Tetrahedron Vol. 41, No. 21, pp. 4909 to 4917, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00
© 1985 Pergamon Press Ltd.

STEREOCHEMISTRY OF SOME REACTIONS BETWEEN ALKYL S-METHYL METHYLPHOSPHONOTHIOATES AND CHIRAL ALKOXIDES

C. RICHARD HALL, THOMAS D. INCH, COLIN POTTAGE
and NANCY E. WILLIAMS

Chemical Defence Establishment, Porton Down,
Salisbury, Wiltshire, SP4 0JQ, Great Britain

(*Received in UK 29 May* 1985)

Abstract - With R-(+) ethyl (or methyl) S-methyl methylphosphonothioate and (+)-pinacolyl alkoxide competitive and highly stereoselective displacements of O-alkyl and S-methyl occur, both reactions being with inversion of configuration. With the enantiomeric S-(-) ethyl (and methyl) S-methyl methylphosphonothioates and (+)-pinacolyl alkoxide the reactions, although still competitive, are no longer stereoselective. In contrast similar reactions with the sodium salt of (-)-menthol, (which might be considered to be the mirror image of (+)-pinacolyl alkoxide) occur highly stereoselectively with the S-(-) but not with R-(+) enantiomers. The displacement of O-alkyl from alkyl S-methyl methylphosphonothioates by ethoxide, pinacolyl alkoxide and menthyl alkoxide is not observed when methoxide is the nucleophile; in this case only displacement of S-alkyl group occurs.

Nucleophilic displacement of S-alkyl groups from phosphorus in alkyl S-alkyl alkylphosphonothioates is usually highly stereoselective occurring with inversion of configuration [1,2]. However, the degree of stereoselectivity is sometimes influenced significantly by reaction conditions or by the nature of substituent groups [3,4,5]. Accordingly it has been suggested,[6] but without proof, that in reactions between alkyl S-alkyl alkylphosphonothioates and acetylcholinesterase, the chiral environment of the enzyme could encourage different reaction pathways for each isomer of an enantiomeric pair. This paper reports, as chemical models for the enzyme-phosphonothioate interactions, studies of reactions between the enantiomers of alkyl S-methyl methylphosphonothiates and the sodium salts of S-(+) pinacolyl alcohol [7] (3,3-dimethylbutan-2-ol) and (-)-menthol (which has a 1R, 3R, 4S configuration [8]).

Experiments were conducted using both R-(+) and S-(-) ethyl and methyl S-methyl methylphosphonothioates which were prepared by conventional resolution procedures [9]. Enantiomeric compositions as determined by n.m.r. chiral shift reagent procedures [5,10] showed the ethyl isomers to be enantiomerically pure but the methyl derivatives to be mixtures of enantiomers.

(The methyl S-methyl methylphosphonothioate hereafter designated R-(+) was a 3.9:1, R:S mixture and the S(-) isomer was a 3.6:1, S:R mixture).

All reactions were monitored by ^{31}P n.m.r. (with heteronuclear decoupling). Product identities were established by addition of appropriate standards to reaction mixtures and by isolation of products for detailed n.m.r. analysis, including examination in the presence of optically active shift reagents.

Experiments with S-(+) pinacolyl alcohol - R-(+) and S-(-) ethyl S-methyl methylphosphonothioate (0.1 g) were separately dissolved in (+)-pinacolyl alcohol, and the sodium salt of the alcohol was added. The reactions were slow and after four days at room temperature about half the starting materials remained. For the R-(+) enantiomer the product was mainly (> 90%) the isomer of ethyl pinacolyl methylphosphonate with a high field phosphorus n.m.r. signal (δp((+)pinOH) 29.0) with just a trace of the low field diastereoisomer (δp((+)PinOH) 29.7) and some diethyl methylphosphonate.

In contrast S(-) ethyl S-methyl methylphosphonothioate afforded both isomers of ethyl pinacolyl methylphosphonate with the low field one (δp 29.7) only slightly in excess. Thus the (+)-pinacolyl alcohol - R(+) methylphosphonothioate reaction was highly stereoselective whereas the (+)-pinacolyl alcohol - S(-) methylphosphonothioate reaction was not.

