433. *Factors in the Formation of Isomerically and Optically Pure Alkyl Halides. Part II.*[1] *Reactions of Straight-chain Alcohols with Hydrogen Halides, and the Preparation of Isomerically Pure 2-Halogeno-octanes.*

By W. Gerrard and H. R. Hudson.

Alkyl rearrangements occurring during formation of alkyl halides from straight-chain alcohol–hydrogen halide interactions have been investigated with the aid of gas chromatography. The effect of zinc halides or concentrated sulphuric acid upon the reaction, and upon the alkyl halides obtained, has also been investigated. Isomerically pure 2-halogeno-octanes were obtained in moderate yields by the controlled interaction of phosphorus trihalides with octan-2-ol.

IN continuation of our investigation of alcohol–hydrogen chloride reaction systems,[1] we find that hydrogen bromide and hydrogen iodide also react with straight-chain primary alcohols (Pr^n, Bu^n, n-pentyl, and n-octyl) to afford pure n-alkyl halides at temperatures up to 100—120°; even at 160° in a sealed tube rearrangement is barely detectable.

The s-alkyl groups (1-methylbutyl, 1-ethylpropyl, and 1-methylheptyl) readily rearranged to other secondary structures even at 20°, in conformity with other reports,[2-4] and the optical purity of the halides obtained from (+)-octan-2-ol was lower than that attainable in phosphorus trihalide systems.[5] Thus, pentan-2-ol or pentan-3-ol, saturated with hydrogen chloride, bromide, or iodide, each afforded about 20% of the rearranged s-isomer when heated (sealed tube) at 100°; with concentrated hydrobromic acid similar results were obtained. At 20°, the much slower reactions gave a smaller proportion of rearrangement, and the presence of pyridine dihydrochloride, although accelerating the reaction[1,6] did not materially alter the percentage of rearrangement.

That rearrangement occurs in the reaction step, and not after halide formation, is indicated by the non-rearrangement and retention of optical purity of 2-chloro-octane added to the pentan-2-ol–hydrogen chloride reaction in a sealed tube at 100°. 2-Bromo- and 2-iodo-octane similarly remained unrearranged in the corresponding pentan-2-ol–hydrogen halide systems, although they lost optical purity, indicative of an S_N2 halogen–halogen exchange[7] resulting from the greater polarisability of C–Br or C–I bonds, and the greater nucleophilic power of bromide or iodide ions. 2-Bromo-octane suffered no loss in optical rotatory power, however, when shaken with concentrated hydrobromic acid or heated with it at 100° (5 hours) in a sealed tube. It has generally been accepted that rearrangement occurs on the formation of a carbonium cation. If each cation of necessity rearranges, then only factors related to its formation need be elucidated; but if there be a probability of non-rearrangement of the cation, then factors related to this have to be evaluated, and these factors may not be in every respect identical with the first set of factors.

That formation of rearranged halides in these preparative systems may occur by initial formation of olefin, which then combines with the hydrogen halide according to Markowni-koff's rule, cannot be entirely discounted, although we consider it to be a minor probability. Whereas the passage of but-1-ene into the n-butanol–zinc chloride–hydrogen chloride

[1] Part I, Gerrard and Hudson, *J.*, 1963, 1059.
[2] Whitmore and Karnatz, *J. Amer. Chem. Soc.*, 1938, **60**, 2536.
[3] Pines, Rudin, and Ipatieff, *J. Amer. Chem. Soc.*, 1952, **74**, 4063.
[4] Cason and Correia, *J. Org. Chem.*, 1961, **26**, 3645.
[5] Gerrard, *J.*, 1940, 1464; 1944, 85; 1945, 848; Berlak and Gerrard, *J.*, 1949, 2309; Brauns, *Rec. Trav. chim.*, 1946, **65**, 799.
[6] Gerrard and Hudson, *Proc. Chem. Soc.*, 1961, 467.
[7] Hughes, Juliusberger, Masterman, Topley, and Weiss, *J.*, 1935, 1525; Hughes, Juliusberger, Scott, Topley, and Weiss, *J.*, 1936, 1173.

