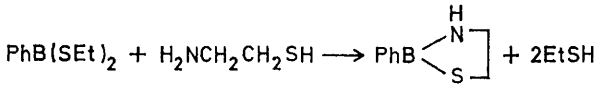
Boron–Sulphur Compounds. Part VI.[1] Organoboron Compounds of Cysteamine (2-Aminoethanethiol)

By **Richard H. Cragg** * and **Alan F. Weston**, The Chemical Laboratory, University of Kent at Canterbury, Canterbury, Kent

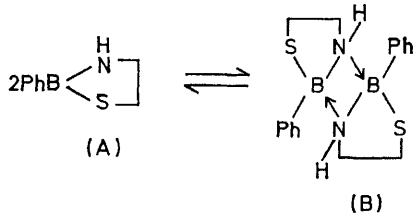
The synthesis and properties of a new class of compounds, based on the $-B-S-CH_2CH_2-NH$ unit, are described. The reaction of trisalkylthioboranes and cysteamine gave a borazine which on reaction with ethylenediamine gave a novel unsymmetrical borazine. The mass spectral fragmentations of these compounds are fully discussed.

THERE has been considerable interest over the last decade in the synthesis and properties of heterocyclic organoboranes. Much of this interest has been concerned mainly with heterocyclic boron–oxygen [2,3] compounds and more recently those containing boron–nitrogen bonds.[4] However organoboron heterocycles containing sulphur and nitrogen in the ring, with the exception of derivatives of 2-aminothiophenol,[5] have been completely ignored and no detailed mass spectral studies of these systems have been previously published. We therefore wish to report our results concerning the organoboron derivatives of cysteamine (2-aminoethanethiol).

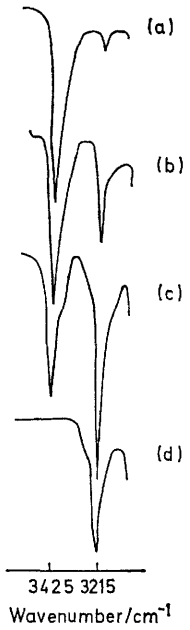
Cysteamine reacted readily with bisethylthiophenylborane to produce 2-phenyl-1,3,2-thiazaborolidine



(A). It is interesting to note that (A) distils over as a monomeric liquid, with a characteristic NH stretching frequency band at 3425 cm^{-1}, and dimerises within a few minutes to a solid (B) with a characteristic NH stretching frequency band at 3215 cm^{-1}. This strongly suggests that the dimerisation is taking place *via* the



nitrogen atom in the ring and is the first example of a phenylorganoheterocyclic borane undergoing such a process. On redistillation of the solid (B) the monomer (A) is obtained. The Figure gives some indication of the change in the NH stretching frequency band, with time, and also shows that when (B) dissolves in benzene



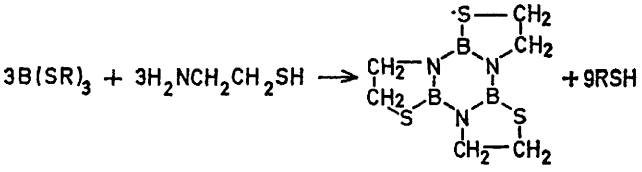
NH Stretching frequency band in i.r. spectrum of liquid, (a), at 0 min; (b), after 5 min; (c), after 10 min; (d), spectrum of the solid in benzene

it still remains in an associated form. However (B) dissolved readily in THF and the i.r. spectrum of this solution showed the presence of free and complexed NH stretching bands. Because of this unusual property we therefore investigated the synthesis and properties of organoboron derivatives of cysteamine.

