Anal. Calcd for $C_{43}H_{62}BO_3P$ (IVa): C, 77.2; H, 9.4; B, 1.6; P, 4.6. Found: C, 77.2; H, 9.7; B, 1.9; P, 4.7.

Bis(2-*t*-butoxyethyl)methylphosphine (V).—To III (78.1 g, 0.33 mole) in ethyl ether (300 ml) was added 154 ml of a 21.3% solution of *n*-butyllithium in *n*-hexane (equivalent to 0.33 mole of C_4H_9Li) over a 30-min period. The temperature was maintained at 17–20° during the addition. Precipitation of a white solid occurred, but no condensate collected in the −80° cold trap. However, upon the dropwise addition of methyl iodide (47.3 g, 0.33 mole) in ether (100 ml) over 45 min with continued stirring for 3 hr, this solid dissolved with the evolution of *n*-butane (17.8 g, 92%). A bright yellow clear solution remained. After cooling to −40° to precipitate the lithium salts, oxygen-free water (200 ml) was added. The ether layer was separated and dried with K_2CO_3. Removal of solvent and distillation yielded V (72.4 g, 88%), bp 146–147° (22 mm), as a colorless oil.

Anal. Calcd for $C_{13}H_{29}O_2P$: C, 62.8; H, 11.8; P, 12.5. Found: C, 62.9; H, 11.8; P, 12.3.

The phosphine was characterized by conversion in methanol first to the methiodide (Va), mp 84–85° (acetone–cyclohexane), and then to the phosphonium tetraphenylborate salt (Vb), mp 185–187° (needles from methanol–benzene).

Anal. Calcd for $C_{14}H_{32}IO_2P$ (Va): C, 43.1; H, 8.3; I, 32.5; P, 7.9. Found: C, 43.1; H, 8.3; I, 32.4; P, 7.9.

Anal. Calcd for $C_{38}H_{52}BO_2P$ (Vb): C, 78.3; H, 9.0; B, 1.9; P, 5.3. Found: C, 78.2; H, 8.9; B, 1.9; P, 5.4.

Bis(2-hydroxyethyl)methylphosphine Hydrochloride (VI).—To the phosphine (V, 45.5 g, 0.18 mole) stirred at 0°, concentrated HCl (168 g, *ca.* 1.7 moles) was added dropwise during 20 min. An exothermic reaction occurred with the formation of a white emulsion. The mixture was stirred for 6.5 hr at 35° and in the cold trap (−80°) *t*-butyl chloride (32.3 g, 95%), bp 50.5°, was obtained. The residual, colorless aqueous phase was concentrated under reduced pressure at 60° to give a quantitative yield of the bis alcohol hydrochloride (VI, colorless syrup) which was characterized by direct conversion in methanol to bis(2-hydroxyethyl)methylphosphonium tetraphenylborate, mp 158–160°, prisms from methanol.

Anal. Calcd for $C_{29}H_{34}BO_2P$: C, 76.3; H, 7.5; B, 2.4; P, 6.8. Found: C, 76.5; H, 7.5; B, 2.4; P, 6.8.

Bis(2-chloroethyl)methylphosphine Hydrochloride (VII).—Compound VI (31.5 g, 0.18 mole) was suspended in dry $CHCl_3$ (300 ml) and cooled to −10° in an ice–acetone bath. Thionyl chloride (87.0 g, 0.73 mole) in $CHCl_3$ (200 ml) was added dropwise to the stirred mixture over 70 min at such a rate that the temperature did not rise above −5°. After the addition was complete, the mixture was stirred for 1 hr during which time it attained room temperature. A yellow insoluble paste separated from solution. Gentle heating at 40–43° for 3 hr caused solution of this paste (clear yellow solution) with the separation of a small amount of colloidal sulfur. Filtration and concentration of the filtrate at 20° (10 mm) gave the phosphine hydrochloride (VII) as a white solid (27.0 g, 71%). This was washed well with dry petroleum ether and dried *in vacuo* (0.05 mm) at room temperature.

Anal. Calcd for $C_5H_{12}Cl_3P$: Cl, 50.9. Found: Cl, 49.9, 52.7.

