

**194.** *Factors in the Formation of Isomerically and Optically Pure Alkyl Halides. Part I. Alcohol-Hydrogen Chloride or -Thionyl Chloride Systems.*

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The slow interaction of hydrogen chloride with straight-chain primary alcohols affords isomerically pure alkyl halides at temperatures up to 120°. Whereas catalysis by zinc chloride can cause considerable rearrangement to the corresponding secondary structures, catalysis by certain bases gives isomerically pure products. Reversible rearrangement between different secondary structures occurs even in the absence of catalysts, and, in the case of (+)-octan-2-ol, considerable loss in optical activity is accompanied by rearrangement to 3- and 4-chloro-octane. Although thionyl chloride affords unrearranged products from all the alcohols studied, it does not give optically pure 2-chloro-octane from (+)-octan-2-ol; the loss may be due to operation of an  $S_Ni$  mechanism.

AIDED by gas chromatography and infrared spectroscopy we have assessed the degree of isomeric purity of alkyl chlorides produced in hydrogen chloride-alcohol systems under

TABLE 1.  
 Alcohol-hydrogen chloride systems.

Alcohol (ROH)		HCl (mol.)	Method * and temp.	Time (months or hr.)	Yield (%)	Alkyl halide (RCl)		Composition (%)
R	Wt. (g.)					B. p.	$n_D^{20}$	R
Bu <sup>a</sup>	7.8	1.0	S.T. 15°	7 mth.	47	76-78°	1.4018	Bu <sup>a</sup>
"	10.2	1.0	S.T. 120	8 hr.	87	67-69	1.4016	"
Bu <sup>a</sup>	7.1	1.0	S.T. 15	5 mth.	44	65-68	1.3968	"
"	7.6	1.0	S.T. 160	10 hr.	67 <sup>a</sup>	65	1.3953	"
"	67.2		R 100	5 hr.	4 <sup>a</sup>	60-70	1.3952	"
Bu <sup>l</sup>	7.7	0.9	S.T. 120	20 hr.	75 <sup>a</sup>		1.3950	Bu <sup>l</sup>
"	47.2		R 106	3 hr.	0			87.5; Bu <sup>l</sup>
Bu <sup>l</sup>	58.2		R 50	1 hr.	66 <sup>a</sup>	51	1.3843	0;
Et <sub>3</sub> CH	8.3	0.9	S.T. 100	10 hr.	53 <sup>b</sup>	94	1.4094	Me-[CH <sub>2</sub> ] <sub>2</sub> -CHMe
n-Octyl	6.9	1.0	S.T. 100	10 hr.	63	73-77/17 mm.	1.4298	20; Et <sub>3</sub> CH
(-)-Me-[CH <sub>2</sub> ] <sub>5</sub> -CHMe	9.3	1.2	S.T. 100	10 hr.	69 <sup>d</sup>	62-65/15 mm.	1.4259	100; Me-[CH <sub>2</sub> ] <sub>5</sub> -CHMe

\* S.T. = sealed tube; R = reflux.

<sup>a</sup> Olefin also formed. <sup>b</sup> Pentene (0.2 g.), b. p. 33°,  $n_D^{20}$  1.3831; a liquid (2.4 g.), b. p. 33-94°,  $n_D^{20}$  1.4070, also collected. <sup>c</sup>  $\alpha_D^{18} + 8.00^\circ$  ( $l = 1$ ). <sup>d</sup>  $\alpha_D^{19} - 18.3^\circ$  ( $l = 1$ ). Freed from octan-2-ol by conversion into sulphite with calculated quantities of thionyl chloride and pyridine, and distilled to give octyl chloride (2.2 g.) (Found: Cl, 23.2%),  $n_D^{20}$  1.4263,  $\alpha_D^{17} - 20.2^\circ$  ( $l = 1$ ), containing 2-chloro-94, 3-chloro-5.5, and 4-chloro-octane 0.5%.

TABLE 2.

Alcohol-hydrogen chloride-zinc chloride systems.

