# **608.** *Esters Containing Boron and Selenium.*

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Tri-(2-fluoroethyl) borate is a toxic liquid, the physiological action of which is attributable to its ready hydrolysis to fluoroethanol. Diethyl ether–boron trifluoride complex reacts with tri-*n*-butyl borate; one of the products appears to be impure di-*n*-butyl fluoroboronate, $F{\cdot}B(OEt)_2$.

2 : 2′-Dichlorodiethyl selenite is a relatively non-toxic low-melting solid.

For certain purposes during the war, we prepared a number of esters containing boron. A convenient starting material for these compounds is boron triacetate, $B(OAc)_3$ (Pictet and Geleznoff, *Ber.*, 1903, **36**, 2219), which is essentially a mixed anhydride of boric acid and acetic acid. In general, heating the triacetate with an alcohol gave the corresponding ester of boric acid. The following were readily obtained in this way: tri-*n*-propyl, tri-*n*-butyl, tri-(2-fluoroethyl), tribenzyl, and tri*cyclo*hexyl borates. Attempts to obtain the *iso*propyl and tertiary esters by alcoholysis of boron triacetate were not very successful (but see below). All these esters, except tri*cyclo*hexyl borate, were readily hydrolysed by water.

Tri-(2-fluoroethyl) borate, $B(O{\cdot}CH_2{\cdot}CH_2F)_3$, was submitted for physiological tests since bisfluoroethyl fluorophosphonate had already been shown to produce a remarkable state of hyperactivity in rats (McCombie and Saunders, *Nature*, 1946, **158**, 382). Batches of rabbits, guinea-pigs, rats, and mice were exposed to the vapour of the borate with the following results:

*Ct.* of 5000 mg./min./m.$^3$ ($t = 10$) killed 74%
,, ,, 2000 ,, ,, ,, 57%
,, ,, 1000 ,, ,, ,, 86% (rabbits and guinea-pigs only exposed)
,, ,, 500 ,, ,, ,, 0% (all varieties)

The symptoms produced were of the " fluoroacetate " type and the above figures suggest that the toxicity of the ester is due almost entirely to the fluoroethanol produced by hydrolysis (cf. Saunders, Stacey, and Wilding, *J.*, 1949, 773).

Schiff (*Annalen*, supplement **5**, 1867, 158) described an alternative method for preparing alkyl borates. He obtained triethyl borate in fair yield by heating boric anhydride and ethyl alcohol in an autoclave for 24 hours : $B_2O_3 + 3EtOH = B(OEt)_3 + B(OH)_3$. We have found that by the use of a rotating autoclave (see Saunders and Stacey, *J.*, 1948, 1773) the time of heating could be reduced to 6 hours and that Schiff's yield could be improved. Tri*iso*propyl borate was easily prepared by this method.

Gasselin (*Ann. Chim. Physique*, 1894, [vii], **3**, 46) prepared diethyl fluoroboronate, $F{\cdot}B(OEt)_2$, by the action of boron trifluoride on triethyl borate. Owing to the difficulty of measuring the calculated quantity of gaseous boron trifluoride necessary to ensure the non-formation of ethyl difluoroboronite, $F_2B{\cdot}OEt$, it seemed to us that a more convenient fluorinating agent might be an ether–boron trifluoride complex. We therefore directed our attention to the formation of such liquid complexes, in particular those from diethyl and di*iso*amyl ether. The latter complex, which does not seem to have been described, is more stable that the diethyl ether complex. The intention was to bring about the reaction $R_2O,BF_3 + 2B(OR')_3 = 3F{\cdot}B(OR')_2 + R_2O$. Diethyl fluoroboronate is described by Gasselin as a very unstable compound, and efforts were therefore made to prepare a more stable member of the series. In attempting to make dibenzyl fluoroboronate the product, however, decomposed on distillation. A smooth reaction took place between the ether complex and tri-*n*-butyl borate and a colourless fuming liquid was obtained which from its reactions seemed to be essentially di-*n*-butyl fluoroboronate, $F{\cdot}B(OBu^n)_2$, but analysis indicated that it tended to decompose after successive distillations. It is probable that it undergoes slow disproportionation into *n*-butyl difluoroboronite and tri-*n*-butyl borate. The ready disproportionation of mixed orthoborates has already been noted by Thomas (*J.*, 1946, 823).

The instability of the di-*n*-butyl fluoroboronate is of interest as the corresponding compound of phosphorus, namely diethyl fluorophosphinate, $F{\cdot}P(OEt)_2$, is also unstable and readily hydrolysed by water. It is worthy of note that the slightly greater stability of tri*cyclo*hexyl borate compared with the trialkyl borates is paralleled approximately by the greater stability of di*cyclo*hexyl hydrogen phosphite compared with the dialkyl hydrogen phosphites towards sodium hydroxide solution.

