# Conformation of the Aryl Amine DNA Adduct 2-Amino-3-methylimidazole-[4,5-f]quinoline $N^2$-deoxyguanine in the NarI Endonuclease Recognition Sequence as Determined by NMR Spectroscopy

By

Kallie Marie Stavros

Dissertation

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

In

Chemical and Physical Biology

May, 2015

Nashville, Tennessee

Approved:
Michael Stone, Ph.D.
Brandt Eichman, Ph.D.
Frederick Guengerich, Ph.D.
Carmelo Rizzo, Ph.D.
Charles Sanders, Ph.D.

**ACKNOWLEDGEMENTS**

I would like to acknowledge everyone who provided support and assistance that made my Ph.D. possible. First of all, I want to thank Dr. Michael Stone for all of his patience and guidance throughout the last five years. I would also like to thank each of my committee members for their time and effort: Dr. Carmelo Rizzo, Dr. Fred Guengerich, Dr. Charles Sanders, and Dr. Brandt Eichmann.

Many members of the lab, both past and present, were instrumental in helping me along the way. Dr. Ewa Kowal and Dr. Marta Szulik were always available for help and advice for NMR calculations and sample preparation. Dr. Markus Voehler and Dr. Donald Stec were very willing to provide their assistance with NMR experiments. Dr. Amritaj Patra taught me how to loop crystals. Dr. Surajit Banerjee spent much of his time over the phone and email to troubleshoot the crystallography as well as collecting diffraction data. I also really appreciate the encouragement I received from the rest of the Stone lab, who have made the journey a pleasant one: Dr. Liang Li, Dennis Kuo, Drew Kellum, and Dustin Politica. I worked with several undergraduate students that have been very helpful, including Patrick Donahue and Reneisha Franklin, who assisted with protein expression, and Ruidan Ma and Sam Lazaroff for help with setting up many, many crystal trays. Amy Millsap taught me to run the extension assays and gel polymerization as well as providing good conversation as a collaborator. I would especially like to remember Ed Hawkins, who synthesized my NMR samples and was always a great resource for really getting me started with the IQ project.

I would also like to acknowledge the National Institutes of Health and Center for Molecular Toxicology for funding my project.

Finally, I want to thank my parents, sister, and Ryan who have been enormously supportive and full of encouragement throughout my graduate career.

**TABLE OF CONTENTS**

## LIST OF TABLES

## LIST OF FIGURES

Figure Page

## LIST OF SCHEMES

Scheme Page

## LIST OF CHARTS

Charts Page

## LIST OF ABBREVIATIONS

| | |
|---|---|
| 1-D | 1-dimensional |
| 2-D | 2-dimensional |
| 3-D | 3-dimensional |
| 8-oxoG | 8-dihydro-8-oxoguanine |
| AAF-dG | N-(2-deoxyguanosin-8-yl)-2-acetylaminofluorene |
| AF-dG | N-(2-deoxyguanosin-8-yl)-2-aminofluorene |
| CORMA | complete relaxation matrix analysis |
| COSY | correlated spectroscopy |
| dA | deoxyadenosine |
| dC | deoxycytosine |
| DNA | deoxyribose nucleic acid |
| dNTP | deoxyribonucleic triphosphate |
| Dpo4 | *Sulfolobus solfataricus* P2 DNA polymerase IV |
| dT | deoxythymidine |
| EDTA | ethylenediaminetetraacetic acid |
| FPLC | fast protein liquid chromatography |
| HCA | heterocyclic amine |
| HPA | hydroxypicolinic acid |
| hpol | human DNA polymerase |
| IPTG | Isopropyl β-D-1-thiogalactopyranoside |
| IQ | 2-amino-3-methylimidazo-[4,5-*f*]quinoline |
| LB | Luria-Bertani |
| MAD | multiple-wavelength anomalous dispersion |
| MALDI-TOF | matrix-assisted laser desorption ionization- time of flight |
| MIR | multiple isomorphous replacement |

| | |
|---|---|
| MR | molecular replacement |
| NaCl | sodium chloride |
| NER | nucleotide excision repair |
| NMR | nuclear magnetic resonance spectroscopy |
| NOESY | nuclear Overhauser effect spectroscopy |
| PEG | polyethylene glycol |
| ppm | parts per million |
| rMD | restrained molecular dynamics |
| rmsd | root mean-square deviation |
| RP-HPLC | reverse phase- high performance liquid chromatography |
| RPA | replication protein A |
| SAD | single-wavelength anomalous dispersion |
| SDS-PAGE | sodium dodecyl sulfate polyacrylamide gel electrophoresis |
| TFIIH | transcription factor IIH |
| $T_m$ | melting temperature |
| UV | ultraviolet |
| XP | xeroderma pigmentosum |

# Chapter I

## INTRODUCTION

### Deoxyribonucleic Acid (DNA)

DNA is the genetic material responsible for coding for proper functioning and development of all living organisms. It does this through a genetic alphabet composed of four nitrogenous bases: adenine (A), cytosine (C), guanine (G), and thymine (T). These bases are attached to a deoxyribose ring and polymerized through a phosphodiester backbone. DNA is typically found in a double helix, where the two antiparallel strands form Watson-Crick hydrogen bonding and coil around each other about an axis[1]. Hydrogen bonding typically occurs between two sets of base pairs, A-T and G-C, shown in Figure 1-1. James Watson and Frances Crick first proposed this structure in 1953[2,3], followed by evidence from H.R. Wilson that it does exist in living organisms[4]. The canonical structure led them to believe that it "suggests a possible copying mechanism for genetic material."[2]

Three forms of DNA shown in Figure 1-2 have been identified. The typical right-handed helix discovered by Watson and Crick is known as B DNA. This is the most common type found in organisms at neutral pH and physiological salt concentrations. However, A-DNA[5] and Z-DNA[5,6] have also been observed in organisms. A form DNA differs by the sugar conformation where it adopts a C3′ endo conformation instead of a C2′ endo like B-DNA[7], which results in shorter linkages of the phosphate backbone and a more compact helix compared to B-DNA[8]. This form is more favorable at high salt concentrations[9]. Z-DNA is the only left-handed helix and tends to be found in CpG islands and involved in transcription regulation[10]. The alternating purine-pyrimidine pattern creates a zig-zag pattern. The conformation of Z-DNA is drastically different from either A or B in that guanine bases are

typically found in the syn conformation[11]. A comparison of duplex geometries can be found in Table 1-1.

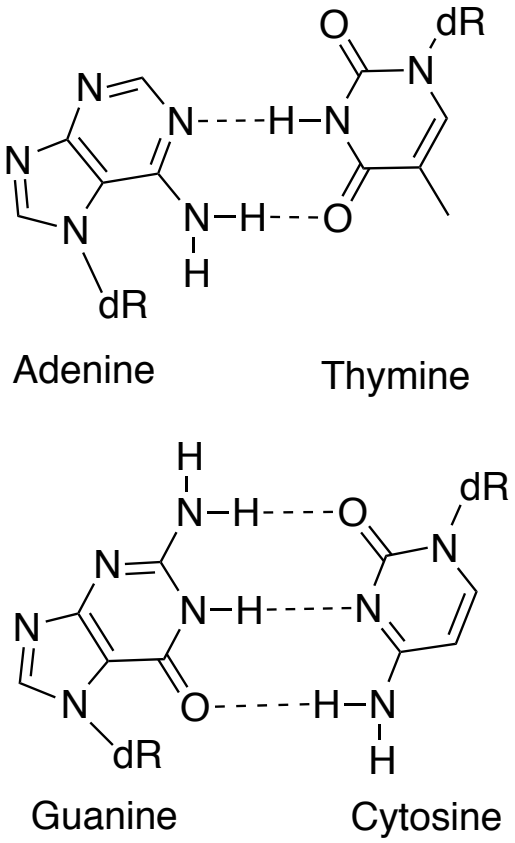



**Figure 1-1.** Watson-Crick hydrogen bonding for A) adenine: thymine and B) guanine: cytosine base pairs.

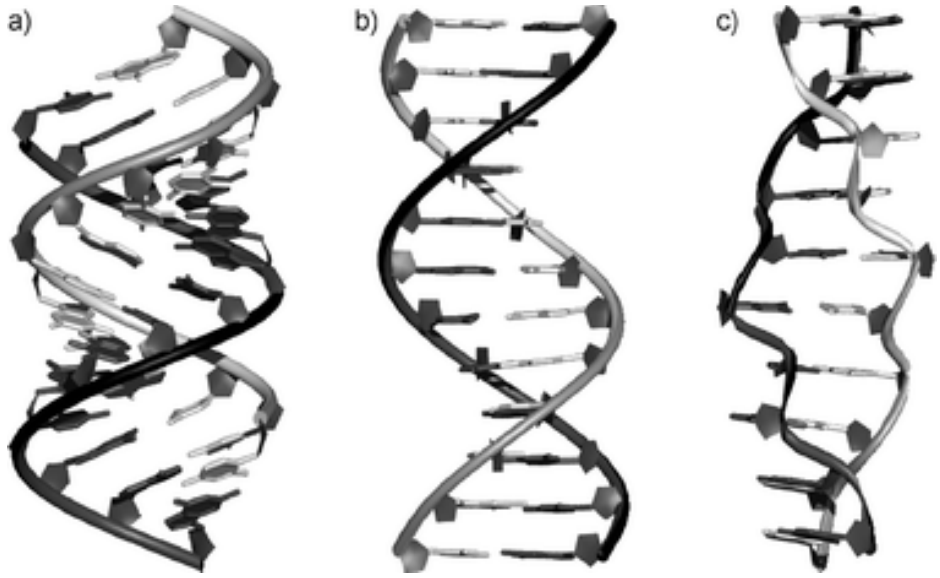



**Figure 1-2.** Structural comparison of A) A-type DNA, B) B-type DNA, and C) Z-type DNA (Reprinted with permission from reference [12] , Copyright (2010) Royal Society of Chemistry).

B-DNA has a number of characteristics that are important for interactions with other biological molecules. The double helical structure results in a wider major groove and a narrower minor groove. The major groove is easily accessible for many DNA binding proteins, while the minor groove provides a more hydrophobic environment that is less solvent exposed

**Table 1-1.** Characteristic parameters for A, B, and Z DNA[13].

| | A DNA | B DNA | Z DNA |
|---|---|---|---|
| Handedness | Right | Right | Left |
| BP per turn | 11 | 10 | 12 |
| Rise per pair (Å) | 2.56 | 3.4 | 3.7 |
| Rotation per pair (°) | 33 | 36 | -30 |
| Helical diameter (Å) | 23 | 19 | 18 |
| Propeller twist (°) | 18 | 16 | 0 |

*DNA Replication*

The order of these bases create a genetic code, where an open reading frame can be transcribed into mRNA and later translated into proteins, required for functioning of living organisms. Three bases are required to code for each amino acid.

In order for cells to divide, proper replication of the genetic code must occur for biological functions to be conserved. This process typically requires high fidelity polymerases that strongly favor insertion of correct nucleotide. Errors for these polymerases are rare, making a mistake an estimated one for every one million bases that are copied[14,15]. Several polymerases are also equipped with a 3′-5′ exonuclease activity which can remove incorrect nucleotides in the event of misincorporation. These polymerases are members of the B family of polymerases, including δ, and ε as well as α, but lacks exonuclease activity, and are responsible for the bulk of DNA replication. During the process of replication in eukaryotes, an MCM2-7 helicase complex[16] must separate the two strands into lagging and leading ssDNA. Synthesis is then initiated by the pol α-primase complex. A polymerase can subsequently bind to the leading strand, inserting the new complementary code in a continuous fashion. The lagging strand, however, is replicated in a series of discontinuous patches of approximately 250 base pairs known as Okazaki fragments. Each fragment must be initiated by pol α-primase activity[17].

There are also other polymerases with more specialized roles important for replication of the nuclear genome. These include a B-family polymerase, ζ, as well as Y-family polymerases η, ι, κ, and Rev1. These polymerases are responsible for bypassing DNA lesions that block the replicative polymerases. The active sites for these polymerases are

much larger, in order to accommodate the extra bulk of the lesions, which this also makes the active site more solvent accessible and lack exonuclease activity. These characteristics make the polymerases more error prone.

Replication fidelity seems to be facilitated by hydrogen bonding ability between the template and incoming dNTP[18]. One idea to explain this is enthalpy-entropy compensation[19], which requires water molecules that are hydrogen-bonded to the base of the dNTP to be desolvated before hydrogen bonding to the template can occur, thus decreasing the entropy of the system. This is consistent with the solvent accessible, error-prone active sites of Y-family polymerases, which behave as though enthalpy-entropy compensation does not contribute to selectivity as demonstrated by kinetic insertion analysis of non-polar base analogs by yeast polη[20].

Nucleotide selectivity also results from the shape complementarity of the newly formed base-pair in the binding pockets[21,22]. Mismatches would likely alter the geometry of the base pair[23,24], which would otherwise fit snugly in the active site. However, the mismatch is presumed to result in steric clashes that would reduce the binding affinity of the incorrect dNTP and reduce the catalysis for proper phosphodiester bond formation.

*DNA Damage, Repair and Bypass*

DNA is subjected to damaging agents on a daily basis. Sources of damage include endogenous factors, such as oxidative damage or deamination, and exogenous causes, including toxic chemicals and radiation[25]. Damaging agents are generally metabolized, resulting in a reactive species that subsequently react with DNA. On average, somewhere between 10,000 to 1,000,000 lesions may form on any given day, where approximately

10,000 lesions alone could be the result of various cellular processes[26]. DNA damage can lead to mutations, which is the initial step in carcinogenesis. Organisms have developed systems to prevent carcinogenesis from occurring. There are a number of pathways in mammalian cells designed to remove potentially dangerous lesions. These pathways include mismatch repair[27], base excision repair[28], and nucleotide excision repair[29]. Some pathways are specialized for specific types of DNA damages; however, proteins involved in each repair process may have overlapping functions in other pathways.

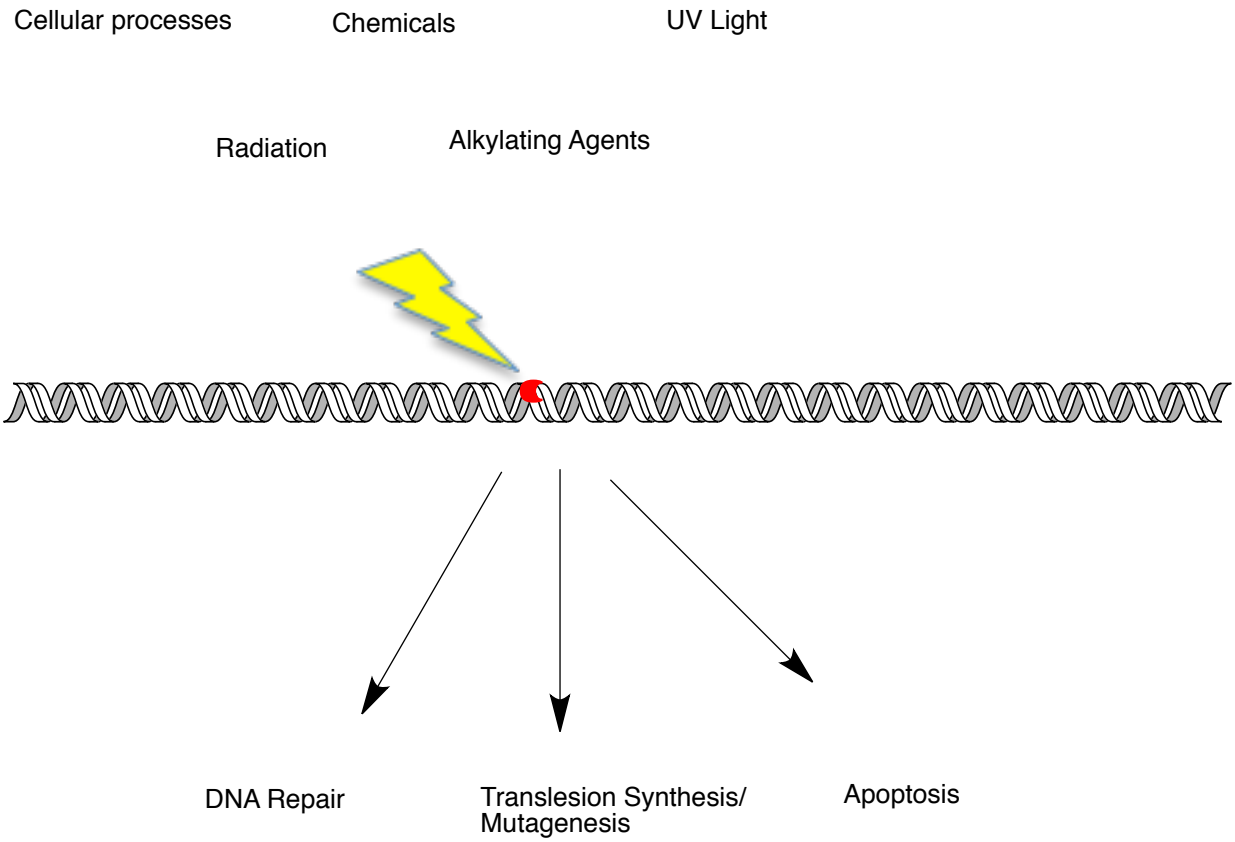



**Figure 1-3.** Types of DNA damage and possible cellular response pathways.

UV radiation DNA damage products are known substrates of the nuclear excision repair pathway (NER). This was discovered from studies of people diagnosed with

xeroderma pigmentosum, or a disease involving deficient activity of one or more of the proteins involved in the NER pathway, are highly sensitive to UV exposure and become prone to skin cancer[30]. This pathway is involved in removing much larger adducts that other pathways may not be able to repair. Human NER requires the orchestration of many proteins to recognize, remove, and repair the damaged DNA. There are two types of NER pathways: transcription coupled repair and global genome repair, which only differ in the initial recognition process.

There are a number of characteristics induced by DNA lesions that are believed to recruit NER proteins to the lesion site. These include DNA unwinding, loss of hydrogen bonding or change in base-pairing geometry, and/or thermal instabilities due to reduced base stacking. The XPC, RAD23B, and centrin 2 protein complex is thought to recognize distortions in the helix induced by a wide array of damage[31,32], while XPE-binding factor more likely recognizes UV radiation damage[33] and stimulates binding of XPC[34,35]. The XPC complex binds to the lesion site and recruits more proteins to verify the presence of the lesion[36]. It does this by associating with transcription initiation factor IIH (TFIIH) complex[37], which is comprised of ten protein subunits. The complex consists of two DNA helicases and TFIIH basal transcription factor complex helicase subunits XPB and XPD that extend the distorted lesion area and likely verify the lesion[38], while XPA is thought to be able to identify altered chemical structures of bases[39]. When the TFIIH complex is loaded on XPC, it performs a 5'→3' scan of the ssDNA[40] and the archaeal orthologue of XPD appears to form an internal channel, where undamaged ssDNA can slide through but damage does not[41,42]. When TFIIH binds to XPC on the damaged DNA, the CDK-activating

kinase subcomplex (CAK) dissociates from TFIIH, which is only essential for the transcription activity of TFIIH but not necessary for repair[43].

Once the lesion has been verified, it must be excised in order to be repaired. The excision is conducted by structure-specific endonucleases, XPF-ERCC1 and XPG, that are able to remove about 22-30 nucleotides around the site of damage, leaving a single-stranded gap[44]. Proper excision is coordinated by the XPA, XPG and replication protein A (RPA)[45] at the location identified by XPC and verified by TFIIH. XPF-ERCC1 is recruited through interactions with XPA[46] and activated by the presence of XPG to make the 5′ excision[47]. Before the XPG-mediated 3′ excision is made, gap filling begins in order to prevent DNA-damage signaling[48]. The gap-filling synthesis can be done by a high fidelity DNA polymerase, usually determined by the proliferative status of the cell[49]. Once repaired, replication and normal cell functioning can continue. Figure 1-3 depicts the series of steps involved in the NER pathway. The NER pathway recognizes the widest variety of DNA damage. It does not detect a specific lesion but instead recognizes changes to the DNA induces by the lesion, such as unwinding and bending, and is probably the most accurate method of repair due to the extensive lesion verification process before removal.

If a repair pathway does not recognize the damage, the cell must have a way to replicate the damaged DNA base, or replication will stall and apoptosis will be induced. Y-family polymerases are typically recruited to bypass lesions, since replicative polymerases cannot accommodate large adducts in their active site. Y-family polymerases can often bypass the lesion; however, many times it will insert an incorrect base opposite the adducted base. When the misinsertion occurs, this results in a mutation. If a mutation

occurs in a critical gene, such as one that regulates cell proliferation, carcinogenesis may be induced if the function of the gene is affected.

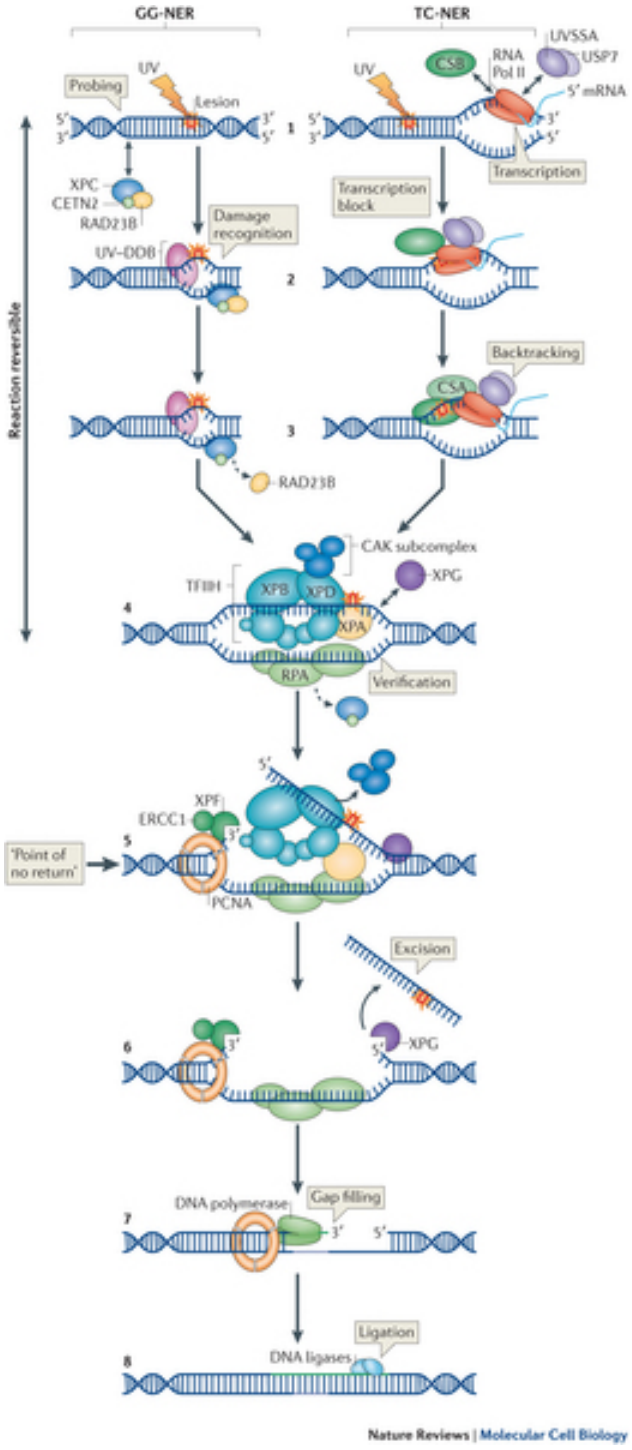
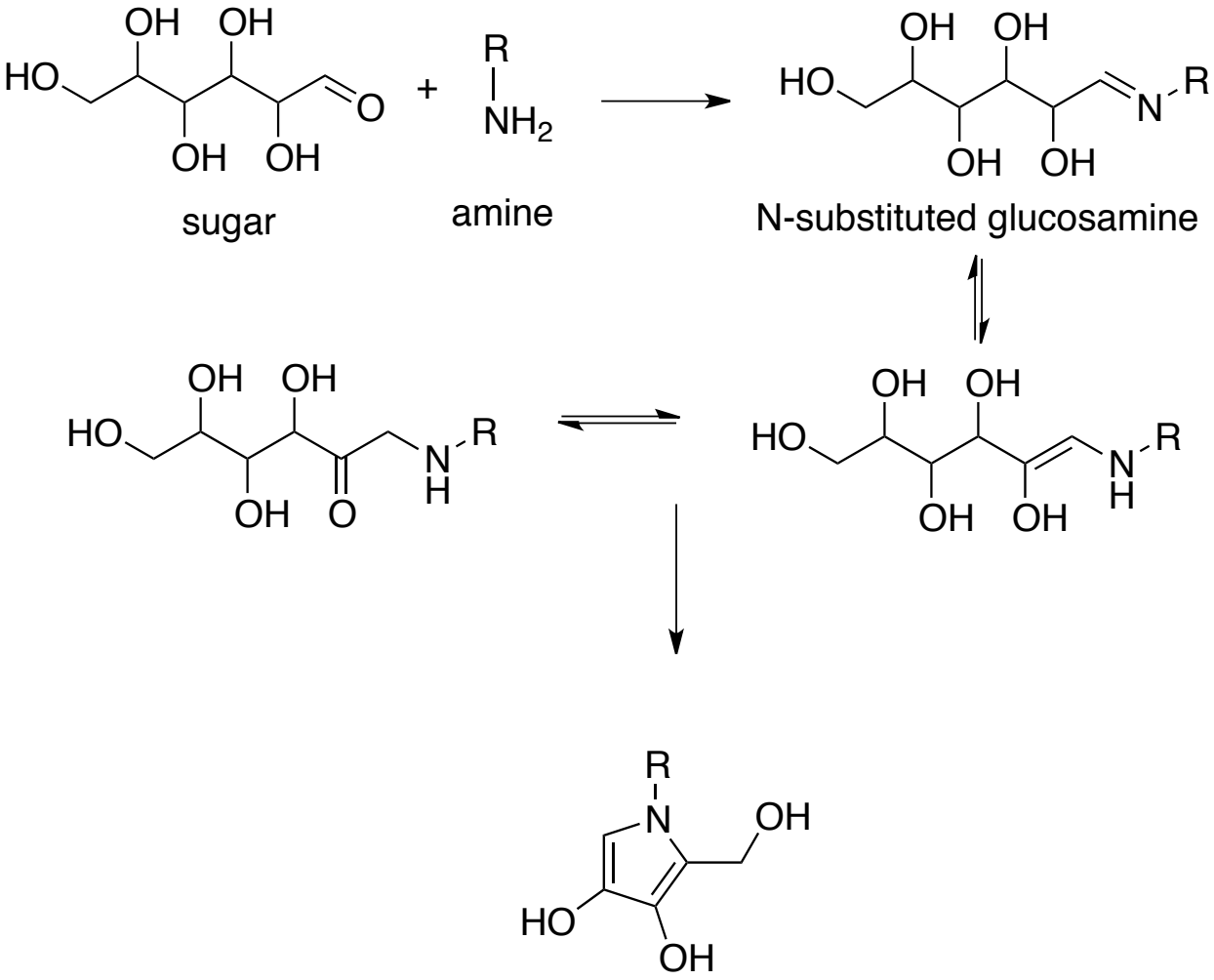



**Figure 1-4**. Steps by which lesions are recognized and removed in the nucleotide excision repair pathway Reprinted with permission from reference[50], Copyright (2014) Nature Publishing Group.

## Heterocyclic Amines

Heterocyclic amines (HCA) are a class of compounds that form in high temperatures when cooking meat through the Maillard reaction[51,52]. The reaction causes amino acids to react with sugars, which is typically induced at high temperatures above 300 °C. However, the reaction could occur at lower temperatures in meats with higher concentrations of amino acids and sugars. Incidentally, the Maillard reaction is also responsible for the browning that occurs during cooking as well as the enticing aroma that emanates from the cooking meat[52] (Scheme 1-1). Approximately more than twenty HCA compounds have been identified. As a class of compounds, they have proved to be mutagenic in Ames assays as well as mammalian *in vitro* and *in vivo* studies. About 25-30% of cancers result from inflammation, smoking, and dietary factors[53,54]. While HCA are difficult to definitively link to human carcinogenesis, they are believed to play a role in pancreatic[55], colon[56], breast[57] and prostate[58]. Studies evaluating HCA formation in meats have been ongoing for over twenty years. Many HCA are classified as either 2A (probable human carcinogens) or 2B (possible human carcinogens) compounds by the International Agency for Research on Cancer (IARC), though many believe these should be upgraded to 1A carcinogens. Methods to reduce HCA intake have already been suggested, such as avoiding cooking meat over an open flame[59], flipping meat often[60] or microwaving[61] as well as marinades or cooking agents rich in polyphenols[57,62,63] have all been shown to reduce the formation of HCAs.




**Scheme 1-1.** Sugars and amino acids react at high temperatures through the Maillard reaction. The carbonyl group on a sugar can react with the amino group to form an N-substituted glycosylamine. The glycosamine undergoes Amadori rearrangement to produce a ketosamine. The ketosamine can react in many possible ways. The products of these reactions can also undergo further reactions for many possible products.

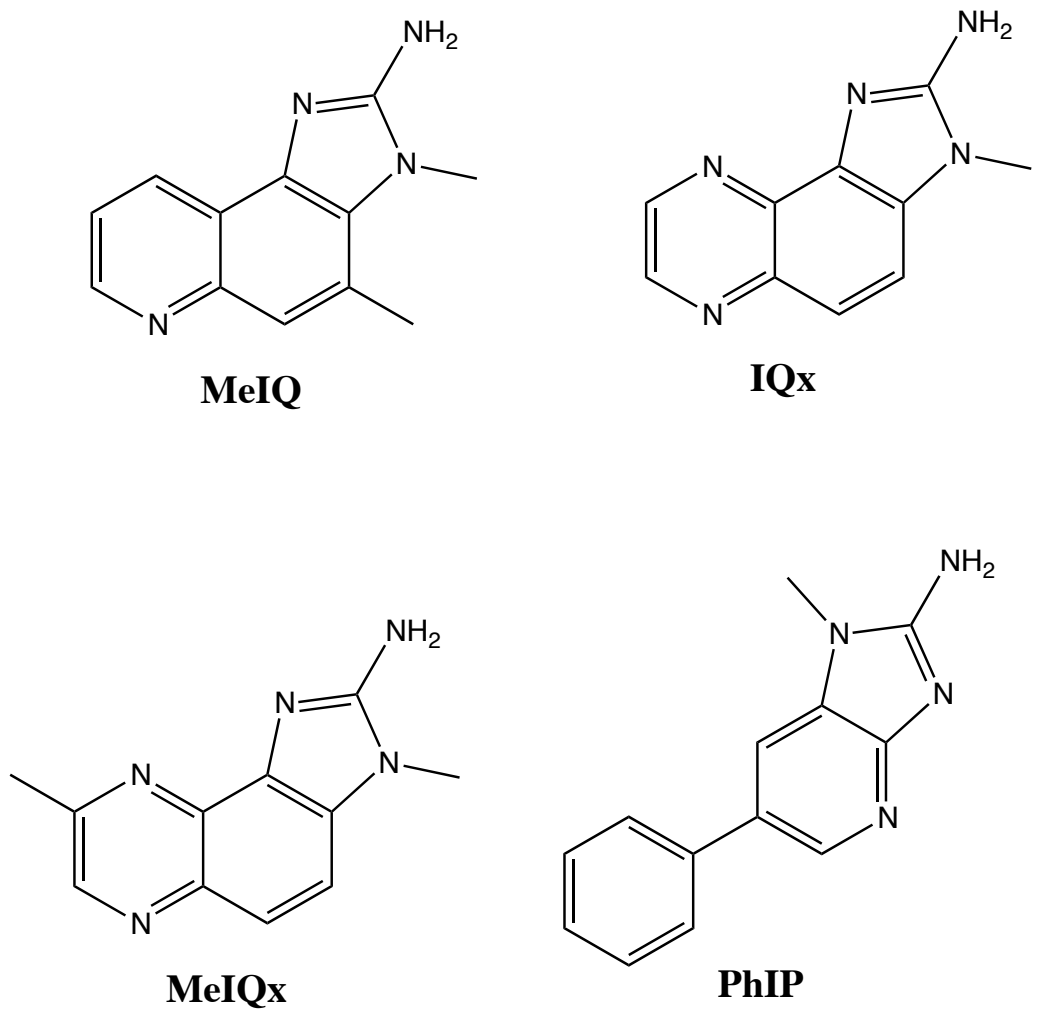
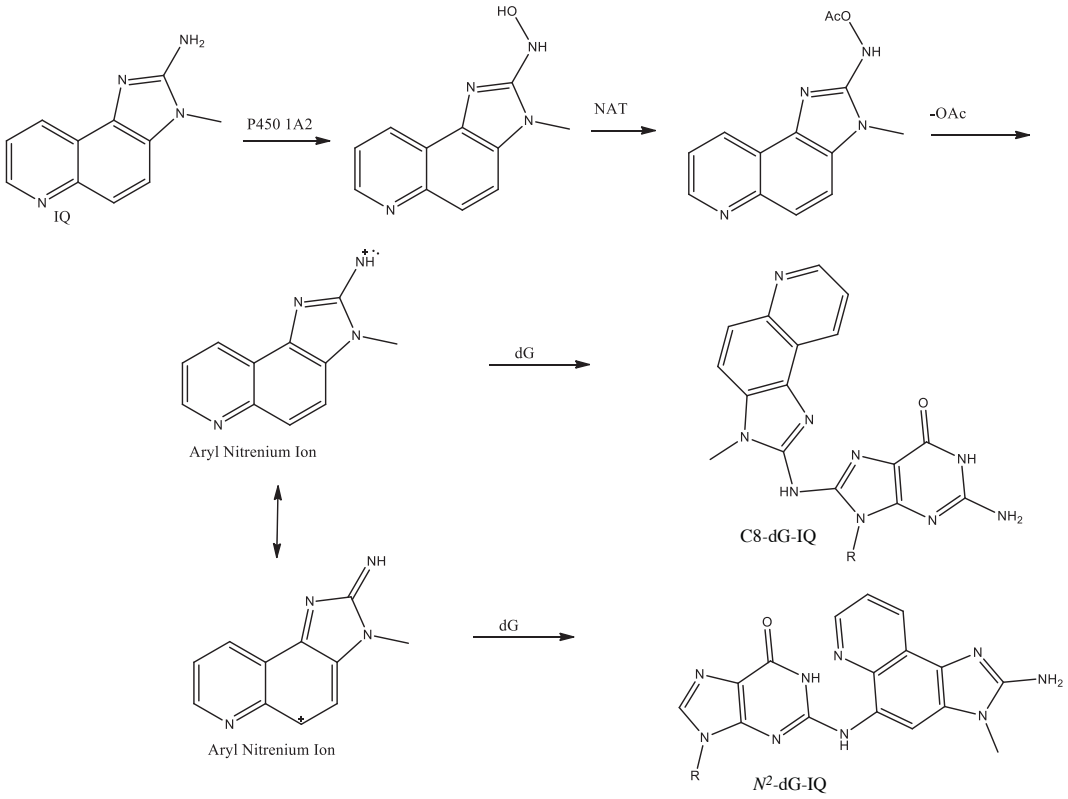



**Figure 1-5.** Examples of identified HCA compounds.

*2-Amino-3-methylimidazo-[4,5-f]quinoline and metabolism*

2-Amino-3-methylimidazo-[4,5-*f*]quinoline (IQ) is one of the most mutagenic of the characterized HCA compounds. IQ is classified as a class 2A carcinogen by the IARC[64], the highest classification of any HCA. Many animal studies have been done that indicated IQ is carcinogenic in animals. One study exposed rats through intragastric intubation and found formation of tumors in mammary glands, liver and ear ducts[65]. Another study fed cynomolgus monkeys IQ and observed hepatocellular carcinomas[66].

IQ is metabolized by cytochrome P450, primarily 1A2, while cytochromes P450 1A1, 1B1, and 3A4 may be involved to a lesser extent[67]. P450 enzymes oxidize the exocyclic amino group to a hydroxylamine. Tissues with active N-acetyltranserase (NAT1 and NAT2) and sulfotransferase enzymes[68] catalyze the acetylation of the hydroxyl group. The reaction can continue without transferase enzymes under acidic conditions. The hydroxylamine may also become protonated, resulting in the loss of this group through solvolysis, resulting in a reactive aryl nitrenium ion. However, the reaction is much more efficient with transferase enzyme catalysis; thus tissues with active NAT2 activity tend to be more prone to IQ adduction.




**Scheme 1-2.** Metabolism pathway for IQ.

*NarI Recognition Sequence*

The *NarI* recognition DNA sequence has been frequently used in relationship to understanding mutagenicity of aromatic amines [69-71]. This sequence consists of a GC dinucleotide repeat, $G^1G^2CG^3CC$, which has been observed to exhibit sequence dependent mutagenic properties in *Eschericia coli* (*E. coli*)[72]. Repeat sequences in general have been observed to produce frameshift mutations with much higher frequencies than non-repeat sequences[73-75]. The *NarI* sequence codes for one of two of the proteins making up the γ subunit of a nitrate reductase enzyme that allows the *E. coli* to use nitrate as an electron acceptor during anaerobic conditions. It is a hotspot for frameshift mutations, which has displayed a mutagenic frequency of $10^7$ in *E. coli* over background when $G^3$ is modified by the aryl amine adduct N-2-acetylaminofluorene (AF)[76]. The frameshift mutation in *E. coli* could reduce the ability of the *NarI* enzyme to bind to the membrane and possibly reduce binding of the heme since this function is associated with the γ subunit[77].

In 1966, Streisinger had predicted that repeat sequences would be hotspots for mutations[78,79]. He hypothesized that that either the template or the daughter strand would be able to slip, resulting in a misalignment of the duplex, thus, the occurence of in frameshift mutations (Figure 1-5)[80]. The Ames tester strain TA98 contains an island of $(CpG)_4$ has verified the idea of his hypothesis.

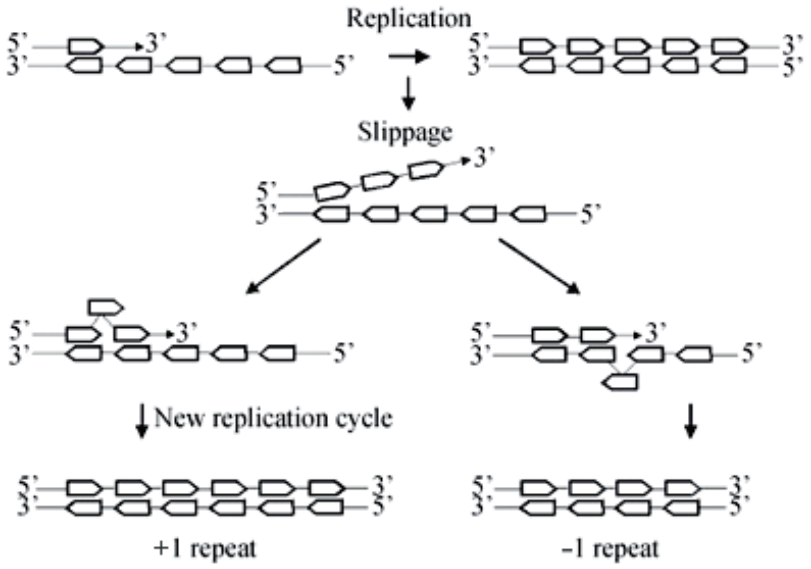



**Figure 1-6**. Streisinger slippage mechanism. Reprinted from reference [81].

Studies also looked at the sequence effect of the *NarI* sequence on the NER pathway in *E. coli*[82]. The incision rates of the C8-AF-dG and C8-AAF-dG by UvrABC were monitored at the $G^1$, $G^2$ and $G^3$ sites in the *NarI* recognition sequence. Rates of incision appeared to be modulated by sequence effect, where the AF adduct was most efficiently cleaved at the $G^3$ and $G^1$ sequence contexts. The AAF adduct, however, was incised more efficiently at the $G^1$ and $G^2$ sites. The incision efficiency can be correlated to the conformers present, which seems to be dictated by the sequence context.

## Structural Biology Techniques for Macromolecules

Structural studies can be an important tool for understanding how biological molecules, such as proteins, DNA, lipids, etc., function. A number of tools have been developed to allow for high-resolution structures for macromolecules to be determined.

The most widely used methods are nuclear magnetic spectroscopy (NMR) and x-ray crystallography.

X-ray crystallography has long been the standard for structure determination. X-ray crystallography can be used for small molecules to macromolecules with no known size restrictions. The only requirement is that they form a stable crystal lattice. Good quality crystals can diffract with a resolution less than 1 Å. However, such a method requires electron density, and hydrogen atoms are not visible in the diffraction pattern. Flexible pieces of molecules may exhibit low density as well and be difficult to place. Also, it is not well known if crystal-packing forces could alter the native structure.

NMR has been considered an alternative to x-ray crystallography for years, but is really a complementary technique to crystallography. However, there is a size limitation to molecules that can be used in NMR. Typically molecules smaller than 40 kDa can be used for structural determination. Larger molecules may be used to obtain certain information, such as global folding; however, in order to obtain this information, a high amount of deuteration is required, meaning a loss of other important structural information as a result. Therefore, it is not likely a full structure can be determined from such large molecules. The largest structure determined by NMR is the 82 kDa *E. coli* protein malate synthase G, which also used small angle x-ray scattering (SAXS) data to improve the resolution[83]. The benefits of NMR include being able to leave the molecules in possibly more native conditions in the solution state, if soluble; although solid state NMR is popular for nonsoluble molecules like membrane proteins. Also, hydrogen atoms are NMR active, which is often another benefit for studying biological molecules such as DNA.

*X-ray Crystallography of Biological Molecules*

Long considered the gold standard of structural biology, x-ray crystallography can be the simplest way to study large proteins and protein complexes in atomic or near atomic resolution. While x-ray crystallography for structure determination of small molecules has been used since 1913 after the structure of NaCl was determined[84], it was not until 1950 that it was used by Sir John Kendrew to determine the structure of the first protein, sperm whale myoglobin[85], earning him a Nobel Prize in Chemistry in 1962. Over the last 30 years, the number of structures determined by x-ray crystallography has increased exponentially, with currently more than 93,000 structures uploaded to the PDB to date[86]. Unlike NMR, there are no size restrictions for crystallography. A molecule typically just has to retain a stable structure under conditions that allow for crystal formation. However, the larger the molecule, the harder it may be to resolve individual atoms.

In macromolecular x-ray crystallography, highly purified samples must be obtained in order to grow crystals. In order to induce nucleation, the sample must be concentrated, generally in a supersaturated state, and allowed to grow over time as the solubility of the sample decreases. Figure 1-7 depicts the states of the sample as a function of concentrations. The vapor diffusion method of growing crystals is based on this curve, where the precipitant should not encourage too much nucleation, but rather growth over time without reaching the precipitation stage too quickly[87].

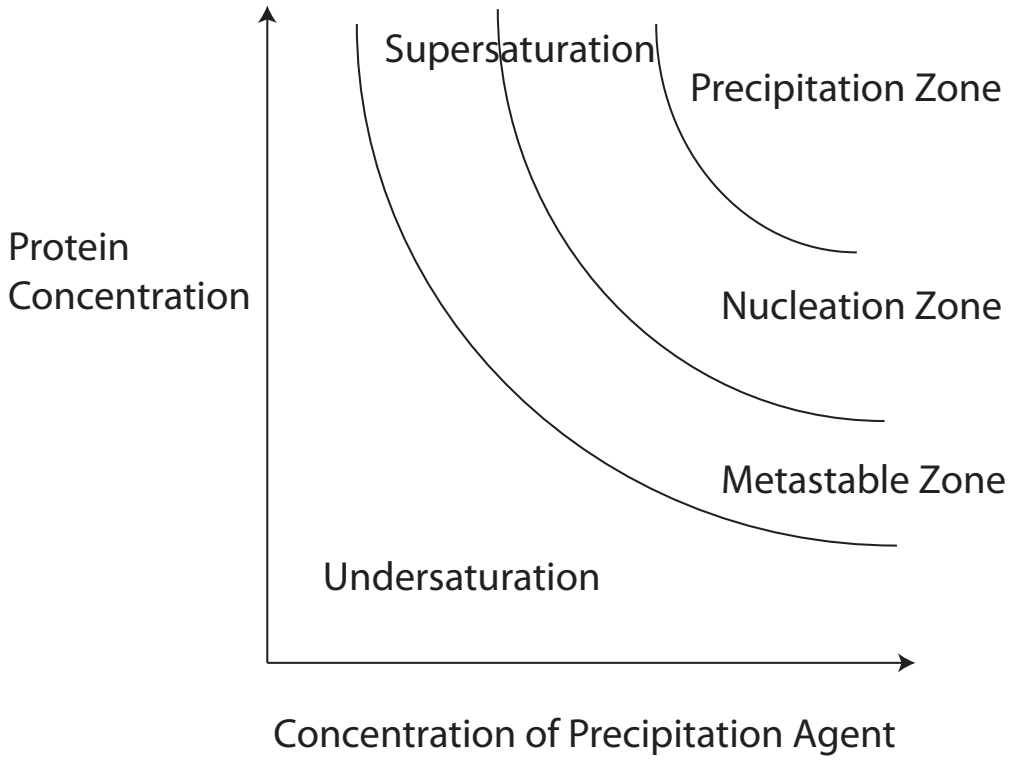



**Figure 1-7.** Stages of solutions in relation to the drop concentration and precipitating agent.

Figure 1-8 is an example of the hanging drop vapor diffusion method, commonly used for growing protein crystals. Other methods include sitting drop and microdialysis. Here the sample is combined with a precipatant and equilibrated against a reservior of the precipitant. As vapor diffuses from the reservoir to the drop, the sample concentration will reach the nucleation zone and crystals begin to form. The sample concentration in the drop decreases while crystals are forming, reaching the metastable zone, allowing the crystals to grow over a period of days to months. Conditions are optimized until sizable crystals are formed.

Once the sample does crystallize, the crystals are mounted in loops, flash frozen in liquid nitrogen and ready to be study by x-rays. X-rays are high energy electromagnetic

radiation with a small wavelength of 0.1-100 Å, with the typical wavelength for crystallography being about 1 Å. These can be generated from accelerating electrons, either from an in house source or synchrotron. When they are focused into a beam, the crystal can be subjected to the beam of x-rays. The goniostat allows the crystal to be properly aligned in the x-ray beam and kept there as the crystal is rotated. The distance between the detector and the crystal must be known and can be adjusted for desired resolution since the resolution is based on the diffraction angles. The greater the diffraction angles, the better the resolution of spots. This is based on the Bragg law defined as:

$$2d \sin \theta = n\lambda$$

where d is the spacing between the planes, θ is the diffaction angle between the incident ray and diffraction planes, n is an integer and λ is the wavelength of the x-ray beam.

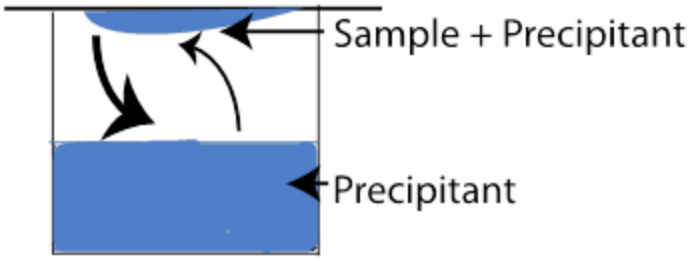



**Figure 1-8.** Hanging drop vapor diffusion where the precipitant in the well is more concentrated then the drop, inducing solvent from the drop to diffuse faster than from the well to the drop and promoting supersaturation of the drop.

When the crystal is exposed to the x-ray beam, the beam scatters when in proximity to electron-rich atoms, producing an observable pattern of reflections on the detector, such as in Figure A-3. The relative intensities of the reflections correspond to the arrangement of the molecules in the crystal. The spacings are dependent on the size of the molecule. The

intensities correlate to both the amplitude of the diffracted waves as well as the phase difference. The amplitudes can be calculated by the square root of the intensities[88]. The phase cannot so easily be determined and, thus, is referred to as solving the phase problem. Reflections should be recorded as the crystal is rotated up to 180°, depending on symmetry, in order to understand the 3-D structure. The data can then be processed.

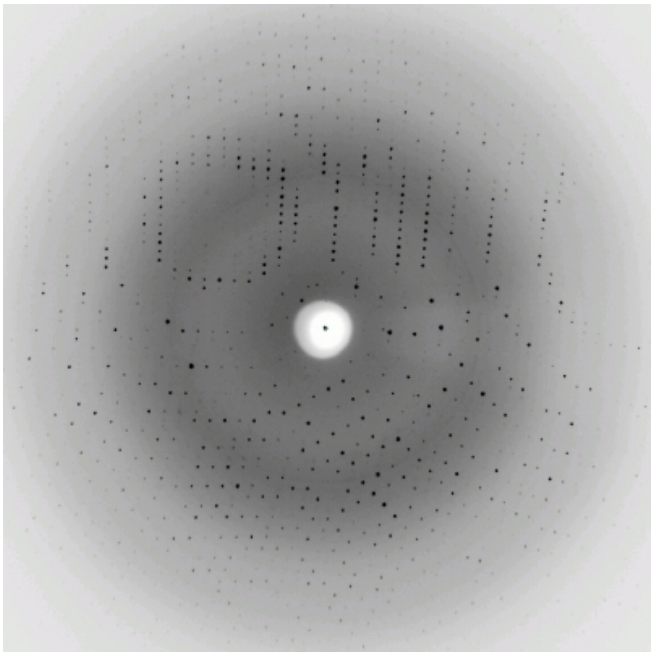


**Figure 1-9.** X-ray diffraction pattern.

The collected data can be analyzed to determine unit cell dimensions, crystal system and space group. The unit cell is described by lengths a, b and c and angles $\alpha$, $\beta$ and $\gamma$. The unit cell shape defines the crystal system. Seven crystal systems are possible and are described in Table 1-2. The space group is determined by the diffraction pattern symmetry. A total of 230 space groups exist, however, only 65 of these are possible for chiral molecules.

**Table 1-2.** Characteristics for each crystal system.

| Crystal System | Conditions of cell geometry | # of space groups |
|---|---|---|
| Triclinic | $a \neq b \neq c$, $\alpha \neq \beta \neq \gamma$ | 2 |
| Monoclinic | $a \neq b \neq c$, $\alpha,\gamma=90°$, $\beta \neq 90°$ | 13 |
| Orthorhombic | $a \neq b \neq c$, $\alpha=\beta=\gamma \neq 90°$ | 59 |
| Tetragonal | $a=b \neq c$, $\alpha=\beta=\gamma=90°$ | 68 |
| Rhombohedal | $a=b=c$, $\alpha=\beta=\gamma \neq 90°$ | 25 |
| Hexagonal | $a=b \neq c$, $\alpha,\beta=90°$, $\gamma=120°$ | 27 |
| Cubic | $a=b=c$, $\alpha,\beta,\gamma=90°$ | 36 |

There are three commonly used methods for solving the phase problem for larger proteins: Molecular replacement (MR)[89,90], anomalous x-ray scattering (MAD or SAD)[91] and multiple isomorphous replacement (MIR)[89]. MR is most commonly used if a homologous structure is available. It is the simplest method since the coordinates and phases of the previously determined structure are used to calculate the new electron density map. The map can then be used for structure determination.

MAD or SAD is usually the next option when a homologous structure is not available. The phases can be solved using a single crystal. In MAD, the crystal is subjected to the x-ray beam multiple times at different wavelengths and allow for direct solution of the phase problem by measuring the dispersive differences, if the crystal is stable enough to remain in the beam that long[92]. SAD, on the other hand, uses a single dataset at a single wavelength. Both work best if an atom in the protein can be substituted for a slightly heavier one, for instance the sulfur in methionine to a selenomethionine[93].

MIR requires the crystal is grown in or soaked in a solution containing heavy, electron-rich atoms that will incorporate in the crystal. The difference between scattering amplitudes caused by the presence of the heavy atom allows the phases to be solved if the

atom does not change the conformation of the protein or crystal shape[94]. MIR, however, requires at least two data sets: one of the sample alone and one with the heavy atoms.

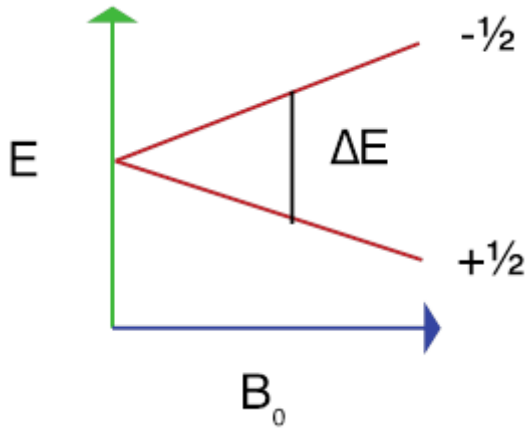
Once the phase problem has been solved, the intensities of the reflections and the phases can be converted to a density map by using the mathematical technique Fourier transform. The electron density map forms a 3-D contour map, where a model can be built in to fit the electron density. The model is used to calculate the phase. Combined with the original intensities of the spots, a new electron density map is constructed, which can be used to improve the model. The cycle continues until changes no longer improve the model. Improvements are determined by measuring R-factors, which compare the observed amplitudes with the calculated amplitudes and are typically 0.15-0.25 for the average size protein. The $R_{free}$ is another way to evaluate model agreement with the data by randomly removing 5-10% of the collected data, known as the test set, to compare to the model. This number is often slightly higher than the R-factor but is believed to be a better representation of an accurate model[95].

*Using NMR to Understand Oligonucleotides*

Technological advances in NMR have made it a useful technique for examining oligonucleotides. The development of superconductoring magnets able to resonate at frequencies as high as 1GHz[96] make NMR a powerful structural biology tool, improving more than thirty times the sensitivity of the original 30 MHz instrument developed in 1950. The common use of cryoprobes has further enhanced the utility of NMR towards structural biology.

NMR samples require NMR active nuclei in order to be detected. The nucleus is composed of protons and neutrons. Nuclei have an intrinsic spin (I) characteristic, determining whether it is NMR active. The spin orientations are defined as either spin up or spin down. For a nucleus to be interesting from an NMR spectroscopist's point-of-view, $I \neq 0$. This excludes atoms with an even mass and even number of neutrons. NMR active nuclei can have an even mass with odd number of neutrons or just an odd mass. The commonly used NMR active nuclei are $^{1}H$, $^{13}C$, $^{15}N$, $^{19}F$, and $^{31}P$. Oligonucleotides are composed of elements $^{1}H$ and $^{31}P$ and have to potential to be $^{13}C$ labled that allow for many possibilities for experiments to obtain structural information.

When a sample is placed in the spectrometer, it is subjected to the high magnetic field, which aligns the spins with or against the axis the magnetic field (Z axis) and separates the spin states so they no longer have the same energies. Scheme 1-3 Depicts the energy difference of the spin states when subjected to magnetic field $B_0$, where $\Delta E$ depends on the strength of the magnetic field. Typically, a 90° RF pulse is applied to flip the spins into the perpendicular (XY) plane, creating coherence between the two spin states and allowing transitions to occur. The nuclei are then allowed to return to the equilibrium state. The transition frequency, also known as chemical shift, as they relax is detected and is dependent on the chemical environment of each atom.




**Scheme 1-3.** Diagram of how the energy states of spin-up and spin-down depend on the magnetic field, which is detected by NMR.

Two types of NMR interactions are commonly measured for structure determination of DNA: scalar coupling interactions and dipolar interactions. Scalar couplings, or J couplings, detect through-bond interactions. 2-D correlated spectroscopy (COSY)[97] experiments are generally used in this project to detect such interactions. Cytosine bases are the only bases that have $^{3}J$ couplings and can easily be used to assess purity of the duplex by examining the aromatic portion of the spectrum. Certain phase-sensitive experiments allow for calculating J-coupling constants, which is based on the orientation of the nuclei relative to each other. $^{3}J$ coupling constants are particularly useful in unambiguously assigning sugar protons on the ring. For instance, the coupling constants for protons of H2′ and H2′′ to H1′ will differ since H2′′ is on the same side of the sugar ring as H1′ and will have a smaller $^{3}J$. Similarly, backbone angles can be determined using $^{3}J$ between $^{31}P$ and nearby protons like H5′ or H5′′.

Dipolar interactions occur when nuclei are closer than 5 Å and occur strictly through space, allowing for distance information to be extracted. Nuclear Overhauser effect

spectroscopy (NOESY)[98] experiments are designed to detect such interactions. In a NOESY experiment, a mixing time of a certain length allows for cross magnetization to occur for protons that are in proximity to each other. The resulting crosspeak is detected between two protons during relaxation. A variety of mixing times tend to be used, ranging from 50 ms to 300 ms. Use of multiple mixing times reduces bias from spin diffusion. The intensities of the peaks are integrated and used for distance values based on Equation 1:

$$r_{ij} = r_{ref} \sqrt[6]{\frac{i_{ref}}{i_{ij}}}$$

where $r_{ref}$ is a known distance, typically between H5 and H6 of cytosine and *i* being the intensity of the reference peak and the peak resulting from spins *i* and *j*.

NOESY spectra for DNA can be divided into characteristic chemical shift regions, as demonstrated in Figure 1-10 The area termed the "walking region" is where the aromatic H6/H8 protons of the bases interact with H1' of the sugar rings, where this interaction can be followed from base 1 to the end of the strand in unmodified DNA. Once this region has been assigned, the sugar protons for each base can usually be identified and assigned according to established protocols[99]. The walking region can be very informative for understanding structural perturbations from adducts because the distances from these protons are well known in B-type DNA. Changes in distances or breaks in the walk are usually identifiable in this region. Chemical shift perturbations can also be informative for understanding where protons are likely located in the DNA duplex. Figure 1-11 demonstrates the typical observable interactions in the walking region, as well as some other NOEs typically observed.

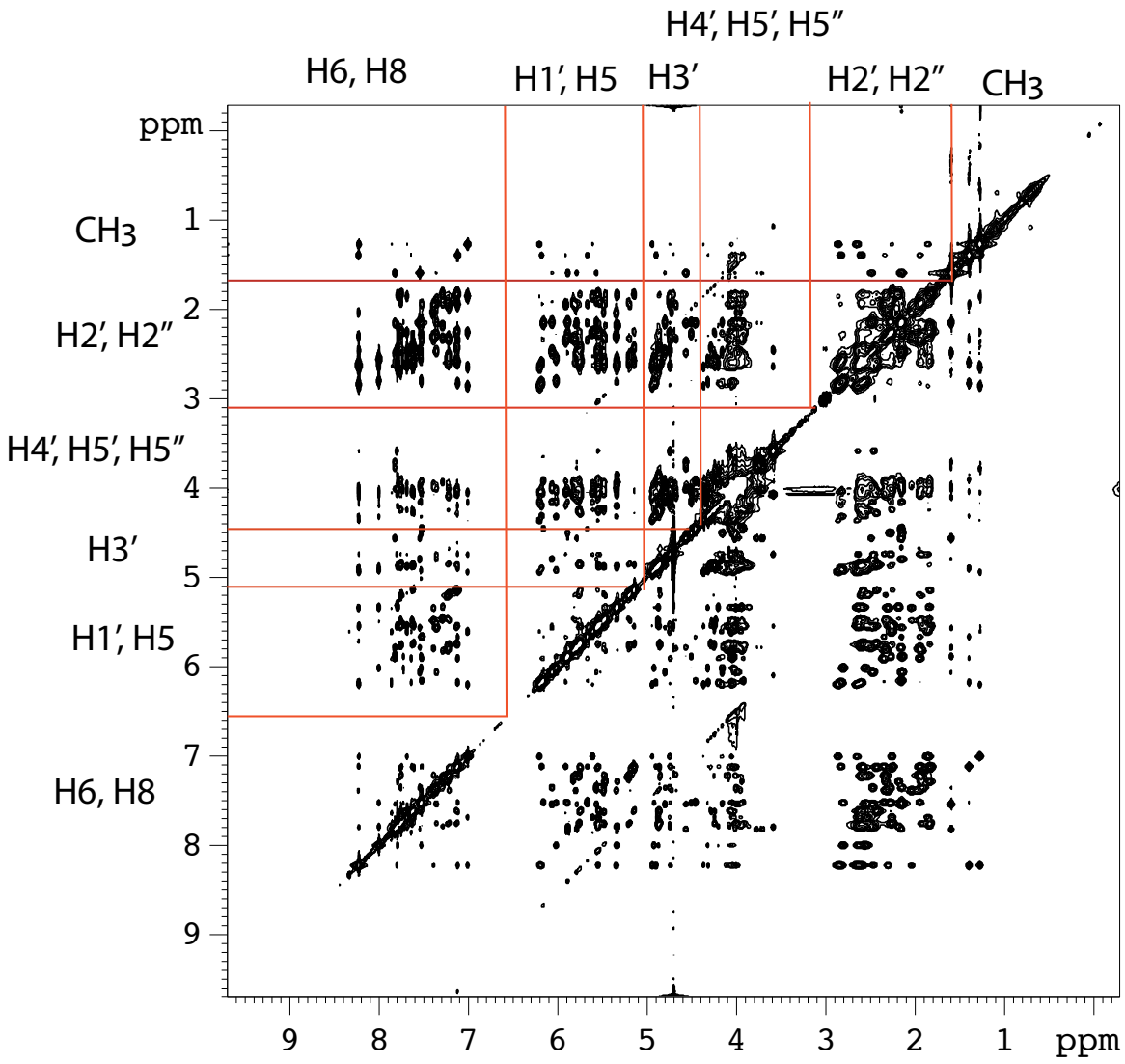



**Figure 1-10**. Chemical shifts for unmodified oligonucleotides are typically found in specific regions labeled on the NOESY spectrum.

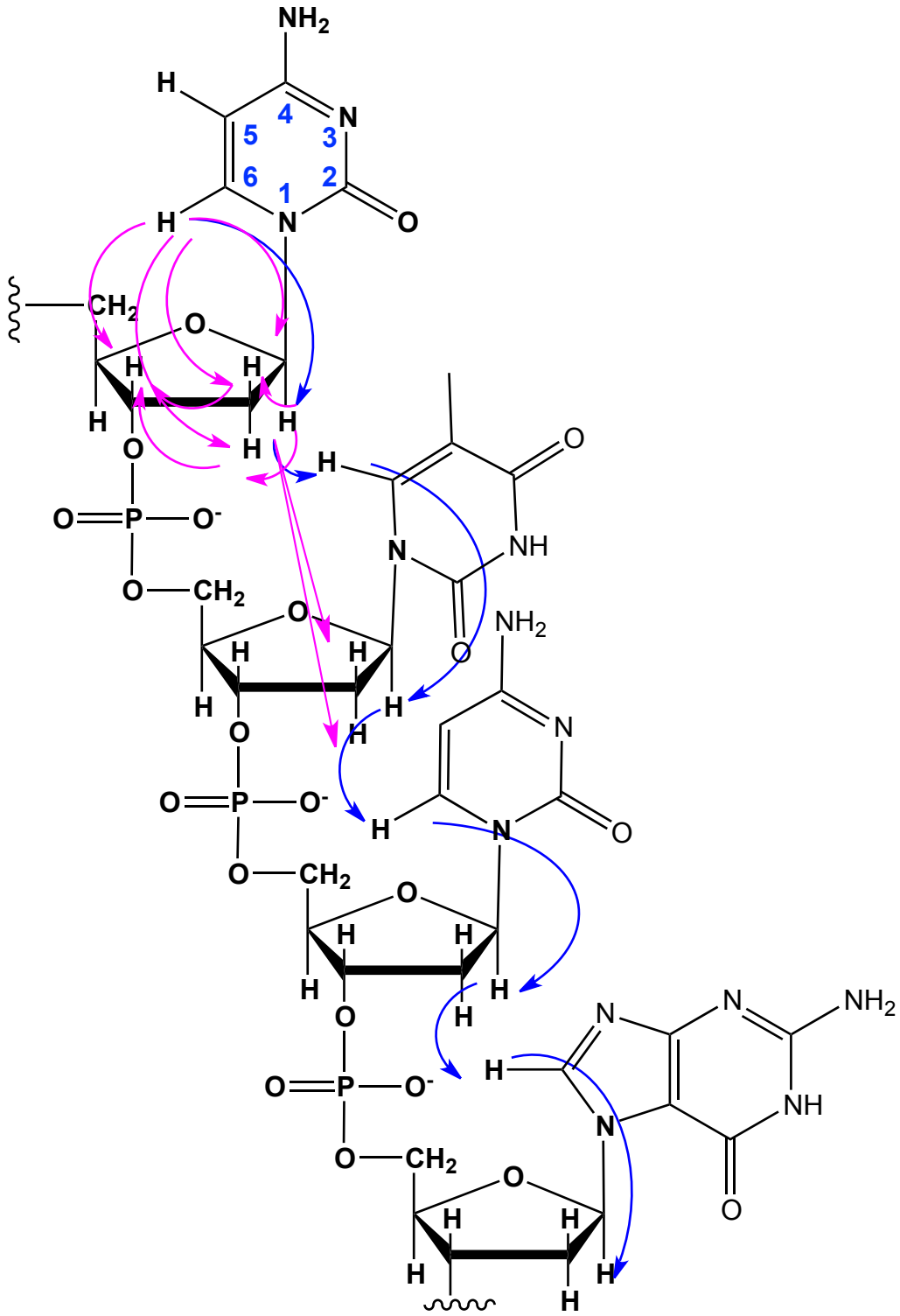


**Figure 1-11.** The walking region consists of the NOESY walk from aromatic base proton to H1' sugar proton, demonstrated in blue. Other NOEs, which can usually be observed, are shown in magenta.

Another important region to study for DNA involves the exchangeable imino and amino protons. The exchange rate for these protons at the nucleoside level are much faster than can typically be observed on the NMR timescale. However, since the N1H proton of guanine and the N3H of thymine are involved in hydrogen bonding when in duplex DNA, the exchange is significantly slower. Therefore, this region can be used to determine if base-stacking and Watson-Crick hydrogen bonding is maintained by being able to identify the chemical shifts of the protons involved in hydrogen bonding. Base-stacking interactions appear much like the connectivities in the walking region of the nonexchangeable region. Since parameters like the rise and twist of B-type DNA remain very characteristic to the duplex, a walk can also be observed in this region from imino to imino proton from the thymines and guanines when normal base-stacking occurs (demonstrated by red arrows in Figure 1-12). The corresponding amino group in the base pair can be identified by the NOEs to the imino proton[100]. Disruption in hydrogen bonding may cause broadening by allowing protons to exchange with the solvent. Hoogsteen or wobble base pairs can also be identified by the chemical shifts of these protons.

Once all NMR data is collected and assigned, NOESY peak volumes can be integrated for Matrix Analysis of Relaxation for Discerning Geometry of an Aqueous Solution (MARDIGRAS)[101,102] calculations to convert volumes to proton-proton distances. Integrating data requires resolved peaks with preferably a Gaussian shape for best accuracy. When integrating, the peaks can manually be selected, thus not accurately being able to define the bounds of overlapped peaks will lead to higher error. Likewise, the integration method assumes a Gaussian peak when integrating; therefore, broad linewidths may also contribute error. The result of the integration is a series of bounds for each

proton-proton distance based on the error value based on noise and intensity errors assigned. This yields the experimentally obtained restraints for calculations. Other restraints include canonical angles for sugars and backbone and distances for Watson-Crick hydrogen bonding. These values can also be adjusted for any deviations that are observed in the NMR data.