reaction mixture at 100° increased the yield of s-butyl chloride slightly, most of the but-1-ene did not react. The possibility of simultaneous bimolecular substitution and rearrangement must also be admitted, *e.g.*,

$$X^- \quad \overset{H}{\underset{}{C}}-C-\overset{H}{\underset{+}{O}}\overset{H}{\underset{H}{}} \longrightarrow X-C-\overset{H}{\underset{}{C}} + H_2O$$

It was important to establish that no rearrangement of secondary to primary alkyl groups occurred in these reactions, as the rearrangement of isopropyl to n-propyl had been reported in the isopropyl bromide–aluminium bromide system [8] (1·3% at 60°) and confirmed by us in this and certain boron systems.[9] We could find no n-isomers in the products from any of the s-alcohols examined, including propan-2-ol, with hydrogen chloride, bromide, or iodide.

Zinc halides are not generally used as catalysts in the preparation of alkyl bromides or iodides, and we found that zinc bromide had indeed no marked effect, and caused no rearrangement (cf. zinc chloride [1]), in the n-propanol–hydrogen bromide reaction, although in its presence the amount of rearrangement in the 1-methylbutyl system was increased from 7 to 18%. Concentrated sulphuric acid is commonly employed as a catalyst in the preparation of n-alkyl bromides,[10] and we have shown it to cause almost no alkyl rearrangement in most cases, although trace quantities of s-isomers were occasionally detectable, *e.g.*, n-propanol gave ~0·3% of isopropyl bromide. Its function is probably to conserve a high concentration of protonated alcohol, ROH_2^+, in the aqueous preparative systems.

The effect of zinc halides, or of concentrated sulphuric acid upon the alkyl halides after formation was also investigated. Zinc chloride has no effect upon n-butyl chloride under reflux,[11] although it will rearrange 2- or 3-chloropentane upon shaking together with concentrated hydrochloric acid in the cold.[2] Zinc bromide caused rearrangement of n-butyl bromide at reflux temperature (11·5% in 8 hours), and finally caused complete decomposition to hydrogen bromide and polymer. Surprisingly, zinc iodide had no effect on n-butyl iodide under reflux.

Concentrated sulphuric acid did not react with n-butyl chloride when heated under reflux, but caused slow decomposition of n-butyl bromide to hydrogen bromide and polymer, and left no isomeric halide. Its ability to isomerise s-alkyl bromides has been reported,[3,4] and we also show that on shaking with 2-chloro-octane at 20° loss in optical purity, and rearrangement to 3- and 4-chloro-octane, occurs together with the evolution of hydrogen chloride. This procedure has been used for the removal of unreacted octan-2-ol from the chloride.[12] When a mixture of n- (87%) and s-butyl chloride (13%) was heated under reflux with concentrated sulphuric acid, the s-isomer gradually decomposed with the evolution of hydrogen chloride, to leave n-butyl chloride of over 99% purity. Sulphuric acid is suggested as a means of removing high-boiling impurities from the crude n-butyl chloride as obtained by the zinc chloride–hydrogen chloride method,[13] and it is likely that this may also have caused the removal of some of the unsuspected s-butyl chloride by-product.

It was necessary to obtain certain s-alkyl halides in a pure state, and for chlorides either the thionyl chloride method [1] or the controlled use of phosphorus trichloride [14] is suitable. The reaction of phosphorus tribromide with secondary alcohols has frequently given rise to rearrangement [4] but it has recently been shown [15] that, by confining dealkyl-

[8] Andreevskii, *Doklady Akad. Nauk. S.S.S.R.*, 1960, **135**, 312.
[9] Gerrard, Hudson, and Murphy, unpublished work.
[10] *Org. Synth.*, 1921, **1**, 1.
[11] Gerrard, Hudson, and Murphy, *J.*, 1962, 1099.
[12] Pickard and Kenyon, *J.*, 1911, **99**, 45.
[13] *Org. Synth.*, 1925, **5**, 27.
[14] Cook, Coulson, Gerrard, and Hudson, *Chem. and Ind.*, 1962, 1506.
[15] Coulson, Gerrard, and Hudson, unpublished work.

