2,4-dimethylpentane-1,3,5-triol or the alternative 2,3-dimethylpentane-1,4,5-triol. The latter was eliminated because X did not take up any periodate. The infrared spectrum of X is identical with that of 2,4-dimethylpentane-1,3,5-triol [m.p. 54–56°, $[\alpha]^{25}D$ −14.0° (*c* 2%, methanol)] isolated as a degradation product of erythromycin.[7] Hence, the triol X is the enantiomorph of the "*act*-triol" from erythromycin.

The above data establish the structure of I as 2,4-dimethyl-3-chalcosyloxy-6-oxoheptanoic acid.

(7) K. Gerzon, E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley, R. Monahan and U. C. Quarck, *J. Am. Chem. Soc.*, **78**, 6396 (1956).

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OPTICALLY ACTIVE AMINES. I. N-ISOPROPYLIDENE DERIVATIVES OF OPTICALLY ACTIVE OPEN CHAIN PRIMARY AMINES AND THEIR ROTATORY POWERS[1]

Sir:

Recently Bergel and co-workers[2] reported that optically active α-amino acid esters and amides containing a primary amino group, and other optically active open chain primary amines examined in ketonic solvents (Table I) exhibit rotatory powers which change greatly with time, eventually reaching a constant value, highly levorotatory for L-α-amino acid esters and amides. They concluded[2b] that the mutarotation is due to the formation in ketonic solvents of unstable Schiff bases, $R_2C{=}NCHR'R''$, (I), and suggested that the maximal rotation of an α-amino acid ester in a ketonic solvent may help to decide its absolute configuration.

TABLE I

MOLECULAR ROTATIONS[a] OF SOME L-α-AMINO ACID DERIVATIVES AND (S)-(+)-AMPHETAMINE[3] IN ETHANOL AND IN ACETONE AS REPORTED BY BERGEL[2]

Code	Compound	$[\phi]^{22}D$ in ethanol	$[\phi]^{22}D$ in acetone	Time to reach constant $[\phi]D$ in acetone, min
IIa	Ethyl L-alaninate	+ 4	−153	160
IIIa	(S)-(+)-Amphetamine	+45	+114	240
IVa	Ethyl L-phenylalaninate	+43	−242	60
IVb	Ethyl L-tyrosinate	+38	−259	60
IVc	L-Tyrosinamide	−41	−133[b]	days

[a] Calculated as $[\alpha]D \times$ mol. wt. of free base/100 from $[\alpha]D$'s reported in Ref. 2. [b] 1:1 methanol–acetone as solvent.

In another connection we had prepared a considerable number of optically active α-amino acid esters and other open chain primary amines, all of known absolute configurations, and it was decided to compare their rotatory powers in ethanol and in acetone (Table II) in order to provide a somewhat broader base for testing the reliability of Bergel's suggested method for assigning the absolute configurations of such open chain compounds.

(1) This work was supported by a grant (G14524) from the National Science Foundation.

(2) (a) F. Bergel and G. E. Lewis, *Chem. and Ind.*, 774 (1955); (b) F. Bergel, G. E. Lewis, S. F. D. Orr and J. Butler, *J. Chem. Soc.*, 1431 (1959); (c) F. Bergel and J. Butler, *ibid.*, 4047 (1961).

(3) Absolute configurational designations according to R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

TABLE II

MOLECULAR ROTATIONS[a] OF SOME OPTICALLY ACTIVE α-AMINO ACID ESTERS AND OTHER OPEN CHAIN PRIMARY AMINES IN ETHANOL AND IN ACETONE

Code	Compound	$[\phi]D^{21-28}$ in ethanol[b]	$[\phi]D^{21-28}$ in acetone	Time to reach constant $[\phi]D$ in acetone, min.
IIa	Ethyl L-alaninate	+ 3	− 70[c]	390
IIb	Ethyl D-phenylglycinate	−217	− 68	350
IIc	(R)-(+)-α-Phenylethylamine	+ 36	+110	1330
IId	(S)-(−)-α-*p*-Tolylethylamine	− 33	−115	1360
IIIb	(S)-(+)-2-Aminobutane	+ 2	+ 72	1210
IVa	Ethyl L-phenylalaninate	+ 43	−249	1170
IVd	Methyl L-tyrosinate	+ 54[d]	−278	1000
IVe	Ethyl L-leucinate	+ 34	−252	1890
IVf	Ethyl L-methioninate	+ 13	−224	540
IVg	Ethyl (S)-(−)-β-aminohydrocinnamate[e]	− 13	−117	330
Va	Ethyl L-isoleucinate	+ 60	−249	1130
Vb	Ethyl L-alloisoleucinate[f]	+ 54	−174	2630

[a] Calculated as $[\alpha]D \times$ mol. wt. of free base/100. [b] No change in $[\phi]D$ with time. [c] 1:1 Ethanol–acetone as solvent. [d] Methanol as solvent. [e] (R)-Isomer used. [f] D-Isomer used.

