The Solvent Effects on the Optical Rotatory Properties of 1,7-Diaryl-5-hydroxy-3-heptanones and Related Compounds

Shinji OHTA
Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Naka-ku, Hiroshima 730
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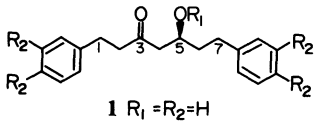
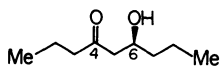
The ORD and CD curves of (*S*)-1,7-diphenyl-5-hydroxy-3-heptanone, (*S*)-1,7-bis(3,4-dimethoxyphenyl)-5-hydroxy-3-heptanone, and the related model compounds were obtained in selected solvents with different polarity. Causing the 1,7-diaryl-5-hydroxy-3-heptanones dextro-rotatory in chloroform was attributed to the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups, regardless of the presence of the phenyl groups. On the other hand, causing the compounds levo-rotatory in methanol was proved to necessitate simultaneously the breaking of the intramolecular hydrogen bond followed by solvation to the carbonyl and/or hydroxyl groups, as well as the presence of the phenyl groups. The ca. 30% of the solvent effect on the optical rotation was based on the change in the rotational strength associated with the $n\rightarrow\pi^*$ transition of the carbonyl group as changing a solvent. The residual 70% was based on the change in the rotational strength associated with the electronic transitions at around 200 nm of the carbonyl and/or hydroxyl groups.

Previously, the absolute structures of five diarylheptanoids isolated from *Alnus serrulatoides* Call.[1,2] and one isolated from *A. sieboldiana* Matsum.[3] were elucidated. In the course of the determination of their absolute configuration, the reversal in the sense of the optical rotation was observed for 1,7-diaryl-5-hydroxy-3-heptanones, such as (*S*)-1,7-diphenyl-5-hydroxy-3-heptanone (**1**)[3] and (*S*)-1,7-bis(3,4-dimethoxyphenyl)-5-hydroxy-3-heptanone (**2**),[1,2] when their optical rotations were measured in the selected solvents, such as chloroform and methanol, with different polarity. The reversal in the sense of the optical rotation is also reported for some natural compounds.[4,5] However, causes for this phenomenon have not been solved yet. In this paper, the author wishes to describe the solvent effects on the optical rotatory properties of the 1,7-diaryl-5-hydroxy-3-heptanones and related compounds. The results are in part outlined in the form of a preliminary communication.[6]



1 $R_1=R_2=H$
2 $R_1=H$, $R_2=OMe$
3 $R_1=Ac$, $R_2=H$
4 $R_1=Ac$, $R_2=OMe$



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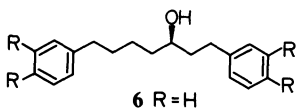
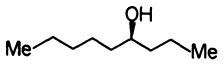


6 R=H
7 R=OMe



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Results and Discussion

The compounds **1** and **2** were dextro-rotatory in chloroform and levo-rotatory in methanol, while their acetates **3** and **4** were dextro-rotatory in both of the solvents (Table 1). These observations suggest that the interaction between the solvent and the β-ketol moiety of the compounds **1** and **2** is responsible for the reversal in the sense of their optical rotations.

The Relationships between the Molecular Rotations

Table 1. Optical Rotations of **1**—**4**

Compound	$[\alpha]_D^{25}$/°	
	Chloroform	Methanol
1	+14.0±0.6	−2.7±0.6
2	+12.0±0.1	−2.3±0.1
3	+3.6±0.3	+4.1±0.3
4	+3.5±0.5	+2.9±0.5

Table 2. Molecular Rotations of **1**, **2** and ^{13}C Chemical Shifts at C-3 of **1**—**4**

Solvent	$[M]_D^{25}$[a]/°		$\delta_{C\text{-}3}$[b]			
	1	**2**	**1**	**2**	**3**	**4**
a Carbon tetrachloride	+48.8	+52.1	27.7	27.6	23.5	23.1
b Chloroform	+39.6	+48.2	29.7	29.1	25.3	25.0
c Dichloromethane	+44.6	+46.0	29.3	29.3	25.2	24.8
d Benzene	+39.6	+48.1	27.7	27.4	23.3	23.1
e Toluene	+34.5	+42.0	27.9	27.3	23.1	22.8
f Diethyl ether	+29.6	+25.7	25.9	c)	22.3	23.3
g Dioxane	+13.5	+19.6	26.9	26.5	24.3	23.9
h Ethyl acetate	+6.7	+9.6	27.0	26.8	23.9	23.7
i Acetone	−2.5	−2.8	27.0	26.7	24.2	24.0
j Acetonitrile	−7.6	−7.2	28.1	27.8	25.3	25.0
k Methanol	−7.6	−9.2	28.3	28.0	26.2	25.7
l Ethanol	−5.1	−6.0	27.9	27.7	25.6	25.2
m 2-Propanol	−3.4	−3.2	28.0	27.8	25.3	25.0

a) 0.025 mol dm^{-3}. b) Ppm with respect to an external reference of $CH_3{}^{13}CO_2Na$. c) It was impossible to measure the spectrum of **2** because of its poor solubility in diethyl ether.

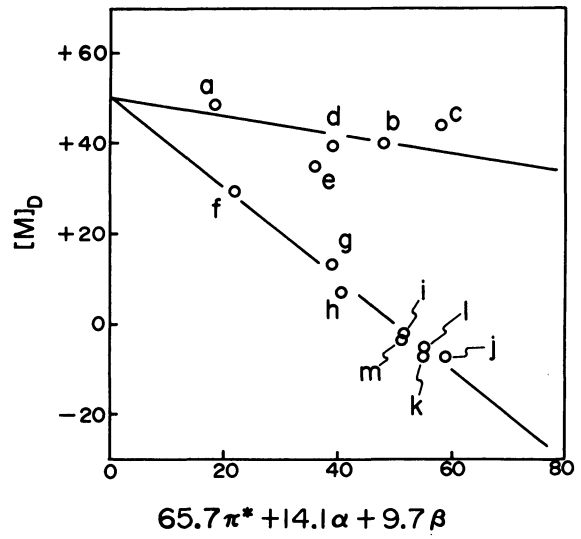

Fig. 1. A plot of $[M]_D$ of **1** vs. $65.7\pi^*+14.1\alpha+9.7\beta$. For the symbols of the data points, see Table 2.

