The simulations were run using a computer program based on a model described previously,[4b] using parameters listed in the caption of Figure 2. The J couplings are smaller than those for bis(alkyl) biradicals of even longer chain length,[4] indicating that delocalizing the electrons into the aromatic rings results in a significant decrease in the interaction between them, as expected. An analysis of the time evolution of all four EPR signals, especially with regard to spin relaxation and chemical reaction rates, is the subject of research in progress. From these preliminary simulations, we can conclude that both correlated and uncorrelated electron dipole–dipole induced spin relaxation plays a strong role in determining the shape of the spectra. Spin–orbit coupling appears to manifest itself only in the overall disappearance of the signals on the microsecond time scale.

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Solution Structure of an Intramolecular Purine·Purine·Pyrimidine DNA Triplex

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The sequence-specific recognition of DNA duplexes by third strands through triplex formation[1] has potential applications ranging from gene regulation[2] to site-specific cleavage of genomic DNA.[3] This effort could be greatly aided by a knowledge of the structural details of DNA triplexes in solution and in the crystalline state. There has been no success in the latter approach to date, and we report below on continued progress in defining the solution structure of DNA triplexes through a combination of NMR experiments and molecular dynamics computations.

The pyrimidine·purine·pyrimidine (Y·RY) DNA triplex has the third pyrimidine strand positioned in the major groove and *parallel* to the purine strand of the Watson–Crick duplex.[4]

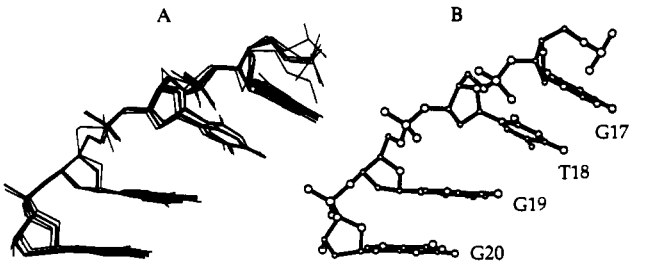
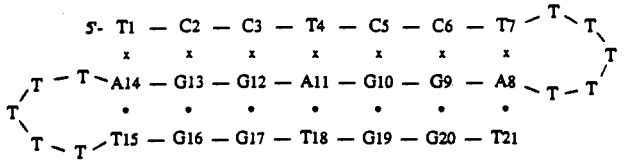


Figure 1. (A) Best fit superposition of the six refined structures. (B) Representative refined structure of the G17-T18-G19-G20 segment of the purine-rich third strand of the R·RY triplex **1**. Note the increase in helical rise between T18 and G19 at the T-G step.

Several Y·RY triplexes containing standard T·AT and C$^+$·GC triples as well as other triplex combinations have been investigated in solution by NMR.[5] We have recently determined the solution structure of a G·TA-containing Y·RY triplex by a combination of experimental NMR constraints and molecular dynamics calculations,[6] in contrast to Y·RY triplex models based on computations alone.[7] The purine·purine·pyrimidine (R·RY) DNA triplex has the third purine-rich strand positioned in the major groove *antiparallel* to the purine strand of the Watson–Crick duplex.[8] This triplex is stabilized by G·GC[8c,8d] and A/T·AT[8d] triples (supplementary Figure 1), and solution NMR studies have established that the third strand bases adopt *anti* glycosidic torsion angles,[9] thus defining the base triple pairing alignments. We report below on a combined NMR–molecular dynamics study which defines the solution structure of an intramolecular R·RY triplex (**1**) and identifies the structural transitions necessary for accommodating thymines in an otherwise guanine-rich third strand.



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The intramolecular[10] R·RY triplex **1**, which contains two partially overlapping T-G-G-T repeats in the third strand, was chosen since it gave narrower exchangeable and nonexchangeable proton spectra (supplementary Figures 2A and 2B) than its

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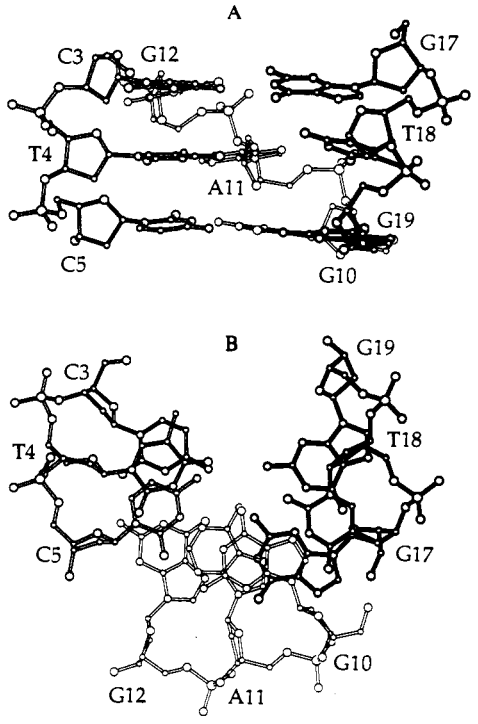

