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X-RAY AND CARBON-13 NUCLEAR MAGNETIC RESONANCE CHARACTERIZATION OF CYCLOPROPANE DERIVATIVES OBTAINED BY SOLVOLYSIS OF (*E*)-3α- AND (*E*)-3β-HYDROXY-5,10-SECO-1(10)-CHOLESTEN-5-ONE TOSYLATES[1]

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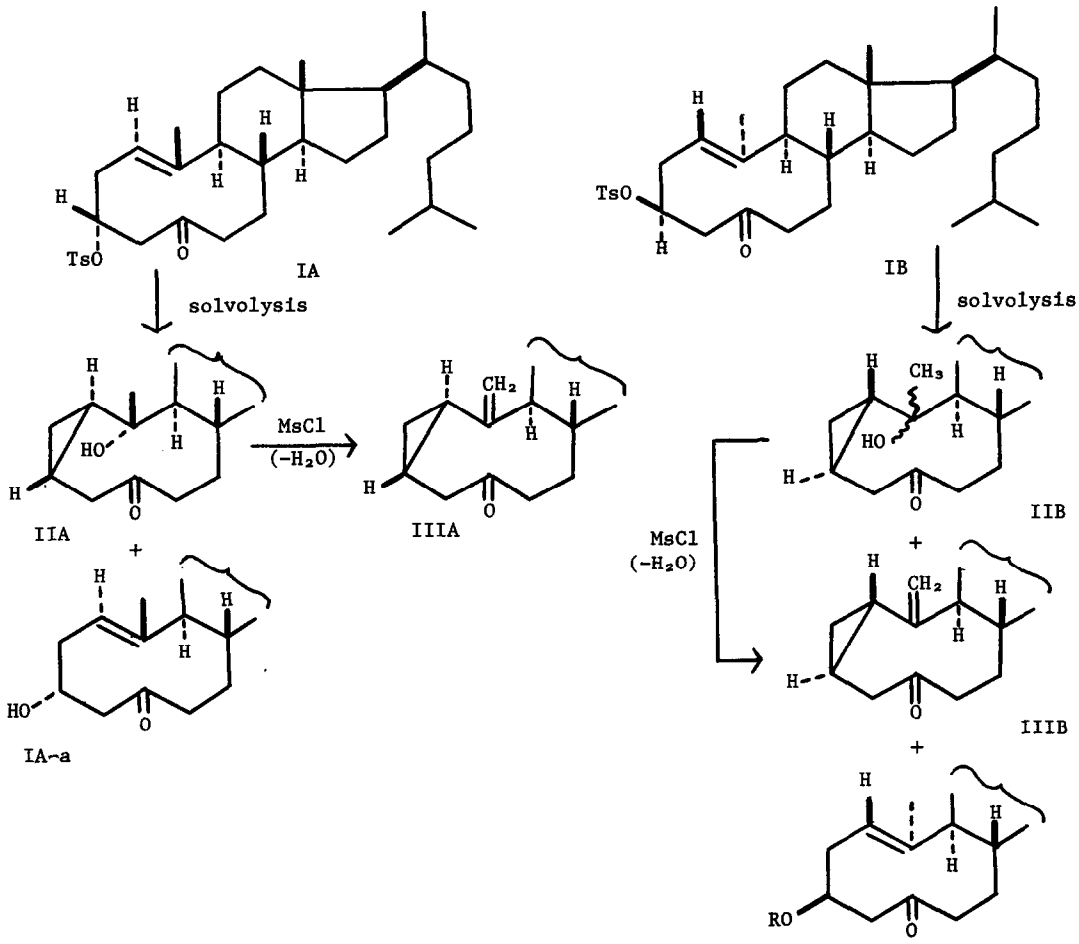
Summary The stereochemistries and conformations of three cyclopropane ring containing compounds derived from (*E*)-3α- and (*E*)-3β-hydroxy-5,10-seco-1(10)-cholesten-5-one tosylates have been determined by *X*-ray methods and the results correlated with ^{13}C nmr chemical shift data.

