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References and Notes

(1) M. S. Foster and J. L. Beauchamp, *J. Am. Chem. Soc.*, **93**, 4924 (1971); *Ibid.*, **97**, 4808, 4814 (1975); J. L. Beauchamp, *J. Chem. Phys.*, **64**, 718, 929 (1976); R. R. Corderman and J. L. Beauchamp, *Inorg. Chem.*, **15**, 665 (1976).

(2) R. C. Dunbar, J. F. Ennever, and J. P. Fackler, Jr., *Inorg. Chem.*, **12**, 2734 (1973); R. D. Bach, J. Gauglhofer, and L. Kevan, *J. Am. Chem. Soc.*, **94**, 6860 (1972); R. D. Bach, J. Patane, and L. Kevan, *J. Org. Chem.*, **40**, 257 (1975).

(3) R. D. Wieting, R. H. Staley, and J. L. Beauchamp, *J. Am. Chem. Soc.*, **97**, 924 (1975); A. D. Williamson and J. L. Beauchamp, *ibid.*, **97**, 5714 (1975).

(4) R. H. Staley and J. L. Beauchamp, *J. Am. Chem. Soc.*, **97**, 5920 (1975).

(5) J. Allison and D. P. Ridge, *J. Organomet. Chem.*, **99**, C11 (1975).

(6) R. R. Corderman and J. L. Beauchamp, *J. Am. Chem. Soc.*, **98**, 3998 (1976).

(7) R. C. Dunbar and B. B. Hutchinson, *J. Am. Chem. Soc.*, **96**, 3816 (1974); J. H. Richardson, L. M. Stephenson, and J. I. Brauman, *ibid.*, **96**, 3671 (1974); B. S. Freiser, R. H. Staley, and J. L. Beauchamp, *Chem. Phys. Lett.* **39**, 49 (1976).

(8) For a review see J. L. Beauchamp, *Annu. Rev. Phys. Chem.*, **22**, 527 (1971).

(9) R. R. Corderman and J. L. Beauchamp, unpublished results.

(10) J. Müller and W. Goll, *Chem. Ber.*, **106**, 1129 (1973); **107**, 2084 (1974).

(11) J. Halpern in "Organotransition Chemistry", Y. Ishii and M. Tsutsui, Ed., Plenum Press, New York, N.Y., 1975, p 109.

(12) C. W. Bird, "Transition Metal Intermediates in Organic Synthesis", Academic Press, New York, N.Y., 1967, p 239; J. Tsuji and K. Ohno, *Tetrahedron Lett.*, 3969 (1965).

(13) J. McCarty, J. Falconer, and R. J. Madix, *J. Catal.*, **30**, 235 (1973); J. T. Yates, Jr., T. E. Madey, and M. J. Dresser, *ibid.*, **30**, 260 (1973).

(14) T. B. McMahon and J. L. Beauchamp, *Rev. Sci. Instrum.*, **43**, 509 (1972).

(15) The abundance of ions from both CH_3CHO alone (A. S. Blair and A. G. Harrison, *Can. J. Chem.*, **51**, 703 (1973)), and $CpNiNOH^+$ are not included in the normalization of data given Figure 1.

(16) J. L. Beauchamp and J. Y. Park, *J. Phys. Chem.*, **80**, 575 (1976); R. J. Blint, T. B. McMahon, and J. L. Beauchamp, *J. Am. Chem. Soc.*, **96**, 1269 (1974); R. H. Staley and J. L. Beauchamp, *J. Chem. Phys.*, **62**, 1998 (1975).

(17) The Langevin, or collision rate constant,[22,23] is calculated to be 8.8×10^{-10} cm^3 $molecule^{-1}$ s^{-1}.

(18) A measure of RCO^+ stability is given by the hydride affinity, or $D[RCO^+-H^-]$, of these cations. Using available thermochemical data, we compute $D[CH_3CO^+-H^-] = 233$ kcal/mol and $D[CH_3CH_2CO^+-H^-] = 225$ kcal/mol, while $D[HCO^+-H^-] = 255$ kcal/mol, for example.

(19) $D[CO-CpNi^+]$ is calculated from the proton affinity of CO, $D[CO-H^+] =$ 143 kcal/mol (A. E. Roche, M. M. Sutton, D. K. Bohme, and N. I. Schiff, *J. Chem. Phys.*, **55**, 5480 (1971)) and the data given in ref 6. An additional 5 kcal/mol was added to account for π-bonding interactions.

(20) The 18-electron intermediate III may be more stable than II, a 16-electron complex, thus providing a driving force for the decarbonylation step II → III (Figure 2).

(21) Camille and Henry Dreyfus Teacher–Scholar, 1971–1976.

(22) G. Gioumousis and D. P. Stevenson, *J. Chem. Phys.*, **29**, 294 (1958).