The hydrochloride salt (VII) is rapidly transformed to an oil at normal temperatures, but it can be kept for indefinite periods below 0° either under a dry nitrogen atmosphere or *in vacuo*. It was characterized by direct conversion with sodium tetraphenylboron in methanol to the corresponding phosphonium salt, mp 134–135°, colorless prisms from methanol.

Anal. Calcd for $C_{29}H_{32}BCl_2P$: C, 70.6; H, 6.5; B, 2.2; Cl, 14.4; P, 6.3. Found: C, 71.4, 69.3; H, 6.5; B, 2.1; Cl, 13.5; P, 5.9.

Results of analysis for carbon, chlorine, and phosphorus, on the above phosphonium salt, were subject to great variation, even on the same analytical sample. The chlorine content was consistently low, and the reason may be ascribed to the instability of the tetraphenylboron derivative. Repeated attempts at recrystallization gave only dark brown oily products.

Acknowledgments.—The authors wish to thank Dr. William H. Sweet, Chief of Neurosurgery, Massachusetts General Hospital, Dr. Thomas C. Hall, Chief of Clinical and Biochemical Pharmacology, Children's Cancer Research Foundation, and Dr. Vernon H. Mark, Chief of Neurosurgery, Boston City Hospital, for their interest and encouragement. The technical assistance of Miss Beverly Whitman and Mr. John Lyons is gratefully acknowledged.

Attempted Synthesis of 2,4-Dihydroxy-4,3-borazaropyridine. Preparation of Aminoalkylboronic Acids[1]

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Received October 21, 1965

Attempts directed toward the synthesis to 2,4-dihydroxy-4,3-borazaropyridine ("4-boranuracil"), a possible antimetabolite of uracil, for use in boron-10 neutron-capture irradiation of brain tumors are described. The preparation and properties of 2-aminoethyl- and 3-aminopropylboronic acids, intermediates in the synthesis, are reported.

As a continuation of the program designed to synthesize boron compounds which could be used for the treatment of cancer by neutron-capture irradiation,[3] the preparation of 2,4-dihydroxy-4,3-borazaropyridine (I) (4-borauracil) was undertaken. The biological rationale for preparing such potential antimetabolites is that a twofold attack on tumors may become feasible, (1) by direct inhibition of the neoplasm itself, and (2) by incorporation of the compound into the nucleic acids of the neoplasm as a consequence of tumor metabolism. A nuclear site for a thermal neutron absorber, such as a boron-10 atom, may permit effective disruption of tumor chromosomes by the radiation procedure.

The chemical basis for the synthesis of such a structure is the fact that two cyclic derivatives IIa[4] and IIb[5] containing this ring system have been described as well as the preparation now of a third one, IIc. Though a definitive proof of structure for IIa–c has as yet not

(1) This research was supported by grants from the John A. Hartfoud Foundation, Inc., The U. S. Atomic Energy Commission (AT(30-1)-3267), and the U. S. Public Health Service (CA-07368).

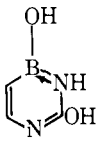
(2) Postdoctoral Fellow of the Harvard Medical School.

(3) A. H. Soloway in "Progress in Boron Chemistry," Vol. 1, A. L. McCloskey and H. Steinberg, Ed., Pergamon Press Inc., New York, N. Y., 1964, pp 203–234.

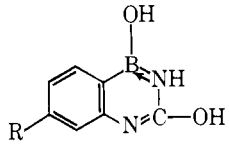
(4) A. H. Soloway, *J. Am. Chem. Soc.*, **82**, 2442 (1960).

(5) M. J. S. Dewar, Advances in Chemistry Series, No. 42, K. Niedenzu, Ed., American Chemical Society, Washington, D. C., 1964, p 241.

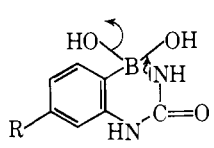
been obtained, the physical and chemical properties best agree with these formulations. As a possible mechanistic intermediate, III would account for the synthesis of these compounds by the reaction of the appropriately substituted 2-aminobenzeneboronic acid with cyanic acid. The high hydrolytic stability of these compounds (IIa–c) as shown by the fact that they were unaltered after recrystallization from water, prompted the attempts at synthesizing the parent heterocycle (I).



