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PERHALOKETONES—XVII[1]

HEXABROMOACETONE AND THE BROMOCHLOROPERHALOACETONES

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Abstract—Hexabromoacetone, and all eight possible bromochloroperhaloacetones, have been prepared by the bromination of acetone, and of the corresponding chloroacetones, respectively, in acetic acid in the presence of sodium acetate. Several of these have also been made by treatment of fluorochloroperhaloacetones with aluminium bromide, but hexachloroacetone with aluminum bromide gave mixtures. The ketones were converted to the corresponding amides.

AS PART of a program on perhaloketones, it was desired to obtain hexabromoacetone and the perhaloacetones containing bromine and chlorine. The former[2] and five of the eight possible ketones of the latter type[2c, 2d, 3, 4] are known, but they have been prepared only by the brominolysis of phenols or of more complex ketones. We have found that all of these compounds can be made in good yields by direct bromination of the corresponding acetones in acetic acid in the presence of sodium acetate, or—in some cases—by treating fluorochloroacetones with aluminum bromide.

Although the partial bromination of acetone,[5] 1,1,1-trifluoroacetone,[6] or acetophenone[7] will occur in the presence of the hydrogen bromide formed, the attainment of complete bromination is difficult under this condition. The addition of sodium acetate as a basic acceptor is therefore either necessary[7] or preferable[6] to achieve complete replacement of available hydrogen, forming the tribromomethyl derivatives of the last two ketones. On the other hand, an attempt to convert chloroacetophenone to dibromochloroacetophenone by this procedure did not succeed,[7] since the product comprised 70% tribromoacetophenone. This result suggested that the method might not be applicable to bromination of the chloroacetones. We have found, however, that the desired compounds were obtained in good yield, as indicated in Table 1.

Treatment of aliphatic chloro compounds with aluminum bromide is a known procedure[8] for replacing chlorine by bromine. It therefore seemed of interest to study the interaction of it with hexachloroacetone for the preparation of the desired compounds. As shown in Table 2, it was found that the reaction yields a mixture of unchanged starting material, the monobromo-ketone IX, and the di-, tri-, and tetrabromoketone isomers which could be separated by distillation or chromatographically only as isomer mixtures. This approach was therefore concluded to be unsuitable for preparative purposes.

As expected, raising the reaction temperature from 45 to 75° reduced, but did not eliminate unreacted starting material, reduced the total yield of crude product, and gave increased conversion to polybromo derivatives at the expense of the monobromo compound. Attempts to attain a higher degree of bromination by using excess

TABLE 1. BROMINATION OF ACETONE AND CHLOROACETONES

Substrate	Product	Yield[a] %	M.p., °C[b]		Calcd., %			Found, %			Amide		
			This study	Lit.	C	H	Total Halogen as Cl	C	H	Total Halogen as Cl	Structure	M.p., °C[b]	
												This study	Lit.
CH_3COCH_3	$Br_3CCOCBr_3$ (I)	80	109	107–9[c]	6·8	0	90·3[d]	7·1	0·3	90·3[d]	Br_3CCONH_2	122	122[e]
$ClCH_2COCH_3$	$ClBr_2CCOCBr_3$ (II)	79	93	91–2[f]	7·4	0	—	7·8	0·2	—	$ClBr_2CCONH_2$	128	128[g]
$ClCH_2COCH_2Cl$	$ClBr_2CCOCBr_2Cl$ (III)	95	81	79·5[h]	8·4	0	—	8·3	0·3	—	$ClBr_2CCONH_2$	128	128[g]
$Cl_2CHCOCH_3$	$Cl_2BrCCOCBr_3$ (IV)	96	69	81[h]	8·1	0	—	8·4	0·2	—	$Cl_2BrCCONH_2$	139	139[j]
$Cl_2CHCOCH_2Cl$	$Cl_2BrCCOCBr_2Cl$ (V)	86	47	57[h]	9·1	0	61·8	9·5	0	61·5	$Cl_2BrCCONH_2$	140	139[j]
Cl_3CCOCH_3	$Cl_3CCOCBr_3$ (VI)	48	45	[i]	9·0	0	61·5	9·3	0·2	61·4	Cl_3CCONH_2	142	141[m]
$Cl_2CHCOCHCl_2$	$Cl_2BrCCOCBrCl_2$ (VII)	93	37	53[n]	10·2	0	66·2	10·4	0	66·2	$Cl_2BrCCONH_2$	140	139[j]
Cl_3CCOCH_2Cl	$Cl_3CCOCBr_2Cl$ (VIII)	97	27	[i]	10·2	0	—	10·1	0·2	—	Cl_3CCONH_2	141	141[m]
$Cl_3CCOCHCl_2$	$Cl_3CCOCBrCl_2$ (IX)	87	92·5–94 (11 mm)[o]	[i]	11·6	0	72·3	11·8	0·1	71·8	Cl_3CCONH_2	142	141[m]