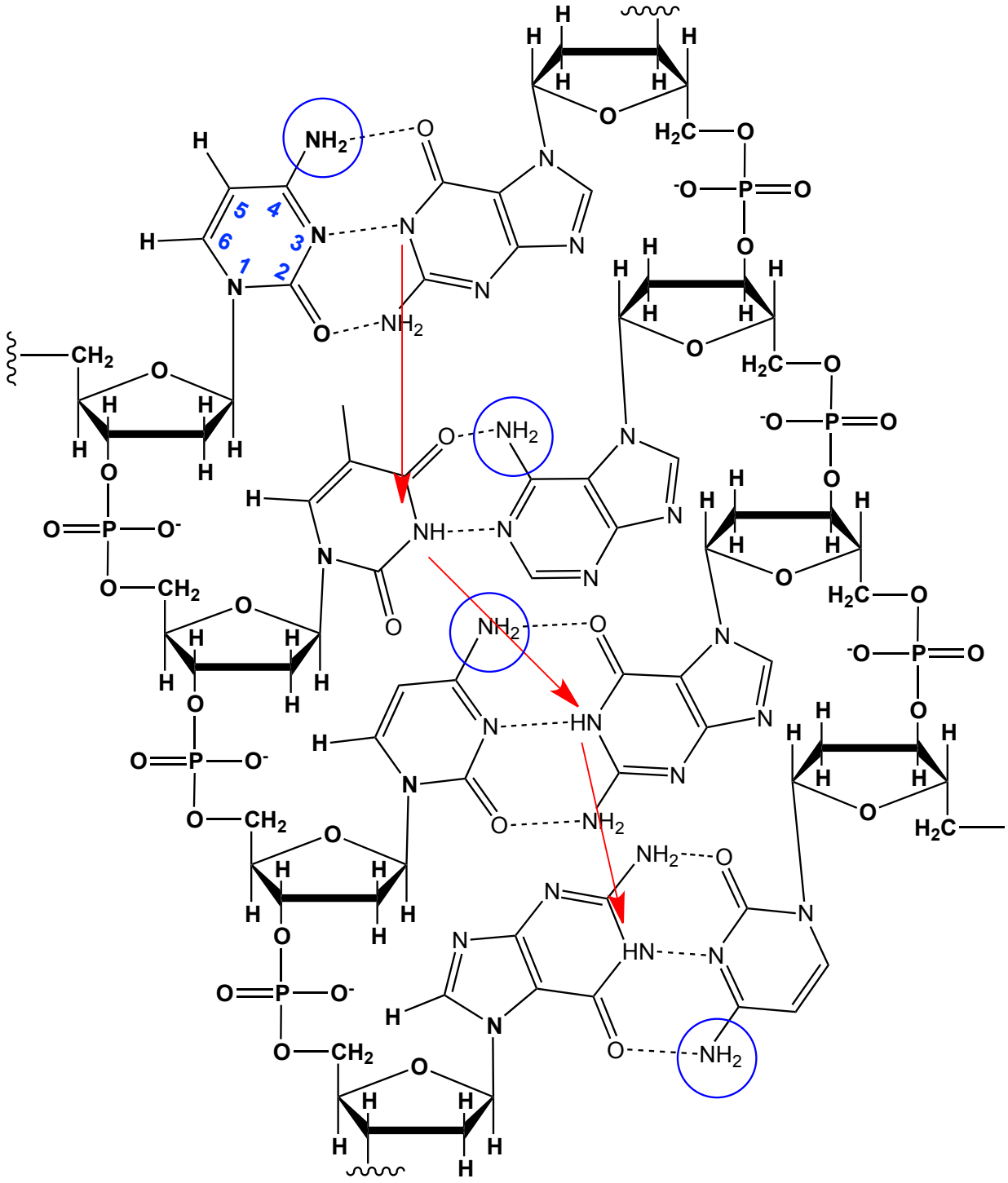
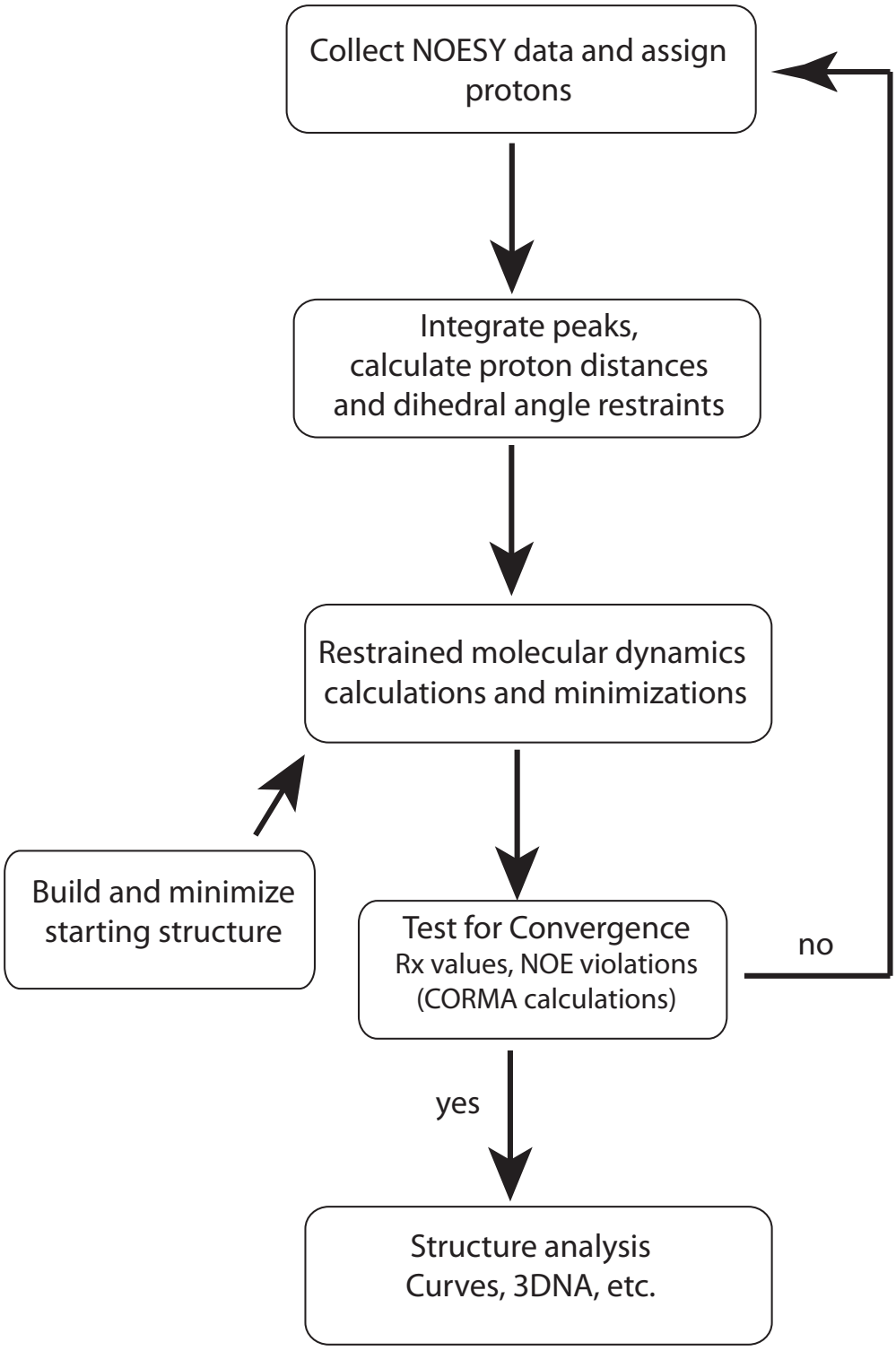


**Figure 1-12.** Exchangeable protons observable in NOESY experiments due to participation in hydrogen bonding.

An initial structure or series of structures can be built to obtain topology and parameter files necessary for structure calculations. Using the topology and parameter information, the structure can be minimized to reach a local energy minimum by randomly sampling a variety of conformational space to find the lowest energy structure. The experimentally obtained restraints can then be applied to the minimized structure through a series of restrained molecular dynamics (rMD) calculations[103]. A simulated annealing protocol[104] is applied, which adds energy to the system, allowing the molecule to overcome energy barriers and increases the number of possible conformations at the higher energy. The system is cooled slowly to allow the molecule to sample probable conformational space to find the most energetically favorable conformation. Slowly cooling the system reduces the risk of becoming stuck in a local minimum. The structure is evaluated based on violations incurred to the NOE restraints, the sixth root residual $R_1^x$ calculated by the program complete relaxation matrix analysis (CORMA)[105-107], which compares calculated data to the experimental data, and root mean square deviation (rmsd) that evaluates the precision of the rMD calculations. Once these factors convey convergence of the calculated structure, helicoidal structure analysis can be performed using programs such as Curves[62,108] or 3DNA[109].




**Scheme 1-4**. Strategy for refining oligonucleotide structures using solution NMR.

*Circular Dichroism*

Circular dichroism (CD) is another technique that can provide information about secondary structure of optically active chiral biological molecules. While the structural information may not be as detailed as x-ray crystallography or NMR, it is much faster and only requires a small amount of sample, approximately 0.3 OD, but is able to detect small changes in secondary structure[110].

CD utilizes the differential absorption of circular right-handed polarized light and left-handed polarized light. When the light passes through the sample, the optically active chiral sample typically absorbs one direction preferentially. The difference in absorption between the two directions is detected. CD detects the degrees of ellipticity of the polarized light, θ. The change in polarization is a function of wavelength as well as sample conformation, which can be dependent on concentration, temperature, pH, etc. CD is typically reported in molar absorptivity:

$$[\theta] = 3298\Delta\varepsilon$$

where $[\theta]$ is the molar ellipticity and $\Delta\varepsilon$ is the molar absorptivity. Correlations between CD and structure have been found[111], making CD a useful tool for the field of structural biology.

## Dissertation Statement

The goal of this project is to structurally characterize the $N^2$-dG-IQ in the DNA duplex containing the GCGC dinucleotide repeat, where a difference in mis-coding potential has been observed with hpol η in *in vitro* assays in different sequence contexts. It is possible that the duplex structures differ between the mutagenic hotspot $G^3$ position where two-base deletions are observed versus the $G^1$ where frameshifts are rarely observed.

Structural studies could shed light why the mis-coding potential differs in the different sequence contexts by allowing the study of its structure-function relationship. It is hypothesized that the sequence context will dictate whether or not the IQ moiety will intercalate into the duplex, much like what was observed with the C8-dG-IQ adduct.

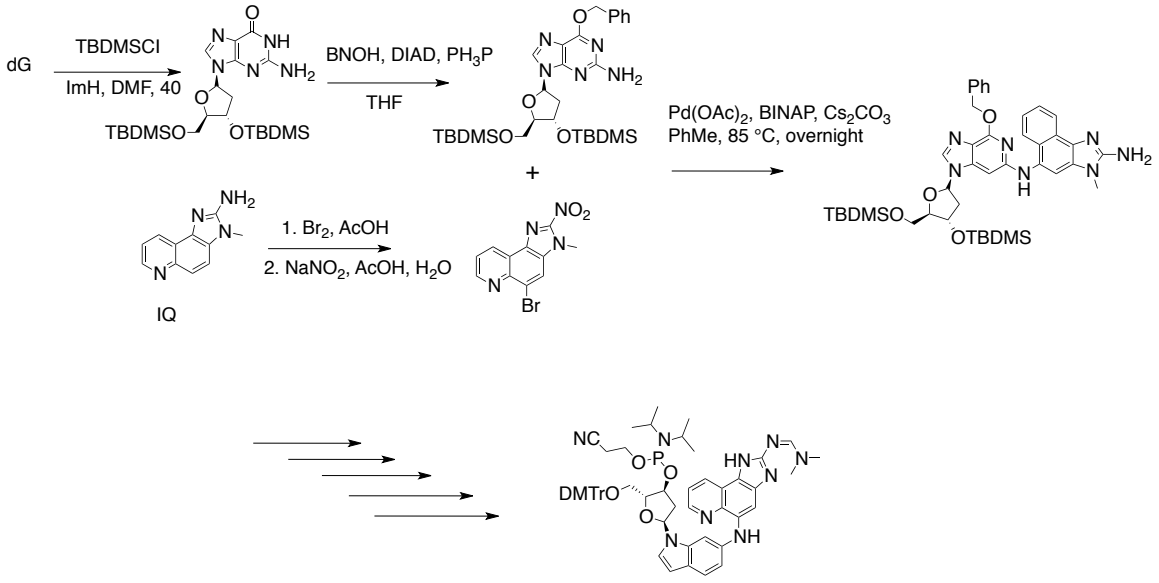
Chapter II describes the materials and methods for this project. Chapter III reveals the solution studies of $N^2$-dG-IQ by NMR at the mutagenic hotspot, $G^3$, in the *NarI* recognition sequence. Chapter IV details the solution studies of $N^2$-dG-IQ by NMR at $G^1$ in the *NarI* recognition sequence. Chapter V concludes the findings for the project as well as the future directions of the work.

## Chapter II

## MATERIALS AND METHODS

### Sample Preparation

Unmodified oligonucleotides were obtained from Midland Certified Reagent Co. (Midland, TX). The oligonucleotides were purified by reverse-phase high performance liquid chromatography (RP-HPLC) using 100 mM ammonium formate buffer at pH 7 with an acetonitrile gradient increasing at a rate of 1% every 2 minutes. The IQ-adducted strands was synthesized as previously published[112] and obtained from Professor Carmelo Rizzo's lab. The scheme depicting the Buchwald Hartwig palladium catalyzed reaction, which is an important step for the synthesis of the phosphoramidite is demonstrated in Scheme 2-1.




**Scheme 2-1.** Synthesis schematic for $N^2$-dG-IQ phosphoroamidite showing the Buchwald Hartwig palladium catalyzed reaction between IQ and dG, followed by five additional reaction steps to produce the phosphoroamidite.

The identity of each oligonucleotide was confirmed by MALDI-TOF mass spectrometry Voyager-DE (PerSeptive Biosystems, Inc.) instrument in the negative ion mode using a matrix consisting of 0.5 M 3-hydroxypicolinic acid (HPA) and 0.1 M ammonium citrate. The concentration of each single strand was determined using the extinction coefficient of 1.10 x $10^5$ $M^{-1}$ $cm^{-1}$ at 260 nm. Each duplex was then annealed at a 1:1 ratio at room temperature in a buffer solution containing 10 mM $NaH_2PO_4$ buffer containing, 100 mM NaCl, and 50 μM EDTA (pH 7). Duplex purities were confirmed by RP-HPLC.

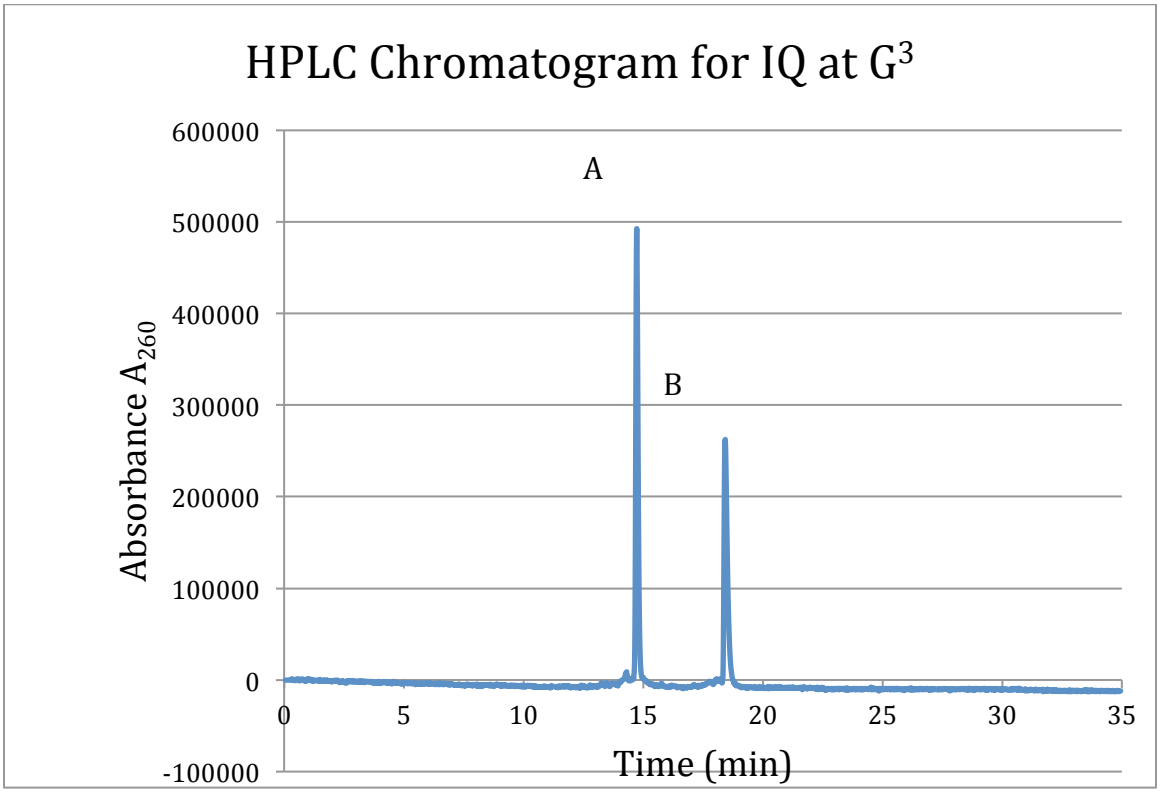



**Figure 2-1**. HPLC chromatogram of *Nar*I modified by IQ at $G^3$ with separation of both strands. Peak A shows the elution of the complement strand, while peak B is the IQ modified strand.

## Thermal Melting Experiments

UV melting temperatures were collected on Cary 100 Bio UV (Varian, Inc. Palo Alto, CA) spectrophotometer, and data was collected in the Cary WinUV Thermal Application (v2.0). Sample in the amount of 0.5 OD (4 μM) of duplex was suspended in 1 mL of solution containing 0.1 M NaCl, 10 mM $NaH_2PO_4$, and 50 μM $Na_2EDTA$ (pH 7.0). The temperature was increased from 25-75 °C at a rate of 1 °C per min and absorbance readings were taken every 0.5 °C. The melting temperature ($T_m$) was extrapolated from the first derivative of absorbance $A_{260}$ versus temperature profiles.

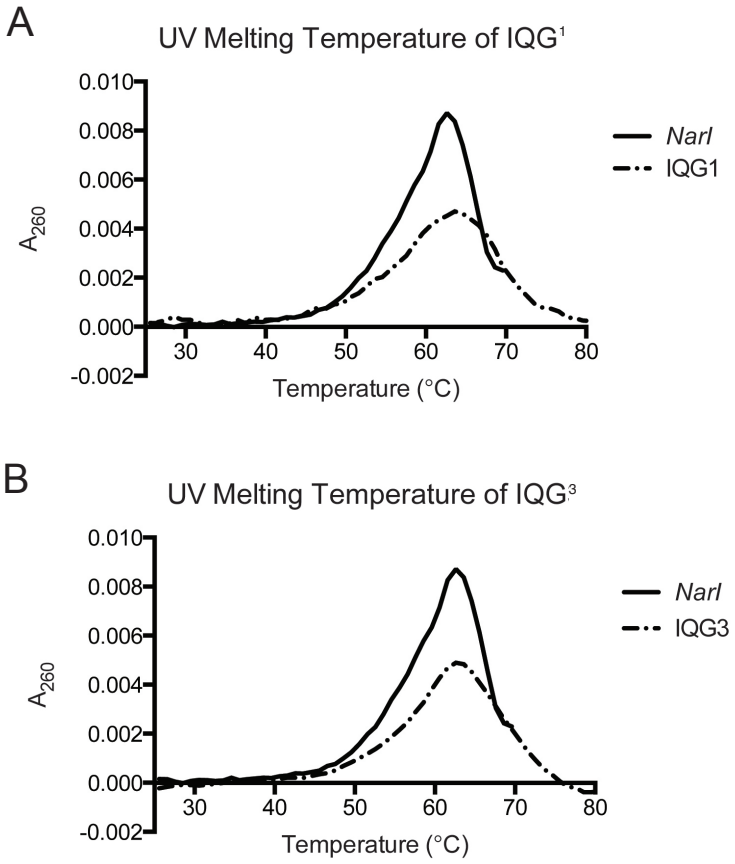



**Figure 2-2**. First derivative curves of UV thermal melting experiments for A) IQ at G1 and B) IQ at G3.

## Circular Dichroism

The samples contained 0.5 OD (4 μM) of duplex in a cuvette with 1 cm pathlength in buffer conditions of 0.1 M NaCl, 10 mM sodium phosphate buffer, and 0.05 mM EDTA at pH 7.0 in 800 μL volumes. Data was collected on Jasco 720 with a response time of 1 second, scan speed of 20 nm/min and step resolution of 1 nm across a wavelength of 400-200 nm over 10 accumulations.

## NMR Spectroscopy

Duplex samples were suspended in 180 μL buffer solution containing 10 mM $NaH_2PO_4$, 100 mM NaCl, 50 μM EDTA at pH 7. In order to observe the nonexchangeable protons, the solvent was exchanged for three rounds by drying the solvent and adding 99.9% pure $D_2O$, followed by an exchange with 99.996% $D_2O$, and finally suspended in 180 μL 99.996% $D_2O$ solution. Experiments to observe exchangeable protons were conducted in 9:1 $H_2O$: $D_2O$. $^1H$ NMR spectra were collected at 600 and 800 MHz. Nonexchangeable protons were observed at 15 °C; exchangeable protons were monitored at 5 °C. Chemical shifts were referenced to the water peak (4.868 ppm at 288 K). The data was processed in TOPSPIN (Bruker Biospin Inc., Billerica, MA).

NOESY data for nonexchangeable protons were collected using States-TPPI[113] phase cycling with a relaxation delay of 1.8 s and mixing times of 150, 200, and 250 ms to account for spin diffusion. Spectra for exchangeable protons were collected with a relaxation delay of 1.2 s and a mixing time of 100 ms. Spectra were recorded with 512 points in the t1 dimension and 2048 points in the t2 dimension, then zero-filled to 2048 x 2048 overall matrix. Water suppression was applied through the WATERGATE sequence[114].

## Distance Restraints

Spectrum analysis and assignments were performed in SPARKY[115]. Intensities of peaks were measured by volume integration using either Gaussian method for regular peaks or box method for irregular or overlapped peaks. Bounds for overlapped peaks were manually adjusted based on typical B-DNA values, unless near the adduct. Noise was assigned half the intensity of the weakest peak and motion was assumed to be isotropic. Experimental intensities were combined with intensities obtained from complete relaxation matrix analysis of starting model to generate a hybrid intensity matrix[116,117]. The intensities were converted to distances with the program MARDIGRAS[102], which refined the hybrid intensity matrix. Calculations were performed using 150, 200, and 250 ms mixing time data and 2, 3, and 4 ns isotropic correlation times. Evaluation of the resulting distance data allowed creation of upper and lower bound distance restraints that were used in restrained molecular dynamics (rMD) calculations.

## Restrained Molecular Dynamics Calculations

An unmodified B-DNA model[118] was used as a starting structure. The guanine at position $G^7$ was replaced by the $N^2$-dG-IQ adduct using the program INSIGHT II (Accelrys Inc., San Diego, CA). Partial charges for the $N^2$-dG-IQ adduct were calculated with the B3LYP/6-31G* basis set in GAUSSIAN[119]. The starting structure was energy minimized for 1000 cycles. Simulated annealing protocols[120] used for the rMD calculations were conducted with the parm99 force field[121], using the program AMBER[122]. Force constants of 32 kcal $mol^{-1}$ $Å^{-2}$ were applied for distance and torsion angle restraints. The generalized

Born model[123] was used for solvation. The NaCl concentration was 0.1 M. The molecule was coupled to the bath temperature to control the temperature during simulated annealing. First, calculations were performed for 20 ps (20000 steps) and recording data every ps by the following protocol: During steps 0 – 1000, the system was heated from 0 to 600 K with a coupling of 0.5 ps. During steps 1001-2000, the system was kept at 600 K. The system was then cooled from 600 K to 100 K during steps 2001 – 18000 with a coupling of 4 ps. Further cooling from 100 K to 0 K occurred during steps 18001 – 20000 with a coupling of 1 ps. After initial cycles of refinement a longer 100 ps (100000 steps) calculation was performed by the following protocol: During steps 0–5000 the system was heated from 0 to 600 K with a coupling of 0.5 ps. During steps 5001-10000 the system was kept at 600 K. The system was cooled from 600 K to 100 K during steps 10001 – 90000 with a coupling of 4 ps. Additional cooling from 100 K to 0 K occurred during steps 90001 – 100000 with a coupling of 1 ps. Structure coordinates were saved after each cycle, and were subjected to potential energy minimization. Complete relaxation matrix analysis (CORMA)[116,117] was used to compare intensities calculated from these emergent structures with the distance restraints. Helicoidal analysis was performed using the CURVES+ web server[124,125].

## Expression and Purification of Dpo4

A glycerol stock of the vector pET22b(+) with plasmid coding for Dpo4 with a c-terminal $(His)_6$ tag with ampicillin resistance in *E. coli* strain BL21(DE3) competent cells (Stratagene, CA) was a gift from Professor Fred Guengerich's lab. A fresh glycerol stock was made from ~1 μL of these cells by adding to 100 mL Luria broth culture and shaking overnight at 37 °C. Seven hundred fifty μL of Luria broth was mixed with 250 μL of

glycerol, flash frozen, and stored at -80 °C. The plasmid was also isolated from remaining cells using QIAprep Spin Mini Prep Kit (Quiagen, Germany) and submitted to the DNA core for sequencing to ensure no mutations had occurred over time.

To express Dpo4, ~1 μL of the glycerol stock of cells was added to a culture flask containing a volume of 25 mL of LB per 1 L flask and shaken overnight (14-16 hrs.) at 37 °C. The overnight flask was then distributed evenly between all flasks containing 1 L LB and 1 mL of ampicillin stock solution of 100 mg/mL. The flasks shook at 37 °C until the optical density at 600 nm ($OD_{600}$) reached 0.6. The cells were then induced by adding 1 mL of 1 M IPTG to each flask. The flasks continued to shake at 37 °C for 3.5 hrs., after which the cell pellets were harvested by centrifugation at 9000 rpm at 4 °C for 45 min. (Beckman, JLA-9.100) in a Beckman Avanti-25 centrifuge and stored at -80 °C until purification.

To purify Dpo4, lysis buffer containing 50 mM Tris-HCl buffer at pH 7.5, 300 mM NaCl, 10% glycerol (v/v), 5 mM β-mercaptoethanol, 1 mg/mL lysozyme, and 1 protease inhibitor tablet (Roche Applied Science) was added to thawed cell pellet and resuspended, bringing the total volume to about 35-40 mL before cooling on ice for 30 min. The cells were lysed through 2-3 intervals of sonication (Branson Sonifier 450, Danbury, CT) (for 1 min. on and one min. off). Cell debris was removed by centrifuging at 10,000 rpm (Beckman, JA-12) at 4 °C for 45 min. The supernatant was removed and heated in water bath to 78 °C for 10 min. The denatured proteins were again spun off at 10,000 rpm (Beckman, JA-12) at 4 °C for 45 min.

The supernatant was loaded on FPLC to a 5 mL HisTrap column (GE Healthcare Life Sciences) equilibrated with Buffer A (50 mM Tris HCl (pH 7.5), 300 mM NaCl, 10% glycerol (v/v) and 5 mM β-mercaptoethanol). The column was washed with 5% Buffer B (Buffer A +

500 mM imidazole) for 5 column volumes, then changed to 100% Buffer B over 2 column volumes and held for 3 column volumes. Dpo4 elution was monitored by $A_{280}$.

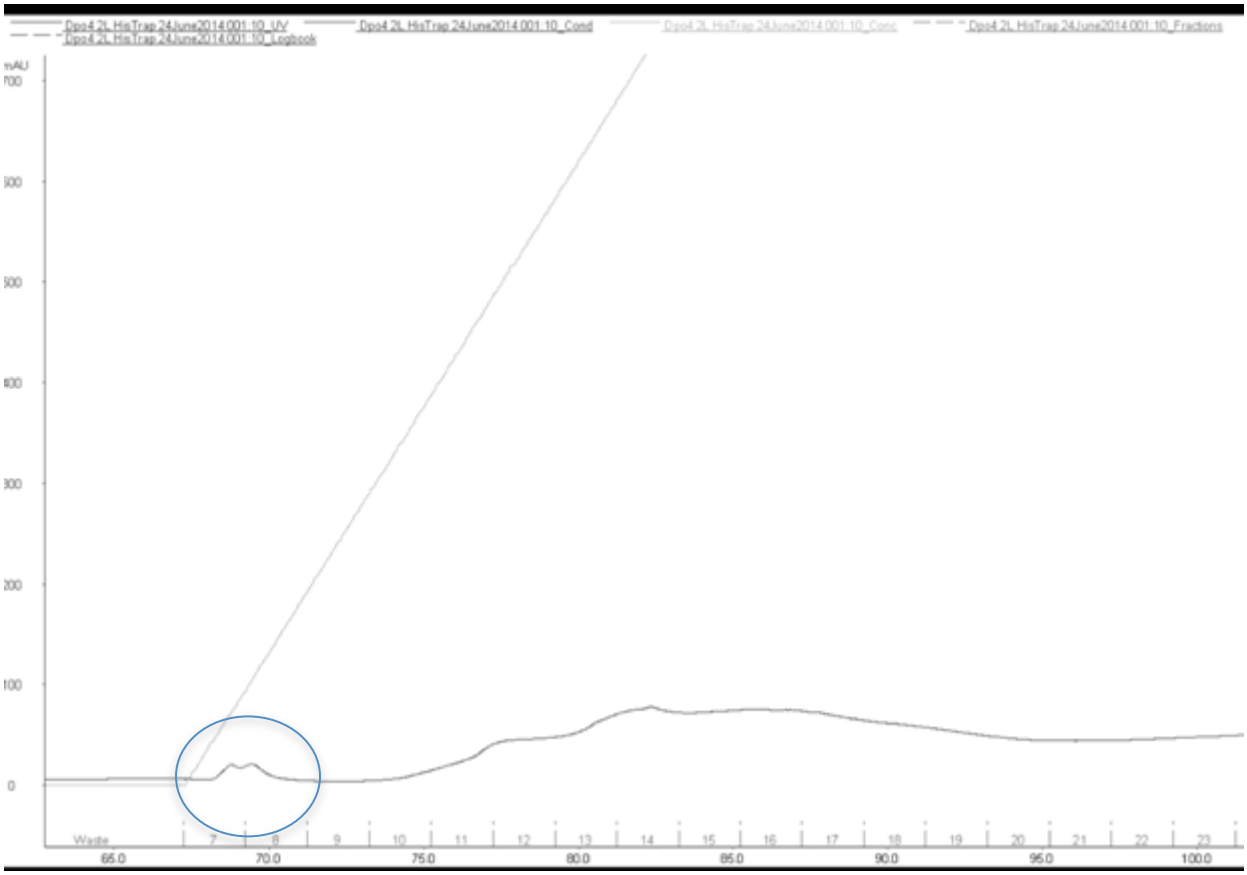



**Figure 2-3.** Dpo4 elution on HisTrap column.

Fractions containing Dpo4 were combined and spun down in 15 mL Millipore centrifuge filter tubes with 30kDa cut off. After the protein reached a volume of about 1-2 mL, it was diluted with Buffer A (50 mM Tris-HCl pH 7.5, 0.5 mM EDTA, 10% glycerol (v/v), and 5 mM β-mercaptoethanol) to about 20-25 mL. The protein solution was loaded onto an 8-mL MonoS column (GE Healthcare) and eluted with Buffer B (Buffer A + 500 mM NaCl) over a linear gradient for 8 column volumes, reaching 100% B. Dpo4 elution was monitored by $A_{280}$.


**Figure 2-4.** MonoS elution profile of Dpo4.

The purity of Dpo4 was assessed by SDS-page gel using pre-cast Nu-Page 4-12% Bis-Tris gels (Life Technologies, NY) (Figure B-3). The protein was concentrated to ~40-50 mg/mL, as determined by the $A_{280}$ and the molar extinction coefficient of 22 $mM^{-1}$ $cm^{1126}$.

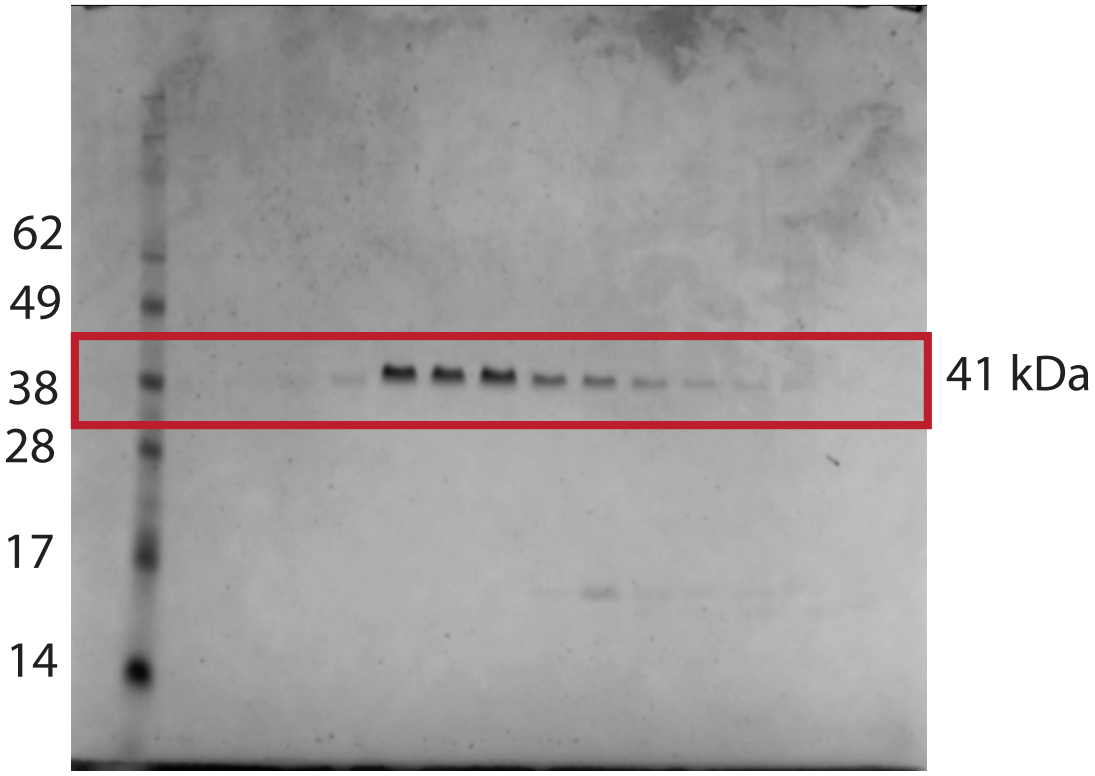



**Figure 2-5.** SDS-PAGE gel of Dpo4 after final purification step showing intended band at about 41 kDa.

## Activity Assay

Unmodified 19mer template strand and 12mer with a 5´ FAM tag were purchased from IDT (Coralville, IA) and purified by HPLC. The duplex was annealed at a 1:1 ratio by placing it in an 85 °C hot water bath for 10 minutes and allowing to cool slowly to room temperature. Dpo4/DNA reactions were run at 10 μM DNA and 100 μM Dpo4 concentrations in a buffer of 25 mM Tris-HCl (pH 7.8), 5 mM DTT, 0.1 $mg{\cdot}mL^{-1}$ BSA, and 5

mM $MgCl_2$, by incubating the mixture at 37 °C with 20 mM total dNTPs. Time points were taken at 0, 2, 5, 10, 20, 40, 60, 75, 90, 105, and 120 min. and quenched with a solution of 20 mM $Na_2EDTA$ in 95% formamide (with bromophenol) and denatured at 90 °C for 10 min. Electrophoresis was used to separate reaction products on a denaturing gel containing 40% acrylamide solution. The gel was imaged on a UV scanner able to detect the fluorescence at 520 nm.

## Crystallization of DNA:Dpo4 Complexes

The sequences 5′-TCAC(8OG)GAATCCTTCCCCC-3’ 18mer template strand and 5’-GGGGGAAGGATTCC-3’ 14mer primer strand were obtained from Midland (Midland, TX) and were based on a previously published structure[127,128].

Dpo4 and DNA sequences were mixed at 1:1.2 molar ratio at final 200 μM protein concentration in a buffer containing 20 mM HEPES (pH7.4), 5 mM DTT, and 100 mM NaCl and incubated on ice for 10 min. Five mM $CaCl_2$ was added to ternary complex solutions and incubated an additional 10 min. Individual 1 mM dNTPs were then added to the ternary complex, and they were incubation was done at 37 °C for 5 min. The complex solutions were finally spun down at 8000 rpm for 5 min. before setting up via hanging drop vapor diffusion with a 1:1 ratio of reservoir solution consisting of 20 mM HEPES (pH 7.4), 100 mM $Ca(OAc)_2$, and 10-20% PEG 4000 (w/v). Plates were incubated at room temperature. Crystals were looped in the mother liquor (plus an additional 25% PEG (4000) and 15% ethylene glycol) and flash frozen in liquid nitrogen.

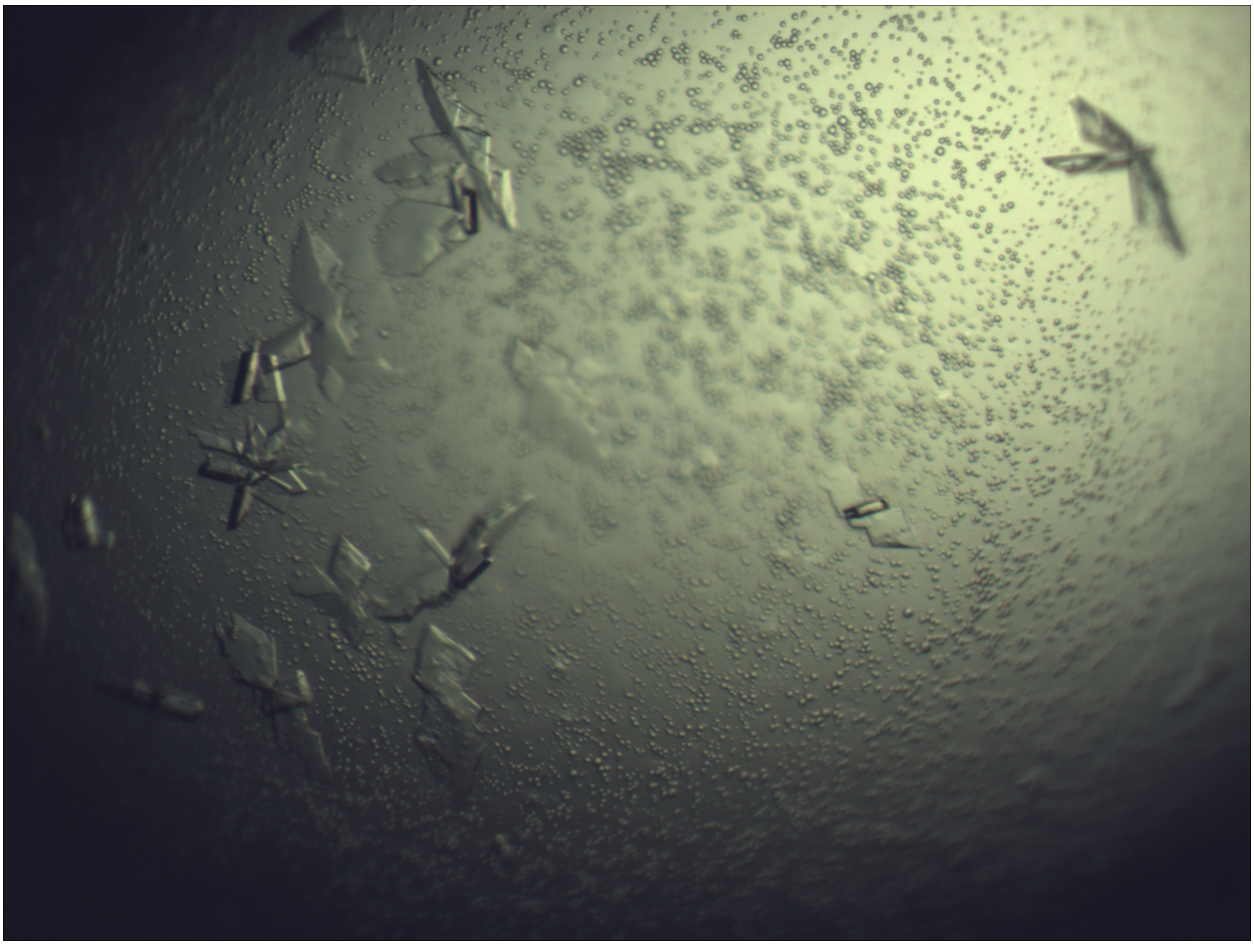


**Figure 2-6.** Typical crystals of Dpo4 with 8-oxoG modified oligonucleotide.

## X-Ray Diffraction Data Collection and Processing

The crystals were shipped to Dr. Surajit Banerjee, who collected diffraction data at 100 K at a wavelength of 1.0 Å on beamline 24-ID-C (Northeast Collaborative Access Team NE-CAT, Advanced Photon Source, Argonne, IL). Indexing and scaling were done using HKL2000[129].

## Structure Determination and Refinement

The starting model came from PDB accession code 2C22[130] without the modified 8-oxoG base (minus the waters) was also created by Dr. Surajit Banerjee. The structure was

refined using CNSsolve (v1.3)[131,132] by rounds of minimization and individual b-factor optimization. A single waterpick was also initially run in CNS. Molecules were manually aligned with the data and water molecules were subsequently placed in positive regions of the $F_o$-$F_c$ Fourier difference electron density in Coot[133]. 10% of the reflections were excluded from the refinement for use in $R_{free}$ calculations. Figures were prepared using Pymol[134].

## Chapter III

## SOLUTION STRUCTURE OF $N^2$-dG-IQ AT THE MUTAGENIC HOTSPOT $G^3$ POSITION IN THE *NARI* SEQUENCE CONTEXT*

### Introduction

The IQ-dG adduct results from the metabolism of IQ upon the consumption of meat cooked at high temperatures. This chapter focuses on the NMR solution studies and characterization of the IQ adduct in the mutagenic hotspot of the 12mer based on the *NarI* recognition sequence, 5'-$C^1T^2C^3G^4G^5C^6X^7C^8C^9A^{10}T^{11}C^{12}$-3' paired with 5'-$G^{13}A^{14}T^{15}G^{16}G^{17}C^{18}G^{19}C^{20}C^{21}G^{22}A^{23}G^{24}$-3'. Thermal melting temperature experiments indicate it is a stable duplex when paired opposite the correct dC base, which does not change from the unmodified duplex. NMR data suggests this is due to intercalation into the duplex, which allows base stacking to occur with base pairs $C^6{\cdot}G^{19}$ and $C^8{\cdot}G^{17}$. This does, however, prevent $C^{18}$ from Watson-Crick hydrogen bonding with $X^7$, since it is flipped into the major groove to allow the IQ moiety to intercalate. The modified base also remains in the *anti* conformation. These results may explain why the $N^2$-dG-IQ is poorly repaired when compared to the C8-dG-IQ adduct.

### Results

*Oligodeoxynucleotide Containing the $N^2$-dG-IQ Adduct*

The $N^2$-dG-IQ adduct was incorporated into 5'-d(CTCGGCXCCATC)-3' using automated solid-phase synthesis[135]. The position of the $N^2$-dG-IQ adduct was located at

---

* Reprinted manuscript with permission from Stavros, KM; Hawkins, EK; Rizzo, CJ; Stone MP, *Nucl. Acid. Res.,* **2014**, 42(5), Copyright (2014) Oxford University Press, 1/6/15.

position $X^7$, corresponding to position $G^3$ in the *NarI* sequence. The modified oligodeoxynucleotide was purified by C18 reversed phase HPLC and characterized by MALDI-TOF mass spectrometry in the negative ion mode [*m/z* 3777.7, calcd for (M – H), 3776.6]. Thermal melting ($T_m$) profiles of 0.5 $A_{260}$ units (4 μM) of the IQ-modified duplex were monitored at 100 mM NaCl (1 mL volume) by its absorbance at 260 nm as a function of temperature. An unmodified duplex was evaluated under the same conditions to provide a basis of comparison. The $T_m$ of the modified duplex was 63 ºC and is within experimental error of the unmodified duplex (Figure S1 in the Supplementary Data). Thus, the $N^2$-dG-IQ adduct did not reduce the stability of this oligodeoxynucleotide. This result differed from our previous report, which had indicated that this adduct destabilized this duplex[135]. Subsequent analysis of the previous sample by mass spectrometry revealed that the complement strand was not correct, accounting for the discrepancy. Table 3-1 lists the correct $T_m$ values of the $N^2$-dG-IQ adduct at the three positions of the *NarI* sequence.

*NMR*

The modified duplex yielded well-resolved NMR spectra with narrow line shapes for the non-exchangeable protons at 15 °C. The best spectral quality for the exchangeable protons was obtained at 5 °C.

**(a) Non-exchangeable DNA Protons.** The base aromatic and deoxyribose anomeric protons were assigned using established procedures (Figure 3-1)[136,137]. The intensity of the $X^7$ H8 to $X^7$ H1' NOE was not changed in the presence of the adduct, indicating minimal change in the conformation of the glycosyl torsion angle. In the complementary strand, the intensity of the NOE between $C^{18}$ H1' and $G^{19}$ H8 was weakened. The $N^2$-dG-IQ adduct did not induce breaks in the sequential pattern of

NOEs between the aromatic base protons and the anomeric protons. With the exception of the adduct site, the internucleotide NOEs were characteristic of a B-type duplex. The adenine H2 protons were assigned based upon NOEs to the thymine imino protons of the respective A:T base pairs. With the deoxyribose H1' assignments in hand, the remainder of the deoxyribose protons were assigned from a combination of NOESY and COSY data. The assignments of the non-exchangeable DNA protons are summarized in the Appendix D.

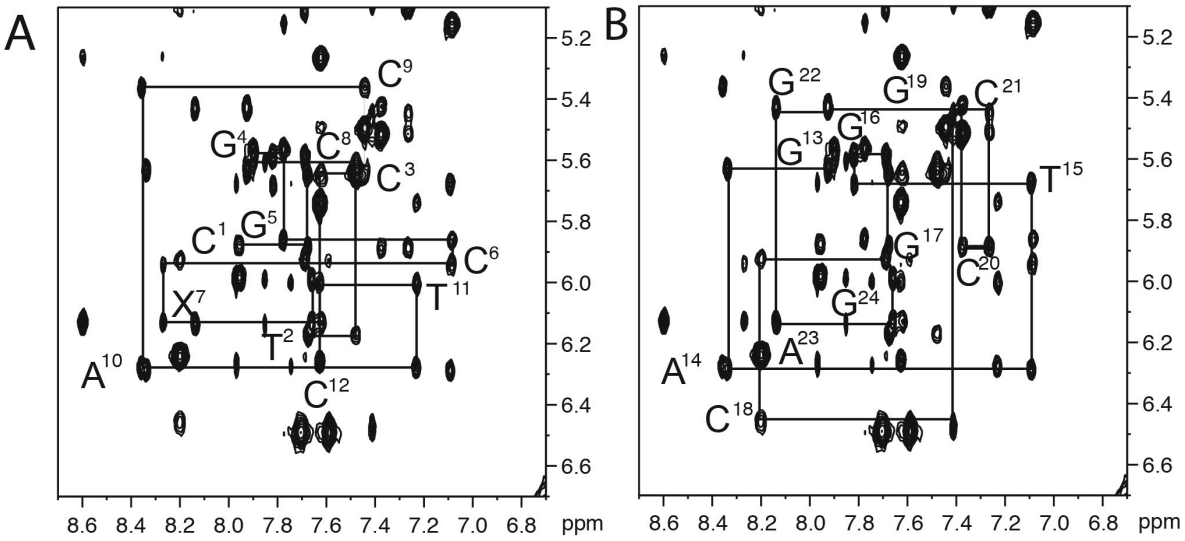



**Figure 3-1.** Expanded plot of the 250 ms NOESY spectrum showing NOEs between the base aromatic and deoxyribose anomeric protons of the *N*$^2$-dG-IQ modified duplex. A. Bases C$^1$ to C$^{12}$ of the modified strand. B. Bases G$^{13}$ to G$^{24}$ of the complementary strand. The spectrum was acquired at 800 MHz at 15 °C.

**(b) Exchangeable DNA Protons.** The imino and amino proton regions of the NOESY spectrum are shown in Figure 3-2. The assignments were made using established methods[100]. The *N*$^2$-dG-IQ adduct perturbed Watson-Crick hydrogen bonding. At the X$^7$:C$^{18}$ base pair, the X$^7$ imino proton resonance was broadened, probably due to an enhanced rate of exchange with water. The amino protons for C$^{18}$ were not

detected. No NOE was observed between the $X^7$ and $G^{19}$ imino protons, perhaps due to the broadening of the $X^7$ imino proton. The chemical shifts of the $X^7$ and $G^{17}$ imino protons were almost isochronous. It was not possible to determine if a NOE between these two protons existed. Figure 3-3 shows the assigned $X^7$ N1H peak visible as a shoulder to $G^{17}$ N1H, which is no longer observable above 5 °C. All other base pairs were assigned, with the exception of the two terminal base pairs $C^1$:$G^{24}$ and $C^{12}$:$G^{13}$. The imino protons from the terminal base pairs were exchange broadened. Overall, the data suggested that the duplex maintained Watson-Crick hydrogen bonding, with the exception of the modified base pair (Figure 3-2B). The assignments of the exchangeable protons are summarized in Appendix D.

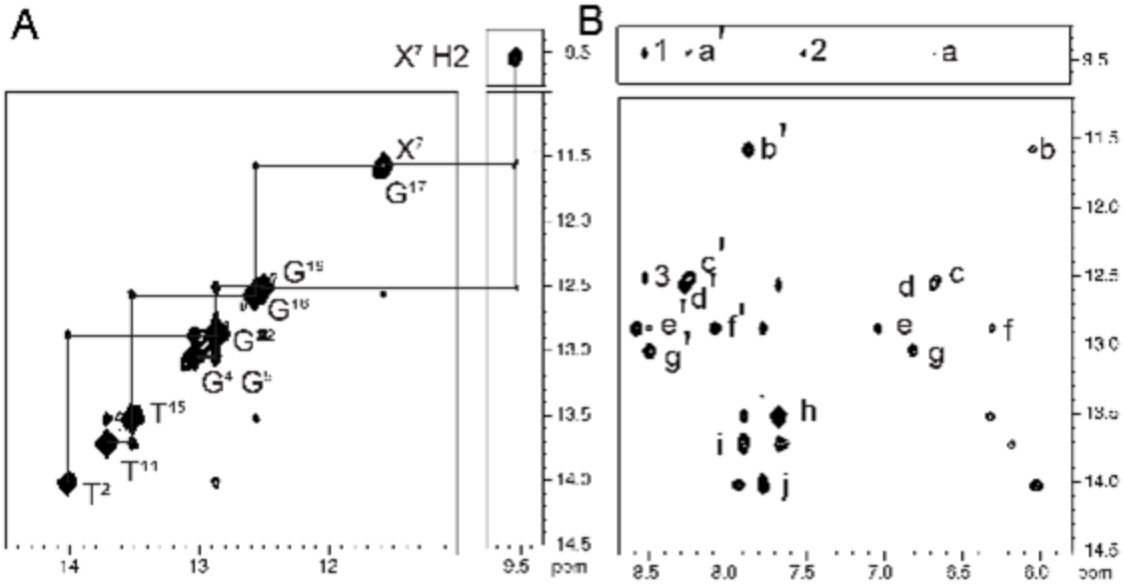



**Figure 3-2.** Expanded plots of the NOESY spectrum, showing the NOEs between the exchangeable imino and amino protons of the *N*²-dG-IQ-modified duplex. A. Sequential NOE connectivity for the imino protons of base pairs $T^2$:$A^{23}$ to $T^{11}$:$A^{14}$. B. NOE connectivity within Watson-Crick base pairs and between the imino protons and the amino protons. The lettered cross-peaks are assigned as follows: a', $X^7$ *N*²H →$C^6$ *N*⁴Hb; a, $X^7$ *N*²H →$C^6$ *N*⁴Ha; b', $G^{17}$ N1H→$C^8$ *N*⁴Ha; b, $G^{17}$ N1H→$C^8$ *N*⁴Hb; c', $G^{19}$ N1H→$C^6$ *N*⁴Hb; c, $G^{19}$ N1H→$C^6$ *N*⁴Ha; d', $G^{16}$ N1H→$C^9$ *N*⁴Hb; d, $G^{16}$ N1H→$C^9$ *N*⁴Ha; e', $G^{22}$ N1H→$C^3$ *N*⁴Hb; e, $G^{22}$ N1H→$C^3$ *N*⁴Ha; f', $G^5$ N1H→$C^{20}$ *N*⁴Hb; f, $G^5$ N1H→$C^{20}$ *N*⁴Ha; g', $G^4$ N1H→$C^{21}$ *N*⁴Hb; g, $G^4$ N1H→$C^{21}$ *N*⁴Ha; h, $T^{15}$ N3H→$A^{10}$ H2; i, $T^{11}$ N3H→$A^{14}$ H2; j, $T^2$ N3H→$A^{23}$ H2; 1, $X^7$ *N*²H→IQ H4a; 2, IQ H7a→$X^7$ *N*²H; 3, $X^{19}$ N1H→IQ H4a. The spectrum was collected at 800 MHz at 5 ºC.

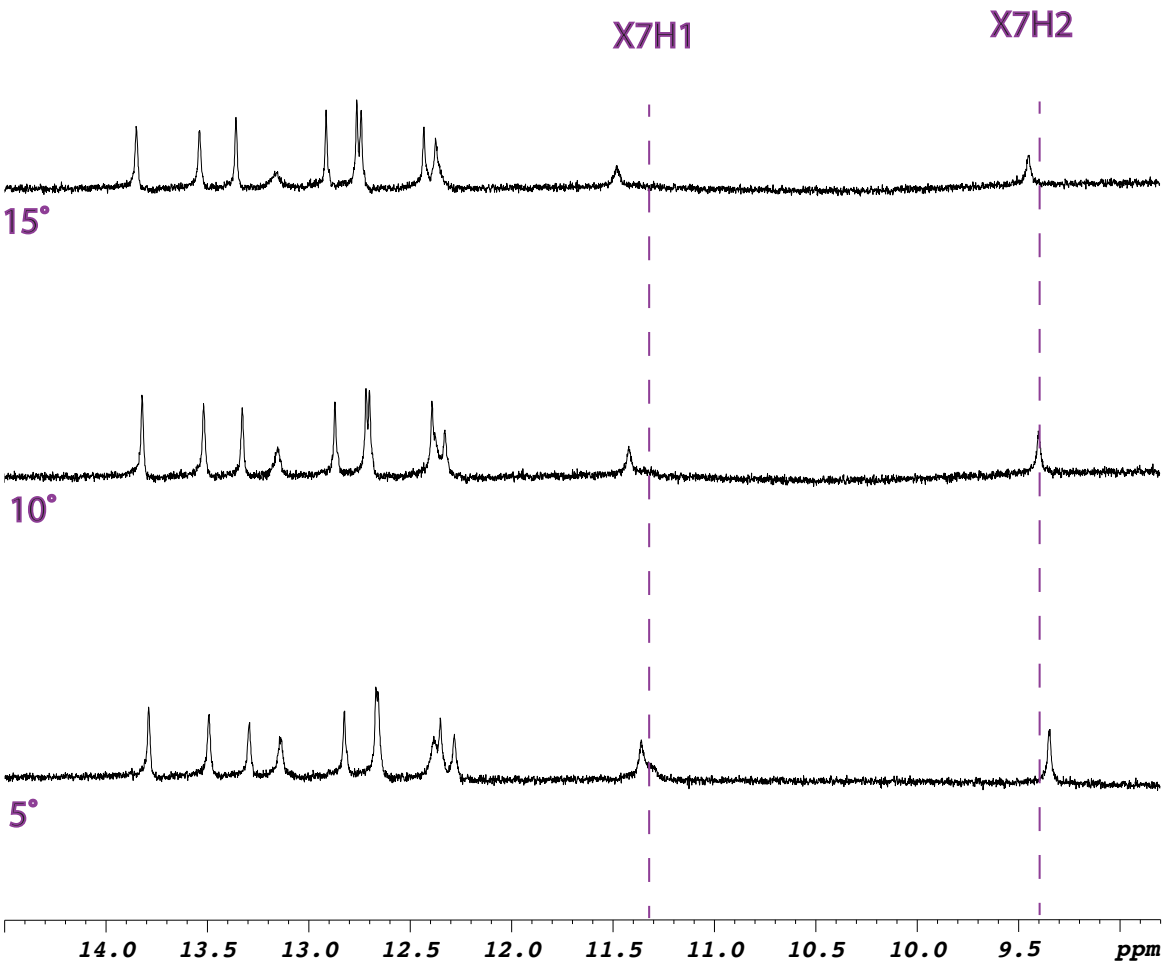



**Figure 3-3.** 1-D spectra of imino exchangeable region at different temperatures showing the broad peak observed at 5 °C believed to be $X^7$ N1H, appearing as a shoulder to $G^{17}$ and quickly disappears as the temperature increases, while the $X^7$ N2H peak is much sharper.

**(c) IQ Protons.** The IQ protons, consisting of the $CH_3$ group, the H4a proton, and the H7a, H8a, and H9a spin system, were assigned from a combination of COSY and NOESY data (Figure 3-3). The $CH_3$ resonance was observed at 3.57 ppm. It displayed an intense NOE to the H4a proton, whose resonance was observed at 8.55 ppm. A $^3J$ coupling between the H8a proton (δ 6.55 ppm) and the H9a proton (δ

7.65 ppm) was observed in the COSY spectrum. The H8a proton also exhibited an NOE to the H7a proton (δ 7.6 ppm). The $^{3}J$ coupling between H8 and H7a exhibited weak intensity in the COSY spectrum. This was attributed to presence of the nitrogen atom in the ring, which broadened the H7a resonance. This effect was also observed for the C8-dG-IQ adduct, for which the COSY cross peak between H7a and H8a was only observed between 25-35 °C [138]. The IQ amine proton was not assigned. Assignments are shown in Figure 3-3.

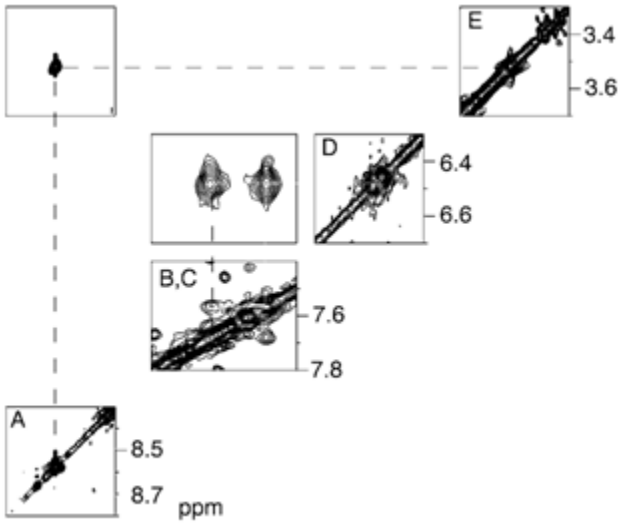



**Figure 3-4.** Expanded tile plot of the 250 ms NOESY spectrum showing the assignments of the IQ ring protons. A. The IQ H4a proton was observed at 8.55 ppm. B. The IQ H9a proton was observed at 7.65 ppm. C. The IQ H7a proton was observed at 7.6 ppm. D. The IQ H8a proton was observed at 6.55 ppm. E. The IQ CH3 protons were observed at 3.57 ppm. The spectrum was collected at 800 MHz at 15 ºC.

**(d) Chemical Shift Perturbations.** The $N^{2}$-dG-IQ adduct resulted in localized chemical shift perturbations, involving the modified base pair $X^{7}$:$C^{18}$ and the neighboring $C^{6}$:$G^{19}$ and $C^{8}$:$G^{17}$ base pairs (Figure 3-5). At the modified $X^{7}$:$C^{18}$ base pair, the $X^{7}$ H8 resonance shifted 0.4 ppm downfield relative to the $G^{7}$ H8 resonance in the

unmodified duplex. In contrast, the $C^{18}$ H6 and $C^{18}$ H1' resonances shifted 1 ppm and 0.8 ppm downfield, respectively. At the 5'-neighbor $C^{6}$:$G^{19}$ base pair, the $C^{6}$ H6 resonance shifted upfield by 0.2 ppm, whereas the $C^{6}$ H1' resonance shifted downfield by 0.4 ppm. The $G^{19}$ H8 and H1' resonances each shifted upfield by 0.4ppm.

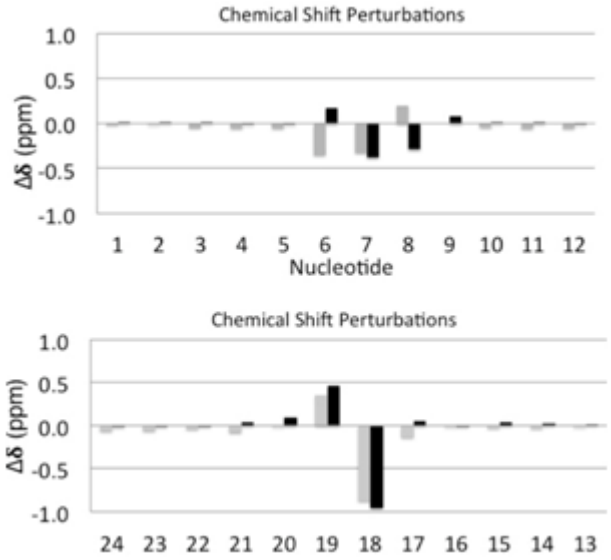



**Figure 3-5.** Chemical shift perturbations of the deoxyribose H1' protons (grey) and the pyrimidine H6 or purine H8 aromatic protons (black), for the $N^{2}$-dG-IQ modified duplex. A. Nucleotides $C^{1}$-$C^{12}$ in the modified strand. B. Nucleotides $G^{13}$-$G^{24}$ in the complementary strand. The Δδ (ppm) values were calculated as δmodified duplex-δunmodified duplex. Positive Δδ values represent upfield chemical shift perturbations. Negative Δδ values represent downfield chemical shift perturbations.

At the 3'-neighbor $C^{8}$:$G^{17}$ base pair, the $C^{8}$ H8 resonance shifted downfield by 0.3 ppm, whereas the $C^{8}$ H1' resonance shifted upfield by 0.2 ppm. The $G^{17}$ H8 resonance shifted downfield 0.1 ppm. The $G^{17}$ H1' resonance showed negligible chemical shift perturbation. The resonances for the remaining base pairs in the duplex also showed negligible chemical shift perturbations. In the imino proton region of the spectrum, the $X^{7}$ and $G^{17}$ N1H imino resonances, at 11.57 and 11.59 ppm, respectively, exhibited upfield chemical shifts of greater than 1 ppm from

those of the unmodified duplex, at 13.24 and 13.16 ppm, respectively. The $X^7$ $N^2$H amine resonance was observed at 9.5 ppm.

**(e) NOEs Between IQ and DNA.** The $CH_3$, H4a, H7a, and H8a protons of IQ exhibited NOEs to the $C^8$, $G^{17}$, $C^{18}$, and $G^{19}$ bases (Table 3-1). The pattern of NOEs involving H9a was difficult to establish due to resonance overlap with $G^{17}$. The $CH_3$ group showed medium strength NOEs to $X^7$ H1' and $C^8$ H6, and weak NOEs to $C^8$ H1' and $C^8$ H5. It also showed an NOE to the $G^{19}$ N1H imino proton. The H4a proton showed a strong NOE to $X^7$ H1', and medium NOEs to $C^8$ H5, the $X^7$ N2H amine proton, and the $G^{19}$ N1H imino proton, and weak NOEs to $X^7$ H2' and $X^7$ H2". The H7a proton exhibited weak NOEs to $G^{17}$ H1', and the $X^7$ N2H amine proton. Three NOEs from $X^7$ to $C^{18}$ were observed; these were of medium strength NOE between H9a and $C^{18}$ H1', and H8a and medium strength between $C^{18}$ H2' and H2''. The H8a proton showed a medium strength NOE to $G^{19}$ H3', and weak NOEs to $G^{17}$ H1' and $G^{19}$ H8. Some 30% of the NOEs from the IQ ring were to protons in the complementary strand, while another 46% were to other IQ protons and protons of the modified base. The remaining 24% of the NOEs were to neighbor bases in the modified strand.

**Table 3-1.** Summary of NOEs observed between $N^2$-dG-IQ adduct protons and oligodeoxynucleotide protons, and their intensities.

| IQ proton | NOEs to Oligodeoxynucleotide Protons |
|---|---|
| **$CH_3$** | $X^7$ H1' - medium; $C^8$ H6 - medium; $C^8$ H1'- weak; $C^8$ H5 - weak |
| **H4a** | $X^7$ H1' - strong; $C^8$ H5 - medium; $X^7$ H2' - weak; $X^7$ H2" - weak; $X^7$ N2H - medium; $G^{19}$ N1H- medium |
| **H7a** | $G^{17}$ H1' - weak, $X^7$ H2 - weak |
| **H8a** | $G^{19}$ H3' - medium; $C^{18}$ H2' - medium; $C^{18}$ H2"- medium; $G^{17}$ H1' – weak, $G^{19}$ H8 - weak; $G^{17}$ H2" - weak |
| **H9a** | $C^{18}$ H1' - medium |

*Conformational Refinement*

After the unmodified duplex was constructed using B-DNA coordinates[139], the guanine at position $G^7$ was replaced by the $N^2$-dG-IQ adduct. The partial charges for the $N^2$-dG-IQ adduct are provided in Figure S2 of the Supplementary Data. Potential energy minimization provided an energy minimized starting duplex. A total of 329 distance restraints consisting of 127 inter- and 202 intra-nucleotide distances (Table 3-2) were obtained using the program MARDIGRAS[140,141], from 15 °C NOESY data. Similar distance restraints were obtained if the data were collected at 150 ms, 200 ms, or 250 ms mixing times. These restraints included 16 DNA-IQ distances. A total of 49 Watson-Crick hydrogen-bonding restraints were applied for all of the base pairs except for the modified $X^7$:$C^{18}$ base pair. An additional 100 phosphodiester backbone and 20 deoxyribose pseudorotation restraints for base pairs not proximal to the site of modification were obtained from canonical values derived from B-DNA[139], consistent with the spectroscopic

data indicating that the duplex maintained a B-DNA like structure. A series of rMD calculations were performed using a simulated annealing protocol in which the generalized Born solvation model[142] was used, with a salt concentration of 0.1 M. The emergent structures were subjected to potential energy minimization before further analysis, which involved a 100 ps rMD calculation using the protocol described above, again followed by potential energy minimization.

**Table 3-2.** NMR restraints used for the $N^2$-dG-IQ structure calculations and refinement statistics.

| NOE restraints | |
|---|---|
| Internucleotide | 127 |
| Intranucleotide | 202 |
| Total | 329 |
| Backbone Torsion Angle Restraints | 100 |
| H-bonding Restraints | 49 |
| Deoxyribose Restraints | 20 |
| Total number of restraints | 498 |
| Refinement Statistics | |
| Number of distance restraint violations | 56 |
| Number of torsion restraint violations | 50 |
| Total distance penalty/Maximum penalty [kcal $mol^{-1}$] | 2.3/0.187 |
| Total torsion penalty/Maximum penalty [kcal $mol^{-1}$] | 2.8/0.177 |
| r.m.s. distances (Å) | 0.012 |
| r.m.s. angles (°) | 2.5 |
| Distance restraint force field [kcal $mol^{-1}$ $Å^{-2}$] | 32 |
| Torsion restraint force field [kcal $mol^{-1}$ $deg^{-2}$] | 32 |

The pairwise rmsd analysis of structures emergent from the rMD calculations was used to measure the precision of the structural refinement. Ten structures were chosen based on the lowest deviations from the experimental distance and dihedral restraints (Figure 3-6). These exhibited an rmsd of 0.012 Å in distances and 2.5° in torsion angles (Table 3-3). There were 56 distance violations with a maximum penalty of 0.187 kcal•$mol^{-1}$

and a total distance penalty of 2.3 kcal•mol$^{-1}$. There were 50 torsion angle violations with a maximum penalty of 0.177 kcal•mol$^{-1}$ and a total torsion angle penalty of 2.8 kcal•mol$^{-1}$. The maximum pairwise rmsd distances were 1.12 Å. These structures were averaged and subjected to potential energy minimization.

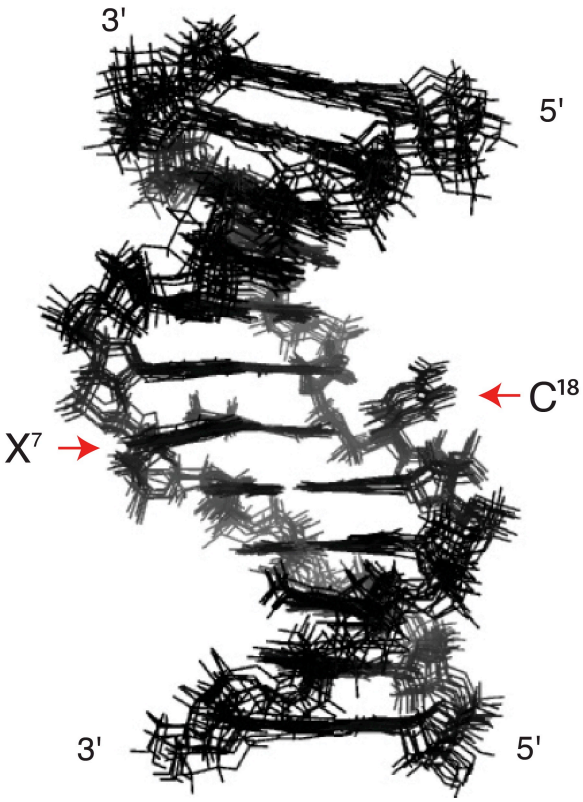



**Figure 3-6.** Superposition of ten potential energy minimized structures emergent from the rMD calculations of the *N*$^2$-dG-IQ modified duplex, using distance restraints from the 250 ms NOESY data. The positions of the modified X$^7$ nucleotide and the C$^{18}$ nucleotide in the complementary strand are as indicated. The maximum pairwise rmsd between these ten structures was 1.12 Å.

The accuracy of the refined structures was assessed by complete relaxation matrix analyses[140,143], which compared intensities calculated from the refined structures with the distance restraints (Figure 3-6). The sixth root residual $R^1_x$ value of the average structure was 8.4%, and the individual values for intra-nucleotide restraints (8.5%) and inter-nucleotide restraints (8.3%) were of similar magnitudes. This indicated agreement with

the NOE data. Nucleotide $G^{19}$ exhibited a greater $R^1_x$ value of 17.1%, suggesting that it was not as well-refined. This was attributed to several NOEs involving $G^{19}$ being overlapped with other resonances. The structural statistics are summarized in Table 3-4.

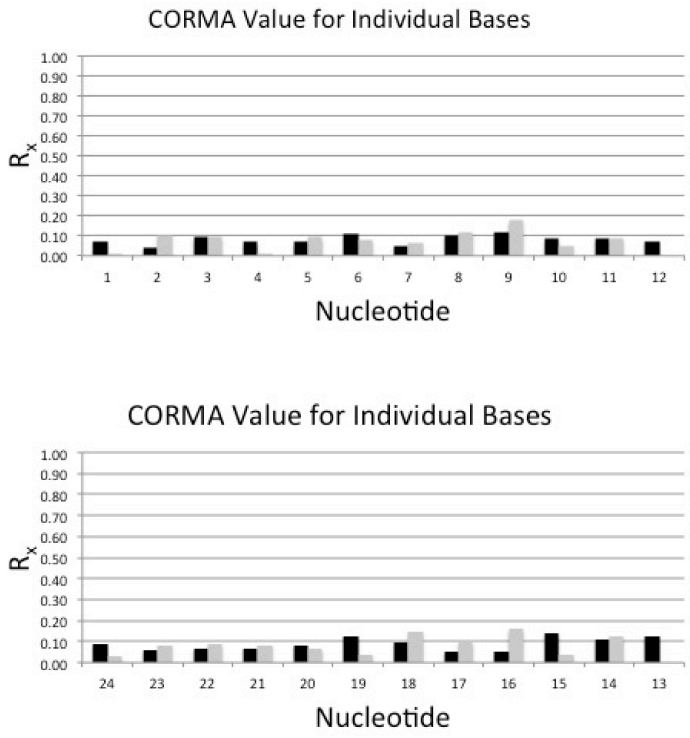



**Figure 3-7.** Sixth root residuals ($R_1^x$) calculated using complete relaxation matrix calculations from the average of ten structures emergent from the rMD calculations of the *N*$^2$-dG-IQ modified duplex. The black bars represent intra-nucleotide sixth root residuals and the grey bars represent inter-nucleotide sixth root residuals. A. Nucleotides C$^1$-C$^{12}$ in the modified strand. B. Nucleotides G$^{13}$-G$^{24}$ in the complementary strand.

