The Addition of the Elements of "BrF" and of "IF" to Unsaturated Carbohydrates

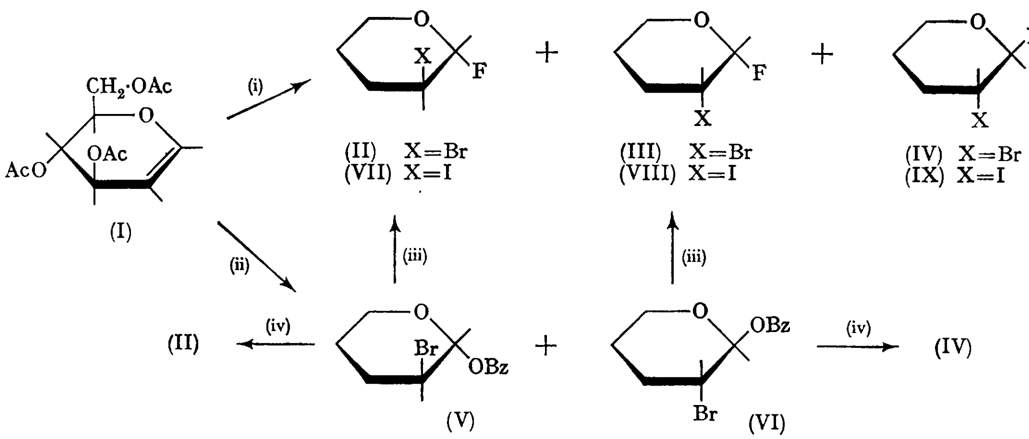
By L. D. HALL* and J. F. MANVILLE

(*Department of Chemistry, The University of British Columbia, Vancouver* 8, *B.C., Canada*)

WE have recently shown that reaction of an alkene with halogen (Br_2 or I_2) in the presence of finely powdered silver monofluoride results in the high yielding addition of the elements of "XF" to the alkene; for cyclohexene the addition occurs exclusively *trans*.[1] We now describe the application of this reaction sequence to a class of unsaturated carbohydrates, the pyranose glycals, for which we observe both *cis*- and *trans*-addition, although the *trans*-adduct(s) always predominates.

For example, 3,4,6-tri-*O*-acetyl-D-glucal (I) with Br_2–AgF affords a mixture containing three "BrF" adducts, all having bromine at C-2 and fluorine at C-1. These are: 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-mannopyranosyl fluoride (II, 70%), m.p. 139—140°, $[\alpha]_D^{22}$ −32·0° (*c*, 1·28 in $CHCl_3$); 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl fluoride (III, 9%), m.p. 120—121°, $[\alpha]_D^{22}$ 134·5° (*c*, 1·80 in $CHCl_3$); and the corresponding β-anomer (21%) which has thus far failed to crystallise. We consider it significant that reaction of (I) with "BrF" generated by the "Bowers" method[2] gives the same three glycopyranosyl fluorides in similar yields: (II), *ca.* 55%, (III), *ca.* 9%, and (IV), *ca.* 30%. These results should be contrasted with those previously reported for this reaction.[3] We find, rather surprisingly,[4] that the Bowers addition of "BrF" also results in significant quantities (*ca.* 7%) of 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl fluoride.[5]

The structures of the adducts (II) to (IV) were



Reagents: (i) X_2 in benzene, AgF in MeCN; (ii) X_2 in benzene, AgOBz in benzene; (iii) HF; (iv) (a) HBr in HOAc, (b) AgF in MeCN.

