

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WASHINGTON STATE UNIVERSITY]

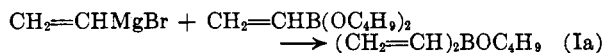
## Synthesis of 4-Butoxy-1-thia-4-boracyclohexane via Dimethylaminoethyl and Butyl Divinylborinates<sup>1</sup>

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Vinylmagnesium bromide converts dibutyl ethyleneboronate to butyl divinylborinate, which has invariably polymerized on attempted isolation but can be transesterified to the stable, chelated dimethylaminoethyl divinylborinate. Radical-catalyzed addition of hydrogen sulfide to either of the two divinylborinate esters in dilute solution yields the corresponding 4-alkoxy-1-thia-4-boracyclohexane. Correlation of the chemistry of the divinylborinates with simple molecular orbital calculations is discussed.

Butyl divinylborinate (Ia) appeared potentially useful for the synthesis of cyclic organoboron compounds and for study of the effects of conjugation across the vacant *p*-orbital of boron.<sup>2</sup> Addition of vinylmagnesium bromide to dibutyl ethyleneboronate<sup>3</sup> leads to butyl divinylborinate as expected.

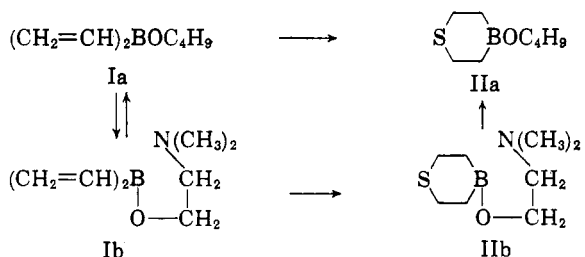


However, all attempts to concentrate solutions of this compound have resulted in its polymerization. The polymer characteristically forms as a clear gel, often with a separable surface film, and dries to a weak, brittle white solid, soluble only in solvents which destroy it, such as sulfuric acid or alkaline hydrogen peroxide. The irritating odor attributed to monomeric Ia persists in polymer dried overnight in air. Evidence that monomeric Ia has been obtained in solution consists in the preparation of the stable derivatives described below, the infrared spectrum, and the ability of the substance to codistill with butanol on rapid vacuum distillation. Fractionation of solutions of Ia under reduced pressure indicates its boiling point to be between those of butanol and dibutyl ethyleneboronate as it should be, but liquid rich in Ia polymerizes rapidly in the column. Thus, even if an inhibitor much more effective than the dubiously active phenothiazine could be found, prospects for isolating Ia, except possibly in high vacuum apparatus, appeared hopeless.

The chelated ethanolamine esters<sup>4</sup> have been used to protect borinic acids from air oxidation and decomposition. Furthermore, for the divinylborinate series, simple molecular orbital calculations indicated that filling the vacant orbital of the boron atom (essentially equivalent to its removal

from conjugation) by chelation with a base should drastically reduce the susceptibility of the vinyl groups to radical attack. The  $\beta$ -dimethylaminoethyl ester was chosen for the present work, as crystallinity was not needed but a derivative easily soluble in nonpolar solvents was desired. As anticipated, dimethylaminoethyl divinylborinate (Ib) is stable even in the absence of radical inhibitor and reflects its chelated, polar character in relatively high melting (6°) and boiling points for a borinic ester of its molecular weight. The dimethylaminoethyl ester Ib is easily reconverted to dilute solutions of the butyl ester Ia in organic solvents by addition of butanol and extraction with dilute acid. The properties of these solutions are described in detail in the Experimental section.