Similar results were obtained when the reactions were performed in DMF rather than in (+)-pinacolyl alcohol as solvent. Under these conditions the reactions proceeded more rapidly and when a slight excess of the sodium salt of (+)-pinacolyl alcohol was used all the starting phosphonothioates reacted. Product ratios were not affected.

Corresponding results were obtained with the enantiomers of methyl S-methyl methylphosphonothioate. An example of the n.m.r. trace from the S(-) enantiomer - (+)-pinacolyl alkoxide reaction in DMF after 100 min is given in Fig 1a. The products were approximately equal amounts of both isomers of methyl (+)-pinacolyl methylphosphonate (δp 29.5, 30.1), dipinacolyl methylphosphonate (δp 30.5), dimethyl methylphosphonate (δp 31.8), the isomers of pinacolyl S-methyl methylphosphonothioate (δp 51.2, 51.9) and some unreacted S-(-) methyl S-methyl methylphosphonothioate (δp 54.9). The above ^{31}P shifts are for the reaction mixture; for pure materials see experimental . Under similar conditions the R-(+) isomer gave the n.m.r. trace in Fig 1b. Taking account of the fact that the R-(+) isomer contained some of the S-(-) isomer initially, it is clear that as for the R-(+) ethyl derivative the displacement of S-methyl was highly stereoselective.

The above results are consistent with the following interpretation (Scheme 1). With the sodium salt of (+)-pinacolyl alcohol, R-(+) methyl S-methyl methylphosphonothioate loses S-methyl stereospecifically with inversion of configuration at phosphorus. (For a discussion of the absolute stereochemistry of the reactions involved see below). In competition with this reaction is the displacement of alkoxy by pinacolyl also with inversion (see below). The methoxide so generated reacts with the starting methylphosphonothioate more readily than pinacolyl alkoxide so that even although the latter may be in excess, dimethyl methylphosphonate is formed. Dipinacolyl methylphosphonate is formed but to a lesser extent than dimethyl methylphosphonate by reaction of pinacolyl S-methyl methylphosphonothioate with pinacolyl alkoxide.

SA = S(-) methyl S-methyl methylphosphonothioate
RA = R(+) methyl S-methyl methylphosphonothioate
B = phosphorus isomers of pinacolyl S-methyl methylphosphonothioate
C = dimethyl methylphosphonate
D = dipinacolyl methylphosphonate
E = phosphorus isomers of methyl pinacolyl methylphosphonate

