(dd, $^1J_{CC}$ = 57.7 Hz and $^2J_{CC}$ = 18.6 Hz, C7a), 134.7, 127.3 (d, J_{CC} = 2.9 Hz), 127.0 (dd, J_{CC} = 3.9 Hz and J_{CC} = 1.9 Hz), 123.5, 36.4 (d, $^1J_{CC}$ = 39.1 Hz, C2), 25.9 (dd, $^1J_{CC}$ = 35.2 Hz and $^2J_{CC}$ = 2.9 Hz, C3).

[2,3-$^{13}C_2$]Bicyclo[3.2.2]nona-3,6,8-trien-2-ol (5).[12] The ketone **29** was reduced with lithium aluminum hydride in diethyl ether at −80 °C and worked up as usual to yield 88% **5**. ^{1}H NMR (CD_2Cl_2): δ 6.88–6.63 (m, 2 H), 6.40–6.06 (m, 3 H), 4.98 (dd, m, $^1J_{CH}$ = 157.2 Hz and J_{HH} = 10.7 Hz, 0.9 H; d, m, J_{CH} = 10.6 Hz, 0.1 H), 4.01 (br d, $^1J_{CH}$ = 147 Hz, 0.9 H; br, 0.1 H), 3.49 (m, 1 H), 3.25 (m, J = 7 Hz, 1 H), 2.20 (br, 1 H). ^{13}C NMR: δ 141.9 (C6 or C9), 140.7 (C6 or C9), 136.6 (d, $^1J_{CC}$ = 70.8 Hz, C4), 128.9 (d, $^1J_{CC}$ = 46.4 Hz, C3), 65.1 (d, $^1J_{CC}$ = 46.4 Hz, C2), 44.6 (d, $^1J_{CC}$ = 35.4 Hz, C1), 37.3 (C5).

2-Methyl[2,3-$^{13}C_2$]bicyclo[3.2.2]nona-3,6,8-trien-2-ol (6).[11a] Methyllithium was prepared by the addition of methyl iodide to lithium wire in ether under argon[25] and was titrated with 1,3-diphenyl-2-propanone tosylhydrazone (Ventron) in tetrahydrofuran, [CH_3Li] = 0.9 M.

The ketone **29** (20 mg, 0.15 mmol) was dissolved in diethyl ether, added to methyllithium (1 mL, 0.9 M) in diethyl ether at 0 °C, and stirred for 4 min. The reaction was quenched with ice and saturated NH_4Cl, extracted with diethyl ether, dried over K_2CO_3, and evaporated, to give 18 mg (0.12 mmol, 80%) of 6. Analysis with TLC and GLC revealed some minor impurities (<2% each). ^{1}H NMR (CD_2Cl_2): δ 6.9–6.5 (d, t, 2 H), 6.3–6.0 (m, 3 H), 4.82 (ddd, $^1J_{CH}$ = 156.6 Hz and J_{HH} = 10.7, 2.2 Hz, 0.9 H; dd, J_{HH} = 10.7, 2.2 Hz, 0.1 H), 3.31 (m, 2 H), 1.91 (br, 1 H), 1.28 (m, 3 H). ^{13}C NMR: δ 141.5 (C6 or C9), 139.3 (C6 or C9), 134.4 (d, $^1J_{CC}$ = 46.4 Hz, C3), 130.8 (C7 or C8), 130.1 (C7 or C8), 68.4 (d, $^1J_{CC}$ = 46.4 Hz, C2), 49.6 (d, $^1J_{CC}$ = 34 Hz, C1), 37.3 (C5), 27.4 (d, $^1J_{CC}$ = 41.5 Hz, CH_3).

Preparation of Ions. Ions were prepared in 5-mm NMR tubes with the ion-generation apparatus of Ahlberg and Engdahl.[11b] Precursor alcohols (ca. 8 mg) were dissolved in $CHCl_2F$ (ca. 100 μL) at −10 °C in a syringe and added to a mixture of FSO_3H–SO_2ClF–SO_2F_2–$CHCl_2F$ (2:7:7:2, v/v/v/v) under nitrogen gas at ca. −135 °C.[12] Rapid mixing gave pale-yellow solutions, which were sealed and stored in liquid nitrogen.

Acknowledgment. We thank the Swedish Natural Science Research Council for support, including a predoctoral fellowship for G.J.

