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Exciton Coupling of the Phthalimide Chromophore: Application to Configurational Assignments†

F. Kaźmierczak, K. Gawrońska, U. Rychlewska and J. Gawroński*
Department of Chemistry, A. Mickiewicz University, 60-780 Poznan, Poland

Abstract: The absolute configuration of chiral β-phenyl substituted primary amines is readily correlated with the exciton Cotton effects resulting from the intramolecular interaction of the electric transition moments of the phthalimide derivative (220 nm π-π* band) with the benzene chromophore (^1L_a band), compounds **1-3**. Similar correlation is applied to the exciton coupling between the π-π* band transition moments of the phthalimide and the benzoate chromophores derived from chiral vicinal amino alcohols, compounds **8-13**.

The primary amino group is present in a large number of chiral molecules, including amino alcohols and phenyl substituted amines, both of natural and synthetic origin. Despite the increasing interest in the synthesis and applications of such compounds, there is no generally accepted chromophoric derivative of the amino group for chiroptical studies, which would allow configurational and conformational assignments in cyclic and acyclic molecules. Exciton coupling of the benzamide and the benzoate chromophores has been used for configurational assignments of amino alcohols[1,2]. In this communication we report that the phthalimide group, widely used as a protective group or a masked amino group in organic synthesis, is also an excellent chromophoric derivative of the amino group for circular dichroism studies.

The advantage of using the phthalimide chromophore is that its π-π* intramolecular charge-transfer band at ca. 220 nm (ε 36000) has the electric dipole transition moment colinear with the C-N bond, i. e. its direction is independent on the rotation of the phthalimide chromophore[3] Thus exciton coupling[4] is observed even with the phenyl chromophore (^1L_a transition at ca. 206 nm) in β-phenyl substituted phthalimides, resulting in strong CD maxima at 219-223 nm and 205-211 nm. For example, phthalimide derivatives of (R)-phenylalanine **1** and its anilide **2**, give positive exciton Cotton effects, resulting from the interaction between the phenyl and the phthalimide chromophores in the conformation shown (planar carbon chain)[5].

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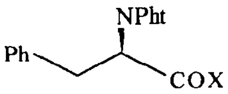
†Dedicated to Professor H. M. Walborsky on the occasion of his 70th birthday.

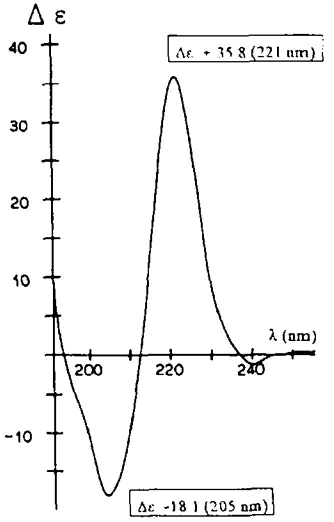


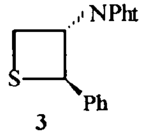
1 X - OH, Δε +44.5 (220 nm)
-6.5 (205 nm)

2 X = NHPh, Δε +36.4 (220 nm)
-5.0 (207 nm)

The cyclic β-phenylphthalimide **3**, derived from (1S,2S)-2-amino-1-phenyl-1,3-propanediol[6] shows strong positive exciton Cotton effect (Fig. 1). This allows to establish its absolute configuration at C(2) as (R).

Fig. 1





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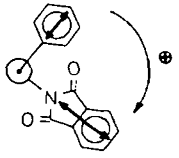
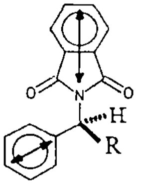


On the other hand weak non-exciton type Cotton effects around 220 nm are observed for α-phenyl phthalimides **4-7** in which the electric dipoletransition moments of the phenyl ^1L_a transition and the phthalimide intramolecular charge-transfer band are coplanar, cf. X-ray determined molecular structure of **6** (Fig. 2)[7].



4 R = CH_3, Δε +3.3 (223 nm)
5 R = CH_2OH, Δε +2.5 (220 nm)
6 R = COOH, Δε +3.8 (225 nm)
7 R = CONHPh, Δε +1.3 (215 nm)

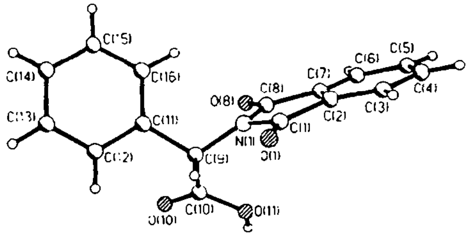
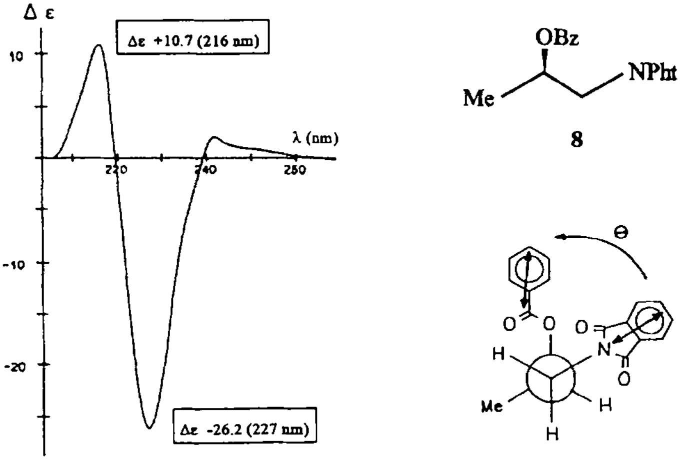