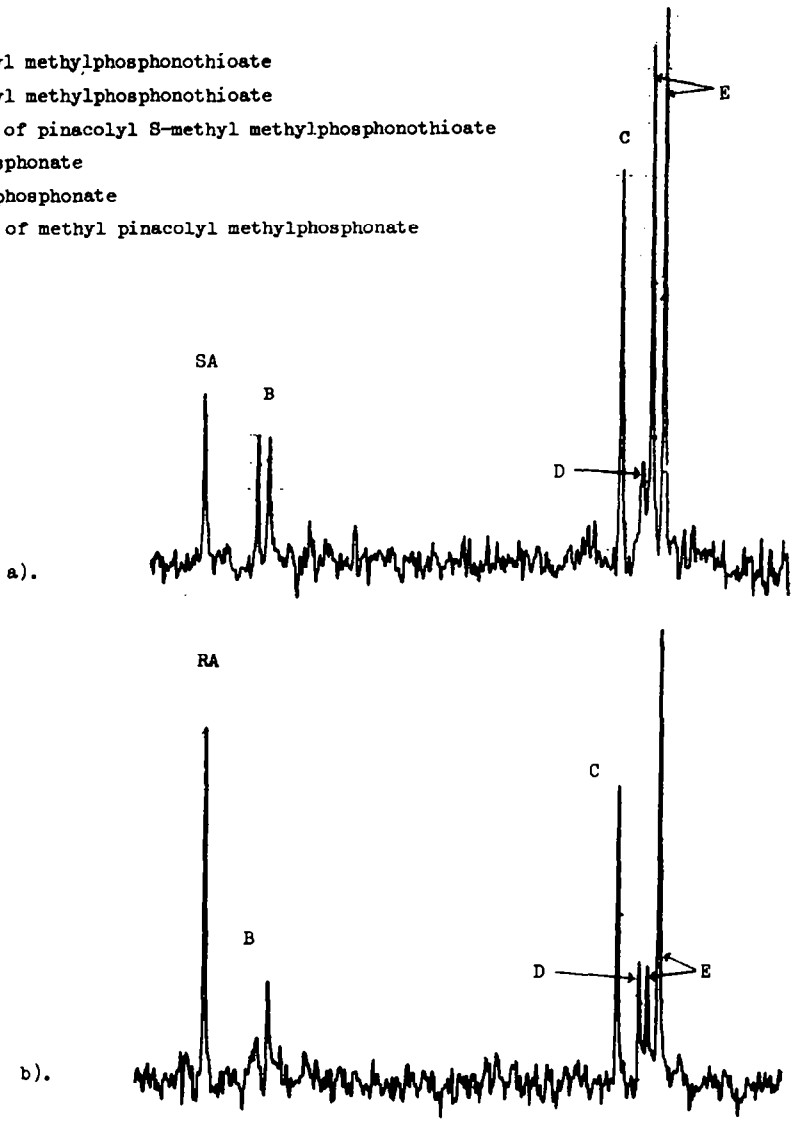
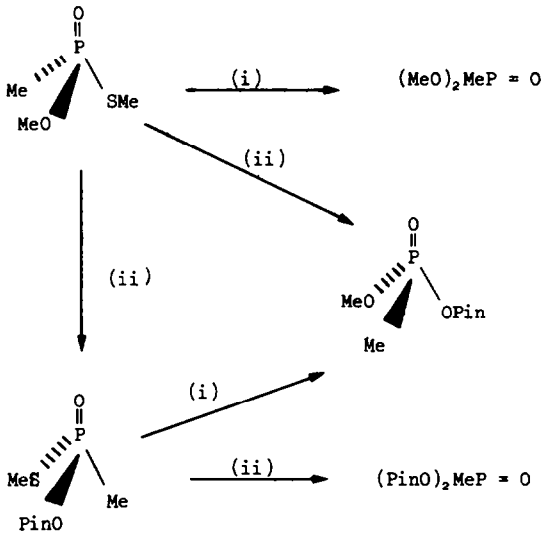


Fig 1 a) ^{31}P spectrum from S(-) methyl S-methyl methylphosphonothioate in DMF following treatment for 100 min at room temperature with the sodium salt of (-) pinacolyl alcohol.

b) corresponding spectrum from R(+)-methyl S-methyl methylphosphonothioate.

The overall pattern of reactions of S(-)-methyl S-methyl methylphosphonothioate were the same as for the R(+) isomer even although the displacements of S-methyl and O-methyl by (+)-pinacolyl alcohol were not stereoselective in this case.



Reagents: (i) sodium methoxide (ii) the sodium salt of (+)-pinacolyl alcohol.

Scheme 1

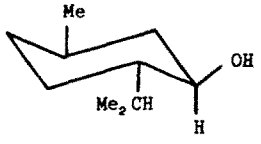
The reactions of the ethyl S-methyl methylphosphonothioate showed slight differences to the methyl analogues but only with respect to the extent of the formation of pinacolyl S-methyl methylphosphonothioate and dipinacolyl methylphosphonate. Although the n.m.r. traces showed the presence of the former (and that it is formed stereospecifically from the R-(+) precursor but nonspecifically for the S-(-) enantiomer) there was never any significant concentration present. Its intermediacy could be inferred by the formation of dimethyl methylphosphonate. Also no significant amounts of dipinacolyl methylphosphonate were observed. These differences can be accounted for by assuming small differences in the rates of the variously competing reactions for the methyl and ethyl derivatives. [Also, although the reactions and products described preponderate in the early stages there are further competing reactions which lead to various phosphorus acid derivatives which attain relatively high proportions when the reaction mixtures are stored for long periods].

Experiments with (-)-menthol - The fact that the sodium salt of S(+)-pinacolyl alcohol behaved similarly as a chiral nucleophile either in (+)-pinacolyl alcohol or in DMF as solvent provided a justification for the use of the sodium salt of (-)-menthol in DMF. The advantage of using (-)-menthol was that it has been used previously in stereochemical studies with phosphonothioates and that good stereochemical correlations have been reported.

