The Stereochemistry and the Circular Dichroism of Several Pinane Derivatives[1]

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The optical rotatory dispersion and the circular dichroism curves were measured for some bicyclo[3.1.1]-heptane derivatives. The applicability of the octant rule to a bicyclo[3.1.1]heptane system was discussed in connection with its preferred conformation; the conformation was determined on the basis of nuclear magnetic resonance spectrum measurements.

Some questions[3-7] have arisen as to the application of the octant rule to the optical rotatory dispersion (ORD) and the circular dichroism (CD) measurements of a pinane system. A combination of the examination of molecular models and physico-chemical study has suggested[8-10] that the preferred conformation of pinane derivatives differ from the chair conformation of an unstrained cyclohexane ring because of the strain caused by the cyclobutane ring. From this point of view, the author now wishes to study the applicability of the octant rule to a bicyclo[3.1.1]heptane system, as well as the preferred conformation of several pinane derivatives.

Results and Discussion

The Preferred Conformation. The preferred conformations of several pinane derivatives were determined on the basis of the anisotropic effect[11-13] of the carbonyl group in the NMR spectrum by comparing the chemical shifts of the sample with those of the corresponding carbonyl-free compound. The conformers, **1a** and **1b**, are proposed as the preferred conformations for (−)-10β-pinan-3-one (**1**). A large upfield shift may be predicted for the C-9 methyl group of **1a**, whereas a downfield one may be predicted for that of **1b**, as is shown in Fig. 1. The signal of the C-9 methyl resonance shows the upfield shift of 0.12 ppm, when the chemical shift of the ketone (**1**) is substracted from that of 10β-pinane (**2**). This fact indicates that **1a** is the preferred conformation of the ketone (**1**). Similarly, the anisotropic effect of the C-9 methyl resonance (Table 1) indicates that the preferred conformations of 10α-pinan-3-one (**3**), 2α-hydroxy-10β-pinan-3-one (**4**), 4α-hydroxy-10α-pinan-3-one (**5**), 4β-acetoxy-10β-pinan-4-one (**8**), 3β-acetoxy-10α-pinan-4-one (**9**), 3β-methylnopinone (**10**), 10β-pinan-4-one (**11**), and nopinone (**12**) are **3a**—**12a** respectively, as is shown in Figs. 2 and 3.

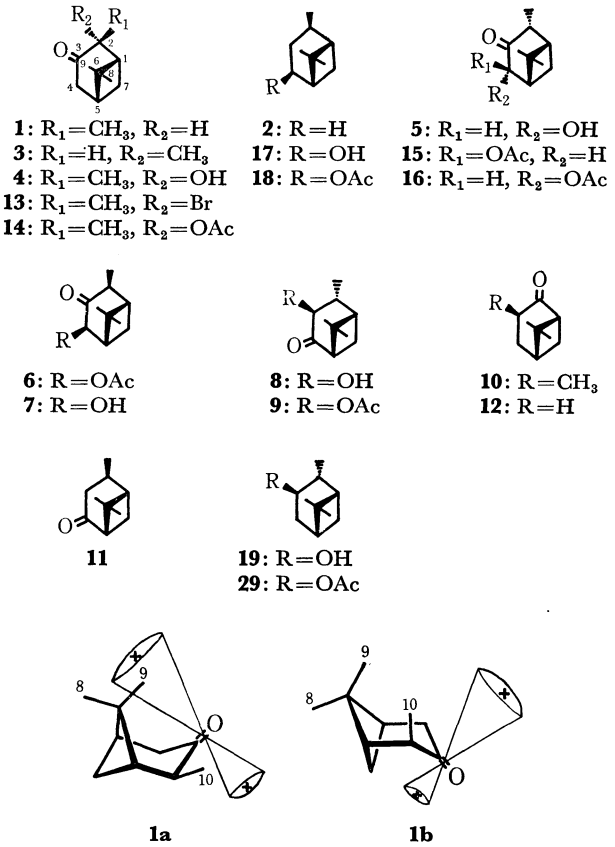

Fig. 1. Possible preferred conformations and predicted anisotropic effect of the carbonyl group for the ketone (**1**).

The proposed preferred conformations were further examined by studying the solvent effect[14-16] of the NMR spectrum. As a general rule, Δ values are positive for protons lying at the back of a reference plane and negative for protons lying in front of the

1) This paper forms Part XX[2] in the Hiroshima University series on "Stereochemical Studies of Monoterpene Compounds." A part of this work has been read at the 23rd Anuual Meeting of the Chemical Society of Japan, Tokyo, April, 1970.

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Table 1. Anisotropic effects of the carbonyl group for methyl group

Compd.	$\Delta\delta$ reference[a]-ketone (ppm)		
	C-8	C-9	C-10
1	−0.13	+0.12	−0.15
3	−0.15	−0.08	−0.18
4	−0.11	+0.07	−0.05
5	−0.15	−0.22	−0.12
6	−0.10	+0.18	−0.16
7	−0.10	+0.30	−0.13
8	−0.17	+0.16	−0.24
9	−0.17	+0.09	−0.18
10	−0.17	+0.07	—
11	−0.16	−0.01	−0.16
12	−0.16	−0.01	—

a) The reported value[8,10,17,18] for methyl signals of 10β-pinane, 10α-pinane, 2α-hydroxy-10β-pinane, 4α-hydroxy-10α-pinane, 3β-methylapopinane, and apopinane, was used as a reference value for the corresponding carbonyl compounds.

Table 2. Solvent effects of NMR spectra for methyl groups

Compd.	$\Delta\delta$ CCl_4–C_6H_6 (ppm)			$\Delta\delta$ CCl_4–C_5H_5N (ppm)		
	C-8	C-9	C-10	C-8	C-9	C-10
1	+0.27	+0.22	0.00	+0.17	+0.15	−0.02
3	+0.29	+0.32	+0.01	+0.17	+0.20	−0.01
4	+0.28	+0.28	−0.04	+0.11	+0.08	−0.25
5	+0.29	+0.34	+0.05	+0.11	+0.17	−0.07
6	+0.34	+0.06	+0.07	+0.14	−0.01	0.00
7	+0.29	+0.02	+0.06	+0.10	−0.20	−0.07
10	+0.34	+0.14	−0.03	+0.19	+0.08	−0.03
13	+0.47	+0.42	+0.05	+0.22	+0.18	−0.03
14	+0.35	+0.31	−0.19	+0.17	+0.12	−0.19
15	+0.35	+0.13	+0.26	+0.19	+0.05	+0.09