Alcohol (ROH)		ZnCl <sub>2</sub> (mol.)	Temp.*	Time † (hr.)	Yield ‡ (%)	Alkyl halide (RCl)		Composition (%)
R	Wt. (g.)						$n_D^{20}$	R
Bu <sup>a</sup>	67.6	0.2	100°	4	10		1.4020	~100;
"			100	3	25		1.4020	99.2; Bu <sup>a</sup>
"			100	2.5	26		1.4020	97.9; "
"			100	2	20		1.4016	93.5; "
Bu <sup>a</sup>	26.8	0.5	100	2	38		1.4018	94.0; "
"			100	2	39		1.4009	85.7; "
"			100	1	20		1.3994	79.0; "
Bu <sup>a</sup>	28.6	1.0	105	0.75	55		1.3950	0;
Bu <sup>a</sup>	41.6	0.2	105	0.25	20		1.3931	0;
Bu <sup>l</sup>	47.2	0.2	105	5	20		1.3939	65.9; Bu <sup>l</sup>
"			105	2	23		1.3915	49.0; "
"			105	Trap	27		1.3888	27.7; "
Pr <sup>a</sup>	36.5	0.2	105	1.5	20		1.3888	~100;
"			105	1	20		1.3880	96.3; Pr <sup>l</sup>
"			105	1.5	15		1.3873	91.1; "

TABLE 2. (Continued.)

Alcohol (ROH)		Wt. (g.)	ZnCl <sub>2</sub> (mol.)	Temp.* (hr.)	Time † (hr.)	Yield ‡ (%)	Alkyl halide (RCl)	
R	R						<i>n</i> <sub>D</sub> <sup>20</sup>	Composition (%)
Pr <sup>l</sup> .....	.....	38.8	0.2	100	2	46	Pr <sup>l</sup>	100; Pr <sup>n</sup> 0
n-Pentyl .....	.....	22.8	0.2	125	1	36	n-Pentyl	~100
				125	1	12	"	~90
				<sup>a</sup>	Trap	5	"	<50
Me-[CH <sub>2</sub> ] <sub>2</sub> -CHMe .....	.....	41.6	0.2	100	1.5	38	Me-[CH <sub>2</sub> ] <sub>2</sub> -CHMe	70; Et <sub>2</sub> CH 30
Et <sub>2</sub> CH .....	.....	25.9	0.2	100	3	52	Me-[CH <sub>2</sub> ] <sub>2</sub> -CHMe	45; Et <sub>2</sub> CH 55
n-Octyl .....	.....	26.1	0.2	120	2	55	n-Octyl	~100
(+)-Me-[CH <sub>2</sub> ] <sub>6</sub> -CHMe <sup>f</sup> ...	.....	6.6	0.2	110	3	66	2-Oc 81, 3-Oc 13, 4-Oc 6	

\* In every case hydrogen chloride was passed into the system under reflux; some olefin was always formed. † Consecutive periods. ‡ Produced during the period.  
<sup>a</sup> Condensed (-80°) from effluent HCl. <sup>b</sup> 2- and 3-Chloropentane also present. <sup>c</sup> Unidentified impurity (small %). <sup>d</sup> Pent-2-ene (*cis*- + *trans*)- (6.7 g.), b. p. 30-40°, *n*<sub>D</sub><sup>20</sup> 1.3802, collected. <sup>e</sup> 2-, 3-, and 4-Chloro-octane, total <1%. <sup>f</sup>  $\alpha_D^{18}$  +8.00° (*l* = 1). <sup>g</sup>  $\alpha_D^{18,15.5}$  -7.80° (*l* = 1). <sup>h</sup> Pent-2-ene (*cis* + *trans*-) (0.85 g.), *n*<sub>D</sub><sup>20</sup> 1.3810, collected.

TABLE 3.

Alcohol-base hydrochloride systems.