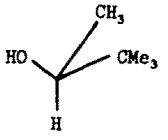
Thus when R(+) methyl S-methyl methylphosphonothioate was treated with (-)-menthol as its sodium salt in DMF the products were mainly dimethyl methylphosphonate and equal amounts of the two isomers (at phosphorus) of menthyl methyl methylphosphonate. In this case it was the S(-) methyl S-methyl methylphosphonothioate which was highly stereoselective in the reaction so that the main product in addition to dimethyl methylphosphonate was the high field menthyl methyl methylphosphonate isomer in a least four fold excess over the low field enantiomer. Except for the reversal in stereoselectivity of the methyl S-methyl methylphosphonothioate isomers, the

reactions with (-)-menthol were similar to those with (+)-pinacolyl alcohol with some formation of menthyl S-methyl methylphosphonothioate and dimethyl methylphosphonate.

When the absolute configuration of S(+)-pinacolyl alcohol and (-)-menthol (Scheme 2) are considered a possible reason for the reversal of stereoselectivity is apparent; these reagents are essentially mirror images with respect to the bulky groups.



(1R, 3R, 4S) (-)-menthol



S-(+)-pinacolyl alcohol

Scheme 2

Preparation and absolute configuration of standards

S-(+) Pinacolyl alcohol series

[S-(+) pinacolyl] methylphosphonothioic acid gave salts with (+) α-methylphenylethylamine and (-) α-methylphenylethylamine with specific rotations of +13.8° (c 1.2 in MeOH) and -4.2° (c 0.8 in MeOH) respectively. By analogy with other phosphonothioic acids [12] the least soluble salt with (+) α-methylphenylethylamine may be assigned the R configuration at phosphorus.

S-methylation of the thioacid salts gave R-(+) [S(+) pinacolyl] S-methyl methylphosphonothioate $[\alpha]_D$ + 56.7 (c 0.9 $CHCl_3$), and S(-) [S(+) pinacolyl] S-methyl methylphosphonothioate $[\alpha]_D$ -47.8 (c 0.9 $CHCl_3$). The R(+) isomer reacted cleanly with sodium methoxide in methanol to give R-(+) [S(+) pinacolyl] methyl methylphosphonate $[\alpha]_D$ + 12.8 (c 0.4 $CHCl_3$). These latter configurations were assigned on the assumption that displacement of S-alkyl occurs with inversion of configuration [1,2].

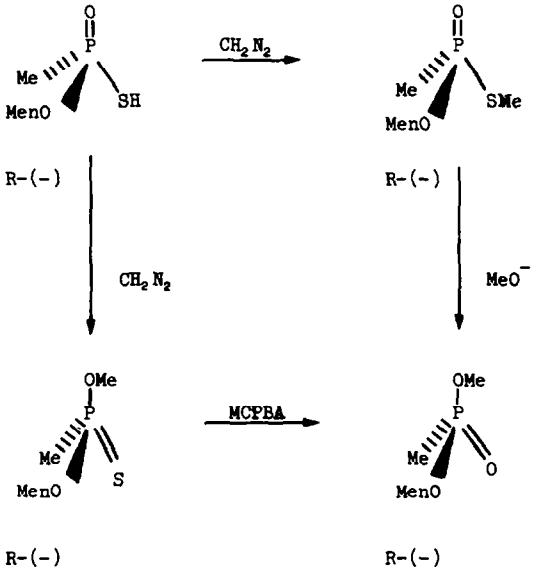
In the series of experiments with (+) pinacolyl alcohol the configurations of the variously derived phosphorus esters are based only on the apparently consistent resolution behaviour of phosphonothioic acids and on the fact that where nucleophilic displacement of S-methyl is highly stereoselective, it occurs with inversion of configuration.

As stated in the introduction, product identities and configuration were assigned by addition of standards to reaction mixtures and observation of peak enhancement.

(-) Menthol series

(-) [(-)-Menthyl] S-methyl methylphosphonothioate m.p. 45°, $[\alpha]_D$ - 37° (in benzene) is a product whose absolute configuration has been much discussed [2,13] but which must now be recognised as having the R configuration [8,12]. (The physical constants are essentially the same as those reported previously mp 45-47°, $[\alpha]_D$ - 37.1 (c 1.4 in benzene)[14] when the S configuration was assigned in error). It is formed from the least soluble salt from [(-)-menthyl] methylphosphonothioic acid and (+) α-methyl phenylethylamine, via the derived R(-) [(-)-menthyl] methylphosphonothioic acid, ($[\alpha]_D$ - 87.3° (benzene)) by S-alkylation with methyliodide.

