Russian Journal of Organic Chemistry, Vol. 38, No. 4, 2002, pp. 484–486. Translated from Zhurnal Organicheskoi Khimii, Vol. 38, No. 4, 2002, pp. 508–510.
Original Russian Text Copyright © 2002 by Kabachnik, Ternovskaya, Zobnina, Beletskaya.

Synthesis of α-Aminophosphonates under Conditions of Phase-transfer Catalysis

M. M. Kabachnik, T. N. Ternovskaya, E. V. Zobnina, and I. P. Beletskaya

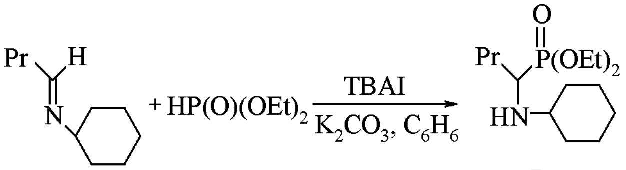
Lomonosov Moscow State University, Moscow, 119899 Russia

Received August 17, 2001

Abstract—An easy preparative synthesis of α-aminophosphonates by reaction of azomethines with diethyl phosphite under conditions of phase-transfer catalysis was developed.

Among various organophosphorus compounds prepared with the use of phase-transfer catalysis (PTC), the most numerous are phosphonates and α-hydroxyphosphonates [1–3]. Yet the α-aminophosphonates have not been synthesized under PTC conditions.

We for the first time carried out a synthesis of α-aminophosphonates under PTS conditions. The reaction conditions were developed using as an example reaction between O,O-diethyl phosphite and *N*-cyclohexylbutyralimine.



Ia

Table 1. Conditions of reaction between O,O-diethyl phosphite and *N*-cyclohexylbutyralimine in benzene (phase-transfer catalyst TBAI, 5 mol%)

Base	Base:diethyl phosphite ratio	Temperature, °C	Time, h	Yield after separation, %
K_2CO_3	1 : 1	20	8	61
K_2CO_3/$NaHCO_3$	2 : 1	20	8	58
Cs_2CO_3	1 : 1	20	6	64
KF^a	1 : 1	20	8	<10
K_2CO_3	2 : 1	20	6	64
K_2CO_3	2 : 1	40–45	5	80
K_2CO_3/Et_3N	2 : 1	40–45	6	70
$K_2CO_3{}^b$	2 : 1	40–45	8	72

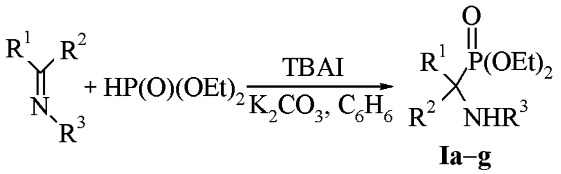
[a] Reaction was performed in THF. [b] With no catalyst.

The reaction was carried out in benzene or THF at the reagents ratio 1 : 1 in the presence of tetrabutylammonium iodide (TBAI, 5 mol%) as a phase-transfer catalyst. As bases were tested K_2CO_3, Cs_2CO_3, and KF. The reaction progress was monitored by IR and ^{31}P NMR spectroscopy. The conditions of the reaction under study (time, temperature, amount of the base used) are listed in Table 1. There are also given the yields of separated α-aminophosphonate **Ia**.

As seen from Table 1, the optimum conditions of the reaction under study require the use of double excess of K_2CO_3, 5.5 mol% of TBAI, heating to 40–45°C for 5 h.

Under the PTC conditions the reaction readily occurs both at slight heating (40–45°C) and at room temperature; the latter is especially important for the synthesis of α-aminophosphonates of the natural structure.

Under the conditions developed we prepared a number of α-aminophosphonates **Ia–g** in 74–80% yield.



Ia–g

I, R^1 = H, R^2 = Pr, R^3 = cyclo-C_6H_{11} (**a**); R^1 = H, R^2 = Pr, R^3 = *t*-Bu (**b**); R^1 = H, R^2 = Ph, R^3 = cyclo-C_6H_{11} (**c**); R^1 = H, R^2 = Ph, R^3 = Ph (**d**); R^1 = H, R^2 = 2-Fu, R^3 = *t*-Bu (**e**); R^1 = H, R^2 = 3-Py, R^3 = Ph (**f**); R^1 = Me, R^2 = Et, R^3 = cyclo-C_6H_{11} (**g**).