ation of the intermediate trialkyl phosphite to the first stage, isomerically pure s-alkyl bromides can be obtained (see also ref. 5). Removal of excess of the hydrogen bromide in a stream of carbon dioxide thus enabled 2-bromo-octane to be prepared in what is most likely an optically pure condition, *viz.*, α_D^{20} $-44 \cdot 0°$ ($l = 1$), whereas in the phosphorus tri-iodide system the use of an excess of the latter (which itself may dealkylate the intermediate phosphite [5]) also gave isomerically pure 2-iodo-octane, but with some loss of rotatory power.

<div align="center">EXPERIMENTAL</div>

Starting Materials.—Alcohols were attested by gas chromatography. In the resolution of octan-2-ol,[16] triethylamine ($0 \cdot 25$ mol.), in addition to pyridine, was used in the preparation of the hydrogen phthalate.[17] Phthalic anhydride (148 g.) was dissolved in hot dry pyridine (80 g.) and cooled, to give a fine suspension which, when heated (100°) for 5 min. with octan-2-ol (130 g.) plus triethylamine (25 g.), afforded the hydrogen phthalate as a clear viscous mass.

<div align="center">TABLE 1.</div>
<div align="center">Primary alkyl systems.</div>

Alcohol (ROH)				Added substance (mol.)	Method * and temp.	Time (hr.)	Alkyl halide (RX)				
R	Wt. (g.)	Reagent (mol.)					Yield (%)	B. p./mm.	n_D^{20}	Composition	(%)
Pr^n	20·0	HBr aq.^{a}	1·25	—	R	80°	3	15	70—72°	1·4328	Pr^n	100
,,	20·0	,,	1·25	H_2SO_4 1·18	R	92	3	73	70—72	1·4335	,,	99·7^b
,,	20·0	,,	1·25	ZnBr$_2$ 0·50	R	92	3	16	68—72	1·4320	,,	100
Bu^n	44·0	,,	1·23	H_2SO_4 1·16	R	118	3	87	101—102	1·4389	Bu^n	~100^c
,,	6·0	HBr anhyd.	1·02	—	S	20	96	62	98—100	1·4369	,,	100
,,	12·0	,,	1·02	—	S	125	7	75	97—100	1·4370	,,	100
,,	3·1	,,	0·93	—	S	160	7	61	99—101	1·4351	,,	~100^d
,,	18·5	HI aq.^{e}	4·0	—	R	118	3	89	129	1·4992	,,	100
,,	18·5	,,	1·25	—	R	118	3	56	126—128	1·4940	,,	100
,,	17·2	,,	1·0	ZnI$_2$ 0·5	R	118	3	44	129—130	1·4959	,,	100
Pe^n	16·3	HBr aq.^{a}	1·23	H_2SO_4 1·16	R	130	3	72	127—128	1·4431	Pe^n	~100^f
Oc^n	9·9	,,	1·24	,, 1·17	R	130	3	73	85—86/12	1·4505	Oc^n	100

<div align="center">* S = sealed tube, R = reflux.</div>

^{a} Concentrated acid (47% w/w). ^{b} Pr^i 0·3%. ^{c} Trace of Bu^{s}Br detectable with very large sample. ^{d} Trace of Bu^{s}Br and possibly Bu^{t}Br. ^{e} Concentrated acid (55% w/w). ^{f} ~1% of mixed 2- and 3-bromopentane.

The crude (+)- or (−)-hydrogen phthalates were finally recrystallised from ether–petroleum (b. p. 60—80°), in place of glacial acetic acid.[17]

Hydrogen bromide and hydrogen iodide were obtained by the interaction of the theoretical quantity of water and phosphorus tribromide or tri-iodide.[18]

Analytical Methods.—Gas-chromatographic analyses were carried out as described previously for the corresponding alkyl chlorides,[1] except that, for the bromo- and iodo-pentanes, column temperatures of 37 and 44°, respectively, were used. Propyl and butyl iodides were analysed on an Argon chromatograph with 10% di-(2-cyanoethyl) ether on Celite at 40°. Replacement of diethyl by di-n-butyl D-tartrate made complete separation of 4- and almost complete separation of 2- and 3-halogeno-octanes, possible. All optical rotations α are for $l = 1$.