**Table 3-3.** Structural statistics for the $N^2$-dG-IQ modified duplex.

| Average structure (obtained from 10 structures) | | | |
|---|---|---|---|
| RMS pairwise difference between structures | 1.12 | | |
| RMS difference from average structure | 0.75 | | |
| CORMA analysis for average structure[a] | | | |
| | Intranucleotide | Internucleotide | Total |
| $R^1_x$ [b] | 0.085 | 0.083 | 0.084 |
| Average error[c] | | | 0.0037 |

*Conformation of the $N^2$-dG-IQ Adduct*

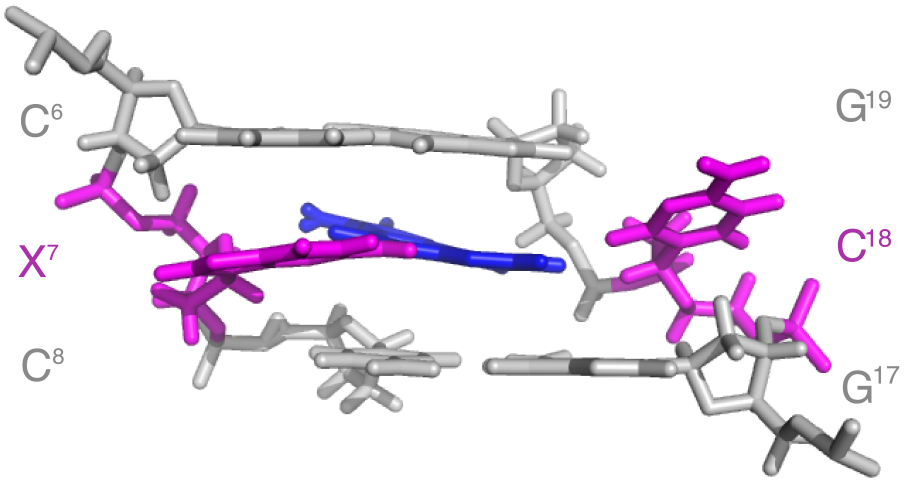



**Figure 3-8.** Expanded view of the average structure calculated from ten structures emergent from the rMD calculations of the $N^2$-dG-IQ modified duplex, showing base pairs $C^6$:$G^{19}$, $X^7$:$C^{18}$, and $C^8$:$G^{17}$. The view is from the major groove. The modified base pair $X^7$:$C^{18}$ is shown in magenta, with the IQ moiety shown in blue.

The nucleotide $X^7$ remained in the *anti* conformation about the glycosyl bond. It was displaced toward the major groove. The IQ ring was intercalated and oriented such that the H4a proton and the $CH_3$ group faced into the minor groove, whereas the H7a, H8a, and H9a protons faced into the major groove (Figure 3-8). The IQ ring was angled by approximately 15° with respect to the modified guanine, but otherwise remained largely in plane with the damaged base. The helix was unwound between $C^6$ and $X^7$, with a reduced helicoidal twist of 30°. This was partially compensated by an increased twist of 9° between $X^7$ and $C^8$. At base pair $X^7$:$C^{18}$ the roll of the $X^7$ purine decreased by 24°. This was compensated at base pair $C^8$:$G^{17}$, where the roll decreased by 12°. Consequently, the $N^2$-dG-IQ adduct induced a bend of 10° to the duplex. The IQ ring exhibited stacking with the flanking base pairs (Figure 3-9). IQ was stacked between $G^{17}$ and $G^{19}$ of the complementary strand of the $C^6$:$G^{19}$ and $C^8$:$G^{17}$ base pairs. The complementary nucleotide, $C^{18}$, extruded

into the major groove and did not exhibit stacking with the neighboring base pairs. The base opening between $X^7$ and $C^{18}$ increased by 76°. This disrupted Watson-Crick hydrogen bonding. The other base pairs maintained Watson-Crick hydrogen bonding. The structural coordinates were deposited in the Protein Data Bank (www.rcsb.org): the PDB ID code for the $N^2$-dG-IQ duplex is 2MAV.

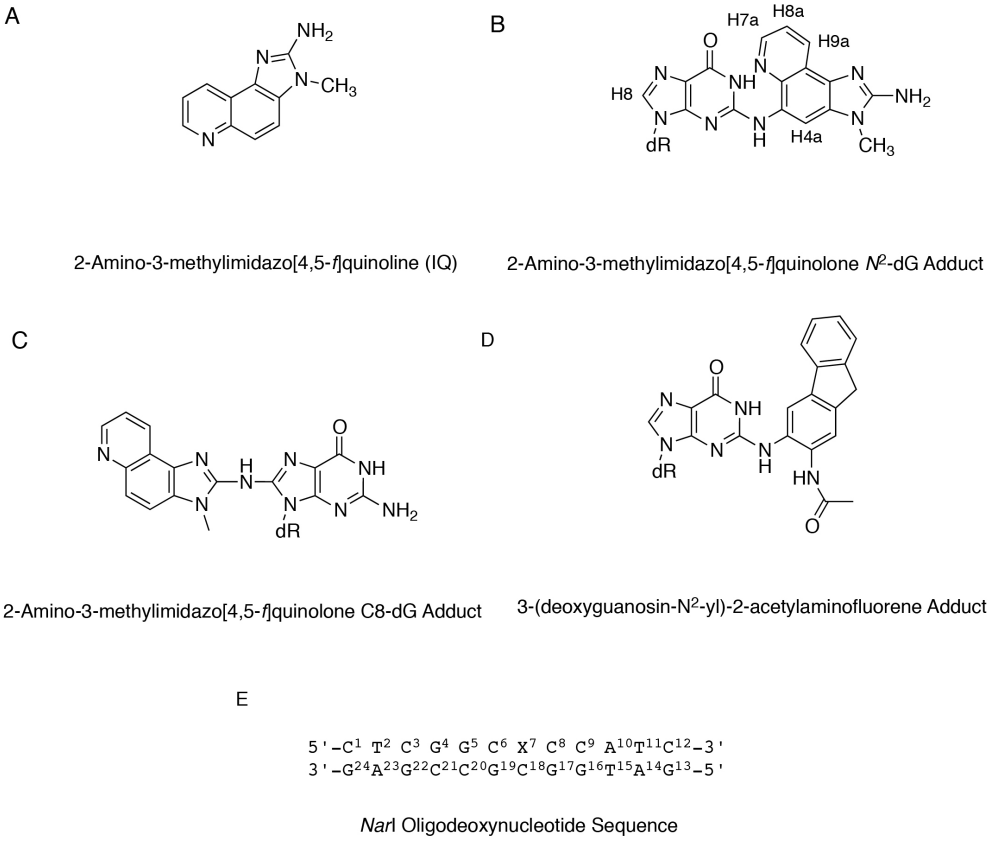
## Discussion

The $N^2$-dG-IQ DNA adduct has been of interest following reports that it is more persistent than the C8-dG-IQ adduct in rodents and primates that were fed IQ in their diet[144]. The synthesis of this adduct and its incorporation into oligodeoxynucleotides[135] has allowed the conformation of the $N^2$-dG-IQ adduct at the $G^3$-position of this sequence to be determined. This is a hot spot for two-base frameshift deletions in bacterial mutagenesis assays[145-150]. Additionally, human DNA polymerase (hpol) η produces two-base deletions when replicating past the $N^2$-dG-IQ adduct at position $G^3$ *in vitro*[151].

### *Conformation of the $N^2$-dG-IQ Adduct*

The IQ ring intercalates when the $N^2$-dG-IQ adduct is positioned at the frameshift-prone $G^3$ position of the *NarI* sequence (Figure 3-7). The strong NOE intensities of the IQ H4a and $CH_3$ protons to the $X^7$ and $C^8$ H1' protons (Table 3-1) indicate that these protons face into the minor groove and establish the conformation about the bond between $N^2$-dG and C5 of the IQ moiety. In contrast, NOEs involving the H8a proton of the IQ ring are primarily to bases $G^{17}$, $C^{18}$, and $G^{19}$ of the complementary strand (Table 3-1). The chemical shifts of the IQ H7a, H8a, and H9a protons are observed between 6.5 and 8.0 ppm, which is

1.3-2.0 ppm upfield as compared to the $N^2$-IQ-dG nucleoside. This is consistent with the intercalated conformation and stacking of the IQ ring below the 5'-neighboring $G^{19}$ of the complementary strand and above the 3'-neighboring $C^8$:$G^{17}$ base pair (Figure 3-8). Chemical shift perturbations corroborate the NOE data (Figure 3-5). The IQ H4a proton resonance, observed at 9.6 ppm, is 0.4 ppm upfield from the resonance observed for the modified $N^2$-dG-IQ nucleoside[135], consistent with its location below $G^{19}$ and above $C^8$ (Figure 3-8). The IQ moiety displaces the complementary $C^{18}$ base from the duplex, and flips it into the major groove. This is supported by smaller perturbations in chemical shifts for the H4a and $CH_3$ protons as compared to the H7a, H8a, and H9a aromatic protons of IQ. The displacement of the modified nucleotide $X^7$ toward the major groove (Figure 3-8) is supported by the downfield chemical shift change of 0.4 ppm for the $X^7$ H8 and H1' protons of the modified base. The $C^8$ H6 proton resonance also experiences a downfield shift of 0.3 ppm. The stacking interactions of the IQ ring with the flanking bases $C^8$, $G^{17}$, and $G^{19}$ are reflected in the thermodynamic analysis of the adduct, in which the thermal melting temperature of 63 °C is unchanged from that of the unmodified duplex.




2-Amino-3-methylimidazo[4,5-*f*]quinoline (IQ)

2-Amino-3-methylimidazo[4,5-*f*]quinolone $N^2$-dG Adduct

2-Amino-3-methylimidazo[4,5-*f*]quinolone C8-dG Adduct

3-(deoxyguanosin-$N^2$-yl)-2-acetylaminofluorene Adduct

*Nar*I Oligodeoxynucleotide Sequence

**Chart 3-1.** Adduct structures: A. Structure of 2-amino-3-methylimidazo[4,5-f]quinolone (IQ). B. Structure of the $N^2$-dG-IQ adduct, showing the numbering of guanine base and IQ protons. C. Structure of the C8-dG-IQ adduct. D. Structure of the $N^2$-dG-AAF adduct. E. The duplex containing the *NarI* sequence, showing the numbering of the nucleotides. The $N^2$-dG-IQ adduct is positioned at $X^7$, which corresponds to the $G^3$ frameshift-prone position of the *NarI* sequence.

### *Comparison to the $N^2$-Acetylaminofluorene-dG Adduct*

The other $N^2$-dG arylamine adduct that has been subjected to conformational analysis, although not in the *NarI* sequence of interest herein, is that arising from *N*-acetylaminofluorene (AAF; Chart 3-1)[152]. The $N^2$-dG-AAF adduct conformation has also been examined using computational approaches[153]. Zaliznyak et al. [152] have shown that the AAF moiety resides in the minor grove with its long axis directed toward the 5'-end of the modified strand. This shields the hydrophobic AAF ring from water. Similar to the $N^2$-dG-IQ adduct, the modified nucleotide maintains the *anti* conformation about the glycosyl

bond. Notably, the $N^2$-dG-AAF adduct increases the stability of the DNA by 6 °C, which has been attributed to a favorable entropic effect[152]. The present data reveal that the base-displaced intercalated conformation of the $N^2$-dG-IQ adduct at position $G^3$ of the *NarI* sequence differs from that of the $N^2$-dG-AAF adduct, suggesting that the conformations of $N^2$-dG arylamine adducts vary rather than following a common motif. At the molecular level, the factors governing whether planar aromatic molecules such as AAF or IQ favor DNA groove binding vs. intercalation are not well established, but may be influenced both by their electronic structures and their respective geometries[154]. Replication bypass studies have revealed that the $N^2$-dG-AAF adduct largely blocked DNA synthesis but when bypassed, mis-incorporation of dATP opposite the lesion was observed[155].

*Comparison to the C8-dG-IQ Adduct*

When the C8-dG-IQ adduct was placed into the *NarI* sequence at the frameshift-prone $G^3$ position, the IQ ring also intercalated into the duplex and the complementary $C^{18}$ base was extruded into the major groove. The conformation of the C8-dG-IQ adduct also was characterized as base-displaced intercalated[156]. Thus, at the $G^3$ position within the *NarI* sequence, both the C8-dG-IQ and $N^2$-dG-IQ adducts share a motif in which the IQ ring intercalates and $C^{18}$ extrudes into the major groove. However, the two conformations are distinctive. Apart from the difference in the regiochemistry of alkylation (C8 vs. $N^2$, Scheme 1-1), a major difference between the C8-dG-IQ and $N^2$-dG-IQ adducts is that the C8-dG-IQ-modified guanine adopts a *syn* conformation about the glycosyl bond, whereas the $N^2$-dG-IQ-modified guanine maintains the *anti* conformation about the glycosyl bond (Figures 3-8 and 3-9). In addition, for the C8-dG-IQ adduct, rotation of the glycosyl bond into the *syn*

conformation places the Watson–Crick hydrogen bonding edge of the modified dG into the major groove. The $X^7$ imino and amino protons are exposed to solvent. The orientation of the IQ ring of the C8-dG-IQ adduct about the linkage between the C8-dG and the $N^2$-IQ atoms also differs, such that the IQ $CH_3$ group and H4a and H5a protons face the major groove rather than the minor groove[156]. The orientation of the C8-dG-IQ adduct in the duplex rotates the bulk of the IQ aromatic ring away from the flanking bases, resulting in a loss of base-stacking interactions, as shown in Figure 3-9. In comparison, the $N^2$-dG-IQ adduct appears to have more favorable stacking interactions with $G^{19}$. These differences may lead to differential processing during both DNA repair and DNA replication.

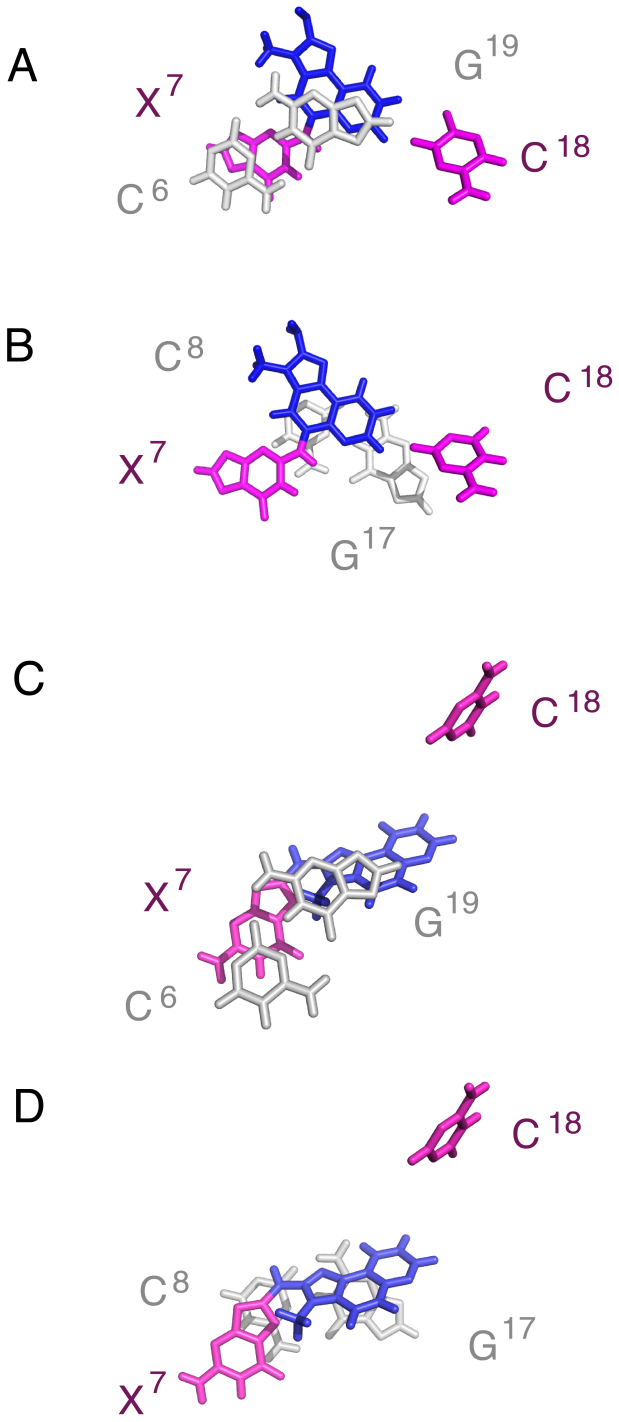



**Figure 3-9.** Expanded views of the average structure calculated from ten structures emergent from the rMD calculations of the *N*$^{2}$-dG-IQ modified duplex. Base-stacking of the modified X$^{7}$:C$^{18}$ base pair with the 5'-neighbor and 3'-neighbor base pairs. A. Stacking of C$^{6}$:G$^{19}$ above X$^{7}$:C$^{18}$. B. Stacking of X$^{7}$:C$^{18}$ above C$^{8}$:G$^{17}$. Expanded views of the average structure of the corresponding C8-dG-IQ adduct at X$^{7}$.$^{75}$ C. Stacking of C$^{6}$:G$^{19}$ above X$^{7}$:C$^{18}$. D. Stacking of X$^{7}$:C$^{18}$ above C$^{8}$:G$^{17}$. In each instance the modified base pair X$^{7}$:C$^{18}$ is shown in magenta, with the IQ moiety shown in blue.

*Structure-Activity Relationships*

The $N^2$-dG-IQ adduct is less efficiently removed from genomic DNA by nucleotide excision repair[144,157]. The NER machinery is thought to recognize bulky DNA damage that is destabilizing and distortive to the duplex[158-161]. It has been proposed that the thermal stabilization of the $N^2$-dG-AAF adduct hinders NER [152]. We observe that the $T_m$ of the $N^2$-dG-IQ adduct at position $G^3$ within the *NarI* sequence does not destabilize the duplex (Table 3-4), correcting our original report[135]. The $T_m$ of the $N^2$-dG-IQ modified duplex is 63° C and does not differ significantly from the unmodified duplex. This is remarkable, given that the intercalated IQ moiety disrupts Watson-Crick hydrogen bonding and that the complementary $C^{18}$ base is displaced into the major groove. The stability of the $N^2$-dG-IQ modified duplex likely arises from favorable stacking between the IQ moiety and the neighboring base pairs (Figure 3-9). It is also interesting to note that unlike the $N^2$-dG-IQ adduct, the C8-dG-IQ adduct (which does not stack with the neighboring bases as well at this position (Figure 3-9)) thermally destabilizes the duplex, reducing the $T_m$ by 4°C. Yeo et al.[162] examined acetylaminofluorene (AAF) and aminofluorene (AF) C8-dG adducts within the *NarI* sequence and observed a correlation between the degree of destabilization induced by the lesions, binding affinities to the damage recognition protein XPC-RAD23B, and overall NER efficiencies. Likewise, Zaliznyak et al. attributed the increased stability of the $N^2$-dG-AAF adduct to its orientation within the minor groove and the entropy-favored release of waters from the duplex[152]. Similar conclusions were reached by Cai et. al.[163] who correlated thermodynamic stabilities and van der Waals interaction energies with repair efficiencies for stereoisomeric intercalated $N^6$-dA PAH adducts. Their studies showed that intercalated adducts with fewer DNA structural distortions and increased van der Waals

interactions with neighboring bases correlated with reduced repair efficiencies. The heterocyclic amine PhIP adduct has been compared with the *cis*-B[*a*]P-$N^2$-dG adduct in duplex DNA and in a nucleotide deletion duplex and it was concluded that local stabilization induced by these adducts governs the ability of the β-hairpins of NER proteins to recognize the damage[164]. In summary, it seems plausible that the thermal stability of the $N^2$-dG-IQ adduct may, in part, explain the persistence of the $N^2$-dG-IQ adduct in rats and primates.

**Table 3-4.** Thermal melting temperatures ($T_m$ measurements) of *NarI* duplexes containing the $N^2$-dG-IQ adducts.

| *NarI* $N^2$-dG-IQ Modified Duplex | $T_m$ °C | $\Delta T_m$* °C |
|---|---|---|
| 5′–CTC<u>X</u>GCGCCATC–3′<br>3′–GAGCCGCGGTAG–5′ | 62 | -1 |
| 5′–CTCG<u>X</u>CGCCATC–3′<br>3′–GAGCCGCGGTAG–5′ | 64 | +1 |
| 5′–CTCGGC<u>X</u>CCATC–3′<br>3′–GAGCCG<u>C</u>GGTAG–5′ | 63 | 0 |

If not repaired, the $N^2$-dG-IQ adduct is anticipated to be genotoxic. Indeed, IQ is an order of magnitude more mutagenic than is aflatoxin $B_1$ in Ames assays. The mutations occur primarily at G:C base pairs[165,166]. The replication of the $N^2$-dG-IQ-adducts within the *NarI* sequence is influenced by the identity of the DNA polymerase. Because the damaged guanine remains in the *anti* conformation about the glycosyl bond (Figures 3-7 and 3-8), one might anticipate that the $N^2$-dG-IQ lesion should block Watson-Crick base pairing with incoming dNTPs during lesion bypass. Stover et al.[167] incorporated the $N^2$-dG-IQ-adduct into the $G^1$- and $G^3$-positions of the *NarI* sequence and examined replication of the oligodeoxynucleotides with Klenow fragment of *E. coli* polymerases (pol) I (exonuclease

deficient), exonuclease deficient pol II, and the *Solfolobus solfataricus* P2 DNA polymerase IV (Dpo4), *in vitro*. At the $G^3$ position the $N^2$-dG-IQ adduct blocked the *E. coli* polymerases. Pol II *exo*$^-$ favored correct incorporation of dCTP over dGTP but was unable to extend either of these initial insertion products. In contrast, the Dpo4 polymerase bypassed the $N^2$-dG-IQ adduct and produced an error-free product. The present studies do not necessarily predict the structure of the $N^2$-dG-IQ adduct during trans-lesion bypass. Consequently, it will be of interest to prepare complexes of bypass polymerases with $N^2$-dG-IQ modified template: primers in an effort to determine how the $N^2$-dG-IQ adduct is accommodated during lesion bypass and how polymerases, e.g., the Dpo4 polymerase[168] allow bypass of this lesion.

Bypass of the $N^2$-dG-IQ adduct has been reported to be dependent upon its position in the *NarI* sequence. Choi et al.[151] have demonstrated that the human DNA polymerase (hpol) η can extend primers beyond template $N^2$-dG-IQ adducts. Pol η correctly inserts dCTP and incorrectly inserts dATP. Analyses of hpol η extension products reveal that a -2 bp deletion occurs with the $G^3$ $N^2$-dG-IQ adduct. In contrast, at the $G^1$ position replication past the $N^2$-dG-IQ adduct results in error-free incorporation of dCTP, but further extension is inhibited and the polymerase stalls. In contrast, hpol η does not yield -2 bp deletions with the C8-dG-IQ adduct located at position $G^3$. While further studies will be necessary to probe the basis for these observations, it is of interest to note that the stability of the $N^2$-dG-IQ adduct placed opposite a 2-bp deletion increases as compared to the fully complementary duplex, suggesting that the adduct may stabilize a 2-bp strand slippage intermediate[135]. At the $G^1$ position, the $N^2$-dG-IQ adduct is bypassed and extended by the *E. coli* polymerases and the Dpo4 polymerase and error-free product is observed. Thus, it will also be of

interest to examine the structure of the $N^2$-dG-IQ adduct when positioned at position $G^1$ of the *NarI* sequence.

*Summary*

Analysis of the $N^2$-dG-IQ adduct placed at position $G^3$ of the *NarI* sequence[145-150], where it has been observed to cause -2 bp deletions when bypassed by hpol η [151], reveals that it adopts a base-displaced intercalated conformation in which the H4a and $CH_3$ protons of the IQ ring face the minor groove and the H7a, H8a, and H9a protons face the major groove. The IQ ring is shielded from water and stacks with the 5'- and 3'-neighbor base pairs. Remarkably, despite this conformational perturbation, the $N^2$-dG-IQ adduct does not destabilize the duplex, which may correlate with the observation that it is refractory to repair by NER[144,157]. Additionally, the IQ moiety disrupts the potential for Watson-Crick hydrogen bonding with incoming dNTPs, which perhaps explains why this lesion blocks DNA synthesis by many polymerases.

## Chapter IV

## SOLUTION STRUCTURE OF $N^2$-dG-IQ AT THE MUTAGENIC HOTSPOT $G^1$ POSITION IN THE *NARI* SEQUENCE CONTEXT

### Introduction

This chapter examines the effect of IQ attached at the $N^2$ position of dG when located at the $G^1$ position in the *NarI* sequence. *In vitro* replication data for this adduct results in error-free bypass for both human and prokaryotic polymerases[169,170]. This result contrasts to IQ at the $G^3$ location, which was observed to be a hotspot for -2 bp deletions. Structural comparisons of the $G^1$ adduct to the $G^3$ adduct could provide suggest possible explanations for the replication data. However, NMR data for the $G^1$ duplex support a similar base-displaced intercalated type structure, providing limited insight to replication results. Cell culture experiments conducted by Basu's lab at the University of Connecticut support similar duplex structures, since his lab has observed bypass to be more polymerase dependent rather than sequence context dependent (communicated by Dr. Basu). These structures do allow the $N^2$ adducts to be differentiated to the C8 adduct and provide a better understanding of the discrepancy in repair efficiencies.

### Results

*Circular Dichroism*

When IQ is located at the $G^1$ and $G^3$ position in the *NarI* sequence, there are distinct shifts for each sequence relative to the unmodified sequence, indicating that both sequences have been perturbed. The adducts at $G^1$ and $G^3$ had a maximum UV absorption at 270 and 269 nm, respectively. These display blue shifts of 4 and 5 nm relative to the

unmodified duplex. They crossed 0 at 260 and 257 nm for $G^1$ and $G^3$ IQ modified sequences and had a minimum at 249 and 248 nm compared to the unmodified at 260 and 249 nm. The intensities of the modified spectra are also reduced with respect to the *NarI* sequence. The absorbance of the IQ moiety would be predicted to be visible between 300-360 nm, according to the results of the C8-IQ-dG single strand[171], although the signal was broad. In all sequences for $N^2$-IQ-dG, there was negligible signal detected in this range as well as in the UV absorption spectrum. The CD spectrum of the $N^2$-AF-dG adduct had a negative ellipticity in the 300-360 nm range at the $G^2$, which was characterized as a groove-bound conformation but positive ellipticity was observed at the $G^1$ or $G^3$ [71]. Since all sequences agree in this range, this could support the hypothesis that all three adducts adopt similar conformations, although the linkage for $N^2$-IQ-dG could broaden the signal, making it difficult to detect and hard to interpret.

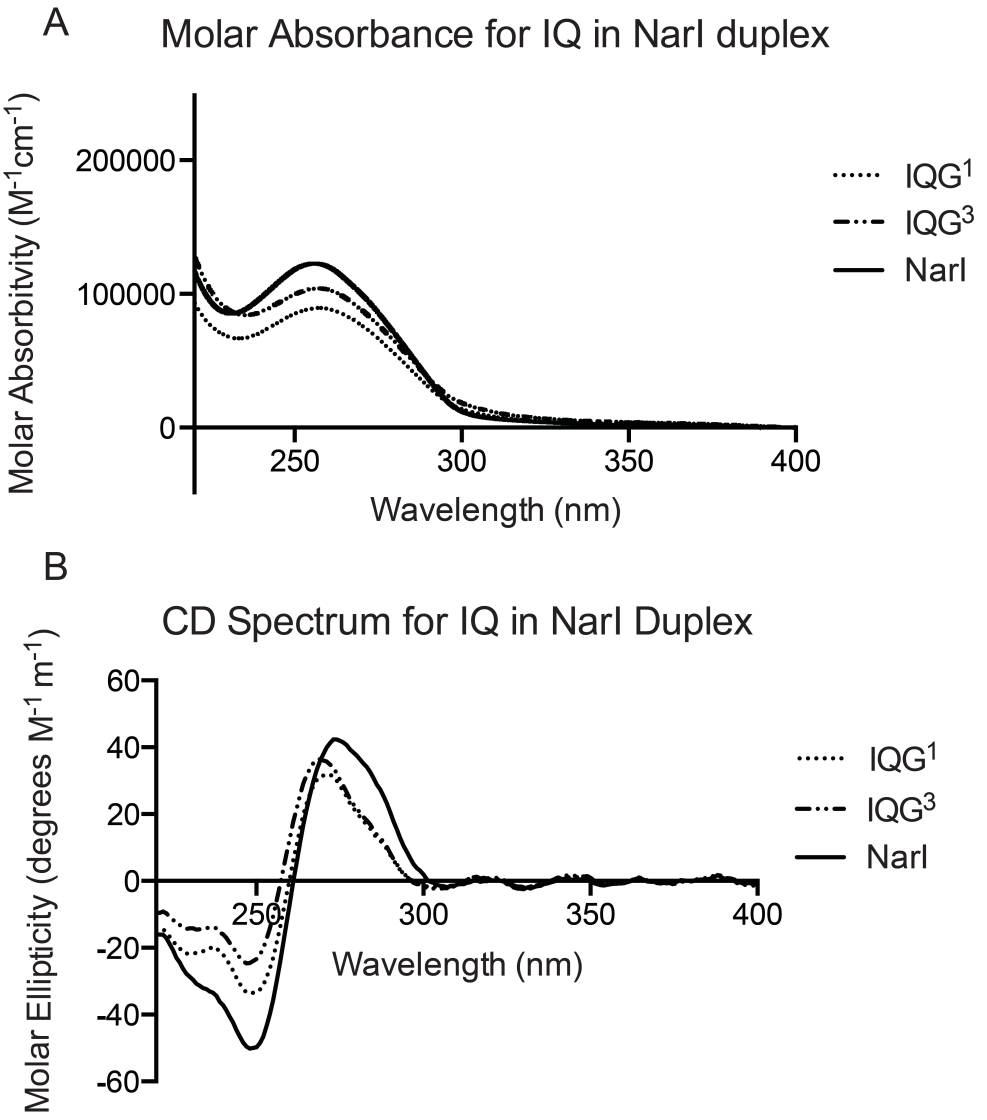



**Figure 4-1.** A) UV and B) CD spectra for $N^2$-dG-IQ at $G^1$ and $G^3$ as well as the unmodified *NarI* sequence.

*NMR*

The IQ-modified duplex yielded sharp, well resolved peaks at 15 °C for nonexchangeable proton spectra that were able to be unambiguously assigned, with the exception of many of the H4', H5' H5'' protons, which were overlapped and the majority were not included in structure calculations, with the exception of $T^2$ and $C^{21}$. Data was

collected at 5 °C for exchangeable protons, which provided optimal resolution and sharpest peaks.

Magnitude COSY experiments helped to identify cytosine shifts as well as the aromatic protons of the IQ adduct with $^{3}J$ coupling. However, crosspeaks between H7a and H8a were broadened due to the presence of the nitrogen atom. This effect was also observed in NMR experiments of the nucleoside[138].

The guanine proton $X^{4}$ H8 was shifted downfield 0.47 ppm relative to the unmodified oligonucleotide and the H1' shifted downfield by 0.74 ppm. The opposite base $C^{21}$H6 and H1' was shifted downfield by 0.81 and 1.26 ppm indicating a deshielding effect for this base. The intensity of the NOE for $C^{21}$ H1' and $G^{22}$ H8 was very weak, indicating the most significant impact on the base opposite the adduct. $C^{3}$ H1' and H6 were shifted 0.51 and 0.46 ppm downfield, while its partner, $G^{22}$, was shifted 0.17 and 0.34 ppm downfield. $G^{5}$ H8 was shifted 0.28 downfield, while $C^{20}$ H6 was shifted 0.19 ppm upfield. These shifts were likely due to a shift in base stacking by the presence of the IQ. The remaining peaks were relatively unaffected by the presence of IQ, shifting less than 0.1 ppm from the unmodified duplex. The relative pattern of chemical shift perturbations closely resembled that of the IQ at $G^{3}$ as well. The base opposite the adduct had the greatest downfield shifts, while the perturbations to the bases to either side of the opposite bases were less than half the magnitude of the base directly opposite, either $C^{18}$ or $C^{21}$ for $G^{3}$ and $G^{1}$. The modified base itself was shifted downfield as well by 0.4 ppm, and the bases flanking it were also perturbed by a similar magnitude.

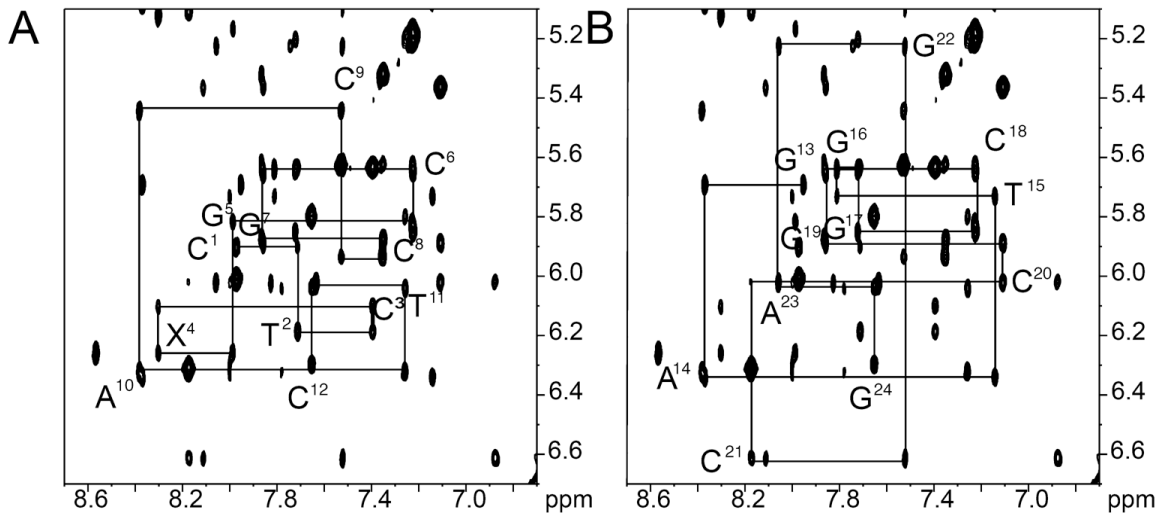



**Figure 4-2.** Plot of NOESY spectrum with 150 ms mixing time showing connectivities between base aromatic protons to deoxyribose anomeric protons for adduct *N*$^2$-dG-IQ located at G$^1$ position. A) Bases C$^1$ to C$^{12}$ for modified strand. B) bases G$^{13}$ to G$^{24}$ for complementary strand. Spectrum was acquired at 900 MHz at 15 °C.

*IQ Proton Assignments*

All chemical shifts for adduct protons have been identified and are shown in Figure 4-2. The IQ $CH_3$ group and H4a had NOEs with protons X$^4$H1' and X$^5$H1' in the minor groove of the duplex indicating the imidazole ring of IQ is oriented into the minor groove. The IQ H8a and H9a protons were identified by the $^3$J coupling in the aromatic region of the COSY spectrum. The IQ H7a to H8a crosspeak is observed in the NOESY spectrum and was easily assigned. These protons had many NOEs to bases from the complementary strand, mostly to C$^{20}$ and C$^{21}$ and a single NOE to G$^{22}$ that was identified. Figure 4-3 depicts the assignments of the IQ ring, while Table 4-1 describes the observed NOEs to the DNA.

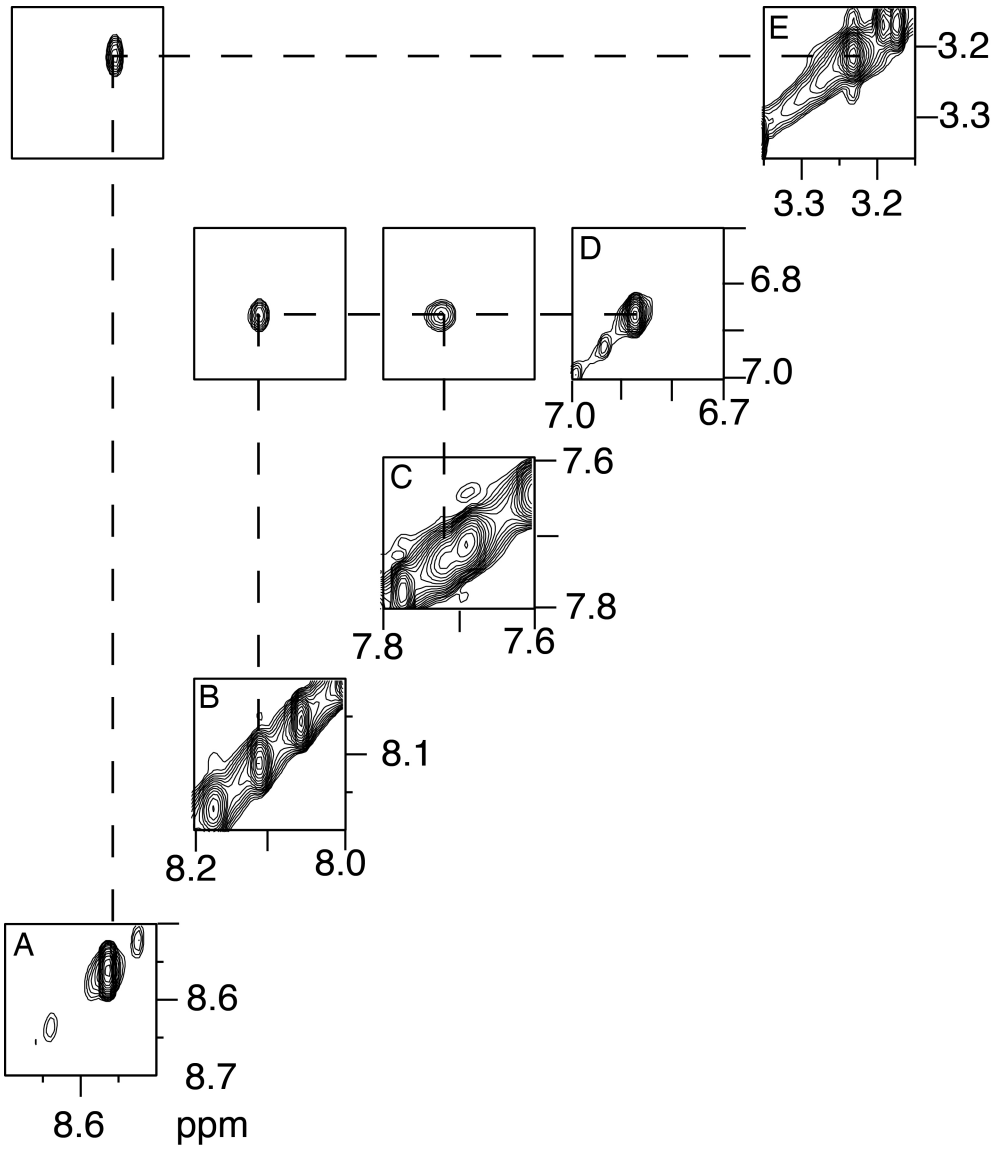



**Figure 4-3.** Plot of NOESY spectrum showing IQ ring proton assignments. A. IQ H4a proton was observed at 8.56 ppm. B. H7a was observed at 8.11 ppm. C. IQ H9a was observed at 7.74 ppm. D. IQ H8a was observed at 6.87 ppm. E. IQ $CH_3$ was observed at 3.23 ppm.

**Table 4-1.** Summary of observed NOEs from IQ to DNA and their intensities.

| IQ proton | NOEs to oligonucleotide protons: |
|---|---|
| $CH_3$ | $X^4$H1' – strong; $G^5$H8 – medium; $X^4$H2''; $X^4$H2'; $G^5$H1' – weak |
| H4a | $X^4$H1' – strong; $X^4$H2'' –weak; $X^4$H2' – weak |
| H7a | $G^{22}$H1' – medium |
| H8a | $C^{21}$H1' – medium; $C^{20}$H1' – medium; $C^{21}$H4' – medium; $C^{20}$H2'' – medium; $G^{22}$H8 – weak; $C^{20}$H6 – weak; $C^{21}$H2' – weak; $C^{21}$H2'' – weak; $C^{21}$H5' – weak; $C^{21}$H5'' – weak |
| H9a | $C^{21}$H1' – medium; $C^{20}$H5 – medium; $C^{20}$H2'' – weak |

*Exchangeable Protons*

The 1D $^1$H spectrum of the imino region of the duplex supported the assignments of the 2D NOESY spectrum. Here we could observe the broadened imino proton peak for the modified base at low temperatures that was too broad to be observed in the NOESY spectrum at 11.8 ppm. The peak quickly broadened in the 1D with increased temperature as shown in Figure 4-4. The sharp upfield peak at 9.5 ppm was assigned as $X^4$ N2H, which is typically not observed. However, the peak was very sharp and persistant and was visible up to a temperature of ~55 °C, when most of the duplex had melted, suggesting a stabilizing effect comes from an intrastrand interaction. This peak also had NOEs to the amino protons of $C^3$ and $C^{21}$ as well as IQ protons H4a and H9a.

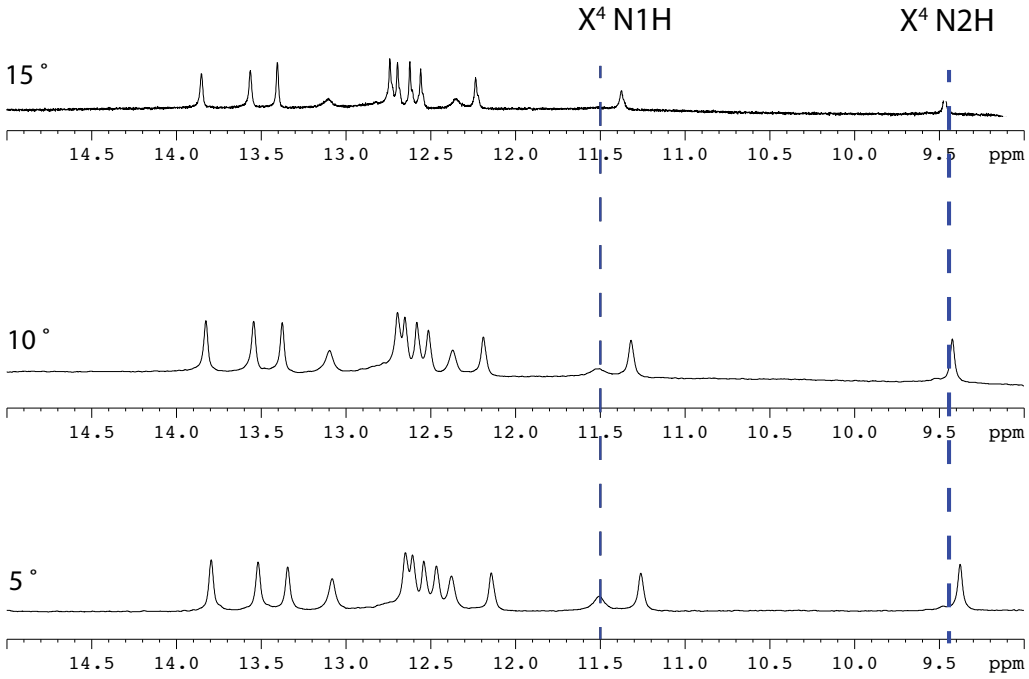



**Figure 4-4.** 1-D spectrum of imino region from 5 °C – 15 °C showing the assignment of $X^4$ N1H proton, which quickly broadens as temperature increases.

The imino/amino proton region of the NOESY spectrum indicated a loss of hydrogen bonding between $X^4$ and $C^{21}$ (Figure 4-5). The imino proton of $X^4$ was visible at 11.8 ppm in the 1D spectrum at 5 °C, but was nearly completely broadened out of the spectrum at 10 °C. $X^4$ N1H does not have crosspeaks to the flanking base-pair imino protons, suggesting a shift in the base stacking at the modified base pair. $X^4$ N1H did have a weak crosspeak to $X^4$ N2H; however, the $X^4$ N1H has broadened, likely due to solvent exchange and was not visible in the NOESY spectrum. All protons involved in hydrogen bonding were observed except for $C^{21}$ amino protons. No other Watson-Crick hydrogen bonding for other base pairs appeared to be affected by the presence of the IQ ring.

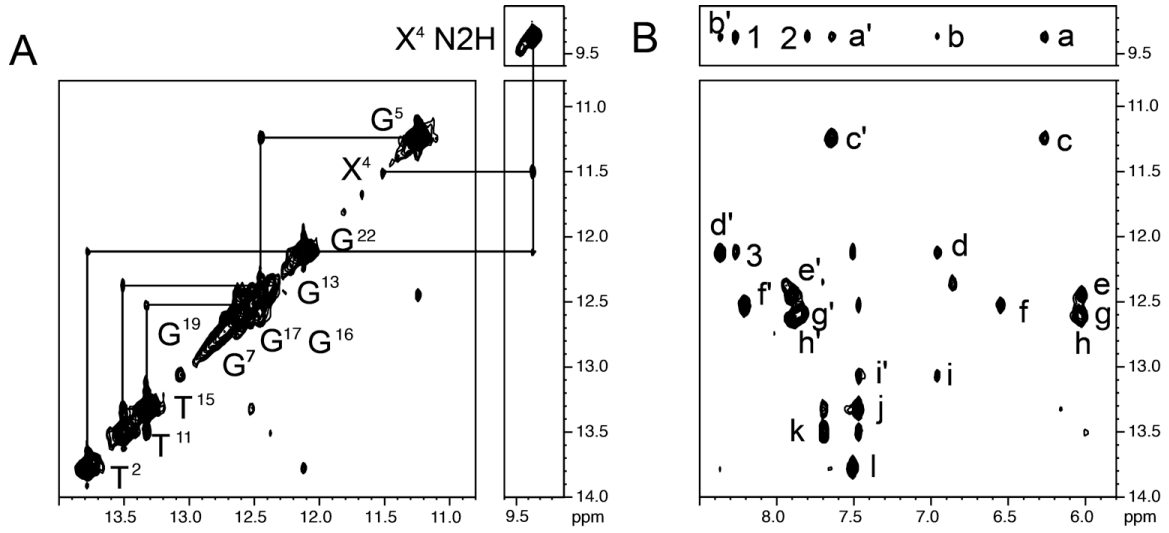



**Figure 4-5.** NOESY plot with exchangeable proton assignments for *N*[2]-dG-IQ modified duplex at position G[1]. A. Sequential connectivity of imino protons from T[2] to T[11]. B. NOE connectivity from imino protons to amino protons involved in Watson-Crick hydrogen bonding: a', X[4]N2H→C[20]H4b; a, X[4]N2H→C[20]H4a; b', X[4]N2H→C[3]H4b; b, X[4]N2H→C[3]H4a; c', G[5]N1H→C[20]H4b; c, G[5]N1H→C[20]H4a; d', G[22]N1H→C[3]H4b; e', G[19]N1H→C[6]N4b; e, G[19]N1H→C[6]N4a; f', G[16]N1H→C[9]H4b; f, G[16]N1H→C[9]H4a; g', G[17]N1H→C[8]N4b; g, G[17]→C[8]N4a; h', G[7]N1H→C[18]N4b; h, G[7]N1H→C[18]H4a; i', G[24]N1H→C[1]N4b; i, G[24]N1H→C[1]N4a; j, T[15]N3H→A[10]H2; k, T[11]N3H→A[14]H2; l, T[2]N3H→A[23]H2; 1, X[4]N2H→IQ H4a; 2, X[4]N2H→IQ H9a; 3, G[22]N2H→IQ H4a.

*Structure Refinement*

A total of 283 NOEs were obtained for structure calculations using NOESY data collected with a mixing time of 150 ms at 15 °C. Twenty-three NOEs were from IQ to DNA. Forty-nine restraints for Watson-Crick hydrogen bonding were applied, omitting restraints for the X[4]:C[21] base pair. Another 100 restraints for the phosphodiester backbone and 20 deoxyribose pseudorotation based on canonical values for B-DNA[118] were applied to bases not immediately surrounding the modification. NOEs from bases G[7] and G[19] were not included in structure calculations due to high amount of overlap between peaks. Similar chemical environments resulted in chemical shifts within 0.02 ppm for all protons of these bases and were unable to be resolved. However, the chemical shifts are ±0.05 ppm of the

unmodified bases and were presumed to be unaffected by the presence of the adduct. Table 4-2 summarizes the total restraints used and refinement statistics.

**Table 4-2.** Refinement statistics for $N^2$-dG-IQ at $G^1$ position in the *NarI* sequence.

| NOE restraints | |
|---|---|
| Internucleotide | 155 |
| Intranucleotide | 128 |
| Total | 283 |
| Backbone Torsion Angle Restraints | 100 |
| H-bonding Restraints | 49 |
| Deoxyribose Restraints | 20 |
| Total number of restraints | 442 |
| Refinement Statistics | |
| Number of distance restraint violations | 70 |
| Number of torsion restraint violations | 46 |
| Total distance penalty/Maximum penalty [kcal $mol^{-1}$] | 3.0/0.24 |
| Total torsion penalty/Maximum penalty [kcal $mol^{-1}$] | 1.7/0.16 |
| r.m.s. distances (Å) | 0.012 |
| r.m.s. angles (°) | 2.5 |
| Distance restraint force field [kcal $mol^{-1}$ $Å^{-2}$] | 32 |
| Torsion restraint force field [kcal $mol^{-1}$ $deg^{-2}$] | 32 |

Ten emergent structures based on the lowest deviation from experimental and dihedral restraints were selected to best represent the structure. The end of the duplex near the adduct appears as if there is poor agreement, presumably because of the unwinding induced by the IQ so close to the end of the duplex. The total distance penalty of was 3.0 kcal • $mol^{-1}$, with a single maximum penalty of 0.245 kcal • $mol^{-1}$. The total torsion penalty was 1.7 kcal • $mol^{-1}$, with a single maximum penalty of 0.161 kcal • $mol^{-1}$.

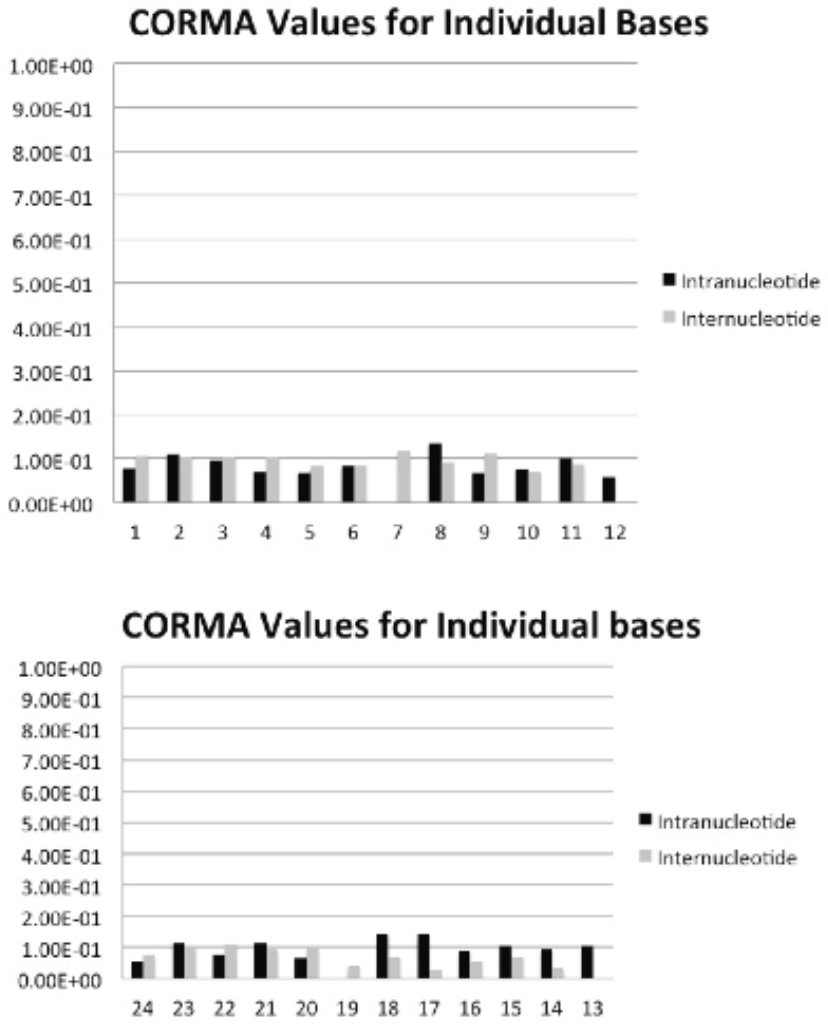



**Figure 4-6**. Sixth root residuals ($R_1^x$) calculated using complete relaxation matrix calculations from the average of ten structures emergent from the rMD calculations of the *N*$^2$-dG-IQ modified duplex. The black bars represent intra-nucleotide sixth root residuals and the grey bars represent inter-nucleotide sixth root residuals. A. Nucleotides $C^1$-$C^{12}$ in the modified strand. B. Nucleotides $G^{13}$-$G^{24}$ in the complementary strand.

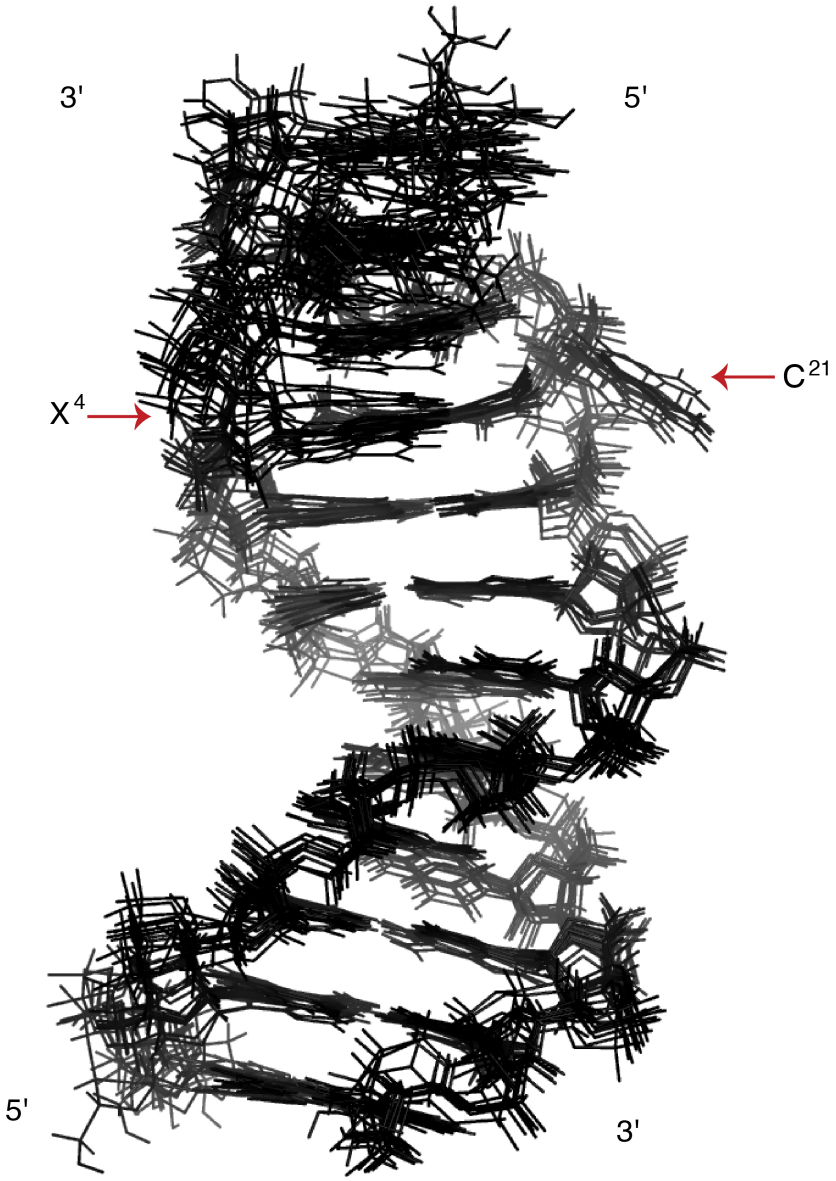



**Figure 4-7.** Ten best fitting structures calculated from NOESY data with 150 ms mixing time superimposed. The modified $X^4$ base and complementary $C^{21}$ are indicated.

*Conformation of $N^2$-dG-IQ at $G^1$*

The imidazole portion containing the methyl group of the IQ ring faced the minor groove of the duplex and is oriented towards the modified strand of the duplex. The quinolone ring intercalates between bases of the complementary strand since all NOEs

came from $C^{20}$, $C^{21}$, and $G^{22}$. The aromatic protons on the quinolone ring, H7a, H8a, and H9a, are oriented towards the major groove. The IQ remained in plane with $X^4$, with a dihedral angle of 178°. It did increase the tilt of $C^3$:$G^{22}$ by 20°. The tilt between $C^3$ and $X^4$ as well as $X^4$ to $G^5$ was decreased by 13° and increased by 23°, respectively. Likewise, the roll between the three bases was altered by -24° and 21°, respectively. The opposite base $C^{21}$ rotated into the major groove and had a base opening that was 98° greater than the unmodified base pair. The modified guanine maintained its *anti* conformation. The adduct induced a bend of 10° into the duplex compared to the unmodified duplex and a localized unwinding effect, increasing the helical twist by 15° at the adduction site.

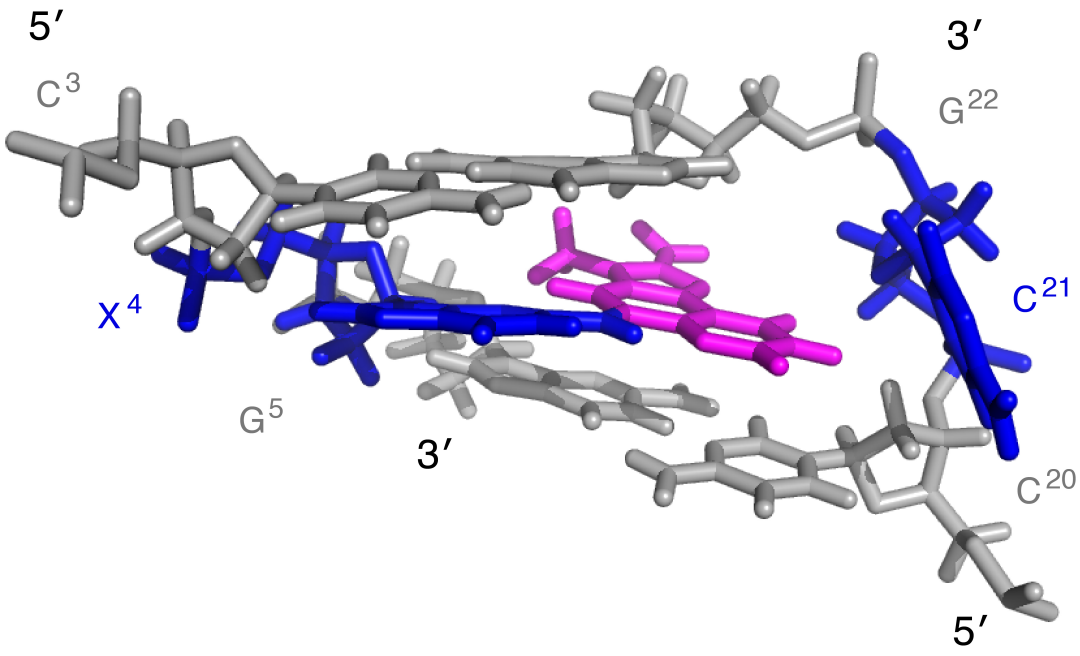



**Figure 4-8.** Expanded view of calculated structure from major groove, showing base pairs $C^3$:$G^{22}$, $X^4$:$C^{21}$, $G^5$:$C^{20}$. The IQ moiety is shown in magenta.

## Discussion

Structural characterization of the $N^2$-dG-IQ adduct is of interest since IQ appears to be one of the most genotoxic substances tested in the Ames assay, being approximately fifteen times more mutagenic than aflatoxin $B_1$, a known human carcinogen[172]. The $N^2$-dG-IQ adduct has been shown to be the more persistent than the C8-dG-IQ adduct and could possibly contribute more towards the carcinogenic properties of the IQ, considering persistence is a factor when assessing human risk[173]. The $N^2$-dG-IQ adduct also induces frameshift mutations when replicated by hpol η as demonstrated in *in vitro* extension assays[174]. Site-specific synthesis of the oligonucleotide containing this adduct has allowed for high resolution structural studies by NMR to understand more of the structure-function relationship of the $N^2$ HCA adducts[112].

The $T_m$ for the $N^2$-dG-IQ adduct at the $G^1$ position did not change the thermal stability of the duplex. The modified duplex has a melting temperature of 62 °C compared to the unmodified duplex, which has a melting temperature of 63 °C, meaning that the adduct has little effect on the overall stability of the duplex[175]. The $N^2$-dG-IQ adduct is able to disrupt the Watson-Crick hydrogen bonding of the modified base pair and maintain thermal stability, likely due to the strong base-stacking interactions which make up for the loss of hydrogen bonding.

The assignments of the N1H and N2H protons of $X^4$ in the water data are based on the observed stabilities of the peaks at different temperatures. $X^4$ N2H is within proximity of the nitrogen atom in the IQ ring allowing for hydrogen bonding interactions, which are able to slow solvent exchange so we can observe this peak on the NMR timescale and

remains sharp until the temperature nearly reaches the $T_m$ of the duplex. The N2H proton has a crosspeak to the broadened peak corresponding to N1H. The N1H proton is visible at 5 °C and quickly broadens as the temperature increases. The N1H proton does not have crosspeaks to $C^{21}$ amino protons, indicating a loss of hydrogen bonding at that base pair. No crosspeaks corresponding to the $C^{21}$ amino groups are visible in the spectrum, indicating that they are likely solvent exposed.

The *N*$^2$-dG-IQ modified base adopts a base-displaced intercalated structure, where the IQ moiety takes the place of the opposite base, $C^{21}$, disrupting base pairing and rotates into the major groove to accommodate the adduct. This is supported by the chemical shift change of 1.3 ppm of the H6 proton downfield relative the unmodified guanine. The IQ ring is accommodated into the duplex and stacks well with the flanking base pairs, as shown in Figure 4-9. NOEs from the IQ adduct to other DNA bases show it is oriented in a specific orientation across the duplex. The protons of the quinolone moiety have NOEs to the opposite strand, while the protons attached to the imidazole ring have NOEs to the same strand. The pla*NarI*ty of the IQ ring may be facilitated by the possible hydrogen bonding interactions between $X^4$ N2H and the nitrogen atom in the IQ ring, which allows the N2H proton to be observed in the NOESY spectrum. The visible N2H proton chemical shift is also observed for the adduct at the $G^3$ position[175].

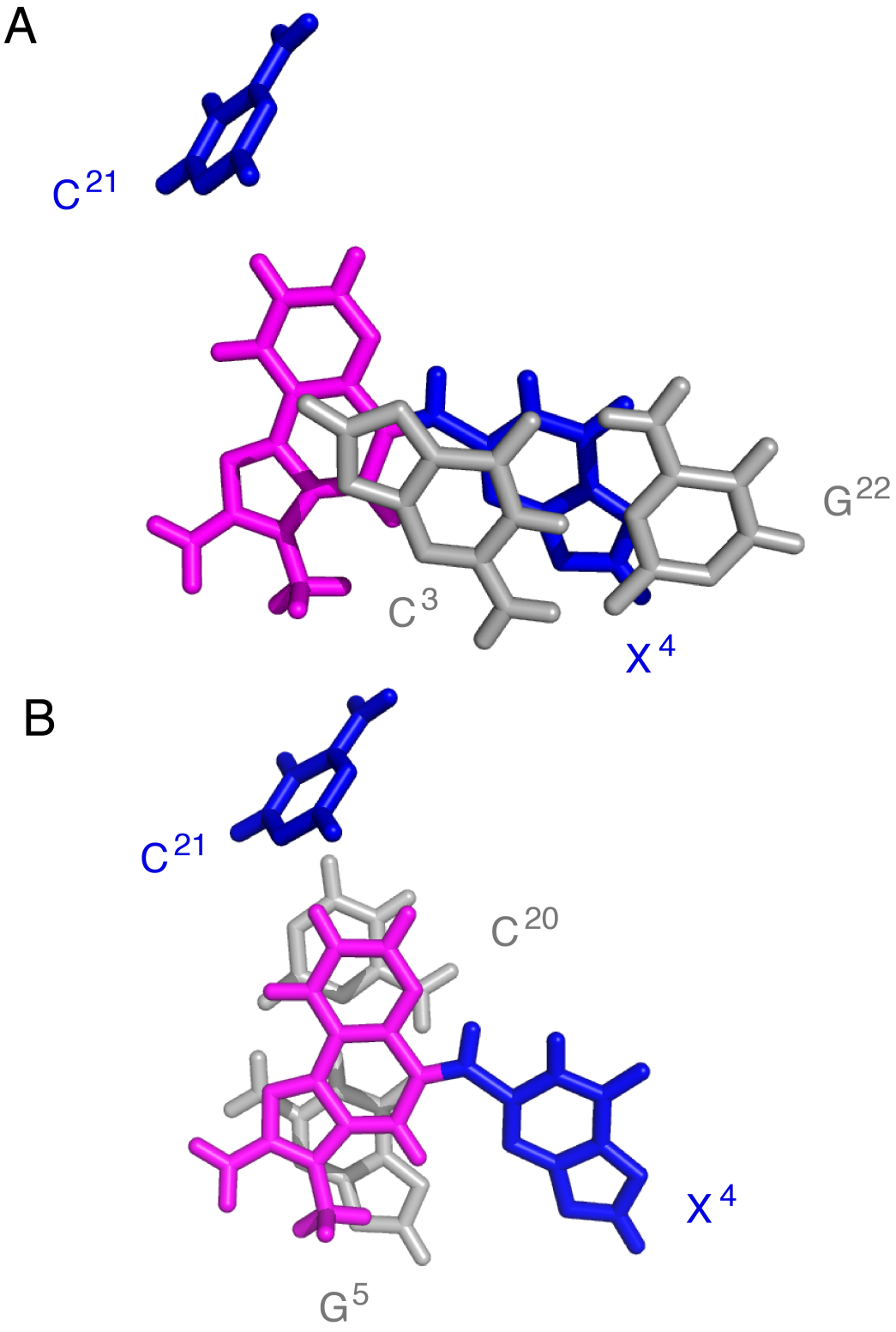



**Figure 4-9.** View from top of duplex looking at base-stacking interactions. A. base pairs $C^3$:$G^{22}$ and $X^4$:$C^{21}$, with IQ shown in magenta. B. Base pairs $X^4$:$C^{21}$ and $G^5$:$C^{20}$.

The aromaticity of the IQ ring allows for strong base-stacking interactions between the other bases in the duplex, and these interactions are reflected in the melting temperature of 62 °C, compared to the unmodified sequence with a melting temperature of 63 °C. Within experimental error, the presence of the adduct does not change the thermal stability of the duplex. The base-stacking interactions are able to overcome the instability introduced by the loss of hydrogen bonding between the modified base pair. Primarily, IQ appears to be stacking with bases $C^{20}$ and $G^{22}$, as shown in Figure 4-9. Similar effects can be observed by other aromatic adducts, demonstrating the importance of base stacking to duplex stability[176].

The chemical shifts of the aromatic IQ protons (H4a, H7a, H8a, H9a) range from 6.87 - 8.56 ppm. These chemical shifts are 0.5 – 0.9 ppm upfield from the nucleoside, indicating a shielding effect from the duplex and supporting intercalation of the IQ ring exhibited by the structure. Likewise, the $CH_3$ proton resonance on the imidazole ring shifts upfield 0.4 ppm, suggesting it might be slightly less shielded and more groove bound than the aromatic protons. This is supported by the refined structure, in which this group is located in the minor groove of the duplex and not in the base stack. $C^{21}$H6 and H1' had the largest downfield shifts. In the structure, this base is extruded into the major groove and is no longer base stacking with neighbor bases, explaining the large chemical perturbations for this base. The bases neighboring $X^4$, namely $C^3$, $G^5$, $G^{22}$ and $C^{20}$, are only shifted several tenths of a ppm from the change in base stacking induced by the presence of the IQ ring that has replace $C^{21}$ in the duplex. This structure resembles other C8 HCA adducts as well as some polyaromatic hydrocarbon adducts (PAH), such as benzo(a)pyrene, whose anti-$N^2$-dG *cis* adduct favors a similar base displaced intercalated conformation[177]. In this solution

structure, the adduct displaces the modified guanine into the major groove and flips the opposite cytosine into the major groove as well. The modified guanine is displaced to a greater extent than with IQ, in order to accommodate the much larger ring system of B[a]P. The B[a]P ring spans the duplex, with the majority of the ring oriented into the major groove.

*Sequence Dependence of $N^2$-dG-IQ in NarI*

The structure at the mutagenic hotspot, $G^3$, in the *NarI* recognition sequence has previously been determined[175]. The conformations of IQ at all three positions adopt similar structures with subtle differences between the positions. The CD spectra indicate each sequence maintains B DNA structure but is perturbed by the presence of the adduct. A lack of a visible signal for all three sequences between 300 and 360 nm, where the IQ-induced signal should occur, could support that the conformation of the modified base adopts a similar conformation in all sequences. However, the lack of signal could also be due to a perturbation of in the IQ chromophore from the linkage at dGuo $N^2$ to the IQ ring.

At the $G^1$ position, the IQ ring intercalates between the $C^3$:$G^{22}$ and $G^5$:$C^{20}$ base pair. $C^{21}$ flips out into the major groove to allow for the intercalation of the IQ ring. Comparable observations were made for $C^{18}$ opposite IQ attached to $X^7$, where the H6 proton resonance of both bases is shifted downfield more than 1 ppm[175]. According to the calculated structures, $C^{21}$ was rotated 20° further out of the duplex than $C^{18}$. A similar effect on the helical twist between the 5' neighbor base to the modified was observed, which was reduced by 30°. However, $G^1$ had a greater unwinding effect from the modified base to the

3' neighbor, with an increase of 15° compared to the 9° increase for $G^3$. The blue shifts in the CD data correspond to adduct-induced twisting and/or bending for both duplexes. The 10° bend observed at $G^3$ likely contributes to the increased differences in shifts by 1-3 at the maximum, 0 and minimum wavelengths.

The chemical shifts of the IQ proton H7a and H9a between $G^1$ and $G^3$ differ by 0.45 and 0.3 ppm further downfield for $G^1$, while all other protons on the IQ ring differed by less than 0.1 ppm, which could indicate this portion of the IQ ring is oriented more towards the major groove than the $G^3$ adduct. One difference in the orientation of IQ is at $G^1$, it maintained pla*NarI*ty with $X^4$. At the $G^3$ position, however, IQ was inserted at a 15° angle relative to $X^7$.

