Halomethyl Metal Compounds. IX.[1] The Reaction of Phenyl(bromodichloromethyl)mercury with Alcohols[2]

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The products obtained when phenyl(bromodichloromethyl)mercury was allowed to react with alcohols in chlorobenzene or ethylbenzene solution at 80–85°, alkyl chloride, alkyl formate, benzene, and chloroform can be rationalized as resulting from an initially formed alkyl dichloromethyl ether (eq 2–5 in text). A mechanism for the formation of the latter involving electrophilic attack of dichlorocarbene at the oxygen atom of the alcohol, followed by proton migration from oxygen to carbon, was suggested on the basis of the lack of reactivity of CF_3CH_2OH and $HCF_2CF_2CH_2OH$ in these reactions and apparent steric effects encountered with *t*-butyl alcohol. Dichloromethylenation of unsaturated alcohols was possible if the hydroxyl function was protected by a trimethylsilyl group.

In 1950 Henne and Snook[5] reported the preparation of ethyl difluoromethyl ether by reaction of potassium hydroxide, bromodifluoromethane, and ethanol. Hine's later studies[6] established that such reactions involved the insertion of difluorocarbene into the O–H bond of the alcohol, *e.g.*, eq 1. This general reaction also has

$$HCF_2Cl + RO^- \xrightarrow{ROH} CF_2 \xrightarrow{ROH} ROCF_2H \quad (1)$$

been used in the difluoromethylenation of phenols and thiophenols.[6b,7-9] Of special interest is the preparation of alkyl difluoromethyl ethers by the reaction of CF_2 as obtained by photolysis of difluorodiazirine with alcohols.[10] No dichlorocarbene-based synthesis of dichloromethyl ethers has been reported to date. Since phenyl(bromodichloromethyl)mercury has been shown to be an excellent CCl_2 transfer agent,[11] an examination of its reactions with alcohols was of interest.

The reaction chosen for initial study was that of *n*-butyl alcohol with phenyl(bromodichloromethyl)mercury. Heating a mixture of 20 mmoles each of these reactants at 80–85° in 30 ml of ethylbenzene under nitrogen caused complete consumption of the mercurial within 30 min, and phenylmercuric bromide precipitated. Analysis of the filtrate by gas–liquid partition chromatography (glpc) showed that *n*-butyl chloride (3.5 mmoles), *n*-butyl formate (8.8 mmoles), chloroform (5.8 mmoles), and benzene (3.34 mmoles) were present. The first two products were reconcilable with the following reaction scheme (eq 2, 3, and 4).

$$C_6H_5HgCCl_2Br + C_4H_9OH \longrightarrow C_6H_5HgBr + C_4H_9OCCl_2H \quad (2)$$

$$C_4H_9OCCl_2H + C_4H_9OH \longrightarrow (C_4H_9O)_2CHCl + HCl \quad (3)$$

$$(C_4H_9O)_2CHCl \longrightarrow C_4H_9Cl + HCOOC_4H_9 \quad (4)$$

Reactions 3 and 4 represent known chemistry of dichloromethyl ethers.[12] If *n*-butyl chloride and *n*-butyl formate had been formed solely by reaction 4, then they would be expected to be present in an equimolar ratio. The large excess of the formate ester must be due in part to another process, possibly adventitious hydrolysis during work-up of a quantity of *n*-butyl dichloromethyl ether which remained after the consumption of the *n*-butyl alcohol. The other products, benzene and chloroform, were formed in the reaction of the hydrogen chloride produced (eq 3) with $C_6H_5HgCCl_2Br$ (eq 5). A separate study of the action

$$C_6H_5HgCCl_2Br + HCl \longrightarrow \begin{cases} C_6H_6 + ClHgCCl_2Br \\ C_6H_5HgBr + HCCl_3 \end{cases} \quad (5)$$

of hydrogen chloride on this mercurial confirmed that both C_6H_5–Hg cleavage by HCl and CCl_2 insertion into the H–Cl linkage occur at 80°.[1]

Reactions of several other alcohols with phenyl(bromodichloromethyl)mercury were studied. With allyl alcohol there was produced allyl chloride, allyl formate, benzene, and chloroform, and in the case of benzyl alcohol the volatile products were benzyl chloride, benzyl formate, benzene, and chloroform. In the reaction of *t*-butyl alcohol with phenyl(bromodichloromethyl)mercury *t*-butyl chloride was obtained, but no *t*-butyl formate. Also present were rather large (up to 26%) amounts of *t*-butyl alcohol upon completion of the reaction. Further products were tetrachloroethylene (in up to 39% yield) and 1,1-dichloro-2,2-dimethylcyclopropane, the dichloromethylenation product of isobutylene. Formation of the latter is believed to result from acid-catalyzed elimination of formic acid from *t*-butyl formate to give the olefin which then reacts with CCl_2 (eq 6).

