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High-Yield Acyl Anion Trapping Reactions: A Synthesis of Acyltrimethylsilanes

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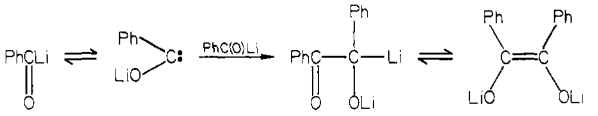
There has been a long-standing interest in the reaction of active metal organometallic compounds (such as RLi and RMgX) with carbon monoxide. The early work on the action of Grignard reagents on carbon monoxide has been summarized by Kharasch and Reinmuth.[2] In 1940, Wittig reported that the reaction of carbon monoxide with phenyllithium gave, after hydrolysis, α,α-diphenylacetophenone.[3] This reaction was examined in detail by Jutzi and Schröder[4,5] who obtained this ketone in 86% yield after hydrolytic workup. Ryang and Tsutsumi developed a synthesis of diaryl and dialkyl ketones based on the introduction of carbon monoxide into an ethereal RLi solution at −70 °C,[6] and diarylalkylcarbinols were prepared in moderate yields by Nudelman and Vitale by the carbonylation at atmospheric pressure of solutions of aryllithium reagents at −78 °C in THF in the presence of bromoalkanes.[7] The mechanism of the PhLi/CO reaction is quite complex, but it seems certain that benzoyllithium, PhC(O)Li, is the first intermediate that is formed.[8] Such reagents most likely were trapped in the diarylalkylcarbinol synthesis (eq 1). An inevitable byproduct in these reactions was ArC(O)CH(OH)Ar, formed via ArC(O)Li "dimerization" (eq 2).[7]

$$\mathrm{ArLi} \xrightarrow{\mathrm{CO}} \mathrm{ArC(O)Li} \xrightarrow{\mathrm{RBr}} \mathrm{ArC(O)R} \xrightarrow{\mathrm{ArLi}} \xrightarrow{\mathrm{H_2O}} \mathrm{Ar_2RCOH} \qquad (1)$$


(2)

Convincing evidence for an RC(O)Li intermediate was provided by Jutzi and Schröder, who bubbled CO into a solution of *tert*-butyllithium in hexane and then added the resulting dark red solution to trimethylchlorosilane in Et$_2$O/THF. Pivaloyltrimethylsilane, Me$_3$SiC(O)CMe$_3$, was produced in 15% yield. A similar experiment with a PhLi/CO reaction mixture gave a mixture of hexamethyldisiloxane, trimethylphenylsilane, and a β-keto silane, Ph$_2$C(SiMe$_3$)C(O)Ph, while a *n*-BuLi/CO reaction mixture, on addition to Me$_3$SiCl, gave *n*-Bu$_2$C(SiMe$_3$)C(O)-*n*-Bu in 16% yield. The β-keto silanes, it was suggested, were the result of further reactions of the acyllithium "dimer" (cf. eq 2). Thus, only in the case of the *tert*-butyllithium/CO reaction did significant amounts of RC(O)Li intermediate accumulate in solution.

Acyl- and aroylsilanes have become of interest as intermediates in organic synthesis, and there are many routes available for their synthesis.[9] All of them are indirect, and many of them require the prior preparation of appropriate organosilicon starting materials. The application of acyl anion equivalents[10] to the preparation of acylsilanes is the most generally practiced strategy.[9] All of them require a subsequent solvolysis step to form the acylsilane, and such solvolysis is not always a facile, high-yield process. If successful, a *direct* synthesis of acylsilanes by reaction of an organolithium reagent, carbon monoxide, and a chlorosilane would be the most expeditious procedure. The work of Jutzi and Schröder[4] showed that such a process in which the reaction of RLi with CO is carried out in a prior step before addition of Me$_3$SiCl is largely unsuccessful. Even when it does proceed as desired as in the case of the *t*-BuLi/CO + Me$_3$SiCl reaction, the yield of the acylsilane is very low.

Table I. Preparation of Acyltrimethylsilanes by the RLi/CO/Me$_3$SiCl Reaction

R in RLi	RC(O)SiMe$_3$ yield[a] GLC yield, %	distillation yield, %[b]
n-C$_4$H$_9$	77	45
n-C$_5$H$_{11}$	71	45
n-C$_6$H$_{13}$	80	71
(CH$_3$)$_2$CHCH$_2$	75	50
(CH$_3$)$_2$CHCH$_2$CH$_2$	87	65
(CH$_3$)$_3$C	50	
(CH$_3$)$_2$CH	28	
C$_2$H$_5$CHCH$_3$	30	

[a] Based on RLi used. [b] Of pure (by GLC and spectroscopically) products.

