The electrochemical properties of **1b** and **2b** were studied in THF and dimethyl sulfoxide (DMSO). Three reversible single electron reduction events are observed for **1b** in THF (−1.53, −2.04, and −2.61 V vs ferrocene/ferrocenium; −1.27 and −1.77 V in DMSO). The anion t-BuC_{60}^- is 0.67 V harder to reduce than C_{60} in THF. For **2b**, three reversible single electron reduction events are also observed (−1.01, −1.57, and −2.18 V in THF; −0.87 V in DMSO), making **2b** 0.15 V harder to reduce than C_{60} (cf. $(C_6H_5)_2CC_{60}$, which is 0.11 V harder to reduce than C_{60}[9]). Evidence is mounting[9b,12] that $(C_6H_5)_2CC_{60}$ is not a fully "opened" structure as was originally proposed,[9] which is in line with the similar reduction potential observed here for t-$BuC_{60}H$.

Protonation of the t-BuC_{60}^- anion can be quantitatively monitored by electrochemistry. From titration behavior using the acids saccharin (pK_a = 4.0), 2,4-dinitrophenol (pK_a = 5.1), and dichloroacetic acid (pK_a = 6.4), a pK_a of 5.7 (±0.1) was determined for t-$BuC_{60}H$.[4] Consistent with this, **2b** can be deprotonated with n-$Bu_4N^+CH_3CO_2^-$ in DMSO to form t-BuC_{60}^-. This ranks t-$BuC_{60}H$ as one of the strongest acids made up of only carbon and hydrogen.[13,14] From the thermodynamic cycle employed by Bordwell,[13] knowing this pK_a value and the t-$BuC_{60}^{\bullet}$/t-BuC_{60}^- reversible potential (−0.33 V vs ferrocene/ferrocenium: +0.33 V vs normal hydrogen electrode), we can calculate the C_{60}–H bond dissociation energy to be 71 ± 2 kcal/mol in DMSO. This is on the low side of measured carbon–hydrogen bond strengths in organic hydrocarbon molecules.

Supplementary Material Available: Details of the measurement of pK_a for t-$BuC_{60}H$ and ^{13}C NMR, ^1H NMR, mass spectral, and elemental analytical data for **1b** and **2b** (8 pages). Ordering information is given on any current masthead page.

(12) Creegan, K. M.; Robbins, J. L.; Robbins, W. K.; Millar, J. M.; Sherwood, R. D.; Tindall, P. J.; Cox, D. M.; Smith, A. B., III; McCauley, J. P., Jr.; Jones, D. R.; Gallagher, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 1103.

(13) (a) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463. (b) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 1229–1231.

(14) We found only one example more acidic than t-$BuC_{60}H$: Kuhn, R.; Rewicki, D. *Justus Liebigs Ann. Chem.* **1967**, *706*, 250–261.

The First Design and Synthesis of a Steroidal Peptidomimetic. The Potential Value of Peptidomimetics in Elucidating the Bioactive Conformation of Peptide Ligands

Ralph Hirschmann,* Paul A. Sprengeler, Tomomi Kawasaki, James W. Leahy, William C. Shakespeare, and Amos B. Smith, III*

Department of Chemistry, University of Pennsylvania Philadelphia, Pennsylvania 19104

Received August 20, 1992

Peptidomimetics have emerged as an active field at the interface of bioorganic, organic, and medicinal chemistry.[1] This interest derives from the expectation that such molecules will have both better biostability and oral bioavailability than their peptide counterparts. Progress to date has come from three distinct approaches: (1) broad screening; (2) the design and synthesis of peptide analogs, wherein one or more of the amide bonds are isosterically replaced; and (3) the design and synthesis of novel scaffolding, with retention of peptidal side chains.

(1) Farmer, P. S. In *Drug Design*; Ariëns, E. J., Ed.; Academic: New York, 1980; Vol X, p 119. Spatola, A. F. In *Chemistry and Biochemistry of Amino Acids, Peptides, and Proteins*; Weinstein, B., Ed.; Marcel Dekker: New York, 1983; p 267. See also: Freidinger, R. M. *TIPS Rev.* **1989**, *10*, 270. Sherman, D. B.; Spatola, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 433. Hirschmann, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1278 and references cited therein.