I



IIa, R = $B(OH)_2$
b, R = H
c, R = $COOC_2H_5$

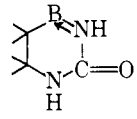


III

Initial attempts to synthesize the six-membered ring system of I involving the reaction of N-vinylurea[6] in diglyme with trimethylamineborane were unsuccessful though similar methods have been utilized[7] in the synthesis of boron–nitrogen heterocycles. The synthesis[8] of β-ureidoethylboronic acid presented a second possible route to the synthesis of 4-borauracil by cyclic dehydration to the dihydro compound V, followed by dehydrogenation to I.

$NH_2CONHCH_2CH_2B(OR)_2$

IVa, R = H
b, R = CH_3



V

Chemical Results and Discussion

Attempted cyclizations of IVa and IVb under a variety of conditions in solvents such as benzene, toluene, diethyleneglycol dimethyl ether (diglyme), dimethyl sulfoxide, and dimethylformamide failed to yield a uniform product and one which was hydrolytically stable. Likewise, reagents such as thionyl chloride, dimethyl sulfate, and phosphorus oxychloride were unsatisfactory. Dehydrogenation of crude intermediates by chemical reagents did not yield any product whose properties could be ascribed to I. With refluxing acetic anhydride IVa was converted to an N-acetylated product and by analogy with N-alkylureas[9] its structure is probably that of VI.

$CH_3CONHCONHCH_2CH_2B(OH)_2$
VI

In order to utilize the probable mechanism shown in III for the synthesis of I, the preparation of 2-aminoethylboronic acid (VII) was developed.[10] Synthesis of such compounds by the acid or base hydrolysis of ureido- or ethylcarbamatoalkylboronic acids, available from the hydroboration of N-olefin-substituted ureas[8] and carbamates,[10] proved to be unsatisfactory. The necessary hydrolytic conditions effected marked deboronation. Cleavage of benzyl carbamates, however, by hydrogen bromide led to the facile production in high yield of the corresponding aminoalkylboronic acid hydrobromides. Thus, 2-(benzyloxycarbamido)-ethylboronic acid and 3-(benzyloxycarbamido)propylboronic acid afforded the hydrobromides of 2-aminoethylboronic acid (VIIa) and 2-aminopropylboronic acid (VIIIa), respectively. Ion-exchange treatment of these compounds liberated the free aminoalkylboronic acids as crystalline dihydrates (VIIb, VIIIb). Acetylation of VIIb gave the N-acetamidoethylboronic acid. Compounds VIIb and VIIIb effloresced to give the anhydrous amino acids from which the dihydrates were readily regenerated by recrystallization from water.

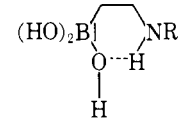
$(HO)_2BCH_2CH_2NH_2 \cdot X$
VIIa, X = HBr
b, X = $2H_2O$
c, X = CH_3COOH

$(HO)_2BCH_2CH_2CH_2NH_2 \cdot X$
VIIIa, X = HBr
b, X = $2H_2O$

These substances are extremely basic in aqueous systems indicating the possibility of an ammonium-type hydroxide. Thus a zwitterionic structure for the aminoalkylboronic acids such as IX would appear to be highly possible.

$(HO)_3\bar{B}(CH_2)_n\overset{+}{N}H_3 \cdot H_2O$
IX, n = 2 or 3

The pmr spectra of these compounds appear to support this contention. In water 2-aminoethylboronic acid (VIIb) showed second-order multiplicity of both the methylene absorptions, typical of the $A_2'X_2'$ pattern.[11] In contrast with the 1.1-ppm absorption for the triplet of the methylene protons adjacent to boron in β-ureidoethylboronic acid,[12] the methylene next to the boron atom of both VIIb and VIIIb suffered considerable quadrapole broadening and absorbed in the vicinity of 0.6 ppm. These observations can be explained by the boron atom in these aminoalkylboronic acids being tetrahedral, as in structure IX with a nonequivalence of the methylene protons. As an added basis for considering the boron atom in such compounds as being tetrahedral is the fact that the typical 1,2-disubstituted ethane pmr spectra for IVa, β-carbethoxyamidoethylboronic acid and β-benzyloxycarbamidoethylboronic acid, are changed by the addition of sodium deuterioxide to ones resembling that of VIIb and VIIIb (Figure 1). In each case the absorptions of the methylene group adjacent to the boron atom moves to a higher field (about 1.1–0.6 ppm) and suffers quadrapole broadening. This again is typical of the $A_2'X_2'$ case and indicates the nonequivalence of these methylene protons. These results could be explained by the existence of a cyclic structure such as X in which conformational stability is conferred