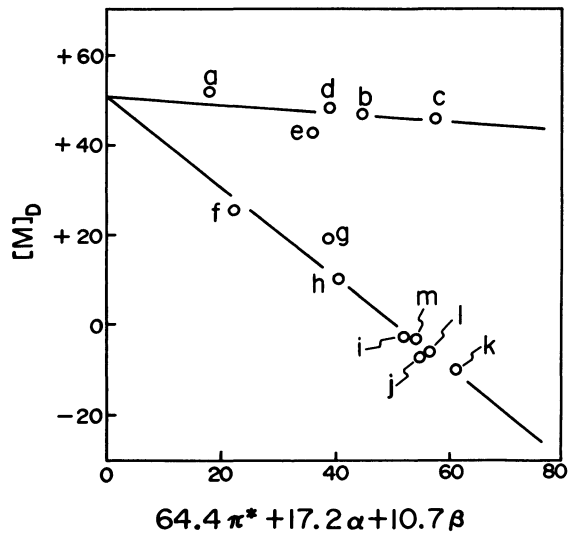

Fig. 2. A plot of $[M]_D$ of **2** vs. $64.4\pi^*+17.2\alpha+10.7\beta$. For the symbols of the data points, see Table 2.

of the Compounds 1 and 2 and Solvatochromic Parameters. The effect of the solvents on the optical rotation of the compounds **1** and **2** were examined by a solvatochromic comparison method[7] with the solvents (a)—(m) given in Table 2. The molecular rotations $[M]_D$ of the compounds **1** and **2** in these solvents were independent of the concentration (0.005—0.1 mol dm^{-3}) and truly constant. The relationship between the $[M]_D$ of the compound **1** (Table 2) and the solvatochromic parameters π^*, α, and β[†] was represented by the following least-squares regression equation,

$$[M]_D=49.6-k_1(65.7\pi^*+14.1\alpha+9.7\beta).$$

A plot of $[M]_D$ vs. $65.7\pi^*+14.1\alpha+9.7\beta$ is shown in Fig. 1, and the constant k_1 was 0.2 for the solvents (a)—(e) and 1.0 for the solvents (f)—(m). Separate correlation lines were observed for the individual solvent families. The similar facts were observed for the compound **2**. The relationship between the $[M]_D$ of the compound **2** (Table 2) and the solvatochromic parameters was represented by the following equation,

$$[M]_D=50.9-k_2(64.4\pi^*+17.2\alpha+10.7\beta).$$

A plot of $[M]_D$ vs. $64.4\pi^*+17.2\alpha+10.7\beta$ is shown in Fig. 2, and the constant k_2 was 0.1 for the solvents (a)—(e) and 1.0 for the solvents (f)—(m). The $[M]_D$ of the both compounds was dextro-rotatory in the solvents (a)—(e). The β values are very small (0—0.11)[7] for the solvents (a)—(e). Thus, the ability of the solvents to accept the proton from the C-5 hydroxyl group of the compounds **1** and **2** is so small that there is a fair chance of the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups in such solvents. On the other hand, the $[M]_D$ obtained in the solvents (f)—(m) changed from dextro-rotatory to levo-rotatory with the change in the values of the solvatochromic parameters. The β values for the solvents (f)—(m) are 0.31—0.95[7] and higher than those for the solvents (a)—(e). In the solvents (f)—(m), therefore, the proton of the C-5 hydroxyl group of the compounds **1** and **2** is strongly attracted to the solvent molecules. Accordingly, there is a fair possibility of the breaking of the intramolecular hydrogen bond in the solvents (f)—(m). Therefore, the variation in the $[M]_D$ of the compounds **1** and **2** in the solvents (f)—(m) can be attributed to the solvation to the β-ketol moiety. The relative contribution of each solvent property to the $[M]_D$ of the compounds **1** and **2** was estimated by the method described in the literature.[8] The relative contributions of the π^*, α, and β were 67, 20, and 13%, respectively, for the compound **1**, and 65, 22, and 13%, respectively, for the compound **2**. The superiority of the contribution of the π^* indicates a great contribution of the ability of the solvents to stabilize the dipole[7] of the compounds **1** and **2** to the variation in the $[M]_D$ of the compounds in the solvents (f)—(m). So, the fact that the compounds **1** and **2** were dextro-rotatory in the solvents (f), (g), and (h) could be rationalized in terms of the very weak interaction of these solvents to the β-ketol moiety of the compounds **1** and **2**. Such a solute/solvent interaction is weakened by the formation of the intramolecular hydrogen bond between the carbonyl and hydroxyl groups. Thus, the variation in the $[M]_D$ of the compounds **1** and **2** is minimized in the solvents (a)—(e).

