[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF NEW HAMPSHIRE]

Rotatory Dispersion Studies. I. Aralkylamines and Alcohols[1]

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The optical rotatory dispersion curves of compounds having an aromatic center attached to an asymmetric carbon bearing a hetero atom have been shown to exhibit Cotton effects. The investigation of this property with a number of aralkylamines and alcohols has led to correlations with the absolute configurations. The portion of the curve in the visible spectrum can be fitted to the Drude equation, and the slopes thus obtained are shown to be an intrinsic property of the asymmetric center and additive.

Compounds which possess a weakly absorbing chromophore, such as the carbonyl group, in the vicinity of an asymmetric center display anomalous variation of optical rotation with wavelength showing Cotton effects in the region of ultraviolet absorption. This property has provided a useful means of assigning relative and absolute configurations to ketonic steroids by Djerassi and co-workers.[3] Steroids such as equilenin[4] which contain one or more aromatic rings gave plain curves leading to the conclusion that the aromatic ring did not produce Cotton effects. In contrast to this, the rotatory dispersion of ergosterol which possesses no aromatic group but conjugated double bonds shows a Cotton effect of pronounced magnitude.[5] On the other hand, the $\Delta^{3,5}$-steroids,[6a] the $\Delta^{7,9(11)}$-steroids[6b] and $\Delta^{11,13(18)}$-and $\Delta^{12,18}$-terpenoids[6c] failed to reveal anomalous RD curves in the region examined.

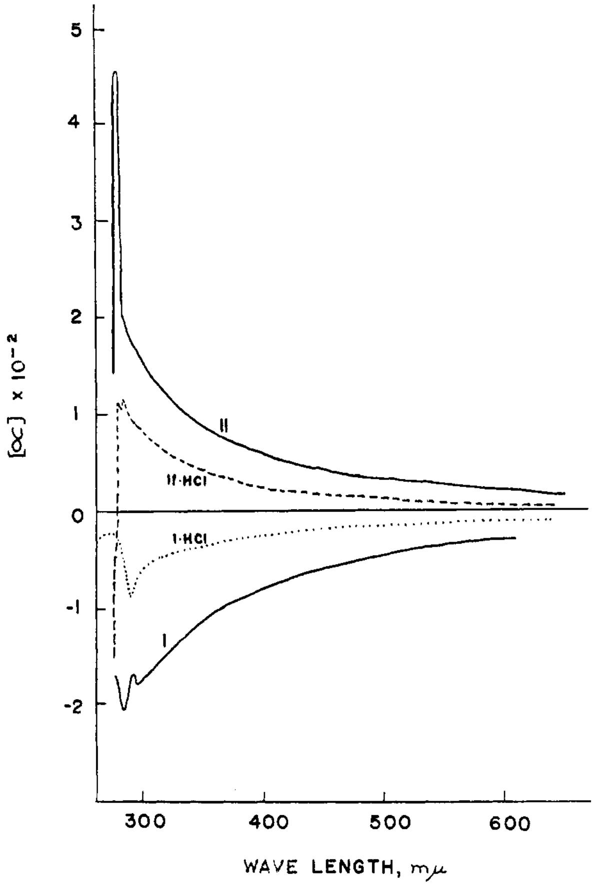

Fig. 1. Optical rotatory dispersion curves of (−)-α-methylbenzylamine (I), (+)-α,*p*-dimethylbenzylamine (II) and their hydrochlorides in ethanol

It seemed likely that an aromatic ring in conjunction with an amino or hydroxyl function would produce optical rotatory dispersion curves exhibiting Cotton effects. The rotatory dispersion curves of relatively few alkaloids have been reported,[5,7,8] and in order to establish a basis for the correlation of configurations with the curves, a group of α-arylalkylkamines and α-arylalkanolamines was examined. When the aromatic ring was attached to an asymmetric center bearing a hydroxyl or amino function, the optical rotatory dispersion curves showed Cotton effects (one exception is discussed below).

The curve (Fig. 1) obtained for (S)-(−)-α-methylbenzylamine (I)[9,10] gave a negative Cotton

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[1] Presented in part before the Organic Division of the American Chemical Society, 136th Meeting, Atlantic City, N. J., September, 1959, p. 71P.

[2] On leave from the University of New Hampshire, 1958–1959. Public Health Service Fellow, 1958–59. Work done at the Laboratory of the Chemistry of Natural Products, National Heart Institute, National Institutes of Health.

[3] C. Djerassi, *Optical Rotatory Dispersion: Applications to Organic Chemistry*, McGraw Hill, New York, 1960.

[4] E. W. Foltz, A. E. Lippman, and C. Djerassi, *J. Am. Chem. Soc.*, **77**, 4359 (1955).

[5] Private communication from Dr. U. Weiss.

[6] (a) A. K. Bose and W. A. Struck, *Chem. & Ind. (London)*, **1959**, 1628; (b) C. Djerassi, O. Halpern, V. Halpern, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 4001 (1958); (c) C. Djerassi, J. Osiecki, and W. Closson, *J. Am. Chem. Soc.*, **81**, 4587 (1959).

[7] T. M. Lowry, *Optical Rotatory Power*, Longmans, Green and Co., London, 1935, p. 326ff.