plane. The reference plane was supposed to go through the carbonyl carbon at right angles with the carbon-oxygen bond of the carbonyl group for a benzene-induced effect, and also through the α-position to the carbonyl group for a pyridine-induced effect. The C-10 methyl protons of ketones, **1**, **3**, **4**, **5**, **7**, **10**, and **13**, suffer only a small shift when the solvent is changed from carbon tetrachloride to benzene, and a downfield shift when a change of the solvent from carbon tetrachloride to pyridine (Table 2). These facts show that the C-10 methyl group of these compounds is equatorial. However, the preferred conformations of 4β-acetoxy-10β-pinan-3-one (**6**), 2α-acetoxy-10β-pinan-3-one (**14**), and 4β-acetoxy-10α-pinan-3-one (**15**) were not determined by means of the solvent effect only because of the disturbance caused by the acetoxyl group. The IR spectra of hydroxyketones, **5**, **7**, and **8**, showed, respectively, an intramolecularly hydrogen-bonded hydroxyl band at 3536, 3540, and 3514 cm^{-1}, assigned to the equatorial hydroxyl group. Although the preferred conformation of the acetate (**14**) was not assigned by these methods, the conformer (**14a**) may be proposed as the preferred conformation, because of the decrease in the steric hindrance of the C-10 methyl group and the stabilization by the dipole-moment of the acetoxyl and the carbonyl groups. In addition, since **4a** and **13a** are the preferred conformations for compounds **4** and **13**, respectively, similar to the compound (**14**), the conformer **14a** seems to be appropriate. On the other hand, conformations keeping the coplanarity of the C-1—C-5 atoms have been considered[6] to hold for pinane derivatives. The coplanar conformation can, however, be rejected on the grounds of the fact that the intramolecular hydrogen bonding is formed in the ketones, **5**, **7**, and **8**. No reason to consider the coplanar conformation for the other ketones has been given by the physico-chemical data.

The Application of the Octant Rule. In order to examine the applicability of the octant rule to a pinanone system, the present author prepared some pinane derivatives belonging to two groups as follows: (A) pinan-2- or 4-one, with the carbonyl group adjacent to the four-membered ring, and (B) pinan-3-one, with the carbonyl group at the symmetric position to the ring.

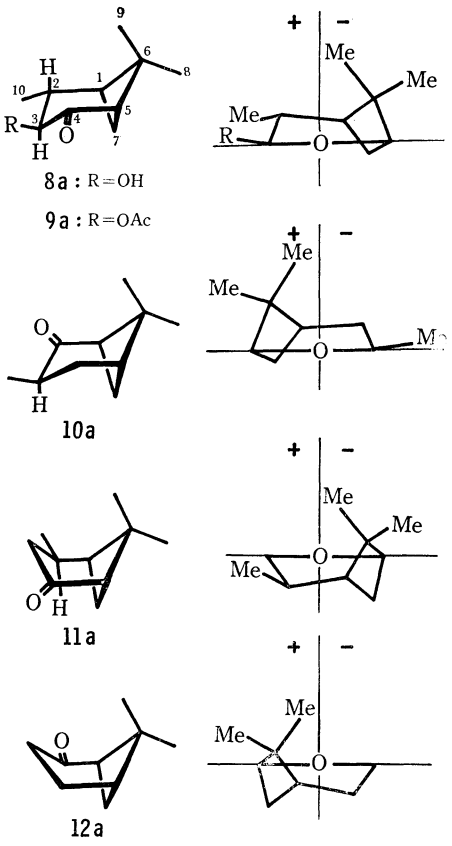

Fig. 2. Preferred conformations and octant projection diagrams for ketones (**8**), (**9**), (**10**), (**11**), and (**12**).

The compounds of the A group are the ketones, **8**, **9**, **10**, **11**, and **12**. Octant projection diagrams for the preferred conformation of these ketones are shown in Fig. 2. The diagrams indicate a large contribution of the C-6 *gem*-dimethyl group to the optical activity. The predicted Cotton effect is negative for **8a**, **9a**, and **11a**, but positive for **10a** and **12a**. Even if the preferred conformation of these compounds is coplanar, the same sign of a Cotton effect can be predicted.

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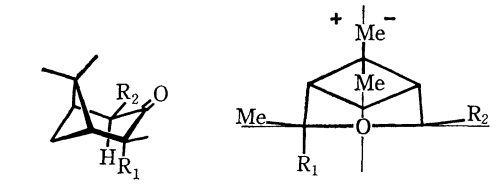
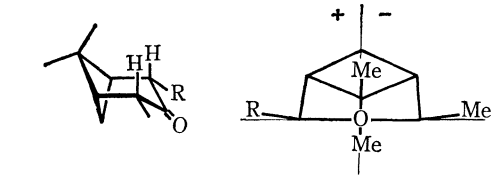
The ORD and the CD curves in both polar and nonpolar solvents showed a large, negative Cotton effect for **8**, **9**, and **11**, and a large, positive one for **10** and **12**. In addition, the same sign of a Cotton effect was observed for various-temperature CD curves in the EPA solvent[19] and in decalin. It was thus established that a Cotton effect for compounds of the A group is in good agreement with the predicted one obtained by applying the octant rule of the cyclohexanone pattern.



1a: R_1,R_2=H
4a: R_1=OH, R_2=H
6a: R_1=H, R_2=OAc

7a: R_1=H,R_2=OH
13a: R_1=Br, R_2=H
14a: R_1=OAc, R_2=H



3a: R=H
5a: R=OH

Fig. 3. Preferred conformations and octant projection diagrams for ketones (**1**), (**3**), (**4**), (**5**), (**6**), (**7**), (**13**), and (**14**).

On the other hand, the direct application of the octant rule to the ketones of the B group presented complicated problems. Octant projection diagrams of the conformers, **1a**, **3a**, **4a**, **5a**, **6a**, **7a**, **13a**, and **14a**, are shown in Fig. 3. The predicted Cotton effect is positive for **1a**, but negative for **3a**, **4a**, **13a**, and **14a**. A Cotton effect for **5a**, **6a**, and **7a** cannot be predicted, since the contribution of the hydroxyl and the acetoxyl groups to the optical rotation can not be compared

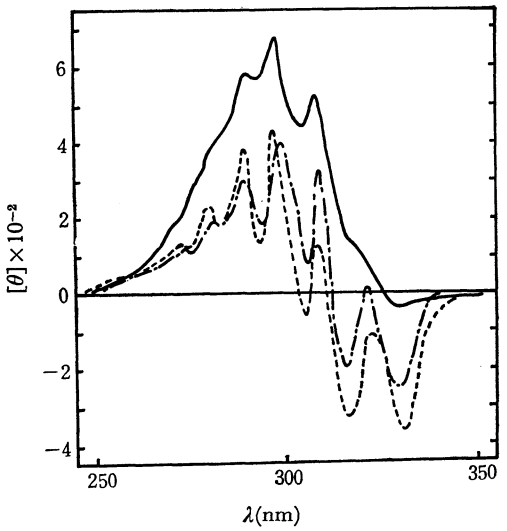
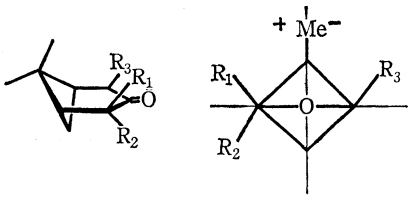


Fig. 4. CD curves of the ketone (**3**) in selected solvents at 25°C: ——, in MeOH; – – –, in isooctane; – – –, in CCl_4.