When the R(-) thioacid was treated with diazomethane both R(-) [(-)-menthyl] S-methyl methylphosphonothioate and (-) [(-) menthyl] methyl methylphosphonothioate were isolated. Oxidation of the latter derivative with m.chloroperbenzoic acid, a reaction which proceeds with retention of configuration [15], gave (-) [(-) menthyl] methyl methylphosphonate, a product indistinguishable from that obtained by treating R(-) [(-) menthyl] S-methyl methylphosphonothioate with sodium methoxide (Scheme 3).



Scheme 3

The above series of experiments provided configurational information about the standards needed for the (-) menthol experiments, that was much more firmly based than for the (+)-pinacolyl experiments.

Stereochemistry of displacement of O-alkyl by alkoxides (but not methoxides in alkyl S-methyl methylphosphonothioates. Although it has been shown that in cyclic phosphonate esters ring opening by alkoxide takes place rapidly and with inversion of configuration [16], examples of nucleophilic displacement of O-alkyl by alkoxide, in acyclic systems are rare and

the stereochemistry of such reactions are not usually recorded.† Thus the observation* that O-alkyl is displaced in reasonable competition to S-alkyl prompted some confirmatory experiments particularly to determine the stereochemistry of the displacement.

R-(+) methyl S-methyl methylphosphonothioate (3.9:1, R:S) was treated with a solution (0.4 M) of sodium ethoxide in ethanol at room temperature until t.l.c. showed that some P-O bond cleavage had occurred, At this stage the major products, ie ethyl S-methyl methylphosphonothioate, ethyl methyl methylphosphonate and diethyl methylphosphonate were separated by chromatography over silica. The methylphosphonothioate, $[\alpha]_D$ - 45.2 ($CHCl_3$), was shown by ^1H n.m.r. in the presence of the chiral shift reagent Eu(hfc), to be a mixture with an S:R isomer ratio of between 3 and 4:1. Thus replacement of methoxide by ethoxide occurs with inversion of configuration.

Discussion

The facility of the displacements of O-methyl and O-ethyl from alkyl S-methyl methylphosphonothioate by ethoxide and pinacolyl alkoxide either in the parent alcohol or in DMF and by the anion of menthol in DMF was a consistent feature of all the reactions. Moreover, for S(+) pinacolyl alcohol and (-)-menthol the stereoselectivity of this displacement paralleled the stereoselectivity of displacement of S-methyl. That is to say for R(+) methyl (or ethyl) S-methyl methylphosphonothioate the reaction was highly stereoselective with (+)-pinacolyl alcohol but not with (-)-menthol with the reverse situation occurring for the S(+) enantiomers. It is perhaps surprising that with different leaving groups and presumably a quite different relation between the apical groups and the basal groups in the intermediate TBP inversion or mixed stereochemistry is apparently independent of whether the leaving group was O-alkyl or S-methyl. (The complexity of these reactions make interesting comparison with those reported in cyclic phosphono- and phosphonothioates [16]). Another surprising feature was the major difference in products when methoxide was the nucleophile. In this case no significant displacement of alkoxy occurred. Thus when ethyl S-methyl methylphosphonothioate was treated with sodium methoxide in methanol the main product was ethyl methyl methylphosphonate. No dimethyl methylphosphonate was detected. This result, which was repeated many times on ethyl-, pinacolyl-, and menthyl S-methyl methylphosphonothioate was inconsistent with a previous result from this laboratory[4] where treatment of methyl 6-deoxy-2,3-di-O-methyl-6-methylacetamido-α-D-glucopyranoside 4-[(R)-S-methyl methylphosphonothioate] and its S isomers resulted in liberation of methyl 6-deoxy-2,3-di-O-methyl-6-methylacetamido-α-D-glucopyranoside by P-O bond cleavage in competition with displacement of S-alkyl in proportions which depended on the configuration at phosphorus. That experiment was carried out in 1M methoxide as opposed to the 0.4 M methoxide used in the current experiments and without the use of ^{31}P n.m.r. to monitor the formation of phosphorus products. Base concentration has now been shown not to affect the situation for

*Stereochemical studies [2] on the displacement of S-methyl from menthyl S-methyl phenylphosphonothioate by methoxide do not describe any competing displacement of methanol. Kinetic studies aimed at determining the mechanism of displacement of S-methyl from alkyl S-methyl phenylphosphonothioate showed that loss of O-alkyl occurs but did not establish the stereochemistry[1].

