and poorly with the 3′-linked base T19 (Figure 1B). More interestingly, unlike the other residues in the triplex, the guanine sugar adopts a typical N-type conformation (C2′-exo). Stereopairs of Figure 1 are included separately as supplementary Figure 2.

In summary, using experimental NMR restraints and molecular dynamics, we have demonstrated the structural features unique to the G·TA triple **2** in an intramolecular Y·RY DNA triplex **1** in solution. The accommodation of the purine base in a homopyrimidine third strand can be attributed to the readjustments in the local structure of the G18 purine base and sugar pucker and an unusual base stacking interaction. One guanine amino proton hydrogen bonds with the thymine carbonyl within the G·TA triple, while the other guanine amino proton weakly hydrogen bonds with the thymine carbonyl of the adjacent T·AT triple. This demonstration that the third strand guanine recognizes local structural features defined by adjacent residues was anticipated in earlier contributions from Dervan's[3b] and Helene's[16] laboratories.

Acknowledgment. We thank Dr. Charles Laughton for helpful discussions. This work was supported, in part, by an NIH Grant GM-34504 to D.J.P. The Molecular Modeling Facility for Molecular Biology at Columbia University was supported under NSF Grant DIR-8720229. The access to the Cray Y-MP Supercomputer at North Carolina provided by Glaxo Inc. Research Institute is gratefully acknowledged.

Supplementary Material Available: Stereoviews of a superposition of six refined structures of the (T17-G18-T19)·(A10-T11-A12)·(T3-A4-T5) central segment of triplex **1** (3 pages). Ordering information is given on any current masthead page.

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A New Synthesis of Methano-Bridged Annulenes: Access to Highly Substituted Derivatives

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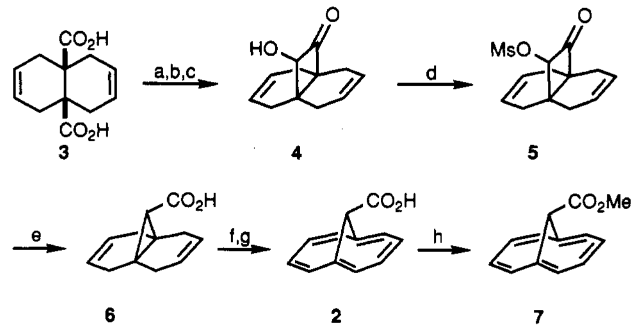
Received February 4, 1992

The synthesis of 1,6-methanol[10]annulene (**1**) was first reported by Vogel and Roth in 1964,[1] and many aspects of the chemistry of the methano-bridged annulenes have been elucidated by the laboratories of Vogel,[2,3] Paquette,[4] and others in the intervening years. We became interested in derivatives of **1** bearing

1

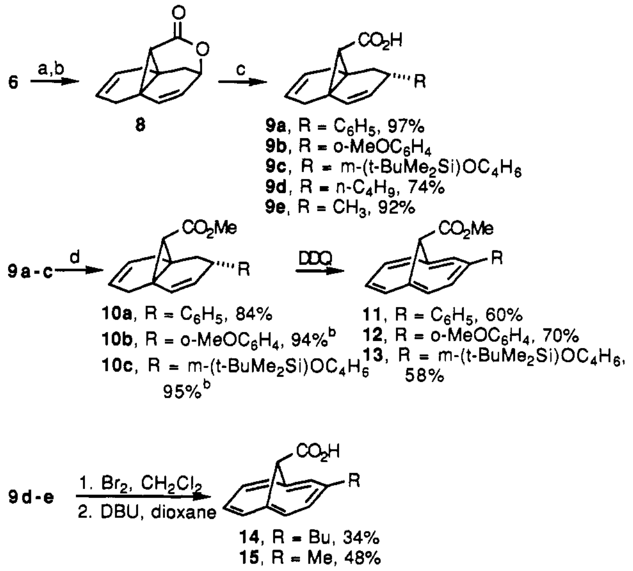
polar substituents on the methylene bridge because of their unusual amphiphilic topology: one face of the rigid structure is nonpolar, and the other face is polar. Incorporation of such double-sided amphiphilic subunits into larger structures should lead to molecules with interesting complexation and/or aggregation properties.[5] In order to employ bridged annulenes as architectural elements in larger structures, however, one requires derivatives bearing functionality on both the methylene bridge and the aromatic platform; no examples of this type of doubly functionalized bridged annulene have been previously reported, to our knowledge. We describe a new synthetic approach to the 1,6-methano[10]annulene framework that provides efficient access to highly substituted derivatives.