[8] (a) C. Djerassi, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956); (b) E. E. van Tamelen, P. E. Aldrich, and J. B. Hester, Jr., *J. Am. Chem. Soc.*, **81**, 6214 (1959); (c) J. M. Bobbitt, U. Weiss, and D. Hanessian, *J. Org. Chem.*, **24**, 1582 (1959); (d) W. Wildman and H. M. Fales, *J. Am. Chem. Soc.*, **80**, 6465 (1958); (e) H. G. Leemann and S. Fabbri, *Helv. Chim. Acta*, **42**, 2696 (1959).

[9] For nomenclature indicating absolute configurations, see R. Cahn, C. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

[10] W. Leithe, *Chem. Ber.*, **64**, 2827 (1931).

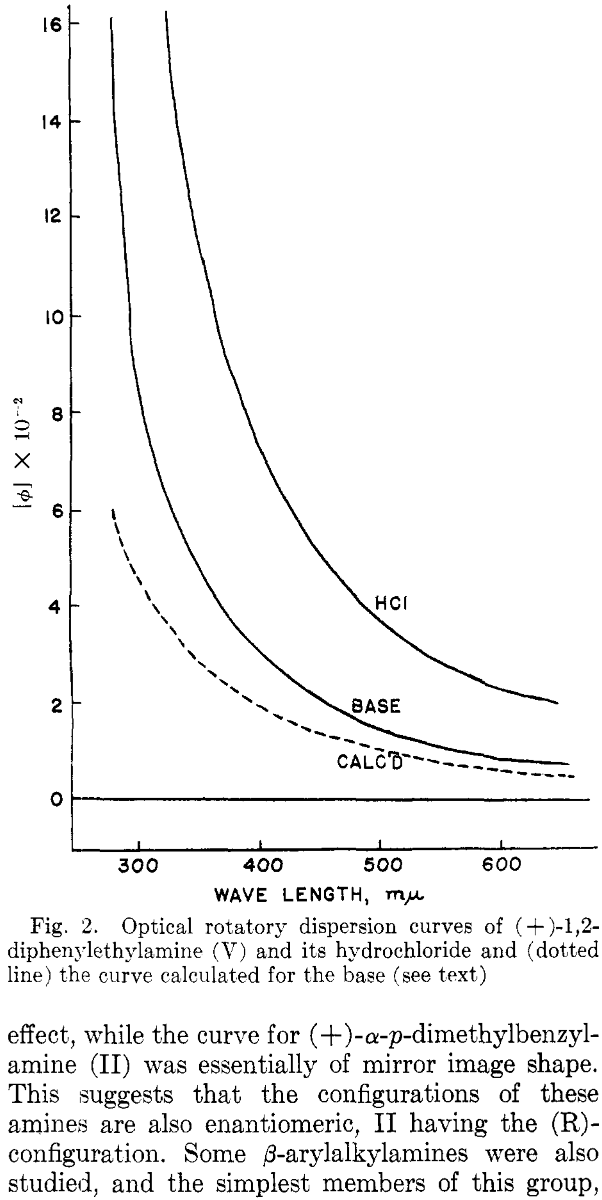


Fig. 2. Optical rotatory dispersion curves of (+)-1,2-diphenylethylamine (V) and its hydrochloride and (dotted line) the curve calculated for the base (see text)

effect, while the curve for (+)-α-*p*-dimethylbenzylamine (II) was essentially of mirror image shape. This suggests that the configurations of these amines are also enantiomeric, II having the (R)-configuration. Some β-arylalkylamines were also studied, and the simplest members of this group, (S)-(+)-amphetamine (III) and (S)-(+)-deoxyephedrine (IV), gave plain curves as the salts in water.[11] Both of these compounds gave anomalous curves, however, when their hydrochlorides were dissolved in ethanol. The shape of the curve was dependent upon the amount of water present in the alcoholic solution, the less the percentage of water, the more apparent the anomalous behavior.

A most interesting result was obtained when the open chain (+)-1,2-diphenylethylamine (V) was examined. The molecule may be considered the summation of (+)-I and (+)-III, as the relative positions of the two aromatic rings would cause the rotation of V to be intensely positive or negative. The curve showed no Cotton effect although V is an α-aralkyl amine. That this was reasonable was shown by calculating a curve for V based on the summation of the molecular rotation values for (+)-I and (+)-III. The two curves are shown in Fig. 2, and the calculated curve shows no Cotton effect in agreement with that found for V. Thus the effects of the phenyl groups appear to be additive even though they are interacting on a single asymmetric center. From these rotatory dispersion data, (+)-V may be assigned the (R)-configuration. Pratesi and co-workers[12] assigned the same configuration to this amine (V) from a relatively complex series of chemical reactions.

