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Reactions of Hydrophosphoryl Compounds with Schiff Bases in the Presence of CdI_2

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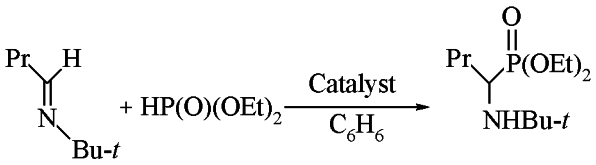
Abstract—The reaction of hydrophosphoryl compounds with aldimines and ketimines in the presence of catalytic amounts of cadmium iodide was investigated. A simple preparative method for the synthesis of α-aminophosphonates, phosphinates, and tertiary phosphine oxides was developed.

We were the first to apply CdI_2 as catalyst in preparation of α-trimethylsiloxyphosphines by reaction of diphenyltrimethylsilylphosphine with ketones [1]. Later several publications appeared on the use of CdI_2 as Lewis acid in various organic processes [2, 3]. In particular, this catalyst was successfully applied to the synthesis of acetals and ketals under microwave irradiation [4].

In this study, a reaction of aldimines and ketimines with hydrophosphoryl compounds (HPC) in the presence of CdI_2 was investigated, and catalytic activity of the latter was compared to that of the other Lewis acids.

The catalytic activity of Lewis acids was compared on an example of reaction between *O,O*-diethyl phosphite with N-*tert*-butylbutyralimine.



Ia

Table 1. Reaction of *O,O*-diethyl phosphite with N-*tert*-butylbutyralimine in the presence of Lewis acids

Catalyst	Time at 20°C, h	Time at 40–45°C, h
–	11 days	36
CdI_2	20	1.5
$ZnCl_2$	>48	4
$PdCl_2$	22	3
$AlCl_3$	20	1.5
$NiCl_2$	–	2
$LaCl_3$	>60	8

The reaction progress was monitored by IR and ^{31}P NMR spectroscopy. The completion of reaction was determined by disappearance of absorption bands in the IR spectra in the regions 1675–1685 (C=N) and 2450–2500 cm^{-1} [P(O)H].

This reaction was studied in the presence of catalytic amounts (2 mol%) of Lewis acids $ZnCl_2$, CdI_2, $PdCl_2$, $NiCl_2$, $AlCl_3$, and $LaCl_3$. The reaction of diethyl phosphite with imine was carried out in anhydrous benzene at reagents ratio 1:1 in the temperature range from 20 to 70°C. The time till reaction completion depending on the catalyst used and temperature is given in Table 1. It was found that at 20°C the process with different Lewis acids completed within 20–60 h. The optimum temperature was 40–45°C, and heating over this temperature virtually did not affect the yield of compound **Ia**.

The best catalysts were CdI_2 and $AlCl_3$ (Table 1). With these catalysts the reaction between diethyl phosphite and *N-tert*-butylbutyralimine is easily finished at 40–45°C in 1.5 h. Yet without catalyst the reaction at room temperature goes to completion for 11 days, and at 40–45°C for 36 h.

Further we used as catalyst cadmium iodide. Note that the addition of diethyl phosphite to *N-tert*-butylbutyralimine in the presence of aluminum chloride strongly depends on the purity of the latter. The best results were obtained with $AlCl_3$ Merk or write common substance subjected to sublimation and drying just before use. The application of CdI_2 is more convenient for preparative targets because the recrystallized and dehydrated salt can be stored for a long time unchanged.

