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**LETTERS TO THE EDITOR**

# (1*R*,2*S*,5*R*)-Menthyl Phosphinate and Its Properties

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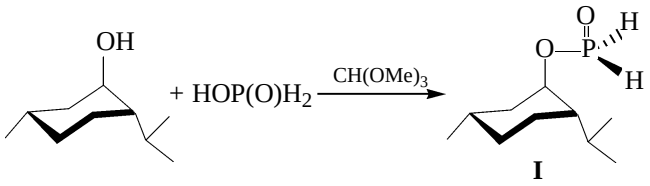
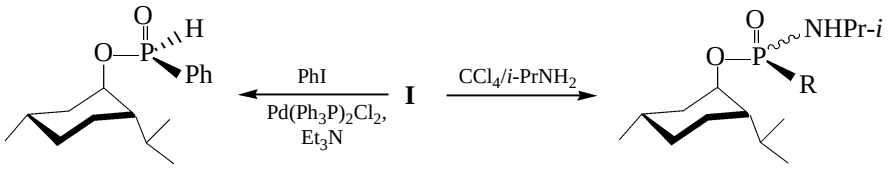
Proceeding with our research into chiral esters of phosphorous acid we synthesized (1*R*,2*S*,5*R*)-menthyl phosphinate (**I**) [1–3]. Compound **I** was prepared by the reaction of anhydrous hypophosphorous acid with (1*R*,2*S*,5*R*)-menthol in the presence of trimethyl orthoformate in THF. The reaction occurred smoothly and completely to give pure (1*R*,2*S*,5*R*)-menthyl phosphinate (**I**) in high yield.




**I**

Unlike known hypophosphites that are quite unstable compounds [4, 5], compound **I** is relatively stable and can be purified by high-vacuum distillation. Its stability is probably explained by the steric effect of the menthyl group. The structure of the product was confirmed by its $^1$H and $^{31}$P NMR spectra and chemical transformations. The $^{31}$P NMR spectrum contains a triplet at 11 ppm ($^1J_{PH}$ 567 Hz) that collapses to a singlet in the $^{31}$P–{$^1$H} spectrum. The $^1$H NMR spectrum contains a doublet of doublets at 7.16 and 7.17 ppm with the same $^1J_{PH}$ constant, corresponding to magnetically nonequivalent $PH_2$ protons. Compound **I** enters the Heck reaction with iodobenzene in the presence of a palladium complex to form in high yield diastereomerically enriched ($S_P$)-(–)-menthyl phenylphosphonite (**II**) that was purified by column chromatography on silica gel.




$S_P$-**II** **IIIa, IIIb**

R = H (**a**), NHPr-*i* (**b**).

The Todd–Atherton reaction of compound **I** with carbon tetrachloride and isopropylamine involves consecutive replacement of the hydrogen atoms at phosphorus by amino groups to produceinitially monoamide **IIIa** (detected by NMR spectroscopy) and then diamide **IIIb** (isolated as crystals). Other transformations of (1*R*,2*S*,5*R*)-menthyl phosphinate (**I**) will be reported in further publications.

**(1*R*,2*S*,5*R*)-Menthyl phosphinate (I).** Anhydrous hypophosphorus acid, 0.05 mol, in THF was treated consecutively with 0.06 mol of trimethyl orthoformate and 0.06 mol of (1*R*,2*S*,5*R*)-menthol. The mixture was kept for 3 h at 20°C, and volatile compounds were removed in vacuo. The residue was a spectroscopically pure compound **I** which can be distilled in a high vacuum if necessary. Yield ~90% (without distillation), bp 85–90°C (0.01 mm Hg). $^1$H NMR spectrum ($C_6D_6$), δ, ppm (*J*, Hz): 0.74 d [3H, $CH_3C$, $^3J_{HH}$ 8]; 0.86, d (3H, $(CH_3)_2C^a$, $^3J_{HH}$ 7); 0.87, d (3H, $(CH_3)_2C^b$, $^3J_{HH}$ 7); 0.8–2.0 m (9H, $CH_2$ + C*H*); 4.1 m (*ABX* system, 1H, C*H*OP); 7.16 d (1H, P*H*, $^1J_{HP}$ 558); 7.17 d (1H, P*H*, $^1J_{HP}$ 559). $^{31}$P NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): $\delta_P$ 10.5, d.t ($^1J_{PH}$ 557, $^3J_{HH}$ 10). Found, %: P 15.06. $C_{10}H_{21}O_2P$. Calculated, %: P 15.16.

