

Circular Dichroism of Some *N*-Monosubstituted and *N,N*-Disubstituted Benzamides

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The circular dichroism (CD) spectra of some *N*-benzoyl-1-alkyl-2-propynylamines and *N*-benzoyl-1-alkyl-2-propenylamines show three Cotton effects (CE's) in the near ultraviolet region. These are assigned to 1L_b , $n \rightarrow \pi^*$ and 1L_a transitions of the *N*-monosubstituted benzamide chromophore. The 1L_b and $n \rightarrow \pi^*$ CE's are negative and positive, respectively, for the *R* configuration. In the *N*-benzoyl-1-alkyl-2-propenylamines, the 1L_a CE's appear to be developed primarily through dipole–dipole coupling between allowed ($\pi \rightarrow \pi^*$) transitions of the benzamide chromophore and the ethenyl group. The benzoyl derivatives of some 2- and 3-substituted pyrrolidines also exhibit three CE's which are assigned to 1L_b , $n \rightarrow \pi^*$ and 1L_a transitions of the *N,N*-disubstituted benzamide chromophore. In benzoyl derivatives of 2-substituted pyrrolidines, these CE's are negative, positive and negative, respectively, for the *D*-proline configuration. The effect of increasing nonplanarity of the phenyl and amide groups, brought about by *ortho*-methyl substitution, on the CD behaviour of both *N*-monosubstituted and *N,N*-disubstituted benzamides is discussed.

Although the chiroptical properties of the aromatic¹ and amide^{2–5} chromophores have been extensively studied, very few systematic studies of the optical rotatory properties of the benzamide chromophore have appeared.^{6–8} The optical rotatory dispersion⁹ (ORD) and circular dichroism¹⁰ (CD) of thiobenzamides, however, have been investigated in more detail.

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Simple benzamides generally show three bands above 200 nm in their electronic absorption (EA) spectra. A relatively weak band in the 270–280 nm region corresponds to the 1L_b band of benzene.^{6,11} The strong band observed at 220–240 nm generally is assigned to an 1L_a aromatic transition^{6,11} although an intramolecular charge-transfer transition has also been proposed as the origin of this band.¹² An intense band just above 200 nm probably results from a transition within the aromatic ring.¹²

The CD study performed by Kreuger *et al.*⁶ showed that only weak optical activity is associated with the electronic transitions of *N*-monosubstituted benzamides derived from saturated aliphatic amines such as 2-butylamine. More intense Cotton effects (CE's) were observed in the CD spectrum of *N*-benzoyl-*trans*-1-amino-2-phenylcyclohexane,⁸ but for this compound the band assignment is complicated by the dichroic absorption of the additional phenyl group. We have previously noted that *N*-salicylidene,¹³ dimedonyl¹⁴ and *N*-2,4-dinitrophenyl¹⁵ derivatives of chiral allylic and propargylic primary amines exhibit CE's of much greater magnitude than the same derivatives of the corresponding saturated amines. Moreover, the presence of an unsaturated linkage in the amine part of these derivatives greatly facilitated band assignments and correlations of absolute configuration with the sign of the observed CE's. With the expectation that a similar enhancement of CE's will occur in the benzamide chromophore, the CD spectra of benzoyl derivatives of some chiral 1-alkyl-2-propynylamines (*I*–4) and 1-alkyl-2-propenylamines (*S*–7) of known absolute con-

figurations have been examined (Table 1). To study the effect of increasing nonplanarity of the phenyl ring and the amide group on the CD behaviour of these benzamides, the 2-methylbenzamides *10* and *12* and the 2,4,6-trimethylbenzamides *11* and *13* were also examined.

N-Monosubstituted benzamides exist almost entirely in the *Z* conformation with respect to the carbonyl carbon–nitrogen bond.¹⁶ However, there is considerable conformational mobility about the bond connecting the nitrogen with the alkyl group. The low CD intensity observed in the near ultraviolet region of most *N*-monosubstituted benzamides presumably is a result, at least in part, of cancellation of intensity among the different conformers present in solution. Benzoyl derivatives of cyclic amines, such as pyrrolidine, should be less flexible because of the rigidity imposed by the ring. Therefore, some benzoyl derivatives (Table 2, *14*–*19*) of chiral substituted pyrrolidines were also investigated.

RESULTS AND DISCUSSION

Electronic Absorption Spectra

N-Monosubstituted benzamides *1*–*13*. The EA spectra of the benzamides *1*–*9* exhibit two relatively weak shoulders at 270–280 nm. The shoulders are more evident in hexane than in methanol solution (Fig. 1) and may be assigned to the ¹L_b transition of the benzamide

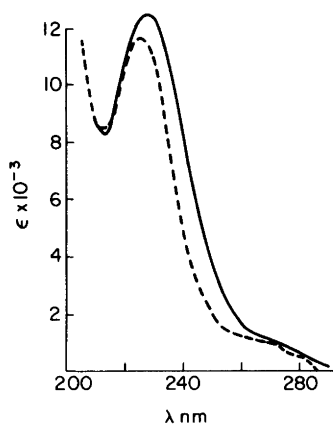


Fig. 1. Electronic absorption spectra of (*R*)-*N*-benzoyl-1-ethyl-2-propynylamine (*2*) in methanol (—) and in hexane (---).

chromophore.^{6,11} An additional band is observed at 226–227 nm (ϵ 10900–12400) in methanol and at 225 nm (ϵ 10200–12400) in hexane solution. In agreement with previous assignments,^{6,11} this band will be referred to as the ¹L_a band.