(23) The value of α used was 4.9×19^{-24} cm^3 from J. Applequist, J. R. Carl, and K.-K. Fung, *J. Am. Chem. Soc.*, **94**, 2952 (1972).

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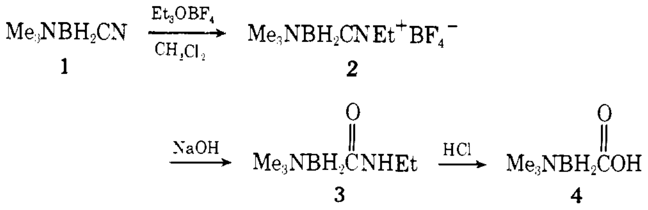
Boron Analogues of Amino Acids. Synthesis and Biological Activity of Boron Analogues of Betaine

Sir:

As a class of compounds, the α-amino acids are of unquestioned importance, being the principal constituents of protein and living matter. The postulation of a series of isoelectronic and isostructural boron analogues of the amino acids would give rise to questions about their chemical stability and the possibility of biological activity. Providing important information on this subject, we wish to report on the synthesis and structure of $Me_3NBH_2CO_2H$ (**4**) the (protonated) boron analogue of the dipolar amino acid betaine, $Me_3N^+CH_2CO_2^-$, and its N-ethylamide derivative (**3**). Further, we wish to issue a preliminary report on the antitumor and hypolipidemic activity of these compounds in mice.

3 and **4** may be obtained by the general scheme shown below.



$$Me_3NBH_2CN \ (\mathbf{1}) \xrightarrow[CH_2Cl_2]{Et_3OBF_4} Me_3NBH_2CNEt^+BF_4^- \ (\mathbf{2}) \xrightarrow{NaOH} Me_3NBH_2\overset{\overset{\displaystyle O}{\|}}{C}NHEt \ (\mathbf{3}) \xrightarrow{HCl} Me_3NBH_2\overset{\overset{\displaystyle O}{\|}}{C}OH \ (\mathbf{4})$$

Although **1** may be prepared by a variety of methods,[1] we have found it to be conveniently prepared by the reaction of $NaBH_3CN$[2] with $Me_3N{\cdot}HCl$ (suspension) in THF.[3] The N-ethylnitrilium salt (**2**) was prepared by refluxing (under dry N_2) a solution of **1** in CH_2Cl_2 with 2 equiv of triethyloxonium tetrafluoroborate for 24 h. **2** was not isolated but a 1.0 N NaOH solution added slowly with vigorous stirring until basic. The organic layer was separated and the aqueous layer extracted three times with CH_2Cl_2. The combined CH_2Cl_2 solutions were dried over $CaCl_2$, concentrated (rotary evaporator), and vacuum distilled at 80 °C and 10^{-3} Torr to give **3**, a clear viscous liquid, in 60% yield: ^1H NMR ($CDCl_3$) δ 1.07 (t, $J = 8$ Hz CH_2CH_3), 2.75 (s, CH_3N), 3.57 (m, CH_2CH_3), 5.43 (broad s, NH); ^{13}C NMR ($CDCl_3$) δ^4 15.3 CH_3CH_2, 31.5 CH_2CH_3, 51.8 CH_3N, 182.8 CO; ^{11}B ($CDCl_3$), 50 °C, δ^{5a} 7.4 (1:2:1 t, $J = 90$ Hz); ir (neat in cm^{-1}) 3289 ν_{NH}, 2915 ν_{CH}, 2330 ν_{BH}, 1590 amide I, 1480 amide II; mass spectral m/e, 144 (M^+, $C_6H_{17}{}^{11}BN_2O$). Anal. ($C_6H_{17}BN_2O$) C, H, B, N.[5b]

To obtain **4**, 0.3 N HCl was added to **3** and refluxed for a period of 8 h. The solution was evaporated to dryness under reduced pressure and the residue washed with CCl_4 and extracted with $CHCl_3$. After evaporation of $CHCl_3$, the residue was fractionally crystallized from H_2O to give a white crystalline solid (dried under vacuum, 1 h), mp (under vacuum) 147 °C with dec. Typical overall yields of **4** from **1** of 25% have been obtained.[6] ^1H NMR (D_2O) δ 2.72 (s CH_3N) 4.65 (s HDO); ir (KBr in cm^{-1}) 3130 ν_{OH} broad and superimposed with ν_{CH} in 2950–3310 region, 2380 ν_{BH}, 1645 ν_{CO}; mass spectral m/e, 118 (M^+, $C_4H_{12}{}^{11}BNO_2$). Anal. ($C_4H_{12}BNO_2$) C, H, B, N.[5b]