19) The EPA solvent is composed of ether–isopentane–ethanol in the ratio 5: 5: 2 by volume.



1b: R_1=CH_3; R_2,R_3=H
3b: R_1, R_3=H; R_2=CH_3
4b: R_1=CH_3, R_2=OH, R_3=H
6b: R_1=CH_3, R_2=H, R_3=OAc
13b: R_1=CH_3, R_2=Br, R_3=H
14b: R_1=CH_3, R_2=OAc, R_3=H

Fig. 5. Octant projection diagram for the coplanar conformer of ketones (**1**), (**3**), (**4**), (**6**), (**13**), and (**14**).

with that of the methyl group. The compound **1** showed a negative Cotton effect, while compounds **4** and **14** showed a positive one. The observed Cotton effect of these samples was not identical with the prediction. The bromoketone (**13**), however, showed a negative Cotton effect which coincides with the prediction. The ketone **3** in the nonpolar solvent exhibited a positive Cotton effect at a shorter wavelength and a weak negative effect at a longer one. However, the negative effect diminished in the polar solvent (Fig. 4). The CD curve of the ketone **3** at lower temperatures (Fig. 7) showed an increase in the positive strength of the shorter wavelength band and a decrease in the negative strength of the longer one; it is temperature-dependent. This double-humped Cotton effect may result from a solvation, because the $n\rightarrow\pi^*$ absorption of a solvated ketone generally appears at a shorter wavelength than that of an unsolvated one. In addition, octant projection diagrams for the coplanar conformations, (**1b**), (**3b**), (**4b**), (**6b**), (**13b**), and (**14b**), may be possible for the ketones **1**, **3**, **4**, **6**, **13**, and **14** respectively, as is shown in Fig. 5. The predicted Cotton effect was positive for **1b** and negative for **3b**, while the signs for **4b**, **6b**, and **14b** could not be predicted, because the rotational strength of the hydroxyl and the acetoxyl groups could not be estimated. A negative Cotton effect, however, was predicted for **13b**, since the bromine atom contributes to a larger extent to the optical rotational strength than the methyl group does. The ketone **15** may be at the equilibrium among the conformers **15a**⇌**15b**⇌**15c**, but the preferred conformation was not implied even by any physico-chemical data. However, all these con-

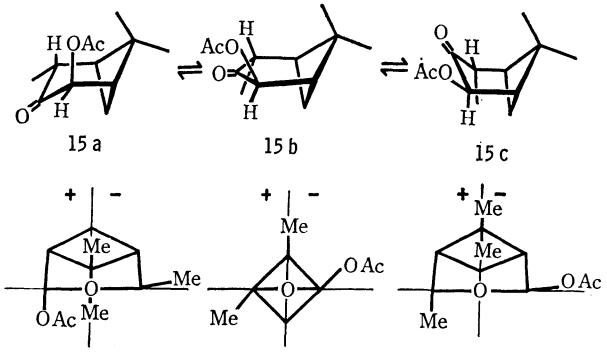


Fig. 6. Possible preferred conformations and octant projection diagrams for the ketone (**15**).

Table 3. Methyl proton signals of the pinane derivatives

Compd.	CCl_4			C_6H_6			C_5H_5N		
	C-8	C-9	C-10	C-8	C-9	C-10	C-8	C-9	C-10
1	1.33	0.90	1.16	1.06	0.68	1.16	1.16	0.75	1.18
3	1.35	0.92	1.05	1.06	0.60	1.04	1.18	0.72	1.06
4	1.35	0.88	1.29	1.07	0.60	1.33	1.24	0.88	1.54
5	1.37	1.00	1.06	1.08	0.66	0.99	1.26	0.83	1.13
6	1.33	0.93	1.21	0.99	0.87	1.13	1.19	0.94	1.21
7	1.32	0.86	1.20	1.03	0.84	1.14	1.22	1.06	1.27
8	1.37	0.74	1.23	0.97	0.62	1.05	1.21	0.83	1.26
9	1.38	0.81	1.15	0.92	0.68	0.92	1.18	0.79	1.08
10	1.34	0.71	1.11	1.00	0.57	1.14	1.15	0.63	1.14
11	1.36	1.02	1.17	1.03	0.80	0.89	1.17	0.88	0.98
12	1.34	0.86	—	1.02	0.65	—	1.14	0.72	—
13	1.41	0.91	1.93	0.94	0.49	1.88	1.19	0.73	1.96
14	1.37	0.86	1.49	1.02	0.55	1.68	1.20	0.74	1.68
15	1.35	0.95	1.14	1.00	0.82	0.88	1.16	0.90	1.05

These data are represented by the δ value in ppm.

formers are capable of predicting a negative Cotton effect, as is shown in Fig. 6. The ORD and CD curves of the compound **15** exhibited a positive Cotton effect; it is not identical with the prediction.

It was also observed that the amplitudes ([θ] *ca.* 300—2000 in methanol) of the CD curves for the B group are considerably small in comparison with those of the A group ([θ] *ca.* 3000—8000). This may be explained as follows: the symmetric skeleton of the compounds of the B group to their carbonyl group necessarily shows a relatively small contribution to the optical rotatory strength, whereas the *gem*-dimethyl bridge occupying unsymmetrically the compounds of the A group shows a large one. These facts suggest that the CD curves of the compounds of the B group are influenced easily by other factors, such as the temperature, the solvation, and the strain of the skeleton. Thus, these observations indicate the necessity of prudent care in the application of the octant rule to the pinan-3-one system.

Experimental

The NMR spectra were taken with a Varian Associates, HA-100 spectrometer, and a Hitachi Perkin-Elmer, R-20, High-resolution spectrometer on solutions in concentrations of 10 per cent, using tetramethylsilane as the internal standard. The signals of the C-8, C-9, and C-10 methyl protons of pinane derivatives are shown in Table 3. The ORD and the CD curves were measured on a Japan Spectroscopic Co., ORD/UV-5, Spectropolarimeter, equipped with a circular dichroism attachment, at 25°C. The variable-temperature CD curves were obtained by the use of the same spectrometer, using a low- and high-temperature cell. The IR spectra in the hydroxyl-stretching region were measured with a Perkin-Elmer, 621, Grating Infrared Spectrometer in a 0.002M carbon tetrachloride solution at a spectral slit-width of less than 2 cm^{-1} at 25°C, using a salt absorption cell 20 mm in length.