Butyl divinylborinate (Ia) in refluxing benzene reacts readily with hydrogen sulfide in the presence of azobisisobutyronitrile to yield 12% of the heterocyclic adduct IIa, 4-butoxy-1-thia-4-boracyclohexane, together with a large amount of polymeric residue. The less reactive dimethylaminoethyl ester Ib requires several times as much azonitrile initiator as Ia under otherwise identical conditions for



complete reaction with hydrogen sulfide, but yields 34% of 4-(2-dimethylaminoethoxy)-1-thia-4-boracyclohexane (IIb). The higher yield and the small polymeric residue are in accord with the expectation<sup>3</sup> of more favorable transfer constants with less reactive vinyl groups. It might appear that the best route to the butyl ester IIa would be *via* the dimethylaminoethyl ester IIb. However, conversion of IIb to IIa proved unexpectedly difficult and could not be accomplished in satisfactory yield. The high stability and moderate water solubility of the chelated spiro structure IIb and the

(1) Supported by National Science Foundation Grant G-9916; presented in part at the 139th American Chemical Society Meeting, St. Louis, March, 1961.

(2) Reported divinylboron compounds, prepared in high vacuum apparatus, include (a) methyldivinylboron, T. D. Parsons, M. B. Silverman, and D. M. Ritter, *J. Am. Chem. Soc.*, **79**, 5091 (1957); (b) chloro- and fluorodivinylboron, F. E. Brinckman and F. G. A. Stone, *J. Am. Chem. Soc.*, **82**, 6218 (1960).

(3) D. S. Matteson, *J. Am. Chem. Soc.*, **82**, 4228 (1960).

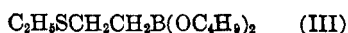
(4) R. L. Letsinger and I. Skoog, *J. Am. Chem. Soc.*, **77**, 2491 (1955).

TABLE I

$\alpha_B - \alpha_C$	(a) $(\text{CH}_2=\text{CH})_2\text{BOH}$		(b) $\text{CH}_2=\text{CH}-\text{B}(\text{OH})_2$			
	Electron Density		Free Valence		Radical Stabilization <sup>3</sup>	
	a	b	a	b	a	b
-0.5 $\beta$	—	0.879	—	0.787	—	0.129 $\beta$
-1.0 $\beta$	0.920	0.932	0.780	0.770	0.139 $\beta$	0.098 $\beta$
-1.5 $\beta$	0.967	0.977	0.766	0.759	0.106 $\beta$	0.076 $\beta$

acid lability of IIa seemed to be the principal causes of difficulty (see Experimental). In addition, purification of IIb was complicated by the unstable, polymeric byproducts and by the reluctance of the compound to crystallize in the presence of solvents or small amounts of impurities.

The following observations confirm the structures of the 4-alkoxy-1-thia-4-boracyclohexanes (II). Passing a butanol solution of IIb through a protonated sulfonic acid ion exchange column partially transesterified it to IIa and partially degraded the heterocycle to dibutyl 2-ethylthioethane-1-boronate (III) (confirmed by synthesis from ethyl



mercaptan and dibutyl ethyleneboronate). Further degradation to butyl borate, inseparable from IIa by distillation but detectable by infrared, also occurred. Unexpectedly, the ring of IIa was also opened on treatment with sulfur at 140–150° for 30 min., yielding nonvolatile material and III, separated by molecular distillation and identified by infrared. For further structure proof, IIb was degraded with potassium hydroxide at 120–130°<sup>3</sup> to yield 60% of the two available  $-\text{CH}_2\text{CH}_2-$  units as ethylene, identity and purity confirmed by infrared.

The successful cycloaddition of hydrogen sulfide to the divinylborinates (I) suggests the possibility of radical catalyzed addition of other bifunctional reagents. After an induction period, carbon tetrabromide reacts vigorously with dimethylaminoethyl divinylborinate (Ib) to yield charred polymer and hydrogen bromide, evidently a result of side reactions at the amino group. Butyl divinylborinate (Ia) and polyhalomethanes yield small amounts of distillable adducts of undetermined structure, which are being studied.

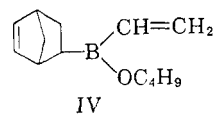
The only readily apparent alternate method for making 1-hetero-4-boracyclohexanes is the addition of an alkylborane to a divinyl compound. Hawthorne<sup>6</sup> has recently reported the addition of *t*-butylborane to divinyl ether and to dimethyldivinylsilane.

