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PRIMARY AMINES VIA ELECTROPHILIC AMINATION OF ORGANOMETALLIC COMPOUNDS WITH O-(DIPHENYLPHOSPHINYL)HYDROXYLAMINE[1]

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Abstract: It is shown that O-(diphenylphosphinyl)hydroxylamine **4a** transforms all kinds of "carbanions" into primary amines; best yields are received with "stabilized anions", e.g. of the benzylic type.

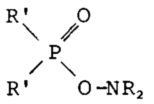
Electrophilic amination reagents like chloramines **1**[2,3], O-alkyl[2a](aryl)hydroxyl=amines **2**[4] and O-sulfonylhydroxylamines **3**[5-8] are being increasingly used for the preparation of all kinds of amino compounds[1-9].

$Cl-NR_2$ **1**

$R'O-NR_2$ **2**

$R'SO_3-NR_2$ **3**

R' = alkyl, aryl
R = H, CH_3 etc.



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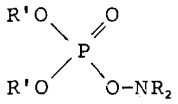

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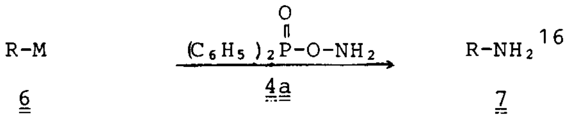
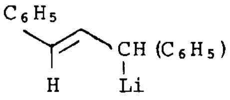
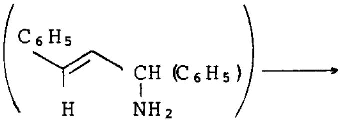
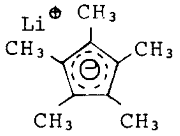
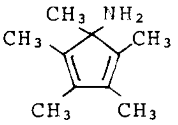
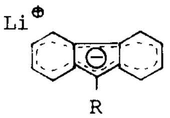
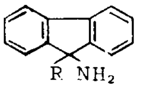
a: R' = C_6H_5, R = H
b: R' = C_6H_5, R = CH_3

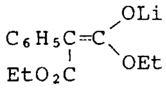
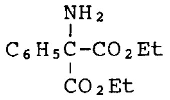
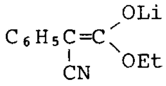
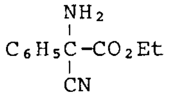
We have recently introduced and successfully applied for that purpose O-phosphinyl- and O-phosphoryl-N,N-dimethylhydroxylamines (**4**[8] and **5**[10a], respectively, R' = aryl, R = CH_3). The determination of the correct structure of O-(diphenylphosphinyl)hydroxylamine **4a** by Harger[11] and the easy access, enhanced stability and low tendency for side reactions[12] of phosphorus compounds like **4** and **5** stimulated the investigation also of the NH_2-compound **4a** as an amination reagent. It is because of two recent communications[13,14] (reaction with N-, P- and S-nucleophiles) that we wish to disclose our results with **4a**: amination of organometallic compounds to yield primary amines[1,15]. Tab. 1 gives a summary of the results.

Tab. 1. Primary amines $\underline{\underline{7}}$ from the reactions of organometallic compounds R-M (M = metal(derivative)) $\underline{\underline{6}}$ with $\underline{\underline{4a}}$:



$$\underset{\underline{\underline{6}}}{R\text{-}M} \xrightarrow[\underline{\underline{4a}}]{(C_6H_5)_2\overset{\overset{O}{\|}}{P}\text{-}O\text{-}NH_2} \underset{\underline{\underline{7}}}{R\text{-}NH_2}{}^{16}$$