In addition to the ¹L_b band at 270–280 nm, the absorption spectra of the 2-methylbenzamides *10* and *12* show a shoulder at 220–225 nm (ϵ 6000–7000) in both methanol and hexane solution. It was previously noted that methyl substitution in the *ortho*-position of benzamide is accompanied by the appearance of the ¹L_a band as a shoulder of reduced intensity.¹¹ Accordingly, the shoulder at 220–225 nm in the spectra of *10* and *12* is assigned to an ¹L_a transition of the 2-methylbenzamide chromophore. Except for the ¹L_b band, the 2,4,6-trimethyl substituted benzamides *11* and *13* have no defined bands above 215 nm. These results are in agreement with those reported for other *N*-monosubstituted 2,4,6-trimethylbenzamides⁶ and indicate reduced conjugation between the phenyl ring and the amide group as a result of steric hindrance.

N,N-Disubstituted benzamides *14*–*19*. The EA spectra of the benzamides *14* and *16* as well as of *N*-benzoylpyrrolidine in methanol exhibit a shoulder at about 216 nm (ϵ 8500). In hexane, a shoulder of lower intensity appears near 245 nm. The 216 nm band may be assigned to the ¹L_a transition of the benzamide chromophore shifted from its position at 226–227 nm in the *N*-monosubstituted benzamides *1*–*9* as a result of steric inhibition of resonance. ¹H NMR data for *1*–*9*, *14*, *16* and *N*-benzoylpyrrolidine support this conclusion. In the *N*-monosubstituted benzamides *1*–*9*, the aromatic protons are non-equivalent and give rise to a complex signal pattern at δ 7.20–7.95 characteristic of a conjugated carbonyl–phenyl group.¹⁷ However, *N*-benzoylpyrrolidine, *14* and *16* show a relatively narrow peak, slightly broadened at the base, at δ 7.37–7.39 in their ¹H NMR spectra, indicating near equivalence of the aromatic protons and thus a substantial departure from coplanarity of the phenyl ring and the amide group.^{17,18} These EA and ¹H NMR results also suggest that the introduction of a methyl group at the 2- or 3-positions of the pyrrolidine ring of *N*-benzoylpyrrolidine (compounds *14* and *16*) has no dramatic effect on the torsional angle between the phenyl and amide groups. This angle has been estimated to 38° in *N*-benzoylpyrrolidine,¹⁹

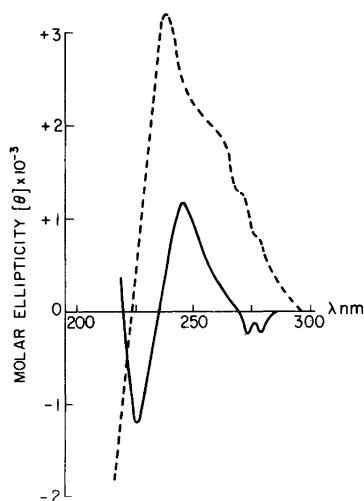


Fig. 2. Circular dichroism spectra of (*R*)-*N*-benzoyl-1-methyl-2-propynylamine (*I*) in methanol (—) and in hexane-dioxane (9:1) (---).

a value substantially larger than that observed for benzamide in the solid state (25°)²⁰ and than that estimated for *N*-methylbenzamide (27°) from ¹³C NMR measurements.¹⁹ From the present CD measurements (*vide infra*), the 245 nm shoulder observed for *14* and *16* in hexane may be assigned to the $n \rightarrow \pi^*$ transition of the benzamide chromophore. The phenyl substituted benzamides *15* and *17* have absorption spectra similar to those of *14* and *16*. Except for the ¹*L*_b band, the highly hindered benzamides *18* and *19* have no defined bands in their EA spectra above 215 nm.

Circular Dichroism Spectra

N-Monosubstituted benzamides 1–13. The CD spectrum of (*R*)-*N*-benzoyl-1-methyl-2-propynylamine (*I*) in methanol (Fig. 2) shows a negative CE with maxima at 273 and 279 nm. This CE coincides with the EA maximum in the 270–280 nm region and can therefore be attributed to the ¹*L*_b transition. In hexane solution, two negative CE's are apparent as positive minima (shoulders) at 269 and 276 nm on the wing of a positive CD band at shorter wavelengths. The positive CE at 245 nm, observed for *I* in methanol, may be assigned to an $n \rightarrow \pi^*$ transition of the benzamide chromophore not detected in the EA spectrum

because of low intensity. A negative CE at 226 nm coincides with the main EA band of *I* and is therefore attributed to the ¹*L*_a transition of the benzamide chromophore. In hexane, the positive $n \rightarrow \pi^*$ CD band is overlapped by a relatively strong positive CE with apparent maximum at 237 nm which may be assigned to the ¹*L*_a transition. The apparent red shift of this CE compared to the EA maximum presumably is due to band distortion from a negative CE below 215 nm (Fig. 2). The reason for the sign reversal of the ¹*L*_a CE of *I* on changing the solvent from methanol to hexane is not clear. An analogous inversion of the sign of the lowest energy $\pi \rightarrow \pi^*$ CE of many thiobenzoyl derivatives has previously been noted and was ascribed to solvent-solute interactions.¹⁰

