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Acid Catalyzed Reactions of 2,2,4,4,6,6-Hexamethyl 1,5-Dihydroxybicyclo[3.1.0]hexane-3-one

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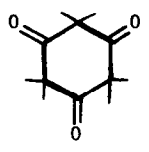
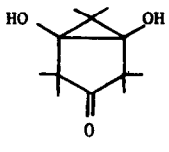
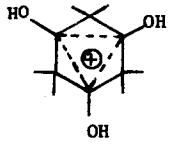
We recently reported the preparation of some vicinal-cyclopropanediol derivatives by the lithium in ammonia reduction of cyclic-1,3-diketones (eg. I → II).[1] In this communication we outline our observations concerning the reaction of 2,2,4,4,6,6-hexamethyl-1,5-dihydroxybicyclo[3.1.0]hexane-3-one (II) with acidic reagents.[2]



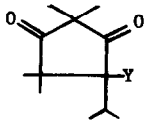
I



II



III



IV Y = OH

V Y = H

The ketodiol II is surprisingly stable to acid treatment. It can be recovered unchanged after eight hours in a methanolic-hydrochloric acid mixture at 25°, and is slowly transformed to the rearranged hydroxydiketone IV in refluxing concentrated hydrochloric acid (1-3 hours).[4] Indeed, the rate of rearrangement is sufficiently slow to permit the isolation of II as the major product (>80%) from Clemmensen reduction of I, by treatment with amalgamated zinc dust in a refluxing ethanol-hydrochloric acid mixture for 2.5 hr. Curphey et al.[5] recently reported the rearrangement of I to IV and V on more vigorous Clemmensen reduction, and were also able to isolate the diacetate derivative of II by reduction of I with zinc powder in acetic anhydride saturated with hydrogen chloride. These results clearly establish the intermediacy of cyclopropanediols in the abnormal Clemmensen reduction of 1,3-diketones.[6]

The unexpected stability of II in acidic media suggests, but does not require, a trishomocyclopropenyl cation structure for the conjugate acid. The evidence supporting less highly substituted cations of this kind as intermediates in solvolysis reactions of 3-substituted bicyclo[3.1.0]hexane derivatives has been reviewed by Winstein et al:[7] however, the importance of steric hinderance by the six methyl groups and charge stabilization by the

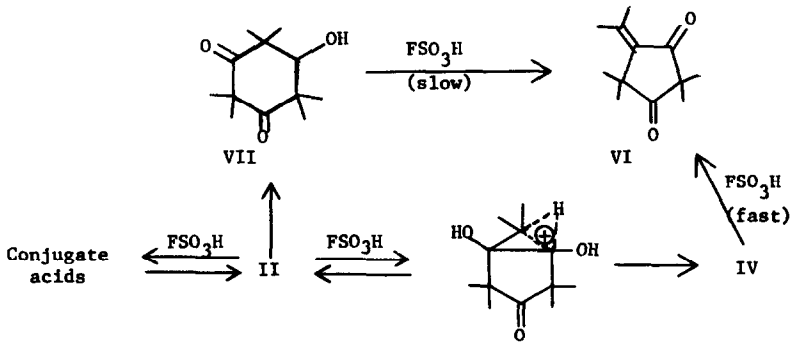
three hydroxyl substituents on III is difficult to estimate. Certainly, the chair-like conformation required by III must suffer serious non-bonded methyl compressions. Furthermore, Olah et al have noted[8] that the positive charge in protonated ketones resides mainly on the oxygen atom; thus the effect of homoaromatic stabilization may be obscured by charge localization on the hydroxyl substituents.

Additional information concerning the question of homoaromatic stabilization of the conjugate acid of II (ie. III), can be obtained from the nmr spectrum of II in strong acids. In the event that III is formed we expect that the C_{3v} symmetry of this species will simplify the characteristic methyl resonance pattern of II (four sharp methyl signals are observed in DMSO or pyridine solution) to either two resonance peaks or a single strong peak, depending on the rate of inversion of III.

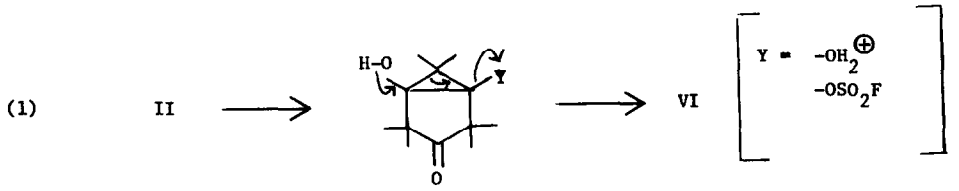
A freshly prepared solution of II in a cold (below -40°) mixture of fluorosulfonic acid and sulfur dioxide showed three well defined methyl signals at δ 1.08 (3H), 1.30 (9H) and 1.50 (6H). When the temperature of this solution increased, five other peaks began to appear; and at 10° eight peaks, falling roughly into three groups with the same 1:3:2 area ratio, were clearly discernable. Cooling the sample to below -40° again caused only a slight broadening of this complex resonance pattern. Finally, the absence of any structural rearrangement was demonstrated by the recovery of unchanged II, upon quenching the nmr sample in ice water. The complex nmr spectrum reported here is probably due to the formation of a mixture of conjugate acids and fluorosulfonate esters. If III is present at all, its concentration at equilibrium must be less than 25% (estimated by assuming that the two most intense methyl signals are generated by this species); consequently, homoaromatic stabilization does not seem to be significant in this system.

A solution of II in fluorosulfonic acid experiences a slow rearrangement to VI, which nmr surveillance shows to be complete after ca. 45 min. at room temperature. The structure of this volatile crystalline substance, mp 34-35.5°, was established by infrared absorption at 1750, 1690 and 1605 cm^{-1}; nmr signals at δ 1.09 (6H), 1.38 (6H), 2.06 (3H) and 2.30 (3H); and the appearance of the parent ion at m/e 194 (P + 1 = 13.8%P, P + 2 = 1.4%P) in the mass spectrum. Retroaldol cleavage of VI in refluxing methanolic potassium hydroxide gave acetone (DNP derivative mp 125-126°) and 2,2,4,4-tetramethylcyclopentan-1,3-dione, a volatile oil characterized by infrared absorption at 1760 and 1725 cm^{-1}, nmr signals at δ 1.16 (6H), 1.26

(6H) and 2.68 (2H), and a parent ion at m/e 154 (P + 1 = 10.9%P, P + 2 = 1.1%P) in the mass spectrum. Catalytic reduction of VI gave V.



Since the rearrangement of II to VI is ostensibly similar to the acid catalyzed transformation of 2,2,5,5-tetramethyl-3-hydroxycyclohexanone to 2-isopropylidene-4,4-dimethylcyclopentanone,[9] we considered the possibility that 2,2,4,4,6,6-hexamethyl-5-hydroxy-1,3-cyclohexanedione (VII) is an intermediate in the former reaction. Although a solution of VII (prepared[1] by base catalyzed ring opening of II) in fluorosulfonic acid does in fact rearrange to VI at a slightly faster rate than the corresponding reaction of II, we have been unable to detect the presence of VII in any acid catalyzed reactions of II. Since IV undergoes rapid dehydration to VI in fluorosulfonic acid and has also been obtained from II by treatment with aqueous acid, we are inclined to favor this pathway for the transformation of II to VI. However, the direct formation of VI from a conjugate acid or a fluorosulfonate ester of II (equation 1)[10] is also possible.



It is clear that parallels exist between the reactions of cyclopropanediols described here and ring opening reactions of cyclopropanols.[11]

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