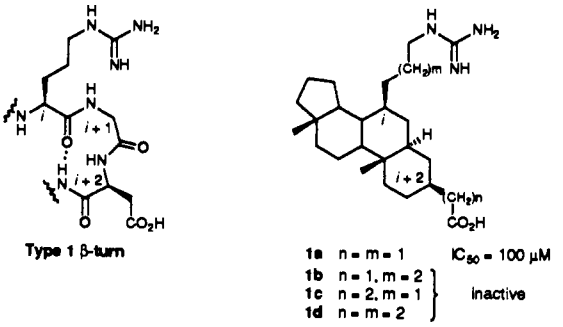


Figure 1.

To our knowledge, bicyclo[2.2.2]octane[2] and β-D-glucose[3] were the first designed scaffoldings successfully employed in the synthesis of a mimetic which is recognized by the targeted endocrine receptor.[4] We now report that the cyclopentanoperhydrophenanthrene skeleton of the steroids can also serve this function. The steroid nucleus was of interest for several reasons: (1) its volume matches that of the backbone of a cyclic hexapeptide;[5] (2) many steroids are drugs with excellent oral bioavailability; (3) the rigid steroid nucleus should reduce the tendency for hydrophobic collapse[6] of appended peptide side chains; and (4) a large body of steroid literature permits regio- and stereoselective introduction of functionality. That steroids offer multiple possibilities for side chain trajectories (i.e., axial, equatorial, quasi-axial and -equatorial, as well as pseudoaxial and -equatorial) was also attractive. This latter consideration, combined with the rigidity of the steroid skeleton, holds the promise that the design and synthesis of steroid-based peptidomimetics may contribute to our understanding of the bioactive conformation of the natural peptidal ligands.

The integrins are a family of cell surface adhesion receptors which include the fibrinogen receptor on blood platelets,[7] a membrane-linked heterodimer (GP IIb/IIIa) which, when activated, initiates platelet aggregation. Antagonists of fibrinogen binding to its receptor are of potential value in the treatment of stroke and heart attacks. Antagonists found in nature and those obtained by design and synthesis contain the sequence Arg-Gly-Asp (RGD), which is thought to be sufficient for binding, provided that it is able to assume the bioactive conformation.[8] Its simplicity led us to explore the potential of the steroid nucleus to serve as a peptidomimetic scaffolding.

Little is known about the bioactive conformation of the peptides which bind to the fibrinogen receptor. Echistatin[9] and kistrin[10-13]

(2) Bélanger, P. C.; Dufresne, C. *Can. J. Chem.* **1986**, *64*, 1514.

(3) Nicolaou, K. C.; Salvino, J. M.; Raynor, K.; Pietranico, S.; Reisine, T.; Freidinger, R. M.; Hirschmann, R. In *Peptides: Chemistry, Structure and Biology*; Rivier, J. E., Marshall, G. R.; Escom: Leiden, 1990; p 881. Hirschmann, R.; Nicolaou, K. C.; Pietranico, S.; Salvino, J.; Leahy, E. M.; Sprengeler, P. A.; Furst, G.; Strader, C. D.; Cascieri, M. A.; Candelore, M. R.; Donaldson, C.; Vale, W.; Maechler, L. *J. Am. Chem. Soc.* **1992**, *114*, 9217–9218.

(4) G. L. Olson (Olson, G. L.; Cheung, H.-C.; Voss, M. E.; Hill, D. E.; Kahn, M.; Madison, V. S.; Cook, C. M.; Sepinwall, J.; Vincent, G. In *Proc. Biotechol. (U.S.A.)*; Conference Management Corporation: Norwalk, CT, 1989; p S.348) reported the conceptually related design of a TRH mimetic which exhibits oral activity in animal models of cognitive dysfunction, but does not bind to the high-affinity endocrine TRH receptor (Olson, G. L. Personal communication). More recently, Pagageorgiou et al. have used a xylofuranose in place of β-D-glucose as a scafolding, see: Papageorgiou, C.; Haltiner, R.; Bruns, C.; Petcher, T. J. *Bioorganic Medicinal Chem. Lett.* **1992**, *2*, 135.