Under the conditions developed for the reaction between diethyl phosphite and *N-tert*-butylbutyralimine in the presence of CdI_2 we involved into this

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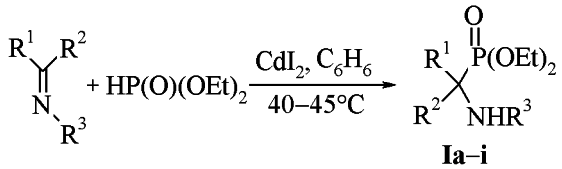
Table 2. Yields, boiling and melting points, n_D^{20} values, and some parameters of ^{31}P and ^{1}H NMR spectra of compounds **Ia–i, IIa, b, III**

Compd. no.	Yield, %	bp, °C (*p*, mm Hg), mp, °C	n_D^{20}	^{31}P NMR spectrum, δ, ppm	^{1}H NMR spectrum, δ, ppm
Ia	77	69–71 (14)	1.4250	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, $C\underline{H}_2CH_2O$), 1.45 m (4H, $CH_3C\underline{H}_2CH_2$), 1.68 m (2H, $CH_3CH_2C\underline{H}_2$), 2.86 m (1H, C<u>H</u>P, *J* 17 Hz), 4.06 q (4H, $CH_3C\underline{H}_2O$)
Ib	81	76–77 (14)	1.4206	29.04	0.96 d [6H, $CH(C\underline{H}_3)_2$], 1.08 s [9H, $C(C\underline{H}_3)_3$], 1.34 t (6H, $C\underline{H}_3CH_2O$), 2.06 m [1H, $C\underline{H}(CH_3)_2$], 2.67 m (1H, C<u>H</u>P, *J* 16.9 Hz), 4.06 q (4H, $CH_3C\underline{H}_2O$)
Ic	80	97–100 (20)	1.4470	29.22	1.1 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.24 t (6H, $C\underline{H}_3CH_2O$), 1.42 m (2H, $C\underline{H}_3CH_2$), 1.78 m (2H, $CH_3C\underline{H}_2$), 2.82 m (1H, C<u>H</u>P, *J* 17 Hz), 4.10 q (4H, $CH_3C\underline{H}_2O$)
Id[a]	80	97–100 (14)	1.4947	29.12	1.24 t (6H, $C\underline{H}_3CH_2O$), 2.15 s (3H, $NHC\underline{H}_3$), 3.98 q (4H, $CH_3C\underline{H}_2O$), 4.64 d (1H, C<u>H</u>P, *J* 17.9 Hz), 7.45, 7.50 m (5H, $CHC_6\underline{H}_5$)
Ie[a]	75	90–91	–	26.20	1.22 t (6H, $C\underline{H}_3CH_2O$), 3.92 q (4H, $CH_3C\underline{H}_2O$), 4.68 d (1H, C<u>H</u>P, *J* 17.9 Hz), 6.55, 7.30 m (5H, $CHC_6\underline{H}_5$), 7.07, 7.43 m (5H, $NHC_6\underline{H}_5$)
If	50	114–116 (8)	–	19.22	1.02 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.15 s (8H, $C_5\underline{H}_8$-cyclo), 1.25 t (6H, $C\underline{H}_3CH_2O$), 4.08 q (4H, $CH_3C\underline{H}_2O$)
Ig	76	96–98 (8)	1.4882	21.42	1.08 m (11H, $C_6\underline{H}_{11}$-cyclo), 1.14 s (10H, $C_6\underline{H}_{10}$-cyclo), 1.24 t (6H, $C\underline{H}_3CH_2O$), 4.01 q (4H, $CH_3C\underline{H}_2O$)
Ih[a]	99	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<u>H</u>P, *J* 16.4 Hz), 7.16 m (5H, $NHC_6\underline{H}_5$), 7.60, 8.40 m (4H, $C_5\underline{H}_4N$)
Ii	81	105–106	–	23.65	1.24 t (6H, $C\underline{H}_3CH_2O$), 2.42 s (3H, $C\underline{H}C_6H_5$), 3.98 q (4H, CH_3CH_2O), 4.68 d (1H, C<u>H</u>P, *J* 17.9 Hz), 6.60, 7.22 m (15H, $CHC_6\underline{H}_5$)
IIa	69	180	–	41.94, 42.53	1.06 s [9H, $C(C\underline{H}_3)_3$], 1.29 t (3H, $C\underline{H}_3CH_2O$), 1.34 d [6H, $C\underline{H}(C\underline{H}_3)_2$], 1.50 m [2H, $CHC\underline{H}_2CH(CH_3)_2$], 1.95 m [1H, $CHCH_2C\underline{H}(CH_3)_2$], 2.36 m (1H, C<u>H</u>P), 4.12 q (4H, $CH_3C\underline{H}_2O$), 7.11 m (5H, $CHC_6\underline{H}_5$)
IIb[a]	78	171	–	40.50, 41.02	1.24 t (3H, $C\underline{H}_3CH_2O$), 4.01 q (4H, $CH_3C\underline{H}_2O$), 4.24 d (1H, C<u>H</u>P, *J* 17.9 Hz), 6.85, 7.22 m (5H, $CHC_6\underline{H}_5$), 7.10, 7.52 m (5H, $NHC_6\underline{H}_5$)
III	52	210	–	19.30	0.96 d [6H, $CH_2CH(C\underline{H}_3)_2$], 1.34 t (6H, $C\underline{H}_3CH_2O$), 2.06 m [1H, $CH_2C\underline{H}(CH_3)_2$], 4.67 m (1H, C<u>H</u>P, *J* 17.9 Hz), 6.44, 7.12 m (10H, $C_6\underline{H}_5$)

