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GENERATION OF THE ENOLATE OF ACETALDEHYDE FROM NON-CARBONYL SUBSTANCES AND ITS C-ALKYLATION, O-ACYLATION AND O-SILYLATION

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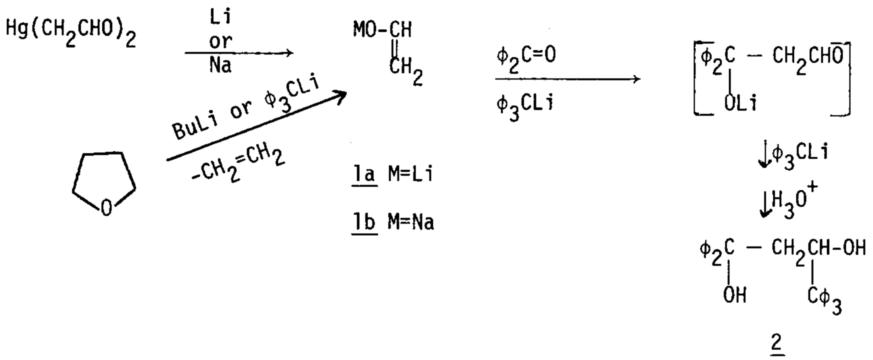
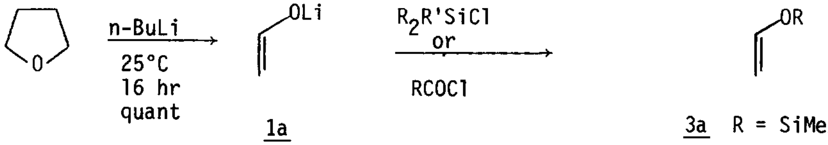
Reaction of the enolates of ketones and aldehydes with a variety of substrates (alkyl and acyl halides, α,β-unsaturated carbonyl compounds, Mannich bases, trialkylsilyl halides, and other compounds) has long been a cornerstone of synthetic organic chemistry.[1] However, this extensive store of reactions cannot be utilized with the enolates of reactive aldehydes (in particular acetaldehyde the simplest carbonyl compound having α-protons) due to facile base-catalyzed polymerization of the starting material and/or products. For these reasons, various indirect methods have been developed for the alkylation of aldehydes, e.g., enamines[2] and imine anions.[3] However, these techniques have never been successfully extended to the alkylation of acetaldehyde. We report now a solution to th theoretical problem, namely experiments which have resulted in improved procedures for the generati of the lithium enolate of acetaldehyde and its O-acylation and O-silylation and a new technique for the C-alkylation of acetaldehyde via its tributyltin enolate.

Several years ago, Nesmeyanov and co-workers prepared the lithium and sodium enolates of aceta dehyde 1ab by reduction of the readily available α-mercurio aldehyde with the respective alkali metals.[4] However, these workers claimed that these compounds 1ab were incapable of clean reaction with various substrates including alkyl and acyl halides.[4] Later, Bates[5] showed that the lithium enolate of acetaldehyde 1a could be formed from treatment of tetrahydrofuran (THF) with n-butyllithium, ethylene being the only other by-product. However, no study of the reactivity of 1a was undertaken. Finally Tomboullian and co-workers reported the generation of 1a from THF by treatment with excess n-butyllithium and trityl lithium and its *in situ* trapping with benzophenone to afford the pentaphenyl diol 2.[6]



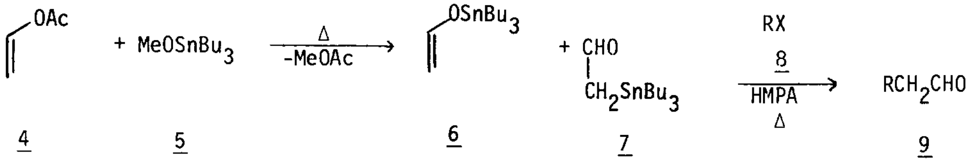
We have found that reaction of n-butyllithium with THF at 25°C for 16 hr under a nitrogen atmosphere affords the desired lithium enolate of acetaldehyde 1a in essentially quantitative yield based on the alkyllithium. Silylation and O-acylation of this enolate could be easily accomplished. Addition of tert-butyldimethylsilyl chloride afforded the silyl enol ether 3a in excellent yield. Due to the small difference in boiling points between THF and trimethylvinyloxysilane 3b, it was more convenient to remove all of the THF from the solution of the enolate 1a, add diglyme and then the silyl chloride, to afford after workup a good yield of the silyl enol ether 3b. In order to effect O-acylation, it was necessary to add a solution of the enolate 1a in THF to 3 equiv. of benzc chloride or pivaloyl chloride at 25°C in 1:1 THF hexamethylphosporic triamide (HMPA) followed by stirring for 5 hr, which furnished excellent yields of the enol esters 3cd.



