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A NOVEL REARRANGEMENT IN C-20 DITERPENE ALKALOIDS. FORMATION OF BRIDGED BICYCLO[4.3.1]DEC-1-ENE SYSTEM

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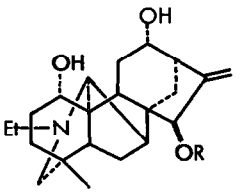
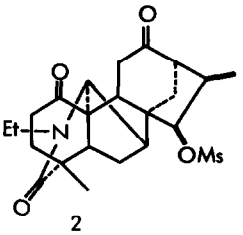
The stability of the compounds having a bridge head double bond has recently received attention, and many of these compounds have been synthesized (1). During the course of chemical transformation directed to the partial synthesis of hexacyclic diterpene alkaloid, napelline 1 (2), we found an interesting rearrangement in which highly strained ring system was produced. The rearrangement might have some significance in the biogenesis of aconane skeleton.

Starting mesylate 2 was prepared from lucidusculine 3 (2) by the following sequence of reactions: i, H_2/PtO_2 in AcOH; ii, CrO_3/py; iii, KOH in MeOH; iv, MsCl/py (3). When mesylate 2 was heated in dry DMSO at 115° for 3.5 hr., two olefinic products 4 and 5 were formed in 68% yield. Since direct separation of 4 and 5 was difficult, the mixture was reduced with ca. 1 equivalent of $NaBH_4$ and separated by silica-gel chromatography to give the keto alcohols 6 and 7 (ca. 1:1). The keto alcohol 6 [m.p. 219-222°, M^+ 355 (base peak), ν (KBr) 3420, 1698, 1621 cm^{-1}, δ ($CDCl_3$) 1.10 (3H, s), 1.18 (3H, t, J=7.0), 1.72 (3H, d, J=1.5), 5.78 (1H, br.s)] afforded by acetylation the keto acetate 8 [amorph., ν ($CHCl_3$) 1737, 1707, 1625 cm^{-1}, δ ($CDCl_3$) 1.12 (3H, s), 1.19 (3H, t, J=7.0), 1.72 (3H, d, J=1.5), 2.04 (OAc), 5.02 (1H, br.t, J=8), 5.79 (1H, br.s)]. The NMR spectrum displayed the presence of a vinyl methyl group and a vinyl proton coupled each other. Thus, 4 was shown to be normal 1,2-elimination product (4). The isomeric keto alcohol 7 [m.p. 195.5-200°, M^+ 355 (base peak), ν ($CHCl_3$) 3350, 1697, 1621 cm^{-1}, δ ($CDCl_3$) 1.15 (3H, t, J=7.0), 1.19 (3H, s)] contained a secondary methyl group (δ 0.98, d, J=7.5) and a vinyl proton (δ 5.31, d, J=2) as well as β,γ-unsaturated 6-



1 : R=H

3 : R=Ac



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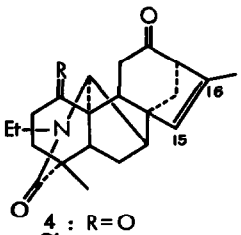
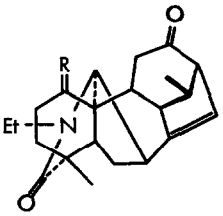


4 : R=O

6 : R=α-OH, β-H

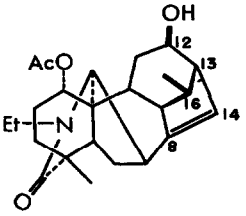
8 : R=α-OAc, β-H



5 : R=O

7 : R=α-OH, β-H

9 : R=α-OAc, β-H



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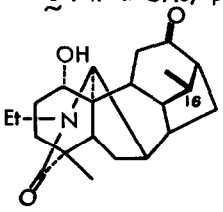

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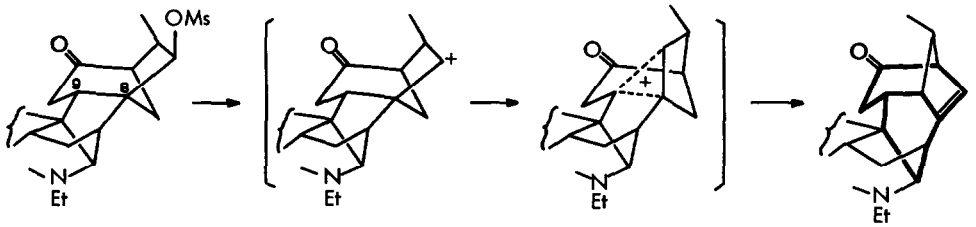
membered ketone chromophor [λmax 298 nm (ε 520)]. The comparison of the NMR spectrum with those of appropriate napelline derivatives disclosed that structural change had taken place only on the rings C and D of the napelline carbon skeleton. Decoupling experiments on the corresponding keto acetate 9 [amorph., ν ($CHCl_3$) 1735, 1705, 1635 cm^{-1}, δ ($CDCl_3$) 0.98 (3H, d, J=7.0), 1.17 (3H, t, J=7.0), 1.20 (3H, s), 2.05 (OAc), 5.04 (1H, br.t, J=8), 5.36 (1H, d, J=2)] established the arrangement of Me-C_{16}H-C_{13}H-C_{14}H=C< (J_{1316}=4 Hz, J_{1314}=2 Hz). The $NaBH_4$ reduction of 9 afforded the corresponding hydroxy acetate 10 [m.p. 99.5-101.5°, M^+ 357, ν (KBr) 3360, 1729, 1620 cm^{-1}, δ ($CDCl_3$) 1.17 (3H, t, J=7.0), 1.21 (3H, s), 1.24 (3H, d, J=7.0), 5.05 (1H, br.t, J=8), 5.30 (1H, d, J=2.0)], while catalytic (Pt) reduction of 7 yielded the corresponding dihydro keto alcohol 11 [amorph., ν ($CHCl_3$) 3350, 1699, 1618 cm^{-1}, δ ($CDCl_3$) 0.93 (3H, d, J=7.0), 1.17 (3H, t, J=7.0), 1.20 (3H, s)]. The following changes in NMR were observed with the aid of NMDR on going from 9 to 10: i) The multiplicity change in the C_{13}-H signal from double doublets to a multiplet (J_{1213}=4 Hz), and ii) a large down-field shift (Δδ=0.26 ppm) of the secondary methyl signal. On the other hand, on going from 7 to 11, practically no change has occurred to the latter (up-field shift by 0.05 ppm), while a large up-field shift (Δδ 0.37 ppm) was observed for C_{16}-H. Furthermore, it was found that the contri-