(−)-10β-Pinane-3-one (1). Following the procedure previously reported,[20] 20 g of (+)-isopinocamphenol (mp 55—57°C, $[\alpha]_D^{25}$ +31.6°) prepared from (−)-α-pinene ($[\alpha]_D^{25}$ −39.9°) through hydrobarotion[21] was oxidized with sodium dichromate to give 17.8 g of 10β-pinane-3-one (**1**): $[\alpha]_D^{25}$ −9.77° (neat) (lit,[21] $[\alpha]_D^{25}$ +10.3°, from (−)-isopinocamphenol); UV (MeOH) 291 nm (ε 17.6), (isooctane) 295 nm (ε 16.6); ORD (*c* 1.1, MeOH) $[\phi]_{400}$ −100, $[\phi]_{319}$ −889, $[\phi]_{276}$ +1200, $[\phi]_{248}$ +960, $[\phi]_{230}$ +1360, (*c* 0.25, isooctane) $[\phi]_{400}$ +30, $[\phi]_{320}$ −617, $[\phi]_{313}$ −440, $[\phi]_{309}$ −617, $[\phi]_{302}$ −65, $[\phi]_{298}$ −216, $[\phi]_{292}$ +277, $[\phi]_{288}$ +205, $[\phi]_{277}$ +617, $[\phi]_{245}$ +404, $[\phi]_{220}$ +645; CD (*c* 1.1, MeOH) $[\theta]_{338}$ 0, $[\theta]_{294}$ −1670, $[\theta]_{247}$ 0, (*c* 0.25, isooctane) $[\theta]_{331}$ 0, $[\theta]_{315}$ −365, $[\theta]_{305}$ −760, $[\theta]_{296}$ −832, $[\theta]_{285}$ −649, $[\theta]_{249}$ 0; variable temp. CD (*c* 0.21, EPA) $[\theta]_{341}^{-192°}$ 0, $[\theta]_{335}$ −105, $[\theta]_{330}$ +176, $[\theta]_{324}$ −491, $[\theta]_{318}$ −175, $[\theta]_{311}$ −1630, $[\theta]_{307}$ −1020, $[\theta]_{301}$ −2380, $[\theta]_{296}$ −1400, $[\theta]_{292}$ −2140, $[\theta]_{286}$ −1160, $[\theta]_{284}$ −1230, $[\theta]_{255}$ 0, $[\theta]_{337}^{+25°}$ 0, $[\theta]_{330}$ +175, $[\theta]_{302}$ −834, $[\theta]_{299}$ −790, $[\theta]_{295}$ −1010, $[\theta]_{256}$ 0,

(−)-10α-Pinan-3-one (3). Following the method in the literature,[21] 0.50 g of (−)-10β-pinan-3-one (**1**) was added to an ethanol solution of sodium ethoxide, which had been prepared by dissolving 0.12 g of metallic sodium in 25 m*l* of absolute ethanol; then the mixture was let to stand for 24 hr at room temperature. The usual treatment of the mixture gave 0.35 g of the ketone (**3**): $[\alpha]_D^{25}$ −18.6° (*c* 1.99, EtOH) (lit,[22] α_J −15°); UV (MeOH) 295 nm (ε 20.0), (isooctane) 318 nm (ε 13.5), 306 (18.0), 296 (18.0); ORD (*c* 0.29, MeOH) $[\phi]_{400}$ −45, $[\phi]_{321}$ +255, $[\phi]_{317}$ +230, $[\phi]_{310}$ +351, $[\phi]_{304}$ +105, $[\phi]_{302}$ +121, $[\phi]_{269}$ −845, $[\phi]_{257}$ −860, $[\phi]_{245}$ −1000, (*c* 0.31, isooctane) $[\phi]_{400}$ −37, $[\phi]_{334}$ −425, $[\phi]_{327}$ +88, $[\phi]_{320}$ −120, $[\phi]_{312}$ +450, $[\phi]_{307}$ −50, $[\phi]_{301}$ +375, $[\phi]_{296}$ −188, $[\phi]_{291}$ +75, $[\phi]_{287}$ −300, $[\phi]_{282}$ −188, $[\phi]_{220}$ −800; CD (*c* 0.29, MeOH), (*c* 0.31, isooctane), and (*c* 0.55, CCl_4) (Fig. 4); variable temp. CD (*c* 0.26, EPA) and (*c* 0.28, decalin) (Fig. 7).

(+)-2α-Hydroxy-10β-pinan-3-one (4). Following the procedure previously reported,[23] (−)-α-pinene ($[\alpha]_D^{25}$ −39.9°) was oxidized with potassium permanganate in 90% aqueous acetone for 8.5 hr at −5°C to obtain the hydroxyketone (**4**) in a 24% yield: mp 34—35°C (lit,[24] mp 34.5—35.3°C), $[\alpha]_D^{25}$ +23.3° (*c* 4.64, EtOH) (lit,[23] $[\alpha]_D^{25}$ −18.56° (*c* 14.44, EtOH) from (+)-α-pinene); UV (MeOH) 308 nm (ε 28.0), (isooctane)

20) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

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23) T. Kuwata, *J. Amer. Chem. Soc.*, **59**, 2509 (1937).

24) H. Schmidt, *Chem. Ber.*, **93**, 2485 (1960).

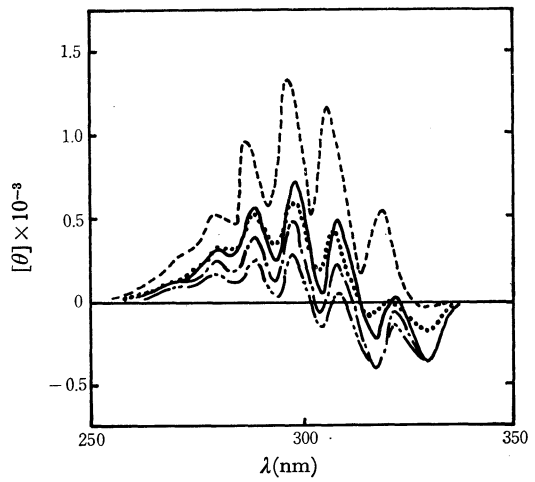

Fig. 7. CD curves of the ketone (**3**) in selected solvents at various temperatures: ——, – – –, and — — —, at −74, +25, and +138°C in decalin, ----- and ·····, at −138 and +25°C in EPA, respectively.

