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A simple protocol for the synthesis of chiral bidentate imidodiphosphoric tetramide ligands: application in the metal-free asymmetric allylation of aldehydes

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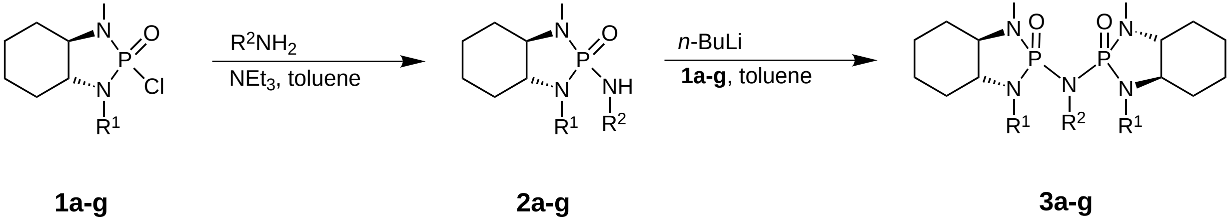
Abstract—The reaction of a series of chiral phosphorus triamides with BuLi and subsequent addition of a phosphoroxychloride diamide afforded the corresponding imidodiphosphoric tetramides in high yield. The use of enantiomerically pure diamides allowed access to bidentate imidodiphosphoric tetramides without loss of optical purity. These bidentate ligands have been used successfully to catalyze the addition of allyltrichlorosilane to aldehydes in an enantioselective fashion up to 60% ee. © 2001 Elsevier Science Ltd. All rights reserved.

Phosphoric triamides have found widespread use in organic chemistry.[1] The strong donor properties and Lewis basicity make them excellent ligands for small and hard metal ions and thus modulate the reactivity of metal centers. Recently, chiral representatives of phosphoric triamides have been considered as strong Lewis bases in asymmetric catalysis in the absence of metals.[2,3] To obtain a rigid chiral environment around a coordinated Lewis acid, chiral bidentate phosphoric triamide-derived ligands may be employed. However, such ligands are hitherto still unknown. In our contribution we would like to present an efficient synthetic approach to that novel class of chiral ligands. It turned out, that these ligands act as highly enantioselective chiral catalysts for the asymmetric allylation of aldehydes in the reaction with trichloroallylsilane.

The reaction of the chiral bicyclic phosphoric diamides **1a**–**g** with primary amines in toluene and in presence of triethylamine proceeds smoothly and gives the phosphoric triamides **2a**–**g** in high yields (see Table 1).[4,5] In a subsequent step, deprotonation of the amides is achieved with *n*-BuLi followed by addition of a second equivalent of **1a**–**g** leading to the final imidophosphoric tetramides **3a**–**g** in high yields.[6] Chiral primary amines as bridging units allowed the synthesis of diastereomeric imido phosphorus tetramides **3d**,**e** in excellent yields. As a suitable test reaction for asymmetric, Lewis-base-promoted catalysis we have chosen the allylation of aldehydes with trichlorosilane (Table 2). The initial observation that Lewis bases are able to accelerate this type of C–C bond-forming reaction, originally reported by Sakurai, stimulated in 1994 Denmark and later Iseki to introduce chiral phosphoric triamides as Lewis-base catalysts for this reaction.[7–13] We reasoned that a bidentate ligand would be better in stabilizing the putative hexa-coordinate siliconate spe-



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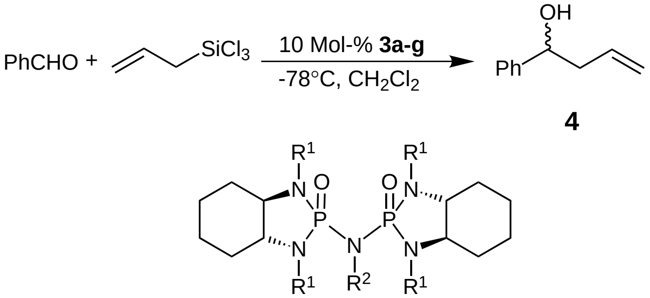

3a-g

cies compared to a monodentate ligand thus inducing higher enantioselectivities.†

Table 1. Synthesis of bidentate imidophosphoric tetramides **3a**–**g**

Catalyst	R^1	R^2	Yield (%)
3a	Me	Ph	83
3b	Me	*p*-CF$_3$-C$_6$H$_4$	87
3c	Me	*p*-MeO-C$_6$H$_4$	76
3d	Me	(*R*)-PhEt	68
3e	Me	(*S*)-PhEt	64
3f	CH$_2$Ph	Ph	79
3g	$(\mathrm{CH_2})_2{}^t\mathrm{Bu}$	Ph	85

Table 2. Allylation of benzaldehyde in presence of **3a**–**g**

Catalyst	R^3	Yield (%)	ee (%)[a]
3a	Ph	63	24
3b	Ph	65	27
3c	Ph	88	18
3d	Ph	15	19
3e	Ph	31	60
3f	Ph	67	49
3g	Ph	65	32

[a] Determined by HPLC (OD-H Daicel).

