222. The Acid-catalyzed Isomerization of an α-Ketoester into β-Ketoesters and the Unusual Fragmentation of an α-Ketoester

Preliminary communication

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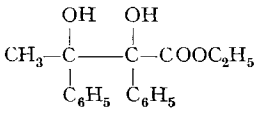
Summary. The first example of an acid-catalyzed isomerization of an α-ketoester into β-ketoesters is described. Ethyl 2-keto-3,3-diphenylbutyrate rearranged in fluorosulfonic acid at 0° into ethyl 2-benzoyl-2-phenylpropionate and ethyl 2,2-diphenylacetoacetate. In contrast, fragmentation of ethyl 3,3-diphenylpyruvate to benzophenone occurred in the same conditions.

Following the discovery that the ethoxycarbonyl group was a good migrating group in the glycidic ester rearrangement [1], a study of its migratory aptitude in the pinacol rearrangement of glyceric esters was initiated [2]. Two unexpected results are reported in this communication.

Ethyl 2,3-diphenyl-2,3-dihydroxy-butyrate (**1**) treated with fluorosulfonic acid at 0° for 3 min yielded as major product ethyl 2-keto-3,3-diphenylbutyrate (**2**), resulting from phenyl migration from the 2- to the 3-position during the pinacol rearrangement. Two very minor products, whose relative concentrations grew with the reaction time, were generated from the initially formed **2** as shown by treating **2** separately under the reaction conditions: it rapidly disappeared at the expense of the above two products **4** and **5**, isolated by preparative TLC. By NMR. and mass



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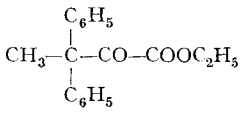
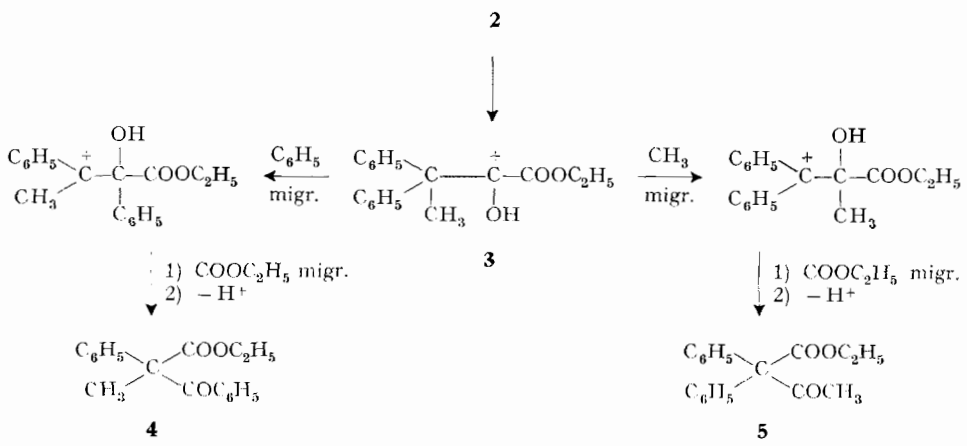


2

spectroscopy they were found to be the two isomeric β-ketoesters ethyl 2-benzoyl-2-phenylpropionate (**4**, M.W. 282, one major peak for $C_6H_5CO^+$ at *m/e* 105, NMR. of the tertiary CH_3 as a singlet at 1.83 ppm in $CDCl_3$) and ethyl 2,2-diphenylacetoacetate (**5**, M.W. 282, one major peak for CH_3CO^+ at *m/e* 43, NMR. of the acetyl at 2.08 ppm). The yields (%) of **2**, **4** and **5** in this order were 76, 16, 12 after 2 min, 38.5, 38.5, 23 after 10 min, and 5, 75, 25 after 20 min.