(25) Schöllkopf, U.; Paust, J.; Patsch, M. R. *Org. Synth. Collect. Vol. V* **1973**, 859–862.

Communications to the Editor

Remarkably Facile Synthesis of an Isoelectronic and Isostructural Boron Analogue of Acetylcholine

Bernard F. Spielvogel,* Fahim U. Ahmed, and Andrew T. McPhail

P. M. Gross Chemical Laboratory, Duke University Durham, North Carolina 27706

Received October 3, 1985

We are interested in the synthesis and characterization of isoelectronic and isostructural boron analogues of biologically important molecules. These may be of use to probe fundamental biochemical events at the molecular level as well as to provide entirely new classes of compounds of potential pharmacological value. Along these lines we have prepared some of the first examples of boron analogues of the α-amino acids[1-3] and their related precursors[4,5] and derivatives.[6,7] These analogues, typified by the protonated glycine analogue[1] $H_3NBH_2CO_2H$, contain 4-coordinate boron and possess appreciable air and hydrolytic stability. They have been found to possess significant pharmacological activity, in particular, antitumor,[8-10] antiarthritic,[11] and hypolipidemic[12,13] activity in animal model studies.

Boron analogues of other important biologically active molecules such as neurotransmitters can be envisioned. In this paper, we wish to report a remarkably facile synthesis of (2-acetoxyethyl)dimethylamine–borane (**1**), an isoelectronic and isostructural

H_3B–$N(CH_2)_2CH_2CH_2OC(=O)CH_3$
1

$[H_3CN(CH_3)_2CH_2CH_2OC(=O)CH_3]^+$
2

boron analogue of the important neurotransmitter the acetylcholine (ACh) cation (**2**).

This boron analogue of ACh is a molecular species since the boron and nitrogen atoms bear canceling formal negative and positive charges, respectively. Thus this analogue may be useful in studies designed to probe the importance of the so-called "anionic" subsite of acetylcholinesterase and ACh receptors. Although **1** belongs to the relatively well-known class of compounds, the amine–boranes, viewed as an analogue of ACh, suggests examination of its activity in novel areas.[14]

(2-Acetoxyethyl)dimethylamine–borane, **1** was prepared by an efficient synthesis shown below in Scheme I.

Scheme I

$$Me_2NCH_2CH_2OH \xrightarrow[CH_2Cl_2]{CH_3COCl} \underset{\mathbf{3}}{Me_2NCH_2CH_2OC(=O)CH_3}\ Cl^- \xrightarrow[Et_4NBH_4]{CH_2Cl_2} \underset{\mathbf{1}}{H_3B\text{–}N(CH_3)_2CH_2CH_2OC(=O)CH_3}$$

The ester hydrochloride **4** was prepared by adding $CH_3C(O)Cl$[15] (10% mol excess) dropwise to an ice-cold solution of