The Formation and Breaking of the Intramolecular Hydrogen Bond. A more definite study for demonstrating the formation and breaking of the intramo-

[†] π^*, α, and β are a measure of solvent dipolarity/polarizability, that of solvent hydrogen bond donor acidity, and that of solvent hydrogen bond acceptor basicity, respectively.[7]

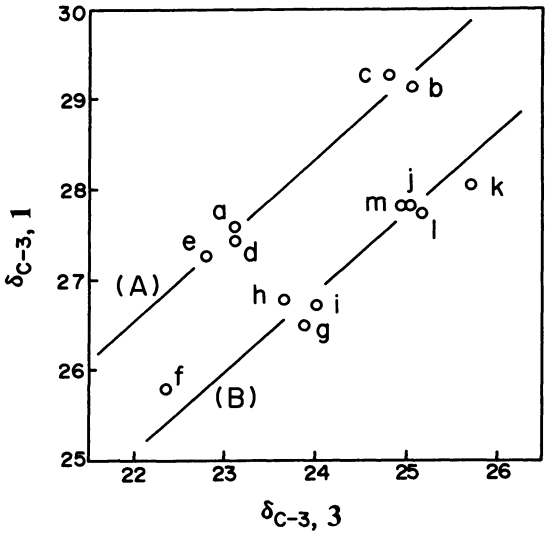

Fig. 3. A plot of δ_{C-3} for **1** vs. δ_{C-3} for **3** in the selected solvents (ppm with respect to an external reference of $CH_3{}^{13}CO_2Na$). For the symbols of the data points, see Table 2.

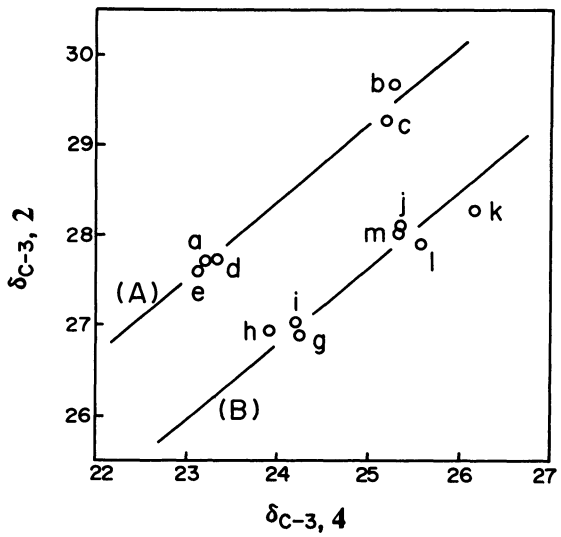

Fig. 4. A plot of δ_{C-3} for **2** vs. δ_{C-3} for **4** in the selected solvents (ppm with respect to an external reference of $CH_3{}^{13}CO_2Na$). For the symbols of the data points, see Table 2.

lecular hydrogen bond in the compounds **1** and **2** was carried out by a combination of IR and ^{13}CNMR spectroscopies. The IR spectra of the compounds **1** and **2** in carbon tetrachloride exhibited the presence of an intramolecular hydrogen-bonded OH absorption band at 3556 and 3563 cm^{-1}, respectively, which were independent of the concentration (0.005—0.1 mol dm^{-3}). Figure 3 shows the relation of the ^{13}CNMR chemical shift (Table 2) between the C-3 carbonyl carbons of the compound **1** and its acetate (**3**) in the solvents (a)—(m). The data points for the solvents (a)—(e) and the solvents (f)—(m) are situated along by lines (A) and (B), respectively. The line (A) is shifted by ca. 1.5 ppm to a lower field, compared with the line (B). The similar relation was also found for the compound **2** and its acetate (**4**) as shown in Fig. 4. These lower-field shifts[9] indicate clearly the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups in the solvents (a)—(e) and the formation of the intermolecular hydrogen bond between the solvent and the β-ketol group in the solvents (f)—(m). It was thus confirmed that the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups causes the compounds **1** and **2** dextro-rotatory in the solvents (a)—(e), while the breaking of the intramolecular hydrogen bond followed by the solvation to the β-ketol moiety causes the compounds **1** and **2** levo-rotatory in the solvents (i)—(m).

The Roles of the β-Ketol Moiety and the Phenyl Groups. The participation of the β-ketol moiety and the phenyl groups in determining the sense of the optical rotation cannot be ignored, and this was examined with the model compounds, such as (*S*)-6-hydroxy-4-nonanone (**5**), (*R*)-1,7-diphenyl-3-heptanol (**6**), (*R*)-1,7-bis(3,4-dimethoxyphenyl)-3-heptanol (**7**), and (*S*)-4-nonanol (**8**) by means of ORD measurements. Figure 5 shows the ORD curves of the compounds **1**, **2**, and **5**—**8** in chloroform and methanol. The ORD curves of the compounds **1**, **2**, and **5** showed the solvent dependence, whereas the curves of the compounds **6**—**8** were not the case. This finding indicates the indispensability of the β-ketol moiety for occurrence of the solvent effect on the optical rotation. On the other hand, the compounds **6** and **7** were levo-rotatory in 400—600 nm in chloroform and methanol, while the compound **8** was dextro-rotatory in these solvents. This fact indicates unambiguously that, in addition to the breaking of the hydrogen bond followed by the solvation, the presence of the phenyl groups in the molecules of the compounds **1**, **2**, **6**, and **7** is essential for the appearance of levo-rotation.

The Conformational Analysis in the β-Ketol Moiety. The variations in the optical rotation are presumably caused by the conformational changes in the β-ketol moiety; the conformational changes are associated with the formation and breaking of the intramolecular hydrogen bond and with the solvational effect. Such conformational changes should be effectively analyzed by means of CD measurement. The CD curves of the compound **1** in the selected solvents were shown in Fig. 6. These CD curves are complicated, because of the overlapping of the CD bands associated with the electronic transitions of the carbonyl and phenyl groups. So, the CD spectra of the model compounds **5** and **6** were examined and shown in Fig. 6. The CD curves of the compound **5** showed remarkable changes as changing the solvent, while the compound **6** showed solvent independent, negative CD maxima at 263—265 and 257—259 nm. These observations indicate that the CD maxima at 263—