Scheme I[a]



[a] Key: (a) $(MeO)_2SO_2$, K_2CO_3, MeCN; (b) Na, K, Me_3SiCl, Et_2O; (c) MeOH; (d) MsCl, Et_3N, CH_2Cl_2; (e) LiOH, THF, H_2O; (f) Br_2, CH_2Cl_2; (g) *t*-BuOK, THF; (h) $(MeO)_2SO_2$, K_2CO_3, MeCN.

Scheme II[a]



[a] Key: (a) I_2, KI, $NaHCO_3$, H_2O; (b) DBU, benzene; (c) cuprate;[9] (d) $(MeO)_2SO_2$, K_2CO_3, MeCN. [b] Yields from **8**.

The merits of the new route are illustrated by the synthesis of acid **2**[3,4] shown in Scheme I. Dicarboxylic acid **3**[6] was converted in three steps (92% overall yield) to propellane **4**,[7,8] which could then be converted quantitatively to the mesylate. The key transformation was a LiOH-induced semi-benzylic Favorskii rearrangement[9] of **5** that produced **6** in 96% yield (the overall yield of **6** from **3** was 88%). The previously reported synthesis of **6** proceeds in three steps and 13% overall yield from isotetralin in a route that requires several chromatographic separations;[4] our synthesis of **6** proceeds in superior yield and requires chromatography of only mesylate **5**. Treatment of **6** with Br_2 yielded a mixture of stereoisomeric tribromo lactones which, when allowed to react with *t*-BuOK, produced annulene **2** in 95% yield (from **6**). Formation of ester **7** from **2** and $(MeO)_2SO_2/K_2CO_3$ was quantitative under standard conditions. Acid **6** has previously

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(7) Propellane **4** has previously been prepared in three steps and 45-55% overall yield from the anhydride of **3**: Bloomfield, J. J.; Irelan, J. R. S. *J. Org. Chem.* **1966**, *31*, 2017 and references therein.

(8) In situ trapping of acyloin condensation products with trimethylsilyl chloride: Bloomfield, J. J.; Melke, J. M. *Org. Synth.* **1977**, *57*, 1.

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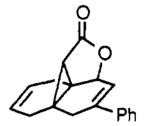
0002-7863/92/1514-6915$03.00/0

been converted to **7** in 64% overall yield via esterification with CH_2N_2 followed by treatment with DDQ.[4]

We have developed an efficient route from acid **6** to 1,6-methano[10]annulene derivatives bearing substituents on both the bridgehead and the 10-membered ring (Scheme II). Treatment of **6** with I_2/KI followed by DBU yielded lactone **8** in 92% yield. This lactone reacted with the appropriate cuprate reagents to produce acids **9a–e** in good yield.[10] Acids **9a–d** could be converted to the corresponding methyl esters **10a–d** by the action of $(MeO)_2SO_2/K_2CO_3$. Ester **10e** was obtained in 94% yield by treatment of **9e** with $BF_3{\cdot}OEt_2$ in MeOH at reflux.[11] ^{1}H NMR data indicated that the substituent was introduced in formal S_N2 fashion during the cuprate reaction. This conclusion was verified crystallographically for **9a**;[12] the crystal structure also showed the expected endo configuration at the site of addition.

Bridged annulenes **11–13** were produced via DDQ oxidation of **10a–c**,[13] but attempts to oxidize esters **10d,e** in this way were unsuccessful. Both DDQ and *o*-chloranil caused **10e** to decompose, and no reaction was observed with *p*-chloranil. Annulenes **14** and **15** could, however, be prepared via the bromination/dehydrobromination route. Treatment of **9e** with Br_2 afforded a mixture of tribromo lactones in quantitative yield. Subsequent treatment of this mixture with *t*-BuOK produced only small quantities of **15**, but DBU (dioxane, reflux, 64 h) provided the desired annulene in 48% yield. An analogous series of reactions produced butyl analogue **14** in 34% yield.

One source of difficulty in these base-mediated eliminations is suggested by the observation that treatment of acid **9a** with I_2/KI followed by DBU led to the regioselective formation of γ-lactone **16** in 75% yield. If γ-lactones are produced by the action of Br_2 on **9d** and **9e**, as suggested by IR data, then subsequent elimination of the carboxylate must ultimately occur in 1,4 fashion. The modest yields of **14** and **15** via the bromination/dehydrobromination route, compared with the success of this route for conversion of **6** to **2**, may result from the harsh conditions required for this 1,4 elimination.



