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A NOVEL FRAGRANT TRICYCLIC KETONE FROM SANTANOLIDE

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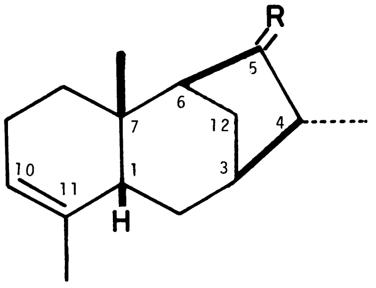
(+)-1β,3α,6αH-4α,7β,11-trimethyltricyclo[5.4.1^{3,6}.0^{1,7}]dodec-10-en-5-one (3) was obtained together with trimethylethanoadamantanone (2) by an unusual reaction of 3-deoxyhexahydrosantonin (1). The structure, conformation and absolute configuration of **3** was determined by X-ray diffraction and CD/ORD spectrometry.

In connection with our study on the cyclization-skeletal rearrangement from a representative eudesmanolide, 3-deoxy-4β,5αH-hexahydro-ℓ-α-santonin (1) to an optically active ethanoadamantanone, (-)-2,5,9-trimethyltetracyclo-[6.3.1.0^{2,6}.0^{5,10}]dodecan-11-one (2),2) we now describe the transformation of the santanolide (1) to a new fragrant ketone, tricycloeudesmenone (3), in the course of the reaction similar to the previous case.2) The structure and conformation together with absolute configuration of **3** have been established on the basis of the X-ray crystallographic analysis of **3** and the CD and ORD spectrometric determination.

The dried sodio salt of the hydroxy acid prepared from **1** (5 g) was heated with boiling phosphoryl chloride (15 ml) as same as earliar.2) A dark violet oil left after removal of the solvent was dissolved in ether, and the ether solution was passed through a column of neutral alumina excluding pre-treatment with aq. ammonia and hot 15% sodium hydroxide in the previous case. A colorless liquid (10.90 g, ∿18%) obtained from the eluate, bp 120-125°C/2 mmHg, was further chromatographed on silica gel. Besides the earliar elution with pentane giving 0.30 g

(∿6%) of hydrocarbons (centered at Rf 0.75, br),[3] elution with 2% ether in pentane afforded 0.44 g (∿9%) of a mixture of oily ketones (Rf 0.52 and 0.48), IR(KBr) ν 1725 cm^{-1}. A solid product isolated from further elutions with 5% ether in pentane was recrystallized from pentane at -15°C to give the pure ketone (3) (0.10 g, ∿2%) as colorless transparent plates (Rf 0.40): mp 99-103°C (with sublimation), $[\alpha]_D^{22}$ +39.3° (EtOH), IR(KBr) ν 1726 cm^{-1} (cyclopentanone), MS m/e(M$^+$) 218.1673 (218.1671 calcd for $C_{15}H_{22}O$),[3] ^{1}H-NMR(CDCl$_3$) δ 0.93 (s, $\geq$C-C$\underline{H}_3$), 1.13 (d, J=7 Hz, $>$CH-C$\underline{H}_3$), 1.63 (br s, $=\overset{|}{C}$-C$\underline{H}_3$), 5.36 (m, -C$\underline{H}$=C$<$). This ketone did not form the corresponding 2,4-dinitrophenylhydrazone, but on LiAlH$_4$ reduction in boiling dry ether afforded stereoselectively the secondary alcohol (4) (Rf 0.18): MS m/e(M$^+$) 220.1837 (220.1827 calcd for $C_{15}H_{24}O$), $[\alpha]_D^{29}$ +38.0° (EtOH), IR(KBr) ν 3347 cm^{-1}, ^{1}H-NMR(CDCl$_3$) δ 1.13 (s, C_7-C$\underline{H}_3$) (Δ +0.20), 1.08 (d, J=7 Hz, C_4-C$\underline{H}_3$) (Δ -0.05). Acetate (5) (Rf 0.38): MS m/e(M$^+$) 262.1904 (262.1931 calcd for $C_{17}H_{26}O_2$), mp 58-59°C, $[\alpha]_D^{28}$ +18.3°(EtOH), IR(KBr) ν 1733 cm^{-1}, ^{1}H-NMR(CDCl$_3$) δ 0.93 (s, C_7-C$\underline{H}_3$) (Δ +0.00), 1.08 (d, J=7 Hz, C_4-C$\underline{H}_3$) (Δ -0.05). The hydroxyl group of **4** should be in a cis relationship to the angular methyl group on the basis of the dishielding and shielding effect on the *t*- and *s*-methyl as shown above, respectively. Elution with 10% ether in pentane furnished a small amount (6 mg, ∿0.1%) of an oil, which then solidified and was found to be trimethylethanoadamantanone (2) (Rf 0.22), mp 37-39°C (mixed mp.).[2] All the spectral data are identical with those of an authentic sample of **2** in every respect. The last elution with ether gave a pasty mass (0.05 g, ∿1%).



