1185. *Fluorocarbohydrates. Part X.* The Structure and Reactions of 2-Bromo-2-deoxy-β-arabinopyranosyl Fluorides of the* D- *and* L-*Series.*

By P. W. Kent and J. E. G. Barnett.

The elements of bromine monofluoride have been added to di-*O*-acetyl-D- and -L-arabinals giving, after deacetylation, 2-bromo-2-deoxy-β-arabinopyranosyl fluorides as stable, crystalline compounds. These were converted into the methyl 2,3-anhydroribosides by the action of hot sodium methoxide. Hydrogenation and hydrolysis of the bromofluoride of the D-series, led to 2-deoxy-D-ribose, whereas methanolysis gave methyl 2-bromo-2-deoxy-α-D-arabinoside. Aqueous acidic hydrolysis of the bromo-fluorides in both series gave the crystalline 2-bromo-2-deoxyarabinoses. 2-Bromo-2-deoxy-D-mannose and its anilide have been prepared from the corresponding acetylated β-fluoride.

The kinetics of hydrolysis of 2-bromo-2-deoxy-β-D-arabinosyl fluoride have been studied polarimetrically in perchloric acid (0·15—2·78N) between 20° and 48° and compared with those of β-L-arabinosyl fluoride. The mechanism is discussed with reference to the direct proportionality of the rate of hydrolysis to the Hammett acidity function, to the calculated entropies of activation, and to the known behaviour of methyl glycopyranosides. The methanolysis of the bromo-fluoride and of β-L-arabinosyl fluoride, studied at several concentrations of acid, proceeds with inversion in both cases. The kinetic results are consistent with an A1 mechanism involving a cyclic carbonium ion.

Recently it has been shown[1] that *N*-bromosuccinimide in liquid hydrogen fluoride adds the elements of bromine monofluoride to tri-*O*-acetyl-D-glucal giving a mixture of tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannosyl fluoride and tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucosyl fluoride. The interesting feature of this addition is the *cis*-nature of the isolable products. In order to establish whether this is a general reaction with acetylated glycals, the addition has now been investigated with di-*O*-acetyl-D- (I) and -L-arabinals.

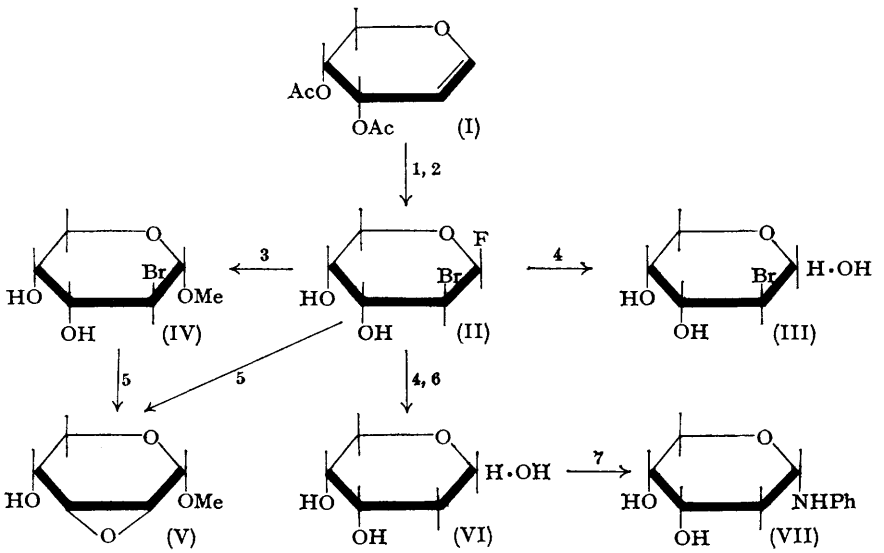
Deacetylation of the bromo-fluoro-adducts of the D-series gave a stable crystalline compound which was shown to be 2-bromo-2-deoxy-β-D-arabinopyranosyl fluoride (II) on the following evidence. Aqueous acidic hydrolysis resulted in quantitative expulsion of fluorine giving 2-bromo-2-deoxy-D-arabinose (III), which reduced Fehling's solution and silver nitrate and gave an orange-red colour with aniline hydrogen phthalate. Methanolysis of (II) led to methyl 2-bromo-2-deoxy-α-D-arabinoside (IV), thus establishing that the bromine is located at C-2 and the fluorine at C-1. The action of hot sodium methoxide converted the methyl bromoarabinoside (IV) into methyl 2,3-anhydro-α-D-riboside (V), thereby demonstrating the *arabino*-configuration of (IV) by *trans*-elimination between the bromine at C-2 and the hydroxyl at C-3. The α-configuration at C-1 may also be inferred from

* Part IX, *J.*, 1964, 2497.

[1] Kent, Robson, and Welch, *J.*, 1963, 3273.

a comparison of its rotation, $[\alpha]_D^{20} -68°$(MeOH), with values for methyl α-D-arabinoside,[2] $[\alpha]_D -17°(H_2O)$ and methyl β-D-arabinoside,[3] $[\alpha]_D -245°(H_2O)$.

