Opening of Cyclic Acetals by Trichloro-, Dichloro-, and Tribromo-borane

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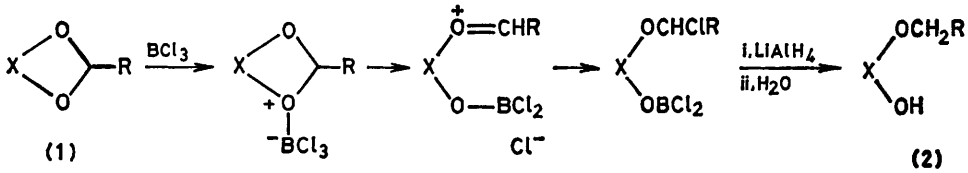
The rate-determining step in the ring opening of cyclic acetals by trichloroborane to yield α-chloro-ethers is shown to be consistent with the formation of an oxocarbenium ion. Subsequent reduction provides a general route for the conversion of a diol into a hydroxy-ether. Tribromoborane is a more powerful and dichloroborane a less powerful reagent than trichloroborane.

ACETALS are opened by dichloroalane [1,2] or chloroalane.[3] The latter reagent with 2-methyl-1,3-dioxolan reversibly [4] co-ordinates with one of the oxygens of the acetal and then intramolecularly [5] reduces the acetal carbon to yield a hydroxy-ether. Treatment of acetals with di- or mono-chloroborane does not seem to have been reported, but 1,3-dioxolan (1, 2, or 3 mol) immediately reacts † with trichloroborane to yield a chloromethoxyethyl ester of boron.[6] Lithium aluminium hydride reduces α-chloro-ethers [7] so that 2,5-*O*-methylene-D-mannitol with trichloroborane, followed by reduction gives a hydroxy-methyl ether (58% overall).[8] The mechanism shown in Scheme 1 (R = H) was proposed.



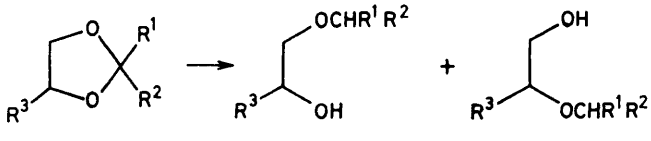
X	R	X	R	X	R
a; $[CH_2]_2$	Pr^n	f; $[CH_2]_3$	CH_2Cl	k; $[CH_2]_5$	Pr^n
b; $[CH_2]_2$	H	g; $[CH_2]_3$	Ph	l; $[CH_2]_5$	H
c; $[CH_2]_2$	CH_2Cl	h; $[CH_2]_4$	Pr^n	m; $[CH_2]_5$	CH_2Cl
d; $[CH_2]_3$	Pr^n	i; $[CH_2]_4$	H	n; $-C_6H_4$-*o*	H
e; $[CH_2]_3$	H	j; $[CH_2]_4$	CH_2Cl	o; $-C_6H_4$-*o*	Ph

SCHEME 1

The present paper gives evidence supporting the ring-opening mechanism and shows the generality of the ring opening–reduction sequence. Table 1 shows that a range of cyclic acetals can be converted into their hydroxy-ethers, using an acetal : trichloroborane ratio of 3 : 1. 1,3-Dioxolan (1b) gave a 90—95% yield of hydroxy-ether with trichloroborane (Table 1), whereas it only gave 60 and 16% yields using chloroalane [3] or borane [9] after 24 h, respectively. With 2-propyl-1,3-dioxan (1d), 1 : 1 and 2 : 1 mol ratios of acetal to trichloroborane gave, as expected, high (>90%) yields of the hydroxy-ether, but with mol ratios of greater than 3 : 1, only 3 mol equiv. of acetal were opened.

Following the reasoning of Leggetter and Brown [3] who opened acetals with chloroalane, if the formation of an oxocarbenium ion (Scheme 1), probably as an ion pair, is the rate-determining step in the production of the α-chloro-ether, then changing R in the sequence Pr^n, H, and CH_2Cl will progressively hinder its formation. It can be seen from Table 1 that for acetals which are opened with difficulty (*e.g.* dioxolans and dioxans) the yields of the opened products do indeed fall in the expected order. The trend is shown more clearly in the two competitive experiments using dioxolan and its derivatives (1 mol equiv. of each of the acetals and 0.2 mol equiv. of trichloroborane).