Figure 2. Representative refined structure of the (C3-T4-C5)·(G10-A11-G12)·(G17-T18-G19) central segment of the R·RY triplex **1**. (A) This view is normal to the helix axis and looks into the major groove of the Watson–Crick duplex segment of the triplex. (B) This view is down the helix axis. Note the reduced twist between T18 and G19 at the T-G step and the absence of base stacking in the third purine-rich strand.

counterpart[9] studied previously. We have assigned the exchangeable and nonexchangeable protons of R·RY triplex **1** following analysis of two-dimensional data sets in H_2O and D_2O solution, respectively. These studies establish formation of G·GC and T·AT triples with pairing alignments discussed previously.[8d,9] The intrastrand NOE connectivities between adjacent nucleotides (base protons to 5′-flanking sugar H1′, H2″ protons) follow patterns characteristic of unperturbed stacked right-handed helical structures for the T1–T7 and the A8–A14 segments of the Watson–Crick duplex part of the R·RY triplex **1**. These connectivities are also observed for the G16–T18 and G19–T21 segments but were not detected for the T-G steps (T15–G16 and T18–G19) in the third strand of the R·RY triplex **1** (supplementary Figures 3A and 3B). Further, the sugar H1′ protons of G16 (4.89 ppm) and G19 (4.78 ppm) and the sugar H2′, H2″ protons of T15 (1.36, 1.94 ppm) and T18 (1.22, 1.61 ppm) in T-G steps in the R·RY triplex **1** are shifted upfield by greater than 1 ppm from their unperturbed values (supplementary Figures 3A and 3B). A set of interstrand NOEs are detected between the imino and CH_3 protons on the third purine-rich strand and between the base and sugar protons on the Watson–Crick purine strand (supplementary Figure 4) which permit the alignment of the third strand in an antiparallel orientation in the major groove of the Watson–Crick duplex.

The structure elucidation was undertaken on the seven base triple segment along with the first and last loop thymines within each loop of the R·RY triplex **1**. The restrained molecular dynamics simulations were based on two starting structures[11] using three different seeds for initial velocity assignments and were guided by the NMR distance constraints[13] (supplementary Figure 5). The starting structures show root mean square deviations (RMSDs) of 2.78 Å for the triplex segment, and this value is reduced to pairwise average RMSDs of 1.01 ± 0.14 Å for the six refined structures (supplementary Figure 6). The helical parameters for all structures (duplex and third strand computed separately) were calculated using the program CURVES.[14] The duplex segment exhibits an average base displacement of −1.8 Å from the helix axis and an average helical twist of 30°. These values for the R·RY triplex **1** are similar to those we reported earlier for the Y·RY triplex[6] but are different from canonical A- and B-DNA forms. The conservation of these features is thus attributable to the structural change that the duplex undergoes in order to accommodate a third strand irrespective of the base pairing alignment and strand direction.

The six refined structures of the G17-T18-G19-G20 segment of the third strand of the R·RY triplex **1** are superpositioned in Figure 1A, and a representative structure is plotted in Figure 1B. This view emphasizes distinct structural differences between the G-G, G-T, and T-G steps in the third strand of the R·RY triplex **1**. The rise and twist parameters for the G-G steps are relatively similar to those observed for the duplex segment. By contrast, the helical rise (average value 5.6 Å) increases significantly, and the axial twist (average value 17°) is reduced significantly for the T-G steps, while the helical rise (average value 2.8 Å) is reduced and the axial twist (average value 40°) increases for the G-T steps. This variation in helical rise and axial twist, predominantly at T-G steps in the third strand of the R·RY triplex **1**, can also be seen in two views of the central (C3-T4-C5)·(G10-A11-G12)·(G17-T18-A19) triplex segment of a representative refined structure in Figure 2. (The corresponding six superpositioned refined structures are plotted in supplementary Figure 7). We note the absence of base stacking at the G17-T18 and T18-G19 steps in the G17-T18-G19 segment of the third strand in contrast to stacking between adjacent bases in the duplex segment (Figure 2B).

