Stereospecific Free-radical Addition of Menthyl Methylphosphinate to Alkenes: Evidence for Inversion of Configuration at Phosphorus

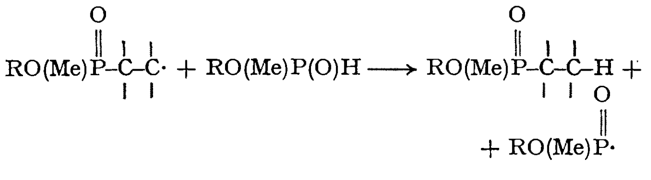
By H. P. BENSCHOP* and D. H. J. M. PLATENBURG

(*Chemical Laboratory of the National Defence Research Organization TNO, Rijswijk, Z.H., The Netherlands*)

Summary Free-radical addition of menthyl methylphosphinate to alkenes and its free-radical reaction with dimethyl disulphide proceed probably with inversion and retention of configuration, respectively.

REPORTS on the racemization of a phosphinium radical cation[1] and on a retention mechanism involving phosphoranyl radicals[2] led us to investigate the stereochemistry of free-radical reactions of optically pure menthyl methylphosphinate (Ia).[3] We have found that the addition of (Ia) to alkenes, initiated by dibenzoyl peroxide or u.v. light, is completely stereospecific, or very nearly so. The free-radical nature of this reaction is well established,[4] presumably involving phosphinyl radicals in the chain-propagating steps:

$$\mathrm{RO(Me)}\overset{\overset{\displaystyle O}{\|}}{P}\cdot + {>}C{=}C{<} \longrightarrow \mathrm{RO(Me)}\overset{\overset{\displaystyle O}{\|}}{P}\text{–}\overset{|}{\underset{|}{C}}\text{–}\overset{|}{\underset{|}{C}}\cdot$$

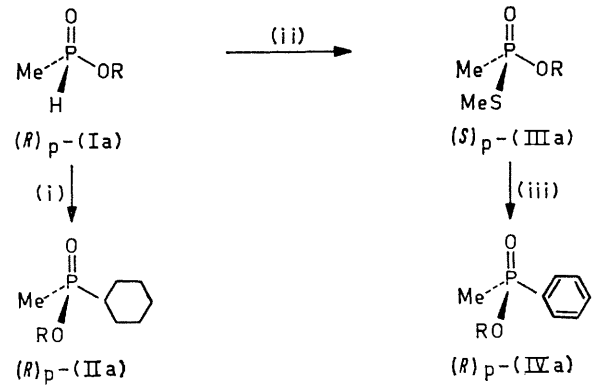


$$\mathrm{RO(Me)}\overset{\overset{\displaystyle O}{\|}}{P}\text{–}\overset{|}{\underset{|}{C}}\text{–}\overset{|}{\underset{|}{C}}\cdot + \mathrm{RO(Me)P(O)H} \longrightarrow \mathrm{RO(Me)}\overset{\overset{\displaystyle O}{\|}}{P}\text{–}\overset{|}{\underset{|}{C}}\text{–}\overset{|}{\underset{|}{C}}\text{–H} + \mathrm{RO(Me)}\overset{\overset{\displaystyle O}{\|}}{P}\cdot$$

Gradual addition of dibenzoyl peroxide (5 mol %) to an equimolar mixture of (Ia) (m.p. 42°)[3] and cyclohexene in n-heptane at 80°, leads to a 95% conversion (g.l.c.) of (Ia) into optically pure $(R)_P$-menthyl cyclohexylmethylphosphinate (IIa).[5,6] The proton-decoupled ^{31}P n.m.r. spectrum of crude $(R)_P$-(IIa) shows a single absorption at −52·2 p.p.m. (in benzene, relative to external 85% H_3PO_4), whereas an additional singlet of approximately equal intensity is observed at −51·0 p.p.m. in the spectrum of (II), obtained from the epimeric mixture of (I). Crystallization of crude $(R)_P$-(IIa) from n-pentane gave analytically pure $(R)_P$-(IIa) {m.p. 110—111°, $[\alpha]_D^{25}$ −54·1° (*c* 0·9, benzene); lit.[5] m.p. 110—111°, $[\alpha]_D$ −54° (benzene)}. Optically pure† $(R)_P$-(IIa) was also obtained from an equimolar mixture of (Ia) and cyclohexene in n-heptane by irradiation with a low-pressure mercury lamp (λ_{max} 253·7 nm) {86% conversion (g.l.c.); m.p. 110—111°, $[\alpha]_D^{25}$ −53·6° (*c* 0·8, benzene), after crystallization from n-pentane}. Similarly, passage of ethylene through a u.v.-irradiated solution of (Ia) in n-heptane gave optically pure† $(R)_P$-menthyl ethylmethylphosphinate[6] {98% conversion (g.l.c.); m.p. 80—81°, $[\alpha]_D^{25}$ −68·8° (*c* 0·7, benzene), after crystallization from n-pentane-isopentane (lit.[6] m.p. 73—76°); ^{1}H n.m.r. (CCl_4, internal Me_4Si) τ 8·71 p.p.m. (CH_3P, J 13·4 Hz); δ^{31}P(benzene) − 51·8 p.p.m.; compare $(S)_P$-epimer: τ 8·68 p.p.m. (CH_3P); δ ^{31}P −51·1 p.p.m. (as derived from the epimeric mixture)}.

