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TERPENOIDS XCII

SYNTHESIS OF 1-OXOEUDESMANES*

Mrs.Emina Siscovic,[1] V.K.Honwad[2] and A.S.Rao
National Chemical Laboratory, Poona-8, India.

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The occurrence in nature of a number of eudesmanic compounds[4] oxygenated at C_1 has prompted us to carry out the transformations described in this communication.

One of the hydrogenation products of santonin is a hydroxy lactone, m.p. 108-110°, $(\alpha)_D + 36^\circ$ for which structure (I) has been assigned by Cocker and McMurry.[5] The arguments in favour of the α-configuration for C-3 hydroxyl are not compelling and available data are best explained by the structure (II). Sodium borohydride reduction of keto-lactone (VIII) furnishes exclusively the hydroxy lactone m.p. 108-110°.[6] Arguing strictly from the steric viewpoint, hydride attack on the C-3 carbonyl of (VIII) from the β-face, which would be necessary for 3-α-ol formation, is prevented by steric interference of C-4 β-methyl group.[7] The hydroxy lactone is also formed

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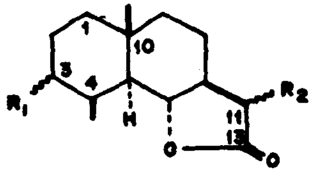
stereospecifically during the catalytic hydrogenation of (VIII)§ due to the shielding of the β-side by the methyl groups at C_4 and C_{10}, the attack is likely to take place from the α-side to furnish 3β-ol. The molecular rotation data is also consistent with the β-configuration for C-3 hydroxyl. The molecular rotation increment ($\Delta M_D = -46$) for acetylation of the hydroxylactone is of the same sign and magnitude as the molecular rotation increment ($\Delta M_D = -95$) for the acetylation of 4β-methyl cholestanol.[8] The NMR[3] spectrum of the acetate (III) prepared from the hydroxy lactone exhibits a broad signal at 5.13τ due to C_3-H and suggests that the C-3 acetate is equatorial.[9]

The elimination reactions of (II) and its esters were studied under a variety of conditions to get the lactene (X) in satisfactory yields. Reaction of (II) with tosyl chloride in dimethyl formamide-collidine mixture in the presence of SO_2[10] at 5-20° furnished the formate (IV) m.p. 195°, $\nu_{max.}$ 1780, 1730, 1190 cm^{-1} (Found: C, 68.1; H, 8.2. $C_{16}H_{24}O_4$ requires: C, 68.54; H, 8.63%); the structure assigned to (IV) is confirmed by its conversion to (II) on treatment with alkali. The tosylate (V)[6] on treatment with KOt-Bu in dimethyl sulfoxide[11] furnished a 5:1 mixture of (XV) and (X) (analysis by NMR and IR spectra). The benzoate (VI) m.p. 185-187°, $(\alpha)_D$ + 68° (c, 3; $CHCl_3$) (Found: C, 73.6; H, 8.04; $C_{22}H_{28}O_4$ requires: C, 74.13; H, 7.92%), on pyrolysis at 350°, furnished in excellent yield, the lactone (X)[5] m.p. 107-108°, Hydrogenation of (X) furnished santanolide C (VII)[12] which has been used in elucidating the structure as well as synthesising some natural products. The route santonin → II → VI → X → VII offers a convenient method for the synthesis of santanolide-C from santonin and is superior to the methods described in literature. Sodium-dichromate oxidation of the lactone (X) in acetic acid at 100° for 6 hrs furnished a mixture, ($\nu_{max.}$ 1775, 1725 and 1665 cm^{-1}) of the starting material and the lactones (XI) and (XVI).[13]

The keto-oxide[14] (IX) on bromination and subsequent dehydrobromination with collidine furnished the α,β-unsaturated ketone (XVII), m.p. 88-90°, $(\alpha)_D$ - 49° (c, 14.8; $CHCl_3$) $\lambda_{max.}$ 227 $m\mu$ (ϵ 9,400), $\nu_{max.}$ 1687 cm^{-1}, NMR[3] signals at 8.96 (d), 8.91 (s), 8.77 (d) (C_{11}, C_{10}, C_4, $-CH_3$), 6.64 (m) (- O - $\underline{CH_2}$ -), 6.02 (t) (C_6 - H), 4.26 (d) and 3.39 (d) (C_1 and C_2 - H ; $J_{1,2}$ = 10 c.p.s.) (Found: C, 77.02; H, 9.61. $C_{15}H_{22}O_2$ requires: C, 76.88; H, 9.46%). The α,β-epoxy ketone (XIX), $(\alpha)_D$ + 40° (c, 4.6; $CHCl_3$), $\nu_{max.}$ 1720 cm^{-1}, NMR signals at 6.86τ (C_1 and C_2 -H), prepared by the epoxidation[15] of (XVII), was reduced with hydrazine[15] to the alcohol (XII) $(\alpha)_D$ + 67° (c, 4.41; $CHCl_3$),