**Molecular Orbital Calculations.** Simple molecular orbital calculations have been carried out for divinylborinic acid with the same parameters and assumptions used previously for ethyleneboronic acid.<sup>3</sup> Results of varying the coulomb integral for

boron,  $\alpha_B$ , are summarized in Table I; these pertain to the terminal-methylene carbon atom and to the radical resulting from addition at that point.

For any given value of  $\alpha_B$  in the range of Table I, the calculated radical stabilization<sup>3</sup> energies (which presumably differ approximately as much as do the transition state energies for radical attack) predict that a given radical will add to divinylborinic acid about ten times faster than to ethyleneboronic acid. However, use of a consistent set of assumptions<sup>3</sup> in these calculations requires that  $\alpha_B$  be reduced by about 0.3  $\beta$ , or 0.1 ( $\alpha_B - \alpha_C$ ), as a consequence of replacing oxygen by carbon in going from the monovinyl to the divinyl compound. This correction for the reduced effective electronegativity of the boron atom reduces the calculated higher reactivity of the divinyl compound somewhat, as may be seen by interpolation in Table I. The magnitude of this parameter adjustment is somewhat arbitrary, but it would seem inconsistent with the observed chemistry to increase the subtraction to 0.6  $\beta$  or 0.2 ( $\alpha_B - \alpha_C$ ), which would lead to the calculation that the divinyl compounds should be no more reactive than the monovinyl series.

The gross difference in polymerization behavior between dibutyl ethyleneboronate and butyl divinylborinate is not all adequately accounted for by the mere factor of 3 to 10 derived from the above calculations. Oxygen, which could not be rigorously excluded from the available apparatus, attacks borinates faster than boronates<sup>6</sup> to yield peroxide intermediates, and does indeed accelerate the polymerization of butyl divinylborinate in solution. If the divinylboron group were actually exceedingly susceptible to radical attack, it should also be somewhat electron deficient (see trends in Table I); these two factors should make it also a very active dienophile. It is not. The yield of the adduct of butyl divinylborinate with cyclopentadiene, butyl vinyl-5-norbornenylborinate (IV), appears to be approximately the same



(allowing for two vinyl groups) as that of the dibutyl ethyleneboronate-cyclopentadiene adduct<sup>7</sup>

(5) M. F. Hawthorne, *J. Am. Chem. Soc.*, **83**, 2541 (1961).

(6) M. F. Lappert, *Chem. Revs.*, **56**, 969 (1956).

(7) Preliminary report: D. S. Matteson and K. Peacock, *J. Am. Chem. Soc.*, **82**, 5759 (1960).

(20%) under identical conditions. Since the rapid reaction of the former adduct with air prevented attainment of an analytical sample, its apparent yield is more properly an upper limit, although there seems to be no reason to doubt the identity of the compound.

#### EXPERIMENTAL

**2-Dimethylaminoethyl divinylborinate (Ib).** A solution of one mole of vinylmagnesium bromide<sup>8</sup> in 360 ml. of tetrahydrofuran was added under nitrogen in 15 min. to a well stirred solution of 184.1 g. (1 mole) of dibutyl ethyleneboronate<sup>3</sup> in 500 ml. of ether kept below  $-60^{\circ}$ . The acidification and workup described for unsaturated boronic esters<sup>3</sup> was used up to and including neutralization of the material with sodium bicarbonate, all scaled up by a factor of two except that the phenothiazine was increased to 1 g. and the butanol decreased to 300 ml. in two portions. Slight polymerization of the product during the extraction procedure, minimized by low temperatures and prompt completion, led to some emulsion formation. The organic phase was then partially dried by washing with 100 ml. of saturated sodium chloride and 108 g. (1.2 mole) of 2-dimethylaminoethanol was added. After concentration at  $25^{\circ}$  with the water pump, fractionation through a 30-cm. column packed with Podbielniak nichrome helices separated butanol-water azeotrope, impure dibutyl ethyleneboronate and considerable forerun at  $60-65^{\circ}$  (0.1 mm.), then yielded 98-101 g. (64-66%) of 2-dimethylaminoethyl divinylborinate (Ib), b.p.  $67-74^{\circ}$  (0.1 mm.), m.p.  $-3$  to  $+3^{\circ}$ . An oil bath was found best for heating the pot, as overheating causes loss of vacuum and discoloration of distillate. A redistilled center cut, b.p.  $71-72^{\circ}$  (0.1 mm.), m.p.  $3-6^{\circ}$ , was analyzed.