Alcohol (ROH)		Wt. (g.)	Base or B,HCl (mol.)	HCl (mol.)	Method *	Time (months or hr.)	Yield (%)	Alkyl halides (RCl)	
R	R							Composition (%)	R
Bu <sup>n</sup> .....	.....	2.8	C <sub>5</sub> H <sub>5</sub> N	3.0 <sup>a</sup>	S.T. 20°	5 mth.	47	Bu <sup>n</sup>	100; Bu <sup>s</sup> 0
" .....	.....	3.4	"	3.0 <sup>a</sup>	S.T. 160	7 hr.	66 <sup>b</sup>	"	94.5; " 5.5
" .....	.....	19.7	"	"	R 105	2 hr.	74	"	100; " 0
" .....	.....	27.0	Me <sub>2</sub> NH,HCl	"	R 105	2.5 hr.	78	"	100; " 0
" .....	.....	17.0	Me <sub>3</sub> N,HCl	"	R 105	3 hr.	44	"	100; " 0
" .....	.....	27.7	MeNH <sub>2</sub> ,HCl	"	R 105	3 hr.	0	"	"
" .....	.....	2.8	C <sub>5</sub> H <sub>5</sub> N,HCl	0	S.T. 100	10 hr.	Bu <sup>n</sup> OH (2.8 g.) recovered, containing Bu <sup>n</sup> Cl (1.8%)	Bu <sup>n</sup> Cl	1.8%
Bu <sup>l</sup> .....	.....	57.0	C <sub>5</sub> H <sub>5</sub> N,HCl	0.95	R 125	12 hr.	51	Bu <sup>l</sup>	99.4; Bu <sup>l</sup> 0.6
Pr <sup>n</sup> .....	.....	45.7	"	"	R 105	Trap	12	"	97.2; " 2.8
" .....	.....	"	"	"	R 105	3 hr.	53	Pr <sup>n</sup>	100; Pr <sup>l</sup> 0
" .....	.....	"	"	"	R 105	Trap	13 <sup>b</sup>	"	100; " 0
n-Pentyl .....	.....	22.9	Me <sub>2</sub> NH,HCl	1.0	R 125	Trap	53	n-Pentyl	100;

\* S.T. = sealed tube, R = reflux.

<sup>a</sup> Clear solution at 20°; white plates of pyridinium hydrogen dichloride (Found: HCl, 46.4%) at 15°. <sup>b</sup> Trace of olefin. <sup>c</sup> Absorbed HCl (27.2 g., 2 mol.) at 20° to give clear solution. <sup>d</sup> Absorbed HCl (18.0 g., 2.1 mol.) at 20° to give clear solution. <sup>e</sup> Absorbed HCl (17.3 g., 1.3 mol.) at 20° without forming solution. <sup>f</sup> Condensed (-80°) from effluent HCl.

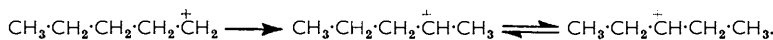
certain relevant conditions.<sup>1</sup> Alcohols of ordinary reactivity, typified by n-butanol, dissolve about one mole of hydrogen chloride per mole of alcohol at 10°. <sup>2</sup> From whatever evidence is available it is plausible to suppose that the system may then be formulated in the simplest terms as:



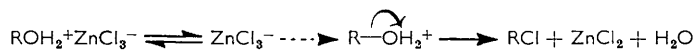
and the product water competes with the alcohol for the proton. There is no available evidence that the unprotonated alcohol can react with the chloride ion, and therefore the product water is a factor involved in the reduction of rate and yield in the formation of alkyl chloride. As the solubility falls quickly with rise in temperature at atmospheric pressure (*e.g.*, 0.66 mole per mole of n-butanol at 45°) and formation of alkyl chloride is very slow at room temperature, three procedures are available to increase the rate. The system can be heated in a sealed tube, or heated under reflux, in the absence or in the presence of a catalyst, whilst hydrogen chloride is continuously passed into the system.