The reaction of trialkylthioboranes with cysteamine

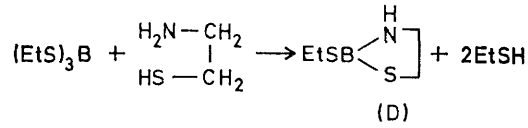
[1] Part V, R. H. Cragg, P. N. Husband, and A. F. Weston, *J. Inorg. Nuclear Chem.*, in the press.
[2] H. Steinberg, 'Organoboron Chemistry,' vol. 1, Interscience, London, 1964.
[3] S. G. Shore, J. L. Crist, B. Lockman, J. R. Long, and A. D. Coon, *J.C.S. Dalton*, 1972, 1123.
[4] K. Niedenzu and C. D. Miller, *Fort. Chem. Forsch.*, 1970, **15**, 191.
[5] K. Niedenzu, J. W. Dawson, P. W. Fritz, and W. Weber, *Chem. Ber.*, 1967, **100**, 1898.

was studied, however, instead of the expected heterocycle (D) a white solid (C) was formed and found to be a trimer consisting of a central borazine ring with three exocyclic borolidine rings attached. The ^{11}B n.m.r.



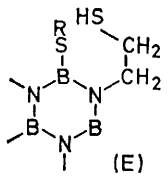
R = Et or Pr^n (C)

spectra, of a benzene solution of (C) using $(MeO)_3B$ as an external standard, showed a peak at −37·5 p.p.m. and ^1H n.m.r. spectra in $CDCl_3$–CCl_4 solution showed two triplets between 6 and 7 p.p.m. where the *N*-CH_2 was further upfield than the *S*-CH_2 from TMS. The mass spectral details are discussed in the mass spectral section. All attempts to prepare the alkylthioborolidines failed and the borazine was obtained in every case. The possibility that the intermediate, in the formation of the borazine, was the alkylthioborane (D) was shown to



(D)

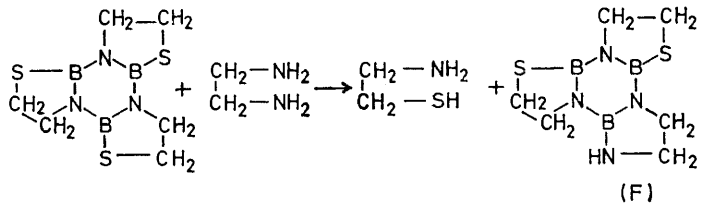
be unlikely. The mass spectrum recorded on the product of an incomplete reaction showed that the mixture contained a borazine with one or two side chains from which thiol elimination (exocyclic ring closure) had not taken place. We therefore suggest that the most likely intermediate is of type (E) from which exocyclic ring closure can then systematically take place.



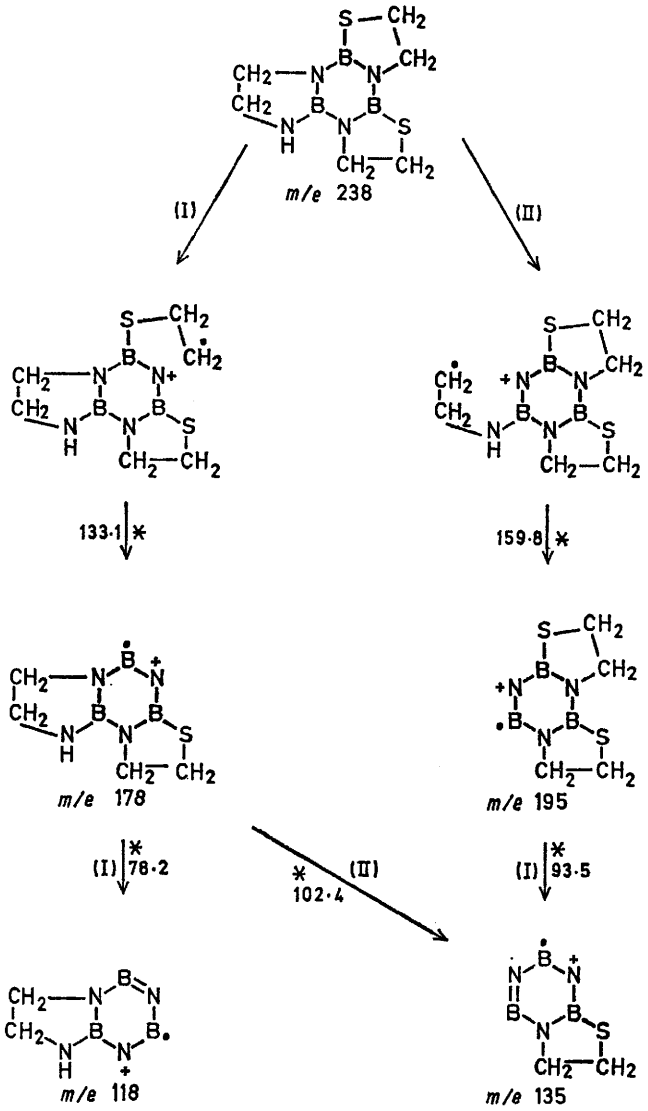
(E)