(1) Spielvogel, B. F.; Das, M. K.; McPhail, A. T.; Onan, K. D.; Hall, I. H. *J. Am. Chem. Soc.* **1980**, *102*, 6343.
(2) Spielvogel, B. F.; Wojnowich, L.; Das, M. K.; McPhail, A. T.; Hargrave, K. D. *J. Am. Chem. Soc.* **1976**, *98*, 5702.
(3) Spielvogel, B. F. "Boron Chemistry-4"; IUPAC, Inorganic Chemistry Division; Parry, R. W. Kodama, G., Eds.; Pergamon Press: New York, 1980; pp 119–129.
(4) Wisian-Neilson, P.; Das, M. K.; Spielvogel, B. F. *Inorg. Chem.* **1978**, *17*, 2327.
(5) Spielvogel, B. F.; Harchelroad, F., Jr.; Wisian-Neilson, P. *J. Inorg. Nucl. Chem.* **1979**, *41*, 123.
(6) Spielvogel, B. F.; Ahmed, F. U.; Morse, K. W.; McPhail, A. T. *Inorg. Chem.* **1984**, *23*, 1776.
(7) Spielvogel, B. F.; Ahmed, F. U.; Silvey, G. L.; Wisian-Neilson, P.; McPhail, A. T. *Inorg. Chem.* **1984**, *23*, 4322.
(8) Hall, I. H.; Spielvogel, B. F.; McPhail, A. T. *J. Pharm. Sci.* **1984**, *73*, 222.
(9) Hall, I. H.; Starnes, C. O.; Spielvogel, B. F.; Wisian-Neilson, P.; Das, M. K.; Wojnowich, L. *J. Pharm. Sci.* **1979**, *68*, 685.
(10) Hall, I. H.; Gilbert, C. J.; McPhail, A. T.; Morse, K. W.; Hasset, K.; Spielvogel, B. F. *J. Pharm. Sci.* **1985**, *74*, 755.
(11) Hall, I. H.; Starnes, C. O.; McPhail, A. T.; Wisian-Neilson, P.; Das, M. K.; Harchelroad, F., Jr.; Spielvogel, B. F. *J. Pharm. Sci.* **1980**, *69*, 1025.
(12) Hall, I. H.; Das, M. K.; Harchelroad, F., Jr.; Wisian-Neilson, P.; McPhail, A. T.; Spielvogel, B. F. *J. Pharm. Sci.* **1981**, *70*, 339.
(13) Hall, I. H.; Williams, W. L., Jr.; Gilbert, C. J.; McPhail, A. T.; Spielvogel, B. F. *J. Pharm. Sci.* **1984**, *73*, 973.
(14) An alkylborinic acid analogue of ACh has been prepared, $Me_3N^+(CH_2)_3B(OH)Me\ Br^-$, whose structure differs significantly from the class under consideration in this paper. Koehler, K. A.; Hess, G. P. *Biochemistry* **1974**, *13*, 5345. A borane adduct of 2-(dimethylamino)ethanol, $H_3BNMe_2CH_2OH$, has been reported which may be considered a boron analogue of choline. However, this analogy was not discussed in the reports. Mancilla, T.; Santiesteban, F.; Contreras, R.; Klaebe, A. *Tetrahedron Lett.* **1982**, *23*, 1561. Brown, H. C.; Murray, L. T. *Inorg. Chem.* **1984**, *23*, 2746.

0002-7863/86/1508-3824$01.50/0 © 1986 American Chemical Society

N,N-dimethylethanolamine (**3**)[15] in CH_2Cl_2 under N_2. After the mixture was stirred overnight at ambient temperature, the solvent was evaporated off under reduced pressure. The white solid thus obtained was repeatedly washed with anhydrous ether to remove any unreacted starting materials and then vacuum pumped overnight to give a 91% yield of the extremely hygroscopic ester hydrochloride **4**: IR ($CDCl_3$) ν_{CO} 1740 (s), ν_{+NH} 2200 (s), 2250 (s), 2400 (br s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (s, CH_3CO), 2.94 (s, $CH_3N^+CH_3$), 3.43 (dist t, CH_2N), 4.48 (dist t, CH_2O). This ester hydrochloride was used as such without further purification considering its extreme hygroscopic behavior.

To obtain **1**, solid Et_4NBH_4[15] (50% mol excess) was slowly added to a stirred solution of **4** in CH_2Cl_2. Vigorous evolution of H_2 gas took place initially. After the reaction had subsided, it was refluxed for 3 h, cooled, and washed 3 times with H_2O. The organic portion was dried over $MgSO_4$ and the solvent removed under reduced pressure to give an 85% yield of **1** (pure by ^1H and ^{11}B NMR spectra); vacuum distillation of the crude product yielded a colorless oil: bp 89–90 °C (0.4 torr); IR (CH_2Cl_2) ν_{CO} 1740 (s), ν_{BH} 2380 (s), 2310 (sh), 2270 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03 (s, CH_3CO), 2.62 (s, CH_3NCH_3), 2.98 (t, J = 6 Hz, CH_2N), 4.38 (t, J = 6 Hz, CH_2O); ^{11}B NMR ($CDCl_3$, BF_3/Et_2O) δ −9.42 (q, J_{BH} = 98 Hz). Anal. Calcd for $C_6H_{16}BNO_2$: C, 49.70; H, 11.12; N, 9.66; B, 7.46. Found: C, 49.63; H, 10.93; N, 9.32; B, 7.25.

When the reaction of **4** was carried out with $NaBH_4$[15] (100% molar excess) for 1 day in refluxing THF, the yield of **1** after workup was only 19%. However, the yield of **1** could be increased up to 74% by carrying out the reaction for 6 days under identical reaction conditions.

In view of the important roles played by acetylcholine and its analogues in the transmission of the nerve impulse, the conformation of these compounds has been extensively studied. It has been postulated that acetylcholine is capable of existence in several conformations. On the basis of various X-ray[16–18] and NMR[19–23] studies, it has been concluded that the predominant conformation of acetylcholine is gauche in solution as well as in the crystalline state.

