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THE FACTORS DOMINATING THE REVERSAL IN THE SENSE OF THE OPTICAL ROTATION OF DIARYLHEPTANOIDS IN THE SOLVENTS OF THE DIFFERENT NATURE

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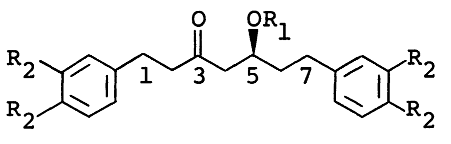
Causing (*S*)-1,7-diphenyl-5-hydroxy-3-heptanone dextrorotatory in chloroform was attributed to the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups, regardless of the presence of the phenyl groups. On the other hand, causing the compound levorotatory in methanol was proved to necessitate simultaneously the breaking of the intramolecular hydrogen bond followed by the solvation to its β-ketol moiety, as well as the presence of the phenyl groups.

It had been reported that some natural compounds[1,2] show the reversal in the sense of their optical rotation when measured in the selected solvents with different polarity. However, causes for this phenomenon have not been solved yet. The reversal in the sense of optical rotation was also 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**).[4,5] In the present letter, we describe the factors dominating the reversal in the sense of the optical rotation of the diarylheptanoid (**1**) in the solvents of the different nature.

The compound **1** was dextrorotatory, $[\alpha]_D^{25}$ +14.0 ± 0.6°, in chloroform and levorotatory, $[\alpha]_D^{25}$ −2.7 ± 0.6°, in methanol, while its acetate (**3**) was dextrorotatory in both solvents, $[\alpha]_D^{25}$ +3.6 ± 0.3° in chloroform and $[\alpha]_D^{25}$ +4.1 ± 0.3° in methanol. These observations suggest that the interaction between the solvent and the β-ketol moiety of the compound **1** is responsible for the reversal in the sense of its optical rotation.

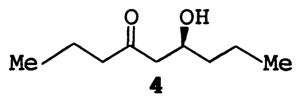
The effect of the solvents on the optical rotation of the compound **1** was examined by a solvatochromic comparison method[6] with the following solvents: (1) carbon tetrachloride, (2) chloroform, (3) dichloromethane, (4) benzene,



1 $R_1=R_2=H$

2 $R_1=H$, $R_2=OMe$

3 $R_1=Ac$, $R_2=H$



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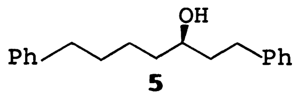

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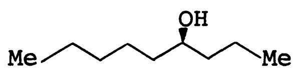

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(5) toluene, (6) dioxane, (7) ethyl acetate, (8) acetone, (9) acetonitrile, (10) methanol, (11) ethanol, and (12) 2-propanol. The molecular rotations $[M]_D$ of the compound 1 in these solvents were independent of the concentration (0.005—0.1 mol dm^{-3}) and truly constant. The relationship between the $[M]_D$ and the solvatochromic parameters π^*, α, and β[6)] was represented by the following least-squares regression equation,

$$[M]_D = 52.2 - k(59.7\pi^* + 7.8\alpha + 24.2\beta).$$

A plot of $[M]_D$ *vs.* $(59.7\pi^* + 7.8\alpha + 24.2\beta)$ is shown in Fig. 1, and k was 0.3 for solvents (1)—(5) and 1.0 for solvents (6)—(12). Separate correlation lines were observed for the individual solvent families. The $[M]_D$ was dextrorotatory in the solvents (1)—(5). The β values representing hydrogen-bond acceptor basicities are very small (0—0.11)[6)] for the solvents (1)—(5). Thus, the ability of the solvents to accept the proton from the C-5 hydroxyl group of the compound 1 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 (6)—(12) changed from dextrorotatory to levorotatory with the change in the values of the solvatochromic parameters. The β values for the solvents (6)—(12) are 0.37—0.95[6)] and higher than those for the solvents (1)—(5). In the solvents (6)—(12), therefore, the proton of the C-5 hydroxyl group of the compound 1 is strongly attracted to the solvent molecules. Accordingly, there is a fair possibility of the breaking of the intramolecular hydrogen bond followed by the solvation to the carbonyl and/or hydroxyl groups in the solvents (6)—(12). Here, the authors note that the compound 1 was dextrorotatory in the solvents (6) and (7). This is probably attributable to the very weak interaction of these solvents to its β-ketol moiety.

