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NOVEL ACID-CATALYZED REARRANGEMENT OF 2,2-DIHALOETHANOLS. A 1,2-HALOGEN SHIFT AFFORDING α-HALOKETONES.

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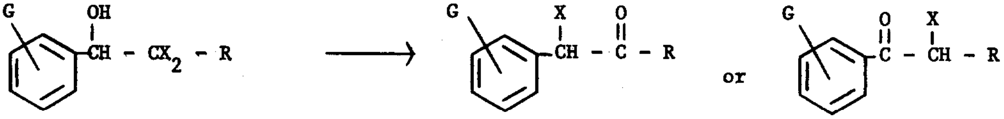
While the chemistry and synthetic utility of 2-haloethanols (halohydrins) has been well established,[1] very little is known about the analogous 2,2-dihaloethanol moiety.[2] Prompted by the initial discovery that 1-(*o*-chlorophenyl)-2,2-dichloro-1-propanol 1a rearranges exclusively to 1-(*o*-chlorophenyl)-1-chloro-2-propanone 2a upon treatment with sulfuric acid, we undertook a systematic study into the scope and limitations of employing 2,2-dihaloethanols as precursors for α-haloketones *via* this novel rearrangement process.[3]

Using 1a → 2a as a model system for this transformation, variations in reaction conditions were performed in an effort to optimize yield. A variety of Lewis acid-solvent combinations at several different temperatures were tried,[4] however, cold concentrated sulfuric acid proved to be the most effective in promoting rearrangement in highest yield. A large number of substituted 2,2-dihaloethanols were subsequently prepared and treated with sulfuric acid.

Through variation of the aryl and alkyl groups attached to the dihaloethanol moiety of compounds 1a-r, considerable differences in reaction behavior were achieved. 1-Aryl-2-alkyl-2,2-dihaloethanols rearranged affording compounds 2 with the yields determined predominantly by the nature of the alkyl side chain, R. Excellent yields of 2 were obtained with methyl substituents, yet, as the length of the alkyl group increased to ethyl or butyl decreased yields resulted. In contrast, replacement of the alkyl substituent with either hydrogen or chlorine, 1n-r, led to the formation of only elimination products. Phenyl substituents, 1k-m, caused the formation of the isomeric α-chloroketones 3. Whereas the substituents R influended the course of the reaction, groups on the aromatic ring had no effect on the type of product which was isolated. However, the rates of reaction were noticeably altered by such groups. The results of these reactions are listed in the Table.

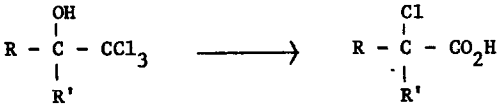
Extending this study into the trichloroethanols 4, we found that again reaction behavior was subtly altered by employing various groups. Methyl substituents led to a nearly quantitative yield of α-chloro acid 5a after aqueous work-up but in the case of the cyclo-

TABLE



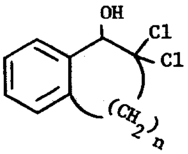
1 2 3

	G	X	R	2 Yield, %[5]	3 Yield, %[5]
a)	o-Cl	Cl	CH_3	74-90	
b)	p-Cl	Cl	CH_3	75	
c)	p-OCH_3	Cl	CH_3	75	
d)	o-CH_3	Cl	CH_3	20	
e)	H	Cl	CH_3	75	
f)	o-Cl	Br	CH_3	15	
g)	H	Cl	CH_3CH_2	25	
h)	o-Cl	Cl	CH_3CH_2	20	
i)	o-Cl	Cl	$CH_3(CH_2)_4$	25	
j)	o-Cl	Cl	ø$(CH_2)_2$	**	
k)	H	Cl	ø		85-90
l)	o-Cl	Cl	ø		55-60
m)	p-Cl	Cl	ø		80-85
n)	H	Cl	Cl	**	
o)	o-Cl	Cl	Cl	**	
p)	o-Cl	Cl	H	**	
q)	m-Cl	Cl	H	**	
r)	p-Cl	Cl	H	**	



4 5

	R	R'	5 Yield, %
a)	CH_3	CH_3	90
b)	cyclohexyl		10



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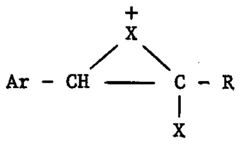
n= 1, 2, 3

hexyl group considerably lower yields were realized. Use of the phenyl substituent, **1n-o**, afforded only a mixture of elimination products.