[a] The constants of compounds **Id, e, h** and **IIb** are identical to published data [8–11].



Ia–i

I, R^1 = H, R^2 = Pr, R^3 = *t*-Bu (**a**); R^1 = H, R^2 = *i*-Pr, R^3 = *t*-Bu (**b**); R^1 = H, R^2 = Et, R^3 = cyclo-C_6H_{11} (**c**); R^1 = H, R^2 = Ph, R^3 = Me (**d**); R^1 = H, R^2 = Ph, R^3 = Ph (**e**); R^1 = H, R^2 = cyclo-C_5H_8, R^3 = cyclo-C_6H_{11} (**f**); R^1 = R^2 = cyclo-C_6H_{10}, R^3 = cyclo-C_6H_{11} (**g**); R^1 = H, R^2 = 3-Py, R^3 = Ph (**h**); R^1 = H, R^2 = Ph, R^3 = $CHPh_2$ (**i**).

process a number of aldimines and ketimines of aliphatic and aromatic series. As show IR and ^{31}P NMR spectroscopy the reaction of aldimines and ketimines with phosphite occurred virtually quantitatively. α-Aminophosphonates **Ia–i** were isolated in 50–99% yield depending on the structure of the Schiff base.

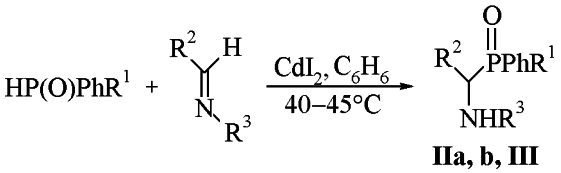
It should be noted that methods of synthesis of α-aminophosphonates are known, and quite a number of publications and reviews treats this topic [5–7]. However up till now no simple and general procedure existed for preparation of these compounds. The method we developed is easy to perform and provides

Table 3. Elemental analyses of compounds **Ia**–**d, f, g, i, IIa, b, III**

Compd. no.	Found, %			Formula	Calculated, %		
	C	H	P		C	H	P
Ia	52.03	10.38	11.69	$C_{12}H_{28}NO_3P$	54.34	10.57	11.70
Ib	53.97	10.51	11.46	$C_{12}H_{28}NO_3P$	54.34	10.57	11.70
Ic	56.15	10.09	11.15	$C_{13}H_{28}NO_3P$	56.32	10.11	11.19
Id	55.97	7.74	11.97	$C_{12}H_{20}NO_3P$	56.03	7.78	12.06
If	59.36	9.84	10.15	$C_{15}H_{30}NO_3P$	59.41	9.90	10.23
Ig	60.50	10.01	9.71	$C_{16}H_{32}NO_3P$	60.57	10.09	9.78
Ii	69.51	6.77	7.55	$C_{24}H_{28}NO_3P$	70.42	6.85	7.58
IIa	65.59	9.35	10.05	$C_{17}H_{30}NO_2P$	65.59	9.64	9.97
IIb	71.81	6.30	8.83	$C_{21}H_{22}NO_2P$	71.79	6.27	8.83
III	73.40	8.65	8.98	$C_{21}H_{30}NOP$	73.47	8.75	9.04

