Conversion of Alkyl Chlorides to Bromides, Selective Reactions of Mixed Bromochloroalkanes, and Halogen Exchange

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Primary alkyl chlorides are quantitatively converted to their corresponding bromides in the presence of ethyl bromide, *N*-methyl-2-pyrrolidinone, and a catalytic amount of metal bromide. A variety of chlorides can be converted. Selective functionalization at bromine of several primary bromochloroalkanes was studied in conjunction with the chloride-bromide conversion for multistep syntheses. Methods for halogen exchange between chloride, bromide, and iodide in the octyl halide series are presented.

Alkyl bromides are often synthetically more useful than are their corresponding chlorides, as for example in the preparation of Grignard[2] and lithium reagents[3] and in copper-catalyzed alkylations.[4] Their convenience in these cases is due to their much higher reactivity.[5] For example, alkyl chlorides, other than for small molecules (*e.g.* butyl chloride), are often virtually inert under conditions for conversion to their Grignard reagents.[2] The reactivity difference between chlorides and bromides in copper-catalyzed alkylations is often large enough so that the chlorides are essentially useless.[4] There are other types of reactions in which the reactivity differences between bromides and chlorides are of practical significance.[6]

In view of the practical implications of these Br–Cl reactivity differences and because many alkyl chlorides are commercially available whereas their corresponding and often more reactive bromides are not, we were interested in a method of direct conversion of acyclic alkyl chlorides to their corresponding bromides. Many such attempts at direct conversion have been reported, for example with octyl chloride (**1**),[7] propargyl chloride (**4**),[8] and 4-chloromethyl-1,3-dioxolane (**11**)[9] (*cf.* Table 1), but in all cases[10] yields were low and the crude bromides were always contaminated with chlorides.[11]

We have discovered a simple, cheap, and efficient conversion of primary alkyl chlorides to their corresponding bromides. We wish to report the method (which can be generalized for all Cl, Br, and I interconversions) along with an indication of its synthetic utility.

Results and Discussion

Chloride-Bromide Equilibria. In our early work we sought a method of conversion of chlorides to bromides based upon the solubility difference between NaBr and NaCl. The utilization of the solubility differences (in acetone) between NaI and NaBr or NaCl to effect conversion of chlorides or bromides to iodides has long been known.[12] In all of our attempts, under various conditions, only partial conversion of chlorides to bromides was realized (see Table 3); in the best case (NaBr/*N*-methyl-2-pyrrolidinone)[13] we achieved an 84% conversion to bromide. In several cases the solvents reacted with the chlorides and bromides (Table 3, entries 2,3,11,17,18).

The limiting factor of this unsuccessful approach is that equilibrium is established between RCl and RBr (*cf.* Table 3, entries 27, 28), and a considerable amount of RCl always remains. We realized, then, that the Cl–Br conversion would have to be carried out in the presence of a solvent, or additive, which would react with Cl^- to yield a product which could easily be removed from the reaction mixture.

$$RCl \xrightarrow[\text{Solvent}\ \text{Additive}\ \Delta]{MBr} RBr \qquad (I)$$

M = metal, Li, K, Na, *etc.*
Additive = alkyl bromides

Scheme 1.

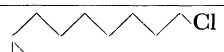
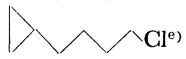
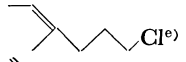
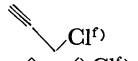
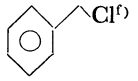
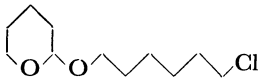
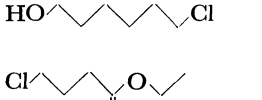
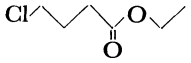
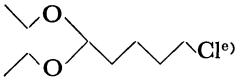
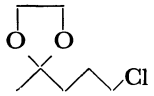
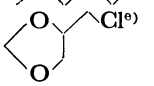
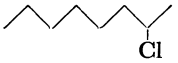
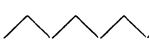
Conversion of Chlorides to Bromides. We found that the conversion (Eq. I) of RCl to RBr was quantitative if an alkyl bromide were added to the mixture of alkyl chloride (RCl), inorganic bromide (MBr), and solvent. We found ethyl bromide (bp 38 °C) to be most convenient since it (and ethyl chloride formed from it) is easily removed after the conversion.

