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FORMATION OF IMINES IN REACTIONS OF PRIMARY AMINES AND LITHIUM REAGENTS

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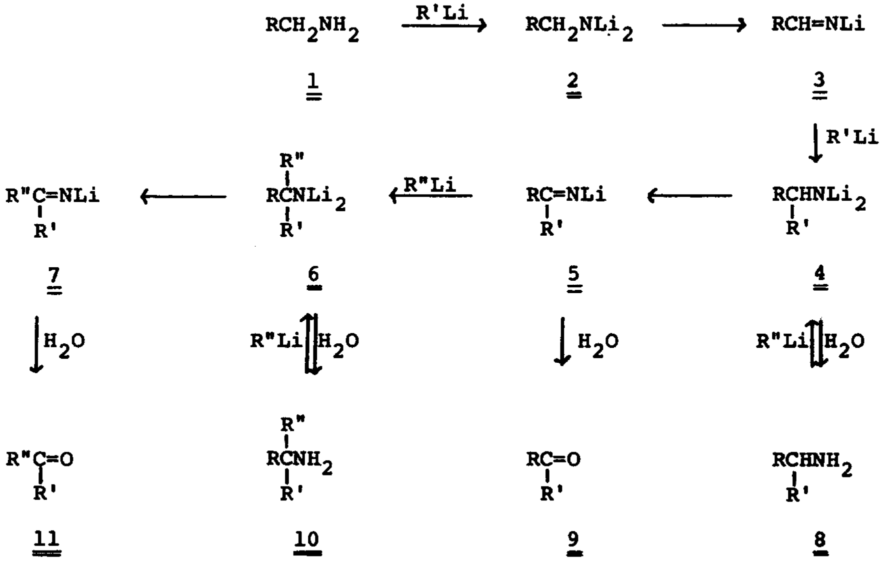
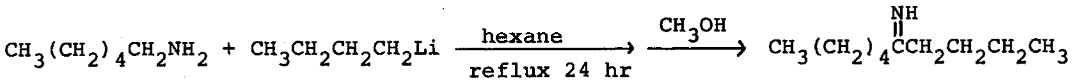
We have isolated imines as significant products from reactions of primary amines with organolithium reagents in excess. This work provides both a new way of synthesizing imines and additional evidence supporting the reaction scheme that we proposed to rationalize the isolation of ketones and α-substituted amines from such reactions.[1]

In the proposed scheme, shown below, eliminations from dilithiated amines



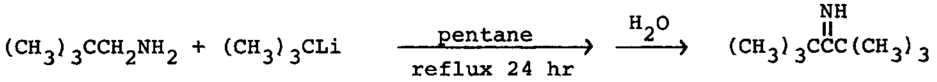
of the elements of lithium hydride or of an organolithium reagent alternate with additions of organolithium reagents to the resultant lithiated imines. If this scheme is correct, then imines instead of ketones (9 or 11) should be isolated by use of a non-hydrolytic work-up. As illustrated by the first example, imines have



$$CH_3(CH_2)_4CH_2NH_2 + CH_3CH_2CH_2CH_2Li \xrightarrow[\text{reflux 24 hr}]{\text{hexane}} \xrightarrow{CH_3OH} CH_3(CH_2)_4\overset{\overset{NH}{\|}}{C}CH_2CH_2CH_2CH_3$$

(1)[2] (3)[2] 12[3]

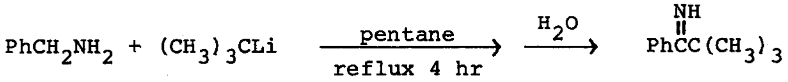
33%[4]



$$(CH_3)_3CCH_2NH_2 + (CH_3)_3CLi \xrightarrow[\text{reflux 24 hr}]{\text{pentane}} \xrightarrow{H_2O} (CH_3)_3C\overset{\overset{NH}{\|}}{C}C(CH_3)_3$$

(1)[2] (3)[2] 13

48%[4]



