Journal of

The Chemical Society,

Chemical Communications

NUMBER 2/1977 19 JANUARY

Route to Chiral Imidate Esters of Phosphorus: Synthesis and Hydrolysis of (*S*)-(+) *O*-Ethyl *N*-t-Butyl Methylphenylphosphinimidate

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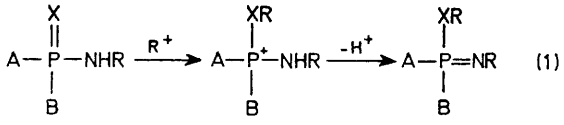
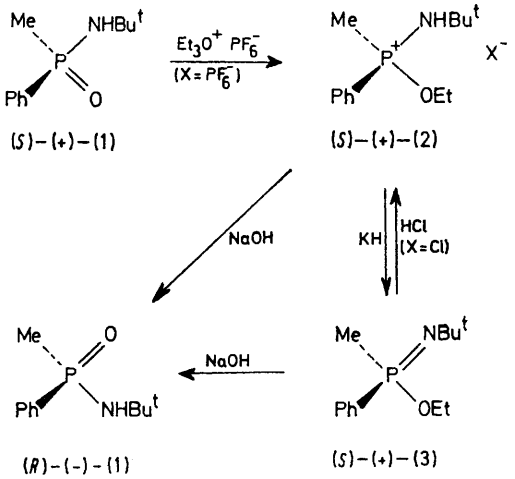
Summary A new synthetic approach to imidate esters of phosphorus was used to prepare optically active (*S*)-(+) *O*-ethyl *N*-t-butyl methylphenylphosphinimidate (**3**) from (*S*)-(+) t-butyl methylphenylphosphinamidate (**1**).

No known synthetic route has yet been recognized to be applicable for generating optically active imidate esters of phosphorus with chirality only at the phosphorus centre.† We report the first synthesis of an optically active phosphinimidate, *O*-ethyl *N*-t-butyl methylphenylphosphinimidate (**3**), by a procedure which should be of quite general utility. The method is shown in equation (1) and requires the readily accessible amidates as precursors.



(1)

(*S*) t-Butyl methylphenylphosphinamidate (**1**), $[\alpha]_D$ + 67° (*c* 2·21, MeOH) was prepared from $(S)_P$ menthyl methylphenylphosphinate[1] ($[\alpha]_D$ −94°, *c* 2·56, benzene) with lithium t-butylamide in tetrahydrofuran.[2] Ethylation on the phosphoryl oxygen of (**1**) with triethyloxonium hexafluorophosphate[3] gave the (*S*) phosphonium hexafluorophosphate (**2**), $[\alpha]_D$ + 1·2° (*c* 1·3, CH_2Cl_2). Under a rigorously dry atmosphere, potassium hydride, previously washed with dry hexanes to remove the mineral oil, was added to an ethereal solution of (**2**) to give, after filtration, concentration, and Kugelrohr distillation (54 °C, 0·03 mm-Hg), the desired (*S*) *O*-ethyl *N*-t-butyl methylphenylphosphinimidate (**3**) 70% yield, $[\alpha]_D$ + 54·9° (*c* 2·68, benzene). This imidate (**3**) was most readily identified by the characteristic 1315 cm^{-1} i.r. absorption for the P=N group. ^1H N.m.r. analysis ($CDCl_3$; Me_4Si reference) showed the presence of a $POCH_2Me$ group [δ 1·33 (t, J_{HCCH} 7 Hz, Me) and 4·02 (two apparent quintets, J_{HCCH} 7, J_{HCOP} 7 Hz, CH_2)] and a splitting of the t-butyl peak [δ 1·28 (d, J_{HCCNP} 1·4 Hz)] which is absent in the amidate