There has been considerable interest concerning substitution reactions of borazines. However in the majority of cases these reactions have been concerned with substitutions taking place at the boron atoms. Ethylene-1,2-diamine was refluxed with (C) in toluene for one week. A white solid collected in the condenser, above the level of the refluxing toluene, and was found to be cysteamine. On removal of the toluene a residue was obtained which on sublimation was found to be an unsymmetrical borazine (F) The ^1H n.m.r. spectra of (F) showed increased *N*-CH_2 contribution but unfortunately the overlap broadened the triplets which became unresolvable and hence integration of the spectrum was of no value. The i.r. spectrum of (F) gave a band at 3380 cm^{-1} characteristic of an NH stretching frequency band. The mass spectrum supported the formulation of (F) giving a parent ion *m/e* 238 and a characteristic fragmentation pattern. There was little evidence for the formulation of borenium ions, instead exocyclic rings were lost from the borazine nucleus. Exocyclic ring loss was achieved either by route (I) or route (II) (Scheme 1), the ratio of the abundance of the ions produced by these routes *m/e* 178 and 195 was **2 : 1**, thus loss of either substituent was equally favoured. This can be explained by consideration of the carbon–nitrogen bond which weakened by nitrogen back donation into the borazine ring, was the first to cleave; boron–nitrogen or boron–sulphur fission was then the secondary process by which a neutral cyclic leaving group was formed (Scheme 1). This was further supported by the ions which had lost a second exocyclic ring *m/e* 135, 118 where the ratio was found to be **1 : 2** as would be expected for random exocyclic loss. These fragmentations were supported by metastable data. The results confirm that not only has substitution taken place at the boron atom but that there has been a replacement of one of the nitrogen atoms in the borazine ring. Although the analysis results were consistent with the formulation of compound (F), the mass spectrum showed the presence of trace amounts of two further compounds where two and three cysteamine groups had been replaced by ethylenediamine. An attempt to obtain the completely substituted tris-ethylenedi-iminoborazine failed due to the fact that the excess of ethylenediamine caused decomposition of the ethylenethioborazine.

The reaction of cysteamine with trisdialkylaminoboranes gave liquid products. Their i.r. spectra gave a band at 3425 cm^{-1} which is characteristic for the N–H stretching frequency band in an unassociated aminoborane. Difficulty was found in the purification of these compounds, by distillation, due to the fact that their boiling points were close to that of the trisaminoboranes. The ^1H n.m.r. spectra showed two triplets due to the ring CH_2 groups around 7 p.p.m. A triplet at 9 p.p.m. assignable to the alkylamino-methyl group overlapped

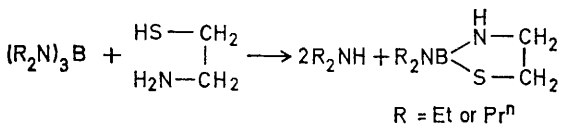


(F)