† It has been reported [5] recently that treatment of (R)-(+) O,S-dimethyl phosphoramidothioate with sodium ethoxide results in competitive P-O and P-S bond cleavage and that both reactions occur with preponderant inversion of configuration at phosphorus.

with 1M methoxide, pinacolyl S-methyl methylphosphonothioate gave only methyl pinacolyl methylphosphonate with no evidence for methyl S-methyl methylphosphonothiate or dimethylphosphonate.

The results reported in this paper provide some support for the suggestion that the stereochemical course of the inhibition of acetylcholinesterase by some alkyl S-alkyl methylphosphonothioates may depend on the absolute configuration of the inhibitor [6] but perhaps more significantly draws attention to the fact that alkoxides with the exception of methoxide can displace other alkoxy groups as easily as S-alkyl from phosphorus.

Experimental

^{1}H-NMR spectra were recorded at 100 MHz (JEOL MH100) with deuteriochloroform as solvent and tetramethylsilane as internal standard. ^{31}P n.m.r. spectra of pure samples were measured for the same solutions (unless otherwise stated) on a JEOL FY40a instrument at 24.15 Hz and shifts are quoted in p.p.m. downfield from phosphoric acid. All phosphonothioate-alkoxide reactions were initially monitored by ^{31}P n.m.r. spectroscopy. A solution of the phosphonothioate (0.15 g) in the appropriate solvent (2 ml) contained in an n.m.r. tube was treated with an excess of a solution (0.4 M) of the alkoxide in the same solvent. Sodium alkoxide solutions were prepared by warming a mixture of the alcohol, solvent (DMF or alcohol) and the required amount of sodium hydride or by direct addition of metallic sodium to the alcohol. Column chromatography was performed over Merck Kieselgel 60, particle size 0.040–0.63 mm, under a slight positive pressure. Optical rotations were measured in chloroform (unless otherwise stated) with a 1dm path length. All solvents and reagents were dried before use and where necessary reactions were carried out under an atmosphere of dry nitrogen.

Chiral O-ethyl and O-methyl hydrogen methylphosphonothioic acids and their esters were prepared and interconverted as previously described [3,9].

S-(+)-Pinacolyl alcohol [7], $[\alpha]_D$ + 8.3° (neat), was resolved by the method of Pickard and Kenyon [11].

(-)-Menthol, $[\alpha]_D$ - 50° (*c* 10 in EtOH) was supplied by Aldrich.

[S-(+)-O-Pinacolyl] Hydrogen Methylphosphonothioic Acid and its Esters

A solution of S-(+) pinacolyl alcohol (7 g) and triethylamine (7 g) in benzene (50 ml) was added dropwise to a cooled solution of methylphosphonous dichloride (8 g) in benzene (100 ml). The mixture was stirred for 4 h then sulphur (2.5 g) was added in small portions. After storing for 48 h the mixture was filtered and the filtrate was concentrated. The residue was dissolved in a mixture of dioxan and an excess of 2 M aqueous sodium hydroxide and the solution was boiled under reflux for 8 h. The mixture was then poured into water and extracted with chloroform. The organic phase was discarded. The aqueous phase was acidified with concentrated hydrochloric acid then again extracted with chloroform. Concentration of the organic solution gave crude [S-(+)-O-pinacolyl] hydrogen methylphosphonothioic acid (7.5 g, 56%).

