

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

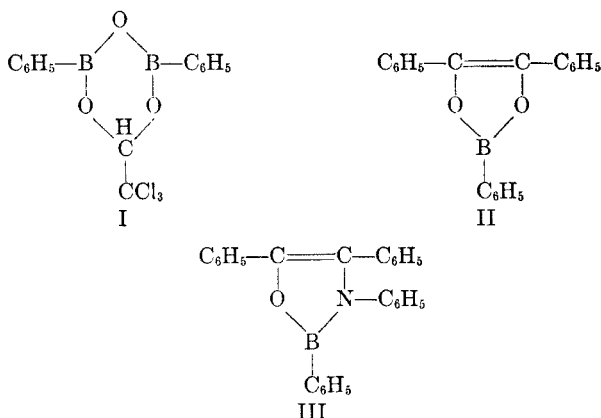
**Organoboron Compounds. XII. Heterocyclic Compounds from Benzeneboronic Acid<sup>1</sup>**

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Received October 13, 1959

New types of compounds were prepared by condensing benzeneboronic acid with chloral hydrate, benzoin, and a mixture of benzoin and aniline. The product from benzoin, 2,4,5-triphenyl-1,3,2-dioxaborole was very readily oxidized to benzil and was relatively resistant to hydrolysis in neutral or acidic solutions.

In view of the smooth conversion of benzeneboronic acid and *o*-phenylenediamine to 2-phenyl-1,3-dihydro-2,1,3-benzoboradiazole,<sup>2</sup> we examined the behavior of benzeneboronic acid with several other substances which might be expected to yield heterocyclic compounds by condensation reactions. New compounds were isolated in high yields from reactions with chloral hydrate, benzoin, and an equimolar mixture of benzoin and aniline.<sup>3</sup> Formulas I-III, respectively, were assigned to these substances on the basis of the mode of formation, analyses, infrared spectra, and chemical behavior.



Compound I is unusual in that the boron-oxygen heterocycle contains carbon at the aldehyde stage of oxidation. Whereas six-membered ring compounds containing either boron and oxygen

(1) For the previous paper in this series see: R. L. Letsinger and J. R. Nazy, *J. Am. Chem. Soc.*, **81**, 3013 (1959).

(2) R. L. Letsinger and S. B. Hamilton, *J. Am. Chem. Soc.*, **80**, 5411 (1958).

(3) A sharp melting substance was also obtained from a reaction of benzeneboronic acid with mandelic acid in toluene. It could be sublimed without decomposition and the analysis corresponded to  $\text{C}_6\text{H}_5\text{CHCOOC}_6\text{H}_5$ ; however, the infrared

spectrum contained in addition to a band at  $5.57 \mu$  (the ring carbonyl group) bands at  $5.82 \mu$  and in the  $2.9-4.0 \mu$  region characteristic of the carboxyl group. It appears that some hydrolysis had occurred in the samples used for the spectral determinations. The ease of hydrolysis of acyloxyboron compounds has been noted by W. Gerrard, M. F. Lappert, and R. Shafferman, *J. Chem. Soc.*, 3648 (1958).

(boroxines) or carbon and oxygen (aldehyde trimers) are well known, a mixed compound of this type does not seem previously to have been described. As expected, compound I was relatively unstable, decomposing slowly to give triphenylboroxine at  $150^\circ$ .

Compound II, 2,4,5-triphenyl-1,3,2-dioxaborole, exhibited several interesting properties. Perhaps the most distinctive feature was the ease of oxidation. Cyclohexane and anhydrous dioxane solutions of compound II were stable indefinitely; however, aqueous dioxane or ethanol solutions rapidly acquired a yellow color due to formation of benzil. The rate of oxidation increased in alkaline solutions which were saturated with oxygen. Table I summarizes data on the oxidation of compound II, benzoin, and an equimolar mixture of benzoin and benzeneboronic acid (hydrolytic products of compound II) by molecular oxygen in alkaline aqueous alcoholic solutions. From experiments 1, 2, and 3 it is seen that compound II was very extensively oxidized under conditions for which benzoin was virtually unchanged and the mixture of benzoin and benzeneboronic acid was attacked to only a minor extent. It is also apparent that compound II was oxidized more rapidly than it was hydrolyzed. Finally, experiments 4 and 5 as well as 2 and 3 demonstrate that benzeneboronic acid accelerated the oxidation of benzoin under these conditions.

