Tetrahedron Letters,Vol.25,No.11,pp 1195-1196,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

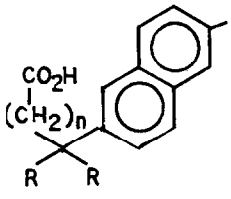
SYNTHESIS, REDUCTION, AND REDUCTIVE ALKYLATION OF A FEW TRICYCLIC α,β-UNSATURATED KETONES

Basudeb Basu, Sukanta Bhattacharyya and Debabrata Mukherjee*

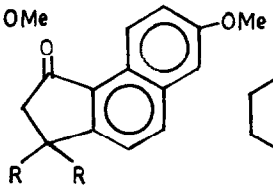
Department of Organic Chemistry
Indian Association for the Cultivation of Science, Calcutta-700 032, India

Summary: Reduction and reductive alkylation of the tricyclic α,β-unsaturated ketones 9-12 afforded the saturated ketones 13-21 in high yields.

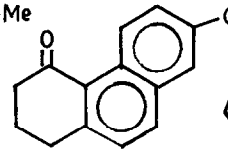
High stereoselectivity usually observed in metal-ammonia reduction and reductive alkylation of various α,β-unsaturated ketones prompted us to undertake the synthesis of several tricyclic enones for studies of their reactions in liquid ammonia. We have found that reductive methylation of the enones 9, 10 and 12 in anhydrous ammonia proceeds stereoselectively to afford in each case a pure isomer of the alkylated saturated product, e.g. 17, 14 and 21 respectively, in 70-80% yields while reductive methylation of the enone 11 furnishes a pure isomer 19 of the methylated product in 56% yield. From studies of the NMR spectra of the products formed during catalytic hydrogenation metal-ammonia reduction and reductive alkylation of the enones 9-12 it is apparent that the high-yield products obtained from metal-ammonia reactions of the enones possess A/B-cis stereochemistry. In view of the recent reports by Ziffer et al.[1] and Ghatak et al.[2] on the RuO_4-catalysed oxidation of aromatic rings, the B/C rings of the aforementioned alkylated products may be considered as latent cyclopentanones. The present study, therefore, not only offers convenient routes to ring-C aromatic tricyclic skeleta having cis-fused 5/6, 6/6 and 7/6 A/B-rings but also promises to provide stereocontrolled routes to cis-fused angularly substituted 5/5, 6/5 and 7/5 bicyclic ring systems.



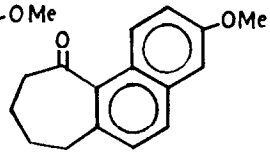
1, R=H, n=1
2, R=Me, n=1
3, R=H, n=2
4, R=H, n=3



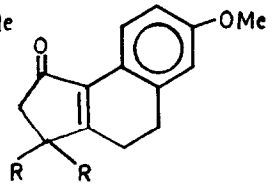
5, R=H
6, R=Me



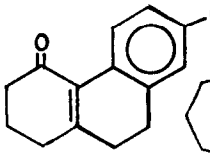
7



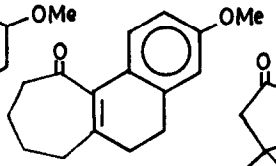
8



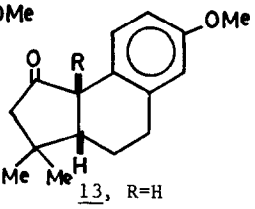
9, R=H
10, R=Me



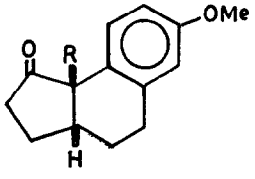
11



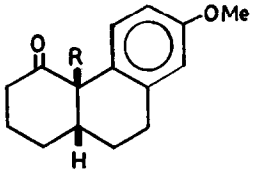
12



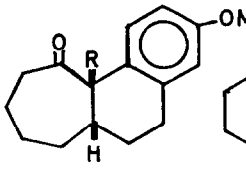
13, R=H
14, R=Me
15, R=CH_2-CH=CH_2



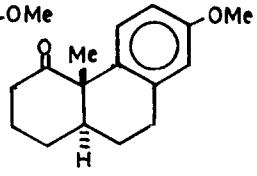
16, R=H
17, R=Me



18, R=H
19, R=Me



20, R=H
21, R=Me



22

The acids 1[3] and 2[4] were cyclised with PPA to give the benzindanones 5[3] and 6, m.p. 124-125° in 75% and 77% yields respectively. Birch reduction of 5 and 6 with Na and EtOH in distilled liquid ammonia according to the procedure of Banerjee et al.[5] afforded the enones 9 (86%), m.p.130° and 10 (85%), m.p. 87-88°. Arndt-Eistert homologation of 1 and subsequent cyclisation of the resulting acid 3 with PPA furnished the ketone 7, m.p. 55-56° in 60% overall yield. Birch reduction[5] of 7 afforded the α,β-unsaturated ketone 11 (85%), m.p. 108° (lit.[6] m.p. 108-108.5°). Condensation of 6-methoxy-2-naphthaldehyde[3] with methyl crotonate in the presence of t-BuOK followed by hydrogenation and hydrolysis of the crude product yielded the acid 4 (70%), m.p. 135°. Cyclisation of 4 with PPA gave the ketone 8 (73%) which on reduction (Na,EtOH, liquid ammonia) furnished the enone 12 (78%), m.p. 56-56.5°.