The crude acid was resolved using the procedure described by Boter and Platenburg [9] for other methylphosphonothioic acids, to give R-(+) [S-(+)-O-pinacolyl] methylphosphonothioic acid as its salt with (+)-phenylethylamine (5 g, 23%), $[\alpha]_D$ + 13.8° (*c* 1,2 in MeOH); δ_H 0.86 (9H,s), 1.20 (3H,d,J = 6.2 Hz), 1.40 (3H, d, J = 14.9 Hz), 1.72 (3H, d, J = 6.5 Hz), 4.10 (1H, dq, J = 11.5 and 6.2 Hz), 4.50 (1H, q, J = 6.5 Hz), δp 74.2; and S-(-) [S-(+)-O-pinacolyl] methylphosphonothioic acid as its salt with (-)-phenylethylamine (4.3 g, 19.8%), $[\alpha]_D$ - 4.2° (*c* 0.8 in MeOH); δ_H 0.88 (9H, s), 1.20 (3H, d, J = 6.4 Hz), 1.60 (3H, d, J = 14.2 Hz), 1.64 (3H, d, J = 6.7 Hz), 4.20 (1H, dq, J = 12.0 and 6.4 Hz) 4.35 (1H, q, J = 6.7 Hz), δp 72.4.

The above acid salts were alkylated with methyl iodide using conventional procedures to give respectively R-(+) [S-(+)-O-pinacolyl] S-methyl methylphosphonothioate, $[\alpha]_D$ + 56.7° (*c* 0.8); δ_H 0.92 (9H, s), 1.35 (3H, d, J = 6.2 Hz), 1.75 (3H, d, J = 15 Hz), 2.32 (3H, d, J = 12.4 Hz), 4.30 (1H dq, J = 9.7 and 6.2 Hz); δp 53.8, and S-(-) [S-(+)-O-pinacolyl] S-methyl methylphosphonothioate, $[\alpha]_D$ - 47.8° (*c* 0.9); δ_H 0.92 (9H, s), 1.30 (3H, d, J = 6.2 Hz), 1.75 (3H, d, J = 15 Hz), 2.30 (3H, d, J = 12.7 Hz), 4.36 (1H, dq, J = 10.6 and 6.2 Hz); δp 53.2.

Storage of solutions of the above methylphosphonothioates in 0.1 M sodium methoxide in methanol for 12 h, followed by conventional processing gave respectively: R-(+) methyl [S-(+)-pinacolyl] methylphosphonate $[\alpha]_D$ + 12.8° (*c* 0.4); δ_H 1.26 (3H, d, J = 6.1 Hz), 1.43 (3H, d,

J = 17 Hz), 3.66 (3H, d, J = 10.9 Hz), 4.20 (1H, m); δp 31.4 and s methyl [S-(+)-pinacolyl] methylphosphonate $[\alpha]_D \sim 0$; δ_H 1.26 (3H, d, J = 6.1 Hz), 1.43 (3H, d, J = 17 Hz), 3.68 (3H, d, J = 10.7 Hz), 4.20 (1H, m); δp 30.7.

Similar reactions but using sodium ethoxide gave R-(+) ethyl [S-(+)-pinacolyl] methylphosphonate [α] + 12.4° (c 0.4); δ_H 0.90 (9H, s), 1.25 (3H, d, J = 6.1 Hz), 1.30 (3H, t, J = 6.8 Hz), 1.44 (3H, d, J = 17 Hz), 4.12 (2H, m), 4.20 (1H, m); δp 30.4 and its S-enantiomer, δ_H indistinguishable (at 100 M Hz) from the R-enantiomer; δp 29.7.

[(-)-O-Menthyl] Hydrogen Methylphosphonothioic Acid and its Esters

A parallel procedure to that described above for the O-pinacolyl thioacid but using (-)-menthol as the alcohol gave hydrogen [(-)-O-menthyl] methylphosphonothioic acid (50%), $[\alpha]_D$ - 86.8° (c 0.6 in benzene), δp 88.0 and 86.5 (concentration dependent).

The acid was resolved using the procedure described by Boter and Platenburg [9] for other methylphosphonothioic acids, to give R-(-) [(-)-O-Menthyl] methylphosphonothiotic acid as its salt with (+)-phenylethylamine, $[\alpha]_D$ - 51° (c 1.0 in MeOH), from which the free acid was liberated using hydrochloric acid, m.p. 82°C (from light petroleum), $[\alpha]_D$ - 87.3° (c 0.5 in benzene), δ_H 0.80 (3H, d, J = 7 Hz), 0.90 (6H, d, J = 7 Hz), 1.82 (3H, d, J = 12.6 Hz), 4.35 (1H, m), δp 86.5 (concentration dependent).