The CD spectra of 2–4 are qualitatively similar to that of *I* (Table 1). In the spectra of 2 and 3 in methanol, the higher intensity of the $n \rightarrow \pi^*$ CE's masks the ¹*L*_b CE's to a large extent. No CE's corresponding to the main EA band at 227 nm of 2 and 3 in methanol are evident above 212 nm. The near Gaussian shape of the $n \rightarrow \pi^*$ CD bands of 2 and 3 in methanol suggests that their position at 239 nm is close to the true location of the weak $n \rightarrow \pi^*$ transition of the *N*-monosubstituted benzamide chromophore. The $n \rightarrow \pi^*$ transition of *N*-monosubstituted acetamides in methanol was previously shown by CD to be located at 210–215 nm³. These results clearly illustrate the usefulness of CD measurements in detecting and locating weak electronic transitions.

The CD spectra of the benzoyl derivatives (5–7) of the 1-alkyl-2-propynylamines in methanol are very similar. As in the 1-alkyl-2-propynylamine derivatives, the ¹*L*_b CE's are negative for the *R* configuration in both methanol and hexane (Table 1). A moderately strong CE at 231–234 nm in methanol is assigned to the ¹*L*_a transition of the benzamide chromophore rather than to an $n \rightarrow \pi^*$ transition on the basis of the observed solvent effect, *i.e.*, shift to shorter wavelengths in hexane (Fig. 3). In methanol, the $n \rightarrow \pi^*$ CE's presumably are hidden under the rather intense ¹*L*_a bands, whereas in hexane they are clearly visible at 244–245 nm.

The relatively strong CE's associated with the ¹*L*_a transition of the *N*-benzoyl-1-alkyl-2-propynylamines (5–7) in methanol contrast to the weak ¹*L*_a CE's of the 1-alkyl-2-propynylamine derivatives (*I*–4) and of the derivatives of the

Table 1. Circular dichroism (CD) maxima of some *N*-monosubstituted benzamides (ArCONHR).

Com- Ar compound	R	Methanol			Hexane-Dioxane (9:1)		
		Abs. con- ¹ <i>L</i> _a fig.	$\lambda_{\text{max}}(\text{[}\theta\text{]})$ <i>n</i> → π^*	¹ <i>L</i> _b	¹ <i>L</i> _a	$\lambda_{\text{max}}(\text{[}\theta\text{]})$ <i>n</i> → π^*	¹ <i>L</i> _b
1	C ₆ H ₅	R	226(-1200)	245(+1200)	273(-240) 279(-230)	237(+3200)	255(+2100) ^a 269(+1300) ^b 276(+870) ^b
2	C ₆ H ₅	R		239(+2700)	280(-90)	235(+4100)	260(+1500) ^a 270(+1100) ^b 276(+810) ^b
3	C ₆ H ₅	R		239(+2300)	280(-60)	235(+3900)	260(+1150) ^a 270(+910) ^b 276(+670) ^b
4	C ₆ H ₅	S	225(+600)	250(-800)	278(+29)		272(+590) ^b
5	C ₆ H ₅	R	231(-5400)		272(-680) 278(-500)	221(-980)	244(+1800) 279(+340) ^b
6	C ₆ H ₅	S	234(+5700)		271(+620) 278(+435)	224(+3100)	245(-500) 270(+140) 277(+100)
7	C ₆ H ₅	R	231(-6500)		271(-660) ^a 278(-380) ^a	224(-2400)	245(+320) 269(-320) 276(-260)
8	C ₆ H ₅	R	226(-1300)		272(-195) 278(-163)		
9	C ₆ H ₅	S		240(-)	280(+36)		
10	2-CH ₃ C ₆ H ₄ ^d	R	215(+3430) ^c	230(+2700)	278(+110)		234(+3200)
11	2,4,6-CH ₃ C ₆ H ₃ ^e	S	215(-3660) ^c	235(-1600)	278(+60)	217(-5110) ^c	237(-4500)
12	2-CH ₃ C ₆ H ₄ ^d	S	216(-1750)	234(+2600)	275(-70)	220(-2600)	257(+280)
13	2,4,6-CH ₃ C ₆ H ₃ ^e	S	217(-3100)	230(+3200)			230(+920)

^a Shoulder. ^b Positive minimum. Actual Cotton effect negative. ^c Maximum not reached. ^d 2-Methylphenyl. ^e 2,4,6-Trimethylphenyl.