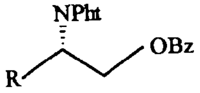
Fig.2. A perspective view of 6.

Exciton coupling between the electric transition moments of the phthalimide (220 nm π-π* band) and the benzoate (227 nm π-π* band) chromophores reflects the absolute configuration of vicinal amino alcohols. For example, strong negative Cotton effect at 224-227 nm followed by a positive Cotton effect at 212-217 nm is obtained for derivative 8 of (R)-1-amino-2-propanol, (Fig. 3).

Fig. 3

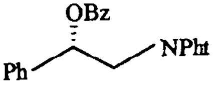


Phthalimide-benzoate derivatives of other amino alcohols give strong exciton Cotton effects reflecting either positive (9-11) or negative (12, 13) dihedral angles between the transition moments, and hence their absolute configuration[8].

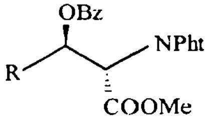


9 R = Me, Δε -7.4 (240 nm), +26.2 (226 nm). -7.4 (214 nm)

10 R = Ph, Δε -8.0 (240 nm), +19.7 (227 nm), -7.3 (216 nm)



11 Δε -3.2 (241 nm), +24.1 (227 nm), -13.7 (217 nm)



12 R = H, Δε +4.2 (240 nm), -28.9 (224 nm), +7.1 (212 nm)
13 R = Me, Δε +7.9 (240 nm), -20.4 (225 nm), +9.6 (212 nm)

Compounds **9**, **10**, derived from L-aminoacids, and **11**, derived from L-mandelic acid, show positive exciton Cotton effects, while **12**, derived from L-serine, gives negative exciton Cotton effect, as expected (CD maxima at 224-227 nm and 212-217 nm). Derivative **13** of L-threonine also gives negative exciton Cotton effect, evidently due to the preference for a bent conformation of the aminoacid chain, as shown As expected, non-benzoylated precursors of phthalimides **8** and **9** do not show exciton-type Cotton effects[9].

In conclusion we have demonstrated that CD measurements allow to determine the absolute configuration of chiral phthalimides, derived from primary amines bearing β-phenyl or β-benzoyloxy substituents[10] Further studies in this area are in progress.

Acknowledgements

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We thank Prof. M D. Rozwadowska for a sample of **3** and Dr. J. Frelek for CD measurements.

References and Notes

1. A. W. Johnson, R. M. Smith, R. D. Guthrie, *J. Chem. Soc., Perkin Trans. I*, **1972**, 2153.
2. M Kawai, U Nagai, M. Katsumi, *Tetrahedron Lett.*, **1975**, 3165.
3. The preferred conformation of the phthalimide group attached to a secondary carbon atom is that in which the phthalimide plane is nearly eclipsed by the C-H bond. In over 20 X-ray structures analyzed the dihedral angle H-C-N-C(O) varies between 4 and 19°
4. N Harada, K Nakanishi, *Circular Dichroic Spectroscopy - Exciton Coupling in Organic Stereochemistry*, University Science Books, Mill Valley 1983.
5. X-ray crystal structure of N-phthaloyl-phenylalanine **1**: A. G. Michel, F. Durant, *Bull. Soc. Chim. Belg.*, **1975**, *54*, 8403.
6. Compound **3** is prepared by treatment of (1S,2S)-1-phenyl-2-phthalimido-1,3-propanediol ditosylate with potassium xantogenate. M D. Rozwadowska, private communication.
7. The nitrogen atom of the phthalimide chromophore in **6** is slightly pyramidalized, but this has insignificant effect on the coplanarity of the C_2 axes of the phenyl and the phthalimide chromophores. Details of the molecular structure of **6** will be published separately. For X-ray structure determination of a related α-(4-methoxyphenyl) phthalimide see: H. Iida, N. Yamazaki, C. Kibayashi, *Tetrahedron Lett.*, **1986**, *27*, 5393
8. The Cotton effects at 240 nm are due to another electronic transition of the phthalimide chromophore (shoulder in the UV spectrum at 240 nm).
9. (R)-1-phthalimido-2-propanol: Δε -1.9 (221 nm); (S)-2-phthalimido-1-propanol: Δε +1.8 (216 nm).
10. All CD spectra reported here were recorded in acetonitrile solution on an AVIV dichrograph.

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