Induced Circular Dichroism of Chiral Amine–Benzoylbenzoic Acid Systems

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Induced circular dichroism for the ion-pair systems of benzoylbenzoic acid–chiral amine displays two typical shapes associated with the origins of the carbonyl *n*–π* transition, *i.e.*, the electronically allowed and vibronically allowed transitions. In the former case the i.c.d. spectra display Gaussian shapes with the sign dependent on the helical structure of the acid. In the latter case the spectra display definite vibrational structure.

BENZOPHENONE derivatives display induced circular dichroism (i.c.d.) in chiral solvents,[1,2] by complex formation with β-cyclodextrin in aqueous solution,[3] and by ion-pair formation with chiral amines in non-polar solvents.[4] The induction of optical activity is remarkable in the latter two cases. However a correlation between the i.c.d. effect and the chemical and/or physical properties of chiral molecules has not been adduced.

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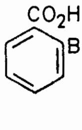
In this paper, attempts in this area are made for the i.c.d. system, chiral amine–benzoylbenzoic acid.

EXPERIMENTAL

The optical procedures were described previously.[4]

Materials.—Methyl esters of L-amino-acids were prepared by the method of Brenner *et al.*[5] from the respective amino-acids. The α-amino-alchohols (17)—(19) were prepared by reduction with lithium aluminium hydride of the respective amino-acid methyl esters.[6] Compounds (21), (22), and (30) were purchased from Aldrich and were purified by distillation before use. Other optically active amines were prepared by the Leuckart reaction of corresponding ketones,[7] or sodium reduction of corresponding ketoxime,[8] followed by optical resolution with L-(+)-tartaric acid; [9] (*S*)-(+)-1-methylpropylamine [10] had $[\alpha]_D$ 4.72° (neat), (*R*)-(−)-1,2-dimethylpropylamine [11] $[\alpha]_D$ −1.47° (*c* 0.9, ethanol), (*R*)-(−)-1-methylbutylamine [11] $[\alpha]_D$ −1.41° (*c* 0.9, ethanol). Racemic 1-(*p*-fluorophenyl)ethylamine was prepared by the conventional method,[7] and was resolved by (+)-tartaric acid.[9] After five recrystallizations from methanol, the less soluble salt, m.p. 193—194.5°, was decomposed by adding 20% aqueous sodium hydroxide to give the (−)-*amine*, b.p. 72° at 21 mmHg, $[\alpha]_D$ −30.7° (neat) (Found: C, 70.55; H, 7.6; N, 10.5. $C_8H_{10}FN$ requires C, 69.05; H, 7.25; N, 10.05%). The *phthalimide derivative* had m.p. 57—58°, $[\alpha]_D$ −35.1° (*c* 1.5, chloroform), c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm) 2 285 (293) in ethanol (Found: C, 71.45; H, 4.6; N, 5.3. $C_{16}H_{12}FNO_2$ requires C, 71.35; H, 4.5; N, 5.2%). The specific rotation and c.d. data predict the (−)-amine to have the *S* configuration.[12] The similarity of the i.c.d. data in Table 2 also leads to the same assumption. The specific rotations of other amines are summarized in Table 2. Secondary amines were prepared by the method of Buck [13] from the optically active amines, and the data for the specific rotation are summarized in Table 3.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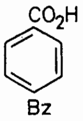
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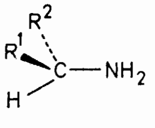
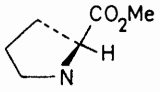


