α-hydrogen or the benzilic methylene as the third group completing the contact. The determination of Michaelis constants using the deuterium labeled substrates might be expected to provide an answer to this problem and such experiments are under way.[14] It is of interest to note that the optical stereospecificity of monoamine oxidase parallels that of D-amino acid oxidase but the significance of this correlation remains to be ascertained.

Acknowledgments.—The authors are grateful to the National Research Council of Canada for the financial support of this work.

[14] See B. Belleau and J. Moran, Abstracts of the American Chemical Society Meeting, September, 1960, New York, N. Y., page 26-C, paper 71, for a preliminary account. In this report, the word "labeled" on line 6 from the bottom (third paragraph) should read "unlabeled."

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RECEIVED JULY 20, 1960

OPTICAL ROTATORY DISPERSION OF PHTHALIMIDES OF p-SUBSTITUTED α-PHENYLETHYLAMINES

Sir:

The rotatory dispersion curves of phthalimides of *para*-substituted (−)(S) α-phenylethylamines (I) show positive Cotton effects superimposed on strong negative backgrounds[1] (Figs. 1 and 2).

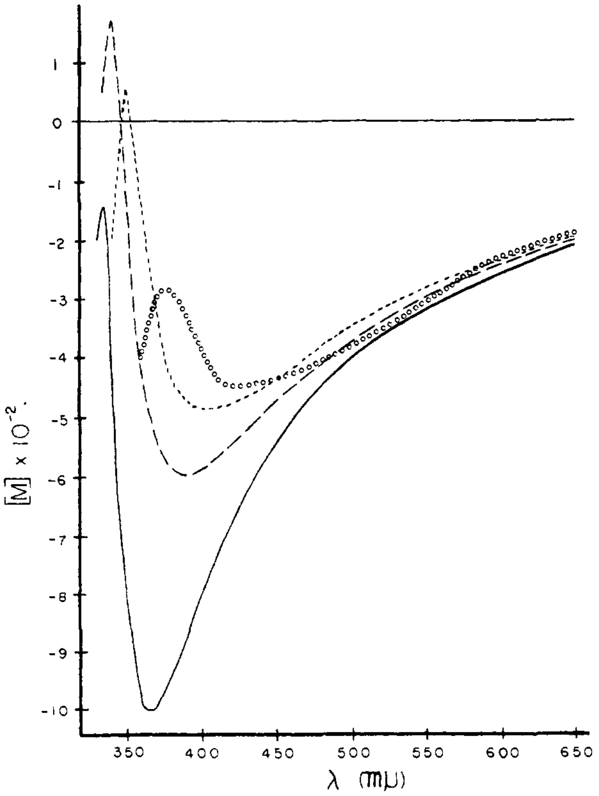

Fig. 1.—The optical rotatory dispersion [M] of phthalimides of p-substituted (−)(S)α-phenylethylamines (II) in chloroform solution; *para* substituents (Z): NO_2, —; Br, - -; OCH_3, - - -; NH_2, oooo.

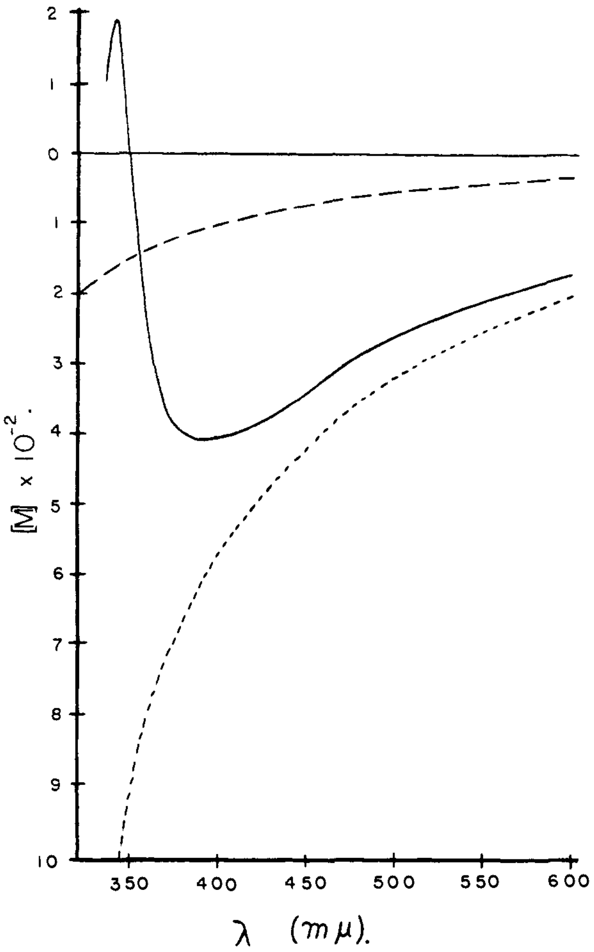

Fig. 2.—The optical rotatory dispersion [M] in chloroform of (−)(S)α-phenylethylamine, - -; its phthalimide, —; its succinimide, - - -.

These curves can be summarized, for the region of transparency (350–700 mμ), by two-term Drude expressions

$$[M] = -\frac{A}{\lambda^2 - x} + \frac{B}{\lambda^2 - y}$$

(see Table I). The positive Cotton effect (first extremum,[1] 335–380 mμ; λ_0, from the Drude constants, about 322 mμ) occurs in the same region of the spectrum as a broad absorption band at 275–350 mμ which is shown by phthalimide and its N-alkyl derivatives but not by α-phenylethylamine or its succinimide; these last compounds show only plain dispersion (Fig. 2). These facts indicate that the phthalimido chromophore produces this Cotton effect.

