

NEW SYNTHESIS OF γ -IONONE

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γ -Ionone was successfully synthesized without accompanying any isomeric substances such as α - and β -ionones by dehydration of a key intermediate, 4-(6-methylene-2,2-dimethylcyclohexyl)-4-hydroxy-2-butanone, prepared from γ -cyclocitral and acetone by the use of di-n-butylboryl trifluoromethanesulfonate and triethylamine as coupling reagents.

Preceding papers presented that TiCl_4 -promoted reaction of silyl enol ether with various acetals or methyl orthoformate successfully gave β -alkoxyketones or β,β -dialkoxyketones¹⁾ and that cross-aldols were obtained in good yields just starting from two different carbonyl compounds by using di-n-butylboryl trifluoromethanesulfonate and tertiary amine.²⁾

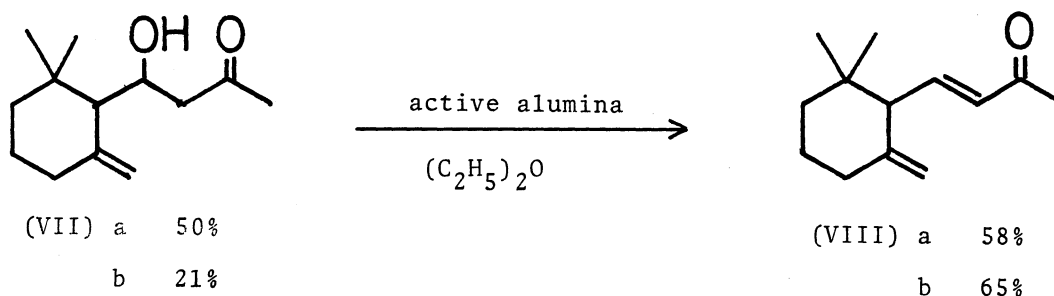
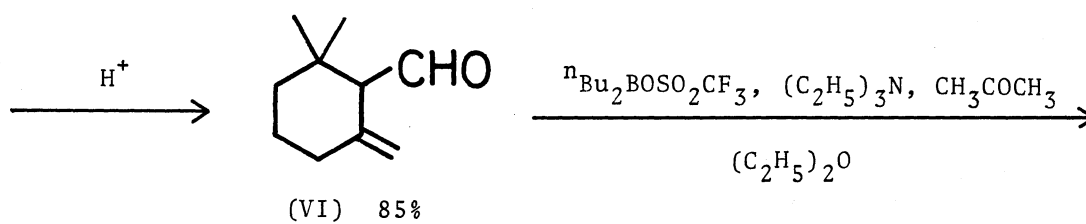
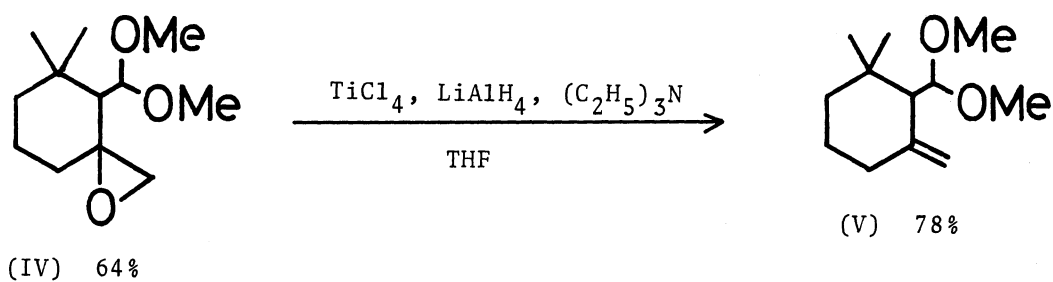
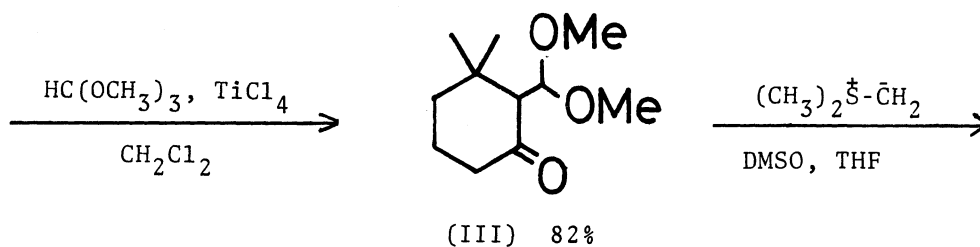
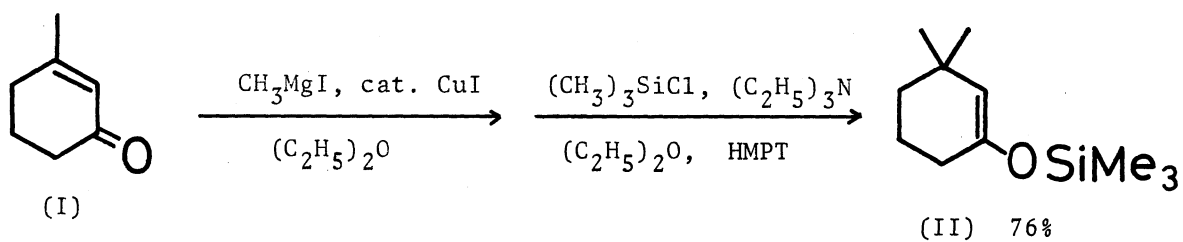
In this communication, we wish to report a new method for the synthesis of γ -ionone³⁾ starting from 3-methyl-2-cyclohexenone (I) by employing two preparative methods mentioned above and a method for the deoxygenation of epoxides to olefins by the action of low valent titanium compound, prepared from TiCl_4 and LiAlH_4 , in each key step. Concerning the synthesis of γ -ionone, several methods have been reported,⁴⁾ but γ -ionone could not be obtained as a sole product, α - and/or β -ionone was usually contaminated with γ -ionone more than 40% of isomers because of the sensitivity of γ -ionone toward strong acid or base. Therefore, it is usually difficult to separate γ -ionone effectively from the isomeric mixture.