(5) Veber, D. F. Private communication. This topic will be addressed in a manuscript currently in preparation.

(6) Wiley, R. A.; Rich, D. H. *Med. Res. Rev.*, in press. See also: Tanford, C. *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*; Wiley-Interscience: New York, 1980.

(7) Ruoslahti, E.; Pierschbacher, M. D. *Science* **1987**, *238*, 491.

(8) Plow, E. F.; Ginsberg, M. H. *Prog. Hemostasis Thromb.* **1989**, *9*, 117.

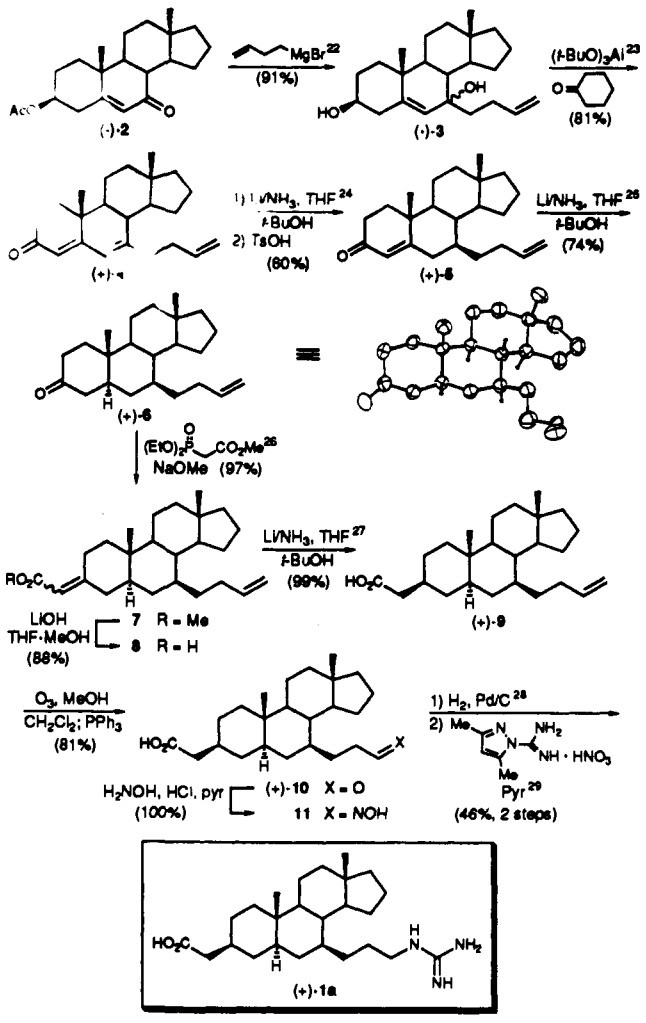
(9) Adler, M.; Lazarus, R. A.; Dennis, M. S.; Wagner, G. *Science* **1991**, *253*, 445.

(10) Chen, Y.; Pitzenberger, S. M.; Garsky, V. M.; Lumma, P. K.; Sanyal, G.; Baum, J. *Biochemistry* **1991**, *30*, 11625.

(11) Cooke, R. M.; Carter, B. G.; Martin, D. M. A.; Murray-Rust, P.; Weir, M. P. *Eur. J. Biochem.* **1991**, *202*, 323.

0002-7863/92/1514-9699$03.00/0 © 1992 American Chemical Society

Scheme I



contain the RGD sequence in highly flexible loop regions of the molecules. It has been suggested[14-18] that RGD is part of a β-turn[19] in its bioactive conformation. On the basis of NMR and CD studies coupled with energy calculations, Reed et al. proposed that the linear peptide GRGDSP adopts a nested set of β-turns initiated at Gly-1 and Arg-2.[14] In addition, Mizutani used NMR studies with c-(GRGDSPA) to suggest that cyclization enforces a β-turn conformation of the RGDS sequence, in which the Gly of RGD also occupies the $i + 1$ position.[17] For these reasons, we undertook the design of a rigid structure to mimic the presentation of the Arg and Asp side chains found in a β-turn with glycine as the $i + 1$ residue.