Finally, the cyclic dihaloalcohols **6** were prepared and caused to react with sulfuric acid. However, no rearrangement products could be isolated and only extensive elimination of HCl, H_2, and HOCl occured as determined by GC-MS analyses.

Following this study, we were prompted to delineate the mechanism of this rearrangement process. Solvolytic rate data was obtained from the acid catalyzed trifluoroacetolysis of the p-toluenesulfonate and p-bromobenzenesulfonate of **1a** indicating carbon-oxygen bond cleavage to be the rate determining step during rearrangement.[6] In addition, rate data gathered from the solvolysis of the trifluoroacetates of **1a** and **1f** in TFA-H_2SO_4 demonstrated that halogen participation occurred in the rate determining step.[7] Based on this evidence, a mechanism for 1,2-halogen shift involving the halonium ion intermediate **7** is in best accord with these observations.



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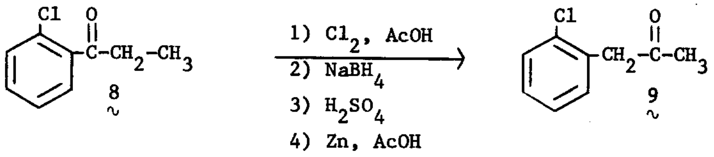
While compounds **2** resulted from 1,2-halogen shift, compounds **3** were probably produced by the thermal elimination of HCl to give initially the enol of **3** since even the vacuum distillation of **1k-m** gave nearly quantitative yields of **3k-m**. It is interesting to note that **1a** affords either **2a**, by reaction with sulfuric acid in 74% yield, or **3a**, by reaction with isopropylmagnesium bromide in 61% yield.[8]

In addition to the use of dihaloethanols as precursors for the synthesis of isomeric α-haloketones, the rearrangement of these compounds has shown some promise as a method for ketone transposition. For example, 1-(o-chlorophenyl)-2-propanone (**9**) can be conveniently prepared in 50-60% overall yield from 1-(o-chlorophenyl)-1-propanone (**8**) using the four-step reaction sequence of α,α-dichlorination, reduction with sodium borohydride, rearrangement in sulfuric acid and dechlorination with zinc in acetic acid.



References and Notes

1. H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, inc., Menlo Park, Calif., 2nd ed., 1972.
2. See, for example, W. Reeve and E. R. Barron, *J. Org. Chem.*, *40*, 1917 (1975);
   P. Blumbergs, M. P. LaMontagne, and J. I. Stevens, *J. Org. Chem.*, *37*, 1247 (1972);
   E. Kiehlmann, *Canad. J. Chem.*, *49*, 2964 (1971);
   C. Weizmann, E. Bergmann, and M. Sulzbacher, *J. Am. Chem. Soc.*, *70*, 1189 (1948).
3. A preliminary account of this work was presented, in part, at the 7th Northeast Regional Meeting of the American Chemical Society, Albany, New York, August 1976, Abstract No. 219.
4. Acid-solvent combinations which were investigated included: H_3PO_4, H_2SO_4-dioxane, PPA, CF_3-CO_2H, HCl-EtOH, TsOH-ϕH, HCl-H_2O, H_2SO_4-H_2O, $BF_3 \cdot Et_2O$, $AlCl_3$-ϕH.
5. a) The IR, NMR, and MS spectral data obtained from the products described here were fully compatible with the structures given in the Table.
   b) All data represent isolated yields after vacuum distillation.
   c) The designation ** denotes a mixture of elimination products as determined by GC-MS analyses.
6. B. L. Jensen and P. E. Peterson, manuscript in preparation.
7. B. L. Jensen, Scott E. Burke, and Susan E. Thomas, manuscript in preparation.
8. For pertinent references, see; A. J. Sisti and G. M. Rusch, *J. Org. Chem.*, *39*, 1182 (1972) and the references cited therein; H. O. House, *J. Am. Chem. Soc.*, *77*, 5083 (1955).