Stereochemical Studies of Monoterpene Compounds. XIV.[1] The Rotational Conformation of the Acetyl and the Formyl Groups of Monoterpene α,β-Unsaturated Carbonyl Compounds

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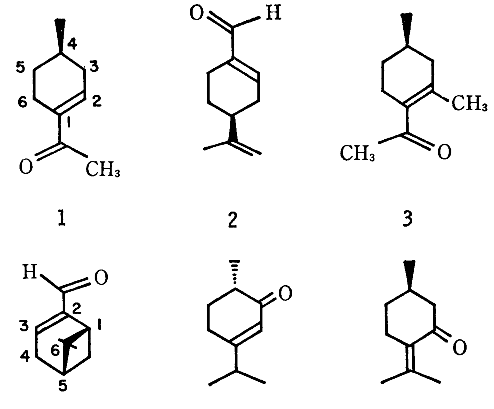
Temperature-dependent circular dichroism measurements in the n-π^* transition enabled us to predict the preferred rotational conformation of the acetyl and the formyl groups of such monoterpene α,β-unsaturated carbonyl compounds as (+)-1-acetyl-4-methylcyclohexene (**1**), (−)-perillaldehyde (**2**), (+)-1-acetyl-2,4-dimethylcyclohexene (**3**), and (−)-myrtenal (**4**).

The geometry of α,β-unsaturated carbonyl compounds has been determined by means of studying the IR, the UV,[2] and the NMR spectra[3] and by dipole-moment measurements.[4] The temperature-dependent circular dichroism (CD) has recently been found to be useful for studying quantitatively the conformational alteration of optically-active, flexible cyclohexanone derivatives.[5] The conformational analysis of α,β-unsaturated carbonyl compounds, particularly flexible ones, is important, because the conformation of the compounds can be expected to affect their chemical reactivity and physicochemical properties. However, only one attempt[6] to make a conformational study of flexible α,β-unsaturated carbonyl compounds has been made. We now wish to deal with the rotational conformation of the acetyl and the formyl groups of four monoterpene α,β-unsaturated carbonyl compounds, (+)-1-acetyl-4-methylcyclohexene (**1**), (−)-perillaldehyde (**2**), (+)-1-acetyl-2,4-dimethylcyclohexene (**3**), and (−)-myrtenal (**4**). The present study was undertaken on the basis of the temperature-dependent circular dichroism and on the basis of the rule[7] of the correlation between the chirality of an enone system and its sign of a Cotton effect for the n-π^* transition.



The absolute configuration of the α,β-unsaturated carbonyl compounds used.

Results and Discussion

For the compounds (**1**), (**2**), and (**3**), but not (**4**), both the conformational exchange of the cyclohexene ring and the rotational conformation of the carbonyl group are suspected to be important factors directly affecting the CD curve. However, since the cyclohexene ring substituted with the bulky group would exist in a stable half-chair conformation,[8] the change in the rotational strength depending on the temperature should be considered to indicate truly the equilibrium of the rotational conformation.

The acetyl group of the compound (**1**) can exist in the *s-trans* or the *s-cis* geometry, which may be stabilized by the orbital overlap interaction of the carbonyl and the ethylenic double donds. The geometry of α,β-unsaturated carbonyl compounds can be elucidated by means of the frequency difference and the intensity ratio between the C=O and the C=C stretching bands in the IR spectrum and by means of the molecular extinction coefficient of the π-π^* transition in the UV spectrum. The compound (**1**) was identified as taknig preferentially the *s-trans* geometry on the basis of the similarity of its values to those of the representative, *s-trans* α,β-unsaturated ketone, (−)-carvenone (**5**) (Table 1). The CD curve of **1** exhibited a positive Cotton effect with a fine structure in the region of the n-π^* transition (Fig. 1). The positive rotational strength was increased linearly with a lowering of the temperature. This observation can be explained in terms of the rotational conformations of the acetyl group. This group may be not coplanar with the ethylenic double bond, but may be rotated out of the plane. Accordingly, the compound (**1**) can exist in two possible rotational conformations, **1a** and **1b** (Fig. 2). Since the octant projection diagram predicts a positive Cotton effect for **1a** and a negative one for **1b**, the temperature-dependency of the CD curve indicated the predominancy of **1a** in the conformational equilibrium between **1a** and **1b**.

