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TRANSFORMATION OF DAVANONE : REDUCTIVE CLEAVAGE OF TETRAHYDROFURAN AND THERMAL CYCLIZATION OF 1:3-DIENE

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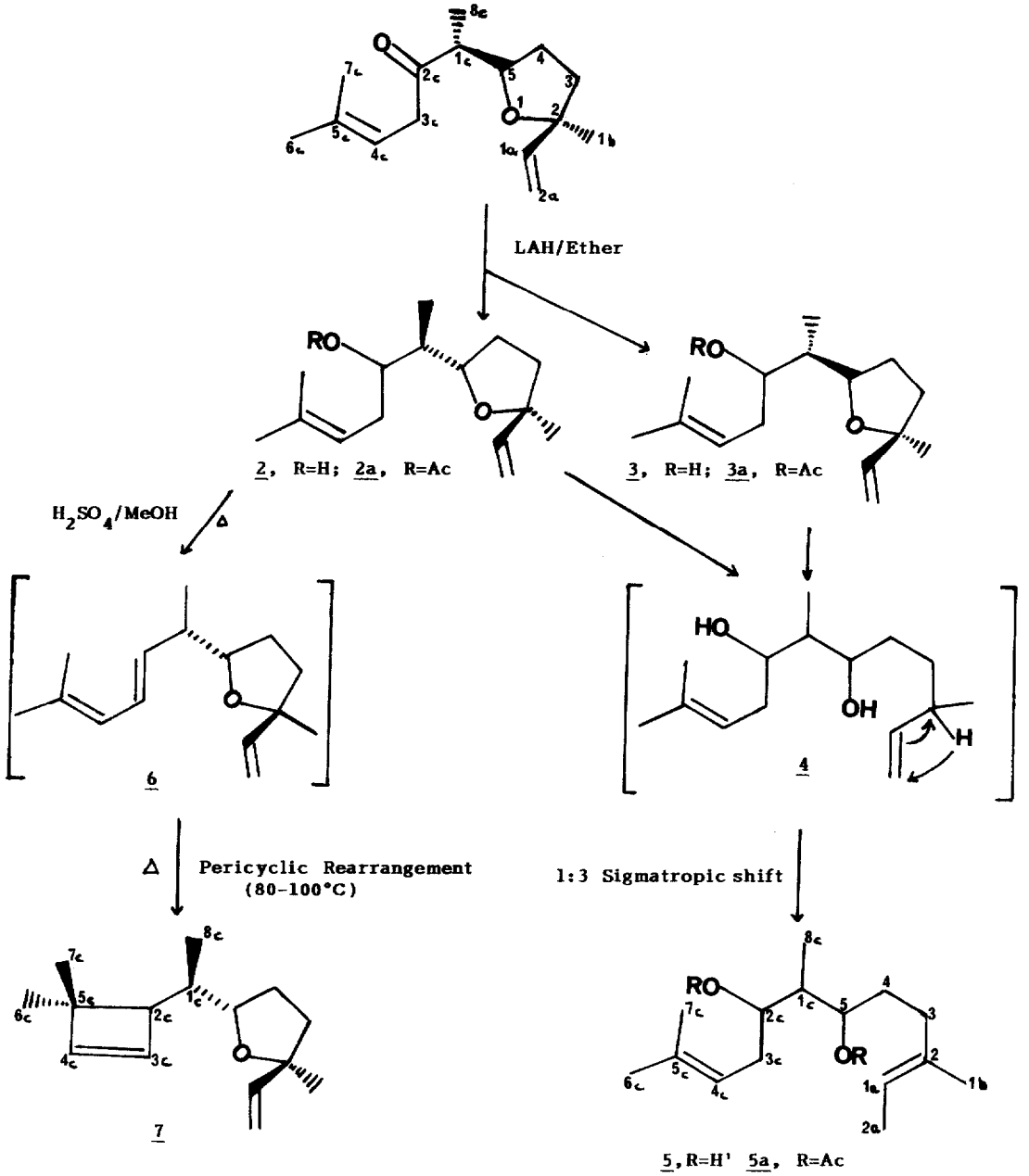
SUMMARY: *Cis- β-davanone (1) the major but odourless component of davana oil (Artemisia pallens) has been converted into various derivatives to yield the compounds with delicate aroma. The $LiAlH_4$ reduction resulted into the unusual cleavage of the tetrahydrofuran ring and the major reduction product (2) after thermal dehydration afforded an unusual electrocyclically rearranged cyclobutene (7).*