Computerized molecular modeling suggested that equatorial substituents at the 3β and 7β positions of an allopregnane have the same spacing and geometry as the i and $i + 2$ amino acid side chains of a β-turn, respectively, and that **1a** ($n = m = 1$) provides the proper side chain lengths for best overlap. Nevertheless, the synthetic plan permitted construction of chain-extended versions of **1a** (i.e., **1b–d**, Figure 1).

3β-Hydroxy-Δ^5-androsten-7-one acetate (**2**)[20] served as our point of departure for the syntheses of **1a–d**. Its conversion to (+)-**6**[21] (Scheme I) was straightforward; the stereochemistry of the 7β and 5α centers was confirmed by single-crystal X-ray analysis. Horner–Emmons olefination[26] with methyl (diethylphosphono)acetate then gave ester **7**[21] as a 1:1 mixture of isomeric olefins. Attempts to reduce the ester directly resulted in mixtures at the 3-position, but the corresponding acid smoothly reduced[27] in nearly quantitative yield to the desired 3β isomer (+)-**9**,[21] which served as the common intermediate for **1a–d**. Completion of the construction of (+)-**1a**[21] (Scheme I) was again unremarkable.

The homologated isomers of **1a** (**1b–d**)[21] were prepared in a similar fashion employing hydroboration for the elaboration of the 7β side chain and the photochemical Arndt–Eisert protocol[30] for the 3β side chain.[5]

Steroid RGD mimetics **1a–d** were tested in an ELISA GP IIb/IIIa–fibrinogen receptor assay.[31] Compound **1a** was found to bind to the GP IIb/IIIa receptor with an IC_{50} of ca. 100 μM using fibrinogen as the ligand. The dose response curve of **1a** resembled that of members of a series of RGD-containing cyclic peptide analogs,[31] with **1a** completely displacing the ligand. Compounds **1b–d** did not bind at 100 μM, thus serving as negative controls. The latter result suggests that **1a** possesses the appropriate distance between the guanidine and acid functionalities. The low binding affinity of **1a** indicates that, although a type 1 β-turn may be involved, glycine probably does not occupy the $i + 1$ position in the bioactive conformation of peptides which bind to the GP IIb/IIIa receptor.

Recent NMR studies of potent, highly constrained peptides from several laboratories suggest that the RGD sequence assumes a geometry[32-34] which is not mimicked by any of our compounds. The design and synthesis of other steroids to test this proposal are now in progress.

After the completion of this work, Venepalli et al.[35] described the isolation of a steroidal natural product which is a substance P antagonist. Taken together, these results show that the steroid nucleus can indeed serve as a scaffold for the attachment of mimics