*$N^2$ vs. C8-dG-IQ*

While the C8 and *$N^2$*–dG-IQ adducts at $G^3$ both intercalate within the duplex, the *$N^2$* at the $G^1$ and $G^2$ positions adopt much more contrasting conformations from that of the C8-dG-IQ adduct. The structures of the C8-dG-IQ adduct at $G^1$ and $G^2$ were groove-bound, where the IQ ring was located in the minor groove of the duplex.

The *$N^2$*-dG-IQ adduct has demonstrated different biological processing from the C8-dG-IQ adduct. Both adducts at the $G^1$ position were able to be bypassed *in vitro* by both prokaryotic[169,174] as well as human polymerases[20], with few instances of frameshift mutations at the $G^1$ position in the *NarI* sequence. Structurally, however, these adopt different conformations in the duplex DNA. The *$N^2$* adduct maintains the *anti* configuration, unlike the C8-dG-IQ adduct which is flipped in the *syn* conformation[178]. The IQ ring of C8-

dG-IQ is located in the minor groove of the duplex. In contrast, the *N*$^{2}$-IQ-dG adduct remains intercalated in the duplex at the G$^{1}$ position, very similar to the G$^{3}$ position. The conformational differences result in adducts which induce various amounts of stabilities to the duplex. C8-dG-IQ decreases the thermal stability by 4-7 °C[171], while *N*$^{2}$ does not significantly change the thermal stability of the duplex at any position[175]. These differences between the two adducts could contribute to the observed discrepancy in repair efficiency since local instabilities induced by the adduct lead to recognition of DNA damage by NER proteins. The structural data provides less insight as to why *N*$^{2}$-dG-IQ results in frameshift mutations when bypassed by polη, yet can bypass C8-dG-IQ. It does, however, provide evidence that the point of attachment for these DNA adducts is important for structure-function relationships.

*Summary*

As a result, this data would suggest that *N*$^{2}$–dG-HCA adducts could have a unique mechanism of biological processing compared to the C8-dG adducts. The structures demonstrate a sequence dependence dictating the whether the C8-dG-IQ adduct is intercalated or groove bound but has little effect on the conformation of the *N*$^{2}$-dG-IQ adduct at the various positions. Yet, bypass by pol η suggests the sequence plays a role in extension beyond the adduct. Therefore, it is likely that the sequence dependence plays a larger role in determining the results of bypass via polymerase interactions for the *N*$^{2}$-dG-IQ than perhaps the structure of the duplex itself. Further experiments looking at the

adduct in a polymerase active site at the ss-ds junction will determine how these interactions differ and lead to sequence dependence mutagenesis.

# CHAPTER V

# CONCLUSIONS AND FUTURE DIRECTIONS

## Conclusions

Structures of IQ have been determined at both the mutagenic hotspot, $G^3$ position, in the *NarI* sequence and the less potent mutagenic $G^1$ position of the *NarI* sequence ($G^1G^2CX^3CC$) by solution NMR. The different sequence contexts are interesting due to exhibited differences in mutagenic results from *in vitro* assays. Based on the different biological processing, it was believed that the duplex structure of the $G^3$ sequence inducing frameshift mutations would differ significantly from the duplex structure when IQ is attached to $G^1$, which is more likely to induce point mutations. Perhaps these differences would suggest possible reasons why hpolη could induce frameshift mutations in one context but not the other.

However, results from solution NMR data collected on both samples indicated a much smaller difference in structure than what was predicted. Both IQ moieties intercalate into the duplex, taking the place of the opposite base, which was relocated to the major groove. The modified base is also displaced to some extent to the major groove to accommodate the IQ in the duplex in such a fashion that does not seem to disrupt the surrounding bases. The thermal stabilities of these duplexes do not change with the presence of the adduct and the CD spectrum for each sequence are comparable, thus supporting the idea that these duplex structures are likely very similar. The placement of the IQ within the duplex is different to some extent, with IQ at $G^3$ at about a 15° angle relative to the modified dG base. This could change its base-stacking ability or position it in

such a way that it interacts with the polymerase active site differently. It is clear, however, that further experiments are necessary to understand the bypass of these adducts.

These structures are interesting in the context of comparing with the C8-dG-IQ adducts, nevertheless. Because the C8-dG-IQ is preferentially repaired and its ability to be bypassed by hpol η but not Dpo4, these adducts would also be predicted to be very different. This work provides a better understanding of the persistence of $N^2$-dG-IQ relative to C8-dG-IQ, since the $N^2$ adduct modifies the duplex with much smaller perturbations to the overall duplex. The IQ has strong base-stacking interactions with flanking bases that allow the duplex to maintain its thermal stability, whereas the C8 adduct is destabilizing and creates far more perturbations to the duplex. The C8 adduct must flip the modified base into the *syn* conformation in order to intercalate, meanwhile bending the backbone as well. These perturbations likely increase the likelihood for the adduct to be recognized by the NER pathway for repair. Determining the Crystal Structure of 8-oxoguanine with Y-family Polymerase Dpo4

## Introduction

Understanding the replication of DNA adducts requires direct observation of structural features of polymerase and DNA at a ss-ds junction. Observing the interactions between the adduct/modified base through x-ray crystallography can be the best way to identify these interactions, which can dictate how likely an adduct is to be mutagenic. Dpo4 is a Y-family polymerase originating from the archaeal bacteria *Sulfolobus solfataricus* that has mechanistic similarities to hpolη. In order to study bypass of IQ, Dpo4 was initially crystallized with the adduct 8-oxoG, which has been published previously[128,179], as a way to develop skills and methods for designing crystal trials using IQ. Results from diffraction of

crystals of the binary complex of correctly paired 8-oxoG:C diffracted with a resolution of 2.7 Å, for which molecular replacement was used to solve the phasing problem. Results reflected those previously published, showing that when 8-oxoG pairs with dC, 8-oxoG maintains the anti configuration in the active site. The quality of data collected is also comparable to published results and ensures the methods are suitable for obtaining useful crystal data.

## Results

*Activity Assay*

Dpo4 is a robust polymerase that is stable both at high temperatures and can be stored at low temperatures for long periods of time and maintain activity. The extension assay was used to test for polymerase activity before setting up crystals to ensure the polymerase maintained its activity and could form active complexes with DNA after purification. Figure 5-1 shows the results of incubating Dpo4 with unmodified DNA in excess dNTPs to allow for full-length extension within a 2 hr. time frame. The starting material is rapidly begun to be extended in the first 5 min. After an hour, more fully extended product, or nearly fully extended, product is visible than initial substrate. At 2 hrs., it still appears as though extension is occurring, although full-length product is clearly the major product at this point, along with a small percent of blunt end extension.

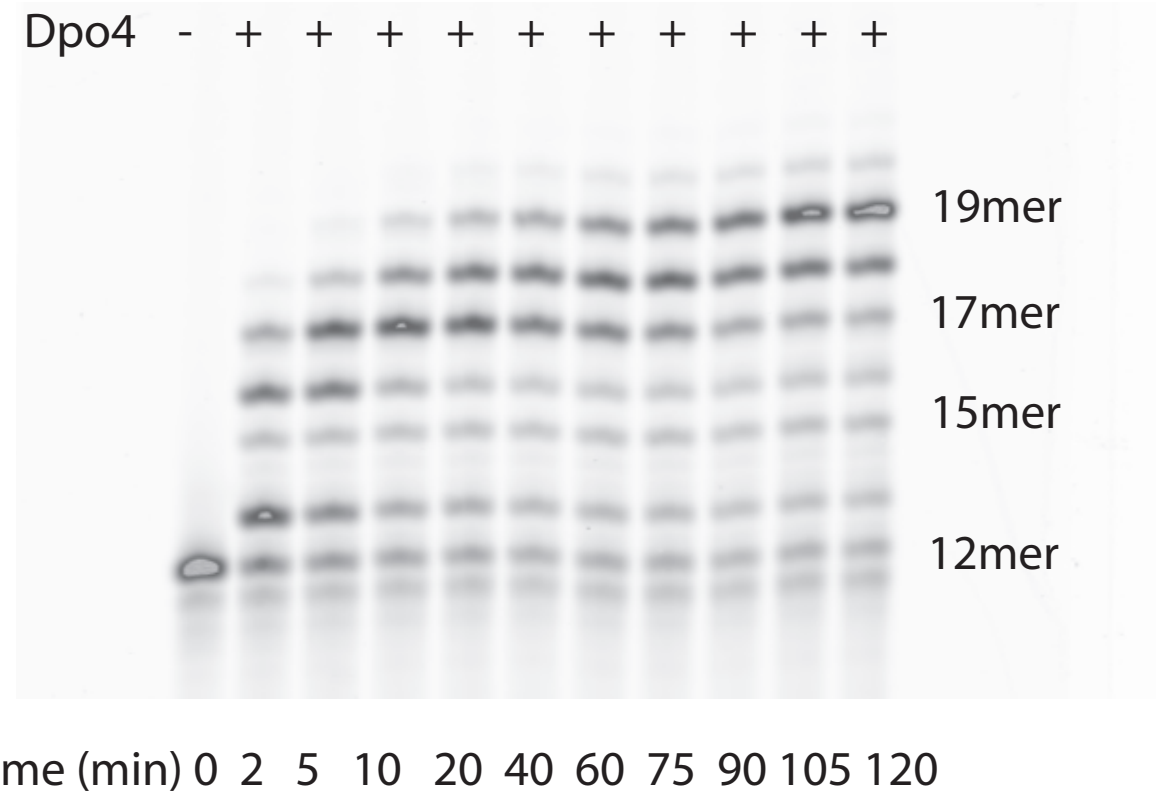



**Figure 5-1.** Extension of unmodified oligonucleotide by Dpo4.

*Crystal Structures of Dpo4:8-oxoG*

Only binary crystal complexes with correct dC opposite the 8-oxoG diffracted with enough data and enough resolution for useful structure determination. The best data set had a resolution of 2.1 Å to a space group of $P_1$. The crystal contained a mosaicity of 0.75. The unit cell contained two molecules and had dimensions of 53.05, 53.12, and 98.85 Å with angles of 80.00°, 77.50°, and 70.33°. The overall completeness was 98.1 and a redundancy of 1.8. A total of 205 images were collected over 205°. The $R_{free}$ for the final structure was 0.30 and the R-value was 0.23.

The crystal structure contains the correctly paired 8-oxoG:C in the active site of Dpo4. The modified 8-oxoG base remains in the *anti* conformation. Because the oxygen modification is located opposite the Watson-Crick hydrogen bonding face of the guanine, the modification does not affect base-pairing. R332 was located 3.8 Å away from the oxygen at C8 of the modified base.

## Discussion

The crystal structure yielded similar results to the previously published structures[128,130,179]. The space groups for the published structures were $P2_12_12$ but were still able to use molecular replacement to phase the data. The R values for the refined structure are also comparable to previously published structures[128,130,179].

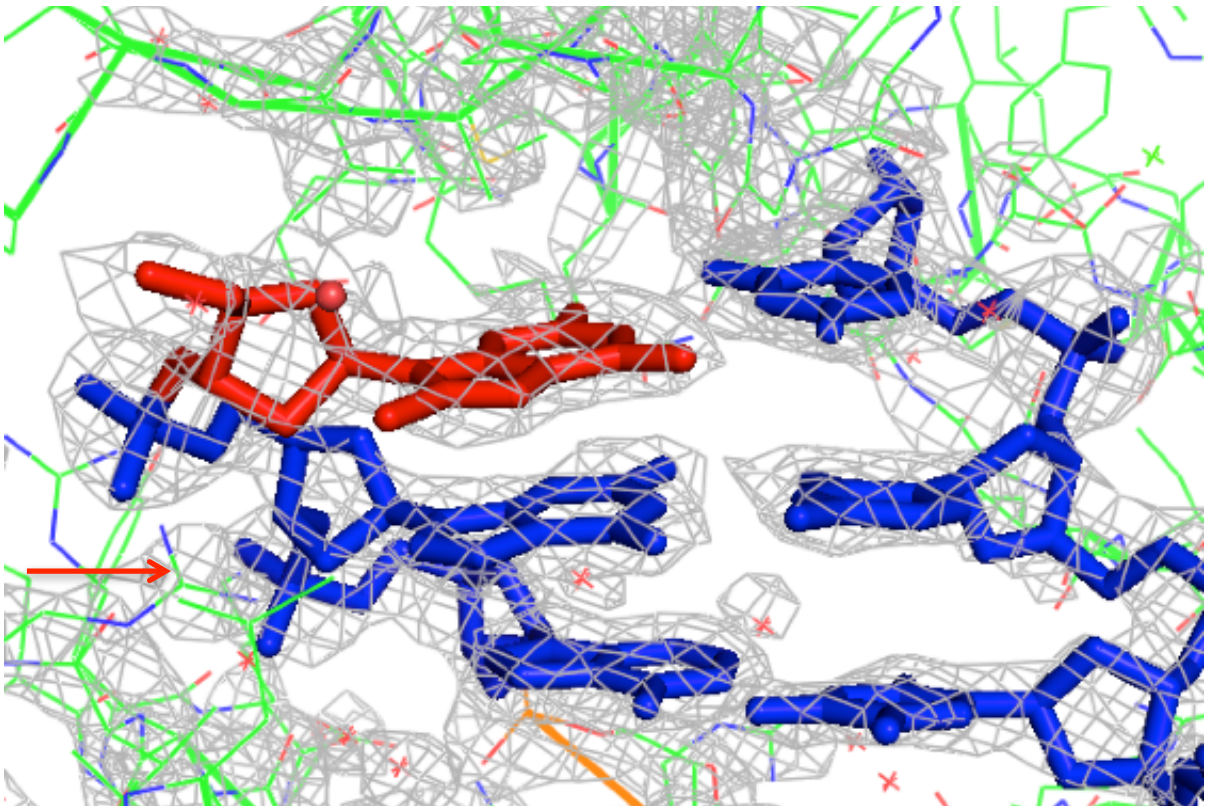


**Figure 5-2**. The active site of Dpo4 containing an 8-oxoG modified DNA sequence (modified base shown in red) paired opposite dC. The arrow highlights residue R332.

Dpo4 has been shown to incorporate dCTP opposite 8-oxoG more than 95% over the mutagenic dATP and can extend the correct pair 4-fold more efficiently[130]. R332 in the active site has been shown to play a role in correct bypass of 8-oxoG through hydrogen bonding with the oxygen of the modified base, which stabilizes the guanine in the *anti* conformation[128]. In this crystal structure, the nitrogen of one of the amine groups of R332 is 3.8 Å from the oxygen, meaning the hydrogen atoms could potentially interact with the oxygen during insertion of dCTP.

While the structure provides no unique information about bypass of 8-oxoG by Dpo4, it does confirm that the purification procedures produce clean, active polymerase, and the crystal setup and buffers are able to yield crystals that diffract with high enough resolution to discern what is happening in the active site. The results are able to confirm that good technique is being used for protein expression and crystallography, as similar techniques are necessary to further investigate the bypass of IQ. Observing the crystal structure of C8-dG-IQ adduct in the active site of Dpo4 would likely involve a similar protocol, despite modifying the DNA sequence to incorporate a GC repeat. The general technique would also be applicable for studying polη complexes with $N^2$-dG-IQ, while more specific protocol details, such as purification and buffers, would be modified. Crystal structures can provide valuable insight into interactions between DNA and polymerase, which can be useful for understanding the miscoding by DNA adducts.

## Future Directions

There are still questions in the field about if duplex structures can directly be related to ss-ds junctions in the polymerase complex. Because the duplex structures of IQ at the $G^1$ and $G^3$ position in the *NarI* DNA recognition sequence appear very similar according to the NMR data, it is especially difficult to predict why the $G^3$ adduct is prone to frameshifts over $G^1$. The only way to answer these questions is to directly examine the DNA•polymerase complex. Crystal structures of IQ in the active site of hpol η would better be able to address why the mutagenesis of these adducts differ because it allows the active site to be visualized and provides a snapshot of what is occurring. This could be a viable experiment since crystals of hpolη have already successfully been obtained and were able to demonstrate the specificity of hpolη to cyclobutane pyrimidine dimers through interactions of the crosslink with hydrophobic residues[180].

However, *in vitro* experiments testing single polymerases may not provide an accurate idea of how the adducts are actually bypassed. Many pathways in human cells involve multiple proteins. Thus, a single polymerase may not be responsible for bypassing IQ. More detailed experiments into the bypass mechanics would, therefore, be needed to understand how relevant the frameshift mutations are in human cells.

## APPENDIX A

## RMD INPUT FILES

### 20 ps Simulated Annealing Protocol

simulated annealing protocol, 18A cut off, 20ps

```
 &cntrl
  imin=0, ntr=0, ntc=2, ntf=2,
  cut=18.0, igb=1, saltcon=0.1, gbsa=0, offset=0.13,
  ntpr=1000, ntwx=1000, nstlim=20000, dt=0.001,
  ntt=1, ntx=1, irest=0, ntb=0, vlimit=20,
  pencut=-0.001, nmropt=1,
 &end



#
#Simple simulated annealing algorithm:
#
#from steps 0 to 1000: heat the system to 600K with short tautp
#from steps 1001 to 2000: keep the temperature at 600K
#from steps 2001 to 18000: cool down the system to 100K with long tautp
#from steps 18001 to 20000: cool down the system to 0K with short tautp
#

 &wt type='TEMP0', istep1=0,istep2=1000,value1=0.0,
         value2=600.0,    &end

 &wt type='TEMP0', istep1=1000,istep2=2000,value1=600.0,
         value2=600.0,    &end

 &wt type='TEMP0', istep1=2001, istep2=18000, value1=600.0,
         value2=100.0,     &end

 &wt type='TEMP0', istep1=18001, istep2=20000, value1=100.0,
         value2=0.0,     &end


 &wt type='TAUTP', istep1=0,istep2=2000,value1=0.5,
         value2=0.5,     &end

 &wt type='TAUTP', istep1=2001,istep2=18000,value1=4.0,
```

```
      value2=4.0,    &end

 &wt type='TAUTP', istep1=18001,istep2=20000,value1=1.0,
      value2=1.0,    &end


 &wt type='REST', istep1=0,istep2=2000,value1=0.1,
      value2=1.0,  &end

 &wt type='REST', istep1=2001,istep2=20000,value1=1.0,
      value2=1.0,  &end


 &wt type='END'  &end
LISTOUT=POUT
DISANG=IQG3.rst
```

**100 ps Simulated Annealing Protocol**

```
simulated annealing protocol, 18A cut off, 100ps

 &cntrl
  imin=0, ntr=0, ntc=2, ntf=2,
  cut=18.0, igb=1, saltcon=0.1, gbsa=0, offset=0.13,
  ntpr=1000, ntwx=1000, nstlim=100000, dt=0.001,
  ntt=1, ntx=1, irest=0, ntb=0, vlimit=20,
  pencut=-0.001, nmropt=1,
 &end

#
#Simple simulated annealing algorithm:
#
#from steps 0 to 5000: heat the system to 600K with short tautp
#from steps 5000 to 10000: keep the temperature at 600K
#from steps 10001 to 90000: cool down the system to 100K with long tautp
#from steps 90001 to 100000: cool down the system to 0K with short tautp
#
 &wt type='TEMP0', istep1=0,istep2=5000,value1=0.0,
      value2=600.0,    &end

 &wt type='TEMP0', istep1=5000,istep2=10000,value1=600.0,
      value2=600.0,    &end

 &wt type='TEMP0', istep1=10001, istep2=90000, value1=600.0,
```

```
      value2=100.0,    &end

 &wt type='TEMP0', istep1=90001, istep2=100000, value1=100.0,
      value2=0.0,    &end

 &wt type='TAUTP', istep1=0,istep2=10000,value1=0.5,
      value2=0.5,    &end

 &wt type='TAUTP', istep1=10001,istep2=90000,value1=4.0,
      value2=4.0,    &end

 &wt type='TAUTP', istep1=90001,istep2=100000,value1=1.0,
      value2=1.0,    &end

 &wt type='REST', istep1=0,istep2=20000,value1=0.1,
      value2=1.0,  &end

 &wt type='REST', istep1=20001,istep2=100000,value1=1.0,
      value2=1.0,  &end

 &wt type='END'  &end
LISTOUT=POUT
DISANG=IQG3.rst
```

## APPENDIX B

## PDB OUTPUT FILES

### $N^2$-dG-IQ at $G^3$

```
REMARK
ATOM      1  H5T DC5     1     -17.117   7.764  23.225
ATOM      2  O5* DC5     1     -16.783   7.198  23.924
ATOM      3  C5* DC5     1     -17.522   7.419  25.116
ATOM      4 1H5* DC5     1     -18.579   7.206  24.958
ATOM      5 2H5* DC5     1     -17.422   8.464  25.409
ATOM      6  C4* DC5     1     -17.049   6.550  26.295
ATOM      7  H4* DC5     1     -17.448   6.981  27.213
ATOM      8  O4* DC5     1     -17.559   5.227  26.215
ATOM      9  C1* DC5     1     -16.492   4.303  26.126
ATOM     10  H1* DC5     1     -16.422   3.774  27.076
ATOM     11  N1  DC5     1     -16.716   3.318  25.016
ATOM     12  C6  DC5     1     -17.050   3.756  23.759
ATOM     13  H6  DC5     1     -17.148   4.817  23.579
ATOM     14  C5  DC5     1     -17.222   2.859  22.760
ATOM     15  H5  DC5     1     -17.451   3.216  21.767
ATOM     16  C4  DC5     1     -17.073   1.473  23.083
ATOM     17  N4  DC5     1     -17.294   0.554  22.198
ATOM     18  H41 DC5     1     -17.519   0.873  21.266
ATOM     19  H42 DC5     1     -17.246  -0.413  22.488
ATOM     20  N3  DC5     1     -16.817   1.033  24.304
ATOM     21  C2  DC5     1     -16.622   1.938  25.288
ATOM     22  O2  DC5     1     -16.363   1.481  26.405
ATOM     23  C3* DC5     1     -15.513   6.467  26.466
ATOM     24  H3* DC5     1     -14.990   7.222  25.880
ATOM     25  C2* DC5     1     -15.194   5.086  25.901
ATOM     26 1H2* DC5     1     -14.349   4.603  26.391
ATOM     27 2H2* DC5     1     -14.980   5.175  24.835
ATOM     28  O3* DC5     1     -15.165   6.597  27.859
ATOM     29  P   DT      2     -13.647   6.762  28.365
ATOM     30  O1P DT      2     -13.706   7.326  29.738
```

```
ATOM     31  O2P DT      2     -12.862   7.493  27.330
ATOM     32  O5* DT      2     -13.083   5.266  28.471
ATOM     33  C5* DT      2     -13.591   4.373  29.451
ATOM     34 1H5* DT      2     -14.680   4.355  29.394
ATOM     35 2H5* DT      2     -13.299   4.773  30.422
ATOM     36  C4* DT      2     -13.096   2.924  29.302
ATOM     37  H4* DT      2     -13.460   2.338  30.146
ATOM     38  O4* DT      2     -13.590   2.321  28.098
ATOM     39  C1* DT      2     -12.583   1.473  27.582
ATOM     40  H1* DT      2     -12.625   0.532  28.131
ATOM     41  N1  DT      2     -12.772   1.246  26.119
ATOM     42  C6  DT      2     -12.874   2.314  25.250
ATOM     43  H6  DT      2     -12.692   3.307  25.633
ATOM     44  C5  DT      2     -13.197   2.140  23.934
ATOM     45  C7  DT      2     -13.263   3.350  23.000
ATOM     46 1H7  DT      2     -14.239   3.417  22.519
ATOM     47 2H7  DT      2     -13.055   4.274  23.540
ATOM     48 3H7  DT      2     -12.521   3.239  22.209
ATOM     49  C4  DT      2     -13.461   0.787  23.414
ATOM     50  O4  DT      2     -13.775   0.468  22.265
ATOM     51  N3  DT      2     -13.324  -0.203  24.349
ATOM     52  H3  DT      2     -13.416  -1.144  23.993
ATOM     53  C2  DT      2     -12.988  -0.051  25.670
ATOM     54  O2  DT      2     -12.870  -1.035  26.390
ATOM     55  C3* DT      2     -11.552   2.805  29.290
ATOM     56  H3* DT      2     -11.075   3.783  29.345
ATOM     57  C2* DT      2     -11.278   2.167  27.919
ATOM     58 1H2* DT      2     -10.454   1.454  27.947
ATOM     59 2H2* DT      2     -11.053   2.953  27.197
ATOM     60  O3* DT      2     -11.117   1.974  30.373
ATOM     61  P   DC      3      -9.538   1.680  30.689
ATOM     62  O1P DC      3      -9.347   1.531  32.156
ATOM     63  O2P DC      3      -8.714   2.697  29.970
ATOM     64  O5* DC      3      -9.344   0.241  29.959
ATOM     65  C5* DC      3     -10.078  -0.898  30.431
ATOM     66 1H5* DC      3     -11.142  -0.683  30.335
```

```
ATOM     67 2H5* DC      3      -9.818  -1.030  31.481
ATOM     68  C4* DC      3      -9.764  -2.204  29.668
ATOM     69  H4* DC      3     -10.267  -3.017  30.191
ATOM     70  O4* DC      3     -10.248  -2.112  28.330
ATOM     71  C1* DC      3      -9.232  -2.489  27.416
ATOM     72  H1* DC      3      -9.286  -3.563  27.237
ATOM     73  N1  DC      3      -9.405  -1.771  26.121
ATOM     74  C6  DC      3      -9.214  -0.409  26.058
ATOM     75  H6  DC      3      -8.895   0.117  26.945
ATOM     76  C5  DC      3      -9.486   0.266  24.915
ATOM     77  H5  DC      3      -9.356   1.336  24.853
ATOM     78  C4  DC      3      -9.955  -0.492  23.817
ATOM     79  N4  DC      3     -10.227   0.117  22.702
ATOM     80  H41 DC      3     -10.014   1.100  22.606
ATOM     81  H42 DC      3     -10.578  -0.434  21.932
ATOM     82  N3  DC      3     -10.128  -1.800  23.838
ATOM     83  C2  DC      3      -9.862  -2.449  24.993
ATOM     84  O2  DC      3     -10.042  -3.668  24.972
ATOM     85  C3* DC      3      -8.253  -2.495  29.599
ATOM     86  H3* DC      3      -7.717  -1.748  30.184
ATOM     87  C2* DC      3      -7.902  -2.272  28.136
ATOM     88 1H2* DC      3      -7.135  -2.950  27.762
ATOM     89 2H2* DC      3      -7.539  -1.254  27.997
ATOM     90  O3* DC      3      -7.818  -3.760  30.134
ATOM     91  P   DG      4      -8.357  -5.242  29.732
ATOM     92  O1P DG      4      -9.830  -5.274  29.659
ATOM     93  O2P DG      4      -7.692  -6.215  30.667
ATOM     94  O5* DG      4      -7.806  -5.522  28.244
ATOM     95  C5* DG      4      -6.435  -5.650  27.977
ATOM     96 1H5* DG      4      -6.039  -6.529  28.485
ATOM     97 2H5* DG      4      -5.886  -4.783  28.344
ATOM     98  C4* DG      4      -6.203  -5.819  26.454
ATOM     99  H4* DG      4      -6.597  -6.787  26.143
ATOM    100  O4* DG      4      -6.829  -4.759  25.735
ATOM    101  C1* DG      4      -5.928  -4.352  24.727
ATOM    102  H1* DG      4      -5.958  -5.086  23.922
```

```
ATOM    103  N9  DG      4      -6.239  -3.031  24.153
ATOM    104  C8  DG      4      -6.041  -1.776  24.673
ATOM    105  H8  DG      4      -5.658  -1.635  25.673
ATOM    106  N7  DG      4      -6.331  -0.800  23.839
ATOM    107  C5  DG      4      -6.769  -1.472  22.680
ATOM    108  C6  DG      4      -7.226  -0.986  21.400
ATOM    109  O6  DG      4      -7.348   0.185  21.013
ATOM    110  N1  DG      4      -7.640  -1.989  20.544
ATOM    111 1H   DG      4      -7.949  -1.694  19.629
ATOM    112  C2  DG      4      -7.578  -3.314  20.841
ATOM    113  N2  DG      4      -7.977  -4.172  19.920
ATOM    114  H21 DG      4      -7.937  -5.154  20.152
ATOM    115  H22 DG      4      -8.326  -3.854  19.028
ATOM    116  N3  DG      4      -7.103  -3.789  21.983
ATOM    117  C4  DG      4      -6.723  -2.831  22.872
ATOM    118  C3* DG      4      -4.685  -5.756  26.133
ATOM    119  H3* DG      4      -4.065  -5.787  27.029
ATOM    120  C2* DG      4      -4.561  -4.416  25.421
ATOM    121 1H2* DG      4      -3.765  -4.418  24.676
ATOM    122 2H2* DG      4      -4.443  -3.611  26.145
ATOM    123  O3* DG      4      -4.295  -6.756  25.209
ATOM    124  P   DG      5      -3.784  -8.217  25.682
ATOM    125  O1P DG      5      -4.738  -8.812  26.665
ATOM    126  O2P DG      5      -2.345  -8.095  26.047
ATOM    127  O5* DG      5      -3.901  -8.988  24.293
ATOM    128  C5* DG      5      -5.126  -9.535  23.807
ATOM    129 1H5* DG      5      -5.949  -8.858  24.036
ATOM    130 2H5* DG      5      -5.329 -10.475  24.320
ATOM    131  C4* DG      5      -5.136  -9.816  22.297
ATOM    132  H4* DG      5      -5.892 -10.584  22.136
ATOM    133  O4* DG      5      -5.455  -8.636  21.573
ATOM    134  C1* DG      5      -4.338  -8.238  20.794
ATOM    135  H1* DG      5      -4.546  -8.491  19.754
ATOM    136  N9  DG      5      -4.112  -6.776  20.917
ATOM    137  C8  DG      5      -3.641  -6.069  21.992
ATOM    138  H8  DG      5      -3.306  -6.524  22.912
```

```
ATOM    139  N7  DG      5      -3.601  -4.780  21.817
ATOM    140  C5  DG      5      -4.147  -4.613  20.529
ATOM    141  C6  DG      5      -4.432  -3.433  19.746
ATOM    142  O6  DG      5      -4.317  -2.246  20.044
ATOM    143  N1  DG      5      -4.886  -3.703  18.468
ATOM    144 1H   DG      5      -5.061  -2.916  17.860
ATOM    145  C2  DG      5      -5.118  -4.957  18.005
ATOM    146  N2  DG      5      -5.532  -5.071  16.775
ATOM    147  H21 DG      5      -5.648  -5.990  16.373
ATOM    148  H22 DG      5      -5.673  -4.236  16.223
ATOM    149  N3  DG      5      -4.887  -6.065  18.695
ATOM    150  C4  DG      5      -4.412  -5.840  19.956
ATOM    151  C3* DG      5      -3.805 -10.353  21.769
ATOM    152  H3* DG      5      -3.233 -10.814  22.574
ATOM    153  C2* DG      5      -3.142  -9.087  21.245
ATOM    154 1H2* DG      5      -2.463  -9.299  20.419
ATOM    155 2H2* DG      5      -2.575  -8.590  22.032
ATOM    156  O3* DG      5      -4.032 -11.350  20.775
ATOM    157  P   DC      6      -2.842 -12.095  19.966
ATOM    158  O1P DC      6      -3.416 -13.342  19.417
ATOM    159  O2P DC      6      -1.627 -12.201  20.834
ATOM    160  O5* DC      6      -2.501 -11.109  18.733
ATOM    161  C5* DC      6      -3.402 -10.960  17.633
ATOM    162 1H5* DC      6      -4.379 -10.665  18.015
ATOM    163 2H5* DC      6      -3.515 -11.919  17.129
ATOM    164  C4* DC      6      -2.913  -9.907  16.628
ATOM    165  H4* DC      6      -3.608  -9.903  15.789
ATOM    166  O4* DC      6      -2.897  -8.597  17.197
ATOM    167  C1* DC      6      -1.772  -7.927  16.712
ATOM    168  H1* DC      6      -1.962  -7.566  15.702
ATOM    169  N1  DC      6      -1.458  -6.775  17.594
ATOM    170  C6  DC      6      -1.018  -6.966  18.884
ATOM    171  H6  DC      6      -0.857  -7.968  19.255
ATOM    172  C5  DC      6      -0.879  -5.909  19.725
ATOM    173  H5  DC      6      -0.571  -6.093  20.744
ATOM    174  C4  DC      6      -1.178  -4.618  19.189
```

```
ATOM    175  N4  DC      6      -1.142  -3.543  19.922
ATOM    176  H41 DC      6      -0.986  -3.621  20.917
ATOM    177  H42 DC      6      -1.393  -2.677  19.468
ATOM    178  N3  DC      6      -1.514  -4.408  17.947
ATOM    179  C2  DC      6      -1.631  -5.462  17.106
ATOM    180  O2  DC      6      -1.966  -5.220  15.948
ATOM    181  C3* DC      6      -1.498 -10.212  16.103
ATOM    182  H3* DC      6      -1.129 -11.141  16.537
ATOM    183  C2* DC      6      -0.692  -9.007  16.605
ATOM    184 1H2* DC      6       0.082  -8.707  15.899
ATOM    185 2H2* DC      6      -0.258  -9.259  17.572
ATOM    186  O3* DC      6      -1.555 -10.303  14.683
ATOM    187  P   DKA     7      -0.358 -10.863  13.750
ATOM    188  O1P DKA     7      -0.930 -11.231  12.419
ATOM    189  O2P DKA     7       0.453 -11.874  14.489
ATOM    190  O5* DKA     7       0.562  -9.568  13.562
ATOM    191  C5* DKA     7       0.143  -8.446  12.784
ATOM    192 1H5* DKA     7      -0.866  -8.145  13.062
ATOM    193 2H5* DKA     7       0.148  -8.754  11.738
ATOM    194  C4* DKA     7       1.103  -7.248  12.931
ATOM    195  H4* DKA     7       0.807  -6.507  12.188
ATOM    196  O4* DKA     7       0.973  -6.702  14.231
ATOM    197  C1* DKA     7       2.282  -6.455  14.720
ATOM    198  H1* DKA     7       2.682  -5.548  14.266
ATOM    199  N9  DKA     7       2.277  -6.337  16.200
ATOM    200  C8  DKA     7       2.655  -7.211  17.190
ATOM    201  H8  DKA     7       2.941  -8.228  16.968
ATOM    202  N7  DKA     7       2.684  -6.678  18.394
ATOM    203  C5  DKA     7       2.278  -5.339  18.165
ATOM    204  C6  DKA     7       2.127  -4.195  19.016
ATOM    205  O6  DKA     7       2.267  -4.119  20.227
ATOM    206  N1  DKA     7       1.754  -3.036  18.353
ATOM    207 1H   DKA     7       1.560  -2.228  18.927
ATOM    208  C2  DKA     7       1.524  -2.964  17.013
ATOM    209  N2  DKA     7       1.228  -1.745  16.552
ATOM    210 2H   DKA     7       1.293  -1.012  17.244
```

```
ATOM    211  C23 DKA     7       0.963  -1.287  15.300
ATOM    212  C22 DKA     7       0.959   0.136  15.063
ATOM    213  N21 DKA     7       1.182   0.982  16.121
ATOM    214  C20 DKA     7       1.047   2.370  15.897
ATOM    215  H20 DKA     7       1.046   3.053  16.734
ATOM    216  C19 DKA     7       0.912   2.851  14.582
ATOM    217  H19 DKA     7       0.852   3.913  14.394
ATOM    218  C18 DKA     7       0.892   1.978  13.492
ATOM    219  H18 DKA     7       0.883   2.352  12.479
ATOM    220  C17 DKA     7       0.750   0.612  13.738
ATOM    221  C16 DKA     7       0.442  -0.251  12.689
ATOM    222  N15 DKA     7       0.228  -0.002  11.362
ATOM    223  C14 DKA     7      -0.092  -1.242  10.847
ATOM    224  N14 DKA     7      -0.416  -1.473   9.511
ATOM    225 1H14 DKA     7      -1.376  -1.760   9.386
ATOM    226 2H14 DKA     7       0.325  -1.949   9.019
ATOM    227  N13 DKA     7      -0.035  -2.279  11.755
ATOM    228  C13 DKA     7      -0.169  -3.714  11.414
ATOM    229 1H13 DKA     7       0.784  -4.121  11.076
ATOM    230 2H13 DKA     7      -0.475  -4.285  12.290
ATOM    231 3H13 DKA     7      -0.946  -3.884  10.668
ATOM    232  C12 DKA     7       0.369  -1.658  12.916
ATOM    233  C11 DKA     7       0.634  -2.134  14.217
ATOM    234  H11 DKA     7       0.562  -3.207  14.318
ATOM    235  N3  DKA     7       1.700  -3.999  16.198
ATOM    236  C4  DKA     7       2.070  -5.142  16.828
ATOM    237  C3* DKA     7       2.568  -7.680  12.726
ATOM    238  H3* DKA     7       2.656  -8.687  12.318
ATOM    239  C2* DKA     7       3.107  -7.605  14.151
ATOM    240 1H2* DKA     7       4.180  -7.417  14.178
ATOM    241 2H2* DKA     7       2.872  -8.533  14.673
ATOM    242  O3* DKA     7       3.280  -6.776  11.897
ATOM    243  P   DC      8       3.086  -6.777  10.303
ATOM    244  O1P DC      8       1.806  -7.420   9.944
ATOM    245  O2P DC      8       4.336  -7.288   9.676
ATOM    246  O5* DC      8       2.920  -5.216   9.959
```

```
ATOM    247  C5* DC      8       4.031  -4.323   9.868
ATOM    248 1H5* DC      8       4.644  -4.603   9.011
ATOM    249 2H5* DC      8       4.641  -4.373  10.771
ATOM    250  C4* DC      8       3.550  -2.876   9.636
ATOM    251  H4* DC      8       2.762  -2.881   8.884
ATOM    252  O4* DC      8       3.044  -2.355  10.863
ATOM    253  C1* DC      8       3.849  -1.265  11.284
ATOM    254  H1* DC      8       3.352  -0.325  11.045
ATOM    255  N1  DC      8       4.109  -1.319  12.761
ATOM    256  C6  DC      8       4.256  -2.520  13.416
ATOM    257  H6  DC      8       4.218  -3.454  12.874
ATOM    258  C5  DC      8       4.471  -2.529  14.759
ATOM    259  H5  DC      8       4.621  -3.466  15.274
ATOM    260  C4  DC      8       4.550  -1.272  15.418
ATOM    261  N4  DC      8       4.762  -1.224  16.714
ATOM    262  H41 DC      8       4.909  -2.068  17.250
ATOM    263  H42 DC      8       4.812  -0.309  17.139
ATOM    264  N3  DC      8       4.381  -0.127  14.826
ATOM    265  C2  DC      8       4.163  -0.107  13.492
ATOM    266  O2  DC      8       3.984   1.004  12.960
ATOM    267  C3* DC      8       4.701  -1.968   9.179
ATOM    268  H3* DC      8       5.500  -2.574   8.751
ATOM    269  C2* DC      8       5.158  -1.336  10.495
ATOM    270 1H2* DC      8       5.595  -0.350  10.340
ATOM    271 2H2* DC      8       5.875  -1.986  10.998
ATOM    272  O3* DC      8       4.222  -1.001   8.259
ATOM    273  P   DC      9       5.182  -0.228   7.196
ATOM    274  O1P DC      9       4.327   0.369   6.140
ATOM    275  O2P DC      9       6.262  -1.162   6.787
ATOM    276  O5* DC      9       5.822   0.950   8.065
ATOM    277  C5* DC      9       5.069   2.068   8.506
ATOM    278 1H5* DC      9       4.226   1.711   9.097
ATOM    279 2H5* DC      9       4.667   2.614   7.653
ATOM    280  C4* DC      9       5.886   3.072   9.348
ATOM    281  H4* DC      9       5.359   4.026   9.308
ATOM    282  O4* DC      9       5.900   2.667  10.696
```

```
ATOM    283  C1* DC      9       7.218   2.795  11.182
ATOM    284  H1* DC      9       7.388   3.844  11.426
ATOM    285  N1  DC      9       7.439   1.970  12.415
ATOM    286  C6  DC      9       7.659   0.618  12.381
ATOM    287  H6  DC      9       7.694   0.118  11.425
ATOM    288  C5  DC      9       7.823  -0.092  13.538
ATOM    289  H5  DC      9       7.994  -1.158  13.494
ATOM    290  C4  DC      9       7.844   0.645  14.752
ATOM    291  N4  DC      9       7.990   0.051  15.896
ATOM    292  H41 DC      9       8.143  -0.945  15.953
ATOM    293  H42 DC      9       7.948   0.612  16.735
ATOM    294  N3  DC      9       7.645   1.946  14.817
ATOM    295  C2  DC      9       7.417   2.617  13.659
ATOM    296  O2  DC      9       7.231   3.819  13.758
ATOM    297  C3* DC      9       7.355   3.252   8.908
ATOM    298  H3* DC      9       7.519   2.845   7.910
ATOM    299  C2* DC      9       8.115   2.506   9.987
ATOM    300 1H2* DC      9       9.133   2.867  10.139
ATOM    301 2H2* DC      9       8.128   1.444   9.744
ATOM    302  O3* DC      9       7.673   4.634   8.945
ATOM    303  P   DA     10       8.942   5.233   8.151
ATOM    304  O1P DA     10       8.430   5.933   6.933
ATOM    305  O2P DA     10       9.974   4.192   8.007
ATOM    306  O5* DA     10       9.475   6.332   9.190
ATOM    307  C5* DA     10       8.712   7.485   9.556
ATOM    308 1H5* DA     10       7.710   7.191   9.871
ATOM    309 2H5* DA     10       8.593   8.146   8.697
ATOM    310  C4* DA     10       9.325   8.269  10.723
ATOM    311  H4* DA     10       8.736   9.179  10.834
ATOM    312  O4* DA     10       9.196   7.526  11.927
ATOM    313  C1* DA     10      10.489   7.289  12.471
ATOM    314  H1* DA     10      10.653   7.907  13.353
ATOM    315  N9  DA     10      10.580   5.878  12.884
ATOM    316  C8  DA     10      10.544   4.769  12.071
ATOM    317  H8  DA     10      10.412   4.884  11.005
ATOM    318  N7  DA     10      10.588   3.620  12.687
```

```
ATOM    319  C5  DA     10      10.726   4.018  14.036
ATOM    320  C6  DA     10      10.852   3.342  15.291
ATOM    321  N6  DA     10      10.892   2.030  15.428
ATOM    322 1H6  DA     10      10.956   1.655  16.363
ATOM    323 2H6  DA     10      10.785   1.416  14.634
ATOM    324  N1  DA     10      10.958   4.007  16.432
ATOM    325  C2  DA     10      10.954   5.324  16.387
ATOM    326  H2  DA     10      11.022   5.805  17.351
ATOM    327  N3  DA     10      10.862   6.102  15.306
ATOM    328  C4  DA     10      10.728   5.378  14.157
ATOM    329  C3* DA     10      10.790   8.670  10.537
ATOM    330  H3* DA     10      11.088   8.578   9.493
ATOM    331  C2* DA     10      11.518   7.641  11.395
ATOM    332 1H2* DA     10      12.442   8.026  11.826
ATOM    333 2H2* DA     10      11.745   6.773  10.777
ATOM    334  O3* DA     10      10.935  10.008  10.971
ATOM    335  P   DT     11      12.312  10.841  10.796
ATOM    336  O1P DT     11      11.980  12.279  10.957
ATOM    337  O2P DT     11      13.003  10.360   9.574
ATOM    338  O5* DT     11      13.190  10.413  12.087
ATOM    339  C5* DT     11      12.792  10.815  13.396
ATOM    340 1H5* DT     11      11.752  10.546  13.580
ATOM    341 2H5* DT     11      12.869  11.898  13.497
ATOM    342  C4* DT     11      13.658  10.153  14.449
ATOM    343  H4* DT     11      13.453  10.590  15.426
ATOM    344  O4* DT     11      13.346   8.751  14.534
ATOM    345  C1* DT     11      14.560   8.057  14.777
ATOM    346  H1* DT     11      14.856   8.161  15.821
ATOM    347  N1  DT     11      14.406   6.600  14.464
ATOM    348  C6  DT     11      14.406   6.125  13.171
ATOM    349  H6  DT     11      14.469   6.820  12.347
ATOM    350  C5  DT     11      14.239   4.807  12.888
ATOM    351  C7  DT     11      14.209   4.347  11.442
ATOM    352 1H7  DT     11      14.321   5.189  10.760
ATOM    353 2H7  DT     11      15.002   3.620  11.261
ATOM    354 3H7  DT     11      13.259   3.856  11.231
```

```
ATOM    355  C4   DT     11      14.096   3.843  13.976
ATOM    356  O4   DT     11      13.936   2.639  13.860
ATOM    357  N3   DT     11      14.134   4.389  15.245
ATOM    358  H3   DT     11      14.112   3.750  16.028
ATOM    359  C2   DT     11      14.274   5.721  15.537
ATOM    360  O2   DT     11      14.288   6.058  16.719
ATOM    361  C3*  DT     11      15.175  10.278  14.157
ATOM    362  H3*  DT     11      15.372  10.882  13.271
ATOM    363  C2*  DT     11      15.594   8.822  13.951
ATOM    364 1H2*  DT     11      16.605   8.628  14.309
ATOM    365 2H2*  DT     11      15.505   8.592  12.889
ATOM    366  O3*  DT     11      15.828  10.897  15.268
ATOM    367  P    DC3    12      17.392  11.312  15.281
ATOM    368  O1P  DC3    12      17.512  12.682  15.838
ATOM    369  O2P  DC3    12      18.010  10.993  13.969
ATOM    370  O5*  DC3    12      17.960  10.242  16.347
ATOM    371  C5*  DC3    12      17.734  10.420  17.740
ATOM    372 1H5*  DC3    12      16.682  10.617  17.946
ATOM    373 2H5*  DC3    12      18.296  11.296  18.064
ATOM    374  C4*  DC3    12      18.188   9.236  18.567
ATOM    375  H4*  DC3    12      18.142   9.519  19.618
ATOM    376  O4*  DC3    12      17.312   8.150  18.363
ATOM    377  C1*  DC3    12      18.002   6.934  18.622
ATOM    378  H1*  DC3    12      17.712   6.559  19.604
ATOM    379  N1   DC3    12      17.769   5.929  17.547
ATOM    380  C6   DC3    12      17.649   6.306  16.231
ATOM    381  H6   DC3    12      17.701   7.352  15.967
ATOM    382  C5   DC3    12      17.522   5.363  15.266
ATOM    383  H5   DC3    12      17.463   5.666  14.230
ATOM    384  C4   DC3    12      17.499   3.997  15.672
ATOM    385  N4   DC3    12      17.413   3.036  14.782
ATOM    386  H41  DC3    12      17.360   3.283  13.804
ATOM    387  H42  DC3    12      17.342   2.088  15.121
ATOM    388  N3   DC3    12      17.565   3.626  16.940
ATOM    389  C2   DC3    12      17.708   4.583  17.892
ATOM    390  O2   DC3    12      17.746   4.214  19.067
```

```
ATOM    391  C3* DC3    12      19.594   8.733  18.241
ATOM    392  H3* DC3    12      19.789   8.734  17.168
ATOM    393  C2* DC3    12      19.490   7.298  18.726
ATOM    394 1H2* DC3    12      19.776   7.241  19.776
ATOM    395 2H2* DC3    12      20.150   6.662  18.136
ATOM    396  O3* DC3    12      20.609   9.422  18.945
ATOM    397  H3T DC3    12      20.765  10.262  18.507
TER
ATOM    398  H5T DG5    13      20.344  -6.206  19.658
ATOM    399  O5* DG5    13      20.094  -6.974  20.177
ATOM    400  C5* DG5    13      18.750  -6.818  20.633
ATOM    401 1H5* DG5    13      18.485  -7.636  21.303
ATOM    402 2H5* DG5    13      18.068  -6.790  19.783
ATOM    403  C4* DG5    13      18.595  -5.520  21.438
ATOM    404  H4* DG5    13      19.315  -5.512  22.256
ATOM    405  O4* DG5    13      18.833  -4.409  20.579
ATOM    406  C1* DG5    13      17.698  -3.571  20.558
ATOM    407  H1* DG5    13      17.784  -2.787  21.310
ATOM    408  N9  DG5    13      17.538  -2.932  19.209
ATOM    409  C8  DG5    13      17.362  -3.529  17.982
ATOM    410  H8  DG5    13      17.283  -4.603  17.897
ATOM    411  N7  DG5    13      17.292  -2.672  16.997
ATOM    412  C5  DG5    13      17.453  -1.403  17.614
ATOM    413  C6  DG5    13      17.513  -0.065  17.081
ATOM    414  O6  DG5    13      17.456   0.311  15.913
ATOM    415  N1  DG5    13      17.653   0.896  18.076
ATOM    416 1H   DG5    13      17.664   1.869  17.806
ATOM    417  C2  DG5    13      17.787   0.619  19.387
ATOM    418  N2  DG5    13      17.897   1.624  20.207
ATOM    419  H21 DG5    13      17.953   1.398  21.190
ATOM    420  H22 DG5    13      17.885   2.575  19.868
ATOM    421  N3  DG5    13      17.777  -0.601  19.911
ATOM    422  C4  DG5    13      17.603  -1.581  18.971
ATOM    423  C3* DG5    13      17.179  -5.361  22.008
ATOM    424  H3* DG5    13      16.671  -6.321  22.095
ATOM    425  C2* DG5    13      16.522  -4.474  20.946
```

```
ATOM    426 1H2* DG5    13      15.695  -3.903  21.368
ATOM    427 2H2* DG5    13      16.207  -5.051  20.077
ATOM    428  O3* DG5    13      17.260  -4.713  23.267
ATOM    429  P   DA     14      15.981  -4.444  24.199
ATOM    430  O1P DA     14      16.417  -4.489  25.615
ATOM    431  O2P DA     14      14.855  -5.297  23.791
ATOM    432  O5* DA     14      15.612  -2.919  23.869
ATOM    433  C5* DA     14      16.434  -1.816  24.263
ATOM    434 1H5* DA     14      17.387  -1.920  23.744
ATOM    435 2H5* DA     14      16.586  -1.875  25.341
ATOM    436  C4* DA     14      15.840  -0.438  23.924
ATOM    437  H4* DA     14      16.393   0.334  24.459
ATOM    438  O4* DA     14      15.926  -0.181  22.510
ATOM    439  C1* DA     14      14.637   0.253  22.067
ATOM    440  H1* DA     14      14.527   1.319  22.267
ATOM    441  N9  DA     14      14.446  -0.016  20.639
ATOM    442  C8  DA     14      14.299  -1.220  20.005
ATOM    443  H8  DA     14      14.330  -2.146  20.560
ATOM    444  N7  DA     14      14.188  -1.127  18.695
ATOM    445  C5  DA     14      14.210   0.258  18.456
ATOM    446  C6  DA     14      14.144   1.103  17.318
ATOM    447  N6  DA     14      13.999   0.676  16.081
ATOM    448 1H6  DA     14      13.976   1.353  15.332
ATOM    449 2H6  DA     14      13.885  -0.311  15.899
ATOM    450  N1  DA     14      14.230   2.426  17.437
ATOM    451  C2  DA     14      14.400   2.944  18.642
ATOM    452  H2  DA     14      14.450   4.021  18.697
ATOM    453  N3  DA     14      14.457   2.290  19.791
ATOM    454  C4  DA     14      14.363   0.937  19.635
ATOM    455  C3* DA     14      14.354  -0.373  24.323
ATOM    456  H3* DA     14      14.072  -1.201  24.973
ATOM    457  C2* DA     14      13.668  -0.504  22.988
ATOM    458 1H2* DA     14      12.675  -0.055  22.979
ATOM    459 2H2* DA     14      13.600  -1.554  22.702
ATOM    460  O3* DA     14      13.978   0.895  24.858
ATOM    461  P   DT     15      14.145   1.283  26.424
```

```
ATOM    462  O1P DT     15      15.593   1.331  26.718
ATOM    463  O2P DT     15      13.264   0.401  27.233
ATOM    464  O5* DT     15      13.599   2.793  26.459
ATOM    465  C5* DT     15      12.237   3.084  26.139
ATOM    466 1H5* DT     15      11.825   3.655  26.971
ATOM    467 2H5* DT     15      11.643   2.176  26.037
ATOM    468  C4* DT     15      12.090   3.912  24.850
ATOM    469  H4* DT     15      12.805   4.735  24.855
ATOM    470  O4* DT     15      12.263   3.122  23.687
ATOM    471  C1* DT     15      11.607   3.823  22.644
ATOM    472  H1* DT     15      12.205   4.693  22.371
ATOM    473  N1  DT     15      11.328   2.991  21.441
ATOM    474  C6  DT     15      10.964   1.672  21.564
ATOM    475  H6  DT     15      10.862   1.269  22.561
ATOM    476  C5  DT     15      10.749   0.882  20.476
ATOM    477  C7  DT     15      10.370  -0.574  20.683
ATOM    478 1H7  DT     15      10.243  -0.799  21.742
ATOM    479 2H7  DT     15       9.432  -0.761  20.160
ATOM    480 3H7  DT     15      11.150  -1.217  20.274
ATOM    481  C4  DT     15      10.919   1.450  19.127
ATOM    482  O4  DT     15      10.792   0.861  18.052
ATOM    483  N3  DT     15      11.234   2.784  19.091
ATOM    484  H3  DT     15      11.330   3.218  18.184
ATOM    485  C2  DT     15      11.433   3.591  20.182
ATOM    486  O2  DT     15      11.697   4.784  20.039
ATOM    487  C3* DT     15      10.677   4.502  24.772
ATOM    488  H3* DT     15       9.975   3.938  25.386
ATOM    489  C2* DT     15      10.321   4.321  23.298
ATOM    490 1H2* DT     15       9.988   5.239  22.815
ATOM    491 2H2* DT     15       9.537   3.569  23.209
ATOM    492  O3* DT     15      10.712   5.881  25.160
ATOM    493  P   DG     16       9.380   6.745  25.487
ATOM    494  O1P DG     16       9.798   7.909  26.291
ATOM    495  O2P DG     16       8.359   5.819  26.045
ATOM    496  O5* DG     16       8.882   7.265  24.025
ATOM    497  C5* DG     16       9.614   8.244  23.312
```

```
ATOM    498 1H5* DG     16      10.574   7.818  23.021
ATOM    499 2H5* DG     16       9.823   9.101  23.953
ATOM    500  C4* DG     16       8.905   8.759  22.040
ATOM    501  H4* DG     16       9.469   9.618  21.676
ATOM    502  O4* DG     16       8.903   7.759  21.022
ATOM    503  C1* DG     16       7.551   7.411  20.713
ATOM    504  H1* DG     16       7.217   7.905  19.800
ATOM    505  N9  DG     16       7.504   5.944  20.523
ATOM    506  C8  DG     16       7.498   4.903  21.427
ATOM    507  H8  DG     16       7.506   5.103  22.488
ATOM    508  N7  DG     16       7.576   3.711  20.891
ATOM    509  C5  DG     16       7.577   3.986  19.513
ATOM    510  C6  DG     16       7.616   3.129  18.354
ATOM    511  O6  DG     16       7.685   1.886  18.290
ATOM    512  N1  DG     16       7.574   3.806  17.154
ATOM    513 1H   DG     16       7.663   3.236  16.324
ATOM    514  C2  DG     16       7.507   5.142  17.043
ATOM    515  N2  DG     16       7.409   5.658  15.843
ATOM    516  H21 DG     16       7.238   6.651  15.775
ATOM    517  H22 DG     16       7.339   5.059  15.033
ATOM    518  N3  DG     16       7.485   5.975  18.085
ATOM    519  C4  DG     16       7.528   5.338  19.295
ATOM    520  C3* DG     16       7.468   9.199  22.272
ATOM    521  H3* DG     16       7.273   9.427  23.320
ATOM    522  C2* DG     16       6.707   7.947  21.847
ATOM    523 1H2* DG     16       5.683   8.145  21.532
ATOM    524 2H2* DG     16       6.696   7.253  22.687
ATOM    525  O3* DG     16       7.214  10.322  21.450
ATOM    526  P   DG     17       5.784  11.028  21.298
ATOM    527  O1P DG     17       5.995  12.440  20.858
ATOM    528  O2P DG     17       4.971  10.788  22.519
ATOM    529  O5* DG     17       5.140  10.187  20.089
ATOM    530  C5* DG     17       5.521  10.363  18.724
ATOM    531 1H5* DG     17       6.567  10.082  18.600
ATOM    532 2H5* DG     17       5.383  11.405  18.434
ATOM    533  C4* DG     17       4.626   9.542  17.764
```

```
ATOM    534  H4* DG    17       4.788   9.913  16.751
ATOM    535  O4* DG    17       4.968   8.153  17.807
ATOM    536  C1* DG    17       3.758   7.437  17.820
ATOM    537  H1* DG    17       3.278   7.458  16.842
ATOM    538  N9  DG    17       3.987   6.015  18.174
ATOM    539  C8  DG    17       4.084   5.472  19.423
ATOM    540  H8  DG    17       4.092   6.097  20.304
ATOM    541  N7  DG    17       4.217   4.173  19.444
ATOM    542  C5  DG    17       4.183   3.824  18.081
ATOM    543  C6  DG    17       4.330   2.550  17.440
ATOM    544  O6  DG    17       4.505   1.441  17.952
ATOM    545  N1  DG    17       4.288   2.628  16.061
ATOM    546 1H   DG    17       4.321   1.755  15.554
ATOM    547  C2  DG    17       4.116   3.778  15.373
ATOM    548  N2  DG    17       3.973   3.666  14.088
ATOM    549  H21 DG    17       3.727   4.478  13.539
ATOM    550  H22 DG    17       4.002   2.740  13.687
ATOM    551  N3  DG    17       3.988   4.997  15.920
ATOM    552  C4  DG    17       4.051   4.950  17.289
ATOM    553  C3* DG    17       3.124   9.630  18.145
ATOM    554  H3* DG    17       2.959  10.413  18.885
ATOM    555  C2* DG    17       2.887   8.250  18.770
ATOM    556 1H2* DG    17       1.846   7.928  18.755
ATOM    557 2H2* DG    17       3.279   8.250  19.787
ATOM    558  O3* DG    17       2.208   9.783  17.064
ATOM    559  P   DC    18       2.260  10.984  15.994
ATOM    560  O1P DC    18       3.320  11.948  16.406
ATOM    561  O2P DC    18       0.868  11.486  15.811
ATOM    562  O5* DC    18       2.727  10.275  14.621
ATOM    563  C5* DC    18       1.830   9.552  13.801
ATOM    564 1H5* DC    18       2.150   9.747  12.777
ATOM    565 2H5* DC    18       0.803   9.902  13.900
ATOM    566  C4* DC    18       1.905   8.024  13.984
ATOM    567  H4* DC    18       2.909   7.693  13.719
ATOM    568  O4* DC    18       1.598   7.670  15.325
ATOM    569  C1* DC    18       0.475   6.804  15.358
```

```
ATOM    570  H1* DC    18       0.856   5.784  15.409
ATOM    571  N1  DC    18      -0.363   7.126  16.547
ATOM    572  C6  DC    18      -0.637   8.428  16.901
ATOM    573  H6  DC    18      -0.274   9.221  16.264
ATOM    574  C5  DC    18      -1.319   8.694  18.039
ATOM    575  H5  DC    18      -1.495   9.723  18.316
ATOM    576  C4  DC    18      -1.755   7.581  18.815
ATOM    577  N4  DC    18      -2.438   7.752  19.910
ATOM    578  H41 DC    18      -2.682   8.684  20.214
ATOM    579  H42 DC    18      -2.714   6.924  20.418
ATOM    580  N3  DC    18      -1.519   6.328  18.513
ATOM    581  C2  DC    18      -0.808   6.078  17.386
ATOM    582  O2  DC    18      -0.618   4.908  17.065
ATOM    583  C3* DC    18       0.873   7.304  13.076
ATOM    584  H3* DC    18       0.578   7.986  12.278
ATOM    585  C2* DC    18      -0.268   7.018  14.053
ATOM    586 1H2* DC    18      -0.854   6.141  13.779
ATOM    587 2H2* DC    18      -0.931   7.883  14.078
ATOM    588  O3* DC    18       1.443   6.111  12.508
ATOM    589  P   DG    19       0.840   5.400  11.186
ATOM    590  O1P DG    19       1.811   4.402  10.700
ATOM    591  O2P DG    19       0.391   6.466  10.251
ATOM    592  O5* DG    19      -0.464   4.648  11.771
ATOM    593  C5* DG    19      -1.249   3.820  10.935
ATOM    594 1H5* DG    19      -0.658   2.983  10.566
ATOM    595 2H5* DG    19      -1.637   4.396  10.095
ATOM    596  C4* DG    19      -2.462   3.241  11.682
ATOM    597  H4* DG    19      -2.990   2.593  10.982
ATOM    598  O4* DG    19      -2.037   2.432  12.775
ATOM    599  C1* DG    19      -3.161   2.207  13.604
ATOM    600  H1* DG    19      -3.785   1.434  13.157
ATOM    601  N9  DG    19      -2.737   1.760  14.956
ATOM    602  C8  DG    19      -2.521   2.478  16.116
ATOM    603  H8  DG    19      -2.601   3.554  16.158
ATOM    604  N7  DG    19      -2.198   1.758  17.161
ATOM    605  C5  DG    19      -2.241   0.447  16.666
```

```
ATOM    606  C6  DG     19      -2.003  -0.806  17.315
ATOM    607  O6  DG     19      -1.650  -1.040  18.478
ATOM    608  N1  DG     19      -2.168  -1.891  16.477
ATOM    609 1H   DG     19      -1.915  -2.803  16.831
ATOM    610  C2  DG     19      -2.513  -1.794  15.162
ATOM    611  N2  DG     19      -2.545  -2.889  14.477
ATOM    612  H21 DG     19      -2.699  -2.822  13.481
ATOM    613  H22 DG     19      -2.367  -3.759  14.959
ATOM    614  N3  DG     19      -2.740  -0.643  14.540
ATOM    615  C4  DG     19      -2.574   0.447  15.328
ATOM    616  C3* DG     19      -3.469   4.252  12.297
ATOM    617  H3* DG     19      -2.887   5.115  12.621
ATOM    618  C2* DG     19      -3.923   3.535  13.567
ATOM    619 1H2* DG     19      -4.995   3.340  13.559
ATOM    620 2H2* DG     19      -3.644   4.173  14.405
ATOM    621  O3* DG     19      -4.597   4.694  11.524
ATOM    622  P   DC     20      -5.369   3.845  10.389
ATOM    623  O1P DC     20      -4.426   3.611   9.272
ATOM    624  O2P DC     20      -6.627   4.582  10.122
ATOM    625  O5* DC     20      -5.769   2.433  11.070
ATOM    626  C5* DC     20      -5.483   1.217  10.406
ATOM    627 1H5* DC     20      -4.408   1.088  10.280
ATOM    628 2H5* DC     20      -5.924   1.246   9.409
ATOM    629  C4* DC     20      -6.077  -0.017  11.126
ATOM    630  H4* DC     20      -5.853  -0.887  10.509
ATOM    631  O4* DC     20      -5.493  -0.168  12.416
ATOM    632  C1* DC     20      -6.477  -0.762  13.242
ATOM    633  H1* DC     20      -6.495  -1.839  13.075
ATOM    634  N1  DC     20      -6.156  -0.479  14.671
ATOM    635  C6  DC     20      -6.096   0.810  15.132
ATOM    636  H6  DC     20      -6.311   1.618  14.449
ATOM    637  C5  DC     20      -5.787   1.041  16.420
ATOM    638  H5  DC     20      -5.738   2.057  16.785
ATOM    639  C4  DC     20      -5.523  -0.082  17.261
ATOM    640  N4  DC     20      -5.197   0.083  18.490
ATOM    641  H41 DC     20      -5.124   1.011  18.883
```

```
ATOM    642  H42 DC     20      -4.969  -0.728  19.047
ATOM    643  N3  DC     20      -5.566  -1.317  16.833
ATOM    644  C2  DC     20      -5.915  -1.542  15.540
ATOM    645  O2  DC     20      -6.004  -2.706  15.182
ATOM    646  C3* DC     20      -7.604   0.056  11.293
ATOM    647  H3* DC     20      -7.955   1.041  10.987
ATOM    648  C2* DC     20      -7.796  -0.145  12.793
ATOM    649 1H2* DC     20      -8.624  -0.812  13.033
ATOM    650 2H2* DC     20      -7.968   0.830  13.249
ATOM    651  O3* DC     20      -8.245  -0.943  10.506
ATOM    652  P   DC     21      -9.856  -1.012  10.288
ATOM    653  O1P DC     21     -10.097  -1.825   9.060
ATOM    654  O2P DC     21     -10.410   0.357  10.360
ATOM    655  O5* DC     21     -10.403  -1.829  11.569
ATOM    656  C5* DC     21     -10.018  -3.181  11.810
ATOM    657 1H5* DC     21      -8.941  -3.277  11.679
ATOM    658 2H5* DC     21     -10.524  -3.835  11.100
ATOM    659  C4* DC     21     -10.415  -3.646  13.212
ATOM    660  H4* DC     21     -10.194  -4.712  13.278
ATOM    661  O4* DC     21      -9.612  -2.954  14.171
ATOM    662  C1* DC     21     -10.456  -2.614  15.261
ATOM    663  H1* DC     21     -10.596  -3.497  15.884
ATOM    664  N1  DC     21      -9.861  -1.528  16.044
ATOM    665  C6  DC     21      -9.921  -0.227  15.636
ATOM    666  H6  DC     21     -10.317   0.028  14.664
ATOM    667  C5  DC     21      -9.443   0.763  16.433
ATOM    668  H5  DC     21      -9.525   1.786  16.098
ATOM    669  C4  DC     21      -8.914   0.373  17.689
ATOM    670  N4  DC     21      -8.484   1.264  18.538
ATOM    671  H41 DC     21      -8.531   2.244  18.298
ATOM    672  H42 DC     21      -8.074   0.917  19.393
ATOM    673  N3  DC     21      -8.817  -0.880  18.090
ATOM    674  C2  DC     21      -9.255  -1.847  17.261
ATOM    675  O2  DC     21      -9.122  -3.021  17.621
ATOM    676  C3* DC     21     -11.901  -3.407  13.580
ATOM    677  H3* DC     21     -12.511  -3.089  12.734
```

```
ATOM    678  C2* DC     21     -11.796  -2.304  14.609
ATOM    679 1H2* DC     21     -12.597  -2.319  15.348
ATOM    680 2H2* DC     21     -11.800  -1.335  14.109
ATOM    681  O3* DC     21     -12.479  -4.537  14.219
ATOM    682  P   DG     22     -13.074  -5.763  13.389
ATOM    683  O1P DG     22     -12.192  -6.104  12.246
ATOM    684  O2P DG     22     -14.505  -5.486  13.093
ATOM    685  O5* DG     22     -13.019  -6.943  14.493
ATOM    686  C5* DG     22     -11.864  -7.718  14.725
ATOM    687 1H5* DG     22     -10.965  -7.140  14.509
ATOM    688 2H5* DG     22     -11.896  -8.576  14.053
ATOM    689  C4* DG     22     -11.745  -8.229  16.170
ATOM    690  H4* DG     22     -11.045  -9.064  16.146
ATOM    691  O4* DG     22     -11.241  -7.209  17.007
ATOM    692  C1* DG     22     -12.142  -6.953  18.064
ATOM    693  H1* DG     22     -11.862  -7.549  18.933
ATOM    694  N9  DG     22     -12.137  -5.500  18.382
ATOM    695  C8  DG     22     -12.570  -4.427  17.649
ATOM    696  H8  DG     22     -13.024  -4.560  16.679
ATOM    697  N7  DG     22     -12.369  -3.259  18.185
ATOM    698  C5  DG     22     -11.748  -3.584  19.409
ATOM    699  C6  DG     22     -11.259  -2.762  20.496
ATOM    700  O6  DG     22     -11.196  -1.545  20.609
ATOM    701  N1  DG     22     -10.832  -3.480  21.586
ATOM    702 1H   DG     22     -10.578  -2.956  22.410
ATOM    703  C2  DG     22     -10.744  -4.850  21.614
ATOM    704  N2  DG     22     -10.294  -5.413  22.698
ATOM    705  H21 DG     22     -10.318  -6.422  22.741
ATOM    706  H22 DG     22     -10.043  -4.851  23.499
ATOM    707  N3  DG     22     -11.125  -5.636  20.609
ATOM    708  C4  DG     22     -11.640  -4.957  19.539
ATOM    709  C3* DG     22     -13.077  -8.714  16.778
ATOM    710  H3* DG     22     -13.830  -8.930  16.020
ATOM    711  C2* DG     22     -13.494  -7.487  17.576
ATOM    712 1H2* DG     22     -14.163  -7.762  18.392
ATOM    713 2H2* DG     22     -14.000  -6.750  16.952
```

```
ATOM    714  O3* DG     22     -12.817  -9.848  17.609
ATOM    715  P   DA     23     -13.975 -10.661  18.389
ATOM    716  O1P DA     23     -13.617 -12.108  18.318
ATOM    717  O2P DA     23     -15.315 -10.218  17.915
ATOM    718  O5* DA     23     -13.830 -10.139  19.913
ATOM    719  C5* DA     23     -12.710 -10.502  20.719
ATOM    720 1H5* DA     23     -11.790 -10.127  20.271
ATOM    721 2H5* DA     23     -12.628 -11.589  20.722
ATOM    722  C4* DA     23     -12.751 -10.025  22.173
ATOM    723  H4* DA     23     -11.889 -10.440  22.694
ATOM    724  O4* DA     23     -12.654  -8.602  22.261
ATOM    725  C1* DA     23     -13.761  -8.067  22.970
ATOM    726  H1* DA     23     -13.501  -7.922  24.019
ATOM    727  N9  DA     23     -14.107  -6.785  22.316
ATOM    728  C8  DA     23     -14.635  -6.581  21.067
ATOM    729  H8  DA     23     -14.892  -7.394  20.403
ATOM    730  N7  DA     23     -14.802  -5.320  20.739
ATOM    731  C5  DA     23     -14.335  -4.653  21.887
ATOM    732  C6  DA     23     -14.192  -3.285  22.250
ATOM    733  N6  DA     23     -14.478  -2.258  21.477
ATOM    734 1H6  DA     23     -14.299  -1.329  21.831
ATOM    735 2H6  DA     23     -14.820  -2.394  20.536
ATOM    736  N1  DA     23     -13.678  -2.933  23.426
ATOM    737  C2  DA     23     -13.278  -3.906  24.238
ATOM    738  H2  DA     23     -12.857  -3.603  25.185
ATOM    739  N3  DA     23     -13.355  -5.221  24.058
ATOM    740  C4  DA     23     -13.884  -5.530  22.834
ATOM    741  C3* DA     23     -14.044 -10.446  22.908
ATOM    742  H3* DA     23     -14.590 -11.226  22.377
ATOM    743  C2* DA     23     -14.833  -9.150  22.907
ATOM    744 1H2* DA     23     -15.506  -9.086  23.762
ATOM    745 2H2* DA     23     -15.391  -9.076  21.973
ATOM    746  O3* DA     23     -13.685 -10.932  24.201
ATOM    747  P   DG3    24     -14.770 -11.471  25.263
ATOM    748  O1P DG3    24     -14.095 -12.467  26.121
ATOM    749  O2P DG3    24     -15.996 -11.887  24.537
```

```
ATOM    750  O5* DG3    24     -15.105 -10.154  26.157
ATOM    751  C5* DG3    24     -14.094  -9.576  26.989
ATOM    752 1H5* DG3    24     -13.211  -9.328  26.401
ATOM    753 2H5* DG3    24     -13.765 -10.311  27.724
ATOM    754  C4* DG3    24     -14.594  -8.317  27.710
ATOM    755  H4* DG3    24     -13.866  -8.082  28.487
ATOM    756  O4* DG3    24     -14.678  -7.237  26.804
ATOM    757  C1* DG3    24     -15.860  -6.506  27.095
ATOM    758  H1* DG3    24     -15.670  -5.822  27.922
ATOM    759  N9  DG3    24     -16.336  -5.733  25.909
ATOM    760  C8  DG3    24     -16.733  -6.194  24.674
ATOM    761  H8  DG3    24     -16.719  -7.250  24.445
ATOM    762  N7  DG3    24     -17.090  -5.264  23.833
ATOM    763  C5  DG3    24     -16.899  -4.070  24.566
ATOM    764  C6  DG3    24     -17.041  -2.686  24.186
ATOM    765  O6  DG3    24     -17.416  -2.215  23.107
ATOM    766  N1  DG3    24     -16.679  -1.794  25.170
ATOM    767 1H   DG3    24     -16.732  -0.810  24.949
ATOM    768  C2  DG3    24     -16.261  -2.188  26.406
ATOM    769  N2  DG3    24     -15.967  -1.226  27.245
ATOM    770  H21 DG3    24     -15.624  -1.469  28.163
ATOM    771  H22 DG3    24     -16.041  -0.252  26.987
ATOM    772  N3  DG3    24     -16.095  -3.447  26.810
ATOM    773  C4  DG3    24     -16.415  -4.360  25.820
ATOM    774  C3* DG3    24     -15.980  -8.455  28.394
ATOM    775  H3* DG3    24     -16.353  -9.478  28.339
ATOM    776  C2* DG3    24     -16.877  -7.535  27.576
ATOM    777 1H2* DG3    24     -17.646  -7.088  28.207
ATOM    778 2H2* DG3    24     -17.326  -8.090  26.752
ATOM    779  O3* DG3    24     -15.930  -8.019  29.747
ATOM    780  H3T DG3    24     -16.765  -8.213  30.180
TER
END
```