The reaction of 3-methyl-2-cyclohexenone (I) with methylmagnesium iodide in ether for 1 hr at 0°C in the presence of catalytic amount of cuprous iodide, followed by quenching with trimethylchlorosilane, triethylamine and hexamethylphosphoric triamide at room temperature, gave 3,3-dimethyl-1-trimethylsiloxy-1-cyclohexene (II)⁵⁾ in 76%

yield by vacuum distillation.⁶⁾ 2-Dimethoxymethyl-3,3-dimethylcyclohexanone (III)⁷⁾ was obtained in 82% yield by the reaction of II with methyl orthoformate in dichloromethane at -78°C for 2 hr in the presence of TiCl_4 .¹⁾ The conversion of III to 4-dimethoxymethyl-5,5-dimethyl-1-oxaspiro[2.5]octane (IV) was carried out according to the literature method⁸⁾, namely, the treatment of III with dimethylsulfonium methylide in the mixed solvent of dimethyl sulfoxide and THF (1 : 6) at -20°C for 1.5 hr gave IV⁹⁾ in 64% yield after purification by silica gel column chromatography. The deoxygenation of IV with low valent titanium compound¹⁰⁾, prepared from TiCl_4 and LiAlH_4 , at room temperature for 1 hr afforded 6-methylene-2,2-dimethylcyclohexanecarbaldehyde dimethyl acetal (V)¹¹⁾ in 78% yield, which was further converted to γ -cyclocitral (VI) in 85% yield by hydrolysis with 2N HCl aqueous solution at room temperature for 24 hr. [VI: bp; $80-81^{\circ}\text{C}/14$ mmHg, ir; 2700, 1720, 1635, 895 cm^{-1} , nmr (δ_{TMS} ppm, in CCl_4); 0.95 (s, 3H), 1.05 (s, 3H), 1.4-1.9 (m, 4H), 2.20 (b, 2H), 2.65 (d, 1H), 4.65 (quasi s, 1H), 4.90 (quasi s, 1H), 9.70 (d, 1H)]