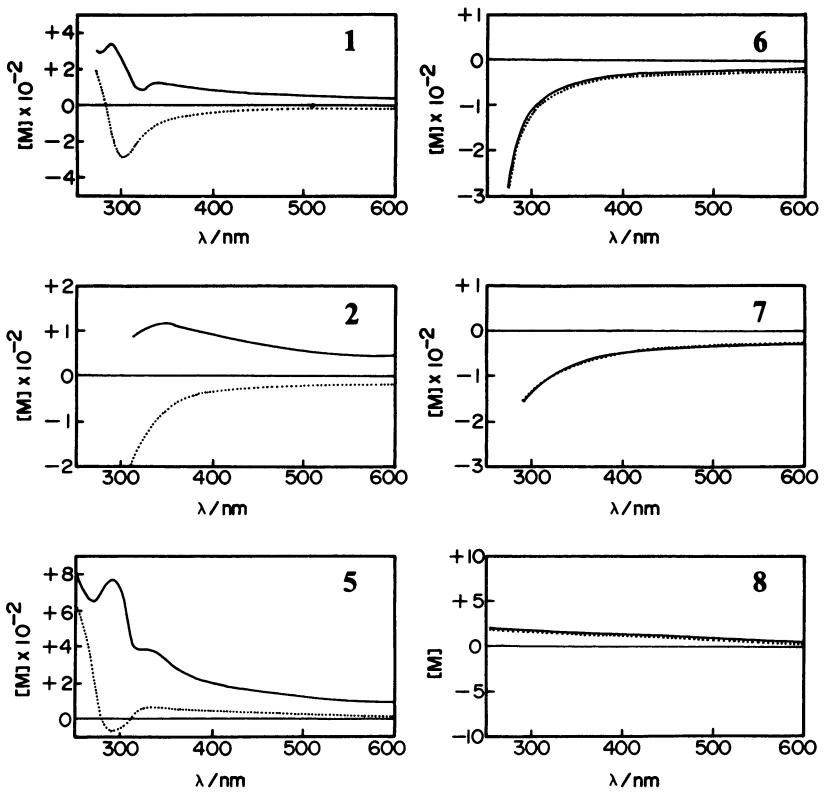

Fig. 5. ORD curves of **1**, **2**, and **5**—**8**: —— in chloroform, ------ in methanol.

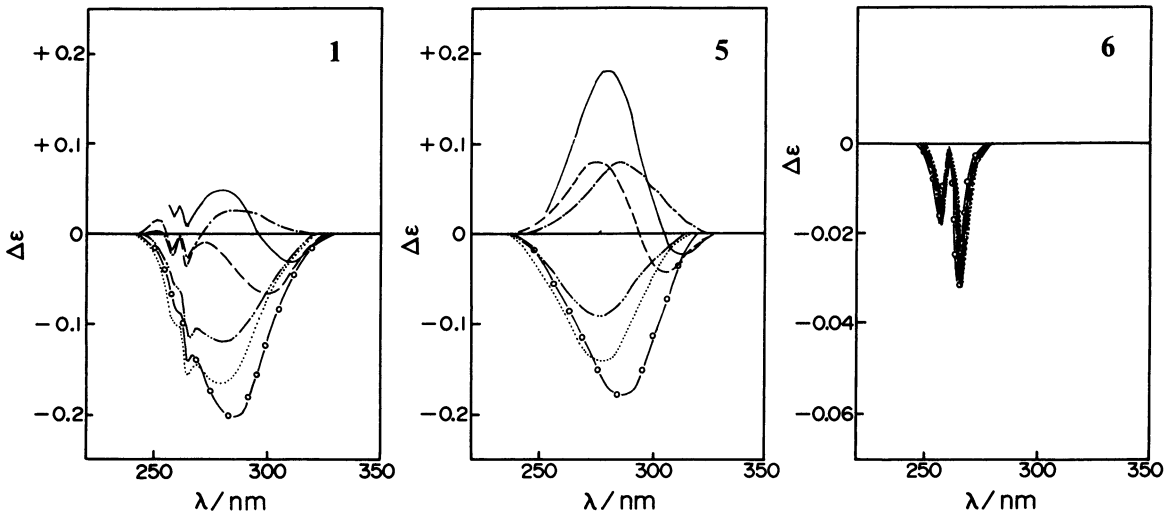

Fig. 6. CD curves of **1**, **5**, and **6**: — in carbon tetrachloride (a), —— in chloroform (b), —·—· in diethyl ether (f), —··—·· in dioxane (g), —o—o in acetonitrile (j), ····· in methanol (k).

265 and 257—259 nm in the compound **1** are associated with the phenyl $\pi \rightarrow \pi^*$ transition and the other CD maxima with the carbonyl $n \rightarrow \pi^*$ transition, only the latter CD maxima vary as changing the solvent. This indication was supported by the good fit between the CD curve of the compound **5** and the CD curve obtained by subtracting the CD curve of the compound **6** from that of the compound **1** in each solvent.

So, the conformational analysis was performed for the compound **5** as follows. The formation of the intramolecular hydrogen bond in the solvents (a) and (b) and the breaking in the solvents (f), (g), (j), and (k) were confirmed by a combination of the IR and ^{13}CNMR spectroscopies. The values for conformational energy differences in the compound **5** were estimated by a semiempirical molecular orbital calculation based upon the CNDO/2 approximation. When the intramolecular hydrogen bond is broken, this compound seems to prefer the eclipsed conformation of the carbonyl and α-alkyl groups. Such a conformation is known to be a predominant one for acyclic carbonyl compounds.[10,11] Thus, three confor-