309 nm (ε 24.6); ORD (*c* 0.61, MeOH) $[\phi]_{400}$ +220, $[\phi]_{337}$ +1680, $[\phi]_{333}$ +1300, $[\phi]_{326}$ +1530, $[\phi]_{316}$ +237, $[\phi]_{304}$ −1010, $[\phi]_{296}$ −1740, $[\phi]_{288}$ −1940, (*c* 0.61, isooctane) $[\phi]_{400}$ +387, $[\phi]_{338}$ +2460, $[\phi]_{332}$ +1520, $[\phi]_{325}$ +2370, $[\phi]_{319}$ +83, $[\phi]_{314}$ +690, $[\phi]_{308}$ −1350, $[\phi]_{304}$ −1100, $[\phi]_{297}$ −2180, $[\phi]_{294}$ −2040, $[\phi]_{290}$ −2320, $[\phi]_{230}$ −900; CD (*c* 0.61, MeOH) $[\theta]_{347}$ 0, $[\theta]_{322}$ +2360, $[\theta]_{313}$ +2740, $[\theta]_{303}$ +2290, $[\theta]_{260}$ 0, (*c* 0.61, isooctane) $[\theta]_{346}$ 0, $[\theta]_{335}$ +1920, $[\theta]_{322}$ +3550, $[\theta]_{310}$ +3780, $[\theta]_{301}$ +3010, $[\theta]_{260}$ 0; variable. temp. CD (*c* 0.68, EPA) and (*c* 0.70, decalin) (Fig. 8).

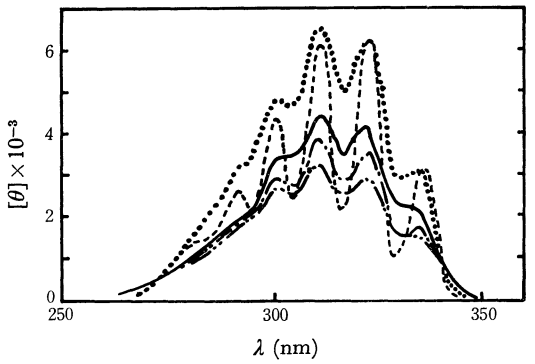

Fig. 8. CD curves of the hydroxyketone (**4**) in selected solvents at various temperatures: ——, – – –, and — — —, at −74, +25, and +138°C in decalin; ----- and ·····, at −138 and +25°C in EPA, respectively.

Acetates (6), (14), (15), and (16). (See Ref. 25 for the details of this reaction) A mixture of (+)-hydroxyketone (**4**) (22.0 g) and acetic anhydride (35.0 g) was refluxed for 6 hr at 160°C. The reaction mixture was then extracted with ether to obtain an oily product (22.9 g), which was composed of (+)-4β-acetoxy-10β-pinan-3-one (**6**) (17% yield), (+)-2α-acetoxy-10β-pinan-3-one (**14**) (14%), (−)-4β-acetoxy-10α-pinan-3-one (*15*) (20%), and (−)-4α-acetocy-10α-pinan-3-one (**16**) (39%).

a) (+)-4β-Acetoxy-10β-pinan-3-one (6): mp 100.5—101.0 °C $[\alpha]_D^{25}$ +66.1° (*c* 6.0, EtOH); UV (MeOH) 292 nm (ε 27.7), (isooctane) 297 nm (ε 24.2); ORD (*c* 1.3, MeOH) $[\phi]_{400}$ +48, $[\phi]_{323}$ +232, $[\phi]_{275}$ −175, $[\phi]_{230}$ −38, (*c* 1.1, isooctane) $[\phi]_{400}$ +29, $[\phi]_{326}$ +151, $[\phi]_{280}$ −99, $[\phi]_{240}$ −30; CD (*c* 1.3, MeOH) $[\theta]_{337}$ 0, $[\theta]_{301}$ +262, $[\theta]_{250}$ 0, (*c* 1.1, isooctane) $[\theta]_{340}$ 0, $[\theta]_{305}$ +147, $[\theta]_{260}$ 0.

b) (+)-2α-Acetoxy-10β-pinan-3-one (14): mp 38—40°C, $[\alpha]_D^{25}$ +23.1° (*c* 0.26, MeOH); UV (MeOH) 300 nm (ε 29.5), (isooctane) 301 nm (ε 23.0); ORD (*c* 0.26, MeOH) $[\phi]_{400}$ +163, $[\phi]_{339}$ +1470, $[\phi]_{328}$ +1840, $[\phi]_{317}$ +990, $[\phi]_{280}$ −2970 $[\phi]_{255}$ −2640, $[\phi]_{240}$ −3010, (*c* 0.19, isooctane) $[\phi]_{400}$ +164, $[\phi]_{344}$ +1470, $[\phi]_{336}$ +1140, $[\phi]_{331}$ +1720, $[\phi]_{322}$ +326, $[\phi]_{319}$ +622, $[\phi]_{309}$ −1080, $[\phi]_{307}$ −982, $[\phi]_{298}$ −2180, $[\phi]_{296}$ −2110, $[\phi]_{289}$ −2540, $[\phi]_{284}$ −2470, $[\phi]_{280}$ −2570, $[\phi]_{257}$ −2210, $[\phi]_{245}$ −2470; CD (*c* 0.26, MeOH) $[\theta]_{340}$ 0, $[\theta]_{317}$ +1120, $[\theta]_{311}$ +1710, $[\theta]_{302}$ +1650, $[\theta]_{260}$ 0, (*c* 0.19, isooctane) $[\theta]_{349}$ 0, $[\theta]_{337}$ +820, $[\theta]_{333}$ +800, $[\theta]_{324}$ +2030, $[\theta]_{319}$ +1770, $[\theta]_{312}$ +2550, $[\theta]_{306}$ +2030, $[\theta]_{302}$ +2200, $[\theta]_{292}$ +1560, $[\theta]_{260}$ 0.

c) (−)-4β-Acetoxy-10α-pinan-3-one (15); $[\alpha]_D^{25}$ −8.5° (*c* 0.37, MeOH); UV (MeOH) 302 nm (ε 27.1), (isooctane) 304 nm (ε 25.4); ORD (*c* 0.37, MeOH) $[\phi]_{400}$ +67.0, $[\phi]_{339}$ +905, $[\phi]_{328}$ +1070, $[\phi]_{279}$ −2180, $[\phi]_{262}$ −2110, $[\phi]_{234}$ −3150, (*c* 0.15, isooctane) $[\phi]_{400}$ +42, $[\phi]_{345}$ +807, $[\phi]_{337}$ +721, $[\phi]_{332}$ +975, $[\phi]_{323}$ +297, $[\phi]_{319}$ +339, $[\phi]_{308}$ −636, $[\phi]_{298}$ −1400, $[\phi]_{272}$ −1780, $[\phi]_{262}$ −1700, $[\phi]_{228}$ −3140; CD (0.37, MeOH) $[\theta]_{347}$ 0, $[\theta]_{309}$ +1790, $[\theta]_{243}$ 0, (*c* 0.15, isooctane) $[\theta]_{351}$ 0, $[\theta]_{338}$ +443, $[\theta]_{325}$ +1100, $[\theta]_{320}$ +1070, $[\theta]_{313}$ +1440, $[\theta]_{307}$ +1230, $[\theta]_{303}$ +1280, $[\theta]_{240}$ 0.