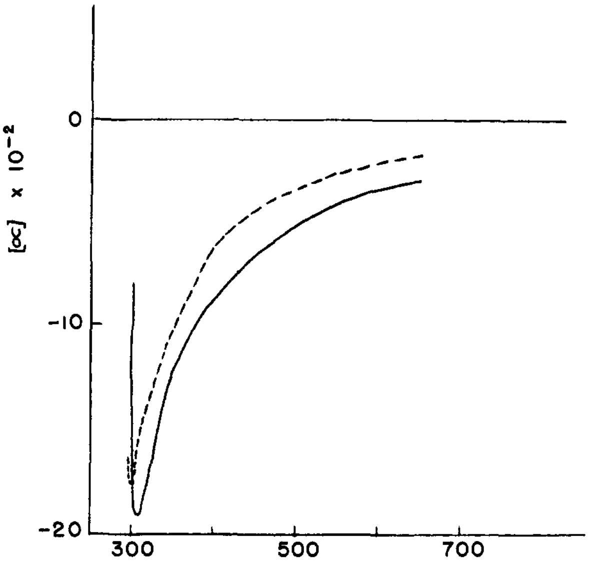
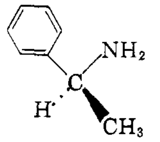
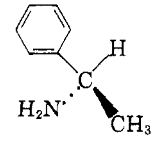


Fig. 3. Optical rotatory dispersion curves of (−)-tetrahydropalmatine (VI) (———) and its hydrochloride (---------)

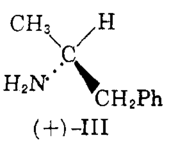
(−)-Tetrahydropalmatine (VI), one of the protoberberine alkaloids, has the amino function *alpha* to one aromatic ring and *beta* to the other and may be compared with (+)-1,2-diphenylethyl-



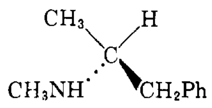
(−)-I



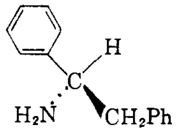
(+)-II



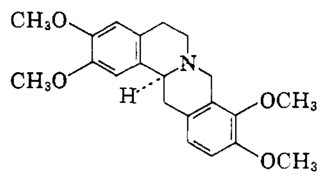
(+)-III



(+)-IV



(+)-V



(−)-VI

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[11] W. Leithe, *Chem. Ber.*, **65**, 660 (1932).

[12] P. Pratesi, A. LaManna, and L. Fontanella, *Il Farmaco (Pavia), Ed. sci.*, **10**, 673 (1955).

amine (V). In this case, however, the aromatic rings are not free to rotate and the confinement in a ring enhances the optical activity. This is in agreement with the discussion of similar open chain and cyclic compounds observed by Kauzmann, Walter, and Eyring.[13] The curve of VI showed a negative Cotton effect of large rotatory power (Fig. 3). The sign of the curve is compatible with its absolute configuration[14] which is enantiomeric to (+)-V and the same as (−)-I.

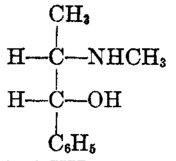
One property of these curves which has found limited application in recent studies is the conversion of the optical rotatory dispersion data to Drude equations.[15] For plain curves, a one-term Drude equation is usually adequate to describe the curve, but for Cotton effect curves, a more complex equation is necessary. In the visible region of the spectrum, however, almost all of the curves can be adequately described by a one-term Drude equation, *i.e.*, $[\phi] = A/(\lambda^2 - \lambda^2_0)$ where $[\phi]$ represents the molecular rotation at a given wave length[16] λ (expressed in microns), and A and λ_0 are characteristic constants of the compound. It is apparent that if a straight line is obtained by plotting $1/[\phi]$ (abscissa), *vs.* λ^2 (ordinate), the slope of this line is A and the intercept is λ_0. The compounds which are reported in this study had values for λ_0 in the far ultraviolet in most cases.

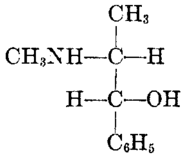
As the slope, A, seemed to be more characteristic of the compounds than the λ_0 values, this quantity was used to determine the configurations. Application of this concept to the amines described above revealed that the values of A for (−)-α-methylbenzylamine (I) and (+)-α,*p*-dimethylbenzylamine (II) were −10.5 and +9.0 respectively. The fact that the slopes are of similar magnitude but of opposite sign lends support to the assignment of configurations (*vide supra*). The substitution of methyl for hydrogen in the *para* position of the aromatic ring in II makes only a small contribution to the rotatory power in the visible region. Nerdel and co-workers[17] examined a group of *m*- and *p*-substituted hydratropic acid derivatives and a similar group of *m*- and *p*-substituted *N*-acetyl-α-methyl benzylamines at five wave lengths in the visible region. The curves of these compounds in alcohol solution were fitted to one-term Drude equations, the A-values of which did not vary with the position of the substituent. In addition, the plot of the A-values as ordinates against Hammett's *sigma* constant[18] as abscissas gave a straight line with a slope of O. The lack of an electronic effect in similar systems permitted the determination of some absolute configurations (*vide infra*).

In the case of (+)-1,2-diphenylethylamine (V), the slope as determined from the Drude equation was +26.3. This value is in good agreement with that calculated from the A-values of the individual components whose curves were summed above. The A-values for (+)-I, +10.5, and (+)-III, +10.4, would predict a value of +20.9 for (+)-V. The hydrochlorides of amphetamine (III) and its *N*-methyl analog (IV) in aqueous solution gave values of close agreement, that of (+)-III hydrochloride being +10.1 and of (+)-IV hydrochloride being +9.9.

