[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE]

ARENEBORONATES FROM DIOLS AND POLYOLS[1]

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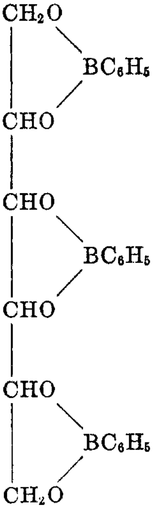
Received October 5, 1953

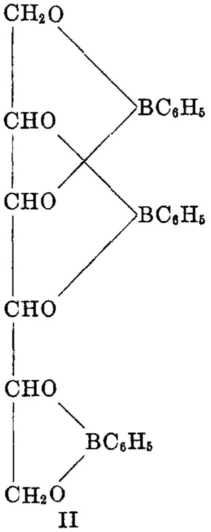
In the course of some investigations with aromatic boronic acids it was observed that when a saturated solution of mannitol was shaken with excess solid benzeneboronic acid the latter did not dissolve, as was expected. Instead the relatively dense boronic acid was replaced by a rather voluminous precipitate. This proved to be a new substance containing boron, as shown by its acidity when dissolved in a solution of mannitol. The neutral equivalent and carbon-hydrogen analyses indicated the formation of an ester of the boronic acid:

$$C_6H_5B(OH)_2 + C_6H_{14}O_6 \rightleftarrows 3\,H_2O + (C_6H_5B)_3O_6C_8H_8.$$

The most probable structure for the product would appear to be I resulting from ester formation involving adjacent hydroxyl groups. At least two alternatives need to be considered, namely a polymeric ester and one involving the formation of six-membered ester rings, such as II. The former can be discarded on the basis of molecular weight determination made on the corresponding product from *p*-tolueneboronic acid which corresponds to the molecular formula of I or II. A structure like II appears to be possible on steric grounds and cannot be rigorously excluded on the basis of available information.



I



II

Esters of this type have been made from mannitol, sorbitol, catechol, pinacol, pentaerythritol, and *cis*-indan-1, 2-diol simply by mixing hot nearly saturated solutions of the reactants. A number of other hydroxylic compounds have been

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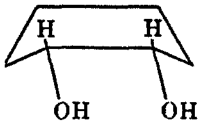
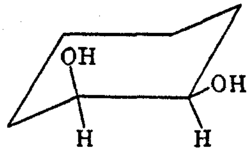
[1] From the M. Sc. thesis of A. H. Keough, September 1951, and the B. Sc. thesis of E. J. Soboczenski, June 1952.

investigated. These include D-glucose, sucrose, maltose, D-fructose, D-galactose, L-ascorbic acid, inositol, D-xylose, D-mannose, D-ribose, gluconic acid, salicylic acid, *o*-aminophenol, diphenacyl D-tartrate, citric acid, and *cis*-cyclohexane-1, 2-diol. In each case one or the other of the reactants precipitated on cooling the reaction mixture. Thus the scope of this simple method of preparing boronates is rather limited. This is not surprising since the separation of the ester from solution will depend on the value of the equilibrium constant for the formation of the ester and the relative solubilities of reactants and ester.

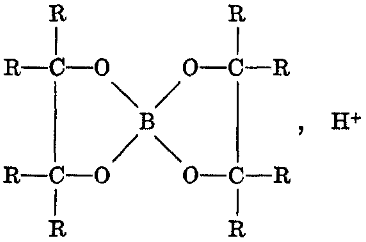
In general, when all of the hydroxyl groups of the di- or poly-ol can become involved in cyclic ester formation (*e.g.*, mannitol, pinacol, diphenacyl D-tartrate) the product should be less soluble than either of the reactants. Consequently the absence of ester formation in the case of *cis*-cyclohexane-1, 2-diol must be due to an unfavorable equilibrium. *cis*-Indan-1, 2-diol, on the other hand, reacts to give an almost quantitative yield of ester. This striking difference must be due to the puckering in the cyclohexane ring. In only one (structure III) of the many possible conformations do the carbon-oxygen bonds lie in the same plane and this requires the unstable boat conformation. In all others, such as IV, the carbon-oxygen bonds lie in different planes; one hydroxyl group is polar and the other is equatorial. The effect of these diols on the conductivity of boric acid solutions provides a close analogy. Bōeseken has shown that *cis*-indan-1, 2-diol increases the conductivity markedly, whereas *cis*-cyclohexane-1, 2-diol decreases it slightly (1). An increase in conductivity is attributed to the formation of a chelate complex, V.



III



IV



V

The stabilities of the esters from mannitol, catechol, sorbitol, and pinacol in water are in accord with the stabilities of the respective boric acid complexes (2, 3).

The benzeneboronate of diethyl D-tartrate was prepared by mixing the reactants and distilling off water. This compound hydrolyzed very rapidly when added to water. Its low stability is in marked contrast to that of the pinacol ester. This is surprising since the cyclic ester from the D-tartrate has the carbethoxy groups in the *trans* configuration.

Of the monosaccharides used D-fructose (3) and α-D-glucose (4) are known to increase the acidity of boric acid. Only one pair of hydroxyl groups in each case is available, by virtue of *cis* configuration, for cyclic ester formation. D-Galactose, if in the α-hemiacetal configuration, has two pairs of hydroxyl groups in the necessary configuration. This would seem to indicate that puckering of the pyranose ring may be an important mitigating factor. In the chair conformation adjacent *cis* groups are alternately polar and equatorial.

No information on borate complexes of tartrate esters appears to be available for comparison with the very low hydrolytic stability of the boronate. The non-appearance of an insoluble compound from salicylic acid is surprising in view of the ease of formation of salicylate-boric acid complexes (5).