(3) R^1=Me, R^2=CO_2Me
(4) R^1=Pr^i, R^2=CO_2Me
(5) R^1=Bu^i, R^2=CO_2Me
(6) R^1=Bu^s, R^2=CO_2Me
(7) R^1=CH_2CH_2SMe, R^2=CO_2Me
(8) R^1=CH_2CH_2SMe, R^2=CO_2Et
(9) R^1=CH_2Ph, R^2=CO_2Me
(10) R^1=$CH_2C_6H_4OH$-*p*, R^2=CO_2Me
(11) R^1=Me, R^2=Et
(12) R^1=Pr^i, R^2=Me
(13) R^1=Pr^n, R^2=Me
(14) R^1=CH_2Ph, R^2=Me
(15) R^1=CH(OH)Me, R^2=CO_2Me
(16) R^1=CH_2CO_2Me, R^2=CO_2Me
(17) R^1=Me, R^2=CH_2OH
(18) R^1=Bu^s, R^2=CH_2OH
(19) R^1=Pr^i, R^2=CH_2OH
(21) R^1=Ph, R^2=Me
(22) R^1=Me, R^2=Ph
(23) R^1=Me, R^2=C_6H_4Me-*p*
(24) R^1=C_6H_4OMe-*p*, R^2=Me
(25) R^1=Me, R^2=C_6H_4F-*p*
(26) R^1=Me, R^2=C_6H_4Cl-*p*
(27) R^1=C_6H_4Br-*p*, R^2=Me
(28) R^1=Me, R^2=C_6H_4CN-*p*
(29) R^1=Et, R^2=Ph
(30) R^1=α-$C_{10}H_7$, R^2=Me
(31) R^1=Ph, R^2=CH_2Ph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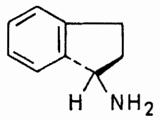
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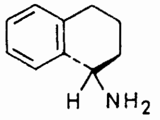
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RESULTS

The i.c.d. spectra arising from the *n*–π* transition of the carbonyl group for the ion-pair systems chiral amine–2-benzoylbenzoic acid (1) display two typical forms with increasing amine concentration (Figure 1a and b). In the former case the spectra show a complicated change in the region $R < 2.0$ where R is [amine] : [acid]. The i.c.d. change is associated with the acid–base equilibrium. When the formation constant K of the ion-pair is >100, the i.c.d. intensity increases almost linearly with increasing amine concentration and becomes constant above R 2.0. However, when the formation constant is relatively small ($K < 50$), plots of θ against λ show a gradual change, as shown in Figure 1a. The spectra of this type exhibit a single maximum at *ca.* 325 nm. The i.c.d. data at R 0.5 and 3.0 are indicated in Table 1.

In the latter case, the shape of the i.c.d. curve seems to be almost independent of the amine concentration, though the intensity increases upon increasing amine concentration. The spectra of this type involve strong vibrational structure; typical examples are indicated in Figure 2. The vibr-

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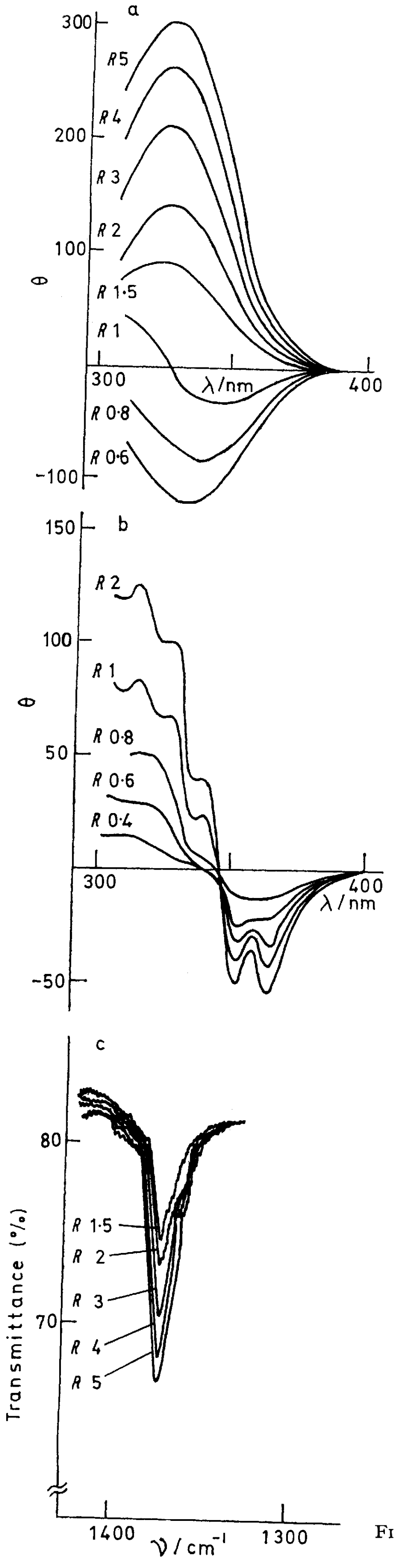


FIGURE 1 a, I.c.d. spectrum of amine (6)–acid (1); b, i.c.d. spectrum of amine (27)–acid (1) (10^{-2}M); c, i.r. spectrum of amine (6)–acid (1) (10^{-2}M) in benzene at 40—50° (0·5 mm path length cell). R = [amine] : [acid]

ational structure is observed in non-polar solvents such as carbon tetrachloride and benzene, and becomes more marked upon lowering the temperature.

