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INDUCED CIRCULAR DICHROISM OF SUBSTITUTED BENZOPHENONES BY COMPLEXATION WITH CHIRAL CROWN ETHERS

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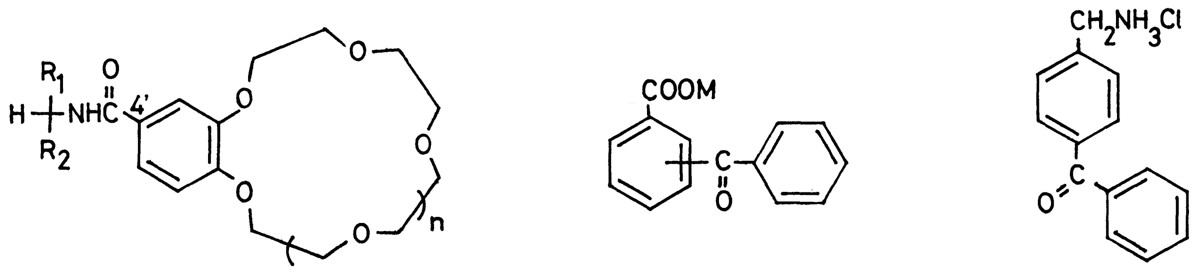
Enhanced induced circular dichroism (ICD) was observed, using ionic benzophenone derivatives as guests and crown compounds containing chiral moieties as hosts. The strength of the ICD spectra was found to depend highly on the solvent polarity and temperature. In methanol-water mixtures the formation constant of crown complexes could be evaluated by the measurement of the ICD.

Benzophenone derivatives have been confirmed to exhibit ICD by interaction with chiral compounds. The chiral induction is attained by various methods such as inclusion complex formation with β-cyclodextrine,[1)] ion-pair formation with chiral amines,[2)] and the use of chiral solvents.[3)] Cyclic polyethers, which are called crown ethers, are known to form complexes with alkali metal cations or others.[4)] With the cyclic peptide or the chiral crown ether the formation constant for cation complexes had been evaluated from the CD spectral change, which is attributed to the conformational change on complex formation.[5)] The present study is concerned with the ICD information on complexes of alkali metal benzoylbenzoates and benzoylbenzylammonium salts with derivatives of benzo-15-crown-5 and benzo-18-crown-6 containing chiral moieties at 4'-position.

Chiral crown ethers and ionic benzophenone derivatives, as shown in Fig. 1, were prepared as follows. Carboxybenzo-15-crown-5 and carboxybenzo-18-crown-6 were converted to the corresponding acid chloride with thionyl chloride in chloroform, and then an excess of thionyl chloride was removed under reduced pressure.



I-a - I-e

II-M (M = Na, K)
ortho, meta, para-forms

III

Fig. 1. Crown ethers and substituted benzophenones used in this study.

To chloroform solution of chiral amines which were L-alanine methyl ester, D-α-phenylethylamine, and L-phenylalanine methyl ester, the chloroform solution of the acid chloride was added dropwise. The mixture was refluxed for 10 hours. The product (I) was purified by recrystallization from toluene.6)

I-a (n=1); $R_1=CH_3$, $R_2=COOCH_3$, $[\alpha]_D^{15}$ +4.2° (c 1.0, MeOH), M^+ 397, mp 164-165 °C, Anal. Calcd. for $C_{19}H_{27}NO_8$: C, 57.43; H, 6.80; N, 3.53. Found: C, 57.13; H, 6.94; N, 3.51.

I-b (n=2); $R_1=CH_3$, $R_2=COOCH_3$, $[\alpha]_D^{15}$ +3.6° (c 1.0, MeOH), M^+ 441, mp 121-122 °C, Anal. Calcd. for $C_{21}H_{31}NO_9$: C, 57.13; H, 7.08; N, 3.17. Found: C, 57.02; H, 7.17; N, 3.15.

I-c (n=1); $R_1=C_6H_5CH_2$, $R_2=COOCH_3$, $[\alpha]_D^{15}$ -52.6° (c 1.0, MeOH), M^+ 473, mp 144-145 °C, Anal. Calcd. for $C_{25}H_{31}NO_8$: C, 63.43; H, 6.55; N, 2.96. Found: C, 63.67; H, 6.58; N, 2.93.

