Stereospecific Reactions of Optically Pure Menthyl Methylphosphinate

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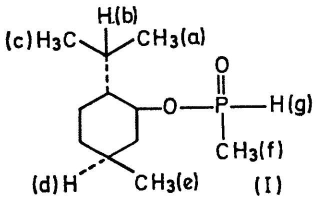
Summary Stereospecific reactions of optically pure menthyl methylphosphinate with sulphur and with *NN*-diethylmethanesulphenamide are described.

Previous attempts to obtain optically-active compounds of the type $R^1(R^2)P(O)H$ (R^1, R^2 = alkyl or alkoxy) have been only partly successful.[1] We report the isolation of an optically pure epimer of menthyl methylphosphinate (I). Fractional crystallization of the epimeric mixture† {280 g; melting range 7—17°; $[\alpha]_{\mathrm{D}}^{25}$ − 71·8° (*c* 1·0, in benzene)} from n-hexane at −25 to −5° gave a high-melting epimer (Ia) {15·5 g; m.p. 42°; $[\alpha]_{\mathrm{D}}^{25}$ − 96·6° (*c* 1·0, in benzene)}.

The optical purity of (Ia) was checked by means of ^{1}H n.m.r. spectroscopy. The Table gives a summary of the n.m.r. data of (Ia) and its epimer (Ib), as deduced from the spectra of (Ia) and the epimeric mixture. Assignment of the doublets originating from the methyl groups of the menthyl moiety (H_a, H_c, and H_e) was made by reference to the investigation of Lewis *et al.*[2] An estimation of the



(I)

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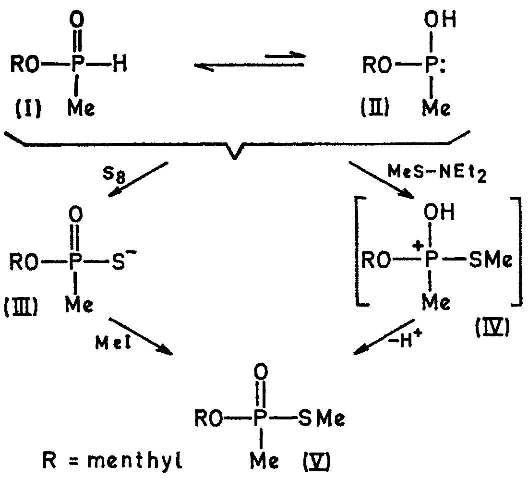
† Prepared *via* the hydrolysis of menthyl methylphosphonochloridite, which was obtained from methylphosphonous dichloride and natural menthol.

TABLE. ^{1}H *chemical shifts* (τ, *p.p.m.*) *and coupling constants* (J,Hz) *of menthyl methylphosphinate*[a]

Epimer	H_a	$J_{H_aH_b}$	H_c	$J_{H_cH_b}$	H_e	$J_{H_eH_d}$	H_f	J_{H_fP}	$J_{H_fH_g}$	H_g	J_{H_gP}
(Ia)	9·15	**6·7**	9·07	**6·7**	9·06	**4·8**	8·49	**14·8**	**2·0**	2·69	536·2
(Ib)	9·18		9·07		9·06		8·47			2·75	534·6

[a] Measured at 60 MHz(Jeol C-60H spectrometer); $CDCl_3$ solution.

ratio of epimers‡ was based on the separation of the upfield part of the H_a doublets of (Ia) and (Ib) ($\Delta\tau$ 0·03 p.p.m.), situated in a region undisturbed by other signals.



SCHEME

The ready availability of optically pure menthyl methylphosphinate gives access to a great variety of stereochemical studies, as shown in the Scheme. Addition of sulphur to the optically pure epimer (Ia) in the presence of dicyclohexylamine in ether under reflux gave the dicyclohexylamine salt of *O*-menthyl hydrogen methylphosphonothioate (IIIa). This product was alkylated with methyl iodide after replacement of ether by benzene as solvent, giving menthyl *S*-methyl methylphosphonothioate {(Va); m.p. 45—47°; $[\alpha]_D^{25}$ − 37·0° (*c* 0·8, in benzene)}. The over-all stereospecificity of the two reaction steps is at least 90%, as estimated from the upfield position of the SCH_3 doublet in the ^{1}H n.m.r. spectrum (60 MHz) ($CDCl_3$) of (Va) (τ 7·69 p.p.m., *J* 12·7 Hz) relative to the corresponding doublet of the other epimer (τ 7·67 p.p.m.) in the spectrum of the epimeric mixture of (V). Since the chiral phosphorus atom is not involved in the alkylation of (III), the observed stereospecificity pertains to the addition of sulphur§ to (I).

Epimer (Va) {optical purity ⩾90%; m.p. 45—47°; $[\alpha]_D^{25}$ − 36·8° (*c* 1·1, in benzene)} was also obtained from a one-step reaction[3] of optically pure (Ia) with an equimolar amount of *NN*-diethylmethanesulphenamide at 130°. Obviously, the reactions of (I) with sulphur and with the sulphenamide follow the same stereochemical course. The latter reaction probably proceeds[3] by means of a nucleophilic attack of (I) in its tervalent form (II) on the sulphur atom of the sulphenamide *via* the phosphonium compound (IV). Consequently, the tervalent form of (I) would be optically stable during its conversion at 130°.

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‡ An estimation of the optical purity of (Ia) is also possible by means of ^{31}P n.m.r. spectroscopy, since the signals of the two epimers are completely separated ($\Delta\delta$ 4·3 p.p.m.): F. H. Meppelder, H. P. Benschop, and G. W. Kraay, submitted for publication in *Chem. Comm.*

§ Very recently, a radical mechanism has been suggested for the addition of sulphur to alkyl methylphosphinates in the presence of amine (see W. A. Mosher and R. R. Irino, *J. Amer. Chem. Soc.*, 1969, **91**, 756).

[1] T. L. Emmick and R. L. Letsinger, *J. Amer. Chem. Soc.*, 1968, **90**, 3459.

[2] R. A. Lewis, O. Korpiun, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4847.

[3] K. A. Petrov, N. K. Bliznyuk, and V. A. Savostenok, *Zhur. obshchei Khim.*, 1961, **31**, 1361.