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**(1*R*,2*S*,5*R*)-Menthyl (*S*)-phenylphosphonate (II).** Bis(triphenylphosphine)palladium dichloride, 0.05 g, was added to a solution of 0.003 mol of menthyl phosphinate **I**, 0.003 mol of iodobenzene, and 0.004 mol of triethylamine in 4 ml of acetonitrile. The mixture was heated for 2–3 h at the bath temperature 100°C. The precipitate that formed was filtered off, the solvent was evaporated, and the residue was subjected to column chromatography on silica gel, eluent hexane–ethyl acetate, 3 : 1. Compound **II** was purified additionally by low-temperature crystallization from hexane. $R_f$ 3.2, Yield 60%, $[\alpha]_D^{20}$ –21 (*c* 4, benzene) [6]. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.60 d [3H, $(CH_3)_2C^a$, $^3J_{HH}$ 8]; 0.61 d [3H, $(CH_3)_2C^b$, $^3J_{HH}$ 8]; 0.8 d [3H, $CH_3$, $^3J_{HH}$ 7); 1.1–2.1 m (9H, C*H* + $CH_2$); 3.5 m (1H, C*H*OP); 7.6 d (1H, P*H*, $^1J_{HP}$ 556); 7.4 m; 7.6 m (5H, $C_6H_5$). $^{31}$P NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): $\delta_P$ 20.5 d.d, $^1J_{HP}$ 557, $^3J_{HH}$ 13.0. Found, %: P 11.16. $C_{16}H_{25}O_2P$. Calculated, %: P 11.05.

**(1*R*,2*S*,5*R*)-Menthyl *N*,*N*'-diisopropylphosphorodiamidate (IIIb).** Carbon tetrachloride, 0.0075 mol, and 0.015 mol of isopropylamine were added to a cooled and stirred solution of 0.01 mol menthyl phosphinate **I** in ether. The $^{31}$P NMR spectrum of the reaction mixture was showed two doublets of doublets corresponding to diastereomeric menthyl isopropylphosphonamidates **IIIa** in a 2 : 1 ratio, $\delta_P$, ppm (*J*, Hz): 11.2 d.d ($^1J_{HP}$ 610, $^3J_{HH}$ 13.5), 8.9 d.d ($^1J_{HP}$ 615, $^3J_{HH}$ 13.0). Additional 0.01 mol of carbon tetrachloride and 0.02 mol of isopropylamine were added to the reaction mixture, isopropylamine hydrochloride was then separated, the solvent was evaporated, and the residue was recrystallized from hexane to obtain compound **IIIb**, yield 70%, mp 128–129°C. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.80 d [3H, $(CH_3C$, $^3J_{HH}$ 7]; 0.87 d [3H, $(CH_3)_2C^a$, $^3J_{HH}$ 7]; 0.89 d [3H, $(CH_3)_2C^b$, $^3J_{HH}$ 7]; 1.0–2.1 m (9H, C*H* + $CH_2$); 2.0 m (2H, N*H*); 3.35 m (2H, C*H*N); 4.15 m (1H, C*H*OP). $^{31}$P NMR spectrum ($CDCl_3$), $\delta_P$ 11.9 ppm. Found, %: N 8.95; P 9.99. $C_{16}H_{35}N_2O_2P$. Calculated, %: N 8.80; P 9.73.

The NMR spectra were measured on a Varian-300 instrument, internal references TMS (1H) and 85% $H_3PO_4$ in $D_2O$ ($^{31}$P).

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