I-d (n=2); $R_1=C_6H_5CH_2$, $R_2=COOCH_3$, $[\alpha]_D^{15}$ -52.4° (c 1.0, MeOH), M^+ 517, mp 127-128 °C, Anal. Calcd. for $C_{27}H_{35}NO_9$: C, 62.66; H, 6.82; N, 2.70. Found: C, 62.54; H, 6.94; N, 2.50.

I-e (n=1); $R_1=C_6H_5$, $R_2=CH_3$, $[\alpha]_D^{15}$ -34.2° (c 1.0, MeOH), M^+ 415, mp 157-159 °C, Anal. Calcd. for $C_{23}H_{29}NO_6$: C, 66.51; H, 6.99; N, 3.37. Found: C, 66.37; H, 7.20; N, 3.19.

One of benzoylbenzoic acid derivatives, 2-benzoylbenzoic acid, was obtained commercially and used without further purification. The other acids, 3- and 4-benzoylbenzoic acids, were prepared by Friedel-Crafts reaction of benzene with iso- and terephthaloyl chloride, respectively.7) Neutralization of the benzoylbenzoic acids by alkali metal hydroxide (Na^+ and K^+) affords the benzoylbenzoates (II). Benzoylbenzylammonium chloride (III) was prepared from 4-iodomethylbenzophenone by Delepine reaction.8)

The UV and CD spectra were measured in chlorobenzene or methanol solution of the chiral crown ethers and ionic benzophenone derivatives, and their data were listed in Table I. Fig. 2 shows the UV and CD spectra of chlorobenzene solution of I-a and meta-II-Na. In nonpolar solvents such as chlorobenzene, enhanced ICD arising from the n-π* electronic transition of the carbonyl group was observed at 320-400 nm. The ICD strength is strongly dependent on the solvent polarity(Table II). Increasing polarity of the solvent reduces the ICD strength. In polar solvents such as methanol, benzoylbenzylammonium complexes showed Cotton effects, while alkali metal benzoylbenzoate complexes did not. From these results it is considered that the interaction of crown ether and ion-pair causes the ICD; crown tightly complexed ion-pair exhibits enhanced ICD in nonpolar solvents and the dissociation of ion-pair reduces the chiral induction. The temperature dependence of the ICD was also studied. The molecular ellipticity $[\theta]_{max}$ decreased with increasing temperature. Fig. 3 shows the plots of $\log[\theta]_{max}$ against 1/T. The curve was approximately extrapolated to give two straight lines and the enthalpy changes for chiral induction were found to be about -4.2 to -42 kJ/mol for these complexes. This nonlinearity may suggest that the equilibrium and intramolecular rotation of the complex also contribute to the chiral induction.9)

Table I. $[\theta]_{max}$ of crown complexes

salt \ crown	I-a	b	c	d	e
o-II-Na	-132 (320)	——	-110 (320)		180 (325)
K	-817 (325)	-236 (320)	-653 (325)		187 (320)
m-II-Na	671 (344)	——	132 (346)		-87 (345)
K	-302 (338)	-126 (348)	-309 (345)		169 (345)
p-II-Na	50*	——	60*		50*
K		-80*			
III		181** (343)		280** (343)	

*: Estimated roughly (because of low S/N).
Solvent: chlorobenzene (**: measured in methanol owing to the poor solubility of the complex),
(λ_{max}: nm), [crown]/[salt]= 2.2,
temperature: 30 °C,
[salt]= 6.00×10^{-3} M.

Table II. Solvent effects on the ICD of I-a-*o*-II-K system

solvent	benzene	chloro-benzene	chloroform	dichloro-methane	acetonitrile	methanol
$[\theta]_{max}$ (λ_{max}: nm)	-1341 (324)	-817 (325)	-632 (324)	-654 (324)	-121 (322)	0

Taking advantage of the concentration-dependent ICD spectral change, it is possible to evaluate the complex formation constant K. In nonpolar solvents K must be too large to detect the slight change of the ion-pair complex concentration with addition of crown ethers. However, in methanol-water mixtures K is small and addition of crown ether gives rise to increase in the CD strength. By applying the Benesi-Hildebrand relation to the ICD data, log K was evaluated as 1.5 ± 0.2 for I-d-III system in methanol-water (54/46 wt%) mixtures at 24 °C. Thus, ICD spectrum may be one of useful methods for evaluation of formation constants of crown ether-cation complexes.

