since in obtaining II from I the 2-proton peak disappeared instantaneously, followed by the slower disappearance of the peak at −100 cycles and a simultaneous diminution of the peak at −104 cycles, we may assign the peaks at −104 and −100 cycles to the 6-proton and the peaks at −104 and −95 cycles to the 4-proton. The above observation also shows that the 2-proton exchanges much faster than the 6-proton.

In the spectrum of III, the 4-proton lines partially disappeared and the 5-proton lines collapsed into a doublet. Therefore, the reduction must have occured at the 4-position.[9]

[9] Westheimer and Hutton recently independently obtained consistent n.m.r. data (to be published).

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CRYSTALLINE POLYMERS OF METHYL METHACRYLATE

Sir:

Recently we have synthesized several crystallizable forms of poly-(methyl methacrylate) by means of stereospecific polymerizations effected by apparently homogeneous free radical and anionic initiating systems. Crystallization was effected by solvent treatment in borderline solvents such as 4-heptanone. Three polymer types (I, II, III) have been characterized by their different X-ray diffraction patterns as well as by differences in their properties, not only in the crystalline but also in the amorphous states (Table I).

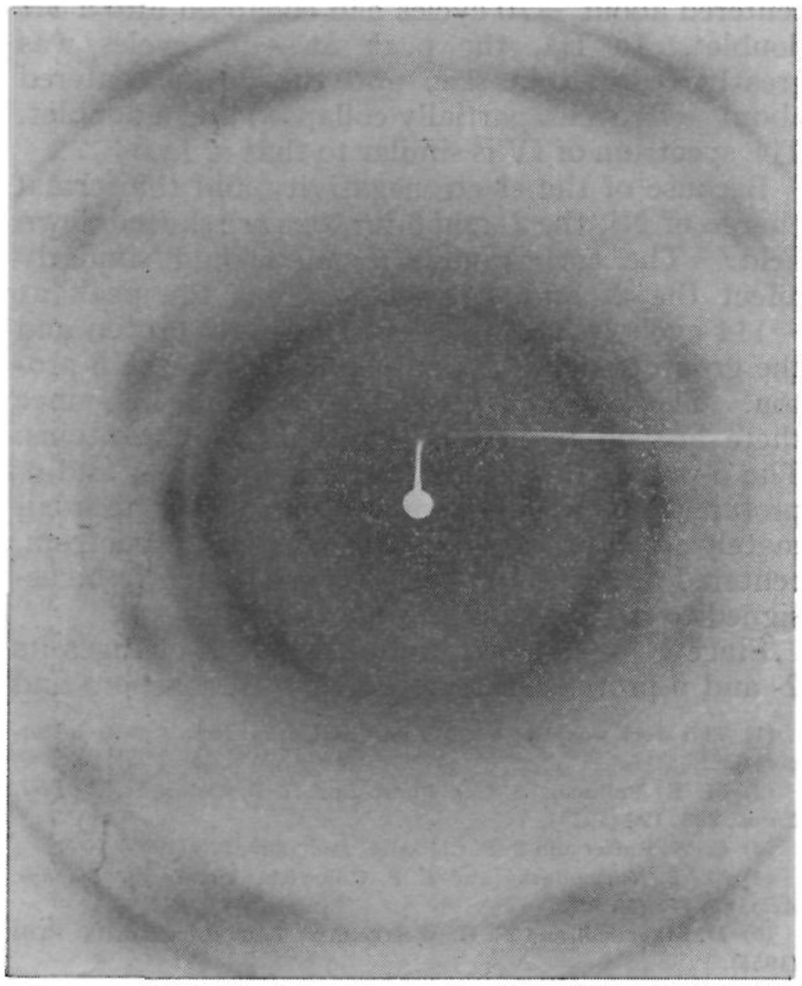

Fig. 1.—X-Ray fiber diffraction pattern of type II PMMA; stretch orientation vertical; exposure calibrated by 2.81 Å.; NaCl line; Ni filtered CuK radiation.

TABLE I

PROPERTIES OF POLYMERS OF METHYL METHACRYLATE

	From vol.-temp. meas.			
Type	Glass temp. T_g, °C.	Melting point, T_m, °C.	Density of amorphous polymer at 30°, g./ml.[3]	Presumed chain configuration
I	115	(>200)[a]	1.19	Isotactic
II	45	160	1.22	Syndiotactic
III	60–95	170	1.20–1.22	Isotactic - syndiotactic block copolymer
Conventional	104	. . .	1.188	Essentially random

[a] Extrapolated from data on concentrated solutions.