We have been able to prepare acyltrimethylsilanes in moderate to excellent yield by application of the in situ procedure, i.e., by generating the acyllithium reagent in the presence of trimethylchlorosilane (eq 3). A typical experiment was carried out as follows.

$$\mathrm{RLi} + \mathrm{CO} \xrightarrow{-110\ ^\circ\mathrm{C}} \underset{\mathbf{1}}{[\mathrm{RC(O)Li}]} \xrightarrow{\mathrm{Me_3SiCl}} \underset{\mathbf{2}}{\mathrm{RC(O)SiMe_3}} \qquad (3)$$

A 500-mL Morton (creased) three-necked flask was equipped with an overhead mechanical stirrer, a Claisen adapter fitted with a gas outlet tube and a low-temperature thermometer, and in the third neck, a rubber septum that held a coarse-fritted gas dispersion tube (for the introduction of CO) and a syringe needle. The latter was connected via polyethylene tubing to an Orion Research Inc. Model 341A syringe pump. The reaction flask was charged with 133 mL each of dry THF and diethyl ether, 33 mL of dry pentane, and 35 mL of trimethylchlorosilane. This mixture was cooled to −110 °C[11] with the aid of a liquid nitrogen filled Dewar flask. After the cooling had been initiated, the introduction of a slow stream of carbon monoxide was started. Carbon monoxide was bubbled into the solution for 30 min, and then *n*-butyllithium (5.0 mL of a 1.35 M solution in hexane; 6.75 mmol) was added at a rate of 0.32 mL/min by means of the syringe pump. The temperature was maintained at −110 ± 5 °C during the course of the addition, and after the addition had been completed, the reaction mixture was stirred under CO for another 2 h at −110 °C. The reaction mixture then was allowed to warm to room temperature over the course of 1 h, with the introduction of CO being continued. After 2 h at room temperature, the mixture was cannulated into a dry 1-L round-bottomed flask. Trap-to-trap distillation (25 °C (0.4 mmHg)) into a liquid nitrogen cooled receiver followed. The residual salts were dissolved in water and extracted with 100 mL of diethyl ether. Fractional distillation of the trap-to-trap distillate and the ether extracts at reduced pressure to remove solvents and the unreacted trimethylchlorosilane obtained in the trap-to-trap distillation was followed by GLC analysis of the high-boiling residues (15% SE-30 silicone rubber gum on Chromosorb P, 90–240 °C program at 6 °C/min). The following products were present: *n*-BuSiMe$_3$ (21% yield); *n*-

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(1) Rhône-Poulenc Graduate Research Fellow, 1982–1983.

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(11) The temperatures cited are corrected values. The Kessler pentane thermometer that was used was of the total immersion variety but was not used as such. An empirical correction of −7 °C was required.

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$BuC(O)SiMe_3$, n^{20}_D 1.4258 (77% yield); and *n*-$Bu_2C(OH)SiMe_3$ (2.7% yield).

An examination of the scope of this reaction (Table I) showed that such $RLi/CO/Me_3SiCl$ acyltrimethylsilane syntheses are very successful when R is a primary alkyl group, linear or with branching in the β position or further out along the chain. With *tert*-butyllithium a 50% yield of pivaloyltrimethylsilane was obtained. With secondary alkyllithium reagents the chemistry is not as clean. Thus, such a reaction in which *sec*-butyllithium was used (with an identical procedure) gave the expected acylsilane, $MeEtCHC(O)SiMe_3$, in only 30% yield. Also formed was the carbinol, $(MeEtCH)_2C(OH)SiMe_3$ (17% yield), and $MeEtCHC(O)CH(OH)CHEtMe$ (9% yield). The latter is the hydrolysis product of the O-silylated acyllithium "dimer", $MeEtCH(OSiMe_3)C{=}C(OSiMe_3)CHEtMe$. Similar byproducts were obtained in the *i*-$PrLi/CO/Me_3SiCl$ reaction, which produced $Me_2CHC(O)SiMe_3$ in 28% yield.

It is clear that the complications of the two-step procedure have not been avoided entirely by using the in situ procedure. However, for the synthesis of acyltrimethylsilanes containing primary alkyl groups and of pivaloyltrimethylsilane, the in situ procedures can be used to good advantage: the reactions are fairly clean and they give satisfactory yields of the desired $RC(O)SiMe_3$ product. The success of this procedure is a consequence of the known[12] low reactivity of trimethylchlorosilane toward many alkyllithium reagents. Thus trimethylchlorosilane may be used in large excess in these $RLi/CO/Me_3SiCl$ reactions. The alkyllithium reacts more rapidly with carbon monoxide (to form the acyllithium) than with Me_3SiCl, even in the presence of a large quantity of the chlorosilane, so that in favorable cases the $RSiMe_3$ byproduct yield is below 25%. At the same time, in the favorable cases, the reaction of $RC(O)Li$ with trimethylchlorosilane is sufficiently rapid at the low temperatures used so that $RC(O)Li$ "dimerization" does not offer serious competition to the formation of $RC(O)SiMe_3$. We emphasize that the practical limits of success are very narrow indeed. The reaction proceeds well when triethylchlorosilane is used in place of trimethylchlorosilane (an 84% yield of *n*-$BuC(O)SiEt_3$ when *n*-BuLi was used), but acylsilane yields fall to zero when the reactivity of the chlorosilane toward nucleophilic attack is increased as a result of more favorable steric (e.g., Me_2HSiCl) or electronic (e.g., $Me_2PhSiCl$) factors. A change from R = alkyl in RLi also can be unproductive. Thus, when phenyllithium was used, not $PhC(O)SiMe_3$ was formed, at least under the conditions that give good product yields when R = primary alkyl. Also, the experimental conditions that result in good $RC(O)SiMe_3$ product yields are crucial. A low reaction temperature must be used, and a controlled, slow (~0.5 mmol/min) rate of addition of the alkyllithium solution is essential.

