Table I. Optimal Geometry, Total Energy, and Energy of the Frontier Orbitals for States 1–3 (T_h) and for State 4 (D_{2h})

	1^a	2^a	3^a	4^a
optimal geometries (Å)				
M_0–Ti[b]	2.701	2.713	2.705	2.745
M_0–C	2.614	2.595	2.592	2.609, 2.748, 2.546
C–C	1.391	1.435	1.402	1.299, 1.392, 1.478
Ti–Ti	3.119	3.133	3.123	3.198, 3.033, 3.275
Ti–C	2.025	2.008	2.013	2.145, 2.067, 1.952
total energy[c]	−0.38279	−0.55345	−0.61641	−0.66187
nature and energy (eV) of the frontier orbitals				
HOMO	$4a_g$ −2.31	$1a_u$ −4.11	$6t_u$ −5.14	$6b_{2u}$ −4.35
POMO		$4t_g$ −1.74	$4t_g$ −3.32	
LUMO	$4t_g$ −0.60	$7t_u$ 1.36	$1a_u$ 0.49	$3a_u$ 0.79

[a] State 1, ^1A_g; state 2, ^3T_g; state 3, ^3T_g; state 4, ^1A_g. See text for a more detailed description. [b] M_0 represents the center of symmetry of the cluster. [c] Hartree; shifted by −7227 hartrees.

A preliminary calculation carried out at the geometry optimal for state 2 yielded the total energy −7227.62241 hartrees. Even though no *geometrical* deformation has been introduced yet, this trial value is already lower than the energy associated with any wave function satisfying the constraints of T_h symmetry.[11]

Finally, a gradient optimization has been carried out on the nine independent geometrical parameters that condition the structure of Ti_8C_{12} in the D_{2h} symmetry. The optimal values and the associated energy are reported in Table I. The distortion with respect to a totally symmetric cage structure is important, especially for the six C–C bonding distances that are split into two "short" bond lengths of 1.30 Å, two "intermediate" ones of 1.39 Å, and two "long" C–C bonds of 1.48 Å. Short C–C bonds are associated with long Ti–C bonds and vice versa (see Figure 1). The HOMO–LUMO gap now amounts to 0.19 hartree (5.2 eV, Table I). This is significantly smaller than the gap computed for C_{60} by Scuseria[12] with a double-ζ basis set (0.28 hartree, 7.6 eV), possibly suggesting less kinetic stability for Ti_8C_{12}. However, the LUMO of Ti_8C_{12} has a positive energy, at variance with that of the strongly electrophilic buckminsterfullerene.[13] With 66% weight on the titanium atoms, the HOMO of the distorted structure ($6b_{2u}$) takes place on the top of a set of 10 occupied orbitals with predominant metal character, spanning the energy range −4.35 to −6.9 eV. This cluster of metal frontier orbitals is separated from the highest carbon π orbital ($9a_g$, −9.2 eV) by an energy gap of 2.3 eV. The Mulliken net charge on the metal atoms is +1.1*e*, and the negative charge is almost equally distributed among the three types of carbon atoms (−0.72, −0.72, and −0.77*e*).

In conclusion, we predict the cage structure assumed for Ti_8C_{12} to be subject to FOJT distortion because of the degenerate character of the triplet ground state characterized under the constraints of T_h symmetry. An important deformation of the cage structure is obtained along the D_{2h} distortion path leading to an energy stabilization of 28.5 kcal mol^{-1} with respect to a wave function satisfying the constraints of the T_h point group.[14] Exploratory extended Hückel calculations carried out on V_8C_{12} with the geometry optimized for triplet state 3 of Ti_8C_{12} (T_h symmetry) suggest that a similar situation should occur for the vanadium cluster.

Acknowledgment. All calculations have been carried out on the CRAY-2 computer of the CCVR (Palaiseau, France) through a grant of computer time from the Conseil Scientifique de Centre de Calcul Vectoriel de la Recherche.