In Part IX on Esters containing Phosphorus (Cook *et al.*, *J.*, 1949, 2921) attention was drawn to the possibility of tautomerism of a hydrogen phosphite with a phosphonate, $H{\cdot}PO(OR)_2 \rightleftharpoons (RO)_2P{\cdot}OH \xrightarrow{OH^-} (RO)_2PO^-$ (the second stage not being reversible). While this is still considered a possibility, it should be emphasised that the action of alkali on certain hydrogen phosphites may also involve the partial hydrolysis of the ester (cf. Milobedzki and Szwejkowka, *Chemik. Polski*, 1917, **15**, 56). On the other hand, Janczak (*Roczniki Chemji*, 1924, **4**, 180) has shown that a hydrogen phosphite can react with its sodium salt according to the equation $(RO)_2P{\cdot}OH + (RO)_2P{\cdot}ONa = (RO)(ONa)P{\cdot}OH + P(OR)_3$.* As a result of this change, Janczak states that the sodium dialkyl phosphite has the same structure as the trialkyl phosphite, *i.e.*, the former contains tervalent phosphorus. This lends some support to the previous observation that one action of alkali on a dialkyl phosphite may perhaps be to facilitate the tautomeric change referred to above. Nevertheless caution must be exercised in drawing definite conclusions from chemical methods. Considerably more work is required on the kinetics of the reaction, and in any case the true structure of the hydrogen phosphites can probably be deduced with certainty only by physical measurements such as infra-red analysis already referred to in Part IX (*loc. cit.*).

Ethoxyselenium oxychloride (or ethyl chloroseleninate), $EtO{\cdot}SeO{\cdot}Cl$, was prepared by a modification of the method of Michaelis and Landmann (*Annalen*, 1887, **241**, 156). It proved to be slightly irritant by inhalation and a *Ct.* of 10,000 mg./min./m.$^3$ ($t = 10$) killed only 3 of a batch of 23 small animals. The toxicity was therefore of a low order.

When selenium oxydichloride and 2 moles of ethylene chlorohydrin were heated together and the product distilled at low pressure in an atmosphere of carbon dioxide, 2 : 2'-dichlorodiethyl selenite, $(ClCH_2{\cdot}CH_2{\cdot}O)_2SeO$, was obtained as a low-melting, deliquescent, white solid. The material when sprayed in ether formed a fine fog which was only slightly irritant. A *Ct.* of 10,000 mg./min./m.$^3$ ($t = 10$) killed only 2 of a batch of 23 small animals.

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* In aqueous solution certain trialkyl phosphites will subsequently be hydrolysed to the alcohol and hydrogen phosphite, and the latter in the presence of alkali will give $(RO)(ONa)P{\cdot}OH$.

## EXPERIMENTAL.

*Boron Triacetate* (cf. Pictet and Geleznoff, *Ber.*, 1903, **36**, 2219).—Boric acid (200 g., 1 mol.) and acetic anhydride (1200 g., 3·5 mols.) were mixed in a three-l., three-necked flask fitted with a reflux condenser and a thermometer. The mixture was warmed gently, and at about 35° the boric acid flocculated and at 45—60° the reaction began. (This was indicated by the appearance of boric acid on the surface of the liquid and it was advisable to stop heating at this juncture, and cool if necessary.) After the reaction had subsided (5—10 minutes), the mixture was heated under reflux until the solid dissolved and then the resultant solution was allowed to cool, whereupon boron triacetate crystallised out. Traces of acetic acid were removed by washing the crystals with dry ether. The product soon developed a smell of acetic acid if exposed to the atmosphere. Further quantities were obtained from the mother-liquor by concentration and by precipitation with ether. The yield was 250 g. (87%). Boron triacetate forms colourless crystals, m. p. 120°, with no smell when pure. It is readily hydrolysed and alcoholysed.

Analyses of the following compounds were carried out (1) by hydrolysis and titration of the boric acid thus formed, in the presence of mannitol and phenolphthalein as indicator, against standardised sodium hydroxide: $B(OR)_3 + NaOH + H_2O = NaBO_2 + 3ROH$, (2) by carbon and hydrogen combustions (in which carbon percentages tended to be erratic), and (3) by determination of fluorine in the case of fluoroethyl borate where it was found that boron did not interfere with the standard analysis as PbClF (Chapman, Heap, and Saunders, *Analyst*, 1948, **73**, 860).

*Tri-*n*-propyl Borate.*—Boron triacetate (30 g., 1 mol.) was dissolved in cold *n*-propyl alcohol (135 g., 3 mols.), and the solution fractionally distilled. The first fraction consisted of acetic acid, b. p. 118°, and the second (which was refractionated) was *n*-propyl borate (18 g., 60%), b. p. 177° (Found: B, 5·9. Calc. for $C_9H_{21}O_3B$: B, 5·85%). Tri-*n*-propyl borate is a colourless liquid possessing a sweet ester-like smell and is readily hydrolysed by water.