We consider that *optimum conditions* on a large scale for the Cl–Br conversion (Eq. I) generally are with 0.2 equivalents of NaBr, 10 equivalents of EtBr, *N*-methyl-2-pyrrolidinone, and usually at 60—70 °C (see Table 1). Under these conditions the conversion is 97—99% complete and occurs within 3—10 days (exception: **11**). The optimum conditions can be varied if complete conversion (≥99.9%) to bromide is desired (*cf.* entry 1, Table 2).

N-Methyl-2-pyrrolidinone was selected as the reaction solvent based upon our preliminary studies (Table 3). *N*,*N*-Dimethylformamide (DMF) was utilized effectively in the Cl–Br conversion in the case of **4**,[8] but not for **7** (chlorohexyl formate forms in that case). The NaBr functions simply as a catalyst in the Cl–Br conversion since octyl chloride is nearly completely converted to octyl bromide with either four equivalents of NaBr or as little as 0.01 equivalents (*cf.* Table 2), although reaction time is considerably longer under catalytic conditions (NaBr is not a unique initiator here, and even if it were omitted, the conversion should eventually proceed if any trace impurities were present which react with ethyl bromide to liberate Br^-). The ethyl bromide additive is convenient, but 2-bromopropane and dibromomethane were found to be useful for the Cl–Br conversion. In principle, many other alkyl bromides could be used.

A general procedure for the conversion is described in the Experimental Section for compound **10**. Some

Table 1. Conversion of alkyl chlorides to bromides (60—70 °C)

	Chloride[a] RCl	% RBr Conv[b]	% RBr Yd[c]	EtBr Equiv	NaBr Equiv	*t* days	RCl (g), Sol (ml)[d]
1		99.7	93	30	4	3	30.0, 550
2		98	95	10	0.2	10	33.5, 335
3		99		10	0.2	7	1, 7.5
4		98	91	10	0.2	6	20.7, 300
5		96		30	1	7	2, 45
6		99	84[g]	30	1	5	11.0, 135
7		>99 98	h) 72[i]	30 20 (>-Br)	1 0.2	13 4	1, 20 26.8, 400
8		97	92	10	0.2	8	30.1, 200
9		99	90	10	0.2	2	20.0, 100
10		99	89	10	0.2	3	101.7, 617
11		98	70	10	0.2	42	36.8, 300
12		~20	j)	30	1	26	1, 18
13		ROH 99.4	72	HOH 20		15	5, 75

a) All chlorides were purified to >98%. b) Conversion determined by GLPC. c) Yield of distilled product. d) Solvent was *N*-methyl-2-pyrrolidinone. e) For preparation, see Experimental Section. f) Conversion was at room temp. g) RBr (RCl prepared from **7**)[24] contained 4% HO⁄⁄⁄⁄⁄⁄Br. h) RBr contained 73% ⁄⁄O⁄⁄⁄⁄⁄⁄Br. i) RBr contained 9% >-O⁄⁄⁄⁄⁄⁄Br which was isolated by column chromatography over Silica Gel (RBr thermally unstable). j) RBr was a complex mixture containing mostly octene isomers, ~20% RBr, and very little **12** (GC/MS evidence).

Table 2. Effect of NaBr on octyl chloride conversion (60 °C)[a]

% Conversion[b] to ⁄⁄⁄⁄⁄⁄Br	Equivalents EtBr	Equivalents NaBr[c]	*t* days
99.9	100	4	7
99.7	30	4	3
99.6	30	2	3
99.3	30	1	3
99.0	30	0.5	3
95.0	30	0.1	3
48.0	30	0.01	3
99.4	30	0.01	10

a) In each case 1 g of octyl chloride was in 18 ml of *N*-methyl-2-pyrrolidinone (exception: 50 ml for the first case). b) Determined by GLPC. c) Solubility in *N*-methyl-2-pyrrolidinone at 70 °C of NaBr=3.52 g/100 ml; of NaCl=0.16 g/100 ml (when EtBr is present the solubility of NaBr drops considerably).

advantages of the process are that it is very simple to carry out even on a large scale, ethyl bromide is inexpensive and easy to remove (and can be recycled), and no solvent is required to extract the product bromide.

