Carbohydrate Research, 32 (1974) 187–193

INTERACTION OF BENZENEBORONIC ANHYDRIDE WITH VICINAL AMINO-ALCOHOLS

IAN R. MCKINLEY, HELMUT WEIGEL,

Department of Chemistry, Royal Holloway College (University of London), Egham, Surrey TW20 OEX (Great Britain)

C. B. BARLOW, AND R. D. GUTHRIE

School of Molecular Sciences, University of Sussex, Brighton BN1 9QT (Great Britain)

(Received March 13th, 1973; accepted for publication September 13th, 1973)

ABSTRACT

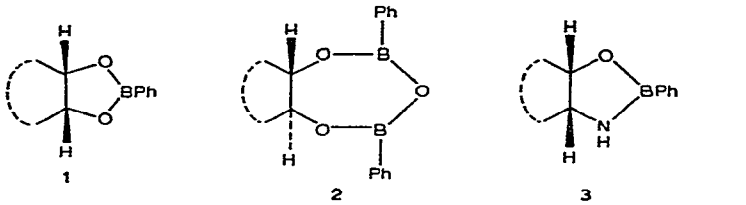
Mass spectrometry has revealed that a vicinal *cis*-amino-alcohol grouping in methyl amino-4,6-*O*-benzylidene-deoxy-α-D-aldopyranosides forms, on treatment with benzeneboronic anhydride, a 2-phenyl-1,3,2-oxazaborolidine ring, whereas the corresponding *trans*-grouping forms a 2,4-diphenyl-1,3,5-dioxaza-2,4-diborepine ring. The conformations of the pyranoid ring in the derivatives thus formed are discussed.

INTRODUCTION

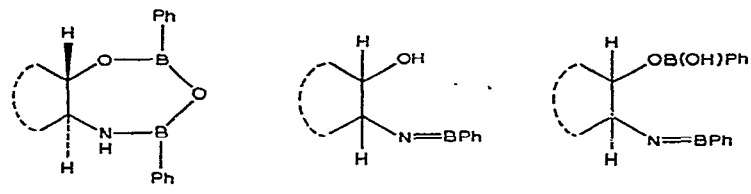
It is known[1,2] that *cis*-cyclohexane-1,2-diol and the *cis*-diol grouping at C-2,C-3 in methyl α-D-mannopyranoside form, on treatment with benzeneboronic anhydride, the 2-phenyl-1,3,2-dioxaborolane ring (**1**), whereas *trans*-cyclohexane-1,2-diol and the *trans*-diol grouping at C-2,C-3 in methyl α-D-glucopyranoside form the 2,4-diphenyl-1,3,5-trioxa-2,4-diborepane ring (**2**)*. It was of interest to investigate whether vicinal amino-alcohol groupings attached to a six-membered ring would behave similarly and form the corresponding 2-phenyl-1,3,2-oxazaborolidine (**3**) and 2,4-diphenyl-1,3,5-dioxaza-2,4-diborepine (**4**) rings. It is conceivable that compounds with structures **3** and **4** also exist in their tautomeric forms **5** and **6**, respectively. This, however, is unlikely in view of the fact that the products obtained from many acyclic amino-alcohols have cyclic structures[1,3–5]; further evidence is provided below. In addition, there does not appear to be any definitely established example of a compound containing a B=N bond[6]. Suitable examples for this investigation are the eight methyl amino-4,6-*O*-benzylidene-deoxy-aldopyranosides (**7**–**14**), which were available in small quantities. In general, benzeneboronates of diols and amino-alcohols can be easily prepared in nearly quantitative yields and are known to produce, under electron impact, relatively stable molecular ions in reasonable abundance. The difference

*Since completion of this work, it has been reported[12] that the *trans*-diol grouping at C-2,C-3 in methyl α-D-galactopyranoside also forms the 2,4-diphenyl-1,3,5-trioxa-2,4-diborepane ring (**2**).

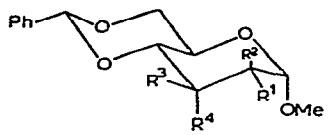
between compounds of types **3** and **4**, when derived from the amino sugars **7–14**, are also manifested in their molecular formulae, *i.e.*, $C_{20}H_{22}BNO_5$ and $C_{26}H_{27}B_2NO_6$, respectively. It was thus conceived that the determination of the molecular formulae of the products of interaction between benzeneboronic anhydride [$(PhBO)_3$] and the amino sugars by high-resolution mass spectrometry might serve to make such a distinction, even though the available amounts of the amino-alcohols **7–14** were too small to allow isolation and conventional characterisation of the products.