When a molecule possesses more than one asymmetric center, the rotation of the molecule has been assumed to be the summation of the rotations of each individual asymmetric center. Attempts to apply the Rule of Optical Superposition[19] to relatively complex molecules using the D-line rotations have met with limited success. The slope of the Drude equation reflects in a single value the rotations over a large number of wavelengths and may also be considered the rotation at a single wave length, one micron. This arises from the fact that if λ^2_0 is relatively small compared with λ^2, the former term may be ignored and the value, A, is approximately equal to the rotation of the molecule at one micron.[20] Application of this hypothesis to a group of alkanolamines indicated the feasibility of this approach.

Examination of two compounds of known absolute configuration,[10] (−)-ephedrine (VII) and (−)-ψ-ephedrine (VIII), showed that these alkaloids gave negative Cotton effect curves, the A-values being −20.9 and −41.4 for the salts of VII and VIII, respectively (Fig. 4). If the contribution of the carbon bearing the amine salt group is ±9.9 (based on IV), the C_1-center would have a contribution of −30.8 in VII and −31.5 in VIII.


(−)-VII


(−)-VIII

Using the shapes of the curves with the presence or absence of Cotton effects as guides and the A-

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[13] W. J. Kauzmann, J. E. Walter, and H. Eyring, *Chem. Rev.*, **26**, 339 (1940).

[14] H. Corrodi and E. Hardegger, *Helv. Chim. Acta*, **39**, 889 (1956).

[15] See ref. 7, p. 120 *et seq.*

[16] Molecular rotation here is defined as in Lowry (ref. 7, p. 22) as one one hundredth of the specific rotation multiplied by the molecular weight. The symbol $[\phi]$ has been suggested by the late Dr. W. Moffitt and Dr. W. Klyne as an appropriate Greek letter to represent rotation rather than the symbol [M] used previously. This proposal is under consideration by the I. U. P. A. C. nomenclature committee.

[17] F. Nerdel and H. Härter, *Ann.*, **621**, 22 (1959); F. Nerdel and H. Würgan, *Ann.*, **621**, 34 (1959); F. Nerdel and H. Liebig, *Ann.*, **621**, 42 (1959).

[18] L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940, p. 184ff.

[19] J. H. van't Hoff, *The Arrangement of Atoms in Space*, 2nd Ed., Longmans, Green and Co., London, 1898, p. 160; P. A. Guye and A. Gauthier, *Compt. rend.*, **119**, 740, 963 (1894).

[20] M. Betti, *Trans. Faraday Soc.*, **26**, 337 (1930).

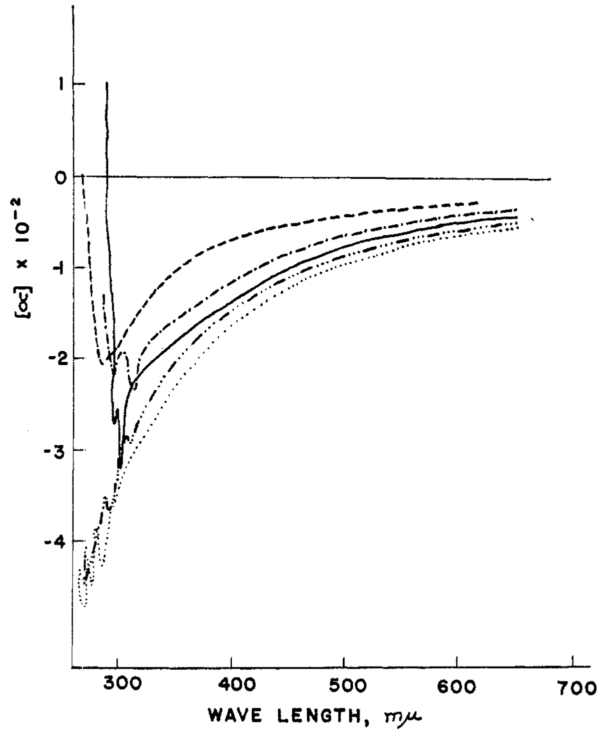


Fig. 4. Rotatory dispersion curves of (−)-ephedrine (VII) sulfate (– – – –), (−)-ψ-ephedrine (VIII) hydrochloride (······), (−)-halostachine (IX) hydrochloride (–···–), (−)-phenylephrine (X) hydrochloride (–·–·–), and (−)-epinephrine (XI) hydrochloride (———)

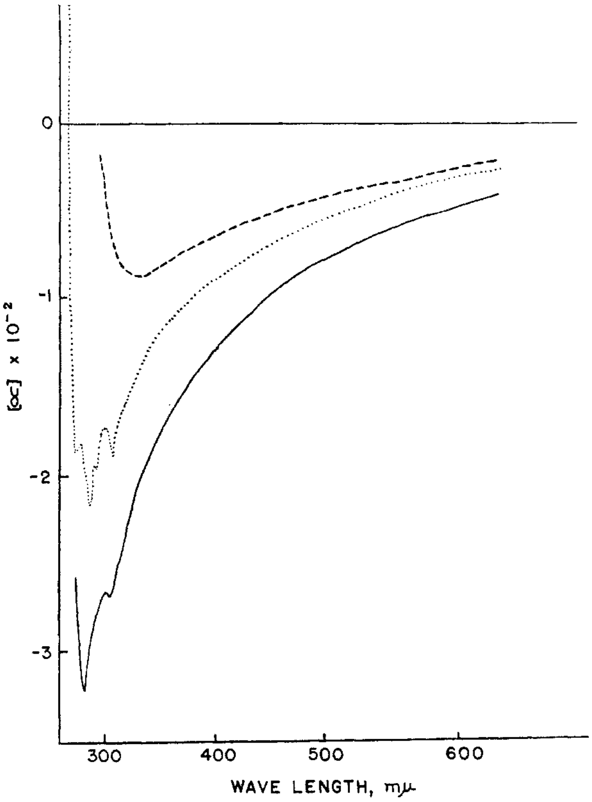
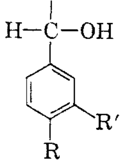