Alcohol–Hydrogen Halide Reactions.—Anhydrous halides were absorbed in the alcohols at 0°, to give saturated solutions which were heated or allowed to stand in sealed tubes for the times stated (Tables). Following the reaction, the halides were separated, washed with water (and with sodium thiosulphate solution to remove free iodine from iodides), dried (K_2CO_3), and distilled.

Preparation of Pure s-Alkyl Halides.—(a) 2-Chloro-octane α_D^{22} $-26 \cdot 55°$ was prepared from octan-2-ol (α_D^{18} $+8 \cdot 00°$), thionyl chloride (2 mol.), and pyridine (2 mol.), by the modified Darzens procedure.[1]

(b) Phosphorus tribromide ($15 \cdot 5$ g., $0 \cdot 33$ mol.) was added dropwise (10 min.) to octan-2-ol ($22 \cdot 4$ g.; α_D^{18} $-8 \cdot 04°$) at $-10°$. After 1 hr. at 20°, the product was poured on to crushed ice,

[16] Pickard and Kenyon, *J.*, 1907, **91**, 2058; Kenyon, *J.*, 1922, **121**, 2540.
[17] Kenyon and Patel, personal communication.
[18] Gerrard, *Res. Correspondence*, 1954, **7**, S20.

View Online

[1964] *Isomerically and Optically Pure Alkyl Halides. Part II.* 2313

TABLE 2.

Secondary alkyl systems.

Alcohol (ROH)			Method* and temp.		Time	Alkyl halide (RX)						
R	Wt. (g.)	Reagent (mol.)				Yield (%)	B. p./mm.	n_D^{20}	Composition (%)			
Pr^i	5·5	HBr anhyd.	0·91	S 20°	144 hr.	30	60°	1·4250	Pr^i	100		
,,	7·2	,,	0·91	S 100	5 hr.	67	60	1·4239	,,	100		
,,	7·3	HI aq.^{a}	4·0	R 100	1 hr.	66	88—90	1·4981	,,	100		
Bu^s	16·9	HBr aq.^{b}	4·0	R 95	1 hr.	82	89—90	1·4359	Bu^s	100		
,,	9·3	HI aq.^{a}	4·0	R 116	1 hr.	81	118—119	1·4993	,,	100		
Pe^2†	21·5	HBr aq.^{b}	4·0	R 115	1 hr.	79	114—116	1·4388	Pe^2	76;	Pe^3	24
,,	7·8	HBr anhyd.	0·93	S 20	144 hr.	40	^{c}		,,	93;	,,	7
,,	10·4	,,	0·93	S 20	144 hr.	62	^{c}		,,	82;	,,	18
,,	8·6	,,	0·93	S 100	3 hr.	80	^{c}		,,	87;	,,	13
,,	6·7	,,	0·88	S 100	10 hr.	58	25—26/20	1·4383	,,	84;	,,	16^d
,,	5·0	HI anhyd.	1·25	S 100	5 hr.	95	44—45/20	1·4946	,,	76;	,,	24^e
,,	11·0	HI aq.^{a}	4·0	R 115	1 hr.	57	40/15	1·4948	,,	72;	,,	28
,,	7·7	HCl anhyd.	1·15	S 100	10 hr.	65	97	1·4065	,,	80;	,,	20^f
,,	3·8	,,	3·42^g	S 25	41 days	60	—	1·4081	,,	92;	,,	8
,,	3·6	,,	3·42^g	S 100	10 hr.	94	97—98	1·4066	,,	83;	,,	17
Pe^3†	8·8	,,	0·92	S 20	8 mth.	76	96—98	1·4083	,,	5;	,,	95
,,	4·4	,,	3·22^g	S 25	39 days	92	—	1·4090	,,	7;	,,	93
,,	3·2	,,	3·22^g	S 100	10 hr.	98	97—98	1·4090	,,	22;	,,	78
,,	18·0	HBr aq.^{b}	4·8	R 115	1 hr.	72	115—118	1·4411	,,	23;	,,	77
,,	15·3	HI aq.^{a}	4·0	R 115	1 hr.	82	49—50/25	1·4978	,,	32;	,,	68
Oc^2†^{h}	6·8	HCl anhyd.	1·15	S 20	8·5 mth.	56^i	64/13	1·4265	Oc^2†	~100;	Oc^3† trace; Oc^4†	—
,, ^{j}	8·1	HBr anhyd.	1·26	S 20	72 hr.	54^k	79/15	1·4482	,,	93;	,,	7;
,, ^{j}	8·6	,,	1·02	S 100	5 hr.	68^l	66/8	1·4479	,,	92;	,,	8; trace
,, ^{m}	2·3	HI anhyd.	1·18	S 20	66 hr.	50^n	102·5/22	1·4878	,,	92;	,,	8;
,, ^{m}	3·0	,,	1·18	S 100	6 hr.	75^p	84/9	1·4871	,,	92;	,,	8;

