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# Regioselective Reductions of 2,3-Epoxy Acetals with Lithium Aluminum Hydride: a Reinvestigation.

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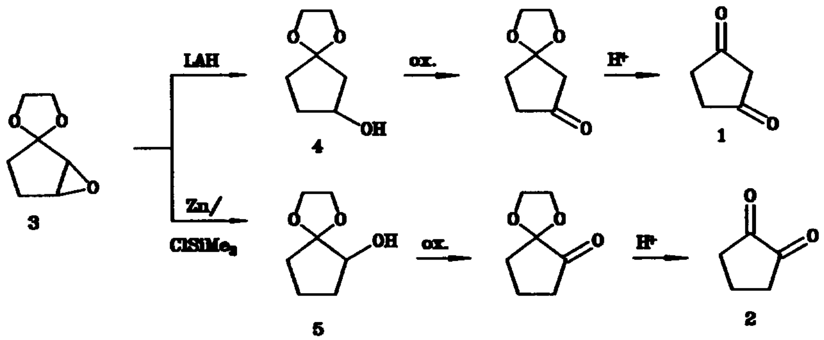
**Abstract:** Treatment of 2,3-epoxy acetals with lithium aluminum hydride gave the corresponding 2-hydroxy acetals, instead of the previously reported 3-hydroxy acetals.

In the course of our studies directed towards the synthesis of barbacenic acid[1], a natural diterpene containing a five-membered ring, we were interested in a large-scale preparation of 1,3-cyclopentanedione (1). Although commercially available, this simple diketone is very expensive, and its employ as starting material for a synthesis is not economically viable.

Among the methods found by us in the literature for synthesizing the diketone 1 [2-4], we have chosen one that appears to be the most economically feasible[2]. The key-step of this method is based on a regioselective opening of the epoxide 3, which can alternatively lead to the regioisomeric alcohols 4 or 5, depending on the employed reagent; a further oxidation of the formed alcohol, followed by deketalization, leads to the corresponding diketone 1 or 2, respectively. The described sequences are outlined in Scheme I.

Scheme I

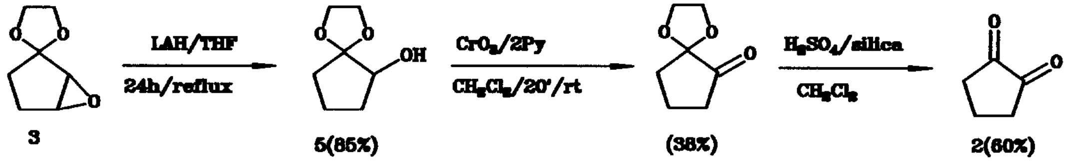


We have then prepared the epoxide 3 by a known methodology[2,5] and we have submitted this epoxide to treatment with lithium aluminum hydride (LAH) in dry tetrahydrofuran (THF), following exactly the experimental procedure described in literature[2].

Surprisingly, the $^{1}H$ and $^{13}C$-NMR spectra[6] of the obtained alcohol were not in accordance with the expected for structure 4, but were consistent with structure 5.

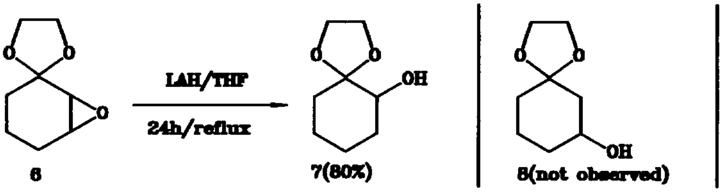
This result was confirmed when the obtained alcohol was submitted to the same sequence of reactions previously described for preparing the diketone 1, as indicated in Scheme II. Analysis of the final product by $^{1}$H and $^{13}$C-NMR, as well as comparison with an authentic sample of the 1,3-diketone 1[7], was sufficient to conclude that this product is in fact the 1,2-diketone 2 (m.p.49-51°C). Therefore, the alcohol formed by the LAH-opening of the epoxide 3 must be the regioisomer 5 (Scheme II).

Scheme II



Similar results, i.e., formation of the alcohol 7[8], were obtained when the homologue epoxide 6 was treated with LAH, also following the conditions described[2] for the preparation of alcohol 8 (Scheme III).

Scheme III



In conclusion, we think that the LAH-opening of the 2,3-epoxy acetals is a convenient method for synthesizing 1,2-diones, not 1,3-diones.

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6. NMR data: $^{1}$H-NMR (200 MHz, CDCl3): 3.97(s, 4H); 3.78(t, J=4.8Hz, 1H);2.2(br, 1H);1.5-2.0(m, 6H) ppm. $^{13}$C-NMR (50 MHz, CDCl3): 18.7(C4), 31.4 and 32.5(C3 and C5), 64.8 and 65.0(-O-CH2-CH2-O), 74.7(C2) and 116.4 (C1) ppm.
7. The 1,3-cyclopentanedione 1 was purchased from Aldrich Co (m.p.151-153°C).
8. NMR data: $^{1}$H-NMR (200 MHz, CDCl3): 4.01(m, 4H); 3.59(dd, J=4.1 and 8.3 Hz, 1H); 2.5(br, 1H); 1.3-1.9(m, 8H) ppm. $^{13}$C-NMR(50 MHz, CDCl3): 21.9 and 23.1(C4 and C5), 31.2 and 32.5(C3 and C6), 64.9 and 65.2(-O-CH2-CH2-O-), 71.9(C2 ) and 109.3(C1) ppm.

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