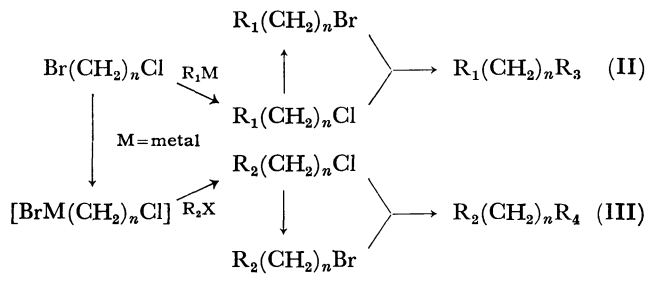
The method appears to be general for *primary* alkyl chlorides (or dichlorides)[14] and several functional groups can be present in the chloride. Certain of the functions are mildly unstable to the conversion conditions; for example, the acetal function in **11** and the tetrahydropyranyl (THP) function in **6**. The hydroxyl function in **7** reacts with ethyl bromide so that 2-bromopropane was used to effect the conversion of **7**. Steric hindrance to the conversion was encountered for the acetal **11** and also for 2-chlorooctane (**12**). Note that although 2-bromopropane readily exchanges Cl^-, 2-chlorooctane (**12**) does not.[15] The tertiary ether 6-chloro-3-methoxy-3-methylhexane (prepared by methoxymercuration of **3**)[17] could not be converted to its bromide; under the conversion conditions it was quickly converted to a mixture of isomers of the unsaturated ether corresponding to **3** (Cl replaced by OCH_3) even in the presence of added sodium hydrogen carbonate, pyridine, 3A molecular sieves or the proton-sponge 1,8-bis(dimethylamino)naphthalene.

Selective Reactions with Mixed Halides. In addition to converting many commercially available chlorides to

Table 3. Chloride-bromide equilibria[a] for octyl chloride (RCl)

MX[b]	Solvent[c]	T	t days	Composition of Mixture[d] RCl	RBr	Other
NaBr	THF/H_2O[e]	boil	23		<0.05	
NaBr	CH_3OH	boil	23	0.17	0.64	0.18 $ROCH_3$
NaBr	CH_3CH_2OH	70	19	0.49	0.34	0.17 $ROCH_2CH_3$
NaBr	CH_3COCH_3	70	21	0.88	0.12	
NaBr	CH_3COCH_3/H_2O[e]	boil	23	0.62	0.38	
LiBr	$CH_3COCH_2CH_3$	70	7	0.64	0.36	
LiBr	$CH_3COCH_2CH_3$, 2TMEDA[f]	70	2	no octyl halides remain		
NaBr	$CH_3COCH_2CH_3$	70	9		<0.05	
KBr	$CH_3COCH_2CH_3$	70	9		<0.05	
NaBr	CH_3CO_2H	70	10		<0.05	
NaBr	CH_3CO_2H	120	12	0.17	0.53	0.30 RO_2CH_3[g]
NaBr	$CH_3(CH_2)_4CO_2H$	120	4		0.05	
NaBr	$CH_3(CH_2)_4CO_2H$	150	8	0.20	0.80	high boiling impurity
NaBr	$HCON(CH_3)_2$ (DMF)	24	3 h		<0.05	
NaBr	DMF[h]	70	7 h	0.50	0.50	
		70	5	0.50	0.50	
		140	3	0.14	0.47	0.27 ROH, 0.12 RO_2CH
NaBr	DMF/H_2O[i]	70	20	0.29		0.35 ROH, 0.36 RO_2CH
3 NaBr, 0.2 KI	DMF	70	21	0.62	0.31	0.07 RI
NaBr[j]	DMF	70	10	0.66	0.34	
NaBr	$CH_3C{\equiv}N$	70	76	0.16	0.84	
3 NaBr, 1 NaI	$CH_3C{\equiv}N$	70	15	0.24	0.07	0.69 RI
NaBr	$CH_3C{\equiv}N$+0.2 18-crown-6[k]	70	28	0.15	0.85	
$CuBr_2$	$CH_3C{\equiv}N$	70	10		<0.05	
LiBr	 (PYRR)	70	28	0.81	0.19	
20 LiBr	PYRR+0.5 18-crown-6[k]	70	17	0.38	0.61	
NaBr	PYRR	70	3	0.13	0.87	
				0.16	0.84	corrected
3 NaBr, 1 NaCl[l]	PYRR	70	3	0.19	0.81	
4 NaBr, 4 LiBr	PYRR	70	2	0.16	0.84	
KBr	PYRR	70	25	0.41	0.59	
RbBr	PYRR	80	12	0.53	0.47	
RbBr	PYRR+0.2 18-crown-6[k]	80	12	0.53	0.47	
NaBr	HMPA	70	10		<0.05	
LiBr	DMSO	70	7		<0.05	
NaCl[m]	CH_3COCH_3	boil	40	0.09		0.91 RI