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TABLE 1. IR AND UV SPECTRAL DATA OF THE α,β-UNSATURATED CARBONYL COMPOUNDS

Compound	IR[a]				UV[b]	
	$\nu_{C=O}$ (cm^{-1})	$\nu_{C=C}$ (cm^{-1})	$\nu_{C=O}-\nu_{C=C}$ (cm^{-1})	ri(C=O/C=C)[c]	λ_{max} (nm)	ε
1	1674	1652	22	2.4	233.5	14,720
2	1688	1652	36	2.3	232	15,120
3	1685	1619	66	0.9	248	6,340
4	1678	1622	56	3.2	239[d]	8,700
5	1681	1637	44	2.5	235	16,950
6	1691	1614	77	0.7	252.5	8,020

a) In liquid film. b) In ethanol. c) Relative intensity. d) In isooctane.

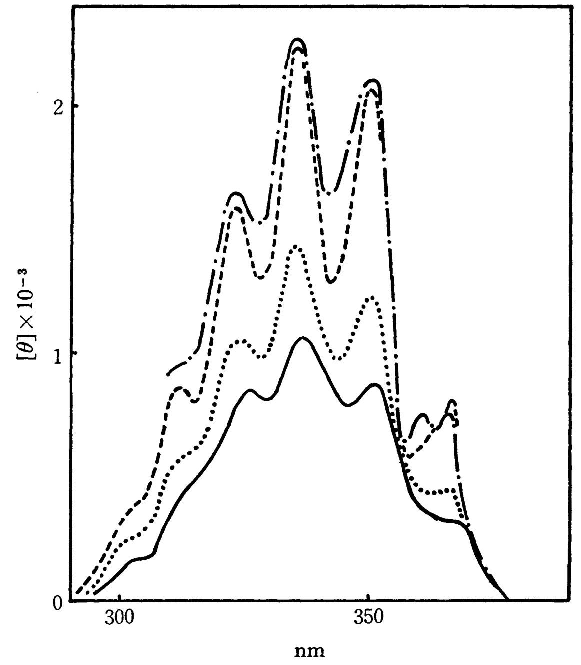
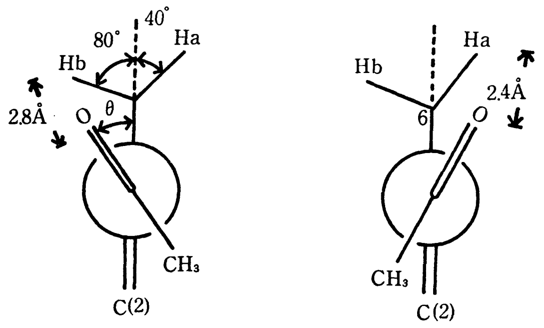
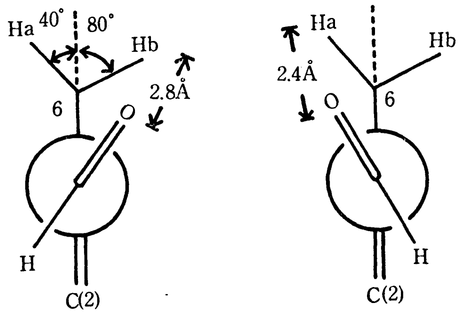


Fig. 1. CD curves of compound **1**: ——, at 25°C, ······, at −26°C, ----, at −127°C, and —·—, at −186°C in MI solvent.



1a **1b**

Fig. 2. The preferred rotational conformation of the acetyl group of compound **1**.



2a **2b**

Fig. 3. The preferred rotational conformation of the formyl group of compound **2**.