(12) Dalvit, C.; Widmer, H.; Bovermann, G.; Breckenridge, R.; Metternich, R. *Eur. J. Biochem.* **1991**, *202*, 315.
(13) Saudek, V.; Atkinson, R. A.; Pelton, J. T. *Biochemistry* **1991**, *30*, 7369.
(14) Reed, J.; Hull, W. E.; von der Lieth, C.-W.; Kübler, D.; Suhai, S.; Kinzel, V. *Eur. J. Biochem.* **1988**, *178*, 141.
(15) Lark, L. R. S. Ph.D. Thesis, The University of Texas Health Science Center at Dallas, Dallas, TX, 1990.
(16) Siahaan, T.; Lark, L. R.; Pierschbacher, M.; Ruoslahti, E.; Gierasch, L. M. In *Proceedings of the 11th American Peptide Symposium*; Escom: Leiden, The Netherlands, 1989; pp 699–701.
(17) Mizutani, R.; Shimada, I.; Ueno, Y.; Yoda, M.; Kumagai, H.; Arata, Y. *Biochem. Biophys. Res. Commun.* **1992**, *182*, 966.
(18) Bogusky, M. J.; Naylor, A. M.; Pitzenberger, S. M.; Nutt, R. F.; Brady, S. F.; Colton, C. D.; Sisko, J. T.; Anderson, P. S.; Veber, D. F. *Int. J. Pept. Protein Res.* **1992**, *39*, 63.
(19) Rose, G. D.; Gierasch, L. M.; Smith, J. A. *Adv. Protein Chem.* **1985**, *37*, 1.
(20) Williams, D. H.; Bhacca, N. S.; Djerassi, C. *J. Am. Chem. Soc.* **1963**, *85*, 2810.
(21) All new compounds gave satisfactory IR, 500-MHz ^{1}H NMR, and 62.9-MHz ^{13}C NMR spectra as well as appropriate parent ion identification by high-resolution mass spectrometry.
(22) Zderic, J. A.; Carpio, H.; Ringold, H. J. *J. Am. Chem. Soc.* **1959**, *81*, 432.
(23) Robinson, C. H.; Gnoj, O.; Charney, W.; Gilmore, M. L.; Oliveto, E. P. *J. Am. Chem. Soc.* **1959**, *81*, 408.
(24) Johnson, F.; Newbold, G. T.; Spring, F. S. *J. Chem. Soc.* **1954**, 1302. Daglish, A. F.; Green, J.; Poole, V. D. *J. Chem. Soc.* **1954**, 2627.
(25) Smith, H. A.; Huff, B. J. L.; Powers, W. J., III; Caine, D. *J. Org. Chem.* **1967**, *32*, 2851.
(26) Bose, A. K.; Dahill, R. T., Jr. *J. Org. Chem.* **1965**, *30*, 505.
(27) Shaw, J. E.; Knutson, K. K. *J. Org. Chem.* **1971**, *36*, 1151.
(28) Hartung, W. H. *J. Am. Chem. Soc.* **1928**, *50*, 3370.
(29) Scott, F. L.; O'Donovan, D. G.; Reilly, J. *J. Am. Chem. Soc.* **1953**, *75*, 4053.
(30) Horner, L.; Spietschka, E. *Chem. Ber.* **1952**, *85*, 225. For a review, see: Meier, H.; Zeller, K.-P. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.
(31) Barker, P. L.; Bullens, S.; Bunting, S.; Burdick, D. J.; Chan, K. S.; Deisher, T.; Eigenbrot, C.; Gadek, T. R.; Gantzos, R.; Lipari, M. T.; Muri, C. D.; Napier, M. A.; Pitti, R. M.; Padua, A.; Quan, C.; Stanley, M.; Struble, M.; Tom, J. Y. K.; Burnier, J. P. *J. Med. Chem.* **1992**, *35*, 2040.
(32) McDowell, R. S.; Gadek, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 9245–9253.
(33) Pieshoff, C. E.; Ali, F. E.; Bean, J. W.; Calvo, R.; D'Ambrosio, C. A.; Eggleston, D. S.; Kline, T. P.; Koster, P. F.; Nichols, A.; Powers, D.; Romoff, T.; Samanen, J. M.; Sadel, J.; Vasko, J. A.; Hwang, S. M.; Kopple, K. D. *J. Med. Chem.* **1992**, *35*, 3962–3969.
(34) Müller, G.; Gurrath, M.; Kessler, H.; Timpl, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 326.
(35) Venepalli, B. R.; Aimone, L. D.; Appell, K. C.; Bell, M. R.; Dority, J. A.; Goswami, R.; Hall, P. L.; Kumar, V.; Lawrence, K. B.; Logan, M. E.; Scensny, P. M.; Seelye, J. A.; Tomczuk, B. E.; Yanni, J. M. *J. Med. Chem.* **1992**, *35*, 374.

of peptide side chains and that the synthesis of peptidomimetics can provide information about the conformation of the natural ligands.

Acknowledgment. We are grateful to Dr. Robert McDowell and Dr. Michael Venuti of the Bioorganic Chemistry Department at Genentech, Inc., South San Francisco, CA, for making the results of their ongoing modeling studies of RGD peptides available to us. We thank Mr. Craig Muir and Mr. Chip Allee of the Biochemical Pharmacology group of the Cell Biology Department at Genentech, Inc., for carrying out the ELISA GP IIb/IIIa-fibrinogen binding assay. In addition, we thank Drs. George Furst and Patrick J. Carroll and Mr. John M. Dykins of the University of Pennsylvania Spectroscopic Service Centers for assistance in securing and interpreting high-field NMR spectra, X-ray crystal structures, and mass spectra, respectively. Financial support was provided by the National Institutes of Health (Institute of General Medical Sciences) through Grant GM-41821 by Bachem, Inc. (Torrance, CA), and by Sterling Winthrop.

