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221. The Migratory Aptitude of the Ethoxycarbonyl Group in the Pinacol Rearrangement

Preliminary communication

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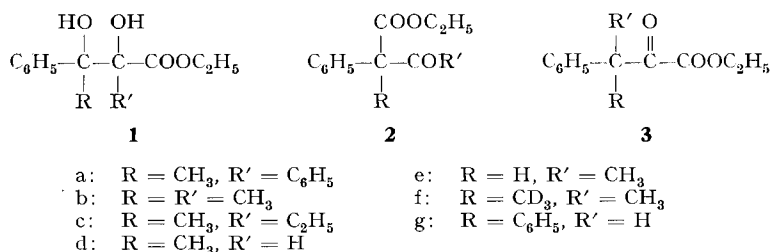
(23. V. 72)

Summary. The migratory aptitude of the ethoxycarbonyl group in the pinacol rearrangement was deduced from the structure of the products observed after treatment of 2-substituted 2,3-dihydroxy-3-phenylbutyrate with fluorosulfonic acid at 0° for 3 minutes. The migratory aptitude of ethoxycarbonyl is comparable to that of ethyl, greater than that of methyl or hydrogen, but smaller than that of phenyl. Cyclization and fragmentation reactions were also observed.

Our recent observation of a ethoxycarbonyl group migration in the acid-catalyzed rearrangement of glycidic esters [1] encouraged us to reinvestigate the classical pinacol rearrangement from the viewpoint of establishing the migratory aptitude of the ethoxycarbonyl group in this reaction¹). In order to minimize the possible influence of the nature of the initial carbonium ion on the course of the reaction, we selected a

series of ethyl 3-phenyl-3-methylglycerates (2,3-dihydroxy-3-phenylbutyrates). This structural feature should favor the initial formation of the 3-carbonium ion, which is benzylic and tertiary, at the expense of the 2-carbonium ion which is destabilized by the adjacent carbonyl group. The ranking of relative migratory aptitudes was established by checking in the products which of the ethoxycarbonyl or C(2) substituent had migrated.

The glyceric esters **1** were prepared from the glycidic esters which were obtained by *Darzens* condensation or by epoxidation of the corresponding unsaturated ester, and they were treated with fluorosulfonic acid at 0° for 3 minutes. The *threo* and *erythro* isomers gave identical results, and the products obtained exclusively by BF₃-catalyzed isomerization of the corresponding glycidic esters [1] were also the major products formed in the pinacol rearrangement.

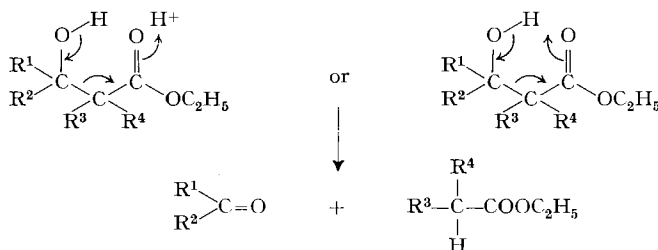


The conversions of **1a** into **3a** (60%), **1b** into **2b** (78%), **1c** into a mixture of **2c** (61%) and **3c** (9%) and of **1d** into **2d** (5%) lead to the conclusions that:

1. The ethoxycarbonyl group can undergo formal 1,2-shifts in the pinacol rearrangement.
2. The migratory aptitudes may be ranked CH₃ and H < COOC₂H₅ and C₂H₅ < C₆H₅.

In the absence of labelling experiments, phenyl migration to the 2-position rather than ethoxycarbonyl migration to the 3-position could not be proven. However, the higher migratory aptitude of ethyl over methyl in pinacol rearrangements [3], as well as that of ethoxycarbonyl over methyl observed in the rearrangement of **1e** to **2e** in the same conditions provided circumstantial evidences for the proposed ranking. It was unequivocally supported by the synthesis and rearrangement of the deuteriated analog **1f** into **2f** (76%), which demonstrated the migration of the ethoxycarbonyl group to the 3-position.

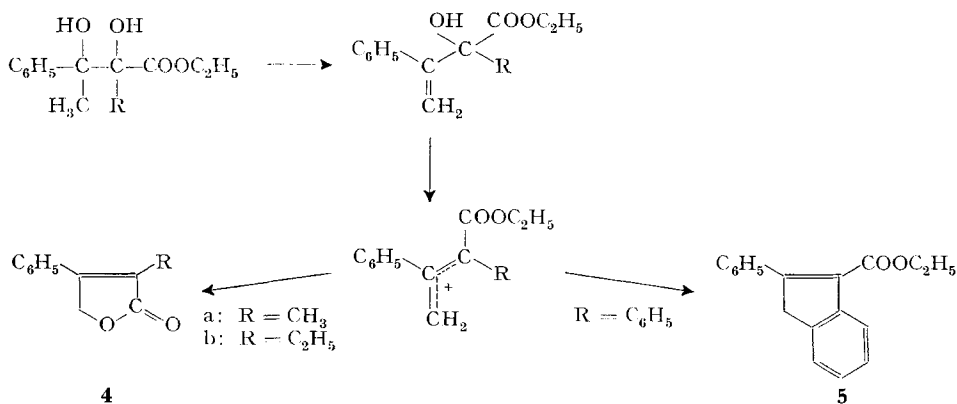
Fragmentation and cyclization reactions were also observed in the fluorosulfonic acid treatment of glyceric (and glycidic) esters. Thus, small amounts (less than 10%)



of acetophenone and benzophenone were obtained in the treatment of **1a–d** and **1g** (to **3g**), respectively. We formulate the reaction as an acid-catalyzed retro-aldol cleavage, following inter- or intramolecular protonation at the carbonyl.

This fragmentation reaction of β -hydroxyesters is well-known in basic medium [4], but with the exception of one report on free β -hydroxybutyric acids [5] this reaction in acid medium does not appear to have been previously described. The quantitative isolation of acetophenone and ethyl phenylacetate in the attempted *Fischer* esterification of 2,3-diphenyl-3-hydroxybutyric acid dramatically proved that the cleavage reaction did not depend on the presence of the α -hydroxyl.

Double dehydration was also observed in the fluorosulfonic acid treatment of **1b**, **1c** and **1a** which yielded small amounts of the lactones **4a** (22%), **4b** (9%) and the indene **5** (10%), respectively. The simplest explanation requires initial dehydration to an allylic alcohol, formation of an allylic cation and intramolecular attack at the oxygen or at the phenyl by the methylene:



Similar reactions of allylic cations have recently been mentioned [6]. The partitioning of the initially formed carbonium ion into rearranged and cyclized products was sensitive to the reaction conditions, and the formation of the fragmentation and cyclization products was suppressed completely by diluting the acid used for the rearrangement.

The acid-catalyzed rearrangements of specifically labelled glyceric and glycidic esters is presently under investigation.

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