a possibility of preparation of a wide range of α-aminophosphonates of versatile structures.

Besides diethyl phosphite the reaction with aldimines was carried out with phenyl ethyl phosphonite and diethenylphosphonous acid.



IIa, b, III

R^1 = EtO, R^2 = *i*-Bu, R^3 = *t*-Bu (**IIa**); R^1 = EtO, R^2 = R^3 = Ph (**IIb**); R^1 = Ph, R^2 = *i*-Bu, R^3 = *t*-Bu (**III**).

In both cases the reaction occurred under standard conditions yielding aminophosphinates **IIa, b** and aminophosphine oxide **III** in 52–78% yield. Compounds **IIa, b** contain asymmetric phosphorus and carbon atoms and form as mixtures of two stereoisomers. In the ^{31}P NMR spectrum of compounds **IIa, b** appeared two signals in the region 40.5–41.9 and 41–42.5 ppm in 1.2 : 1 ratio.

Physico-chemical characteristics, some parameters of ^{31}P and ^{1}H NMR spectra, and elemental analyses of compounds synthesized are given in Tables 2 and 3.

EXPERIMENTAL

^{1}H 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 of O,O-diethyl phosphite with *N*-*tert*-butylbutyralimine in the presence of Lewis acids (Ia) (general procedure). To 0.06 mol (8.3 g, 7.7 ml) of O,O-diethyl phosphite in 20 ml of anhydrous benzene was added 0.44 g of cadmium iodide, and the mixture was stirred to complete dissolution of the catalyst. Then was added 0.06 mol (7.6 g, 9.3 ml) of *N*-*tert*-butylbutyralimine. The reaction was carried out at 40–45°C for 1.5 h. The solvent was removed, the residue was distilled in a vacuum. Yield of compound **Ia** 12.3 g (77%).

Reaction of *O,O*-diethyl phosphite with *N*-*tert*-butyl-iso-butyralimine (Ib). Likewise was obtained compound **Ib** from 0.06 mol (8.3 g, 7.7 ml) of O,O-diethyl phosphite and 0.06 mol (7.6 g, 9.2 ml) of *N*-*tert*-butyl-*iso*-butyralimine. Yield 12.8 g (81%).

Reaction of *O,O*-diethyl phosphite with *N*-cyclohexylpropylideneimine (Ic). Likewise was obtained compound **Ic** from 0.06 mol (8.3 g, 7.7 ml) of *O,O*-diethyl phosphite and 0.06 mol (8.3 g, 10.6 ml) of *N*-cyclohexylpropylideneimine. Yield 13.4 g (80%).

Reaction of *O,O*-diethyl phosphite with *N*-methylbenzalimine (Id). Likewise was obtained compound **Id** from 0.06 mol (8.3 g, 7.4 ml) of *O,O*-diethyl phosphite and 0.06 mol (7.1 g, 7.4 ml) of N-methylbenzalimine. Yield 12.3 g (80%).

Reaction of *O,O*-diethyl phosphite with *N*-phenylbenzalimine (Ie). The reaction was carried out as above using 0.06 mol (8.3 g, 7.7 ml) of O,O-diethyl phosphite and 0.06 mol (10.9 g) of *N*-phenylbenzalimine. The reaction mixture was cooled to room temperature, 20 ml of ether was added, and the mixture was stirred for 3 h. The precipitate of phosphonate was filtered off and recrystallized from alcohol. Yield of compound **Ie** 14,4 g (75%).