$$(CH_3)_3COCH \xrightarrow{HCl} HCOOH + CH_2{=}C(CH_3)_2 \xrightarrow{C_6H_5HgCCl_2Br} CH_2\text{—}C(CH_3)_2 \text{ (with } CCl_2 \text{ bridge)} \quad (6)$$

The reactions of two fluorinated alcohols, CF_3CH_2OH and $HCF_2CF_2CH_2OH$, with phenyl(bromodichloromethyl)mercury gave only small amounts of benzene and chloroform. The corresponding chlorides and formates were not detected, but recovered yields of the alcohols were high (~70%) and tetrachloroethylene was produced in yields of up to 55%.

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(11) D. Seyferth in "Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research. IX. Organometallic Compounds," Robert A. Welch Foundation, Houston, Texas, 1966, pp 89–135.

(12) A. Rieche and H. Gross, *Chem. Ber.*, **92**, 83 (1959).

It would appear from these results that these alcohols are quite inert to attack by CCl_2. Tetrachloroethylene usually is found when phenyl(bromodichloromethyl)-mercury decomposes in the absence of species reactive toward CCl_2 and is believed to arise by the process outlined in eq 7.

$$C_6H_5HgCCl_2Br \xrightarrow{CCl_2} C_6H_5HgCCl_2CCl_2Br \longrightarrow C_6H_5HgBr + CCl_2{=}CCl_2 \quad (7)$$

In terms of mechanistic considerations, the reactions of phenyl(bromodichloromethyl)mercury with 2,2,2-trifluoroethanol and 2,2,3,3-tetrafluoropropanol, as well as with *t*-butyl alcohol, are of some significance. Two main mechanisms can be considered for the $C_6H_5HgCCl_2Br$ + alcohol reactions (which are rapid only at temperatures at which CCl_2 transfer from $C_6H_5HgCCl_2Br$ is rapid): (a) electrophilic attack by CCl_2 at the oxygen atom of the alcohol, followed by proton migration from oxygen to carbon (eq 8), or (b) nucleophilic attack by CCl_2 at the proton of the alcohol (eq 9). In principle, singlet state CCl_2 should be capable of either electrophilic or nucleophilic behavior, since it has

$$C_6H_5HgCCl_2Br + ROH \rightarrow \left[\begin{array}{c} Cl \\ \diagdown \\ C \\ \uparrow \\ O \\ \diagup \quad \diagdown \\ R \quad H \end{array}\right] \rightarrow ROCCl_2H \quad (8)$$

$$C_6H_5HgCCl_2Br + ROH \rightarrow [RO]^-[HCCl_2]^+ \rightarrow ROCCl_2H \quad (9)$$

both a vacant p orbital and a lone electron pair in an sp^2 orbital. The fact that fluorinated alcohols are so unreactive can be rationalized in terms of mechanism a, but not in terms of b. The strong −I effect of the trifluoroethyl and tetrafluoropropyl groups should decrease electron availability at oxygen[13] but increase the protonic character of the alcohol hydrogen atom. Thus if proton abstraction by CCl_2 were occurring as in b, the fluorinated alcohols should be very reactive. The results of the reaction of *t*-butyl alcohol with phenyl(bromodichloromethyl)mercury also are in agreement with mechanism a. While *t*-butyl chloride and *t*-butyl formate derived 1,1-dichloro-2,2-dimethylcyclopropane were formed in low (<15%) yields, recovery of *t*-butyl alcohol and the yield of tetrachloroethylene were, as mentioned above, quite high. This lack of reactivity on the part of *t*-butyl alcohol can be explained in terms of steric hindrance to CCl_2 attack at oxygen by the three-methyl substituents on the adjacent carbon atom. A marked steric effect would not be expected in the case of mechanism b. The results of the study of Mitsch and Robertson[10] on the competition of methanol and 2,2,2-trifluoroethanol for a deficiency of difluorodiazirine in the gas phase led them to a similar conclusion in the case of the difluorocarbene–alcohol reaction. Only CH_3OCF_2H was formed; thus the more nucleophilic of the two competing alcohols was the more reactive.