Fig. 5. Optical rotatory dispersion curves of (−)-ψ-ephedrine (VIII) (———), (−)-halostachine (IX) (······), and (−)-phenylephrine (X) (– – – –) in ethanol

values as significant confirmatory evidence, a group of α-arylalkanolamines was examined. One of the compounds failed to give adequate curves except as the salt because of racemization. The three compounds examined [halostachine (IX)[21] phenylephrine (X), and epinephrine (XI)] are all of physiological interest, the levorotatory isomer being the more active.[22,23] The absolute configuration of epinephrine (XI) has been assigned as (R) on the basis of unequivocal chemical correlations.[24] This configuration is the same as that of the C_1-center of (−)-ephedrine, a fact of significant physiological interest. The other two alkanolamines (IX and X) were of unknown configuration.



(—)-IX R = R′ = H
(—)-X R = H; R′—OH
(—)-XI R = R′ = OH

The optical rotatory dispersion curves of the salts of IX, X, and XI showed negative Cotton effects (Fig. 4). Of similar shape were the curves for the bases of IX and X (Fig. 5). Determination of the A-values for the salts of IX, X and XI gave, respectively, −34.9, −31.7, and −36.7 which are in good agreement with the calculated value of the C_1-center of ephedrine (VII) and ψ-ephedrine (VIII). The shapes of the curves and the A-values are strong evidence for assuming that all three of these compounds, IX, X, and XI, have the same absolute configuration, that is, the (R)-configuration.

Confirmation of the assignment (R) to (−)-halostachine (IX) was obtained unequivocally. The conversion of (R)-(−)-mandelic acid to the (−)-*N*-methylamide (XII) was effected through the acetonide with retention of activity. Attempts to form the amide from the ester gave a poor yield of XII with a large amount of racemization. Reduction of XII, of 34% optical purity, with an excess of lithium aluminum hydride in tetrahydrofuran gave (−)-halostachine (IX). The product was approximately 54% optically pure, the degree of purity being increased by the isolation procedure. The amine crystallized from the reaction mixture with only 15% activity, and the oil remaining possessed the greater activity. The infrared absorption spectra of pure (±)-amine and all fractions from the reduction were identical with that of pure (+)-IX, obtained by resolution of synthetic material. As the (−)-halostachine prepared from

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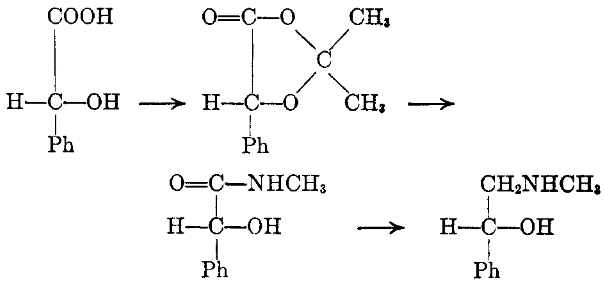
(21) G. P Men'shikov and M. M. Rubinshtein, *J. Gen. Chem.* (*USSR*), **13**, 801 (1943); *Chem. Abstr.*, **39**, 1172 (1945).

(22) W. Osten, *Arzneimittel.-Forsch.*, **5**, 84, 146 (1955).

(23) E. Voss, *Am. Profess. Pharmacist*, **19**, 633, 719, 722, 751 (1953).

(24) P. Pratesi, A. LaManna, A. Campiglio, and V. Ghislandi, *J. Chem. Soc.*, 2069 (1958).

(−)-mandelic acid possessed the (R)-configuration, as XI does also, the absolute configuration of (−)-phenylephrine (X) must also be (R).



XII IX

EXPERIMENTAL

All measurements of rotations were made on a Rudolph spectropolarimeter equipped with a rocking polarizer using zirconium and xenon arcs. The concentrations were not varied over the region investigated, but the path length ranged from 0.5 cm. to 2.0 dcm. The solvent was ethanol or water in the proportions specified, and the temperature was essentially constant between 22 and 25°. Measurements of the blank solutions were made at every wave length read, except in a few cases when averages were obtained from readings at every 5 mμ.

(−)-*α-Methylbenzylamine* (I). R. D. (Fig. 1) in ethanol (*c*, 2.70): $[\alpha]_{610}$ −26.8°, $[\alpha]_{589}$ −29.3°, $[\alpha]_{295}$ −176°, $[\alpha]_{290}$ −167°, $[\alpha]_{284}$ −203°, $[\alpha]_{274}$ −163°. A = −10.5.