Three competitive experiments were performed on mixtures containing 2-propyl acetals (1 mol equiv. each) and trichloroborane (0.25 mol equiv.) to see the effect of ring size. Table 1 shows that the rates of ring opening are 5 ≈ 6 ≪ 7 ≈ 8 (numbers refer the number of ring atoms). These results can be compared with the relative reactivity of 2-methyl-1,3-acetals towards acid-catalysed ring-opening [10] where 5 > 6 ≪ 7 ≪ 8.



a; $R^1 = R^2 = H$, $R^3 = Me$
b; $R^1 = R^2 = H$, $R^3 = CH_2Cl$
c; $R^1 = R^2 = R^3 = Me$
d; $R^1 = R^2 = Me$, $R^3 = CH_2Cl$

SCHEME 2

In the reaction of chloroalane with 4-substituted 1,3-dioxolans the ring usually opened in such a way as to produce the more stabilised oxocarbenium ion (Scheme 2).[3] Table 2 shows the marked similarity between opening by trichloroborane and by chloroalane. The exception is the trimethyl derivative when the product (predicted as mainly the primary alcohol) is mixed

† We thank a referee for bringing this to our notice.

TABLE 1

Acetal (1)	Lewis acid (mol)	Reaction time (h)	Recovered products (%) (2)	(1)	other [c]
a	BCl_3	0.2	>95	0	
b	BCl_3	0.2	90—95	<1	
c	BCl_3	0.2	67	33	
d	BCl_3	0.2	>95	0	
d	$BHCl_2$	1	*ca.* 99	*ca.* 1	
d	BBr_3 (0.33)	0.03	95	0	
e	BCl_3	0.2	90—95	<1	
e	$BHCl_2$	12	70	30	
e	BBr_3 (0.33)	0.03	87		(4) 13
f	BCl_3	0.2	49	44	
f	$BHCl_2$	48	*ca.* 0	*ca.* 100	
f	BBr_3 (0.33)	0.25	82		(4) 18
g	$BHCl_2$	0.05—0.08	*ca.* 99	*ca.* 1	
h	BCl_3	0.2	>95	0	
i	BCl_3	0.2	95	0	
j	BCl_3	0.2	95	<1	
k	BCl_3	0.2	98	0	
l	BCl_3	0.2	95	0	
m	BCl_3	0.2	95	0	
n	BBr_3 (1)	5	70 [a]	*ca.* 14 [a]	
o	BBr_3 (1)	0.25	83 [a]	0	pyrocatechol 17 [a]
a + b } 1.84 g	BCl_3	0.2	35.8	22.3	(3) 3.5 } 1.64 g
			<1	38.1	
b + c } 1.67 g	BCl_3	0.2	27.4	10.1	(3) 2.0 } 1.35 g
			2.4	58.1	
a (4.64 g) + d (5.2 g)	BCl_3	0.2	40.6		(3) 2.3 } 8.86 g
			54.7	*b*	(4) 2.5
d (4.24 g) + h (4.71 g)	BCl_3	0.2	2.7		(4) <1 } 8.41 g
			90.8	*b*	(5) 6.4
h (5.39 g) + k (5.92 g)	BCl_3	0.2	46.1		(5) 3.8 } 9.95 g
			46.8	*b*	(6) 3.3

[a] Isolated yield. [b] The yields of unchanged acetals in the last 3 competitive experiments are excluded. [c] Other products were the diols $HO\cdot[CH_2]_n\cdot OH$: (3; $n = 2$), (4; $n = 3$), (5; $n = 4$), and (6; $n = 5$).

2,2,4,4-Tetramethyl-1,3-dioxolan opens [11] with chloroalane to give the less stabilised oxocarbenium ion, a result explained as due to steric crowding in the transition state. Acid hydrolysis of similar dioxolans is also subject [12] to such interactions. Perhaps the trimethyl acetal–trichloroborane reaction also experiences similar congestions.

TABLE 2

Acetal (7)	Reaction time [a] (min)	Amount recovered [b] (g)	Recovered alcohol (%) BCl_3 [c] (9) [d]	(8)	AlH_2Cl [e] (9)	(8)
a (0.72 g)	10	0.68	95	5	93	7
b (1.13 g)	10	1.03	7	93	10	90
c (1.16 g)	2	1.09	44	56	82	18
d (1.31 g)	2	1.15	5	95	5	95

[a] Time in contact with BCl_3. [b] After $LiAlH_4$ reduction. [c] No acetal remained, but a small amount of the appropriate diols was present. [d] Identity of peak on g.l.c. established by repetition of AlH_2Cl–acetal reaction (ref. 3). [e] Ref. 3.