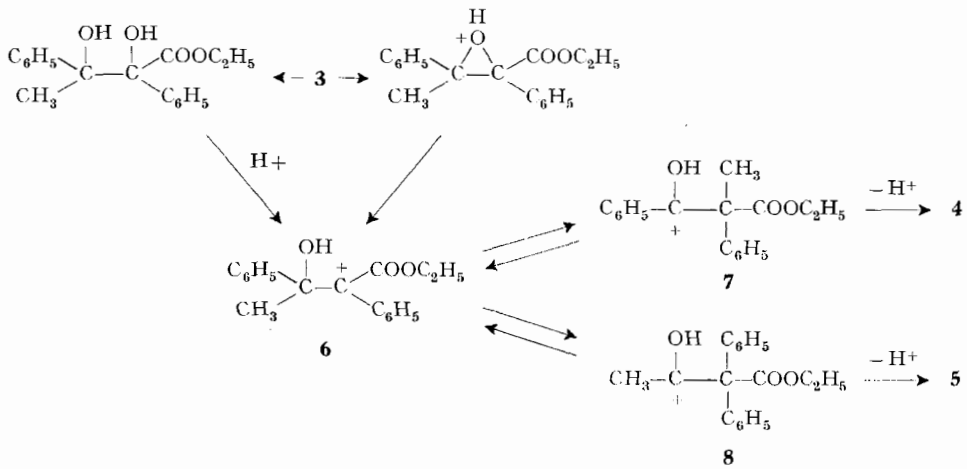
This acid-catalyzed isomerization of an α-ketoester into β-ketoesters is unprecedented. We tentatively explain it by a sequence of two migrations from the protonated ketoester **3** as shown in schemes 1 and 2. In scheme 1, the predominance of product arising from initial phenyl over methyl migration is in line with the known order of migratory aptitudes for these substituents in other carbonium ion rearrangements [3].

Scheme 1



Alternatively, the isomerization reaction could have followed the formation of the benzylic 2-carbonium ion **6**, either by a retropinacol rearrangement or by way of the protonated epoxide, as shown in Scheme 2.

Scheme 2

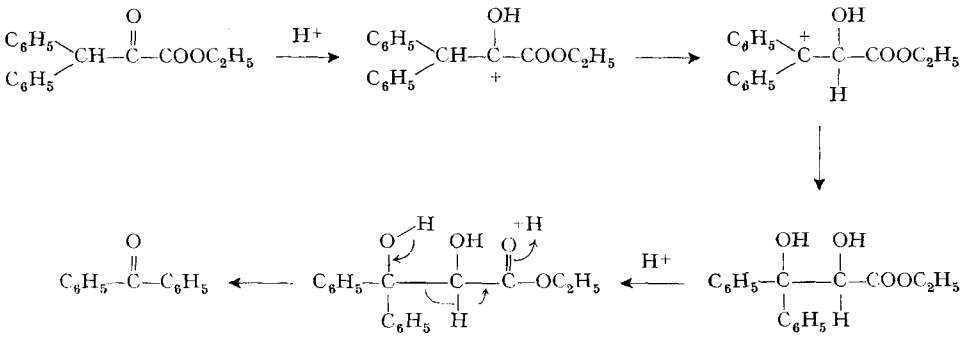


Competitive migration of the methyl and phenyl groups to the adjacent carbonium ion in **6** would yield **7** and **8**, the conjugate acids of **4** and **5** respectively. The observed predominance of **4** over **5** is readily explained by the benzylic nature of the carbonium ion **7**, which must favor this species in the equilibrium **7** $\rightleftarrows$ **6** $\rightleftarrows$ **8**, even though the intrinsic migratory aptitude of a phenyl is greater than that of a methyl in carbonium ion rearrangements [3].

The isomerization of an α into a β-ketoester does not appear to be a general process since it did not take place with ethyl diphenylpyruvate. Instead, cleavage

yielding benzophenone was observed, which is best explained by a retro-pinacol reaction as shown in Scheme 3.

Scheme **3**



The acid-catalyzed retro-aldol cleavage postulated in the last step has also been found to be a common feature in the chemistry of ethyl phenylglycerates [2].

A detailed mechanistic study of the above reactions will be performed with specifically labelled precursors.

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[2] *J. Kagan, D. A. Agdeppa, Jr. & S. P. Singh*, Helv. *55*, 2252 (1972).
[3] *D. Bethel & V. Gold*, 'Carbonium Ions, An Introduction', Academic Press, New York N.Y., p. 217 (1967).

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223. Über das Lipoxygenase-«Lipoperoxidase»-System in Cerealien: III. Zur Kinetik des enzymatischen Abbaues von Linolsäurehydroperoxiden[1])

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Zusammenfassung. Durch Untersuchung der Kinetik der Peroxidase-katalysierten Linolsäurehydroperoxid (LHPO)-Abbaureaktion mit einem Hafer-Ammoniumsulfatpräparat wird gezeigt, dass es sich um eine bimolekulare Reaktion in zwei Ein-Elektron-Schritten des Peroxidase-Hydroperoxid-Komplexes mit dem Wasserstoffdonator handelt. Der Nachweis wird durch die Übereinstimmung der Versuchswerte mit einer aus der Theorie der binären Komplexbildung abgeleiteten mathematischen Funktion erbracht.

Nachdem wir durch die Untersuchungen von Enzym-Reaktionen [1] und der dabei gebildeten Umsetzungsprodukte [2] zeigen konnten, dass der Abbau von

[1]) II. Mitteilung: s. [1].