The CCl_2–alcohol reaction thus has no preparative utility. The dichloromethyl ethers which apparently are formed initially are consumed in further reaction with alcohol, and even the yields of the secondary products, alkyl halide and alkyl formate, are not high. Furthermore, a significant portion of the starting mercurial is destroyed by the HCl formed in the secondary alcoholysis reaction.

This study thus has provided an explanation of our previous failure in the attempted direct conversion of allyl alcohol to 1,1-dichloro-2-hydroxymethylcyclopropane by the mercurial route. The trimethylsilyl group can be used to protect OH, NHR, and NH_2 functions in chemical synthesis, and in most cases the original functional groups are regenerated easily by mild hydrolysis. We have used this technique to prepare 1,1-dichloro-2-hydroxymethylcyclopropane, 1,1-dibromo-2-hydroxymethylcyclopropane, and 1,1-dichloro-2-hydroxymethyl-3-methylcyclopropane, *e.g.*, eq 10. Hydrolysis of the *gem*-dihalocyclopropanes derived from $CH_2{=}CHOSi(CH_3)_3$ and $(CH_3)_3SiOCH_2CH{=}CHCH_2OSi(CH_3)_3$ did not give the expected dihalocyclopropyl-substituted alcohols, but the reasons for this failure were not ascertained.

$$CH_2{=}CHCH_2OH \xrightarrow{(Me_3Si)_2NH} CH_2{=}CHCH_2OSiMe_3 \xrightarrow[(X = Cl, Br)]{C_6H_5HgCX_2Br} \begin{array}{c} CH_2 \text{———} CHCH_2OSiMe_3 \\ \diagdown \quad \diagup \\ CX_2 \\ \downarrow H_2O \\ CH_2 \text{———} CHCH_2OH \\ \diagdown \quad \diagup \\ CX_2 \end{array} \quad (10)$$

Experimental Section

General Comments.—All reactions were carried out under an atmosphere of prepurified nitrogen. The alcohols used were commercial products and were distilled from metallic sodium or barium oxide immediately before use. Phenyl(trihalomethyl)-mercury compounds were prepared as described in part I of this series.[15] Infrared spectra were recorded using a Perkin-Elmer Infracord 337 spectrophotometer.

Reaction of Phenyl(bromodichloromethyl)mercury with Alcohols.—The reaction with *n*-butyl alcohol is described as an example of the procedure used.

The mercurial (8.81 g, 20 mmoles) and 1.48 g (20 mmoles) of *n*-butyl alcohol were allowed to react in 30 ml of ethylbenzene at 80–85° for 30 min in a 100-ml, three-necked flask equipped with reflux condenser, thermometer, magnetic stirring assembly, and nitrogen inlet tube. The phenylmercuric bromide which precipitated during this time (7.15 g, 85% yield) was filtered; its melting point of 277–280° attested to contamination with other solids. Glpc analysis of the filtrate (7-ft glass column, 8-mm o.d., 20% General Electric Co. SE-30 silicone rubber gum on Chromosorb P, jacket at 90°, 15 psi of helium, MIT isothermal gas chromatograph) showed the presence of benzene (3.34 mmoles, 16.7%), chloroform (5.8 mmoles, 29%), *n*-butyl chloride (3.50 mmoles, 17.5%), and *n*-butyl formate (8.8 mmoles, 44%). The same reaction was repeated in chlorobenzene solution; the yields of these products were 21, 22, 19, and 42%, respectively. A third reaction was carried out in 30 ml of chlorobenzene using 30 mmoles of mercurial and 10 mmoles of *n*-butyl alcohol, with the latter being added slowly to the mercurial solution which was maintained at 80–85°. The yields obtained were: benzene, 13%; chloroform, 37%; *n*-butyl chloride, 11%; *n*-butyl formate, 46%. In a fourth experiment, the

(13) The effect of fluorinated alkyl groups on the donor properties of a lone-pair atom is illustrated by the finding[14] that replacement of a CH_3 group in trimethylamine by a CF_3CH_2 group very greatly decreases the donor power of the amine toward trigonal boron compounds.

(14) N. E. Miller, Ph.D. Thesis, University of Nebraska, 1958; data quoted by T. D. Coyle and F. G. A. Stone, *Progr. Boron Chem.*, **1**, 83 (1964), Table 4, p 104.

(15) D. Seyferth and J. M. Burlitch, *J. Organometal. Chem.* (Amsterdam), **4**, 127 (1965).

same reaction was repeated, but with 10 mmoles of mercurial and 30 mmoles of *n*-butyl alcohol. The yields of chloroform and *n*-butyl formate were 8 and 45%, respectively. The benzene and *n*-butyl chloride peaks were obscured by the unconverted *n*-butyl alcohol. The products in these experiments were identified by comparison of their glpc retention times and their infrared spectra with those of authentic samples.