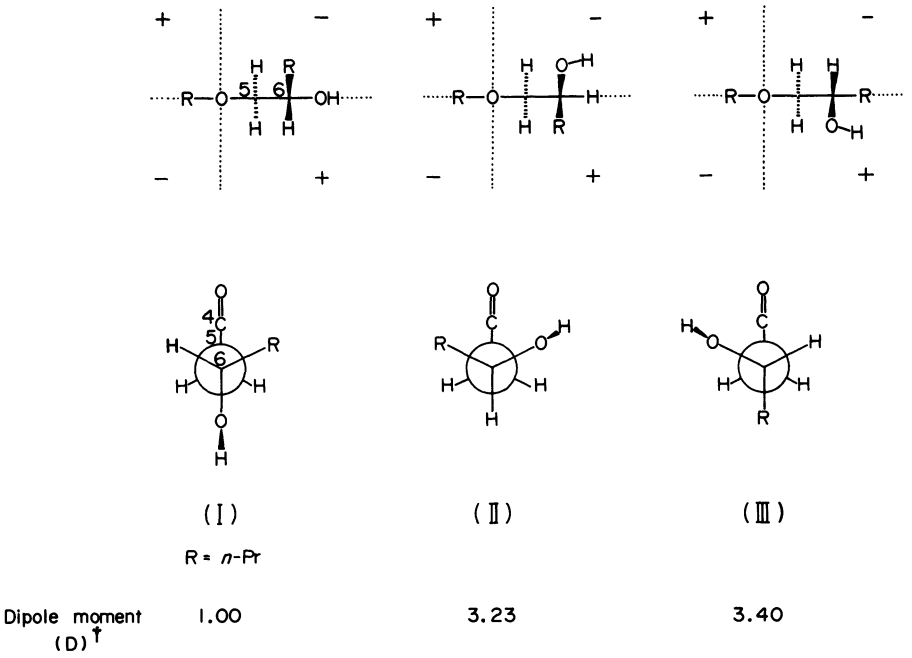

Fig. 7. Conformational isomers of **5** in the case that the intramolecular hydrogen bond is broken.
† 1 D=3.335×10^{-30} C m.

mational isomers(I)—(III) with respect to the C(5)–C(6) bond could be considered as stable ones, as illustrated in Fig. 7. The conformer(I) having the hydroxyl group in the trans position with respect to the carbonyl bond is 0.4 and 0.7 kcal mol^{-1}†† more stable than the conformers(II) and (III) having the gauche hydroxyl group, respectively. The signs for the Cotton effect of the conformers(I) and (III) can be predicted to be positive and negative, respectively, by assuming that the alkyl group R in the conformer(I) and the hydroxyl group in the conformer(III) fall into the front octants as shown in Fig. 7. For the conformer(II), its Cotton effect is predicted to be nearly nil. Hence, the Cotton effect of the compound **5** should be positive in the isolated state when the intramolecular hydrogen bond is broken. This predicted sign for the Cotton effect is in agreement with the sign observed in the solvent (f) as shown in Fig. 6. So, the positive CD band observed in the solvent (f) can be attributed to the conformer(I). However, the negative Cotton effect was observed in the solvents (g), (j), and (k). Since the conformers(II) and (III) are more dipolar than the conformer(I) as shown in Fig. 7, the relative stabilities of the conformers(II) and (III) are predicted to be enhanced by the strong solvational effect in solution.[12] Therefore, the negative CD band is expected to be attributed to the conformer(III) stabilized by the solvational energies. On the other hand, the conformer(IV) is the most predominant one in the case that the intramolecular hydrogen bond between the carbonyl and hydroxyl groups is formed as shown in Fig. 8. The conformer(IV) is 3.9 kcal mol^{-1} more

†† 1 cal=4.184 J.

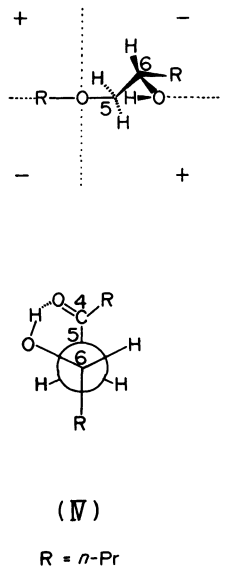

Fig. 8. The most stable conformation of **5** in the case that the intramolecular hydrogen bond is formed.

stable than the conformer(I). In the conformer(IV), the hydroxyl group is coplanar to the carbonyl one. The positive CD band at shorter wavelength in the solvents (a) and (b) can be attributed to the conformer(IV), while the negative one at longer wavelength is presumably attributed to the conformer(III) which is stabilized by the large solvational energies.

Accordingly, there is the conformational equilibrium between the intramolecularly hydrogen-bonded and solvated forms in the solvents (a) and (b), and the former hydrogen-bonded form is predominant. On the other hand, there is the conformational equi-

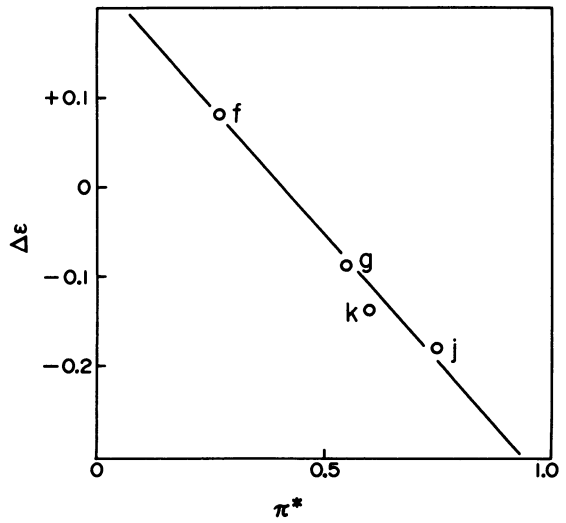

Fig. 9. A plot of CD maximum ($\Delta\varepsilon$) for **5** vs. π^* in the selected solvents. For the symbols of the data points, see Table 2.

librium among the three solvated forms in the solvents (f), (g), (j), and (k). This conformational equilibrium is dominated by the solvational effect, which is supported by the existence of a good correlation between the CD maximum ($\Delta\varepsilon$) and the solvatochromic parameter π^* as shown in Fig. 9. These results were also the case for the compound **1**.