	$\underline{\underline{6}}$		$\underline{\underline{7}}$	[%]
a.	C_6H_5-MgBr		C_6H_5-NH_2	22
b.	C_6H_5-MgCl		C_6H_5-NH_2	35
c.	1-Naphthyl-MgBr		1-Naphthyl-NH_2	31
d.	$C_6H_5CH_2$-MgBr		$C_6H_5CH_2$-NH_2	51
e.	$C_6H_5CH_2$-MgCl		$C_6H_5CH_2$-NH_2	70
f.	$C_6H_5(CH_2)_2$-MgBr		$C_6H_5(CH_2)_2$-NH_2	40
g.	$[C_6H_5(CH_2)_2]_3B$		$C_6H_5(CH_2)_2$-NH_2	36α)
h.	$C_6H_5CH_2$-Li		$C_6H_5CH_2$-NH_2	30
i.	$(C_6H_5)_2CH$-Li		$(C_6H_5)_2CH$-NH_2	41
j.	$(C_6H_5)_3C$-Li		$(C_6H_5)_3C$-NH_2	30
k.			$C_6H_5(CH_2)_2\text{-}\overset{\overset{O}{\|}}{C}\text{-}C_6H_5$ β)	31
l.				37
m.			R = H R = CO_2CH_3 R = CO_2-t-Bu	30 47 78
n.	$C_6H_5CH{=}C\begin{array}{l}\diagup OLi\\ \diagdown OEt\end{array}$		$C_6H_5CH\begin{array}{l}\diagup NH_2\\ \diagdown CO_2Et\end{array}$	45
o.	$C_6H_5\overset{\overset{Li}{\vert}}{C}H\text{-}CN$		$C_6H_5CH\begin{array}{l}\diagup NH_2\\ \diagdown CN\end{array}$	37
p.	$(C_6H_5)_2\overset{\overset{Li}{\vert}}{C}\text{-}CN$		$(C_6H_5)_2C\begin{array}{l}\diagup NH_2\\ \diagdown CN\end{array}$	67

q.	 $C_6H_5\underset{EtO_2C}{C}=C(OLi)(OEt)$		 $C_6H_5\overset{NH_2}{\underset{CO_2Et}{C}}-CO_2Et$	31
r.	 $C_6H_5\underset{CN}{C}=C(OLi)(OEt)$		 $C_6H_5\overset{NH_2}{\underset{CN}{C}}-CO_2Et$	>96
s.	$(C_6H_5-C\equiv C)_2CuLi$	$\left(C_6H_5-C\equiv C-NH_2\right) \longrightarrow$	$C_6H_5CH_2-C\equiv N$ γ)	38

α) The yield is related to all three R groups in 6g; ß) 1,3-diphenylpropan-1-one is the product of the allyl amine 7k, which rearranges to the corresponding primary enamine, this rearranges to the imine, which then is hydrolysed; γ) benzylcyanide results from the primary ynamine 7s[17].

It is apparent from Tab. 1, that with aryl and alkyl "carbanions" (e.g. 7a-c,f,g) 4a leads only to moderate amine yields. The generally higher yields with the N,N-dimethyl reagent 4b[10a] suggested that protonation of these rather basic carbon nucleophiles by the NH_2-group of 4a reduces the amine yields, which we observed. In the case of "activated" organometallic compounds, especially of the benzylic type[17], however, 4a competes favourably with other amination reagents, leading to primary amines[18].

In summary, 4a, which is easily prepared[11,13], rather stable (not explosive![6b]) and which aminates N-, P-, S-nucleophiles[13,14], is also a reagent for the electrophilic amination of organometallic compounds to give primary amines.

General procedure: To 0.02 mol of the metallorganic species (Grignard reagents were prepared in the normal way; deprotonations were performed with 1.1 equivalents of n-butyllithium (n-Buli) or lithium diisopropylamide (LDA) at -15°C) in 100 ml tetrahydrofuran (THF), 4.66 g (0.02 mol) 4a was added in several portions at -20°C and the suspension stirred vigorously for 12 h at room temperature. After hydrolysing the reaction mixture with 100 ml 2 N HCl, purification and isolation of the amines 7[16] succeeded by the usual acid/base treatment.

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