Tetrahedron Letters,Vol.23,No.37,pp 3839-3840,1982 0040-4039/82/373839-02$03.00/0
Printed in Great Britain

SEQUENTIAL CLAISEN AND COPE REARRANGEMENT FOR FORMATION OF 3-(1-METHYLETHYL)-SUBSTITUTED α,β-UNSATURATED ALDEHYDES

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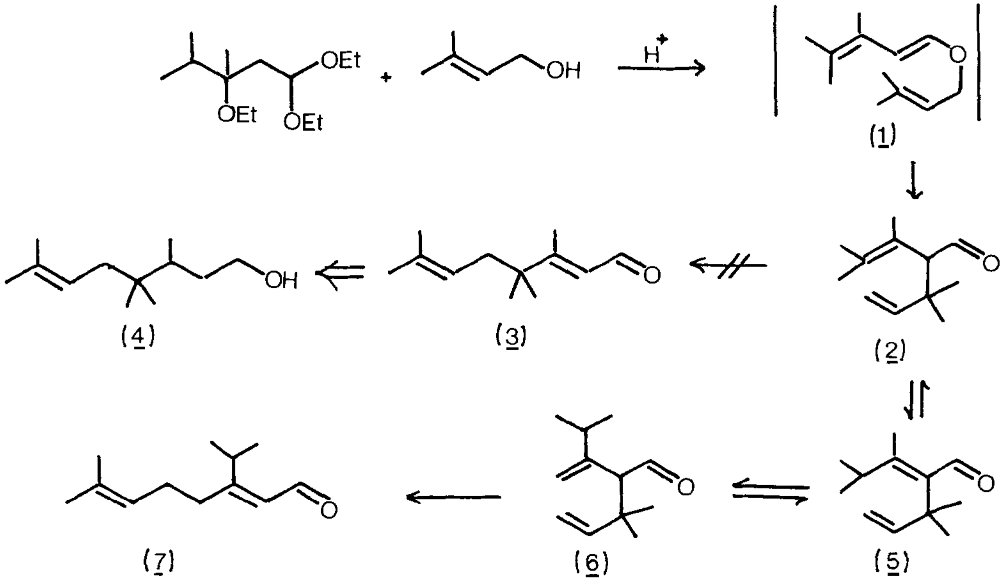
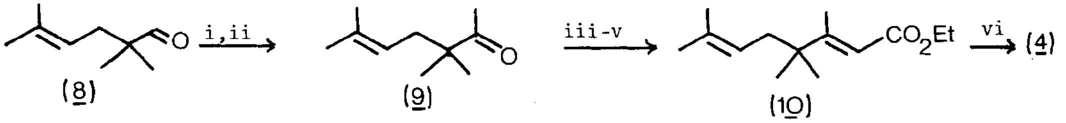
3-(1-Methylethyl)-7-methyl-2,6-octadienal, was prepared from 1,1,3-triethoxy-3,4-dimethylpentane and 3-methyl-2-buten-1-ol in a one-pot procedure utilising Claisen and Cope rearrangements of an intermediate dienol-allyl ether.

The use of sequential Claisen and Cope rearrangements for the preparation of α,β-unsaturated aldehydes was pioneered by Thomas, who applied the reaction for the synthesis of the natural products torreyal[1] and β-sinensal.[2] In connection with our studies on insect pheromones we required a sample of the alcohol (4): successive Claisen and Cope rearrangements of the dienol-allyl ether (1) would provide a convenient synthesis of the corresponding α,β-unsaturated aldehyde (3). This reaction did not, however, proceed as anticipated.