The possible confirmation of Bergel's simple method seems especially important because for many of these compounds the direction and magnitude of the optical rotation is not certainly predicted with rules, such as the Atomic and Conformational Asymmetry Rules of Brewster.[4]

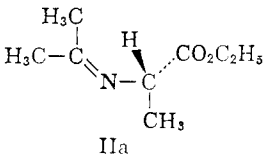
As seen by an inspection of Tables I and II, our results where comparable are essentially the same as those reported by Bergel, except that the times required for the attainment of constant optical rotations in acetone were somewhat longer, due perhaps to the prevailing humidity, traces of water in the acetone being known[2] to diminish the rate of change of rotatory power. Evidently the cause of these slower rates had no great effect on the magnitudes of the the rotatory powers finally observed in acetone (*cf.* IVa in Tables I and II).

From an inspection of Table II it is clear that at least one D-α-amino acid ester is highly levorotatory in acetone. The rotatory power of ethyl D-phenylglycinate in acetone is, indeed, displaced in a positive direction but is still nevertheless levorotatory. The work of Bergel[2] and these data indicate, however, that the absolute configurations of these Schiff bases formed in acetone can be related to their rotatory powers using Brewster's Atomic and Conformational Asymmetry Rules[4] and thus measurements of this kind will be useful in the deduction of the absolute configurations of amines of this type.

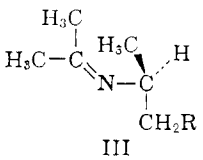
Thus, using Brewster's rules in conjunction with the rotational ranks tabulated by him[4] and considering the rotatory powers of the N-isopropylidene derivatives of code II (Tables I and II), all expected to show atomic asymmetry and the simplest type of conformational asymmetry, one obtains the empirical polarizability sequence of the substituent attachment atoms as decreasing in the order

(4) J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5475 (1959); *Tetrahedron* **13**, 106 (1961).

$N{=}C(CH_3)_2 > C_6H_5 > CO_2R > CH_3 > H$.[5] As shown in the projection of the N-isopropylidene derivative of ethyl L-alaninate (IIa), the contribution to the rotatory power due to atomic asymmetry is negative. An additional negative contribution results from the preferred orientation, also shown in projection IIa, of the isopropylideneamino moiety about its attachment bond. For the other derivatives of code II both of these contributions are not as reinforcing, and in IIb at least, the contribution due to atomic asymmetry appears to be the more important. These derivatives all display substantially lower rotatory powers than that of ethyl L-alaninate (*cf.* Table I).[7]



IIa



III

For the derivatives of code III, the preferred conformation of the isopropylideneamino group is as shown in III, and as a result of the flexible chains (CH_2R), additional conformational asymmetry contributions come into play. With the above sequence of polarizabilities, these derivatives are correctly predicted, using only the Conformational Asymmetry Rule, to be dextrorotatory. Similarly for those of codes IV and V, the same atomic and conformational symmetries present in IIa make, except for IVg, reinforcing negative contributions to the rotatory powers, and as in those of code III, the flexible chains give rise to additional conformational contributions. These contributions considered, the derivatives of code IV and V are all correctly predicted to be highly levorotatory, the additional asymmetric centers in those of code V making, as predicted, only small contributions to the rotatory powers.

These same considerations can also be extended to the rotatory powers of similar Schiff bases formed in other ketonic solvents,[2] and we are currently extending this work to include optically active cyclic amines.

(5) This sequence cannot be deduced uniquely from the data in Tables I and II. The priority of the isopropylideneamino group is assigned, however, on the basis of the atomic refraction (polarizability) of nitrogen in Schiff bases of this type.[6]

(6) S. S. Batsanov, "Refractometry and Chemical Structure" Consultants Bureau, New York, N. Y., 1961, p. 22.

(7) Here and in what follows, the somewhat justifiable assumption is made that no significant contributions to the rotatory powers arise from preferred orientations of the carbethoxy, carbomethoxy and carbamoyl groups about their attachment bonds.

