Synthesis of 1,1,2-Trichloro-1,2-dialkoxyalkanes and their Conversion into 1,1,1,2,2-Pentaalkoxyalkanes

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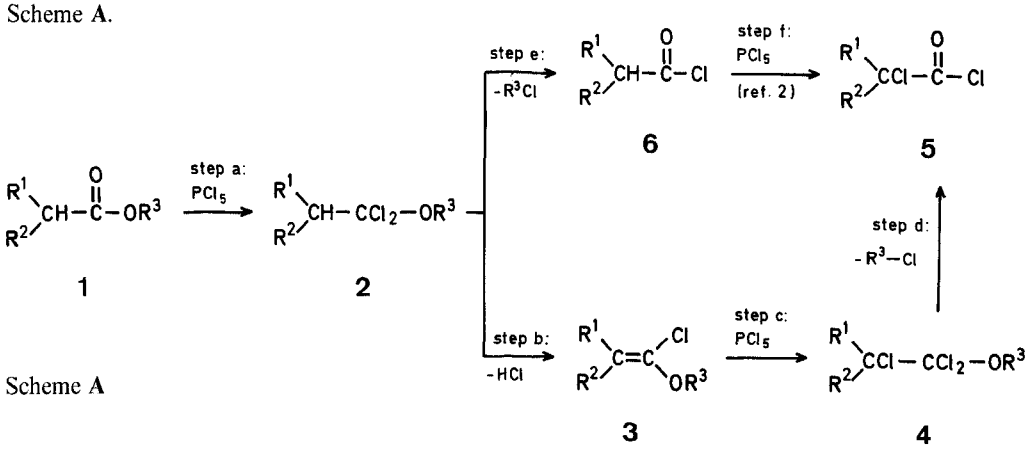
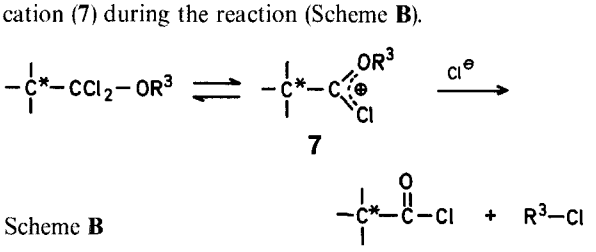
The nature of the reaction product from reactions between esters and phosphorus pentachloride depends on the composition of the ester used as can be explained by the following Scheme A.



Scheme A

Usually esters of carboxylic acids give α-chlorinated acyl chlorides[1,2] (**5**), whereas esters of acids without α-hydrogen atoms (*e.g.* alkyl benzoates) yield unsubstituted acyl chlorides[3] (**6**) as the ultimate product. Since the decomposition of α,α-dichloroethers (steps d and e) cannot occur when R^3 is not sensitive for nucleophilic attack[4,5], phenyl esters give α,β-chlorinated ethers[6] (**4**), and phenyl formate yields α,α-dichloroethers[7] (**2**). The last mentioned type of product is also obtained, however, from alkyl formates[8] and from oxalic esters[9]. This illustrates the fact that the decomposition (steps e, d) is also retarded by the presence of substituents at C* which can sufficiently destabilise the intermediate cation (**7**) during the reaction (Scheme **B**).



Scheme B

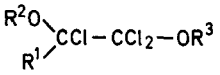
In agreement with this explanation we found that gentle heating of α-alkoxycarboxylic esters (**1** with OR^2 instead of R^2) with phosphorus pentachloride gave 1,1,2-trichloro-1,2-dialkoxyalkanes in good yields (Table 1). R^1 may be hydrogen or aryl; for R^1 = methyl, a higher chlorinated 1,1,2,3-tetrachloro-1,2-dialkoxypropane is isolated.

Baganz has previously reported[10] that 1,1,2-trichloro-1,2-dialkoxyethanes (**8**), obtained *via* a more elaborate method, can be converted into hexaalkoxyethanes (**11**) by elimination of hydrogen chloride with sodium hydroxide, followed by addition of chlorine and substitution of the chlorine atoms by alkanolate residues. The end-products, now more simply available, may be of synthetic value because of the presence of two adjacent highly reactive ortho ester functions in the same molecule (Scheme **C**).

