The Clemmensen Reduction of β-Diketones

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The Clemmensen reduction of β -diketones has been under investigation as part of our study of carbon-carbon bond-forming reactions of the type

 $A^+ + B^+ \longrightarrow A - B$. Recent renewed interest in such reductions^{1,2} and the bearing of our early research results on the mechanism of the reduction process³ prompt the present communication.

Exposure of a refluxing aqueous, methanolic solution of hydrochloric acid and diketone $(I)^4$ to zinc amalgam for fifteen minutes has led to the ketones (IIa⁵ and b⁶) in 43% and 18% yields, respectively. Longer reaction time increased the yield of (IIb) at the expense of (IIa), an observation in consonance with the known tendency of α -hydroxy-ketones to be reduced by zinc and acid.⁷ The severe structural change involved in the conversion of (I) into (IIa) can be rationalized most readily by assuming the intermediacy of cyclopropanediol (III) and its subsequent acid-induced ring rupture. Since cyclopropanols have been shown to undergo cleavage in acid media with retention of configuration,^{8,9} the formation of only one diastereomeric hydroxy-ketone and, further, of the configuration depicted in (IIa) is not surprising.

The latest general review of the mechanism of the Clemmensen reduction³ offered an analysis of the reaction path of the reduction of dimedone (IVa),¹⁰ a well-documented example of the limited

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² M. Quadrat-I-Khuda, M. Manzoor-I-Khuda, and N. A. Jeelani, Pakistan J. Sci. Res., 1964, 7, 81

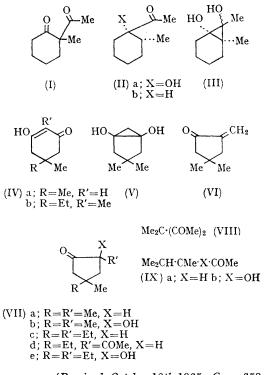
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- ⁴ G. B. Payne, J. Org. Chem., 1961, 26, 4793.
 ⁵ Y. N. Nazarov and A. A. Akhrem, Zhur. obshchei Khim., 1958, 28, 1791.

⁶ Y. N. Nazarov and A. A. Akhrein, *Leur. oushenet Rumm.*, 1936, 26, 1161.
⁶ R. B. Turner, *J. Amer. Chem. Soc.*, 1950, 72, 878.
⁷ Inter alia, W. T. Smith, Jr., *J. Org. Chem.*, 1951, 73, 1883.
⁸ C. H. DePuy and F. W. Breitbeil, *J. Amer. Chem. Soc.*, 1963, 85, 2176.
⁹ A. Nickon, J. H. Hammons, J. L. Lambert, S. J. and R. O. Williams, *J. Amer. Chem. Soc.*, 1963, 85, 3713.
¹⁰ M. Quadrat-I-Khuda, Nature, 1933, 132, 210; A. N. Day and R. P. Linstead, *J. Chem. Soc.*, 1935, 1063; M. Under J. Khuda, Nukhori, J. Mainer, Chem. Soc. 1046, 23, 435. Quadrat-I-Khuda and A. Mukherji, J. Indian Chem. Soc., 1946, 23, 435.

number of published cases of β -diketone reductions. The transformation of (IVa) into (VIIa) was considered to be the consequence of initial reduction leading to the cyclopropane derivative (V), acid-catalysed 1,3-elimination of the diol yielding the unsaturated ketone (VI) and, finally, reduction of the olefinic intermediate. While our data are compatible with the formulation of (V) as primary, albeit acid-labile product of the reduction of dimedone (IVa), they are at variance with the formulation of (VI) as second reaction intermediate and suggest instead the hydroxyketone (VIIb) as immediate precursor of the final reduction product. The Clemmensen reduction of a dimedone homologue (IVb) has been shown recently to yield the ketones, 3-ethyl-3,6-dimethylcyclohexanone, (VIIc) and a hydroxy-ketone formulated as (VIId monoenol).² The latter may be the mechanistically crucial α -hydroxy-ketone (VIIe), since the limited structural data are incompatible with formula (VIId monoenol) while not contradicting (VIIe). Finally, the Clemmensen reduction of a dimedone analogue in the camphor series has been reported to yield monoketone and hydroxy-ketone products.11 While their structures were not elucidated, they probably are of the (VIIa) and (VIIb) types, respectively.

A recent report of the Clemmensen reduction of acyclic β -diketones¹ mentioned *inter alia* the conversion of (VIII) into (IXa) and interpreted the structural changes in terms of the Staschewski mechanism.³ Repetition of the reduction of (VIII) has yielded now not only (IXa) but also (IXb)¹² in

low yield. Thus skeletally-rearranged α -hydroxyketones appear to be potentially trappable intermediates of the zinc-acid reductions of β -diketones.¹³



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¹³ While all products of the present study are of known constitution, their identities were established by direct comparison with authentic samples or by infrared and proton magnetic resonance analysis.