The anhydro-compound (V), m. p. 83°, $[\alpha]_D^{20} +165°$, was also obtained directly from 2-bromo-2-deoxy-β-D-arabinosyl fluoride by the action of hot sodium methoxide. The L-enantiomer, obtained in the same way from the corresponding L-bromo-fluoride, had R_F, mixed melting point, infrared spectrum, and *X*-ray diffraction pattern identical with the anhydro-compound made from methyl 2-*O*-methanesulphonyl-α-L-arabinoside. The L-anhydro-compound, hitherto poorly characterized,[4] has now been obtained in a pure form.



1. *N*-Bromosuccinimide–HF 2. NaOMe (cold) 3. MeOH–HCl
4. H_2SO_4 5. NaOMe (hot) 6. Ni–H_2 7. $PhNH_2$

Recently, the D-isomer (m. p. 84—86°, $[\alpha]_D^{20} +164{\cdot}5°$), assumed to be the α-glycoside from its dissimilarity to methyl 2,3-anhydro-β-D-riboside, has been synthesized from methyl 3,4-di-*O*-acetyl-2-chloro-2-deoxy-α-D-arabinoside.[5]

Hydrogenation of the D-bromo-fluoride (II) with Raney nickel in methanol at room temperature gave methyl 2-deoxy-αβ-D-ribosides, which gave the expected colour yield in the Dische diphenylamine test.[6] On aqueous hydrolysis, the free deoxy-sugar (VI) resulted, chromatographically identical with authentic 2-deoxy-D-ribose, from which the known[7] crystalline anilide (VII) was prepared.

The β-anomeric configuration of the adduct (II), which must be a 2-bromo-2-deoxy-arabinosyl fluoride, follows from a comparative application of Hudson's rules (Table 1), to this and related compounds of known configuration (β-D-arabinosyl fluoride being synthesized by deacetylation of tri-*O*-acetyl-β-L-arabinosyl fluoride[8]).

The pyranose structure of (II) was confirmed by periodate oxidation,[9] 0·94 mol. being consumed after 3 hr. In the same way, methyl 2-bromo-2-deoxy-α-D-arabinoside (IV) was also found to be in the pyranose form.

[2] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994.
[3] Cadotte, Smith, and Spriesterback, *J. Amer. Chem. Soc.*, 1952, **74**, 1501.
[4] Mukherjee and Todd, *J.*, 1947, 969.
[5] Vargha and Kuszmann, *Chem. Ber.*, 1963, **96**, 411.
[6] Burton, *Biochem. J.*, 1956, **62**, 315.
[7] Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433.
[8] Brauns, *J. Amer. Chem. Soc.*, 1926, **48**, 2776.
[9] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.

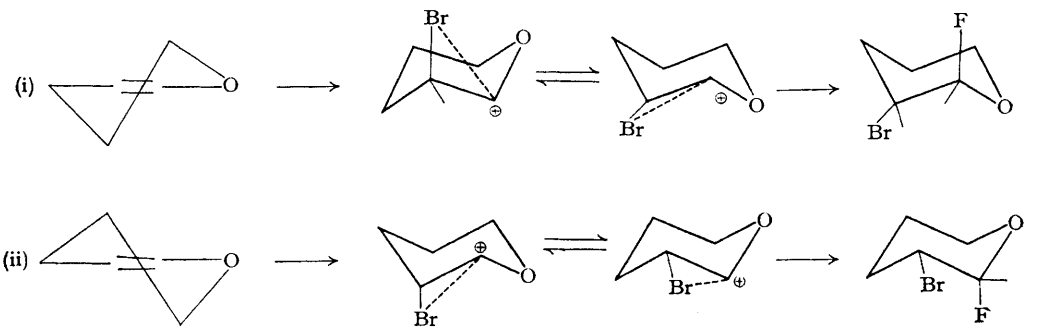
TABLE 1.

Molecular rotations of arabinosides and arabinosyl fluorides.

Compound	M_D	Compound	M_D
β-L-Arabinosyl fluoride	+26,000	2-Bromo-2-deoxy-β-D-arabinosyl fluoride	−38,500
Methyl α-L-arabinoside	+2800	Methyl 2-bromo-2-deoxy-α-D-arabinoside	−15,500
Difference for L-series (β-F) − (α-OMe)	+23,200	Difference for D-series (β-F) − (α-OMe)	−23,000

In contrast to the lability of other dihalogeno-adducts of acetylated glycals,[5,10,11] the present bromo-fluorides exhibit marked stability even in the deacetylated form. A crystalline dichloro-adduct of triacetyl-D-glucal has subsequently been shown to be tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucosyl chloride.[12] The non-crystalline products resulting from the reaction of diacetyl-D-arabinal with chlorine have recently been shown to contain 3,4-di-*O*-acetyl-2-chloro-2-deoxy-β-D-arabinosyl chloride.[5] Addition of bromine to triacetyl-D-glucal and methanolysis gives two isomeric glycosides, one of which can be inferred to be methyl 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-glucoside derived from the α-bromide.[11] The reported[13] ease of conversion of the second bromo-glucoside into the first compound by crystallization from water at 100° casts some doubt on its true configuration, although this second compound is probably methyl tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannoside derived from tri-*O*-acetyl-2-bromo-2-deoxy-α-D-mannosyl bromide. Of the 1,2-dihalogeno-compounds whose structure has been elucidated, the latter compound is the only one with *trans*-halogen atoms.