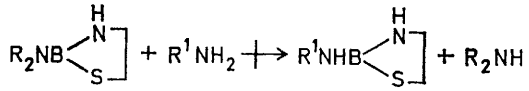


SCHEME 1 Fragmentation pattern for 1,2:3,4-bisethylenethio-5,6-ethyleneiminoborazine

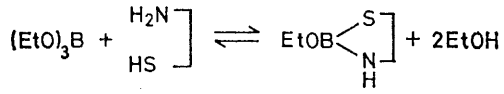
with the CH_2 quartet. Integration of the spectrum gave the correct ratio. These two compounds represent further examples of a class of compounds in which there is an exocyclic dialkylamino-group attached to boron as well as an NH group. Only one example of this class of compounds has previously been reported.[6] Compounds of this type generally eliminate amine to give the borazine. For example the reaction between trisaminoboranes and *o*-aminothiophenol gave the borazine (G) as the only product.[5]



2-Dialkylamino-1,3,2-thiazaborolidines were found to be unstable: they decompose, with trace amounts of moisture, to cysteamine. Transamination reactions, with primary amines, failed to give the required products. On addition of the primary amine a white solid was produced, the mass spectral analysis of which showed it to be mainly cysteamine. Hence ring cleavage appeared to be the major reaction rather than substitution.

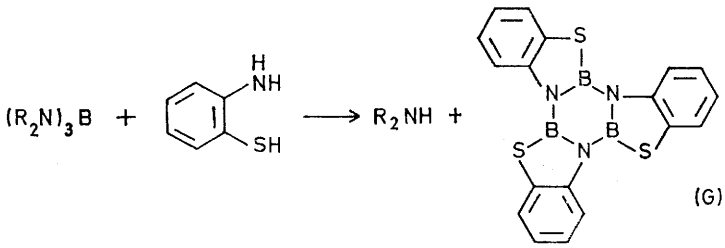


Triethyl borate was refluxed with cysteamine in toluene, in the expectancy that the equilibrium of the reaction to produce the ethoxoborolidine could be pushed over in its favour by the elimination of ethanol vapour from the solution. However after three hours the resultant liquid and solid were separated, and purified, and found to be the starting materials.



It is of interest that the boron atom in the dialkylamino-compounds appears not to be electron deficient. Solutions of the borolidine (11% concentration) and γ-picoline were made up in carbon tetrachloride. No change in the γ-picoline proton resonances were observed suggesting that no complex was formed. It was noted that the borolidines decomposed over a period of a few hours. This result demonstrates that an exocyclic dialkylamino-group causes a loss of the electron deficiency of the boron atom. This is in contrast to the dimeric nature of the phenyl derivative.

Hydrogen chloride was bubbled through a solution of a dialkylamino-derivative in benzene. A white precipitate was formed, the mass spectrum of which showed it to be a mixture of cysteamine hydrochloride and amine hydrochloride. Hence, even for chlorinated borolidines the effect of such a powerful reagent as hydrogen



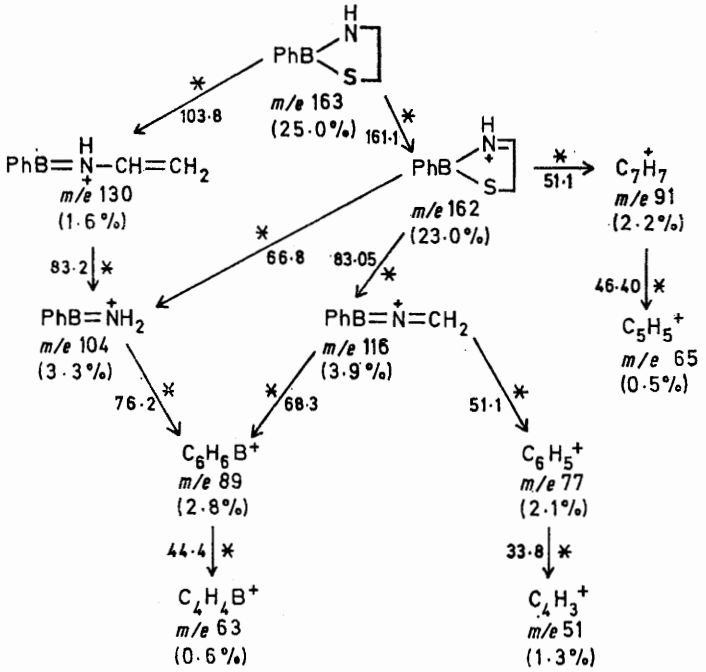
[6] K. Niedenzu and P. Fritz, *Z. anorg. Chem.*, 1965, **340**, 329.