With hydrogen chloride alone (sealed tube) (Table 1), at temperatures up to 120°, isomerically pure alkyl chlorides were obtained from the n-alcohols (butyl and octyl). *s*-Butyl alcohol gave only the *s*-isomer, but pentan-3-ol afforded the isomeric 2- and 3-chloro-derivatives (*cf.* ref. 3). (+)-Octan-2-ol gave mainly (–)-2-chloro-octane, although rearrangement (*ca.* 6%) to 3- and 4-chloro-octane occurred. Loss in optical purity <sup>4</sup> could be due to the  $S_N1$  mechanism; but there could be concurrence of the  $S_N2$  and  $S_Ni$  mechanisms.

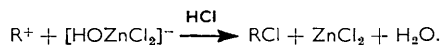
By the distillation procedure, zinc chloride (0.2 mol.) gave, with n-butanol, an increasing proportion of *s*-butyl chloride during each of the consecutive periods of operation (Table 2), 0.5 mol. causing more rearrangement, and 1.0 mol. still more. n-Propanol and n-pentanol behaved similarly, although with n-octanol there was <1% rearrangement. *s*-Butyl alcohol and propan-2-ol gave only the *s*-isomer; but pentan-2-ol and pentan-3-ol both gave 2- and 3-chloropentane, and octan-2-ol afforded the 2- (mainly) but also the 3- and the 4-isomer. Rearrangement in pentan-2- or -3-ol was more extensive than with (+)-octan-2-ol, although the optical purity of the (–)-2-chloro-octane was low. Rearrangement of a straight-chain group was always from normal to secondary, although different secondary structures were interconvertible, *e.g.*,



We believe that the function of zinc chloride is to conserve the concentration of "hydrogen chloride" and hence of the protonated alcohol, by forming  $\text{ZnCl}_3^-$  and  $\text{ZnCl}_4^{2-}$  ions, *e.g.*, as



This need not lead to rearrangement; but in the presence of a larger proportion of zinc chloride, the structure  $\text{R}(\text{H})\text{O}^+-\text{Zn}^-\text{Cl}_2$  becomes important and leads to the  $S_N1$  mechanism:



In Table 3 we show the influence of certain base hydrochlorides.<sup>5</sup> It is significant that bases which form dihydrochlorides<sup>6</sup> are effective, and that pyridinium hydrogen dichloride  $[\text{C}_5\text{H}_5\text{NH}]^+[\text{HCl}_2]^-$  was separated from the n-butanol-hydrogen chloride system. Almost no butyl chloride was formed by heating pyridinium chloride,  $\text{C}_5\text{H}_5\text{NH}^+\text{Cl}^-$ , with

<sup>1</sup> See Gerrard, Hudson, and Murphy, *J.*, 1962, 1099.

<sup>2</sup> Gerrard, Madden, and Tolcher, *J. Appl. Chem.*, 1955, 5, 28; Gerrard and Macklen, *ibid.*, 1956, 6, 241.

<sup>3</sup> Whitmore and Karnatz, *J. Amer. Chem. Soc.*, 1938, 60, 2536.

<sup>4</sup> See Pickard and Kenyon, *J.*, 1911, 99, 45.

<sup>5</sup> Gerrard and Hudson, *Proc. Chem. Soc.*, 1961, 467.

<sup>6</sup> Kaufler and Kunz, *Ber.*, 1909, 42, 385.

n-butanol in the absence of an excess of hydrogen chloride. Although these bases strongly catalyse the formation of alkyl chloride, the n-alcohols showed no rearrangement, and isobutanol gave isobutyl chloride mixed with a relatively small proportion of the t-butyl isomer. Attention is drawn to the remarkable slowness of the formation of isobutyl chloride from isobutanol and hydrogen chloride alone.