EXPERIMENTAL

Mannityl tri-p-bromobenzeneboronate. To a warm solution of 3.7 g. (0.018 mole) of *p*-bromobenzeneboronic acid in 10 ml. of methanol was added a solution of 1.2 g. (0.007 mole) of mannitol in 10 ml. of water. A white solid appeared immediately. After 10 minutes the product was filtered, washed with hot water followed by cold methanol, and then dried at 105–110°. The dry solid was then crystallized from 20 ml. of 1:1 methanol-benzene. This procedure was used in making the indandiol, mannitol, and sorbitol esters.

It is important to add the mannitol solution to the boronic acid solution in order to maintain an excess of boronic acid in the reaction mixture. If the addition is reversed the boronate ester contains fewer than three boronate residues per molecule.

With benzeneboronic acid, water can be used as solvent. This was done in the reactions with catechol and pentaerythritol.

Pinacyl benzeneboronate. Pinacol hydrate (10 g., 0.044 mole) and 4.7 g. (0.045 mole) of benzeneboronic anhydride were placed in a 50-ml. Claisen flask and warmed on the steam cone. When the mixture became liquid the flask was fitted with a capillary and the water

TABLE I

ARENEBORONATES *via* $RB(OH)_2$ + AN ALCOHOL

R	ALCOHOL	YIELD, %	M.P., °C[a].	$[\alpha]_D^{25\pm1°}$	FORMULA	ANALYSES					
						Neut. Equiv.		C[b]		H	
						Calc'd	Found	Calc'd	Found	Calc'd	Found
C_6H_5-	Sorbitol	66	187–190	+39.6	$C_{24}H_{23}B_3O_6$	146.6	150.6	65.53	63.02	5.27	5.34
C_6H_5-	Mannitol	66	134–135	+53.4	$C_{24}H_{23}B_3O_6$	146.6	148.4	65.53	64.76	5.27	5.18
p-$CH_3C_6H_4$-	Mannitol	70	162–164	+45.9	$C_{27}H_{29}B_3O_6$[c]	160.6	165.2	67.29	66.19	6.06	6.05
p-ClC_6H_4-	Mannitol	73	184–185	+45.4	$C_{24}H_{20}B_3Cl_3O_6$	180.7	182.6	53.15	50.28	3.70	3.97
p-BrC_6H_4	Mannitol	74	204–205	+35.1	$C_{24}H_{20}B_3Br_3O_6$	225.6	222.9	42.60	42.55	2.98	3.34
C_6H_5-	Pinacol	59	29–30[d]	—	$C_{12}H_{17}BO_2$	204.1	205.5	70.62	67.88	8.40	8.35
C_6H_5-	*cis*-Indan-1,2-diol	96	107.5–108.5	—	$C_{15}H_{13}BO_2$	237.1	236.8	76.31	74.93	5.55	6.17
C_6H_5-	Diethyl D-tartrate	89	46–48[e]	—	$C_{14}H_{17}BO_6$	292.1	292.3	57.56	56.15	5.87	6.20
C_6H_5-	Catechol	57	111–112	—	$C_{12}H_9BO_2$	196.01	[f]	73.51	73.44	4.63	4.63
C_6H_5-	Pentaerythritol	93	207–208	—	$C_{17}H_{18}B_2O_4$	154.0	156.3	66,08	66.38	5.93	5.88

[a] Melting points are uncorrected. [b] Low values for carbon are often obtained in analysis of boronic acid derivatives due to formation of boron carbide which is oxidized with difficulty even at 1000°, *cf.*, Snyder and Weaver, *J. Am. Chem. Soc.*, **70**, 232 (1948). [c] Molecular weight: Calc'd, 482.1; Found, 453 (benzene). [d] B.p. 128–130°/20 mm. [e] B.p. 197°/11 mm. [f] Catechol apparently interferes with the titration leading to low values.

was removed at reduced pressure (aspirator). After 2 to 3 hours the steam cone was replaced by an oil-bath and the boronate was distilled twice yielding 5.6 g. (59%), b.p. 128–130°/20 mm. Upon standing in the refrigerator for a few days the product solidified. It was dissolved in petroleum ether, cooled in a Dry Ice-acetone bath and the liquid was removed with a filter stick. The crystals were dried in air, m.p. 29–30°.

This distillation procedure was used also in preparing the boronate from diethyl D-tartrate. The middle fraction (b.p. 197°/11 mm.) from a third distillation of the product crystallized, m.p. 46–48°. This compound reacted very readily and with considerable evolution of heat with water.

Neutral equivalents. The boronate was dissolved in 10–15 ml. of boiling methanol. Then 10 g. of mannitol in 75 ml. of water was added with continued heating. The resulting solution was cooled and titrated with standard base (0.02 N) to a phenolphthalein end point. Pinacyl benzeneboronate gave high results by this method due to incomplete hydrolysis. However, when the ester was allowed to stand for a week in the alcoholic mannitol solution (tightly stoppered flask) good results were obtained.

Optical rotations. These were measured with a Schmidt and Haensch triple field polarimeter. A 1-dm. tube was used. The rotation of each compound was measured at two different concentrations. Mean values of the specific rotations which usually agreed to within 0.5° are listed in Table I.

SUMMARY

The preparation and properties of ten solid esters (areneboronates) from areneboronic acids and di- and poly-ols are described. The alcohols involved are mannitol, sorbitol, pinacol, *cis*-indan-1,2-diol, catechol, pentaerythritol, and diethyl D-tartrate. The scope of the simpler of the two methods of preparation described is discussed.

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