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A SYNTHESIS OF 1,3-DIOXEPANE-5,6-DIONE

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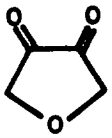
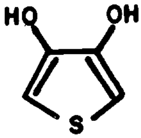
To our knowledge only one unsubstituted heteroalicyclic vicinal diketone I has been prepared, and it was made by a method unique to that structure(1). While II is known(2,3) and is formally a dienolic diketone, apparently it lacks ketonic character. The 6-membered and 7-membered ring compounds are especially inaccessible since, under the alkaline conditions of the ester condensations or the acyloin reactions commonly used in efforts to prepare them, β-eliminations and ring cleavages occur.

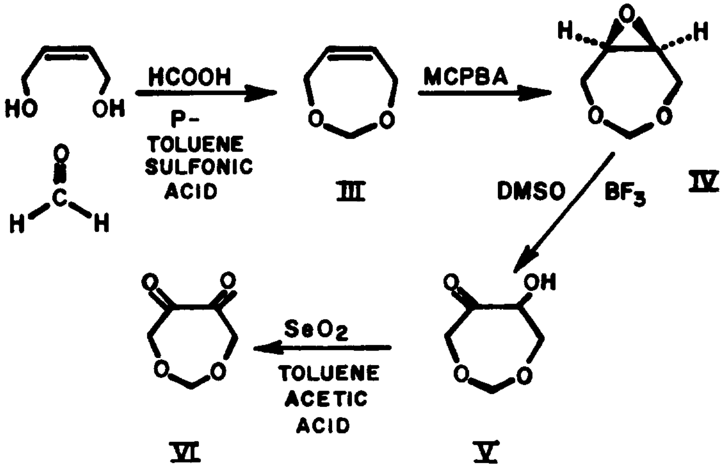


I



II

We report here the synthesis of a second unsubstituted heteroalicyclic vicinal diketone, 1,3-dioxepane-5,6-dione VI, by a route which is novel and perhaps widely applicable to the series since acidic conditions are used in the critical stages. The synthetic sequence is shown below:

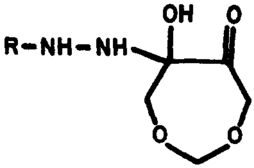


The 1,3-dioxep-5-ene III was prepared in 70% yield by a known method(4). Oxidation of III with meta-chloroperbenzoic acid in chloroform gave 3,5,8-trioxbicyclo[5.1.0] octane IV, m.p. 55-57° also in 70% yield in agreement with a subsequently published report(5). Conversion of IV to 6-hydroxy-1,3-dioxepan-5-one V in 22% yield was accomplished by a method(6) which has been used in acyclic and alicyclic cases. The crude acyloin (yellow due to presence of some VI) was purified by fractional distillation, bp. 58-60° (0.05 mm), and the crystalline distillate melted at 45-48°(7). IR ($CHCl_3$) carbonyl absorption was at 5.80 μ and there was a hydroxyl absorption band at 2.87 μ.