Tri-*n*-butyl borate was similarly prepared in 70% yield, and had b. p. 115°/15 mm. (Found: C, 61·9; H, 12·0; B, 5·0. Calc. for $C_{12}H_{27}O_3B$: C, 62·9; H, 11·8; B, 4·8%).

*Tri-(2-fluoroethyl) Borate.*—Boron triacetate (30 g., 1 mol.) was dissolved in cold fluoroethyl alcohol (131 g., 3 mols.) and fractionated. There was some difficulty in distillation as much decomposition was experienced initially. Eventually a small yield of the pure *fluoroethyl borate*, b. p. 173°, was obtained (Found: C, 36·9; H, 5·9; F, 27·0; B, 5·7. $C_6H_{12}O_3F_3B$ requires C, 36·0; H, 6·0; F, 27·5; B, 5·5%). It was readily hydrolysed by cold water.

*Tri*cyclo*hexyl Borate.*—Boron triacetate (30 g., 3 mols.) was dissolved in *cyclo*hexanol (50 g., 3 mols.) by gentle warming. The liquid was fractionally distilled; the residue, after removal of acetic acid, solidified. The borate (25 g., 80%), recrystallised from light petroleum (b. p. 100—120°), had m. p. 54°, b. p. 203°/17 mm. Tri*cyclo*hexyl borate forms white crystals, slowly hydrolysed by water (Found: C, 69·0; H, 10·4; B, 3·6. Calc. for $C_{18}H_{33}O_3B$: C, 70·0; H, 10·6; B, 3·55%).

*Tribenzyl borate*, prepared in a similar manner (88%), had b. p. 255°/17 mm. (Found: B, 3·3. $C_{21}H_{21}O_3B$ requires B, 3·3%). It shows a slight blue fluorescence, is rather viscous, has a sweet smell, and is readily hydrolysed.

*Preparation of Triethyl Borate in a Rotating Autoclave.*—Boric anhydride (75 g., slight excess) was heated with ethyl alcohol (128 g.) in a rotating autoclave at 100—110° for 6 hours. The product was extracted with ether, the solution filtered, and the ether distilled off. Unchanged alcohol (20 g.) was obtained in the range 75—117°. After two distillations of the residue, 44 g. (30%) of the borate of b. p. 117—118° were obtained (Found: C, 49·7; H, 10·7; B, 7·6. Calc. for $C_6H_{15}O_3B$: C, 49·5; H, 10·2; B, 7·5%).

Tri*iso*propyl borate, prepared in a similar manner from boric anhydride (75 g.) and *iso*propyl alcohol (180 g.) at 125—135° for 6 hours (yield, 40 g.), had b. p. 139—140° (Found: B, 6·0; 6·0. Calc. for $C_9H_{21}O_3B$: B, 5·85%).

*Boron Trifluoride.*—Boron trifluoride was obtained by heating potassium borofluoride with an excess of concentrated sulphuric acid. The issuing gases were first passed up a reflux condenser, then through a wash-bottle containing concentrated sulphuric acid saturated with boric oxide and boron trifluoride, and finally through glass wool into the substance under experiment, contained in a vessel readily detachable for weighing purposes. Ground-glass joints were used throughout, as rubber connections were readily attacked.

*Complex between Diethyl Ether and Boron Trifluoride.*—Boron trifluoride was passed into anhydrous diethyl ether (150 g., 1 mol.) and after 4 hours an uptake of 55 g. was obtained. Heat was evolved during the reaction. The solution was distilled and a fraction, b. p. 126—127° (195 g.), obtained. Redistilled, this had b. p. 126°. Further quantities of boron trifluoride were passed through the compound which then again distilled at 126° and, under reduced pressure in an atmosphere of nitrogen, at 75°/70 mm. The complex is a colourless fuming liquid, immediately hydrolysed by cold water, depositing boric acid which dissolves in excess of water.

*Complex between Di*iso*amyl Ether and Boron Trifluoride.*—Pure di*iso*amyl ether, obtained by drying over metallic sodium followed by distillation, had b. p. 170—171°. Boron trifluoride was passed, as above, into *iso*amyl ether (20 g., 1 mol.) and in 30 minutes an uptake of 8·6 g. (1 mol.) was obtained. The solution was distilled under reduced pressure in an atmosphere of nitrogen. The uptake was theoretical for a compound $(C_5H_{11})_2O,BF_3$. The complex, a colourless liquid, b. p. 78—79°/22 mm., with a sweet smell resembling that of the pure ether, is completely hydrolysed by excess of cold water in 5 minutes.

