

Aroyl Anion Trapping Reactions. A Preliminary Study of Direct Nucleophilic Aroylation by Means of Low Temperature, in situ (CH₃)_{n-6}H_{5-n}Li/CO Systems.

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Summary. Results of studies of the in situ nucleophilic aroylation of PhCO₂Me, Me₃CCO₂Me and Ph₂CO by several low temperature ArLi/CO systems (Ar = C₆H₅, p-CH₃C₆H₄, o-CH₃C₆H₄, 2,6-(CH₃)₂C₆H₃ and 2,4,6-(CH₃)₃C₆H₂) are reported. The experiments with C₆H₅Li were unsuccessful and the best results were obtained with 2,6-(CH₃)₂-C₆H₃Li.

Our previous studies of the low temperature, in situ RLi/CO (R = n-Bu, sec-Bu, tert-Bu) systems have shown them to be applicable to the direct nucleophilic acylation of aldehydes, ketones, esters, lactones, trialkylchlorosilanes, diorgano disulfides and elemental sulfur.²⁻⁶ We report here our initial studies of the use of in situ ArLi/CO systems in the direct nucleophilic aroylation of esters and benzophenone.

Much of the previous work relating to direct nucleophilic acylation by RLi/CO systems has focused on reactions of phenyllithium. Thus the earliest report of a study of the interaction of an organolithium reagent with carbon monoxide was the brief comment by Wittig that the action of CO on a solution of phenyllithium resulted in formation of PhC(O)CHPh₂.⁷ This reaction received further attention some 30 years later by Jutzi and Schröder.⁸ The most detailed study of the interaction of CO with an organolithium reagent was that of Whitesides and his coworkers of the PhLi/CO system.⁹ Although no useful synthetic chemistry resulted from this investigation, the complications which arise in such RLi/CO systems were well delineated. In a synthetically useful procedure, other workers prepared diaryl-alkylcarbinols by the atmospheric pressure carbonylation of aryllithium reagents at -78°C in THF in the presence of bromoalkanes.¹⁰ (Note, however, that it was a secondary product, not the direct nucleophilic aroylation product, which was isolated in this process.)

We have applied the direct nucleophilic acylation procedure which we have developed²⁻⁶ to a study of nucleophilic aroylation using phenyllithium, p-tolyl-lithium, o-tolyl-lithium, 2,6-dimethylphenyllithium and mesityllithium. Since we

wished to obtain a rough idea where the synthetic potential lies in this series of aryllithiums and what the major problems are, we restricted our initial study to three organic electrophilic substrates: methyl benzoate, methyl pivalate and benzophenone.

In these reactions a solution of the organic electrophile in a solvent mixture of 4 volumes of THF, 4 volumes of Et₂O and 1 volume of pentane was cooled (under nitrogen or argon) to -110°C and then carbon monoxide was bubbled into this solution by means of a gas dispersion tube for about 30 min. While the temperature was maintained at -110°C by external cooling and the CO stream was continued, a solution of the aryllithium in diethyl ether (one molar equivalent per equivalent of the organic electrophile) was added, with stirring, slowly by means of a syringe pump (ca. 0.3-0.6 mmol/min when the reactions were carried out on a 9 mmol scale). After the addition had been completed, the CO stream was continued and the reaction mixture was stirred and allowed to warm slowly to room temperature. Hydrolysis with saturated ammonium chloride solution was followed by separation, drying and work-up of the organic layer. New products were characterized by C/H analysis and IR and proton NMR spectroscopy. The results of these experiments are summarized in Table 1.

It is clear that direct nucleophilic benzoylation with the PhLi/CO system, at least of esters and ketones, is not a useful process. Direct attack by phenyllithium at the C=O function of the organic substrate predominates. The case of *p*-tolyllithium looks equally unpromising. However, the aryoylation of the two esters studied was successful in the case of *o*-tolyllithium, although benzophenone reacted directly with this lithium reagent. The still more hindered 2,6-dimethylphenyllithium, on the other hand, served well in the direct nucleophilic aryoylation of all three substrates, giving clean reactions in which only the desired product was formed. Even with this aryllithium reagent, however, there are problems. This was shown in reactions in which CH₃CO₂CH₃ was the substrate used: at -110°C and even at -135°C, deprotonation to form the arene in substantial yield (73% at -135°C) was the predominant process, and the expected α-diketone, 2,6-Me₂C₆H₃C(O)C(O)CH₃, was formed in only low yield (9% at -135°C). Better product yields were obtained as the number of protons α to the C=O group was decreased. Methyl *n*-butyrate reacted with the 2,6-dimethylphenyllithium/CO system at -135°C to give the expected α-diketone, 2,6-Me₂C₆H₃C(O)C(O)C₃H₇-*n* in 66% yield, while a similar reaction with CH₃CH₂CH(CH₃)CO₂Et gave 2,6-Me₂C₆H₃C(O)C(O)CH(CH₃)C₂H₅ in 84% yield.