The structure readily explains the absence of NOE connectivities between the base protons of guanine and the sugar H1′ and H2″ protons of the 5′-linked thymine in the T15-G16 and T18-G19 steps and can be attributed to the increase in axial rise observed at this step (Figures 1B, 2A, and 2B). Further, the structure also readily explains the unusually large upfield shifts for specific sugar protons in T-G steps in the third strand presented earlier. The sugar H1′ protons of G19 (and G16) is stacked directly over the purine ring of G20 (and G17), while the sugar H2′, 2″ protons of T18 (and T15) are stacked directly over the purine ring of G19 (and G16) (Figure 1B) so that these protons experience upfield ring current contributions.

Our NMR–molecular dynamics studies on R·RY triplex **1** establish that a purine-rich third strand can be readily positioned in the major groove in an antiparallel orientation with G·GC and T·AT pairing alignments. The thymines in an otherwise guanine-rich third strand are accommodated by localized structural transitions (increase in helical rise and decrease in axial twist) at T-G steps.

Acknowledgment. This research was supported by NIH grant GM-34504 to D.J.P. The Molecular Modeling Facility for

(11) The starting structures for the duplex portion of the molecule were constructed from the fiber-diffraction coordinates for the A′-form[12c] and B-form[12] DNA. The third strand was constructed by docking individual nucleotides at hydrogen-bonding positions from the purine second strand. The starting structures were then subjected to 300 steps of conjugate gradient minimization in X-PLOR.

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Supplementary Material Available: Table of procedures for estimating distance restraints; a set of figures showing base triple pairing alignments, one-dimensional proton spectra in H_2O and D_2O, expanded NOESY contour plots in D_2O, interstrand NOE correlations, distribution of distance restraints, and superpositioned distance refined structures for the entire triplex and the central segment (11 pages). Ordering information is given on any current masthead page.

*Book Reviews**

Synthesis and Chemistry of Agrochemicals III. ACS Symposium Series 504. Edited by Don R. Baker (ICI Americas), Joseph G. Fenyes (Buckman Laboratories International, Inc.), and James J. Steffens (E.I. du Pont de Nemours and Company). ACS: Washington, DC. 1992. xii + 468 pp. $109.95. ISBN 0-8412-2473-0.

This book was developed from symposia sponsored by the Division of Agrochemicals of the ACS and organized by the editors of this monograph. It is organized like the others in that the first chapters deal with the discovery of new plant control agents, the second section with control of insects, acarids, and nematodes, and the final section with control of fungal diseases. It is introduced by a chapter entitled Progress in a Time of Change, written by the editors, and concludes with an author index, affiliation index, and subject index.

Lange's Handbook of Chemistry. Fourteenth Edition. By John A. Dean (University of Tennessee). McGraw-Hill: New York. 1992. xvi + 1381 pp. $79.50. ISBN 0-07-016104-1.

This edition of the classic handbook is organized under the following sections: (1) Organic Compounds; (2) General Information, Conversion Tables, and Mathematics; (3) Inorganic Chemistry; (4) Properties of Atoms, Radicals, and Bonds; (5) Physical Properties; (6) Thermodynamic Properties; (7) Spectroscopy; (8) Electrolytes, Electromotive Force, and Chemical Equilibrium; (9) Physicochemical Relationships; (10) Polymers, Rubbers, Fats, Oils, and Waxes; and (11) Practical Laboratory Information. There are prefaces to the 14th, 13th, and 1st editions and a 24-page index.

Supramolecular Photochemistry. By Vincenzo Balzani (University of Bologna) and Franco Scandola (University of Ferrara). Ellis Horwood, Ltd.: London (Available in North America from Prentice-Hall: New York.). 1991. 427 pp. $83.00. ISBN 0-13-877531-1.

This book is a most welcome addition to the photochemistry literature. One of its aims is to provide "the concepts for a rational and unified view of supramolecular photochemistry," and it succeeds admirably. The authors are, of course, very well-known to inorganic photochemists around the world. A unique aspect of this work, however, is that it covers both inorganic and organic supermolecules. This is done in a systematic way by comparing, often side by side, examples of both types that have the same number of components and are of similar size.