Note Added in Proof. After this communication had been accepted for publication, calculations on Ti_8C_{12} and Si_8C_{12} were published by R. W. Grimes and J. D. Gale (*J. Chem. Soc., Chem. Commun.* **1992**, 1222). The calculations, based on the local density approximation, have been carried out on the cage structures with T_h symmetry and the triplet ground state reported for Ti_8C_{12} correlates with state 3 of the present work. The optimized geometrical parameters (C–C = 1.40 Å, M_0–C = 2.57 Å, M_0–Ti = 2.65 Å) are also quite similar to those reported for state 3 in Table I. However, the authors did not consider the FOJT distortion.

Registry No. Ti_8C_{12}, 141344-40-3.

---

(10) Another deformation path should be considered by retaining one C_3 axis and the inversion center as unique symmetry elements (S_6 point group). An investigation of this type of distortion with the present basis set is unfortunately beyond our computational capabilities. We intend to carry out a complete exploration of both distortion pathways using a STO-3G basis set. The calculation of the force constants will then indicate whether the optimal geometries belonging to the D_{2h} and S_6 point groups correspond to true distinct minima or not. If negative eigenvalues are generated by the diagonalization of the Hessian matrices, then a conformation with lower symmetry and lower energy is to be found.

(11) Even though the effect of electron correlation has not been investigated in the present study, it can be predicted that the correlation energy of the $4b_{1g}$ and $4b_{2g}$ electron pairs will increase the energy gap in favor of closed-shell state 4.

(12) Scuseria, G. E. *Chem. Phys. Lett.* **1991**, *176*, 423.

(13) Koga, N.; Morokuma, K. *Chem. Phys. Lett.* **1992**, *196*, 191 and references therein. Note that the geometrical distortion due to FOJT in C_{60}^- leads to an energy stabilization of ~2 kcal mol^{-1} only with respect to a totally symmetric I_h wave function.

(14) Another energy difference of interest should be computed with respect to the *broken symmetry wave function* with lowest energy obtained with a T_h geometry.

Synthesis, Chemistry, and Properties of a Monoalkylated Buckminsterfullerene Derivative, *t*-BuC_{60} Anion

Paul J. Fagan,*,[†] Paul J. Krusic,[†] Dennis H. Evans,*,[‡] Susan A. Lerke,[‡] and Eric Johnston[†]

Central Research and Development Department
E. I. du Pont de Nemours and Co., Inc.[§]
Experimental Station, P.O. Box 80328
Wilmington, Delaware 19880-0328
Department of Chemistry and Biochemistry
University of Delaware, Newark, Delaware 19716

Received July 28, 1992

Although the reactions of lithium and Grignard reagents with buckminsterfullerene (C_{60})[1,2] forming alkylated or arylated products[3] have been reported, no structurally well-defined anionic product has been isolated. The compounds $(R_3P)_2M(\eta^2\text{-}C_{60})$ (M = Ni, Pd, Pt) were 0.36 V harder to reduce than C_{60}, indicating that the electron affinity and reactivity of the C_{60} cluster toward

---

[†] E. I. du Pont de Nemours and Co., Inc.

[‡] University of Delaware.

[§] Contribution No. 6344.

