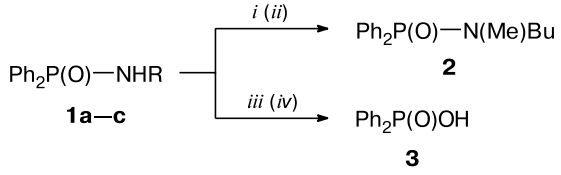
The P—N bond cleavage during the phase transfer alkylation of *N*-alkyldiphenylphosphinic amides

*A. V. Kharlamov, A. G. Vendilo, and N. A. Bondarenko**

State Research Institute of Chemical Reagents and High Purity Substances,
3 Bogorodskii val, 107076 Moscow, Russian Federation.
Fax: +7 (495) 963 7071. E-mail: bond039@mail.ru

Phase transfer NH-alkylation of *N*-alkyldiphenylphosphinic amides **1** is successful in the presence of an aqueous 50% [1] or solid[2] alkali and a phase transfer catalyst. It is worth noting that the reaction can proceed in the absence of a phase transfer catalyst, as demonstrated earlier[3] for alkylation of P(O)H acids. We synthesized the known[4] dialkylamide **2** in high yield from *N*-methylamide **1a** in benzene without phase transfer catalyst, using aqueous 50% alkali or the anhydrous heterogeneous system $NaOH—K_2CO_3/CH_2Cl_2$ (Scheme 1). However, attempted alkylation of amide **1a** with methyloxirane in aqueous alkali (50% $NaOH—CH_2Cl_2$) failed: we recovered the starting reagent only. With systems of stronger basicity, reactions of amide **1a** with ethylene chlorohydrin ($NaOH—K_2CO_3/C_6H_6$) and methyloxirane (50% NaOH/DMSO) did not yield the expected *N*-(2-hydroxyalkyl) derivatives; instead, we obtained diphenylphosphinic acid* (**3**) as a major reaction product (78—90%) arising from cleavage of the P—N bond. Attempted alkylation of *N*-(2-hydroxyethyl)diphenylphosphinic amide (**1b**) with methyl iodide ($NaOH—K_2CO_3$/DMSO, 35 °C, 5 h) also gave acid **3** in 76% yield.

Scheme 1



1: R = Me (**a**), CH_2CH_2OH (**b**), $C_{12}H_{25}$ (**c**)

i. $NaOH—K_2CO_3/CH_2Cl_2$/BuBr;
ii. 50% NaOH/C_6H_6/BuBr;
iii. $NaOH—K_2CO_3/C_6H_6/ClCH_2CH_2OH$;
iv. 50% NaOH/DMSO/methyloxirane

* Under alkaline conditions, the reaction yields the corresponding phosphinate $Ph_2P(O)ONa$,[5] which can be converted into acid **3** by standard aqueous workup followed by acidification.

The P—N bond in diphenylphosphinic amides is known to be resistant[5] to the nucleophilic attack, which allows their reactions in basic media.[6] Indeed, heating of amide **1c** with aqueous 50% alkali in toluene (100 °C, 8 h) and heating of amide **1a** in a superbasic medium (NaOH or KOH in DMSO, 40 °C, 3 h) did not result in cleavage of the P—N bond, and we recovered the starting amides. Under analogous conditions ($NaOH—K_2CO_3$/DMSO, 35 °C, 3 h), amide **1b** did quantitatively yield acid **3**. The P—N bond cleavage in the reactions studied can be associated with the presence of the *N*-(2-hydroxyalkyl) fragment in either the intermediate or starting amide. Apparently, the formation of the anion N—C—C—O^- under basic conditions is accompanied by its intramolecular attack on the P atom. This causes cleavage of the P—N bond and gives rise to the corresponding diphenylphosphinate with a ester bond readily cleavable in this medium.

^1H and ^{31}P NMR spectra were recorded on a Bruker Avance 300 spectrometer (300.13 and 121.495 MHz, respectively) in $CDCl_3$ with reference to Me_4Si and 85% H_3PO_4.