1 **2** **3**



4 **5** **6**



7 $R^1 = NH_2$, $R^4 = OH$, $R^2 = R^3 = H$ **11** $R^1 = NH_2$, $R^3 = OH$, $R^2 = R^4 = H$
8 $R^2 = NH_2$, $R^3 = OH$, $R^1 = R^4 = H$ **12** $R^2 = NH_2$, $R^4 = OH$, $R^1 = R^3 = H$
9 $R^3 = NH_2$, $R^2 = OH$, $R^1 = R^4 = H$ **13** $R^3 = NH_2$, $R^1 = OH$, $R^2 = R^4 = H$
10 $R^4 = NH_2$, $R^1 = OH$, $R^2 = R^3 = H$ **14** $R^4 = NH_2$, $R^2 = OH$, $R^1 = R^3 = H$

DISCUSSION

The eight amino sugars (**7–14**) produced, under electron impact and albeit in very low abundance, molecular ions [*m/e* 281 ($C_{14}H_{19}NO_5^{+\cdot}$)] and (M+1) ions [*m/e* 282 ($C_{14}H_{20}NO_5^{+}$)] (Table I). It was not possible to assign fragmentation modes unambiguously as no metastable ions could be detected. However, it is likely that the ions with *m/e* 59 ($C_2H_5NO^+$), 190 ($C_{11}H_{12}NO_2^+$), and 207 ($C_{11}H_{13}NO_3^+$) arise by fragmentation as indicated in Fig. 1. Although the ions with *m/e* 74 ($C_3H_6O_2^+$) and 101 ($C_4H_7NO_2^+$) could arise from the 3-amino compounds (**9**, **10**, **13**, and **14**) by the fragmentation modes *a–e* shown in Fig. 1, they could not be produced by these modes from the 2-amino sugars (**7**, **8**, **11**, and **12**). It is likely that these ions arise through molecular rearrangements.

TABLE I

PRINCIPAL IONS PRODUCED FROM METHYL AMINO-4,6-*O*-BENZYLIDENE-DEOXY-α-D-ALDOSIDES

Compound	*Abundances of ions*[a]						
	$C_{14}H_{19}NO_5^{+\cdot}$ m/e *281*	$C_{14}H_{20}NO_5^{+}$ m/e *282*	$C_{11}H_{13}NO_3^{+}$ m/e *207*	$C_{11}H_{12}NO_2^{+}$ m/e *190*	$C_4H_7NO_2^{+}$ m/e *101*	$C_3H_6O_2^{+}$ m/e *74*	$C_2H_5NO^{+}$ m/e *59*
2-amino							
7	0.0	0.2	0.0	0.0	0.0	0.9	22.3
8	0.2	0.0	0.0	0.0	0.4	1.0	24.7
11	0.2	0.1	0.0	0.0	0.4	1.0	21.4
12	0.1	0.1	0.0	0.0	0.0	0.8	19.2
3-amino							
9	0.1	0.1	1.1	1.5	4.8	2.8	4.7
10	0.1	0.1	1.1	1.4	5.5	2.9	6.6
13	0.1	0.1	1.0	1.5	6.2	4.7	5.5
14	0.1	0.1	0.7	1.2	7.3	3.0	4.5

[a] $\%\Sigma_{40}$.