Alkylation of the above acid with diazomethane using conventional procedures gave R-(-) [(-)-O-menthyl] O-methyl methylphosphonothioate (8%), $[\alpha]_D$ - 75° (c 0.2), δ_H 0.80 (3H, d, J = 7 Hz), 0.90 (6H, d, J = 7 Hz), 1.75 (3H, d, J = 15 Hz), 3.65 (3H, d, J = 13.6 Hz), 4.30 (1H, m), δp 91.8, and R-(-) [(-)-O-menthyl] S-methyl methylphosphonothioate (82%) M.P. 45°C (from di-isopropylether-benzene), $[\alpha]_D$ - 31.1° (c 0.9), δ_H 0.85 (3H, d, J = 7 Hz), 0.90 (6 H, d, J = 6.8 Hz), 1.72 (3H, d, J = 15 Hz), 2.28 (3H, d, J = 12.6 Hz), 4.35 (1H, m), δp 50.8.

Oxidation of R-(-) [(-)-O-menthyl] O-methyl methylphosphonothioate with m-chloroperbenzoic acid using conventional procedures gave R-(-) [(-)-menthyl] methyl methylphosphonate (83%), $[\alpha]_D$ - 59° (c 0.4), δ_H 0.80 (3H, d, J = 7 Hz), 0.90 (6H, d, J = 7 Hz), 1.44 (3H, d, J = 17 Hz), 3.68 (3H, d, J = 10.8 Hz), 4.20 (1H, m), δp (31.7).

Storage of a solution of R-(-) [(-)-O-menthyl] S-methyl methylphosphonothioate in 0.4 M sodium methoxide in methanol for 12 h, followed by conventional processing gave R-(-) [(-)-menthyl] methyl methylphosphonate as essentially the only product.

References

1. K.E. DEBRUIN and D.M. JOHNSON, J. Amer. Chem. Soc. 1973, 95, 7921.
2. W.B. FARNHAM, D. MISLOW, N, MANDEL and J. DONOHUE, J.C.S. Chem. Commun, 1972, 120.
3. D.B. COOPER, C.R. HALL, J.M. HARRISON and T.D. INCH, J. Chem. Soc. Perkin Trans. I, 1977, 1969.
4. T.D. INCH and G.J. LEWIS, Carbohydrate Res., 1975, 45 65.
5. C.R. HALL, T.D. INCH, G. PEACOCK, C. POTTAGE and N.E. WILLIAMS. J. Chem. Soc., Perkin Trans I, 1984, 669.
6. M.C. FRENCH, C.R. HALL, J.M. HARRISON, T.D. INCH, D.J. SELLERS, A.P. SMITH, D.G. UPSHALL and P. WATTS, Pesticide Biochem. and Physiol., 1985, in press.
7. J. JACOBUS, Z. MAYERSKI, K. MISLOW, P. VAN RAQUE SCHLEYAR, J. Amer. Chem. Soc., 1969, 91, 1998.
8. J. DONOHUE, N. MANDELL, W.B. FARNHAM, R.K. MURRAY, K. MISLOW and H.P. BENSCHOP, J. Amer. Chem. Soc. 1971, 93, 3792.
9. H.L. BOTER and D.H.J.M. PLATENBURG, Rec. Trav. Chim. Pays-Bas, 1967, 86, 399.
10. C.R. HALL and T.D. INCH, Phosphorus and Sulphur, 1979, 7, 171.
11. R.H. PICKARD and T. KENYON, J. Chem. Soc., 1914, 1115.
12. M. MIKOLAJCZYK, J. OMELANCYUK and M. PARA, Tetrahedron, 1972, 28, 3855.
13. W.B. FARHAM, R.K. MURRAY and K. MISLOW, J.C.S. Chem. Commn. 1971, 605.
14. H.P. BENSCHOP, D.H.J.M. PLATENBURG, F.H. MEPPELDER and H.L. BOTER, J.C.S. Chem. Commn., 1970, 33. H.P. BENSCHOP and D.H.J.M. PLATENBURG, J.C.S. Chem. Commn., 1970, 1098.
15. A.W. HERRIOT, J. Amer. Chem. Soc., 1971, 93, 3304.
16. D.B. COOPER, J.M. HARRISON, T.D. INCH and G.J. LEWIS, J. Chem. Soc., Perkin I, 1974, 1058.