methylthiocarbamyl peptide was activated and coupled to the resin as described above. After the first trifluoroacetic acid treatment (which removed the N-terminal amino acid), the residual peptide had the analysis: $Phe_{0.98}Val_{0.93}Ala_{0.99}Pro_{0.93}Leu_{1.00}Gly_{0.99}$.

The data in Figure 2 show that it is possible to determine the sequence of 0.5 μmole (or less) of a simple heptapeptide in a relatively short time (in fact, the rate-determining factor in this case was amino acid analysis of the residual peptides), even though the amino acids were not liberated quantitatively at each stage. The reason for these nonquantitative results may be that the carboxyl end of the peptide has become buried in the resin, and that reaction is inhibited because of steric hindrance. However, it should be possible to obtain more unambiguous results by analysis of the thiazolinones, since the nonreactive peptides will not release large amounts of contaminating thiazolinones.

The reaction conditions described here are not optimal, and it is clear that more work is required to find the proper reaction times, solvents, polymer characteristics, etc. Furthermore, the peptide model used in these experiments contains only amino acids with nonfunctional side chains, so other models will have to be examined. The problem of blocking the carboxyl groups of peptides containing glutamic and aspartic acids can probably be overcome in many cases by total esterification followed by deesterification, specifically, of the C-terminal carboxyl with a proteolytic enzyme (*e.g.*, in the case of peptides obtained by digestion of a protein with trypsin or chymotrypsin) prior to attachment of the peptide to the resin. These problems are under investigation.

In recent years Edman has developed an automated version[7] of the phenyl isothiocyanate degradation in which it has been possible to remove as many as 60 amino acids[8] from the N terminus of a protein. Thiazolinones are separated from the protein by an elegant extraction procedure. However, as with the more classical extraction procedures, problems of solubility cause the method to be less satisfactory with small peptides.[8] It is hoped that the solid-state modification will help to compensate for this deficiency. Alternatively, it should be possible to use the chemistry discussed here to attach a lipophobic "tail" which will prevent the peptide from being extracted into organic solvents, and in this way make the analysis of small peptides amenable to the automated procedure of Edman.

Acknowledgment. The initial stages of this investigation were supported by a grant (GM-04714) from the National Institutes of Health to F. H. Westheimer. I wish to express my gratitude to Professor Westheimer for his encouragement and support of this project.

(7) P. Edman, *Thromb. Diath. Haemorrhag., Suppl.*, 13 (1963).
(8) P. Edman, personal communication.
(9) Address to which requests for reprints should be sent.

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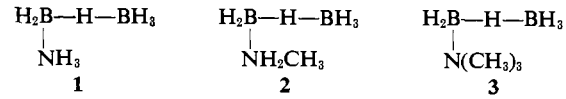
Structural Evidence for Singly Hydrogen-Bridged Boranes. Their Relationship to Symmetrical and Unsymmetrical Cleavage Reactions of Diborane

Sir:

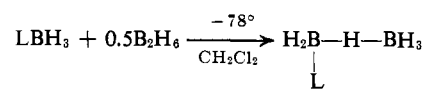
The existence of the singly hydrogen-bridged borane (**1**) as an intermediate in the reaction of diborane with ammonia has been suggested by chemical[1] and cryoscopic[2] evidence. Using procedures similar to those of Brown, Stehle, and Tierney,[3] who report a series of compounds which are believed to be singly bridged structures, we have prepared **1–3** and have obtained



1 **2** **3**

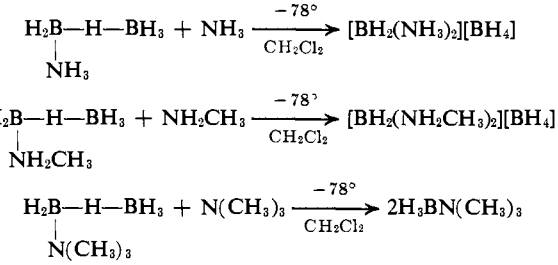
boron-11 nmr spectra which support the proposed structural formulations.