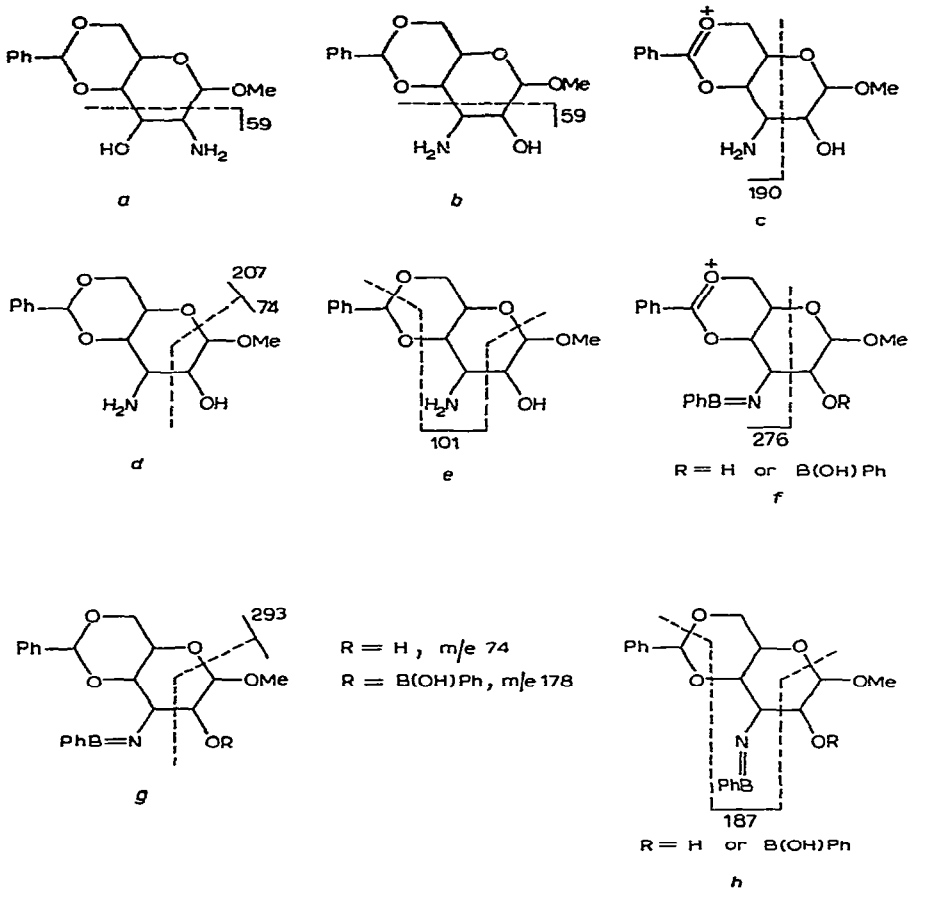


Fig. 1. Fragmentation modes of methyl amino-4,6-*O*-benzylidene-deoxy-aldopyranosides.

The abundances of ions produced by electron impact from the benzeneboronates of compounds **7–14** are shown in Table II. Ions arising by fragmentation modes *f–h* (Fig. 1), *i.e.*, similar to those of the amino sugars **9**, **10**, **13**, and **14** (Fig. 1, *c–e*), could not be detected. This is further evidence that the tautomeric structures **5** and **6** do not occur to any significant extent. The ions with *m/e* 367 and 471 correspond to the molecular ions of monobenzeneboronates ($C_{20}H_{22}BNO_5^{+\cdot}$) and dibenzenepyroboronates ($C_{26}H_{27}B_2NO_6^{+\cdot}$), respectively. It is thus apparent that the benzeneboronates of the compounds (**7–10**) with a vicinal *cis*-amino-alcohol grouping possess the 2-phenyl-1,3,2-oxazaborolidine ring and have structures **15*** (from **7** and **8**) and **16*** (from **9** and **10**), whereas those of the compounds (**11–14**) with a vicinal *trans*-amino-alcohol grouping possess the 2,4-diphenyl-1,3,5-dioxaza-2,4-diborepine ring and have structures **17*** (from **11** and **12**) and **18*** (from **13** and **14**). Further evidence for the

*In structures **15–18**, the stereochemistry at C-2 and C-3 of the amino-sugar portions is not shown.

assignment of structures **17** or **18** to the derivatives formed from the *trans* isomers is the formation of ions with *m/e* 249 ($C_{14}H_{13}B_2NO_2^+$), containing two boron atoms. They arise, most likely, by the fragmentation indicated in Fig. 2. Similarly, ions with *m/e* 145 ($C_8H_8BNO^+$) are produced from the derivatives of the *cis* isomers (Fig. 2). However, a fragment with *m/e* 145 ($C_8H_8BNO^+$) also arises from the compounds (**17** and **18**) possessing the 2,4-diphenyl-1,3,5-dioxaza-2,4-diborepine ring but in lower abundance. From these structures, it is produced by elimination of PhBO from $C_{14}H_{13}B_2NO_2^+$, as evidenced by a metastable ion with *m/e* 84.4.