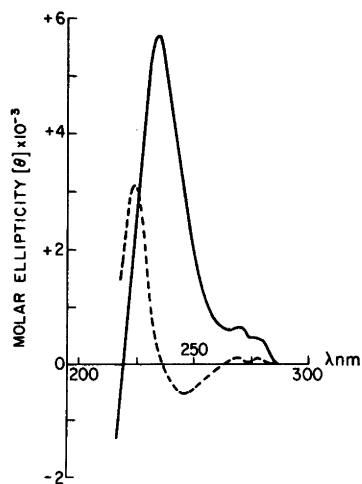
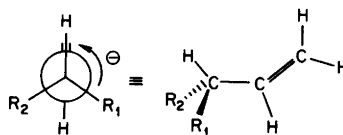


Fig. 3. Circular dichroism spectra of (*S*)-*N*-benzoyl-1-ethyl-2-propenylamine (θ) in methanol (—) and in hexane-dioxane (9:1) (---).

saturated amines (8–9). Since the 1L_a absorption band of benzamides has high intensity (*vide supra*) and since the ethenyl group has its lowest energy $\pi \rightarrow \pi^*$ transition (allowed) at *ca.* 185 nm (red shifted by alkyl substitution),²¹ a substantial part of the rotatory strength of the 1L_a transition of 5–7 should be developed by the dipole-dipole coupling mechanism in a non-degenerate system.²² It is known that the intensity of the CE's associated with coupled chromophores generally decreases when the energy difference between the transitions of the component chromophores becomes larger.²³ The lowest energy $\pi \rightarrow \pi^*$ transition (allowed) of the ethynyl group is located at *ca.* 152 nm.²⁴ Therefore, the coupled oscillator contribution to the 1L_a CE of the 1-alkyl-2-propynylamine derivatives should be smaller than in the case of the 1-alkyl-2-propenylamine derivatives, in agreement with the observed weak 1L_a CE's of the former.

According to the coupled oscillator theory, the sign of the observed CE is determined by the chirality of the coupled oscillators.²² This chirality depends on the absolute configuration and the preferred conformation of the compound as well as on the polarization of the electric transition moments in the coupling groups. In 5–7, the electric transition moment of the 1L_a transition is nearly parallel to the nitrogen-chiral carbon

bond (benzamide chromophore attachment bond)⁷ and the moment of the lowest energy $\pi \rightarrow \pi^*$ transition of the ethenyl group is directed along the double bond.²⁴ As in the corresponding *N*-2,4-dinitrophenyl¹⁵ and *N*-salicylidene¹³ derivatives, the conformational preference around the ethenyl group attachment bond of an (*R*)-*N*-benzoyl-1-alkyl-2-propenylamine may be depicted as in (*R*)-20*a*. Analogous conformations have been demonstrated for 3,3-dialkylpropenes²⁵ and for *p*-bromobenzoates of secondary allylic alcohols, (*R*)-20*b*.²⁶



(*R*)-20*a* $R_1 = C_6H_5CONH$

(*R*)-20*b* $R_1 = p\text{-}BrC_6H_4COO$

The chirality (right-handed screw for positive chirality) of the benzamide chromophore attachment bond and the C=C bond in (*R*)-20*a* is negative. Since the observed 1L_a CE's of 5–7 are negative for the *R* configuration (Table 1), the relationship between the chirality of the coupling moments and the sign of the CE is the same as for the 1L_a band of the closely related benzoyl derivatives of secondary allylic alcohols.^{26,27} As shown for the benzoates,^{26,27} these results are in agreement with the predictions made from the exciton theory for non-degenerate systems.

All of the benzamides 1–7 exhibit 1L_b , $n \rightarrow \pi^*$, or 1L_a CE's in either methanol or hexane. The signs of the 1L_b and $n \rightarrow \pi^*$ CE's appear to be the most reliable guide to the absolute configuration of these derivatives. Thus the CE's are negative and positive, respectively, for the *R* configuration. The same relationship seems to apply also to benzoyl derivatives (*e.g.* 8 and 9) of saturated primary amines.⁶ Since different mechanisms apparently are involved in the generation of the 1L_a CE's of 1–9, a correlation between the sign of this CE and the absolute configuration is not expected for the whole series of compounds.

The 2-methyl- and 2,4,6-trimethylbenzamides 10–13 would be expected to have their 1L_a and $n \rightarrow \pi^*$ CE's at somewhat shorter wavelengths than 1–9 because of diminished conjugation between the phenyl and amide groups as evident from the EA spectra. These expectations are

generally fulfilled (Table 1). For example, the $n \rightarrow \pi^*$ CE's of *10* and *11* in methanol are hypsochromically displaced by 4–9 nm compared to the position of the $n \rightarrow \pi^*$ CE of the corresponding benzamide (2). Similarly, the 1L_a CE's of *12* and *13* in methanol are shifted by about 15 nm compared to the position in the parent benzamide (7). For the same absolute configuration, the signs of the 1L_a CE's of *12* and *13* and of the 1L_b CE's of *10* and *12* are opposite to those of the corresponding CE's of the parent molecules. Similar reversal of the sign of aromatic CE's on *ortho*-methyl substitution has previously been observed²⁸ and may be due to a change of the preferred conformation or to a change in the orientation of the transition moments caused by a perturbation of the aromatic chromophore by the methyl group(s). On the other hand, the signs of the $n \rightarrow \pi^*$ CE's of *10* and *11* agree, for the same absolute configuration, with that of the $n \rightarrow \pi^*$ CE of the parent benzamide.