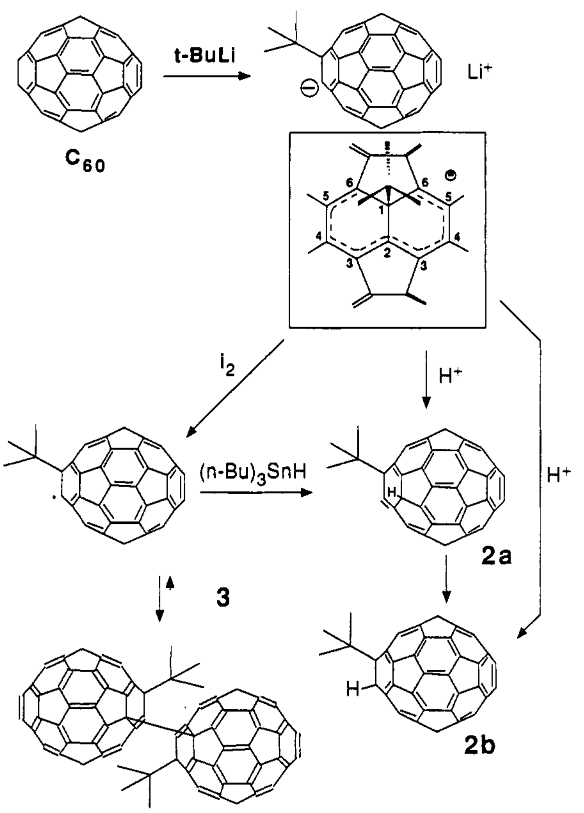
(1) For reviews of C_{60} research, see: McLafferty, F., Ed. *Acc. Chem. Res.* **1992**, *25*, 95. Also see: Schwarz, H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 293.

(2) Wudl, F.; Hirsch, A.; Khemani, K. C.; Suzuki, T.; Allemand, P.-M.; Koch, A.; Eckert, H.; Srdanov, G.; Webb, H. M. In *Fullerenes*; Hammond, G. S., Kuck, V. J., Eds.; ACS Symposium Series 481; American Chemical Society: Washington, DC, 1992; pp 161–175.

(3) (a) Bausch, J. W.; Prakash, G. K. S.; Olah, G. A.; Tse, D. S.; Lorents, D. C.; Bae, Young K.; Malhotra, R. *J. Am. Chem. Soc.* **1991**, *113*, 3205–3206. (b) Krusic, P. J.; Wasserman, E.; Keizer, P. N.; Morton, J. R.; Preston, K. F. *Science* **1991**, *254*, 1183–1185. (c) Morton, J. R.; Preston, K. F.; Krusic, P. J.; Hill, S. A.; Wasserman, E. *J. Phys. Chem.* **1992**, *96*, 3576–3578.

0002-7863/92/1514-9697$03.00/0

Scheme I



nucleophiles is reduced.[4] We reasoned that addition of a single alkyl anion to produce RC_{60}^- should be possible. Independently, Hirsch et al. recently reported that $t\text{-BuC}_{60}H$ could be obtained upon protonation of the reaction of *tert*-butyllithium and C_{60}, suggesting the presence of $t\text{-BuC}_{60}^-$.[5] The compound $C_{60}H^-$ $Li^+{\cdot}9H_2O$ has been reported, but other than elemental analysis, no spectroscopic or structural data could be obtained.[2] Here we report the synthesis and properties of the *tert*-butyllithium adduct of C_{60} isolated in impure form as $t\text{-BuC}_{60}^-Li^+{\cdot}3\text{–}4THF$ (**1a**), and in pure form as $t\text{-BuC}_{60}^-Li^+{\cdot}4CH_3CN$ (**1b**). Protonation of **1b** yields a mixture of isomers of $t\text{-BuC}_{60}H$ (**2a** and **2b**) with **2a** converting to **2b** over time (Scheme I). The compound $t\text{-BuC}_{60}H$ is one of the strongest acids made up of only carbon and hydrogen and has a relatively weak C_{60}–H bond.