Supplementary Material Available: Listings of complete spectral data for **1a-d** and **3-11** and tables of experimental details, positional parameters, and thermal parameters for the X-ray analysis of **6** (14 pages). Ordering information is given on any current masthead page.

Aggregation of Hexa(phenylacetylene) Macrocycles in Solution: A Model System for Studying $\pi-\pi$ Interactions†

Jinshan Zhang and Jeffrey S. Moore*

The Willard H. Dow Laboratories, Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109-1055

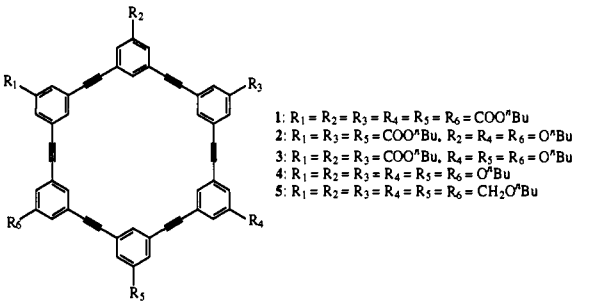
Received June 25, 1992

π-Stacking interactions between aromatic rings have received a great deal of attention[1] due to their importance in such diverse areas as molecular recognition,[2] stereocontrol of organic reactions,[3] structure of biological molecules,[4] and solid-state packing of organic molecules.[5] Specific details on the nature of these interactions, especially regarding the contributions of various noncovalent bonding forces, remain unclear. Although substituents on the π-systems are known to strongly influence stacking tendencies, these effects cannot always be explained in terms of simply donor-acceptor interactions.[1g] Here we would like to report on the self-association of phenylacetylene macrocycles (PAMs) in solution. These compounds should be useful as models for quantitatively studying substituent effects on $\pi-\pi$ interactions. Moreover, depending on the geometry of the aggregate, self-association of toroidal-shaped macrocycles represents the initiation of a noncovalently bound molecular channel. Thus, a better understanding of these interactions may be useful for designing novel, tubular mesophases,[6] porous organic solids, and molecular monolayers for controlling transport properties at surfaces.[7]

Table I. Thermodynamic Data for Dimerization of **1-5** in Chloroform-*d*

compd	K_{assoc} (M^{-1})[a]	ΔG (kcal mol^{-1})[a]	ΔH (kcal mol^{-1})	ΔS (cal mol^{-1} K^{-1})
1	60	-2.4	-5.0 ± 0.2	-9.2 ± 0.8
2	18	-1.7	-5.6 ± 0.3	-13.6 ± 1.0
3	26	-1.9	-5.1 ± 0.3	-10.8 ± 1.0
4	*b*	*b*	*b*	*b*
5	*b*	*b*	*b*	*b*

[a] At 293 K. [b] No evidence for dimerization was observed.



Using our previously reported synthetic methods,[8] we have synthesized compounds **1-5**.[9] It was found that the chemical shifts (δ) of the aromatic protons of **1** depended strongly on concentration. At ambient temperature, the chemical shifts (in $CDCl_3$) of the two aromatic protons of **1** varied from 8.12 to 7.23 ppm and from 7.81 to 6.79 ppm, respectively, as the concentration changed from 0.83 to 106 mM. This indicates that PAM **1** self-associates in solution.[10,11] If we assume that monomer-dimer equilibrium is the predominant process of this self-association,[12] ^1H NMR measurements at different concentrations can be used to determine the dimerization constant, K_{assoc}, using a reported procedure.[13] By this method, K_{assoc} was found to be 60 M^{-1} at 20 °C, which is of the same order as porphyrin dimerization in $CDCl_3$.[14] Since **1** has no functionality to engage in hydrogen bonding, we believe that the observed behavior results from π-stacking interactions. This idea is supported by the observation that only the protons directly attached to the aromatics show significant concentration-dependent chemical shifts. It is also consistent with the fact that we observed no evidence for self-association in benzene-d_6.[15] We suspect that the well-defined,

† Nanoarchitectures. 3. Part 2: see ref 8b.