N,N-Disubstituted benzamides 14–19. The CD spectra of the benzamides 14–17 are qualitatively similar (Fig. 4). The CE's at 215–218 nm in methanol and at 211–220 nm in hexane (Table 2) may be assigned to the 1L_a transition of the benzamide chromophore, in agreement with the

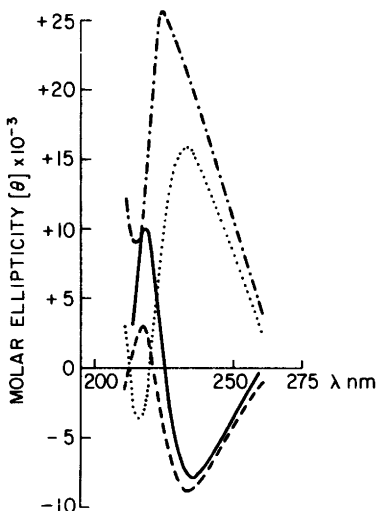


Fig. 4. Circular dichroism spectra of (*S*)-*N*-benzoyl-2-methylpyrrolidine (*14*) (···), (*R*)-*N*-benzoyl-2-phenylpyrrolidine (*15*) (-·-·), (*S*)-*N*-benzoyl-3-methylpyrrolidine (*16*) (---) and (*R*)-*N*-benzoyl-3-phenylpyrrolidine (*17*) (—) in methanol.

assignment for the shoulder around 216 nm in the EA spectra. A rather broad band at 233–235 nm in methanol, shifted to 252 nm in hexane, is attributed to the $n \rightarrow \pi^*$ transition of the benzamide chromophore.

The benzoyl derivatives of 2-methylpyrrolidine (*14*) and 2-phenylpyrrolidine (*15*) are configurationally related as are the derivatives of 3-methylpyrrolidine (*16*) and 3-phenylpyrrolidine (*17*), although the absolute configurations are opposite in the *RS* convention. At first sight, the CD spectrum of *15* may appear to show some anomalies compared to that of *14* (Fig. 4). However, the ellipticity given for the 215 nm CD band of *15* in methanol (Table 2) refers to a positive minimum on a strong positive CE at shorter wavelengths. The latter most probably originates from the 1L_a transition of the phenyl group attached to the pyrrolidine ring. The observation⁵ that the acetyl derivative of (*R*)-2-phenylpyrrolidine displays an intense positive 1L_a CE at 206 nm in ethanol strongly supports this suggestion. The strong positive CE of *15* inferred below 215 nm presumably also is responsible for the apparent blue shift of the $n \rightarrow \pi^*$ band (Table 2). The interpretation of the 1L_b region in the CD spectra of *14*–*17* is complicated by considerable overlap from the broad $n \rightarrow \pi^*$ band, especially in hexane solution. The dichroic absorption at 260–300 nm of *14*–*17* in methanol is illustrated in Fig. 5. Both *14* and *15* display negative CE's

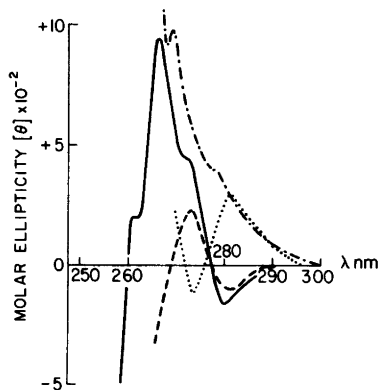
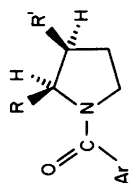


Fig. 5. Circular dichroism maxima in the 1L_b region of (*S*)-*N*-benzoyl-2-methylpyrrolidine (*14*) (···), (*R*)-*N*-benzoyl-2-phenylpyrrolidine (*15*) (-·-·), (*S*)-*N*-benzoyl-3-methylpyrrolidine (*16*) (---) and (*R*)-*N*-benzoyl-3-phenylpyrrolidine (*17*) (—) in methanol.

Table 2. Circular dichroism (CD) maxima of some *N,N*-disubstituted benzamides.

Com- pound	Ar	R	R'	Abs. con- fig.	Methanol		Hexane		
					1L_a	$\lambda_{\text{max}} ([\theta])$ $n \rightarrow \pi^*$	1L_b	1L_a	$\lambda_{\text{max}} ([\theta])$ $n \rightarrow \pi^*$
14	C ₆ H ₅	CH ₃	H	S	216(-3600)	233(+15800)	273(-120) 281(+300) ^a 269(+980) ^b 278(+400) ^b	220(-14800)	252(+16200)
15	C ₆ H ₅	C ₆ H ₅	H	R	215(+9000) ^b	224(+25600)	273(+230) 281(-100) ^a	211(-400)	227(+14600)
16	C ₆ H ₅	H	CH ₃	S	217(+3000)	233(-8800)	261(+200) ^c 266(+940)	220(+6200)	252(-8000)
17	C ₆ H ₅	H	C ₆ H ₅	R	218(+10000)	235(-7900)	272(+450) ^c 280(-160) ^a 267(-420)	220(+16000)	252(-7600)
18	2-CH ₃ C ₆ H ₄ ^d	CH ₃	H	S	217(+16500)	(+)	273(-500)		242(+8500)
19	2,4,6-CH ₃ C ₆ H ₂ ^e	CH ₃	H	S	214(+19800)	(+)	270(-390) 277(-580)	218(+14500)	240(+6600)