The *cis*-nature of the other adducts can be explained either by conformational changes in the carbonium-ion intermediate (Scheme 1) or by equilibrium anomerization except in the case of tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannosyl fluoride. Recently, a ring intermediate has been postulated[14] to explain *cis*-chlorine addition to phenanthrene and acenaphthene.



SCHEME 1

The general procedure for the preparation of bromo-sugars from the corresponding acetylated fluorides, applied to tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannosyl fluoride gave 2-bromo-2-deoxymannose from which the crystalline anilide was prepared.

Results, and Discussion of Kinetic Data.—The mechanisms of methanolysis of acetylated, benzoylated,[15] and methylated[16,17] glycosyl halides and of hydrolysis of methyl glyco-

[10] Fischer, Bergmann, and Schotte, *Ber.*, 1920, **53**, 509.
[11] Bergmann and Schotte, *Ber.*, 1921, **54**, 440.
[12] Richtmeyer, *Adv. Carbohydrate Chem.*, 1945, **1**, 58.
[13] Manolopoulos, Mednick, and Lichtin, *J. Amer. Chem. Soc.*, 1962, **84**, 2203.
[14] de la Mare, Klassen, and Koenigsberger, *J.*, 1961, 5285.
[15] Capon and Overend, *Adv. Carbohydrate Chem.*, 1960, **15**, 39.
[16] Banks, Meinwald, Rhind-Tutt, Sheft, and Vernon, *J.*, 1961, 3240.
[17] Rhind-Tutt and Vernon, *J.*, 1960, 4637.

sides[18,19] have been extensively investigated. The relationship of the two types of reaction has been difficult to investigate hitherto due to the instability of the unprotected glycosyl halides other than fluorides. The latter we find to be suitable compounds for kinetic investigation in both aqueous and non-aqueous media. With 2-bromo-2-deoxy-β-D-arabinosyl fluoride (II) and β-L-arabinosyl fluoride in aqueous perchloric acid, good first-order rate curves were obtained in all cases. The apparent rate constants (k_1) were calculated (Table 2)

TABLE 2.

Rates of hydrolysis in aqueous perchloric acid (at 20·5°).

			2-Bromo-2-deoxy-β-D-arabinosyl fluoride		β-L-Arabinosyl fluoride	
Normality	pH	H_0	$k_1 \times 10^3$ (min.$^{-1}$)	3+ ($\log_{10} k_1$)	$k_1 \times 10^3$ (min.$^{-1}$)	3+ ($\log_{10} k_1$)
0·15	0·825	0·825	2·42	0·384	15·35	1·186
0·75	0·125	0·04	17·1	1·233	71·6	1·855
1·04	−0·017	−0·14	23·3	1·367	138·4	2·131
1·39	−0·14	−0·36			211·0	2·324
1·50	−0·176	−0·43	42·9	1·636		
1·73	−0·243	−0·57	51·9	1·715		
2·08	−0·318	−0·735	86·5	1·937		
2·78	−0·444	−1·035	153·5	2·186		

using the expression $\ln x = k_1 t$, where x, the concentration of glycosyl halide remaining, is proportional to $(\alpha_t - \alpha_\infty)$ and assumes that no other slow reactions occur. In Fig. 1, $\log_{10}$ (rate) at 20·5° is plotted against pH and against H_0 (defined as $-\log_{10} h_0$, the Hammett acidity function[20]) from the data in Table 2. Values of H_0 were taken from the results

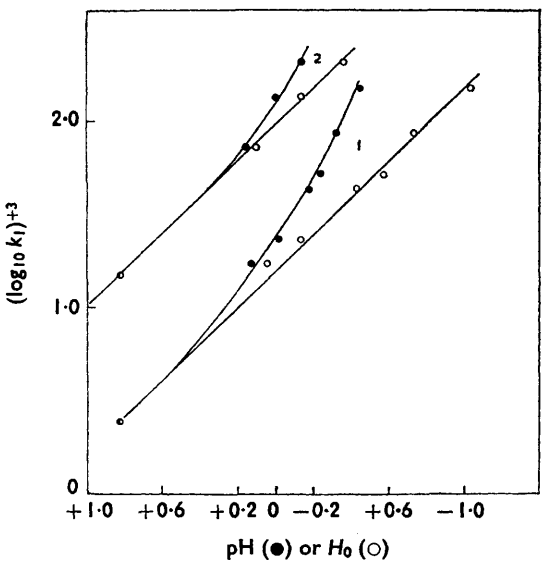


FIG. 1. Plot of $\log_{10} k$ against pH and H_0 for the rates of hydrolysis of (1) 2-bromo-2-deoxy-β-arabinosyl fluoride and (2) β-arabinosyl fluoride at 20·5° in perchloric acid.