X, R = H, $CONH_2$, $COOC_2H_5$, $COOCH_2C_6H_5$

(6) R. Hart, *Bull. Soc. Chim. Belges*, **66**, 229 (1957).
(7) (a) D. G. White, *J. Am. Chem. Soc.*, **85**, 3634 (1963); (b) M. N. Greenwood, J. H. Morris, and J. C. Wright, *J. Chem. Soc.*, 4753 (1964); (c) M. J. S. Dewar, G. J. Gleicher, and B. P. Robinson, *J. Am. Chem. Soc.*, **86**, 5699 (1964).
(8) D. N. Butler and A. H. Soloway, *ibid.*, **86**, 2961 (1964).
(9) E. Rodd, "Chemistry of Carbon Compounds," Vol. Ib, Elsevier Publishing Co., New York, N. Y., 1952, p 913.
(10) D. N. Butler and A. H. Soloway, *Chem. Commun.*, **15**, 333 (1965).
(11) R. H. Bible, "Interpretation of NMR Spectra," Plenum Press, New York, N. Y., 1965, pp 77–104.
(12) D. N. Butler and A. H. Soloway, *J. Am. Chem. Soc.*, **88**, 484 (1966).

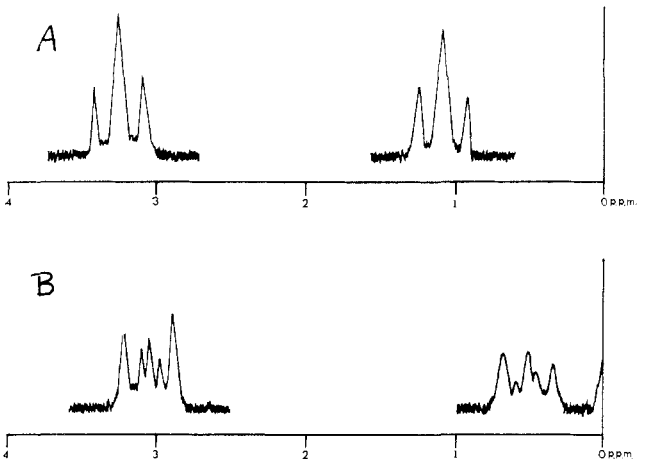


Figure 1.—A: Pmr spectrum of 2-ureidoethylboronic acid in D_2O. B: Pmr spectrum of 2-aminoethylboronic acid or alkaline 2-ureidoethylboronic acid in D_2O.

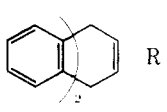
by hydrogen bonding. However, there is not direct evidence for such a structure.

Synthesis and structure proof of VII permitted the utilization of the mechanism shown by III for the attempted synthesis of I. Reaction of VIIb, however, with potassium cyanate in aqueous acetic acid solution yielded only the acetate salt VIIc, as a result of the high basicity of the amino function in this molecule. Reaction of the hydrobromide VIIa with silver cyanate afforded in nearly quantitative yield β-ureidoethylboronic acid, isolated as its iminodiethanol derivative.

These failures to synthesize a dihydro compound of I in contrast with the high stability of II indicate that the chemical stability of these latter compounds is due primarily to resonance stabilization rather than the presence of a cyclic structure. On this basis it would appear highly unlikely that the dihydro compound of I would be hydrolytically stable in cyclic form but more likely that it would readily hydrolyze to IVa. Consequently subsequent efforts have been directed toward the synthesis of 2-ureidovinylboronic acid (XI) which in its *cis* form would most probably exist as I. Attempts to hydroborate *trans*-2-chlorovinylurea[12] to generate a boronic acid, which after dehydrohalogenation would yield 2-ureidovinylboronic acid, failed. The preparation of the bridged vinylurea (XIIc), preliminary to hydroboration and a reverse Diels-Alder reaction to produce XI, was unsuccessful as well. However, further attempts to produce XI are

$NH_2CONHCH{=}CHB(OH)_2$

XI



XIIa, R = COCl
b, R = N=C=O
c, R = $NHCONH_2$

underway since this compound would appear to be a feasible way to synthesize the desired boron analog (I) of uracil.

