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The Stereochemistry of (+)-Occidentalol. Further Support for the Revised Structure

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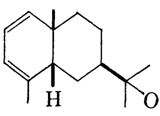
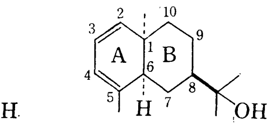
(+)-Occidentalol, an eudalene-type sesquiterpene alcohol isolated from the heartwood of *Thuja occidentalis* L., has been shown[1] to possess *cis* ring-fusion[2] and a 1,3-diene system. The optical rotatory dispersion (ORD) study[3,4] of its related compounds has led to the acceptance of structure **1** of two structures **1** and **2** possible for (+)-occidentalol. However, recently the structure has been revised to **2** on the basis of nuclear magnetic resonance (NMR) spin-decoupling[5] and synthesis[6] of the antipode of (+)-occidentalol from α-santonin. We now wish to present additional evidence supporting absolute configuration (**2**), and to describe the conformational study of (+)-occidentalol and its dehydration products (**5**) and (**6**) by circular dichroism (CD) measurements at various temperatures.



1



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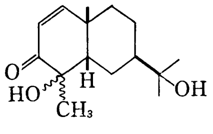
Results and Discussion

Further Support for the Absolute Configuration of (+)-Occidentalol. According to Mislow's suggestion,[3]



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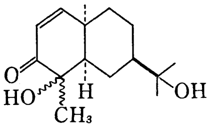
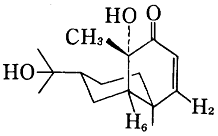
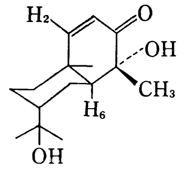


4

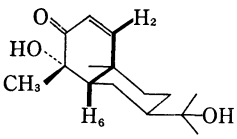
the structure possible for (+)-5-hydroxy-8-(1-hydroxy-1-methylethyl)-1,5-dimethylbicyclo-[4.4.0]-2-decen-4-one[7] derived from (+)-occidentalol may be **3** or **4**, each of which can take two possible conformations **3a** and **3b**, and **4a** and **4b**. The infrared spectrum of the α′-hydroxy-α,β-unsaturated ketone in the hydroxyl-stretching region indicated four absorption bands at 3635 (ε 34), 3622 (ε 66), 3592 (ε 80), and 3490 cm^{-1} (ε 6) in 0.0042M carbon tetrachloride solution. The two high-frequency bands can be attributed to free hydroxyl stretching due to the hydroxyisopropyl group and the hydroxyl group at C-5. The third band was assigned to the $\mathrm{OH}\cdots\pi$ intramolecularly-interacted hydroxyl group and the fourth to the $\mathrm{OH}\cdots\mathrm{O}$ interacted hydroxyl group adjacent to the carbonyl group.[8] Since the A-ring of the four conformers has been postulated to exist in the most stable half chair conformation,[9] the hydroxyl group at C-5 should be in the axial orientation and will easily form the $\mathrm{OH}\cdots\pi$ hydrogen bond. Accordingly, in the conformational equilibrium between **3a** and **3b** and between **4a** and **4b**, conformers **3a** and **4a** may be expected to predominate because they suffer the less 1,3-diaxial interaction.



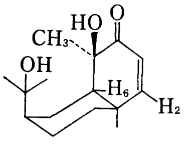
3a



3b



4a



4b

Long range coupling of the W or the M type[10] between H-2 and H-6 may be expected for **4a**, since the H-2, C-2, C-1, C-6, and H-6 portion of this conformer is in a coplanar zigzag spatial arrangement; this is not the case for the conformer (**3a**). The NMR spectrum (60 MHz) of compound **4** showed the characteristic resonance pattern for olefinic protons of H-2 and H-3 at 6.59 and 5.95 ppm respectively. Upon irradiation of the signal due to H-6 at 1.82 ppm, the spin-coupling pattern due to H-2 at 6.59 ppm (dd, $J_{2,3}$=10.5 Hz and $J_{2,6}$=2.0 Hz) was transformed to a doublet ($J_{2,3}$=10.5 Hz). This observation of the long range coupling ($J_{2,6}$=2.0 Hz) indicates that the compound (**4**) exists in the preferred conformation (**4a**).

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[9] E. Toromanoff, "Topics in Stereochemistry," Vol. 2, ed. by N. L. Allinger and E. L. Eliel, Interscience Publishers, New York (1967), p. 157.

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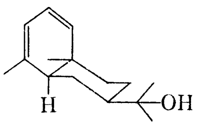
Table 1. The percentage change of molecular ellipticity of compounds **2**, **5**, and **6** in the MI solvent and decalin

Compds.	MI solvent[a)]			Decalin		
	$[\theta](\lambda_{max})\times10^{-4}$ at 25°C (T_2)	$[\theta]$ $(\lambda_{max})\times10^{-4}$ at -180 ± 2°C (T_1)	$I^{T_1}_{T_2}$	$[\theta]$ $(\lambda_{max})\times10^{-4}$ at 143 ± 1°C (T_2)	$[\theta]$ $(\lambda_{max})\times10^{-4}$ at 25°C (T_2)	$I^{T_1}_{T_2}$
2	6.10	6.65	− 8.3	6.21	6.61	− 6.1
5	5.16	6.19	−16.6	4.53	5.60	−19.1
6	7.49	8.81	−15.0	6.32	7.76	−18.6

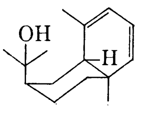
a) The MI solvent is composed of methylcyclohexane–isopentane in the ratio 1:3 by volume.