We found that **8** undergoes mainly substitution rather than elimination on treatment with a dilute solution of sodium methanolate at 0°. In this way pentaalkoxyethanes such as **12** can be obtained in about 60% yield, and a similar procedure can be used for the preparation of 1,1,1,2,2-pentaalkoxy derivatives of higher hydrocarbons (Table 2). On treatment of **8** with other alkoxides, and at higher temperatures, elimination again predominates over substitution, giving 1,2-dialkoxy-1,2-dichloroethenes (**9**).

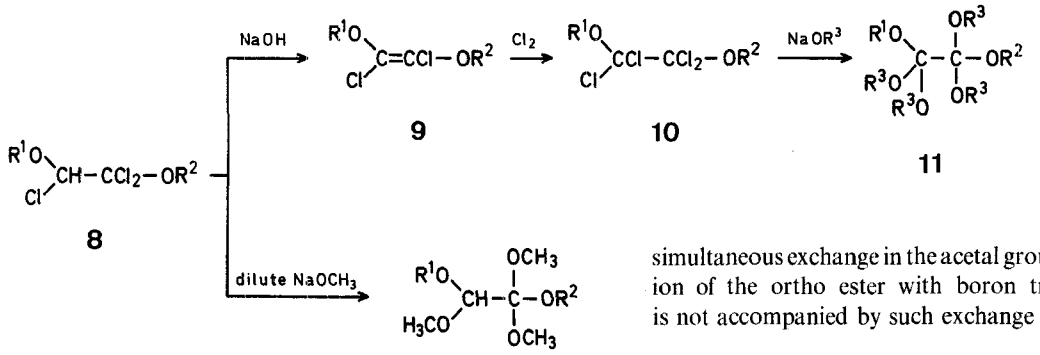
The reactivities of the acetal and ortho ester function in **12** show a remarkably large difference which may make it possible to employ these compounds in a variety of ortho ester reactions without interference from the acetal group. This appeared to be the case with the methoxy groups at the ortho ester side in **13** which could be exchanged for other alkoxy groups in the presence of an acid without

Table 1. Preparation of 1,1,2-Trichloro-1,2-dialkoxyalkanes

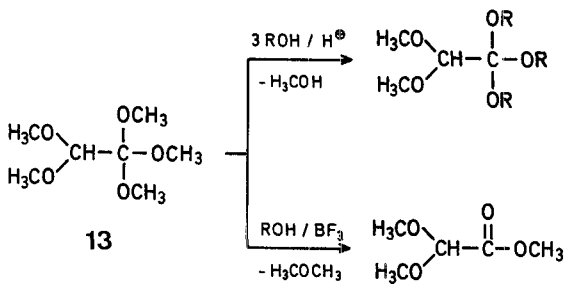


R^1	R^2	R^3	Yield (%)	B.p.	^{1}H-N.M.R. δ ppm for R^1 = H
H	CH_3	CH_3	75	91°/20 torr	5.55
H	CH_3	C_2H_5	80	96°/20 torr	5.60
H	CH_3	i-C_3H_7	80	52°/0.2 torr	5.60
H	C_2H_5	C_2H_5	85	96°/15 torr[a]	5.60
H	C_2H_5	$CH_2CH_2-O-CH_3$	80	120°/20 torr	5.70
	CH_3	CH_3	75	108°/0.3 torr	–

[a] Lit.[12]: 91.5°/12 torr.



Scheme C



simultaneous exchange in the acetal group. Even decomposition of the ortho ester with boron trifluoride in alcohol is not accompanied by such exchange reactions.

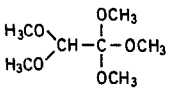
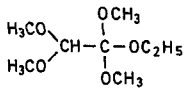
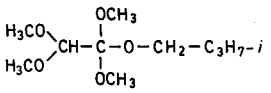
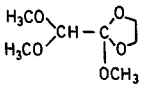
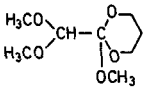
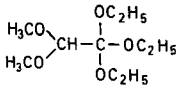
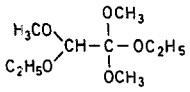
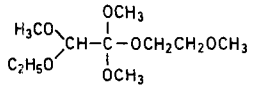
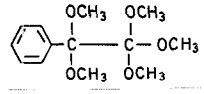
The α-alkoxycarboxylic esters used as starting compounds were obtained from α-bromo- or α-chlorocarboxylic acids by nucleophilic substitution of the halogen atom by the relevant alkoxide group, followed by acid-catalysed esterification[11].

