and the two very predominant alcohol products are produced completely stereospecifically as the *cis* epimers. The "trishomocyclopropenyl" cation VIII provides an explanation for the reactivity and the observed stereochemistry.

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CONTRIBUTION NO. 1647   S. WINSTEIN
DEPARTMENT OF CHEMISTRY   P. BRUCK
UNIVERSITY OF CALIFORNIA   PHILLIP RADLICK[9]
LOS ANGELES 24, CALIFORNIA   R. BAKER

Boron-Substituted Pyrimidines[1]

Sir:

It has been reported that when boron is localized within cancerous tissue in the form of some suitable derivatives,[2] the tumor cells are destroyed by the dissipation of α-particles resulting from the neutron-induced disintegration of B^{10} (naturally occurring boron contains 18.84% of B^{10} isotope). Many investigators have since synthesized a number of boron-containing organic compounds including azo dyes,[3] diboronic acids,[4] bromine-, sulfur-, or nitrogen-substituted aromatic boronic acids,[5] amino acids,[6] boronic anhydrides,[7] as well as many heterocyclic boron compounds.[8] Some of these compounds have already been evaluated in animals[9b,d] and in human patients,[9a,c,e] and a few have shown to be promising.[9b,c] As the future success of neutron-capture therapy may well depend on the design of boron-substituted antimetabolites (which can be preferentially bound or incorporated into the structures of growing neoplasms),[10] a program involving the

synthesis of boron-substituted nitrogen heterocyclic compounds has been initiated in our laboratories. We now wish to report the synthesis of some boron-substituted pyrimidines. Compounds of this type have not been prepared previously.[11]

Treatment of 5-bromo-2,4-dihydroxypyrimidine[12] with phosphorus oxychloride and N,N'-dimethylaniline gave 5-bromo-2,4-dichloropyrimidine (I),[12] b.p. 75–80° (0.4 mm.), in 91% yield. Sodium methoxide readily converted I to 5-bromo-2,4-dimethoxypyrimidine (IIa),[12] m.p. 63–64°. The lithium compound IIIa, prepared by Langley's method,[13] was caused to react *in situ* with freshly distilled trimethyl borate or tributyl borate to give 2,4-dimethoxy-5-pyrimidineboronic acid (IVa), m.p. 115–117°. *Anal.* Calcd. for $C_6H_9BN_2O_4 \cdot 0.5H_2O$: C, 37.3; H, 5.18; N, 14.5. Found: C, 37.1; H, 5.23; N, 14.5. An infrared spectrum of IVa had bands at 1350 and 1250 cm.$^{-1}$, which were assigned to the B–O and B–C stretching frequencies, respectively. The B–O deformation mode was located near 810 cm.$^{-1}$ and the boron–aryl sharp absorption band was also noted at 1435 cm.$^{-1}$.[14]
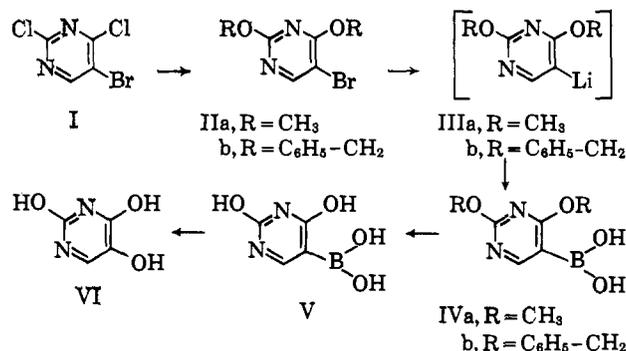
2,4-Dibenzyloxy-5-pyrimidineboronic acid (IVb) was similarly prepared from I *via* 2,4-dibenzyloxy-5-bromopyrimidine (IIb; 59% yield, m.p. 87–89°. *Anal.* Calcd. for $C_{18}H_{15}BrN_2O_2$: C, 58.2; H, 4.04; N, 7.55. Found: C, 58.2; H, 4.00; N, 7.50) and the lithium derivative IIIb. Since IVb was difficult to purify, it was converted directly to 5-uracilboronic acid (V) by catalytic hydrogenation. Compound V was isolated as a hemihydrate. *Anal.* Calcd. for $C_4H_5BN_2O_4 \cdot 0.5H_2O$: C, 29.1; H, 3.64; N, 17.0. Found: C, 29.3; H, 3.54; N, 17.4. Ultraviolet properties of V showed maxima at 262 mμ (ϵ 10,600, pH 1) and at 284 mμ (ϵ 5600, pH 11). The product decomposed slowly around 330°. The structure of 5-uracilboronic acid (V) was further confirmed by oxidation to 5-hydroxyuracil (VI) according to the procedure of Letsinger and Dandegaonker for the conversion of 8-quinolineboronic acid to 8-hydroxyquinoline.[15] Compound VI was identical with

(1) This investigation was supported by the Cancer Chemotherapy National Service Center, National Cancer Institute of the National Institutes of Health, Public Health Service (Contract SA-43-ph-3025).