## $N^2$-dG-IQ at $G^1$

```
REMARK  99
REMARK  99 MOE v2012.10 (Chemical Computing Group Inc.) Fri Feb 14
14:14:16 2014
LINK         O3* DC5     1                 P    DT     2     1555
1555  1.63
LINK         O3'  DC     3                 P   DKA     4     1555
1555  1.63
LINK         O3* DKA     4                 P    DG     5     1555
1555  1.64
LINK         O3'  DT    11                 P   DC3    12     1555
1555  1.64
LINK         O3* DG5    13                 P    DA    14     1555
1555  1.63
LINK         O3'  DA    23                 P   DG3    24     1555
1555  1.63
CRYST1   10.000   10.000   10.000  90.00  90.00  90.00 P1
HETATM    1  O5* DC5     1     -13.629  18.420  22.409  0.00  0.00
HETATM    2  C5* DC5     1     -14.816  17.820  22.920  0.00  0.00
HETATM    3  C4* DC5     1     -14.931  16.355  22.496  0.00  0.00
HETATM    4  O4* DC5     1     -15.211  16.291  21.072  0.00  0.00
HETATM    5  C1* DC5     1     -14.336  15.294  20.510  0.00  0.00
HETATM    6  N1  DC5     1     -14.106  15.543  19.086  0.00  0.00
HETATM    7  C6  DC5     1     -13.808  16.816  18.651  0.00  0.00
HETATM    8  C5  DC5     1     -13.585  17.076  17.364  0.00  0.00
HETATM    9  C4  DC5     1     -13.668  15.925  16.439  0.00  0.00
HETATM   10  N4  DC5     1     -13.443  16.123  15.107  0.00  0.00
HETATM   11  N3  DC5     1     -13.950  14.719  16.840  0.00  0.00
HETATM   12  C2  DC5     1     -14.188  14.476  18.181  0.00  0.00
HETATM   13  O2  DC5     1     -14.478  13.331  18.532  0.00  0.00
HETATM   14  C3* DC5     1     -13.655  15.545  22.745  0.00  0.00
HETATM   15  C2* DC5     1     -13.076  15.365  21.360  0.00  0.00
HETATM   16  O3* DC5     1     -14.019  14.254  23.223  0.00  0.00
HETATM   17 'HO5 DC5     1     -13.567  19.306  22.809  0.00  0.00
HETATM   18  H5* DC5     1     -15.668  18.395  22.545  0.00  0.00
HETATM   19 'H5* DC5     1     -14.786  17.891  24.012  0.00  0.00
HETATM   20  H4* DC5     1     -15.793  15.908  23.006  0.00  0.00
```

```
HETATM   21  H1* DC5     1     -14.829  14.323  20.643  0.00  0.00
HETATM   22  H6  DC5     1     -13.768  17.599  19.401  0.00  0.00
HETATM   23  H5  DC5     1     -13.353  18.062  16.989  0.00  0.00
HETATM   24  H41 DC5     1     -13.236  17.026  14.704  0.00  0.00
HETATM   25  H42 DC5     1     -13.479  15.317  14.468  0.00  0.00
HETATM   26  H3* DC5     1     -12.968  16.024  23.449  0.00  0.00
HETATM   27  H2* DC5     1     -12.468  14.466  21.251  0.00  0.00
HETATM   28 'H2* DC5     1     -12.466  16.236  21.097  0.00  0.00
ATOM     29  P    DT      2     -13.148  13.620  24.450  0.00  0.00
ATOM     30  OP1  DT      2     -13.712  14.145  25.752  0.00  0.00
ATOM     31  OP2  DT      2     -11.685  13.775  24.096  0.00  0.00
ATOM     32  O5'  DT      2     -13.527  12.045  24.237  0.00  0.00
ATOM     33  C5'  DT      2     -14.885  11.635  24.293  0.00  0.00
ATOM     34  C4'  DT      2     -15.156  10.424  23.380  0.00  0.00
ATOM     35  O4'  DT      2     -14.862  10.789  22.002  0.00  0.00
ATOM     36  C1'  DT      2     -14.038   9.745  21.456  0.00  0.00
ATOM     37  N1   DT      2     -13.188  10.244  20.378  0.00  0.00
ATOM     38  C6   DT      2     -12.334  11.307  20.610  0.00  0.00
ATOM     39  C5   DT      2     -11.475  11.764  19.691  0.00  0.00
ATOM     40  C7   DT      2     -10.516  12.887  19.911  0.00  0.00
ATOM     41  C4   DT      2     -11.446  11.090  18.374  0.00  0.00
ATOM     42  O4   DT      2     -10.681  11.446  17.479  0.00  0.00
ATOM     43  N3   DT      2     -12.323  10.054  18.208  0.00  0.00
ATOM     44  C2   DT      2     -13.247   9.612  19.132  0.00  0.00
ATOM     45  O2   DT      2     -14.065   8.754  18.796  0.00  0.00
ATOM     46  C3'  DT      2     -14.328   9.166  23.700  0.00  0.00
ATOM     47  C2'  DT      2     -13.258   9.193  22.639  0.00  0.00
ATOM     48  O3'  DT      2     -15.150   8.008  23.499  0.00  0.00
ATOM     49  H5'  DT      2     -15.533  12.462  23.983  0.00  0.00
ATOM     50 'H5'  DT      2     -15.124  11.385  25.331  0.00  0.00
ATOM     51  H4'  DT      2     -16.227  10.196  23.425  0.00  0.00
ATOM     52  H1'  DT      2     -14.716   8.977  21.065  0.00  0.00
ATOM     53  H6   DT      2     -12.391  11.764  21.597  0.00  0.00
ATOM     54 1H7   DT      2      -9.496  12.583  19.656  0.00  0.00
ATOM     55 2H7   DT      2     -10.787  13.747  19.291  0.00  0.00
ATOM     56 3H7   DT      2     -10.503  13.210  20.957  0.00  0.00
```

```
ATOM     57  H3   DT     2     -12.311   9.571  17.314  0.00  0.00
ATOM     58  H3'  DT     2     -13.944   9.176  24.723  0.00  0.00
ATOM     59  H2'  DT     2     -12.815   8.225  22.409  0.00  0.00
ATOM     60 'H2'  DT     2     -12.453   9.867  22.950  0.00  0.00
ATOM     61  P    DC     3     -14.675   6.563  24.105  0.00  0.00
ATOM     62  OP1  DC     3     -15.891   5.662  24.177  0.00  0.00
ATOM     63  OP2  DC     3     -13.848   6.827  25.343  0.00  0.00
ATOM     64  O5'  DC     3     -13.715   6.013  22.888  0.00  0.00
ATOM     65  C5'  DC     3     -14.395   5.541  21.725  0.00  0.00
ATOM     66  C4'  DC     3     -13.477   5.211  20.537  0.00  0.00
ATOM     67  O4'  DC     3     -12.749   6.408  20.150  0.00  0.00
ATOM     68  C1'  DC     3     -11.416   5.968  19.860  0.00  0.00
ATOM     69  N1   DC     3     -10.512   7.096  19.804  0.00  0.00
ATOM     70  C6   DC     3     -10.181   7.816  20.927  0.00  0.00
ATOM     71  C5   DC     3      -9.321   8.833  20.864  0.00  0.00
ATOM     72  C4   DC     3      -8.750   9.110  19.532  0.00  0.00
ATOM     73  N4   DC     3      -7.819  10.086  19.364  0.00  0.00
ATOM     74  N3   DC     3      -9.090   8.458  18.462  0.00  0.00
ATOM     75  C2   DC     3      -9.994   7.428  18.554  0.00  0.00
ATOM     76  O2   DC     3     -10.294   6.828  17.521  0.00  0.00
ATOM     77  C3'  DC     3     -12.427   4.097  20.753  0.00  0.00
ATOM     78  C2'  DC     3     -11.147   4.896  20.901  0.00  0.00
ATOM     79  O3'  DC     3     -12.328   3.332  19.534  0.00  0.00
ATOM     80  H5'  DC     3     -15.100   6.320  21.411  0.00  0.00
ATOM     81 'H5'  DC     3     -14.964   4.644  21.992  0.00  0.00
ATOM     82  H4'  DC     3     -14.119   4.950  19.686  0.00  0.00
ATOM     83  H1'  DC     3     -11.455   5.498  18.870  0.00  0.00
ATOM     84  H6   DC     3     -10.647   7.530  21.863  0.00  0.00
ATOM     85  H5   DC     3      -9.040   9.431  21.718  0.00  0.00
ATOM     86  H41  DC     3      -7.507  10.680  20.118  0.00  0.00
ATOM     87  H42  DC     3      -7.412  10.216  18.432  0.00  0.00
ATOM     88  H3'  DC     3     -12.664   3.433  21.589  0.00  0.00
ATOM     89  H2'  DC     3     -10.235   4.339  20.685  0.00  0.00
ATOM     90 'H2'  DC     3     -11.082   5.306  21.914  0.00  0.00
HETATM   91  P   DKA     4     -11.571   1.884  19.536  0.00  0.00
HETATM   92  O1P DKA     4     -12.564   0.831  19.109  0.00  0.00
```

```
HETATM   93  O2P DKA     4     -10.785   1.750  20.819  0.00  0.00
HETATM   94  O5* DKA     4     -10.510   2.120  18.311  0.00  0.00
HETATM   95  C5* DKA     4     -10.979   2.102  16.969  0.00  0.00
HETATM   96  C4* DKA     4      -9.809   1.942  15.980  0.00  0.00
HETATM   97  O4* DKA     4      -9.020   3.157  15.976  0.00  0.00
HETATM   98  C1* DKA     4      -7.718   2.872  16.516  0.00  0.00
HETATM   99  N9  DKA     4      -7.408   3.929  17.465  0.00  0.00
HETATM  100  C8  DKA     4      -8.013   4.118  18.688  0.00  0.00
HETATM  101  N7  DKA     4      -7.554   5.169  19.333  0.00  0.00
HETATM  102  C5  DKA     4      -6.609   5.667  18.495  0.00  0.00
HETATM  103  C6  DKA     4      -5.760   6.807  18.694  0.00  0.00
HETATM  104  O6  DKA     4      -5.708   7.503  19.703  0.00  0.00
HETATM  105  N1  DKA     4      -4.936   7.023  17.604  0.00  0.00
HETATM  106  C2  DKA     4      -4.881   6.202  16.471  0.00  0.00
HETATM  107  N2  DKA     4      -3.794   6.632  15.440  0.00  0.00
HETATM  108  C23 DKA     4      -3.524   6.261  14.240  0.00  0.00
HETATM  109  C22 DKA     4      -2.318   6.924  13.670  0.00  0.00
HETATM  110  N21 DKA     4      -1.734   7.793  14.541  0.00  0.00
HETATM  111  C20 DKA     4      -0.638   8.431  14.074  0.00  0.00
HETATM  112  C19 DKA     4      -0.104   8.218  12.811  0.00  0.00
HETATM  113  C18 DKA     4      -0.736   7.327  11.946  0.00  0.00
HETATM  114  C17 DKA     4      -1.868   6.667  12.391  0.00  0.00
HETATM  115  C16 DKA     4      -2.612   5.742  11.580  0.00  0.00
HETATM  116  N15 DKA     4      -2.404   5.370  10.349  0.00  0.00
HETATM  117  C14 DKA     4      -3.457   4.550  10.040  0.00  0.00
HETATM  118  N14 DKA     4      -3.602   4.100   8.822  0.00  0.00
HETATM  119  N13 DKA     4      -4.272   4.306  11.092  0.00  0.00
HETATM  120  C13 DKA     4      -5.454   3.452  11.107  0.00  0.00
HETATM  121  C12 DKA     4      -3.812   5.085  12.138  0.00  0.00
HETATM  122  C11 DKA     4      -4.265   5.292  13.382  0.00  0.00
HETATM  123  N3  DKA     4      -5.641   5.160  16.283  0.00  0.00
HETATM  124  C4  DKA     4      -6.488   4.937  17.327  0.00  0.00
HETATM  125  C3* DKA     4      -8.858   0.783  16.316  0.00  0.00
HETATM  126  C2* DKA     4      -7.752   1.461  17.101  0.00  0.00
HETATM  127  O3* DKA     4      -8.246   0.227  15.149  0.00  0.00
HETATM  128 1H5* DKA     4     -11.505   3.044  16.784  0.00  0.00
```

```
HETATM  129 2H5* DKA     4     -11.674   1.269  16.831  0.00  0.00
HETATM  130  H4* DKA     4     -10.226   1.868  14.976  0.00  0.00
HETATM  131  H1* DKA     4      -7.001   2.928  15.689  0.00  0.00
HETATM  132  H8  DKA     4      -8.784   3.462  19.067  0.00  0.00
HETATM  133 1H   DKA     4      -4.361   7.850  17.699  0.00  0.00
HETATM  134 2H   DKA     4      -3.127   7.352  15.767  0.00  0.00
HETATM  135  H20 DKA     4      -0.176   9.138  14.754  0.00  0.00
HETATM  136  H19 DKA     4       0.795   8.742  12.505  0.00  0.00
HETATM  137  H18 DKA     4      -0.346   7.161  10.946  0.00  0.00
HETATM  138 H141 DKA     4      -2.942   4.370   8.111  1.00  0.00
HETATM  139 H142 DKA     4      -4.573   3.765   8.511  1.00  0.00
HETATM  140 1H13 DKA     4      -5.650   3.087  12.118  0.00  0.00
HETATM  141 2H13 DKA     4      -6.325   4.026  10.785  0.00  0.00
HETATM  142 3H13 DKA     4      -5.305   2.591  10.451  0.00  0.00
HETATM  143  H11 DKA     4      -5.151   4.795  13.759  0.00  0.00
HETATM  144  H3* DKA     4      -9.335  -0.023  16.882  0.00  0.00
HETATM  145 1H2* DKA     4      -6.777   0.972  16.999  0.00  0.00
HETATM  146 2H2* DKA     4      -8.001   1.462  18.167  0.00  0.00
ATOM    147  P    DG      5      -9.120  -0.865  14.292  0.00  0.00
ATOM    148  OP1  DG      5     -10.218  -0.064  13.635  0.00  0.00
ATOM    149  OP2  DG      5      -9.423  -2.057  15.170  0.00  0.00
ATOM    150  O5'  DG      5      -7.967  -1.254  13.191  0.00  0.00
ATOM    151  C5'  DG      5      -8.329  -1.172  11.817  0.00  0.00
ATOM    152  C4'  DG      5      -7.115  -1.274  10.885  0.00  0.00
ATOM    153  O4'  DG      5      -6.270  -0.114  11.096  0.00  0.00
ATOM    154  C1'  DG      5      -4.962  -0.570  11.483  0.00  0.00
ATOM    155  N9   DG      5      -4.448   0.352  12.482  0.00  0.00
ATOM    156  C8   DG      5      -5.023   0.620  13.706  0.00  0.00
ATOM    157  N7   DG      5      -4.337   1.504  14.407  0.00  0.00
ATOM    158  C5   DG      5      -3.273   1.805  13.602  0.00  0.00
ATOM    159  C6   DG      5      -2.182   2.720  13.827  0.00  0.00
ATOM    160  O6   DG      5      -2.044   3.457  14.806  0.00  0.00
ATOM    161  N1   DG      5      -1.311   2.761  12.751  0.00  0.00
ATOM    162  C2   DG      5      -1.482   2.075  11.558  0.00  0.00
ATOM    163  N2   DG      5      -0.542   2.347  10.618  0.00  0.00
ATOM    164  N3   DG      5      -2.479   1.255  11.343  0.00  0.00
```

```
ATOM    165  C4   DG     5      -3.326   1.136  12.397  0.00  0.00
ATOM    166  C3'  DG     5      -6.251  -2.520  11.099  0.00  0.00
ATOM    167  C2'  DG     5      -5.119  -2.006  11.959  0.00  0.00
ATOM    168  O3'  DG     5      -5.759  -2.962   9.829  0.00  0.00
ATOM    169  H5'  DG     5      -8.811  -0.205  11.637  0.00  0.00
ATOM    170 'H5'  DG     5      -9.042  -1.973  11.599  0.00  0.00
ATOM    171  H4'  DG     5      -7.471  -1.219   9.850  0.00  0.00
ATOM    172  H1'  DG     5      -4.320  -0.520  10.597  0.00  0.00
ATOM    173  H8   DG     5      -5.943   0.146  14.024  0.00  0.00
ATOM    174 1H    DG     5      -0.491   3.359  12.857  0.00  0.00
ATOM    175  H21  DG     5      -0.547   1.803   9.762  0.00  0.00
ATOM    176  H22  DG     5       0.173   3.078  10.745  0.00  0.00
ATOM    177  H3'  DG     5      -6.821  -3.327  11.568  0.00  0.00
ATOM    178  H2'  DG     5      -4.189  -2.562  11.851  0.00  0.00
ATOM    179 'H2'  DG     5      -5.412  -2.050  13.013  0.00  0.00
ATOM    180  P    DC     6      -5.154  -4.478   9.691  0.00  0.00
ATOM    181  OP1  DC     6      -5.212  -4.909   8.238  0.00  0.00
ATOM    182  OP2  DC     6      -5.780  -5.339  10.764  0.00  0.00
ATOM    183  O5'  DC     6      -3.593  -4.173  10.079  0.00  0.00
ATOM    184  C5'  DC     6      -2.828  -3.482   9.098  0.00  0.00
ATOM    185  C4'  DC     6      -1.401  -3.215   9.568  0.00  0.00
ATOM    186  O4'  DC     6      -1.408  -2.142  10.554  0.00  0.00
ATOM    187  C1'  DC     6      -0.448  -2.529  11.565  0.00  0.00
ATOM    188  N1   DC     6      -0.629  -1.738  12.782  0.00  0.00
ATOM    189  C6   DC     6      -1.733  -1.930  13.581  0.00  0.00
ATOM    190  C5   DC     6      -1.924  -1.227  14.695  0.00  0.00
ATOM    191  C4   DC     6      -0.899  -0.217  15.008  0.00  0.00
ATOM    192  N4   DC     6      -1.038   0.558  16.124  0.00  0.00
ATOM    193  N3   DC     6       0.145  -0.009  14.260  0.00  0.00
ATOM    194  C2   DC     6       0.338  -0.774  13.120  0.00  0.00
ATOM    195  O2   DC     6       1.366  -0.577  12.467  0.00  0.00
ATOM    196  C3'  DC     6      -0.717  -4.428  10.218  0.00  0.00
ATOM    197  C2'  DC     6      -0.661  -4.037  11.682  0.00  0.00
ATOM    198  O3'  DC     6       0.628  -4.505   9.748  0.00  0.00
ATOM    199  H5'  DC     6      -3.327  -2.536   8.863  0.00  0.00
ATOM    200 'H5'  DC     6      -2.789  -4.098   8.193  0.00  0.00
```

```
ATOM    201  H4'  DC     6      -0.818  -2.843   8.717  0.00  0.00
ATOM    202  H1'  DC     6       0.546  -2.324  11.150  0.00  0.00
ATOM    203  H6   DC     6      -2.456  -2.675  13.275  0.00  0.00
ATOM    204  H5   DC     6      -2.787  -1.346  15.333  0.00  0.00
ATOM    205  H41  DC     6      -1.873   0.537  16.699  0.00  0.00
ATOM    206  H42  DC     6      -0.271   1.190  16.403  0.00  0.00
ATOM    207  H3'  DC     6      -1.232  -5.375  10.030  0.00  0.00
ATOM    208  H2'  DC     6       0.132  -4.528  12.248  0.00  0.00
ATOM    209 'H2'  DC     6      -1.621  -4.285  12.146  0.00  0.00
ATOM    210  P    DG     7       1.278  -5.980   9.491  0.00  0.00
ATOM    211  OP1  DG     7       0.893  -6.426   8.099  0.00  0.00
ATOM    212  OP2  DG     7       0.967  -6.839  10.694  0.00  0.00
ATOM    213  O5'  DG     7       2.867  -5.569   9.532  0.00  0.00
ATOM    214  C5'  DG     7       3.354  -4.736   8.484  0.00  0.00
ATOM    215  C4'  DG     7       4.517  -3.841   8.947  0.00  0.00
ATOM    216  O4'  DG     7       4.033  -2.990  10.015  0.00  0.00
ATOM    217  C1'  DG     7       4.867  -3.194  11.174  0.00  0.00
ATOM    218  N9   DG     7       4.042  -3.152  12.368  0.00  0.00
ATOM    219  C8   DG     7       2.888  -3.873  12.565  0.00  0.00
ATOM    220  N7   DG     7       2.326  -3.620  13.731  0.00  0.00
ATOM    221  C5   DG     7       3.157  -2.700  14.306  0.00  0.00
ATOM    222  C6   DG     7       3.052  -2.044  15.588  0.00  0.00
ATOM    223  O6   DG     7       2.146  -2.186  16.409  0.00  0.00
ATOM    224  N1   DG     7       4.142  -1.216  15.826  0.00  0.00
ATOM    225  C2   DG     7       5.212  -1.025  14.959  0.00  0.00
ATOM    226  N2   DG     7       6.194  -0.198  15.406  0.00  0.00
ATOM    227  N3   DG     7       5.294  -1.603  13.786  0.00  0.00
ATOM    228  C4   DG     7       4.244  -2.416  13.506  0.00  0.00
ATOM    229  C3'  DG     7       5.744  -4.596   9.472  0.00  0.00
ATOM    230  C2'  DG     7       5.583  -4.520  10.971  0.00  0.00
ATOM    231  O3'  DG     7       6.939  -3.903   9.077  0.00  0.00
ATOM    232  H5'  DG     7       2.542  -4.096   8.122  0.00  0.00
ATOM    233 'H5'  DG     7       3.677  -5.380   7.660  0.00  0.00
ATOM    234  H4'  DG     7       4.797  -3.185   8.115  0.00  0.00
ATOM    235  H1'  DG     7       5.579  -2.362  11.213  0.00  0.00
ATOM    236  H8   DG     7       2.506  -4.562  11.823  0.00  0.00
```

```
ATOM    237 1H    DG    7       4.132  -0.728  16.723  0.00  0.00
ATOM    238  H21  DG    7       7.021  -0.086  14.831  0.00  0.00
ATOM    239  H22  DG    7       6.143   0.327  16.297  0.00  0.00
ATOM    240  H3'  DG    7       5.773  -5.621   9.094  0.00  0.00
ATOM    241  H2'  DG    7       6.527  -4.546  11.515  0.00  0.00
ATOM    242 'H2'  DG    7       4.970  -5.360  11.317  0.00  0.00
ATOM    243  P    DC    8       8.363  -4.720   8.999  0.00  0.00
ATOM    244  OP1  DC    8       9.288  -4.002   8.036  0.00  0.00
ATOM    245  OP2  DC    8       8.056  -6.188   8.801  0.00  0.00
ATOM    246  O5'  DC    8       8.918  -4.472  10.529  0.00  0.00
ATOM    247  C5'  DC    8       9.487  -3.188  10.790  0.00  0.00
ATOM    248  C4'  DC    8      10.045  -3.024  12.211  0.00  0.00
ATOM    249  O4'  DC    8       8.954  -2.870  13.150  0.00  0.00
ATOM    250  C1'  DC    8       9.302  -3.602  14.343  0.00  0.00
ATOM    251  N1   DC    8       8.063  -3.938  15.061  0.00  0.00
ATOM    252  C6   DC    8       7.132  -4.753  14.459  0.00  0.00
ATOM    253  C5   DC    8       5.978  -5.050  15.047  0.00  0.00
ATOM    254  C4   DC    8       5.743  -4.450  16.374  0.00  0.00
ATOM    255  N4   DC    8       4.544  -4.707  16.979  0.00  0.00
ATOM    256  N3   DC    8       6.612  -3.693  16.980  0.00  0.00
ATOM    257  C2   DC    8       7.810  -3.399  16.338  0.00  0.00
ATOM    258  O2   DC    8       8.593  -2.636  16.909  0.00  0.00
ATOM    259  C3'  DC    8      10.945  -4.166  12.718  0.00  0.00
ATOM    260  C2'  DC    8      10.120  -4.784  13.832  0.00  0.00
ATOM    261  O3'  DC    8      12.156  -3.599  13.230  0.00  0.00
ATOM    262  H5'  DC    8       8.716  -2.432  10.608  0.00  0.00
ATOM    263 'H5'  DC    8      10.311  -3.030  10.087  0.00  0.00
ATOM    264  H4'  DC    8      10.592  -2.073  12.237  0.00  0.00
ATOM    265  H1'  DC    8       9.928  -2.944  14.957  0.00  0.00
ATOM    266  H6   DC    8       7.362  -5.131  13.471  0.00  0.00
ATOM    267  H5   DC    8       5.219  -5.665  14.586  0.00  0.00
ATOM    268  H41  DC    8       3.815  -5.251  16.532  0.00  0.00
ATOM    269  H42  DC    8       4.332  -4.344  17.919  0.00  0.00
ATOM    270  H3'  DC    8      11.200  -4.875  11.924  0.00  0.00
ATOM    271  H2'  DC    8      10.698  -5.246  14.630  0.00  0.00
ATOM    272 'H2'  DC    8       9.484  -5.560  13.395  0.00  0.00
```

```
ATOM    273  P    DC     9      13.402  -4.573  13.664  0.00  0.00
ATOM    274  OP1  DC     9      14.684  -3.767  13.615  0.00  0.00
ATOM    275  OP2  DC     9      13.286  -5.877  12.909  0.00  0.00
ATOM    276  O5'  DC     9      13.015  -4.808  15.236  0.00  0.00
ATOM    277  C5'  DC     9      13.097  -3.656  16.067  0.00  0.00
ATOM    278  C4'  DC     9      12.528  -3.916  17.456  0.00  0.00
ATOM    279  O4'  DC     9      11.105  -4.197  17.355  0.00  0.00
ATOM    280  C1'  DC     9      10.849  -5.191  18.360  0.00  0.00
ATOM    281  N1   DC     9       9.560  -5.824  18.170  0.00  0.00
ATOM    282  C6   DC     9       9.339  -6.646  17.090  0.00  0.00
ATOM    283  C5   DC     9       8.213  -7.340  16.968  0.00  0.00
ATOM    284  C4   DC     9       7.234  -7.167  18.055  0.00  0.00
ATOM    285  N4   DC     9       6.103  -7.919  18.042  0.00  0.00
ATOM    286  N3   DC     9       7.388  -6.318  19.027  0.00  0.00
ATOM    287  C2   DC     9       8.555  -5.583  19.119  0.00  0.00
ATOM    288  O2   DC     9       8.658  -4.753  20.026  0.00  0.00
ATOM    289  C3'  DC     9      13.158  -5.103  18.194  0.00  0.00
ATOM    290  C2'  DC     9      12.046  -6.122  18.234  0.00  0.00
ATOM    291  O3'  DC     9      13.395  -4.719  19.547  0.00  0.00
ATOM    292  H5'  DC     9      12.537  -2.839  15.599  0.00  0.00
ATOM    293 'H5'  DC     9      14.148  -3.359  16.153  0.00  0.00
ATOM    294  H4'  DC     9      12.625  -2.996  18.046  0.00  0.00
ATOM    295  H1'  DC     9      10.865  -4.681  19.330  0.00  0.00
ATOM    296  H6   DC     9      10.114  -6.711  16.334  0.00  0.00
ATOM    297  H5   DC     9       8.002  -7.986  16.131  0.00  0.00
ATOM    298  H41  DC     9       5.909  -8.621  17.345  0.00  0.00
ATOM    299  H42  DC     9       5.387  -7.780  18.769  0.00  0.00
ATOM    300  H3'  DC     9      14.084  -5.466  17.735  0.00  0.00
ATOM    301  H2'  DC     9      12.090  -6.832  19.063  0.00  0.00
ATOM    302 'H2'  DC     9      12.049  -6.682  17.293  0.00  0.00
ATOM    303  P    DA    10      14.613  -5.484  20.310  0.00  0.00
ATOM    304  OP1  DA    10      15.898  -4.855  19.827  0.00  0.00
ATOM    305  OP2  DA    10      14.378  -6.971  20.198  0.00  0.00
ATOM    306  O5'  DA    10      14.309  -5.034  21.851  0.00  0.00
ATOM    307  C5'  DA    10      14.395  -3.654  22.183  0.00  0.00
ATOM    308  C4'  DA    10      13.444  -3.306  23.341  0.00  0.00
```

```
ATOM    309  O4'  DA    10      12.092  -3.616  22.911  0.00  0.00
ATOM    310  C1'  DA    10      11.543  -4.579  23.830  0.00  0.00
ATOM    311  N9   DA    10      10.714  -5.534  23.123  0.00  0.00
ATOM    312  C8   DA    10      11.033  -6.208  21.974  0.00  0.00
ATOM    313  N7   DA    10      10.102  -7.073  21.626  0.00  0.00
ATOM    314  C5   DA    10       9.130  -6.943  22.600  0.00  0.00
ATOM    315  C6   DA    10       7.899  -7.596  22.791  0.00  0.00
ATOM    316  N6   DA    10       7.445  -8.543  21.900  0.00  0.00
ATOM    317  N1   DA    10       7.141  -7.249  23.869  0.00  0.00
ATOM    318  C2   DA    10       7.586  -6.230  24.657  0.00  0.00
ATOM    319  N3   DA    10       8.735  -5.529  24.547  0.00  0.00
ATOM    320  C4   DA    10       9.471  -5.958  23.510  0.00  0.00
ATOM    321  C3'  DA    10      13.705  -4.092  24.632  0.00  0.00
ATOM    322  C2'  DA    10      12.720  -5.230  24.534  0.00  0.00
ATOM    323  O3'  DA    10      13.393  -3.273  25.769  0.00  0.00
ATOM    324  H5'  DA    10      14.126  -3.051  21.310  0.00  0.00
ATOM    325 'H5'  DA    10      15.430  -3.427  22.457  0.00  0.00
ATOM    326  H4'  DA    10      13.488  -2.226  23.523  0.00  0.00
ATOM    327  H1'  DA    10      10.914  -4.027  24.538  0.00  0.00
ATOM    328  H8   DA    10      11.957  -6.038  21.439  0.00  0.00
ATOM    329 1H6   DA    10       6.532  -8.999  21.983  0.00  0.00
ATOM    330 2H6   DA    10       8.049  -8.804  21.132  0.00  0.00
ATOM    331  H2   DA    10       6.930  -5.943  25.474  0.00  0.00
ATOM    332  H3'  DA    10      14.748  -4.412  24.708  0.00  0.00
ATOM    333  H2'  DA    10      12.425  -5.647  25.495  0.00  0.00
ATOM    334 'H2'  DA    10      13.147  -6.041  23.935  0.00  0.00
ATOM    335  P    DT    11      13.776  -3.818  27.270  0.00  0.00
ATOM    336  OP1  DT    11      14.167  -2.643  28.142  0.00  0.00
ATOM    337  OP2  DT    11      14.695  -5.010  27.120  0.00  0.00
ATOM    338  O5'  DT    11      12.310  -4.348  27.763  0.00  0.00
ATOM    339  C5'  DT    11      11.287  -3.378  27.954  0.00  0.00
ATOM    340  C4'  DT    11      10.039  -3.981  28.613  0.00  0.00
ATOM    341  O4'  DT    11       9.476  -4.964  27.708  0.00  0.00
ATOM    342  C1'  DT    11       9.405  -6.209  28.420  0.00  0.00
ATOM    343  N1   DT    11       9.534  -7.324  27.492  0.00  0.00
ATOM    344  C6   DT    11      10.734  -7.581  26.860  0.00  0.00
```

```
ATOM    345  C5   DT    11      10.900  -8.591  25.998  0.00  0.00
ATOM    346  C7   DT    11      12.173  -8.893  25.280  0.00  0.00
ATOM    347  C4   DT    11       9.740  -9.470  25.738  0.00  0.00
ATOM    348  O4   DT    11       9.811 -10.427  24.971  0.00  0.00
ATOM    349  N3   DT    11       8.582  -9.159  26.389  0.00  0.00
ATOM    350  C2   DT    11       8.402  -8.097  27.240  0.00  0.00
ATOM    351  O2   DT    11       7.282  -7.871  27.695  0.00  0.00
ATOM    352  C3'  DT    11      10.297  -4.694  29.949  0.00  0.00
ATOM    353  C2'  DT    11      10.454  -6.133  29.517  0.00  0.00
ATOM    354  O3'  DT    11       9.132  -4.565  30.781  0.00  0.00
ATOM    355  H5'  DT    11      11.021  -2.973  26.972  0.00  0.00
ATOM    356 'H5'  DT    11      11.666  -2.565  28.581  0.00  0.00
ATOM    357  H4'  DT    11       9.288  -3.191  28.732  0.00  0.00
ATOM    358  H1'  DT    11       8.412  -6.237  28.882  0.00  0.00
ATOM    359  H6   DT    11      11.552  -6.903  27.083  0.00  0.00
ATOM    360 1H7   DT    11      12.037  -8.788  24.199  0.00  0.00
ATOM    361 2H7   DT    11      12.981  -8.219  25.583  0.00  0.00
ATOM    362 3H7   DT    11      12.502  -9.916  25.492  0.00  0.00
ATOM    363  H3   DT    11       7.765  -9.741  26.227  0.00  0.00
ATOM    364  H3'  DT    11      11.159  -4.285  30.483  0.00  0.00
ATOM    365  H2'  DT    11      10.272  -6.866  30.300  0.00  0.00
ATOM    366 'H2'  DT    11      11.470  -6.296  29.149  0.00  0.00
HETATM  367  P   DC3    12       9.166  -5.212  32.284  0.00  0.00
HETATM  368  OP1 DC3    12       8.351  -4.358  33.231  0.00  0.00
HETATM  369  OP2 DC3    12      10.586  -5.605  32.617  0.00  0.00
HETATM  370  O5* DC3    12       8.338  -6.586  31.993  0.00  0.00
HETATM  371  C5* DC3    12       6.960  -6.473  31.671  0.00  0.00
HETATM  372  C4* DC3    12       6.274  -7.839  31.701  0.00  0.00
HETATM  373  O4* DC3    12       6.794  -8.661  30.633  0.00  0.00
HETATM  374  C1* DC3    12       7.189  -9.927  31.188  0.00  0.00
HETATM  375  N1  DC3    12       8.269 -10.486  30.384  0.00  0.00
HETATM  376  C6  DC3    12       9.437  -9.777  30.232  0.00  0.00
HETATM  377  C5  DC3    12      10.422 -10.215  29.454  0.00  0.00
HETATM  378  C4  DC3    12      10.166 -11.481  28.740  0.00  0.00
HETATM  379  N4  DC3    12      11.098 -11.919  27.845  0.00  0.00
HETATM  380  N3  DC3    12       9.086 -12.188  28.913  0.00  0.00
```

```
HETATM  381  C2  DC3    12       8.097 -11.723  29.758  0.00  0.00
HETATM  382  O2  DC3    12       7.092 -12.418  29.918  0.00  0.00
HETATM  383  C3* DC3    12       6.485  -8.620  32.996  0.00  0.00
HETATM  384  C2* DC3    12       7.535  -9.648  32.644  0.00  0.00
HETATM  385  O3* DC3    12       5.278  -9.326  33.304  0.00  0.00
HETATM  386  H5* DC3    12       6.874  -6.034  30.672  0.00  0.00
HETATM  387 'H5* DC3    12       6.468  -5.810  32.390  0.00  0.00
HETATM  388  H4* DC3    12       5.206  -7.694  31.496  0.00  0.00
HETATM  389  H1* DC3    12       6.308 -10.578  31.136  0.00  0.00
HETATM  390  H6  DC3    12       9.516  -8.834  30.760  0.00  0.00
HETATM  391  H5  DC3    12      11.346  -9.676  29.306  0.00  0.00
HETATM  392  H41 DC3    12      11.916 -11.380  27.590  0.00  0.00
HETATM  393  H42 DC3    12      10.972 -12.833  27.387  0.00  0.00
HETATM  394  H3* DC3    12       6.738  -7.994  33.856  0.00  0.00
HETATM  395  H2* DC3    12       7.493 -10.561  33.247  0.00  0.00
HETATM  396 'H2* DC3    12       8.531  -9.208  32.757  0.00  0.00
HETATM  397 'HO3 DC3    12       5.407  -9.737  34.178  0.00  0.00
TER     398      DC3    12
HETATM  399  O5* DG5    13       6.757 -20.608  21.392  0.00  0.00
HETATM  400  C5* DG5    13       5.810 -21.001  22.380  0.00  0.00
HETATM  401  C4* DG5    13       5.540 -19.876  23.372  0.00  0.00
HETATM  402  O4* DG5    13       6.769 -19.445  23.992  0.00  0.00
HETATM  403  C1* DG5    13       6.422 -18.195  24.635  0.00  0.00
HETATM  404  N9  DG5    13       7.604 -17.398  24.902  0.00  0.00
HETATM  405  C8  DG5    13       8.848 -17.518  24.333  0.00  0.00
HETATM  406  N7  DG5    13       9.712 -16.647  24.824  0.00  0.00
HETATM  407  C5  DG5    13       8.987 -15.928  25.739  0.00  0.00
HETATM  408  C6  DG5    13       9.390 -14.838  26.603  0.00  0.00
HETATM  409  O6  DG5    13      10.520 -14.355  26.693  0.00  0.00
HETATM  410  N1  DG5    13       8.324 -14.376  27.365  0.00  0.00
HETATM  411  C2  DG5    13       7.038 -14.904  27.346  0.00  0.00
HETATM  412  N2  DG5    13       6.159 -14.288  28.174  0.00  0.00
HETATM  413  N3  DG5    13       6.675 -15.905  26.584  0.00  0.00
HETATM  414  C4  DG5    13       7.682 -16.369  25.804  0.00  0.00
HETATM  415  C3* DG5    13       4.956 -18.611  22.758  0.00  0.00
HETATM  416  C2* DG5    13       5.383 -17.530  23.737  0.00  0.00
```

```
HETATM  417  O3* DG5    13       3.550 -18.741  22.655  0.00  0.00
HETATM  418 'HO5 DG5    13       7.531 -20.271  21.880  0.00  0.00
HETATM  419  H5* DG5    13       6.228 -21.870  22.898  0.00  0.00
HETATM  420 'H5* DG5    13       4.890 -21.308  21.873  0.00  0.00
HETATM  421  H4* DG5    13       4.877 -20.267  24.157  0.00  0.00
HETATM  422  H1* DG5    13       5.983 -18.450  25.608  0.00  0.00
HETATM  423  H8  DG5    13       9.068 -18.261  23.576  0.00  0.00
HETATM  424 1H   DG5    13       8.535 -13.582  27.973  0.00  0.00
HETATM  425  H21 DG5    13       5.176 -14.525  28.112  0.00  0.00
HETATM  426  H22 DG5    13       6.448 -13.575  28.855  0.00  0.00
HETATM  427  H3* DG5    13       5.396 -18.423  21.772  0.00  0.00
HETATM  428  H2* DG5    13       4.552 -17.143  24.335  0.00  0.00
HETATM  429 'H2* DG5    13       5.812 -16.686  23.186  0.00  0.00
ATOM    430  P    DA     14       2.695 -17.678  21.755  0.00  0.00
ATOM    431  OP1  DA     14       1.520 -18.414  21.162  0.00  0.00
ATOM    432  OP2  DA     14       3.649 -16.871  20.905  0.00  0.00
ATOM    433  O5'  DA     14       2.149 -16.690  22.932  0.00  0.00
ATOM    434  C5'  DA     14       1.292 -17.218  23.930  0.00  0.00
ATOM    435  C4'  DA     14       0.901 -16.135  24.948  0.00  0.00
ATOM    436  O4'  DA     14       2.111 -15.556  25.499  0.00  0.00
ATOM    437  C1'  DA     14       2.171 -14.165  25.118  0.00  0.00
ATOM    438  N9   DA     14       3.532 -13.821  24.740  0.00  0.00
ATOM    439  C8   DA     14       4.234 -14.305  23.666  0.00  0.00
ATOM    440  N7   DA     14       5.454 -13.813  23.593  0.00  0.00
ATOM    441  C5   DA     14       5.530 -12.927  24.644  0.00  0.00
ATOM    442  C6   DA     14       6.553 -12.052  25.058  0.00  0.00
ATOM    443  N6   DA     14       7.754 -11.983  24.388  0.00  0.00
ATOM    444  N1   DA     14       6.319 -11.237  26.121  0.00  0.00
ATOM    445  C2   DA     14       5.120 -11.356  26.749  0.00  0.00
ATOM    446  N3   DA     14       4.098 -12.193  26.471  0.00  0.00
ATOM    447  C4   DA     14       4.357 -12.931  25.381  0.00  0.00
ATOM    448  C3'  DA     14       0.078 -14.978  24.370  0.00  0.00
ATOM    449  C2'  DA     14       1.137 -13.958  24.020  0.00  0.00
ATOM    450  O3'  DA     14      -0.784 -14.497  25.407  0.00  0.00
ATOM    451  H5'  DA     14       1.829 -18.017  24.452  0.00  0.00
ATOM    452 'H5'  DA     14       0.396 -17.641  23.465  0.00  0.00
```

```
ATOM    453  H4'  DA    14       0.366 -16.615  25.775  0.00  0.00
ATOM    454  H1'  DA    14       1.908 -13.581  26.006  0.00  0.00
ATOM    455  H8   DA    14       3.817 -15.009  22.960  0.00  0.00
ATOM    456 1H6   DA    14       8.528 -11.373  24.673  0.00  0.00
ATOM    457 2H6   DA    14       7.870 -12.566  23.569  0.00  0.00
ATOM    458  H2   DA    14       4.962 -10.681  27.587  0.00  0.00
ATOM    459  H3'  DA    14      -0.536 -15.288  23.519  0.00  0.00
ATOM    460  H2'  DA    14       0.782 -12.928  23.995  0.00  0.00
ATOM    461 'H2'  DA    14       1.545 -14.179  23.029  0.00  0.00
ATOM    462  P    DT    15      -1.848 -13.296  25.093  0.00  0.00
ATOM    463  OP1  DT    15      -3.016 -13.433  26.048  0.00  0.00
ATOM    464  OP2  DT    15      -2.064 -13.231  23.598  0.00  0.00
ATOM    465  O5'  DT    15      -0.955 -11.999  25.561  0.00  0.00
ATOM    466  C5'  DT    15      -0.627 -11.919  26.945  0.00  0.00
ATOM    467  C4'  DT    15       0.166 -10.659  27.318  0.00  0.00
ATOM    468  O4'  DT    15       1.446 -10.659  26.643  0.00  0.00
ATOM    469  C1'  DT    15       1.631  -9.354  26.063  0.00  0.00
ATOM    470  N1   DT    15       2.525  -9.467  24.919  0.00  0.00
ATOM    471  C6   DT    15       2.151 -10.209  23.817  0.00  0.00
ATOM    472  C5   DT    15       2.938 -10.379  22.750  0.00  0.00
ATOM    473  C7   DT    15       2.570 -11.174  21.542  0.00  0.00
ATOM    474  C4   DT    15       4.264  -9.730  22.779  0.00  0.00
ATOM    475  O4   DT    15       5.060  -9.827  21.847  0.00  0.00
ATOM    476  N3   DT    15       4.573  -9.008  23.896  0.00  0.00
ATOM    477  C2   DT    15       3.764  -8.834  24.990  0.00  0.00
ATOM    478  O2   DT    15       4.193  -8.190  25.946  0.00  0.00
ATOM    479  C3'  DT    15      -0.517  -9.326  26.990  0.00  0.00
ATOM    480  C2'  DT    15       0.227  -8.851  25.763  0.00  0.00
ATOM    481  O3'  DT    15      -0.261  -8.435  28.084  0.00  0.00
ATOM    482  H5'  DT    15      -0.032 -12.801  27.205  0.00  0.00
ATOM    483 'H5'  DT    15      -1.551 -11.941  27.532  0.00  0.00
ATOM    484  H4'  DT    15       0.386 -10.717  28.392  0.00  0.00
ATOM    485  H1'  DT    15       2.090  -8.728  26.837  0.00  0.00
ATOM    486  H6   DT    15       1.169 -10.670  23.855  0.00  0.00
ATOM    487 1H7   DT    15       1.566 -11.603  21.628  0.00  0.00
ATOM    488 2H7   DT    15       2.586 -10.542  20.648  0.00  0.00
```

```
ATOM    489 3H7   DT    15       3.274 -12.000  21.397  0.00  0.00
ATOM    490  H3   DT    15       5.477  -8.547  23.951  0.00  0.00
ATOM    491  H3'  DT    15      -1.595  -9.435  26.849  0.00  0.00
ATOM    492  H2'  DT    15       0.211  -7.772  25.603  0.00  0.00
ATOM    493 'H2'  DT    15      -0.207  -9.328  24.879  0.00  0.00
ATOM    494  P    DG    16      -1.085  -7.030  28.189  0.00  0.00
ATOM    495  OP1  DG    16      -1.101  -6.605  29.642  0.00  0.00
ATOM    496  OP2  DG    16      -2.353  -7.168  27.384  0.00  0.00
ATOM    497  O5'  DG    16      -0.048  -6.059  27.379  0.00  0.00
ATOM    498  C5'  DG    16       1.166  -5.726  28.036  0.00  0.00
ATOM    499  C4'  DG    16       2.068  -4.865  27.156  0.00  0.00
ATOM    500  O4'  DG    16       2.591  -5.658  26.056  0.00  0.00
ATOM    501  C1'  DG    16       2.591  -4.788  24.909  0.00  0.00
ATOM    502  N9   DG    16       2.748  -5.548  23.691  0.00  0.00
ATOM    503  C8   DG    16       1.844  -6.411  23.123  0.00  0.00
ATOM    504  N7   DG    16       2.273  -6.907  21.977  0.00  0.00
ATOM    505  C5   DG    16       3.515  -6.357  21.822  0.00  0.00
ATOM    506  C6   DG    16       4.485  -6.556  20.775  0.00  0.00
ATOM    507  O6   DG    16       4.345  -7.312  19.814  0.00  0.00
ATOM    508  N1   DG    16       5.634  -5.809  20.994  0.00  0.00
ATOM    509  C2   DG    16       5.848  -4.969  22.080  0.00  0.00
ATOM    510  N2   DG    16       7.027  -4.295  22.078  0.00  0.00
ATOM    511  N3   DG    16       4.978  -4.806  23.042  0.00  0.00
ATOM    512  C4   DG    16       3.840  -5.522  22.866  0.00  0.00
ATOM    513  C3'  DG    16       1.380  -3.653  26.523  0.00  0.00
ATOM    514  C2'  DG    16       1.290  -4.024  25.056  0.00  0.00
ATOM    515  O3'  DG    16       2.273  -2.543  26.618  0.00  0.00
ATOM    516  H5'  DG    16       1.687  -6.651  28.306  0.00  0.00
ATOM    517 'H5'  DG    16       0.928  -5.173  28.951  0.00  0.00
ATOM    518  H4'  DG    16       2.936  -4.557  27.753  0.00  0.00
ATOM    519  H1'  DG    16       3.455  -4.118  24.997  0.00  0.00
ATOM    520  H8   DG    16       0.891  -6.637  23.583  0.00  0.00
ATOM    521 1H    DG    16       6.360  -5.922  20.284  0.00  0.00
ATOM    522  H21  DG    16       7.264  -3.676  22.849  0.00  0.00
ATOM    523  H22  DG    16       7.713  -4.384  21.312  0.00  0.00
ATOM    524  H3'  DG    16       0.419  -3.402  26.982  0.00  0.00
```

```
ATOM    525  H2'  DG    16       1.240  -3.177  24.368  0.00  0.00
ATOM    526 'H2'  DG    16       0.419  -4.668  24.892  0.00  0.00
ATOM    527  P    DG    17       1.594  -1.069  26.685  0.00  0.00
ATOM    528  OP1  DG    17       1.157  -0.819  28.108  0.00  0.00
ATOM    529  OP2  DG    17       0.628  -0.954  25.528  0.00  0.00
ATOM    530  O5'  DG    17       2.885  -0.151  26.291  0.00  0.00
ATOM    531  C5'  DG    17       4.036  -0.131  27.113  0.00  0.00
ATOM    532  C4'  DG    17       5.278   0.318  26.315  0.00  0.00
ATOM    533  O4'  DG    17       5.567  -0.685  25.303  0.00  0.00
ATOM    534  C1'  DG    17       5.532  -0.052  24.003  0.00  0.00
ATOM    535  N9   DG    17       4.918  -0.944  23.027  0.00  0.00
ATOM    536  C8   DG    17       3.668  -1.515  23.154  0.00  0.00
ATOM    537  N7   DG    17       3.324  -2.234  22.103  0.00  0.00
ATOM    538  C5   DG    17       4.421  -2.155  21.284  0.00  0.00
ATOM    539  C6   DG    17       4.650  -2.778  20.001  0.00  0.00
ATOM    540  O6   DG    17       3.900  -3.560  19.415  0.00  0.00
ATOM    541  N1   DG    17       5.870  -2.409  19.454  0.00  0.00
ATOM    542  C2   DG    17       6.798  -1.574  20.056  0.00  0.00
ATOM    543  N2   DG    17       7.909  -1.335  19.306  0.00  0.00
ATOM    544  N3   DG    17       6.622  -1.046  21.245  0.00  0.00
ATOM    545  C4   DG    17       5.421  -1.359  21.814  0.00  0.00
ATOM    546  C3'  DG    17       5.130   1.664  25.591  0.00  0.00
ATOM    547  C2'  DG    17       4.772   1.255  24.183  0.00  0.00
ATOM    548  O3'  DG    17       6.392   2.340  25.594  0.00  0.00
ATOM    549  H5'  DG    17       4.210  -1.133  27.518  0.00  0.00
ATOM    550 'H5'  DG    17       3.854   0.557  27.945  0.00  0.00
ATOM    551  H4'  DG    17       6.137   0.334  26.996  0.00  0.00
ATOM    552  H1'  DG    17       6.569   0.130  23.699  0.00  0.00
ATOM    553  H8   DG    17       3.050  -1.357  24.029  0.00  0.00
ATOM    554 1H    DG    17       6.082  -2.795  18.536  0.00  0.00
ATOM    555  H21  DG    17       8.575  -0.652  19.646  0.00  0.00
ATOM    556  H22  DG    17       8.129  -1.821  18.423  0.00  0.00
ATOM    557  H3'  DG    17       4.373   2.294  26.065  0.00  0.00
ATOM    558  H2'  DG    17       5.048   1.983  23.423  0.00  0.00
ATOM    559 'H2'  DG    17       3.689   1.102  24.111  0.00  0.00
ATOM    560  P    DC    18       6.439   3.962  25.374  0.00  0.00
```

```
ATOM    561  OP1  DC    18       7.784   4.474  25.852  0.00  0.00
ATOM    562  OP2  DC    18       5.160   4.554  25.916  0.00  0.00
ATOM    563  O5'  DC    18       6.414   4.020  23.745  0.00  0.00
ATOM    564  C5'  DC    18       7.640   3.718  23.091  0.00  0.00
ATOM    565  C4'  DC    18       7.436   3.522  21.599  0.00  0.00
ATOM    566  O4'  DC    18       6.667   2.329  21.347  0.00  0.00
ATOM    567  C1'  DC    18       6.254   2.446  19.974  0.00  0.00
ATOM    568  N1   DC    18       5.064   1.658  19.697  0.00  0.00
ATOM    569  C6   DC    18       3.980   1.681  20.543  0.00  0.00
ATOM    570  C5   DC    18       2.916   0.910  20.321  0.00  0.00
ATOM    571  C4   DC    18       2.996   0.017  19.145  0.00  0.00
ATOM    572  N4   DC    18       1.994  -0.871  18.889  0.00  0.00
ATOM    573  N3   DC    18       3.999   0.023  18.316  0.00  0.00
ATOM    574  C2   DC    18       5.043   0.900  18.528  0.00  0.00
ATOM    575  O2   DC    18       5.923   0.987  17.669  0.00  0.00
ATOM    576  C3'  DC    18       6.675   4.638  20.893  0.00  0.00
ATOM    577  C2'  DC    18       6.077   3.928  19.699  0.00  0.00
ATOM    578  O3'  DC    18       7.543   5.694  20.519  0.00  0.00
ATOM    579  H5'  DC    18       8.059   2.804  23.526  0.00  0.00
ATOM    580 'H5'  DC    18       8.335   4.547  23.262  0.00  0.00
ATOM    581  H4'  DC    18       8.425   3.382  21.140  0.00  0.00
ATOM    582  H1'  DC    18       7.093   2.069  19.375  0.00  0.00
ATOM    583  H6   DC    18       4.025   2.357  21.390  0.00  0.00
ATOM    584  H5   DC    18       2.049   0.887  20.964  0.00  0.00
ATOM    585  H41  DC    18       1.222  -1.012  19.526  0.00  0.00
ATOM    586  H42  DC    18       2.024  -1.427  18.024  0.00  0.00
ATOM    587  H3'  DC    18       5.875   5.033  21.530  0.00  0.00
ATOM    588  H2'  DC    18       6.562   4.178  18.756  0.00  0.00
ATOM    589 'H2'  DC    18       5.021   4.203  19.617  0.00  0.00
ATOM    590  P    DG    19       6.934   7.006  19.755  0.00  0.00
ATOM    591  OP1  DG    19       7.872   8.166  19.983  0.00  0.00
ATOM    592  OP2  DG    19       5.455   7.127  20.044  0.00  0.00
ATOM    593  O5'  DG    19       7.075   6.546  18.194  0.00  0.00
ATOM    594  C5'  DG    19       8.361   6.222  17.683  0.00  0.00
ATOM    595  C4'  DG    19       8.270   5.718  16.230  0.00  0.00
ATOM    596  O4'  DG    19       7.370   4.579  16.206  0.00  0.00
```

```
ATOM    597  C1'  DG    19       6.272   4.895  15.326  0.00  0.00
ATOM    598  N9   DG    19       5.044   4.358  15.889  0.00  0.00
ATOM    599  C8   DG    19       4.429   4.784  17.044  0.00  0.00
ATOM    600  N7   DG    19       3.331   4.106  17.322  0.00  0.00
ATOM    601  C5   DG    19       3.231   3.213  16.291  0.00  0.00
ATOM    602  C6   DG    19       2.181   2.264  16.003  0.00  0.00
ATOM    603  O6   DG    19       1.170   2.075  16.681  0.00  0.00
ATOM    604  N1   DG    19       2.397   1.613  14.799  0.00  0.00
ATOM    605  C2   DG    19       3.479   1.827  13.956  0.00  0.00
ATOM    606  N2   DG    19       3.475   1.080  12.823  0.00  0.00
ATOM    607  N3   DG    19       4.433   2.685  14.215  0.00  0.00
ATOM    608  C4   DG    19       4.261   3.351  15.384  0.00  0.00
ATOM    609  C3'  DG    19       7.737   6.754  15.229  0.00  0.00
ATOM    610  C2'  DG    19       6.274   6.403  15.124  0.00  0.00
ATOM    611  O3'  DG    19       8.372   6.571  13.953  0.00  0.00
ATOM    612  H5'  DG    19       8.790   5.431  18.306  0.00  0.00
ATOM    613 'H5'  DG    19       9.009   7.103  17.739  0.00  0.00
ATOM    614  H4'  DG    19       9.259   5.357  15.923  0.00  0.00
ATOM    615  H1'  DG    19       6.465   4.384  14.375  0.00  0.00
ATOM    616  H8   DG    19       4.826   5.593  17.647  0.00  0.00
ATOM    617 1H    DG    19       1.679   0.939  14.533  0.00  0.00
ATOM    618  H21  DG    19       4.234   1.174  12.159  0.00  0.00
ATOM    619  H22  DG    19       2.741   0.391  12.601  0.00  0.00
ATOM    620  H3'  DG    19       7.914   7.772  15.582  0.00  0.00
ATOM    621  H2'  DG    19       5.824   6.671  14.169  0.00  0.00
ATOM    622 'H2'  DG    19       5.717   6.922  15.911  0.00  0.00
ATOM    623  P    DC    20       8.368   7.809  12.873  0.00  0.00
ATOM    624  OP1  DC    20       9.494   7.597  11.883  0.00  0.00
ATOM    625  OP2  DC    20       8.255   9.104  13.646  0.00  0.00
ATOM    626  O5'  DC    20       6.930   7.536  12.126  0.00  0.00
ATOM    627  C5'  DC    20       6.917   6.601  11.052  0.00  0.00
ATOM    628  C4'  DC    20       5.511   6.313  10.495  0.00  0.00
ATOM    629  O4'  DC    20       4.745   5.585  11.502  0.00  0.00
ATOM    630  C1'  DC    20       3.402   6.073  11.367  0.00  0.00
ATOM    631  N1   DC    20       2.577   5.740  12.515  0.00  0.00
ATOM    632  C6   DC    20       2.831   6.313  13.737  0.00  0.00
```

```
ATOM    633  C5   DC    20       2.059   6.070  14.789  0.00  0.00
ATOM    634  C4   DC    20       0.956   5.123  14.566  0.00  0.00
ATOM    635  N4   DC    20       0.150   4.802  15.611  0.00  0.00
ATOM    636  N3   DC    20       0.703   4.553  13.427  0.00  0.00
ATOM    637  C2   DC    20       1.513   4.842  12.345  0.00  0.00
ATOM    638  O2   DC    20       1.228   4.322  11.263  0.00  0.00
ATOM    639  C3'  DC    20       4.652   7.534  10.072  0.00  0.00
ATOM    640  C2'  DC    20       3.587   7.567  11.137  0.00  0.00
ATOM    641  O3'  DC    20       3.946   7.241   8.857  0.00  0.00
ATOM    642  H5'  DC    20       7.359   5.666  11.413  0.00  0.00
ATOM    643 'H5'  DC    20       7.539   6.999  10.244  0.00  0.00
ATOM    644  H4'  DC    20       5.624   5.629   9.644  0.00  0.00
ATOM    645  H1'  DC    20       2.977   5.601  10.473  0.00  0.00
ATOM    646  H6   DC    20       3.674   6.986  13.815  0.00  0.00
ATOM    647  H5   DC    20       2.226   6.505  15.764  0.00  0.00
ATOM    648  H41  DC    20       0.351   5.088  16.564  0.00  0.00
ATOM    649  H42  DC    20      -0.676   4.209  15.439  0.00  0.00
ATOM    650  H3'  DC    20       5.227   8.458   9.981  0.00  0.00
ATOM    651  H2'  DC    20       2.649   8.037  10.839  0.00  0.00
ATOM    652 'H2'  DC    20       3.982   8.087  12.015  0.00  0.00
ATOM    653  P    DC    21       3.588   8.428   7.790  0.00  0.00
ATOM    654  OP1  DC    21       3.056   7.772   6.532  0.00  0.00
ATOM    655  OP2  DC    21       4.776   9.361   7.754  0.00  0.00
ATOM    656  O5'  DC    21       2.360   9.206   8.552  0.00  0.00
ATOM    657  C5'  DC    21       1.031   8.715   8.396  0.00  0.00
ATOM    658  C4'  DC    21      -0.051   9.660   8.978  0.00  0.00
ATOM    659  O4'  DC    21       0.265   9.956  10.366  0.00  0.00
ATOM    660  C1'  DC    21       0.304  11.391  10.517  0.00  0.00
ATOM    661  N1   DC    21       1.260  11.777  11.559  0.00  0.00
ATOM    662  C6   DC    21       2.492  11.164  11.606  0.00  0.00
ATOM    663  C5   DC    21       3.386  11.462  12.544  0.00  0.00
ATOM    664  C4   DC    21       2.979  12.492  13.520  0.00  0.00
ATOM    665  N4   DC    21       3.852  12.827  14.517  0.00  0.00
ATOM    666  N3   DC    21       1.835  13.109  13.470  0.00  0.00
ATOM    667  C2   DC    21       0.918  12.787  12.481  0.00  0.00
ATOM    668  O2   DC    21      -0.171  13.363  12.433  0.00  0.00
```

```
ATOM    669  C3'  DC    21      -0.203  11.012   8.266  0.00  0.00
ATOM    670  C2'  DC    21       0.641  11.928   9.132  0.00  0.00
ATOM    671  O3'  DC    21      -1.531  11.546   8.364  0.00  0.00
ATOM    672  H5'  DC    21       0.983   7.753   8.917  0.00  0.00
ATOM    673 'H5'  DC    21       0.818   8.547   7.336  0.00  0.00
ATOM    674  H4'  DC    21      -0.998   9.114   8.982  0.00  0.00
ATOM    675  H1'  DC    21      -0.703  11.704  10.816  0.00  0.00
ATOM    676  H6   DC    21       2.714  10.427  10.841  0.00  0.00
ATOM    677  H5   DC    21       4.367  11.009  12.598  0.00  0.00
ATOM    678  H41  DC    21       4.720  12.325  14.665  0.00  0.00
ATOM    679  H42  DC    21       3.627  13.603  15.129  0.00  0.00
ATOM    680  H3'  DC    21       0.102  11.007   7.216  0.00  0.00
ATOM    681  H2'  DC    21       0.389  12.989   9.040  0.00  0.00
ATOM    682 'H2'  DC    21       1.703  11.800   8.897  0.00  0.00
ATOM    683  P    DG    22      -2.790  10.873   7.574  0.00  0.00
ATOM    684  OP1  DG    22      -2.259   9.893   6.555  0.00  0.00
ATOM    685  OP2  DG    22      -3.771  11.969   7.216  0.00  0.00
ATOM    686  O5'  DG    22      -3.409  10.010   8.815  0.00  0.00
ATOM    687  C5'  DG    22      -4.744   9.535   8.683  0.00  0.00
ATOM    688  C4'  DG    22      -4.842   8.095   9.203  0.00  0.00
ATOM    689  O4'  DG    22      -4.610   8.063  10.644  0.00  0.00
ATOM    690  C1'  DG    22      -5.871   7.781  11.305  0.00  0.00
ATOM    691  N9   DG    22      -5.953   8.540  12.535  0.00  0.00
ATOM    692  C8   DG    22      -5.208   9.654  12.850  0.00  0.00
ATOM    693  N7   DG    22      -5.409  10.060  14.088  0.00  0.00
ATOM    694  C5   DG    22      -6.389   9.233  14.555  0.00  0.00
ATOM    695  C6   DG    22      -7.025   9.220  15.851  0.00  0.00
ATOM    696  O6   DG    22      -6.694   9.910  16.812  0.00  0.00
ATOM    697  N1   DG    22      -8.001   8.238  15.921  0.00  0.00
ATOM    698  C2   DG    22      -8.266   7.291  14.932  0.00  0.00
ATOM    699  N2   DG    22      -9.245   6.404  15.233  0.00  0.00
ATOM    700  N3   DG    22      -7.625   7.251  13.787  0.00  0.00
ATOM    701  C4   DG    22      -6.732   8.265  13.634  0.00  0.00
ATOM    702  C3'  DG    22      -6.236   7.495   9.005  0.00  0.00
ATOM    703  C2'  DG    22      -6.952   7.973  10.258  0.00  0.00
ATOM    704  O3'  DG    22      -6.089   6.081   9.088  0.00  0.00
```

```
ATOM    705  H5'  DG    22      -5.051   9.571   7.633  0.00  0.00
ATOM    706 'H5'  DG    22      -5.380  10.211   9.261  0.00  0.00
ATOM    707  H4'  DG    22      -4.058   7.480   8.747  0.00  0.00
ATOM    708  H1'  DG    22      -5.849   6.729  11.601  0.00  0.00
ATOM    709  H8   DG    22      -4.515  10.103  12.147  0.00  0.00
ATOM    710 1H    DG    22      -8.545   8.226  16.788  0.00  0.00
ATOM    711  H21  DG    22      -9.505   5.683  14.568  0.00  0.00
ATOM    712  H22  DG    22      -9.763   6.444  16.127  0.00  0.00
ATOM    713  H3'  DG    22      -6.727   7.792   8.075  0.00  0.00
ATOM    714  H2'  DG    22      -7.837   7.383  10.500  0.00  0.00
ATOM    715 'H2'  DG    22      -7.236   9.027  10.170  0.00  0.00
ATOM    716  P    DA    23      -6.592   5.041   7.941  0.00  0.00
ATOM    717  OP1  DA    23      -5.725   3.800   8.175  0.00  0.00
ATOM    718  OP2  DA    23      -6.618   5.724   6.599  0.00  0.00
ATOM    719  O5'  DA    23      -8.095   4.754   8.505  0.00  0.00
ATOM    720  C5'  DA    23      -9.199   5.570   8.092  0.00  0.00
ATOM    721  C4'  DA    23     -10.378   5.347   9.062  0.00  0.00
ATOM    722  O4'  DA    23     -10.117   6.105  10.279  0.00  0.00
ATOM    723  C1'  DA    23     -11.327   6.804  10.645  0.00  0.00
ATOM    724  N9   DA    23     -10.978   7.955  11.462  0.00  0.00
ATOM    725  C8   DA    23     -10.203   9.020  11.075  0.00  0.00
ATOM    726  N7   DA    23      -9.990   9.875  12.055  0.00  0.00
ATOM    727  C5   DA    23     -10.710   9.373  13.121  0.00  0.00
ATOM    728  C6   DA    23     -10.891   9.840  14.442  0.00  0.00
ATOM    729  N6   DA    23     -10.259  10.965  14.932  0.00  0.00
ATOM    730  N1   DA    23     -11.701   9.130  15.270  0.00  0.00
ATOM    731  C2   DA    23     -12.260   7.993  14.789  0.00  0.00
ATOM    732  N3   DA    23     -12.123   7.437  13.566  0.00  0.00
ATOM    733  C4   DA    23     -11.342   8.187  12.769  0.00  0.00
ATOM    734  C3'  DA    23     -11.761   5.809   8.545  0.00  0.00
ATOM    735  C2'  DA    23     -12.001   7.098   9.313  0.00  0.00
ATOM    736  O3'  DA    23     -12.716   4.812   8.924  0.00  0.00
ATOM    737  H5'  DA    23      -9.471   5.261   7.079  0.00  0.00
ATOM    738 'H5'  DA    23      -8.893   6.620   8.088  0.00  0.00
ATOM    739  H4'  DA    23     -10.405   4.291   9.357  0.00  0.00
ATOM    740  H1'  DA    23     -11.931   6.123  11.255  0.00  0.00
```

```
ATOM    741  H8   DA    23      -9.809   9.114  10.071  0.00  0.00
ATOM    742 1H6   DA    23     -10.410  11.233  15.915  0.00  0.00
ATOM    743 2H6   DA    23      -9.658  11.503  14.324  0.00  0.00
ATOM    744  H2   DA    23     -12.905   7.456  15.476  0.00  0.00
ATOM    745  H3'  DA    23     -11.782   5.932   7.459  0.00  0.00
ATOM    746  H2'  DA    23     -13.051   7.369   9.436  0.00  0.00
ATOM    747 'H2'  DA    23     -11.496   7.920   8.791  0.00  0.00
HETATM  748  P   DG3    24     -14.230   4.794   8.312  0.00  0.00
HETATM  749  OP1 DG3    24     -14.772   3.383   8.419  0.00  0.00
HETATM  750  OP2 DG3    24     -14.262   5.555   7.007  0.00  0.00
HETATM  751  O5* DG3    24     -14.986   5.707   9.432  0.00  0.00
HETATM  752  C5* DG3    24     -15.051   5.173  10.746  0.00  0.00
HETATM  753  C4* DG3    24     -15.515   6.223  11.735  0.00  0.00
HETATM  754  O4* DG3    24     -14.654   7.383  11.752  0.00  0.00
HETATM  755  C1* DG3    24     -15.401   8.312  12.563  0.00  0.00
HETATM  756  N9  DG3    24     -14.842   9.644  12.500  0.00  0.00
HETATM  757  C8  DG3    24     -14.351  10.297  11.398  0.00  0.00
HETATM  758  N7  DG3    24     -13.951  11.525  11.683  0.00  0.00
HETATM  759  C5  DG3    24     -14.176  11.650  13.032  0.00  0.00
HETATM  760  C6  DG3    24     -13.963  12.770  13.925  0.00  0.00
HETATM  761  O6  DG3    24     -13.574  13.892  13.598  0.00  0.00
HETATM  762  N1  DG3    24     -14.324  12.470  15.233  0.00  0.00
HETATM  763  C2  DG3    24     -14.853  11.256  15.653  0.00  0.00
HETATM  764  N2  DG3    24     -15.123  11.173  16.979  0.00  0.00
HETATM  765  N3  DG3    24     -15.085  10.256  14.841  0.00  0.00
HETATM  766  C4  DG3    24     -14.725  10.503  13.559  0.00  0.00
HETATM  767  C3* DG3    24     -16.900   6.798  11.461  0.00  0.00
HETATM  768  C2* DG3    24     -16.840   8.195  12.068  0.00  0.00
HETATM  769  O3* DG3    24     -17.908   6.012  12.081  0.00  0.00
HETATM  770  H5* DG3    24     -14.057   4.822  11.039  0.00  0.00
HETATM  771 'H5* DG3    24     -15.739   4.321  10.749  0.00  0.00
HETATM  772  H4* DG3    24     -15.485   5.764  12.734  0.00  0.00
HETATM  773  H1* DG3    24     -15.325   7.968  13.603  0.00  0.00
HETATM  774  H8  DG3    24     -14.324   9.835  10.418  0.00  0.00
HETATM  775 1H   DG3    24     -14.187  13.225  15.906  0.00  0.00
HETATM  776  H21 DG3    24     -15.473  10.310  17.380  0.00  0.00
```

```
HETATM  777  H22 DG3    24      -14.966  11.949  17.635  0.00  0.00
HETATM  778  H3* DG3    24      -17.115   6.860  10.388  0.00  0.00
HETATM  779  H2* DG3    24      -17.559   8.360  12.877  0.00  0.00
HETATM  780 'H2* DG3    24      -17.049   8.937  11.288  0.00  0.00
HETATM  781 'HO3 DG3    24      -18.768   6.331  11.757  0.00  0.00
TER     782      DG3    24
CONECT    1   17    2
CONECT    2    1   18   19    3
CONECT    3    2   20    4   14
CONECT    4    3    5
CONECT    5    4   21    6   15
CONECT    6    5    7   12
CONECT    7    6   22    8    8
CONECT    8    7    7   23    9
CONECT    9    8   10   11   11
CONECT   10    9   24   25
CONECT   11    9    9   12
CONECT   12    6   11   13   13
CONECT   13   12   12
CONECT   14    3   26   15   16
CONECT   15    5   14   27   28
CONECT   16   14   29
CONECT   17    1
CONECT   18    2
CONECT   19    2
CONECT   20    3
CONECT   21    5
CONECT   22    7
CONECT   23    8
CONECT   24   10
CONECT   25   10
CONECT   26   14
CONECT   27   15
CONECT   28   15
CONECT   29   16   30   31   32
CONECT   30   29
```

```
CONECT   31   29
CONECT   32   29   33
CONECT   33   32   49   50   34
CONECT   34   33   51   35   46
CONECT   35   34   36
CONECT   36   35   52   37   47
CONECT   37   36   38   44
CONECT   38   37   53   39   39
CONECT   39   38   38   40   41
CONECT   40   39   54   55   56
CONECT   41   39   42   42   43
CONECT   42   41   41
CONECT   43   41   57   44
CONECT   44   37   43   45   45
CONECT   45   44   44
CONECT   46   34   58   47   48
CONECT   47   36   46   59   60
CONECT   48   46
CONECT   49   33
CONECT   50   33
CONECT   51   34
CONECT   52   36
CONECT   53   38
CONECT   54   40
CONECT   55   40
CONECT   56   40
CONECT   57   43
CONECT   58   46
CONECT   59   47
CONECT   60   47
CONECT   61   62   63   64
CONECT   62   61
CONECT   63   61
CONECT   64   61   65
CONECT   65   64   80   81   66
CONECT   66   65   82   67   77
```

```
CONECT   67   66   68
CONECT   68   67   83   69   78
CONECT   69   68   70   75
CONECT   70   69   84   71   71
CONECT   71   70   70   85   72
CONECT   72   71   73   74   74
CONECT   73   72   86   87
CONECT   74   72   72   75
CONECT   75   69   74   76   76
CONECT   76   75   75
CONECT   77   66   88   78   79
CONECT   78   68   77   89   90
CONECT   79   77   91
CONECT   80   65
CONECT   81   65
CONECT   82   66
CONECT   83   68
CONECT   84   70
CONECT   85   71
CONECT   86   73
CONECT   87   73
CONECT   88   77
CONECT   89   78
CONECT   90   78
CONECT   91   79   92   93   94
CONECT   92   91
CONECT   93   91
CONECT   94   91   95
CONECT   95   94  128  129   96
CONECT   96   95  130   97  125
CONECT   97   96   98
CONECT   98   97  131   99  126
CONECT   99   98  100  124
CONECT  100   99  132  101  101
CONECT  101  100  100  102
CONECT  102  101  103  124  124
```

```
CONECT  103  102  104  104  105
CONECT  104  103  103
CONECT  105  103  133  106
CONECT  106  105  107  123  123
CONECT  107  106  134  108  108
CONECT  108  107  107  109  122
CONECT  109  108  110  114  114
CONECT  110  109  111  111
CONECT  111  110  110  135  112
CONECT  112  111  136  113  113
CONECT  113  112  112  137  114
CONECT  114  109  109  113  115
CONECT  115  114  116  116  121
CONECT  116  115  115  117
CONECT  117  116  118  118  119
CONECT  118  117  117  138  139
CONECT  119  117  120  121
CONECT  120  119  140  141  142
CONECT  121  115  119  122  122
CONECT  122  108  121  121  143
CONECT  123  106  106  124
CONECT  124   99  102  102  123
CONECT  125   96  144  126  127
CONECT  126   98  125  145  146
CONECT  127  125  147
CONECT  128   95
CONECT  129   95
CONECT  130   96
CONECT  131   98
CONECT  132  100
CONECT  133  105
CONECT  134  107
CONECT  135  111
CONECT  136  112
CONECT  137  113
CONECT  138  118
```

```
CONECT  139  118
CONECT  140  120
CONECT  141  120
CONECT  142  120
CONECT  143  122
CONECT  144  125
CONECT  145  126
CONECT  146  126
CONECT  147  127  148  149  150
CONECT  148  147
CONECT  149  147
CONECT  150  147  151
CONECT  151  150  169  170  152
CONECT  152  151  171  153  166
CONECT  153  152  154
CONECT  154  153  172  155  167
CONECT  155  154  156  165
CONECT  156  155  173  157  157
CONECT  157  156  156  158
CONECT  158  157  159  165  165
CONECT  159  158  160  160  161
CONECT  160  159  159
CONECT  161  159  174  162
CONECT  162  161  163  164  164
CONECT  163  162  175  176
CONECT  164  162  162  165
CONECT  165  155  158  158  164
CONECT  166  152  177  167  168
CONECT  167  154  166  178  179
CONECT  168  166
CONECT  169  151
CONECT  170  151
CONECT  171  152
CONECT  172  154
CONECT  173  156
CONECT  174  161
```

```
CONECT  175  163
CONECT  176  163
CONECT  177  166
CONECT  178  167
CONECT  179  167
CONECT  180  181  182  183
CONECT  181  180
CONECT  182  180
CONECT  183  180  184
CONECT  184  183  199  200  185
CONECT  185  184  201  186  196
CONECT  186  185  187
CONECT  187  186  202  188  197
CONECT  188  187  189  194
CONECT  189  188  203  190  190
CONECT  190  189  189  204  191
CONECT  191  190  192  193  193
CONECT  192  191  205  206
CONECT  193  191  191  194
CONECT  194  188  193  195  195
CONECT  195  194  194
CONECT  196  185  207  197  198
CONECT  197  187  196  208  209
CONECT  198  196
CONECT  199  184
CONECT  200  184
CONECT  201  185
CONECT  202  187
CONECT  203  189
CONECT  204  190
CONECT  205  192
CONECT  206  192
CONECT  207  196
CONECT  208  197
CONECT  209  197
CONECT  210  211  212  213
```

```
CONECT  211  210
CONECT  212  210
CONECT  213  210  214
CONECT  214  213  232  233  215
CONECT  215  214  234  216  229
CONECT  216  215  217
CONECT  217  216  235  218  230
CONECT  218  217  219  228
CONECT  219  218  236  220  220
CONECT  220  219  219  221
CONECT  221  220  222  228  228
CONECT  222  221  223  223  224
CONECT  223  222  222
CONECT  224  222  237  225
CONECT  225  224  226  227  227
CONECT  226  225  238  239
CONECT  227  225  225  228
CONECT  228  218  221  221  227
CONECT  229  215  240  230  231
CONECT  230  217  229  241  242
CONECT  231  229
CONECT  232  214
CONECT  233  214
CONECT  234  215
CONECT  235  217
CONECT  236  219
CONECT  237  224
CONECT  238  226
CONECT  239  226
CONECT  240  229
CONECT  241  230
CONECT  242  230
CONECT  243  244  245  246
CONECT  244  243
CONECT  245  243
CONECT  246  243  247
```

```
CONECT  247  246  262  263  248
CONECT  248  247  264  249  259
CONECT  249  248  250
CONECT  250  249  265  251  260
CONECT  251  250  252  257
CONECT  252  251  266  253  253
CONECT  253  252  252  267  254
CONECT  254  253  255  256  256
CONECT  255  254  268  269
CONECT  256  254  254  257
CONECT  257  251  256  258  258
CONECT  258  257  257
CONECT  259  248  270  260  261
CONECT  260  250  259  271  272
CONECT  261  259
CONECT  262  247
CONECT  263  247
CONECT  264  248
CONECT  265  250
CONECT  266  252
CONECT  267  253
CONECT  268  255
CONECT  269  255
CONECT  270  259
CONECT  271  260
CONECT  272  260
CONECT  273  274  275  276
CONECT  274  273
CONECT  275  273
CONECT  276  273  277
CONECT  277  276  292  293  278
CONECT  278  277  294  279  289
CONECT  279  278  280
CONECT  280  279  295  281  290
CONECT  281  280  282  287
CONECT  282  281  296  283  283
```

```
CONECT  283  282  282  297  284
CONECT  284  283  285  286  286
CONECT  285  284  298  299
CONECT  286  284  284  287
CONECT  287  281  286  288  288
CONECT  288  287  287
CONECT  289  278  300  290  291
CONECT  290  280  289  301  302
CONECT  291  289
CONECT  292  277
CONECT  293  277
CONECT  294  278
CONECT  295  280
CONECT  296  282
CONECT  297  283
CONECT  298  285
CONECT  299  285
CONECT  300  289
CONECT  301  290
CONECT  302  290
CONECT  303  304  305  306
CONECT  304  303
CONECT  305  303
CONECT  306  303  307
CONECT  307  306  324  325  308
CONECT  308  307  326  309  321
CONECT  309  308  310
CONECT  310  309  327  311  322
CONECT  311  310  312  320
CONECT  312  311  328  313  313
CONECT  313  312  312  314
CONECT  314  313  315  320  320
CONECT  315  314  316  317  317
CONECT  316  315  329  330
CONECT  317  315  315  318
CONECT  318  317  331  319  319
```

```
CONECT  319  318  318  320
CONECT  320  311  314  314  319
CONECT  321  308  332  322  323
CONECT  322  310  321  333  334
CONECT  323  321
CONECT  324  307
CONECT  325  307
CONECT  326  308
CONECT  327  310
CONECT  328  312
CONECT  329  316
CONECT  330  316
CONECT  331  318
CONECT  332  321
CONECT  333  322
CONECT  334  322
CONECT  335  336  337  338
CONECT  336  335
CONECT  337  335
CONECT  338  335  339
CONECT  339  338  355  356  340
CONECT  340  339  357  341  352
CONECT  341  340  342
CONECT  342  341  358  343  353
CONECT  343  342  344  350
CONECT  344  343  359  345  345
CONECT  345  344  344  346  347
CONECT  346  345  360  361  362
CONECT  347  345  348  348  349
CONECT  348  347  347
CONECT  349  347  363  350
CONECT  350  343  349  351  351
CONECT  351  350  350
CONECT  352  340  364  353  354
CONECT  353  342  352  365  366
CONECT  354  352  367
```

```
CONECT  355  339
CONECT  356  339
CONECT  357  340
CONECT  358  342
CONECT  359  344
CONECT  360  346
CONECT  361  346
CONECT  362  346
CONECT  363  349
CONECT  364  352
CONECT  365  353
CONECT  366  353
CONECT  367  354  368  369  370
CONECT  368  367
CONECT  369  367
CONECT  370  367  371
CONECT  371  370  386  387  372
CONECT  372  371  388  373  383
CONECT  373  372  374
CONECT  374  373  389  375  384
CONECT  375  374  376  381
CONECT  376  375  390  377  377
CONECT  377  376  376  391  378
CONECT  378  377  379  380  380
CONECT  379  378  392  393
CONECT  380  378  378  381
CONECT  381  375  380  382  382
CONECT  382  381  381
CONECT  383  372  394  384  385
CONECT  384  374  383  395  396
CONECT  385  383  397
CONECT  386  371
CONECT  387  371
CONECT  388  372
CONECT  389  374
CONECT  390  376
```

```
CONECT  391  377
CONECT  392  379
CONECT  393  379
CONECT  394  383
CONECT  395  384
CONECT  396  384
CONECT  397  385
CONECT  399  418  400
CONECT  400  399  419  420  401
CONECT  401  400  421  402  415
CONECT  402  401  403
CONECT  403  402  422  404  416
CONECT  404  403  405  414
CONECT  405  404  423  406  406
CONECT  406  405  405  407
CONECT  407  406  408  414  414
CONECT  408  407  409  409  410
CONECT  409  408  408
CONECT  410  408  424  411
CONECT  411  410  412  413  413
CONECT  412  411  425  426
CONECT  413  411  411  414
CONECT  414  404  407  407  413
CONECT  415  401  427  416  417
CONECT  416  403  415  428  429
CONECT  417  415  430
CONECT  418  399
CONECT  419  400
CONECT  420  400
CONECT  421  401
CONECT  422  403
CONECT  423  405
CONECT  424  410
CONECT  425  412
CONECT  426  412
CONECT  427  415
```

```
CONECT  428  416
CONECT  429  416
CONECT  430  417  431  432  433
CONECT  431  430
CONECT  432  430
CONECT  433  430  434
CONECT  434  433  451  452  435
CONECT  435  434  453  436  448
CONECT  436  435  437
CONECT  437  436  454  438  449
CONECT  438  437  439  447
CONECT  439  438  455  440  440
CONECT  440  439  439  441
CONECT  441  440  442  447  447
CONECT  442  441  443  444  444
CONECT  443  442  456  457
CONECT  444  442  442  445
CONECT  445  444  458  446  446
CONECT  446  445  445  447
CONECT  447  438  441  441  446
CONECT  448  435  459  449  450
CONECT  449  437  448  460  461
CONECT  450  448
CONECT  451  434
CONECT  452  434
CONECT  453  435
CONECT  454  437
CONECT  455  439
CONECT  456  443
CONECT  457  443
CONECT  458  445
CONECT  459  448
CONECT  460  449
CONECT  461  449
CONECT  462  463  464  465
CONECT  463  462
```

```
CONECT  464  462
CONECT  465  462  466
CONECT  466  465  482  483  467
CONECT  467  466  484  468  479
CONECT  468  467  469
CONECT  469  468  485  470  480
CONECT  470  469  471  477
CONECT  471  470  486  472  472
CONECT  472  471  471  473  474
CONECT  473  472  487  488  489
CONECT  474  472  475  475  476
CONECT  475  474  474
CONECT  476  474  490  477
CONECT  477  470  476  478  478
CONECT  478  477  477
CONECT  479  467  491  480  481
CONECT  480  469  479  492  493
CONECT  481  479
CONECT  482  466
CONECT  483  466
CONECT  484  467
CONECT  485  469
CONECT  486  471
CONECT  487  473
CONECT  488  473
CONECT  489  473
CONECT  490  476
CONECT  491  479
CONECT  492  480
CONECT  493  480
CONECT  494  495  496  497
CONECT  495  494
CONECT  496  494
CONECT  497  494  498
CONECT  498  497  516  517  499
CONECT  499  498  518  500  513
```

```
CONECT  500  499  501
CONECT  501  500  519  502  514
CONECT  502  501  503  512
CONECT  503  502  520  504  504
CONECT  504  503  503  505
CONECT  505  504  506  512  512
CONECT  506  505  507  507  508
CONECT  507  506  506
CONECT  508  506  521  509
CONECT  509  508  510  511  511
CONECT  510  509  522  523
CONECT  511  509  509  512
CONECT  512  502  505  505  511
CONECT  513  499  524  514  515
CONECT  514  501  513  525  526
CONECT  515  513
CONECT  516  498
CONECT  517  498
CONECT  518  499
CONECT  519  501
CONECT  520  503
CONECT  521  508
CONECT  522  510
CONECT  523  510
CONECT  524  513
CONECT  525  514
CONECT  526  514
CONECT  527  528  529  530
CONECT  528  527
CONECT  529  527
CONECT  530  527  531
CONECT  531  530  549  550  532
CONECT  532  531  551  533  546
CONECT  533  532  534
CONECT  534  533  552  535  547
CONECT  535  534  536  545
```

```
CONECT  536  535  553  537  537
CONECT  537  536  536  538
CONECT  538  537  539  545  545
CONECT  539  538  540  540  541
CONECT  540  539  539
CONECT  541  539  554  542
CONECT  542  541  543  544  544
CONECT  543  542  555  556
CONECT  544  542  542  545
CONECT  545  535  538  538  544
CONECT  546  532  557  547  548
CONECT  547  534  546  558  559
CONECT  548  546
CONECT  549  531
CONECT  550  531
CONECT  551  532
CONECT  552  534
CONECT  553  536
CONECT  554  541
CONECT  555  543
CONECT  556  543
CONECT  557  546
CONECT  558  547
CONECT  559  547
CONECT  560  561  562  563
CONECT  561  560
CONECT  562  560
CONECT  563  560  564
CONECT  564  563  579  580  565
CONECT  565  564  581  566  576
CONECT  566  565  567
CONECT  567  566  582  568  577
CONECT  568  567  569  574
CONECT  569  568  583  570  570
CONECT  570  569  569  584  571
CONECT  571  570  572  573  573
```

```
CONECT  572  571  585  586
CONECT  573  571  571  574
CONECT  574  568  573  575  575
CONECT  575  574  574
CONECT  576  565  587  577  578
CONECT  577  567  576  588  589
CONECT  578  576
CONECT  579  564
CONECT  580  564
CONECT  581  565
CONECT  582  567
CONECT  583  569
CONECT  584  570
CONECT  585  572
CONECT  586  572
CONECT  587  576
CONECT  588  577
CONECT  589  577
CONECT  590  591  592  593
CONECT  591  590
CONECT  592  590
CONECT  593  590  594
CONECT  594  593  612  613  595
CONECT  595  594  614  596  609
CONECT  596  595  597
CONECT  597  596  615  598  610
CONECT  598  597  599  608
CONECT  599  598  616  600  600
CONECT  600  599  599  601
CONECT  601  600  602  608  608
CONECT  602  601  603  603  604
CONECT  603  602  602
CONECT  604  602  617  605
CONECT  605  604  606  607  607
CONECT  606  605  618  619
CONECT  607  605  605  608
```

```
CONECT  608  598  601  601  607
CONECT  609  595  620  610  611
CONECT  610  597  609  621  622
CONECT  611  609
CONECT  612  594
CONECT  613  594
CONECT  614  595
CONECT  615  597
CONECT  616  599
CONECT  617  604
CONECT  618  606
CONECT  619  606
CONECT  620  609
CONECT  621  610
CONECT  622  610
CONECT  623  624  625  626
CONECT  624  623
CONECT  625  623
CONECT  626  623  627
CONECT  627  626  642  643  628
CONECT  628  627  644  629  639
CONECT  629  628  630
CONECT  630  629  645  631  640
CONECT  631  630  632  637
CONECT  632  631  646  633  633
CONECT  633  632  632  647  634
CONECT  634  633  635  636  636
CONECT  635  634  648  649
CONECT  636  634  634  637
CONECT  637  631  636  638  638
CONECT  638  637  637
CONECT  639  628  650  640  641
CONECT  640  630  639  651  652
CONECT  641  639
CONECT  642  627
CONECT  643  627
```

```
CONECT  644  628
CONECT  645  630
CONECT  646  632
CONECT  647  633
CONECT  648  635
CONECT  649  635
CONECT  650  639
CONECT  651  640
CONECT  652  640
CONECT  653  654  655  656
CONECT  654  653
CONECT  655  653
CONECT  656  653  657
CONECT  657  656  672  673  658
CONECT  658  657  674  659  669
CONECT  659  658  660
CONECT  660  659  675  661  670
CONECT  661  660  662  667
CONECT  662  661  676  663  663
CONECT  663  662  662  677  664
CONECT  664  663  665  666  666
CONECT  665  664  678  679
CONECT  666  664  664  667
CONECT  667  661  666  668  668
CONECT  668  667  667
CONECT  669  658  680  670  671
CONECT  670  660  669  681  682
CONECT  671  669
CONECT  672  657
CONECT  673  657
CONECT  674  658
CONECT  675  660
CONECT  676  662
CONECT  677  663
CONECT  678  665
CONECT  679  665
```