Singly hydrogen-bridged species were formed by adding diborane to appropriate amine boranes by means of tensiometric titrations at −78° in methylene chloride



where L = amine. In each case the break in the titration curve corresponded to the molar ratio of 1 amine borane/0.5 B_2H_6, and the boron-11 nmr spectrum established the presence of a BH_2 and BH_3 unit.

Addition of 1 mole of amine per mole of singly hydrogen-bridged species gave the products cited in the equations below. X-Ray powder diffraction data confirmed the formation of $[BH_2(NH_3)_2][BH_4]$ and $H_3BN(CH_3)_3$, while $[H_2B(NH_2CH_3)_2][BH_4]$ was identified by its boron-11 nmr spectrum.[4] The products formed in these reactions are the same products formed when diborane reacts with an excess quantity of

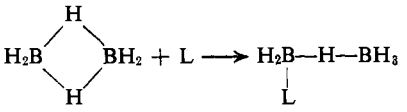


amine.[4-6] Thus, so-called "unsymmetrical cleavage"[5] products are obtained in the first two reactions while a "symmetrical cleavage" product is observed in the latter case.

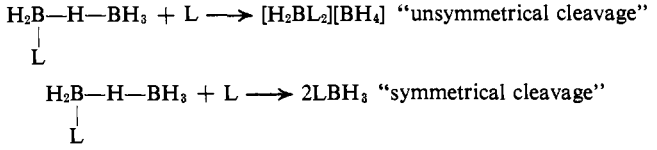
In view of the results presented above, plus the fact that there exists evidence for analogous intermediates in related systems,[5,7-10] it is not unreasonable to sup-

(1) R. W. Parry and S. G. Shore, *J. Am. Chem. Soc.*, **80**, 15 (1958).
(2) B. Z. Egan and S. G. Shore, *ibid.*, **83**, 4717 (1961).
(3) H. C. Brown, P. F. Stehle, and P. A. Tierney, *ibid.*, **79**, 2020 (1957).
(4) S. G. Shore, C. W. Hickam, Jr., and D. Cowles, *ibid.*, **87**, 2755 (1965).
(5) R. W. Parry, in collaboration with D. R. Schultz, S. G. Shore, and P. R. Girardot, *J. Am. Chem. Soc.*, **80**, 4, 8, 15, 20 (1958).
(6) O. T. Beachley, Jr., *Inorg. Chem.*, **4**, 1823 (1965).
(7) A. B. Burg and G. W. Campbell, *J. Am. Chem. Soc.*, **74**, 3744 (1952).
(8) S. H. Bauer, J. V. Martinez, D. Price, and W. D. Jones, Advances in Chemistry Series, No. 42, American Chemical Society, Washington, D. C., 1964, p 35.

pose that diborane reacts with a ligand in a stepwise fashion, the first step involving the displacement of one hydrogen from the bridge position.



The second step, involving displacement of hydrogen from the remaining bridge, would determine the type of product produced.



Such a scheme is consistent with the observation that with increasing steric bulk of methyl-substituted amine the yield of symmetrical cleavage product increases.[4]

It has been suggested that reactions of diborane with Lewis bases at low temperature can involve unsymmetrical cleavage, but that the product can readily rearrange to a symmetrical cleavage product, depending upon which form is more stable, thermodynamically, at a particular temperature.[6] There is no evidence for facile rearrangements in amine diborane systems. Thus, H_3NBH_3 and $[H_2B(NH_3)_2][BH_4]$ show no tendency toward interconversion in liquid ammonia.[5]

Boron-11 nmr spectra of singly hydrogen-bridged boranes are markedly temperature dependent. At about $-25°$ each spectrum consists of a broad singlet, suggesting rapid proton exchange. As the temperature is lowered, fine structure in the spectrum becomes evident, until at about $-60°$ seven lines can be observed. The BH_3 group produces a quartet which overlaps a triplet produced by the BH_2 group. In each spectrum the B–H coupling constant for the quartet appears to be significantly smaller than that for the triplet.[11] Figure 1 shows a typical low-temperature spectrum. Table I reports chemical shifts and coupling constants