***N*-Butyl-*N*-methyldiphenylphosphinic amide (2).** A powdered mixture of NaOH (27.7 mmol) and anhydrous K_2CO_3 (27.7 mmol) was added at 20 °C to a stirred solution of *N*-methyldiphenylphosphinic amide[5] (**1a**) (13.8 mmol) in CH_2Cl_2 (10 mL). Then BuBr (17.3 mmol) was added dropwise. The reaction mixture was heated at 45—50 °C for 12 h and diluted with water (10 mL). The organic layer was separated, washed with water (2×5 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on silica gel (Aldrich, 130—270 mesh, 60 Å) with $CHCl_3$—MeOH (20 : 1) as an eluent. The yield of amide **2** was 3.7 g (94%). With aqueous 50% NaOH (C_6H_6, 65—70 °C, 12 h), the yield of amide **2** was 91%. ^1H NMR, δ: 0.79 (t, 3 H, Me); 1.12—1.28 (m, 2 H, $C\underline{H}_2Me$); 1.47—1.60 (m, 2 H, $C\underline{H}_2CH_2Me$); 2.63 (d, 3 H, NMe, $J_{H,P}$ = 11.1 Hz); 2.89 (q, 2 H, NCH_2, $^3J_{H,H}$ = 8.5 Hz, $^3J_{H,P}$ = 7.0 Hz); 7.35—7.54 (m, 6 H, Ph); 7.74—7.92 (m, 4 H, Ph). ^{31}P NMR, δ: 31.4.

The reaction of amide **1a** (9.1 mmol) with ethylene chlorohydrin (13.6 mmol) was carried out analogously in the presence of a mixture of NaOH (18.2 mmol) and anhydrous K_2CO_3 (18.2 mmol) (benzene, 75—80 °C, 10 h). The starting amide **1a** (0.4 g, 17%) was recovered. ^1H NMR, δ: 2.73, 2.75 (both d,

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3 H each, NMe, $^3J_{H,P}$ = 12.3 Hz); 2.80—2.89 (m, 1 H, NH); 7.47—7.60 (m, 6 H, Ph); 7.91—8.01 (m, 4 H, Ph). ^{31}P NMR, δ: 25.4. Acidification of the aqueous layer gave acid **3** (1.6 g, 78%), m.p. 193—195 °C (*cf.* Ref. 7: m.p. 194—196 °C).

Reaction of amide 1a with methyloxirane. Analogously, stirring of a mixture of amide **1a**, methyloxirane, and aqueous 50% KOH in the ratio 1 : 2 : 1 in DMSO at 35—40 °C for 3 h gave acid **3** in 90% yield.

References

1. A. Zwierzak and I. Podstawczynska, *Angew. Chem., Int. Ed.*, 1977, **16**, 702.
2. E. Slusarska and A. Zwierzak, *Synthesis,* 1980, 717.
3. E. N. Tsvetkov and A. V. Kharitonov, *Zh. Obshch. Khim.*, 1985, **55**, 2481 [*J. Gen. Chem. USSR*, 1985, **55** (Engl. Transl.)]; N. A. Bondarenko, M. V. Rudomino, and E. N. Tsvetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 1196 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 1076 (Engl. Transl.)].
4. N. L. Smith and G. H. Sisler, *J. Org. Chem.*, 1961, **26**, 5145.
5. T. Koizumi and P. Haake, *J. Am. Chem. Soc.*, 1973, **95**, 8073.
6. M. I. Kabachnik and T. A. Mastryukova, *Mezhfaznyi kataliz v fosfororganicheskoi khimii* [*Phase Transfer Catalysis in Organophosphorus Chemistry*], URSS, Moscow, 2002, 204 pp. (in Russian).
7. E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Zh. Obshch. Khim.*, 1985, **55**, 11 [*J. Gen. Chem. USSR*, 1985, **55** (Engl. Transl.)]; E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Synthesis*, 1986, 198.

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