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An Improved Preparation of O-(Diphenylphosphinyl)hydroxylamine

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An Improved Preparation of *O*-(Diphenylphosphinyl)hydroxylamine

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O-(Diphenylphosphinyl)hydroxylamine (DPPH) is a versatile electrophilic amination reagent that has been used widely for the amination of stable carbanions, Grignard reagents and π -electron-rich nitrogen heterocycles.^{1–4} More recently, Armstrong *et al.* have used DPPH for the aziridination of enones.⁵ Compared to other hydroxylamine derivatives that typically are stored as hydrochloride salts, this activated phosphinyl reagent exhibits good stability and can be stored indefinitely at 0°C.

DPPH is prepared in a single step from hydroxylamine hydrochloride and diphenylphosphinic chloride (1).⁶ However, the general and most used procedure, developed by Colvin *et al.*,¹ is not reliable. Yields ranging from 42% to a maximum of 70% have been reported using this method.^{7,8} In our hands, we found Colvin's method to be sensitive to reaction scale, with multigram attempts generally delivering DPPH in *ca.* 30–60% yield. Our interest in aminooxy chemistry⁹ led us to develop a reproducible, higher yield synthesis of DPPH. We report herein a convenient procedure for the preparation of DPPH on multigram scale.

Adaptation of Schotten-Baumann conditions¹⁰ using a two-phase solvent system helped minimize hydrolysis of starting chloride **1** prior to its reaction with hydroxylamine and afforded DPPH in 78% yield on a 10-gram scale. The yield of DPPH formed using these conditions did not vary significantly when the reaction scale was decreased (*e. g.*, 4-gram scale gave an 84% yield of DPPH). Product purity, generally compromised by the presence of Ph₂P(O)OH prior to base treatment, was readily assessed using ³¹P NMR (CDCl₃): DPPH, δ 37.5; Ph₂P(O)OH δ 28.3.

Experimental Section

To a stirred solution (mechanical stirring) of hydroxylamine hydrochloride (6.46 g, 93.0 mmol) in water (20 mL) at -10° C was added a solution of sodium hydroxide (3.55 g,

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Figure Conditions: *i*. HONH₂·HCl (2.2 equiv.), NaOH (2.1 equiv.), 4.5:1 Et₂O:H₂O, -15° to -0° C, 25 min; *ii*. 0.25 M NaOH, 0° C, 30 min.

88.7 mmol) in water (20 mL). Diethyl ether (180 mL) was then added and the biphasic mixture was further cooled using an ice-methanol bath (*ca.* -15° C). Diphenylphosphinic chloride (10.0 g, 42.3 mmol) was added rapidly via syringe, and the reaction mixture was stirred vigorously for 10 min, and then warmed to 0°C and stirred an additional 15 min. The resultant white slurry was filtered and the retentate was washed successively with cold water (60 mL) and Et₂O (70 mL). The resultant amorphous paste was dried under vacuum to afford a white powder that then was treated with aq. NaOH (0.25 M, 120 mL) at 0°C for 30 min. The slurry was filtered and the resultant amorphous solid was washed with cold water (40 mL), and was dried under vacuum 10 h to afford the title compound (7.68 g, 78%) with >97% purity by ³¹P nmr. Recrystallization of an analytical sample from methanol delivered DPPH in crystalline form, mp. 140–141°C, lit.^{6,7} (uncrystallized sample) 130°C (dec); all spectral data were in agreement with published values: ¹H NMR (400 MHz, CDCl₃): δ 7.87–7.82 (4H, m), 7.57–7.53 (2H, m), 7.49–7.47 (4H, m), 5.84 (2H, br) ppm; ³¹P NMR (162 MHz, CDCl₃): δ 37.5 ppm.

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