In the course of investigations on the influence which the configuration at C(3) and the cyclodecene ring conformation have on homoallylic π-bond participation and internal 1,3 C-C bond formation, we earlier presented a preliminary account[2] of the partial results of the solvolysis of diastereomeric (*E*)-3α, (*E*)-3β, (*Z*)-3α, (*Z*)-3β-hydroxy-5,10-seco-1(10)-cholesten-5-one tosylates, but the product stereochemistries remained to be defined. We now report on *X*-ray and ^{13}C nmr structural characterizations of three of the cyclopropane derivatives obtained from the (*E*)-3α- and (*E*)-3β-tosylates[3] (IA and IB) by solvolysis in acetone-water (90:10 v/v) solution at reflux temperature in the presence of one mol equivalent of anhydrous potassium acetate (IIA and IIIB) and by further reaction (IIIA).

Tosylates IA and IB[1] were prepared from the corresponding alcohols IA-a and IB-b[5] in the usual way by reaction with *p*-toluenesulfonyl chloride in pyridine. Solvolysis of IA yielded a cyclopropane ring containing product IIA[6](60%) as well as the original alcohol IA-a (34%); starting from IB, however, two cyclopropane derivatives IIB (*ca.*1%) and IIIB (32%), in addition to IB-a (30%) and its acetate, IB-b (35%), were obtained. Separation and isolation of the products was achieved by direct crystallization and/or column chromatography. Dehydration of IIA and IIB with methanesulfonyl chloride (MsCl) in dimethylformamide-pyridine for 3 h at room temperature gave IIIA and IIIB, respectively. When it became apparent that ^{13}C nmr spectroscopy could not yield the cyclopropane ring configurations of IIA, IIIA, and IIIB, we resorted to single-crystal *X*-ray analysis for unequivocal proof of structure and stereochemistry.

Crystal Data : (IIA), $C_{27}H_{46}O_2$, m.p. 174 °C (from acetone-MeOH), M = 402.7, Orthorhombic, a = 15.062(7), b = 20.364(10), c = 8.249(4) Å, U = 2530.2 Å^3, Z = 4, D_c = 1.057 g cm^{-3}, space

group $P2_12_12_1$. (IIIA), $C_{27}H_{44}O$, m.p. 154-155 °C (from acetone-MeOH), M = 384.7, Monoclinic, a = 7.685(4), b = 6.578(4), c = 24.148(11) Å, β = 96.57(3)°, U = 1212.7 Å^3, Z = 2, D_c = 1.053 g cm^{-3}, space group $P2_1$. (IIIB), $C_{27}H_{44}O$, m.p. 103 °C (from acetone), M = 384.7, Monoclinic, a = 7.888(5), b = 8.441(5), c = 18.884(10) Å, β = 91.47(4)°, U = 1256.9 Å^3, Z = 2, D_c = 1.016 g cm^{-3}, space group $P2_1$. Intensity data to θ = 67° were recorded for each compound on an Enraf-Nonius CAD-3 automated diffractometer (Ni-filtered Cu-K_α radiation, λ = 1.5418 Å) by use of the θ-2θ scanning procedure. All three crystal structures were solved by direct methods using MULTAN.[7] Atomic positional[8] and thermal parameters (anisotropic C, O; isotropic H) were refined by full-matrix least-squares calculations to R 0.071 (IIA), 0.067 (IIIA), and 0.070 (IIIB), over 1694, 2051, and 1143 statistically-significant [$I > 2.0\sigma(I)$] reflections.



The carbon shifts of IIA, IIIA, and IIIB were assigned on the basis of the chemical shifts of cholesterol[9] and from the results of relaxation and deuteration studies (Table 1). Whereas a carbon shift analysis of IB (as its 3β-acetate equivalent) had revealed that at -60 °C to above room temperature its ten-membered ring exists in two solution conformations;[10] one identified by *X*-ray analysis as the crystalline state conformer (IB as its 3β-*p*-bromobenzoate equivalent),[10] the ^{13}C nmr spectra of IIIA and IIIB now were found to be temperature independent from -120 to 30 °C, thereby indicating the existence of either one large-ring conformer or a conformer mixture equilibrating with a low energy barrier. The close similarity of the chemical shifts of IIA and IIIA, except for carbons in the vicinity of C(10), showed that these compounds possessed the same solution conformation. Introduction of β-effects by the C(10) substituents in IIA caused deshielding of C(1) and C(9) with respect to IIIA.[11]

Table 1. ^{13}C NMR Chemical Shifts and Relaxation Times of IIA, IIIA, and IIIB[a]