By contrast, in the ^1H NMR spectrum[24] of **1** in $CDCl_3$, an apparently perfect A_2X_2 system, was observed for the CH_2CH_2 moiety as evidenced by the symmetrical 1:2:1 intensity distribution of the CH_2 multiplets with coupling constant J = 6 Hz. This implies that the two "A" protons are magnetically equivalent and, likewise, the two "X" protons. No observable difference exists in the free energy of the gauche and trans conformations.[25] This conclusion is supported by the fact that the spectrum of **1** did not change upon decreasing the temperature to −60 °C.

This boron analogue, like other tertiary amine–boranes, is thermally and hydrolytically stable (no hydrolysis of B–H bond in pure H_2O). Also, since amine–boranes do not normally reduce esters,[26] this possible decomposition mode has not presented any difficulties.

The foregoing synthetic route readily lends itself to the preparation of substituted acetylcholines and a number of these, together with **1**, have been prepared. Additional efforts are under way involving the synthesis of analogues with boron in other positions of substitution. An LD_{50} > 750 mg/kg (male mice) for **1** has been obtained indicating a relatively nontoxic compound.[27] Investigation in various biological activity studies is under way.

Acknowledgment. We thank the U.S. Army Research Office for financial support.

Registry No. 1, 100898-92-8; **2**, 51-84-3; **3**, 108-01-0; **4**, 17210-49-0; Et_4NBH_4, 17083-85-1.

(15) CH_3COCl, $Me_2NCH_2CH_2OH$, and $NaBH_4$ were obtained commercially from Aldrich Chemical Co. and used without further purification. Et_4NBH_4 was prepared from $NaBH_4$ and Et_4NOH by a standard method described previously: Gibson, D. H.; Ahmed, F. U.; Phillips, K. R. *J. Organomet. Chem.* **1981**, *218*, 325.

(16) Canepa, F. P.; Pauling, P.; Sorm, H. *Nature (London)* **1966**, *210*, 907.

(17) Chotia, C.; Pauling, P. *Nature (London)* **1968**, *219*, 1156.

(18) Herdklotz, J. K.; Sass, R. L. *Bichem. Biophys. Res. Commun.* **1970**, *40*, 583.

(19) Culvenor, C. C. J.; Ham, N. S. *Chem. Commun.* **1966**, 537.

(20) Cushley, R. J.; Mautner, H. G. *Tetrahedron* **1970**, *26*, 2151.

(21) Terui, Y.; Ueyama, M.; Satoh, S.; Tori, K. *Tetrahedron* **1974**, *30*, 1465.

(22) Lichtenberg, D.; Kroon, P. A.; Chan, S. I. *J. Am. Chem. Soc.* **1974**, *96*, 5934.

(23) Partington, P.; Feeney, J.; Burgen, A. S. V. *Mol. Pharmacol.* **1972**, *8*, 269.

(24) ^1H NMR spectrum of **1** was recorded at 60 MHz in $CDCl_3$ solution on a Varian EM 360 Spectrometer.

(25) The conformational behavior of metocloramide and its protonated analogues was investigated recently by NMR spectroscopy (Anker, L.; Lauterwein, J.; Van de Waterbeemd, H.; Testa, B. *Helv. Chim. Acta* **1984**, *67*, 706). For these compounds with their protonated aminoethyl side chain, the gauche and trans rotamers have observable identical energies in D_2O as well as in $CDCl_3$ solutions and an apparently perfect A_2X_2 system was observed for the CH_2CH_2 moiety (e.g., 1:2:1 symmetrical triplet for CH_2 resonance, J = 6 Hz). These studies are very similar to what we have observed for **1**.

(26) Lane, C. F. *Aldrichimica Acta* **1973**, *6*, 51. Also see the bulletin: "Amine-Boranes"; Callery Chemical Co.: Callery, PA, 1977.

(27) Private communication: Hall, I. H. Department of Medicinal Chemistry, University of North Carolina, Chapel Hill, NC 27514.