The results obtained with mesityllithium were poorer than expected, possibly as a result of the low solubility of this reagent at very low temperatures. If any of its reactions do not occur until it becomes soluble when higher temperatures are reached, then the occurrence of competitive, undesirable reactions is more likely.

Our preliminary studies suggest that direct nucleophilic aryoylation with low

TABLE 1. Direct Nucleophilic Aroylation Reactions.^a

ArLi	Organic Electrophile	Product(s) (% Yield)
C_6H_5Li	$C_6H_5CO_2Me$	$(C_6H_5)_2CO$ (94)
	Me_3CCO_2Me	$C_6H_5C(O)CMe_3$ (61) + $C_6H_5C(O)C(O)CMe_3$ (11)
	$(C_6H_5)_2CO$	$(C_6H_5)_3COH$ (80)
$p\text{-}CH_3C_6H_4Li$	$C_6H_5CO_2Me$	$p\text{-}CH_3C_6H_4C(O)C_6H_5$ (95)
	Me_3CCO_2Me	$p\text{-}CH_3C_6H_4C(O)CMe_3$ (67) + $p\text{-}CH_3C_6H_4C(O)C(O)CMe_3$ (11)
	$(C_6H_5)_2CO$	$p\text{-}CH_3C_6H_4C(OH)(C_6H_5)_2$ (80)
$o\text{-}CH_3C_6H_4Li$	$C_6H_5CO_2Me$	$o\text{-}CH_3C_6H_4C(O)C_6H_5$ ^b (30) + $o\text{-}CH_3C_6H_4C(O)C(O)C_6H_5$ ^c (60)
	Me_3CCO_2Me	$o\text{-}CH_3C_6H_4C(O)C(O)CMe_3$ (87)
	$(C_6H_5)_2CO$	$o\text{-}CH_3C_6H_4C(OH)(C_6H_5)_2$ (75)
$2,6\text{-}(CH_3)_2C_6H_3Li$	$C_6H_5CO_2Me$	$2,6\text{-}(CH_3)_2C_6H_3C(O)C(O)C_6H_5$ (79)
	Me_3CCO_2Me	$2,6\text{-}(CH_3)_2C_6H_3C(O)C(O)CMe_3$ (96)
	$(C_6H_5)_2CO$	$2,6\text{-}(CH_3)_2C_6H_3C(O)C(OH)(C_6H_5)_2$ (90)
$2,4,6\text{-}(CH_3)_3C_6H_2Li$ ^d	$C_6H_5CO_2Me$	$2,4,6\text{-}(CH_3)_3C_6H_2C(O)C(O)C_6H_5$ (86)
	Me_3CCO_2Me	$2,4,6\text{-}(CH_3)_3C_6H_2C(O)CMe_3$ (9) + $2,4,6\text{-}(CH_3)_3C_6H_2C(O)C(O)CMe_3$ (35)
	$(C_6H_5)_2CO$	$2,4,6\text{-}(CH_3)_3C_6H_2C(O)C(OH)(C_6H_5)_2$ (15)

^aInitial reaction temperature -110°C as described in the text.

^b25% Yield when initial reaction temperature was -135°C.

^c40% Yield when initial reaction temperature was -135°C.

^dThe reaction mixture was white and milky due to insolubility of mesityllithium until the temperature rose to about -50°C. It is likely that at -110°C much of the mesityllithium did not react and that at -50°C deprotonation reactions became competitive.

temperature in situ ArLi/CO systems will be of much less general applicability than such processes with alkylolithium reagents. However, good results appear realizable when steric hindrance can be introduced into the aryllithium reagent, the organic electrophile, or both. Thus we may expect the in situ ArLi/CO systems to show synthetic utility, however, with limitations.

More detailed studies of these and other ArLi/CO systems are in progress.

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