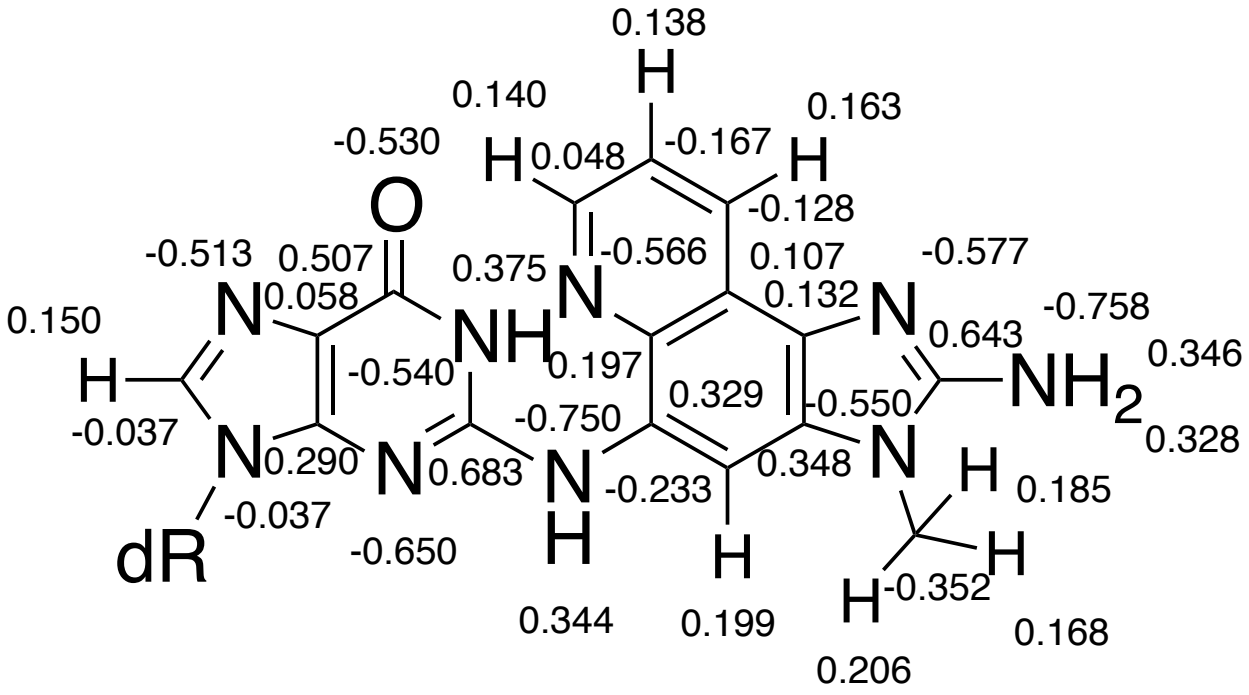
```
CONECT  680  669
CONECT  681  670
CONECT  682  670
CONECT  683  684  685  686
CONECT  684  683
CONECT  685  683
CONECT  686  683  687
CONECT  687  686  705  706  688
CONECT  688  687  707  689  702
CONECT  689  688  690
CONECT  690  689  708  691  703
CONECT  691  690  692  701
CONECT  692  691  709  693  693
CONECT  693  692  692  694
CONECT  694  693  695  701  701
CONECT  695  694  696  696  697
CONECT  696  695  695
CONECT  697  695  710  698
CONECT  698  697  699  700  700
CONECT  699  698  711  712
CONECT  700  698  698  701
CONECT  701  691  694  694  700
CONECT  702  688  713  703  704
CONECT  703  690  702  714  715
CONECT  704  702
CONECT  705  687
CONECT  706  687
CONECT  707  688
CONECT  708  690
CONECT  709  692
CONECT  710  697
CONECT  711  699
CONECT  712  699
CONECT  713  702
CONECT  714  703
CONECT  715  703
```

```
CONECT  716  717  718  719
CONECT  717  716
CONECT  718  716
CONECT  719  716  720
CONECT  720  719  737  738  721
CONECT  721  720  739  722  734
CONECT  722  721  723
CONECT  723  722  740  724  735
CONECT  724  723  725  733
CONECT  725  724  741  726  726
CONECT  726  725  725  727
CONECT  727  726  728  733  733
CONECT  728  727  729  730  730
CONECT  729  728  742  743
CONECT  730  728  728  731
CONECT  731  730  744  732  732
CONECT  732  731  731  733
CONECT  733  724  727  727  732
CONECT  734  721  745  735  736
CONECT  735  723  734  746  747
CONECT  736  734  748
CONECT  737  720
CONECT  738  720
CONECT  739  721
CONECT  740  723
CONECT  741  725
CONECT  742  729
CONECT  743  729
CONECT  744  731
CONECT  745  734
CONECT  746  735
CONECT  747  735
CONECT  748  736  749  750  751
CONECT  749  748
CONECT  750  748
CONECT  751  748  752
```

```
CONECT  752  751  770  771  753
CONECT  753  752  772  754  767
CONECT  754  753  755
CONECT  755  754  773  756  768
CONECT  756  755  757  766
CONECT  757  756  774  758  758
CONECT  758  757  757  759
CONECT  759  758  760  766  766
CONECT  760  759  761  761  762
CONECT  761  760  760
CONECT  762  760  775  763
CONECT  763  762  764  765  765
CONECT  764  763  776  777
CONECT  765  763  763  766
CONECT  766  756  759  759  765
CONECT  767  753  778  768  769
CONECT  768  755  767  779  780
CONECT  769  767  781
CONECT  770  752
CONECT  771  752
CONECT  772  753
CONECT  773  755
CONECT  774  757
CONECT  775  762
CONECT  776  764
CONECT  777  764
CONECT  778  767
CONECT  779  768
CONECT  780  768
CONECT  781  769
END
```

**APPENDIX C**

**PARTIAL CHARGES FOR MODIFIED BASE**



## APPENDIX D

## CHEMICAL SHIFTS

### Nonexchangeable protons for IQ modified duplex at $G^3$

| | H1' | H2' | H2'' | H3' | H8/H6 | H5/H2 |
|---|---|---|---|---|---|---|
| $C^1$ | 5.72 | 2.10 | 2.43 | 4.49 | 7.73 | 5.78 |
| $T^2$ | 5.96 | 2.39 | 2.05 | 4.49 | 7.45 | 1.51 |
| $C^3$ | 5.45 | 2.21 | 1.86 | 4.64 | 7.25 | 5.44 |
| $G^4$ | 5.40 | 2.56 | 2.52 | 4.85 | 7.67 | |
| $G^5$ | 5.70 | 2.35 | 2.51 | 4.82 | 7.55 | |
| $C^6$ | 5.78 | 1.48 | 2.21 | 4.64 | 6.85 | 4.98 |
| $X^7$ | 5.96 | 2.65 | 2.45 | 4.88 | 8.04 | |
| $C^8$ | 5.48 | 2.23 | 1.76 | 4.41 | 7.40 | 5.05 |
| $C^9$ | 5.20 | 2.23 | 1.95 | 4.66 | 7.21 | 5.31 |
| $A^{10}$ | 6.11 | 2.56 | 2.77 | 4.87 | 8.13 | 7.52 |
| $T^{11}$ | 5.84 | 2.29 | 1.87 | 4.88 | 7.00 | 1.32 |
| $C^{12}$ | 6.09 | 2.06 | 2.09 | 4.41 | 7.40 | 5.58 |
| $G^{13}$ | 5.47 | 2.56 | 2.41 | 4.67 | 7.70 | |
| $A^{14}$ | 6.12 | 2.77 | 2.57 | 4.88 | 8.11 | 7.74 |
| $T^{15}$ | 5.52 | 2.17 | 1.75 | 4.64 | 6.87 | 1.14 |
| $G^{16}$ | 5.42 | 2.50 | 2.55 | 4.85 | 7.59 | |
| $G^{17}$ | 5.76 | 2.37 | 2.45 | 4.94 | 7.46 | |
| $C^{18}$ | 6.29 | 2.61 | 2.11 | 4.88 | 7.98 | 6.08 |
| $G^{19}$ | 5.28 | 2.05 | 2.42 | 4.42 | 7.18 | |
| $C^{20}$ | 5.72 | 2.23 | 1.87 | 4.64 | 7.04 | 4.93 |
| $C^{21}$ | 5.26 | 2.11 | 1.76 | 4.63 | 7.15 | 5.35 |
| $G^{22}$ | 5.27 | 2.58 | 2.53 | 4.83 | 7.70 | |
| $A^{23}$ | 5.97 | 2.76 | 2.51 | 4.87 | 7.91 | 7.62 |
| $G^{24}$ | 5.83 | 2.08 | 2.22 | 4.45 | 7.44 | |

**Exchangeable protons for IQ modified duplex at $G^3$**

| | N1H/N3H | H4a | H4b |
|---|---|---|---|
| $C^1$•$G^{24}$ | 13.37 | 7.21 | 7.79 |
| $T^2$•$A^{23}$ | 14.02 | | |
| $C^3$•$G^{22}$ | 12.90 | 7.04 | 8.61 |
| $G^4$•$C^{21}$ | 13.05 | 6.81 | 8.53 |
| $G^5$•$C^{20}$ | 12.89 | 6.29 | 8.14 |
| $C^6$•$G^{19}$ | 12.52 | 6.66 | 8.30 |
| $X^7$•$C^{18}$ | 11.56 | | |
| $C^8$•$G^{17}$ | 11.59 | 6.05 | 7.89 |
| $C^9$•$G^{16}$ | 12.58 | 6.68 | 8.30 |
| $A^{10}$•$T^{15}$ | 13.52 | | |
| $T^{11}$•$A^{14}$ | 13.72 | | |
| $C^{12}$•$G^{13}$ | 12.61 | 7.11 | 8.19 |

## Chemical Shifts for IQ ring for $G^3$ modified base

| IQ Proton | δ (ppm) |
|---|---|
| H4a | 8.37 |
| H7a | 7.48 |
| H8a | 6.33 |
| H9a | 7.36 |
| CH3 | 3.35 |

## Nonexchangeable Protons for IQ modified duplex at G[1]

| | H1' | H2' | H2'' | H3' | H6/H8 | H2/H5 |
|---|---|---|---|---|---|---|
| $C^{1}$ | 5.90 | 2.32 | 2.63 | 4.70 | 7.93 | 6.01 |
| $T^{2}$ | 6.18 | 2.28 | 2.61 | 4.94 | 7.71 | 1.76 |
| $C^{3}$ | 6.10 | 1.76 | 2.39 | 4.94 | 7.39 | 5.63 |
| $G^{4}$ | 6.26 | 2.91 | 2.77 | 5.12 | 8.30 | |
| $G^{5}$ | 5.81 | 2.562 | 2.72 | 5.03 | 7.98 | |
| $C^{6}$ | 5.62 | 2.01 | 2.38 | 4.98 | 7.22 | 5.17 |
| $G^{7}$ | 5.87 | 2.64 | 2.72 | 5.00 | 7.86 | |
| $C^{8}$ | 5.93 | 2.08 | 2.46 | 4.82 | 7.35 | 5.32 |
| $C^{9}$ | 5.44 | 2.17 | 2.43 | 4.94 | 7.52 | 5.62 |
| $A^{10}$ | 6.32 | 2.74 | 2.97 | 5.05 | 8.38 | 7.78 |
| $T^{11}$ | 6.04 | 2.07 | 2.48 | 5.04 | 7.25 | 1.53 |
| $C^{12}$ | 6.30 | 2.28 | 2.29 | 4.60 | 7.65 | 5.80 |
| $G^{13}$ | 5.69 | 2.61 | 2.78 | | 7.95 | |
| $A^{14}$ | 6.34 | 2.78 | 2.99 | 5.08 | 8.37 | 8.00 |
| $T^{15}$ | 5.73 | 1.97 | 2.36 | 5.08 | 7.14 | 1.39 |
| $G^{16}$ | 5.64 | 2.65 | 2.73 | 5.00 | 7.81 | |
| $G^{17}$ | 5.85 | 2.68 | 2.68 | 2.54 | 7.72 | |
| $C^{18}$ | 5.65 | 1.95 | 2.37 | 4.83 | 7.22 | 5.20 |
| $G^{19}$ | 5.89 | 2.63 | 2.74 | 5.02 | 7.86 | |
| $C^{20}$ | 6.02 | 2.17 | 2.50 | 5.00 | 7.10 | 5.36 |
| $C^{21}$ | 6.61 | 2.43 | 2.71 | 5.11 | 8.17 | 6.31 |
| $G^{22}$ | 5.22 | 2.05 | 2.44 | 4.93 | 7.52 | |
| $A^{23}$ | 6.02 | 2.65 | 2.89 | 5.01 | 8.05 | 7.82 |
| $G^{24}$ | 6.01 | 2.27 | 2.40 | 4.63 | 7.63 | |

**Exchangeable protons for IQ modified duplex at G[1]**

| | N1H/N3H | H4a | H4b |
|---|---|---|---|
| $C^{1}$•$G^{24}$ | 13.35 | 7.24 | 7.76 |
| $T^{2}$•$A^{23}$ | 14.06 | | |
| $C^{3}$•$G^{22}$ | 12.41 | 7.23 | 8.65 |
| $X^{4}$•$C^{21}$ | 11.79 | | |
| $G^{5}$•$C^{20}$ | 11.53 | 6.55 | 7.93 |
| $C^{6}$•$G^{19}$ | 12.74 | 6.32 | 8.18 |
| $G^{7}$•$C^{18}$ | 11.56 | 6.31 | 7.71 |
| $C^{8}$•$G^{17}$ | 12.88 | 6.32 | 8.14 |
| $C^{9}$•$G^{16}$ | 12.81 | 6.83 | 8.50 |
| $A^{10}$•$T^{15}$ | 13.61 | | |
| $T^{11}$•$A^{14}$ | 13.79 | | |
| $C^{12}$•$G^{13}$ | 12.65 | 7.14 | 8.22 |

## Chemical Shifts for IQ modified G[1]

| IQ Proton | δ (ppm) |
|---|---|
| H4a | 8.568 |
| H7a | 8.114 |
| H8a | 6.877 |
| H9a | 7.744 |
| $CH_3$ | 3.233 |