$\nu_{max.}$ 3390 cm^{-1}. Jones oxidation of (XII) furnished 1-oxo-4,6,11β (H), 5,7α(H)-eudesm-2-en-6,13 -oxide (XIII), (α)$_D$ - 50° (c, 8.7; CHCl$_3$) $\lambda_{max.}$ 227 mμ (ε 9100); $\nu_{max.}$ 1689 cm^{-1}. NMR signals at 8.98 (d), 8.96 (s), 8.72 (d) (C$_{11}$, C$_{10}$ and C$_4$ - CH$_3$), 6.65 (m) (-O-CH$_2$-), 6.02 (t) (C$_6$ - H), 4.27 (q) and 3.53 (q) τ (C$_2$ and C$_3$ -H) (Found: C, 76.47; H, 9.94%). Keto oxide (XIII) was hydrogenated with Pd-C to yield (XXI), (α)$_D$ + 6° (c, 5; CHCl$_3$) $\nu_{max.}$ 1725 cm^{-1} (Found: C, 76.25; H, 10.68. $C_{15}H_{24}O_2$ requires: C, 76.22; H, 10.24%).

Epoxidation of (XVIII)^{16} furnished the α,β - epoxyketone (XX), m.p.124-127°, (α)$_D$ + 120° (c, 0.78; CHCl$_3$) $\nu_{max.}$ 1780, 1720 cm^{-1}. NMR signals at 6.77 τ (C$_1$ and C$_2$ -H) (Found: C, 68.19; H, 7.70. $C_{15}H_{20}O_4$ requires: C, 68.16; H, 7.63%). The hydrazine reduction of (XX) to the allylic alcohol (XIV) did not proceed satisfactorily.



I R_1 = α-OH, R_2 = β-Me

II R_1 = β-OH, R_2 = α-Me

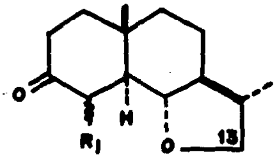
III R_1 = β-OAC, R_2 = α-Me

IV R_1 = β-O-$\underset{\underset{O}{\|}}{C}$-H, R_2 = α-Me

V R_1 = β-Tosyl, R_2 =α-Me

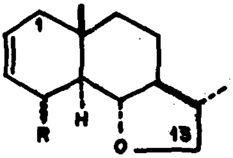
VI R_1 = β-O-$\underset{\underset{O}{\|}}{C}$-$C_6H_5$, R_2=α-Me

VII R_1= H, R_2 = α-Me



VIII R_1 = β-Me, 13-oxo

IX R_1 = α-Me



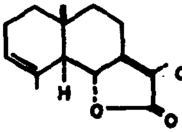
X R=β-Me, 13-oxo

XI R= β -Me, 1-oxo,13-oxo

XII R = α-Me, 1-α-OH

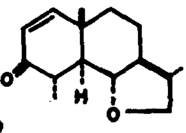
XIII R = α-Me, 1-oxo

XIV R= α-Me, 1-α-OH,13-oxo



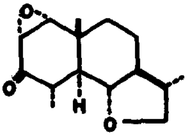
XV

XVI 1-oxo



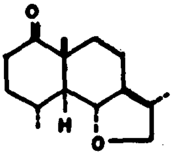
XVII

XVIII 13-oxo



XIX

XX 13-oxo



XXI

REFERENCES

1. Recipient of a scholarship from the Ministry of Education, Government of India.

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3. NMR spectra are taken at 60 megacycles using tetramethylsilane as internal standard in CCl_4 (except the acetate (III) which was taken in $CHCl_3$); (s) singlet, (d) doublet, (t) triplet, (q) quadruplet and (m) multiplet.

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