16

Treatment of **13** with KF (cat. HBr, DMF)[14] provided the desilylated phenol in 91% yield, the hydroxyl group of which could be alkylated under standard conditions[15] (e.g., 2 equiv of *n*-PrI, K_2CO_3, MeCN, reflux, 6 days; 98%). This type of alkylation, and other attachment strategies involving substituents on the 10-membered ring, should allow the incorporation of amphiphilic bridged annulenes into larger structures. The preparation and characterization of such molecules, based on the synthetic route we have presented here, are underway in our laboratory.

Acknowledgment. We thank Professor Reinhardt Brückner, Professor Howard W. Whitlock, and Mr. John Cochran for helpful suggestions and Ms. Elizabeth Gallo, Mr. Kevin Enzweiler, and Mr. Thomas Stein for technical assistance. This research was supported by the National Institutes of Health (GM-41825) and, in the initial phases, by Cambridge NeuroScience Research, Inc. S.H.G. thanks the Searle Scholars Program, the American Cancer Society (Junior Faculty Research Award), the National Science Foundation Presidential Young Investigator Program, the Eastman-Kodak Company, and Eli Lilly and Company for support.

Supplementary Material Available: Complete description of the synthesis of compounds **7**, **11**, and **15** (9 pages). Ordering information is given on any current masthead page.

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[10] Success of cuprate additions to **8** is dependent upon the conditions under which the cuprate reagents are generated. Since optimum conditions vary with the cuprate used, reaction times and temperatures are listed below. Organolithium reagents, when not commercially available, were prepared via halogen metal exchange between the appropriate bromides and *n*-butyllithium. Solutions of the organolithium reagents were then added to a slurry of cuprous bromide–methyl sulfide complex in a 1:1 mixture of ether and methyl sulfide at 0 °C (Me_2CuLi), −78 °C [Ph_2CuLi, Bu_2CuLi, $(o\text{-}MeOC_6H_4)_2CuLi$], or −45 °C $\{[m\text{-}(t\text{-}BuMe_2SiO)C_6H_4]_2CuLi\}$. After 5 min ($Me_2CuLi$), 10 min ($Ph_2CuLi$, Bu_2CuLi), or 30 min [$(o\text{-}MeOC_6H_4)_2CuLi$], a solution of **8** in THF, equilibrated to the temperature of the cuprate, was added. After 60 min, a solution of $\{[m\text{-}(t\text{-}BuMe_2SiO)C_6H_4]_2CuLi\}$ was cooled to −78 °C before addition of **8**. After 2–3 h at low temperature, the reaction mixtures were allowed to come to room temperature overnight, and the crude product was isolated by aqueous workup. Copper salts were removed by ammonium chloride washes.

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[13] Optimal conditions for the oxidations were as follows: Compound **11**, **12** or **13** was stirred in the presence of 1.5 equiv of DDQ in dioxane at 60–70 °C for 24–48 h; a further 1.5 equiv of DDQ was then added, and the mixture was heated at reflux for 24 h. Along with the major product, a second annulene was usually isolated in ca. 5% yield upon chromatographic purification. Spectroscopic studies suggest this minor product to be the epimer at the bridge position.

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Photoinduced Electron Transfer in Multimetal Complexes. Observations on Electronically Forbidden Back Electron Transfers

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Received September 20, 1991
Revised Manuscript Received June 15, 1992

There has been much recent interest in the use of light to promote charge separation in simple molecular systems.[1-6] One requirement for the generation of useful charge-separated intermediates is a relatively slow back-electron-transfer (BET) rate. A potential approach which has received little attention capitalizes on electronic selection rules to retard the BET rate. We have investigated this issue by using light-promoted reactions to generate a high-energy electron-transfer intermediate in complexes containing a light-absorbing ruthenium(II) complex (excited-state electron donor) covalently linked to cobalt(III) electron acceptors which form high-spin ($^4T_2$ in O_h symmetry) Co(II) products. While the resulting spin-forbidden and orbitally forbidden BET process might be expected to be relatively slow, the effects of such electronic factors on observed electron-transfer rates have long been a subject of discussion and controversy.[7,8] The work reported

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