* S = sealed tube, R = reflux. † Pe = pentyl, Oc = octyl (all straight carbon chain).

^{a} Concentrated acid (55% w/w). ^{b} Concentrated acid (47% w/w). ^{c} Yields from gas chromatography. ^{d} 2-Bromo-octane (2·02 g.), $\alpha_D^{18·5}$ +40·24°, added; recovered (1·08 g.) (Found: Br, 41·0. Calc. for $C_8H_{17}Br$: Br, 41·4%), b. p. 83°/20 mm., n_D^{20} 1·4475, α_D^{17} +27·56°. ^{e} 2-Iodo-octane (2·96 g.), α_D^{17} +42·32°, added; recovered (1·73 g.) (Found: I, 51·8. Calc. for $C_8H_{17}I$: I, 52·9%), b. p. 98—99°/20 mm., n_D^{20} 1·4880, α_D^{19} +38·06°. ^{f} 2-Chloro-octane (1·0 g.), α_D^{22} −26·55° added; recovered (0·72 g.), b. p. 63°/13 mm., n_D^{20} 1·4239, α_D^{20} −23·92°, containing 2-chloro-octane (90%); equivalent to no loss in rotatory power. ^{g} Pyridine (1 mol.) added. ^{h} α_D^{18} +8·00°. ^{i} α_D^{19} −25·98° (Found: Cl, 23·4%). ^{j} α_D^{20} −8·00°. ^{k} α_D^{20} +33·02°. ^{l} α_D^{18} +26·20°. ^{m} α_D^{20} −7·62°. ^{n} α_D^{15} +49·88°. ^{p} α_D^{17} +11·42°.

made alkaline with sodium carbonate solution, extracted with ether, dried (MgSO$_4$), and distilled, to give: (i) 5·1 g., b. p. 66—67°/8 mm., n_D^{20} 1·4480, α_D^{19} +39·32°; (ii) 7·5 g., b. p. 67°/8 mm., n_D^{19} 1·4490, α_D^{19} +40·24°, and a residue (2·32 g.), n_D^{20} 1·4380. Fractions (i) and (ii) consisted of 2-bromo-octane (38% yield) containing 3-bromo-octane (~2%) but no detectable 4-isomer.

Whilst phosphorus tribromide (7·1 g., 0·34 mol.) was added (10 min. at −10°) to octan-2-ol (10·0 g.; α_D^{15} +8·07), dry carbon dioxide was passed through the reaction liquid, and then for 2 hr. at 20°. 2-Bromo-octane (3·4 g., 23%), b. p. 66—67°/9 mm., n_D^{20} 1·4491, α_D^{20} −44·0°, completely free from 3- or 4-bromo-octane, was obtained.