The reactions with other alcohols were carried out in chlorobenzene using 7.5 mmoles of $C_6H_5HgCCl_2Br$ and 5 mmoles of the respective alcohol. The products and their yields, as obtained using glpc, follow below. They represent the average of two or more experiments.

Allyl alcohol gave 11% benzene, 36% chloroform, 12% allyl alcohol, 9% allyl chloride, and 9% allyl formate.

Benzyl alcohol gave 9% benzene, 20% chloroform, 9% benzyl chloride, and 3% benzyl formate.

***t*-Butyl alcohol** gave 11% benzene, 19% chloroform, 37% tetrachloroethylene, 11% *t*-butyl chloride, 24% *t*-butyl alcohol, and 11% 1,1-dichloro-2,2-dimethylcyclopropane.

2,2,2-Trifluoroethanol produced 10% benzene, 3% chloroform, 49% tetrachloroethylene, and 53% 2,2,2-trifluoroethanol. In another reaction the recovery of unconverted alcohol was 73% and the tetrachloroethylene yield was 37%.

2,2,3,3-Tetrafluoropropanol gave 5% benzene, 8% chloroform, 55% tetrachloroethylene, and 70% recovered alcohol.

Preparation of 1,1-Dichloro-2-hydroxymethylcyclopropane.—To a 50-ml, three-necked flask equipped with reflux condenser, a thermometer, and a drying tube was added 0.2 mole of allyl alcohol and 0.1 mole of hexamethyldisilazane (Peninsular Chem Research, Inc.), together with 2 drops of trimethylchlorosilane. A small amount of white precipitate formed and evolution of ammonia commenced. The mixture was heated at reflux for 10 hr, then was distilled to give 22 g (85%) of allyloxytrimethylsilane: bp 98–101°, $n^{25}D$ 1.3939 (lit.[16] bp 100°, $n^{30}D$ 1.3904). Its nmr spectrum (CCl_4 solution) showed a 9 H singlet at 0.11, a 2 H sextuplet centered at 4.14, a 2 H multiplet centered at 5.19, and a 1 H multiplet centered at 5.90 ppm downfield from tetramethylsilane.

A solution of 20.1 g (0.0456 mole) of phenyl(bromodichloromethyl)mercury and 14.9 g (0.114 mole) of allyloxytrimethylsilane in 50 ml of dry benzene was heated at reflux under nitrogen with stirring for 6 hr. The precipitated phenylmercuric bromide (15.54 g, 95%) was filtered. The filtrate was distilled at 0.05 mm into a receiver at −78°, pot temperature to 70°. Glpc analysis of the filtrate (20% SE-30 Chromosorb W, jacket at 145°, 10 psi of helium) showed that 1,1-dichloro-2-trimethylsiloxymethylcyclopropane had been produced in 50% yield. Pure samples were isolated by preparative glpc, $n^{25}D$ 1.4454. The nmr spectrum showed a singlet (9 H) at 0.10, a multiplet (1 H) centered at 1.12, a multiplet (2 H) centered at 1.64, and a doublet (J = 6.2 cps) (2 H) at 3.68 ppm.

Anal. Calcd for $C_7H_{14}Cl_2OSi$: C, 39.45; H, 6.61; Cl, 33.25. Found: C, 39.44; H, 6.65; Cl, 33.12.

A mixture of 2.94 g (13.8 mmoles) of 1,1-dichloro-2-trimethylsiloxymethylcyclopropane and 3 ml of benzene was stirred at reflux with 0.198 g (11 mmoles) of distilled water and sufficient methanol to produce a homogeneous solution for 3.5 hr. The low-boiling materials were removed at atmospheric pressure. The higher boiling liquid was distilled at 0.05 mm into a trap at −78°. Glpc analysis of the distillate showed that 1,1-dichloro-2-hydroxymethylcyclopropane had been produced in 88% yield. Pure samples were isolated by glpc. They had $n^{25}D$ 1.4844. The nmr spectrum (CCl_4) showed a multiplet from 1.10 to 2.28 (3 H) and a multiplet (2 H) centered at 3.78 ppm. The hydroxyl proton appeared as a broad singlet at 4.04 ppm.

Anal. Calcd for $C_4H_6Cl_2O$: C, 34.07; H, 4.22; Cl, 50.30. Found: C, 33.89; H, 4.49; Cl, 50.15.