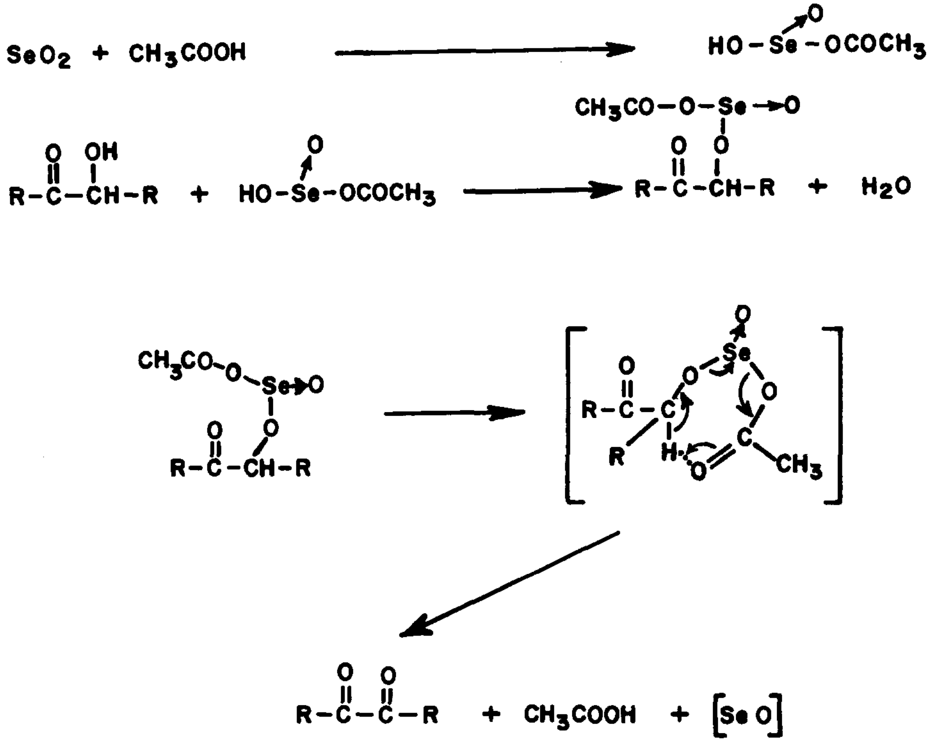
Oxidation of V to VI proved difficult, particularly since it was necessary to avoid protic solvents, which add rapidly to the carbonyl groups of the vicinal diketone as it is formed. In our hands cupric acetate, bismuth oxide, manganese dioxide, lead dioxide, lead tetraacetate, chromic acid, dinitrogen tetroxide, dimethyl sulfoxide-acetic anhydride in a variety of solvents all were unsuccessful in oxidizing V to isolable VI. Selenium dioxide also failed in several solvents, but in refluxing toluene with a little acetic acid present and a reaction time of 4 hours a 41% yield of yellow 1,3-dioxepane-5,6-dione VI, m.p. 94-96°, was obtained. It was purified by recrystallization from isopropyl ether and by sublimation. The IR ($CHCl_3$) showed a single strong carbonyl band at 5.71 μ with not more than a few percent of hydroxyl absorption at 2.87 μ. In the UV (CH_3CN) the carbonyl $n \rightarrow \pi^*$ absorption appeared at 386 mμ (ε=30). The second peak occurred at 275 mμ (ε=38). In constrast to the approximate 20 peaks in the complex NMR spectrum of V the diketone VI in $CDCl_3$ showed only two signals, one at 5.69 τ (4H) and one at 4.99 τ (2H).

On dissolution at ordinary temperatures in protic solvents (H_2O, CH_3OH) the disappearance of the yellow color of the diketone due to solvent addition could be measured in seconds. As reported for I(1) and for cycloheptane-1,2-dione(8) there is a high degree of stabilization of VI in the dione form. Cyrstalline material was unchanged after ordinary storage for a period of several weeks. It has remained unchanged after more than a year of storage at 0°C.

While VI can form conventional derivatives with hydrazide carbonyl reagents under suitable conditions, in an aprotic solvent such as acetonitrile such reagents form colorless hydrated derivatives of the type:



Selenium dioxide conventionally is not used as an acyloin oxidant, but is commonly used to convert α-methylene ketones to vicinal diketones(9,10). The mechanism of this reaction has been studied, particularly for the deoxybenzoin type(11). Acetic acid must participate in our reaction since there was little oxidation without it. Anhydrous selenium dioxide was used, and at 100° conditions are favorable both for removal of water produced by esterification and for cleavage of selenium-oxygen bonds. It is possible, then, to envisage the following speculative mechanism for the oxidation-reduction process:



Under the reaction conditions it is likely that SeO would disproportionate to Se and SeO_2, and in fact selenium was present among the products.

It is interesting that the yields in this reaction are similar to the yields obtained in, *e.g.* the oxidation of cyclohexanone to cyclohexane-1,2-dione by selenium dioxide(10).

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