*Action of Diethyl Ether–Boron Trifluoride Complex on Benzyl Borate.*—The formula, $Et_2O,BF_3$, was assumed, and an excess of benzyl borate to favour the formation of dibenzyl fluoroboronate was used. The complex (4 g., 1 mol.) and benzyl borate (20 g., 2·2 mols.) were dissolved in ether (10 c.c.), and the solution heated under reflux for 4 hours. After removal of ether, attempts were made to distil the resultant liquid, but a violent reaction occurred at about 100°.

*Action of Diethyl Ether–Boron Trifluoride Complex on* n-*Butyl Borate*.—The complex (6 g., 1 mol.) and butyl borate (21 g., 2·2 mols.) were dissolved in absolute ether (20 c.c.), and the solution heated under reflux for 6 hours. The ether was removed and the residual liquid fractionated under reduced pressure. Fractions were obtained as follows : (i) b. p. 50°/30 mm. (ether–boron trifluoride complex) ; (ii) b. p. 72°/15 mm. ; (iii) b. p. 120°/15 mm. (*n*-butyl borate). Fraction (ii) was redistilled giving a liquid of b. p. 77°/18 mm. This *product* was a colourless fuming liquid, immediately hydrolysed by cold water, and its general reactions were in accordance with the formula, $F\cdot B(OBu^n)_2$ (Found : F, 10·0. $C_8H_{18}OFB$ requires F, 10·8%. $C_4H_9OBF_2$ requires F, 31·2%). Redistillation of the product did not alter the b. p. appreciably, but the fluorine content tended to rise above the theoretical value for di-*n*-butyl fluoroboronate. At the same time a fraction of higher b. p. and lower fluorine content was also obtained. This was probably due to a disproportionation. (It should be noted that the b. p.s of diethyl fluoroboronate and ethyl difluoroboronite are only 4° apart.)

Ether–boron trifluoride complex (10 g., 1 mol.) and butyl borate (30 g., 2·2 mols.), initially immiscible, were heated under reflux until homogeneous (20 hours). The resultant liquid was distilled under reduced pressure in an atmosphere of nitrogen, giving as above a middle fraction, b. p. 90°/40 mm., together with large fractions of unchanged reactants. The middle fraction was distilled and gave a liquid of b. p. 77°/20 mm.

*Ethyl Chloroseleninate*.—To ethyl alcohol (138·2 g., 3·0 mols.) was added slowly selenium oxydichloride (33·2 g., 0·2 mol.). The mixture was heated under reflux on the water-bath for 30 minutes and then the excess of alcohol was distilled off. The clear orange-coloured residue was distilled under reduced pressure in a stream of carbon dioxide in an all-glass apparatus. After the last traces of alcohol had come over, the remainder of the liquid distilled at 86—88°/17 mm., a quantity of brownish solid being deposited on the sides of the distilling-flask. The yield was 29·4 g. (83%). Redistillation gave a product of b. p. 89·5°/17 mm. (Found : Cl, 20·9. Calc. for $C_2H_5O_2ClSe$ : Cl, 20·2%).

2 : 2′-*Dichlorodiethyl Selenite*.—To ethylene chlorohydrin placed under reflux, selenium oxydichloride (24·9 g., 0·15 mol.) was slowly added. The mixture was heated in an oil-bath at 130° for 30 minutes during which hydrogen chloride was evolved. The excess of ethylene chlorohydrin was distilled off under reduced pressure in a stream of carbon dioxide. The residual oil, after filtration, was distilled in an all-glass apparatus. The distillate was collected in the following fractions : a small quantity below 87°/0·1 mm. ; a brown viscous liquid, b. p. 87—126°, as the pressure changed from 0·1 to 0·3 mm. ; and a larger fraction at 126°/0·3 mm. The last fraction gave white crystals on cooling (16·8 g.) ; on redistillation, the greater part came over at 118°/0·15 mm. In all these distillations dry carbon dioxide was admitted through the air-leak and decomposition was then almost negligible, although discoloration caused by traces of free selenium was observed. The product, which was extremely deliquescent, could be recrystallised, giving white needles from a mixture of carbon tetrachloride and light petroleum (b. p. 60—80°), but this was not very satisfactory owing to the rapidity with which water was taken up. The m. p. of the 2 : 2′-*dichlorodiethyl selenite* was 44—45° (Found : Cl, 27·3; Se, 31·3. $C_4H_8O_3Cl_2Se$ requires Cl, 27·9; Se, 31·1%). The selenium was estimated by Bauer's method (*Ber*., 1915, **48**, 507) after breaking the compound down to selenious acid by heating it in a sealed tube with fuming nitric acid for 6 hours at 280°. Addition of aqueous silver nitrate to the aqueous solution of the selenite gave a white precipitate which redissolved on addition of concentrated nitric acid.

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