Scheme

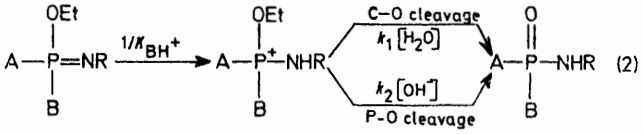
† Optically active phosphine imines with chirality at phosphorus have been prepared (L. Horner and H. Winkler, *Tetrahedron Letters*, 1964, 175, 455; C. R. Hall and D. J. H. Smith, *ibid.*, 1974, 1693).

precursor (**1**) (δ 1·29). The *P*Me and *P*Ph regions have similar chemical shifts and coupling constants to those for (**1**) (PMe δ 1·63, d, J_{HCP} 14 Hz).

When the imidate (**3**) was submitted to alkaline hydrolysis with 0·05 M NaOH in 50% aqueous acetonitrile, the amidate (**1**) ($[\alpha]_D$ −67°, *c* 2·06, MeOH) could be recovered within 10 min at 25 °C in near quantitative yield. As shown in the Scheme, this hydrolysis proceeds with complete inversion of configuration at phosphorus, ruling out any C–O bond cleavage. A similar result was observed in the alkaline hydrolysis of the phosphonium salt (**2**), giving (**1**) with inversion ($[\alpha]_D$ −63°, *c* 1·95, MeOH). At present, we have not determined whether hydrolysis of the imidate (**3**) proceeds through the protonated species (phosphonium salt **2**) or directly by a base-catalysed route to the amidate (**1**).‡

Under acidic conditions (0·05 M HCl, 50% aqueous acetonitrile), (**3**) is immediately converted into the phosphonium salt (**2**; X = Cl), which is totally resistant to further hydrolysis during 60 h at 25 °C. It can be extracted from solution and is identical (^{1}H n.m.r. spectroscopy) with (**2**) prepared directly from (**1**; X = PF_6^-). Also, an authentic sample of (**2**; X = PF_6^-), prepared from (**1**), when placed in the above acidic solution, was similarly inert and could be recovered from the solution.

The limiting values for the observed rate constants for acid ($k_{H^+} < 10^{-6}$ s^{-1}) and base ($k_{OH^-} > 10^{-3}$ s^{-1}) hydrolysis of (**3**) at 25 °C are markedly different from the values obtained by other workers[4] for the hydrolysis of triethyl *N*-phenylphosphorimidate [(**4**), $(EtO)_3P{=}NPh$] extrapolated to the same acid or base concentrations in the same solvent at 30 °C (k_{H^+} 3·3 × 10^{-4} s^{-1}; k_{OH^-} 2·8 × 10^{-6} s^{-1}). If the general mechanism shown in equation (2) holds for both compounds (**3**) and (**4**), the acceleration (> 10^3) in the rate of (**3**) over (**4**) under basic conditions is consistent with (**3**)



(2)

having a larger pK_{BH^+} owing to the t-butyl substituent on nitrogen.‡ Under acid conditions, where presumably both (**3**) and (**4**) are in the protonated forms (phosphonium salt), attack by water on carbon with C–O bond cleavage is 10^3 times slower for protonated (**3**) than protonated (**4**). This rate ratio was independently verified by synthesis of the phosphonium salts (X = PF_6^-) from the corresponding amidates and submitting them to the acidic conditions. Thus, the reaction is remarkably sensitive to the leaving group, *i.e.*, whether an *N*-t-butyl-phosphinamidate (**1**) as opposed to an *N*-phenyl-phosphoramidate is formed.§

We thank the National Institutes of Health and the National Cancer Society for support of this work.

(*Received*, 20*th September* 1976; *Com.* 1074.)

‡ We estimate the pK_{BH^+} of protonated (**3**) (*i.e.*, **2**) to be *ca.* 10 ± 5 (ref. **4** and also M. I. Kabachnik, *Phosphorus*, 1971, **1**, 117).

§ Supporting this is our observation that phosphinamidates are alkylated on oxygen more readily than phosphoramidates by $Et_3O^+PF_6^-$.

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