of Hammett.[21,22] The procedure was inapplicable to methanolysis since the values for acidity function are not valid for methanolic solutions.[23]

[18] Capon and Overend, *Adv. Carbohydrate Chem.*, 1960, **15**, 33.
[19] Overend, Rees, and Sequeira, *J.*, 1962, 3429.
[20] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 237.
[21] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[22] Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827.
[23] Bunton, Ley, Rhind-Tutt, and Vernon, *J.*, 1957, 2327.

The temperature-dependence of rate constants (k_1) led (Table 3) to the true rate constant (k_2), where (rate) $= k_2 h_0 x$. This can be evaluated from the relations $\log_{10} k_2 = \log_{10} k_1 + H_0$ and $k_1 = k_2 h_0$. The entropy change ($\Delta S^\ddagger$) and heat of activation (E) were calculated from the relation $\ln k_2 = \ln kT/h - E/RT + \Delta S^\ddagger/R$.

TABLE 3.

Temperature-dependence of rates of hydrolysis of glycosyl fluorides.

2-Bromo-2-deoxy-β-D-arabinosyl fluoride

Temp.	20·5°	26·0	31·8	38·0	42·0	48·0
(1) 0·15N-Perchloric acid						
$k_1 \times 10^3$ (min.$^{-1}$)	2·42	5·68	10·82	21·02	33·90	52·0
$\log_{10} k_2$ (sec.$^{-1}$) + 4	0·431	0·801	1·101	1·370	1·577	1·863
$k_2 \times 10^4$ (sec.$^{-1}$)	2·70	6·32	12·62	23·44	37·76	72·95
(2) 0·69N-Perchloric acid						
$k_1 \times 10^3$ (min.$^{-1}$)	13·4	30·0	58·4	110·9	184·8	
$\log_{10} k_2$ (sec.$^{-1}$) + 4	0·429	0·772	1·078	1·347	1·568	
$k_2 \times 10^4$ (sec.$^{-1}$)	2·69	5·92	11·97	22·23	37·07	

β-L-*Arabinosyl fluoride* (0·15N-perchloric acid)

$k_1 \times 10^3$ (min.$^{-1}$)	15·35	26·3	105·1	198·5	
$\log_{10} k_2$ (sec.$^{-1}$) + 4	1·233	1·467	2·069	2·349	
$k_2 \times 10^4$ (sec.$^{-1}$)	17·1	29·31	117·2	223·4	

The plots of $\log_{10} k_2$ against $1/T$ (Fig. 2) were presumed to be linear, and their gradients were determined by the method of least squares. The results are summarized in Table 4.

TABLE 4.

Activation parameters for aqueous hydrolysis of glycosyl fluorides.

	$\log_{10} A$	E (kcal.)	$\Delta S^\ddagger$ at 20°	$\log_{10} k_1/H_0$
2-Bromo-2-deoxy-β-D-arabinosyl fluoride	12·97	22·18	−1·1	−0·99
β-L-Arabinosyl fluoride	13·32	21·85	+0·45	−0·98

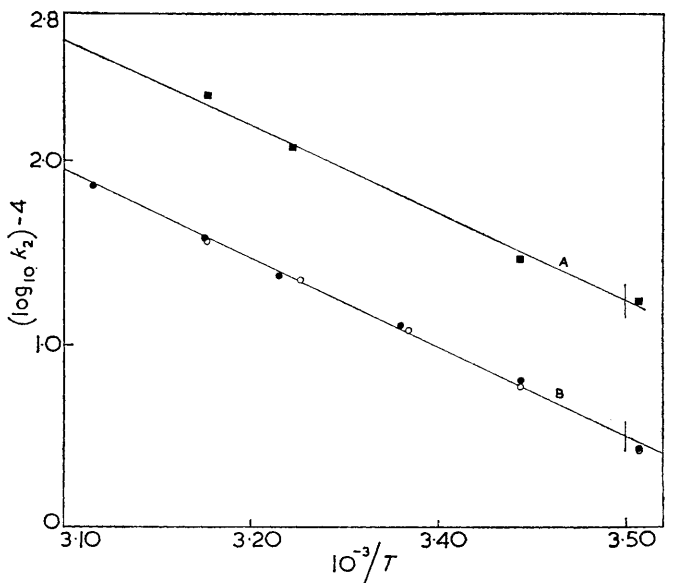


FIG. 2. Plot of $\log_{10} k_2$ against $1/T$ for the rates of hydrolysis of (B) 2-bromo-2-deoxy-β-arabinosyl fluoride and (A) β-arabinosyl fluoride between 20° and 48° in perchloric acid.

○, ■, 0·15N-$HClO_4$;
●, 0·7N-$HClO_4$.

