

Favorsky Rearrangements

III. Syntheses of *cis*-3-Halogenoacrylic Acids from 1,1,3-Trihalogenoacetones

CHRISTOFFER RAPPE

Institute of Chemistry, University of Uppsala, Uppsala, Sweden

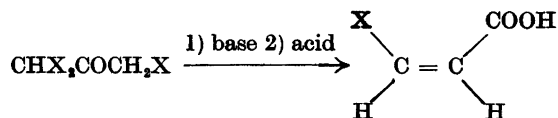
Good yields of *cis*-3-chloro- and *cis*-3-bromoacrylic acids are prepared from the Favorsky rearrangement of 1,1,3-trihaloacetones with carbonates or bicarbonates as bases.

The Favorsky rearrangement of halogenated ketones has found many applications in syntheses of organic acids. Kende gives more than 140 examples of this reaction in his review article.¹ Most examples are rearrangements of either mono- or dihalogeno ketones and only nine examples are given for rearrangements of trihalogeno ketones.

When α,α,α' -trihalo ketones are treated under Favorsky conditions, the result can be either a 2- or a 3-halogeno substituted 2-enoic acid. An example of a 2-substituted acid is 2-bromo-3-methyl-2-butenic acid, which is formed in 10 % yield from 1,1,3-tribromo-3-methyl-2-butanone.² A 3-halogeno substituted acid is 2-bromocyclohepten-1-carboxylic acid which is formed in 83 % yield from 2,2,8-tribromocyclooctanone.³ This apparent lack of symmetry can be explained by the structures of the ketones studied, as these have either been branched or cyclic compounds. In each case investigated there was only one theoretical possibility open, in some cases the 2-substituted acid and in other cases the 3-substituted acid. With 3-substituted acids only cyclic acids are obtained and the possibility of geometric isomerism is not discussed.

Ketones which theoretically can give three different acids (2-, *cis*-3- and *trans*-3-) are the 1,1,3-trihaloacetones, and the present investigation deals with the rearrangements of 1,1,3-trichloro- and 1,1,3-tribromoacetone.

The latter ketones have been treated with various inorganic bases in aqueous solution. The reactions can be written in the following way:



Detectable amounts of the *trans*-isomers could not be found in the reactions. The yields are good, usually about 60–75 %, see Table 1.

The two *cis*-halogenoacrylic acids prepared in this reaction have previously been prepared from the addition of hydrogen halides to propiolic acid.^{4,5} The more stable *trans*-isomers were usually obtained together with the *cis*-isomers. Although Cu_2Cl_2 as catalyst yields the *cis*-isomers exclusively,⁶ the route used in the present work seems preferable. Recently the two acids, and especially *cis*-3-chloroacrylic acid, have found use as potent defoliant and crop desiccants.⁶

It is interesting to notice that geometric specificity was found in the rearrangement of trihaloacetones. The Favorsky rearrangement has been reported as giving no geometric specificity,⁷ but it was recently found by the present author that several 1,3-dibromo-2-ones give high yields of pure *cis*-2-enoic acids when treated with weak bases.⁸ It is desirable to study other α, α, α' -tribromoketones to establish whether geometric specificity is general in the rearrangements of trihaloketones.

The mechanism of the Favorsky rearrangement is not yet completely understood. Three mechanisms are still discussed, the cyclopropanone mechanism proposed by Loftfield,⁹ the polar intermediates proposed by Aston and Newkirk,¹⁰ and the semibenzilic mechanism proposed by Tchoubar and Sackur.¹¹ Conia and Salaün have recently shown the latter to be valid for the rearrangements of 2-bromocyclobutanone.¹² The geometric specificity is not in accordance

Table 1.

Haloacetone	Purity % (NMR)	Base	Equiv. haloacetone/ base	Temp. °C	Time h	Yield ^a %	M.p. °C
$\text{CHCl}_2\text{COCH}_2\text{Cl}$	80	NaHCO_3	1:7.5	20	6	65	58–62 ^b
„	90	„	1:7.5	20	4	74	51–56 ^c
„	80	KHCO_3	1:7.5	20	6	65	58–62 ^b
„	80	CaCO_3	1:4	70	4	63	57–61 ^b
„	90	NaOH	1:4	30	1/4	—	—
$\text{CHBr}_2\text{COCH}_2\text{Br}$	95	NaHCO_3	1:7.5	20	4	68	56–59 ^c
„	95	Na_2CO_3	1:5	20	2	63	53–59 ^c
„	95	KHCO_3	1:7.5	20	1 1/2	69	56–59 ^c

^a Counted on 1,1,3-trihaloacetone present.

^b Recrystallized product.

^c Crude product.

with any of these mechanisms as presently formulated. More experimental work is needed to clarify the situation.