All compounds synthesised were identified from ^{1}H-N.M.R.-spectra which substantiated the proposed structure as well as the purity of the products. The methyne proton shifts in the ^{1}H-N.M.R.-spectra were always between $\delta = 4.0$ and 4.2 (in CCl_4). The mass spectra of all pentaalkoxyethanes showed strong peaks for $[M-1]^{\oplus}$, $[M-OCH_3]^{\oplus}$ and $[M-HC(OCH_3)OR]^{\oplus}$.

1,1,2-Trichloro-1,2-dialkoxyalkanes (Table 1):

One equivalent of an alkyl α-alkoxycarboxylate is added to 1.8 equivalents of powdered phosphorus pentachloride, and the mixture is kept at 85–90° for 12 h. Unreacted phosphorus pentachloride is destroyed by addition of a small amount of methyl formate.

Table 2. Preparation of Pentaalkoxyalkanes

Product	Method	Yield (%)	B.p.	n_D^{25}
	A	60	64°/15 torr[a]	1.4129
	A	60	72°/15 torr	1.4100
	A	65	40°/0.3 torr	1.4133
	C	55	96°/13 torr	1.4290
	C	50	50°/0.1 torr	1.4401
	B	50	81°/15 torr	1.4096
	A	60	78°/15 torr	1.4122
	A	50	105°/15 torr	1.4308
	A	70[b]	88°/0.3 torr	1.4908

[a] Lit.[14]: b.p. 85°/25 torr; ^{1}H-N.M.R. (CCl_4): $\delta = 4.1$ ppm (HC(OCH$_3$)$_2$–).

[b] Mass spectrum: $m/e = 225$ (90%, $M^{\oplus} - OCH_3$), 179 (36%, $M^{\oplus} - C_6H_5$), 151 (100%, $M^{\oplus} - C(OCH_3)_3$), 105 (100%, $M^{\oplus} - C(OCH_3)_2(C_6H_5)$).

Then phosphorus trichloride and phosphorus oxychloride are removed by fractionation at low pressure (15 torr) over a well-fractionating column, thus avoiding the possibility that the desired product distils over with the volatile halides. Distillation of the residue yields the trichlorodialkoxyalkanes.

Baganz[1,2] has previously shown that decomposition of **4** (R^1 = H, R^2 = ethoxy, R^3 = ethyl) according to step d is strongly influenced by the presence of small amounts of aluminium chloride. Boiling stones also accelerated this decomposition. In some experiments we isolated larger amounts of acid chlorides (**5**) which must be ascribed to the unnoticed presence of such catalysts.

According to this procedure methyl 2-methoxypropanoate yields *1,1,2,3-tetrachloro-1,2-dimethoxypropane* as the main product; yield: 35%; b.p. 60°/0.3 torr.

^{1}H-N.M.R. (CCl_4): δ = 4.2 (s, 2H), 3.85 (s, 3H), 3.75 ppm (s, 3H).

Mass spectrum: *m/e* = 239 (7%), 241 (7%), 243 (4%), 245 (1%) $(M-1)^{\oplus}$; 205 (100%), 207 (100%), 209 (66%), 211 (10%) $(M-Cl)^{\oplus}$; 191 (95%), 193 (95%), 195 (50%), 197 (8%) $(M-CH_2Cl)^{\oplus}$.

1,1,1,2,2-Pentaalkoxyalkanes (Table 2):

Method A: By substitution of chlorine in $(R^2O)CR^1Cl-CCl_2(OR^3)$. Over a period of about 3 h a 1,1,2-trichloro-1,2-dialkoxyalkane (0.2 mol) is dropped into a solution of sodium methoxide (0.8 mol) in methanol (400 ml) at 0°. The reaction mixture is left for 12h at room temperature. Methanol is distilled off through a small fractionating column, and the residue is extracted several times with pentane. The extract is distilled, first at normal pressure to remove pentane, then at reduced pressure. Pentaalkoxyalkanes containing various alkoxy groups at the ortho ester side are distilled and stored in alkaline washed vessels to avoid disproportionation[13].

Method B: By exchange reactions from $(CH_3O)_2CH-C(OCH_3)_3$. A small amount of *p*-toluenesulphonic acid is added to a mixture of pentamethoxyethane and 10 equivalents of an alcohol. Methanol is distilled off from the mixture over a well-fractionating column. The residue is neutralised by addition of a small piece of sodium and distilled at low pressure.

Method C: By exchange reactions with a diol. Equivalent amounts of a pentaalkoxyethane and a diol are heated for 20 minutes at 70° in the presence of 1 mole percent of *p*-toluenesulphonic acid. The mixture is worked up as in the previous preparation.

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