The stereochemical course of the free-radical alkylations of (Ia) was compared with that of the free-radical reaction of (Ia) with dimethyl disulphide.[7] No reaction occurred when (Ia) was heated with a five-fold molar excess of dimethyl disulphide in n-heptane at 50°. However, u.v. irradiation of (Ia) for 5 h at 50° resulted in a complete conversion of (Ia) into the earlier reported[3] optically pure† epimer of menthyl *S*-methyl methylphosphonothioate (IIIa) {m.p. 45—47°, $[\alpha]_D^{25}$ −37·1° (*c* 1·4, benzene)}, with evolution of methanethiol.‡ Reaction of (IIIa) with phenylmagnesium bromide[8] gave optically pure† $(R)_P$-menthyl methylphenylphosphinate (IVa)[5] {m.p. 87—88°, $[\alpha]_D^{25}$ −16·0° (*c* 0·6, benzene); lit.[5] m.p. 89°, $[\alpha]_D$ −16° (benzene)}.

Since the formation of $(R)_P$-(IVa) from (IIIa) proceeds with inversion,[8] the chirality of (IIIa) is $(S)_P$. This assignment is confirmed by the negative Cotton effects (trough at 215 nm, EtOH) in the o.r.d. spectra of menthyl methylphosphonothioic acid, from which (IIIa) is obtained by methylation with retention,[3] and of (+)-$(S)_P$-isopropyl methylphosphonothioic acid.[8,9] Based on the tentative assignment of the $(R)_P$-chirality to (Ia) by Meppelder *et al.*,[10] we suggest that the free-radical reaction of (Ia) with dimethyl disulphide, and the addition of sulphur[3] to (Ia), occur with retention. This conclusion is supported by the recently reported retention mechanism for the addition of sulphur to *cis*-4-methyl-1,3,2-dioxaphosphorinan 2-oxide.[11] Consequently (see Scheme), the free-radical addition of (Ia) to cyclohexene (and ethylene) would lead to inversion of configuration at phosphorus.



SCHEME. R = Menthyl. Reagents: (i) Cyclohexene in n-heptane with 5 mol % of dibenzoyl peroxide (15 h at 80°) or u.v. irradiation for 15 h at 50°; (ii) Dimethyl disulphide in n-heptane with u.v. irradiation for 5 h. at 50°; (iii) PhMgBr in tetrahydrofuran, 30 min under reflux.

It has been assumed that phosphinyl radicals [RO(Me)-P(O)·] are involved in the aforementioned reactions of (I) with alkenes[4] and with dimethyl disulphide.[7]§ If this is so,

---

† An epimeric mixture of starting materials yields an epimeric mixture of reaction products.

‡ The formation of (III) also occurs readily upon u.v. irradiation of (I) and dimethyl disulphide in a molar ratio of 2 : 1. Molecular hydrogen is evolved from the reaction mixture under these conditions.

§ *A priori*, the reaction could also proceed *via* the phosphoranyl radical RO(Me)P(OH)SMe, by addition of a thiyl radical to the tervalent form of (I) (see ref. 2 and ref. 4, pp. 22 and 34).

our experiments show that these free radicals are chiral and, unlike phosphinium radical cations,[1] sufficiently optically stable to give completely, or almost completely, stereospecific reactions. E.s.r. evidence for the non-planarity of the related free radical $(EtO)_2P(O)\cdot$ is consistent with our stereochemical studies.[12] Similar results were recently reported on silyl radicals.[13]

The stereospecific addition of (Ia) to alkenes represents a synthetically useful extension to Mislow's method for the preparation of optically active phosphine oxides from menthyl phosphinates.[5,6] Further studies will be necessary to clarify the mechanism of the addition reaction, which to our knowledge provides the first evidence for inversion of configuration in a free-radical process.[14]

We thank Dr. L. Maat, Laboratory of Organic Chemistry, Technische Hogeschool, Delft, for the o.r.d. measurements.

(*Received, July 13th*, 1970; *Com.* 1111.)

---

[1] R. L. Powell and C. D. Hall, *J. Amer. Chem. Soc.*, 1969, **91**, 5403.

[2] W. G. Bentrude, J. H. Hargis, and P. E. Rusek, *Chem. Comm.*, 1969, 296.

[3] H. P. Benschop, D. H. J. M. Platenburg, F. H. Meppelder, and H. L. Boter, *Chem. Comm.*, 1970, 33.

[4] C. Walling, in "Topics in Phosphorus Chemistry," ed. E. J. Griffith and M. Grayson, Interscience, New York, 1966, vol. 3, p. 10.

[5] O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4842.

[6] R. A. Lewis and K. Mislow, *J. Amer. Chem. Soc.*, 1969, **91**, 7009.

[7] W. A. Mosher and R. R. Irino, *J. Amer. Chem. Soc.*, 1969, **91**, 756.

[8] H. P. Benschop, G. R. Van den Berg, and H. L. Boter, *Rec. Trav. chim.*, 1968, **87**, 387.

[9] M. Mikolajczyk and M. Para, *Chem. Comm.*, 1969, 1192.

[10] F. H. Meppelder, H. P. Benschop, and G. W. Kraay, *Chem. Comm.*, 1970, 431.

[11] M. Mikolajczyk, *Chem. Comm.*, 1969, 1221.

[12] K. Terauchi and H. Sakurai, *Bull. Chem. Soc. Japan*, 1968, **41**, 1736.

[13] H. Sakurai, M. Murakami, and M. Kumada, *J. Amer. Chem. Soc.*, 1969, **91**, 519; A. G. Brook and J. M. Duff, *ibid.*, p. 2118; S. W. Bennett, C. Eaborn, A. Hudson, R. A. Jackson, and K. D. J. Root, *J. Chem. Soc.* (*A*), 1970, 348.

[14] R. A. Herrmann and R. M. Noyes, *J. Amer. Chem. Soc.*, 1956, **78**, 5764; but compare S. W. Benson, *J. Chem. Phys.*, 1963, **38**, 1945.