[a] Mole per cent yield of crude product.
[b] On purified samples.
[c] Ref. 2.
[d] Per cent bromine.
[e] Ref. 2a.
[f] Ref. 3. F. Henle, *Liebigs Ann.* **350**, 330 (1906) gives m.p. 99°, but presents no supporting data.
[g] T. Zincke and O. Kegel, *Ber. Dtsch. Chem. Ges.* **23**, 1706 (1890). Anal. Calcd.: N, 5·6. Found: 5·6.
[h] Ref. 2c.
[i] Ref. 3.
[j] R. Neumeister, *Ber. Dtsch. Chem. Ges.* **15**, 603 (1882). Anal. Calcd.: N, 6·8. Found: 6·9.
[k] Ref. 2d.
[l] New compound.
[m] T. Zincke and O. Kegel, *Ber. Dtsch. Chem. Ges.***23**, 230 (1890). The compound showed no depression of m.p. when mixed with Cl_3CCONH_2 made from hexachloroacetone.
[n] Ref. 4; b.p. 110–111° (11 mm).
[o] B.p.

aluminum bromide and/or higher reaction temperatures resulted in excessive decomposition.

A recent study[9] has shown that boron tribromide in the presence of a trace of aluminum is an excellent reagent for the total replacement of chlorine in hexachlorocyclopentadiene by bromine. This reagent system gave incomplete replacement of chlorine in hexachloroacetone (cf. Table 2), although the degree of bromination and

TABLE 2. REACTION OF HEXACHLOROACETONE WITH ALUMINUM BROMIDE

	Yield[a]		
Compounds formed[b]	40–45°	70–75°	80–85°[c]
Total	45[d]	35[d]	117[d]
$Cl_3CCOCCl_3$ (recovered)	9·0	3·4	0
$Cl_3CCOCBrCl_2$ (IX)	30·9	17·9	0·6
Di- (VII and VIII)	17·3[e]	28·1[f]	21·2[f]
Tri- (V and VI)	27·1[g]	33·8[f]	41·6[f]
Tetra- (III and IV)	11·1[f]	14·5[f]	26·9[f]
Residue	4·1	2·4	9·7

[a] Weight per cent in product mixture by GLC, except as indicated.

[b] At temperatures given.

[c] Using boron tribromide with a trace of aluminum bromide.

[d] Weight per cent based on $Cl_3CCOCCl_3$ used.

[e] Analysis of a vacuum-distilled sample by GLC and mass spectrum showed a 2:1 wt. ratio of VII to VIII.

[f] Isomer composition of this fraction was not determined.

[g] Mass spectral analysis of a sample made by preparative GLC showed about 80% content of V.

the total yield were considerably higher than those noted with aluminum bromide alone. Boron tribromide alone did not react, as has been noted also with hexachlorocyclopentadiene.[9] Presumably aluminum bromide functions in a cyclic manner as the effective brominating agent, with boron tribromide effecting regeneration.

Although carbon disulfide has been successfully used in the past as the reaction solvent for aluminum bromide exchange reactions,[8] attempts to employ it in the present study were not encouraging, since sulfur-containing compounds of indefinite composition were obtained as the major product. 1,2-Dichloroethane was successfully used as reaction solvent with aluminum bromide–boron tribromide.

As indicated in Scheme I and Table 3, treatment of two fluorochloroacetones with aluminum bromide* gave stepwise or partial replacement of fluorine, with the degree of bromination in one case being determined by appropriate adjustment of reagent ratios and reaction conditions. Previous work by other on the interaction of fluorine compounds with aluminum bromide showed *only* complete replacement of *all* the

* These experiments were conducted by Dr. B. S. Farah.

fluorine atoms in certain cyclic olefins,[11] and in the preparation of brominated cyclobutenones.[11] Efforts to react hexafluoroacetone with aluminum bromide were unsuccessful.