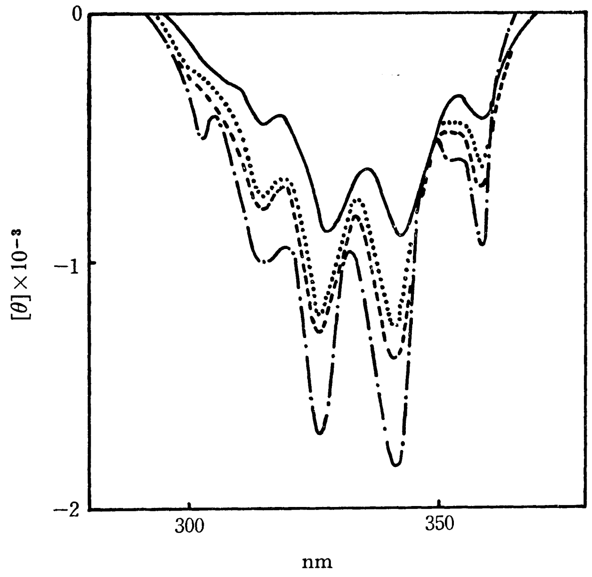
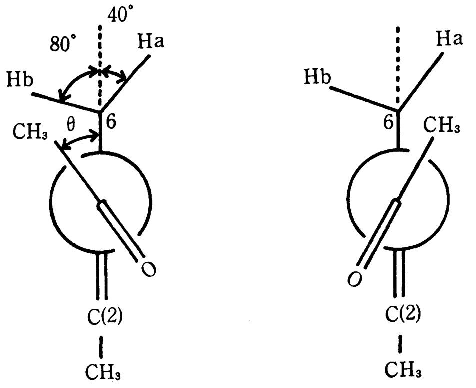


Fig. 4. CD curves of compound **2**: ——, at 25°C, ······, at −25°C, ----, at −76°C, and —·—, at −115°C in MI solvent.

For the compound (**2**), the **2a** and **2b** conformations (Fig. 3) with the skewed *s-trans* geometry may be favored, as has been discussed above. The temperature-dependency of the CD curve (Fig. 4) showed the presence of the conformational equilibrium between **2a** and **2b**, with a negative and a positive Cotton effect respectively. The increase in the negative rotational strength with the lowering of the temperature indicated the predominance of the **2a** conformer.

According to the Dreiding Model, two allylic hydrogen atoms, (Ha) and (Hb), at the C-6 position are located dissymmetrically in relation to the plane of the ethylenic double bond, keeping the angles of 40 and 80° respectively (Figs. 2 and 3). For the **1b** and **2b** conformers, accordingly, the internuclear distance (2.4 Å) between the Ha and the oxygen atom of the carbonyl group is shorter than the sum of the van der Waals radius[9] of the hydrogen atom (1.2 Å) and that of the oxygen atom (1.4 Å). On the other hand, the distance between the Hb and the oxygen atom is 2.8 Å for the **1a** and **2a** conformers. These conformers suffer no van der Waals interaction. Thus, the similarity of the temperature-dependent CD curve of the compound (**1**) to that of the compound (**2**) seems to indicate that the bulkiness of the alkyl group (the hydrogen atom or the methyl group) of the carbonyl side chain does not significantly affect the rotational conformation.

The similarity of the IR and the UV spectral data of the compound (**3**) (Table 1) to those of (+)-pulegone (**6**) with a *s-cis*, α,β-unsaturated ketone moiety suggests **3a** and **3b** with a skewed *s-cis* geometry (Fig. 5), as the preferred conformation of **3**. From the discussion, compared with the compound (**1**), it seems that the steric hindrance of the methyl group at C-2 could enable the compound (**3**) to take the preferred conformation with the *s-cis* moiety. According to the octant projection diagram, a positive Cotton effect can be predicted for **3a**, and a negative one, for **3b**. The CD curve of the compound (**3**) exhibited a weak negative Cotton effect at 25°C. However, with a lowering of the temperature, a strong positive curve appeared in the long-wavelength region at the expense of the negative one (Fig. 6). This result suggests the predominance of the **3a** conformer. This is supported by the fact that the dihedral angle, θ, of the the compound (**3**) between the plane of the ethylenic double bond and that of the carbonyl double bond is larger than that of the compounds (**1**) and (**2**), because the van der Waals radius of the methyl group (2.0 Å) is larger than that of the oxygen atom.