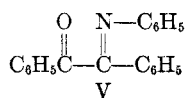
Weissberger<sup>4</sup> postulated that oxidation of benzoin in alkaline solution involved a slow, rate-determining enolization followed by reaction of the enolate ion with molecular oxygen. An extension of this mechanism to the oxidation of compound II seems plausible. According to this the rate determining step would be generation of an enolate ion (IV) by attack of hydroxide ion on boron, a reaction which could well be much faster than removal of the  $\alpha$ -hydrogen in benzoin by hydroxide ion. The activating effect of benzeneboronic acid on the oxidation of benzoic (exp. 5) may depend upon formation in solution of a low concentration of compound II or a related charged complex which can yield IV.

(4) A. Weissberger, *Ber.*, **65**, 1815 (1932).



TABLE II

| Wt. Cpd. II, g. | Organic Solvent    | Solvent Added                        | Cpd. II Recovered |    |
|-----------------|--------------------|--------------------------------------|-------------------|----|
|                 |                    |                                      | g.                | %  |
| 0.50            | 20 ml. 95% ethanol | 5 ml. water                          | 0.481             | 96 |
| 0.50            | 50 ml. 95% ethanol | 5 ml. water + 5 ml. of aq. 0.08M HCl | 0.45              | 90 |
| 0.65            | 35 ml. acetic acid | 15 ml. water                         | 0.58              | 89 |



crystallize compound III from ethanol-water solutions likewise yielded benzil anil.

The synthesis of compound III provides another example of formation of a boron-nitrogen bond at the expense of a boron-oxygen bond.<sup>2</sup> With respect to the reaction path leading to the oxazaborole, two stable substances, benzoin anil and compound II, appeared to be possible intermediates. Evidence that neither is in fact an intermediate was gained by heating toluene solutions of (a) benzoin anil and benzeneboronic anhydride and (b) compound II and aniline. In neither case was compound III formed; the starting materials were isolated in high yield. It is also of interest that compound II failed to react with *o*-phenylene diamine in hot toluene. By contrast, the boronic acids and their esters generally react readily with *o*-phenylenediamine to give dihydrobenzoboradiazoles.<sup>2</sup>

#### EXPERIMENTAL

Melting points were taken on a Fisher-Johns melting point block and are uncorrected. Carbon, hydrogen, and nitrogen analyses were performed by Miss Hilda Beck unless otherwise indicated. The infrared spectra were determined with a Baird double-beam recording spectrophotometer with the sample in potassium bromide, and the ultraviolet spectra were taken with a Beckman ratio recording spectrophotometer, Model DK-2.

**Reaction with chloral hydrate.** A solution containing 2.0 g. of benzeneboronic acid and 2.71 g. of chloral hydrate in 50 ml. of chloroform was partially distilled below 30° at reduced pressure to remove the water liberated in the reaction. Pentane was added, the solution filtered, and pentane removed at reduced pressure until a crystalline product (I) appeared: 2.44 g. (84%), m.p. 116–117°. The infrared spectrum had neither hydroxyl nor carbonyl bands, but showed absorption at 7.4  $\mu$  (B—O). Strong bands present at 8.8, 11.9, 12.1, 14.9, and 15.1  $\mu$  were absent in the spectrum of benzeneboronic anhydride. Conversely, the anhydride absorbed strongly at 9.15  $\mu$  while compound I did not.

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{11}\text{O}_2\text{Cl}_2\text{B}$ : C, 47.4; H, 3.12; neut. equiv., 177.6; mol. wt., 355.2. Found: C, 47.4; H, 3.21; neut. equiv. (with mannitol) 179; mol. wt. 361.

A sample of compound I (0.5203 g.) was heated at 150–160° for 18 hr. in a nitrogen atmosphere; weight after heating, 0.2744 g. (90% calcd. as the boroxine); m.p. 210–215°. After sublimation at reduced pressure the boroxine melted at 214–216° and did not depress the melting point of an authentic sample of triphenylboroxine (benzeneboronic anhydride).

**2,4,5-Triphenyl-1,3,2-dioxaborole (III).** A toluene solution (50 ml.) containing 2.44 g. of benzeneboronic acid and 4.24 g. of benzoin was heated in a flask fitted with a take-off adapter to remove the water azeotrope. Toluene was then

removed *in vacuo* until the product solidified. Recrystallization from pentane yielded 5.43 g. (91%) of purified material, m.p. 112–113°;  $\lambda_{\text{max}}$  (in cyclohexane), 285  $\text{m}\mu$  ( $\epsilon$  16,500), 242  $\text{m}\mu$  ( $\epsilon$  12,800), 220  $\text{m}\mu$  ( $\epsilon$  25,000). The wave length and intensity of the main band (285) were greater than for closely related substances such as *cis*-stilbene- $\alpha,\beta$ -diol diacetate,<sup>10</sup> catechol benzeneboronate ( $\lambda_{\text{max}}$  273  $\text{m}\mu$ ,  $\epsilon$  14,720, in cyclohexane), and *meso*-hydrobenzoin benzeneboronate ( $\lambda_{\text{max}}$  268  $\text{m}\mu$ ,  $\epsilon$  865, in cyclohexane), in accord with the idea that the dioxaborole system possesses a degree of aromatic character. The infrared spectrum had bands at 6.1  $\mu$  (C=C) and 7.4  $\mu$  (B—O) and no bands in the hydroxyl or carbonyl regions.