d) (−)-4α-Acetoxy-10α-pinan-3-one (16): $[\alpha]_D^{25}$ −78.1° (*c* 0.49, MeOH); UV (MeOH) 298 nm (ε 30.2), (isooctane) 294 nm (ε 28.4), 302 (27.1); ORD (*c* 0.49, MeOH) $[\phi]_{400}$ −596, $[\phi]_{340}$ −2680, $[\phi]_{329}$ −3020, $[\phi]_{282}$ +3150, $[\phi]_{230}$ +1450, (*c* 0.32, isooctane) $[\phi]_{400}$ −463, $[\phi]_{343}$ −2580, $[\phi]_{338}$ −2450, $[\phi]_{330}$ −2970, $[\phi]_{320}$ −1390, $[\phi]_{308}$ +859, $[\phi]_{298}$ +2640, $[\phi]_{285}$ +3370, $[\phi]_{215}$ +1720; CD (*c* 0.49, MeOH) $[\theta]_{350}$ 0, $[\theta]_{309}$ −4440, $[\theta]_{250}$ 0, (*c* 0.32, isooctane) $[\theta]_{348}$ 0, $[\theta]_{323}$ −3400, $[\theta]_{313}$ −4540, $[\theta]_{303}$ −4190, $[\theta]_{294}$ −3230, $[\theta]_{254}$ 0.

(−)-4α-Hydroxy-10α-pinan-3-one (5) and (−)-3β-Hydroxy-10α-pinan-4-one (8).[25] The acetate (**16**) was hydrolyzed by methanolic potassium hydroxide at room temperature overnight to give hydroxyketones (**5**) and (**8**) (67% and 33% yields respectively).

a) (−)-4α-Hydroxy-10α-pinan-3-one (5): $[\alpha]_D^{25}$ −52.8° (*c* 0.55, MeOH); IR (CCl_4) 3536 cm^{-1} (intramol. bonded OH); UV (MeOH) 285 nm (ε 29.7), (isooctane) 283 nm (ε 35.3); ORD (*c* 0.55, MeOH) $[\phi]_{400}$ −337, $[\phi]_{340}$ −1470, $[\phi]_{330}$ −1500, $[\phi]_{281}$ +1620, $[\phi]_{247}$ +1220, $[\phi]_{225}$ +1590, (*c* 0.71, isooctane) $[\phi]_{400}$ −294, $[\phi]_{325}$ −1850, $[\phi]_{273}$+2530, $[\phi]_{245}$ +2320, $[\phi]_{220}$ +5470; CD (*c* 0.55, MeOH) $[\theta]_{346}$ 0, $[\theta]_{309}$ −2220, $[\theta]_{250}$ 0, (*c* 0.71, isooctane) $[\theta]_{346}$ 0, $[\theta]_{298}$ −3080, $[\theta]_{240}$ 0.

b) (−)-3β-Hydroxy-10α-pinan-4-one (8): mp 44—45°C, $[\alpha]_D^{25}$ −147.7° (*c* 0.27, MeOH); IR (CCl_4) 3514 cm^{-1}(intermol. bonded OH); UV (MeOH) 282 nm (ε 36.9), (isooctane) 284 nm (ε 37.9); ORD (*c* 0.27, MeOH) $[\phi]_{400}$ −689, $[\phi]_{302}$ −5570, $[\phi]_{264}$ +5200, $[\phi]_{220}$ +751, (*c* 0.17, isooctane) $[\phi]_{400}$ −778, $[\phi]_{299}$ −6610, $[\phi]_{258}$ +7100, $[\phi]_{227}$ +4670, $[\phi]_{215}$ +6610; CD (*c* 0.27, MeOH) $[\theta]_{321}$ 0, $[\theta]_{282}$ −8020, $[\theta]_{245}$ 0, (*c* 0.17, isooctane) $[\theta]_{315}$ 0, $[\theta]_{281}$ −9860, $[\theta]_{224}$ 0.

(+)-4β-Hydroxy-10β-pinan-3-one (7). The hydrolysis of the acetate (**6**) (420 mg) with methanolic sodium hydroxide gave the hydroxyketone (**7**) (292 mg): mp 67—68°C, $[\alpha]_D^{25}$ +33.5° (*c* 0.25, MeOH); IR (CCl_4) 3540 cm^{-1} (intramol. bonded OH); UV (MeOH) 288 nm (ε 29.8), (isooctane) 283 nm (ε 31.5); ORD (*c* 0.25, MeOH) $[\phi]_{400}$ +332, $[\phi]_{322}$ +1660, $[\phi]_{279}$ −1990, $[\phi]_{253}$ −1590, $[\phi]_{225}$ −3380, (*c* 0.22, isooctane) $[\phi]_{400}$ +375, $[\phi]_{317}$ +2480, $[\phi]_{273}$ −3300, $[\phi]_{248}$ −2100, $[\phi]_{225}$ −6000; CD (*c* 0.25, MeOH) $[\theta]_{344}$ 0, $[\theta]_{301}$ +1880, $[\theta]_{250}$ 0, (*c* 0.22, isooctane) $[\theta]_{331}$ 0, $[\theta]_{296}$ +2770,

25) T. Hirata, This Bulletin, **45**, 599 (1972).

$[\theta]_{247}$ 0.

(−)-3β-Acetoxy-10α-pinan-4-one (9). The acetylation of the hydroxyketone (**8**) (100 mg) with acetic anhydride in pyridine gave the acetate (**9**) (95 mg): mp 38—39°C; $[\alpha]_D^{25}$ −135.2° (*c* 0.49, MeOH); UV (MeOH); 284 nm (ε 54.9), (isooctane) 290 nm (ε 63.0); ORD (*c* 0.14, MeOH) $[\phi]_{400}$ −1200, $[\phi]_{303}$ −7410, $[\phi]_{263}$ +5560, $[\phi]_{230}$ +1390, (*c* 0.20, isooctane) $[\phi]_{400}$ −685, $[\phi]_{308}$ −5000, $[\phi]_{267}$ +4660, $[\phi]_{230}$ +2330; CD (*c* 0.14, MeOH) $[\theta]_{322}$ 0, $[\theta]_{285}$ −6830, $[\theta]_{237}$ 0, (*c* 0.20, isooctane) $[\theta]_{326}$ 0, $[\theta]_{290}$ −4870, $[\theta]_{245}$ 0.

