Tetrahedron Letters No. 47, pp 4731 - 4734.

0040-4039/78/1115-4731$02.00/0

SOLID NaOH/K_2CO_3 - A NEW HIGHLY EFFECTIVE BASE FOR PHASE-TRANSFER CATALYSED N-ALKYLATION OF DIPHENYLPHOSPHINIC HYDRAZIDE

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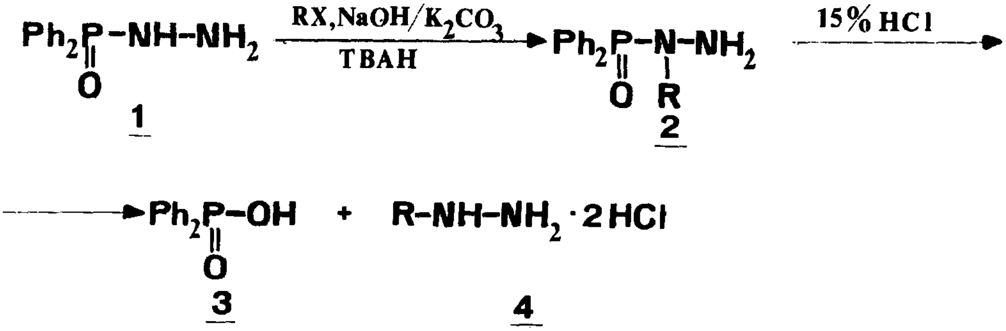
In view of the strongly electron-withdrawing property of the phosphoryl group, attempted N-alkylation of some diphenylphosphinic hydrazides was unsuccessful under conventional conditions[1]. Recently, a number of various N-alkylated amides and hydrazides have been, however, successfully prepared by using PTC technique[2].

We have found that diphenylphosphinic hydrazide 1 [3] cannot be efficiently and regioselectively monoalkylated under conventional PTC conditions. Such reaction can be, however, carried out easily when 50% aqueous NaOH solution is replaced by solid, powdered NaOH/K_2CO_3 mixture. High efficiency of this base in solid-liquid PTC alkylation is propably attributed to the limited amount of water in the system which strongly enhances the reaction rate by effective solvation control. The specific role of potassium carbonate is not quite clear. Evidently it prevents aggregation of sodium hydroxide particles in the presence of water formed by deprotonation of 1 ; it can also possibly act as a mild base under reaction conditions[4].



$$Ph_2P(O)\text{-}NH\text{-}NH_2 \ (\underline{1}) \xrightarrow[TBAH]{RX,NaOH/K_2CO_3} Ph_2P(O)\text{-}N(R)\text{-}NH_2 \ (\underline{2}) \xrightarrow{15\%\ HCl} Ph_2P(O)\text{-}OH \ (\underline{3}) + R\text{-}NH\text{-}NH_2\cdot 2HCl \ (\underline{4})$$

Table 1

N-substituted diphenylphosphinic hydrazides 2 and monoalkylhydrazine dihydrochlorides 4.

	2		4	
R	Yield % [a]	m.p. °C	Yield %	m.p. °C
CH_3	27 /56/[b]	174-176	-	-
C_2H_5	96[c]	164-165	99	145-147
n-C_3H_7	93	115-116	82	129-131/dec./
i-C_3H_7	46 /40/[d]	133-135	99	70-79 /dec./
n-C_4H_9	91	100-101	97	97-110/dec./
i-C_4H_9	87	135-137	[e]	-
sec-C_4H_9	42/35/[d]	127-130	[e]	-
$CH_2=CH-CH_2$	88	121-122	96	128-130/dec./
$CH\equiv C-CH_2$	61	134-138	-	-
$PhCH_2$	94	176-177		135-141/dec./

[a] Yield of recovered 1 given in parenthesis. [b] In chlorobenzene at 90-100°C

[c] Yield - 50% /41% recovery of 1/ in the presence of benzyltriethylammonium chloride and 70% in the presence of tetra-n-butylammonium chloride.

[d] 1.5 mole of RX per 1 mole of 1 added over a period of 2h, 20 mol % catalyst.

[e] Deprotection followed by elimination affording hydrazine hydrochloride.

N-Alkyl diphenylphosphinic hydrazides 2 /Table 1/ were obtained when a small excess of the corresponding alkyl bromide /0.022 mole/ was added slowly /1.5h - 2h/ to the mixture of 1 /0.02 mole/, finely powdered NaOH /0.08 mole/, and potasium carbonate /0.03 mole/ suspended in boiling benzene /60 ml/. The reaction proceeded even without a catalyst /22% yield of 2, R = Et, after 2h/ but was strongly accelerated in the presence of 10 mol % of tetraalkylammonium salts, especially tetra-n-butylammonium hydrogen sulphate /TBAH/. It confirms the essential role of transferring into the organic phase the anion of 1 which is probably initially formed at the solid-liquid interface. To isolate the alkylation product 2 the reaction mixture was filtered, the solid precipitate dissolved in water /50 ml/, and the solution extracted with methylene chloride /3 x 30 ml/. On evaporation of the extracts combined with the filtrate crude 2 were obtained. All samples of 2, when recrystallized from benzene, gave correct elemental analyses, IR and ^{1}H-NMR spectra /Table 2/. The structure of 2 /R = Et/ was additionally confirmed by condensation with benzaldehyde affording N-benzylidene derivative /m.p. 104-105°, yield - 97%/.