SCHEME I

$$Cl_2FCCOCFCl_2 \xrightarrow{AlBr_3} \begin{cases} Cl_2FCCOCBrCl_2\ (X) \\ + \\ Cl_2BrCCOCBrCl_2\ (VII) \end{cases}$$

$$ClF_2CCOCF_2Cl \xrightarrow{AlBr_3} ClF_2CCOCBr_2Cl\ (XI)$$

$$F_3CCOCF_3 \xrightarrow{AlBr_3} \text{No reaction}$$

An earler report from this laboratory[12] on the interaction of aluminum chloride with *sym*-tetrafluorodichloroacetone and with hexafluoroacetone gave results generally similar to those observed in the present study using aluminum bromide. The latter ketone did not react, and in the former compound both F atoms on one C atom were replaced by chlorine, while the other two were inert. These results appear consistent with the well-known stabilizing effect of one F atom upon another located on the same C atom, and with the lability of the ClF_2CCO-group in contrast to the stability of the F_3CCO-moiety, as noted in other studies at this laboratory.[13]

Haloform cleavage of perhalogenated acetones with ammonia to the corresponding solid amides has in the past proved a convenient method of identification, and this approach was used to advantage in the present study (Table 1). With the symmetrical ketones, e.g. III, only one amide can be formed:

$$ClBr_2CCOCBr_2Cl \xrightarrow{NH_3} ClBr_2CCONH_2 + \underset{III}{HCBr_2Cl}$$

The unsymmetrical ketones are capable of forming two amides, and II has in fact been reported to form a 4:1 molar mixture of $ClBr_2CCONH_2$ and Br_3CCONH_2,[3] as indicated by m.p. and analytical data. GLC examination of the haloform product from II has indeed shown that a mixture is produced, but under our conditions at a ratio of 7·1:1. One recrystallization of the crude amide product gave pure $ClBr_2CCONH_2$, as indicated in Table 1.

TABLE 3. REACTIONS OF FLUOROCHLOROACETONES WITH ALUMINIUM BROMIDE

Substrate	Compound(s) formed[a]	Moles $AlBr_3$ per mole substrate	Conditions	
			Addition	Digestion
$Cl_2FCCOCFCl_2$	X[b]: 13%; VII: 21%	0·5	2 hr: 0–5°	1 hr: 100°
	VII: 30%	0·9	1 hr: 25–130°	2 hr: 130°
ClF_2CCOCF_2Cl	XI[c]: 22–27%	0·5	3 hr: 0–5°	16 hr: 25°; 1 hr: 60°

[a] Conversion in mole per cent bases substrate used.

[b] Anal. Calcd.: F, 6·5. Found: 5·9. B.p. 84–88° (20 mm).

[c] Anal. Calcd.: F, 11·8. Found: 11·5. Hydrolysis gave the expected CBr_2ClH of correct b.p. and IR spectrum. With aniline it gave the expected $F_2ClCCONHC_6H_5$, m.p. 72–73° (lit. (I. L. Knunyants, B. L. Dyatkin, L. S. German and M. P. Mochalina, *Izv. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk* 231 (1960); *Chem. Abstr.*, **54**, 20871 (1960)) gives 72–73°). Anal. Calcd.: Cl, 17·3; F, 18·5; N, 6·8. Found: 17·2; 18·7; 6·7. B.p. 55–56° (12 mm).

EXPERIMENTAL

M.ps were taken in capillary tubes on a Mel-temp block and are uncorrected. IR spectra were recorded on a Perkin–Elmer Infracord Model 137 Spectrophotometer. Mass spectra were obtained with a CEC 21–103 (modified) spectrometer equipped with a stainless steel inlet maintained at 150°; the source temp was 250°, and 70-eV ionizing electrons were used. Sources for the ketones used were as follows: hexachloroacetone and the fluorochloroketones—Specialty Chemicals Division, Allied Chemical Corp., Morristown, N.J.; monochloro- and 1,3-dichloroacetones—Eastman Organic Chemicals, Rochester, N.Y.; the other six chloroacetones—courtesy of Mr. W. Keith Langdon, Wyandotte Chemicals Corporation, Wyandotte, Michigan. All ketones were used as received, except monochloroacetone, which was redistilled before use.

Bromination of 1,3-*dichloroacetone.* Anhyd NaOAc (35 g) was mixed with 100 ml glacial AcOH in a laboratory reaction flask equipped with dropping funnel, reflux condenser, stirrer, thermometer and heater. The mixture was heated to 60°, and 1,3-dichloroacetone (13 g) was added, followed by the dropwise addition of Br_2 (70 g) over a 10 min period with stirring. The Br_2 reacted immediately, and the reaction was mildly exothermic such that no external cooling was needed to maintain a temp of 60–70°. The mixture was then heated to 95° and held there for ¾ hr, after which it was cooled to room temp and mixed with 500 ml water to precipitate the desired product (III) as a heavy red oil which soon solidified. After air drying it weight 42 g, 95% of theoretical. After one recrystallization from hexane, it melted at 81°, lit. 79–81° (cf. Table 1).