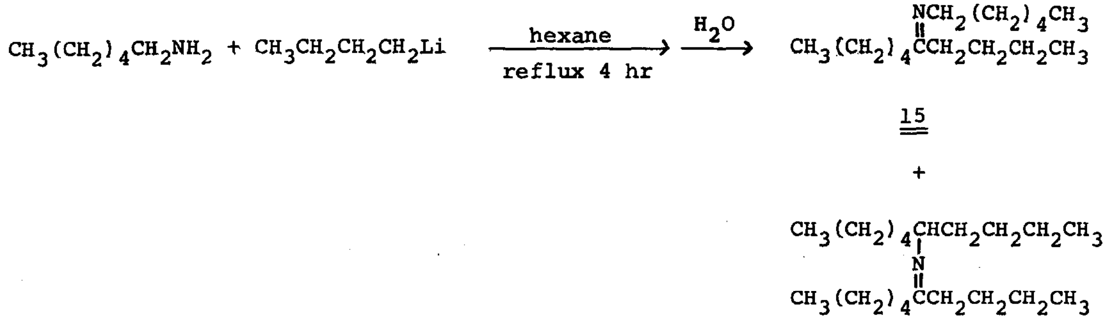
$$PhCH_2NH_2 + (CH_3)_3CLi \xrightarrow[\text{reflux 4 hr}]{\text{pentane}} \xrightarrow{H_2O} Ph\overset{\overset{NH}{\|}}{C}C(CH_3)_3$$

(1)[2] (6)[2] 14

63%[4]

now been found to be major products of reaction mixtures quenched with methanol. Imines sometimes are observed when the reactions are quenched with water, but generally in amounts that are erratic and smaller than the amounts of the corresponding ketones. However, if the imine function is quite hindered, as in 13 and 14, then even hydrolysis of a reaction mixture furnishes an imine in good yield.

N-alkylimines, 15 and 16, for example, often are noted as minor products from the reactions of organolithium reagents with primary amines. The N-alkylimines most probably arise (following quenching of the reaction mixtures) by condensations between imines such as 12-14 and primary amines.[5] In fact, N-alkylimines are found to be major products when the reaction conditions favor the presence of a primary amine on quenching. For example, 15 is the major



$$CH_3(CH_2)_4CH_2NH_2 + CH_3CH_2CH_2CH_2Li \xrightarrow[\text{reflux 4 hr}]{\text{hexane}} \xrightarrow{H_2O} CH_3(CH_2)_4\overset{NCH_2(CH_2)_4CH_3}{\overset{\|}{C}}CH_2CH_2CH_2CH_3$$

15

+

$$\begin{array}{c} CH_3(CH_2)_4CHCH_2CH_2CH_2CH_3 \\ | \\ N \\ \| \\ CH_3(CH_2)_4CCH_2CH_2CH_2CH_3 \end{array}$$

16

product in a reaction in which the lithium reagent and amine are used in a ratio of 2:1; a reactant ratio of 3:1 is required[6] according to the proposed reaction scheme for conversion of all of an amine (1) to ketimine precursor 5. At lower ratios of lithium reagent to amine (or at low temperatures or with short reaction times), it is reasonable that primary amines 1 and 8 necessary for the formation of 15 and 16 would be present following quenching.

N-Benzylidenebenzylamine (17), accompanied by sizeable amounts of unreacted benzylamine, was isolated from a reaction of benzylamine with methyllithium.

$$\underset{(1)^2}{PhCH_2NH_2} + \underset{(3)^2}{CH_3Li} \xrightarrow[\text{reflux 4 hr}]{\text{ether}} \xrightarrow{H_2O} \underset{17}{PhCH{=}NCH_2Ph}$$

Under these conditions, this reaction did not proceed past 3 in the proposed reaction scheme, perhaps because methyllithium, a relatively unreactive lithium reagent, was unable to add rapidly to 3. The imine (or aldehyde) formed from 3 on quenching was trapped by unreacted benzylamine.

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References

1. H. G. Richey, Jr., W. F. Erickson, and A. S. Heyn, Tetrahedron Lett., 2187 (1971).
2. The relative molar amounts of amine and lithium reagent.
3. The spectral properties of this new compound are in accord with the structural assignment.
4. The yield (on the basis of the amine) is of distilled product; since the reactions were run on a small scale, losses in workup and distillation probably were significant, and the amounts of products formed greater than the indicated yields.
5. Condensations between amines and the ketones formed by hydrolysis of the imines furnish the same products. However, probably in some instances, these condensations are not sufficiently rapid to account for the amounts of N-alkylimines that are observed.
6. Assuming that the lithium hydride formed by elimination (and any organolithium reagents that may form by elimination from lithiated amines with tertiary alkyl groups)[1] do not enter into the reaction scheme.