a) Equilibria here only implies reversibility except for entries 27 and 28 which are true equilibrium values. b) Four equivalents used in all cases except as noted. c) 7.5 ml solvent/mmol RCl. d) Values are mole fractions determined by GLPC and are uncorrected (except entry 27) for response ratio=(Br/Cl)=0.8. e) Biphasic. f) TMEDA=$Me_2N(CH_2)_2NMe_2$. g) *Cf.* S. Akabori and M. Ohtomi, *Bull. Chem. Soc. Jpn.*, **48**, 2991 (1975). h) After 7 h the mixture was filtered and 3 NaBr added; after additional 5 days, no change in RCl/RBr. i) Monophasic. j) Carried out on initial mixture of 0.8 RCl+0.2 RBr. k) 18-Crown-6=crown ether catalyst; see: C. J. Pederson, *J. Am. Chem. Soc.*, **89**, 7017 (1967); *cf.* also Ref. 22a, D. J. Sam and H. E. Simmons, *ibid.*, p. 2252, and C.L. Liotta and E. E. Grisdale, *Tetrahedron Lett.*, **1975**, 4203. l) Octyl bromide (RBr) used here. m) Octyl iodide (RI) used here.



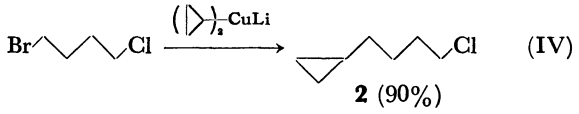
R_1, R_2, R_3, R_4=alkyl, aryl, other

Scheme 2.

their commercially unavailable and more reactive bromides we were interested in utilizing the Cl–Br conversion and the reactivity difference of bromide *vs.* chloride for multistep synthetic schemes (*cf.* Scheme 2).

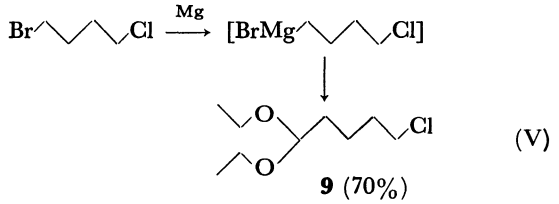
We have found that certain bromochloroalkanes behave, *towards alkylation and metallation with magnesium*, as if they were simple bromoalkanes; in these cases the chlorine is essentially inert. For example, we found that 1-bromo-4-chlorobutane could be selectively functionalized at the bromine according to the plan of Scheme 2. Thus reaction of 1-bromo-4-chlorobutane with lithium dicyclopropylcuprate (Eq. IV)[18] yields

1-chloro-4-cyclopropylbutane exclusively and quantitatively; 1-bromo-3-chloropropane likewise yields 1-chloro-3-cyclopropylpropane.[26] (The corresponding reaction using bromochloromethane yields cyclopropylmethyl chloride but in low yield.) Chloride **3** (Table 1) was also selectively prepared from lithium di-2-butenylcuprate and 1-bromo-3-chloropropane. The



2 (90%) (IV)

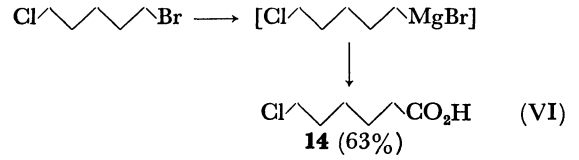
reaction of bromochlorobutane with magnesium yields chlorobutylmagnesium bromide[19] which, when treated with diethyl phenyl orthoformate (Eq. V)[20] yields 5-chloro-1,1-diethoxypentane (**9**); acetal **9** has previously



9 (70%) (V)

been prepared (48% yield) from 5-chlorovaleryl chloride.[21a] The hexyl and heptyl chloroacetals corresponding to **9** were likewise formed from the five and six-carbon bromochloroalkanes, respectively (see Experimental Section). We found that for similar acetal functionalization (*cf.* Eq. V) of the chloro-THP **6** it was first necessary to convert to the bromide. Thus, while **6** (Table 1) was exceedingly unreactive with magnesium in tetrahydrofuran, the bromide of **6** reacted readily to yield $THPO(CH_2)_6MgBr$ which, after treatment with $PhOCH(OCH_2CH_3)_2$, yielded $THPO(CH_2)_6CH(OCH_2CH_3)_2$.