(2) For "neutron-capture" theory, see, *e.g.*: (a) P. G. Kruger, *Proc. Natl. Acad. Sci.*, **26**, 181 (1940); (b) P. A. Zahl and F. S. Cooper, *Science*, **93**, 64 (1941); (c) P. A. Zahl and F. S. Cooper, *Radiology*, **37**, 673 (1941); (d) W. H. Sweet and M. Javid, *J. Neurosurg.*, **9**, 200 (1952); (e) P. G. Kruger, *Radiation Res.*, **3**, 1 (1955); (f) W. Gerrard, "The Organic Chemistry of Boron," Academic Press, New York, N. Y., 1961, pp. 76–201; (g) G. Milhaud, *Maroc Med.*, **41**, 295 (1962).

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(4) (a) H. R. Snyder and S. L. Meisel, *ibid.*, **70**, 774 (1948); (b) D. R. Nielsen and W. E. McEwen, *ibid.*, **79**, 3081 (1957); (c) A. H. Soloway, *ibid.*, **82**, 2442 (1960).

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(15) R. L. Letsinger and S. H. Dandegaonker, *J. Am. Chem. Soc.*, **81**, 498 (1959).

that reported by Albert and Phillips[16] and Wang,[17] indicating that the boron atom was originally substituted at the 5-position of the pyrimidine ring system.

(16) A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956).
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MIDWEST RESEARCH INSTITUTE   T. K. LIAO
KANSAS CITY, MISSOURI 64110   EUGENE G. PODREBARAC
                                                    C. C. CHENG

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C^{13} and H^1 Nuclear Magnetic Resonance Spectra of Cycloalkanes

Sir:

We have measured C^{13} and H^1 n.m.r. spectra of the cycloalkanes from cyclopropane to cycloheptadecane, as well as those of several n-alkanes from hexadecane to dotriacontane. The results are presented in Table I along with data on some of the same compounds reported elsewhere. The C^{13} spectra were measured as previously reported.[1] Solid samples were dissolved
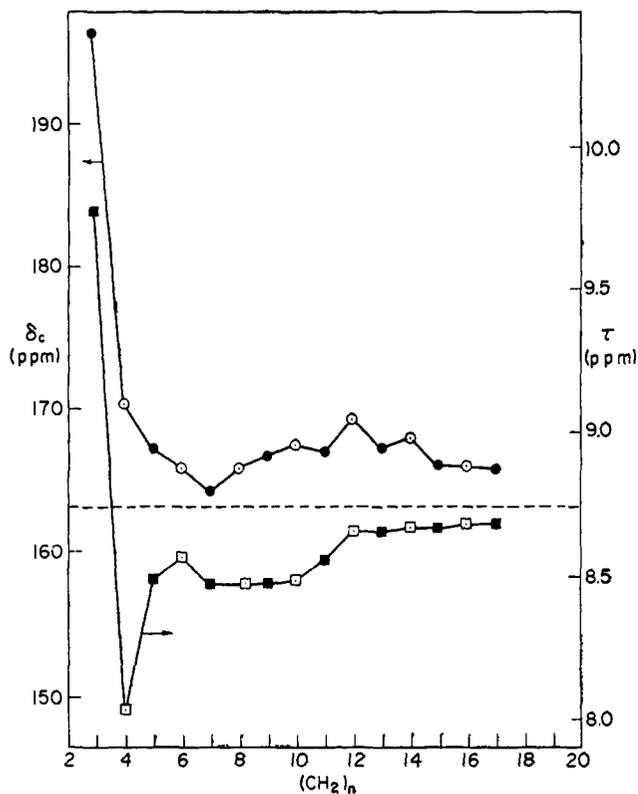

Fig. 1.—Nuclear magnetic shieldings in cycloalkanes: carbon (O,●); hydrogen (□,■); central CH_2 groups in long-chain n-alkanes for both carbon and hydrogen (– – – –).

in CS_2 and their shieldings corrected to neat liquid values. All measurements were referred to external CS_2. The H^1 spectra were obtained with a Varian A-60 spectrometer and referred to internal tetramethylsilane.[2] Corrections to infinite dilution were made for the cycloalkanes and n-alkanes in carbon tetrachloride.