Physico-chemical constants, yields, ^{31}P and ^1H NMR spectral data, and elemental analyses of α-aminophosphonates **Ia–g** are given in Tables 2, 3.

1070-4280/01/3804-484$27.00 © 2002 MAIK “Nauka/Interperiodica”

Table 2. Yield, boiling and melting points, and some spectral data of compounds **Ia**–**g**

Compd. no.	Yield, %	bp, °C (*p*, mm Hg), mp, °C	^{31}P NMR spectrum, δ, ppm	^1H NMR spectrum ($CDCl_3$), δ, ppm
Ia	80	108–110 (10)	29.05	0.98 s (3H, $C\underline{H}_3CH_2CH_2$), 1.1 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.24 t (6H, $C\underline{H}_3CH_2O$), 1.42 m (2H, $CH_3C\underline{H}_2CH_2$), 1.78 m (2H, $CH_3CH_2C\underline{H}_2$), 2.82 m (1H, $C\underline{H}P$, *J* 17 Hz), 4.10 q (4H, $CH_3C\underline{H}_2O$)
Ib	77	70 (15)	29.09	0.87 s (3H, $C\underline{H}_3CH_2CH_2$), 1.04 s [9H, $C(C\underline{H}_3)_3$], 1.26 t (6H, $C\underline{H}_3CH_2O$), 1.45 m (2H, $CH_3C\underline{H}_2CH_2$), 1.68 m (2H, $CH_3CH_2C\underline{H}_2$), 2.86 m (1H, $C\underline{H}P$, *J* 17 Hz), 4.06 q (4H, $CH_3C\underline{H}_2O$)
Ic	74	124 (8)	25.30	1.12 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.28 t (6H, $C\underline{H}_3CH_2O$), 4.14 q (4H, $CH_3C\underline{H}_2O$), 4.66 d (1H, $C\underline{H}P$, *J* 17.9 Hz), 6.41, 7.18 m (5H, $CHC_6\underline{H}_5$)
Id[a]	79	90–91	22.92	1.22 t (6H, $C\underline{H}_3CH_2O$), 3.92 q (4H, $CH_3C\underline{H}_2O$), 4.68 d (1H, $C\underline{H}P$, *J* 17.9 Hz), 6.55, 7.30 m (5H, $CHC_6\underline{H}_5$), 7.07, 7.43 m (5H, $NHC_6\underline{H}_5$)
Ie	76	86 (8)	21.61	1.04 s [9H, $C(C\underline{H}_3)_3$], 1.24 t (6H, $C\underline{H}_3CH_2O$), 3.98 q (4H, $CH_3C\underline{H}_2O$), 4.68 d (1H, $C\underline{H}P$, *J* 17.9 Hz), 6.99, 7.57 m (3H, C_4H_3æ)
If[a]	78	121–122	22.60	1.22 t (6H, $C\underline{H}_3CH_2O$), 4.08 q (4H, $CH_3C\underline{H}_2O$), 4.54 d (1H, $C\underline{H}P$, *J* 16.4 Hz), 7.16 m (5H, $NHC_6\underline{H}_5$), 7.60, 8.40 m (4H, $C_5\underline{H}_4N$)
Ig	77	Oily substance	28.52	0.94 s (3H, $C\underline{H}_3$), 1.04 c (3H, $C\underline{H}_3CH_2$), 1.12 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.28 t (6H, $C\underline{H}_3CH_2O$), 1.51 m (2H, $CH_3C\underline{H}_2$), 4.14 q (4H, $CH_3C\underline{H}_2O$)

[a] Constants of compounds **Id** and **If** are identical to published data [4, 5].

Table 3. Elemental analyses of compounds **Ia**–**c, Ie, Ig**

Compd. no.	Found, %			Formula	Calculated, %		
	C	H	P		C	H	P
Ia	57.31	10.31	10.62	$C_{14}H_{30}NO_3P$	57.73	10.31	10.65
Ib	54.10	10.89	11.83	$C_{12}H_{28}NO_3P$	54.34	10.57	11.70
Ic	62.70	8.58	9.57	$C_{17}H_{28}NO_3P$	62.77	8.61	9.54
Ie	53.93	8.92	10.56	$C_{13}H_{24}NO_4P$	53.97	8.30	10.72
Ig	57.70	10.00	10.52	$C_{14}H_{30}NO_3P$	57.73	10.31	10.65

EXPERIMENTAL

^1H NMR spectra were recorded on spectrometer Tesla BS-147 with TMS as external reference. ^{31}P NMR spectra were registered on Varian FT-80 instrument with TMS as internal reference, 85% H_3PO_4 as external reference.