A ca. 0.15 M solution[7] of **4** in distilled H_2O (in an evacuated flask) was stable towards H_2 evolution for a period of 1 month. After standing for 1 week (in an evacuated flask) a ca. 0.15 M solution of **4** in 1 N HCl gave a 25.7% theoretical yield of H_2 and 52.8% after 3 weeks.[8] No changes in the ir spectra of **4** were noted after exposure to the atmosphere for a period of 2 months.[9]

Attempts to prepare **4** directly by acid or base hydrolysis of **1** were unsuccessful giving either boric acid or borate salts. This result is consistent with the kinetic study by Kelly[1c] on the hydrolysis of **1** to yield $B(OH)_4^-$. Structures **3** and **4** may also be viewed as trimethylamine derivatives of boranocarbamate, $H_3BC(O)NHR^-$, and boranocarbonate, $H_3BCO_2{}^{2-}$, ions as synthesized by Parry and co-workers.[10]

The molecular geometry of **4** was established by single-crystal x-ray analysis. Orthorhombic crystals of **4**, grown by slow evaporation of an aqueous solution, belong to the space group $Pna2_1$, with: $a = 12.59$ (1), $b = 5.95$ (1), $c = 19.54$ (1) Å, $U = 1464$ Å^3, d_m (flotation in heptane-CCl_4) $= 1.05$ g cm^{-3}, $Z = 8$, $d_c = 1.061$ g cm^{-3}. Weissenberg photographs of the reciprocal lattice levels recorded from several crystals rotating about the a axis consistently showed that diffuse streaking was present along festoons with constant k when h was odd; the origin of this observation is under further investigation. For the x-ray analysis the intensities of 1288 reflections with $\theta < 65°$ were recorded at 25 °C on an Enraf-Nonius

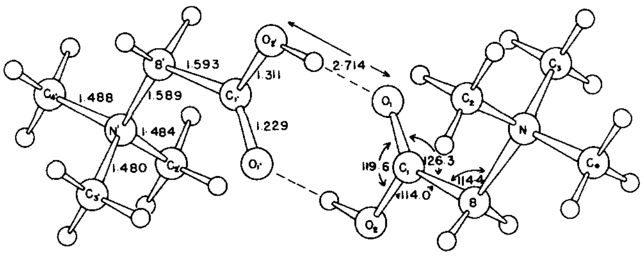


Figure 1. Conformation, interatomic distances (±0.017 Å), and valency angles (±1.0°), averaged according to C_i symmetry, in the asymmetric crystal unit of $Me_3NBH_2CO_2H$; valency angles around nitrogen do not deviate significantly from tetrahedral. Small circles denote calculated hydrogen atom positions.

CAD 3 automated diffractometer using Ni-filtered Cu K_α radiation (λ 1.5418 Å) and the θ-2θ scanning procedure as described previously.[11] The structure was solved by direct methods using the MULTAN program package.[12] Refinement of atomic positional and thermal parameters (anisotropic B, C, N, O; fixed H contributions) converged at $R = 0.109$ over 625 statistically significant $[I > 2.0\sigma(I)]$ reflections. The conformation and mean dimensions of the asymmetric crystal unit which comprises a hydrogen-bonded dimer with approximate C_{2h} symmetry are shown in Figure 1. Although the crystal structure of the corresponding carboxylic acid, 3,3-dimethylbutanoic acid, which lacks the $^-B-N^+$ dipole and consequently has a much lower melting point of 6–7 °C, has not been studied the dimensions of **4** may be compared with those of other carboxylic acids. The bond length and valency angle pattern at the carboxyl group in **4** are similar to that in simple carboxylic acids,[13] but the O-H···O hydrogen bonded distance at 2.714 Å in the dimer is slightly longer than the corresponding distance of ca. 2.64 Å in that same class of compounds. The remaining dimensions and molecular conformation reveal no unusual features.

Preliminary in vivo antitumor screens[14] in mice have demonstrated significant antitumor activity for **3** and **4** in the Ehrlich Ascites screen and for **3** in the P_{388} Lymphocytic Leukemia screen. In the Ehrlich screen, dosages of 33.3 mg/kg per day into CF_1 male mice resulted in inhibition of tumor growth[15] of 82.4% for **4** and 69.4% for **3**. In the P_{388} screen, using standard NCI protocols,[16] compound **3** at a dosage of 50 mg/kg per day into DBA/2 male mice exhibited a T/C of 132 compared to the control 5-fluorouracil of 126. Although no specific toxic dose studies have been completed, there have been no signs of toxicity exhibited in the tests at these dosage levels.

Betaine and choline have been implicated as cofactors in the liver for synthesis of cholesterol. Examinations of the serum blood cholesterol levels[14] of male mice after dosing with **4** for 1 week at 1 mg/day resulted in a lowering of serum cholesterol by 29%,[17] considered to be a significant reduction in the mouse.