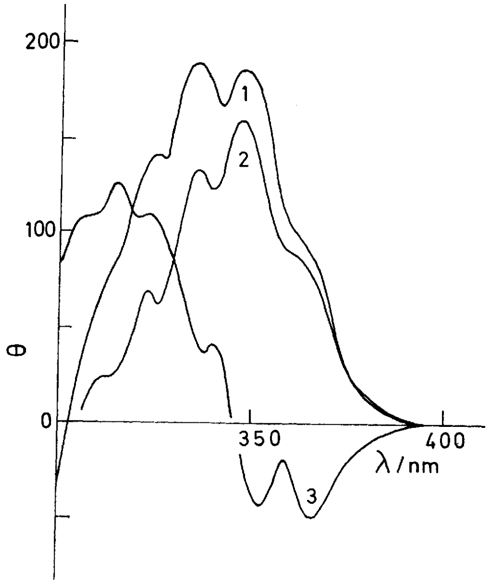


FIGURE 2 I.c.d. spectra of 1, amine (22)–acid (1) (0.5θ); 2, amine (25)–acid (1); and 3, amine (27)–acid (1) in benzene at 22°, [amine] 2 × 10^{-2}M, [acid] 10^{-2}M

TABLE 1

Spectral data for chiral amine–(1) and –(2) systems

		I.c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm)		
		Acid (1)		Acid (2)
Amine	K	R 0.4	R 3.0	R 2.0
(3)	77 ± 7	59 (327)	−597 (324)	49 (347)
(4)	16 ± 4	−109 (336)	135 (324)	0
(5)	18 ± 3	−63 (336)	251 (326)	41 (334)
(6)	32 ± 6	−102 (336)	221 (326)	20 (345)
(7)	16 ± 2	−7 (334)	139 (331)	0
(8)		−32 (333)	55 (333)	
(9)	6.5 ± 0.5	76 (326)	122 (326)	76 (345)
(10)	>100	640 (326)	2 000 (327)	0
(11)			−493 (325)	−33 (342)
(12)			346 (324)	0
(13)			288 (324)	
(14)	>100		1 161 (322)	95 (345)
(15)	>100	−33 (330)	−216 (330)	0
(16)	12 ± 1	−181 (328)	−287 (328)	38 (346)
(17)		58 (332)	243 (330)	
(18)		475 (326)	534 (329)	
(19)		495 (327)	271 (329)	
(20)	>100	581 (326)	528 (326)	0

Experimental condition: [benzoylbenzoic acid] 1 × 10^{-2}M; [chiral amine] 0.4 × 10^{-2} (R 0.4), 2 × 10^{-2} (R 2), 3 × 10^{-2}M (R 3) in benzene at 22 ± 1°.

The i.c.d. spectra for the chiral amine–4-benzoylbenzoic acid (2) systems also exhibit similar shapes. The i.c.d. data are summarized in Tables 1—3. The equilibrium constants for the ion-pair indicated in Table 1 were evaluated from the change of absorbance at 1 370 cm^{-1} (Figure

TABLE 2

Spectral data for α-aralkylamine–(1) and –(2) systems

Amine	$[\alpha]\theta/°$ [a]	I.c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm) Acid (1)	I.c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm) Acid (2)
(21) [b]	37	−375 (334)	350 (347)
(22) [b]	−37	367 (334)	−355 (347)
(23) [c]	−9.1	190 (335)	−102 (347)
(24) [c]	10.2	−285 (333)	57 (347)
(25) [d]	−30.7	311 (348)	−832 (347)
(26) [c]	−27.4	106 (351)	−528 (346)
(27) [c]	−26.5	−52 (367)	294 (345)
(28) [e]	−29.4	79 (351)	
(29) [f]	−13.0	725 (333)	−518 (347)
(30) [g]	78	−882 (340)	23 (345)
(31) [h]	−13.3	−910 (324)	155 (347)
(32) [i]	25.0	−1 780 (320)	581 (347)
(33) [j]	35.5	−2 035 (317)	541 (346)

Experimental conditions are as in Table 1.