Table I. Boron-11 Nmr Data at $-65°$

	δ, ± 0.5 ppm[a]	$J(BH_3)$, ± 3 cps[b]
$H_2B(NH_3)H_2BH_3$	−17.7	84
$H_2B(NH_2CH_3)H_2BH_3$	−18.0	89
$H_2B[N(CH_3)_3]H_2BH_3$	−17.0	91

[a] $BF_3O(C_2H_5)_2$ external reference. [b] The coupling constant $J(BH_2)$ is not reported at this time because of difficulty in locating the exact positions of the outer peaks of the triplet.

observed. Bridge hydrogen is expected to couple with each boron with the coupling constant for the

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(10) R. W. Parry, R. W. Rudolph, and D. F. Shriver, *ibid.*, 3, 1479 (1964).
(11) Gaines[9] observed a seven-line spectrum for diborane in ether solutions at elevated temperatures and suggested that all six B–H hydrogens are equivalent. Considering the temperatures at which his work was performed plus the fact that only one coupling constant was observed for the seven-line spectrum, his interpretation is reasonable and does not conflict with the present study.

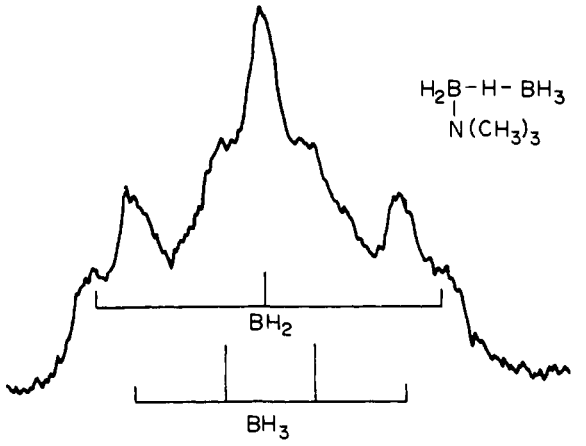

Figure 1. Boron-11 nmr spectrum at $-65°$ in methylene chloride.

B–H–B bond being smaller than that for the B–H bond. Each component of the quartet and of the triplet should, therefore, be split into a doublet. Such coupling appeared to be present on one sample of **2** in which each component of the quartet was split into a doublet, with an apparent coupling constant of only several cycles. In general, however, coupling with bridge hydrogen was not detected.[12]

Acknowledgment. Support of this work by the National Science Foundation is gratefully acknowledged.

(12) Bridge coupling was not detected in H_3B–H–BH_3^-.[9]

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The "Size" of a Lone Pair of Electrons. Evidence for an Axial *t*-Butyl Group[1]

Sir:

For some years there has been interest in the effective size of a lone pair of electrons.[2] Recently evidence has accumulated that the lone pair is smaller than a bonded hydrogen atom,[3,4] although a contrary indication has also been recorded.[5] We present here a striking demonstration that the space requirements of a free pair are, in fact, much smaller than those of a bonded hydrogen atom, the evidence being that *cis*-2-alkyl-5-*t*-butyl-1,3-dioxanes (I, Figure 1) exist very largely in the conformation Ia in which the *t*-butyl group is axial. Apparently this is the first instance where a *t*-butyl group is found to assume the axial position in a six-membered ring system.

Equilibration of *cis*- and *trans*-2-alkyl-4-methyl-1,3-dioxanes[6] (Figure 2) indicates that the conformational

(1) This work was supported by National Science Foundation Grant GP-2096 and by a grant from the Air Force Office of Scientific Research (AF-AFOSR-772-65).
(2) *Cf.* E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Division, John Wiley and Sons, Inc., New York, N. Y., 1965, p 245.
(3) N. L. Allinger and J. C. Tai, *J. Am. Chem. Soc.*, 87, 1227 (1965); N. L. Allinger, J. G. D. Carpenter, and F. M. Karkowski, *ibid.*, 87, 1232 (1965).
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