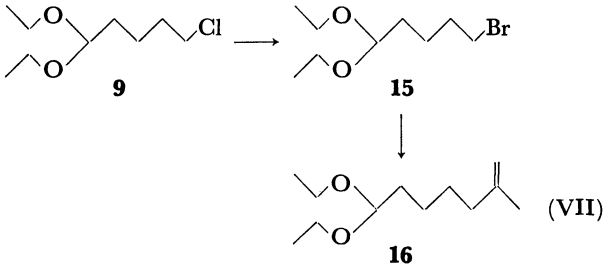
Treatment of 1-bromo-5-chloropentane with magnesium, followed by carbon dioxide, yielded high purity 6-chlorohexanoic acid (Eq. VI).



14 (63%) (VI)

In an effort to find other metals which would selectively attack bromine (*cf.* Scheme 2), we attempted to selectively metallate 1-bromo-6-chlorohexane with lithium in ether; a complex mixture was obtained.

The products of reactions IV and V can be directly utilized for further reactions typical of alkyl chlorides, or can be converted to their corresponding bromides if more reactive molecules are desired for reactions typical of bromides (*cf.* Scheme 2). For example, 5-chloro-1,1-diethoxypentane (**9**, Eq. V) was converted to its bromide which was alkylated with lithium di-2-propenylcuprate to yield 1,1-diethoxy-6-methyl-6-heptene (Eq. VII).



(VII)

Direct reaction of the cuprate with the chloride (**9**) was expected to be poor[18] since the corresponding reaction of lithium di-2-propenylcuprate with 6-chloro-3-methoxy-3-methylhexane (prepared from **3**) was very poor.

Hydrolysis. As part of our study we also found that octyl bromide (**13**) could be directly converted to 1-octanol (*cf.* Table 1). Under the conditions of this hydrolysis, 11-bromoundecanoic acid was completely converted to 11-hydroxyundecanoic acid (see Experimental Section).[29b] However, we were unable to convert ethyl 4-bromobutyrate (from **8**) to ethyl 4-hydroxybutyrate; butyrolactone was apparently formed in that case.

Halogen Exchange. We found that the conversion procedure (Scheme 1) used for the chlorides of Table 1 is also apparently general for all halogen exchanges involving *primary* Cl, Br, and I (see Table 4); similar exchanges to produce fluorides are also known.[22]

Experimental

Spinning-band distillations were with a Normagteflon

Table 4. Interconversion of octyl halides (60—70 °C)[12b]

$R_1X \xrightarrow[NaY]{R_2Y} R_1Y$ X, Y = Cl, Br, I; R_1 = octyl

R_1X[a]	R_2Y	NaY	% R_1Y	*t*/h
Cl	30 EtBr	0.5 NaBr	99.0	3 (days)
Cl[b,d]	10 MeI	0.2 NaI	99.7	10
Br	20 *i*-PrCl	0.2 NaCl	91	32 (days)
Br[c,d]	20 MeI	0.2 NaI	94	2
I	30 *n*-PrCl	0.2 NaCl	97	20 (days)
I	20 EtBr	0.2 NaBr	96	0.25

a) Except for entry 1 (*cf.* Table 2) all conversions were carried out with 1 ml *N*-methyl-2-pyrrolidinone/mmol R_1X, and % R_1Y was determined by GLPC (response ratios were taken as = 1.0). One gram samples of R_1X were used (except for the 2nd and 4th entries) and yields were not determined. b) Distilled yield of octyl iodide (bp 36.5—38 °C/0.01 mmHg) from 50 g of octyl chloride here was 98%. c) Distilled yield of octyl iodide (bp 80 °C/1.4 mmHg) from 50 g of octyl bromide here was 98%. d) This method in these two cases is more convenient, and of about equal expense (since most of the MeI is recovered and is recyclable: 93% by volume of MeI was recovered from the 4th entry) compared to the original Finkelstein method.[12]

apparatus (40 theoretical plates) from Norell Chemical Co. NMR spectra were recorded on a Varian T-60 instrument and infrared spectra on a Beckman Acculab 4 instrument. All solvents and organic reagents were dried over activated 4A molecular sieves prior to use. The bromochloroalkanes[23] were purchased from Fairfield Chemical Co., Blythewood, S.C. 29016, USA. All compounds not commercially available (described below) were characterized by their IR, NMR, and mass spectra.