The Contribution of the Carbonyl n→π* Cotton Effect to the Molecular Rotation. The contribution of the Cotton effect associated with the n→π* transition of a carbonyl chromophore to the molecular rotation was calculated by a simplified Kronig-Kramer's equation.[13,14] When a CD band of the compound **1** overlapped with a benzenoid band of the phenyl group, Gaussian band associated with an only n→π* transition of the carbonyl group was obtained by a graphic method. The relationships between the contribution to the molecular rotation, $[M]_D$(n→π* component), and the observed molecular rotation, $[M]_D$(obsd), were obtained for the compounds **1** and **5** in the selected solvents (a), (b), (f), (g), (j), and (k). As shown in Fig. 10, the $[M]_D$(n→π* component) was correlated with the $[M]_D$(obsd) for both the compounds. The slope of the correlation line represents the contribution of the solvent effect on the Cotton effect to the solvent effect on the molecular rotation. Both the slopes for the compounds **1** and **5** were ca. 0.3. Accordingly, ca. 30% of the solvent effect on the molecular rotations of these β-hydroxy ketones is found to be based on the solvent effect on the Cotton effect associated with the n→π* transition of the carbonyl group. The residual 70% of the solvent effect on the molecular rotation was probably based on the solvent effect on the Cotton effect at shorter wavelength (below 230 nm) associated with the electronic transitions of the carbonyl and/or hydroxyl groups. Here, it is noted that the deviation in the correlation is too large to be ignored, as shown in Fig. 10. This deviation might be

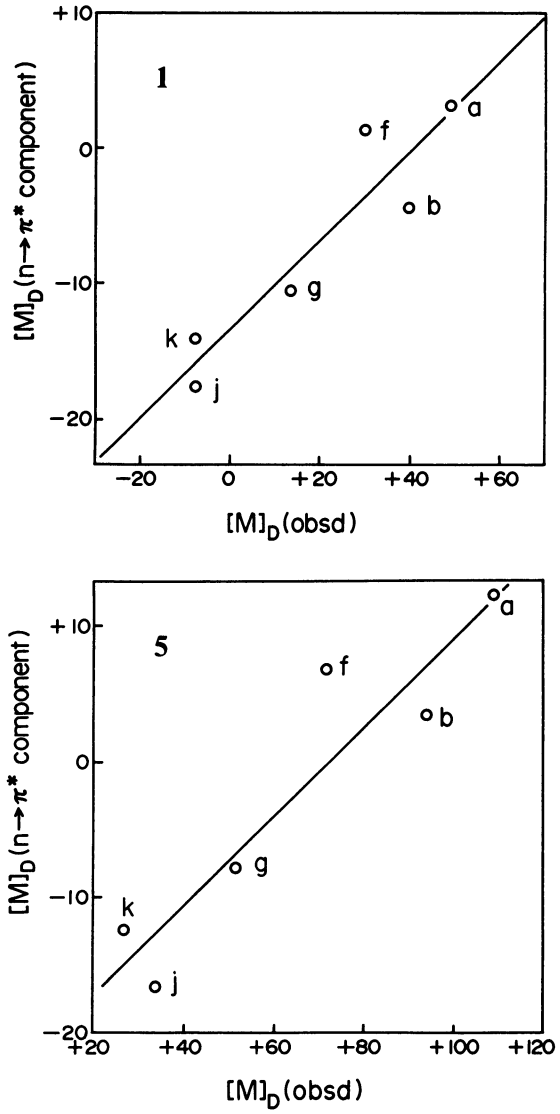

Fig. 10. A plot of $[M]_D$(n→π* component) vs. $[M]_D$(obsd) for **1** and **5**. For the symbols of the data points, see Table 2.

due to the difference in the nature between the solvent effect on the Cotton effect at 280 nm and that on the Cotton effect below 230 nm.

The Wavelength of the Cotton Effect below 230 nm. Since there is a good correlation between the $[M]_D$ of the compound **1** and that of the compound **5** in the selected solvents (a), (b), (f), (g), (j), and (k), the Cotton effect below 230 nm was examined for the compound **5** free of the phenyl group, instead of the compound **1**. The wavelength (λc) of the Cotton effect below 230 nm was calculated by use of a one-term Drude equation[15] as follows. The ORD data, [M(λ)](dif), used in the Drude analysis were derived from the difference between the observed ORD data, [M(λ)](obsd), and the contribution of the carbonyl n→π* Cotton effect to the molecular rotation, [M(λ)](n→π* component), in both chloroform and methanol. The [M(λ)](n→π* component) were calculated by use of the simplified Kronig-Kramer's equation described above. The [M(λ)]-

(dif) in the wavelength region of 340 to 600 nm were used for the calculation, because the compound **5** showed a plain ORD curve in the region in both the solvents. When the λc was assumed to be 200±10 nm, the [M(λ)](dif) from 340 to 600 nm fit the one-term Drude equation well in both chloroform and methanol. This suggests that a strong Cotton effect presents at around 200 nm, and the solvent effect on the Cotton effect largely affects the solvent effect on the optical rotation at sodium-D line. This CD band will probably correspond to carbonyl and/or hydroxyl CD bands at 185—200 nm.[16,17] The similar results is expected for the compound **1**, because there is the good correlation between $[M]_D$ of the compound **1** and that of the compound **5** as mentioned above.

In conclusion, it was found that causing the 1,7-diaryl-5-hydroxy-3-heptanones dextro-rotatory in chloroform was attributed to the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups in the molecules, and the presence of the phenyl groups did not affect the determination of the sense of their optical rotations. On the other hand, causing the compounds levo-rotatory in methanol was proved to be attributed to the breaking of the intramolecular hydrogen bond followed by solvation to the carbonyl and/or hydroxyl groups, as well as the presence of the phenyl groups. The ca. 30% of the solvent effect on the optical rotation is based on the change in the rotational strength associated with the $n\rightarrow\pi^*$ transition of the carbonyl group as changing a solvent. This change is caused by the conformational equilibrium. The formation and breaking of the intramolecular hydrogen bond is dominated by the ability of the solvents to accept the proton from the C-5 hydroxyl group of the compounds. When the intramolecular hydrogen bond is broken, the conformation of the compounds is dominated by the dielectric effect of the solvents. The residual 70% of the solvent effect on the optical rotation is based on the change in the rotational strength associated with the electronic transitions at around 200 nm of the carbonyl and/or hydroxyl groups.

