

A NOVEL *N*-DEALKYLATION REACTION OF *N,N*-DIALKYLARYLCARBOXAMIDES PROMOTED BY ELECTRON TRANSFER FROM ALKALI METALS

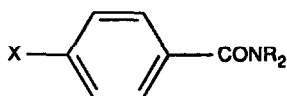
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Summary: Reactions of some *N,N*-dialkylarylcaboxamides with either lithium or sodium metals in dry tetrahydrofuran (THF) promoted by ultrasound waves afforded the corresponding *N*-monoalkylarylcaboxamides in good yields. In the cases of *N,N*-diethylarylcaboxamides the products obtained were derived from coupling reactions rather than from *N*-dealkylation reactions.

Cleavages of various compounds such as ethers, heterocyclics, arylamines, arylphosphines and sulfonamides with alkali metals are well documented and have proven to be a valuable tool in synthesis and structure proof.¹ Interest in *N*-dealkylation reactions of tertiary amines by electron transfer and other methods continues to rise,² but, with the exception of strained *N*-benzoylaziridines,³ to our knowledge there appear to be no reports in the literature on *N*-dealkylation reactions of *N,N*-dialkylarylcaboxamides.

During the course of our studies on electron-transfer reactions of carbonyl compounds,⁴ we have found a new and simple method for *N*-dealkylation of some *N,N*-dialkylarylcaboxamides. A typical procedure is as follows: a solution of *N,N*-dialkylarylcaboxamide (1, 20 mmol) in dry THF (50 mL) was added to Na or Li metal (40 milligram atom) and the reaction mixture was placed in a laboratory ultrasonic bath and sonicated at room temperature under nitrogen atmosphere for five hours. The progress of the reaction was accompanied by color changes (colorless \Rightarrow green \Rightarrow reddish brown) and was monitored by TLC and GC/MS methods. Quenching with dilute hydrochloric acid, extraction with dichloromethane, and separation by flash chromatography afforded as products the corresponding *N*-alkylarylcaboxamides (4) in good yields (Table). Examination of the Table reveals that amides with secondary, tertiary, or benzylic R groups undergo *N*-dealkylation reactions, whereas those with primary alkyl groups (R = ethyl) undergo reductive coupling reactions to benzoin (7) and amides (9).

The results described are fully consistent with the mechanism shown in the Scheme. The first step is electron transfer from lithium or sodium to amide 1.^{3,5} In the second step intermediate 2 can undergo two different reaction types, a *N*-dealkylation reaction (2 \Rightarrow 3 \Rightarrow 4) or a coupling reaction (2 \Rightarrow 6 \Rightarrow 7 or 2 \Rightarrow 8 \Rightarrow 9). The thermodynamic stability of the alkyl radical (R \cdot) should play a dominant role



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a; X = H, R = ethyl; b; X = H, R = cyclohexyl
 c; X = H, R = isopropyl; d; X = methyl, R = ethyl
 e; X = methyl, R = isopropyl; f; X = H, R = benzyl
 g; X = methyl, R = benzyl

in the designation of the reaction path. In the cases where R is isopropyl, cyclohexyl, or benzyl, the *N*-dealkylation reaction is preferable. These results are in accord with the stability order of free radicals (benzylic > tertiary > secondary > primary).