(1) For general references, see: (a) Tucker, E. E.; Christian, S. D. *J. Phys. Chem.* **1979**, *83*, 426. (b) Ravishanker, G.; Beveridge, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 2565. (c) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768. (d) Tucker, J. A.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1990**, *112*, 5465. (e) Linse, P. *J. Am. Chem. Soc.* **1992**, *114*, 4366. (f) Leighton, P.; Cowan, J. A.; Abraham, R. J.; Sanders, J. K. M. *J. Org. Chem.* **1988**, *53*, 733. (g) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525. (h) Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773. (i) Anderson, H. L.; Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5780.

(2) (a) Benzing, T.; Tjivikua, T.; Wolfe, J.; Rebek, J., Jr. *Science* **1988**, *242*, 266. (b) Muehldorf, A. V.; Van Engen, D.; Warner, J. C.; Hamilton, A. D. *J. Am. Chem. Soc.* **1988**, *110*, 6561. (c) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054. (d) Cochran, J. E.; Parrott, T. J.; Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1992**, *114*, 2269.

(3) (a) Trost, B. M.; O'Krongly, D.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595. (b) Evans, D. A.; Chapman, K. T.; Hung, D. T.; Kawaguchi, A. T. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1184.

(4) (a) Burley, S. K.; Pestko, G. A. *Adv. Protein Chem.* **1988**, *39*, 125. (b) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984.

(5) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989.

(6) Lehn, J.-M.; Malthete, J.; Levelut, A.-M. *J. Chem. Soc., Chem. Commun.* **1985**, 1794.

(7) Markowitz, M. A.; Janout, V.; Castner, D. G.; Regen, S. L. *J. Am. Chem. Soc.* **1989**, *111*, 8192.

(8) (a) Zhang, J.; Moore, J. S.; Xu, Z.; Aguirre, R. A. *J. Am. Chem. Soc.* **1992**, *114*, 2273. (b) Moore, J. S.; Zhang, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 922.

(9) All compounds give satisfactory ^1H NMR, ^{13}C NMR, mass, and element analyses (characterization data are given in the supplementary material).

(10) Self-association of porphyrins in solution has long been recognized and extensively studied. (a) Alexander, A. E. *J. Chem. Soc.* **1937**, 1813. (b) Hughes, A. *Proc. R. Soc. London, Ser. A* **1936**, *155*, 710-711. (c) Abraham, R. J.; Eivazi, F.; Pearson, H.; Smith, K. M. *J. Chem. Soc., Chem. Commun.* 1976, 698 and 699. (d) White, W. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. V, Chapter 7.

(11) For the dimerization of other large organic molecules, see: Cram, D. J.; Choi, H.-J.; Bryant, J. A.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7748.

(12) (a) Saunders, M.; Hyne, J. B. *J. Chem. Phys.* **1958**, *29*, 1319. (b) Marcus, S. H.; Miller, S. I. *J. Am. Chem. Soc.* **1966**, *88*, 3719. Saunder-Hyne analysis of our NMR data has shown that the monomer-dimer model gives the best fit. For fitting comparisons of our data to various models, see the supplementary material.

(13) Horman, I.; Dreux, B. *Helv. Chim. Acta* **1984**, *67*, 754.

(14) (a) Doughty, D. A.; Dwiggins, C. W., Jr. *J. Phys. Chem.* **1969**, *73*, 423. (b) Abraham, R. J.; Barnett, G. H.; Bretschneider, E. S.; Smith, K. M. *Tetrahedron* **1973**, *29*, 553.

(15) For a similar example, see: Sanders, G. M.; van Dijk, M.; van Veldhuizen, A.; van der Plas, H. C.; Hofstra, U.; Schaafsma, T. J. *J. Org. Chem.* **1988**, *53*, 5272.

0002-7863/92/1514-9701$03.00/0 © 1992 American Chemical Society