Experimental

General. The ^{1}H NMR spectra were obtained on a Hitachi R-600 FT NMR (60 MHz) spectrometer using TMS as an internal standard. The ^{13}C NMR spectra were obtained on a Hitachi R-42 FT NMR (22.6 MHz) spectrometer. Tris[3-(2,2,2-trifluoro-1-hydroxyethylidene)-*d*-camphorato]europium [Eu(tfc)$_3$] was obtained from Merck. The mass spectra were obtained on a Shimadzu QP-1000 spectrometer with an EI ion source at 70 eV and a CI ion source with isobutane. The analytical GLC was carried out with a Shimadzu GC-6A gas chromatograph using a glass column (3 mm×2 m) packed with 2% OV-17 on Chromosorb W (AW-DMCS; 80—100 mesh). The optical rotation was measured with a JASCO DIP-360 digital polarimeter, using a 1.0-dm cell. The CD spectra were recorded on a JASCO J-40 spectropolarimeter. The ORD curves were recorded on a JASCO ORD/UV-5 spectropolarimeter at 25 °C in a quartz cell of 1.0-cm path length. The UV spectra were obtained on a Shimadzu UV-240 spectrometer. Solvents were either spectrophotometric grade or distilled immediately before use.

(*S*)-6-Hydroxy-4-nonanone (5). Into a slurry of pyridinium chlorochromate (710 mg) in 10 cm^3 of dry dichloromethane, (4*S*,6*S*)-4,6-nonanediol (506 mg) (see below) dissolved in 10 cm^3 of dry dichloromethane was added all at once, after which the mixture was kept for 3 h with stirring at room temperature. The reaction mixture was then added to dry diethyl ether (30 cm^3), and the resulting slurry was kept for another hour under stirring. The slurry was then passed through a column packed with 20 g of Florisil, and the eluate was concentrated under a reduced pressure at room temperature. The condensate was purified on a silica-gel column with diethyl ether–hexane (1:4) and then distilled at 88 °C (bath temperature) at 5 Torr (1 Torr=133.322 Pa) through a short-path distillation apparatus to afford **5** (313 mg, 63%) as colorless oil: $[\alpha]_D^{25}$ +59.3±0.5° (*c* 0.39, chloroform); $[\alpha]_D^{25}$ +16.9±0.5° (*c* 0.40, methanol); IR (neat) 3420 (OH) and 1705 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.92 (6H, t, *J*=7 Hz, Me×2), 1.23—1.90 (6H, m, >CH_2×3), 2.29—2.57 (4H, m, >CH_2×2), 3.04 (1H, brs, OH), and 4.04 (1H, m, >C<u>H</u>OH); EI-MS *m/z* (rel intensity) 140 (2, M^+-H_2O), 115 (14), 97 (10), 71 (65), and 43 (100); CI-MS *m/z* (rel intensity) 159 (62, M^++H) and 141 (100, M^+-H_2O+H). The GLC (90 °C) showed a single peak (retention time 16 min). The optical purity of **5** was determined by measuring the ^{1}H NMR with a soln of its acetate (5 mg) and Eu(tfc)$_3$ (3 molar equivalents to the acetate) in $CDCl_3$ (0.4 cm^3). The acetate showed no detectable signal of the enantiomer.

Preparation of (4*S*,6*S*)-4,6-Nonanediol. 4,6-Nonanedione (5.96 g), prepared from methyl butyrate and 2-pentanone by the method previously reported,[18] was hydrogenated with an asymmetrically modified Raney nickel [(*S*,*S*)-TA-NaBr-MRNi][19,20] followed by crystallization from hexane to afford (4*S*,6*S*)-4,6-nonanediol (1.04 g, 17%) as colorless needles: mp 52—53 °C (lit,[20] 58—59 °C); $[\alpha]_D^{25}$ +20.5±0.2° (*c* 10, ethanol) (lit,[20] $[\alpha]_D^{20}$ +21.2°); IR (KBr) 3340 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$) δ=0.74—1.12 (6H, m, Me×2), 1.18—1.68 (10H, m, >CH_2×5), 2.50—2.67 (2H, br, OH×2), 3.93 (2H, m, >C<u>H</u>OH×2); EI-MS *m/z* (rel intensity) 117 (16, M^+-43), 99 (35), 81 (83), and 73 (100); CI-MS *m/z* (rel intensity) 161 (17, M^++H), 160 (14, M^+), 143 (27, M^+-H_2O+H), and 125 (100, M^+-2H_2O+H). Found: C, 67.65; H, 12.76%. Calcd for $C_9H_{20}O_2$: C, 67.45; H, 12.58%. The GLC (120 °C) showed a single peak (retention time 8 min).

(*R*)-1,7-Diphenyl-3-heptanol (6). A solution of *p*-toluenesulfonyl chloride (220 mg) in dry pyridine (3 cm^3) was added to a solution of (3*S*,5*S*)-1,7-diphenyl-3,5-heptanediol (300 mg), prepared as shown below, in dry pyridine at 0 °C. The solution was allowed to stand at 4 °C for 3 d, poured into ice-cold 5% HCl, and then extracted with diethyl ether. The solution was washed with cold 5% HCl, 5% $NaHCO_3$, and saturated NaCl solutions, successively, and then dried over Na_2SO_4 followed by concentration in vacuo. The tosylate obtained was used for the next preparation without further purification. A solution of the optically active tosylate in dry THF (20 cm^3) was added to a slurry of $LiAlH_4$ (0.5 g) in dry THF (10 cm^3). The mixture was then heated under reflux for 5 h. An excess of $LiAlH_4$ was decomposed with a solution of methanol in diethyl ether and then 5% HCl.