Experimental conditions are summarized in Table 1. Strong bases as sodium hydroxide gave no crystallizable products. Among the weak bases, carbonates and bicarbonates gave 60–75 % yields of *cis*-3-halogenoacrylic acid. Contrary to the rearrangement of 1,3-dibromobutanone-2, in which bicarbonates gave 15 % higher yields than carbonates,⁸ no significant difference could be found in the present case. Sodium, potassium and calcium salts gave all about the same yields. It can be relevant to note that carbonates and bicarbonates have found limited use in the rearrangement of monohaloketones, for which strong bases as alkoxides and hydroxides are mostly used.¹

The NMR-spectra of *cis*-3-chloro- and *cis*-3-bromoacrylic acids were recorded together with the two *trans*-isomers. The results are collected in Table 2. Both the chemical shifts and the coupling constants are of interest.

The coupling constants were found to be lower than expected. The values of 8–11 cycles/sec and 17–18 cycles/sec are given for *cis*- and *trans*-isomers of ethylenic compounds,¹³ and recently several aliphatic and aromatic α,β -unsaturated acids were found to have values within these limits.¹⁴ In the present case the *cis*-acids were found to have values of 8–8.5 cycles/sec and the *trans*-acids a value of 13–14 cycles/sec.

The chemical shifts of the α -protons were about the same for the *cis*- and *trans*-acids, but the shifts of the *cis*- β and the *trans*- β -protons were appreciably different. The *cis*-protons (*trans*-acids) have about 0.5–0.6 ppm higher δ -

Table 2.

Acid	2-H ppm	3-H ppm	J_{HH} cps
$\begin{array}{c} \text{Cl} \quad \quad \text{COOH} \\ \quad \quad \diagdown \quad / \\ \quad \quad \text{C}=\text{C} \\ \quad \quad / \quad \quad \diagdown \\ \text{H} \quad \quad \quad \text{H} \end{array}$	6.29	6.92	8.2
$\begin{array}{c} \text{H} \quad \quad \quad \text{COOH} \\ \quad \quad \diagdown \quad / \\ \quad \quad \text{C}=\text{C} \\ \quad \quad / \quad \quad \diagdown \\ \text{Cl} \quad \quad \quad \text{H} \end{array}$	6.35	7.57	13.3
$\begin{array}{c} \text{Br} \quad \quad \quad \text{COOH} \\ \quad \quad \diagdown \quad / \\ \quad \quad \text{C}=\text{C} \\ \quad \quad / \quad \quad \diagdown \\ \text{H} \quad \quad \quad \text{H} \end{array}$	6.75	7.30	8.4
$\begin{array}{c} \text{H} \quad \quad \quad \text{COOH} \\ \quad \quad \diagdown \quad / \\ \quad \quad \text{C}=\text{C} \\ \quad \quad / \quad \quad \diagdown \\ \text{Br} \quad \quad \quad \text{H} \end{array}$	6.64	7.85	13.8

values. This is in accordance with the spectrum of α -methylacrylic acid where the *cis*-proton is found to have a 0.58 ppm higher δ -value than the *trans*-proton.¹⁵ This feature can be of interest for the determination of the geometrical structure of 3-halo-2-enoic acids.¹⁶

EXPERIMENTAL

The NMR-spectra were recorded on a Varian model A-60 spectrometer, solvent carbon tetrachloride + TMS.

1,1,3-Trichloroacetone. This substance was prepared by the chlorination of 1,3-dichloroacetone. Two preparations were made and their purity according to NMR-analyses were 80 % and 90 %. B.p. 62°C/10 mm, $n_D^{25} = 1.4909$ (90 %).

1,1,3-Tribromoacetone. This substance was prepared according to Rappe¹⁷ from the bromination of acetone with three moles of bromine. B.p. 107–107.5°C/9 mm, m.p. 30.0–30.5°C, $n_D^{25} = 1.5874$.

cis-3-Haloacrylic acid

General procedure. The trihaloacetone was added to a well stirred aqueous solution or suspension of the base kept at room temperature. The mixture was thoroughly stirred and, when constant titration-values against methyl orange were obtained, the solution was extracted with ether (2 × 100 ml), acidified with hydrochloric acid, and again extracted with ether (6 × 100 ml). After drying, the ether phase was evaporated and the last traces of ether were removed with an oil pump. The yields of the crystallized crude products or recrystallized acids are given in Table 1.

The crude products were recrystallized from heptane. The chloro acid had the m.p. 61.5–63.5°C, Backer and Beute report the m.p. 63–64°C.⁴ The bromo acid had the m.p. 63–65°C, Alder *et al.* gave the m.p. 55°C,⁵ and Herret and Kurtz reported 60.5–62.8°C.⁶

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