First-order acid-catalysed solvolyses may proceed by two types of mechanism:

$$A1 \qquad X + H^+ \rightleftharpoons XH^+ \text{ (equilibrium)}$$
$$XH^+ \longrightarrow Y^+ \text{ (slow)}$$
$$Y^+ + H_2O \longrightarrow \text{Products (fast)}$$
$$A2 \qquad X + H^+ \rightleftharpoons XH^+ \text{ (equilibrium)}$$
$$XH^+ + H_2O \longrightarrow \text{Products (slow)}$$

A generally observed characteristic of the $A1$ mechanism is the linear relationship of $\log_{10} k_1$ with H_0, having a gradient of approximately -1. For $A2$ mechanisms, $\log_{10} k_1$ is linearly related[24–26] to pH. The entropy of activation ($\Delta S^\ddagger$) for an $A1$ mechanism is generally positive and of the order of 20—30 cal./degree higher than that for an $A2$ mechanism in the same series of compounds.[27] This difference has been attributed[26] to a more ordered transition state in the $A2$ mechanism.

With both glycosyl fluorides under investigation, the linearity of log(rate) with H_0 (Fig. 1) and the values of $\Delta S^\ddagger$ (Table 4) favour an $A1$ mechanism. The low values of $\Delta S^\ddagger$, in contrast to the values for methyl glucosides,[19] may be due to the high hydration state of the released fluoride ions (or hydrogen fluoride).

The $A1$ mechanism may involve either an open chain or cyclic carbonium ion.[26–27] Methanolysis of both glycosyl fluorides (Table 5) proceeded with optical inversion, the ratio

TABLE 5.

Rates of methanolysis of 2-bromo-2-deoxy-β-D-arabinosyl fluoride (at 20·5°).

Normality (H^+)	0·096	0·192	0·384	0·576
$k_1 \times 10^4$ (sec.$^{-1}$)	1·12	2·22	3·63	6·95
$[\alpha]_D^{20·5}$ (equilib.)*	−77°	−70	−77	−88

* Corrected throughout for methyl glycoside.

(α/β) of methyl arabinosides produced from β-L-arabinosyl fluorides was 9:1 at 20°, in 0·48N-hydrochloric acid. No mutarotation of pure methyl α- or β-arabinopyranosides was observed under the same conditions. In the case of the bromoarabinosyl fluorides, the final α/β ratio of methyl glycosides could not be calculated, because methyl 2-bromo-2-deoxy-β-arabinoside has not yet been isolated in a sufficiently pure form for determination of $[\alpha]_D$. The methyl bromoarabinosides were not observed to mutarotate in methanolic 0·25N-hydrochloric acid.

The occurrence of inversion suggests that, if hydrolysis and methanolysis proceed by the same mechanism, a cyclic ion intermediate intervenes and that the attacking anion approaches from the side remote from the leaving ion.[28]

The rate of hydrolysis of β-L-arabinosyl fluoride by aqueous acid is about seven times greater than that of 2-bromo-2-deoxy-β-D-arabinosyl fluoride at 20°. Such differences between related compounds have been explained by both steric[29] and inductive factors[30] for cyclic intermediates. For arabinosides, which exist in the 1C conformation,[31] conversion into the carbonium ion, which has the half-chair conformation, causes the group at position 2 to be twisted from the equatorial position. Thus, the bromine atom, which is much larger than the hydroxyl group, may cause the carbonium ion to be less stable. Conversely, the inductive

[24] Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791.
[25] Long, *Proc. Chem. Soc.*, 1957, 220.
[26] Bunton, Lewis, Llewellyn, and Vernon., *J.*, 1955, 4419.
[27] Long, Pritchard, and Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 2362.
[28] Lemieux and Huber, *Canad. J. Chem.*, 1955, **33**, 128.
[29] Edward, *Chem. and Ind.*, 1955, 1102.
[30] Richards, *Chem. and Ind.*, 1955, 228.
[31] Reeves, *J. Amer. Chem. Soc.*, 1950, **72**, 1499.

effect of the hydroxyl group is greater than that of the bromine atom so that the bromo-compound will, from this effect, have the more stable carbonium ion. Thus, the steric effect must be the predominant one and favours a cyclic ionic intermediate.

Experimental

Paper chromatography was by downward elution on Whatman No. 1 paper with the water-poor phase of butan-1-ol–ethanol–water (4:1:5). Sugars were detected by alkaline silver nitrate,[32] aniline hydrogen phthalate,[33] or by sodium periodate followed by 0·5% benzidine in methanol,[34] and anhydro-sugars by naphthoresorcinol.[35] Rotations were measured by using a Bendix–Ericsson photoelectric polarimeter or by a Hilger Standard Polarimeter Mark III with 5, 10, or 20 cm. cells. Fluorine analyses were performed by the method of Belcher, Leonard, and West.[36]