Biological Results.—The need for compounds which will leave the vascular supply and become incorporated into tumor has become essential if neutron-capture therapy is to be utilized in man. For this purpose multiple injections of a compound have been followed by the animal's sacrifice several days following the last injection.[13]

With the hydrobromides of both 2-aminoethylboronic acid and 3-aminopropylboronic acid and the dihydrate of the former compound itself, doses as high as 140 μg of boron/g were well tolerated in C3H mice. However, there was no selective binding of these compounds to tumor in contrast with blood, brain, and muscle by the method used for their evaluation.[13] Consequently, such compounds would not appear to be of value as potential agents for use in neutron-capture irradiation.

Experimental Section[14]

2-Nitro-4-carbethoxybenzeneboronic Acid.—To 14.0 g of 2-nitro-4-carboxybenzeneboronic acid[15] was added 60 ml of absolute ethanol containing 8 g of dry HCl. The solution was refluxed for 6 hr and then poured into 500 ml of an ice-water mixture. The filtered yellow product was washed with water and dried to yield 14.0 g, mp 70–79°. Recrystallization from ethanol-water gave long yellow needles, mp 78–83°.

Anal. Calcd for $C_9H_{10}BNO_6 \cdot H_2O$: C, 42.06; H, 4.71; B, 4.21; N, 5.45. Found: C, 42.32; H, 4.88; B, 4.27; N, 5.67.

Deboronation of the compound by ammoniacal silver nitrate yielded ethyl *m*-nitrobenzoate.

7-Carbethoxy-4-hydroxy-4,3-borazaro-2-quinolone (IIc).—To a solution of 2 g of 2-nitro-4-carbethoxybenzeneboronic acid in 25 ml of 95% ethanol was added 34 mg of PtO_2. The solution was reduced in a Parr shaker until the uptake of hydrogen was complete. During the course of the reduction, a solid precipitated out of the solution. To this mixture of Pt and amine was added 25 ml of glacial acetic acid. Upon solution of the amine the mixture was filtered to remove the metal, and an aqueous solution of 2 g of KCNO in 10 ml of water was added. A precipitate began to form immediately, and upon completion of the reaction, the mixture was cooled, filtered, washed with water, and dried. The product (1.0 g) was recrystallized from ethanol-water; mp >350°.

Anal. Calcd for $C_{10}H_{11}BN_2O_4$: C, 51.32; H, 4.74; B, 4.62; N, 11.97. Found: C, 51.48; H, 4.73; B, 4.70; N, 11.97.

N-Acetyl-8-ureidoethylboronic Acid (VI).—A suspension of 2.0 g of β-ureidoethylboronic acid in 50 ml of acetic anhydride was refluxed overnight. The clear dark brown solution was concentrated under reduced pressure to a small volume. Water was added and the concentration procedure was repeated until no acetic anhydride remained. From this small volume the product crystallized on cooling. The precipitate was filtered, washed with 2 ml of an acetone–ethyl ether mixture, and dried. The crude solid (757 mg) was recrystallized successively from acetone–ether to give a crystalline solid, mp 227–228°.

Anal. Calcd for $C_5H_{11}BN_2O_4$: C, 34.52; H, 6.32; B, 6.22; N, 16.10. Found: C, 34.01; H, 6.40; B, 6.38; N, 15.90.

The iminodiethanol derivative, recrystallized from DMF, had mp 234–235°.

Anal. Calcd for $C_9H_{18}BN_3O_4$: C, 44.46; H, 7.46; B, 4.45; N, 17.28. Found: C, 44.14; H, 7.65; B, 4.47; N, 16.74.