Next, a more definite study for demonstrating the formation and breaking of the intramolecular hydrogen bond was carried out by a combination of IR and ^{13}C NMR spectroscopies. The IR spectrum of the compound 1 in a carbon tetrachloride solution exhibited the presence of intramolecularly hydrogen-

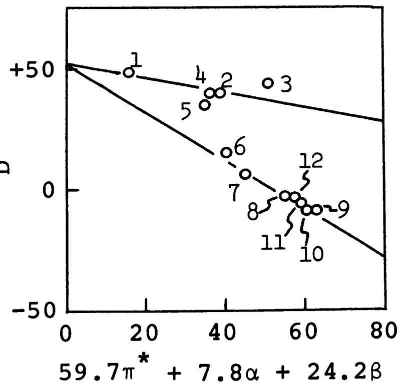

Fig. 1. A plot of $[M]_D$ of **1** *vs.* $59.7\pi^* + 7.8\alpha + 24.2\beta$. Numbering of the data points is as in text.

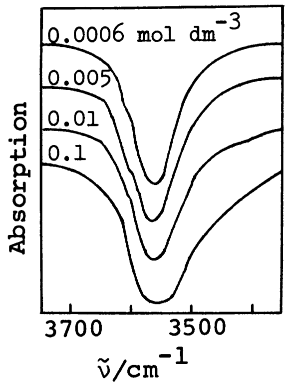

Fig. 2. IR spectra of **1** in carbon tetrachloride solution ranging in concentration from 0.0006 to 0.1 mol dm^{-3}.

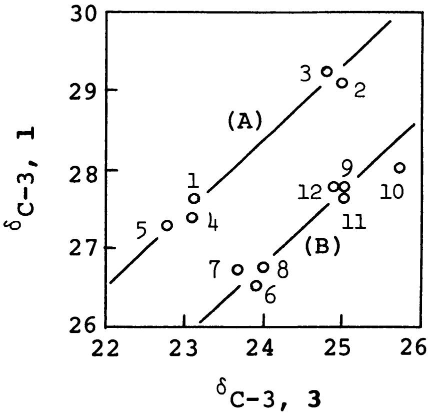

Fig. 3. A plot of δ_{C-3} for **1** *vs.* δ_{C-3} for **3** in the selected solvents (ppm with respect to an external reference of $CH_3{}^{13}CO_2Na$). Numbering of the data points is as in text.

bonded OH absorption band at 3556 cm^{-1} which was independent of the concentration (0.0006—0.1 mol dm^{-3}), as shown in Fig. 2. Figure 3 shows the relation of the ^{13}C NMR chemical shift between the C-3 carbonyl carbons of the compound **1** and its acetate (**3**) in twelve solvents (1)—(12). The data points for the solvents (1)—(5) and the solvents (6)—(12) 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). This lower-field shift7) indicates clearly that the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups is formed in the solvents (1)—(5) and the intermolecular hydrogen bond between the solvent and the β-ketol group occurs in the solvents (6)—(12). It was thus found that the formation of the intramolecular hydrogen bond between the C-3 carbonyl and C-5 hydroxyl groups causes the compound **1** dextrorotatory in the solvents (1)—(5), while the breaking of the intramolecular hydrogen bond followed by the solvation to the carbonyl and/or hydroxyl groups causes the compound **1** levorotatory in the solvents (8)—(12).

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 (**4**),8) (*R*)-1,7-diphenyl-3-heptanol (**5**),9) and (*S*)-4-nonanol (**6**),10) by means of optical rotatory dispersion (ORD) measurements. Figure 4 shows the ORD curves of the compounds **1** and **4**—**6** in chloroform and methanol. The ORD curves of the compounds **1** and **4** showed the solvent dependence, whereas the ORD curves of the compounds **5** and **6** were not the case. This indicates the indispensability of the β-ketol moiety for occurrence of the solvent effect on the optical rotation. On the other hand, the compound **5** was levorotatory in 400—600 nm in chloroform and methanol, while the compound **6** was