chloride was sufficient to cause decomposition of the ring.

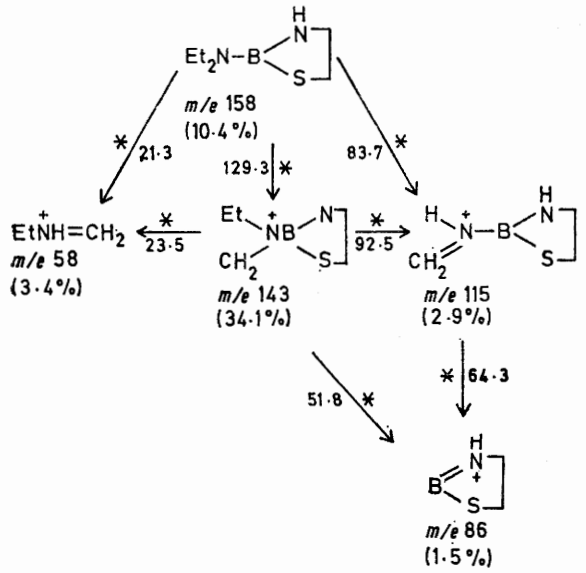
Mass Spectra.—With the synthesis of a new class of heterocyclic organoboranes we were in a position to study the mass spectral fragmentations of these compounds. Detail fragmentation patterns based on metastable scanning are given in Schemes 2—5 and include the approximate percentages of the total ionisation arising from the ions in the respective Schemes.

(a) 2-*Phenyl*-1,3,2-*thiazaborolidine.*—The recorded spectrum of this compound showed the parent peak to be smaller than the $P - 1$ peak. However when the monoisotopic spectrum was calculated the parent became the base peak. The major route for fragmentation was *via* the $P - 1$ ion. It was this ion, not the parent, which rearranged to give the tropylium ion; this was checked by precise mass measurement. No metastable was found for the parent fragmenting to *m/e* 91. The other major fragment associated to the fragmentation of the $P - 1$ ion was at *m/e* 116. This ion lost HCN to give the boratropylium ion which further fragmented to give the boracyclopentadienyl ion. These three ions were characterised by metastable scanning and precise mass determination.

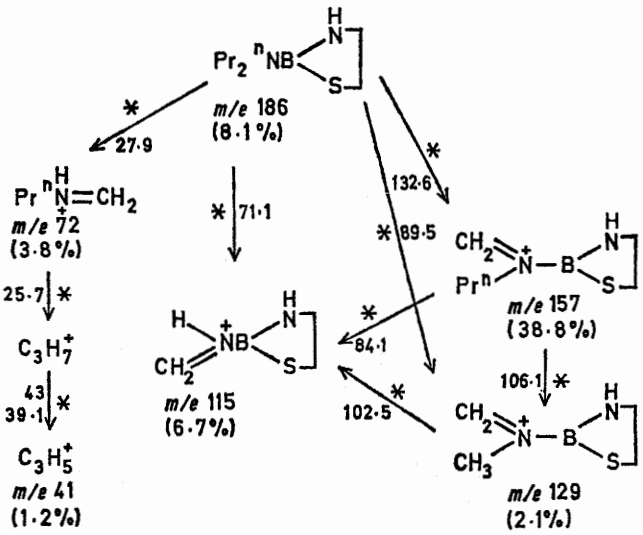
The fragments of the ring, observed in high abundance