A majority of N-alkyl diphenylphosphinic hydrazides 2 could be easily and almost quantitatively deprotected by refluxing with 15% hydrochloric acid for 5h. Separation of the insoluble 3 by filtration and evaporation of the filtrate followed by drying the residue in vacuo over P_2O_5 gave monoalkylhydrazine dihydrochloride 4 as crystaline, strongly hygroscopic solid. The structures of 4 which were contaminated with monohydrochlorides and could not be satisfactority analyzed, were confirmed by MS, IR and ^{1}H-NMR spectroscopy.

The alkylation - deprotection two-step sequence offers a new approach to the synthesis of pure monoalkylhydrazines, free from contamination by polyalkylated materials.

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(Received in UK 18 September 1978)

Table 2

^{1}H-NMR and IR data of N-alkyl diphenylphosphinic hydrazides 2

R	IR , max in cm^{-1} /KBr/	^{1}H-NMR , in ppm, J in Hz /CDCl$_3$/
CH_3	3450,3340,3200/νNH/; 2980,2940,2830/νCH/; 1640/δNH_2/;1490,1400/δCH/;1190/νP=0/.	2,85/d,J=11.0,3H/; 3.20/br.s.,2H/; 7.37-7.57 /m,6H/; 7.75-8.02/m,4H/
C_2H_5	3440/νNHbr./; 2970,2940,2870/νCH/;1620 /δNH_2/ 1480,1460,1380/δCH/; 1200,1175 /νP=0/.	1.18/t,J=7.0,3H/; 3.08/at., J=7.0,2H/; 3.45 /br.s,2H/; 7.35-7.62/m,6H/;7.75-8.07/m,4H/.
n-C_3H_7	3430,3340,3200/νNH/;2950,2880/νCH/;1620 /δNH_2/ 1485,1470,1385/δCH/; 1200,1175 /νP=0/.	0.85/t,J=7.0, 3H/; 1.65/sex., J=7.0, 2H/; 3.00/dist.q., J=7.0, 2H/; 3.35/br.s., 2H/; 7.37-7.56/m, 6H/; 7.75-8.05/m, 4H/.
i-C_3H_7	3420,3340,3200/νNH/; 2980,2930,2880/νCH/; 1630/δNH_2/; 1480,1460,1390,1370/δCH/; 1220,1180/νP=0/.	1.15/d, J=6.7, 6H/; 3.37-3.90/m,1H/; 3.12 /br.s., 1H/; 7.31-7.50/m,6H/;7.72-8.02/m, 4H/.
n-C_4H_9	3440,3340,3200/νNH/;2990,2870/νCH/;1615 /δNH_2/ 1485,1470,1360,1340/δCH/; 1190, 1170/νP=0/.	0.81/dist.t., J=6.5, 3H/; 1.01-1.81/m,4H/; 3.00/dist.q., J=6.5, 2H/; 3.35/br.s.,2H/; 7.31-7.50/m,6H/; 7.75-8.02/m, 4H/.
i-C_4H_9	3420,3330,3200/νNH/; 2950,2870/νCH/; 1618/δNH_2/ 1480,1465,1380,1365/δCH/; 1190,1175/νP=0/.	0.87/d,J=6.5,6H/; 1.62-2.45/m,1H/;2.80/dd., J=7.0,J=5.0, 2H/; 3.30/br.s.,2H/;7.35-7.50 /m,6H/;7.75-7.80/m,4H/.
sec-C_4H_9	3420,3340,3200/νNH/; 2970,2880/νCH/; 1620/δNH_2/ 1485,1465,1380/δCH/; 1220, 1180/νP=0/ .	0.87/dist.t,J=7.0,3H/; 1.17/dist.t.,J=6.5,3H/; 1.25-1.87/m,2H/; 2.87-3.50/m, 1H/; 3.07/br.s., 2H/;7.35-7.55/m,6H/;7.70-8.02/m,4H/.
CH_2=CH-CH_2	3420,3320,3200/νNH/;2920,2860/νCH/; 1640/νC=C/; 1620/δNH_2/;1480/δCH/;1190 /νP=0/.	3.30/br.s.,2H/;3.67/t,J=6.2,2H/;5.10-5.37/m, 2H/; 5.57-6.12/m,1H/; 7.35-7.57/m,6H/; 7.75-8.05/m, 4H/.
CH≡C-CH_2	3440,3320,3200/νNH/; 2990,2860/νCH/; 2120/νC≡C/,1630/δNH_2/;1490/δCH/; 1195/νP=0/.	2,30/dist.t,J=2,0, 1H/; 3.57/br.s.,2H/;4.10 /dd.,J=7.5,J=2,0,2H/; 7.25-7.60/m,6H/;7.75-8.07/m,4H/.
PhCH_2	3420,3320,3200/νNH/;2920/νCH/;1625 /δNH_2/, 1485,1460/νCH/,1190/νP=0/.	3.17/br.s.,2H/;4.23/d,J=5.0,2H/;7.20-7.55/m, 11H/7.77-8.10/m,4H/.