Addition all at once of 1.20 mL of 1.2 M *tert*-butyllithium (1.44 mmol) to 1.200 g (1.665 mmol) of C_{60} (completely dissolved overnight in 1 L of benzene) followed by evaporation of the solvent yielded a dark brown residue. The residue was washed with benzene, extracted with tetrahydrofuran, and filtered. Concentration to ca. 10 mL and addition of hexane precipitated a black glassy solid (0.746 g). The ^1H NMR spectrum (THF-d_8) of this air-sensitive compound (**1a**) has a singlet at δ 2.37 ppm (*t*-Bu group) with impurity peaks between 1.7 and 2.3 ppm (ca. 30% of the intensity of the *tert*-butyl resonance). The impurities are presumably isomers of $(t\text{-Bu})_2C_{60}^{2-}$ and $(t\text{-Bu})_3C_{60}^{3-}$ since protonation of **1a** yields a brown solid which by FAB mass spectroscopy contains $t\text{-BuC}_{60}H$, $(t\text{-Bu})_2C_{60}H_2$, and $(t\text{-Bu})_3C_{60}H_3$.

The anion $t\text{-BuC}_{60}^-$ was purified by dissolving **1a** in acetonitrile, filtering, concentrating, and cooling to −25 °C. A green crystalline material was isolated, which upon drying in vacuo loses its crystalline appearance to yield **1b** as a green powder (0.40 g, 25% yield).[6] The product has the expected ^{13}C NMR spectrum for a C_{60} derivative with C_s symmetry.[6] Upon cooling, the *tert*-butyl resonance in the ^1H NMR spectrum (500 MHz, THF-d_8, −99 °C) splits into two resonances (δ 2.22, 6 H; 2.59, 3 H) owing to hindered rotation of the *tert*-butyl group. Simulation of line shapes yields $\Delta G^{\ddagger} = 9.3$ (±0.1) kcal/mol at −60 °C. Hindered rotation in the radical $t\text{-BuC}_{60}^{\bullet}$ has also been observed.[7]

Protonation of **1b** with acetic acid in THF yields a brown solid after solvent removal. Extraction with benzene, filtration, and concentration of the filtrate yields a brown microcrystalline product. Spectroscopy reveals this product to be a mixture of **2a** and **2b** in a 1:10 ratio respectively (Scheme I).[8] With saccharin as the acid, a 1:1 ratio of **2a** and **2b** is formed. Isomer **2a** is unstable and, after ca. 12 h at 25 °C, rearranges to **2b**[8] (Scheme I). An NOE intensity enhancement (^1H NMR) of the C_{60}–H resonance for **2b** at 6.08 ppm upon irradiation of the *tert*-butyl resonance suggests that the C_{60}-bound hydrogen and *tert*-butyl group are in close proximity. Hindered rotation of the *tert*-butyl group is observed for **2b** in the ^1H NMR spectrum (300 MHz, −90 °C, toluene-d_8: δ 1.60 and 1.51 in a 2:1 intensity ratio) and is consistent with the molecule containing a mirror plane. Hindered rotation is also seen for **2a** in which the *tert*-butyl resonance splits into three resonances in a 1:1:1 intensity ratio at low temperature. This corresponds to an isomer with no symmetry elements and is tentatively assigned structure **2a** in Scheme I (vide infra).

All resonances expected for the C_s symmetry isomer **2b** (Scheme I) are observed in the ^{13}C NMR spectrum.[6] Hirsch et al. had proposed this structure on the basis of a theoretical calculation,[5] and the data reported here provides definitive experimental evidence that this is the correct structure. Opening of the sphere[9] does not occur as the shift for the protonated C_{60}-carbon is at δ 57.3 with $J_{C-H} = 135$ Hz, consistent with sp^3 hybridization.

Oxidation of **1b** in THF with 1 equiv of I_2 leads to a brown product which contains some $t\text{-BuC}_{60}H$. Repeated washing with benzene removes $t\text{-BuC}_{60}H$, leaving a slightly soluble dark brown powder. EPR studies of this powder dissolved in CS_2 or toluene reveal the presence of the $t\text{-BuC}_{60}^{\bullet}$ radical (**3**).[10] Addition of $n\text{-Bu}_3SnH$ to this powder in toluene produces exclusively **2a**, which subsequently rearranges to **2b** as determined by ^1H NMR spectroscopy. Solutions of $t\text{-BuC}_{60}^{\bullet}$ generated by photolysis of C_{60} in the presence of $t\text{-Bu}_2Hg$ also react with tri-*n*-butyltin hydride to generate **2a**.