The mixture was extracted with diethyl ether. The diethyl ether solution was washed with 5% HCl and saturated NaCl solutions, successively, and then dried (Na_2SO_4) followed by concentration in vacuo. The residue was purified on a silica-gel column with a mixture of ethyl acetate and hexane (1:4) to afford **6** (170 mg, 60%) as colorless needles: mp 60—61 °C; $[\alpha]_D^{25}$ −5.8±0.1° (*c* 1.70, chloroform) (lit,[21] $[\alpha]_D^{25}$ −4.3±2.9° (*c* 0.14, chloroform)); $[\alpha]_D^{25}$ −7.3±0.1° (*c* 1.70, methanol); UV (ethanol) 268 (log ε 2.51), 261 (2.64), 255 (2.57), 248 (2.44), and 243 nm (2.29); IR (KBr) 3340 (OH), 1598 and 1492 cm^{-1} (aromatic ring); ^1H NMR (CCl_4) δ= 1.06 (1H, brs, OH), 1.30—1.84 (8H, m, $>CH_2$×4), 2.45—2.81 (4H, m, $>CH_2$×2), 3.48 (1H, m, >CHOH), 7.13 (10H, m, aromatic H); EI-MS *m/z* (rel intensity) 250 (62, M^+-H_2O), 159 (10), 145 (8), 131 (9), 117 (31), 104 (57), and 91 (100); CI-MS *m/z* (rel intensity) 267 (65, M^+-H) and 251 (100, M^+-H_2O+H). Found: C, 85.25; H, 9.21%. Calcd for $C_{19}H_{24}O$: C, 85.02; H, 9.01%. The optical purity of **6** was determined by the same method as described for the determination of the optical purity of **5**. The acetate derived from **6** showed no detectable signal of the enantiomer.

Preparation of (3*S*,5*S*)-1,7-Diphenyl-3,5-heptanediol. 1,7-Diphenyl-3,5-heptanedione (2.70 g) prepared with the method previously reported[22] was hydrogenated with the asymmetrically modified Raney nickel described for the preparation of (4*S*,6*S*)-4,6-nonanediol followed by crystallization from hexane to afford (3*S*,5*S*)-1,7-diphenyl-3,5-heptanediol (1.10 g, 40%) as colorless needles: mp 89.5—90.5 °C; $[\alpha]_D^{25}$ −11.1±0.2° (*c* 1.06, ethanol); UV (ethanol) 268 (log ε 2.50), 261 (2.63), 255 (2.55), 249 (2.39), 243 nm (2.16); IR (KBr) 3350 (OH), 1600 and 1490 cm^{-1} (aromatic ring); ^1H NMR (CCl_4) δ=1.45—1.88 (6H, m, $>CH_2$×3), 2.52—2.81 (6H, m, $>CH_2$×2 and OH×2), 3.87 (2H, m, >CHOH×2), 7.13 (10H, m, aromatic H); EI-MS *m/z* (rel intensity) 266 (9, M^+-H_2O), 248 (17, M^+-2H_2O), and 91 (100); CI-MS *m/z* (rel intensity) 285 (50, M^++H), 267 (72, M^+-H_2O+H), and 249 (100, M^+-2H_2O+H). Found: C, 80.41; H, 8.77%. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51%. The optical purity of this diol was determined by measuring the ^1H NMR with a soln of its diacetate (5 mg) and Eu(tfc)$_3$ (3 molar equivalents to the diacetate) in $CDCl_3$ (0.4 cm^3). The diacetate showed no detectable signal of the enantiomer.

(*R*)-1,7-Bis(3,4-dimethoxyphenyl)-3-heptanol (7). Compound **7** was prepared following the previously reported method.[21] The reduction of the carbonyl group of the compound **2** (69 mg) with $TsNHNH_2$ (35 mg) and $NaBH_4$ (300 mg) in methanol gave **7** (51 mg, 77%): mp 67—69 °C; $[\alpha]_D^{25}$ −4.7±0.4° (*c* 0.51, chloroform); $[\alpha]_D^{25}$ −5.5±0.4° (*c* 0.51, methanol); UV (ethanol) 280 (log ε 3.70), 229 nm (4.13); IR (KBr) 3430 (OH), 1587 and 1515 cm^{-1} (aromatic ring); ^1H NMR ($CDCl_3$) δ=1.25—1.90 (8H, m, $>CH_2$×4), 1.70 (1H, brs, OH), 2.38—2.81 (4H, m, $>CH_2$×2), 3.60 (1H, m, >CHOH), 3.84 and 3.85 (12H, each s, OMe×4), 6.68—6.82 (6H, m, aromatic H); EI-MS *m/z* (rel intensity) 388 (32, M^+), 370 (2, M^+-H_2O), 177 (8), 164 (7), and 151 (100). Found: C, 71.14; H, 8.29%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%.

(*S*)-4-Nonanol (8). The tosylation of (4*S*,6*S*)-4,6-nonanediol (465 mg), prepared as shown above, followed by the reduction with $LiAlH_4$ was carried out in the same manner described for the preparation of **6**. The distillation of the product at 68 °C (bath temperature) at 4 Torr through a short-path distillation apparatus afforded **8** (191 mg, 46%) as colorless oil: $[\alpha]_D^{25}$ +0.6±0.2° (*c* 2.25, chloroform); $[\alpha]_D^{25}$ +0.5±0.2° (*c* 2.25, methanol) (lit,[23] $[\alpha]_D^{25}$ +0.57°); IR (neat) 3350 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ=0.70—1.04 (6H, m, Me×2), 1.16—1.53 (12H, m, $>CH_2$×6), 1.73 (1H, brs, OH), 3.61 (1H, m, >CHOH); EI-MS *m/z* (rel intensity) 126 (1, M^+-H_2O), 101 (9), 83 (34), 73 (40), and 55 (100); CI-MS *m/z* (rel intensity) 143 (11, M^+-H) and 127 (100, M^+-H_2O+H). The GLC (90 °C) showed a single peak at 6 min of retention time.

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