Aminoalkylboronic Acids.—The alkylboronic acids, 2-(benzyloxycarbamido)ethylboronic acid or 3-(benzyloxycarbamido)propylboronic acid (10 g), were suspended in 100 ml of glacial acetic acid to which was added 30 ml of 30% HBr in acetic acid. A yellow solution formed and the mixture was allowed to remain overnight at room temperature. The solution was poured with stirring into 1 l. of anhydrous ethyl ether, and the off-white precipitate of the hydrobromide was washed twice with anhydrous ether, filtered, and recrystallized from glacial acetic acid. In

(13) D. S. Matteson, A. H. Soloway, D. W. Tomlinson, J. D. Campbell, and G. A. Nixon, *J. Med. Chem.*, **7**, 640 (1964).

(14) Analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. All melting points and boiling points are listed as they were observed. Nmr results were obtained using an analytical A-60 Varian spectrometer.

(15) A. H. Soloway, *J. Am. Chem. Soc.*, **81**, 3017 (1959).

this manner both **2-aminoethylboronic acid hydrobromide (VIIa)** (6.2 g, 82%), mp 106–108°, and **3-aminopropylboronic acid hydrobromide (VIIIa)** (6.5 g, 83%), mp 98–103°, were prepared.

Anal. Calcd for $C_2H_9BBrNO_2$ (VIIa): C, 14.15; H, 5.34; B, 6.49; Br, 47.04; N, 8.25. Found: C, 14.66; H, 5.60; B, 6.49; Br, 46.00; N, 8.07.

The iminodiethanol derivative of this compound had mp 168–170°.

Anal. Calcd for $C_6H_{16}BBrN_2O_2$: C, 30.16; H, 6.75; B, 4.53; Br, 33.44; N, 11.73. Found: C, 30.05; H, 6.84; B, 4.78; Br, 33.21; N, 11.76.

Anal. Calcd for $C_3H_{11}BBrNO_2$ (VIIIa): C, 19.60; H, 6.03; B, 6.02; Br, 43.46; N, 7.62. Found: C, 19.71; H, 6.18; B, 6.09; Br, 43.49; N, 7.89.

The iminodiethanol compound obtained from VIIIa had mp 172–173°.

Anal. Calcd for $C_7H_{18}BBrN_2O_2$: C, 33.24; H, 7.17; B, 4.28; Br, 31.59; N, 11.08. Found: C, 33.19; H, 7.48; B, 4.55; Br, 31.83; N, 11.29.

The hydrobromide, VIIa or VIIIa (1 g), was dissolved in 4 ml of water and the solution was allowed to percolate slowly through a column (1 × 12 cm) of Amberlite IRA 400 ion-exchange resin (OH^- form). The column was then washed with 300 ml of water until the chromatographic effluent was neutral. The total alkaline eluate was combined and evaporated under reduced pressure to dryness. Recrystallization of the residue (0.7 g) from water gave the **aminoethylboronic acid dihydrate** VIIb or VIIIb.

2-Aminoethylboronic acid dihydrate (VIIb) had no definitive melting point but decomposed in the range of 160°.

Anal. Calcd for $C_2H_{12}BNO_4$: C, 19.23; H, 9.68; B, 8.66; N, 11.21. Found: C, 19.22; H, 9.70; B, 8.66; N, 11.11.

3-Aminopropylboronic acid dihydrate (VIIIb) dehydrated near 100° with the formation of a microcrystalline product, mp 148–149°.

Anal. Calcd for $C_3H_{14}BNO_4$ (the dihydrate): C, 25.92; H, 10.15; B, 7.78; N, 10.08. Found: C, 25.98; H, 10.44; B, 7.52; N, 9.83.

Drying VIIIb at 100° (0.1 mm) for several hours gave 3-aminopropylboronic acid, mp 148–149°.

Anal. Calcd for $C_3H_{10}BNO_2$: C, 35.01; H, 9.79; B, 10.50; N, 13.61. Found: C, 35.11; H, 9.52; B, 10.62; N, 13.27.

Reaction of VIIb in a 1:1 refluxing mixture of acetic acid–acetic anhydride (1 hr) furnished, after evaporation and successive recrystallization from water, **2-N-acetylaminoethylboronic acid**, mp 90–95°.