(c) Phosphorus tri-iodide (32·3 g., 1·02 mol.) was prepared, in carbon disulphide (160 ml.), from yellow phosphorus and iodine, and added to octan-2-ol (10·0 g.; α_D^{20} −7·62°) at −10°. After 24 hr. at 20°, the product was poured on to crushed ice; the carbon disulphide layer was washed with sodium carbonate solution, sodium thiosulphate solution, and water, dried (K$_2$CO$_3$), and distilled, to give 2-iodo-octane (5·7 g., 31%), b. p. 93—95°/15 mm., n_D^{20} 1·4872, α_D^{17} +42·32°, free from 3- or 4-iodo-octane.

Action of Zinc Halides on Alkyl Halides.—(a) n-Butyl bromide (9·3 g.) was heated under reflux (8 hr.) with zinc bromide (7·7 g., 0·5 mol.). Hydrogen bromide was evolved, to leave a liquid, n_D^{20} 1·4338 (Bu^{n}Br, 88·5; Bu^{s}Br, 11·5%). Further heating (16 hr.) gave more hydrogen

4 F

bromide (total 2·1 g., 0·38 mol.) and a small dark residue containing resinous products and at least 14 volatile components (gas chromatography), but no n-butyl bromide.

(*b*) n-Butyl iodide (9·2 g.) and zinc iodide (7·9 g., 0·5 mol.) were heated under reflux (4 hr.). No hydrogen iodide was evolved and the n-isomer, n_D^{20} 1·4985, remained.

Action of Concentrated Sulphuric Acid on Alkyl Halides.—n-Butyl chloride (17·7 g.) was heated under reflux (30 min.) with the acid (20 ml.). No hydrogen chloride was evolved, and distillation then afforded n-butyl chloride (15·9 g.), b. p. 77—78°, n_D^{20} 1·4010. n-Butyl bromide (13·0 g.) and the acid (10 ml.) evolved some hydrogen bromide upon heating under reflux (60 min.) but distillation gave only n-butyl bromide (10·3 g.), b. p. 101°, n_D^{20} 1·4388. A dark resin remained. A mixture (17·6 g.) of n-butyl chloride (87%) and s-butyl chloride (13%) was heated under reflux with the acid (10 ml.). During 8 hr., hydrogen chloride (0·73 g., 0·08 mol.) and butyl chloride, n_D^{20} 1·4018 (Bu^n, 99·2; Bu^s, 0·8%), were isolated.

2-Chloro-octane (0·85 g.; α_D^{18} +30·15°) was shaken (1 hr.) with an equal volume of concentrated sulphuric acid. The acid layer became brown and hydrogen chloride was evolved. The washed halide (0·61 g.) (Found: Cl, 23·5. Calc. for $C_8H_{17}Cl$: Cl, 23·9%), n_D^{20} 1·4267, $\alpha_D^{19·5°}$ +24·06°, then contained: Oc^{2}Cl, 96·5; Oc^{3}Cl, 3·5; Oc^{4}Cl, 0·5%.

2-Bromo-octane (1·0 g.; α_D^{19} +40·18°) was shaken with concentrated hydrobromic acid (7 hr. at 20°), and then heated in a sealed tube (5 hr. at 100°). The pure 2-isomer, α_D^{15} +40·34°, n_D^{20} 1·4497, was isolated.

Introduction of But-1-ene into the Butyl Chloride Preparation.—n-Butanol (68·1 g.) containing zinc chloride (25·3 g., 0·2 mol.) was heated (100—110°) while hydrogen chloride and but-1-ene were passed in. During 1 hr., but-1-ene (9·1 g.) was fed in, to give a distillate (17·3 g.) (Bu^{n}Cl, 89; Bu^{s}Cl, 4·5; but-1-ene, 6·5%) and at −80° a trap condensate (10·4 g.) consisting mainly of but-1-ene. During a further 4 hr., but-1-ene (11·6 g.) was introduced, and butyl chlorides (53·1 g.) (Bu^{n}Cl, 91; Bu^{s}Cl, 7·5; but-1-ene, 1·5%) distilled; the trap condensate (16·6 g.) consisted mainly of unreacted olefin (infrared).