	IIA[b]		IIIA[c]		IIIB[d]			IIA[b]		IIIA[c]		IIIB[d]	
	δ	T_1	δ	T_1	δ	T_1		δ	T_1	δ	T_1	δ	T_1
C(1)	33.5	0.36	28.6	0.47	22.0	0.29	C(15)	23.6	0.20	24.4	0.25	24.4	0.17
C(2)	8.6	0.19	11.4	0.28	10.3	0.16	C(16)	27.7	0.57	28.3	0.32	28.5	0.15
C(3)	16.9	0.36	25.4	0.48	19.3	0.25	C(17)	56.1	0.38	56.9	0.52	56.5	0.30
C(4)	47.8	0.19	48.8[e]	0.27	48.9	0.18	C(18)	12.0	1.13	12.2	0.78	12.0	0.77
C(5)	211.1		211.7		211.4		C(19)	15.6	0.37	101.4	0.23	105.5	0.13
C(6)	35.2	0.19	34.9[e]	0.28	43.4	0.16	C(20)	35.6	0.38	35.6	0.49	35.8	0.30
C(7)	23.8	0.17	28.0	0.32	31.0	0.16	C(21)	18.4	0.58	18.5	0.54	18.5	0.44
C(8)	37.7	0.37	42.6	0.50	35.6	0.29	C(22)	35.8	0.25	35.9	0.34	36.0	0.21
C(9)	53.1	0.37	49.9	0.52	53.1	0.27	C(23)	23.8	0.30	23.7	0.35	23.7	0.25
C(10)	73.6		153.3		153.6		C(24)	39.2	0.57	39.3	0.61	39.3	0.38
C(11)	23.8	0.19	23.7	0.35	28.0	0.17	C(25)	27.7	0.57	27.9	0.68	27.8	0.80
C(12)	39.9	0.18	40.1	0.28	39.8	0.17	C(26)	22.4	1.08	22.5	0.74	22.5	0.90
C(13)	42.9		43.2		43.1		C(27)	22.6	1.00	22.7	0.74	22.7	0.86
C(14)	53.4	0.37	53.2	0.51	55.8	0.31							

[a]Shifts in ppm downfield from TMS; δ(TMS) = δ($CDCl_3$) + 76.9 ppm. Relaxation times in seconds; [b]150 mg/0.4 ml $CDCl_3$; [c]90 mg/0.4 ml $CDCl_3$; [d]140 mg/0.4 ml $CDCl_3$; [e]Signal disappeared on deuteration.

Despite the large chemical shift differences between the corresponding carbon centers in the bicyclo[7.1.0]decanone systems in IIIA and IIIB, configurational assignments proved to be impossible in the absence of independent knowledge of the cyclononanone ring conformations. The results of the *X*-ray analyses not only establish the nature of the fusions of the three- and nine-membered rings in these products to be as shown, but they also furnish details of the solid-state conformations which, in turn, permit evaluation of the carbon chemical shifts in conformational terms. The cyclononanone rings are characterized by endocyclic torsion angles

$\omega_{1,3}$ -135, $\omega_{3,4}$ 70, $\omega_{4,5}$ -33, $\omega_{5,6}$ 75, $\omega_{6,7}$ -150, $\omega_{7,8}$ 57, $\omega_{8,9}$ 50, $\omega_{9,10}$ -78, and $\omega_{1,10}$ 103° in IIA with corresponding values of -127, 80, -47, 86, -149, 59, 47, -91, and 107° in IIIA, and 129, -61, -45, 71, 53, -142, 57, 33, and -100° in IIIB. Thus, the nine-membered rings in IIA and IIIA have very similar conformations which approximate to twist-chair-chair[12] (C_2) forms with the two-fold axis passing through C(8) and the mid-point of the C(3)-C(4) bond, whereas in IIIB the corresponding ring is best considered as a distorted chair-boat (C_s) form in which a mirror plane of symmetry passes through C(9) and the mid-point of the C(4)-C(5) bond. The conformations found in the solid state indicate that intramolecular non-bonded interactions, *i.e.* γ-effects would be expected between C(6) and C(9), C(6) and C(14), C(11) and C(19) in IIIA as well as between C(2) and C(8) in IIIB. The observed shielding of C(6), C(9), C(11), C(14), and C(19), and deshielding of C(2) and C(8) of IIIA compared to IIIB thus attest to the fact that the solid-state conformations of these compounds also represent their spatial orientation in solution.

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