Anal. Calcd for $C_4H_{10}BNO_3$: C, 36.69; H, 7.70; B, 8.26; N, 10.70. Found: C, 36.82; H, 7.98; B, 8.38; N, 10.61.

An iminodiethanol derivative of this compound was prepared and recrystallized from DMF; mp 218–220°.

Anal. Calcd for $C_8H_{17}BN_2O_3$: C, 48.05; H, 8.57; B, 5.41; N, 14.01. Found: C, 48.44; H, 8.72; B, 5.61; N, 14.23.

To a solution of 2.5 g of VIIb in 6.5 ml of 40% acetic acid was added in small portions a solution of 1.25 g of KCNO in 3 ml of water. After standing for 30 min, the mixture was evaporated under reduced pressure to dryness and the residue was recrystallized from a small volume of water to yield 2.2 g of **2-aminoethylboronic acid acetate (VIIc)** (instead of the expected dihydro derivative of 4-borauracil), mp 126–127°.

Anal. Calcd for $C_4H_{12}BNO_4$: C, 32.25; H, 8.12; B, 7.26; N, 9.40. Found: C, 32.36; H, 8.30; B, 7.40; N, 9.80.

A further attempt at synthesizing the dihydro derivative of 4-borauracil was carried out by treating a magnetically stirred suspension of 7.0 g of AgCNO and 5.0 g of VIIa in 25 ml of anhydrous DMF. After stirring for 15 min, the mixture remained at room temperature overnight prior to the removal of AgBr by filtration. The filtrate was concentrated under pressure to an oil. The residue was diluted with 50 ml of DMF and to this was added 3.1 g of iminodiethanol. An immediate precipitate of the iminodiethanol derivative of β-ureidoethylboronic acid formed in quantitative yield, mp 237–238°, as determined by its infrared spectra.

Dibenzo[2.2.2]bicyclooctatriene-2-carbonyl Chloride (XIIa).—A mixture of 27 g of dibenzo[2.2.2]bicyclooctatriene-2-carboxylic acid,[16] 40 ml of $SOCl_2$, and 120 ml of benzene was refluxed for 4 hr and then evaporated to dryness under reduced pressure. The residue was dissolved in 60 ml of benzene, filtered, and diluted with an excess of petroleum ether (bp 30–60°) to yield 17 g of the crystalline acid chloride (XIIa), mp 196–198°.

Anal. Calcd for $C_{17}H_{11}ClO$: C, 76.54; H, 4.16; Cl, 13.29. Found: C, 76.89; H, 4.07; Cl, 13.60.

The acid chloride XIIa (17 g) was dissolved in 300 ml of toluene and added dropwise to a vigorously stirred solution of 12.6 g of sodium azide in water (100 ml) maintained at 0°. This mixture was stirred vigorously for 3.5 hr at this same temperature. The toluene layer was separated and washed successively with two 50-ml portions of ice-cold 10% $NaHCO_3$ and two 100-ml portions of water. The toluene phase was then dried ($CaCl_2$) in the refrigerator.

Without prior isolation, this acyl azide solution was added dropwise into 30 ml of refluxing toluene containing 1 g of *m*-dinitrobenzene as a polymerization inhibitor. The rate of addition was such as to maintain a steady evolution of nitrogen. Upon completion of the reaction, the mixture was cooled and filtered. A strong band in the infrared spectra at 2150 cm^{-1} of the toluene solution of the product (XIIb) was indicative of the presence of the isocyanate function, but in view of the ready polymerization of such vinyl isocyanates the compound was not isolated as such. This solution was added to an ether–liquid NH_3 mixture at −40° in the same manner that had resulted in the preparation vinylureas. In contrast with these the reaction of dibenzo[2.2.2]bicyclooctatriene 2-isocyanate with NH_3 resulted in the loss of the vinylic proton absorption at 6.4 ppm in the pmr spectra. This is certainly indicative of an abnormal addition reaction of ammonia involving the carbon–carbon double bond conjugated with the isocyanate moiety.

Acknowledgments.—The authors wish to thank Dr. William H. Sweet, Chief, Neurosurgical Service, Massachusetts General Hospital, for his interest, encouragement, and support; Mr. J. E. Lyons for his technical assistance; and Professor W. N. Lipscomb of Harvard University for helpful discussions.

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