^a Long-wavelength tail of the $n \rightarrow \pi^*$ CD band. ^b Positive minimum. Actual Cotton effect negative. ^c Shoulder. ^d 2-Methylphenyl. ^e 2,4,6-Trimethylphenyl.

for the 1L_b transition of the benzamide chromophore. The apparent positive band of *14* at 281 nm constitutes the long-wavelength tail of the relatively strong positive $n \rightarrow \pi^*$ band. In the spectrum of *15*, the negative 1L_b CE is visible as positive minima on the strong positive $n \rightarrow \pi^*$ band. Compounds *16* and *17* show positive CE's for the 1L_b transition of the benzamide chromophore. The spectra of both compounds contain the long-wavelength tail of the $n \rightarrow \pi^*$ band observed for *14*. Benzamide *17* also shows a positive CE with maxima at 261 and 266 nm which may be assigned to the 1L_b transition of the phenyl group attached to the pyrrolidine ring. The sign and position of this CE agree with those observed for the 1L_b CE of acetyl (*R*)-3-phenylpyrrolidine.⁵

From these results, it appears that the absolute configuration of 2- and 3-substituted pyrrolidines may be determined from the signs of the 1L_b , $n \rightarrow \pi^*$ and 1L_a CE's of their benzoyl derivatives. Thus in 2-substituted pyrrolidines, the CE's are negative, positive and negative, respectively, for the *D*-proline configuration. In agreement with these findings, *N*-benzoyl-*D*-proline exhibits a positive $n \rightarrow \pi^*$ CD band.⁴

The $n \rightarrow \pi^*$ CE's of chiral *N*-acetyl- and *N*-pivaloylpyrrolidines in methanol are located around 222 nm⁵ compared to their location at 233 nm in *N*-benzoyl-pyrrolidines (Table 2). Furthermore, the sign of the $n \rightarrow \pi^*$ CE's of acetyl^{4,5} and benzoyl derivatives of 2-substituted pyrrolidines is opposite at equal absolute configurations. On the other hand, acetyl⁵ and benzoyl derivatives of 3-substituted pyrrolidines display $n \rightarrow \pi^*$ CD bands of the same sign. The reason for this behaviour is not known.

The torsional angle between the aromatic and amide groups in 2,4,6-trimethylbenzamide has been estimated¹¹ to 64°. Compound *19*, being an *N,N*-disubstituted 2,4,6-trimethylbenzamide, should have an even larger torsional angle resulting in virtually complete steric inhibition of resonance between the amide and phenyl groups which, accordingly, may be regarded as separate chromophores. The blue shift of the 1L_a transition of *19* as compared to its position in *14*, expected as a result of loss of conjugation, may be offset by the red shift caused by the three methyl groups attached to the phenyl group.²⁹ On this basis, we ascribe the 214 and 218 nm CE's of *19* in methanol and hexane, respectively, to

the 1L_a transition of the isolated 2,4,6-trimethylphenyl group. The appearance of the 1L_a absorption band of mesitylene around 215 nm²⁹ supports this assignment (Table 2). As in the case of the methyl substituted benzamides *12* and *13*, the sign of the 1L_a CE's of *18* and *19* is opposite to that of the 1L_a CE of the configurationally related parent benzamide *14*. In methanol solution, the $n \rightarrow \pi^*$ CE's of *18* and *19* are partially hidden under the relatively intense 1L_a CE's of the same sign. In hexane, the $n \rightarrow \pi^*$ band experiences the expected blue shift as compared to the position of the corresponding band of *14* (Table 2). As observed for *10* and *11*, the sign of the $n \rightarrow \pi^*$ CE's of *18* and *19* is the same as that of the $n \rightarrow \pi^*$ CE of the parent benzamide.

Unsymmetrical *N,N*-disubstituted benzamides normally exist in solution as equilibrium mixtures of *Z* and *E* conformers as shown by NMR measurements.¹⁸ However, the barrier to rotation about the C–N bond of the amide group in benzamides is lower than in aliphatic amides.¹⁶ Because of band overlap and coalescence temperatures below the operating temperature (37 °C) of the NMR instrument used in the present study, no *ZE* ratios could be assigned to benzamides *14*–*17*. It may be assumed, however, that, as for the closely related *N*-benzoylproline (*ZE* ratio 4:1),¹⁸ the *Z* conformer predominates in solution. The ${}^1\text{H}$ NMR spectra of *18* and *19* in carbon tetrachloride exhibit two well isolated doublets at δ 0.83–0.84 and 1.29–1.30. The former may be assigned to the protons of the pyrrolidine methyl group of the *E* conformer and the latter to the corresponding protons of the *Z* conformer. This assignment is based on the location of the pyrrolidine methyl group of the *E* conformers in the shielding region of the aromatic ring, which is twisted out of the plane of the amide group.³⁰ The *ZE* ratio of both *18* and *19* in carbon tetrachloride (37 °C), obtained by integration over the signals around δ 0.84 and 1.30, is about 3:1. In benzene-*d*₆, the high-field doublet of *19* is shifted to δ 0.57, whereas the low-field doublet remains at δ 1.30. This solvent effect is in agreement with the above peak assignment.³¹