The position of the first extremum[1] appears to be influenced by the ability of the substituent Z (I) to attract or release electrons. Measurements of the electrical properties of substituents on aromatic nuclei might, thus, be made in this and related systems by use of optical rotatory dispersion methods. Since it is the *position* rather than the magnitude of the Cotton effect which is important, such measurements could be made on substances of unknown optical purity and absolute configuration and would require neither the precise data nor

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[1] C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., New York, N. Y., 1960, pp. 11–17.

TABLE I

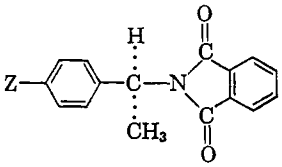
DISPERSION CONSTANTS FOR PHTHALIMIDES OF (−)(S) α-PHENYLETHYLAMINES (CHLOROFORM SOLUTION)

$$[M] = -\frac{A}{\lambda^2 - x} + \frac{B}{\lambda_2 - y}$$

Z	A	x (μ^2)	B	y (μ^2)	$[M]_D$	Trough λ (mμ)	Trough [M]	Peak λ (mμ)	Peak [M]
NO_2	111	0.085	38	0.104	−267	365	−995	335	−150
H	85	.070	30	.104	−180	400	−410	340	+190
Cl	114	.070	38	.104	−253	390	−590	340	+200
Br	114	.070	38	.104	−255	390	−600	340	+170
I	117	.070	38	.104	−275	390	−640	340	+100
OCH_3	125	.070	50	.104	−250	400	−510	350	+ 50
NH_2	186	.075	100	.104	−245	425	−450	380	−290

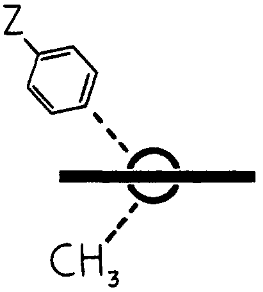
These compounds were prepared from the phthalimide of optically pure (−)S)α-phenylethylamine *via* nitration, reduction and diazotization; they gave correct analyses. The Drude constants are presented only as a concise means of summarizing the dispersion curves and do not represent unique solutions of the two-term equations. The constants for the positive term are the more reliable since measurements could be made to the beginning of the positive Cotton effect. All rotations were measured using a manual Rudolph spectrophotopolarimeter (see ref. 1, pp. 18–26) purchased with funds from the Indiana Elks, the American Cancer Society, the National Institute of Health and the Research Corporation.

the elaborate computations needed for the determination of "reduced rotational strengths."[2]

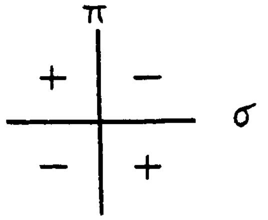


I

The phthalimide group has one plane of symmetry containing the atoms and *sigma* bonds (the σ plane) and another bisecting both rings and lying parallel to the *pi* orbitals (the π plane). In a particular conformation atoms which are



II



III

distributed asymmetrically among the quadrants defined by those planes could produce a dissymmetric perturbation of an electronic transition of the phthalimido group and so cause a Cotton effect at the absorption band corresponding to that transition.[3,4,5] We assume, tentatively, that the sign of the contribution of an atom or group to the phthalimido Cotton effect of a particular conformation is determined simply by the quadrant in which it lies. The observed Cotton effect will be a summation of those of the individual conformations; it is necessary (but not sufficient) that certain conformations be more abundant than others for any Cotton effect to be observed at all. Models indicate that the oxygen atoms would produce severe steric stress in certain conformations and that, in the present series of compounds, only the conformation shown in II[6] will be reasonably free of such stress. It thus appears that atoms in the quadrant occupied by the phenyl group in II make positive contributions to this Cotton effect; signs may be given to the other quadrants on the basis of their symmetry relationships to this one (III). It is at least an interesting coincidence that the same σ-π plane diagram (III) can be used for predicting ketonic Cotton effect by use of the Octant Rule.[4]

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(2) Ref. 1, pp. 150–177 (Chapter by A. Moscowitz).

(3) This analysis is parallel to one used in a theoretical treatment of ketonic Cotton effects.[2]

(4) See ref. 1, pp. 178–190.

(5) The question of whether there is a third plane cutting each of these quadrants into two octants is, for the present, academic and will be left open.

(6) The horizontal bar represents the σ plane of the phthalimido group projecting forward from the asymmetric carbon atom.

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OPTICAL ROTATORY DISPERSION STUDIES. XLIII.[1] ABSOLUTE CONFIGURATIONAL ASSIGNMENT OF α-SUBSTITUTED CARBOXYLIC ACIDS BY ANOMALOUS ROTATORY DISPERSION OF THEIR ACYLTHIOUREA DERIVATIVES[2]

Sir:

Our recent investigations[3] have amply demonstrated the utility of anomalous rotatory dispersion measurements for the solution of a variety of organic chemical problems. As Cotton effect curves are only shown by substances containing an optically active chromophore (*e.g.*, carbonyl group) with suitable spectral characteristics (usually low intensity maximal absorption in an accessible spectral range), there are a number of important classes of organic compounds (*e.g.*, alcohols, amines, carboxylic acids) that do not lend themselves to this anomalous rotatory dispersion approach because of their unsuitable spectral properties. In order to circumvent this problem, we have been searching for easily prepared derivatives which absorb in the near ultraviolet or visible

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(1) Paper XLII, C. Djerassi, A. Fregda and B. Sjöberg, in press.

(2) Supported by grant No. CRTY-5061 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service, and by the National Science Foundation.

(3) For a detailed summary see C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960.