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A Novel Rearrangement from Eudesmanolide to Adamantanone*1

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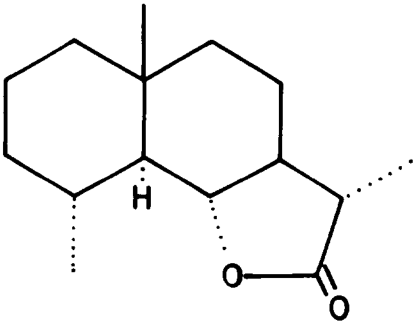
Summary: A novel cyclization-skeletal rearrangement from a eudesmanolide, 3-desoxy-4β, 5αH-hexahydro-ℓ-α-santonin(1) to an adamantanone, 2, 5, 9-trimethyltetracyclo[6. 3. 1. $0^{2,6}$. $0^{5,10}$]dodecan-11-one(2) was found to occur as the result of a most unusual reaction. The structure of 2 was elucidated by the X-ray diffraction method.

In the course of our medico-chemical investigation, a unique cyclization-skeletal rearrangement from santanolide to ethanoadamantanone has been found to occur in a most unusual reaction as described below.



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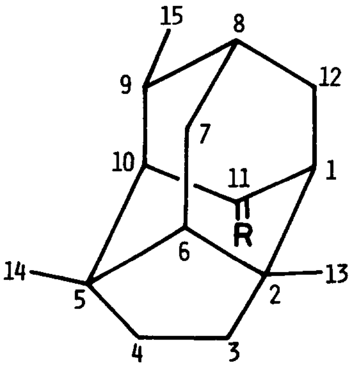

2 R=O, 3 R= $<^{H}_{OH}$, 4 R= $<^{H}_{OCOCH_3}$

The dried sodio salt of the acid derived from a representative eudesmanolide, 3-desoxy-4β, 5αH-hexahydro-ℓ-α-santonin(1)1) was heated to reflux for 3 hr in excess of phosphorus oxychloride. The oily product obtained after removal of the excess reagent in vacuo, neutralization with conc. aq. ammonia, and evaporation of the ether extraction, was further treated with hot 15% sodium hydroxide to remove a trace of the unreacted lactone. Distillation of the ether extract obtained from the above alkali treatment afforded a colorless liquid(ca. 15% from 1), bp_2 110-114°, which was subjected to a chromatography over silisic acid. Besides the successive elutions with pentane(ca. 55%, Rf 0.75[*4])(oily hydrocarbons and chlorohydrocarbons), 2% ether-pentane(ca. 8%, Rf 0.49)(oily ketone), 5% ether-pentane(ca. 3%, Rf 0.36)(oily ketone), and ether (ca. 16%)(viscous oil), the middle one with 10% ether-pentane gave a solid compound(2)(ca. 18%, Rf 0.21), $C_{15}H_{22}O$[*5], m/e(M^+) 218.1659(Calcd 218.1669), mp 37-39°, $[\alpha]_D^{27}$ -3.33°(c, 0.867; EtOH). The ^{1}H-nmr($CDCl_3$)(δppm) disclosed the presence of one sec-methyl(0.87, d, 7), two tert-methyl(1.13, s), four methylenes(1.45, s), and two different types of five methine groups(1.90, s, 2H; 1.93, s, 3H). Ultraviolet(EtOH)[λmax 294 nm(ε 22.4)] and infrared absorptions(KBr)[1708 cm^{-1}] indicate the presence of a six membered ketone, which was supported by the stereoselective formation of the corresponding sec-alcohol (3)(Rf 0.14) on lithium aluminum hydride reduction of 2 in dry boiling ether; mp 67-69°, $C_{15}H_{24}O$, m/e(M^+) 220.1825, $[\alpha]_D^{22}$ +56.2°(c, 0.911; EtOH), ir(KBr) absorption(ν 3318 cm^{-1}) and ^{1}H-nmr signal($CDCl_3$)(1.56, s; 4.12∿4.25, m). The acetate of 3[ν(KBr) 1734 cm^{-1}, Rf 0.49] was obtained by the usual manner, mp 29-31°, $[\alpha]_D^{20}$ -21.7°(c, 0.737; EtOH), $C_{17}H_{26}O_2$, m/e 202.0(M^+-CH_3COOH).