The fact that separate NMR signals were observed for the *Z* and *E* conformers of *18* and *19* at 37 °C indicates a higher barrier to rotation about the amide bond of these compounds than in compounds *14*–*17*. Under suitable conditions amide *19* crystallizes as the pure *Z* conformer.

Studies are now in progress to determine the barrier to C–N rotation in 19 using polarimetric and NMR techniques. Compound 19 also offers the possibility to investigate the *Z–E* conformational dependence of the circular dichroism of an *N,N*-disubstituted amide.

EXPERIMENTAL

Optical rotations at the sodium *D* line were measured in a 1-dm tube with a Perkin-Elmer 141 spectropolarimeter. Electronic absorption spectra were obtained with a Zeiss Spektralfotometer Pm QII. Circular dichroism (CD) spectra were recorded on a Jasco J-41 spectropolarimeter at 20 °C. For the CD measurements below 265 nm, the concentration of the amide solution was normally about 1 mg/10 ml and the cell lengths 0.5–2 mm. Above 265 nm the concentration was about 10 mg/10 ml and the cell lengths 2 or 5 mm. Because of limited solubility of the *N*-monosubstituted benzamides 1–13 in hydrocarbon solvents, a mixture of hexane–dioxane (9:1) was used instead of hexane for the CD measurements in a nonpolar solvent. In regions of strong absorption and weak optical activity (below 240 nm for some *N*-monosubstituted benzamides), at least three separate CD curves were obtained and averaged. ¹H NMR spectra were recorded at 37 °C and 60 MHz with a Perkin-Elmer R 12 B spectrometer. Elemental analyses were done at the Microanalytical Laboratory, Royal Agricultural College, Uppsala, Sweden.

N-Monosubstituted benzamides. Benzamides 1–9 were prepared from the resolved amines or their hydrogen tartrates under customary Schotten-Baumann conditions as previously described.^{14,32,33}

N-Monosubstituted 2-methyl- and 2,4,6-trimethylbenzamides. 2-Methylbenzoyl chloride and 2,4,6-trimethylbenzoyl chloride were prepared from their corresponding acids as follows: 1 g of the acid was refluxed for 1 h with 2 ml of SOCl₂. Anhydrous benzene (10 ml) was added and evaporated *in vacuo*. This procedure was repeated twice to ensure complete removal of SOCl₂. The acid chlorides obtained were used without further purification in a Schotten-Baumann reaction with the appropriate resolved primary amine to yield 10–13 which were all recrystallized from light petroleum (b.p. 60–80 °C).

(*R*)-*N*-(2-Methylbenzoyl)-1-ethyl-2-propynylamine (10), yield 75 %, m.p. 87–88 °C, $[\alpha]_D^{22} +51.8^\circ$ (*c* 1.0, methanol). ¹H NMR (CDCl₃): δ 1.05 (3 H,t,CH₂,CH₃), 1.78 (2 H,m,CH₂CH₃),

2.28 (1 H, d, *J*=2.3 Hz, ≡CH), 2.43 (3 H,s,ArCH₃), 4.85 (1 H, doublet of quartets, *J*₁=6.9 and *J*₂=2.3 Hz, NCH), 6.15 (1 H,d,NH), 7.20–7.40 (4 H,m,ArH). Anal. C₁₃H₁₅NO: C,H,N.

(*S*)-*N*-(2,4,6-Trimethylbenzoyl)-1-ethyl-2-propynylamine (11), yield 65 %, m.p. 109.5–110.5 °C, $[\alpha]_D^{22} -48.2^\circ$ (*c* 1.4, methanol). ¹H NMR (CDCl₃): δ 1.04 (3 H,t, CH₂CH₃), 1.70 (2 H,m,CH₂CH₃), 2.26 (9 H,s,ArCH₃), 4.82 (1 H,m,NCH), 6.08 (1 H,d,NH), 6.81 (2 H,s,ArH). Anal. C₁₅H₁₉NO: C,H,N.

(*S*)-*N*-(2-Methylbenzoyl)-1-propyl-2-propenylamine (12), yield 76 %, m.p. 84.5–85.5 °C, $[\alpha]_D^{22} +14.5^\circ$ (*c* 0.9, ethanol). ¹H NMR (CDCl₃): δ 2.40 (3 H,s, ArCH₃), 7.18–7.38 (4 H,m,ArH). Anal. C₁₄H₁₉NO: C,H,N.

(*S*)-*N*-(2,4,6-Trimethylbenzoyl)-1-propyl-2-propenylamine (13), yield 71 %, no defined m.p., $[\alpha]_D^{22} +13.7^\circ$ (*c* 1.1, ethanol). ¹H NMR (CDCl₃): δ 2.27 (9 H,s, ArCH₃), 6.82 (2 H,s,ArH). Anal. C₁₆H₂₃NO: C,H,N.