Cis- β-davanone (1) which constituted nearly 45% of the davana oil has been reported to be odourless in its purest form[1]. Our continued interest in finding out[1,2] new aroma chemicals and their further derivatizations, prompted us to investigate davana oil and reduce 1 with $NaBH_4$[3] resulting in the formation of the fragrant 2 and 3 with camphoraceous undertone which after acetylation[4] gave 2a and 3a having better floral odor. But the reduction[5] of 1 by $LiAlH_4$ yielded 5 (5.62%) alongwith 2 (52.5%) and 3 (17.5%). 5 And 5a also imparted delicate floral-fruity odour. The formation of 2 in addition to 3 could be explained through the isomerization of the reduced chain at C-5, but the formation of 5 is of considerable importance as the reduction with $LiAlH_4$ has caused the cleavage of tetrahydrofuran ring. Earlier, it was observed that the tetrahydrofurans cleaved with $LiAlH_4$ in the presence of $AlCl_3$[6]. It has also been generalized that the unsaturation in alkyl moiety near the ether linkage is an essential feature for significant hydrogenolysis by catalyzed $LiAlH_4$[6]. Therefore, the formation of 5 may be explained as 2 and 3 after further reduction and cleavage would have afforded 4, which after 1:3-sigmatropic shift or allylic rearrangement[7] would have yielded 5.

After CC and TLC separations of the reduction products 2, 3 and 5 were obtained in pure form[5]. The ^1H NMR spectrum[8] of 3 was almost similar to that of 1 with the exception of the upfield shifting of H-3e and appearance of a new multiplet at δ 4.18. On the

other hand, the difference in the ^{1}H NMR spectrum of 2 existed at H-2c (δ 3.45) as well as H-5 (δ 3.70, ddd, J=8, 6.5 and 3Hz). Cis-davanone and its stereoanalogue (3) showed $J_{5,1c}$ = 9.0Hz for the β-orientation of the side chain[1]. Whereas the smaller magnitude of coupling between H-5 and H-1c (J = 6.5Hz) in case of 2 suggested that the side chain has assumed α-orientation. The ^{13}C NMR, IR and MS were also in complete agreement[9] with the structure 2.



Contrary to 2 and 3, the ^{1}H NMR spectrum of 5 lacked the characteristic signals for vinylic protons (H-1a and H-2a) and the furanoid nucleus (H-5 and H-1b). Instead of that the spectrum showed signals for four vinylic Me (δ 1.63, 1.68, 1.68 and 2.05), two vinylic H (δ 5.45, t, J=7Hz and 5.15q, J=7.0Hz) and two H-C-OH (δ 4.12, overlapping multiplets). The remaining signals in ^{1}H NMR and the ^{13}C NMR, IR and MS spectral data of 5 and 5a were in full agreement[10] for the structure proposed.

Our further attempt to convert 2 into 6 for possible better fragrance, yielded[11] (80%) a highly unusual product 7 instead of 6, imparting fruity odor with spicy undertone. 2 After dehydration with conc. H_2SO_4 may have yielded 6 which owing to the thermal treatment would have undergone the electrocyclic rearrangement through pericyclic reaction. Dehydration reaction would have created the usual double bond between C-8 and C-9 in Z form which would have facilitated the cyclization leading to a gem-dimethyl cyclobutene system. The thermal cyclization of 1:3-diene to cyclobutenes has been earlier reported and conclusion drawn[12] that the substituted dienes with steric constraints lead to facile cyclization, though rare in comparison to the kinetically favoured reverse processes. The ^{1}H NMR spectrum of 7 showed usual signals for 2-vinyl-2-methyl-5-substituted tetrahydrofuran moiety. The doublet for H-8c was also present at δ 0.80. Further, the two singlets at δ 1.28 and 1.25 and the overlapping multiplets at δ 6.08 supported the geminal dimethyl cyclobutene ring. Its ^{13}C NMR also showed signals at δ 27.0 and 27.6 (2Me), 137.5 and 132.0 (C=C) and δ 38.4 and 37.7 for cyclobutene moiety. The CIMS of 7 showed $[M+1]^{+}$ ion at m/z 221 confirming the mol. formula $C_{15}H_{24}O$ for 7. These alongwith the remaining[13] spectral data substantiated its structure as 7.