Catalytic hydrogenation (H_2, 10% Pd-C) and metal ammonia reduction (Li, NH_3,NH_4Cl) of 10 afforded the same product 13, m.p. 96-97° in 90% and 81% yields respectively. Reductive methylation and reductive allylation of 10 in anhydrous ammonia furnished the ketones 14 (82%) $/^{-1}$H-NMR (CCl_4): δ 0.93 (s,3H), 1.13 (s,3H), 1.3 (s,3H), 1.5-2.8 (m,7H), 3.68 (s,3H), 6.42 (d,1H,J=2Hz), 6.55 (d of d, 1H,J=8,2 Hz), 7.4 (d,1H,J=8 Hz)$\_/$ and 15 (82%) $/^{-1}$H-NMR (CCl_4): δ 0.97 (s,3H), 1.17 (s,3H), 1.4-2.8 (m,9H), 3.7 (s,3H), 4.65-5.62 (m,3H), 6.42 (d,1H,J=2Hz), 6.58 (d of d,1H,J=8,2 Hz), 7.47 (d,1H, J=8 Hz) $\_/$ respectively. In the NMR spectra of the ketones 13-15 the close similarity of the aromatic regions is attributable to identical ring fusion since A/B-trans and A/B-cis fused compounds in this series are expected to differ[7] appreciably in the aromatic region due to the presence of the carbonyl group in the ring A. Furthermore, the ketone 13 was isolated as the only product from both catalytic hydrogenation and metal-ammonia reduction of 10. It is, therefore, highly probable that the stereochemistry of the A/B ring fusion is cis in compounds 13-15. Catalytic hydrogenation of 9, 11 and 12 afforded the corresponding cis-fused ketones 16 (90%; m.p. 92-93°), 18 (87%; m.p. 82-83°) and 20 (90%; m.p. 57-58°) respectively. Reductive methylation of 9 and 12 afforded the ketones 17 (72%) $/^{-1}$H-NMR (CCl_4): δ 1.3 (s,3H), 1.53-2.93 (m,9H), 3.68 (s,3H), 6.36 (d,1H,J=3Hz), 6.53 (d of d,1H,J=8,3 Hz), 7.2 (d,1H,J=8Hz)$\_/$ and 21 (80%) $/^{-1}$H-NMR ($CDCl_3$): δ 1.38 (s,3H),1.45-2.95 (m,13H), 3.77 (s,3H), 6.55-6.95 (m,3H)$\_/$ respectively. Cis stereochemistry for 17 and 21 seems more likely for the reasons given earlier for 14. Reductive methylation of 11 furnished two products in 56% and 18% yields. In the NMR spectra the aromatic pattern of the major product 19 $/^{-1}$H-NMR (CCl_4): δ 1.28 (s,3H), 1.42-2.93 (m,11H), 3.7 (s,3H), 6.28-6.58 (m,3H)$\_/$ is similar to that of 18 but the minor product 22 $/^{-1}$H-NMR (CCl_4): δ 1.4 (s,3H), 1.47-2.93 (m,11H), 3.68 (s,3H), 6.27-6.63 (m,2H), 7.05 (d,1H,J=9Hz)$\_/$ shows considerable difference. Cis and trans stereochemistry have been tentatively assigned to 19 and 22 respectively from chromatographic behaviour and NMR spectra.

We thank Prof. B.M.Trost of the University of Wisconsin,U.S.A. for the comparison spectra of 11.

References:

1 M. Kasai and H. Ziffer, *J. Org. Chem.*, 48, 2346 (1983).

2 A.K. Chakraborti and U.R. Ghatak, *Synthesis*, 746 (1983).

3 P. McCloskey, *J. Chem. Soc.*, 3811 (1965).

4 S. Bhattacharyya and D. Mukherjee, *Tetrahedron Letters*, 23, 4175 (1982).

5 D.K. Banerjee, E.J. Jacob and N. Mahishi, *Steroids*, 16, 733 (1970).

6 B.M. Trost and E. Murayama, *Tetrahedron Letters*, 23, 1047 (1982).

7 T. Kametani, T. Honda, Y. Shiratori and K. Fukumoto, *Tetrahedron Letters*, 21, 1665 (1980).

(Received in UK 3 January 1984)