(−)-*α-Methylbenzylamine* (I) *hydrochloride*. R. D. (Fig. 1) in 87% ethanol-water (*c*, 2.13): $[\alpha]_{650}$ −4.18°, $[\alpha]_{589}$ −5.97°, $[\alpha]_{290}$ −82.7°, $[\alpha]_{276}$ −23.5°. A = −2.2.

(+)-*α,p-Dimethylbenzylamine* (II). R. D. (Fig. 1) in ethanol (*c*, 2.68): $[\alpha]_{650}$ 17.8°, $[\alpha]_{589}$ 22.7°, $[\alpha]_{278}$ 455°, $[\alpha]_{275}$ 144°. A = +9.0.

(+)-*α,p-Dimethylbenzylamine* (II) *hydrochloride*. R. D. (Fig. 1) in ethanol (*c*, 4.25): $[\alpha]_{650}$ 8.22°, $[\alpha]_{589}$ 10.1°, $[\alpha]_{285}$ 118°, $[\alpha]_{282}$ 106°, $[\alpha]_{281}$ 113°, $[\alpha]_{275}$ −150°. A = +5.1.

(+)-*Amphetamine* (III). R. D. in ethanol (*c*, 2.81): $[\alpha]_{650}$ 20.9°, $[\alpha]_{589}$ 26.3°, $[\alpha]_{275}$ 300°. A = +10.4.

(+)-*Amphetamine* (III) *hydrochloride*. R. D. in water (*c*, 0.785): $[\alpha]_{650}$ 16.5°, $[\alpha]_{589}$ 20.1°, $[\alpha]_{267}$ 293°. A = +10.1. R. D. in ethanol (*c*, 2.484): $[\alpha]_{589}$ −0.54°, $[\alpha]_{330}$ −4.67°, $[\alpha]_{280}$ 23.83°. R. D. in 50% ethanol-water (*c*, 1.241): $[\alpha]_{610}$ 3.86°, $[\alpha]_{589}$ 4.40°, $[\alpha]_{340}$ 20.06°.

(+)-*Deoxyephedrine* (IV). R. D. in ethanol (*c*, 1.956): $[\alpha]_{700}$ 12.4°, $[\alpha]_{589}$ 17.7°, $[\alpha]_{280}$ 138°. A = +8.9.

(+)-*Deoxyephedrine* (IV) *hydrochloride*. R. D. in water (*c*, 2.94): $[\alpha]_{650}$ 13.8°, $[\alpha]_{589}$ 17.1°, $[\alpha]_{310-304}$ 90° (sh,), $[\alpha]_{293-290}$ 108° (sh.), $[\alpha]_{273}$ 147°. A = +9.9. R. D. in ethanol (*c*, 2.26 to 400 mμ, *c*, 3.23, 400–276 mμ): $[\alpha]_{650}$ −4.98°, $[\alpha]_{589}$ −6.14°, $[\alpha]_{305}$ −32.7°, $[\alpha]_{300}$ −28.6°, $[\alpha]_{290}$ −32.3°, $[\alpha]_{276}$ −18.1°.

(+)-*1,2-Diphenylethylamine* (V). R. D. (Fig. 2) in ethanol (*c*, 2.68): $[\alpha]_{650}$ 37.5°, $[\alpha]_{589}$ 47.9°, $[\alpha]_{275}$ 795°. A = +26.3.

(+)-*1,2-Diphenylethylamine* (V) *hydrochloride*. R. D. (Fig. 2) in ethanol (*c*, 1.02): $[\alpha]_{650}$ 102°, $[\alpha]_{589}$ 128°, $[\alpha]_{275}$ 1720°. A = +86.7.

(−)-*Tetrahydropalmatine* (VI). R. D. (Fig. 3) in ethanol (*c*, 0.635): $[\alpha]_{650}$ −232°, $[\alpha]_{589}$ −290°, $[\alpha]_{305}$ −1920°, $[\alpha]_{298}$ −891°. A = −310.

(−)-*Tetrahydropalmatine* (VI) *hydrochloride*. R. D. (Fig. 3) in 95% ethanol (*c*, 0.412): $[\alpha]_{650}$ −183°, $[\alpha]_{589}$ −227°, $[\alpha]_{300}$ −1710°, $[\alpha]_{298}$ −1583°, $[\alpha]_{297}$ −1730°, $[\alpha]_{296.5}$ −1670°. A = −269.

(−)-*Ephedrine* (VII). R. D. in ethanol (*c*, 3.16): $[\alpha]_{650}$ −2.36°, $[\alpha]_{589}$ −2.65°, $[\alpha]_{460}$ −3.20° (broad trough), $[\alpha]_{330}$ 4.54°. This substance was not absolutely pure, containing some water of hydration.

(−)-*Ephedrine* (VII) *sulfate*. R. D. (Fig. 4) in 80% ethanol-water (*c*, 5.15): $[\alpha]_{610}$ −28.1°, $[\alpha]_{589}$ −30.4°, $[\alpha]_{290}$ −207° (broad trough), $[\alpha]_{272}$ −99°. A = −20.9.

(−)-*Pseudoephedrine* (VIII). R. D. (Fig. 5) in ethanol (*c*, 1.60): $[\alpha]_{650}$ −42.6°, $[\alpha]_{589}$ −52.5°, $[\alpha]_{305}$ −268° (sh), $[\alpha]_{280}$ −323°, $[\alpha]_{273}$ −256°. A = −27.5.