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THE CHEMISTRY OF ACTINOSPECTACIN. I. ACTINAMINE

Sir:

Actinospectacin,[1,2,3] a new broad spectrum antibiotic produced by an actinomycete, *Streptomyces spectabilis*, is a basic compound with the molecular formula $C_{14}H_{24}N_2O_7$. Hydrolysis of this antibiotic with boiling 6.0 *N* hydrochloric acid gives actinamine (I) isolated as its dihydrochloride which has the molecular formula $C_8H_{18}N_2O_4 \cdot 2HCl$, m.p. 315° dec., optically inactive. *Anal.* Calcd. for $C_8H_{18}N_2O_4 \cdot 2HCl$: C, 34.41; H, 7.12; N, 10.05; Cl, 25.45; O, 22.93; mol. wt., 279.2. Found: C, 34.46, 34.39; H, 7.12, 7.07; N, 10.02, 9.83; Cl, 25.31; O, 21.23; mol. wt. (electr. titr.), 280. Treatment of the dihydrochloride with an anion exchange resin (Dowex 2) gave the free base, m.p. 129°. *Anal.* Calcd. for $C_8H_{18}N_2O_4$: C, 46.60; H, 8.74; N, 13.59; O, 31.07; mol. wt., 206.2. Found: C, 46.99; H, 8.99; N, 14.06; O, 31.00; mol. wt. (electr. titr.), 204. The free base in water is optically inactive in the range 310 to 589 mμ and shows only end absorption in the ultraviolet region. A strong band at 3200 cm.$^{-1}$ in the infrared spectrum of actinamine is indicative of hydroxyl and/or amino groups, but there are no bands attributable to unsaturation of any type. Both nitrogen atoms are present as methylamino groups as shown by pK_a' values of 7.2 and 8.9 and isolation of two moles of methylamine, identified as its *p*-hydroxyazobenzene-*p'*-sulfonic acid salt, from each mole of actinamine dihydrochloride after periodate oxidation. Acetylation of actinamine dihydrochloride with acetic anhydride and sodium acetate gave a hexaacetyl derivative (II), m.p. 196–198°, optically inactive. *Anal.* Calcd. for $C_{20}H_{30}N_2O_{10}(6CH_3C)$: C, 52.40; H, 6.53; N, 6.11; O, 34.93; CH_3C, 19.6. Found: C, 52.34; H, 6.71; N, 6.20; O, 34.46; CH_3C, 18.9. The infrared spectrum of this compound has bands indicative of ester carbonyl (1750 cm.$^{-1}$) and amide carbonyl (1650 cm.$^{-1}$) but no bands in the OH/NH region. The formation of hexaacetylactinamine established that all the oxygen atoms were present as hydroxyl groups.

Actinamine dihydrochloride consumed six moles of periodate per mole with no formation of formaldehyde. The periodate consumption data coupled with analysis and functional group determination point unequivocally to a bis-(methylamino)-tetrahydroxycyclohexane structure for actinamine. There are three possible positional isomers aside from stereoisomers having such a structure. These are 1,2-bis-(methylamino)-, 1,3-bis-(methylamino)- and 1,4-bis-(methylamino)-tetrahydroxycyclohexane. That actinamine is the 1,3-isomer was shown by a study of the periodate oxidation of N,N'-diacetylactinamine (III, prepared by methanolysis of hexaacetylactinamine), m.p. 250–252° dec., infrared absorption bands at 3280 cm.$^{-1}$ and 3180 cm.$^{-1}$ (hydroxyl) and at 1635 cm.$^{-1}$ (amide carbonyl). *Anal.* Calcd. for $C_{12}H_{22}N_2O_6$ ($2CH_3CO$): C, 49.65; H, 7.58; N, 9.65; CH_3CO, 29.6. Found C, 49.77; H, 7.65; N, 9.47; CH_3CO, 23.3. This diacetyl compound consumed two moles of periodate per mole with formation of one mole of formic acid, conclusively establishing structure I for actinamine.

Actinamine and all of its derivatives are optically inactive, indicating a *meso* compound. There are

(1) The trade name of The Upjohn Company for actinospectacin is Trobicin.

(2) D. J. Mason, A. Dietz and R. M. Smith, *Antibiotics and Chemotherapy*, **11**, 118 (1961).

(3) M. E. Bergy, T. E. Eble, and R. R. Herr, *ibid.*, **11**, 661 (1961).