(+)-3β-Methylnopinone (10). To a stirred solution of potassium hydroxide (7.0 g) in methanol (20 m*l*), was added a sample of (−)-10β-pinan-2α,3α-diol monotosylate (6.2 g) which had been prepared in our previous work.[26] The solution was heated to 65°C for 3 hr had then kept further at room temperature overnight. The reaction mixture was extracted with ether to give an oily product (2.5 g), which was subsequently subjected to chromatography on a silica-gel column to isolate the ketone (**10**) in an 8.5% yield: $[\alpha]_D^{25}$ +59.7° (neat); UV (MeOH) 275 nm (ε 30.1); ORD (*c* 0.64, MeOH) $[\phi]_{400}$ +380, $[\phi]_{301}$ +3550, $[\phi]_{265}$ −3380, $[\phi]_{230}$ −1080, (*c* 0.77, isooctane) $[\phi]_{400}$ +157, $[\phi]_{304}$ +1490, $[\phi]_{268}$ −1530, $[\phi]_{230}$ −315; CD (*c* 0.64, MeOH) $[\theta]_{317}$ 0, $[\theta]_{285}$ +2740, $[\theta]_{240}$ 0, (*c* 0.77, isooctane) $[\theta]_{322}$ 0, $[\theta]_{290}$ +1240, $[\theta]_{238}$ 0; variable temp. CD (*c* 0.61, EPA) $[\theta]_{323}^{-192°}$ 0, $[\theta]_{289}$ +2940, $[\theta]_{248}$ 0, $[\theta]_{320}^{+25°}$ 0, $[\theta]_{283}$ +2410, $[\theta]_{250}$ 0, (*c* 0.59, decalin) $[\theta]_{317}^{-74°}$ 0, $[\theta]_{287}$ +2580, $[\theta]_{254}$ 0, $[\theta]_{316}^{+25°}$ 0, $[\theta]_{288}$ +1630, $[\theta]_{254}$ 0, $[\theta]_{317}^{+137°}$ 0, $[\theta]_{288}$ +1920, $[\theta]_{253}$ 0.

(−)-10β-Pinan-4-one (11). *a) Preparation of (−)-verbenone*: To a stirred sample of 100 g of (−)-α-pinene ($[\alpha]_D^{25}$ −39.9°), was added a *t*-butyl chromate solution, which had been prepared from chromiun trioxide (220.5 g), *t*-butyl alcohol (330 g), benzene (500 m*l*), glacial acetic acid (150 g), and acetic anhydride (150 g) following the method in the literature.[27] The mixture was stirred for 12 hr at room temperature in an atmosphere of nitrogen, and then it was treated with water and oxalic acid as usual.[27] The reaction product extracted with benzene was subjected to distillation and then to column chromatography to isolate (−)-verbenone (39.4 g); bp 80—84°C/9 mmHg, $[\alpha]_D^{25}$ −208.6° (neat).

b) Preparation of Ketone 11: (−)-verbenone (1.3 g) in ethanol was hydrogenated in the presence of palladium hydroxide on calcium carbonate, under an atmospheric pressure, to yield an oily product (1.2 g). The product was rectified by distillation under a reduced pressure to give the ketone (**11**) (1.0 g): bp 59—61°C/11 mmHg, $[\alpha]_D^{25}$ −47.8° (neat), d_D^{25} 0.9693, n_D^{25} 1.4751; UV (MeOH) 274 nm (ε 34.5), (isooctane) 285 nm (ε 20.2); ORD (*c* 0.15, MeOH) $[\phi]_{400}$ −250, $[\phi]_{305}$ −2620, $[\phi]_{266}$ +2720, $[\phi]_{235}$ +1250, (*c* 0.17, isooctane) $[\phi]_{400}$ −250, $[\phi]_{317}$ −1670, $[\phi]_{314}$ −1450, $[\phi]_{307}$ −1800, $[\phi]_{270}$ +1800, $[\phi]_{230}$ +710; CD (*c* 0.15, MeOH) $[\theta]_{320}$ 0, $[\theta]_{285}$ −3550, $[\theta]_{230}$ 0, (*c* 0.35, isooctane) $[\theta]_{324}$ 0, $[\theta]_{294}$ −2380, $[\theta]_{250}$ 0; variable temp. CD (*c* 0.20, EPA) and (*c* 0.27, decalin) (Fig. 9); the semicarbazone derivative, mp 222—223°C.

(+)-Nopinone (12). Into a solution of 5.0 g of (−)-β-pinene ($[\alpha]_D^{25}$ −21.8°) in 30 m*l* of dichloromethane, was passed ozonized oxygen at −60°C. The solution was subjected to steam distillation, and then extraction with chloroform to give 2.8 g of an oily product. The distillation of the product gave 14.5 g of (+)-nopinone (**12**): bp 76.5—77.5°C /7 mmHg, $[\alpha]_D^{25}$ +18.9° (neat), d_D^{25} 0.9786, n_D^{25} 1.4761; IR (liq.) 1713 cm^{-1} (C=O); UV (MeOH) 273 nm (ε 30.2),

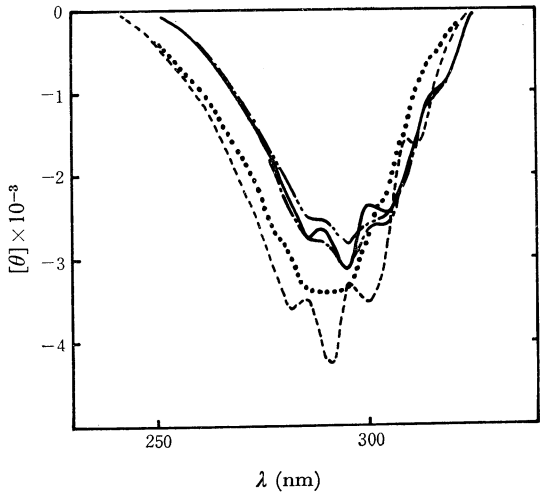

Fig. 9. CD curves of the ketone (**11**) in selected solvents at various temperatures: ——, – – –, and ——, at −74, +20, and +138°C in decalin; – – – – and ·····, at −192 and +25°C in EPA, respectively.