Heating the dienol-allyl ether (1) (generated in situ from 1,1,3-triethoxy-3,4-dimethyl pentane and 3-methyl-2-buten-1-ol) in refluxing xylene resulted in formation of the sole product 3-(1-methylethyl)-7-methyl-2,6-octadienal (7). This product resulted from Cope rearrangement of the β,γ-unsaturated aldehyde (6), itself arising from acid catalysed rearrangement of the β,γ-unsaturated aldehyde (2). Reaction of 3-methyl-2,2-diethoxybutane with ethyl vinyl ether in presence of boron trifluoride-ether complex[2] gave 1,1,3-triethoxy-3,4-dimethylpentane (b.p. 110°, 16mm; 40%; calculated for $C_{13}H_{28}O_3$, C = 67.12, H = 12.15; found C = 67.27, H = 12.19; δ(CCl_4), 4.60 (1H,t,J=5Hz,CH), 3.80-3.15 (6H,m,3xCH_2-O), 1.70 (2H,d,J=5Hz,CH_2), 1.30-1.00 (12H,m,4xCH_3), 0.85 (6H,d,J=8Hz, CH-$(CH_3)_2$). The Claisen-Cope rearrangement was conducted using a modified form of the procedure described by Cookson and Rogers.[3] 1,1,3-Triethoxy-3,4-dimethylpentane (2.15mmol) and *o*-nitrobenzoic acid (12mg) were refluxed in sodium-dried xylene (50ml) for 24 hours.[4] The crude reaction mixture was reduced with sodium borohydride (3mmol) in methanol to give, after column chromatography (silica, petrol:ether 9:1), 3-(1-methylethyl)-7-methyl-2,6-octadienal (298mg, 76%) as a 70:30 mixture of the E and Z-isomers; δ(CCl_4), 5.35 (1H,t,J=7Hz,C=CH-CH_2-O), 5.10 (1H,broad s,C=CH), 4.02 (2H,d,J=7Hz,CH_2-OH), 2.57 (1H,s,OH), 2.05 (4H,m,CH_2), 1.70 (3H,s,CH_3), 1.61 (3H,s,CH_3), 1.03 (6H,d,J=7Hz,CH-C$(CH_3)_2$); high resolution mass spectrum 182.1697 (calculated 182.1671).

Although initial formation of (2) would be expected, the lower steric requirements of the Cope rearrangement of (6) direct the reaction to proceed via this pathway.[6] The Claisen-Cope procedure described provides a valuable method of forming 3-(1-methylethyl)-substituted α,β-unsaturated aldehydes. The alcohol (4) was finally obtained from the known aldehyde (8)[7] by conventional methodology. Thus Grignard reaction and oxidation gave the ketone (9) and application of the Reformatsky acylation/elimination procedure of Schmalzl and Mirrington[8] gave the ester (10). Finally reduction with lithium in liquid ammonia gave the alcohol (4) (b.p. 72-75°C, 1mm; calculated for $C_{12}H_{24}O$, C = 78.2, H = 13.13; found C = 77.94, H = 13.24; 20% from (8)), δ($CDCl_3$), 5.19 (1H,t,J=8Hz,C=CH-), 3.62 (2H,m,CH_2-O), 1.92 (2H,d,J=8Hz,C=CH-CH_2), 1.72 (3H,s,CH_3), 1.66 (1H,s,OH), 1.61 (3H,s,CH_3), 1.40-1.00 (3H,m,CH-CH_2-), 0.83 (3H, d,J=4Hz,CH-CH_3), 0.82 (6H,s,C$(CH_3)_2$).



i) MeMgI; ii) PCC; iii) Zn,$BrCH_2COOEt$; iv) CH_3COCl; v) NaOEt; vi) Li/liq. NH_3

Acknowledgements: Thank are due to S.E.R.C. and Cyanamid of Great Britain Limited for a CASE award and other financial assistance.

References and Notes

1. A.F. Thomas, J.C.S. Chem. Comm., 1968, 1657.
2. A.F. Thomas, J. Amer. Chem. Soc., 1969, 91, 3281.
3. R.C. Cookson and N.R. Rogers, J.C.S. Perkin I, 1973, 2746.
4. Optimum reaction time. Isolation at this stage gave the aldehydes in only 85% purity (contaminated by hydrolysed triethoxy compound).
5. No spectral or chromatographic (GLC) evidence could be obtained for formation of (3).
6. P. Cresson, Bull. Soc. Chim. Fr., 1964, 2618.
7. K.J. Schmalzl and R.N. Mirrington, Tetrahedron Letters, 1970, 3219; see also J. Org. Chem. 1972, 37, 2873.

(Received in UK 25 June 1982)