3 R=O, 4 R=<$^{H}_{OH}$, 5 R=<$^{H}_{OCOCH_3}$

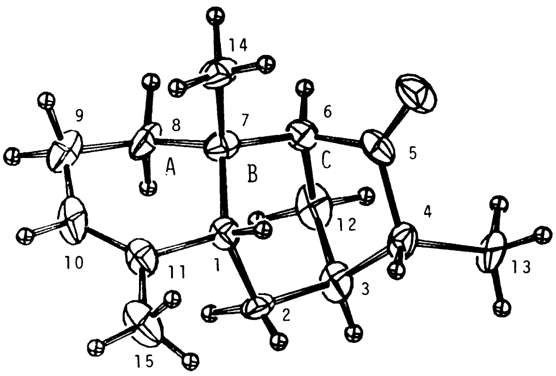


FIG. 1 PERSPECTIVE VIEW OF THE MOLECULAR STRUCTURE OF 3

A direct X-ray crystallographic analysis for the structure determination of **3** was carried out with a specimen of the crystal grown as above as colorless plates flattered on (010). The lattice constants and intensities were measured on a Philips PW 1100 diffractometer using graphite monochromated CuKα radiation. Most of the crystals showed interpenetrate twinning about the twin axis [101] on a twin plane ($\bar{1}01$). A crystal of approximate dimensions of 0.05 X 0.07 X 0.02 mm was able to find by chance which exhibited predominant intensities for one of the twinned fragments. The crystal data are shown below. M.W. 218.2, monoclinic, space group $P2_1$, Z= 2, Dx= 1.128 g.cm^{-3}. a= 10.843(5), b= 9.019(4), c= 7.560(4) Å, β= 102.55(2)°, U= 641.7 Å^3. Within a 2θ range of 6°-156°, intensities of 1318 reflexions were measured for one of the fragments as above the 2σ(I) level. The structure factors were then derived by correcting the intensities for Lorentz and polarization factors but no absorption corrections were applied.

Although the accuracy of the intensity measurement was considered to be greatly affected by the twinning, the agreement between various symmetry related reflexions was good enough to proceed the analysis. The crystal structure was solved by the direct method using MULTAN$^{4)}$ and refined by the method of block-diagonal least-squares. Most of the $\bar{h}kh$ reflexions which are common for the twinned fragments were excluded from the refinement. The final R factor was 0.067 for 1198 reflexions including hydrogen atom contributions. Fig. 1 illustrates a perspective view of the molecular structure of **3** drawn by the ORTEP program.$^{5)}$

The structure of **3** has been thus disclosed to be (+)-1β,3α,6αH-4α,7β,11-trimethyltricyclo[5.4.1^{3,6}.0^{1,7}]dodec-10-en-5-one. With respect to the conformation of **3**, a chair form cyclohexane B-ring and an envelope type cylopentane C-ring puckered at C(12) are rigidly fixed. The hydrogen atoms of the ring junction at C(3) and C(6) take α-equatorial configuration in the B-ring with *trans* relationship to β-equatrial methyl group at C(7). A half chair form cyclohexene A-ring, in which C(8) is situated downward from the plane of the *cis* butene, takes a non-steroid type *cis* A/B ring fused system with the rigid B-ring.

The absolute configuration of **3** shown in the above structure, can be deduced from a strong negative sign of the Cotton effect exhibited in the CD and ORD curves as follows: CD $[\theta]_{303}$ -2931 and $[\theta]_{314}$ -1801, ORD $[\phi]_{319}$ -2205, $[\phi]_{272}$ +949 (a= -31.5) and $[\phi]_{327}$ -1502, $[\phi]_{287}$ +384 (a= -18.9) (in MeOH and hexane, respectively). Finally the configuration thus defined is coincident with that predicted from the conventional octant sector diagram.$^{6)}$

It seems most plausible to assume that the product (3) should be transformed from the acid chloride of **1** through a non-steroidal *cis* octalin intermediate. The detailed reaction mechanism will be discussed in the subsequent paper in relation to the structure elucidation of other products in the present reaction.

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References and Notes

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