Alkyl Bromides, General Procedure. The conversion of chloride **10** to its corresponding bromide is described as a representative example. A mixture of 101.7 g (0.62 mol) of 2-(3-chloropropyl)-2-methyl-1,3-dioxolane (**10**; Aldrich Chem. Co.), 617 ml of *N*-methyl-2-pyrrolidinone, 461 ml (6.2 mol) of ethyl bromide, and 12.7 g (0.124 mol) of sodium bromide (Mallinckrodt) was heated at 65 °C, in a 1-neck flask under a Friedrich condenser, for 3 days. The mixture was then cooled and poured into a mixture prepared from 1 liter each of ice, water, and brine, and contained in a separatory funnel. The lower layer, after shaking, was removed and washed with a mixture of 1 liter of water and 1 liter of brine. The organic phase was again removed and distilled (without drying) through a 45 cm Vigreaux column. Ethyl bromide (containing some ethyl chloride) was collected at 38—40 °C (1 atm). The remaining material was then distilled under vacuum. There was obtained 114.6 g (89%) of 2-(3-bromopropyl)-2-methyl-1,3-dioxolane, of 97% purity, bp 65 °C/3.5 mm Hg (lit,[25] 98—101 °C/13 mm Hg).

Highly volatile halides (*e.g.* **4**) were isolated by spinning-band distillation and thermally unstable ones (*e.g.* **7**) by column chromatography.

In the case of the chlorodioxolane **11** (Table 1) the total conversion time was shortened to 30 days by addition of the EtBr (at 0 °C) after the Cl–Br conversion had proceeded to *ca.* 67% RBr after 2 days at 65 °C in *N*-methyl-2-pyrrolidinone alone.

1-Chloro-4-cyclopropylbutane (2). A solution of 1.1 M cyclopropyllithium in ether (660 ml) was added over 45 min, at −35 °C, to a mixture of 73 g (0.38 mol) of copper (I) iodide and 660 ml of tetrahydrofuran (THF) After a Gilman test was negative, 1-bromo-4-chlorobutane (54 g, 0.32 mol) was rapidly added to the mixture which was held at −35 °C for 1.5 h. Aqueous satd. $(NH_4)_2SO_4$ (NH_4Cl yielded poor quality precipitates) was then added and the mixture was filtered. The product was extracted with 2 liters of 1:1 ether–pentane. The organic layer was washed several times with water, then with brine. After drying ($CaSO_4$) the extract was distilled through a 45 cm Vigreaux column to remove solvents. The pot residue was then short-path distilled to yield 37.4 g (90%) of 1-chloro-4-cyclopropylbutane (**2**):[26] bp 58—59 °C/17 mmHg; IR (neat): 3084 (▷), 3008, 2941, 2864, and 1024 cm^{-1}; NMR (CCl_4): δ 3.48 (t, J=6 Hz, 2H, $C\underline{H}_2Cl$); mass spectrum (70 eV): base peak *m/e* 55 ($\overset{+\cdot}{\triangle}$).

1-Chloro-3-cyclopropylpropane[26] was prepared from 1-bromo-3-chloropropane in the same manner as above, but was isolated by spinning-band distillation: bp 73 °C/85 mmHg.

Chloride **2** was converted to 1-bromo-4-cyclopropylbutane (as described above for **10**): bp 71—72 °C/15 mmHg; IR (neat): 3086 (▷), 3010, 2936, 2866, and 1023 cm^{-1}; NMR (CCl_4): δ 3.35 (t, J=6 Hz, 2H, $C\underline{H}_2Br$); mass spectrum (70 eV): base peak *m/e* 55 ($\overset{+\cdot}{\triangle}$).

Found: C, 47.39; H, 7.27; Br, 45.03%. Calcd for $C_7H_{13}Br$: C, 47.48; H, 7.40; Br, 45.12%.