Reaction between *O,O*-diethyl phosphite and *N*-cyclohexylbutyralimine (**Ia**) (general procedure). To 0.025 mol (3.5 g, 3.2 ml) of *O,O*-diethyl phosphite in 10 ml of anhydrous benzene was added 0.05 mol (6.9 g) of freshly calcined powder of potassium carbonate and 5 mol% TBAI. The mixture was stirred for 15 min at room temperature, then 0.025 mol (3.8 g, 4.5 ml) of N-cyclohexylbutyralimine was added. The reaction mixture was heated to 40–45°C for 5 h. Then to the solution was added 15 ml of water, and the mixture was stirred till K_2CO_3 dissolved. The organic layer was separated, the water layer was extracted with chloroform (3 × 5 ml). The solvent was distilled off, the residue was distilled in a vacuum. Yield of compound **Ia** 5.8 g (80%).

Reaction of *O,O*-diethyl phosphite with *N-tert*-butylbutyralimine (Ib). The reaction was carried out as described above using 0.025 mol (3.5 g, 3.2 ml) of *O,O*-diethyl phosphite and 0.025 mol (3.2 g, 3.9 ml) of *N-tert*-butylbutyralimine. Yield of compound **Ib** 5.1 g (77%).

Reaction of *O,O*-diethyl phosphite with *N*-cyclohexylbenzalimine (Ic). The reaction was carried out as described above using 0.012 mol (1.7 g, 1.6 ml) of *O,O*-diethyl phosphite and 0.012 mol (2.3 g) of *N*-cyclohexylbenzalimine. Yield of compound **Ic** 2.9 g (74%).

Reaction of *O,O*-diethyl phosphite with *N*-phenylbenzalimine (Id). The reaction was carried out as described above using 0.025 mol (3.5 g, 3.2 ml) of *O,O*-diethyl phosphite and 0.025 mol (4.5 g) of **N**-phenylbenzalimine. Yield of compound **Id** 6.3 g (79%).

Reaction of *O,O*-diethyl phosphite with *N-tert*-butylfurfuralimine (Ie). The reaction was carried out as described above using 0.025 mol (3.5 g, 3.2 ml) of *O,O*-diethyl phosphite and 0.025 mol (4.5 g) of *N-tert*-butylfurfuralimine. Yield of compound **Ie** 3.7 g (76%).

Reaction of *O,O*-diethyl phosphite with *N*-phenyl-3-pyridinecarboxaldimine (If). Likewise was performed a reaction of 0.11 mol (15.2 g, 14.2 ml) of *O,O*-diethyl phosphite and 0.11 mol (20 g) of *N*-phenyl-3-pyridinecarboxaldimine. The precipitate was filtered off, the compound obtained was purified by recrystallization from hexane–toluene mixture (1 : 1). Yield of compound **If** 27.6 g (78%).

Reaction of *O,O*-diethyl phosphite with *N*-cyclohexylbutylidene-2-imine (Ig). The reaction was carried out as described above using 0.0125 mol (1.85 g, 1.6 ml) of *O,O*-diethyl phosphite and 0.0125 mol (1.9 g) of *N*-cyclohexylbutylidene-2-imine at room temperature for 18 h. To the solution was added 10 ml of water, and the mixture was stirred till K_2CO_3 dissolved. The organic layer was separated, the water layer was extracted with chloroform (3 × 5 ml). The solvent was distilled off, the residue was treated with ether (3 × 10 ml). Yield of compound **Ig** 2.8 g (77%).

REFERENCES

1. Texier-Boullet, F. and Foucaud, A., *Tetrahedron Lett.*, 1980, pp. 2161; Texier-Boullet, F. and Foucaud, A., *Synthesis*, 1982, p. 916.
2. Kossev, K., Troev, K., and Roundhill, D.M., *Phosphorus, Sulfur, Silicon*, 1993, vol. 81, p. 1.
3. Changtao, Q. and Taisheng, H., *J. Org. Chem.*, 1998, vol. 63, p. 4125.
4. Pudovik, A.N., *Dokl. Akad Nauk SSSR*, 1952, vol. 83, pp. 865–868.
5. Boduszek, B., *Tetrahedron*, 1996, vol. 52, pp. 12483–12494.