The provenance of the $R_2C(OH)SiMe_3$ byproduct is not certain. It could derive from RLi addition to the C=O bond of the acylsilane (a known reaction[9a,13]) or from reaction of a $[R_2CO]Li_2$ intermediate (of the type suggested to obtain in the PhLi/CO reaction[8]) with trimethylchlorosilane. It is not yet clear why the $RLi/CO/Me_3SiCl$ reaction does not proceed as well with secondary alkyllithium reagents.

The reactions described in this communication are the first examples of the successful trapping of acyllithium reagents in high yield in which the products isolated are those formed initially, and a useful, one-step synthesis of primary acyltrimethylsilanes from readily accessible alkyllithiums, carbon monoxide, and trimethylchlorosilane is now in hand. Further examination of the scope of this new acyltrimethylsilane synthesis is in progress.

New compounds have been characterized by combustion analysis and by proton NMR and IR spectroscopy. Yields were determined by gas–liquid chromatography using the internal standard method.

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Note Added in Proof. We have found recently that trimethylchlorosilane does not need to be present in large excess in order to obtain satisfactory yields of an acyltrimethylsilane. For example, a reaction in which 2 mL (15.8 mmol) of Me_3SiCl and 7.0 mmol of *n*-BuLi were used gave a 65% yield (GLC) of *n*-$BuC(O)SiMe_3$. A reaction in which 11 mL (88 mmol) of Me_3SiCl and 7.0 mmol of *n*-BuLi were used gave a 67% yield of this product. Thus this acylsilane synthesis may be applied to reactions in which trialkylchlorosilanes other than the readily available and cheap Me_3SiCl are used.

Registry No. *n*-$C_4H_9C(O)SiMe_3$, 82903-02-4; *n*-$C_5H_{11}C(O)SiMe_3$, 63578-18-7; *n*-$C_6H_{13}C(O)SiMe_3$, 82903-03-5; $(CH_3)_2CHCH_2C(O)SiMe_3$, 63578-20-1; $(CH_3)_2CHCH_2CH_2C(O)SiMe_3$, 71821-71-1; $(CH_3)_3CC(O)SiMe_3$, 13411-49-9; $(CH_3)_2CHC(O)SiMe_3$, 56583-93-8; $C_2H_5CH(CH_3)C(O)SiMe_3$, 82903-04-6; *n*-C_4H_9Li, 109-72-8; *n*-$C_5H_{11}Li$, 3525-31-3; *n*-$C_6H_{13}Li$, 21369-64-2; $(CH_3)_2CHCH_2Li$, 920-36-5; $(CH_3)_2CHCH_2CH_2Li$, 7488-31-5; $(CH_3)_3CLi$, 594-19-4; $(CH_3)_2CHLi$, 1888-75-1; $C_2H_5CH(CH_3)Li$, 598-30-1; CO, 630-08-0; Me_3SiCl, 75-77-4.

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Picosecond Dynamics of Hydride Transfer

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The mechanisms of carbonyl reduction by hydride-donating reagents has been extensively investigated.[1] The net transfer of a hydride may be conceived as proceeding through one of three mechanisms: direct hydride transfer or stepwise via an initial one-electron transfer followed by either a hydrogen atom transfer or a proton–electron transfer process. For the reducing reagents nicotinamide[2] and the metal hydrides,[3] there is supporting evidence for the initial transfer of an electron during the reduction of aromatic carbonyls. However, for these reactions there is no direct evidence pertaining to the pathway of subsequent hydrogen atom transfer, as in most instances the initial electron transfer is rate limiting, and thus subsequent transformations are relatively fast and the intermediates difficult to detect. If the rate of the initial electron transfer could be enhanced so that it were no longer rate limiting, these subsequent intermediates might then be detectable. A method for accelerating charge transfer is the photoexcitation of the oxidant, resulting in a lowering of its reduction potential by the energy of its excited state,[4] a method recently employed in our study of the photochemical reduction of benzophenone by aromatic amines.[5] In this communication we examined the photoinduced hydride reduction of benzophenone (Bph) and fluorenone (Fl) by *N*-methylacridan (NMA)[6] in order to deter-

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