NOTES AND REFERENCES

1. Chandra,A., Misra,L.N. and Thakur,R.S., Tetrahedron Letters, 28(50), 6377 (1987) and references therein.

2. (a) Ahmad,A., Siddiqui,M.S. and Misra,L.N., Phytochemistry, 27, 1065-67 (1988) (b) Misra,L.N., Shawl,A.S. and Raina,V.K., Planta Med., 54, 165-66 (1988) (c) Garg,S.N., Misra,L.N. and Agarwal,S.K., Phytochemistry, in press (d) Ahmad,A., Misra,L.N. and Thakur,R.S., Planta Med., in press (e) Misra,L.N., Tyagi,B.R. and Thakur,R.S., Planta Med., communicated.

3. 800 Mg 1 was taken in 5 ml MeOH at 0°C and 1g $NaBH_4$ was added gradually. After usual work up and TLC separations 2 (400mg) and 3 (180mg) were obtained.

4. 50 Mg 2 and 3 were individually taken in 1 ml pyridine and 1ml Ac_2O and kept at R.T. overnight. After usual work up 2a (40mg) and 3a (40mg) were obtained.

5. 800 Mg 1 was taken in 5ml ether and 200g $LiAlH_4$ were added gradually while stirring at R.T. After usual work up and TLC separations 2 (420mg), 3 (140mg), and 5 (45mg) were obtained.

6. a) Bailey,W.J. and Marktscheffel,F., J.Org.Chem., 25, 1797 (1960) (b) Tweedie,V.L. and Cuscurida,M., J.Am.Chem.Soc., 79, 5463 (1957) (c) Tweedie,V.L. and Barron,B.G., J.Org.Chem. 25, 2023 (1960).

7. a) Charlwood,B.V. and Banthorpe,D.V. in 'Progress in Phytochemistry', Vol.5, p.75 eds. Reinhold,L., Harborne,J.B. and Swain,T., Pergamon Press, Oxford (1978)

(b) March,J., 'Advanced Organic Chemistry', pp.1014, Wiley Eastern Ltd., New Delhi (1985).

8. 3, IR $\nu_{max}^{cm^{-1}}$: 3500-3450 (OH), 1448, 1420, 1380, 1248, 1200, 1110. MS m/z (rel.int.): 238 [M^+, $C_{15}H_{26}O_2$] (48), 223 [M-CH_3]$^+$ (27), 220 [M-H_2O]$^+$ (15). ^{1}H NMR ($CDCl_3$) δ:5.28 (dd, J = 18.0 and 2.0Hz, H-2a), 4.91 (dd, J = 10.5 and 2.0Hz, H-2a'), 5.88 (dd, J=18 and 10.5Hz, H-1a), 1.26 (s, H-1b), 3.80 (ddd, J=9.0, 8.0, 3.0, H-5), 0.86 (d, J = 7.0Hz, H-8c), 4.18 (m, H-2c), 2.27-2.20 (m, H-3c), 5.28 (t, J = 7.0Hz, H-4c), 1.72 and 1.64 (s each, H-6c and 7c). ^{13}C NMR: ($CDCl_3$): 111.5 (C-2a), 144.6 (C-1a), 83.0 (C-2), 26.5 (C-1b), 32.4 and 31.0 (C-3 and C-4), 82.0 (C-5), 43.0 (C-1c), 11.8 (C-8c), 73.2 (C-2c), 37.9 (C-3c), 121.8 (C-4c), 131.0 (C-5c), 18.0 and 25.9 (C-6c and C-7c).