The synthesis of other boron analogues of amino acids and biological activity studies are in progress.

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References and Notes

(1) (a) B. F. Spielvogel, J. M. Purser, and C. G. Moreland, Abstracts Southeast Regional Meeting, American Chemical Society, Richmond, Va., Nov 1969; *Chem. Eng. News*, **33** (Nov. 10, 1969); (b) S. S. Uppal and H. C. Kelly, *Chem. Commun.*, 1619 (1970); (c) C. Weidlg, S. S. Uppal, and H. C. Kelly, *Inorg. Chem.*, **13**, 1763 (1974); (d) B. F. Spielvogel, R. F. Bratton, and C. G. Moreland, *J. Am. Chem. Soc.*, **94**, 8597 (1972); (e) P. J. Bratt, M. P. Brown, and K. R. Seddon, *J. Chem. Soc., Dalton Trans.*, 2161 (1974).

(2) Obtainable commercially from Aldrich Chemical Co., and Ventron Corporation.

(3) B. F. Spielvogel, M. K. Das, and R. F. Bratton, manuscript in preparation.

(4) In ppm from internal Me_4Si, positive sign indicates downfield from standard.

(5) (a) In ppm from external $BF_3{\cdot}Et_2O$, positive sign indicates upfield from standard. (b) Analyses for indicated elements within ±0.3% were obtained.

(6) It is not necessary to vacuum distill **3** before proceeding with the hydrolysis if only **4** is desired.

(7) A saturated solution of **4** in water is ca. 0.67 M.

(8) After warming the solution for several days at 50–55 °C, eventually over 90% of the theoretical yield of H_2 was obtained.

(9) A decrease in the melting point (with decomposition) is noted after prolonged vacuum or desiccator drying but may be increased close to the original value by allowing the sample to stand in a H_2O saturated atmosphere. This process is currently under investigation. Essentially no change was observed in the elemental analysis of a sample stored in air in a stoppered flask after 4 months.

(10) (a) J. C. Carter and R. W. Parry, *J. Am. Chem. Soc.*, **87**, 2354 (1965); (b) L. J. Malone and R. W. Parry, *Inorg. Chem.*, **6**, 817 (1967).

(11) D. L. McFadden and A. T. McPhail, *J. Chem. Soc., Dalton Trans.*, 363 (1971).

(12) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).

(13) I. Nahringbauer, *Acta Chem. Scand.*, **24**, 453 (1970); F. J. Strieter D. H. Templeton, R. F. Scheuerman, and R. L. Sass, *Acta Crystallogr.*, **15**, 1233 (1962); F. J. Strieter and D. H. Templeton, *Ibid.*, **15**, 1240 (1962); R. F. Scheuerman and R. L. Sass, *Ibid.*, **15**, 1244 (1962).

(14) Private communication, I. H. Hall, Department of Medicinal Chemistry, University of North Carolina, Chapel Hill, N.C.

(15) According to standard procedures; see C. Piantadosi, C. S. Kim, and J. L. Irwin, *J. Pharm. Sci.*, **58**, 821 (1969). The control in these screens, 6-mercaptopurine, showed 99.7% inhibition.

(16) R. I. Geran, N. H. Greenberg, M. M. Macdonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 2*, **3**, 9 (1972).

(17) Hyperlipidemia is a problem in cancer patients.[18] Design of a drug which has both characteristics, i.e., antitumor and hypolipidemic activity is desirable.

(18) M. R. Grigor, M. L. Blank, and F. Snyder, *Cancer Res.*, **33**, 1870 (1973).

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9,10-Dehydroanthracene. A Derivative of 1,4-Dehydrobenzene

Sir:

Dehydrobenzenes have fascinated chemists since the suggestion of 1,2-dehydrobenzene (benzyne) as a reaction intermediate.[1] Benzyne is now a well-characterized molecule[2,3] with a clearly defined triple bond[4] and a singlet ground state.[5] The isomeric 1,4-dehydrobenzene which has been reported as a transient in time-of-flight mass spectrometry[6] poses a particularly intriguing theoretical problem in that diradical (singlet or triplet) and bicyclic structures are possible.[7-13] It has, in fact, been suggested that the diradical structure for 1,4-dehydrobenzene and the butalene structure may each represent minima on the C_6H_4 energy surface.[13] Chemical trapping evidence has been obtained for a 1,4-dehydrobenzene with a diradical structure (benzene-1,4-diyl)[14] and for a 1,4-dehydrobenzene with the butalene structure.[15,16] We wish to describe the synthesis, spectroscopic observation, and chemical characterization of 9,10-dehydroanthracene, a derivative of 1,4-dehydrobenzene.