		Yield (%)
3a	R = $SiMe_2$t-Bu	77
3b	R = $SiMe_3$	83
3c	R = COϕ	80
3d	R = COt-Bu	83

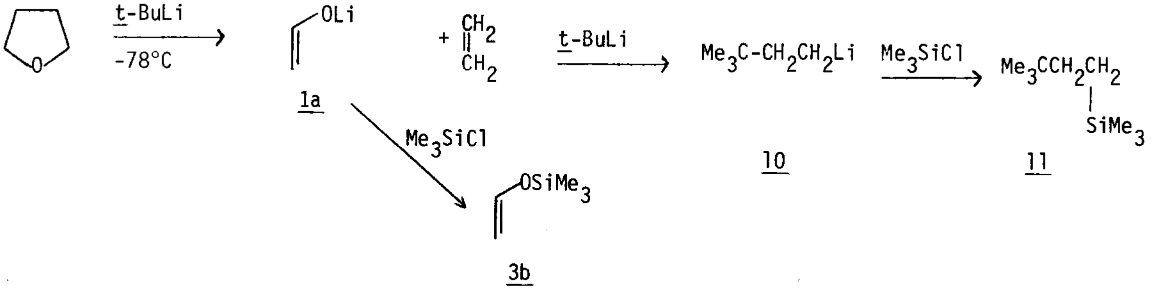
Attempted C-alkylation of the lithium enolate 1a afforded mainly polymeric material under nearl all experimental conditions. However by the use of the tributyltin enolate 6 (and its C-stannylatec isomer 7), C-alkylation could be successfully accomplished.[7] Pereyre, Valade, and co-workers have reported that 6 could not be prepared by the usual procedure of reacting vinyl acetate 4 with methoxytributylstannane 5,[8] echoing similar statements of Nesmeyanov and his associates.[9] However we have found that under carefully controlled conditions[10] one can prepare a 2.5:1 mixture of tributylvinyloxystannane 6 and α-tributylstannylacetaldehyde 7 in quantitative yield from 4 and 5.[11]

Heating a solution of 6 and 7 with an alkyl halide 8a-d in HMPA in a sealed tube at 110°C (75°C for 8a) for 10 min (for 8ab), 30 min (for 8d) or 1 hr (for 8c) affords fair to good yields of the C-alkylation products 9a-d.[12] Thus this method permits the C-alkylation of the simplest carbonyl compound with α-protons.



	Yield
a R = Me	61
b R = Et	40
c R = $PhCH_2$	68
d R = $CH_2{=}CHCH_2$	41

In addition to trapping the lithium enolate of acetaldehyde from the decomposition of THF with alkyllithium, we have also successfully trapped the ethylene by-product. When a solution of excess trimethylchlorosilane in THF was treated at -78°C with 2 eq of tert-butyllithium, several products were obtained, two of which were clearly identified (NMR, IR, MS) as the silyl enol ether 3b and trimethyl 4,4-dimethylbutylsilane 11.[13] Thus the ethylene generated from the THF was trapped by tert-butyllithium to give the primary anion 10 which was then silylated. This is the first example of the trapping of ethylene from THF.



The techniques described herein should now allow synthetic chemists to use acetaldehyde in a large variety of alkylation and acylation reactions.

References and Notes

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10. A solution of the methoxystannane *5* in excess vinyl acetate *4* is stirred under reduced pressure at 25°C to remove methyl acetate as it is formed. When the removal of methyl acetate is comple the excess vinyl acetate is evaporated at 25°C under reduced pressure to leave a mixture of *6* and *7*. It is absolutely necessary that the reagents are scrupulously dried and that the reactio be carried out under an inert atmosphere. Compounds *6* and *7* could not be formed cleanly by the trapping of the lithium enolate *1a* with tributyltin chloride.
11. Spectral data for the mixture of *6* and *7*: NMR (CDCl$_3$) δ:9.27 (t, J = 5.5 Hz), 6.37 (dd, J = 7 Hz), 3.4 (m, J = 7 Hz), 2.05 (d, J = 5.5 Hz), 1.75-0.55 (m, Bu$_3$Sn) IR (liquid film) cm^{-1}: 2950, 1695, 1675, 1625, 1470, 1375, 1200.
12. Yields were determined by gas chromatographic (gc) analysis of the crude reaction mixtures utilizing three columns: a 9' x 18" 20% Carbowax 20M on 60-80 mesh Chromosorb W (for *9a*), a 6' x 1/8" 20% AgNO$_3$/benzyl cyanide on 100-120 mesh Chromosorb W (for *9b*), and a 6' x 1/8" SE-30 on 60-80 mesh Chromosorb W (for *9cd*). The internal standards used were: for *9a*: THF; for *9b*, heptane; for *9c*, toluene; and for *9d*, 1-octene. The alkylated products were identified by their gc retention times and mass spectral analysis.
13. Spectral data for *11*: NMR (CDCl$_3$) δ:1.2 (m, 2H), 0.98 (s, 9H), 0.4 (m, 2H), 0.05 (s, 9H); IR: (liquid film) cm^{-1}: 2850, 1500, 1385, 1275, 1170. MS (M$^+$, 70ev) 158, 143, 101, 74, 73, 59.