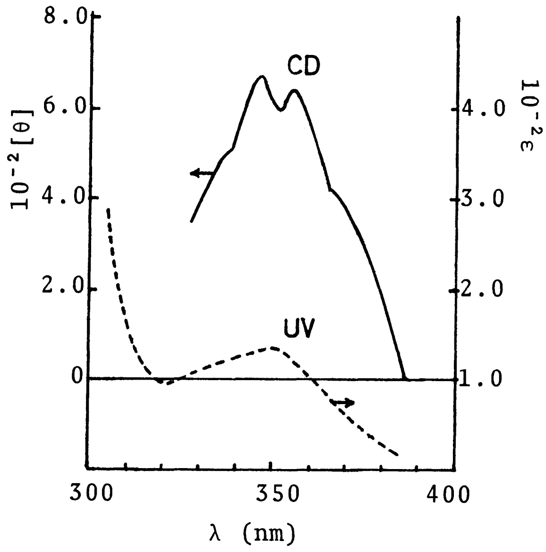


Fig. 2. CD and UV spectra of benzoylbenzoate (*m*-II-Na; 6.00 $\times 10^{-3}$ M) with crown ether (I-a; 1.32 $\times 10^{-2}$ M) in chlorobenzene at 30 °C.

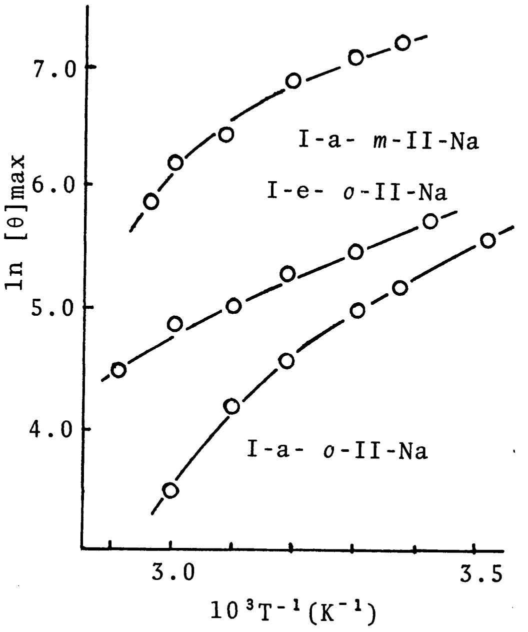


Fig. 3. Temperature dependence of ICD for crown complexes in benzene: [crown] / [salt] = 2.2, [salt] = 8.00×10^{-3} M.

References

1) N. Matsuura, S. Takenaka, and N. Tokura, J. Chem. Soc., Perkin Trans. 2, 1977, 1419.

2) S. Takenaka, M. Ako, T. Kotani, A. Matsubara, and N. Tokura, ibid., 1978, 95.

3) B. Bosnich, J. Am. Chem. Soc., 89, 6143 (1967).
L. D. Hayward and R. N. Totty, Can. J. Chem., 49, 624 (1971).

4) J. J. Christensen, D. J. Eatough, and R. M. Izatt, Chem. Rev., 74, 351 (1974).

5) V. Madison, C. M. Deber, and E. R. Blout, J. Am. Chem. Soc., 99, 4788 (1977).
M. P. Mack, R. R. Hendrixson, R. A. Palmer, and R. G. Ghirardelli, ibid., 98, 7830 (1976).

6) R. Ungaro, B. El Haj, and J. Smid, ibid., 98, 5198 (1976).

7) M. E. Smith, ibid., 43, 1921 (1921).

8) F. F. Blicke and W. M. Lilienfeld, ibid., 65, 2281 (1943).

9) S. Takenaka, K. Kondo, and N. Tokura, J. Chem. Soc., Perkin Trans. 2, 1974, 1749.

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