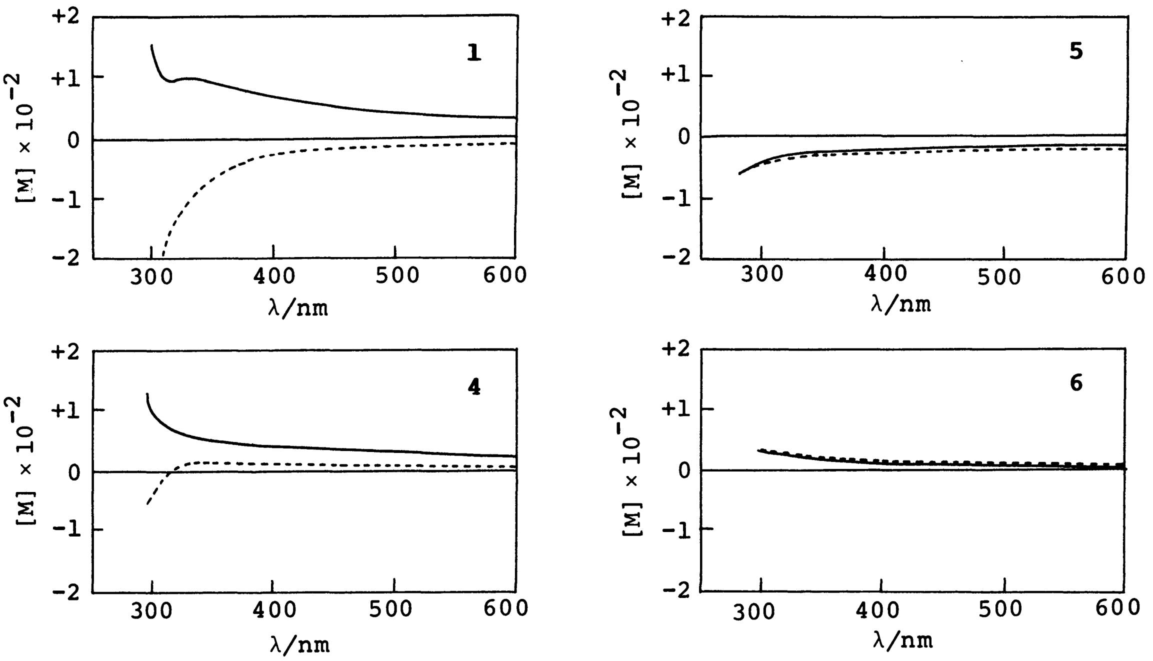

Fig. 4. ORD curves of **1** and **4**—**6**: ——— in chloroform, ------ in methanol.

dextrorotatory in these solvents. This fact indicates unambiguously that, in addition to the breaking of the hydrogen bond followed by solvation, the presence of the phenyl groups in the molecules of the compounds **1** and **5** is essential for the appearance of levorotation.

Thus, a dominant factor causing the 1,7-diphenyl-5-hydroxy-3-heptanone (**1**) dextrorotatory in chloroform was proved to be the formation of the intramolecular hydrogen bond between the carbonyl and hydroxyl groups in the molecule, and the presence of the phenyl groups has no connection with determining the sense of its optical rotation. For causing the compound levorotatory in methanol, on the other hand, a dominant factor was the breaking of the intramolecular hydrogen bond followed by the solvation to the carbonyl and/or hydroxyl groups, as well as the presence of the phenyl groups was indispensable. Further examinations for the effect of solvents on the sense of the optical rotation is in progress.

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8) Asymmetric partial hydrogenation[11) of 4,6-nonanedione afforded **4** as colorless oil, bp 101 °C (bath temp) (12 mmHg); $[\alpha]_D^{25}$ +12.7 ± 0.8° (*c* 2.67, chloroform); $[\alpha]_D^{25}$ +3.5 ± 0.8° (*c* 2.55, methanol); *ca.* 50% ee.12)
9) Asymmetric reduction13) of 1,7-diphenyl-4-hepten-3-one, followed by catalytic hydrogenation over 10% Pd-C, afforded **5** as colorless needles, mp 44—45 °C (from hexane); $[\alpha]_D^{25}$ -3.2 ± 1.1° (*c* 1.87, chloroform); $[\alpha]_D^{25}$ -5.4 ± 1.1° (*c* 1.87, methanol); *ca.* 50% ee.12)
10) Actually an *R* enantiomer14) was used, and the ORD curves of **6** in Fig. 4 are drawn after the sign of ORD curves of the *R* enantiomer were reversed. (*S*)-4-Nonanol is now in preparation.
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14) Asymmetric reduction13) of 2-nonen-4-one, followed by catalytic hydrogenation over 10% Pd-C, afforded (*R*)-4-nonanol as colorless oil, $[\alpha]_D^{25}$ -0.5 ± 0.2° (*c* 8.79, chloroform); $[\alpha]_D^{25}$ -0.6 ± 0.2° (*c* 8.67, methanol) [lit.15) $[\alpha]_D^{25}$ +0.57° for *S* enantiomer].
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