From ESR studies of $t\text{-BuC}_{60}^{\bullet}$, the greatest amount of spin density is at C2 (Scheme I), with less at C4 and C6.[10] For steric reasons, this radical was proposed to dimerize at C4.[10] We tentatively suggest that C4 is the site of kinetic hydrogen atom addition with $n\text{-Bu}_3SnH$. It is likely that negative charge delocalization in $t\text{-BuC}_{60}^-$ is similar to unpaired spin delocalization in $t\text{-BuC}_{60}^{\bullet}$. Although protonation of C2 is most likely, for steric reasons we propose that, depending on conditions and the acid, kinetic protonation occurs at both C2 and C4 forming **2a** and **2b**. Rearrangement of **2a** to **2b** (by an as yet unknown mechanism) would be thermodynamically favorable as this removes a double bond from within a C_{60} five-membered ring. Calculations on isomers of $C_{60}H_2$ find that the "1,2" addition product has the lowest energy.[11]

The results we have obtained are summarized in Scheme I. These results provide good experimental evidence that the negative charge upon addition of a nucleophile (or the electron spin upon addition of a radical) is localized near the point of attack on C_{60}. Regioselective chemistry on the C_{60} surface should be possible.

---

(4) (a) Lerke, S. A.; Evans, D.; Fagan, P. J.; Parkinson, B. *J. Am. Chem. Soc.*, in press. (b) Fagan, P. J.; Calabrese, J. C.; Malone, B. *Acc. Chem. Res.* **1992**, *25*, 134–142.

(5) Hirsch, A.; Soi, A.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 766–768.

(6) See supplementary material.

(7) Krusic, P. J.; Roe, D. C.; Johnston, E.; Keizer, P. N.; Morton, J. R.; Preston, K. F. Submitted for publication.

(8) ^1H NMR (300 MHz, toluene-d_8, 25 °C) for **2a**: δ 1.63 (s, 9 H, *t*-Bu), 5.46 (s, 1 H, $C_{60}H$). For **2b**: δ 1.70 (s, 9 H, *t*-Bu), 6.08 (s, 1 H, $C_{60}H$).

(9) (a) Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, Ö. *Science* **1991**, *254*, 1186–1188. (b) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157. (c) Suzuki, T.; Khemani, K. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 7300–7301. (d) Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 7301–7302.

(10) Morton, J.; Preston, K. F.; Krusic, P. J.; Hill, S. A.; Wasserman, E. *J. Am. Chem. Soc.* **1992**, *114*, 5454–5455.

(11) Matsuzawa, N.; Dixon, D. A.; Fukunaga, T. *J. Phys. Chem.* **1992**, *96*, 7594–7604.

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$_6$H$_5$)$_2$CC$_{60}$, which is 0.11 V harder to reduce than C$_{60}$[9]). Evidence is mounting[9b,12] that (C$_6$H$_5$)$_2$CC$_{60}$ 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$_4$N$^+$CH$_3$CO$_2^-$ 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, ^{1}H 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.

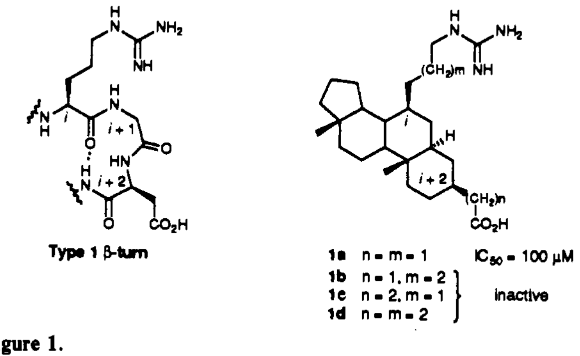


Figure 1.

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]

---

[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.

[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.