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DIPOLE-STABILIZED CARBANIONS: PREPARATION OF A LITHIOMETHYL AMIDE, A LITHIOETHYL AMIDE, A LITHIOMETHYL THIOESTER, AND A LITHIOETHYL THIOESTER BY DIRECT METALATION

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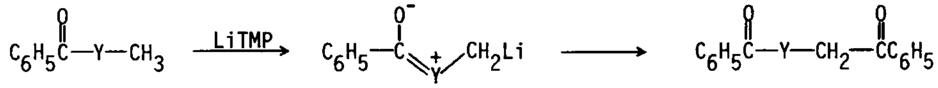
The conversions of *N*,*N*-dimethylbenzamide to *N*-methyl-*N*-phenacylbenzamide and of methyl thiobenzoate to dibenzoylmethane with lithium 2,2,6,6-tetramethylpiperidide have been postulated to involve proton removal from the methyl groups to form the formally dipole-stabilized carbanions **1** and **2** as transient intermediates (Scheme 1). Under the conditions used these species subsequently add to the carbonyl group of the starting material to give products of self-condensation.[1,2] We now wish to report that structural inhibition of the addition step allows preparation of a lithiomethyl amide and a lithioethyl amide from the corresponding tertiary benzamides, and a lithiomethyl thioester and a lithioethyl thioester from the corresponding thioesters. These α-heterocarbanions[3] have been trapped with a variety of electrophiles.