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{15}\text{BO}_2$ : C, 80.58; H, 5.07; neut. equiv., 298. Found: C, 80.64; H, 5.16; neut. equiv. (titration in the presence of mannitol), 294.

Compound II neither dissolved directly in cold, concd. sulfuric acid nor was it extracted from a pentane solution which was shaken with sulfuric acid. By contrast, benzoin and hydrobenzoin readily dissolved in sulfuric acid to give deeply colored solutions.

Solid samples of compound II which were exposed to sunlight in the presence of air acquired a deep yellow color on the surface after a few days, presumably as a result of conversion to benzil.

**Alkaline oxidation of compound II and benzoin.** Data on yields, quantities of reagents, and times of reaction are given in Table I. The conditions were the same in all cases except where noted in the table. As a representative example, the reaction of compound II is described in detail.

Compound II (1.50 g.) was dissolved in 75 ml. of hot 95% ethanol into which oxygen was bubbling. After addition of 20 ml. of 0.074M sodium hydroxide (an intense yellow color appeared when the alkali was added) the solution was refluxed for 5 min., diluted with water to precipitate neutral organic products, cooled, concentrated at reduced pressure, and filtered. The precipitate, 0.72 g., m.p. 95.5–96.5°, did not depress the melting point of an authentic sample of benzil. A second crop of crystals, obtained by further concentration of the solution, yielded on fractional crystallization from pentane 0.025 g. of benzil and 0.08 g. of benzoin. Acidification of the aqueous solution and extraction with ether afforded a white solid which on drying gave 0.28 g. of benzeneboronic anhydride, identified by its melting point (214–216°) and infrared spectrum.

**Nitric acid oxidation of compound II.** To 0.50 g. of the dioxaborole suspended in 10 ml. of glacial acetic acid at 30° was added a mixture of 1 ml. of concentrated nitric acid and 4 ml. of acetic acid. The dioxaborole rapidly dissolved and the solution became intensely yellow. After 3 min. benzil was precipitated by dilution with water; 0.34 g., m.p. 94–95°. Partial neutralization (to about pH 6) of the filtrate with sodium hydroxide and ether extraction gave 0.17 g. (98%) of benzeneboronic anhydride, m.p. 214–216°.

A sample of benzoin (0.36 g.) in a mixture of 14 ml. of acetic acid and 1 ml. of nitric acid did not produce a yellow

(10) L. F. Fieser, *Experiments in Organic Chemistry*, 3rd Ed., D. C. Heath and Co., (1957), pp. 170–180.

(11) The carbon analysis was performed by the Huffman Microanalytical Laboratory, Wheatridge, Colo., by the "moist oxygen" technique. Conventional combustion analysis for carbon was unsatisfactory.

color within an hour period. Addition of water then reprecipitated benzoin, 0.35 g. (98% recovery).

*meso-Hydrobenzoin benzeneboronate.* This compound was prepared in the same manner as compound II except that 2.13 g. of *meso*-hydrobenzoin and 1.22 g. of benzeneboronic acid were used as reactants; weight, 2.58 g. (90%), m.p. 92–93°.

*Anal.* Calcd. for  $C_{20}H_{17}BO_2$ : C, 80.2; H, 5.72; neut. equiv., 300. Found: C, 81.0; H, 5.80; neut. equiv. (titration in presence of mannitol), 304.

A sample of ester (0.4085 g.) was dissolved in 50 ml. of ether and shaken with 20 ml. of 1M sodium hydroxide. By conventional procedures there were obtained 0.283 g. (98%) of *meso*-hydrobenzoin, m.p. 133.5–135°, from the ether layer and 0.14 g. (99%) of benzeneboronic anhydride, m.p. 218–220°, from the aqueous layer.

*Recrystallization of compound II from hydroxylic solvents.* (See Table II.) These recrystallizations were carried out with solvents which had previously been boiled to remove dissolved oxygen. Thereafter a slow stream of nitrogen was bubbled through the solutions and a nitrogen atmosphere maintained until the precipitate had been collected. In each case compound II was dissolved in the hot organic solvent; water or dilute hydrochloric acid was then added and the resulting solution was boiled for a few minutes and allowed to cool. Compound II crystallized and was collected by filtration, m.p. 113–114°.