For comparison, we give relevant results with thionyl chloride. No rearrangements were detected in any such system, when pyridine was absent or present (cf. refs. 3 and 7); but, although pure 2-chloro-octane was thus obtained there was slight loss of optical purity. From octan-2-ol,  $\alpha_D^{20} + 8.0^\circ$  ( $l = 1$ ) the highest rotation we could obtain for attested (by gas-chromatography) 2-chloro-octane was  $[\alpha]_D^{17} - 33.3^\circ$  in the presence of pyridine, and  $[\alpha]_D^{21} - 30.1^\circ$  in its absence, compared to  $[\alpha]_D^{20} - 35.2^\circ$  for product obtained by the dealkylation of trioctyl phosphite.<sup>8</sup> By a previously reported thionyl chloride procedure,<sup>9</sup> we could not obtain 2-chloro-octane having  $[\alpha]_D^{20} 36.0^\circ$ , and it is possible that the slight loss occurring in these systems is due to the operation of an  $S_Ni$  mechanism in the chloro-sulphinate decomposition.

## EXPERIMENTAL

*Analysis by Gas-Liquid Chromatography.*—The alcohols were attested on a 10% poly(ethylene glycol) 400 column with argon carrier-gas at 75–80°. The isomers of propyl and butyl chloride were separable on a 30% dinonyl phthalate-Celite column at 60°, with hydrogen carrier gas, except that isobutyl and s-butyl chloride could not be separated, and the exclusion of either had to be established by infrared spectroscopy. Peak areas were measured for determination of the proportion of the particular isomer present in the product. Chloropentanes (1-, 2-, or 3-) were analysed on 10–20% squalane-Celite columns with argon gas at ambient temperature. For the 2- and the 3-isomer quantitative data are approximate because of overlap of the peaks. Whereas 1-chloro-octane was entirely separated, the 2-, 3-, and 4-isomers were only partly separated by a 10% diethyl tartrate-Celite column (argon carrier-gas) at 45°.

TABLE 4.  
Alcohol-thionyl chloride systems.

Alcohol (ROH)	Wt. (g.)	SOCl <sub>2</sub> (mol.)	Pyridine (mol.)	Method	Alkyl halide (RCl)				
					Yield (%)	B. p.	$n_D^{20}$	Composition (%)	
Bu <sup>a</sup> .....	30.3	1.0	0	A	54	78–79°	1.4015	Bu <sup>a</sup>	100
Bu <sup>b</sup> .....	24.3	2.0	1.0	B	64	78–79°	1.4019	Bu <sup>a</sup>	100
Et <sub>2</sub> CH .....	19.1	1.3	1.1	B	29 <sup>c</sup>	95–97°	1.4100	Et <sub>2</sub> CH	100
(+)-Me·[CH <sub>2</sub> ] <sub>6</sub> ·CHMe <sup>b</sup>	10.0	3.3	0	C	0 <sup>e</sup>				
„ „	20.0	3.3	0	C <sup>d</sup>	46 <sup>e</sup>	62–66/ 15 mm.		Me·[CH <sub>2</sub> ] <sub>6</sub> ·CHMe	100
„ „	20.1	1.0	1.0	D	48 <sup>f</sup>	60–62/ 12 mm.	1.4259	Me·[CH <sub>2</sub> ] <sub>6</sub> ·CHMe	100

