

The introduction of a second double bond between C₁ and C₂ has no uniform effect on the solubilisation. In the case of cortisone the double bond slightly increases the solubility, but in the case of hydrocortisone an opposite effect is noted. In this respect also considerable quantitative differences are observed with different colloids. Furthermore, the data for *Δ*¹-cortisone and *Δ*¹-hydrocortisone are less reliable than those for the other steroids, since turbid solutions were often formed around the CMC. This phenomenon is possibly due to the formation of a mesomorphous phase, as in the case of cholesterol and association colloid solutions.⁵ As with all the other steroids studied perfectly clear solutions were obtained at all colloid concentrations, it may be suggested that a double bond in certain positions of the steroid skeleton contributes to the formation of a mesomorphous phase.

At last, the solubility values for 9-fluoro-16-methyl-*Δ*¹-hydrocortisone indicate, that the methyl group and fluorine are of little importance for the solubilisation.

The systematic investigations of the solubilisation of steroids is being continued and the results presented here will be discussed later in more detail together with other data.

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Favorsky Rearrangements

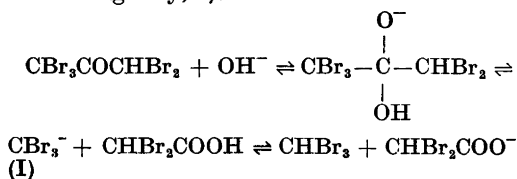
II. Attempts to Rearrange Pentabromoacetone

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Recently it has been found that the reaction between di-, tri- and tetrahalo ketones and weak bases such as carbonates or bicarbonates give good yields of Favorsky rearranged products. In most cases the reaction showed geometric specificity.¹⁻⁶ Continuing these studies it appeared interesting to study the effect of the same weak bases on the related pentabromo ketones. In this connection Wagner, Kloosterziel and Bickel found that small amounts of Favorsky rearranged products were isolated from the reaction between penta- and hexachloroacetone and sodium trichloroacetate.⁷

Since only α -halo ketones having at least one α -hydrogen can undergo the Favorsky rearrangement⁸ it was necessary to use pentabromoacetone. Accordingly pentabromoacetone was treated with excess aqueous bicarbonate and the reaction mixture was extracted with ether, acidified and then once again extracted with ether. From the acidic extract an acid could be isolated. However, it was not the expected 2,2,3-tribromoacrylic acid but dibromoacetic acid. This acid could be isolated in 64 % yield. The basic extract was distilled and from this extract bromoform could be isolated in 67 % yield. The reaction is probably an example of a haloform reaction and it can be visualized in the following way, cf. Ref.⁹



Attempts to use water, a still weaker base, instead of bicarbonate for the reaction (at 80°C for 4 days) resulted in the isolation of small amounts of crude materials, which consisted partly of dibromoacetic acid and bromoform.

It had been found earlier that pentachloroacetone can undergo a similar reaction. From the reaction between this compound and aluminium ethylate, chloroform and ethyl dichloroacetate were isolated.¹⁰ The reaction between a base and a halo ketone can occur by attack on either the α -carbon or the carbonyl group. In the former case the result will be either a Favorsky rearrangement, a hydroxy-ketone or an epoxide. See, for example, the review by Kende⁸ and also Refs.¹⁻⁶

On the other hand, a reaction between the base and the carbonyl group will give a haloform reaction. This kind of reaction occurs with α, α, α -tri-,¹¹ $\alpha, \alpha, \alpha, \alpha'$ -tetra-,¹² penta-,¹⁰ and hexachloro ketones,¹⁰ and even with 2,2-dichloroacetoacetic ester.¹³ When all three α -hydrogens are replaced by electron-attracting groups (halogens, carbethoxy) the reaction will be a haloform reaction. The anion (I) is stabilized by the three electron-attracting groups, forcing the equilibria to the right. When only two hydrogens are substituted a Favorsky rearrangement usually occurs,⁴⁻⁶ although the tetrabromo ketone, 2,2,4,4-tetrabromocyclobutanone, was found to undergo a haloform reaction. Conia and Ripoll isolated 2,2,4,4-tetrabromobutyric acid from the reaction between this ketone and sodium carbonate.¹⁴

Pentabromoacetone was prepared in 50 % yield according to the general method for the preparation of polybromo ketones.¹⁵ Shah and Pishawikar have reported a yield of 28 % from the bromination in the absence of solvent.¹⁶

Experimental. Pentabromo acetone. To a cooled mixture of 29.0 g of acetone (0.5 mole) in 50 ml of 48 % hydrobromic acid, 400 g (2.5 moles) of bromine were added dropwise. In the beginning of the reaction the bromine was decoloured immediately, but later the bromine colour persisted. After standing five days 500 ml of water was added and a heavy, brown-coloured oil separated which crystallized on standing. It was recrystallized from ethanol (2 ml/g) and gave 114 g (50 %) of long broad white needles, m.p. 68–70°C. Repeated crystallization from ethanol raised the m.p. to 72–73°C. Shah *et al.*¹⁵ reported m.p. 72–73°C.

Reaction between pentabromo acetone and sodium bicarbonate. Pentabromoacetone (45.3 g, 0.1 mole) were added to a solution of 68 g (0.8 mole) of sodium bicarbonate in 1 l of water. The reaction mixture was kept at 80°C for 45 h. After cooling, the water phase was

extracted with ether (3 × 150 ml), acidified with hydrochloric acid and once again extracted with ether (5 × 150 ml). From the basic extract, 17.0 g (67 %) of bromoform could be distilled, b.p. 42–43°C at 14 mm, $n_D^{22} = 1.5925$. Values reported for bromoform are b.p. 46°C at 15 mm and $n_D^{19} = 1.5980$. From the acidic extract 14.0 g (64 %) of dibromoacetic acid could be collected, b.p. 122–127°C at 10 mm. The boiling point of this compound has been given as 128–130°C at 16 mm.¹⁷ The identity of the products were proved by IR-spectra.

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