The other ketones were brominated similarly, as summarized in Table 1. The IR spectra of all the products showed CO absorption at 1750–1775 cm^{-1}, the absence of hydrogen, and strong C–Cl stretching in the 835 cm^{-1} range. Ketones containing fluorine showed C–F stretching at 1175 cm^{-1}.

Compounds III–IX were subjected to GLC analysis, which was done at 100° on a 5 ft × ¼ in column packed with 60–80 mesh "Chromosorb W" loaded with 10 wt% "Silicone QF1". It was found that this column was incapable of distinguishing between isomers, but did give sharp separation on the basis of Br content. The products were found to be essentially pure on this basis. (Isomer content was determined by mass spectral analysis or by haloform cleavage, as mentioned below.)

The ketones were converted to amides by the following typical procedure:

Dibromochloroacetamide. Compound III (8·8 g) was dissolved in 100 ml diethyl ether, and the soln was cooled to 10° with stirring. 30% NH_4OH (1·5 ml) was added, after which stirring was continued for 5 min. The ether soln was washed with water, dried over $MgSO_4$, and evaporated to dryness, yielding the crude solid amide, 4·7 g, 94 of theory. After one recrystallization from benzene, it melted at 128°, lit. 128° (cf. Table 1).

GLC analysis of the ether solns from the amide preparations gave the identity and amount of the haloforms produced, from which the composition of the ketone (or ketone mixture) could be determined. This was effected at 60° on a 10 ft × ¼ in column packed with 60–80 mesh "Chromosorb W" loaded with 20 wt% "Silicone Gum Rubber SE-30". The ketones listed in Table I were thus found to be of good purity.

Reaction of hexachloroacetone with aluminum bromide. Aluminum bromide (anhydrous technical lump—133 g) was added portionwise over a 20 min period with stirring to hexachloroacetone (200 g), preheated to 45°. Care was taken to break up the lumps of bromide as added. A slightly exothermic reaction occurred and the mixture turned red. The temp was kept at 40–45° during the period of addition by external cooling as needed, and stirring was continued for 4 hr afterward as the mixture gradually cooled to room temp. The product was mixed with ice water and extracted with 150 ml CCl_4. The extract was washed with three portions of cold water, and dried over $MgSO_2$. Removal of the solvent gave 90 g clear yellow oil. A similar run made at 70–75° gave 70 g. The products were examined by GLC, as shown in Table 2. Limited examination by haloform cleavage and mass spectral analysis shows at least some of the fractions to be isomer mixtures.

Reaction of hexachloroacetone with boron tribromide and aluminum bromide. Hexachloroacetone (9 g), boron tribromide (25 g), $AlBr_3$ (0·25 g), and 1,2-dichloroethane (25 ml) were mixed and refluxed for 8 hr, with steadily rising temp and evolution of boron halides as reaction progressed. The reaction mixture was cooled and mixed with ice water. The organic layer was dried over $MgSO_4$. Removal of the solvent gave 10·5 g brown oil which crystallized on standing. The results of GLC analysis are given in Table 2. No reaction occurred without the addition of $AlBr_3$.

Reaction of sym-tetrafluoridichloroacetone with aluminum bromide. Aluminum bromide (134 g) was added portionwise at 0–5° to the stirred ketone (200 g) over 3 hr. The mixture was held at room temp for 16 hr and was then heated to 60° to distill unreacted ketone (b.p. 45°—34 g). The reaction mixture was cooled and worked up as before.

Reaction of sym-difluorotetrachloroacetone with aluminum bromide. Aluminium bromide (500 g) was added portionwise with stirring and external cooling to the ketone (480 g) over 1 hr as the temp rose to 130°. The mixture was then digested 2 hr with external heating at 130°. It was cooled, mixed with an equal volume of CH_2Cl_2, treated with ice water, washed with cold water, and dried with $MgSO_4$. The product, after removal of the solvent, was mixed with an equal volume of hexane and chilled in an acetone–dry ice bath to induce crystallization. The solid was filtered, washed with fresh chilled hexane, and air dried. The yield of crude VII was 214 g.

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