N,N-Disubstituted benzamides. To a solution of pyrrolidine, (*S*)-2-methylpyrrolidine,³⁴ (*S*)-3-methylpyrrolidine,³⁴ (*R*)-2-phenylpyrrolidine^{14,35} or (*R*)-3-phenylpyrrolidine^{14,36} (0.005 mol) and triethylamine (0.005 mol) in anhydrous ether was added a solution of benzoyl chloride (0.005 mol) in anhydrous ether. The mixture was refluxed for 2 h and filtered. After evaporation of the ether, the product was distilled or recrystallized.

N-Benzoylpyrrolidine, yield 84 %, m.p. 52–53 °C (from light petroleum). Lit.³⁷ m.p. 46–47 °C. ¹H NMR (CCl₄): δ 1.72–2.05 (4 H, m, CCH₂CH₂C), 3.30–3.65 (4 H, m, CH₂NCH₂), 7.28–7.50 (5 H,broad s,ArH). Anal. C₁₁H₁₃NO: C,H,N.

(*S*)-*N*-Benzoyl-2-methylpyrrolidine (14), yield 73 %, b.p. 115 °C (0.5 mm Hg), $[\alpha]_D^{22} +138^\circ$ (*c* 0.8, methanol). ¹H NMR (CCl₄): δ 1.20 (3 H,d,CH₃), 1.45–2.20 (4 H,m,CCH₂CH₂C), 3.40 (2 H,t,NCH₂), 3.88–4.40 (1 H,m,NCH), 7.30–7.55 (5 H, broad s,ArH). Anal. C₁₂H₁₅NO: C,H,N.

(*R*)-*N*-Benzoyl-2-phenylpyrrolidine (15), yield 68 %, m.p. 70–75 °C (from methanol–water), $[\alpha]_D^{22} +151^\circ$ (*c* 0.9, methanol). Anal. C₁₇H₁₇NO: C,H,N.

(*S*)-*N*-Benzoyl-3-methylpyrrolidine (16), yield 72 %, m.p. 66–67 °C (from light petroleum), $[\alpha]_D^{22} -66.6^\circ$ (*c* 1.5, methanol). Lit.³⁴ m.p. 66–67 °C, $[\alpha]_D^{22} -69.3^\circ$ (*c* 1.5, methanol). ¹H NMR (CCl₄): δ 1.05 (3 H,d,CH₃), 7.28–7.56 (5 H, broad s,ArH).

(*R*)-*N*-Benzoyl-3-phenylpyrrolidine (17), yield 70 %, m.p. 88–89 °C (from methanol–water), $[\alpha]_D^{22} -16.4^\circ$ (*c* 1.3, methanol). Anal. C₁₇H₁₇NO.

0.5 H₂O: C, H, N.

N,N-Disubstituted 2-methyl- and 2,4,6-trimethylbenzamides. These compounds were prepared from 2-methyl- and 2,4,6-trimethylbenzoyl chloride and (*S*)-2-methylpyrrolidine as described above for the *N,N*-disubstituted benzamides. However, anhydrous tetrahydrofuran was used instead of ether as solvent and the reaction time was 12 h.

(*S*)-*N*-(2-Methylbenzoyl)-2-methylpyrrolidine (18), yield 80 %, b.p. 120 °C (0.4 mm Hg), $[\alpha]_D^{25} +71.6^\circ$ (c 0.1, methanol). ¹H NMR (CCl₄): δ 0.84 (0.7 H, d, *E*-NCCH₃), 1.29 (2.3 H, d, *Z*-NCCH₃), 1.50–2.10 (4 H, m, CCH₂CH₂C), 2.24 (3 H, s, ArCH₃), 3.09 (1.6 H, t, *Z*-NCH₂), 3.40–3.80 (0.6 H, m, *E*-NCH₂ and *E*-NCH), 4.05–4.45 (0.8 H, m, *Z*-NCH), 7.12 (4 H, s, ArH). Anal. C₁₃H₁₇NO: C, H, N.

(*S*)-*N*-(2,4,6-Trimethylbenzoyl)-2-methylpyrrolidine (19), yield 85 %, b.p. 120 °C (0.2 mm Hg), $[\alpha]_D^{25} +48.9^\circ$ (c 1.3, methanol). ¹H NMR (CCl₄): δ 0.83 (0.7 H, d, *E*-NCCH₃), 1.30 (2.3 H, d, *Z*-NCCH₃), 1.45–2.05 (4 H, m, CCH₂CH₂C), 2.05–2.35 (9 H, m, ArCH₃), 2.97 (1.6 H, t, *Z*-NCH₂), 3.30–3.80 (0.7 H, m, *E*-NCH₂ and *E*-NCH), 3.90–4.40 (0.7 H, m, *Z*-NCH), 6.73 (2 H, s, ArH). ¹H NMR (C₆D₆): δ 0.57 (d, *E*-NCCH₃), 1.30 (d, *Z*-NCCH₃).

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