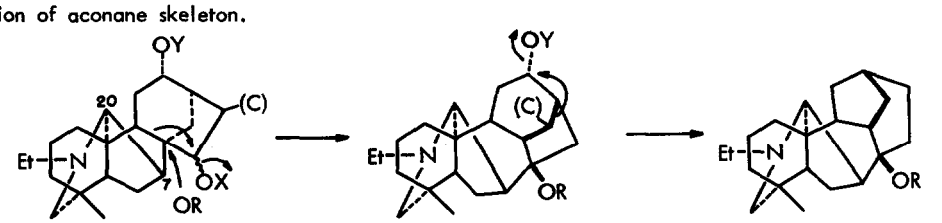
bution of C_8=C_{14} double bond to the CD spectrum of 7 [$\Delta[\theta] = [\theta]_7 - [\theta]_{11}$ = -58900 (304) - (+600 (280)) = -59500] is strongly negative and opposite to that of C_{15}=C_{16} bond in 6 [$[\theta]_6 - [\theta]_{H_2-6}$ = +37400 (301) - (-7900 (304)) = +45300]. All of these observations combined established the stereochemistry of the compound 7 as shown.

In contrast to the rearrangement known in the related ring systems (5) in which antiparallel bond migrates to the less-strained bicyclo[4.4.1]undec-1-ene system, conversion of 2 to 5 has some significance in that it involves the migration of unfavorable cis C_8-C_9 bond to the leaving group and that the product 5 contains highly strained ring system, a bicyclo[4.3.1]dec-1-ene with an one-carbon and a two-carbon bridges. Both points may be rationalized by the ground state strain in the starting 2 caused by the fusion of a bicyclo[2.2.1]heptane and a bicyclo[3.2.1]octane. Thus, when the carbonium ion A (possibly stabilized by solvent) which is also the precursor of 4, is formed, C_8-C_9 bond migrates via the bridged ion B in non-concerted fashion in order to release the strain of the bicyclo[2.2.1]heptane system and gain the overall stabilization.



2 A B 5

The rearrangement is also interesting in connection with the biogenesis of aconane type alkaloids. In the proposed mechanism (6), C_7-C_{20} bridge is formed after the rearrangement in C and D rings has been completed. However, natural occurrence of bridged alkaloids such as napelline 1 and denudatine (7), a 7,20-bridged alkaloid of atisine type, suggests that the bridging between C-7 and C-20 is independent to the skeletal rearrangement (8). On the basis of the facile rearrangement discussed here in the 7,20-bridged veatchine system, the pathway depicted below might also have to be considered for the formation of aconane skeleton.



References and Footnotes

1) J.A. Marshall and H. Faubl, J. Am. Chem. Soc., 89, 5965 (1967); J.R. Wiseman, ibid., 89, 5966 (1967); J.R. Wiseman, H.F. Chan and C.J. Ahola, ibid., 91, 2812 (1969); J.R. Wiseman and J.A. Chong, ibid., 91, 7775 (1969); J.R. Wiseman and W.A. Pletcher, ibid., 92, 956 (1970); C.B. Quinn and J.R. Wiseman, ibid., 95, 1342 (1973); W.G. Dauben and J. Ipaktschi, ibid., 95, 5088 (1973).

2) T. Sugasawa, Chem. Pharm. Bull., 9, 897 (1961); T. Okamoto, M. Natsume, Y. Iitaka, A. Yoshino and T. Amiya, ibid., 13, 1270 (1965) and references therein.

3) Full part of the conversion will be reported separately.

4) In fact, napelline 1 was derived from 4 by a series of chemical transformation. S. Itô, M. Kodama, H. Kurihara and T. Sato, to be published.

5) W.A. Ayer and P.D. Deshpande, Can. J. Chem., 51, 77 (1973); K. Wiesner, T.Y.R. Tsai, K. Huber, S.E. Bolton and R. Vlahov, J. Am. Chem. Soc., 96, 4990 (1974).

6) R.C. Cookson and M.E. Trevelt, J. Chem. Soc., 3121 (1956); Z. Valenta and K. Wiesner, Chem. & Ind., 354 (1956); O.E. Edwards, Chem. Comm., 318 (1965).

7) M. Götz and K. Wiesner, Tetrahedron Letters, 4369 (1969); F. Brisse, ibid., 4373 (1969); L.H. Wright, M.G. Newton, S.W. Pelletier and L.H. Singh, Chem. Comm., 359 (1970).

8) Biogenetic significance of C_7-C_{20} bond has also been implied by Johnston and Overton [J. Chem. Soc. Perkin 1, 1490 (1972)].