TABLE II

IONS PRODUCED FROM BENZENEBORONATES OF METHYL AMINO-4,6-*O*-BENZYLIDENE-α-D-ALDOSIDES

Aldoside	$C_8H_8BNO^+$ (*Base Peak*)		$C_{14}H_{13}B_2NO_2^+$		$C_{20}H_{22}BNO_5^{\ddagger}$		$C_{26}H_{27}B_2NO_6^{\ddagger}$	
	Abundance[a]	(m/e)	*Abundance*[a]	(m/e)	*Abundance*[a]	(m/e)	*Abundance*[a]	(m/e)
7	37.7	145.0703	zero		0.6	367.1590	zero	
8	38.3	145.0695	zero		0.6	367.1593	zero	
9	15.8	145.0694	zero		0.5	367.1590	zero	
10	18.3	145.0697	zero		0.1	367.1595	zero	
11	9.7	145.0697	6.1	249.1138	zero		0.4	471.2030
12	2.3	145.0698	0.5	249.1131	zero		0.04	471.2020
13	12.8	145.0695	4.1	249.1131	zero		5.2	471.2030
14	7.2	145.0695	2.9	249.1127	zero		0.4	471.2019

[a] $\%\Sigma_{40}$; the mass spectrum of benzeneboronic anhydride was subtracted before calculation of Σ_{40}.

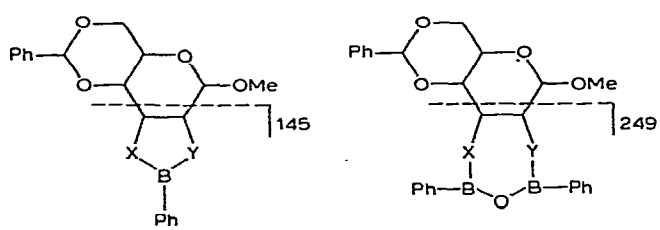
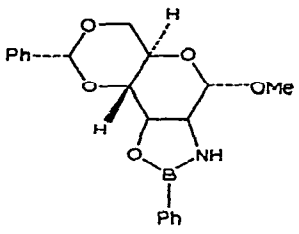
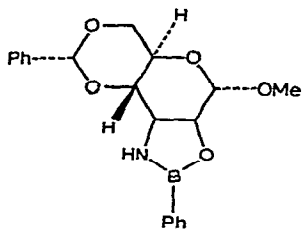


Fig. 2. Fragmentation modes of benzeneboronates of methyl amino-4,6-*O*-benzylidene-deoxy-aldopyranosides; X = O, Y = NH; or X = NH, Y = O.

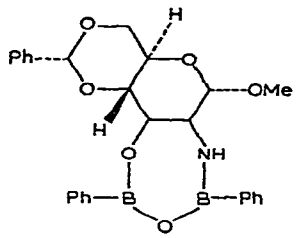
Some conclusions concerning the conformation of the pyranoid ring in the benzeneboronates of the amino sugars **7–14** may be drawn as a result of the above observations. Interatomic distances and bond angles in compounds of the types **3** and **4** have, to our knowledge, not been reported. If, in the as yet unknown compound $PhB(OH)NH_2$, the N–B–O bond angle were the same as the O–B–O and N–B–N bond angles in boric acid[7] and 2,4,6-trimethylborazine[8], respectively (generally 120 ±1°), and if the B–O and B–N bond lengths were the same as in boric acid[7] (1.36 Å) and



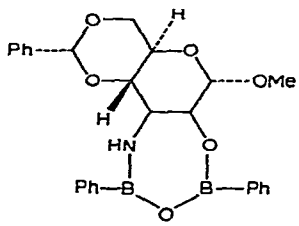
15



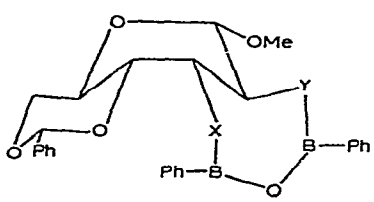
16



17



18



19

2,4,6-trimethylborazine[8] (1.42 Å), respectively, the O–N distance can be calculated to be 2.41 Å. A 2-phenyl-1,3,2-oxazaborolidine ring is thus expected to be formed readily when the O–N separating distance in the vicinal amino-alcohol grouping is near to this value. This situation is most closely approached (2.50 Å) when the dihedral angle between the C–O and C–N bonds is 0°. In calculating this value, the C–C, C–O, and C–N bond-lengths were taken to be 1.54, 1.42, and 1.47 Å, respectively. Although the dihedral angles in the vicinal *cis*-amino-alcohol (*i.e.*, in compounds **7–10**) and vicinal *trans*(*eq,eq*)-amino-alcohol groupings (*i.e.*, compounds **11** and **13**) are nominally the same, *i.e.*, 60°, only in the *cis* series can this value be reduced towards 0° without affecting normal bond lengths and angles. The fact that the esters obtained only from compounds **7–10** contain the five-membered 1,3,2-oxazaborolidine ring is in agreement with many other examples in carbohydrate and alicyclic chemistry, which show that the movement of *ax,eq*-groups on a six-membered ring towards coplanarity is a much less energetic process than it is for the corresponding *eq,eq*-system. The vicinal *trans*(*eq,eq*) N and O atoms can only be spanned by forming the seven-membered 1,3,5-dioxaza-2,4-diborepine ring.