*Anal.* Calcd. for  $C_8H_{16}BNO$ : C, 62.78; H, 10.54; B, 7.07; N, 9.16. Found<sup>2</sup>: C, 62.57; H, 10.69; B, 7.24; N, 9.02.

When the dibutyl ethyleneboronate was added to the vinylmagnesium bromide and the above procedure otherwise followed, only a small yield of impure, noncrystallizable Ib was obtained. Addition of one mole of methyl borate to two of vinylmagnesium bromide yielded 14% of Ib, partially crystalline at  $-15^{\circ}$ . The insolubility of vinylmagnesium bromide at  $-70^{\circ}$  probably contributes to the failure of these procedures. The latter reaction did proceed as far as precipitation of the 1:1 adduct of vinylmagnesium bromide and methyl borate, as evidenced by a high yield of mixed esters of ethyleneboronic acid, b.p. approx.  $30^{\circ}$  (0.1 mm.), and the apparent absence of *tris-2-dimethylaminoethyl borate*. This borate ester has been prepared in 69% yield by simple distillation of methanol and, unavoidably, some methyl borate, from a stoichiometric mixture of 2-dimethylaminoethanol and methyl borate, b.p.  $80^{\circ}$  (0.1 mm.).

*Anal.* Calcd. for  $C_{12}H_{20}BN_2O_3$ : C, 52.4; H, 10.9; B, 3.9; N, 15.3. Found: C, 52.0; H, 11.4; B, 4.1; N, 14.7.

Addition of 2 moles of vinylmagnesium bromide to 0.33 mole of *tris-2-dimethylaminoethyl borate* and 0.67 mole of methyl borate did not yield the divinyl compound Ib, but impure dibutyl ethyleneboronate on workup. Further discouragement to attempted one step synthesis of Ib is the

observation that the boiling point of *tris-2-dimethylaminoethyl borate*, a likely byproduct, is too close to that of Ib to permit separation.

**Butyl divinylborinate (Ia) solutions.** Extraction of a solution of 15.3 g. (0.1 mole) of dimethylaminoethyl divinylborinate (Ib) and 12 ml. of 1-butanol in 300 ml. of benzene with 250 ml. of 0.5M hydrochloric acid, then 100 ml. of 0.2 M acid, followed by washing with 50 ml. of saturated sodium bicarbonate and drying over sodium sulfate yielded butyl divinylborinate (Ia) in solution without noticeable polymerization. Methylene chloride solutions of Ia are somewhat less stable and some polymer forms during their preparation; higher concentrations of acid lead to extensive polymerization. In butanol, Ia polymerizes shortly after exposure to air. The boiling point of Ia, not accurately measurable because of rapid polymerization of the concentrated liquid at room temperature, is slightly higher than that of butanol, with which it easily codistills, and distinctly lower than that of dibutyl ethyleneboronate; it probably is between  $45$  and  $65^{\circ}$  (15 mm.). Divinylborinic acid in benzene, prepared by omission of butanol in the procedure above, is a volatile, noxious substance which begins to polymerize at once; it is undoubtedly the impurity that makes direct preparation of ethyleneboronic acid<sup>3</sup> from vinylmagnesium chloride and methyl borate impractical. It was demonstrated that the dimethylaminoethyl group protects Ib by chelation, not by acting as a radical inhibitor or acid scavenger, by concentrating a methylene chloride solution of Ia and 20-30% as much added Ib; as usual, the Ia promptly polymerized. The infrared spectrum of Ia in methylene chloride has a strong C=C band at  $1610\text{ cm.}^{-1}$  and a probable vinyl CH bending band at  $970\text{ cm.}^{-1}$  with an overtone at  $1935\text{ cm.}^{-1}$ . The corresponding bands for the dimethylaminoethyl ester Ib consist of a several times weaker pair at 1610 and  $1630\text{ cm.}^{-1}$  (without solvent, single band at 1610) and a pair at 940 and  $950\text{ cm.}^{-1}$  with an overtone at  $1875\text{ cm.}^{-1}$ . In the ultraviolet (Cary Model 14 Spectrophotometer), Ib in 2,2,4-trimethylpentane appears to have a maximum about 189 m $\mu$ ,  $\epsilon_{\text{max}}$  about 13,000, but the absorption of the solvent is so near 100% in this region that the data are unreliable. Treatment of the solution to convert Ib to Ia did not increase  $\lambda_{\text{max}}$ , shifted  $\epsilon_{\text{max}}$  upward roughly 20%.