Synthesis and Structural-Magnetic Study of a New Type of High-Nuclearity Metal Carbonyl Cluster Possessing an 11-Atom Rh_5Ni_6 Core: Formation of a Heterometallic Core via Nickel Capping of a Pentarhodium Trigonal-Bipyramidal Kernel

Dick A. Nagaki,[1a,b] John V. Badding,[1c] Angelica M. Stacy,*[1c] and Lawrence F. Dahl*[1b]

Department of Chemistry
University of Wisconsin—Madison
Madison, Wisconsin 53706
Department of Chemistry, University of California
Berkeley, California 94720

Received January 15, 1986

In connection with our extensive exploratory studies[2] of the chemistry of the $[Ni_6(CO)_{12}]^{2-}$ dianion,[3] we report herein the preparation and characterization of the $[Rh_5Ni_6(CO)_{21}H_x]^{3-}$ trianion (**1**). This cluster, which represents the third example[4] of an 11-atom heterometallic species,[5] possesses a heretofore unknown close-packed 11-vertex D_{3h} polyhedron which has not been theoretically predicted[6] and which is geometrically and

(1) (a) Based in part on the Ph.D. thesis of D. A. Nagaki at the University of Wisconsin—Madison, 1986. (b) University of Wisconsin—Madison. (c) University of California—Berkeley.

(2) (a) Lower, L. D.; Dahl, L. F. *J. Am. Chem. Soc.* **1976**, *98*, 5046–5047. (b) Montag, R. A., Ph.D. Thesis 1980, University of Wisconsin—Madison. (c) Rieck, D. F.; Montag, R. A.; McKechnie, T. S.; Dahl, L. F. *J. Am. Chem. Soc.* **1986**, *108*, 1330–1331. (d) Nagaki, D. A.; Lower, L. M.; Ceriotti, A.; Longoni, G.; Chini, P.; Dahl, L. F. *Organometallics*, in press. (e) Nagaki, D. A.; Dahl, L. F.; unpublished results.

(3) Calabrese, J. C.; Dahl, L. F.; Cavalieri, A.; Chini, P.; Longoni, G.; Martinengo, S. *J. Am. Chem. Soc.* **1974**, *96*, 2616–2618.

(4) (a) $[PtRh_{10}(CO)_{21}N]^{3-}$ (C_{2v} $PtRh_{10}$ polyhedron): Martinengo, S.; Ciani, G. *J. Am. Chem. Soc.* **1982**, *104*, 328–330. (b) $[Pt_2Rh_9(CO)_{22}]^{3-}$ (D_{3h} Pt_2Rh_9 polyhedron): Fumagalli, A.; Martinengo, S.; Ciani, G. *J. Organomet. Chem.* **1984**, *273*, C46–C48.

(5) Reports of homonuclear species with 11-atom polyhedra include (a) $[Rh_{11}(CO)_{23}]^{3-}$ (D_{3h} Rh_{11} polyhedron) (Fumagalli, A.; Martinengo, S.; Ciani, G.; Sironi, A. *J. Chem. Soc., Chem. Commun* **1983**, 453–455), (b) $[Os_{11}(CO)_{27}C]^{2-}$ (C_{2v} Os_{11} polyhedron) (Braga, D.; Henrick, K.; Johnson, B. F. G.; Lewis, J.; McPartlin, M.; Nelson, W. J. H.; Sironi, A.; Vargas, M. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1131–1133), (c) $[Co_{11}(CO)_{22}C_2]^{3-}$ (C_s Co_{11} polyhedron) (Albano, V. G.; Braga, D.; Ciani, G.; Martinengo, S. *J. Organomet. Chem.* **1981**, *213*, 293–301), (d) $[B_{11}H_{11}]^{2-}$ (C_{2v} B_{11} polyhedron) (Klanberg, F.; Muetterties, E. L. *Inorg. Chem.* **1966**, *5*, 1955–1960), (e) P_{11}^{3-} (D_3 P_{11} polyhedron) (Wichelhaus, W.; von Schnering, H. G. *Naturwissenschaften* **1973**, *60*, 104), (f) As_{11}^{3-} (D_3 As_{11} polyhedron) (Belin, C. H. E. *J. Am. Chem. Soc.* **1980**, *102*, 6036–6040), and (g) (D_3)-trishomocubane (D_3 C_{11} polyhedron) (Godleski, S. A.; Schleyer, P. v. R.; Osawa, E.; Kent, G. J. *J. Chem. Soc., Chem. Commun.* **1974**, 976–977).

0002-7863/86/1508-3825$01.50/0 © 1986 American Chemical Society