established by detailed ^1H and ^{19}F n.m.r. studies, and confirmed by the following syntheses. Triacetyl-D-glucal (I) reacted with bromine and silver benzoate[6] in benzene solution to give the bromobenzoates (V, 31%), m.p. 168—169°, $[\alpha]_D^{28}$ 62·3° (*c*, 1·54 $CHCl_3$); corresponding α-D-*gluco*-isomer (27%), m.p. 112—113°, $[\alpha]_D^{25}$ 212·6° (*c*, 0·89 $CHCl_3$) and (VI, 42%), m.p. 161—162°, $[\alpha]_D^{28}$ 15·3° (*c*, 0·72 $CHCl_3$); reaction of the α-D-*manno*-derivative (V) with anhydrous liquid HF under conditions known[7] to give preferentially α-D-hexopyranosyl fluorides afforded, as sole product, material which was identical in all respects with a sample of (II) obtained *via* the Br_2–AgF sequence. Under identical conditions the β-D-*gluco*-derivative (VI) gave a mixture of (III) and (IV); since (IV) isomerized readily to (III), we assign these the β- and α-configurations, respectively. Another stereospecific synthesis of (II) and (IV), followed the separate conversion of the bromo-benzoates (V) and (VI) into the corresponding α-D-glycopyranosyl bromides, which were reacted without isolation with AgF to give (II) and (IV), respectively. Both of these reactions afforded *exclusively* the *trans*-fluoride, presumably as a result of the participation of the bromine substituent at C-2. Further, indirect evidence supporting the assignment of the α-configuration to (II) followed from a partial hydrogenolysis of this derivative at room temperature (10% palladium–charcoal catalyst) to give (n.m.r. evidence[5]), 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl fluoride.

To a first approximation, these "XF" reactions follow closely the rationale of electrophilic addition reactions presented by Lemieux and Frazer-Reid.[8] The contrast between the above results and the exclusive *trans*-addition observed for cyclohexene indicates the important role played by the ring-oxygen substituent during the addition of electrophiles to cyclic, vinyl ethers.

Similarly, we have added the elements of "IF" to (I) and have obtained a similar set of derivatives which have the following physical constants: α-D-*manno*- (VII, 60%), m.p. 155—156°, $[\alpha]_D^{22}$ −46·1° (*c*, 2·54 in $CHCl_3$); α-D-*gluco*- (VIII, 6%), m.p. 143—144°, $[\alpha]_D^{22}$ 180·5° (*c*, 2·72 in $CHCl_3$); β-D-*gluco*- (IX, 34%). The structure of compounds (VII) and (VIII) have also been confirmed by independent syntheses. We have also synthesised the "ClF" adducts of (I): α-D-*manno*-, m.p. 120—121°, $[\alpha]_D^{25}$ −23·4° (*c*, 0·96 in $CHCl_3$); α-D-*gluco*-, m.p. 95—97°, $[\alpha]_D^{25}$ 203° (*c*, 1·13 in $CHCl_3$); β-D-*gluco*-, m.p. 77—78°, $[\alpha]_D^{25}$ 124° (*c*, 2·10 in $CHCl_3$).

We acknowledge financial assistance from the National Cancer Institute of Canada and the National Research Council of Canada.

(*Received, October* 30*th*, 1967; *Com.* 1166.)

---

[1] L. D. Hall, D. L. Jones, and J. F. Manville, *Chem. and Ind.*, 1967, 1787.

[2] A. Bowers, L. C. Ibanez, E. Denot, and R. Becerra, *J. Amer. Chem. Soc.*, 1960, **82**, 4001.

[3] P. W. Kent, F. O. Robson, and V. A. Welch, *J. Chem. Soc.*, 1963, 3273; K. R. Wood, P. W. Kent, and D. Fisher, *J. Chem. Soc.*, (*C*), 1966, 912.

[4] I. Lundt and C. Pedersen, *Acta Chem. Scand.*, 1966, **20**, 1369.

[5] L. D. Hall and J. F. Manville, *Canad. J. Chem.*, 1967, **45**, 1299.

[6] R. U. Lemieux and S. Levine, *Canad. J. Chem.*, 1962, **40**, 1926, and references therein.

[7] F. Micheel and A. Klemer, *Adv. Carbohydrate Chem.*, 1961, **16**, 85.

[8] R. U. Lemieux and B. Frazer-Reid, *Canad. J. Chem.*, 1965, **43**, 1460.