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ELECTROPHILIC AMINATION OF ACYL ANION EQUIVALENTS: MILD OXIDATION OF ALDEHYDES TO AMIDES VIA O-(TRIMETHYLSILYL)ALDEHYDE CYANOHYDRIN ANIONS

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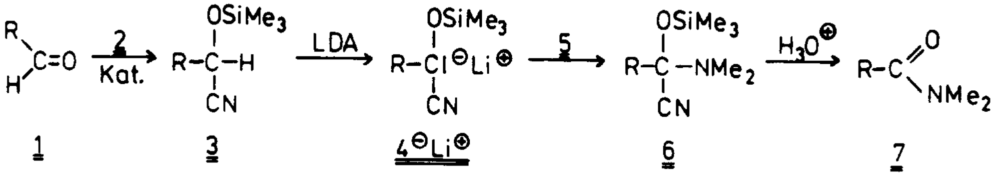
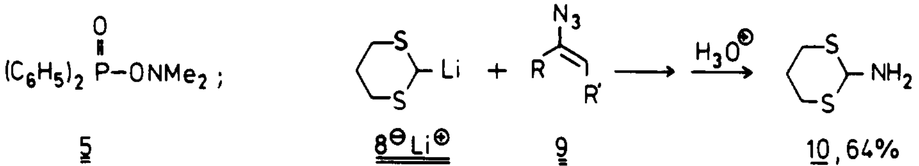
Summary: The O-(trimethylsilyl)aldehyde cyanohydrin anions $4a\text{-}p^{\ominus}Li^{\oplus}$ react with 5 to the amines 6. This electrophilic amination corresponds to a mild and specific oxidation of the aldehydes 1a-p to the amides 7a-p.

Nucleophilic acylation has become an important method for CC-bond formation in recent years[1]. In this context, O-(trimethylsilyl)aldehyde cyanohydrins 3 and their lithio compounds $4^{\ominus}Li^{\oplus}$ turned out to be of special preparative value for two reasons: 1. anions like $4^{\ominus}Li^{\oplus}$ are easily accessible from aldehydes 1 (R=(het)ar, α,ß-unsatur.), trimethylsilyl cyanide 2 and lithium diisopropylamide (LDA); 2. there is no work-up-problem for the reaction products of $4^{\ominus}Li^{\oplus}$ with electrophiles[2,3].

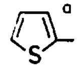
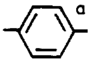
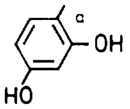
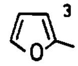
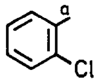
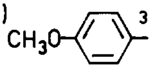
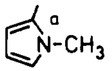
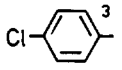
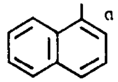
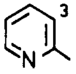
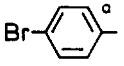
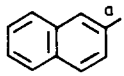
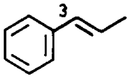
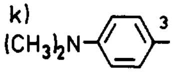
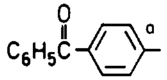
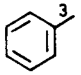




The increasing importance of the electrophilic amination of carbanions[4-6], especially a recent communication[6] in which Hassner, Munger and Belinka reported, i.a., on the reaction of $8^{\ominus}Li^{\oplus}$ with the vinyl azide 9 to give the amine 10, prompts us to disclose similar reactions of $4a\text{-}p^{\ominus}Li^{\oplus}$ with N,N-dimethyl-O-(diphenylphosphinyl)hydroxyl amine 5[5b].

$4a\text{-}p^{\ominus}Li^{\oplus}$, prepared from the aldehydes 1a-p via 3a-p[3], were reacted with 5 between -78 and 20°C for 5 hours and then hydrolyzed (2n HCl) to the amides 7a-p without isolating 6a-p, s. Tab. 1.

Tab. 1. Reaction of the aldehydes 1a-p with 2 to 3a-p, deprotonation of 3a-p with LDA to $4a\text{-}p^{\ominus}Li^{\oplus}$, followed by amination of $4a\text{-}p^{\ominus}Li^{\oplus}$ with 5 and hydrolysis of the resulting 6a-p with 2n HCl. Amide yield: related to 3a-p. Indices: [3]: the cyanohydrin is described in lit.[3]; $^{a(b)}$: the cyanohydrin 3 (amide 7) is new and completely characterized.

	7 (R-)	Yield (%)		**7** (R-)	Yield (%)		**7** (R-)	Yield (%)
a)		80	g)		36	l)		67^{b}
b)		77	h)		92	m)		75
c)		68^{b}	i)		95	n)		80
d)		96	j)		91	o)		90
e)		35	k)		98	p)		51^{b}
f)		76						

Although there is ample literature on the oxidation of aldehydes to carboxylic acids[7], one should point out that the electrophilic amination of the cyanohydrin anions 4a-p$^{\ominus}$Li$^{\oplus}$ is an extraordinary mild and selective oxidation, which proceeds in basic medium. Furthermore, oxidations of carbanions are often related with electron transfer to the corresponding radicals[8], especially if the radicals (as in the case of 4a-p$^{\ominus}$Li$^{\oplus}$!) would be stabilized by capto-dative substituents[9]. We do, however, not observe typical radical reactions. It is also remarkable that the substituents R in 4a-c$^{\ominus}$Li$^{\oplus}$ and 4k-m$^{\ominus}$Li$^{\oplus}$, which are very susceptible to oxidation[10], are not oxidized by 5.

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