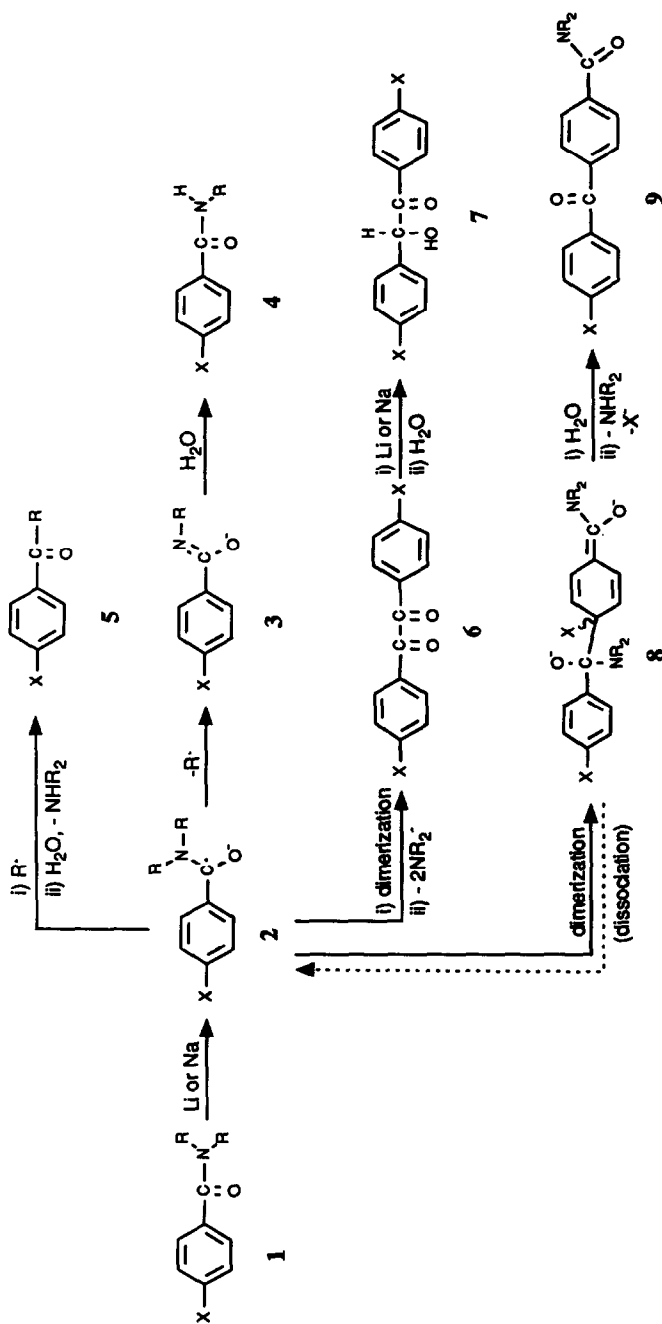
Table. Reductions of *N,N*-dialkylarylcarboxamides with Lithium or Sodium in THF

Entry	Substrate (1)	Metal	% Yield of Products ^d			
			<i>N</i> -Alkylaryl- carboxamide (4)	Ketone (5)	Benzoin (7)	Amide (9)
1 ^b	a	Li	--	--	30	44
2	a	Na	--	--	--	68
3	b	Li	63	--	trace	--
4 ^c	b	Na	42	--	30	--
5	c	Li	72	--	--	--
6	c	Na	83	--	--	--
7 ^d	d	Li	--	--	43	--
8 ^e	d	Na	--	--	45	--
9	e	Li	84	--	--	--
10	e	Na	95	--	--	--
11	f	Li	54	20	--	--
12	f	Na	66	12	--	--
13	g	Li	62	18	--	--
14	g	Na	72	11	--	--

^aIsolated yields. The products were identified by ¹H and ¹³C NMR and GC/MS spectral methods. ^b*p*-Benzoylbenzaldehyde was also obtained in 16% yield. ^cBenzylphenyl ketone was also obtained in 19% yield. ^d*p*-Tolualdehyde was also obtained in 24% yield. ^e*p*-Tolualdehyde was also obtained in 22% yield.

In order to gain further insight into the modes of the reaction, experiments 13 and 14 were repeated in the same manner and were quenched with either D₂O or CO₂. Upon quenching with D₂O, *N*-benzyltoluamide-*N-d*₇ and unlabeled toluene were obtained.⁶ Quenching with CO₂ produced *N*-benzyltoluamide (4g) and toluene. In neither case was carboxylic acid obtained, as judged by GC/MS analysis.⁷ The formation of ketones (5) in experiments 11-14 is thus very likely a result of the coupling reaction of the benzyl radical and intermediate 2 (see the Table and the Scheme) and not of benzyl anion with substrate 1.

The discrepancy between the reactions of amides 1a and 1d with alkali metals may have several causes. Factors to be considered include both blockage of the *para* position in 1d and reversibility of head-to-tail radical dimerization because of the poor leaving group qualities of methyl compared to



Scheme

hydrogen in dimer 8. Thus when the substituent group X is hydrogen, amides (9) may be formed and when X is methyl, benzoin (7) are obtained instead. In addition, the substitution of a ring hydrogen for an electron-donating alkyl group may affect the ability of the carboxamide to accept electrons. Additional work will have to be performed to determine the relative importance of these factors.

The reductions of tertiary amides with various metal hydride reducing agents, such as lithium aluminum hydride,⁸ diborane,⁹ sodium borohydride in the presence of PCl_5 ,¹⁰ and lithium triethylborohydride¹¹ or alkaline earth metals such as zinc in the presence of POCl_3 ,¹² proceed with carbonyl carbon-oxygen or carbonyl carbon-nitrogen bond fissions to give the corresponding amines or alcohols. By contrast, the work reported in this paper forms a novel method for reductions of tertiary amides with alkali metals which proceeds with alkyl carbon-nitrogen bond fission to furnish the corresponding *N*-dealkylated amides.

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