*Attempted preparation of compound II in aqueous ethanol.* A solution containing 0.205 g. of benzeneboronic acid, 0.365 g. of benzoin, 20 ml. of 95% ethanol, and 5 ml. of water was refluxed for 5 min. and then cooled in an ice bath. No crystals formed; if compound II had been present it should have separated at this stage (see previous experiment on recrystallization of compound II). On addition of 40 ml. of distilled water benzoin, 0.350 g. (98%), m.p. 127–131°, separated; it did not depress the melting point of an authentic sample of benzoin.

*Hydrolysis of compound II. (a) In alkaline solution.* Nitrogen gas was passed through a hot solution consisting of 25 ml. of 95% ethanol, 5 ml. of distilled water, and 5 ml. of 0.074M sodium hydroxide. Compound II (0.50 g.) was added and the resulting solution cooled. From the mixture were isolated compound II (28%), benzoin and benzeneboronic anhydride (products from hydrolysis of II) in 42% and 52% yield, respectively, and benzil (product of oxidation) in 11% yield.

*(b) Estimation of minimum half-life of hydrolysis.* (Method of Steinberg and Hunter<sup>6</sup>). In each case a solution containing 70 ml. of dioxane, 5 ml. of distilled water, 2.72 ml. of 0.0740M solution hydroxide (0.200 mmole), and 2.0 g. of mannitol was heated to the boiling point, saturated with nitrogen gas, and cooled to 15°. Three drops of a phenolphthalein indi-

cator solution and 0.400 mmole of the boronic acid derivative were added in succession. The boron compounds dissolved almost immediately. The time lapse between addition of the sample and the disappearance of the indicator color was too short to measure for the catechol and *meso*-hydrobenzoin esters of benzeneboronic acid. For compound II it was 24 sec.

*2,3,4,5-Tetraphenyl-1,3,2-oxazaborole (III).* A toluene solution (50 ml.) containing 1.22 g. of benzeneboronic acid, 2.12 g. of benzoin, and 0.93 g. of aniline was heated to reflux at room temperature, the water azeotrope removed, and the toluene removed at reduced pressure. Recrystallization of the resulting solid from hexane yielded 3.07 g. (77%) of a white crystalline product (III); m.p. in a sealed capillary tube in a nitrogen atmosphere, 183–185°; m.p. on a Fisher-Johns block in air, 134–167° (slow heating), 164–175° (rapid heating). Evaporation of the hexane mother liquors and recrystallization of the resulting solid from ethanol-water afforded 0.53 g. (17%) of compound II, m.p. 112–113°. The infrared spectrum of product III had bands at 6.1  $\mu$  (C=C) and 7.4  $\mu$  (B—O or B—N) and no bands attributable to OH, NH, or C=O; it differed also from the spectrum of compound II. The ultraviolet spectrum resembled that of compound II in having a broad absorption band with  $\lambda_{max}$  284 m $\mu$ ,  $\epsilon$  24,200 (in cyclohexane) and a minimum about 245 m $\mu$ , however, it lacked a second maximum in the region of 242 m $\mu$ .

*Anal.* Calcd. for  $C_{28}H_{20}ONB$ : C, 83.7; H, 5.40; N, 3.75. Found: C, 83.4;<sup>10</sup> H, 5.02; N, 3.15.

Compound III (0.50 g.) was dissolved in 20 ml. of benzene and allowed to stand for 4 days in the presence of air. Ether was added and the solution extracted with dilute sodium hydroxide. The organic layer was dried with magnesium sulfate, treated with charcoal to reduce the color, and distilled at reduced pressure until crystallization set in. On recrystallization from pentane 0.29 g. (75%) of benzil anil, m.p. 106–107.5° (lit.<sup>12</sup> m.p. 106–108°), was obtained.

*Reaction with mandelic acid.* Equimolar quantities of benzeneboronic acid (1.22 g.) and mandelic acid (1.52 g.) were heated to reflux in 25 ml. of toluene and the water azeotrope removed. The solid obtained on concentrating the solution afforded, after recrystallization from pentane, 1.44 g. (60%) of a compound melting at 124–125° (see footnote 3).

*Anal.* Calcd. for  $C_{14}H_{11}O_3B$ : C, 70.6; H, 4.66; neut. equiv., 116. Found: C, 70.7; H, 4.82; neut. equiv. (mannitol present), 118.

EVANSTON, ILL.

(12) M. Siegfried, *Ber.*, 25, 2600 (1892).