2-Bromo-2-deoxy-β-D-arabinopyranosyl Fluoride (II).—3,4-Di-*O*-acetyl-D-arabinal (I) (10 g.), b. p. 56—59°/0·004 mm., n_D^{20} 1·4620, in ether (20 ml.) and *N*-bromosuccinimide (11 g.) were added to a stirred mixture of ether (10 ml.) and anhydrous hydrogen fluoride (25 g.) in a polyethylene vessel at −70°. After 2 hr. the temperature was raised to 0° for a further 2 hr. and the solution was then poured into ether (500 ml.) and saturated sodium carbonate (150 ml.). The ethereal layer was separated, the aqueous layer was washed with a total of 1 l. of ether, and the combined ethereal layer washed with sodium hydrogen carbonate and water, and dried. Removal of the ether gave a syrupy mixture of 3,4-di-*O*-acetyl-2-bromo-2-deoxy-D-pentosyl fluorides (13·5 g.), n_D^{20} 1·4770 (Found: Br, 27·0; F, 6·4. Calc. for $C_9H_{12}BrFO_5$: Br, 26·7; F, 6·4%), which was dissolved in dry methanol (150 ml.). Sodium methoxide (1N; 5 ml.) was added (α −3·4°→ +2·66°, constant after 1 hr.) and, after 1½ hr., the solution was neutralized (CO_2), evaporated to dryness, extracted with ethyl acetate, filtered, and concentrated, giving *2-bromo-2-deoxy-β-D-arabinopyranosyl fluoride* (2·8 g., 24%) which, after recrystallization from dry methanol, decomposed, without melting, at 140—145°, $[\alpha]_D^{20}$ −181° (*c* 1·47, MeOH), R_F 0·76 (Found: C, 27·4; H, 3·7; Br, 37·6; F, 9·1. $C_5H_8BrFO_3$ required C, 27·9; H, 3·7; Br, 37·1; F, 8·8%).

2-Bromo-2-deoxy-β-L-arabinopyranosyl Fluoride.—Di-*O*-acetyl-L-arabinal (2·0 g.), b. p. 61—64°/0·006 mm., n_D^{20} 1·4620, $[\alpha]_D^{-20}$ −252° (*c* 1·2, $CHCl_3$),[37] gave, by the same procedure, a syrupy mixture of 3,4-di-*O*-acetyl-2-bromo-2-deoxy-L-pentosyl fluorides (2·7 g.), n_D^{20} 1·4712 (Found: Br, 27·3; F, 7·0. Calc. for $C_9H_{12}BrFO_5$: Br, 26·7; F, 6·4%), and deacetylation gave *2-bromo-2-deoxy-β-L-arabinopyranosyl fluoride* (0·4 g.), decomposing at 140—145°, $[\alpha]_D^{20}$ +186° (*c* 0·33, MeOH), R_F 0·76 (Found: C, 28·2; H, 4·1; Br, 37·0; F, 8·9%).

2-Bromo-2-deoxy-D-arabinose (III).—The bromo-fluoride (II) (277 mg.), dissolved in 0·1N-sulphuric acid (10 ml.), was maintained at 100° for 15 min. when the fluorine was quantitatively expelled. The solution was deionized with Dowex 1 (CO_3^{2-}), filtered, and freeze-dried to a glass which slowly crystallized. Two crystallizations from ethanol–ether gave *2-bromo-2-deoxy-D-arabinose* (238 mg.), m. p. 125°, $[\alpha]_D^{18}$ −121° (*c* 0·49 in H_2O after 5 min.) (Found: C, 28·7, H, 4·4; Br, 37·8. $C_5H_9BrO_4$ requires C, 28·2; H, 4·2; Br, 37·5%).

2-Bromo-2-deoxy-L-arabinose.—The bromo-fluoride of the L-series gave, by the same procedure, *2-bromo-2-deoxy-L-arabinose*, m. p. 122°, $[\alpha]_D^{20}$ +116° (*c* 0·29, H_2O) (Found: C, 28·6; H, 4·4; Br, 37·0.

Methyl 2-Bromo-2-deoxy-α-D-arabinopyranoside (IV).—The bromo-fluoride (II) (230 mg.), dissolved in 1% (w/w) methanolic hydrogen chloride (10 ml.), was refluxed for 2 hr. (α −4·05° → −2·29°). The solution was neutralized with silver carbonate and calcium oxide, or with Dowex 1 (CO_3^{2-}), and was taken to dryness, giving a syrup which crystallized at 0°. The product had m. p. 91—92° (from ethyl acetate), $[\alpha]_D^{20}$ −68° (*c* 0·3, MeOH), R_F 0·68 (Found: C, 32·2; H, 5·0; Br, 35·2; OMe, 13·4. $C_6H_{11}BrO_4$ requires C, 31·7; H, 4·8; Br, 35·2; OMe, 13·6%). The compound consumed 0·94 mol. of periodate after 3 hr.[9]

Methyl 2,3-Anhydro-α-D-ribopyranoside (V).—(*a*) The bromo-glycoside (IV) (12 mg.) was heated with 0·11N-sodium methoxide (1 ml.) at 60° for 2 hr. The solution was neutralized with carbon dioxide, evaporated to dryness, extracted with ethyl acetate, and evaporated to dryness

[32] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[33] Partridge, *Nature*, 1949, **164**, 443.
[34] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.
[35] Yapke, *Canad. J. Microbiol.*, 1957, **3**, 987.
[36] Belcher, Leonard, and West, *J.*, 1959, 3577.
[37] Austin and Humaller, *J. Amer. Chem. Soc.*, 1934, **56**, 1152.

giving the anhydro-sugar (8 mg.), m. p. 83·5° (from ether), alone or mixed with the product obtained in (*b*).