Preparation of 1,1-Dibromo-2-hydroxymethylcyclopropane.—Essentially the same reaction sequence was carried out, with phenyl(tribromomethyl)mercury replacing the mercurial used in the experiment described above. 1,1-Dibromo-2-trimethylsiloxymethylcyclopropane, $n^{25}D$ 1.4846, was obtained in 31% yield. This low yield possibly results from limited thermal stability of this compound.

Anal. Calcd for $C_7H_{14}Br_2OSi$: C, 27.83; H, 4.67; Br, 52.92. Found: C, 27.80; H, 4.75; Br, 52.53.

Hydrolysis of this product gave 1,1-dibromo-2-hydroxymethylcyclopropane in nearly quantitative yield. Both the nmr and infrared spectrum were consistent with this structure.

Anal. Calcd for $C_4H_6Br_2O$: C, 20.88; H, 2.64; Br, 69.51. Found: C, 20.47; H, 2.90; Br, 69.75.

Preparation of 1,1-Dichloro-2-hydroxymethyl-3-methylcyclopropane.—Crotyloxytrimethylsilane, 98% pure by glpc, $n^{25}D$ 1.4063, was prepared by reaction of crotyl alcohol with hexamethyldisilazane with trimethylchlorosilane catalyst in 65% yield, bp 126–128.5°. Treatment with phenyl(bromodichloromethyl)mercury in benzene at 80° gave 1,1-dichloro-2-methyl-3-trimethylsiloxymethylcyclopropane, $n^{25}D$ 1.4487, in 87% yield. A mixture of isomers (*cis* and *trans*) was present, with a (presumed) *trans/cis* ratio of 4:3.

Anal. Calcd for $C_8H_{16}Cl_2OSi$: C, 42.22; H, 7.11; Cl, 31.22. Found: (combined isomers) C, 42.17; H, 7.21 (major isomer); C, 41.97; H, 6.85; Cl, 31.05.

Since the mercurial–olefin reaction is known to occur with retention of geometric configuration[11] this isomer ratio very probably reflects the *trans/cis* ratio in the crotyloxytrimethylsilane.

Hydrolysis of the cyclopropanation product gave 1,1-dichloro-2-hydroxymethyl-3-methylcyclopropane in 70% yield, $n^{25}D$ 1.4820.

Anal. Calcd for $C_5H_8Cl_2O$: C, 38.72; H, 5.21; Cl, 45.76. Found: C, 39.20; H, 5.39; Cl, 45.50.

The (presumed) *trans/cis* isomer ratio was 3:4.

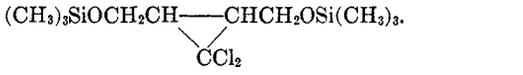
Preparation of 1,1-Dichloro-2-trimethylsiloxycyclopropane.—Vinyloxytrimethylsilane was prepared by reaction of $Hg(CH_2CHO)_2$[17] with trimethylchlorosilane.[18] The product had $n^{25}D$ 1.3856 (lit.[18] $n^{20}D$ 1.3885). Its nmr spectrum (CCl_4) showed a singlet (9 H) at 0.21, a doublet (1 H, J = 5.1 cps) at 4.08, a doublet (1 H, J = 13.6 cps) at 4.36, and a quartet centered at 6.33 ppm (1 H). Reaction of vinyloxytrimethylsilane with phenyl(bromodichloromethyl)mercury in benzene at 80° on a 46-mmole scale gave 1,1-dichloro-2-trimethylsiloxycyclopropane, $n^{20}D$ 1.4372, bp 32–33° (3 mm), in 77% yield. Its nmr spectrum showed a nine-proton singlet at 0.16, a two-proton multiplet centered at 1.12, and a one-proton quartet centered at 3.35 ppm.

Anal. Calcd for $C_6H_{12}Cl_2OSi$: C, 36.18; H, 6.08; Cl, 35.60. Found: C, 36.10; H, 5.98; Cl, 35.29.

Preparation of 1,1-Dichloro-2,3-bis(trimethylsiloxymethyl)cyclopropane.—1,4-Bis(trimethylsiloxy)-2-butene was prepared from 2-butene-1,4-diol and hexamethyldisilazane. It then was treated with phenyl(bromodichloromethyl)mercury in benzene at 80°. Samples of the product, $n^{25}D$ 1.4476, were isolated by glpc.

Anal. Calcd for $C_{11}H_{24}Cl_2O_2Si_2$: C, 41.87; H, 7.67; Cl, 22.49. Found: C, 41.62; H, 7.41; Cl, 22.80.

The nmr and infrared spectra were in agreement with its assumed structure as shown.



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