SCHEME 2 Fragmentation pattern for 2-phenyl-1,3,2-thiazaborolidine

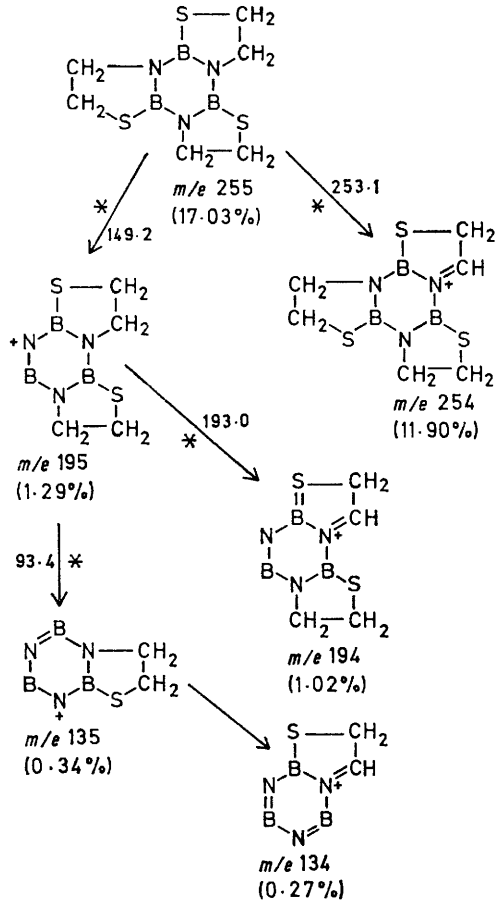


SCHEME 3 Fragmentation pattern for 2-diethylamino-1,3,2-thiazaborolidines



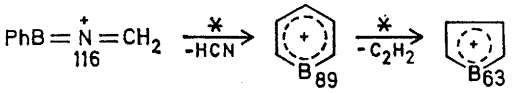
SCHEME 4 Fragmentation pattern for 2-di-n-propylamino-1,3,2-thiazaborolidine

all contained nitrogen but not sulphur. This can be explained by the fact that the boron–sulphur bond was



SCHEME 5 Fragmentation pattern for trisethylenethioborazine

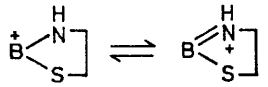
the weakest bond in the ring and was also in a position to be β cleaved by nitrogen. The few sulphur fragments



present were in about 2% of base abundance. It is of interest to note that ion *m/e* 134 PhB(N)(S) was only 3% abundant in contrast to the relatively high abundance for the symmetrical cases PhB(S)(S)[7] and PhB(N)(N).[8]

(b) 2-*Diethylamino*-1,3,2-*thiazaborolidine*.—The mass spectrum of this compound showed the presence of trisdiethylaminoborane as an impurity. However the spectrum was obtained pure by the removal of the peaks due to trisdimethylaminoborane by computer analysis. The dimethylaminoborolidine produced the base peak by β cleavage of the exocyclic amino-group by the elimination of CH_3. In all the major boron-containing fragments the ring remained intact and the elements of the side chain were lost. The formulation of *m/e* 115 as (H) and not (I) is based on the analogy with the previous compound where no ions of the type B(N)(S) or B(NH)(S) were observed and also that elimination of C_2H_4 is a normal fragmentation route for an amine. The ion of

most interest is *m/e* 86. Precise mass measurement supports the formulation (J). This is the first example of a bivalent borenium cation formed from a five-membered heterocyclic precursor and is in contrast to previously published work[9] which comments on the fact that such ions do not appear in the spectra of



heterocycles of this type. The other fragmentations observed are due to various N β cleavages leaving the charge on the exocyclic amine group.