The ability of these polymers to crystallize is ascribed to unusually uniform chain structure resulting from isotactic or syndiotactic[1] arrangement of configurations at the pseudoasymmetric carbon atoms. In this respect they are similar to certain crystallizable linear polymers prepared by Natta[1] by means of heterogeneous solid catalysts. A preliminary assignment of the configuration of the various types of poly-(methyl methacrylate), based on evidence to be published later, is shown in Table I.

Type I poly-(methyl methacrylate) results from free radical polymerizations conducted at low temperature, as well as from anionic polymerizations in highly solvating media, such as those initiated by 9-fluorenyllithium in 1,2-dimethoxyethane at −60°. The stereospecificity of these polymerizations is believed to arise from small differences in the free energies of the two transition states, such as the differences which may result from interaction of the groups of the last and penultimate monomer units at each monomer addition step.

Type II poly-(methyl methacrylate) is prepared by anionic polymerizations initiated by organolithium compounds in hydrocarbons. Thus 9-fluorenyllithium at −60° in toluene produces quantitative yields of type II polymers. Under these conditions chain propagation involves an ion pair rather than free ions; the lithium counterion apparently is involved intimately in the transition state.[2] An X-ray diffraction pattern of a crystalline type II fiber is shown in Fig. 1.

Anionic polymerizations at low temperature in media of moderate solvating power for cations produce poly-(methyl methacrylate) of type III. Such polymers are produced by 9-fluorenyllithium at −70° in toluene containing small amounts of dioxane. These conditions are intermediate between those leading to types I and II. Intimate mixtures of types I and II crystallize to give the same diffraction patterns as those obtained from type III. However, while the mixtures may be separated by fractionations under special conditions, it has not been possible to obtain an equivalent separation of type III polymers prepared directly. This evidence suggests that the latter polymers consist of alternating sequences of isotactic and syndiotactic structures. This "block

[1] *Cf.* G. Natta and P. Corradini, *Atti acad. nazl. Lincei* (Series 8), **18**, 19–27 (1955); G. Natta, F. Danusso, and G. Moraglio, *Makromol. Chem.*, **20**, 37–45 (1956); G. Natta, *Angew. Chem.*, **68**, 393–403 (1956).

[2] *Cf.* F. W. Stavely and co-workers, *Ind. Eng. Chem.*, **48**, 77 (1956); H. Hsieh and A. V. Tobolsky, *J. Polymer Sci.*, **25**, 245 (1957).

copolymer" character presumably is responsible for the variation in X-ray and physical property data observed with type III poly-(methyl methacrylate). The exact nature of the crystals themselves is under more intensive investigation.

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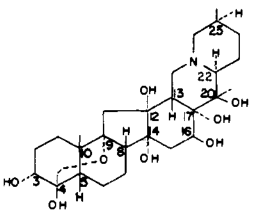
THE CONFIGURATION OF CEVINE

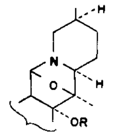
Sir:

The configurations of nine (C_3, C_4, C_5, C_9, C_{10}, C_{12}, C_{14}, C_{17}, C_{25}) of the fourteen asymmetric centers of cevine were established almost simultaneously with the climactic structure elucidation in 1954–55.[1–3] Recent work in our laboratory made possible assignment of configuration at C_{16} and C_{20} and provides support for previously considered[1] configurational assignments at C_8 and C_{13}.[4] Evidence is presented herewith for assignment of configuration at the remaining asymmetric center (C_{22}) of cevine which now can be represented completely by formula I. It is highly probable that closely related alkaloids, such as zygadenine and germine, also have this basic configuration.