## APPENDIX E

## DISTANCE RESTRAINTS FILES

### IQ at $G^3$

```
#
#   7 DKA H2    6 DC  H42   3.930   4.780
 &rst
  ixpk= 0, nxpk= 0, iat= 210, 177, r1= 3.43, r2= 3.93, r3= 4.78, r4= 5.28,
     rk2=20.0, rk3=20.0, ir6=1, ialtd=0,
 &end
#
#   7 DKA H2    6 DC  H41   4.520   6.300
 &rst
  ixpk= 0, nxpk= 0, iat= 210, 176, r1= 4.02, r2= 4.52, r3= 6.30, r4= 6.80,  &end
#
#   7 DKA H20   7 DKA H2                4.160   5.270   (#165 4.660   6.270  )
 &rst
  ixpk= 4, nxpk= 0, iat= 215, 210, r1= 3.66, r2= 4.16, r3= 5.27, r4= 5.77,  &end
#
#   7 DKA H11   7 DKA H2                3.710   5.770   (#4.310   5.770  )
 &rst
  ixpk= 5, nxpk= 0, iat= 234, 210, r1= 3.21, r2= 3.71, r3= 5.77, r4= 6.27,  &end
#
#   1 DC5 H2'2   1 DC5 H1'   1.780   3.050      (#op 6,13,17,54  1.680   2.250)
 &rst
  ixpk= 6, nxpk= 0, iat=  27,  10, r1= 1.28, r2= 1.78, r3= 3.05, r4= 3.55,  &end
#
#   1 DC5 H2'1   1 DC5 H1'   2.030   2.530
 &rst
  ixpk= 6, nxpk= 0, iat=  26,  10, r1= 1.53, r2= 2.03, r3= 2.53, r4= 3.03,  &end
#
#   1 DC5 H3'    1 DC5 H2'2  2.340   4.640    (#59  2.440   4.640   )
 &rst
  ixpk= 2, nxpk= 0, iat=  24,  27, r1= 1.84, r2= 2.34, r3= 4.64, r4= 5.14,  &end
#
#   1 DC5 H3'    1 DC5 H2'1  2.130   2.750    (#42,74  2.130   2.550  )
 &rst
  ixpk= 2, nxpk= 0, iat=  24,  26, r1= 1.63, r2= 2.13, r3= 2.75, r4= 3.25,  &end
#
#   1 DC5 H5'1   1 DC5 H1'   3.170   5.720
 &rst
  ixpk= 2, nxpk= 0, iat=   4,  10, r1= 2.67, r2= 3.17, r3= 5.72, r4= 6.22,  &end
#
#   1 DC5 H5'2   1 DC5 H1'   3.680   5.700
 &rst
  ixpk= 2, nxpk= 0, iat=   5,  10, r1= 3.18, r2= 3.68, r3= 5.70, r4= 6.20,  &end
#
#   1 DC5 H6    1 DC5 H1'   2.340   3.880
 &rst
  ixpk= 2, nxpk= 0, iat=  13,  10, r1= 1.84, r2= 2.34, r3= 3.88, r4= 4.38,  &end
#
#   1 DC5 H6    1 DC5 H2'2  1.850   2.910
```

```
 &rst
  ixpk= 2, nxpk= 0, iat=  13,  27, r1= 1.35, r2= 1.85, r3= 2.91, r4= 3.41,  &end
#
#   1 DC5 H6    1 DC5 H2'1  2.120   4.030    (#61,85,105  2.120   3.730  )
 &rst
  ixpk= 2, nxpk= 0, iat=  13,  26, r1= 1.62, r2= 2.12, r3= 4.03, r4= 4.53,  &end
#
#   1 DC5 H6    1 DC5 H3'   3.260   5.610
 &rst
  ixpk= 2, nxpk= 0, iat=  13,  24, r1= 2.76, r2= 3.26, r3= 5.61, r4= 6.11,  &end
#
#   1 DC5 H6    1 DC5 H5'1  2.460   3.110   (#132  2.460   3.010    )
 &rst
  ixpk= 2, nxpk= 0, iat=  13,   4, r1= 1.96, r2= 2.46, r3= 3.11, r4= 3.61,  &end
#
#   1 DC5 H6    1 DC5 H5'2  2.830   4.320
 &rst
  ixpk= 2, nxpk= 0, iat=  13,   5, r1= 2.33, r2= 2.83, r3= 4.32, r4= 4.82,  &end
#
#   1 DC5 H5    1 DC5 H3'   3.450   6.380   (#90,94,112  3.450   6.080   )
 &rst
  ixpk= 3, nxpk= 0, iat=  15,  24, r1= 2.95, r2= 3.45, r3= 6.38, r4= 6.88,  &end
#
#   1 DC5 H5    1 DC5 H5'2  3.670   6.470   (#63,72,91,126,141  3.670   5.970    )
 &rst
  ixpk= 3, nxpk= 0, iat=  15,   5, r1= 3.17, r2= 3.67, r3= 6.47, r4= 6.97,  &end
#
#   2 DT  H2'2   2 DT  H1'   2.840   4.760
 &rst
  ixpk= 3, nxpk= 0, iat=  59,  40, r1= 2.34, r2= 2.84, r3= 4.76, r4= 5.26,  &end
#
#   2 DT  H2'1   2 DT  H1'   2.130   2.940
 &rst
  ixpk= 3, nxpk= 0, iat=  58,  40, r1= 1.63, r2= 2.13, r3= 2.94, r4= 3.44,  &end
#
#   2 DT  H6    1 DC5 H1'   3.580   4.670
 &rst
  ixpk= 3, nxpk= 0, iat=  43,  10, r1= 3.08, r2= 3.58, r3= 4.67, r4= 5.17,  &end
#
#   2 DT  H6    2 DT  H3'   3.080   4.550   (#op 58,76,83,100 3.080   3.850 )
 &rst
  ixpk= 58, nxpk= 0, iat=  43,  56, r1= 2.58, r2= 3.08, r3= 4.55, r4= 5.05,  &end
#
#   2 DT  H6    2 DT  H1'   2.030   3.680    (#21,71,92  2.030   2.580  (*3.780))
 &rst
  ixpk= 2, nxpk= 0, iat=  43,  40, r1= 1.53, r2= 2.03, r3= 3.68, r4= 4.18,  &end
#
#   2 DT  Q5    1 DC5 H1'   2.690   5.260
 &rst
  ixpk= 2, nxpk= 0, iat=  -1,  10, r1= 2.19, r2= 2.69, r3= 6.32, r4= 6.82,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H2'2  2.680   4.410   (#64,68,82,88,97  3.280   4.410    )
 &rst
```

```
 ixpk= 3, nxpk= 0, iat=  -1,  27, r1= 2.18, r2= 2.68, r3= 5.30, r4= 5.80,
igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H3'   3.050   3.970    (#104,114,123  3.050   3.770(*4.770)   )
 &rst
 ixpk= 3, nxpk= 0, iat=  -1,  24, r1= 2.55, r2= 3.05, r3= 4.77, r4= 5.27,
igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H6    2.420   4.020
 &rst
 ixpk= 3, nxpk= 0, iat=  -1,  13, r1= 1.92, r2= 2.42, r3= 4.83, r4= 5.33,
igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H5    2.610   5.980
 &rst
 ixpk= 3, nxpk= 0, iat=  -1,  15, r1= 2.11, r2= 2.61, r3= 7.18, r4= 7.68,
igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    2 DT  H2'2  2.280   4.060    (#78,86,91,105  2.280   3.660  )
 &rst
 ixpk= 2, nxpk= 0, iat=  -1,  59, r1= 1.78, r2= 2.28, r3= 4.88, r4= 5.38,
igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    2 DT  H6    2.700   5.690    (#18,26,52,79  3.200   5.690 )
 &rst
 ixpk= 3, nxpk= 0, iat=  -1,  43, r1= 2.20, r2= 2.70, r3= 6.83, r4= 7.33,
igr1=  46,  47,  48,
 &end
#
#   3 DC  H2'2   3 DC  H1'   1.740   3.080    (#op 7,15,23,28,55,117  1.740   2.380)
 &rst
 ixpk= 7, nxpk= 0, iat=  89,  72, r1= 1.24, r2= 1.74, r3= 3.08, r4= 3.58,  &end
#
#   3 DC  H2'1   3 DC  H1'   1.980   2.580
(#3 DC  H2'1   2 DT  H2'2  1.950   2.540     near diagonal)
 &rst
 ixpk= 7, nxpk= 0, iat=  88,  72, r1= 1.48, r2= 1.98, r3= 2.58, r4= 3.08,  &end
#
#   3 DC  H6    2 DT  H1'   3.070   5.200
 &rst
 ixpk= 7, nxpk= 0, iat=  75,  40, r1= 2.57, r2= 3.07, r3= 5.20, r4= 5.70,  &end
#
#   3 DC  H6    2 DT  H2'2  2.150   3.780
 &rst
 ixpk= 7, nxpk= 0, iat=  75,  59, r1= 1.65, r2= 2.15, r3= 3.78, r4= 4.28,  &end
#
#   3 DC  H6    2 DT  H2'1  2.250   5.520    (#87,121  2.450   5.520  )
 &rst
 ixpk= 2, nxpk= 0, iat=  75,  58, r1= 1.75, r2= 2.25, r3= 5.52, r4= 6.02,  &end
#
```

```
#   3 DC  H6    2 DT  H6    3.240   5.300    (#60,69  3.240   5.100   )
 &rst
  ixpk= 3, nxpk= 0, iat=  75,  43, r1= 2.74, r2= 3.24, r3= 5.30, r4= 5.80,  &end
#
#   3 DC  H6    3 DC  H1'   2.980   3.780   (#op 1,2,10,13,54,92   1.780   2.680 ci)
 &rst
  ixpk= 1, nxpk= 0, iat=  75,  72, r1= 2.48, r2= 2.98, r3= 3.78, r4= 4.28,  &end
#
#   3 DC  H6    3 DC  H2'2  2.170   3.180    (#op 56  2.270   3.180   )
 &rst
  ixpk= 56, nxpk= 0, iat=  75,  89, r1= 1.67, r2= 2.17, r3= 3.18, r4= 3.68,  &end
#
#   3 DC  H6    3 DC  H2'1  2.290   3.730    (#45,53,98,129  2.290   3.330   )
 &rst
  ixpk= 2, nxpk= 0, iat=  75,  88, r1= 1.79, r2= 2.29, r3= 3.73, r4= 4.23,  &end
#
#   3 DC  H5    2 DT  H1'   3.910   5.690
 &rst
  ixpk= 2, nxpk= 0, iat=  77,  40, r1= 3.41, r2= 3.91, r3= 5.69, r4= 6.19,  &end
#
#   3 DC  H5    2 DT  H2'1  2.910   4.380
 &rst
  ixpk= 2, nxpk= 0, iat=  77,  58, r1= 2.41, r2= 2.91, r3= 4.38, r4= 4.88,  &end
#
#   3 DC  H5    2 DT  H6    3.720   5.960
 &rst
  ixpk= 2, nxpk= 0, iat=  77,  43, r1= 3.22, r2= 3.72, r3= 5.96, r4= 6.46,  &end
#
#   3 DC  H5    2 DT  Q5    3.220   4.540
 &rst
  ixpk= 2, nxpk= 0, iat=  77,  -1, r1= 2.72, r2= 3.22, r3= 5.45, r4= 5.95,
 igr2=  46,  47,  48,
 &end
#
#   8 DC  H1'   8 DC  H2'1  2.330   2.960      (#op)
 &rst
  ixpk= 2, nxpk= 0, iat= 254, 270, r1= 1.83, r2= 2.33, r3= 2.96, r4= 3.46,  &end
#
#   4 DG  H3'   3 DC  H2'1  3.280   4.230    (#65,100  3.280   4.030   )
 &rst
  ixpk= 3, nxpk= 0, iat= 119,  88, r1= 2.78, r2= 3.28, r3= 4.23, r4= 4.73,  &end
#
#   4 DG  H3'   4 DG  H1'   2.780   4.400
 &rst
  ixpk= 3, nxpk= 0, iat= 119, 102, r1= 2.28, r2= 2.78, r3= 4.40, r4= 4.90,  &end
#
#   4 DG  H8    3 DC  H1'   2.820   4.380   (#op 57,73,75,76,82,103  2.520   3.780 )
 &rst
  ixpk= 57, nxpk= 0, iat= 105,  72, r1= 2.32, r2= 2.82, r3= 4.38, r4= 4.88,  &end
#
#   4 DG  H8    3 DC  H2'2  2.810   3.450
 &rst
  ixpk= 57, nxpk= 0, iat= 105,  89, r1= 2.31, r2= 2.81, r3= 3.45, r4= 3.95,  &end
#
#   4 DG  H8    3 DC  H2'1  2.820   4.160   (#93,126,138  3.120   4.160    )
```

```
 &rst
  ixpk= 3, nxpk= 0, iat= 105,  88, r1= 2.32, r2= 2.82, r3= 4.16, r4= 4.66,  &end
#
#   4 DG  H8    4 DG  H1'   2.760   4.050
 &rst
  ixpk= 3, nxpk= 0, iat= 105, 102, r1= 2.26, r2= 2.76, r3= 4.05, r4= 4.55,  &end
#
#   4 DG  H8    4 DG  H3'   3.000   5.740
 &rst
  ixpk= 3, nxpk= 0, iat= 105, 119, r1= 2.50, r2= 3.00, r3= 5.74, r4= 6.24,  &end
#
#   4 DG  H8    4 DG  H4'   4.510   5.450   (#14,19,58,62,74  3.310   4.350  ci)
 &rst
  ixpk= 3, nxpk= 0, iat= 105,  99, r1= 4.01, r2= 4.51, r3= 5.45, r4= 5.95,  &end
#
#   4 DG  H8    4 DG  H5'1  4.080   6.300
 &rst
  ixpk= 3, nxpk= 0, iat= 105,  96, r1= 3.58, r2= 4.08, r3= 6.30, r4= 6.80,  &end
#
#   4 DG  H8    4 DG  H5'2  3.370   4.220
 &rst
  ixpk= 3, nxpk= 0, iat= 105,  97, r1= 2.87, r2= 3.37, r3= 4.22, r4= 4.72,  &end
#
#   5 DG  H2'2   5 DC  H1'   2.080   3.070   (#op 52,81,117  2.080   2.770    )
 &rst
  ixpk= 52, nxpk= 0, iat= 155, 135, r1= 1.58, r2= 2.08, r3= 3.07, r4= 3.57,  &end
#
#   5 DG  H2'1   5 DC  H1'   2.180   3.410
 &rst
  ixpk= 52, nxpk= 0, iat= 154, 135, r1= 1.68, r2= 2.18, r3= 3.41, r4= 3.91,  &end
#
#   5 DG  H3'    5 DC  H1'   3.320   5.460
 &rst
  ixpk= 52, nxpk= 0, iat= 152, 135, r1= 2.82, r2= 3.32, r3= 5.46, r4= 5.96,  &end
#
#   5 DG  H3'    5 DG  H2'1  2.440   3.140
 &rst
  ixpk= 52, nxpk= 0, iat= 152, 154, r1= 1.94, r2= 2.44, r3= 3.14, r4= 3.64,  &end
#
#   5 DG  H8    4 DG  H1'   2.590   3.560   (#66,133  2.590   3.360   )
 &rst
  ixpk= 2, nxpk= 0, iat= 138, 102, r1= 2.09, r2= 2.59, r3= 3.56, r4= 4.06,  &end
#
#   5 DG  H8    4 DG  H3'   3.680   6.720
 &rst
  ixpk= 2, nxpk= 0, iat= 138, 119, r1= 3.18, r2= 3.68, r3= 6.72, r4= 7.22,  &end
#
#   5 DG  H8    5 DG  H1'   2.870   4.060
 &rst
  ixpk= 2, nxpk= 0, iat= 138, 135, r1= 2.37, r2= 2.87, r3= 4.06, r4= 4.56,  &end
#
#   5 DG  H8    5 DG  H2'1  2.110   3.870   (#1,13,18,27,34,49,61,90 2.110   2.570   )
 &rst
  ixpk= 2, nxpk= 0, iat= 138, 154, r1= 1.61, r2= 2.11, r3= 3.87, r4= 4.37,  &end
#
```

```
#   5 DG  H8    5 DG  H3'   3.430   5.560
 &rst
  ixpk= 2, nxpk= 0, iat= 138, 152, r1= 2.93, r2= 3.43, r3= 5.56, r4= 6.06,  &end
#
#   6 DC  H2'2   6 DC  H1'   2.140   3.010     (#16,69  2.140   2.610 )
 &rst
  ixpk= 2, nxpk= 0, iat= 185, 168, r1= 1.64, r2= 2.14, r3= 3.01, r4= 3.51,  &end
#
#   6 DC  H2'1   6 DC  H1'   2.360   3.820    (#30,52,57  2.660   3.820   )
 &rst
  ixpk= 2, nxpk= 0, iat= 184, 168, r1= 1.86, r2= 2.36, r3= 3.82, r4= 4.32,  &end
#
#   6 DC  H3'    6 DC  H2'1  2.780   4.000
 (#21 DC  H3'   20 DC  H2'1  1.830   2.860   #wa,op? 166,167 1.830   2.560   )
 &rst
  ixpk= 2, nxpk= 0, iat= 182, 184, r1= 2.28, r2= 2.78, r3= 4.00, r4= 4.50,  &end
#
#   6 DC  H6    5 DG  H1'   2.820   4.160    (#17,31,40,48,139  2.820   3.560  )
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 135, r1= 2.32, r2= 2.82, r3= 4.16, r4= 4.66,  &end
#
#   6 DC  H6    5 DG  H2'2  2.300   3.350    (#op 53,83  2.300   3.050   )
 &rst
  ixpk= 53, nxpk= 0, iat= 171, 155, r1= 1.80, r2= 2.30, r3= 3.35, r4= 3.85,  &end
#
#   6 DC  H6    5 DG  H2'1  2.350   4.300   (#op 2,6,9,11,15,26,78,97 3.350   4.900)
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 154, r1= 1.85, r2= 2.35, r3= 4.30, r4= 4.80,  &end
#
#   6 DC  H6    5 DG  H3'   4.870   6.720
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 152, r1= 4.37, r2= 4.87, r3= 6.72, r4= 7.22,  &end
#
#   6 DC  H6    5 DG  H8    3.640   4.600    (#62,119  3.640   4.400  )
 &rst
  ixpk= 3, nxpk= 0, iat= 171, 138, r1= 3.14, r2= 3.64, r3= 4.60, r4= 5.10,  &end
#
#   6 DC  H6    6 DC  H1'   2.930   3.720    (#28,54,63,72  2.930   3.320   )
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 168, r1= 2.43, r2= 2.93, r3= 3.72, r4= 4.22,  &end
#
#   6 DC  H6    6 DC  H2'2  2.050   3.460    (#op 29,32,60  2.350   3.460  )
 &rst
  ixpk= 29, nxpk= 0, iat= 171, 185, r1= 1.55, r2= 2.05, r3= 3.46, r4= 3.96,  &end
#
#   6 DC  H6    6 DC  H2'1  2.330   3.750    (#51,55,64,77,81,93  2.330   2.850)
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 184, r1= 1.83, r2= 2.33, r3= 3.75, r4= 4.25,  &end
#
#   6 DC  H6    6 DC  H3'   3.680   6.060
 &rst
  ixpk= 2, nxpk= 0, iat= 171, 182, r1= 3.18, r2= 3.68, r3= 6.06, r4= 6.56,  &end
#
#   6 DC  H5    5 DG  H1'   3.690   5.010
 &rst
```

```
 ixpk= 2, nxpk= 0, iat= 173, 135, r1= 3.19, r2= 3.69, r3= 5.01, r4= 5.51,  &end
#
#   6 DC  H5    5 DG  H2'2  2.890   3.940
 &rst
 ixpk= 2, nxpk= 0, iat= 173, 155, r1= 2.39, r2= 2.89, r3= 3.94, r4= 4.44,  &end
#
#   6 DC  H5    5 DG  H2'1  2.840   3.750   (#OP 96  2.840   3.750   )
 &rst
 ixpk= 96, nxpk= 0, iat= 173, 154, r1= 2.34, r2= 2.84, r3= 3.75, r4= 4.25,  &end
#
#   6 DC  H5    5 DG  H8    3.370   4.000
 &rst
 ixpk= 96, nxpk= 0, iat= 173, 138, r1= 2.87, r2= 3.37, r3= 4.00, r4= 4.50,  &end
#
#   6 DC  H5    6 DC  H2'2  3.350   4.500
 &rst
 ixpk= 96, nxpk= 0, iat= 173, 185, r1= 2.85, r2= 3.35, r3= 4.50, r4= 5.00,  &end
#
#   7 DKA H1'   6 DC  H2'2  4.870   5.870    (#wp 33,34  4.870   5.670   )
 &rst
 ixpk= 33, nxpk= 0, iat= 198, 185, r1= 4.37, r2= 4.87, r3= 5.87, r4= 6.37,  &end
#
#   7 DKA H2'2   7 DKA H1'   3.060   3.900    (#op 37  3.160   3.900   )
 &rst
 ixpk= 37, nxpk= 0, iat= 241, 198, r1= 2.56, r2= 3.06, r3= 3.90, r4= 4.40,  &end
#
#   7 DKA H2'1   7 DKA H1'   2.300   4.020      (#6,12,13,27,38,57,70 3.300   4.120)
 &rst
 ixpk= 3, nxpk= 0, iat= 240, 198, r1= 1.80, r2= 2.30, r3= 4.02, r4= 4.52,  &end
#
#   7 DKA H3'   7 DKA H1'   3.310   3.990
(#7 DKA H2'1   7 DKA H2'2  2.240   2.680     near diagonal)
 &rst
 ixpk= 3, nxpk= 0, iat= 238, 198, r1= 2.81, r2= 3.31, r3= 3.99, r4= 4.49,  &end
#
#   7 DKA H8    6 DC  H1'   3.430   5.120    (#19,45,56,59,68,73,76  3.330   3.720  )
 &rst
 ixpk= 3, nxpk= 0, iat= 201, 168, r1= 2.93, r2= 3.43, r3= 5.12, r4= 5.62,  &end
#
#   7 DKA H8    6 DC  H2'2  2.730   3.810    (#1,10,35  2.730   3.210   )
 &rst
 ixpk= 2, nxpk= 0, iat= 201, 185, r1= 2.23, r2= 2.73, r3= 3.81, r4= 4.31,  &end
#
#   7 DKA H8    6 DC  H2'1  2.670   3.800    (#7,17,18 3.070   3.800  )
 &rst
 ixpk= 3, nxpk= 0, iat= 201, 184, r1= 2.17, r2= 2.67, r3= 3.80, r4= 4.30,  &end
#
#   7 DKA H8    6 DC  H3'   4.040   6.290
 &rst
 ixpk= 3, nxpk= 0, iat= 201, 182, r1= 3.54, r2= 4.04, r3= 6.29, r4= 6.79,  &end
#
#   7 DKA H8    6 DC  H6    3.900   4.770
 &rst
 ixpk= 3, nxpk= 0, iat= 201, 171, r1= 3.40, r2= 3.90, r3= 4.77, r4= 5.27,  &end
#
```

```
#   7 DKA H8    7 DKA H1'   3.690   4.190
 &rst
  ixpk= 3, nxpk= 0, iat= 201, 198, r1= 3.19, r2= 3.69, r3= 4.19, r4= 4.69,  &end
#
#   7 DKA H8    7 DKA H2'2  2.290   3.630    (#2,66,79,93,106  2.690   3.430)
 &rst
  ixpk= 2, nxpk= 0, iat= 201, 241, r1= 1.79, r2= 2.29, r3= 3.63, r4= 4.13,  &end
#
#   7 DKA H8    7 DKA H3'   3.260   6.180
 &rst
  ixpk= 2, nxpk= 0, iat= 201, 238, r1= 2.76, r2= 3.26, r3= 6.18, r4= 6.68,  &end
#
#   7 DKA H8    7 DKA H4'   4.100   6.350
 &rst
  ixpk= 2, nxpk= 0, iat= 201, 195, r1= 3.60, r2= 4.10, r3= 6.35, r4= 6.85,  &end
#
#   7 DKA H19   7 DKA H18   2.170   2.730
 &rst
  ixpk= 2, nxpk= 0, iat= 217, 219, r1= 1.67, r2= 2.17, r3= 2.73, r4= 3.23,  &end
#
#   7 DKA H20   7 DKA H19   2.210   2.510
 &rst
  ixpk= 2, nxpk= 0, iat= 215, 217, r1= 1.71, r2= 2.21, r3= 2.51, r4= 3.01,  &end
#
#   7 DKA Q13   7 DKA H1'   3.720   4.190
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 198, r1= 3.22, r2= 3.72, r3= 5.03, r4= 5.53,
 igr1= 229, 230, 231,
 &end
#
#   7 DKA H11   7 DKA H1'   2.960   4.110     (#2,8,21,45,61 3.660   4.110 )
 &rst
  ixpk= 3, nxpk= 0, iat= 234, 198, r1= 2.46, r2= 2.96, r3= 4.11, r4= 4.61,  &end
#
#   7 DKA H11   7 DKA H2'1  4.130   6.740
 &rst
  ixpk= 3, nxpk= 0, iat= 234, 240, r1= 3.63, r2= 4.13, r3= 6.74, r4= 7.24,  &end
#
#   7 DKA H11   7 DKA H2'2  3.860   5.740   (#85,97,103,122  3.860   5.240   )
 &rst
  ixpk= 3, nxpk= 0, iat= 234, 241, r1= 3.36, r2= 3.86, r3= 5.74, r4= 6.24,  &end
#
#   7 DKA H11   7 DKA H5'1  4.820   6.540
 &rst
  ixpk= 3, nxpk= 0, iat= 234, 192, r1= 4.32, r2= 4.82, r3= 6.54, r4= 7.04,  &end
#
#   7 DKA H11   7 DKA H4'   3.580   4.450    (#25,28,31,35,41  3.580   4.250  )
 &rst
  ixpk= 3, nxpk= 0, iat= 234, 195, r1= 3.08, r2= 3.58, r3= 4.45, r4= 4.95,  &end
#
#   7 DKA H11   7 DKA Q13   2.290   3.020
 &rst
  ixpk= 3, nxpk= 0, iat= 234,  -1, r1= 1.79, r2= 2.29, r3= 3.63, r4= 4.13,
 igr2= 229, 230, 231,
 &end
```

```
#
#   8 DC  H1'    7 DKA Q13   2.810   4.360
 &rst
  ixpk= 3, nxpk= 0, iat= 254,  -1, r1= 2.31, r2= 2.81, r3= 5.24, r4= 5.74,
 igr2= 229, 230, 231,
 &end
#
#   8 DC  H2'1   8 DC  H1'   2.280   3.720    (#op 54  2.380   3.720   )
 &rst
  ixpk= 54, nxpk= 0, iat= 270, 254, r1= 1.78, r2= 2.28, r3= 3.72, r4= 4.22,  &end
#
#   8 DC  H6     7 DKA H1'   2.090   2.930  (#op 88,114,120  2.090   2.530    )
 &rst
  ixpk= 88, nxpk= 0, iat= 257, 198, r1= 1.59, r2= 2.09, r3= 2.93, r4= 3.43,  &end
#
#   8 DC  H6     7 DKA H2'1  2.700   4.120    (#4,22,26,29,50,166 3.100   3.720    )
 &rst
  ixpk= 3, nxpk= 0, iat= 257, 240, r1= 2.20, r2= 2.70, r3= 4.12, r4= 4.62,  &end
#
#   8 DC  H6     7 DKA Q13   3.950   4.570
 &rst
  ixpk= 3, nxpk= 0, iat= 257,  -1, r1= 3.45, r2= 3.95, r3= 5.49, r4= 5.99,
 igr2= 229, 230, 231,
 &end
#
#   8 DC  H6     8 DC  H1'   3.680   6.420
 &rst
  ixpk= 3, nxpk= 0, iat= 257, 254, r1= 3.18, r2= 3.68, r3= 6.42, r4= 6.92,  &end
#
#   8 DC  H6     8 DC  H2'2  2.670   4.070   (#op 98,118,123,128  3.270   4.270    )
 &rst
  ixpk= 98, nxpk= 0, iat= 257, 271, r1= 2.17, r2= 2.67, r3= 4.07, r4= 4.57,  &end
#
#   8 DC  H6     8 DC  H2'1  3.210   5.620
 &rst
  ixpk= 98, nxpk= 0, iat= 257, 270, r1= 2.71, r2= 3.21, r3= 5.62, r4= 6.12,  &end
#
#   8 DC  H5     7 DKA H1'   2.900   3.310
 &rst
  ixpk= 98, nxpk= 0, iat= 259, 198, r1= 2.40, r2= 2.90, r3= 3.31, r4= 3.81,  &end
#
#   8 DC  H5     7 DKA H2'1  3.550   4.300   (#111,137  3.550   4.100    )
 &rst
  ixpk= 3, nxpk= 0, iat= 259, 240, r1= 3.05, r2= 3.55, r3= 4.30, r4= 4.80,  &end
#
#   8 DC  H5     7 DKA H8    3.970   6.610
 &rst
  ixpk= 3, nxpk= 0, iat= 259, 201, r1= 3.47, r2= 3.97, r3= 6.61, r4= 7.11,  &end
#
#   8 DC  H5     7 DKA Q13   4.520   6.150
 &rst
  ixpk= 3, nxpk= 0, iat= 259,  -1, r1= 4.02, r2= 4.52, r3= 7.39, r4= 7.89,
 igr2= 229, 230, 231,
 &end
#
```

```
#   8 DC  H5    7 DKA H11   3.320   4.610   (#167 3.320   4.510    )
 &rst
  ixpk= 3, nxpk= 0, iat= 259, 234, r1= 2.82, r2= 3.32, r3= 4.61, r4= 5.11,  &end
#
#   9 DC  H2'2   9 DC  H1'   2.100   2.970   (#23,32,48,66,93  2.100   2.370    )
 &rst
  ixpk= 2, nxpk= 0, iat= 301, 284, r1= 1.60, r2= 2.10, r3= 2.97, r4= 3.47,  &end
#
#   9 DC  H2'1   9 DC  H1'   2.210   3.660    (#28,33,37  2.510   3.660   )
 &rst
  ixpk= 2, nxpk= 0, iat= 300, 284, r1= 1.71, r2= 2.21, r3= 3.66, r4= 4.16,  &end
#
#   9 DC  H3'    9 DC  H1'   3.140   5.370
 &rst
  ixpk= 2, nxpk= 0, iat= 298, 284, r1= 2.64, r2= 3.14, r3= 5.37, r4= 5.87,  &end
#
#   9 DC  H3'    9 DC  H2'1  2.780   3.680
 &rst
  ixpk= 2, nxpk= 0, iat= 298, 300, r1= 2.28, r2= 2.78, r3= 3.68, r4= 4.18,  &end
#
#  19 DG  H8    7 DKA H20   3.070   4.000    (#1,10,13,26,31,36,44 3.070   3.400   )
 &rst
  ixpk= 3, nxpk= 0, iat= 603, 215, r1= 2.57, r2= 3.07, r3= 4.00, r4= 4.50,  &end
#
#   9 DC  H6    8 DC  H1'   3.300   4.350    (#76,78  3.100   4.250   )
 &rst
  ixpk= 3, nxpk= 0, iat= 287, 254, r1= 2.80, r2= 3.30, r3= 4.35, r4= 4.85,  &end
#
#   9 DC  H6    8 DC  H2'1  2.240   4.410   (#41,46,55,57,59,61,65  3.240   4.410   )
 &rst
  ixpk= 3, nxpk= 0, iat= 287, 270, r1= 1.74, r2= 2.24, r3= 4.41, r4= 4.91,  &end
#
#   9 DC  H6    8 DC  H6    3.890   5.790
 &rst
  ixpk= 3, nxpk= 0, iat= 287, 257, r1= 3.39, r2= 3.89, r3= 5.79, r4= 6.29,  &end
#
#   9 DC  H6    9 DC  H1'   2.790   3.750    (#18,104  2.790   3.350   )
 &rst
  ixpk= 2, nxpk= 0, iat= 287, 284, r1= 2.29, r2= 2.79, r3= 3.75, r4= 4.25,  &end
#
#   9 DC  H6    9 DC  H3'   2.750   5.530   (#42,49,57,62,70,73,74  3.450   5.530  )
 &rst
  ixpk= 3, nxpk= 0, iat= 287, 298, r1= 2.25, r2= 2.75, r3= 5.53, r4= 6.03,  &end
#
#   9 DC  H5    8 DC  H2'1  2.640   4.170    (#op 102,140  2.640   3.870   )
 &rst
  ixpk= 102, nxpk= 0, iat= 289, 270, r1= 2.14, r2= 2.64, r3= 4.17, r4= 4.67,  &end
#
#   9 DC  H5    8 DC  H6    3.900   4.800   (#3.900   4.700    )
 &rst
  ixpk= 4, nxpk= 0, iat= 289, 257, r1= 3.40, r2= 3.90, r3= 4.80, r4= 5.30,  &end
#
#   9 DC  H5    8 DC  H5    3.880   4.970
 &rst
  ixpk= 4, nxpk= 0, iat= 289, 259, r1= 3.38, r2= 3.88, r3= 4.97, r4= 5.47,  &end
```

```
#
#  9 DC  H5    9 DC  H2'2  2.450   4.570   (#op 48,68,77,80,83,92  2.450   3.470   )
 &rst
  ixpk= 48, nxpk= 0, iat= 289, 301, r1= 1.95, r2= 2.45, r3= 4.57, r4= 5.07,  &end
#
#  9 DC  H5    9 DC  H2'1  3.030   6.050
 &rst
  ixpk= 48, nxpk= 0, iat= 289, 300, r1= 2.53, r2= 3.03, r3= 6.05, r4= 6.55,  &end
#
#  21 DC  H5   20 DC  H3'   3.940   5.760  (#broad  46,60,64,67,69,72 3.640   4.260)
 &rst
  ixpk= 46, nxpk= 0, iat= 668, 647, r1= 3.44, r2= 3.94, r3= 5.76, r4= 6.26,  &end
#
#  10 DA  H2'2  10 DA  H1'   1.690   3.960
 &rst
  ixpk= 46, nxpk= 0, iat= 333, 314, r1= 1.19, r2= 1.69, r3= 3.96, r4= 4.46,  &end
#
#  10 DA  H3'   10 DA  H2'2  1.680   2.380    (#71,93,135  1.680   2.080   )
 &rst
  ixpk= 1, nxpk= 0, iat= 330, 333, r1= 1.18, r2= 1.68, r3= 2.38, r4= 2.88,  &end
#
#  10 DA  H4'   10 DA  H1'   2.980   5.570   (#119  3.080   5.570    )
 &rst
  ixpk= 3, nxpk= 0, iat= 311, 314, r1= 2.48, r2= 2.98, r3= 5.57, r4= 6.07,  &end
#
#  10 DA  H8    9 DC  H1'   2.980   4.560   (#26,29,30,33,36,40,43  2.580   3.460  )
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 284, r1= 2.48, r2= 2.98, r3= 4.56, r4= 5.06,  &end
#
#  10 DA  H8    9 DC  H2'2  2.560   5.540
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 301, r1= 2.06, r2= 2.56, r3= 5.54, r4= 6.04,  &end
#
#  10 DA  H8    9 DC  H2'1  2.570   5.870    (#35,38,45,47*  2.970   5.270   )
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 300, r1= 2.07, r2= 2.57, r3= 5.87, r4= 6.37,  &end
#
#  10 DA  H8   10 DA  H3'   2.600   4.220
 (#10 DA  H8   10 DA  H1'   1.790   2.760     #op)
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 330, r1= 2.10, r2= 2.60, r3= 4.22, r4= 4.72,  &end
#
#  10 DA  H8   10 DA  H4'   3.730   6.150
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 311, r1= 3.23, r2= 3.73, r3= 6.15, r4= 6.65,  &end
#
#  10 DA  H8   10 DA  H5'2  3.380   5.400
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 309, r1= 2.88, r2= 3.38, r3= 5.40, r4= 5.90,  &end
#
#  11 DT  H2'2  11 DT  H1'   2.420   3.020
 &rst
  ixpk= 2, nxpk= 0, iat= 365, 346, r1= 1.92, r2= 2.42, r3= 3.02, r4= 3.52,  &end
#
#  11 DT  H2'1  11 DT  H1'   2.310   3.130   (#52,102  2.610   3.130    )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 364, 346, r1= 1.81, r2= 2.31, r3= 3.13, r4= 3.63,  &end
#
#  11 DT  H3'   11 DT  H2'1  2.730   3.250
 &rst
  ixpk= 2, nxpk= 0, iat= 362, 364, r1= 2.23, r2= 2.73, r3= 3.25, r4= 3.75,  &end
#
#  20 DC  H5    20 DC  H2'2  2.840   4.290   (#11,15,17,51,63,77  3.140   3.990    )
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 650, r1= 2.34, r2= 2.84, r3= 4.29, r4= 4.79,  &end
#
#  11 DT  H6    10 DA  H1'   2.970   4.430   (#19,38,41,42,46,62,65  2.370   3.130   )
 &rst
  ixpk= 2, nxpk= 0, iat= 349, 314, r1= 2.47, r2= 2.97, r3= 4.43, r4= 4.93,  &end
#
#  11 DT  H6    10 DA  H2'2  2.250   3.400   (#50,57,75,101,110  2.250   2.800   )
 &rst
  ixpk= 2, nxpk= 0, iat= 349, 333, r1= 1.75, r2= 2.25, r3= 3.40, r4= 3.90,  &end
#
#  11 DT  H6    10 DA  H2'1  2.440   5.090   (#14,37,42,126,129  3.040   5.190    )
 &rst
  ixpk= 3, nxpk= 0, iat= 349, 332, r1= 1.94, r2= 2.44, r3= 5.09, r4= 5.59,  &end
#
#  11 DT  H6    10 DA  H8    3.360   6.460
 &rst
  ixpk= 3, nxpk= 0, iat= 349, 317, r1= 2.86, r2= 3.36, r3= 6.46, r4= 6.96,  &end
#
#  11 DT  H6    11 DT  H1'   3.090   3.800
 &rst
  ixpk= 3, nxpk= 0, iat= 349, 346, r1= 2.59, r2= 3.09, r3= 3.80, r4= 4.30,  &end
#
#  11 DT  H6    11 DT  H2'2  1.980   3.120    (#op 39,66,103,105  2.380   3.120   )
 &rst
  ixpk= 39, nxpk= 0, iat= 349, 365, r1= 1.48, r2= 1.98, r3= 3.12, r4= 3.62,  &end
#
#  11 DT  H6    11 DT  H2'1  2.090   3.380    (#op 78,80,113,121  2.090   2.880   )
 &rst
  ixpk= 78, nxpk= 0, iat= 349, 364, r1= 1.59, r2= 2.09, r3= 3.38, r4= 3.88,  &end
#
#  11 DT  H6    11 DT  H3'   3.930   6.050
 &rst
  ixpk= 78, nxpk= 0, iat= 349, 362, r1= 3.43, r2= 3.93, r3= 6.05, r4= 6.55,  &end
#
#  11 DT  Q5    10 DA  H2'2  3.120   4.710
 &rst
  ixpk= 78, nxpk= 0, iat=  -1, 333, r1= 2.62, r2= 3.12, r3= 5.66, r4= 6.16,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5    10 DA  H2'1  2.770   3.970
 &rst
  ixpk= 78, nxpk= 0, iat=  -1, 332, r1= 2.27, r2= 2.77, r3= 4.77, r4= 5.27,
 igr1= 352, 353, 354,
 &end
#
```

```
#  11 DT  Q5    10 DA  H8    2.480   3.320   (#170 2.480   3.220    )
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 317, r1= 1.98, r2= 2.48, r3= 3.99, r4= 4.49,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5    11 DT  H1'   4.410   5.560
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 346, r1= 3.91, r2= 4.41, r3= 6.68, r4= 7.18,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5    11 DT  H2'2  2.880   4.320
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 365, r1= 2.38, r2= 2.88, r3= 5.19, r4= 5.69,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5    11 DT  H6    2.440   3.100
 (#11 DT  Q5    11 DT  H3'   3.600   5.370  #2,3,4,9,23,27,28,31   3.600   4.170 )
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 349, r1= 1.94, r2= 2.44, r3= 3.72, r4= 4.22,
 igr1= 352, 353, 354,
 &end
#
#  12 DC3 H3'   12 DC3 H1'   3.240   5.470
 (#12 DC3 H1'   11 DT  Q5    3.250   4.250   #33,34,40,42,45  3.250   3.750   )
 &rst
  ixpk= 2, nxpk= 0, iat= 392, 378, r1= 2.74, r2= 3.24, r3= 5.47, r4= 5.97,  &end
#
#  12 DC3 H3'   12 DC3 H2'2  1.560   2.360              (#op, 1,2,3 1.560   2.060     )
 &rst
  ixpk= 1, nxpk= 0, iat= 392, 395, r1= 1.06, r2= 1.56, r3= 2.36, r4= 2.86,  &end
#
#  12 DC3 H6    11 DT  H1'   2.030   2.920    (#op 99,124,141  2.030   2.520   )
 &rst
  ixpk= 99, nxpk= 0, iat= 381, 346, r1= 1.53, r2= 2.03, r3= 2.92, r4= 3.42,  &end
#
#  12 DC3 H6    11 DT  H2'1  2.390   4.560      (#18,67,84,116,127  2.890   4.560)
 &rst
  ixpk= 2, nxpk= 0, iat= 381, 364, r1= 1.89, r2= 2.39, r3= 4.56, r4= 5.06,  &end
#
#  12 DC3 H6    11 DT  H6    3.250   4.960   (#48,73,92,114,117,130  3.250   4.260   )
 &rst
  ixpk= 3, nxpk= 0, iat= 381, 349, r1= 2.75, r2= 3.25, r3= 4.96, r4= 5.46,  &end
#
#  12 DC3 H6    12 DC3 H1'   3.020   3.780    (#81  3.020   3.580   )
 &rst
  ixpk= 3, nxpk= 0, iat= 381, 378, r1= 2.52, r2= 3.02, r3= 3.78, r4= 4.28,  &end
#
#  12 DC3 H6    12 DC3 H3'   2.700   3.220    (#134  2.800   3.220   )
 &rst
  ixpk= 2, nxpk= 0, iat= 381, 392, r1= 2.20, r2= 2.70, r3= 3.22, r4= 3.72,  &end
#
#  12 DC3 H5    11 DT  H1'   2.900   3.920   (#44,45,55,56,60,64,74  2.700   3.120  )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 383, 346, r1= 2.40, r2= 2.90, r3= 3.92, r4= 4.42,  &end
#
#  12 DC3 H5    11 DT  H2'2  3.680   4.910
 &rst
  ixpk= 2, nxpk= 0, iat= 383, 365, r1= 3.18, r2= 3.68, r3= 4.91, r4= 5.41,  &end
#
#  12 DC3 H5    11 DT  H2'1  2.970   3.830   (#88,104  3.170   3.830    )
 &rst
  ixpk= 3, nxpk= 0, iat= 383, 364, r1= 2.47, r2= 2.97, r3= 3.83, r4= 4.33,  &end
#
#  12 DC3 H5    11 DT  H6    3.040   3.770     (#13,26  3.040   3.570)
 &rst
  ixpk= 3, nxpk= 0, iat= 383, 349, r1= 2.54, r2= 3.04, r3= 3.77, r4= 4.27,  &end
#
#  12 DC3 H5    11 DT  Q5    3.600   4.610
 &rst
  ixpk= 3, nxpk= 0, iat= 383,  -1, r1= 3.10, r2= 3.60, r3= 5.54, r4= 6.04,
 igr2= 352, 353, 354,
 &end
#
#  12 DC3 H5    12 DC3 H3'   3.230   5.660
 &rst
  ixpk= 3, nxpk= 0, iat= 383, 392, r1= 2.73, r2= 3.23, r3= 5.66, r4= 6.16,  &end
#
#  13 DG5 H3'   13 DG5 H1'   3.130   5.400
 &rst
  ixpk= 3, nxpk= 0, iat= 424, 407, r1= 2.63, r2= 3.13, r3= 5.40, r4= 5.90,  &end
#
#  13 DG5 H3'   13 DG5 H2'2  2.400   4.420    (#near ws 54,92  IQG3.dist2.600   4.420   )
 &rst
  ixpk= 3, nxpk= 0, iat= 424, 427, r1= 1.90, r2= 2.40, r3= 4.42, r4= 4.92,  &end
#
#  13 DG5 H3'   13 DG5 H2'1  2.700   4.360    (#41,42,57,93  3.100   4.360  )
 &rst
  ixpk= 3, nxpk= 0, iat= 424, 426, r1= 2.20, r2= 2.70, r3= 4.36, r4= 4.86,  &end
#
#  13 DG5 H8    13 DG5 H1'   2.750   4.240
 &rst
  ixpk= 3, nxpk= 0, iat= 410, 407, r1= 2.25, r2= 2.75, r3= 4.24, r4= 4.74,  &end
#
#  14 DA  H8    13 DG5 H1'   2.410   3.600   (#102,103  2.410   3.300    )
 &rst
  ixpk= 2, nxpk= 0, iat= 443, 407, r1= 1.91, r2= 2.41, r3= 3.60, r4= 4.10,  &end
#
#  14 DA  H8    13 DG5 H2'1  2.100   4.130   (#141  2.200   4.130    )
 &rst
  ixpk= 2, nxpk= 0, iat= 443, 426, r1= 1.60, r2= 2.10, r3= 4.13, r4= 4.63,  &end
#
#  14 DA  H8    14 DA  H1'   2.730   3.840   (#op   )
 &rst
  ixpk= 2, nxpk= 0, iat= 443, 440, r1= 2.23, r2= 2.73, r3= 3.84, r4= 4.34,  &end
#
#  14 DA  H8    14 DA  H3'   2.330   4.520    (#21  2.330   4.020  )
 &rst
```

```
 ixpk= 2, nxpk= 0, iat= 443, 456, r1= 1.83, r2= 2.33, r3= 4.52, r4= 5.02,  &end
#
#  14 DA  H8    14 DA  H5'2  2.800   6.490
 &rst
 ixpk= 2, nxpk= 0, iat= 443, 435, r1= 2.30, r2= 2.80, r3= 6.49, r4= 6.99,  &end
#
#  15 DT  H2'2  15 DT  H1'   1.960   3.020    (#4,7,10,11,18,30,60 1.960   2.320)
 &rst
 ixpk= 1, nxpk= 0, iat= 491, 472, r1= 1.46, r2= 1.96, r3= 3.02, r4= 3.52,  &end
#
#  15 DT  H2'1  15 DT  H1'   2.270   3.570
 &rst
 ixpk= 1, nxpk= 0, iat= 490, 472, r1= 1.77, r2= 2.27, r3= 3.57, r4= 4.07,  &end
#
#  15 DT  H3'   15 DT  H2'2  2.250   3.330    (#op 26,32,66,70,81  2.750   3.330   )
 &rst
 ixpk= 26, nxpk= 0, iat= 488, 491, r1= 1.75, r2= 2.25, r3= 3.33, r4= 3.83,  &end
#
#  15 DT  H3'   15 DT  H2'1  2.710   3.650    (#105  2.810   3.650   )
 &rst
 ixpk= 2, nxpk= 0, iat= 488, 490, r1= 2.21, r2= 2.71, r3= 3.65, r4= 4.15,  &end
#
#  15 DT  H6    14 DA  H1'   2.350   3.690    (#104,114   2.350   3.390)
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 440, r1= 1.85, r2= 2.35, r3= 3.69, r4= 4.19,  &end
#
#  15 DT  H6    14 DA  H2'2  2.550   3.880
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 459, r1= 2.05, r2= 2.55, r3= 3.88, r4= 4.38,  &end
#
#  15 DT  H6    14 DA  H2'1  2.180   3.570
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 458, r1= 1.68, r2= 2.18, r3= 3.57, r4= 4.07,  &end
#
#  15 DT  H6    15 DT  H1'   2.680   3.880    (#21  2.680   3.380   )
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 472, r1= 2.18, r2= 2.68, r3= 3.88, r4= 4.38,  &end
#
#  15 DT  H6    15 DT  H2'2  2.220   3.720     (#14  2.320   3.720 )
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 491, r1= 1.72, r2= 2.22, r3= 3.72, r4= 4.22,  &end
#
#  15 DT  H6    15 DT  H3'   3.450   5.630    (#op 97  3.550   5.630   )
 &rst
 ixpk= 97, nxpk= 0, iat= 475, 488, r1= 2.95, r2= 3.45, r3= 5.63, r4= 6.13,  &end
#
#  15 DT  Q5    14 DA  H1'   2.800   4.460
 &rst
 ixpk= 97, nxpk= 0, iat=  -1, 440, r1= 2.30, r2= 2.80, r3= 5.36, r4= 5.86,
igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    14 DA  H2'2  2.740   4.880
 &rst
 ixpk= 97, nxpk= 0, iat=  -1, 459, r1= 2.24, r2= 2.74, r3= 5.86, r4= 6.36,
```

```
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    14 DA  H2'1  3.130   4.720   (#103  3.230   4.720    )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 458, r1= 2.63, r2= 3.13, r3= 5.67, r4= 6.17,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    14 DA  H8    2.160   4.290
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 443, r1= 1.66, r2= 2.16, r3= 5.15, r4= 5.65,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    15 DT  H1'   3.090   6.090
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 472, r1= 2.59, r2= 3.09, r3= 7.31, r4= 7.81,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    15 DT  H2'2  3.140   6.490
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 491, r1= 2.64, r2= 3.14, r3= 7.79, r4= 8.29,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5    15 DT  H6    2.400   2.990
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 475, r1= 1.90, r2= 2.40, r3= 3.59, r4= 4.09,
 igr1= 478, 479, 480,
 &end
#
#  16 DG  H3'   16 DG  H1'   2.780   4.450
 (#16 DG  H3'   15 DT  Q5    3.110   4.300    #22,23,31,33,35,38  3.110   3.600 )
 &rst
  ixpk= 3, nxpk= 0, iat= 521, 504, r1= 2.28, r2= 2.78, r3= 4.45, r4= 4.95,  &end
#
#  16 DG  H8    15 DT  H1'   4.440   5.210
 &rst
  ixpk= 3, nxpk= 0, iat= 507, 472, r1= 3.94, r2= 4.44, r3= 5.21, r4= 5.71,  &end
#
#  16 DG  H8    15 DT  H2'2  2.620   3.180    (#64  2.620   3.080    )
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 491, r1= 2.12, r2= 2.62, r3= 3.18, r4= 3.68,  &end
#
#  16 DG  H8    15 DT  H2'1  2.490   3.650    (#60,61,63,72,117  2.990   3.650  )
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 490, r1= 1.99, r2= 2.49, r3= 3.65, r4= 4.15,  &end
#
#  16 DG  H8    15 DT  H6    3.720   5.290
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 475, r1= 3.22, r2= 3.72, r3= 5.29, r4= 5.79,  &end
#
#  16 DG  H8    16 DG  H1'   2.720   3.910    (#16  2.720   3.310   ci)
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 504, r1= 2.22, r2= 2.72, r3= 3.91, r4= 4.41,  &end
#
#  16 DG  H8    16 DG  H3'   2.870   5.570
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 521, r1= 2.37, r2= 2.87, r3= 5.57, r4= 6.07,  &end
#
#  16 DG  H8    16 DG  H4'   4.380   6.650
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 501, r1= 3.88, r2= 4.38, r3= 6.65, r4= 7.15,  &end
#
#  16 DG  H8    16 DG  H5'1  2.980   4.100   (#82,93,95,96,101,113,119 2.980   3.300     )
 &rst
  ixpk= 2, nxpk= 0, iat= 507, 498, r1= 2.48, r2= 2.98, r3= 4.10, r4= 4.60,  &end
#
#  17 DG  H1'    7 DKA H19   3.430   5.060    (#17,26,28,36,37,97  3.430   4.360  )
 &rst
  ixpk= 3, nxpk= 0, iat= 537, 217, r1= 2.93, r2= 3.43, r3= 5.06, r4= 5.56,  &end
#
#  17 DG  H2'2  17 DG  H1'   1.730   3.160      (#op 11,13,92  1.730   2.360  ci)
 &rst
  ixpk= 11, nxpk= 0, iat= 557, 537, r1= 1.23, r2= 1.73, r3= 3.16, r4= 3.66,  &end
#
#  17 DG  H2'1  16 DG  H1'   2.900   5.410  (#broad 53,57,67,69,79,83  2.800   3.810   )
 &rst
  ixpk= 53, nxpk= 0, iat= 556, 504, r1= 2.40, r2= 2.90, r3= 5.41, r4= 5.91,  &end
#
#  17 DG  H2'1  17 DG  H1'   2.110   3.750
 &rst
  ixpk= 53, nxpk= 0, iat= 556, 537, r1= 1.61, r2= 2.11, r3= 3.75, r4= 4.25,  &end
#
#  17 DG  H3'   17 DG  H1'   2.980   5.180
 &rst
  ixpk= 53, nxpk= 0, iat= 554, 537, r1= 2.48, r2= 2.98, r3= 5.18, r4= 5.68,  &end
#
#  17 DG  H3'   17 DG  H2'2  2.170   3.880
 &rst
  ixpk= 53, nxpk= 0, iat= 554, 557, r1= 1.67, r2= 2.17, r3= 3.88, r4= 4.38,  &end
#
#  17 DG  H3'   17 DG  H2'1  2.160   2.960
 &rst
  ixpk= 53, nxpk= 0, iat= 554, 556, r1= 1.66, r2= 2.16, r3= 2.96, r4= 3.46,  &end
#
#  17 DG  H8    16 DG  H1'   2.690   3.620  (#100,130   2.690   3.320     )
 &rst
  ixpk= 2, nxpk= 0, iat= 540, 504, r1= 2.19, r2= 2.69, r3= 3.62, r4= 4.12,  &end
#
#  17 DG  H8    17 DG  H1'   2.670   3.790   (#71  2.670   3.590    )
 &rst
  ixpk= 2, nxpk= 0, iat= 540, 537, r1= 2.17, r2= 2.67, r3= 3.79, r4= 4.29,  &end
#
#  17 DG  H8    17 DG  H3'   3.340   5.580
 &rst
  ixpk= 2, nxpk= 0, iat= 540, 554, r1= 2.84, r2= 3.34, r3= 5.58, r4= 6.08,  &end
#
```

```
#  18 DC  H2'2   7 DKA H19   2.770   4.460   (#op 3,10,14,22,24,25,88  2.470   3.060    )
 &rst
  ixpk= 3, nxpk= 0, iat= 587, 217, r1= 2.27, r2= 2.77, r3= 4.46, r4= 4.96,  &end
#
#  18 DC  H2'2  17 DG  H1'   3.310   5.200
 &rst
  ixpk= 3, nxpk= 0, iat= 587, 537, r1= 2.81, r2= 3.31, r3= 5.20, r4= 5.70,  &end
#
#  18 DC  H2'2  18 DC  H1'   2.090   3.330    (#ci  2.090   2.430  )
 &rst
  ixpk= 2, nxpk= 0, iat= 587, 570, r1= 1.59, r2= 2.09, r3= 3.33, r4= 3.83,  &end
#
#  18 DC  H2'1   7 DKA H19   2.880   5.520    (#23,45,50,53  3.180   4.920  )
 &rst
  ixpk= 3, nxpk= 0, iat= 586, 217, r1= 2.38, r2= 2.88, r3= 5.52, r4= 6.02,  &end
#
#  18 DC  H2'1  18 DC  H1'   2.290   5.070    (#170 2.390   5.170   )
 &rst
  ixpk= 2, nxpk= 0, iat= 586, 570, r1= 1.79, r2= 2.29, r3= 5.07, r4= 5.57,  &end
#
#  18 DC  H3'   18 DC  H1'   3.730   5.320
 &rst
  ixpk= 2, nxpk= 0, iat= 584, 570, r1= 3.23, r2= 3.73, r3= 5.32, r4= 5.82,  &end
#
#  18 DC  H5'2  18 DC  H1'   2.170   4.750    (#18, 20  2.170   3.550   ci)
 &rst
  ixpk= 20, nxpk= 0, iat= 565, 570, r1= 1.67, r2= 2.17, r3= 4.75, r4= 5.25,  &end
#
#  18 DC  H6    17 DG  H1'   2.760   3.960   (#51,57,68,81,107,110  2.760   3.160    )
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 537, r1= 2.26, r2= 2.76, r3= 3.96, r4= 4.46,  &end
#
#  18 DC  H6    17 DG  H2'2  3.360   5.350
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 557, r1= 2.86, r2= 3.36, r3= 5.35, r4= 5.85,  &end
#
#  18 DC  H6    17 DG  H2'1  3.510   5.760    (#73,95,111  3.810   5.760   )
 &rst
  ixpk= 3, nxpk= 0, iat= 573, 556, r1= 3.01, r2= 3.51, r3= 5.76, r4= 6.26,  &end
#
#  18 DC  H6    17 DG  H3'   3.330   4.620    (#30,45,46,74,87,112  3.330   3.820   )
 &rst
  ixpk= 3, nxpk= 0, iat= 573, 554, r1= 2.83, r2= 3.33, r3= 4.62, r4= 5.12,  &end
#
#  18 DC  H6    18 DC  H1'   2.770   3.980      (#9  2.770   3.180  ci)
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 570, r1= 2.27, r2= 2.77, r3= 3.98, r4= 4.48,  &end
#
#  18 DC  H6    18 DC  H2'2  2.450   4.020    (#36,77  2.650   4.020   )
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 587, r1= 1.95, r2= 2.45, r3= 4.02, r4= 4.52,  &end
#
#  18 DC  H6    18 DC  H2'1  2.760   4.010    (#2,29,31,52,117  2.760   3.310)
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 586, r1= 2.26, r2= 2.76, r3= 4.01, r4= 4.51,  &end
```

```
#
#  18 DC  H6    18 DC  H3'   3.420   4.920
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 584, r1= 2.92, r2= 3.42, r3= 4.92, r4= 5.42,  &end
#
#  18 DC  H6    18 DC  H4'   3.660   4.650
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 567, r1= 3.16, r2= 3.66, r3= 4.65, r4= 5.15,  &end
#
#  18 DC  H6    18 DC  H5'1  3.480   5.610
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 564, r1= 2.98, r2= 3.48, r3= 5.61, r4= 6.11,  &end
#
#  18 DC  H6    18 DC  H5'2  2.650   4.690   (#98,101,103,109,115  3.350   4.690    )
 &rst
  ixpk= 3, nxpk= 0, iat= 573, 565, r1= 2.15, r2= 2.65, r3= 4.69, r4= 5.19,  &end
#
#  18 DC  H5    17 DG  H1'   3.930   5.440   (#1,21,32,39,54,59,60,70  2.930   3.440   )
 &rst
  ixpk= 2, nxpk= 0, iat= 575, 537, r1= 3.43, r2= 3.93, r3= 5.44, r4= 5.94,  &end
#
#  18 DC  H5    17 DG  H3'   3.380   4.520   (#96,100,121  3.380   4.220     )
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 554, r1= 2.88, r2= 3.38, r3= 4.52, r4= 5.02,  &end
#
#  19 DG  H2'2  19 DG  H1'   1.960   3.060    (#op 92  1.960   2.960   )
 &rst
  ixpk= 92, nxpk= 0, iat= 620, 600, r1= 1.46, r2= 1.96, r3= 3.06, r4= 3.56,  &end
#
#  19 DG  H2'1  19 DG  H1'   2.240   3.250
 &rst
  ixpk= 92, nxpk= 0, iat= 619, 600, r1= 1.74, r2= 2.24, r3= 3.25, r4= 3.75,  &end
#
#  19 DG  H3'    7 DKA H19   3.240   4.640    (#op 95  3.240   4.540   )
 &rst
  ixpk= 95, nxpk= 0, iat= 617, 217, r1= 2.74, r2= 3.24, r3= 4.64, r4= 5.14,  &end
#
#  19 DG  H3'   18 DC  H1'   3.110   5.170
 &rst
  ixpk= 95, nxpk= 0, iat= 617, 570, r1= 2.61, r2= 3.11, r3= 5.17, r4= 5.67,  &end
#
#  19 DG  H3'   18 DC  H6    4.480   6.180   (#102,104,125  4.480   5.880    )
 &rst
  ixpk= 4, nxpk= 0, iat= 617, 573, r1= 3.98, r2= 4.48, r3= 6.18, r4= 6.68,  &end
#
#  19 DG  H3'   19 DG  H2'1  2.810   3.510    (#75  2.910   3.510   )
 &rst
  ixpk= 2, nxpk= 0, iat= 617, 619, r1= 2.31, r2= 2.81, r3= 3.51, r4= 4.01,  &end
#
#  19 DG  H8     7 DKA H19   2.930   3.890    (#114  2.930   3.790   )
 &rst
  ixpk= 2, nxpk= 0, iat= 603, 217, r1= 2.43, r2= 2.93, r3= 3.89, r4= 4.39,  &end
#
#  19 DG  H8    18 DC  H1'   2.870   5.230
 &rst
```

```
 ixpk= 2, nxpk= 0, iat= 603, 570, r1= 2.37, r2= 2.87, r3= 5.23, r4= 5.73,  &end
#
#  19 DG  H8    18 DC  H2'2  3.850   5.120   (#93  3.850   4.920    )
 &rst
 ixpk= 3, nxpk= 0, iat= 603, 587, r1= 3.35, r2= 3.85, r3= 5.12, r4= 5.62,  &end
#
#  19 DG  H8    19 DG  H2'1  1.960   3.520   (#op 64,76,90,91,99  1.960   2.820    )
 &rst
 ixpk= 64, nxpk= 0, iat= 603, 619, r1= 1.46, r2= 1.96, r3= 3.52, r4= 4.02,  &end
#
#  19 DG  H8    19 DG  H3'   3.870   6.470
 &rst
 ixpk= 64, nxpk= 0, iat= 603, 617, r1= 3.37, r2= 3.87, r3= 6.47, r4= 6.97,  &end
#
#  20 DC  H2'2  20 DC  H1'   1.860   3.030   (#op 1,3,22,26,34,56,66 1.760   2.130)
 &rst
 ixpk= 1, nxpk= 0, iat= 650, 633, r1= 1.36, r2= 1.86, r3= 3.03, r4= 3.53,  &end
#
#  20 DC  H2'1  20 DC  H1'   2.250   4.050      (#4,11,15,16,24  2.750   4.950)
 &rst
 ixpk= 2, nxpk= 0, iat= 649, 633, r1= 1.75, r2= 2.25, r3= 4.05, r4= 4.55,  &end
#
#  20 DC  H3'   20 DC  H1'   3.380   5.460
 &rst
 ixpk= 2, nxpk= 0, iat= 647, 633, r1= 2.88, r2= 3.38, r3= 5.46, r4= 5.96,  &end
#
#  20 DC  H3'   20 DC  H2'2  2.210   3.200
 &rst
 ixpk= 2, nxpk= 0, iat= 647, 650, r1= 1.71, r2= 2.21, r3= 3.20, r4= 3.70,  &end
#
#  20 DC  H6    19 DG  H1'   2.780   3.150
 &rst
 ixpk= 2, nxpk= 0, iat= 636, 600, r1= 2.28, r2= 2.78, r3= 3.15, r4= 3.65,  &end
#
#  20 DC  H6    19 DG  H2'2  2.690   3.910    (#30,42,43,48,60,94  2.690   3.110  )
 &rst
 ixpk= 2, nxpk= 0, iat= 636, 620, r1= 2.19, r2= 2.69, r3= 3.91, r4= 4.41,  &end
#
#  20 DC  H6    19 DG  H8    3.140   4.480   (#79,81,85,87,96,98  2.940   3.480   )
 &rst
 ixpk= 2, nxpk= 0, iat= 636, 603, r1= 2.64, r2= 3.14, r3= 4.48, r4= 4.98,  &end
#
#  20 DC  H6    20 DC  H1'   2.560   3.740   (#51,59,89  2.560   3.340   )
 &rst
 ixpk= 2, nxpk= 0, iat= 636, 633, r1= 2.06, r2= 2.56, r3= 3.74, r4= 4.24,  &end
#
#  20 DC  H6    20 DC  H2'2  2.120   5.880   (#op 73  2.320   5.880   )
 &rst
 ixpk= 73, nxpk= 0, iat= 636, 650, r1= 1.62, r2= 2.12, r3= 5.88, r4= 6.38,  &end
#
#  20 DC  H6    20 DC  H2'1  1.860   3.730   (#op 49,63,80,82,83,84  1.860   2.530   )
 &rst
 ixpk= 49, nxpk= 0, iat= 636, 649, r1= 1.36, r2= 1.86, r3= 3.73, r4= 4.23,  &end
#
#  20 DC  H6    20 DC  H3'   3.860   6.310
```

```
 &rst
  ixpk= 49, nxpk= 0, iat= 636, 647, r1= 3.36, r2= 3.86, r3= 6.31, r4= 6.81,  &end
#
#  20 DC  H6    20 DC  H4'   4.400   6.780
 &rst
  ixpk= 49, nxpk= 0, iat= 636, 630, r1= 3.90, r2= 4.40, r3= 6.78, r4= 7.28,  &end
#
#  20 DC  H6    20 DC  H5'1  3.650   6.020
 &rst
  ixpk= 49, nxpk= 0, iat= 636, 627, r1= 3.15, r2= 3.65, r3= 6.02, r4= 6.52,  &end
#
#  20 DC  H6    20 DC  H5'2  3.970   5.060   (#61,65,68,72  3.570   4.660    )
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 628, r1= 3.47, r2= 3.97, r3= 5.06, r4= 5.56,  &end
#
#  20 DC  H5    19 DG  H2'1  3.000   4.390    (#17,27,40   3.000   3.990   )
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 619, r1= 2.50, r2= 3.00, r3= 4.39, r4= 4.89,  &end
#
#  20 DC  H5    19 DG  H8    3.370   4.930   (#95  3.470   4.930    )
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 603, r1= 2.87, r2= 3.37, r3= 4.93, r4= 5.43,  &end
#
#  20 DC  H5    20 DC  H2'2  3.270   4.770
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 650, r1= 2.77, r2= 3.27, r3= 4.77, r4= 5.27,  &end
#
#  20 DC  H5    20 DC  H2'1  3.410   5.530   (#100,103  3.410   5.330    )
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 649, r1= 2.91, r2= 3.41, r3= 5.53, r4= 6.03,  &end
#
#  21 DC  H2'1  21 DC  H1'   2.010   2.600
 (#21 DC  H1'   20 DC  H5    3.140   4.350  #2,3,4,38,41,42,70 3.140   3.450  )
 &rst
  ixpk= 3, nxpk= 0, iat= 679, 663, r1= 1.51, r2= 2.01, r3= 2.60, r4= 3.10,  &end
#
#  21 DC  H3'   21 DC  H2'2  2.280   2.810
 &rst
  ixpk= 3, nxpk= 0, iat= 677, 680, r1= 1.78, r2= 2.28, r3= 2.81, r4= 3.31,  &end
#
#  21 DC  H3'   21 DC  H2'1  2.510   4.230
 &rst
  ixpk= 3, nxpk= 0, iat= 677, 679, r1= 2.01, r2= 2.51, r3= 4.23, r4= 4.73,  &end
#
#  21 DC  H6    20 DC  H2'2  2.140   2.950
 (#21 DC  H6    20 DC  H1'   2.540   4.130  #10,14,19,23,29,32,35  2.640   3.630  )
 &rst
  ixpk= 3, nxpk= 0, iat= 666, 650, r1= 1.64, r2= 2.14, r3= 2.95, r4= 3.45,  &end
#
#  21 DC  H6    20 DC  H2'1  2.400   3.930    (#31  2.500   3.930   )
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 649, r1= 1.90, r2= 2.40, r3= 3.93, r4= 4.43,  &end
#
#  21 DC  H6    20 DC  H6    3.100   4.290   (#107,119  3.100   4.090    )
 &rst
```

```
 ixpk= 3, nxpk= 0, iat= 666, 636, r1= 2.60, r2= 3.10, r3= 4.29, r4= 4.79,  &end
#
#  21 DC  H6    21 DC  H1'   2.860   4.170
 &rst
 ixpk= 3, nxpk= 0, iat= 666, 663, r1= 2.36, r2= 2.86, r3= 4.17, r4= 4.67,  &end
#
#  21 DC  H6    21 DC  H2'2  2.110   4.140   (#op 55  2.210   4.140    )
 &rst
 ixpk= 55, nxpk= 0, iat= 666, 680, r1= 1.61, r2= 2.11, r3= 4.14, r4= 4.64,  &end
#
#  21 DC  H6    21 DC  H2'1  1.770   3.290   (#28,33,43,57,74,75,105  1.770   2.290    )
 &rst
 ixpk= 1, nxpk= 0, iat= 666, 679, r1= 1.27, r2= 1.77, r3= 3.29, r4= 3.79,  &end
#
#  21 DC  H6    21 DC  H3'   2.960   4.530   (#13,18,20,46,65,97  2.960   3.630    )
 &rst
 ixpk= 2, nxpk= 0, iat= 666, 677, r1= 2.46, r2= 2.96, r3= 4.53, r4= 5.03,  &end
#
#  21 DC  H5    20 DC  H2'2  2.380   3.790
 (#21 DC  H5    20 DC  H1'   3.300   6.010  #25,30,36,45,47,49,50,62  3.300   #5.210   )
 &rst
 ixpk= 2, nxpk= 0, iat= 668, 650, r1= 1.88, r2= 2.38, r3= 3.79, r4= 4.29,  &end
#
#  21 DC  H5    20 DC  H2'1  2.770   4.600   (#69  2.770   4.500    )
 &rst
 ixpk= 2, nxpk= 0, iat= 668, 649, r1= 2.27, r2= 2.77, r3= 4.60, r4= 5.10,  &end
#
#  21 DC  H5    20 DC  H6    3.020   3.650   (#114  3.020   3.550    )
 &rst
 ixpk= 3, nxpk= 0, iat= 668, 636, r1= 2.52, r2= 3.02, r3= 3.65, r4= 4.15,  &end
#
#  21 DC  H5    20 DC  H5    3.690   5.980    (#78,79,92,93  4.090   5.980   )
 &rst
 ixpk= 4, nxpk= 0, iat= 668, 638, r1= 3.19, r2= 3.69, r3= 5.98, r4= 6.48,  &end
#
#  21 DC  H5    21 DC  H2'2  2.910   4.530
 &rst
 ixpk= 4, nxpk= 0, iat= 668, 680, r1= 2.41, r2= 2.91, r3= 4.53, r4= 5.03,  &end
#
#  21 DC  H5    21 DC  H2'1  2.820   5.150   (#45,48,51,59,101,109,154  2.620   4.450    )
 &rst
 ixpk= 2, nxpk= 0, iat= 668, 679, r1= 2.32, r2= 2.82, r3= 5.15, r4= 5.65,  &end
#
#  22 DG  H2'2  22 DG  H1'   1.680   3.030    (#op 22,27,42,63  1.680   2.530    )
 &rst
 ixpk= 22, nxpk= 0, iat= 713, 693, r1= 1.18, r2= 1.68, r3= 3.03, r4= 3.53,  &end
#
#  22 DG  H2'1  22 DG  H1'   2.130   3.800
 &rst
 ixpk= 22, nxpk= 0, iat= 712, 693, r1= 1.63, r2= 2.13, r3= 3.80, r4= 4.30,  &end
#
#  22 DG  H3'   22 DG  H1'   2.910   3.950
 &rst
 ixpk= 22, nxpk= 0, iat= 710, 693, r1= 2.41, r2= 2.91, r3= 3.95, r4= 4.45,  &end
#
```

```
#  22 DG  H8    21 DC  H1'   2.610   3.540
 &rst
  ixpk= 22, nxpk= 0, iat= 696, 663, r1= 2.11, r2= 2.61, r3= 3.54, r4= 4.04,  &end
#
#  22 DG  H8    21 DC  H2'2  2.620   4.370   (#40,116,167  2.620   4.070    )
 &rst
  ixpk= 2, nxpk= 0, iat= 696, 680, r1= 2.12, r2= 2.62, r3= 4.37, r4= 4.87,  &end
#
#  22 DG  H8    21 DC  H2'1  2.400   4.090    (#25,60,85,125  2.800   4.090   )
 &rst
  ixpk= 2, nxpk= 0, iat= 696, 679, r1= 1.90, r2= 2.40, r3= 4.09, r4= 4.59,  &end
#
#  22 DG  H8    21 DC  H3'   3.600   5.020
 &rst
  ixpk= 2, nxpk= 0, iat= 696, 677, r1= 3.10, r2= 3.60, r3= 5.02, r4= 5.52,  &end
#
#  22 DG  H8    22 DG  H1'   2.570   3.870
 (#22 DG  H8    21 DC  H6    3.300   5.120   #72,91,95,96,99,110 3.300   4.120 )
 &rst
  ixpk= 2, nxpk= 0, iat= 696, 693, r1= 2.07, r2= 2.57, r3= 3.87, r4= 4.37,  &end
#
#  22 DG  H8    22 DG  H3'   2.730   4.830    (#op 32,37,53,57,68,89  2.730   4.130   )
 &rst
  ixpk= 32, nxpk= 0, iat= 696, 710, r1= 2.23, r2= 2.73, r3= 4.83, r4= 5.33,  &end
#
#  23 DA  H2'2  23 DA  H1'   1.970   3.070    (#22,26,52,112  1.970   2.570   )
 &rst
  ixpk= 1, nxpk= 0, iat= 745, 726, r1= 1.47, r2= 1.97, r3= 3.07, r4= 3.57,  &end
#
#  23 DA  H2'1  23 DA  H1'   2.330   4.500   (#82  2.430   4.500    )
 &rst
  ixpk= 2, nxpk= 0, iat= 744, 726, r1= 1.83, r2= 2.33, r3= 4.50, r4= 5.00,  &end
#
#  23 DA  H8    22 DG  H1'   2.570   3.350
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 693, r1= 2.07, r2= 2.57, r3= 3.35, r4= 3.85,  &end
#
#  23 DA  H8    22 DG  H3'   3.920   6.440
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 710, r1= 3.42, r2= 3.92, r3= 6.44, r4= 6.94,  &end
#
#  23 DA  H8    23 DA  H1'   2.580   4.010      (#9,19  2.580   3.210  ci)
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 726, r1= 2.08, r2= 2.58, r3= 4.01, r4= 4.51,  &end
#
#  23 DA  H8    23 DA  H2'2  2.270   2.900
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 745, r1= 1.77, r2= 2.27, r3= 2.90, r4= 3.40,  &end
#
#  23 DA  H8    23 DA  H3'   3.050   4.530      (#20  3.050   4.430)
 &rst
  ixpk= 3, nxpk= 0, iat= 729, 742, r1= 2.55, r2= 3.05, r3= 4.53, r4= 5.03,  &end
#
#  23 DA  H8    23 DA  H4'   3.910   5.890
 &rst
```

```
 ixpk= 3, nxpk= 0, iat= 729, 723, r1= 3.41, r2= 3.91, r3= 5.89, r4= 6.39,  &end
#
#  23 DA  H8    23 DA  H5'1  3.320   6.040
 &rst
 ixpk= 3, nxpk= 0, iat= 729, 720, r1= 2.82, r2= 3.32, r3= 6.04, r4= 6.54,  &end
#
#  23 DA  H8    23 DA  H5'2  3.610   5.680
 &rst
 ixpk= 3, nxpk= 0, iat= 729, 721, r1= 3.11, r2= 3.61, r3= 5.68, r4= 6.18,  &end
#
#  24 DG3 H2'2  24 DG3 H1'   2.110   3.010     (#op 12,16,18,54  2.110   2.610 )
 &rst
 ixpk= 12, nxpk= 0, iat= 778, 758, r1= 1.61, r2= 2.11, r3= 3.01, r4= 3.51,  &end
#
#  24 DG3 H3'   24 DG3 H1'   2.820   3.820
 &rst
 ixpk= 12, nxpk= 0, iat= 775, 758, r1= 2.32, r2= 2.82, r3= 3.82, r4= 4.32,  &end
#
#  24 DG3 H8    23 DA  H1'   1.860   3.310  (#op 66,67,70,71,84,93,94* 1.760   2.210   )
 &rst
 ixpk= 66, nxpk= 0, iat= 761, 726, r1= 1.36, r2= 1.86, r3= 3.31, r4= 3.81,  &end
#
#  24 DG3 H8    23 DA  H2'2  2.420   3.810     (#15,17,31,41,73  2.420   3.210)
 &rst
 ixpk= 2, nxpk= 0, iat= 761, 745, r1= 1.92, r2= 2.42, r3= 3.81, r4= 4.31,  &end
#
#  24 DG3 H8    23 DA  H3'   3.440   5.890
 &rst
 ixpk= 2, nxpk= 0, iat= 761, 742, r1= 2.94, r2= 3.44, r3= 5.89, r4= 6.39,  &end
#
#  24 DG3 H8    23 DA  H8    3.410   5.300
 &rst
 ixpk= 2, nxpk= 0, iat= 761, 729, r1= 2.91, r2= 3.41, r3= 5.30, r4= 5.80,  &end
#
#  24 DG3 H8    24 DG3 H1'   2.690   3.890
 &rst
 ixpk= 2, nxpk= 0, iat= 761, 758, r1= 2.19, r2= 2.69, r3= 3.89, r4= 4.39,  &end
#
#  24 DG3 H8    24 DG3 H2'2  1.930   2.930    (#op 32 1.930   2.830   )
 &rst
 ixpk= 32, nxpk= 0, iat= 761, 778, r1= 1.43, r2= 1.93, r3= 2.93, r4= 3.43,  &end
#
#  24 DG3 H8    24 DG3 H3'   2.950   6.050
 &rst
 ixpk= 32, nxpk= 0, iat= 761, 775, r1= 2.45, r2= 2.95, r3= 6.05, r4= 6.55,  &end
```