The behaviour of the two compounds (**12** and **14**) with a *trans*(*ax,ax*)-amino-alcohol grouping is of special interest. When the sugar portion of these compounds adopts the $^4C_1$ conformation, the dihedral angle between the functional groups is 180°, and formation of five-membered (1,3,2-oxazaborolidine) or seven-membered (1,3,5-dioxaza-2,4-diborepine) rings is not possible. It is interesting to note that these compounds do not form complexes with cuprammonium[9] and are very resistant to oxidation by periodate[10]. The corresponding diol, methyl 4,6-*O*-benzylidene-α-D-altropyranoside, behaves similarly[11]. However, that compounds **12** and **14** react with benzeneboronic anhydride to give derivatives with a 1,3,5-dioxazadiborepine ring

suggests that, in these derivatives, the pyranose ring is in a conformation resembling the $B_{2,5}$ form (**19a**; X = O, Y = NH; or X = NH, Y = O), where the dihedral angle between the C–O and C–N bonds is close or equal to 60°. The O–N separating distance then represents again, without distortion of bond angles and bond lengths, the closest distance of approach (2.85 Å), and the O and N atoms can only be spanned by forming the seven-membered 1,3,5-dioxaza-2,4-diborepine ring. Apparently, and in contrast to cuprammonium complex formation and oxidation by periodate, the free energy of the reaction giving the 1,3,5-dioxaza-2,4-diborepine ring is sufficiently large to offset the conformational energy associated with boat conformations. It is anticipated that methyl 4,6-*O*-benzylidene-α-D-altropyranoside will react with benzeneboronic anhydride to give a 1,3,5-trioxa-2,4-diborepane derivative (**19b**; X = Y = O). The suggestions made here will be verified by more conventional methods.

EXPERIMENTAL

Mass spectra were obtained, using an A.E.I. MS902 instrument, operating at 70 eV, by the direct-insertion technique and an ion-source temperature of 160–230°. All assignments of atomic composition were deduced from precise mass measurements.

Methyl amino-4,6-*O*-benzylidene-deoxy-α-D-aldosides were available from previous work[10]. Benzeneboronate derivatives were prepared by allowing the aldoside (~10 mg) to condense with benzeneboronic anhydride [$(PhBO)_3$, 0.8 mol.] in 2-methoxyethanol (1 ml) at room temperature for 10 min. Solvents were evaporated under diminished pressure.

ACKNOWLEDGMENT

The authors thank Ranks Hovis McDougall (Research) Ltd. for financial support.

REFERENCES

1 J. M. SUGIHARA AND C. M. BOWMAN, *J. Amer. Chem. Soc.*, 80 (1958) 2443.
2 R. J. FERRIER, *J. Chem. Soc.*, (1961) 2325.
3 M. PAILER AND M. HUEMER, *Monatsh. Chem.*, 95 (1964) 373.
4 C. J. W. BROOKS, B. S. MIDDLEDITCH, AND G. M. ANTHONY, *Org. Mass Spectrom.*, 2 (1969) 1023.
5 G. M. ANTHONY, C. J. W. BROOKS, I. MACLEAN, AND I. SANGSTER, *J. Chromatogr. Sci.*, 7 (1969) 623.
6 W. GERRARD, *The Organic Chemistry of Boron*, Academic Press, London, 1961, p. 174.
7 W. H. ZACHARIASEN, *Acta. Crystallogr.*, 7 (1954) 305.
8 K. P. COFFIN AND S. H. BAUER, *J. Phys. Chem.*, 59 (1955) 193.
9 C. B. BARLOW AND R. D. GUTHRIE, *J. Chem. Soc.*, (1967) 1194.
10 C. B. BARLOW, R. D. GUTHRIE, AND A. M. PRIOR, *Chem. Commun.*, (1966) 268.
11 J. HONEYMAN AND C. J. G. SHAW, *J. Chem. Soc.*, (1959) 2454.
12 D. S. ROBINSON AND J. EAGLES, *Carbohyd. Res.*, 26 (1973) 204.