**4-(2-Dimethylaminoethoxy)-1-thia-4-boracyclohexane (IIB).** A solution of 15.3 g. (0.1 mole) of dimethylaminoethyl divinylborinate (Ib) in 300 ml. of benzene was refluxed and stirred 6 hr. while a slow stream of hydrogen sulfide was bubbled through, and 0.4 g. portions of azobisisobutyronitrile were introduced after 0, 1.5, and 3 hr. After concentration (water pump), the viscous residue was distilled at 0.1-0.3 mm. from a flask immersed almost to the side arm in an oil bath at about  $170^{\circ}$ . Distillation was very slow (4 hr. or more required); molecular distillation below  $110^{\circ}$  appeared satisfactory and would be preferable if a large enough molecular still were available. The crude distillate (11 g.) had to be fractionated to yield the thiaboracyclohexane IIB, b.p.  $126-131^{\circ}$  (0.1 mm.), 6.4 g. (34%). A carefully fractionated center cut, b.p.  $123-125^{\circ}$  (0.1 mm.), crystallized. Not all the impurities could be removed by distillation and attempted recrystallization from solvents was unsuccessful. The analytical sample, m.p.  $40-51^{\circ}$ , was prepared by tedious manual zone melting in a 4 mm. diameter glass tube closed at one end.

*Anal.* Calcd. for  $C_8H_{16}BNOS$ : C, 51.35; H, 9.70; B, 5.78; N, 7.49; S, 17.14. Found: C, 51.09; H, 9.69; B, 5.85; N, 7.64; S, 16.99.

Higher dilution failed to increase the ratio of IIB to polymer significantly, but decreased the conversion of Ib. Substitution of *t*-butyl alcohol for benzene as the solvent also decreased the conversion of Ib.

The infrared spectrum of IIB is consistent with the assigned structure. Although IIB shows a very weak band similar to but somewhat weaker than a typical thiol group absorption at  $2540\text{ cm.}^{-1}$ , the sulfur-free analog Ib shows a similar band at  $2530\text{ cm.}^{-1}$ . A test for free thiol with lead

(8) Resorted to after complete frustration in attempts to make vinylmagnesium chloride by previously successful<sup>8</sup> procedures from pure vinyl chloride purchased in 1960 from the Matheson Company, which appeared to be completely inert even in the presence of a vigorous Grignard reaction with vinyl bromide, neither participating in nor inhibiting that reaction. Commercial vinylmagnesium chloride proved unstable on storage. Vinyl bromide: Peninsular ChemResearch, Gainesville, Fla.

(9) Microanalyses by Galbraith Laboratories, Knoxville, Tenn.

acetate was negative (other heavy metal ions precipitate borinates).

*4-Butoxy-1-thia-4-boracyclohexane* (IIa). A solution of 2.97 g. of 4-(2-dimethylaminoethoxy)-1-thia-4-boracyclohexane (IIb) in 25 ml. of methylene chloride and 5 ml. of butanol was extracted with 30 ml. of 2 *M* hydrochloric acid, the aqueous phase washed with four 25 ml. portions of 4% butanol in methylene chloride, the combined organic phase washed with another 30 ml. portion of 2 *M* acid, then 20 ml. sat. sodium chloride, dried with magnesium sulfate, and distilled, crude yield 1.1 g., b.p. 55–70° (0.1 mm.). Fractionation yielded 0.8 g. of pure IIa; a center cut, b.p. 45–46° (0.1 mm.),  $n_D^{25}$  1.4835, was analyzed.