(isooctane) 286 nm (ε 18.9); ORD (*c* 1.3, MeOH) $[\phi]_{400}$ +150, $[\phi]_{301}$ +3440, $[\phi]_{262}$ −4140, $[\phi]_{220}$ −1800, (*c* 0.30, isooctane) $[\phi]_{400}$ +125, $[\phi]_{316}$ +1680, $[\phi]_{312}$ +1600, $[\phi]_{306}$ +1850, $[\phi]_{265}$ −2230, $[\phi]_{230}$ −1010; CD (*c* 1.3, MeOH) $[\theta]_{304}$ 0, $[\theta]_{283}$ +4390, $[\theta]_{235}$ 0, (*c* 30, isooctane) $[\theta]_{354}$ 0, $[\theta]_{292}$ +2220, $[\theta]_{284}$ 2150, $[\theta]_{233}$ 0; variable temp. CD (*c* 0.41, EPA) $[\theta]_{323}^{-192°}$ 0, $[\theta]_{289}$ −4500, $[\theta]_{238}$ 0, $[\theta]_{322}^{0°}$ 0, $[\theta]_{283}$ −4090, $[\theta]_{322}$ 0, (*c* 0.36, decalin) $[\theta]_{320}^{-74°}$ 0, $[\theta]_{292}$ +3150, $[\theta]_{288}$ +3000, $[\theta]_{285}$ +3300, $[\theta]_{250}$ 0, $[\theta]_{320}^{+25°}$ 0, $[\theta]_{290}$ +2710, $[\theta]_{250}$ 0, $[\theta]_{320}^{+140°}$ 0, $[\theta]_{321}$ +2560, $[\theta]_{250}$ 0.

(−)-2α-Bromo-10β-pinan-3-one (13).[28] *a) Preparation of 3-Acetoxy-pin-2-ene*: Following the method in the reference,[3] the treatment of (−)-10β-pinan-3-one (**1**) with acetic anhydride in the presence of perchloric acid afforded (−)-3-acetoxy-pin-2-ene in a 76% yield: $[\alpha]_D^{25}$ −35.0° (*c* 0.29, MeOH) (lit,[3] $[\alpha]_D^{25}$ +36° (*c* 1.00), derived from (+)-10β-pinan-3-one).

b) Preparation of Bromoketone 13: Bromine (0.94 g) dissolved in carbon tetrachloride (4 m*l*) was added to a stirred suspension of (−)-3-acetoxy-pin-2-ene (1.08 g) and anhydrous sodium carbonate (1.00 g) in carbon tetrachloride (5 m*l*) over a 5 min period at 0°C. After stirring for a further 5 min, the ether extract gave 1.13 g of an oily product, which was composed of 84% of the bromoketone (**13**): $[\alpha]_D^{25}$ −101.8° (*c* 1.18, MeOH); IR (liq.) 1722 cm^{-1} (C=O); UV (MeOH) 313 nm (ε 135.3); ORD (*c* 1.18, MeOH) $[\phi]_{400}$ −638, $[\phi]_{335}$ −1620, $[\phi]_{305}$ −1080, $[\phi]_{250}$ −3430, $[\phi]_{230}$ −1720, (*c* 0.24, isooctane) $[\phi]_{400}$ −692, $[\phi]_{349}$ −1800, $[\phi]_{302}$ −143, $[\phi]_{250}$ −2240, $[\phi]_{230}$ −1190; CD (*c* 1.18, MeOH) $[\theta]_{365}$ 0, $[\theta]_{317}$ −1000, $[\theta]_{293}$ −227, $[\theta]_{258}$ −1000, (*c* 0.24, isooctane) $[\theta]_{364}$ 0, $[\theta]_{318}$ −1700, $[\theta]_{285}$ −315.

(−)-4β-Hydroxy-10β-pinane (17) and Its Acetate (18). A solution of 1.0 g of (−)-10β-pinan-4-one (**11**) in 20 m*l* of ether was stirred into a suspension of 0.3 g of lithium aluminum hydride in 50 m*l* of ether. The mixture was then refluxed for 2 hr. The reaction mixture, after having been treated in the usual manner, afforded 1.0 g of **17**. The subsequent acetylation of **17** (100 mg) with acetic anhydride in pyridine gave the acetate (**18**) (95 mg).

a) 4β-Hydroxy-10β-pinane (17): Mp 72—73°C, $[\alpha]_D^{25}$ −5.1° (*c* 4.0, benzene); NMR (CCl_4) δ 1.22 (s, C_8-3H), 1.16, (s, C_9-3H), 1.07 (d, J=7.0 Hz, C_{10}-3H), and 4.22 ppm (m,

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27) T. Matsuura and K. Fujita, *J. Sci. Hiroshima Univ. Ser. A-II*, **16**, 173 (1952).

28) T. Hirata and T. Suga, This Bulletin, **44**, 2833 (1971).

C_4-H).

b) 4β-Acetoxy-10β-pinane (18): IR (liq.) 1745 cm^{-1} ($OCOCH_3$); NMR (CCl_4) δ 1.23 (s, C_8-3H), 1.11 (s, C_9-3H), 1.05 (d, J=7.0 Hz, C_{10}-3H), 1.91 (s, $OCOCH_3$), and 5.08 ppm (m, C_4-H).

(−)-3β-Hydroxy-10α-pinane (19) and Its Acetate (20). Into a stirred suspension of 120 mg of lithium aluminum hydride in 15 m*l* of ether, was added a solution of 950 mg of (−)-10α-pinan-3-one (**3**) in 15 m*l* of ether, and then the mixture was stirred for 1 hr at room temperature. After a usual treatment, the ether extract gave 590 mg of a crystalline product, which was subsequently chromatographed on a silica-gel column with a mixture of *n*-hexane and ethyl acetate to yield 50 mg of (+)-3α-hydroxy-10α-pinane (mp 26—27°C, $[\alpha]_D^{25}$ +15.8° (*c* 0.20, MeOH)) and 400 mg of (−)-3β-hydroxy-10α-pinane (**19**). The acetylation of **19** (100 mg) with acetic anhydride in pyridine gave the acetate (**20**) (92 mg)

a) 3β-Hydroxy-10α-pinane (19): Mp 66—67°C (lit,[29] mp 67°C), $[\alpha]_D^{25}$ −59.0° (*c* 0.40, MeOH); NMR (CCl_4) δ 1.21 (s, C_8-3H), 0.77 (s, C_9-3H), 0.93 (d, J=7.0 Hz, C_{10}-3H), and 3.99 ppm (t, J=6.5 Hz, C_3-H); 3,5-dinitrobenzoate, mp 118—119°C (lit,[30] mp 118—119°C).

b) 3β-Acetoxy-10α-pinane (20): IR (liq.) 1744 cm^{-1} ($OCOCH_3$); NMR (CCl_4) δ 1.21 (s, C_8-3H), 0.90 (s, C_9-3H), 0.97 (d, J=7.0 Hz, C_{10}-3H), 1.99 (s, $OCOCH_3$), and 4.66 ppm (m, C_3-H).

The author wishes to express his hearty gratitude to Dr. Takayuki Suga of Hiroshima University for his guidance and encouragement, and to Dr. E. von Rudloff for measuring the NMR spectra by a Varian Associates, HA-100, Spectrometer.

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30) T. Takemoto, G. Kusano, and H. Hikino, *Yakugaku Zasshi*, **86**, 1162 (1966).