(c) 2-*Di*-n-*propylamino*-1,3,2-*thiazaborolidine*.— The fragmentation pattern of this compound was similar to the previous compound. The base peak was produced by β cleavage in the exocyclic amino-group and in all boron-containing ions the ring remained intact. Non-boron-containing fragments were the other dominant ions and were formed by ring boron β cleavage leaving the charge on the exocyclic N. The peak at *m/e* 86 was also observed although it was only 3% of the base.

(d) *Trisethylenethioborazine*.—The mass spectrum of this compound has been briefly commented upon.[10] In this compound the $P - 1$ peak was the most intense, however when the monoisotopic spectrum was calculated the parent peak became the base peak. This compound was very stable to fragmentation. Apart from the P and $P - 1$ peaks all other peaks were less than 5% of the base peak. Metastable assignments were complicated by the large number of isotopes which all decomposed giving metastables at near the same position. The main fragmentation process involved the loss of exocyclic groups and fragments which would have been expected if the borazine ring had fragmented were not observed. One minor route involved the loss of H_2S from the parent followed by loss of acetylene.

The overall features of the fragmentation of these

[7] R. H. Cragg, G. Lawson, and J. F. J. Todd, *J.C.S. Dalton*, 1972, 878.
[8] R. H. Cragg and A. F. Weston, unpublished observations.
[9] J. C. Kotz, R. J. Vander Zanden, and R. G. Cooks, *Chem. Comm.*, 1970, 923.
[10] R. H. Cragg and A. F. Weston, *J.C.S. Chem. Comm.*, 1972, 79.

compounds are (i) where the ring is broken the nitrogen fragments are the most abundant, (ii) in compounds containing exocyclic amino-groups the ring remained intact in all boron fragments even producing the borenium cation, (iii) the borazine ring was very stable and the main fragmentations involved the loss of complete exocyclic groups leaving the borazine nucleus intact.

EXPERIMENTAL

General Procedures.—Solvents were dried over sodium wire and distilled before use. The ^{11}B n.m.r. spectra were recorded on neat liquids or solutions in benzene, with methyl borate as an external standard, using a Perkin-Elmer R10 spectrometer. Mass spectra were recorded using an A.E.I. MS 902 mass spectrometer at 70 eV. The source was maintained at 170 °C and the compounds were introduced as neat liquids or solids using a cooled direct-insertion probe. In general only those peaks of relative intensity of greater than 5% were considered. The usual precautions were taken with air-sensitive starting materials and products.

Trisdiethylaminoborane,[11] trisdi-n-propylaminoborane,[12] bisethylthiophenylborane,[13] trisethylthioborane,[14] and tris-n-propylthioborane [15] were prepared by established methods.

Preparation of 2-Phenyl-1,3,2-thiazaborolidine.—Bisethylthiophenylborane (2·25 g, 0·01 mol) and cysteamine (0·82 g, 0·01 mol) were refluxed for 24 h. Distillation of the residue afforded *2-phenyl-1,3,2-thiazaborolidine* (1·22 g, 71·2%), b.p. 92°, 0·5 mmHg (Found: C, 58·35; H, 6·45; N, 7·85; *M*, 163. $C_8H_{10}BNS$ requires C, 59·0; H, 6·15; N, 8·6%; *M*, 163). The compound distilled over as a liquid and quickly dimerised to give a solid, m.p. 82°, within 10 min.

Preparation of Trisethylenethioborazine.—Tris-n-propylthioborane (23·399 g, 0·099 mol) and cysteamine (7·65 g, 0·099 mol) were refluxed in benzene for 3 h. On removal of the solvent a residue was obtained which on sublimation (70°, 0·6 mmHg) yielded *trisethylenethioborazine* (5·25 g, 73%), m.p. 190° (Found: C, 28·05; H, 4·7; N, 16·35; *M*, 225. $C_6H_{12}B_3N_3S_3$ requires C, 28·2; H, 4·7; N, 16·45%; *M*, 225). The reaction of trisethylthioborane and cysteamine, under the same conditions, also gave trisethylenethioborazine (75% yield).