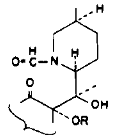
Oxidation of veracevine D-orthoacetate triacetate (IIa)[5] (pK_a' 7.4) with N-bromosuccinimide[6] yielded a dehydro compound (m.p. 280–282° dec., $[\alpha]_D$ +33° diox.; found, C, 63.51; H, 7.35; Ac, 25.52), evidently the bridged oxide IIIa for the following reasons. (1) The pK_a' (found, 3.8) was in the lower range expected for a stable carbinolamine ether.[7] (2) The infrared spectrum showed no absorption in the hydroxyl region. (3) The 16-acetate group survived prolonged treatment with methanol and triethylamine, an indication of the absence of an axial hydroxyl at C_{20} to facilitate methanolysis.[4] (4) Chromic anhydride-pyridine oxidation of IIIa afforded a neutral product (m.p. 263–264° dec., $[\alpha]_D$ +54° diox., λ_{max}^{chf} 6.07 μ, –NCO–, found, C, 60.59; H, 7.17), evidently the formamido ketone IVa. Acid hydrolysis afforded one mole equivalent of formic acid. Alkaline hydrolysis of the corresponding formamido ketone IVb (m.p. 288° dec., $[\alpha]_D$ +52° py., λ_{max}^{chf} 6.07 μ; found, C, 60.98; H, 7.08) derived from cevine gave the desacetyl-formamido-ketone IVc (m.p. 259–260° dec., $[\alpha]_D$ +22° py., found, C, 61.66; H, 7.24). In addition to the amide band, the infrared spectrum of this substance exhibited normal ketone absorption at 5.85 μ.



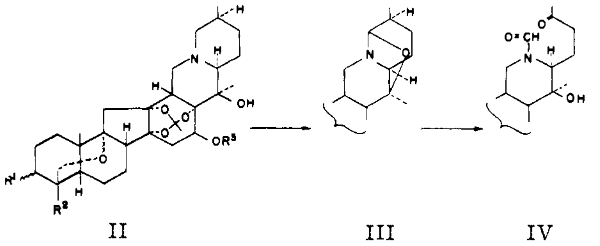
I



V



VI



II III IV

a (R^1 = β-OAc, R^2 = OAc; R^3 = Ac)
b (R^1 = α-OAc, R^2 = OAc; R^3 = Ac)
c (R^1 = α-OH, R^2 = OH; R^3 = H)

The alternative formulations V and VI for the oxide and formamido ketone were excluded on the basis of the following evidence. (1) The formamido ketone IVb derived from cevine readily formed a semicarbazone (m.p. 273–274° dec.; found, C, 57.91; H, 6.80, N, 6.93). (2) The formamido ketone IVa showed active methylene group reactivity in the Zimmermann test[8] and upon treatment in alkaline solution with furfural. (3) The corresponding formamido ketone (m.p. 253–255° dec., $[\alpha]_D$ −83° diox.; found, D, 60.96; H, 7.10) from cevagenine-C-orthoacetate diacetate[5] was, like the parent alkaloid, stable to lead tetraacetate. This behavior is characteristic of a rigid *trans* diaxial glycol system at C_{17}, C_{20}, a situation clearly not satisfied by VI.

The bridged *β-oriented* oxide structure of IIIa and b requires that the hydrogen at C_{22} be α-oriented. That the stereochemical integrity of the molecule was preserved during the oxide formation was demonstrated by catalytic hydrogenation of IIIa over platinum in acetic acid. Two mole-equivalents of hydrogen was absorbed to give a substance identical with the product of hydrogenation (one mole-equivalent uptake) of IIa, namely veracevine-D-dihydroorthoacetate triacetate (m.p. 299–300° dec., $[\alpha]_D$ +21° diox.; found, C, 63.53; H, 7.85; Ac, 19.98).[1,9]

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[1] D. H. R. Barton, C. J. W. Brooks and P. De Mayo, *J. Chem. Soc.*, 3950 (1954).

[2] F. Gautschi, O. Jeger, V. Prelog and R. B. Woodward, *Helv. Chim. Acta*, **38**, 296 (1955).

[3] S. M. Kupchan, THIS JOURNAL, **77**, 686 (1955).

[4] S. M. Kupchan and W. S. Johnson, *ibid.*, **78**, 3864 (1956).

[5] S. M. Kupchan, D. Lavie, C. V. Deliwala and B. Y. A. Andoh, *ibid.*, **75**, 5519 (1953).

[6] *Cf.* O. E. Edwards, F. H. Clarke and B. Douglas, *Can. J. Chem.*, **32**, 235 (1954).

[7] H. Bloom and L. H. Briggs, *J. Chem. Soc.*, 3591 (1952).

[8] W. Zimmermann, *Z. physiol. Chem.*, **233**, 257 (1935); D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 887 (1954).

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RECEIVED JANUARY 27, 1958

16α-CHLORO- AND 16α-IODOESTRONE METHYL ETHER, NEW AND POTENT LIPID-SHIFTING AGENTS

Sir:

The problem of finding estrogen-like substances capable of altering blood lipid composition, and which at the same time are not feminizing, is important in clinical treatment of atherosclerosis. A