## IQ at G[1]

```
#
#   1 DC5 H2'1  1 DC5 H1'   2.210   3.980
 &rst
  ixpk= 0, nxpk= 0, iat=  26,  10, r1= 1.71, r2= 2.21, r3= 3.98, r4= 4.48,
     rk2=20.0, rk3=20.0, ir6=1, ialtd=0,
 &end
#
#   1 DC5 H3'   1 DC5 H1'   3.450   5.910
 &rst
  ixpk= 0, nxpk= 0, iat=  24,  10, r1= 2.95, r2= 3.45, r3= 5.91, r4= 6.41,  &end
#
#   1 DC5 H3'   1 DC5 H2'2  2.380   4.610   (#1  3.080   4.610   )
 &rst
  ixpk= 3, nxpk= 0, iat=  24,  27, r1= 1.88, r2= 2.38, r3= 4.61, r4= 5.11,  &end
#
#   1 DC5 H3'   1 DC5 H2'1  2.320   2.620
 &rst
  ixpk= 3, nxpk= 0, iat=  24,  26, r1= 1.82, r2= 2.32, r3= 2.62, r4= 3.12,  &end
#
#   1 DC5 H6    1 DC5 H1'   3.000   5.700
 &rst
  ixpk= 3, nxpk= 0, iat=  13,  10, r1= 2.50, r2= 3.00, r3= 5.70, r4= 6.20,  &end
#
#   1 DC5 H6    1 DC5 H2'1  2.950   5.310   (#1,7,8,57  3.850   5.310   )
 &rst
  ixpk= 3, nxpk= 0, iat=  13,  26, r1= 2.45, r2= 2.95, r3= 5.31, r4= 5.81,  &end
#
#   1 DC5 H6    1 DC5 H3'   4.290   5.580   (#1,28,59  5.390   6.580 )
 &rst
  ixpk= 5, nxpk= 0, iat=  13,  24, r1= 3.79, r2= 4.29, r3= 5.58, r4= 6.08,  &end
#
#   1 DC5 H5    1 DC5 H6   2.100   2.600     (#ma    )
 &rst
  ixpk= 5, nxpk= 0, iat=  15,  13, r1= 1.60, r2= 2.10, r3= 2.60, r4= 3.10,  &end
#
#   2 DT  H2'2  2 DT  H1'   2.120   2.960   (#1,5  2.120   2.360  )
 &rst
  ixpk= 2, nxpk= 0, iat=  59,  40, r1= 1.62, r2= 2.12, r3= 2.96, r4= 3.46,  &end
#
#   2 DT  H2'1  2 DT  H1'   2.350   3.630   (#1  2.650   3.630   )
 &rst
  ixpk= 2, nxpk= 0, iat=  58,  40, r1= 1.85, r2= 2.35, r3= 3.63, r4= 4.13,  &end
#
#   2 DT  H3'   2 DT  H1'   3.620   5.210
 &rst
  ixpk= 2, nxpk= 0, iat=  56,  40, r1= 3.12, r2= 3.62, r3= 5.21, r4= 5.71,  &end
#
#   2 DT  H3'   2 DT  H2'2  2.340   3.360   (#15,41  2.540   3.360   )
 &rst
  ixpk= 2, nxpk= 0, iat=  56,  59, r1= 1.84, r2= 2.34, r3= 3.36, r4= 3.86,  &end
#
#   2 DT  H3'   2 DT  H2'1  2.300   2.740   (#34,53  2.300   2.640   )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat=  56,  58, r1= 1.80, r2= 2.30, r3= 2.74, r4= 3.24,  &end
#
#   2 DT  H4'   2 DT  H1'   2.650   3.220    (#61 2.650   2.920  )
 &rst
  ixpk= 2, nxpk= 0, iat=  37,  40, r1= 2.15, r2= 2.65, r3= 3.22, r4= 3.72,  &end
#
#   2 DT  H6    1 DC5 H1'   1.480   3.140    (#op 1,18,46,61  1.480   1.940  )
 &rst
  ixpk= 1, nxpk= 0, iat=  43,  10, r1= 0.98, r2= 1.48, r3= 3.14, r4= 3.64,  &end
#
#   2 DT  H6    1 DC5 H3'   3.100   4.670   (#22,59  3.100   4.470   )
 &rst
  ixpk= 3, nxpk= 0, iat=  43,  24, r1= 2.60, r2= 3.10, r3= 4.67, r4= 5.17,  &end
#
#   2 DT  H6    2 DT  H1'   3.050   5.770
 &rst
  ixpk= 3, nxpk= 0, iat=  43,  40, r1= 2.55, r2= 3.05, r3= 5.77, r4= 6.27,  &end
#
#   2 DT  H6    2 DT  H3'   3.210   5.240
 &rst
  ixpk= 3, nxpk= 0, iat=  43,  56, r1= 2.71, r2= 3.21, r3= 5.24, r4= 5.74,  &end
#
#   2 DT  Q5    1 DC5 H1'   2.530   4.500
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  10, r1= 2.03, r2= 2.53, r3= 5.40, r4= 5.90,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H3'   3.270   4.350   (#1,61  3.270   3.750   )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  24, r1= 2.77, r2= 3.27, r3= 5.22, r4= 5.72,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H6    3.390   5.100
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  13, r1= 2.89, r2= 3.39, r3= 6.12, r4= 6.62,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H5    3.200   3.840   (#53,59  3.200   3.540   )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  15, r1= 2.70, r2= 3.20, r3= 4.61, r4= 5.11,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    2 DT  H6    2.310   5.320
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  43, r1= 1.81, r2= 2.31, r3= 6.39, r4= 6.89,
 igr1=  46,  47,  48,
 &end
#
#   2 DT  Q5    1 DC5 H2'2  2.500   3.500   (#ma     )
 &rst
```

```
 ixpk= 3, nxpk= 0, iat=  -1,  27, r1= 2.00, r2= 2.50, r3= 4.20, r4= 4.70,
igr1=  46,  47,  48,
 &end
#
#   3 DC  H2'2  3 DC  H1'   2.030   3.030   (#1,51  2.330   2.530    )
 &rst
  ixpk= 2, nxpk= 0, iat=  89,  72, r1= 1.53, r2= 2.03, r3= 3.03, r4= 3.53,  &end
#
#   2 DT  Q5    2 DT  H1'   4.900   6.160   (#1,4,6,27,33  3.900   5.360 ca 3 H2'  )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1,  40, r1= 4.40, r2= 4.90, r3= 7.40, r4= 7.90,
igr1=  46,  47,  48,
 &end
#
#   3 DC  H2'1  3 DC  H1'   2.460   3.790   (#1,32  3.060   5.790  )
 &rst
  ixpk= 3, nxpk= 0, iat=  88,  72, r1= 1.96, r2= 2.46, r3= 3.79, r4= 4.29,  &end
#
#   3 DC  H6    2 DT  H1'   3.540   4.320   (#30,37  3.540   4.120   )
 &rst
  ixpk= 3, nxpk= 0, iat=  75,  40, r1= 3.04, r2= 3.54, r3= 4.32, r4= 4.82,  &end
#
#   3 DC  H6    2 DT  H2'1  2.260   4.440   (#1,23,24  3.060   4.440)
 &rst
  ixpk= 3, nxpk= 0, iat=  75,  58, r1= 1.76, r2= 2.26, r3= 4.44, r4= 4.94,  &end
#
#   3 DC  H6    3 DC  H1'   3.390   3.760   (#53  3.390   3.560  )
 &rst
  ixpk= 3, nxpk= 0, iat=  75,  72, r1= 2.89, r2= 3.39, r3= 3.76, r4= 4.26,  &end
#
#   3 DC  H6    3 DC  H2'1  2.300   3.660   (#10,35,59,62  2.300   2.560   )
 &rst
  ixpk= 2, nxpk= 0, iat=  75,  88, r1= 1.80, r2= 2.30, r3= 3.66, r4= 4.16,  &end
#
#   3 DC  H6    3 DC  H3'   4.170   5.630
 &rst
  ixpk= 2, nxpk= 0, iat=  75,  86, r1= 3.67, r2= 4.17, r3= 5.63, r4= 6.13,  &end
#
#   3 DC  H5    2 DT  H1'   3.910   4.940
 &rst
  ixpk= 2, nxpk= 0, iat=  77,  40, r1= 3.41, r2= 3.91, r3= 4.94, r4= 5.44,  &end
#
#   3 DC  H5    2 DT  H2'1  3.070   3.970   (#op 17,61  3.070   3.870   )
 &rst
  ixpk= 17, nxpk= 0, iat=  77,  58, r1= 2.57, r2= 3.07, r3= 3.97, r4= 4.47,  &end
#
#   3 DC  H5    2 DT  Q5    3.030   5.150   (#1,21,38  3.030   3.250 ca 3 H2')
 &rst
  ixpk= 3, nxpk= 0, iat=  77,  -1, r1= 2.53, r2= 3.03, r3= 6.18, r4= 6.68,
igr2=  46,  47,  48,
 &end
#
#   3 DC  H5    3 DC  H6    2.100   2.600   (#ma   )
 &rst
  ixpk= 3, nxpk= 0, iat=  77,  75, r1= 1.60, r2= 2.10, r3= 2.60, r4= 3.10,  &end
```

```
#
#   4 DKA H2'2  4 DKA H1'   2.070   3.060   (#op 1,42 2.070   2.460   )
 &rst
  ixpk= 1, nxpk= 0, iat= 105, 102, r1= 1.57, r2= 2.07, r3= 3.06, r4= 3.56,  &end
#
#   4 DKA H2'1  4 DKA H1'   2.390   4.490   (#br 1,14,59  3.090   4.490    )
 &rst
  ixpk= 1, nxpk= 0, iat= 104, 102, r1= 1.89, r2= 2.39, r3= 4.49, r4= 4.99,  &end
#
#   4 DKA H3'   4 DKA H1'   3.780   5.540   (#11  3.880   5.540   )
 &rst
  ixpk= 3, nxpk= 0, iat= 145, 102, r1= 3.28, r2= 3.78, r3= 5.54, r4= 6.04,  &end
#
#   4 DKA H3'   4 DKA H2'1  2.470   2.780
 &rst
  ixpk= 3, nxpk= 0, iat= 145, 104, r1= 1.97, r2= 2.47, r3= 2.78, r4= 3.28,  &end
#
#   4 DKA H19   4 DKA H20   2.370   2.750
 &rst
  ixpk= 3, nxpk= 0, iat= 125, 127, r1= 1.87, r2= 2.37, r3= 2.75, r4= 3.25,  &end
#
#   4 DKA H11   4 DKA H1'   2.820   3.580
 &rst
  ixpk= 3, nxpk= 0, iat= 118, 102, r1= 2.32, r2= 2.82, r3= 3.58, r4= 4.08,  &end
#
#   4 DKA H11   4 DKA H2'2  3.300   6.090   (#br 1,20,43  3.300   4.690 )
 &rst
  ixpk= 1, nxpk= 0, iat= 118, 105, r1= 2.80, r2= 3.30, r3= 6.09, r4= 6.59,  &end
#
#   4 DKA H11   4 DKA H2'1  5.110   6.060   (#53,61,62  5.410   6.560   )
 &rst
  ixpk= 5, nxpk= 0, iat= 118, 104, r1= 4.61, r2= 5.11, r3= 6.06, r4= 6.56,  &end
#
#   4 DKA Q13   4 DKA H11   2.970   3.500   (#1,61  3.370   3.500)
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 118, r1= 2.47, r2= 2.97, r3= 4.20, r4= 4.70,
 igr1= 136, 137, 138,
 &end
#
#   4 DKA Q13   4 DKA H1'   3.400   4.800   (#ma     )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 102, r1= 2.90, r2= 3.40, r3= 5.76, r4= 6.26,
 igr1= 136, 137, 138,
 &end
#
#   4 DKA H18   4 DKA H19   2.330   2.530
 &rst
  ixpk= 3, nxpk= 0, iat= 123, 125, r1= 1.83, r2= 2.33, r3= 2.53, r4= 3.03,  &end
#
#   4 DKA H8    3 DC  H1'   3.920   4.180   (#61 3.920   4.180   )
 &rst
  ixpk= 3, nxpk= 0, iat= 143,  72, r1= 3.42, r2= 3.92, r3= 4.18, r4= 4.68,  &end
#
#   4 DKA H8    3 DC  H2'2  3.000   4.550   (#1,25  3.000   3.150   )
 &rst
```

```
 ixpk= 3, nxpk= 0, iat= 143,  89, r1= 2.50, r2= 3.00, r3= 4.55, r4= 5.05,  &end
#
#   4 DKA H8    3 DC  H2'1  2.350   4.040   (#1,36,61,63  3.350   4.040   )
 &rst
 ixpk= 3, nxpk= 0, iat= 143,  88, r1= 1.85, r2= 2.35, r3= 4.04, r4= 4.54,  &end
#
#   4 DKA H8    3 DC  H6    4.330   5.260   (#40,63  4.330   5.060   )
 &rst
 ixpk= 4, nxpk= 0, iat= 143,  75, r1= 3.83, r2= 4.33, r3= 5.26, r4= 5.76,  &end
#
#   4 DKA H8    4 DKA H1'   3.340   3.960   (#53  3.340   3.760   )
 &rst
 ixpk= 3, nxpk= 0, iat= 143, 102, r1= 2.84, r2= 3.34, r3= 3.96, r4= 4.46,  &end
#
#   4 DKA H8    4 DKA H2'2  2.200   5.440   (#1,13  2.900   5.440    )
 &rst
 ixpk= 2, nxpk= 0, iat= 143, 105, r1= 1.70, r2= 2.20, r3= 5.44, r4= 5.94,  &end
#
#   4 DKA H8    4 DKA H3'   3.350   4.570   (#1,26  3.350   3.970    )
 &rst
 ixpk= 3, nxpk= 0, iat= 143, 145, r1= 2.85, r2= 3.35, r3= 4.57, r4= 5.07,  &end
#
#   5 DG  H1'   4 DKA Q13   4.290   5.650   (#59 4.390   5.650   )
 &rst
 ixpk= 4, nxpk= 0, iat= 158,  -1, r1= 3.79, r2= 4.29, r3= 6.79, r4= 7.29,
igr2= 136, 137, 138,
 &end
#
#   5 DG  H2'2  5 DG  H1'   2.250   3.050
 &rst
 ixpk= 4, nxpk= 0, iat= 178, 158, r1= 1.75, r2= 2.25, r3= 3.05, r4= 3.55,  &end
#
#   5 DG  H2'1  5 DG  H1'   2.350   3.970   (#op 1,19  2.650   3.970   )
 &rst
 ixpk= 1, nxpk= 0, iat= 177, 158, r1= 1.85, r2= 2.35, r3= 3.97, r4= 4.47,  &end
#
#   5 DG  H3'   5 DG  H1'   3.610   4.900
 &rst
 ixpk= 1, nxpk= 0, iat= 175, 158, r1= 3.11, r2= 3.61, r3= 4.90, r4= 5.40,  &end
#
#   5 DG  H8    4 DKA H1'   4.030   4.640
 &rst
 ixpk= 1, nxpk= 0, iat= 161, 102, r1= 3.53, r2= 4.03, r3= 4.64, r4= 5.14,  &end
#
#   5 DG  H8    4 DKA Q13   4.540   5.340
 &rst
 ixpk= 1, nxpk= 0, iat= 161,  -1, r1= 4.04, r2= 4.54, r3= 6.41, r4= 6.91,
igr2= 136, 137, 138,
 &end
#
#   5 DG  H8    5 DG  H1'   3.440   3.850   (#53  3.440   3.750   )
 &rst
 ixpk= 3, nxpk= 0, iat= 161, 158, r1= 2.94, r2= 3.44, r3= 3.85, r4= 4.35,  &end
#
#   5 DG  H8    5 DG  H2'1  2.520   3.610   (#op 1  2.320   2.810   )
```

```
 &rst
  ixpk= 1, nxpk= 0, iat= 161, 177, r1= 2.02, r2= 2.52, r3= 3.61, r4= 4.11,  &end
#
#   5 DG  H8    5 DG  H3'   3.680   5.150
 &rst
  ixpk= 1, nxpk= 0, iat= 161, 175, r1= 3.18, r2= 3.68, r3= 5.15, r4= 5.65,  &end
#
#   5 DG  H8    4 DKA H2'1  3.800   5.000   (#ma     )
 &rst
  ixpk= 1, nxpk= 0, iat= 161, 104, r1= 3.30, r2= 3.80, r3= 5.00, r4= 5.50,  &end
#
#   6 DC  H2'1  6 DC  H1'   2.120   3.080   (#op 1  2.120   2.780   )
 &rst
  ixpk= 1, nxpk= 0, iat= 207, 191, r1= 1.62, r2= 2.12, r3= 3.08, r4= 3.58,  &end
#
#   6 DC  H2'2  6 DC  H1'   2.400   4.810   (#1,6,45  3.000   4.810   )
 &rst
  ixpk= 3, nxpk= 0, iat= 208, 191, r1= 1.90, r2= 2.40, r3= 4.81, r4= 5.31,  &end
#
#   6 DC  H6    5 DG  H3'   5.360   6.840   (#wk 2,34,59 6.260   6.840    )
 &rst
  ixpk= 2, nxpk= 0, iat= 194, 175, r1= 4.86, r2= 5.36, r3= 6.84, r4= 7.34,  &end
#
#   6 DC  H6    5 DG  H8    4.480   5.930   (#61 4.580   6.930   )
 &rst
  ixpk= 4, nxpk= 0, iat= 194, 161, r1= 3.98, r2= 4.48, r3= 5.93, r4= 6.43,  &end
#
#   6 DC  H6    6 DC  H2'2  2.180   3.040  (#op 22,30  2.180   2.640)
 &rst
  ixpk= 22, nxpk= 0, iat= 194, 208, r1= 1.68, r2= 2.18, r3= 3.04, r4= 3.54,  &end
#
#   6 DC  H6    6 DC  H3'   4.300   5.000  (#ma  6,62  4.700   6.000 )
 &rst
  ixpk= 6, nxpk= 0, iat= 194, 205, r1= 3.80, r2= 4.30, r3= 5.00, r4= 5.50,  &end
#
#   6 DC  H5    5 DG  H1'   4.500   5.420
 &rst
  ixpk= 6, nxpk= 0, iat= 196, 158, r1= 4.00, r2= 4.50, r3= 5.42, r4= 5.92,  &end
#
#   6 DC  H5    5 DG  H2'2  3.270   4.240   (#1  3.270   3.840   )
 &rst
  ixpk= 3, nxpk= 0, iat= 196, 178, r1= 2.77, r2= 3.27, r3= 4.24, r4= 4.74,  &end
#
#   6 DC  H5    5 DG  H2'1  3.620   4.570   (#53  3.620   4.270    )
 &rst
  ixpk= 3, nxpk= 0, iat= 196, 177, r1= 3.12, r2= 3.62, r3= 4.57, r4= 5.07,  &end
#
#   6 DC  H5    5 DG  H8    3.730   4.100
 &rst
  ixpk= 3, nxpk= 0, iat= 196, 161, r1= 3.23, r2= 3.73, r3= 4.10, r4= 4.60,  &end
#
#   6 DC  H5    6 DC  H2'2  3.540   5.260
 &rst
  ixpk= 3, nxpk= 0, iat= 196, 208, r1= 3.04, r2= 3.54, r3= 5.26, r4= 5.76,  &end
#
```

```
#   7 DG  H8    6 DC  H1'   3.320   4.400  (#op 17 3.520   4.400)
 &rst
  ixpk= 17, nxpk= 0, iat= 224, 191, r1= 2.82, r2= 3.32, r3= 4.40, r4= 4.90,  &end
#
#   7 DG  H8    6 DC  H2'2  3.100   3.900  (#ma    )
 &rst
  ixpk= 17, nxpk= 0, iat= 224, 208, r1= 2.60, r2= 3.10, r3= 3.90, r4= 4.40,  &end
#
#   8 DC  H2'2  8 DC  H1'   1.790   3.100    (#1,38  1.790   2.300  )
 &rst
  ixpk= 1, nxpk= 0, iat= 271, 254, r1= 1.29, r2= 1.79, r3= 3.10, r4= 3.60,  &end
#
#   8 DC  H2'1  8 DC  H1'   2.450   3.690   (#1,10  3.150   3.590   )
 &rst
  ixpk= 3, nxpk= 0, iat= 270, 254, r1= 1.95, r2= 2.45, r3= 3.69, r4= 4.19,  &end
#
#   8 DC  H3'   8 DC  H1'   3.670   5.480   (#7  3.870   5.480   )
 &rst
  ixpk= 3, nxpk= 0, iat= 268, 254, r1= 3.17, r2= 3.67, r3= 5.48, r4= 5.98,  &end
#
#   8 DC  H3'   8 DC  H2'2  2.390   3.450   (#1,2,3,32  2.790   3.450   )
 &rst
  ixpk= 2, nxpk= 0, iat= 268, 271, r1= 1.89, r2= 2.39, r3= 3.45, r4= 3.95,  &end
#
#   8 DC  H3'   8 DC  H2'1  2.500   2.920
 &rst
  ixpk= 2, nxpk= 0, iat= 268, 270, r1= 2.00, r2= 2.50, r3= 2.92, r4= 3.42,  &end
#
#   8 DC  H6    7 DG  H1'   3.050   4.300   (#op 1,19,23,59  2.050   2.500   )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 221, r1= 2.55, r2= 3.05, r3= 4.30, r4= 4.80,  &end
#
#   8 DC  H6    7 DG  H2'2  2.420   3.270   (#op 1  2.420   3.070   )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 241, r1= 1.92, r2= 2.42, r3= 3.27, r4= 3.77,  &end
#
#   8 DC  H6    7 DG  H2'1  2.480   4.400   (#op 1,61  2.780   5.400   )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 240, r1= 1.98, r2= 2.48, r3= 4.40, r4= 4.90,  &end
#
#   8 DC  H6    7 DG  H8    3.640   4.430
 (#8 DC  H6    7 DG  H3'   5.090   6.040  #br 29  5.190   6.840   )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 224, r1= 3.14, r2= 3.64, r3= 4.43, r4= 4.93,  &end
#
#   8 DC  H6    8 DC  H1'   2.870   3.770    (#op 1,25  1.870   2.470  )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 254, r1= 2.37, r2= 2.87, r3= 3.77, r4= 4.27,  &end
#
#   8 DC  H6    8 DC  H2'2  2.090   4.250   (#op 1 2.890   4.250    )
 &rst
  ixpk= 1, nxpk= 0, iat= 257, 271, r1= 1.59, r2= 2.09, r3= 4.25, r4= 4.75,  &end
#
#   8 DC  H6    8 DC  H2'1  1.830   3.320   (#br 1,11,14,40,61  1.830   2.420   )
 &rst
```

```
 ixpk= 1, nxpk= 0, iat= 257, 270, r1= 1.33, r2= 1.83, r3= 3.32, r4= 3.82,  &end
#
#   8 DC  H6    8 DC  H3'   3.710   6.030
 &rst
 ixpk= 1, nxpk= 0, iat= 257, 268, r1= 3.21, r2= 3.71, r3= 6.03, r4= 6.53,  &end
#
#   8 DC  H5    7 DG  H1'   4.850   5.450   (#53  3.850   5.350    )
 &rst
 ixpk= 3, nxpk= 0, iat= 259, 221, r1= 4.35, r2= 4.85, r3= 5.45, r4= 5.95,  &end
#
#   8 DC  H5    7 DG  H2'2  3.090   3.900    (#op 1  3.090   3.500  )
 &rst
 ixpk= 1, nxpk= 0, iat= 259, 241, r1= 2.59, r2= 3.09, r3= 3.90, r4= 4.40,  &end
#
#   8 DC  H5    7 DG  H2'1  3.500   4.970
 &rst
 ixpk= 1, nxpk= 0, iat= 259, 240, r1= 3.00, r2= 3.50, r3= 4.97, r4= 5.47,  &end
#
#   8 DC  H5    7 DG  H8    3.510   4.330  (#op 53  3.610   4.330    )
 &rst
 ixpk= 53, nxpk= 0, iat= 259, 224, r1= 3.01, r2= 3.51, r3= 4.33, r4= 4.83,  &end
#
#   8 DC  H5    8 DC  H2'2  2.940   6.700
 &rst
 ixpk= 53, nxpk= 0, iat= 259, 271, r1= 2.44, r2= 2.94, r3= 6.70, r4= 7.20,  &end
#
#   8 DC  H5    8 DC  H2'1  3.370   5.280
 &rst
 ixpk= 53, nxpk= 0, iat= 259, 270, r1= 2.87, r2= 3.37, r3= 5.28, r4= 5.78,  &end
#
#   8 DC  H5    8 DC  H6    2.000   2.600  (#ma     )
 &rst
 ixpk= 53, nxpk= 0, iat= 259, 257, r1= 1.50, r2= 2.00, r3= 2.60, r4= 3.10,  &end
#
#   9 DC  H2'2  9 DC  H1'   2.200   3.010   (#1,5  2.200   2.410   )
 &rst
 ixpk= 2, nxpk= 0, iat= 301, 284, r1= 1.70, r2= 2.20, r3= 3.01, r4= 3.51,  &end
#
#   9 DC  H2'1  9 DC  H1'   2.470   5.080   (#1  3.170   5.580   )
 &rst
 ixpk= 3, nxpk= 0, iat= 300, 284, r1= 1.97, r2= 2.47, r3= 5.08, r4= 5.58,  &end
#
#   9 DC  H6    8 DC  H1'   4.050   4.660
 &rst
 ixpk= 3, nxpk= 0, iat= 287, 254, r1= 3.55, r2= 4.05, r3= 4.66, r4= 5.16,  &end
#
#   9 DC  H6    8 DC  H3'   4.740   5.630   (#53  4.840   6.630   )
 &rst
 ixpk= 4, nxpk= 0, iat= 287, 268, r1= 4.24, r2= 4.74, r3= 5.63, r4= 6.13,  &end
#
#   9 DC  H6    9 DC  H1'   3.290   3.460
 &rst
 ixpk= 4, nxpk= 0, iat= 287, 284, r1= 2.79, r2= 3.29, r3= 3.46, r4= 3.96,  &end
#
#   9 DC  H6    9 DC  H2'1  2.160   2.560   (#59 2.160   2.460   )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 287, 300, r1= 1.66, r2= 2.16, r3= 2.56, r4= 3.06,  &end
#
#   9 DC  H5    8 DC  H2'2  3.300   4.870
 &rst
  ixpk= 2, nxpk= 0, iat= 289, 271, r1= 2.80, r2= 3.30, r3= 4.87, r4= 5.37,  &end
#
#   9 DC  H5    8 DC  H2'1  3.010   4.010
 &rst
  ixpk= 2, nxpk= 0, iat= 289, 270, r1= 2.51, r2= 3.01, r3= 4.01, r4= 4.51,  &end
#
#   9 DC  H5    8 DC  H6    3.340   4.380   (#61 3.340   4.280   )
 &rst
  ixpk= 3, nxpk= 0, iat= 289, 257, r1= 2.84, r2= 3.34, r3= 4.38, r4= 4.88,  &end
#
#   9 DC  H5    9 DC  H2'1  3.460   4.750  (#53,59  3.460   4.550)
 &rst
  ixpk= 3, nxpk= 0, iat= 289, 300, r1= 2.96, r2= 3.46, r3= 4.75, r4= 5.25,  &end
#
#   9 DC  H5    9 DC  H6    2.000   2.600  (#ma     )
 &rst
  ixpk= 3, nxpk= 0, iat= 289, 287, r1= 1.50, r2= 2.00, r3= 2.60, r4= 3.10,  &end
#
#  10 DA  H2'1 10 DA  H1'   2.260   3.450
 &rst
  ixpk= 3, nxpk= 0, iat= 332, 314, r1= 1.76, r2= 2.26, r3= 3.45, r4= 3.95,  &end
#
#  10 DA  H3'  10 DA  H1'   3.250   4.990
 &rst
  ixpk= 3, nxpk= 0, iat= 330, 314, r1= 2.75, r2= 3.25, r3= 4.99, r4= 5.49,  &end
#
#  10 DA  H3'  10 DA  H2'2  2.320   3.450  (#op 12,41  2.520   3.450    )
 &rst
  ixpk= 12, nxpk= 0, iat= 330, 333, r1= 1.82, r2= 2.32, r3= 3.45, r4= 3.95,  &end
#
#  10 DA  H8    9 DC  H1'   2.980   3.600  (#24,37  3.280   3.600    )
 &rst
  ixpk= 3, nxpk= 0, iat= 317, 284, r1= 2.48, r2= 2.98, r3= 3.60, r4= 4.10,  &end
#
#  10 DA  H8    9 DC  H2'2  3.850   5.100  (#1,8 2.950   3.100    )
 &rst
  ixpk= 2, nxpk= 0, iat= 317, 301, r1= 3.35, r2= 3.85, r3= 5.10, r4= 5.60,  &end
#
#  10 DA  H8    9 DC  H2'1  3.340   5.120   (#1,53,59  3.740   6.120   )
 &rst
  ixpk= 3, nxpk= 0, iat= 317, 300, r1= 2.84, r2= 3.34, r3= 5.12, r4= 5.62,  &end
#
#  10 DA  H8    9 DC  H6    4.480   5.660
 &rst
  ixpk= 3, nxpk= 0, iat= 317, 287, r1= 3.98, r2= 4.48, r3= 5.66, r4= 6.16,  &end
#
#  10 DA  H8   10 DA  H3'   4.150   6.080
 &rst
  ixpk= 3, nxpk= 0, iat= 317, 330, r1= 3.65, r2= 4.15, r3= 6.08, r4= 6.58,  &end
#
```

```
#  11 DT  H2'1 11 DT  H1'   2.330   3.310   (#1  2.730   3.310   )
 &rst
  ixpk= 2, nxpk= 0, iat= 364, 346, r1= 1.83, r2= 2.33, r3= 3.31, r4= 3.81,  &end
#
#  11 DT  H6   10 DA  H1'   3.320   3.860
 &rst
  ixpk= 2, nxpk= 0, iat= 349, 314, r1= 2.82, r2= 3.32, r3= 3.86, r4= 4.36,  &end
#
#  11 DT  H6   10 DA  H2'2  2.460   3.210   (#5,10,33  2.460   2.710   )
 &rst
  ixpk= 2, nxpk= 0, iat= 349, 333, r1= 1.96, r2= 2.46, r3= 3.21, r4= 3.71,  &end
#
#  11 DT  H6   10 DA  H2'1  2.220   4.090   (#op 1,15  2.720   4.090   )
 &rst
  ixpk= 1, nxpk= 0, iat= 349, 332, r1= 1.72, r2= 2.22, r3= 4.09, r4= 4.59,  &end
#
#  11 DT  H6   10 DA  H8    4.640   6.090   (#29  4.740   6.090   )
 &rst
  ixpk= 4, nxpk= 0, iat= 349, 317, r1= 4.14, r2= 4.64, r3= 6.09, r4= 6.59,  &end
#
#  11 DT  H6   11 DT  H1'   3.300   3.740   (#4  3.300   3.540   )
 &rst
  ixpk= 3, nxpk= 0, iat= 349, 346, r1= 2.80, r2= 3.30, r3= 3.74, r4= 4.24,  &end
#
#  11 DT  H6   11 DT  H2'2  2.410   4.370   (#1,6,61  2.910   4.370   )
 &rst
  ixpk= 2, nxpk= 0, iat= 349, 365, r1= 1.91, r2= 2.41, r3= 4.37, r4= 4.87,  &end
#
#  11 DT  H6   11 DT  H2'1  2.540   3.880    (#op 1  2.040   2.580  )
 &rst
  ixpk= 1, nxpk= 0, iat= 349, 364, r1= 2.04, r2= 2.54, r3= 3.88, r4= 4.38,  &end
#
#  11 DT  Q5   10 DA  H2'1  3.400   3.550   (#53  3.500   3.550   )
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 332, r1= 2.90, r2= 3.40, r3= 4.26, r4= 4.76,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5   10 DA  H3'   3.880   4.350
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 330, r1= 3.38, r2= 3.88, r3= 5.22, r4= 5.72,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5   10 DA  H8    2.830   3.080
 &rst
  ixpk= 3, nxpk= 0, iat=  -1, 317, r1= 2.33, r2= 2.83, r3= 3.70, r4= 4.20,
 igr1= 352, 353, 354,
 &end
#
#  11 DT  Q5   11 DT  H6    2.740   3.100  (#22  2.840   3.100)
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 349, r1= 2.24, r2= 2.74, r3= 3.72, r4= 4.22,
 igr1= 352, 353, 354,
 &end
```

```
#
#  11 DT  Q5   10 DA  H2'2  3.000   4.500  (#ma    )
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 333, r1= 2.50, r2= 3.00, r3= 5.40, r4= 5.90,
 igr1= 352, 353, 354,
 &end
#
#  12 DC3 H3'  12 DC3 H1'   3.760   5.680   (#1  4.060   5.680   )
 &rst
  ixpk= 4, nxpk= 0, iat= 392, 378, r1= 3.26, r2= 3.76, r3= 5.68, r4= 6.18,  &end
#
#  12 DC3 H6   11 DT  H2'2  2.660   3.150
 &rst
  ixpk= 4, nxpk= 0, iat= 381, 365, r1= 2.16, r2= 2.66, r3= 3.15, r4= 3.65,  &end
#
#  12 DC3 H6   11 DT  H2'1  2.260   3.680    (#1,16,18,31  3.060   3.680  )
 &rst
  ixpk= 3, nxpk= 0, iat= 381, 364, r1= 1.76, r2= 2.26, r3= 3.68, r4= 4.18,  &end
#
#  12 DC3 H6   12 DC3 H1'   3.300   5.450
 &rst
  ixpk= 3, nxpk= 0, iat= 381, 378, r1= 2.80, r2= 3.30, r3= 5.45, r4= 5.95,  &end
#
#  12 DC3 H5   11 DT  H1'   3.850   4.930   (#20,56,59  3.850   4.630   )
 &rst
  ixpk= 3, nxpk= 0, iat= 383, 346, r1= 3.35, r2= 3.85, r3= 4.93, r4= 5.43,  &end
#
#  12 DC3 H5   11 DT  H2'2  3.200   4.120   (#op 21  3.400   4.120   )
 &rst
  ixpk= 21, nxpk= 0, iat= 383, 365, r1= 2.70, r2= 3.20, r3= 4.12, r4= 4.62,  &end
#
#  12 DC3 H5   11 DT  H2'1  3.370   3.700
 &rst
  ixpk= 21, nxpk= 0, iat= 383, 364, r1= 2.87, r2= 3.37, r3= 3.70, r4= 4.20,  &end
#
#  12 DC3 H5   11 DT  H6    3.640   3.950
 &rst
  ixpk= 21, nxpk= 0, iat= 383, 349, r1= 3.14, r2= 3.64, r3= 3.95, r4= 4.45,  &end
#
#  12 DC3 H5   11 DT  Q5    4.070   4.500
 &rst
  ixpk= 21, nxpk= 0, iat= 383,  -1, r1= 3.57, r2= 4.07, r3= 5.40, r4= 5.90,
 igr2= 352, 353, 354,
 &end
#
#  12 DC3 H5   12 DC3 H6    2.000   2.600  (#ma    )
 &rst
  ixpk= 21, nxpk= 0, iat= 383, 381, r1= 1.50, r2= 2.00, r3= 2.60, r4= 3.10,  &end
#
#  13 DG5 H2'2 13 DG5 H1'   2.050   3.090  (#op 1  2.050   2.490    )
 &rst
  ixpk= 1, nxpk= 0, iat= 427, 407, r1= 1.55, r2= 2.05, r3= 3.09, r4= 3.59,  &end
#
#  13 DG5 H2'1 13 DG5 H1'   2.350   2.920
 &rst
```

```
 ixpk= 1, nxpk= 0, iat= 426, 407, r1= 1.85, r2= 2.35, r3= 2.92, r4= 3.42,  &end
#
#  13 DG5 H8   13 DG5 H1'   3.130   3.940   (#1,63  3.130   3.540   )
 &rst
 ixpk= 3, nxpk= 0, iat= 410, 407, r1= 2.63, r2= 3.13, r3= 3.94, r4= 4.44,  &end
#
#  13 DG5 H8   13 DG5 H2'2  2.670   4.390   (#op 7,32,59  3.170   4.390   )
 &rst
 ixpk= 7, nxpk= 0, iat= 410, 427, r1= 2.17, r2= 2.67, r3= 4.39, r4= 4.89,  &end
#
#  10 DA  H1'  11 DT  Q5    3.300   4.250   (#58,61 3.300   4.050   )
 &rst
 ixpk= 3, nxpk= 0, iat= 314,  -1, r1= 2.80, r2= 3.30, r3= 5.10, r4= 5.60,
igr2= 352, 353, 354,
 &end
#
#  14 DA  H2'1 14 DA  H1'   2.340   3.660   (#op 26  2.540   3.660   )
 &rst
 ixpk= 26, nxpk= 0, iat= 458, 440, r1= 1.84, r2= 2.34, r3= 3.66, r4= 4.16,  &end
#
#  14 DA  H3'  14 DA  H1'   3.190   4.600
 &rst
 ixpk= 26, nxpk= 0, iat= 456, 440, r1= 2.69, r2= 3.19, r3= 4.60, r4= 5.10,  &end
#
#  14 DA  H3'  14 DA  H2'2  2.340   3.260   (#op 11,14  2.540   3.260   )
 &rst
 ixpk= 11, nxpk= 0, iat= 456, 459, r1= 1.84, r2= 2.34, r3= 3.26, r4= 3.76,  &end
#
#  14 DA  H8   13 DG5 H1'   2.980   3.790   (#40  3.180   3.690   )
 &rst
 ixpk= 3, nxpk= 0, iat= 443, 407, r1= 2.48, r2= 2.98, r3= 3.79, r4= 4.29,  &end
#
#  14 DA  H8   14 DA  H3'   3.330   5.060
 &rst
 ixpk= 3, nxpk= 0, iat= 443, 456, r1= 2.83, r2= 3.33, r3= 5.06, r4= 5.56,  &end
#
#  15 DT  H2'2 15 DT  H1'   2.170   2.980   (#1  2.170   2.480   )
 &rst
 ixpk= 2, nxpk= 0, iat= 491, 472, r1= 1.67, r2= 2.17, r3= 2.98, r4= 3.48,  &end
#
#  15 DT  H2'1 15 DT  H1'   2.200   5.590   (#1  3.000   5.590   )
 &rst
 ixpk= 3, nxpk= 0, iat= 490, 472, r1= 1.70, r2= 2.20, r3= 5.59, r4= 6.09,  &end
#
#  15 DT  H6   14 DA  H1'   3.420   3.860   (#62 3.420   3.860   )
 &rst
 ixpk= 3, nxpk= 0, iat= 475, 440, r1= 2.92, r2= 3.42, r3= 3.86, r4= 4.36,  &end
#
#  15 DT  H6   14 DA  H2'2  2.590   3.060   (#53  2.590   2.760   )
 &rst
 ixpk= 2, nxpk= 0, iat= 475, 459, r1= 2.09, r2= 2.59, r3= 3.06, r4= 3.56,  &end
#
#  15 DT  H6   14 DA  H2'1  2.200   4.210   (#op 1,57  3.000   4.210   )
 &rst
 ixpk= 1, nxpk= 0, iat= 475, 458, r1= 1.70, r2= 2.20, r3= 4.21, r4= 4.71,  &end
```

```
#
#  15 DT  H6   14 DA  H8    4.570   6.190
 &rst
  ixpk= 1, nxpk= 0, iat= 475, 443, r1= 4.07, r2= 4.57, r3= 6.19, r4= 6.69,  &end
#
#  15 DT  H6   15 DT  H1'   3.280   3.800   (#9,59  3.280   3.500   )
 &rst
  ixpk= 3, nxpk= 0, iat= 475, 472, r1= 2.78, r2= 3.28, r3= 3.80, r4= 4.30,  &end
#
#  15 DT  H6   15 DT  H2'2  2.550   4.720   (#13,18,30,34,36,38,59  3.350   4.720   )
 &rst
  ixpk= 3, nxpk= 0, iat= 475, 491, r1= 2.05, r2= 2.55, r3= 4.72, r4= 5.22,  &end
#
#  15 DT  H6   15 DT  H2'1  2.330   4.400    (#1  2.330   2.500  )
 &rst
  ixpk= 2, nxpk= 0, iat= 475, 490, r1= 1.83, r2= 2.33, r3= 4.40, r4= 4.90,  &end
#
#  15 DT  Q5   14 DA  H1'   3.890   5.020
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 440, r1= 3.39, r2= 3.89, r3= 6.03, r4= 6.53,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5   14 DA  H2'1  3.250   4.110
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 458, r1= 2.75, r2= 3.25, r3= 4.94, r4= 5.44,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5   14 DA  H3'   4.400   4.860
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 456, r1= 3.90, r2= 4.40, r3= 5.84, r4= 6.34,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5   14 DA  H8    3.280   5.570
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 443, r1= 2.78, r2= 3.28, r3= 6.69, r4= 7.19,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5   15 DT  H6    2.770   3.070  (#20  2.870   3.070)
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 475, r1= 2.27, r2= 2.77, r3= 3.69, r4= 4.19,
 igr1= 478, 479, 480,
 &end
#
#  15 DT  Q5   14 DA  H2'2  2.900   4.300  (#ma    )
 &rst
  ixpk= 2, nxpk= 0, iat=  -1, 459, r1= 2.40, r2= 2.90, r3= 5.16, r4= 5.66,
 igr1= 478, 479, 480,
 &end
#
#  16 DG  H2'2 16 DG  H1'   2.160   3.060   (#op 1  2.160   2.460   )
 &rst
```

```
 ixpk= 1, nxpk= 0, iat= 524, 504, r1= 1.66, r2= 2.16, r3= 3.06, r4= 3.56,  &end
#
#  16 DG  H3'  16 DG  H1'   3.240   4.300
 &rst
 ixpk= 1, nxpk= 0, iat= 521, 504, r1= 2.74, r2= 3.24, r3= 4.30, r4= 4.80,  &end
#
#  16 DG  H8   15 DT  H1'   4.030   5.130   (#1,25,61  4.030   4.330   )
 &rst
 ixpk= 4, nxpk= 0, iat= 507, 472, r1= 3.53, r2= 4.03, r3= 5.13, r4= 5.63,  &end
#
#  16 DG  H8   15 DT  H2'2  3.000   3.130
 &rst
 ixpk= 4, nxpk= 0, iat= 507, 491, r1= 2.50, r2= 3.00, r3= 3.13, r4= 3.63,  &end
#
#  16 DG  H8   15 DT  H2'1  3.000   3.900   (#1  3.300   3.900   )
 &rst
 ixpk= 3, nxpk= 0, iat= 507, 490, r1= 2.50, r2= 3.00, r3= 3.90, r4= 4.40,  &end
#
#  16 DG  H8   15 DT  H6    4.460   5.190
 &rst
 ixpk= 3, nxpk= 0, iat= 507, 475, r1= 3.96, r2= 4.46, r3= 5.19, r4= 5.69,  &end
#
#  16 DG  H8   16 DG  H1'   3.330   3.890   (#37 3.330   3.690  )
 &rst
 ixpk= 3, nxpk= 0, iat= 507, 504, r1= 2.83, r2= 3.33, r3= 3.89, r4= 4.39,  &end
#
#  16 DG  H8   16 DG  H2'2  2.280   3.310   (#op 10,12  2.580   4.310  )
 &rst
 ixpk= 10, nxpk= 0, iat= 507, 524, r1= 1.78, r2= 2.28, r3= 3.31, r4= 3.81,  &end
#
#  16 DG  H8   16 DG  H2'1  2.040   3.200   (#op 8,17,29,63  2.040   2.600   )
 &rst
 ixpk= 8, nxpk= 0, iat= 507, 523, r1= 1.54, r2= 2.04, r3= 3.20, r4= 3.70,  &end
#
#  16 DG  H8   16 DG  H3'   3.820   6.200
 &rst
 ixpk= 8, nxpk= 0, iat= 507, 521, r1= 3.32, r2= 3.82, r3= 6.20, r4= 6.70,  &end
#
#  17 DG  H2'1 17 DG  H1'   2.360   3.760    (#op 1,14  2.460   3.460  )
 &rst
 ixpk= 1, nxpk= 0, iat= 556, 537, r1= 1.86, r2= 2.36, r3= 3.76, r4= 4.26,  &end
#
#  17 DG  H8   16 DG  H1'   2.940   3.430
 &rst
 ixpk= 1, nxpk= 0, iat= 540, 504, r1= 2.44, r2= 2.94, r3= 3.43, r4= 3.93,  &end
#
#  17 DG  H8   17 DG  H1'   2.670   3.880   (#op 1,22,60  2.670   2.880  )
 &rst
 ixpk= 1, nxpk= 0, iat= 540, 537, r1= 2.17, r2= 2.67, r3= 3.88, r4= 4.38,  &end
#
#  17 DG  H8   17 DG  H2'1  2.170   3.830   (#op 1,23  2.170   2.530   )
 &rst
 ixpk= 1, nxpk= 0, iat= 540, 556, r1= 1.67, r2= 2.17, r3= 3.83, r4= 4.33,  &end
#
#  17 DG  H8   17 DG  H3'   3.220   5.290
```

```
 &rst
  ixpk= 1, nxpk= 0, iat= 540, 554, r1= 2.72, r2= 3.22, r3= 5.29, r4= 5.79,  &end
#
#  18 DC  H2'2 18 DC  H1'   1.920   3.080   (#op 1,24  1.920   2.480  )
 &rst
  ixpk= 1, nxpk= 0, iat= 587, 570, r1= 1.42, r2= 1.92, r3= 3.08, r4= 3.58,  &end
#
#  18 DC  H2'1 18 DC  H1'   2.420   4.200   (#1,61  2.820   4.200   )
 &rst
  ixpk= 2, nxpk= 0, iat= 586, 570, r1= 1.92, r2= 2.42, r3= 4.20, r4= 4.70,  &end
#
#  18 DC  H3'  18 DC  H1'   3.680   5.610   (#wk 1  4.080   5.610   )
 &rst
  ixpk= 1, nxpk= 0, iat= 584, 570, r1= 3.18, r2= 3.68, r3= 5.61, r4= 6.11,  &end
#
#  18 DC  H3'  18 DC  H2'2  2.320   3.560   (#1  2.820   3.560    )
 &rst
  ixpk= 2, nxpk= 0, iat= 584, 587, r1= 1.82, r2= 2.32, r3= 3.56, r4= 4.06,  &end
#
#  18 DC  H3'  18 DC  H2'1  2.620   2.950
 &rst
  ixpk= 2, nxpk= 0, iat= 584, 586, r1= 2.12, r2= 2.62, r3= 2.95, r4= 3.45,  &end
#
#  18 DC  H6   17 DG  H1'   3.180   4.480
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 537, r1= 2.68, r2= 3.18, r3= 4.48, r4= 4.98,  &end
#
#  18 DC  H6   17 DG  H8    3.930   5.920
 &rst
  ixpk= 2, nxpk= 0, iat= 573, 540, r1= 3.43, r2= 3.93, r3= 5.92, r4= 6.42,  &end
#
#  18 DC  H6   18 DC  H2'1  2.150   3.130   (#op 3,42,57,62  2.150   2.530   )
 &rst
  ixpk= 3, nxpk= 0, iat= 573, 586, r1= 1.65, r2= 2.15, r3= 3.13, r4= 3.63,  &end
#
#  18 DC  H6   18 DC  H3'   4.310   6.130
 &rst
  ixpk= 3, nxpk= 0, iat= 573, 584, r1= 3.81, r2= 4.31, r3= 6.13, r4= 6.63,  &end
#
#  18 DC  H5   17 DG  H1'   3.570   4.490   (#15,20,31,59  3.570   3.890   )
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 537, r1= 3.07, r2= 3.57, r3= 4.49, r4= 4.99,  &end
#
#  18 DC  H5   17 DG  H2'2  3.100   3.420
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 557, r1= 2.60, r2= 3.10, r3= 3.42, r4= 3.92,  &end
#
#  18 DC  H5   17 DG  H2'1  3.380   5.460  (#1  3.680   5.460    )
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 556, r1= 2.88, r2= 3.38, r3= 5.46, r4= 5.96,  &end
#
#  18 DC  H5   17 DG  H8    3.700   4.100
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 540, r1= 3.20, r2= 3.70, r3= 4.10, r4= 4.60,  &end
#
```

```
#  18 DC  H5   18 DC  H2'2  4.460   4.990   (#1,6,13  5.360   5.990   )
 &rst
  ixpk= 5, nxpk= 0, iat= 575, 587, r1= 3.96, r2= 4.46, r3= 4.99, r4= 5.49,  &end
#
#  18 DC  H5   18 DC  H2'1  3.900   5.240   (#5,27,33,61  3.400   4.840   )
 &rst
  ixpk= 3, nxpk= 0, iat= 575, 586, r1= 3.40, r2= 3.90, r3= 5.24, r4= 5.74,  &end
#
#  19 DG  H8   18 DC  H1'   3.530   4.240
 &rst
  ixpk= 3, nxpk= 0, iat= 603, 570, r1= 3.03, r2= 3.53, r3= 4.24, r4= 4.74,  &end
#
#  19 DG  H8   18 DC  H3'   5.020   6.580
 &rst
  ixpk= 3, nxpk= 0, iat= 603, 584, r1= 4.52, r2= 5.02, r3= 6.58, r4= 7.08,  &end
#
#  19 DG  H8   18 DC  H6    3.420   3.820   (#53  3.520   3.820)
 &rst
  ixpk= 3, nxpk= 0, iat= 603, 573, r1= 2.92, r2= 3.42, r3= 3.82, r4= 4.32,  &end
#
#  19 DG  H8   18 DC  H2'1  3.000   3.500  (#ma     )
 &rst
  ixpk= 3, nxpk= 0, iat= 603, 586, r1= 2.50, r2= 3.00, r3= 3.50, r4= 4.00,  &end
#
#  20 DC  H1'   4 DKA H19   2.620   3.250
 &rst
  ixpk= 3, nxpk= 0, iat= 633, 125, r1= 2.12, r2= 2.62, r3= 3.25, r4= 3.75,  &end
#
#  20 DC  H2'2  4 DKA H19   2.340   4.880    (#op 1  2.340   3.180  )
 &rst
  ixpk= 1, nxpk= 0, iat= 650, 125, r1= 1.84, r2= 2.34, r3= 4.88, r4= 5.38,  &end
#
#  20 DC  H2'2  4 DKA H18   3.080   5.070   (#1,23,32,35,38  3.080   4.370   )
 &rst
  ixpk= 3, nxpk= 0, iat= 650, 123, r1= 2.58, r2= 3.08, r3= 5.07, r4= 5.57,  &end
#
#  20 DC  H2'1  4 DKA H19   2.590   3.770
 &rst
  ixpk= 3, nxpk= 0, iat= 649, 125, r1= 2.09, r2= 2.59, r3= 3.77, r4= 4.27,  &end
#
#  20 DC  H2'1  4 DKA H18   3.340   4.610
 &rst
  ixpk= 3, nxpk= 0, iat= 649, 123, r1= 2.84, r2= 3.34, r3= 4.61, r4= 5.11,  &end
#
#  20 DC  H2'1 20 DC  H1'   2.430   3.820  (#op 1,17 2.730   3.820   )
 &rst
  ixpk= 1, nxpk= 0, iat= 649, 633, r1= 1.93, r2= 2.43, r3= 3.82, r4= 4.32,  &end
#
#  20 DC  H3'  20 DC  H2'1  2.540   2.870
 &rst
  ixpk= 1, nxpk= 0, iat= 647, 649, r1= 2.04, r2= 2.54, r3= 2.87, r4= 3.37,  &end
#
#  20 DC  H6    4 DKA H19   2.900   3.770
 &rst
  ixpk= 1, nxpk= 0, iat= 636, 125, r1= 2.40, r2= 2.90, r3= 3.77, r4= 4.27,  &end
```

```
#
#  20 DC  H6    4 DKA H18   3.430   4.500
 &rst
  ixpk= 1, nxpk= 0, iat= 636, 123, r1= 2.93, r2= 3.43, r3= 4.50, r4= 5.00,  &end
#
#  20 DC  H6   19 DG  H1'   3.210   4.720  (#1,19  3.210   3.620    )
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 600, r1= 2.71, r2= 3.21, r3= 4.72, r4= 5.22,  &end
#
#  20 DC  H6   19 DG  H2'2  2.480   2.970   (#63 2.580   2.970   )
 &rst
  ixpk= 2, nxpk= 0, iat= 636, 620, r1= 1.98, r2= 2.48, r3= 2.97, r4= 3.47,  &end
#
#  20 DC  H6   19 DG  H2'1  2.670   4.440    (#1  3.270   4.840  )
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 619, r1= 2.17, r2= 2.67, r3= 4.44, r4= 4.94,  &end
#
#  20 DC  H6   19 DG  H8    3.980   4.590
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 603, r1= 3.48, r2= 3.98, r3= 4.59, r4= 5.09,  &end
#
#  20 DC  H6   20 DC  H1'   3.230   3.530   (#62 3.230   3.430   )
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 633, r1= 2.73, r2= 3.23, r3= 3.53, r4= 4.03,  &end
#
#  20 DC  H6   20 DC  H2'2  2.230   3.060   (#1,7,16,34,50  3.330   5.660    )
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 650, r1= 1.73, r2= 2.23, r3= 3.06, r4= 3.56,  &end
#
#  20 DC  H6   20 DC  H2'1  2.350   2.520
 &rst
  ixpk= 3, nxpk= 0, iat= 636, 649, r1= 1.85, r2= 2.35, r3= 2.52, r4= 3.02,  &end
#
#  20 DC  H5    4 DKA H18   4.380   5.180   (#1,2,26,28,37,61  3.380   3.680   )
 &rst
  ixpk= 3, nxpk= 0, iat= 638, 123, r1= 3.88, r2= 4.38, r3= 5.18, r4= 5.68,  &end
#
#  20 DC  H5   19 DG  H1'   3.800   5.380    (#op 1,39  3.800   4.680  )
 &rst
  ixpk= 1, nxpk= 0, iat= 638, 600, r1= 3.30, r2= 3.80, r3= 5.38, r4= 5.88,  &end
#
#  20 DC  H5   19 DG  H2'2  3.240   3.540
 &rst
  ixpk= 1, nxpk= 0, iat= 638, 620, r1= 2.74, r2= 3.24, r3= 3.54, r4= 4.04,  &end
#
#  20 DC  H5   19 DG  H2'1  3.460   4.220   (#op 29,53,62  3.460   3.920   )
 &rst
  ixpk= 29, nxpk= 0, iat= 638, 619, r1= 2.96, r2= 3.46, r3= 4.22, r4= 4.72,  &end
#
#  20 DC  H5   19 DG  H8    3.440   4.090
 &rst
  ixpk= 29, nxpk= 0, iat= 638, 603, r1= 2.94, r2= 3.44, r3= 4.09, r4= 4.59,  &end
#
#  20 DC  H5   20 DC  H2'1  3.500   4.710   (#br 1  3.500   4.110)
 &rst
```

```
 ixpk= 1, nxpk= 0, iat= 638, 649, r1= 3.00, r2= 3.50, r3= 4.71, r4= 5.21,  &end
#
#  20 DC  H5   20 DC  H6    2.100   2.700  (#ma    )
 &rst
 ixpk= 1, nxpk= 0, iat= 638, 636, r1= 1.60, r2= 2.10, r3= 2.70, r4= 3.20,  &end
#
#  21 DC  H1'   4 DKA H19   2.300   3.050  (#op 1,47  2.500   3.350    )
 &rst
 ixpk= 1, nxpk= 0, iat= 663, 125, r1= 1.80, r2= 2.30, r3= 3.05, r4= 3.55,  &end
#
#  21 DC  H1'   4 DKA H18   2.910   4.260   (#53 2.910   4.060   )
 &rst
 ixpk= 2, nxpk= 0, iat= 663, 123, r1= 2.41, r2= 2.91, r3= 4.26, r4= 4.76,  &end
#
#  21 DC  H2'2  4 DKA H19   3.540   6.110
 &rst
 ixpk= 2, nxpk= 0, iat= 680, 125, r1= 3.04, r2= 3.54, r3= 6.11, r4= 6.61,  &end
#
#  21 DC  H2'2 21 DC  H1'   2.300   3.040   (#1,9,40  2.300   2.540   )
 &rst
 ixpk= 2, nxpk= 0, iat= 680, 663, r1= 1.80, r2= 2.30, r3= 3.04, r4= 3.54,  &end
#
#  21 DC  H2'1  4 DKA H19   3.300   4.570   (#56   )
 &rst
 ixpk= 2, nxpk= 0, iat= 679, 125, r1= 2.80, r2= 3.30, r3= 4.57, r4= 5.07,  &end
#
#  21 DC  H2'1 21 DC  H1'   2.370   5.210   (#1  3.070   5.210   )
 &rst
 ixpk= 3, nxpk= 0, iat= 679, 663, r1= 1.87, r2= 2.37, r3= 5.21, r4= 5.71,  &end
#
#  21 DC  H3'  21 DC  H1'   3.890   5.380   (#60,61 4.090   5.380   )
 &rst
 ixpk= 4, nxpk= 0, iat= 677, 663, r1= 3.39, r2= 3.89, r3= 5.38, r4= 5.88,  &end
#
#  21 DC  H3'  21 DC  H2'2  2.340   3.540   (#op 1,25  2.640   3.840   )
 &rst
 ixpk= 1, nxpk= 0, iat= 677, 680, r1= 1.84, r2= 2.34, r3= 3.54, r4= 4.04,  &end
#
#  21 DC  H3'  21 DC  H2'1  2.480   2.900   (#ws 6  2.480   2.700  )
 &rst
 ixpk= 6, nxpk= 0, iat= 677, 679, r1= 1.98, r2= 2.48, r3= 2.90, r4= 3.40,  &end
#
#  21 DC  H4'   4 DKA H19   3.340   3.880   (#6  3.340   3.680   )
 &rst
 ixpk= 3, nxpk= 0, iat= 660, 125, r1= 2.84, r2= 3.34, r3= 3.88, r4= 4.38,  &end
#
#  21 DC  H4'  21 DC  H1'   2.940   3.620    (#1  3.340   3.620  )
 &rst
 ixpk= 3, nxpk= 0, iat= 660, 663, r1= 2.44, r2= 2.94, r3= 3.62, r4= 4.12,  &end
#
#  21 DC  H5'1 21 DC  H1'   2.680   4.390    (#1,4,21  2.680   3.190)
 &rst
 ixpk= 2, nxpk= 0, iat= 657, 663, r1= 2.18, r2= 2.68, r3= 4.39, r4= 4.89,  &end
#
#  21 DC  H5'1  4 DKA H19   4.000   5.500  (#ma  )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 657, 125, r1= 3.50, r2= 4.00, r3= 5.50, r4= 6.00,  &end
#
#  21 DC  H5'2  4 DKA H19   2.980   5.510   (#30  2.980   5.410   )
 &rst
  ixpk= 2, nxpk= 0, iat= 658, 125, r1= 2.48, r2= 2.98, r3= 5.51, r4= 6.01,  &end
#
#  21 DC  H6   20 DC  H1'   3.470   4.210   (#br 53  3.470   4.010   )
 &rst
  ixpk= 53, nxpk= 0, iat= 666, 633, r1= 2.97, r2= 3.47, r3= 4.21, r4= 4.71,  &end
#
#  21 DC  H6   20 DC  H2'2  3.340   4.260   (#op 3  3.340   3.960   )
 &rst
  ixpk= 3, nxpk= 0, iat= 666, 650, r1= 2.84, r2= 3.34, r3= 4.26, r4= 4.76,  &end
#
#  21 DC  H6   20 DC  H2'1  2.860   6.040    (#br 1  4.260   6.740  )
 &rst
  ixpk= 1, nxpk= 0, iat= 666, 649, r1= 2.36, r2= 2.86, r3= 6.04, r4= 6.54,  &end
#
#  21 DC  H6   20 DC  H3'   2.960   3.250    (#53  2.960   3.150  )
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 647, r1= 2.46, r2= 2.96, r3= 3.25, r4= 3.75,  &end
#
#  21 DC  H6   21 DC  H1'   3.380   3.620
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 663, r1= 2.88, r2= 3.38, r3= 3.62, r4= 4.12,  &end
#
#  21 DC  H6   21 DC  H2'2  2.780   4.190
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 680, r1= 2.28, r2= 2.78, r3= 4.19, r4= 4.69,  &end
#
#  21 DC  H6   21 DC  H2'1  3.050   4.000    (#1,24,49  2.250   2.600  )
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 679, r1= 2.55, r2= 3.05, r3= 4.00, r4= 4.50,  &end
#
#  21 DC  H6   21 DC  H3'   3.560   4.410
 &rst
  ixpk= 2, nxpk= 0, iat= 666, 677, r1= 3.06, r2= 3.56, r3= 4.41, r4= 4.91,  &end
#
#  21 DC  H6   21 DC  H4'   4.240   5.660   (#22  4.340   5.660   )
 &rst
  ixpk= 4, nxpk= 0, iat= 666, 660, r1= 3.74, r2= 4.24, r3= 5.66, r4= 6.16,  &end
#
#  21 DC  H6   21 DC  H5'1  3.020   3.820    (#10,52,57,63  3.120   3.320  )
 &rst
  ixpk= 3, nxpk= 0, iat= 666, 657, r1= 2.52, r2= 3.02, r3= 3.82, r4= 4.32,  &end
#
#  21 DC  H6   21 DC  H5'2  3.860   5.900
 &rst
  ixpk= 3, nxpk= 0, iat= 666, 658, r1= 3.36, r2= 3.86, r3= 5.90, r4= 6.40,  &end
#
#  21 DC  H5   20 DC  H3'   3.070   3.650   (#53  3.170   3.650   )
 &rst
  ixpk= 3, nxpk= 0, iat= 668, 647, r1= 2.57, r2= 3.07, r3= 3.65, r4= 4.15,  &end
#
```

```
#  21 DC  H5   21 DC  H2'1  3.770   5.750   (#wk,27 1  3.770   5.150)
 &rst
  ixpk= 1, nxpk= 0, iat= 668, 679, r1= 3.27, r2= 3.77, r3= 5.75, r4= 6.25,  &end
#
#  21 DC  H5   20 DC  H2'2  4.000   5.300
 &rst
  ixpk= 1, nxpk= 0, iat= 668, 650, r1= 3.50, r2= 4.00, r3= 5.30, r4= 5.80,  &end
#
#  21 DC  H5   21 DC  H6    2.100   2.700  (#ma    )
 &rst
  ixpk= 1, nxpk= 0, iat= 668, 666, r1= 1.60, r2= 2.10, r3= 2.70, r4= 3.20,  &end
#
#  22 DG  H1'   4 DKA H20   3.660   4.400   (#op 53 3.660   4.000   )
 &rst
  ixpk= 53, nxpk= 0, iat= 693, 127, r1= 3.16, r2= 3.66, r3= 4.40, r4= 4.90,  &end
#
#  22 DG  H2'2 22 DG  H1'   2.250   3.050   (#1  2.250   2.450   )
 &rst
  ixpk= 2, nxpk= 0, iat= 713, 693, r1= 1.75, r2= 2.25, r3= 3.05, r4= 3.55,  &end
#
#  22 DG  H2'1 22 DG  H1'   2.330   3.760   (#1,31  2.830   3.760   )
 &rst
  ixpk= 2, nxpk= 0, iat= 712, 693, r1= 1.83, r2= 2.33, r3= 3.76, r4= 4.26,  &end
#
#  22 DG  H3'  22 DG  H1'   3.850   5.170    (#1   4.050   5.170  )
 &rst
  ixpk= 4, nxpk= 0, iat= 710, 693, r1= 3.35, r2= 3.85, r3= 5.17, r4= 5.67,  &end
#
#  22 DG  H3'  22 DG  H2'2  2.310   4.030   (#ws 1,14  2.710   4.030  )
 &rst
  ixpk= 1, nxpk= 0, iat= 710, 713, r1= 1.81, r2= 2.31, r3= 4.03, r4= 4.53,  &end
#
#  22 DG  H3'  22 DG  H2'1  2.470   2.930
 &rst
  ixpk= 1, nxpk= 0, iat= 710, 712, r1= 1.97, r2= 2.47, r3= 2.93, r4= 3.43,  &end
#
#  22 DG  H8    4 DKA H19   3.350   4.590   (#1  3.350   3.690   )
 &rst
  ixpk= 3, nxpk= 0, iat= 696, 125, r1= 2.85, r2= 3.35, r3= 4.59, r4= 5.09,  &end
#
#  22 DG  H8   21 DC  H1'   2.890   3.660   (#1,59  3.390   3.660   )
 &rst
  ixpk= 3, nxpk= 0, iat= 696, 663, r1= 2.39, r2= 2.89, r3= 3.66, r4= 4.16,  &end
#
#  22 DG  H8   21 DC  H3'   4.850   6.550
 &rst
  ixpk= 3, nxpk= 0, iat= 696, 677, r1= 4.35, r2= 4.85, r3= 6.55, r4= 7.05,  &end
#
#  22 DG  H8   22 DG  H1'   3.600   4.190
 &rst
  ixpk= 3, nxpk= 0, iat= 696, 693, r1= 3.10, r2= 3.60, r3= 4.19, r4= 4.69,  &end
#
#  22 DG  H8   21 DC  H2'2  4.300   5.300  (#ma    )
 &rst
  ixpk= 3, nxpk= 0, iat= 696, 680, r1= 3.80, r2= 4.30, r3= 5.30, r4= 5.80,  &end
```

```
#
#  23 DA  H2'2 23 DA  H1'   2.180   3.060   (#1,7,57  2.180   2.360   )
 &rst
  ixpk= 2, nxpk= 0, iat= 745, 726, r1= 1.68, r2= 2.18, r3= 3.06, r4= 3.56,  &end
#
#  23 DA  H2'1 23 DA  H1'   2.280   3.410   (#1  2.580   3.500   )
 &rst
  ixpk= 2, nxpk= 0, iat= 744, 726, r1= 1.78, r2= 2.28, r3= 3.41, r4= 3.91,  &end
#
#  23 DA  H3'  23 DA  H2'2  2.280   3.500
 &rst
  ixpk= 2, nxpk= 0, iat= 742, 745, r1= 1.78, r2= 2.28, r3= 3.50, r4= 4.00,  &end
#
#  23 DA  H8   22 DG  H1'   3.620   4.960   (#1,12  3.620   4.160   )
 &rst
  ixpk= 3, nxpk= 0, iat= 729, 693, r1= 3.12, r2= 3.62, r3= 4.96, r4= 5.46,  &end
#
#  23 DA  H8   22 DG  H2'2  2.270   2.830   (#13,18  2.670   2.830   )
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 713, r1= 1.77, r2= 2.27, r3= 2.83, r4= 3.33,  &end
#
#  23 DA  H8   22 DG  H2'1  3.180   4.220
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 712, r1= 2.68, r2= 3.18, r3= 4.22, r4= 4.72,  &end
#
#  23 DA  H8   22 DG  H3'   3.950   4.460
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 710, r1= 3.45, r2= 3.95, r3= 4.46, r4= 4.96,  &end
#
#  23 DA  H8   23 DA  H1'   3.390   3.860
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 726, r1= 2.89, r2= 3.39, r3= 3.86, r4= 4.36,  &end
#
#  23 DA  H8   23 DA  H2'2  2.570   4.640   (#1,33  2.770   4.640  )
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 745, r1= 2.07, r2= 2.57, r3= 4.64, r4= 5.14,  &end
#
#  23 DA  H8   23 DA  H3'   3.540   5.240
 (#23 DA  H8   23 DA  H2'1  2.660   3.920  #op 1,48,61  2.060   2.420   )
 &rst
  ixpk= 2, nxpk= 0, iat= 729, 742, r1= 3.04, r2= 3.54, r3= 5.24, r4= 5.74,  &end
#
#  24 DG3 H2'2 24 DG3 H1'   2.650   4.670
 &rst
  ixpk= 2, nxpk= 0, iat= 778, 758, r1= 2.15, r2= 2.65, r3= 4.67, r4= 5.17,  &end
#
#  24 DG3 H2'1 24 DG3 H1'   2.060   2.320
 &rst
  ixpk= 2, nxpk= 0, iat= 777, 758, r1= 1.56, r2= 2.06, r3= 2.32, r4= 2.82,  &end
#
#  24 DG3 H3'  24 DG3 H1'   3.440   4.210
 &rst
  ixpk= 2, nxpk= 0, iat= 775, 758, r1= 2.94, r2= 3.44, r3= 4.21, r4= 4.71,  &end
#
#  24 DG3 H3'  24 DG3 H2'2  2.210   2.630    (#62 2.310   2.630 )
```

```
 &rst
  ixpk= 2, nxpk= 0, iat= 775, 778, r1= 1.71, r2= 2.21, r3= 2.63, r4= 3.13,  &end
#
#  24 DG3 H3'  24 DG3 H2'1  2.530   3.700
 &rst
  ixpk= 2, nxpk= 0, iat= 775, 777, r1= 2.03, r2= 2.53, r3= 3.70, r4= 4.20,  &end
#
#  24 DG3 H8   23 DA  H2'2  2.770   3.160   (#20,23  2.770   2.960    )
 &rst
  ixpk= 2, nxpk= 0, iat= 761, 745, r1= 2.27, r2= 2.77, r3= 3.16, r4= 3.66,  &end
#
#  24 DG3 H8   23 DA  H2'1  2.650   3.510   (#1,59  3.050   3.510   )
 &rst
  ixpk= 3, nxpk= 0, iat= 761, 744, r1= 2.15, r2= 2.65, r3= 3.51, r4= 4.01,  &end
#
#  24 DG3 H8   23 DA  H3'   4.410   6.120
 &rst
  ixpk= 3, nxpk= 0, iat= 761, 742, r1= 3.91, r2= 4.41, r3= 6.12, r4= 6.62,  &end
#
#  24 DG3 H8   23 DA  H8    3.770   4.260
 &rst
  ixpk= 3, nxpk= 0, iat= 761, 729, r1= 3.27, r2= 3.77, r3= 4.26, r4= 4.76,  &end
#
#  24 DG3 H8   24 DG3 H2'2  2.360   3.740
 &rst
  ixpk= 3, nxpk= 0, iat= 761, 778, r1= 1.86, r2= 2.36, r3= 3.74, r4= 4.24,  &end
#
#  24 DG3 H8   24 DG3 H3'   3.110   4.620
 &rst
  ixpk= 3, nxpk= 0, iat= 761, 775, r1= 2.61, r2= 3.11, r3= 4.62, r4= 5.12,  &end
```

## REFERENCES


(1) Dickerson, R.; Drew, H.; Conner, B.; Wing, R.; Fratini, A.; Kopka, M. *Science* **1982**, *216*, 475.

(2) Watson, J.; Crick, F. *Nature* **1953**, *171*, 737.

(3) Watson, J.; Crick, F. *Nature* **1953**, *171*, 964.

(4) Wilkins, M.; Stokes, A.; Wilson, H. *Nature* **1953**, *171*, 738.

(5) Paleček, E.; Rašovská, E.; Boublíková, P. *Biochem. Biophys. Res. Comm.* **1988**, *150*, 731.

(6) Jiang, H.; Zacharias, W.; Amirhaeri, S. *Nucl. Acids Res.* **1991**, *19*, 6943.

(7) Lua, X.; Shakkedb, Z.; Olson, W. *J. Mol. Biol.* **2000**, *300*, 819.

(8) Wahl, M.; Sundaralingam, M. *Biopolymers* **1997**, *44*, 45.

(9) Pohl, F.; Jovin, T. *J. Mol. Biol.* **1972**, *67*, 375.

(10) Oh, D.; Kim, Y.; Rich, A. *Proc. Natl. Acad. U.S.A.* **2002**, *99*, 16666.

(11) Wang, A.; Quigley, G.; Kolpak, F.; Crawford, J.; Boom, J. v.; Marel, G. v. d.; Rich, A. *Nature* **1979**, *282*, 680.

(12) Muller, J. *Metallomics* **2010**, *2*, 318.

(13) Sinden, R. *DNA Structure and Function*; Elsevier, 2012.

(14) Thomas, D.; Roberts, J.; Sabatino, R.; Meyers, T.; Tan, C.; Downey, K.; So, A.; Bambera, A.; Kunkel, T. *Biochem.* **1991**, *30*, 11751.

(15) Schaaper, R. *J. Biol. Chem.* **1993**, *268*, 23762.

(16) Garg, P.; Burgers, P. *Crit. Rev. Mol. Biol.* **2005**, *40*, 115.

(17) Johnson, A.; O'Donnel, M. *Annu. Rev. Biochem.* **2005**, *74*, 283.

(18) Kool, E. *Annu. Rev. Biochem.* **2002**, *71*, 191.

(19) Goodman, M.; Creighton, S.; Bloom, L.; Petruska, J. *Crit. Rev. Biochem. Mol. Biol.* **1993**, *28*, 83.

(20) Washington, M.; Helquist, S.; Prakash, L.; Prakash, S. *Mol. Cell Biol.* **2003**, *23*, 5107.

(21) Echols, H.; Goodman, M. *Annu. Rev. Biochem.* **1991**, *60*, 477.

(22) Kunkel, T.; Bebenek, K. *Annu. Rev. Biochem.* **2000**, *69*, 487.

(23) Goodman, M. *Proc. Natl. Acad. U.S.A.* **1997**, *94*, 10493.

(24) Johnson, S.; Beese, L. *Cell* **2004**, *116*, 803.

(25) Altieri, F.; Grillo, C.; Maceroni, M.; Chichiarelli, S. *Antioxid. Redox Signaling* **2008**, *10*, 891.

(26) Gupta, R.; Lutz, W. *Mutat. Res* **1999**, *424*, 1.

(27) Iyer, R.; Pluciennik, A.; Burdett, V.; Modrich, P. *Chem. Rev.* **2006**, *106*, 302.

(28) Kim, Y.; Wilson, D. *Curr. Mol. Pharmocol.* **2012**, *5*, 3.

(29) Sancar, A. *Annu. Rev. Biochem.* **1996**, *65*, 43.

(30) Spivak, G. *Mutat. Res* **2008**, *577*, 162.

(31) Masutani, C.; Sugasawa, K.; Yanagisawa, J.; Sonoyama, T.; Ui, M.; Enomoto, T.; Takio, K.; Tanaka, K.; Spek, P. v. d.; Bootsma, D. *EMBO J.* **1994**, *13*, 1831.

(32) Nishi, R.; Okuda, Y.; Watanabe, E.; Mori, T.; Iwai, S.; Masutani, C.; Sugasawa, K.; Hanaoka, F. *Mol. Cell Biol.* **2005**, *25*, 5664.

(33) Chu, G.; Chang, E. *Science* **1988**, *242*, 564.

(34) Wakasugi, M.; Kawashima, A.; Morioka, H.; Linn, S.; Sancar, A.; Mori, T.; Nikaido, O.; Matsunaga, T. *J. Biol. Chem.* **2002**, *277*, 1637.

(35) Scrima, A.; Konickova, R.; Czyzewski, B.; Kawasaki, Y.; Jeffrey, P.; Groisman, R.; Nakatani, Y.; Iwai, S.; Pavletich, N.; Thoma, N. *Cell* **2008**, *135*, 1213.

(36) Sugasawa, K.; Okamoto, T.; Shimizu, Y.; Masutani, C.; Iwai, S.; Hanaoka, F. *Genes Dev.* **2001**, *15*, 507.

(37) Yokoi, M.; Masutani, C.; Maekawa, T.; Sugasawa, K.; Ohkuma, Y.; Hanaoka, F. *J. Biol. Chem.* **2000**, *275*, 9870.

(38) Compe, E.; Egly, J. *Nature Rev. Mol. Cell Biol.* **2012**, *13*, 343.

(39) Camenisch, U.; Dip, R.; Schumacher, S.; Schuler, B.; Naegeli, H. *Nature Struct. and Mol. Biol.* **2006**, *13*, 278.

(40) Sugasawa, K.; Akagi, J.; Nishi, R.; Iwai, S.; Hanaoka, F. *Mol. Cell Biol.* **2009**, *36*, 642.

(41) Wolski, S.; Kuper, J.; Hanzelmann, P.; Truglio, J.; Croteau, D.; Houten, B.; Kisker, C. *PLoS Biol* **2008**, *6*.

(42) Matheiu, N.; Kaczmarek, N.; Ruthemann, P.; Luch, A.; Naegeli, H. *Curr. Biol.* **2013**, *23*, 2014.

(43) Coin, F.; Oksenych, V.; Mocquet, V.; Groh, S.; Blattner, C.; Egly, J. *Mol. Cell Biol.* **2008**, *31*, 9.

(44) Fagbemi, A.; Orelli, B.; Scharer, O. *DNA Repair* **2011**, *10*, 722.

(45) Mocquet, V.; Laine, J.; Riedl, T.; Yajin, Z.; Lee, M.; Egly, J. *EMBO J.* **2008**, *27*, 155.

(46) Orelli, B.; McClendon, T.; Tsodikov, O.; Ellenberger, T.; Niedernhofer, L.; Scharer, O. *J. Biol. Chem.* **2010**, *285*.

(47) Dunand-Sauthier, I.; Hohl, M.; Thorel, F.; Jaquier-Gubler, P.; Clarkson, S.; Scharer, O. *J. Biol. Chem.* **2005**, *280*, 7030.

(48) Staresincic, L.; Fagbemi, A.; Enzlin, J.; Gourdin, A.; Wijgers, N.; Dunand-Sauthier, I.; Giglia-Mari, G.; Clarkson, S.; Vermeulen, W.; Scharer, O. *EMBO J.* **2009**, *28*, 1111.

(49) Ogi, T.; Limsirichaikul, S.; Overmeer, R.; Volker, M.; Takenaka, K.; Cloney, R.; Nakazawa, Y.; Niimi, A.; Miki, Y.; Jaspers, N.; Mullenders, L.; Yamashita, S.; Fousteri, M.; Lehmann, A. *Mol Cell Biol* **37**, *37*, 714.

(50) Marteijn, J.; Lans, H.; Vermeulen, W.; Hoeijmakers, J. *Nature Rev. Mol. Cell Biol.* **2014**, *15*, 465.

(51) Somoza, V.; Fogliano, V. *J. Agric. Food Chem.* **2013**, *61*, 10197.

(52) Hodge, J. *J. Agric. Food Chem.* **1953**, *1*, 928.

(53) Doll, R.; Peto, R. *J. Natl. Cancer Inst* **1981**, *66*, 1191.

(54) Parkin, D. *Lancet Oncol.* **2001**, *2*, 533.

(55) Anderson, K.; Mongin, S.; Sinha, R.; Stolzenberg-Solomon, R.; Gross, M.; Ziegler, R.; Mabie, J.; Risch, A.; Kazin, S.; Church, T. *Mol. Carcinog.* **2011**, *51*, 128.

(56) Lang, N.; Butler, M.; Massengill, J.; Lawson, M.; Stotts, R.; Hauer-Jenson, M.; Kadlubar, F. *Cancer Epidemiol. Biomarkers Prev.* **1994**, *3*.

(57) Snyderwine, E. *Cancer Res.* **1994**, *74*, 1070.

(58) Shirai, T.; Sano, M.; Tamano, S.; Takahashi, S.; Hirose, M.; Futakuchi, M.; Hasegawa, R.; Imaida, K.; Matsumoto, K.; Wakabayashi, K. *Cancer Res.* **1997**, *57*, 195.

(59) Persson, E.; Sjoholm, I.; Skog, K. *J. Agric. Food Chem.* **2003**, *51*, 4472.

(60) Salmon, C.; Kinze, M.; Panteleakos, F.; Wu, R.; Nelson, D.; Felton, J. *J. Natl. Cancer Inst* **2000**, *92*, 1773.

(61) Felton, J.; Jägerstad, M.; Knize, M.; Skog, K.; Wakabayashi, K. In *Food borne carcinogens: Heterocyclic amines*; Nagao M, S. T., e, Ed.; John Wiley & Sons Ltd;: Chichester, 2000, p 31.

(62) Stofer, E.; Lavery, R. *Biopolymers* **1994**, *34*, 337.

(63) Smith, J.; Ameri, F.; Gadgil, P. *J. Food Sci.* **2008**, *73*, T100.

(64) IARC *World Health Organization* **1993**, *56*, 165.

(65) Tanaka, T.; Barnes, W.; Williams, G.; Weisburger., J. *Gann* **1985**, *76*, 570.

(66) Adamson, R.; Thorgeirsson, U.; Snyderwine, E.; Thorgeirsson, S.; Reeves, J.; Dalgard, D.; Takayama, S.; Sugimura, T. *Jpn. J. Canc. Res.* **1990**, *81*, 10.

(67) Turesky, R. *Current Drug Metabolism*; Bentham Science Publishers; Vol. 5.

(68) Koutros, S.; Berndt, S.; Sinha, R.; Ma, X.; Chatterjee, N.; Alavanja, M.; Zheng, T.; Huang, W.; Hayes, R.; Cross, A. *Cancer Res.* **2009**, *69*, 1877.

(69) Milhe, C.; Fuchs, R.; Lefevre, J. *Eur. J. Biochem.* **1996**, *235*, 120.

(70) Koehl, P.; Burnouf, D.; Fuchs, R. *Environ. Sci. Res.* **1990**, *40*, 105.

(71) Jain, N.; Li, Y.; Zhang, L.; Meneni, S.; Cho, B. *Biochem.* **2007**, *46*, 13310.

(72) Koffel-Schwartz, N.; Fuchs, R. *Mol. Gen. Genet.* **1989**, *215*, 306.

(73) Okada, Y.; Streisinger, G.; Owen, J.; Newton, J.; Tsugita, A.; Inouye, M. *Nature* **1972**, *236*, 338.

(74) Prinbow, D.; Sigurdson, D.; Gold, L.; Singer, B.; Napoli, C.; Brosius, J.; Dull, T.; Noller, H. *J. Mol. Biol.* **1981**, *149*, 337.

(75) Farabaugh, P.; Schmeissner, U.; Hofer, M.; Miller, J. *J. Mol. Biol.* **1978**, *126*, 847.

(76) Broschard, T.; Koffel-Schwartz, N.; Fuchs, R. *J. Mol. Biol.* **1999**, *288*, 191.

(77) Sodergren, E.; DeMoss, J. *J. Bacteriol.* **1988**, *170*, 1721.

(78) Streisinger, G.; Okada, Y.; Emrich, J.; Newton, J.; Tsugita, A.; Terzaghi, E.; Inoye, M. *Cold Spring Harb. Symp. Quant. Biol.* **1966**, *31*, 77.

(79) Drake, J.; Glickman, B.; Ripley, L. *Am. Scient.* **1983**, *71*, 621.

(80) Streisinger, G.; Owen, J. *Genetics* **1985**, *109*, 6330.

(81) Oliveira, E.; Padua, J.; Zucchi, M.; Vencovsky, R.; Viera, M. *Genet. Mol. Biol.* **2006**, *29*.

(82) Jain, V.; Hilton, B.; Patnaik, S.; Zou, Y.; Chiarelli, M.; Cho, B. *Nucl. Acids Res.* **2012**, *40*, 3939.

(83) Grishaev, A.; Tugarinov, V.; Kay, L.; Trewhella, J.; Bax, A. *J. Biomol. NMR* **2008**, *40*, 95.

(84) Bragg, W. *Proc. R. Soc. Lond.* **1913**, *A89*, 248.

(85) Kendrew, J.; Bodo, G.; Dintzis, H.; Parrish, R.; Wyckoff, H. *Nature* **1958**, *181*, 662.

(86) Bioinformatics, R. C. f. S. 2014.

(87) Ducruix, A.; Giege, R. *Crystallization of nucleic acids and proteins. A practical approach*; Oxford University Press: New York, 1992.

(88) Yaffe, M. *Critical Care Medicine* **2005**, *33*, S435.

(89) Taylor, G. *Acta Cryst.* **2003**, *D 59*.

(90) Rossman, M. *Acta Cryst. A.* **1990**, *46*, 73.

(91) Ealick, S. *Curr. Opin. Struct. Biol.* **2000**, *4*, 495.

(92) Hendrickson, W. *Trans. ACA* **1985**, *21*.

(93) Rice, L.; Earnest, T.; Brunger, A. *Acta Cryst. D. Biol. Crystallogr.* **2000**, *56*, 1413.

(94) Wells, A. F. *Structural Inorganic Chemistry*; 5 ed.; Oxford University Press, 1984.

(95) Kleywegt, G.; Brunger, A. *Structure* **1996**, *15*, 897.

(96) Bhattacharya, A. *Nature* **2010**, *463*, 605.

(97) Marion, D.; Wuthrich, K. *Biochem. Biophys. Res. Comm.* **1983**, *113*, 967.

(98) Broido, M.; Zon, G.; James, T. *Biochem. Biophys. Res. Comm.* **1984**, *119*, 663.

(99) Scheek, R.; Russo, N.; Boelens, R.; Kaptein, R.; Boom, J. V. *J. Am. Chem. Soc.* **1983**, *105*, 2914.

(100) Boelens, R.; Scheek, R.; Dijkstra, K.; Kaptein, R. *J. Magn. Reson.* **1985**, *62*, 378.

(101) Borgias, B.; James, T. *Meth. in Enzymol.* **1989**, *176*, 169.

(102) Borgias, B.; James, T. *J. Magn. Reson.* **1990**, *87*, 475.

(103) Bassolino-Klimas, D.; Tejero, R.; Krystek, S.; Metzler, W.; Montelione, G.; Bruccoleri, R. *Protein Sci.* **1996**, *5*, 593.

(104) P. Khandelwal; Panchal, S.; Hosur, R. *Nucl. Acids Res.* **2001**, *29*, 499.

(105) James, T.; Basus, V. *Annu. Rev. Phys. Chem.* **1991**, *42*, 501.

(106) Schmitz, U.; Pearlman, D.; James, T. *J. Mol. Biol.* **1991**, *221*, 271.

(107) Madrid, M.; Llinas, E.; Llinas, M. *J. Magn. Reson.* **1991**, *93*, 329.

(108) Lavery, R.; Sklenar, H. *J. Biomol. Struct. Dyn.* **1989**, *6*, 655.

(109) Lu, X.; Olson, W. *Nucl. Acids Res.* **2003**, *31*, 5108.

(110) Bishop, G.; Chaires, J. *Current Protocols in Nucleic Acid Chemistry* **2003**, *11:7.11:7.11.1–7.11.8.*

(111) Polavarapu, P.; Zhao, C. *Fresenius J. Anal. Chem.* **2000**, *366*, 727.

(112) Stover, J.; Rizzo, C. *Chem. Res. Toxicol.* **2007**, *20*, 1972.

(113) Wu, Y.; Ghosh, A.; Szyperski, T. *J. Struct. Funct. Genomics* **2009**, *10*, 227.

(114) Piotto, M.; Saudek, V.; Sklenar, V. *J. Biomol. NMR* **1992**, *2*, 661.

(115) Goddard, T.; Kneller, D. University of California, San Francisco, 2006.

(116) James, T. *Curr. Opin. Struct. Biol.* **1991**, *1*, 1042.

(117) Keepers, J.; James, T. *J. Magn. Reson.* **1984**, *57*, 404.

(118) Arnott, S. H., D. W. L. *Biochem. Biophys. Res. Comm.* **1972**, *47*, 1504.

(119) Frisch, M. J. T., G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Pomelli, J.; Ochterski, W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewska, V. G.; Daniels, A. D.; Farkas, O.; Rabuck, A. D.; Raghavachari, K.; Ortiz, J. V. Wallingford, CT, 2004.

(120) Kirkpatrick, S. G., C. D., Jr.; Vecchi, M. P. *Science* **1983**, *220*, 671.

(121) Wang, J.; Wolf, R.; Caldwell, J.; Kollman, P.; Case, D. *J. Comput. Chem.* **2004**, *25*, 1157.

(122) Case, D.; Darden, T.; Cheatham, T.; III, C. S.; Wang, J.; Duke, R.; Luo, R.; Crowley, M.; Walker, R.; Zhang, W.; Merz, K.; B.Wang; Hayik, S.; Roitberg, A.; Seabra, G.; Kolossváry, I.; Wong, K.; Paesani, F.; Vanicek, J.; Wu, X.; Brozell, S.; Steinbrecher, T.; Gohlke, H.; Yang, L.; Tan, C.; Mongan, J.; Hornak, V.; Cui, G.; Mathews, D.; Seetin, M.; Sagui, C.; Babin, V.; Kollman, P. University of California, San Francisco, 2008.

(123) Bashford, D.; Case, D. *Annu. Rev. Phys. Chem.* **2000**, *51*, 129.

(124) Lavery, R.; Moakher, M.; Maddocks, J.; Petkeviciute, D.; Zakrzewska, K. *Nucl. Acids Res.* **2009**, *37*, 5917.

(125) Blanchet, C.; Pasi, M.; Zakrzewska, K.; Lavery, R. *Nucl. Acids Res.* **2011**, *39*, W68.

(126) Pace, C. N.; Vajdos, F.; Fee, L.; Grimsley, G. *Protein Sci.* **1995**, *4*, 2411.

(127) R. Eoff, A. I., K. Angel, M. Egli, F. Guengerich *J. Biol. Chem.* **2007**, *282*.

(128) Eoff, R.; Irmia, A.; Angel, K.; Egli, M.; Guengerich, F. *J. Biol. Chem.* **2007**, *282*, 19831.

(129) Otwinowski, Z.; Minor, W. *Meth. in Enzymol.* **1997**, *276*, 307.

(130) Zang, H.; Irimia, A.; Choi, J.; Angel, K.; Loukachevitch, L.; Egli, M.; Guengerich, F. *J. Biol. Chem.* **2006**, *281*, 2358.

(131) Brunger, A.; Adams, P.; Clore, G.; Delano, W.; Gros, P.; Grosse-Kunstleve, R.; Jiang, J.; Krahn, J.; Kuszewski, J.; Nilges, M.; Pannu, N.; Read, R.; Rice, L.; Schroeder, G.; Simonson, T.; Warren, G. *Acta Cryst.* **1998**, *54*, 905.

(132) Brunger, A. *Nature Protocols* **2007**, *2*, 2728.

(133) Emsley, P.; Lohkamp, B.; Scott, W.; Cowtan, K. *Acta Crystal. Section D - Biol. Crystallog.* **2010**, *66*, 486.

(134) DeLano, W.; DeLano Scientific, LLC: Palo Alto, CA, 2008.

(135) Stover, J. S.; Rizzo, C. J. *Chem. Res. Toxicol.* **2007**, *20*, 1972.

(136) Patel, D. J.; Shapiro, L.; Hare, D. *Q. Rev. Biophys.* **1987**, *20*, 35.

(137) Reid, B. R. *Q. Rev. Biophys.* **1987**, *20*, 2.

(138) Elmquist, E.; Wang, F.; Stover, J.; Stone, M.; Rizzo, C. *Chem. Res. Toxicol.* **2007**, *20*, 445.

(139) Arnott, S.; Hukins, D. W. L. *Biochem. Biophys. Res. Comm.* **1972**, *47*, 1504.

(140) Keepers, J. W.; James, T. L. *J. Magn. Reson.* **1984**, *57*, 404.

(141) Borgias, B. A.; James, T. L. *J. Magn. Reson.* **1990**, *87*, 475.

(142) Bashford, D.; Case, D. A. *Annu. Rev. Phys. Chem.* **2000**, *51*, 129.

(143) James, T. L. *Curr. Opin. Struct. Biol.* **1991**, *1*, 1042.

(144) Turesky, R. J.; Markovic, J.; Aeschlimann, J. M. *Chem. Res. Toxicol.* **1996**, *9*, 397.

(145) Fuchs, R. P.; Schwartz, N.; Daune, M. P. *Nature* **1981**, *294*, 657.

(146) Koffel-Schwartz, N.; Verdier, J. M.; Bichara, M.; Freund, A. M.; Daune, M. P.; Fuchs, R. P. P. *J. Mol. Biol.* **1984**, *177*, 33.

(147) Koehl, P.; Burnouf, D.; Fuchs, R. P. P. *J. Mol. Biol.* **1989**, *207*, 355.

(148) Koehl, P.; Valladier, P.; Lefevre, J. F.; Fuchs, R. P. *Nucleic Acids Res.* **1989**, *17*, 9531.

(149) Broschard, T. H.; Koffel-Schwartz, N.; Fuchs, R. P. *J. Mol. Biol.* **1999**, *288*, 191.

(150) Hoffmann, G. R.; Fuchs, R. P. *Chem. Res. Toxicol.* **1997**, *10*, 347.

(151) Choi, J. Y.; Stover, J. S.; Angel, K. C.; Chowdhury, G.; Rizzo, C. J.; Guengerich, F. P. *J. Biol. Chem.* **2006**, *281*, 25297.

(152) Zaliznyak, T.; Bonala, R.; Johnson, F.; de los Santos, C. *Chem. Res. Toxicol.* **2006**, *19*, 745.

(153) Grad, R.; Shapiro, R.; Hingerty, B. E.; Broyde, S. *Chem. Res. Toxicol.* **1997**, *10*, 1123.

(154) Brown, K.; Hingerty, B. E.; Guenther, E. A.; Krishnan, V. V.; Broyde, S.; Turteltaub, K. W.; Cosman, M. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 8507.

(155) Shibutani, S.; Grollman, A. P. *Chem. Res.Toxicol.* **1993**, *6*, 819.

(156) Wang, F.; Demuro, N. E.; Elmquist, C. E.; Stover, J. S.; Rizzo, C. J.; Stone, M. P. *J. Am. Chem. Soc.* **2006**, *128*, 10085.

(157) Turesky, R. J.; Box, R. M.; Markovic, J.; Gremaud, E.; Snyderwine, E. G. *Mutat. Res.* **1997**, *376*, 235.

(158) Gunz, D.; Hess, M. T.; Naegeli, H. *J. Biol. Chem.* **1996**, *271*, 25089.

(159) Batty, D. P.; Wood, R. D. *Gene* **2000**, *241*, 193.

(160) Sugasawa, K.; Okamoto, T.; Shimizu, Y.; Masutani, C.; Iwai, S.; Hanaoka, F. *Genes Dev.* **2001**, *15*, 507.

(161) Geacintov, N. E.; Broyde, S.; Buterin, T.; Naegeli, H.; Wu, M.; Yan, S.; Patel, D. J. *Biopolymers* **2002**, *65*, 202.

(162) Yeo, J. E.; Khoo, A.; Fagbemi, A. F.; Scharer, O. D. *Chem. Res. Toxicol.* **2012**, *25*, 2462.

(163) Cai, Y.; Geacintov, N. E.; Broyde, S. *Biochemistry* **2012**, *51*, 1486.

(164) Reeves, D. A.; Mu, H.; Kropachev, K.; Cai, Y.; Ding, S.; Kolbanovskiy, A.; Kolbanovskiy, M.; Chen, Y.; Krzeminski, J.; Amin, S.; Patel, D. J.; Broyde, S.; Geacintov, N. E. *Nucleic Acids Res.* **2011**, *39*, 8752.

(165) Kosakarn, P.; Halliday, J. A.; Glickman, B. W.; Josephy, P. D. *Carcinogenesis* **1993**, *14*, 511.

(166) Watanabe, M.; Ohta, T. *Carcinogenesis* **1993**, *14*, 1149.

(167) Stover, J. S.; Chowdhury, G.; Zang, H.; Guengerich, F. P.; Rizzo, C. J. *Chem. Res. Toxicol.* **2006**, *19*, 1506.

(168) Ling, H.; Boudsocq, F.; Woodgate, R.; Yang, W. *Cell* **2001**, *107*, 91.

(169) Stover, J.; Chowdhury, G.; Zang, H.; Guengerich, F.; Rizzo, C. *Chem. Res. Toxicol.* **2006**, *19*, 1506.

(170) Zang, H.; Goodenough, A.; Choi, J.; Irimia, A.; Loukachevitch, L.; Kozekov, I.; Angel, K.; Rizzo, C.; Egli, M.; Guengerich, F. *J. Biol. Chem.* **2005**, *280*, 29750.

(171) Elmquist, C.; Stover, J.; Wang, Z.; Rizzo, C. *J. Am. Chem. Soc.* **2004**, *126*, 11189.

(172) IARC **1993**, *56*, 245.

(173) Poirier'pt, M.; Beland, F. *Chem. Res. Toxicol.* **1992**, *5*, 749.

(174) Choi, J.; Stover, J.; Angel, K.; Chowdhury, G.; Rizzo, C.; Guengerich, F. *J. Biol. Chem.* **2006**, *281*, 25297.

(175) Stavros, K.; Hawkins, E.; Rizzo, C.; Stone, M. *Nucl. Acids Res.* **2014**, *42*, 3450.

(176) Ruan, Q.; Kolbanovskiy, A.; Zhuang, P.; Chen, J.; Krzeminski, J.; Amin, S.; Geacintov, N. *Chem. Res. Toxicol.* **2002**, *15*, 249.

(177) Cosman, M.; Hingerty, B.; Luneva, N.; Amin, S.; Geacintov, N.; Broyde, S.; Patel, D. *Biochem.* **1996**, *35*, 9850.

(178) Wang, F.; Elmquist, C.; Stover, J.; Rizzo, C.; Stone, M. *Biochemistry* **2007**, *46*, 8498.

(179) Rechkoblit, O.; Malinina, L.; Cheng, Y.; Geacintov, N.; Broyde, S.; Patel, D. *Structure* **2009**, *17*, 725.

(180) Biertumpfel, C.; Zhao, Y.; Kondo, Y.; Ramon-Maiques, S.; Gregory, M.; Lee, J.; Masutani, C.; Lehmann, A.; Hanaoka, F.; Yang, W. *Nature* **2010**, *465*, 1044.