*Anal.* Calcd. for  $C_8H_{17}BOS$ : C, 55.83; H, 9.96; B, 6.29; S, 18.63. Found: C, 55.55; H, 10.13; B, 6.47; S, 18.79.

Losses in the above procedure appear to be due both to the relatively high water solubility of IIb and to its stability; some unreacted IIb was recovered after the extraction procedure. In the hope of avoiding such losses, a butanol solution of IIb was chromatographed on sulfonic acid ion exchange resin. However, only a small conversion was obtained over coarse resin. Fine resin (Dowex 50, 4% cross-linked, 200–400 mesh) yielded incomplete conversion and recovery in a batch process or required many hours of contact for chromatography, still yielding incomplete recovery and resulting in ring opening of a third of the heterocycle II to *dibutyl 2-ethylthioethane-1-boronate* (III), an authentic sample of which was prepared by ultraviolet irradiation of ethyl mercaptan and dibutyl ethyleneboronate at room temperature, b.p. 79–80° (0.06 mm.), and proved identical by infrared.

*Anal.* Calcd. for  $C_{12}H_{27}BO_2S$ : C, 58.54; H, 11.05; B, 4.39; S, 13.02. Found: C, 58.32; H, 11.23; B, 4.37; S, 12.89.

Further degradation to tributyl borate occurred as well; this was inseparable from IIa by distillation but readily detected by its characteristic strong infrared band at 665  $cm^{-1}$ .

Direct preparation of IIa from 0.1 mole of Ia in 300 ml. of benzene (solution prepared as described above) was accomplished by refluxing 3 hr. in a stream of hydrogen sulfide and adding 0.1 g. of azobisisobutyronitrile after 0 and 1.5 hr. This effected complete conversion of the divinyl compound

to 12 g. of viscous polymeric adducts as well as 2.9 g. of crude IIa, which distilled with little decomposition of the byproducts from an oil bath at 80–100°, b.p. 60–67° (0.2 mm.), yield on fractionation 2.05 g. (11.9%), identity and purity confirmed by infrared.

Attempted improvement of the above procedure by portionwise addition of a dilute solution of the divinylborinate Ia to the hydrogen sulfide-saturated refluxing benzene was complicated by the tendency of Ia to polymerize on standing and, with the same total quantity of initiator, considerable unreacted Ia remained at the end as evidenced by its polymerization during distillation; the yield of IIa was reduced.

*Butyl Vinyl-5-norbornenylborinate* (IV). A solution of 0.0167 mole of butyl divinylborinate (Ia) in 50 ml. of benzene (prepared as described above) was refluxed under nitrogen with 4 ml. of cyclopentadiene, then concentrated under vacuum and fractionated through a short column to yield 1.12 g. (33%) of butyl vinyl-5-norbornenylborinate, b.p. 56–58° (0.2 mm.), and 0.42 g. of largely polymeric residue. The adduct evolved much heat and polymerized on contact with air. A center cut (transferred with a hypodermic syringe to minimize air exposure) partially polymerized before analysis. The erratic results are attributed to contamination with starting material (Ia, too low boiling to represent the bulk of the sample) and air oxidation.

*Anal.* Calcd. for  $C_{13}H_{21}BO$ : C, 76.49; H, 10.37; B, 5.30. Found: C, 71.15, 71.48; H, 10.18, 9.70; B, 6.36, 6.60.

The infrared spectrum showed bands due to unsaturation which decreased in intensity after a few minutes as the material polymerized between the sodium chloride plates. With excess hydrogen peroxide and 0.2 g. of 2,4-dinitrophenylhydrazine in acidic aqueous methanol,<sup>8</sup> 0.2 ml. of the freshly prepared adduct yielded 0.15 g. of acetaldehyde 2,4-dinitrophenylhydrazone, m.p. 147–150°, confirmed by mixture m.p.

Under the same conditions as those described above, 0.0167 mole of dibutyl ethyleneboronate yielded 20% of the cyclopentadiene adduct,<sup>7</sup> confirmed by infrared comparison.

PULLMAN, WASH.