6-Chloro-3-methyl-2-hexene (3). This compound was prepared from lithium di-2-butenylcuprate and 1-bromo-3-chloropropane as described above for **2**. The product (mixture of *cis/trans* isomers) was isolated in 80% yield by spinning band distillation: bp 51—52 °C/15 mmHg; IR (neat): 2874, 1449, 1382, 828, and 727 cm^{-1}; NMR (CCl_4): δ 3.47 (t, J=6 Hz, 2H, $C\underline{H}_2Cl$).

Found: C, 63.16; H, 9.88%. Calcd for $C_7H_{13}Cl$: C, 63.39; H, 9.88%.

Chloride **3** was converted to 6-bromo-3-methyl-2-hexene (as described above for **10**): bp 69—70 °C/17 mmHg; IR (neat): 2867, 1451, 1383, and 824 cm^{-1}; NMR (CCl_4): δ 3.34 (t, J=6 Hz, 2H, $C\underline{H}_2Br$).

Found: C, 47.42; H, 7.48; Br, 45.08%. Calcd for $C_7H_{13}Br$: C, 47.48; H, 7.40; Br, 45.12%.

5-Chloro-1,1-diethoxypentane (9). 1-Bromo-4-chlorobutane (77.1 g, 0.45 mol) was added to 12.1g (0.496 mol) of magnesium metal (10% excess) in 150 ml of THF as follows: about 2 ml of bromochlorobutane was added at 50 °C and when spontaneous reaction began the mixture was cooled to 0 °C and the rest of the bromochlorobutane was added in five equal portions, followed each time by 150 ml of THF, over a 1 h period. The mixture was stirred 2 h at 0 °C, 2 h at room temperature, then re-cooled to 0 °C. Diethyl phenyl orthoformate (88.4 g, 0.45 mol) was then added to the mixture which was stirred 2 h at 0 °C, overnight at room temperature, then filtered. The filter-cake was washed with 200 ml of ether and the filtrate was evaporated to remove solvents. The residue was diluted with ether (700 ml) and water (300 ml). The ether layer, after shaking, was removed and successively washed three times with aq. 50% sodium hydroxide (50 ml), twice with water (250 ml), once with brine (100 ml), then dried ($CaSO_4$) and evaporated to yield 83.0 g of colorless liquid which was purified by distillation through a 45 cm Vigreaux column. There was obtained from the product fraction 61.0 g (70%) of chloroacetal **9**, of 96% purity: bp 103—105 °C/15 mmHg (lit,[21a] 84—86 °C/5 mmHg); IR (neat): 2992, 2894, 1451, 1381, 1352, 1141, 1082, and 1018 cm^{-1}; NMR (CCl_4): δ 1.16 (t, J=7 Hz, 6H, $OCH_2C\underline{H}_3$) and 4.38 (t, J=5 Hz, 1H, $C\underline{H}(OCH_2CH_3)_2$); mass spectrum (70 eV): *m/e* (rel intensity) 151 (17), 149 (44), 121 (26), 103 (100, $CH_3CH_2OCH{=}OCH_2CH_3^+$), 85 (21), 75 (54, $HOCH{=}OCH_2CH_3^+$), and 47 (53).

Found: C, 55.67; H, 9.90; Cl, 18.10%. Calcd for $C_9H_{19}ClO_2$: C, 55.53; H, 9.77; Cl, 18.25%.

The pot residue (18.0 g, 15%) was high purity 1,1,6,6-tetraethoxyhexane: IR (neat): 2990, 2892, 1448, 1381, 1351, 1134, 1074, and 1019 cm^{-1}; NMR (CCl_4): δ 1.15 (t, J=6.5 Hz, 12H, $OCH_2C\underline{H}_3$) and 4.35 (t, J=4.5 Hz, 2H, $C\underline{H}(OCH_2CH_3)_2$); mass spectrum (70 eV): *m/e* (rel intensity) 170 (5), 127 (60), 103 (100), 81 (50), 75 (60), 73 (35), 59 (37), 47 (33), and 45 (33).

Found: C, 64.22; H, 11.29%. Calcd for $C_{14}H_{30}O_4$: C, 64.09; H, 11.52%.