Preparation of 1,2:3,4-Bisethylenethio-5,6-ethyleneiminoborazine.—Trisethylenethioborazine (3·010 g, 0·012 mol) and ethylenediamine (2·117 g, 0·012 mol) were refluxed in toluene for 7 days. During this time a white solid condensed above the level of the refluxing toluene. The solid was removed and found to be cysteamine (0·680 g, 75%) by comparison of its mass spectrum with that of cysteamine. On removal of the toluene a solid product was obtained which on sublimation was found to be the *bisethylenethioethyleneiminoborazine* (1·204 g, 43%), m.p. 110° (Found: C, 29·45; H, 6·7; N, 24·8; *M*, 238. $C_6H_{13}B_3N_4S_2$ requires C, 30·25; H, 5·5; N, 24·55%; *M*, 238). The above reaction was repeated using an excess of ethylenediamine, and no identifiable product was obtained.

Preparation of 2-Diethylamino-1,3,2-thiazaborolidine.—Cysteamine (2·694 g, 0·012 mol) and trisdiethylaminoborane (0·91 g, 0·012 mol) were refluxed in benzene for 12 h. On removal of the solvent the residue afforded on distillation *2-diethylamino-1,3,2-thiazaborolidine* (1·189 g, 63%), b.p. 52°, 0·3 mmHg (Found: C, 47·45; H, 10·1; N, 16·8; S, 19·5; *M*, 158. $C_6H_{15}BN_2S$ requires C, 45·6; H, 9·5; N, 17·7; S, 20·25%; *M*, 158). The analyses are low due to the fact that the product was difficult to separate from trisdimethylaminoborane. The mass spectrum of the compound showed it to be about 90% pure.

Preparation of 2-Di-n-propylamino-1,3,2-thiazaborolidine.—Trisdi-n-propylaminoborane (6·927 g, 0·022 mol) and cysteamine (1·7319 g, 0·022 mol) were refluxed in benzene for 3 h. After removal of the volatiles the residue afforded on distillation *2-di-n-propylamino-1,3,2-thiazaborolidine* (2·048 g, 49·5%), b.p. 80°, 0·25 mmHg. The mass spectra showed some trisaminoborane as impurity. The precise mass of the compound was determined (Found: 186·13324. $C_8H_{19}BN_2S$ requires 186·136195).

Attempted Synthesis of 2-Ethoxy-1,3,2-thiazaborolidine.—Triethoxyborane (4 mol) and cysteamine (1 mol) were refluxed in toluene, using a Dean–Stark apparatus, for 3 h. The volatiles were removed and the residue was found to be cysteamine.

^1H N.m.r. Study with γ-Picoline.—Solutions containing γ-picoline (11·3%) and 2-diethylamino-1,3,2-thiazaborolidine (11·3%) in carbon tetrachloride were mixed and the ^1H n.m.r. of the resulting solution recorded. No shift in the spectrum of γ-picoline was observed showing that there was no complex formed. The boron compound decomposed to cysteamine after 2—3 h.

Reaction of 2-Diethylamino-1,3,2-thiazaborolidine with HCl.—HCl gas was bubbled through a benzene solution of 2-diethylamino-1,3,2-thiazaborolidine for 3 h. A white solid was formed, filtered off, and found to be boric oxide. On removal of the solvent the filtrate afforded a mixture of diethylamine hydrochloride and cysteamine (confirmed by mass spectrometry). This suggests that trace amounts of water in the HCl were sufficient to decompose the product.

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[12] D. W. Aubrey, W. Gerrard, and E. F. Mooney, *J. Chem. Soc.*, 1962, 1786.
[13] R. H. Cragg, M. F. Lappert, and B. P. Tilley, *J. Chem. Soc. (A)*, 1967, 947.
[14] J. Brault and J. M. Lelancette, *Canad. J. Chem.*, 1964, **42**, 2093.
[15] B. M. Mikhailov and Yu. N. Bubnov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1962, 1378.