By analogy with dichloroalane, dichloroborane also opens cyclic acetals, as shown in Table 1. 1,3-Dioxans were treated with 1 : 3 mol ratios of dichloroborane in diethyl ether and recovery yields were 85—90%; only traces of diol were present. As expected, dichloroborane is a milder reagent than trichloroborane, but it seems to have a slightly better ring-opening ability than chloroalane, which reduces 93% of 2-phenyl-1,3-dioxan (1g) in 15 min at ambient temperature and 28% of 1,3-dioxan (1e) in 24 h.[13]

Tribromoborane is a more powerful Lewis acid [14] than trichloroborane, as indicated in particular by the results for 2-chloromethyl-1,3-dioxan (1f) (Table 1). The acetal : tribromoborane ratio for the three dioxans studied was 3 : 1 and the recovery in each case was 85—90%. When 2-propyl-1,3-dioxan (1d) was treated with tribromoborane (3 : 1 mol ratio) in carbon tetrachloride the acetal-proton triplet at δ 4.5 in the ^1H n.m.r. spectrum was replaced by a one-proton triplet at δ 5.6. In 1-chloro-1-ethoxypropane 1-H resonates at δ 5.9.[15] The same experiment using 2-phenyl-1,3-benzo[*d*]dioxole (1o) gave a one-proton singlet at δ 6.7, and on work-up yielded 83% of 2-benzyloxyphenol. It seems likely, therefore, that tribromoborane is acting similarly to trichloroborane. With the more de-activated 1,3-benzo[*d*]-dioxole (1n) the normal acetal : tribromoborane ratio (3 : 1) gave, after 5 h, only 27% of the reduced product. The yield increased to 68—74% using 1 : 1-, 1 : 2-, or 1 : 3-mol ratios. In the 3 : 1-mol ratio experiment it

seems likely that the reduced Lewis acidity of the boron in the dibromoaryloxyborane formed after 1 mol equiv. of acetal has been opened, is insufficient to open a second mol equiv. of acetal.

EXPERIMENTAL

Chemical-ionisation mass spectra were obtained using an isobutane plasma in a VG Micromass 12F spectrometer. ^{1}H N.m.r. spectra were recorded on a Varian EM360 60 MHz spectrometer, using deuteriochloroform as solvent.

Preparation of Acetals and Hydroxy-ethers.—These were prepared by standard procedures and the purity of liquids was checked by g.l.c. and, when available, by comparing with boiling points given in the literature, except for the compounds given below. Yields of liquids are those obtained after the first distillation. Chiral compounds were obtained as their racemates.

2-Propyl-1,3-acetals were made by method B of Astle *et al.*[16] *2-Propyl-1,3-dioxocan* (1k), 28%, had b.p. 42 °C/2 mmHg (Found: C, 68.2; H, 11.6. $C_9H_{18}O_2$ requires C, 68.3; H, 11.4%). 2-Chloromethyl-1,3-acetals were made as for 2-chloromethyl-1,3-dioxolan (1c).[3] *2-Chloromethyl-1,3-dioxepan* (1j), 76%, had b.p. 98—102 °C/14 mmHg (lit.,[17] b.p. 77 °C/15 mmHg) (Found: C, 48.0; H, 7.6. $C_6H_{11}ClO_2$ requires C, 47.8; H, 7.4%), and *2-chloromethyl-1,3-dioxocan* (1m), 62%, had b.p. 40—45 °C/0.5 mmHg (Found: C, 50.9; H, 8.55; Cl, 21.7. $C_7H_{13}ClO_2$ requires C, 51.1; H, 8.0; Cl, 21.5%).