(*b*) The bromo-fluoride (II) (145 mg.) was treated with 0·11N-sodium methoxide (8 ml.) as described above, for 5 hr (α −5·1°→1·78° const.). After removal of solvent, the product (V) (94 mg.) had m. p. 83° (from ether), $[\alpha]_D^{20}$ +165° ± 5° (*c* 0·21, $CHCl_3$), R_F 0·68 (Found: C, 49·7; H, 6·75; OMe, 21·4. Calc. for $C_6H_{10}O_4$: C, 49·3; H, 6·9; OMe, 21·2%) (lit.,[5] m. p. 84—86°, $[\alpha]_D$ +164·5°).

Methyl 2,3-Anhydro-α-L-ribopyranoside.—(*a*) Methyl 3,4-*O*-isopropylidene-2-*O*-methanesulphonyl-α-L-arabinopyranoside (280 mg.), m. p. 141—142°, $[\alpha]_D^{20}$ +33·4° (*c* 0·63, $CHCl_3$) {cf. m. p. 144—145°, $[\alpha]_D^{20}$ −33·1 (*c* 0·54, $CHCl_3$) for the enantiomer[38]}, dissolved in acetone (0·4 ml.) and 0·1N-sulphuric acid (10 ml.), was heated to 100° for 2 hr., cooled, and deionized with Dowex 1 (CO_3^{2-}). The solution was evaporated to dryness giving methyl 2-*O*-methanesulphonyl-α-L-arabinopyranoside (90 mg.), m. p. 114° (from ethanol), $[\alpha]_D^{20}$ +6·5° (*c* 1·4, MeOH). The methanesulphonate (70 mg.) was treated with 0·11N-sodium methoxide in methanol (1·5 ml.) at 60° for 2 hr. (α +0·18°→ +2·91° const.) and methyl 2,3-anhydro-α-L-ribopyranoside (35 mg.), m. p. 82°, R_F 0·68, $[\alpha]_D^{20}$ −161° ± 5° (*c* 0·17, $CHCl_3$) {lit.,[4] m. p. *ca.* 73°, $[\alpha]_D^{20}$ −145° ± 3° (*c* 1·9, $CHCl_3$)} (Found: C, 49·6; H, 6·7. Calc. for $C_6H_{10}O_4$: C, 49·2; H, 6·9%) was isolated as described for the above D-isomer.

(*b*) The bromo-fluoride (II) (70 mg.) in the L-series was treated as described for the D-isomer and the product (47 mg.), R_F 0·68, crystallized twice from ether, had m. p. 82° alone or in admixture with the preceding product.

2-Deoxy-N-phenyl-α-D-ribosylamine.—The bromo-fluoride (II) (117 mg.) in methanol (10 ml.) was added to Raney nickel[39] (2 g.) in dry methanol (5 ml.) and magnetically stirred in an atmosphere of hydrogen for 5 hr. The solution was filtered, neutralized with silver carbonate and calcium oxide, and evaporated to dryness. Extraction with ethyl acetate gave, on evaporation, a syrup from which a mixture of methyl 2-deoxy-D-ribosides crystallized spontaneously. The Dische test[6] showed a quantitative yield of 2-deoxy-sugar, calculated as methyl 2-deoxyriboside. In a control test, methyl 2-bromo-2-deoxyarabinoside gave no colour in 100-fold excess. The crude methyl 2-deoxyribosides (16 mg.) in 0·1N-sulphuric acid (1 ml.) were heated at 100° for 115 min., cooled, deionized with Dowex 1 (CO_3^{2-}), and freeze-dried to a syrup of 2-deoxy-D-ribose (VI), R_F 0·39. The sugar (VI) (11 mg.) was dissolved in ethanol (10·5 ml.) and redistilled aniline (10 μl.) added. The solution was refluxed for 15 min. giving 2-deoxy-*N*-phenyl-α-D-ribosylamine (VII), m. p. 170—171° (from ethanol), alone or in admixture with an authentic specimen (lit.,[7] m. p. 172—173°, 173—174°).