[a] Neat at 25°. [b] W. Leithe, *Ber.*, 1931, **64**, 2827. [c] J. H. Brewster and S. F. Osman, *J. Amer. Chem. Soc.*, 1960, **82**, 5754. [d] See Experimental section. [e] G. Gottarelli and B. Samori, *J. Chem. Soc. (B)*, 1971, 2418. [f] M. E. Warren, jun., and H. E. Smith, *J. Amer. Chem. Soc.*, 1965, **87**, 1757. [g] H. Wolf, E. Bunnenberg, and C. Djerassi, *Ber.*, 1964, **97**, 533. [h] H. E. Smith and T. C. Willis, *J. Amer. Chem. Soc.*, 1971, **93**, 2282. [i] J. H. Brewster and J. G. Buta, *J. Amer. Chem. Soc.*, 1966, **88**, 2233. [j] Ref. 15.

TABLE 3

Spectral data for secondary amine–(1) systems

Parent amine	Substituent on nitrogen	$[\alpha]_D/°$ [a]	I.c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm) R 0.5	I.c.d. $\theta_{max.}$ ($\lambda_{max.}$/nm) R 2.0
(22)	Me	58.0	−208 (330)	788 (334)
	Et	−23.2	−1 145 (330)	−817 (331)
	Pr^n	−20.0	−1 152 (329)	−868 (331)
	Pr^i	−29.2	−2 423 (329)	−3 134 (332)
	Bu^n	−84.0	−1 181 (329)	−1 418 (329)
	Bu^i	−33.6	−1 207 (329)	−2 075 (330)
	CH_2Ph	−30.5	−1 707 (328)	−1 921 (328)
	C_6H_{11}	−35.4	−3 008 (331)	−4 288 (331)
	$CH_2C_{10}H_7$-β	−14.0	−581 (332)	−1 067 (330)
(26)	Me	−71.0	−181 (330)	203 (330)
	C_6H_{11}	−28.0	−2 652 (330)	−4 387 (331)
	CH_2Ph	−61.8	−1 491 (330)	−1 839 (330)
(30)	Me	132.4	221 (333)	−177 (330)
	C_6H_{11}	66.8	6 234 (330)	7 191 (328)
	CH_2Ph	17.7	1 262 (330)	2 012 (327)
(32)	Me	31.8	32 (340)	226 (350)
	C_6H_{11}	47.3	−825 (328)	1 651 (331)
	CH_2Ph	2.4	367 (335)	1 102 (331)
(5)	Me	−6.4	17 (334)	10 (328)
	C_6H_{11}	−0.3	−374 (330)	−507 (330)
	CH_2Ph	−49.2	115 (328)	259 (328)
(9)	Me	−23.3	10 (337)	43 (336)
	C_6H_{11}	−15.6	−449 (330)	−647 (329)
	CH_2Ph	−0.1	14 (331)	11 (330)

Experimental conditions are as in Table 1.

1c) due to $\nu_{CO_2^-}$ by the crude equilibrium expression (1)

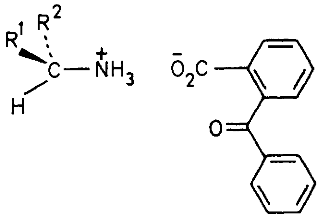
$$RCO_2H + B \overset{K}{\rightleftharpoons} RCO_2^-,BH^+ \qquad (1)$$

where RCO_2H = 2-benzoylbenzoic acid and B = chiral amine.

DISCUSSION

It has been shown that the formation of contact and solvent separated ion-pairs is indispensable for the induction of optical activity in chiral amine–2-benzoylbenzoic acid systems, and the i.c.d. arising from the n–π^* electronic transition of the carbonyl group in the region $R > 2$ originates mainly from the 1 : 1 ion-pair.[4] The solvent, temperature, and salt concentration effects on the i.c.d. have been successfully correlated with those for the ion-pair equilibria.[14] On the other hand, the formation of complex ions $(RCO_2H)_n(R'NH_2)$ where $n = 2$ or 3 is known for the low R region.[15] As is evident from comparison of the i.c.d. changes [16] with the formation constants in Table 1, the complicated change in the region $R < 2$ is related to the formation of the complex ions. Therefore, the i.c.d. in this region is not treated further.