3a **3b**

Fig. 5. The preferred rotational conformation of the acetyl group of compound **3**.

As is shown in Table 1, the IR and the UV spectral data of the compound (**4**), except for the value of the relative intensity, showed an intermediate value between those of the compounds (**5**) and (**6**). This seems to imply that the formyl group may exist in an equilibrium between the *s-trans* and the *s-cis* forms. For the compounds (**1**) and (**2**), however, the conformation with the *s-trans* geometry must be predominant over that with *s-cis*, as has been described above. In addition, it has been pointed out[10,11] that, for butadiene, the *s-trans* form is more stable than the *s-cis* one because of the unfavorable arrangement of the pi orbitals of the latter. Accordingly, the **4a** and **4b** conformations with the skewed *s-trans* geometry are favored for the compound (**4**) (Fig. 7). A positive Cotton effect can be predicted for the **4a** conformer and an opposite one for the **4b** conformer. Actually, the CD curve of **4** exhibited a positive Cotton effect at room temperature. This seems to indicate the preference of the **4a** conformer. However, the compound (**4**) showed unusual variable-temperature CD curves; with a lowering of the temperature, the positive rotational strength in the shorter-wavelength region increased, together with the negative one in the longer-wavelength region (Fig. 8). This indicates the existence of an equilibrium containing more than two rotational conformations, which is considered to show that the conformer population of **4a**, together

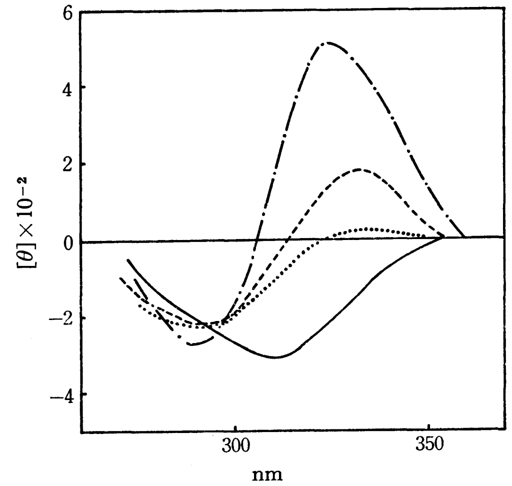
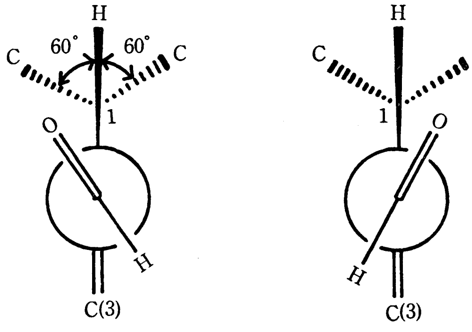


Fig. 6. C.D. curves of compound **3**: ——, at 25°C, ······, at −57°C, ----, at −136°C, and —·—, at −190°C in MI solvent.



4a **4b**

Fig. 7. The preferred rotational conformation of the formyl group compound **4**.

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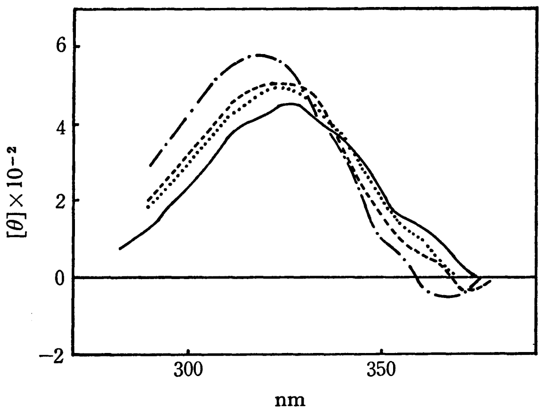

