Journal of Organometallic Chemistry 177 (1979) 35—38

REACTION OF DILITHIOOXIMES WITH EPOXIDES· A NOVEL ROUTE TO 1,4-DIKETONES AND ITS APPLICATION TO DIHYDROJASMONE SYNTHESIS

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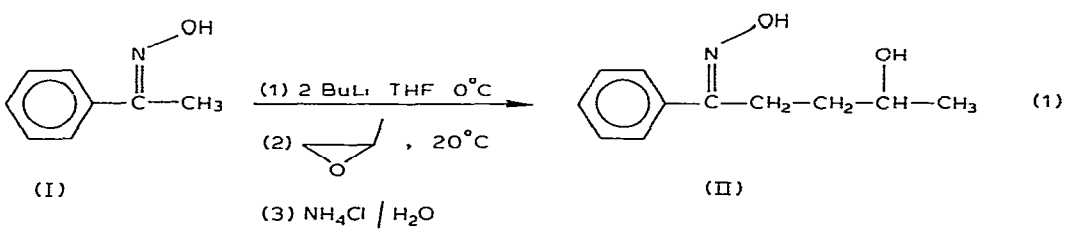
(Received March 30th 1979)

Summary

Dilithiooximes react with epoxides at room temperature in THF to give, after neutral hydrolysis, the corresponding γ-hydroxyoximes These latter can be deoximated and oxidized to lead to the expected 1,4-diketones This approach is successfully applied to the dihydrojasmone synthesis

During the last ten years it has become increasingly clear that dilithiooximes are highly useful in organic synthesis [1—7] However, to our knowledge, the action of these dilithiooximes on epoxides have not been studied We show in this paper that this reaction can be applied to the synthesis of 1,4-diketones

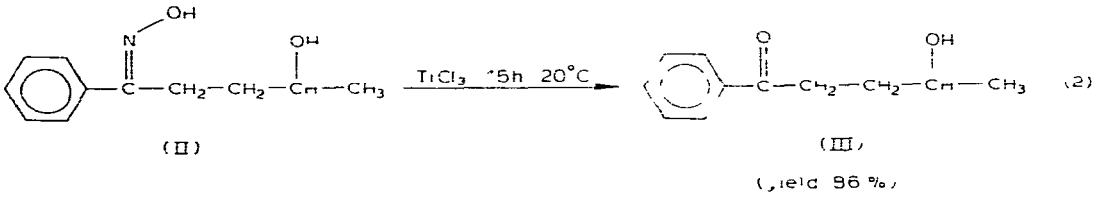
Treatment of acetophenone oxime (I) with two equivalents of n-butyllithium in THF at 0°C followed by the addition of propylene oxide lead, after hydrolysis, to the γ-hydroxyoxime II in 93% yield (eq. 1).



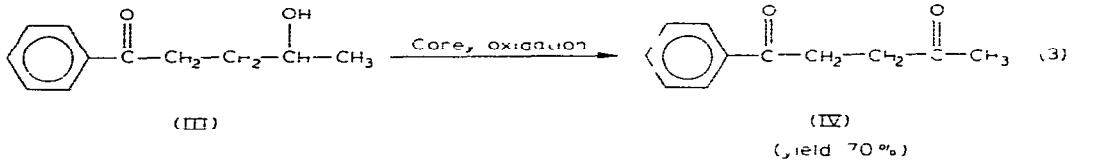
(I) (II) (1)

The product II is then deoximated with titanium trichloride [8] to give the γ-hydroxyketone III (eq. 2)

* Dédie au Professeur H Normant à l'occasion de son 72ème anniversaire le 25 juin 1979

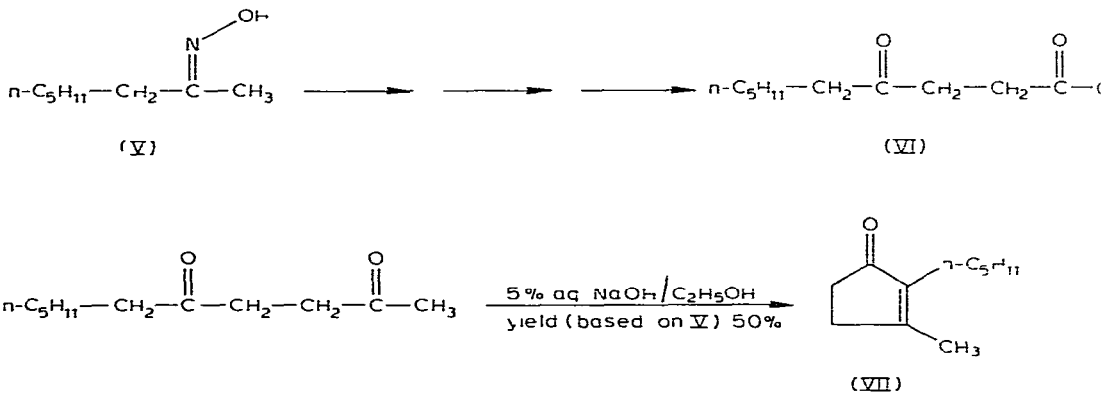


Since this type of compound changes to an unidentified material during distillation [9], the crude compound III is directly oxidized with Corey reagent [10] to give 1,4-diketone (IV) which is readily purified by distillation (eq 3)



This approach is successfully applied to the dihydrojasmone synthesis as shown in Scheme 1.