β-L-Arabinosyl Fluoride.—Tri-*O*-acetyl-β-L-arabinosyl fluoride (560 mg.), m. p. 115°, $[\alpha]_D^{20}$ +131° (*c* 2·2, MeOH) (lit.,[8] m. p. 117—118°, $[\alpha]_D^{28}$ +138·0°), in methanol (15 ml.) was added to N-sodium methoxide (0·1 ml.) (α +2·91° → +2·41°, const. 5 min.). After 15 min. the solution was deionized with methanol-washed Amberlite IR-120 (H^+) and evaporated to dryness. The *product* (153 mg.) was crystallized from dry methanol and decomposed at 92—96°, $[\alpha]_D^{20}$ −170° (*c* 0·4, H_2O) (Found; F, 12·2. $C_5H_9O_4F$ requires F, 12·5%) {cf. lit.,[40] m. p. 95—96° (decomp.), $[\alpha]_D$ −182° for the β-D-fluoride}.

2-Bromo-2-deoxy-D-mannose.—Tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannosyl fluoride[1] (330 mg.) in methanol (25 ml.) was added to 1·0N-sodium methoxide (1 ml.) (α −0·32° → +0·05° const. 5 min.). After 30 min. the solution was deionized with Amberlite IR-120 (H^+) and evaporated to dryness, giving syrupy 2-bromo-2-deoxy-β-D-mannosyl fluoride. The syrup, dissolved in 0·1N-sulphuric acid, was heated to 100° for 15 min. After neutralization with Dowex 1 (CO_3^{2-}), the solution was shown to give two chromatographic spots, R_F 0·14 and 0·44, the slower of which was much fainter and corresponded to glucose. The solution was freeze-dried and the mixture was separated on a cellulose column (2·5 × 45 cm.) eluted with butan-1-ol–ethanol–water (4:1:5). The faster fraction, on evaporation to dryness and trituration with ethanol, gave *2-bromo-2-deoxy-mannose*, m. p. 120°, $[\alpha]_D^{18}$ +2·72° (*c* 0·6, H_2O, 5 min.) (Found: C, 30·4; H, 4·7; Br, 32·7. $C_6H_{11}BrO$ requires C, 29·7; H. 4·4; Br, 32·8%).

2-Bromo-2-deoxy-N-phenylmannosylamine had m. p. 118—119° (Found: N, 4·5. $C_{12}H_{16}BrNO_4$ requires N, 4·4%).

Kinetic Measurements.—Methanol was dried over magnesium methoxide and redistilled. Methanolic hydrogen chloride solutions were freshly made by dilution of a 10% (w/w) stock solu-

[38] Wood and Fletcher, *J. Amer. Chem. Soc.*, 1958, **80**, 5242.
[39] *Org. Synth.*, Coll. Vol. III, 1955, p. 181.
[40] Micheel and Klemer, *Adv. Carbohydrate Chem.*, 1962, **16**, 98.

tion kept at 0° and standardized periodically with sodium hydroxide. Perchloric acid solutions were made by dilution of 70% AnalaR aqueous perchloric acid (*d* 1·70) and standardization against aqueous sodium hydroxide before and after the series of experiments.

Polarimetric Method.—Rotations were measured using a Bendix–Ericsson ETL–NPL automatic polarimeter type 143 A coupled with a Sunvic potentiometric recorder type 10S (AEI Ltd.) using 1 cm. or 2 cm. glass or Polythene cells. Water from a thermostat bath was rapidly circulated and the internal temperature of the cell measured before and after each experiment. The inlet and outlet temperatures of the circulating water remained constant. Reagents and the reaction vessel were immersed in the bath for at least 1 hr. before an experiment. The sugar (25 mg.) was dissolved in the solvent, re-equilibrated for 5 min. in the bath, and acid added so that the total volume was 5 ml. Measurements were taken after 4 min., allowing the apparatus to stabilize. Precautions were taken to avoid stray light, dust, and bubbles. The system was calibrated by using standard sucrose solutions.

Release of Fluoride Ion.—A solution of the bromoarabinosyl fluoride (II) in 1·4N-perchloric acid was placed in the thermostat bath, a portion being analysed by the above polarimetric method. Portions contained 10—30 μg. of free fluoride were withdrawn at intervals and transferred into 50 ml. of water containing acetate buffer (2 ml.; pH 4·3), thus effectively stopping the reaction. The fluoride ion was then measured by the method of Belcher *et al.*[36] The resulting rate curve agreed to within 4% with that obtained polarimetrically.

Methanolysis of 2-Bromo-2-deoxy-β-D-arabinosyl Fluoride.—Each solution remaining after kinetic investigation was deionized with Dowex 1 (CO_3^{2-}), and a portion was analysed chromatographically, giving only one spot (R_F 0·68) in each case, and the remainder evaporated to dryness and recrystallized from ethyl acetate gave methyl 2-bromo-2-deoxy-α-D-arabinoside, m. p. 91—92°, alone or mixed with authentic compound (R_F 0·68).

Methanolysis of β-L-Arabinosyl Fluoride.—The solutions remaining after each kinetic experiment were treated as described above, giving a crystalline product, m. p. 110—124°, in high yield which, after recrystallization from ethyl acetate, gave methyl α-L-arabinoside, m. p. 127—128°, alone or mixed with the authentic compound.

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