Fig. 8. CD curves of compound **4**: ——, at 25°C, ······, at −27°C, ----, at −92°C, and —·—, at −184°C in MI solvent.

with that of **4b**, increased at the expense of the *s-cis* form. This can be explained by the symmetry of the spatial arrangement of the allylic carbon-carbon single bonds at the C-1 position to the planes of C-1, C-2, and C-3, a symmetry resulting from the insertion of a cyclobutane ring into the cyclohexene ring, as has been shown in the cases of **4a** and **4b**. Thus, the stabilities of the **4a** and **4b** conformers are nearly equal.

For the cyclohexene derivatives, thus, the predominance of the conformation has been concluded to depend on the dissymmetry on the allylic carbon of the ethylenic double bond.

Experimental

Measurements. The temperature-dependent CD curves were measured by means of a Japan Spectroscopic Co., Ltd., automatically-recording spectropolarimeter, Model ORD/UV-5, equipped with a CD attachment in the MI solvent (methylcyclohexane - isopentane, 1 : 3 by volume) and in the EPA solvent (ether - isopentane - ethanol, 5 : 5 : 2 by volume), using a variable temperature CD cell designed and constructed by the authors.

Materials. (+)-*1-Acetyl-4-methylcyclohexene (**1**)*: (−)-10-Nor-8-oxomenthol[12] was treated with a mixture of hydrochloric acid and ethyl alcohol (1 : 4 by volume) overnight to convert it to **1**. The crude oil was then refined by column chromatography over silica gel. The compound (**1**) (100% pure by analytical glc) thus obtained showed the following properties: bp 84.0—85.0°C/5 mmHg, n_D^{25} 1.4786, d_4^{25} 0.9384, $[\alpha]_D^{25}$ +184.4° (neat); NMR δ($CDCl_3$, 60 MHz) 0.98 (d, J=6 Hz, $-CH-C\underline{H}_3$), 2.15 (s, $-CO-C\underline{H}_3$), 6.64 ppm (m, $-C{=}C\underline{H}-$).

(−)-*Perillaldehyde (**2**)*: A commercial sample was purified by distillation to give a 99.0% pure compound (**2**), which showed the following properties: bp 89.0—90.0°C/9 mmHg n_D^{25} 1.5036, d_4^{25} 0.9610, $[\alpha]_D^{25}$ −126.5° (neat).

(+)-*1-Acetyl-2,4-dimethylcyclohexene (**3**)*: The compound (**3**) was synthesized from (+)-isopulegone (bp 96.0-96.5°C/14 mmHg, n_D^{25} 1.4715, d_4^{25} 0.9745, $[\alpha]_D^{25}$ +9.65° (neat); 90% pure by analytical glc) by the Grignard reaction, followed by ozonization and the dehydration with thionyl chloride. Column chromatography over silica gel impregnated with 15% (v/v) silver nitrate gave a compound (**3**) with the following properties: bp 64.0°C/4 mmHg, $[\alpha]_D^{25}$ +119.0° (c 0.185, ethanol); NMR δ($CDCl_3$, 60MHz) 0.96 (d, J=6 Hz, $-CH-C\underline{H}_3$), 1.80 (s, $-C{=}C-C\underline{H}_3$), 2.11 ppm (s, $-CO-C\underline{H}_3$).

(−)-*Myrtenal (**4**)*: Following the method in the literature,[13] the oxidation of β-pinene, bp 164.0°C/760 mmHg, n_D^{25} 1.4782, d_4^{25} 0.8692, $[\alpha]_D^{25}$ −19.9° (neat), with selenium dioxide gave a crude compound (**4**), which was then subjected to column chromatography. The pure sample (100% pure by the analytical glc) showed the following properties: bp 58.5°C/4 mmHg, n_D^{25} 1.5002, d_4^{25} 0.9845, $[\alpha]_D^{25}$ −15.8° (neat).

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