(−)-*Pseudoephedrine* (VIII) *hydrochloride*. R. D. (Fig. 4) in ethanol (*c*, 1.57): $[\alpha]_{650}$ −53.1°, $[\alpha]_{589}$ −65.6°, $[\alpha]_{290}$ −434°, $[\alpha]_{284}$ −381°, $[\alpha]_{278}$ −444°, $[\alpha]_{276}$ −415°, $[\alpha]_{274}$ −471°, $[\alpha]_{269}$ −414°. A = −41.4.

(−)-*Phenylephrine* (X). R. D. (Fig. 5) in ethanol (*c*, 0.276): $[\alpha]_{650}$ −22.8°, $[\alpha]_{589}$ −29.5°, $[\alpha]_{335}$ −88.4°, $[\alpha]_{298}$ −22.5°. A = −15.8.

(−)-*Phenylephrine* (X) *hydrochloride*. R. D. (Fig. 4) in ethanol (*c*, 1.22): $[\alpha]_{650}$ −39.3°, $[\alpha]_{589}$ −48.4°, $[\alpha]_{318}$ −232°, $[\alpha]_{315}$ −190°, $[\alpha]_{300}$ −220°, $[\alpha]_{290}$ −133°. A = −31.7.

(−)-*Epinephrine* (XI). R. D. (Fig. 4) in 0.5*N* hydrochloric acid (*c*, 1.20): $[\alpha]_{650}$ −43.7°, $[\alpha]_{589}$ −53.2°, $[\alpha]_{303}$ −325°, $[\alpha]_{299}$ −250°, $[\alpha]_{298}$ −273°, $[\alpha]_{290}$ 732°. A = −36.7.

(R)-(−)-*N-Methylmandelamide* (XII). A solution of 1.46 g. (0.0096 mole) of mandelic acid ($[\alpha]^{23}_{D}$ −60°, 37% optically pure) in 4.5 ml. of acetone was cooled to −10° in an ice-salt bath, and 1.0 g. of concd. sulfuric acid was added dropwise with stirring keeping the temperature below −5°. The solution was added slowly to an ice-cold solution of 2.1 g. of sodium carbonate in 20 ml. of water. The flocculent precipitate was separated by filtration, washed with ice water, and dried under reduced pressure over calcium sulfate. The acetonide which was contaminated with inorganic salts melted at 61–69°.

The crude acetonide was added in portions to a solution of 0.86 g. of methylamine in 8 ml. of methanol, and the mixture was allowed to stand at room temperature for 2 hr. The insoluble material was separated by filtration, washed with methanol, and discarded. The filtrate was concentrated yielding 0.85 g. (59.3%) of (−)-*N-methylmandelamide*, m.p. 86–94°, $[\alpha]^{23}_{D}$ −26.1° (acetone, *c*, 1.32). The pure (±)-amide, prepared in a similar manner, melted at 96–98° after recrystallization from benzene; lit.[25] m.p. of (+)-*N*-methylmandelamide, 94–95°, $[\alpha]_{D}$ not given. The infrared spectra in chloroform of the (±)-amide and the (−)-amide (XII) were identical, 3400 cm.$^{-1}$ (OH, NH), 1675 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_9H_{11}NO_3$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.43; H, 6.51; N, 8.34.

(R)-(−)-*Halostachine* (XI). A suspension of 1.0 g. of lithium aluminum hydride in 20 ml. of tetrahydrofuran was mixed with a solution of 0.61 g. (0.004 mole) of (−)-*N*-methylmandelamide ($[\alpha]^{23}_{D}$ −26.1°) in 30 ml. of tetrahydrofuran, and the mixture was heated under reflux for 18 hr. The reaction mixture was decomposed with 5 drops of water, and an excess of 30% sodium hydroxide was added until the organic layer separated. The tetrahydrofuran solution was decanted and the inorganic residue was triturated twice with the same solvent. The combined organic solutions were concentrated and hexane was added to the residue. The precipitate (0.3 g.) was separated by filtration, m.p. 39–70°, and on recrystallization from hexane yielded 130 mg. of hexane-insoluble material whose infrared spectrum indicated unreduced amide and 91 mg. of hexane-soluble crystals, m.p. 70–76°, $[\alpha]^{23}_{D}$ −4.60° (ethanol, *c*, 1.50, 15% optically pure), lit.[26] m.p. 75–76° [(±)-α-methylaminomethylbenzyl alcohol].

The filtrate from the 0.3 g. precipitate deposited 16 mg. of the amino alcohol, $[\alpha]^{23}_{D}$ −10.9° (ethanol, *c*, 0.80, 28.9% active). Concentration of the filtrate gave 73 mg. of an oil which failed to crystallize but whose infrared spectrum in chloroform was identical with the two crystalline fractions

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(25) I. Heilbron, *Dictionary of Organic Compounds*, Vol. III, Oxford University Press, New York, 1953, p. 211.