The i.c.d. systems may be divided into two types depending on the spectral shape. Type A consists of a series of ion-pair systems displaying a symmetrical i.c.d. curve with a single maximum at *ca.* 325 nm. Typical representative spectra in this class are illustrated in Figure 1a (R 3—5) where the vibrational structure (Type B) is weak. The ion-pair systems which belong to this class comprise acid (1) with amines (3)—(20), (32), and (33) and the secondary amines in Table 3 except for the N-methyl derivative of (32). The i.c.d. effect of benzophenone–α-cyclodextrin systems [3] also belongs to Type A. The spectral shape indicates that the electronically allowed n–π^* transition conclusively demonstrated by Vala and Tanaka [17] is the origin of the i.c.d. intensity. In this transition the presence of the helical structure of the benzophenone skeleton [18] is necessary for the i.c.d. effect, *i.e.*, the apparent i.c.d. intensity is proportional to the ratio of the concentration of the P rotational isomer to that of the M isomer,* *vice versa.* The displacement of the equilibrium between these isomers must be caused by steric hindrance between the benzoyl group and the substituents R^1 and R^2 on the chiral amine in the ion-pairs.



For the amines in Table 1 the i.c.d. sign is positive when the R^1 group is larger than R^2, except for (15)—(19) which behave as secondary amines due to the presence of an intramolecular hydrogen bond.[19] Although such a simple correlation for secondary amine–(1) systems is not so easy to find, it is apparent that the i.c.d. sign is reversed by N-alkyl groups except for methyl and the intensity becomes large upon increasing the size of the alkyl group; N-aryl

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* For an account of P and M isomerism see R. Bentley, 'Molecular Asymmetry in Biology,' Academic Press, London, 1969, vol. 1, p. 60.

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groups decrease the intensity or reverse the sign. Consequently, the i.c.d. is strongly dependent on both the steric and electronic effects of the substituents on the chiral amines.

Type B spectra display a definitive vibrational structure in the n–π^* region (Figure 2) with maxima at *ca.* 335, 350, or 365 nm. The vibrational structure indicates that the vibronically allowed n–π^* transition of the carbonyl group [20] is responsible for the induction of optical activity. The α-aralkylamines (21)—(31) and the *N*-methyl derivative of (32) with acid (1) and all chiral amine–(2) systems belong to this class. In type B systems with acid (1) an i.c.d. effect associated with the helical structure is not observed, though the helical structure of (1) should be retained in the ion-pairs as in the case of Type A. The spectral comparisons of amines (21), (23)—(28)–acid (1) with (32), and (33)–acid (1), or of (22), (26), and (30)–acid (1) with their secondary derivatives–acid (1), or of amine (32)–acid (1) with the *N*-methyl derivative–acid (1) indicate that the absence of i.c.d. associated with the helical structure of (1) is related to the orientation of the aryl group relative to (1) in the ion-pairs. Therefore the simple sector rule based on the presence of a helix is inapplicable for these systems. However, the i.c.d. sign for the longest wavelength (Table 2) seems to be determined by the presence of an aryl group; *i.e.*, the i.c.d. sign is negative when R^1 = aryl.

In Type B systems with acid (2) steric repulsion between the benzoyl group of (2) and the substituents R^1 and R^2 of the amine in the ion-pairs is too small to freeze the optically active conformation. Therefore, i.c.d. associated with a helix is absent and asymmetric perturbation of the n–π^* transition of the carbonyl group in a specified direction is the only source of i.c.d. In fact, the i.c.d. spectra of all chiral amine–(2) systems display strong vibronic structure. A simple sector rule for these systems cannot be found. On the other hand, the intense i.c.d. in 4-benzoylbenzoic acid–β-cyclodextrin arises from the presence of a helix due to freezing of the optically active conformation in the cavity [21] and the spectra belong to Type A.

This classification of the spectra corresponds to Bosnich's hypothesis.[22] Consequently, the helical structure of the benzophenone skeleton in ion-pair systems of 2-benzoylbenzoic acid–chiral amine is preserved on a time-averaged basis, and gives rise to two typical spectral features associated with the origins of optical activity. On the other hand, the benzophenone skeleton in 4-benzoylbenzoic acid–chiral amine systems is optically inactive and the optical activity arises exclusively from the asymmetric perturbation due to the chiral amine for the vibronically allowed n–π^* transition of the carbonyl group.

[6/2034 *Received, 2nd November,* 1976]

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