Di-n-butylisopropenyloxyborane, formed in situ from acetone and di-n-butylboryl trifluoromethanesulfonate in the presence of triethylamine in ether at -78°C ²⁾, reacted with VI in ether at -78°C for 5 hr to give two isomers (VIIa and VIIb) which showed different Rf values on silica gel thin layer chromatography. Their ir and nmr spectra resembled each other and indicated that they were two stereoisomers of 4-(6-methylene-2,2-dimethylcyclohexyl)-4-hydroxy-2-butanone. [VIIa; ir; 3500, 3050, 1700, $1635, 890\text{ cm}^{-1}$, nmr (δ_{TMS} ppm, in CCl_4); 0.90 (s, 3H), 1.10 (s, 3H), 1.4-2.3 (m, 7H), 2.10 (s, 3H), 2.50 (m, 2H), 3.20 (b, 1H), 4.35 (m, 1H), 4.50 (quasi s, 1H), 4.80 (quasi s, 1H). VIIb: ir; 3470, 3050, 1700, 1640, 890 cm^{-1} , nmr (δ_{TMS} ppm, in CCl_4); 0.90 (s, 3H), 1.05 (s, 3H), 1.3-2.1 (m, 7H), 2.10 (s, 3H), 2.40 (d, 2H), 3.20 (b, 1H), 4.15 (m, 1H), 4.60 (quasi s, 1H), 4.70 (quasi s, 1H)] The yields of VIIa and VIIb were 50% and 21%, respectively, based on γ -cyclocitral.

The aldols, VIIa and VIIb, were converted to γ -ionone (VIII) on treatment with active alumina in ether at room temperature for 24 hr in 58% and 65% yields, respectively. [VIII: ir; 1670, 1620, 890 cm^{-1} , nmr (δ_{TMS} ppm, in CCl_4); 0.87 (s, 3H), 0.90 (s, 3H), 2.18 (s, 3H), 1.2-2.3 (m, 6H), 2.55 (d, 1H), 4.55 (b, 1H), 4.78 (b, 1H), 6.00 (d, 1H), 6.85 (dd, 1H)] Spectral data of γ -ionone were consistent with those in the literature.¹²⁾



References and Notes

- 1) T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 15 (1974).
- 2) T. Mukaiyama and T. Inoue, *Chem. Lett.*, 559 (1976).
- 3) *l*-Ionone is a terpenoid and one of the most important perfumes.
- 4) B. Willhalm, U. Steiner, and H. Schinz, *Helv. Chim. Acta*, 41, 1359 (1958); G. Ohloff and S. Mignat, *Ann. Chem.*, 652, 115 (1962); G. Ohloff and G. Schade, *Angew. Chem.*, 74, 944 (1962).
- 5) II: bp; 80-81°C/ 15 mmHg, ir; 1655 cm⁻¹, nmr(δ_{TMS} ppm, in CCl₄); 0.15 (s, 9H), 0.95 (s, 6H), 1.2-2.0 (m, 6H), 4.55 (s, 1H)
- 6) The reaction was carried out according to the literature with some modifications. G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, 90, 4462 (1968).
- 7) III: bp; 82°C/ 2 mmHg, ir; 1710 cm⁻¹, nmr(δ_{TMS} ppm, in CCl₄); 0.95 (s, 3H), 0.98 (s, 3H), 1.3-2.6 (m, 7H), 3.25 (s, 3H), 3.30 (s, 3H), 4.70 (d, 1H)
- 8) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 87, 1353 (1965).
- 9) IV: nmr(δ_{TMS} ppm, in CCl₄); 1.00 (s, 3H), 1.05 (s, 3H), 1.4-2.2 (m, 7H), 2.45 (s, 2H), 3.30 (s, 3H), 3.40 (s, 3H), 4.40 (d, 1H)
- 10) To a solution of TiCl₄ in THF was added LiAlH₄ at room temperature under argon with stirring. After the mixture was stirred for 1 hr, triethylamine was added at room temperature.
- 11) V: bp; 88-89°C/ 10 mmHg, nmr(δ_{TMS} ppm, in CCl₄); 0.90 (s, 6H), 1.2-1.8 (m, 4H), 1.9-2.3 (m, 3H), 3.20 (s, 3H), 3.25 (s, 3H), 4.45 (d, 1H), 4.60 (quasi s, 1H), 4.80 (quasi s, 1H)
- 12) D. Felix, G. Ohloff, and E. sz. Kováts, *Ann. Chem.*, 652, 126 (1962).

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