SCHEME 1



Experimental

Preparation of oximes I and V

Acetophenone oxime (I) and hexylmethyl oxime (V) were prepared by the usual method from the corresponding ketone, hydroxylamine hydrochloride and sodium hydroxide. Acetophenone oxime was recrystallized from hexane after distillation.

Preparation of γ-hydroxyoxime (II)

To a stirred solution of 13 5 g (0.1 mol) of acetophenone oxime in 300 ml of tetrahydrofuran, at 0° C and under nitrogen atmosphere, was added during 15 min 0 22 mol of butyllithium. After 1 h, 6.4 g (0.11 mol) of propylene oxide were added to the clear orange-yellow solution of dilithioacetophenone oxime. The mixture was then allowed to stand at room temperature until thin

layer chromatography showed no starting acetophenone oxime (about 3 h) Then, 100 ml of saturated ammonium chloride solution were added and the aqueous layer was extracted twice with ether, the organic layers were combined and dried over magnesium sulphate After evaporation of the solvent under vacuum, the γ-hydroxyoxime II was isolated as a viscous liquid (17 9 g, yield 93%)

IR ν_{max} (cm^{-1}) 1628 (C=N), 1602, 1580 

^1H NMR ($CDCl_3$, TMS) δ 7 50 (m, 5 H, C_6H_5), 3 80 (m, 1 H, CH—O), 2 85 (t, 2 H, N=C—CH_2) 1 70 (m, 2 H, CH_2—CH) and 1 15 ppm (d, 3 H, CH_3)

Preparation of γ-hydroxyketone III

The γ-hydroxyoxime II was dissolved in acetone (200 ml) Ammonium acetate (100 g) and 50% aqueous acetic acid (50 ml) were added The mixture was stirred and aqueous titanium trichloride (200 ml, 0 2 mol) added gradually at room temperature After standing overnight at the same temperature, the product was poured into 200 ml of water, extracted three times with ether, washed several times with $NaHCO_3$ and dried over $MgSO_4$ The solvent was removed under reduced pressure and 15 3 g of crude compound III were obtained (yield 86%) IR ν_{max} (cm^{-1}) 3400 (OH), 1680 (C=O) ^1H NMR ($CDCl_3$, TMS) δ 8 05 (m, 2 H, C_6H_5), 7 50 (m, 3 H, C_6H_5), 3 90 (m, 1 H, CH—O), 3 13 (t, 2 H, O=C—CH_2), 2 90 (s (br), 1 H, OH), 1 90 (m, 2 H, CH_2—CH) and 1 25 ppm, (d, 3 H, CH_3)

Preparation of 1,4-diketone IV

To 25 g of pyridinium chlorochromate (prepared as indicated in the reference 10) in 100 ml of CH_2Cl_2 was rapidly added, at room temperature, the crude γ-hydroxyketone III (in 100 ml of CH_2Cl_2) After three hours, 500 ml of dry ether were added with vigorous stirring The mixture was then filtered and the gummy residue was washed with anhydrous ether until it became a granular solid The ethereal layers were combined and the solvent removed Distillation gave 12 3 g of pure 1,4-diketone IV (yield 70%) B p 113°C/0 1 mmHg IR ν_{max} (cm^{-1}) 1717 (C=O non-conjugated) 1677 (C=O conjugated) ^1H NMR ($CDCl_3$, TMS) δ 8 50 (m, 2 H, C_6H_5), 7 50 (m, 3 H, C_6H_5), 3 25 (m, 2 H, C_6H_5—CO—CH_2), 2.80 (m, 2 H, CH_2—CO—CH_3), 2.10 (s, 3 H, CH_3).

Preparation of dihydrojasmone VII

Diketone VI obtained as indicated above for compound IV but without any purification at the different steps, was refluxed for eight hours in a mixture of 5% aqueous sodium hydroxide (25 ml) and ethanol (100 ml) The solution was then acidified with 6 *N* hydrochloric acid (10 ml) and extracted with ether. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. After removal of the solvent, the residual oil was distilled to give 8 2 g of pure dihydrojasmone VII (yield 49.3%, based on V) B.p. 71°C/ 0 1 mmHg (Analysis found. C, 79.20, H, 11 00. $C_{11}H_{18}O$ calcd.. C, 79 47, H, 10.93%.) IR ν_{max} (cm^{-1}): 1703 (C=C); 1654 (C=C) ^1H NMR (CCl_4, TMS)· δ 0.90 (t, 3 H, CH_2—CH_3), 1.30 (s (br), 6 H, $(CH_2)_3$), 2.10 (s, 3 H, C=C—CH_3) and 2 20—2.60 ppm (m, 6 H)

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