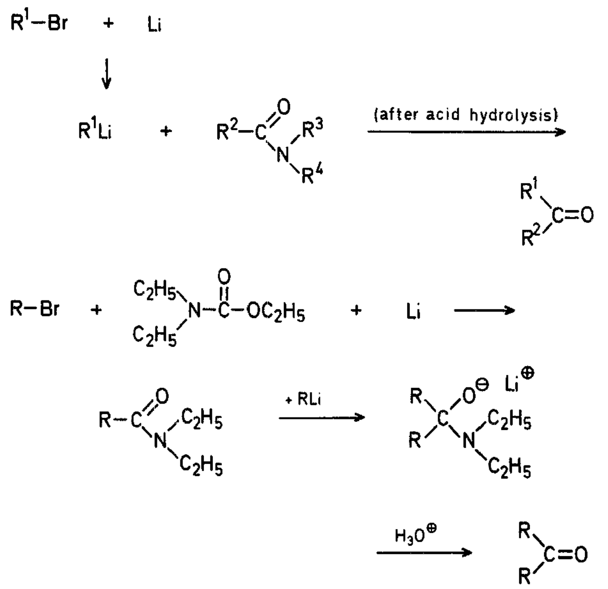
The Preparation of Aldehydes and Ketones via the *in situ* Reaction of Organolithium Compounds with Carboxamides or Carbamates

N. F. Scilly

Explosives Research and Development Establishment, Ministry of Defence, Waltham Abbey, Essex, England

Recently, we described an alternative synthetic procedure to the Grignard reaction for the preparation of alcohols from organic halides and carbonyl compounds using lithium metal in a one-step process[1]. This process, which resembles the Barbier synthesis, consists of the formation of an organolithium derivative in the presence of a carbonyl compound and their subsequent reaction to produce an alcohol. In this communication, the use of this method to prepare aldehydes and ketones from the reaction of organic halides with certain amide derivatives is described.

The reaction procedure is similar to that described previously, namely, the dropwise addition of a mixture of the amide and organic halide (present in ~15–20% excess) to a stirred suspension of lithium pieces in dry tetrahydrofuran at a temperature below 0°.



Typical yields obtained are shown in Tables 1 and 2.

Table 1. Preparation of Aldehydes and Ketones from Carboxamides and Organolithium Compounds *in situ*

R^1	R^2	R^3	R^4	Yield (%)[a]
C_6H_5	H	CH_3	CH_3	78
n-C_7H_{15}	H	CH_3	CH_3	56
C_6H_5	H	CH_3	C_6H_5	56
n-C_7H_{15}	H	CH_3	C_6H_5	73
C_6H_5	C_6H_5	C_2H_5	C_2H_5	76
C_2H_5	C_6H_5	C_2H_5	C_2H_5	79
C_6H_5	CH_3	C_2H_5	C_2H_5	11
n-C_7H_{15}	CH_3	C_2H_5	C_2H_5	10
C_6H_5	n-C_4H_9	C_2H_5	C_2H_5	23

[a] Yields were determined by G.L.C. using an internal standard.

Table 2. Preparation of Symmetrical Ketones from Ethyl N,N-Diethylcarbamate and Organolithium Compounds *in situ*

R	Yield (%)[a]
C_6H_5	82
n-C_7H_{15}	23 (+70% of N,N-diethyloctanamide)

[a] Yields were determined by G.L.C. using an internal standard.

It is apparent from the tables that aromatic amides react smoothly in this process to give ketones in good yield but the reaction with aliphatic amides is not an efficient process. Attempts to promote this reaction by increasing the reactivity of the organolithium reagent by the use of complexing agents such as N,N,N′,N′-tetramethylethylenediamine have so far been unsuccessful.

The preparation of aldehydes and ketones by the reaction of organolithium reagents with carboxamides has been previously described[2] and is a good synthetic route when the organometallic reagent is readily accessible. The reaction of carbamates with organometallic derivatives has not been previously reported and appears to involve the intermediate formation of a carboxamide. It is interesting to note that in the reaction of 1-bromoheptane with ethyl N,N-diethylcarbamate the principal product is a carboxamide. This is unexpected since it would seem reasonable to assume that amides might be more reactive towards organometallic derivatives than carbamates.

General Remarks:

All experiments were conducted under nitrogen; tetrahydrofuran was purified and dried by distillation from sodium-naphthalene.

Preparation of Octanal:

A mixture of 1-bromoheptane (53.7 g, 0.3 mol) and N-methylformanilide (33.8 g, 0.25 mol) was added dropwise, over 1 hr, to a stirred suspension of lithium (5.0 g, 0.7 g-atom) in tetrahydrofuran (200 ml) at −15°. The reaction mixture was maintained at this temperature for 30 min and then filtered to remove excess lithium. The solvent was removed in vacuo and the residue acidified with dilute acid and extracted with ether. The ether extract was dried ($MgSO_4$) and evaporated and the residue distilled in vacuo; yield: 21.4 g (67%); b.p. 70°/15 torr.

Preparation of Benzophenone:

A mixture of bromobenzene (110 g, 0.7 mol) and ethyl N,N-diethylcarbamate (43.5 g, 0.3 mol) was added, dropwise and with stirring over a period of 1 hr, to a suspension of lithium (11.2 g, 1.6 g-atom) in tetrahydrofuran (600 ml) at −15°. The reaction mixture was worked up as in the previous example; yield: 41.0 g (75%); b.p. 187–190°/15 torr.

Received: November 10, 1972

---

[1] P.J. Pearce, D.H. Richards, N.F. Scilly, *Chem. Commun.* **1970**, 1160; *J. Chem. Soc. Perkin Trans. I* **1972**, 1655.

[2] E.A. Evans, *J. Chem. Soc.* **1956**, 4691.
P.T. Izzo, S.R. Safir, *J. Org. Chem.* **24**, 701 (1959).