(26) G. P. Men'shikov and G. M. Borodina, *J. Gen. Chem.* (*USSR*), **17**, 1569 (1947); *Chem. Abstr.*, **42**, 2245 (1948).

and with the optically pure amine (*vide infra*), 3300–3400 cm.$^{-1}$ (OH, NH), no carbonyl band, $[\alpha]^{23}_{D}$ $-20.0°$ (ethanol, *c*, 2.48, 53.5% active). The total yield of amine was 30%; lit.[21,26] m.p. for halostachine, 43–45°, $[\alpha]_{D}$ $-47.03°$ (no solvent given).

Resolution of ($\pm$)*-halostachine.* A solution of 2.3 g. of ($\pm$)-halostachine in acetone was added to an acetone solution containing 3.48 g. of (+)-10-camphorsulfonic acid (total volume = 60 cc.). On addition of ether, 3.64 g. of crystalline salt was obtained, m.p. 109–112°, $[\alpha]^{23}_{D}$ $+28.21°$ (acetone, *c*, 1.74). Three recrystallizations from acetone-ether gave 0.65 g. of pure salt, m.p. 132–134°, $[\alpha]^{23}_{D}$ $+49.41°$.

The amine (IX) was obtained from the salt by passage over ethyl acetate-washed Merck alumina using chloroform as solvent and 10% ethanol-chloroform as eluent. From 650 mg. of salt 64.2 mg. of pure amine, $[\alpha]^{25}_{D}$ $+37.43°$ (ethanol, *c*, 2.37), was obtained. R. D. (Fig. 5) in ethanol: $[\alpha]_{650}$ 30.21°, $[\alpha]_{589}$ 37.43°, $[\alpha]_{314}$ 172°, $[\alpha]_{306}$ 176°, $[\alpha]_{295}$ 203°, $[\alpha]_{292}$ 193°, $[\alpha]_{288}$ 219°, $[\alpha]_{280}$ 182°, $[\alpha]_{276}$ 187°, $[\alpha]_{271}$ 41°. A = +18.0. A total of 151 mg. (74%) of the base was recovered from the salt.

The hydrochloride of IX melted at 108–111°, $[\alpha]^{25}_{D}$ $+53.20°$ (water, *c*, 0.750): lit.[26] m.p. 113–114°, $[\alpha]_{D}$ $+52.46°$. R. D. (Fig. 4) in ethanol (*c*, 1.57): $[\alpha]_{650}$ 48.6°, $[\alpha]_{589}$ 59.1°, $[\alpha]_{292}$ 362°, $[\alpha]_{290}$ 346°, $[\alpha]_{284}$ 392° (sh.), $[\alpha]_{274}$ 447°, $[\alpha]_{272}$ 411°. A = +34.9.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Intramolecular-Intermolecular Polymerizations of Some Phenyl Substituted Nonconjugated Diolefins[1]

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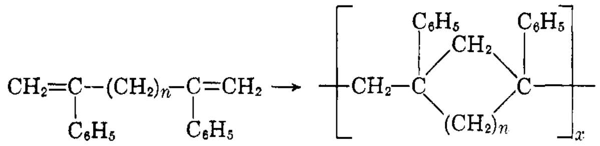
The three hydrocarbons 2,5-diphenylhexadiene-1,5, 2,6-diphenylheptadiene-1,6 and 2,7-diphenyloctadiene-1,7 have been synthesized and polymerized to yield polymers with cyclic recurring units. The evidence indicates that five- and seven-membered rings form less readily than does the six-membered ring in such polymerization reactions.

The work reported here was undertaken to determine whether phenyl substituted nonconjugated diolefins of the type shown in formula I would undergo the intramolecular-intermolecular polymerization reaction which has been successfully applied in a number of instances.[2] While the work was in progress, we learned of the work of Field,[3] who has found that the heptadiene derivative (Ib) readily yields a polymer with a cyclic recurring unit (IIb) by all standard types of initiation. We have confirmed his experience.



Ia. $n = 2$
Ib. $n = 3$
Ic. $n = 4$

IIa. $n = 2$
IIb. $n = 3$
IIc. $n = 4$

The two homologous dienes (Ia and Ic) have been synthesized from the corresponding diketones by application of the Wittig reaction.[3,4] They polymerize to yield soluble, powdery solids which are rather low melting and have low inherent viscosities. These polymers show very little absorption in the infrared in the carbon-carbon double bond region. It seems obvious that these are low molecular weight polymers of the cyclic structures expected (IIa and IIc). It is quite evident however, that there is less tendency to yield five-or seven-membered recurring units than is the case for six-membered recurring units.

EXPERIMENTAL

Melting points are uncorrected.

Monomers: 2,6-Diphenylheptadiene-1,6 (Ib). This monomer was prepared according to the procedure reported by Field[3] and previously reported by us.[5]

2,7-Diphenyloctadiene-1,7 (Ic). 1,4-Dibenzoylbutane was prepared according to the procedure reported by Fuson and Walker.[6]

The conversion of 1,4-dibenzoylbutane to 2,7-diphenyloctadiene-1,7 (Ic) was similar to that described earlier for the preparation of 2,6-diphenylheptadiene-1,6 (Ib). Phenyllithium was prepared in the usual way from 86.4 g. (0.55 mole) of bromobenzene and 9.7 g. (1.4 g.-atoms) of lithium metal in dry diethyl ether in 94.5% yield. A solution of 0.455 mole of phenyl lithium was added to a slurry of 146 g.

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