Firstly, catalyst **3a** led to a high yield but only a low ee of 24% in the product alcohol **4**. The introduction of electron-withdrawing substituents in the *para*-position of the aromatic bridging unit in **3b** reduced the catalytic activity and only moderate yields were accessible (25%) accompanied by a ee of 27%. Electron-donating substituents in this position had a tremendous effect on the rate and the yield of the reaction, almost after 45 min the reaction was complete and high yields of **4** were generated. Again the enantioselectivity had not changed. The introduction of chiral-bridging amines in the diastereomeric catalysts **3d**,**e** gave raise to a high ee with **3e** (60% ee, 31% yield, matched case) and to a low ee with **3d** (19% ee, 15% yield, mismatched case), but in general moderate yields. The replacement of the *N*-methyl groups in the five-membered heterocycle by more bulky benzyl groups in **3f** led to a good ee of 49% and high yield (67%), in contrast to the introduction of $(\mathrm{CH_2})_2{}^t\mathrm{Bu}$ groups, which led only to 32% ee (65% yield).

In summary we have shown the bidentate imidophosphoric triamides are easily accessible in a few steps. These compounds act as enantioselective catalysts in the allylation of benzaldehydes with allyltrichlorosilane. Further studies focus on the use of Lewis-base catalysts in metal-free epoxide openings.[14]

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† Typical procedure: To a solution of 260 mg (0.62 mmol) (S,S)-**2g** in 20 ml toluene, 0.25 ml (0.68 mmol) of *n*-BuLi (2.8 M in *n*-hexane) was added at −78°C. After 1 h a solution of 224 mg (0.62 mmol) **1g** in 1 ml toluene was added dropwise to the reaction mixture. The reaction mixture was refluxed for 12 h. The solvent was removed in vacuo and the resulting brown oil was purified by columm chromatography (hexane/ethyl acetate = 1:1), which afforded **3g** as a colorless solid (390 mg, 85%). Experimental data for **3g**: $R_f = 0.7$ (hexane/ethyl acetate = 1:1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.82 (s, 36H), 1.15–2.01 (m, 24H), 2.58–2.69 (bm, 2H), 2.71–3.15 (m, 8H), 3.51–3.64 (m, 2H), 6.62 (m, 2H), 6.69 (m, 1H), 7.05 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 23.95, 24.34, 24.81, 28.16, 28.56, 28.94, 29.21, 29.33, 29.39, 29.67, 29.75, 29.92, 30.08, 30.16, 38.32, 38.69, 39.20, 39.42, 39.91, 40.72, 41.82, 42.21, 43.15, 60.74, 61.43, 61.94, 62.03, 62.14, 62.23, 126.67, 128.09, 131.32, 140.14. ^{31}P NMR (202 MHz, CDCl$_3$, OP(OPh)$_3$ as external standard δ −18): δ 18.37, 21.30. MS (EI, 70 eV) m/z (%) = 746 [M]$^+$(15), 671 (23), 420 (58). IR (KBr): 2934, 2863, 2812, 1212, 1004 cm^{-1}. Typical allylation procedure: To a solution of 200 mg (1.88 mmol) benzaldehyde and 150 mg (0.19 mmol) **3g** in 5 ml dry CH$_2$Cl$_2$, 0.27 ml (1.88 mmol) of trichloroallylsilane was added at −78°C. After 4 h, 2 ml methanol were added dropwise to the reaction mixture, the stirring was continued for 30 min at −78°C and the solution was then treated with saturated NaHCO$_3$ solution followed by extraction with ethyl acetate. The organic layer was dried over Na$_2$SO$_4$ and the solvent was removed in vacuo. The resulting yellow oil was purified by columm chromatography (hexane/ethyl acetate = 10:1), which afforded **4a** as a colorless oil (32% ee, 180 mg, 65%). Experimental data for **4a**: $R_f = 0.1$ (hexane/ethyl acetate = 10:1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 2.07 (bs, 1H), 2.4–2.45 (m, 2H), 4.63–4.65 (m, 1H), 5.04–5.10 (m, 2H), 5.68–5.75 (m, 1H), 7.16–7.28 (m, 5H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 43.77, 73.24, 118.35, 125.76, 127.49, 128.36, 134.41, 143.81. MS (FAB) m/z (%) = 148 [M]$^+$ (26), 123 (47), 109 (38). Anal. calcd for C$_{10}$H$_{12}$O: C, 81.04; H, 8.16. Found: C, 80.63; H, 8.50.

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