Reaction of *O,O*-diethyl phosphite with *N*-cyclohexylcyclopentylideneamine (If). The reaction was

carried out as above using 0.06 mol (8.3 g, 7.7 ml) of *O,O*-diethyl phosphite and 0.06 mol (6.6 g, 6.6 ml) of *N*-cyclohexylcyclopentylideneamine. The heating to 40–45°C continued for 4.5 h. Yield of compound **If** 6 g (50%).

Reaction of *O,O*-diethyl phosphite with *N*-cyclohexylcyclohexylideneamine (Ig). The reaction was carried out as above using 0.015 mol (2 g, 1.9 ml) of O,O-diethyl phosphite and 0.01 mol (1.8 g, 1.8 ml) of N-cyclohexylcyclohexylideneamine. The heating to 40–45°C continued for 7 h. Yield of compound **Ig** 2.4 g (76%).

Reaction of *O,O*-diethyl phosphite with *N*-phenyl-3-pyridinecarboxaldimine (Ih). To a solution of 0.11 mol (11.8 g, 10.4 ml) of nicotinaldehyde in toluene (50 ml) was added 0.11 mol (10.2 g, 10 ml) of aniline. The mixture was stirred for 1 h, and the solvent was removed on a rotary evaporator. The imine thus obtained was mixed with 0.11 mol (15.2 g, 14.2 ml) of *O,O*-diethyl phosphite, the reaction mixture was heated for 1 h at 40–45°C in the presence of 2 mol% of CdI_2. The mixture was cooled to room temperature, 30 ml of ether was added, and the mixture was stirred for 3 h. The precipitate was filtered off and recrystallized from a mixture hexane–toluene (1 : 1). Yield of compound **Ih** 35 g (99%).

Reaction of *O,O*-diethyl phosphite with *N*-benzhydrylbenzalimine (Ii). The reaction was carried out as in the synthesis of compound **Ia** using 0.06 mol (8.3 g, 7.7 ml) of *O,O*-diethyl phosphite and 0.06 mol 16.3 g) of *N*-benzhydrylbenzalimine. After heating the reaction mixture was cooled to room temperature, 20 ml of water was added, and the mixture was stirred for 3 h. The organic layer was separated, benzene was removed on a rotary evaporator. The compound obtained was purified by recrystallization from alcohol. Yield of compound **Ii** 20 g (81%).

Reaction of phenyl ethyl phosphonite with *N-tert*-butyl-*iso*-pentalimine (IIa) (general procedure). To a solution of 0.025 mol (4.25 g, 3.7 ml) of phenyl ethyl phosphonite in benzene (5 ml) was added 0.183 g of cadmium iodide. The mixture was stirred at room temperature till complete dissolution of the catalyst. Then 0.025 mol (3.53 g, 4.1 ml) of *N-tert*-butyl-*iso*-pentalimine was added. The reaction was carried out at 40–45°C for 4 h. Then to the reaction mixture was added 4 ml of hexane. The separated precipitate was filtered off, 15 ml of ether was added, and the mixture was stirred 3 h at room temperature. The compound obtained was purified by recrystallization from alcohol. Yield of compound **IIa** 5.36 g (69%).

Reaction of phenyl ethyl phosphonite with *N*-phenylbenzalimine (IIb). Likewise from 0.025 mol (4.25 g, 3.7 ml) of phenyl ethyl phosphonite and 0.025 mol (3.53 g, 4.1 ml) of *N*-phenylbenzalimine was obtained compound **IIb**, yield 6.9 g (78%).

Reaction of diphenylphosphinous acid with *N-tert*-butyl-*iso*-pentalimine (III). The reaction was carried out as above using 0.005 mol (1.01 g) of diphenylphosphinous acid and 0.005 mol of *N-tert*-butyl-*iso*-pentalimine. Phosphine oxide **III** was recrystallized from alcohol. Yield of compound **III** 0.89 g (52%).

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