3-Butoxypropan-1-ol (2d), 42%, b.p. 43—45 °C/0.1 mmHg (lit.,[18] b.p. 78—79 °C/10 mmHg), was synthesised as for 3-methoxypropan-1-ol (2e),[13] except that refluxing was used to dissolve the sodium in the n-butanol. ω-(2-Chloroethoxy)-n-alkan-1-ols were isolated from the reaction of trichloroborane–lithium aluminium hydride with the appropriate 2-chloromethyl-1,3-acetal. *3-(2-Chloroethoxy)propan-1-ol* (2f) had b.p. 68—70 °C/2 mmHg (Found: C, 43.55; H, 8.2. $C_5H_{11}ClO_2$ requires C, 43.3; H, 8.0%); *m/e* 139 and 141 $(M + 1)^+$; δ 3.8—3.3 (m, 8 H), 2.9 (s, 1 H), and 1.9 (q, 2 H). *4-(2-Chloroethoxy)butan-1-ol* (2j) had b.p. 86—90 °C/0.15 mmHg (Found: C, 47.4; H, 8.8; Cl, 23.7. $C_6H_{13}ClO_2$ requires C, 47.2; H, 8.6; Cl, 23.2%); *m/e* 153 and 155 $(M + 1)^+$; δ 4.25 (s, 1 H), 3.8—3.3 (m, 8 H), and 1.7—1.4 (m, 4 H). *5-(2-Chloroethoxy)pentan-1-ol* (2m) had b.p. 100—104 °C/0.5 mmHg (Found: C, 50.8; H, 9.25; Cl, 21.7. $C_7H_{15}ClO_2$ requires C, 50.45; H, 9.1; Cl, 21.3%); *m/e* 167 and 169 $(M + 1)^+$; δ 3.8—3.3 (m, 8 H), 2.9 (s, 1 H), and 1.7—1.3 (m, 6 H). ω-Methoxy- and ω-butoxyalkan-1-ols were made from the appropriate diols using 1,2-dimethoxyethane as solvent.[19] 5-Methoxypentan-1-ol (2l), 55%, had b.p. 102—104 °C/12 mmHg (lit.,[20] b.p. 83—84 °C/9 mmHg).

General Procedure for the Reaction of a 1,3-Cyclic Acetal with Trichloroborane, followed by Addition of Lithium Aluminium Hydride.—Dried ($CaCl_2$) dichloromethane was added to a flask immersed in an ice–water bath and trichloroborane was allowed to distil into the stirred solvent. The weight of trichloroborane was determined by weighing before and after the addition. The acetal in dry dichloromethane was added, *via* a separating funnel, to the trichloroborane solution. After the required reaction time the ice–water was removed and a suspension of lithium aluminium hydride in dry diethyl ether was added. When the effervescence ceased (*ca.* 30 min), the mixture was poured into ice-cold aqueous methanol and was made neutral by the addition of 4M-aqueous sodium hydroxide. After filtering the suspension, the filtrate was evaporated, more methanol was added, and this was also removed. This process was repeated twice more to remove the boron. Chloroform was added to the syrup and the suspension was centrifuged. The supernatant solution and the chloroform washings of the residue were combined and the extract was dried (Na_2SO_4) and analysed by g.l.c. using a Pye 104 chromatograph with a flame-ionisation detector and with nitrogen as carrier gas. Stationary phases, normally at *ca.* 200 °C, were (*a*) Apiezon K (7.5%) on Chromasorb W and (*b*) OV-225 (3%) on Chromasorb W. Relative peak-areas (Hewlett-Packard 3370B integrator) were used directly as quantitative measures of the products; differences in the detector response were assumed to be insignificant.

Reaction of Dichloroborane with the 1,3-Dioxans.—Dichloroborane was prepared by addition of lithium borohydride (1 mol) to trichloroborane (3 mol) in diethyl ether at 0 °C (*cf.* ref. 21). The 1,3-dioxan (1 mol) in diethyl ether was slowly added to dichloroborane (3 mol) in diethyl ether at room temperature. Aliquots were quenched by aqueous methanol and analysed by g.l.c. as above. The times given in Table 1 correspond to complete consumption of the acetal or to no further reaction.

Reaction of Tribromoborane with Cyclic Acetals.—The acetal (1 mol) in dichloromethane was added to a stirred solution of tribromoborane (for the amount see Table 1) in dichloromethane at 0 °C. A suspension of lithium aluminium hydride (1 mol) in diethyl ether was added after the time given in Table 1 and the reaction was worked up as above. With 1,3-benzo[*d*]dioxole (1n), the crude product (84%) in chloroform was extracted with 1M-sodium hydroxide. The chloroform layer contained unchanged acetal. The alkaline extracts were acidified and extracted with chloroform. Evaporation of the chloroform gave the phenol. With 2-phenyl-1,3-benzo[*d*]dioxole (1o), the crude product (85%) was separated on a silica-gel column [toluene–methanol (9 : 1) used as eluant].

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