<sup>a</sup> Pentene (0.25 g.), b. p. 30–40°,  $n_D^{20}$  1.3814; and inter-fraction (1.9 g.), b. p. 40–95°,  $n_D^{20}$  1.4019, also collected. <sup>b</sup>  $\alpha_D^{18} + 8.00^\circ$  ( $l = 1$ ). <sup>c</sup> Washed product gave octan-2-ol (0.8 g.), b. p. 68°/6 mm.,  $n_D^{20}$  1.4259,  $\alpha_D^{20} + 6.3^\circ$  ( $l = 1$ ), a fraction (0.3 g.), b. p. 80–120°/0.1 mm.,  $n_D^{20}$  1.4311,  $\alpha_D^{20} + 1.1^\circ$  ( $l = 1$ ), and di-(1-methylheptyl) sulphite (6.0 g.), b. p. 120°/0.1 mm.,  $n_D^{20}$  1.4430,  $\alpha_D^{20} - 16.0^\circ$  ( $l = 1$ ). <sup>d</sup> Followed by heating (14 hr. at 80°/15 mm.) to liberate SO<sub>2</sub>. <sup>e</sup>  $\alpha_D^{21} - 23.9^\circ$ ; redistilled three times to give a trace of octene, and (–)-2-chloro-octane (2.2 g.) (Found: Cl, 23.9. Calc. for C<sub>8</sub>H<sub>17</sub>Cl: 23.9%), b. p. 62.5°/13 mm.,  $n_D^{20}$  1.4260,  $d_4^{15}$  0.872,  $d_4^{20}$  0.866,  $d_4^{25}$  0.861,  $\alpha_D^{21} - 26.0^\circ$  ( $l = 1$ ),  $[\alpha]_D^{21} - 30.1^\circ$ . <sup>f</sup>  $\alpha_D^{19}$  27.9°. Redistillation afforded (–)-2-chloro-octane (7.2 g.) (Found: Cl, 23.5%, b. p. 63°/13 mm.,  $n_D^{20}$  1.4260,  $d_4^{15}$  0.869,  $d_4^{20}$  0.865,  $d_4^{25}$  0.859,  $\alpha_D^{17} - 28.9^\circ$  ( $l = 1$ ),  $[\alpha]_D^{17} - 33.3^\circ$ . Also obtained: octene (2.6 g.), b. p. 30–40°/15 mm.,  $n_D^{20}$  1.4133, and a fraction (3.8 g.), b. p. 40–62°/15 mm.,  $n_D^{20}$  1.4202.

*Characterisation of Chlorides.*—In addition to the foregoing techniques, chemical and infrared spectroscopic analyses and certain physical constants were used; but, except for special reasons, these are not recorded. B. p. and  $n_D$  are given for comparison with the scattered data in the literature.

<sup>7</sup> Cason and Correia, *J. Org. Chem.*, 1961, **26**, 3645.

<sup>8</sup> Gerrard, *J.*, 1945, 851; Gerrard and Cook, unpublished work.

<sup>9</sup> Houssa, Kenyon, and Phillips, *J.*, 1929, 1700.

*Alcohol-Hydrogen Chloride System.*—The alcohol, alone or with added catalyst, was saturated with hydrogen chloride at room temperature, and the system was either sealed in a glass tube or heated under reflux, hydrogen chloride being continuously passed in. In the latter procedure, the flask (250 ml.) was fitted with a 6 in. column packed with Fenske helices, and the product was gradually removed from the still-head as formed. Products (except t-butyl chloride) were washed with water and dried ( $K_2CO_3$ ) before redistillation and characterisation (Tables 1—3).

*Alcohol-Thionyl Chloride System.*—Reactions carried out in the absence or in the presence of pyridine are shown in Table 4. Procedures adopted were: *A*, alcohol was added dropwise to thionyl chloride at  $20^\circ$ , followed by reflux (2 hr.); *B*, thionyl chloride was added dropwise to the alcohol-pyridine mixture at  $0^\circ$ , followed by reflux for 1—2 hr. (Darzens's procedure); <sup>3,10</sup> *C*, thionyl chloride in light petroleum (b. p.  $30-40^\circ$ ) was added (3 hr.) to the alcohol in the same solvent at  $0^\circ$ ; volatile materials were then removed at 15 mm./ $20^\circ$ ; <sup>9</sup> *D*, a modified Darzens procedure (see Gerrard *et al.*<sup>11</sup>) in which the sulphite was first formed by addition of thionyl chloride (0.5 mol.) in ether to the alcohol-pyridine mixture in ether, at  $0^\circ$ . Filtration removed the bulk of the pyridinium chloride, and, after removal of ether from the filtrate ( $20^\circ/15$  mm.), the latter was heated at  $80^\circ$  (6 hr.) with more thionyl chloride (0.5 mol.) until sulphur dioxide evolution ceased.

Products were, unless otherwise stated, washed with water and/or dilute sodium carbonate solution, dried ( $K_2CO_3$ ), and distilled.

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<sup>10</sup> Darzens, *Compt. rend.*, 1911, **152**, 1314, 1601.

<sup>11</sup> Gerrard and French, *Nature*, 1947, **159**, 263; *J.*, 1949, 3326.

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