This further supports the revised absolute configuration of (+)-occidentalol (**2**).

The Conformation of (+)-Occidentalol (2) and Its Dehydration Products (5) and (6). (+)-Occidentalol (**2**) may take two possible preferred conformations (**2a**) and (**2b**). The diene system of the conformer (**2a**) is skewed in the sense of a right-handed helix, whereas the system of **2b** in the sense of a left-handed helix. The helicity rule[11)] predicts a positive Cotton effect for the conformer (**2a**) and a negative one for the conformer (**2b**). The CD curve of **2** exhibited a positive Cotton effect at 25°C, keeping the sign with the same rotational strength as above in a range of +140 to −180°C. The percentage change of molecular ellipticity[12)] expressed as $I^{T_1}_{T_2}=([\theta](T_2)-[\theta](T_1))\times100\%/[\theta](T_1)$ is small, being almost within the deviation (6.1%) (Table 1). The result indicates the predominance of the conformer (**2a**). Furthermore, the population of the conformer (**2a**) is deduced to be more than 99% at room temperature,[13)] because the difference between the conformational energies of **2a** and **2b** is more than 3.85 kcal/mol, as estimated by summation of the conformational energies of the methyl (1.70 kcal/mol)[14)] and the isopropyl (2.15 kcal/mol)[14)] groups.



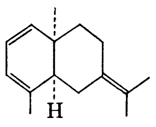
2a



2b

Additional evidence in favor of the stability of the conformer (**2a**) was obtained by means of the NMR spectrum of the three olefinic protons H-2 (5.21 ppm), H-3 (5.74 ppm), and H-4 (5.49 ppm), and the H-6 proton (1.65 ppm), at various temperatures. The spectrum showed the same spin-coupling pattern[5)] at +50, −10, and even −60°C in deuterochloroform.

The dehydration products, (**5**) and (**6**), of occidentalol can exist in two interconvertible conformations (**5a**) and (**5b**), and (**6a**) and (**6b**), respectively, where the A-ring of the conformers (**5a**) and (**6a**) has a skewed diene system in the sense of a right-handed helix, whereas the diene system of the conformers (**5b**) and (**6b**) is skewed in a left-handed helix. The temperature-dependence of the CD curve of these compounds (Table 1) showed the presence of the conformational equilibrium between **5a** and **5b** and between **6a** and **6b**, since the percentage change of the molecular ellipticity for these compounds are about two times as large as that of **2**. The increase in the positive rotational strength with a lowering of the temperature indicated the predominance of the conformers (**5a**) and (**6a**).



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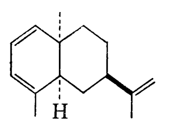

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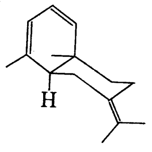
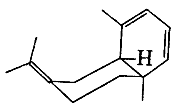
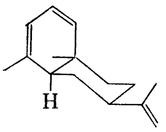


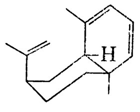
5a



5b



6a



6b

Experimental

(+)-Occidentalol (2). The same sample of (+)-occidentalol as described in the previous report[2)] was used.

Dehydration of (+)-Occidentalol (2). *8-Isopropylidene-1,5-dimethylbicyclo[4.4.0]-2,4-decadiene (5):* To the solution of 0.3 g of (+)-occidentalol in 6 m*l* of pyridine was added dropwise phosphorus oxychloride (0.6 m*l*), and the mixture was left to stand at 5—10°C for 5 hrs and then treated in the usual way. The oily product (0.23 g) obtained was separated into two fractions by column-chromatography on silica-gel (Merck Kieselgel G, less than 0.08 mm) impregnated with 20% (w/w) silver nitrate. The first fraction gave the dehydration product (**5**) as a viscous oil: $[\alpha]^{25}_{D}$ +698° (*c* 0.034, EtOH); λ_{max} (EtOH) 269 nm (ε 4720); δ ($CDCl_3$) 0.82 (s, 3H, methyl), 1.63 (s, 6H, two vinylic methyls), 1.76 (s, 3H, vinylic methyl), 5.32 (d, *J*=9.0 Hz, 1H, vinyl), 5.55 (b, 1H, vinyl), and 5.85 ppm (dd, *J*=9.0 and 5.0 Hz, 1H, vinyl).

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*8-Isopropenyl-1,5-dimethylbicyclo[4.4.0]-2,4-decadiene (**6**)*: The second fraction gave the dehydration product (**6**) as a viscous oil: $[\alpha]_D^{25}$ +674° (c 0.036, EtOH); ν_{max} (liq. film) 3100, 1645, 1586, 892, and 735 (vinyl) cm^{-1}; λ_{max} (EtOH) 265 nm (ε 4920); δ ($CDCl_3$) 0.84 (s, 3H, methyl), 1.63 (d, J=1.0 Hz, 3H, vinylic methyl), 1.74 (d, J=1.0 Hz, vinylic methyl), 4.63 (s, 2H, vinyl), 5.25 (d, J=9.0 Hz, 1H, vinyl), 5.55 (b, 1H, vinyl), and 5.80 ppm (dd, J=9.0 and 5.0 Hz, 1H, vinyl).