The Above spectral data detailed, however, no carbon framework of 2 or 3, but the ^{1}H-nmr spectra for 2, 3 and 4 seem to suggest a relatively high symmetricity of the molecule. Hence, a direct X-ray crystallographic analysis was undertaken with a specimen of the crystal of 2 for the structure determination. The crystals grown in pentane solutions were aggregates of thin needles elongated along the b axis. As the crystals were deliquescent in air, X-ray specimens were sealed in glass capillaries. A single crystal of approximate dimentions of 0.05 x 0.06 x 6 mm was chosen from the aggregates by repeated trials. The lattice trials. The lattice parameter and intensities were measured on a Philips PW-1100 diffractometer with monochromated CuKα radiation. The crystal data are shown below. M.W. 218.3, monoclinic, $P2_1$. a= 7.960(4), b= 11.505(6), c= 7.482(4) Å, β= 113.38(2)°, U= 629.0 Å, Z= 2, D_x= 1.153 $g.cm^{-3}$. Intensities of 1322 reflections were measured within 2θ range of 6° through 156°, in which 985 independent reflections with I>2σ(I) were used for the structure determination. The structure was solved by the direct method using MULTAN[2)]. Refinement by the

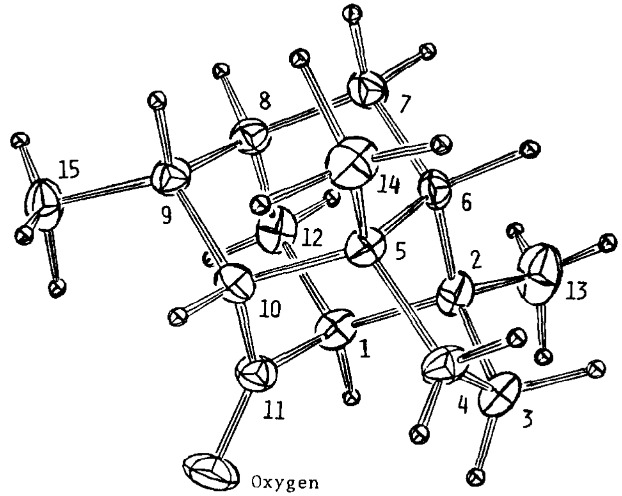

FIG. 1 PERSPECTIVE VIEW OF THE MOLECULAR STRUCTURE OF 2

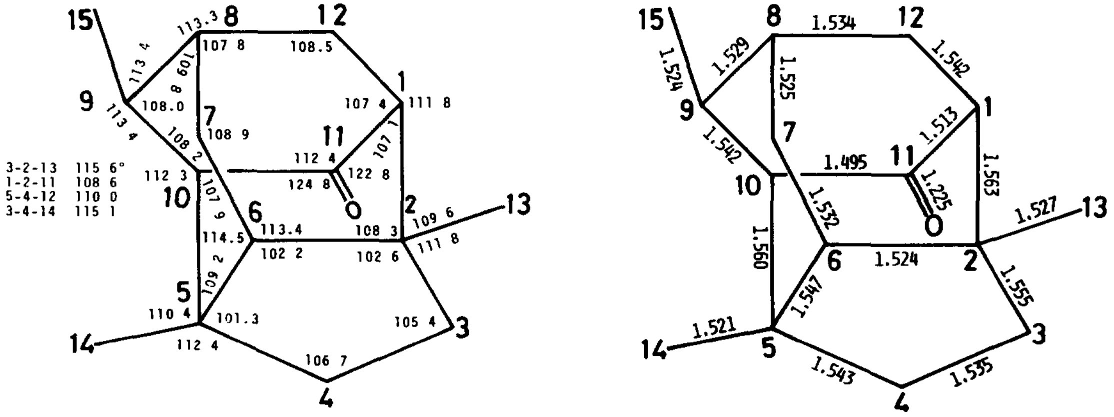

FIG. 2 BOND ANGLES AND LENGTHS OF 2

block-matrix least-squares method yielded the final R value of 0.06 with anisotropic thermal parameters. All hydrogen atoms are included with isotropic thermal parameters*6. The perspective view of the molecular structure of 2 drawn by the ORTEP program3) is illustrated in Fig. 1. The bond lengths and angles are shown in Fig. 2.

The structure of 2 thus defined has been disclosed to be 2, 5, 9-trimethyltetracyclo[6. 3. 1. $0^{2,6}$. $0^{5,10}$]dodecan-11-one possessing an ethanoadamantane framework in the molecule. Further studies on the reaction mechanism and the absolute configuration of 2 are now under progress.

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Notes and References

*1 Presented to the ACS/CSJ Chemical Congress, Apr. 1-6, Honolulu, 1979.

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*4 All the thin layer chromatographies(TLC) were performed in 10% ether-pentane using silica gel(Merck) plate.

*5 Satisfactory analytical data were obtained for all the new compounds described in this paper.

*6 A list of atomic coordinates is deposited at the Cambridge Crystallographic Data Centre.

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