Scheme 1

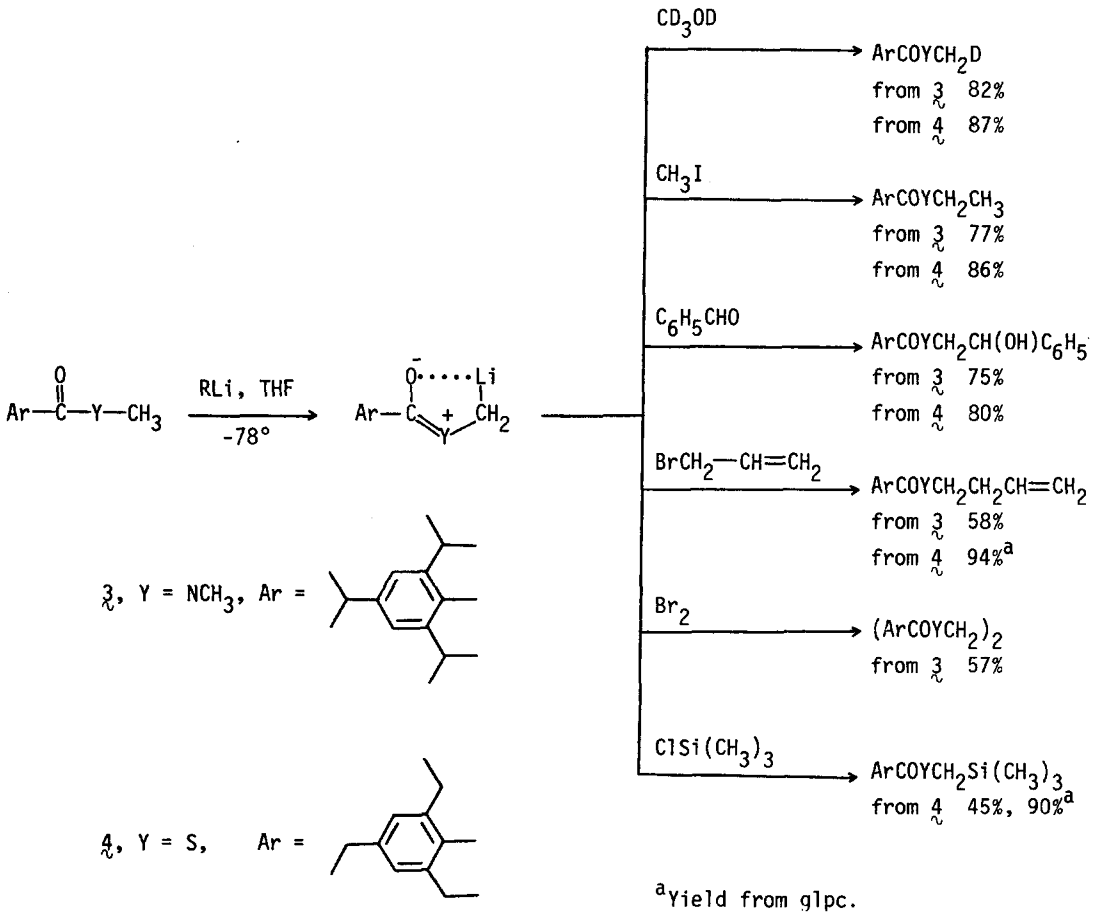


1, Y = NCH_3

2, Y = S

Reaction of *N*,*N*-dimethyl-2,4,6-triisopropylbenzamide (**3**)[4] with *sec*-butyllithium/-tetramethylethylenediamine at -78° for five minutes followed by addition of the electrophilic trapping reagent gave the products of substitution of the N-methyl group as shown in Scheme 2 in the yields indicated.[5] Similarly, reaction of methyl 2,4,6-triethylthiobenzoate (**4**) with *n*-butyllithium at -78° followed by reaction with an electrophilic species gave the products of substitution on the thiomethyl group in the isolated yields indicated in Scheme 2. In both cases the trappable intermediate may be formulated as a dipole-stabilized carbanion which is also stabilized by intramolecular coordination of lithium with the carbonyl oxygen.[6]

Scheme 2

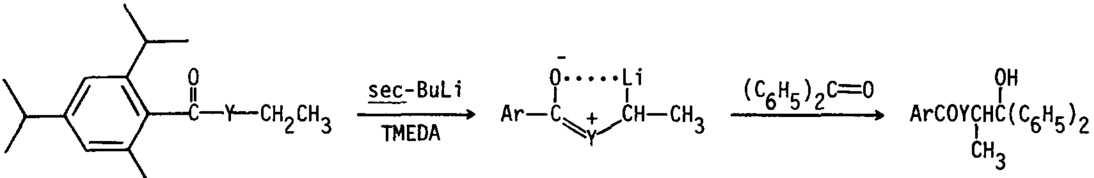


[a] Yield from glpc.

A typical synthetic conversion is illustrated by the reaction of the carbanion from **4** with benzyl bromide to a thioester (78%) which can be reduced with lithium aluminum hydride to give 2-phenylethyl mercaptan (77%).[7] This sequence illustrates the potential of **4** as a synthon for α-lithiomethyl mercaptan. A corresponding use of **3** has been frustrated by resistance of that amide to hydrolysis.

This approach can be extended. Reactions of the tertiary ethyl amide **5** and the ethyl thioester **6** with sec-butyllithium/tetramethylethylenediamine at -45° and -95°, respectively, followed by addition of benzophenone gives the alcohols[5] shown in Scheme 3 in the yields indicated.

Scheme 3



5, Y = NCH_2CH_3
6, Y = S

from **5** 55%
from **6** 86%

The metalations of the ethyl groups appear to be unique for carbonyl activated systems. However, the metalation of N,N-dimethylpivaloylthioamide at the methyl group has been recently reported by Seebach and Lubosch[8] and analogous reactions are known for thioimidates and thiocarbonates from the work of Hirai,[9] Johnson,[10] and Meyers.[6f,6g] The ready hydrolysis of the amides reported by Seebach suggests the pivaloylthioamides may prove more useful synthetically in nucleophilic amino methylations than the carbanion from **3**. On the other hand, the reaction of the ethyl amide **5** raises the prospect that a modified version of this function could provide an alternative to the hazardous but generally useful nitroso function for such activation.[11] The fact that the intermediates resulting from attack of the anion from **4** on carbonyl functions do not undergo rearrangement leading to thiiranes[6f,6g,10] suggests the present case complements the earlier work. Investigation of the stability, structures, and synthetic potential of these novel species is continuing.

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References and Notes

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3. D. J. Peterson, *Organometal. Chem. Res. A*, **7**, 295 (1972).
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