The hydrogen and carbon shieldings are plotted against ring size in Fig. 1. The latter values display

(1) P. C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 1838 (1961).
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TABLE I

Alkane	δ_c,[e] p.p.m.	J_{C-H}, c.p.s. This work	J_{C-H}, c.p.s. Other work[a]	τ, p.p.m. This work[g]	τ, p.p.m. Other work
C_3H_6	196.3	162 ± 2	161		$9.778,^b 9.78^c$
C_4H_8	170.4	136 ± 1	134		$8.02,^d 8.04^c$
C_5H_{10}	167.2	131 ± 2	128	8.494^h	$8.492,^b 8.49^d$ 8.49^c
C_6H_{12}	165.9	127 ± 2	124	8.566	$8.564,^b 8.56^c$
C_7H_{14}	164.3	126 ± 2	123	8.474	$8.470,^b 8.46^c$
C_8H_{16}	165.9	127 ± 2	122	8.470	8.46^c
C_9H_{18}	166.7	125 ± 2		8.473	
$C_{10}H_{20}$	167.5	126 ± 2	118	8.486	
$C_{11}H_{22}$	167.1	126 ± 2		8.555	
$C_{12}H_{24}$	169.3^f	123 ± 3	123	8.658	
$C_{13}H_{26}$	167.3^f	127 ± 2		8.652	
$C_{14}H_{28}$	167.9^f	126 ± 2		8.670	
$C_{15}H_{30}$	166.1^f	126 ± 2		8.666	
$C_{16}H_{32}$	166.0^f	126 ± 3		8.681	
$C_{17}H_{34}$	165.8^f	126 ± 2		8.684	
n-$C_{16}H_{34}$	163.1			8.743	
n-$C_{20}H_{42}$	163.7^f	128 ± 3		8.745	
n-$C_{22}H_{46}$	163.3^f	127 ± 2		8.744	
n-$C_{28}H_{58}$	163.9^f	128 ± 2		8.745	
n-$C_{32}H_{66}$	163.0^f	124 ± 4		8.747	

^{a} Ref. 10. ^{b} Tables of τ values for a variety of organic compounds, G. V. D. Tiers, Minnesota Mining and Mfg. Co., 1958. ^{c} K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, **83**, 1226 (1961). ^{d} E. Lippert and H. Prigge, *Ber. Bunsenges. Physik. Chem.*, **67**, 415 (1963). ^{e} Standard deviation ± 0.3 p.p.m. for cyclics; standard deviation ± 0.5 p.p.m. for n-alkanes. ^{f} Measured in CS_2 and corrected as described in text. ^{g} Standard deviation ± 0.001 p.p.m. for cyclics; standard deviation ± 0.002 p.p.m. for n-alkanes; all measurements made in carbon tetrachloride and corrected as described in text. ^{h} Standard deviation ± 0.003 p.p.m.

an oscillatory behavior for medium rings, but smooth curves can be drawn through the points for odd- and even-membered rings separately. This oscillatory phenomenon, which is also observed for other properties such as heats of combustion[3a] and refractions,[3b] suggests that the ease with which conformational changes occur is reflected in the carbon shieldings. There appears to be no corresponding effect on the hydrogen shieldings, which parallel those of carbon only in the extremely high shieldings observed in cyclopropane. In an attempt to account for the cyclopropane spectra, we have turned to the ring-current model previously used to explain hydrogen shieldings in molecules containing three-membered rings.[4,5] The hydrogen and carbon shieldings, relative to those in central methylene groups in long-chain n-alkanes, are 1.0 and 33 p.p.m., respectively. As the assumed current radius is increased from 0.88 Å.,[4,5] the calculated carbon shielding[6] decreases and that for the protons increases until their *ratio* becomes 33 for a radius of 1.10 Å. The *values* of the shieldings are reproduced by assuming that a current corresponding to 3.5 electrons flows in the 1.10-Å. ring. The equivalent dipole of this current is about 20% larger than that of the 4.5-electron, 0.88-Å., current assumed by Winstein, Boikess, and Brauman[5]; the difference would not markedly affect their correlations for distant protons. The magnetic susceptibility of cyclopropane can be similarly calculated by assuming

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(4) D. J. Patel, M. E. H. Howden, and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 3218 (1963).
(5) S. Winstein, R. S. Boikess, and J. I. Brauman, private communication.
(6) The calculations were performed by J. I. Brauman.