α-KETO EPOXIDES AND THEIR REACTIONS

COMMUNICATION 6. α-KETO EPOXIDES FROM CYCLIC KETONES

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In previous communications [1] we described the preparation of aliphatic α-keto epoxides and keto di-epoxides by the oxidation of the corresponding α,β-unsaturated ketones with alkaline hydrogen peroxide. It was considered to be of interest to apply this reaction also for the oxidation of α,β-unsaturated cyclic ketones with the object of obtaining cyclic α-keto epoxides, because only isolated members of this class of compounds—mainly α-keto epoxides from unsaturated cyclic ketones of the terpene series [2-4]—have been prepared. It should be noted that, until recently, the view was prevalent in the literature that α,β-unsaturated cyclic ketones are difficult to oxidize with alkaline hydrogen peroxide [5] and that the cyclic α-keto epoxides that are formed in small amount in this reaction are unstable compounds, which readily lose their epoxide oxygen during distillation [2]. Interest in cyclic epoxides has grown appreciably recently in connection with work on the partial synthesis of corticosteroids, in particular, cortisone [6], which are known to have a hydroxy or carbonyl group at C-11 and also a hydroxy group at C-17.

We began by studying the oxidation of the simplest cyclic α,β-unsaturated ketones with the intention of proceeding further to the oxidation of more complex polycyclic systems, including tetracyclic ketones related to steroids. Oxidation of 2-methyl-2-cyclopenten-1-one (I) with alkaline hydrogen peroxide in methanol gave 2,3-epoxy-2-methylcyclopentanone (II) in a yield of about 40%. Hydrolysis of this product with hot 3% hydrochloric acid gave a low yield of a crystalline substance of m.p. 104-105°, which corresponded in analysis to a diketone of formula (IV) or (V):

![Chemical structures](image)

The product is acid to Congo red, and with aqueous ferric chloride it gives a violet coloration that changes to red on addition of sodium acetate. The hydrolysis of the α-keto epoxide (II) is probably accompanied by rearrangement of the resulting keto glycol (III) with migration of the methyl group and formation of the α-diketone (IV) instead of the expected β-diketone (V). According to the literature [7], the α-diketone (IV) melts at 105-106°, whereas the β-diketone (V) melts at 212° [8]. We did not succeed in isolating the corresponding keto glycol (III) in the pure state.

By the action of alkaline hydrogen peroxide on 2,4-dimethyl-2-cyclopenten-1-one (VI) [9] in methanol solution, 2,3-epoxy-2,4-dimethylcyclopentanone (VII) was obtained in a yield of about 30%.

![Chemical structures](image)
Hydrolysis of the keto epoxide (VII) with dilute hydrochloric acid gave a product of m.p. 84-87° corresponding in analysis to the diketone (IX) or (X). In this case, together with the diketone, we obtained also the keto glycol (VIII), which probably consisted of a mixture of geometric isomers.

The oxidation of 3,5-dimethyl-2-cyclo penten-1-one (XI) [10] was more difficult, and we did not succeed in isolating the α-keto epoxide (XII) in the pure state; it was characterized only in the form of its semicarbazon. In the oxidation of the ketone (XI), the formation of the keto epoxide (XII) was accompanied by the formation of a small amount of the hydroxy keto epoxide (XIII), m.p. 68°, corresponding to the further oxidation of the keto epoxide (XII):

We met a similar oxidation previously in the case of mesityl oxide [11].

Oxidation of 2-cyclohexen-1-one (XIV) with alkaline hydrogen peroxide gave a 50% yield of the corresponding α-keto epoxide (XV), which was hydrolyzed by water in the cold with formation of the crystalline α-keto glycol (XVI), probably in the transconfiguration.

In the hydrolysis of the keto epoxide (XV), a crystal hydrate of (XVI), m.p. 115°, was first formed. This hydrate contained one molecule of water to every six of the glycol, and this water was lost when the hydrate was sublimed with formation of the anhydrous keto glycol (XVI), m.p. 87°. According to the results of Kötz and Richter [12], 2-cyclohexen-1-one (XIV) cannot be oxidized with hydrogen peroxide.

Oxidation of 2-methyl-2-cyclohexen-1-one (XVII) with alkaline hydrogen peroxide gave the corresponding α-keto epoxide (XVIII) in a yield of about 70%. Hydrolysis of the product with dilute hydrochloric acid gave the keto glycol (XIX), which solidified after distillation as a gumlike mass:

**EXPERIMENTAL**

**Preparation of the α-Keto Epoxide (II)**

In the course of 45 minutes, 50 ml of 12% hydrogen peroxide and 3.5 ml of 4 N NaOH were added simultaneously from two dropping funnels to a continuously stirred cooled (to -8° with ice and salt) solution of 15 g of 2-methyl-2-cyclo penten-1-one (I) [b.p. 49° (13 mm); nD 1.4780] [13] in 100 ml of methanol. Reaction proceeded with appreciable evolution of heat; at first the temperature rose rapidly by 14° (from -8° to +6°), but