The term "supramolecular" (adj) is defined as pertaining to systems that are made up of molecular components in the same way that molecules are made up of atoms. The distinction between a "large molecule" and a "supermolecule" (n.) is that the latter retains properties that are related to those of the individual components in addition to acquiring new properties that derive from intercomponent processes. An example would be a linked electron donor-acceptor (DA) assembly in which, e.g., the spectroscopy and electrochemistry are essentially those of the D and A moieties, but the photophysical and/or photochemical behavior reflect(s) interactions that occur because of the juxtaposition of the constituents not only in space but also in energy and time. Other examples abound throughout this well-written and very useful volume.

The first four chapters (Scope and Limitations; Principles of Molecular Photochemistry; Supramolecular Properties; Control and Tuning of Excited-State Properties of Molecular Components) are introductory and comparatively brief. Chapters 5–10 (Covalently Linked Systems: Photoinduced Electron Transfer; Covalently Linked Systems: Electronic Energy Transfer; Structural Changes in Photoflexible Systems; Ion Pairs; Electron Donor-Acceptor Complexes and Exciplexes; Host-Guest Systems) are the most detailed in terms of their subject matter and the citations of the literature. Chapter 11 (Other Systems) discusses some miscellaneous types of systems (e.g., caged ions, catenanes, rotaxanes, helicates, proton-transfer reactions), the photoprocesses of which have generally been studied less extensively than those discussed in the earlier chapters. Finally, Chapter 12 (Photochemical Molecular Devices) provides some very interesting insights into several kinds of practical devices (e.g., electron- and energy-transfer relays, molecular switches, and other electronic devices on the nanometer scale) that might be developed in the future. The stated goal is that each chapter be essentially self-sufficient but, with extensive cross-references, give a unified view of the field. In this the authors have also realized their expectations.

There is something of value here for everyone currently—or considering—working in this rapidly developing area, from the experienced photochemist to the new graduate student. Just as supramolecular assemblies are built from their constituent parts, so too do the research groups working in this field tend to rely on the cooperative skills of chemists with different backgrounds. In this respect the first few chapters of *Supramolecular Photochemistry* will serve as an excellent tutorial for those not already versed in the fundamental principles of electronic spectroscopy and photophysics. The more detailed chapters are of equal value to experts in the photoprocesses of organic compounds who wish to learn about inorganic systems and vice versa.

Naturally, in a work of this complexity (that is, nevertheless, concise) there are some shortcomings. SI units are used in the introductory chapters but tend to be neglected in the detailed discussions. The terminology is generally clear and straightforward, but there are a few clumsy symbols such as "A.B", which represents a linked, two-component species; this abbreviation becomes somewhat cumbersome when it is further punctuated to indicate an excited state or ionic intermediate. Similarly, there are some awkward terms (e.g., "endoergonic" and "exoergonic", page 47) that later revert to their more familiar counterparts ("endergonic" and "exergonic", page 365) and several spelling inconsistencies (e.g., "dyad" in the index but "diad" [*sic*] in the text). The molecular structures tend to be somewhat uneven in appearance and quality, probably because they were taken from the literature.

On a more substantive note, there is very little to criticize in terms of the content. I would have liked to have seen some discussion of the strengths and limitations of dielectric continuum theory to predict reaction energetics when experimental data (e.g., redox potentials) are not available. Similarly, in the otherwise clear discussion of Marcus theory, it would have been useful to inform the novice that it is due to the properties of symmetric parabolae that the activation energy for a weakly coupled, "isoergonic" electron-transfer reaction is exactly one-fourth of the reorganization energy. In a work of this kind, one does not expect an exhaustive review of the literature; nevertheless, the discussion of some topics (e.g., thermodynamics of excited states, Chapter 2) would have been greatly improved if some of the more recent literature had been cited.

The authors and the publisher are to be congratulated for the layout (e.g., chapter headings on even-numbered pages and section headings opposite) and for the liberal use of clear and generally unambiguous figures. There is also a three-page section of frequently used abbreviations for easy reference. Over 1600 papers (through early 1990) are cited in the references at the end of each chapter, and about 2300 names are listed in the author index, although with some duplication in both because of cross-referencing. The subject index is less generous, with only about 500 entries.

Readers will be delighted with the excellent use of English and fluid style, for which the authors are well known. Some of the spellings and sentence construction (especially, "which" vs "that") as well as punctuation reflect the country of publication. There are also a few unusual variations on commonly used words (e.g., "applicative" vice "applied"), but these are minor annoyances. The text is, for the most part, remarkably free of typographical errors, but the author index contains many incorrectly and/or inconsistently spelled names. There is also at least one erroneous journal citation (*J. Chem. Phys.* instead of *J. Phys.*

*Unsigned book reviews are by the Book Review Editor.