The reactions of $Br(CH_2)_nCl$, where n=5 and n=6, with magnesium (10% excess) in THF (0 °C), followed by $PhOCH(OCH_2CH_3)_2$, according to the above conditions for preparation of **9**, similarly led to products in which the ratio of $(CH_3CH_2O)_2CH(CH_2)_nCl$: $(CH_3CH_2O)_2CH(CH_2)_nCH(OCH_2CH_3)_2$ was 89 : 11 for n=5 and 88 : 12 for n=6.

The reaction of 1 mole of $Cl(CH_2)_5Br$ with magnesium in THF (as above), followed by CO_2 gas (24 °C, 3 h),[2] yielded after distillation, 94.9 g (63%) of $Cl(CH_2)_5CO_2H$ (**14**) of 98% purity: mp 27.5—28 °C (lit,[27a] 24—26 °C); IR (neat): 3600—2400 (CO_2H), 1711 (C=O), 1463, 1416, 1283, and 946 cm^{-1}; NMR ($CDCl_3$): δ 2.39 (t, J=6 Hz, 2H, $C\underline{H}_2CO_2H$) and 3.56 (t, J=6.5 Hz, 2H, $ClC\underline{H}_2$).[30]

Chloride **9** was converted to 5-bromo-1,1-diethoxypentane (**15**; as described above for **10**): bp 98 °C/8 mmHg; IR (neat): 2988, 2894, 1448, 1380, 1351, 1138, 1072, and 1015 cm^{-1};

NMR (CCl_4): δ 1.17 (t, J=7 Hz, 6H, $OCH_2C\underline{H}_3$) and 4.39 (t, J=5 Hz, 1H, $C\underline{H}(OCH_2CH_3)_2$); mass spectrum (70 eV): *m/e* (rel intensity) 239 (1, M^+), 194 (41, $Br(CH_2)_4CH{=}OCH_2{-}CH_3^+$), 166 (15, $Br(CH_2)_4CH{=}OH^+$), 148 (6), 103 (100, $CH_3CH_2OCH{=}OCH_2CH_3^+$), 85 (31), 75 (72), and 47 (65).

Found: C, 45.37; H, 8.01; Br, 33.69%. Calcd for $C_9H_{19}BrO_2$: C, 45.21; H, 7.95; Br, 33.44%.

*4-Chloromethyl-1,3-dioxolane (**11**)* was prepared, in 70% yield, from chloropropanediol and paraformaldehyde in dichloromethane:[28] bp 150—151 °C (lit,[9a] 144—146 °C; 150 °C[9b]).

*1,1-Diethoxy-6-methyl-6-heptene (**16**)* was prepared from the bromoacetal **15** and lithium di-2-propenylcuprate as described above for **2**. The product was isolated in 72% yield (94% purity by GLPC): bp 55 °C/0.3 mmHg; IR (neat): 3091 (>=), 1455, 1382, 1353, 1144, 1074, 1019, and 900 cm^{-1}; NMR (CCl_4): δ 1.17 (t, J=7 Hz, 6H, $OCH_2C\underline{H}_3$), 4.37 (t, J=4.5 Hz, 1H, $C\underline{H}(OCH_2CH_3)_2$) and 4.66 (br s, 2H, $=C\underline{H}_2$).

Found: C, 72.10; H, 12.06%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%.

11-Hydroxyundecanoic Acid. A mixture of 5.0 g (0.019 mol) of 11-bromoundecanoic acid, 7 ml (20×0.019 mol) of water, and 50 ml of *N*-methyl-2-pyrrolidinone was heated, at 60 °C, for 24 days. The mixture was then poured into 300 ml of water and extracted three times with 75 ml-portions of ether–pentane (1:1). The combined extracts were washed with water and brine, then dried ($CaSO_4$) and evaporated to yield a solid which was recrystallized from toluene. There was obtained 2.9 g (76%) of white solid, mp 66—67 °C (lit,[29a] 65.5—66 °C); IR (neat): 1708 (C=O) cm^{-1}; NMR ($CDCl_3$): δ 1.30 (br s, 16H, chain $\underline{H}$), 2.33 (t, J=6 Hz, 2H, $C\underline{H}_2CO_2H$) and 3.63 (t, J=6 Hz, 2H, $HOC\underline{H}_2$).

Hydrolysis of bromooctane (**13**) under similar conditions yielded 72% of 1-octanol (*cf.* Table 1).

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