9. 2, IR $\nu_{max}^{cm^{-1}}$: 3500(OH), 1450, 1390, 1237, 1119. MS m/z (rel.int.): 238 [M^+, $C_{15}H_{26}O_2$] (18), 220 [M-H_2O]$^+$ (5). ^{1}H NMR ($CDCl_3$)δ:5.12 (dd, J=18.0 and 2.0Hz, H-2a), 4.75 (dd, J=10.5, 2.0Hz, H-2a'), 5.72 (dd, J=18 and 10.5Hz, H-1a), 1.14 (s, H-1b), 3.70 (ddd, J=8.0, 6.5 and 3.0Hz,H-5), 0.62 (d, J=7.0Hz, H-8c), 3.45 (m, H-2c), 5.20 (t, J=7.0Hz, H-4c), 1.56 and 1.47 (s each, H-6c and 7c). ^{13}C NMR ($CDCl_3$) δ : 111.0 (C-2a), 143.8 (C-1a), 83.0 (C-2), 26.0 (C-1b), 32.1, 30.9 (C-3, C-4), 84.0 (C-5), 43.4 (C-1c), 12.0 (C-8c), 75.3 (C-2c), 36.9 (C-3c), 120.2 (C-4c), 132.0 (C-5c), 17.2 and 25.2 (C-6c and 7c).

10. 5, IR $\nu_{max}^{cm^{-1}}$: 3400(OH), 1630, 1460, 1278, 1215, 1100, MS m/z (rel.int.): 240 [M^+, $C_{15}H_{28}O_2$] (2), 222 [M-H_2O]$^+$ (1.5), 204 [222-H_2O]$^+$ (32). ^{1}H NMR ($CDCl_3$) δ : 1.63 (d, J = 7Hz, H-2a), 5.15 (q, J=7Hz, H-1a), 2.05 (s, H-1b), 4.12 (overlapping m, H-5 and H-2c), 0.91 (d, J=7Hz, H-8c), 5.45 (t, J=7Hz, H-4c), 1.68 (s, H-6c and 7c). ^{13}C NMR ($CDCl_3$) δ : 16.0, 25.4, 26.0 and 17.4 (C-2a, 1b, 6c and 7c), 123.0 and 123.6 (C-1a and C-4c),144.0 and 142.5 (C-5c and C-2), 81.2 and 73.0 (C-5 and C-2c), 11.4 (C-8c), 39.4, 37.8 and 32.0 (C-3, C-4 and C-3c), 44.0 (C-1c).

11. 50mg (2) was refluxed with methanolic H_2SO_4 [5 drops in 5ml MeOH] for 4 hrs. The reaction mixture after usual work up yielded 7 (40mg; petrol-EtOAc, 4:1, Rf 0.75).

12. a) Shumate,K.M., Neuman,P.N. and Fonken,G.J. J.Am.Chem.Soc., 87, 3996 (1965); b) Steiner,R.P. and Michl,J. J.Am.Chem.Soc., 100, 6413 (1978); c) Gil-Av,E and Herling,J.Tet.Lett. 1 (1967); d) Woodward,R.B. and Hoffmann,R. J.Am.Chem. Soc., 87, 395 (1965).

13. 7, IR $\nu_{max}^{cm^{-1}}$: 1640, 1240, 1120, 1040. CIMS m/z (methane) (rel.int.): 221 [M+1]$^+$ (6.5), ^{1}H NMR ($CDCl_3$) δ : 5.12 (dd, J = 18.0 and 2.0Hz, H-2a), 4.90 (dd, J = 10.5, 2.0Hz, H-2a'), 5.89 (dd, J=18 and 10.5Hz, H-1a), 1.25 (s, H-1b), 3.98 (ddd, J=8.0, 6.5 and 3Hz, H-5), 0.80 (d, J=7Hz, H-8c), 6.08 (overlapping m, H-3c and 4c), 1.25 and 1.28 (sbr, H-6c and 7c), ^{13}C NMR ($CDCl_3$) δ : 110.8 (C-2a), 144.9 (C-1a), 79.4 (C-2), 26.0, 27.0 and 27.6 (C-1b, 6c and 7c), 28.4 and 28.0 (C-3 and C-4), 80.4 (C-5), 41.4 (C-1c), 9.3 (C-8c), 37.7 and 38.4 (C-2c and C-5c), 137.5 and 132.0 (C-3c and C-4c).

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