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CONJUGATE ADDITION OF N-SUBSTITUTED ORGANO(SILYLIMINOMETHYL)COPPER(I) TO α,β-UNSATURATED CARBONYL COMPOUNDS

Masahiro Murakami, Takaharu Matsuura and Yoshihiko Ito*
Department of Synthetic Chemistry, Kyoto University,
Yoshida, Kyoto 606, Japan

Summary: The organocopper reagent prepared from [(2,6-xylylimino)-(trialkylsilyl)methyl]lithium undergoes the conjugate addition to α,β-unsaturated carbonyl compounds to produce γ-(2,6-xylylimino)-γ-(trialkylsilyl)carbonyl compounds or the organosilyl ethers of their enols.

Nucleophilic introduction of acyl groups in organic synthesis has been often achieved by use of synthetic equivalents of acyl anions. Although acylmetals may be potentially useful for this purpose, synthetic application of acylmetals has been so far limited,$^{1)}$ probably due to unavailability and instability of acylmetals. Recently, we reported that [(2,6-xylylimino)-(trialkylsilyl)methyl]lithium (2) generated in situ by transmetallation of [(2,6-xylylimino)(trialkylsilyl)methyl]trialkylstannane (1) is able to react with electrophiles as a synthetic equivalent of organosilylcarbonyl anion and carbonyl dianion.$^{2)}$ The reactions with 2 have provided a new access to organosilylimine derivatives. Herein, we wish to report the conjugate addition of organocopper reagents derived by transmetallation of 1 via 2 to α,β-unsaturated carbonyl compounds.

[(2,6-Xylylimino)(trialkylsilyl)methyl]lithium (2) generated in situ in THF at -78°C reacted with 2-cyclohexenone to give only 1,2-adduct, 3-[(2,6-xylylimino)methyl]-3-(trialkylsilyloxy)-1-cyclohexene (3),$^{3)}$ after hydrolysis, in a moderate yield. In contrast, the reactions of [(2,6-xylylimino)-(trialkylsilyl)methyl]copper reagents (4) derived from 2 with 2-cyclohexenone produced the conjugate addition products (6 or 7) under various reaction conditions (Runs 1-5 of Table). [(2,6-Xylylimino)(trialkylsilyl)methyl]copper reagent (**4i**) prepared from 2 and copper(I) bromide dimethylsulfide was rather unreactive and did not afford the conjugate addition product with 2-cyclohexenone. However, Lewis acid and chlorotrialkylsilane efficiently promoted the conjugate addition, giving 3-[(2,6-xylylimino)(trialkylsilyl)methyl]-cyclohexanone (**6i**) and trialkylsilyl ether (**7i**) of its enol, respectively, in 30% and 46% yields (Runs 1,2). The use of a mixed cuprate (**4ii**) prepared from 2 and copper(I) acetylide remarkably improved the conjugate addition, i.e. **6i** was obtained in 83% yield without any additive, and the respective trialkylsilyl enol ethers [**7i** (75%) and **7ii** (68%)] were obtained in the presence of chlorotrialkylsilanes.

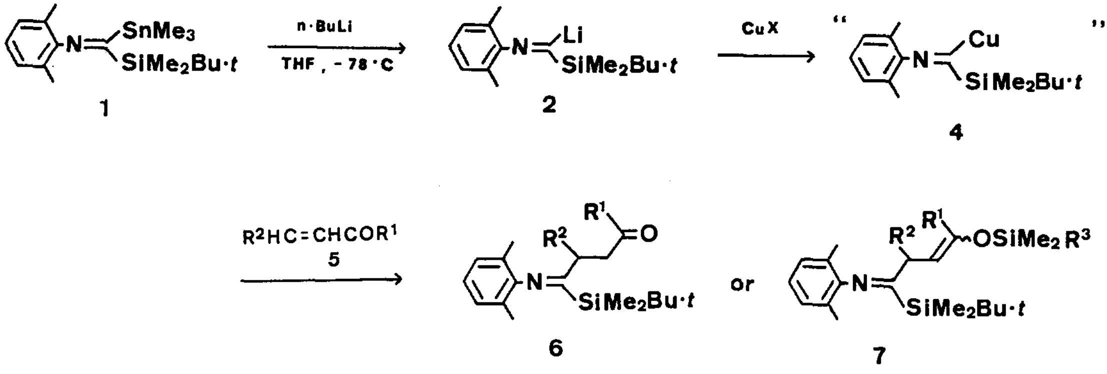
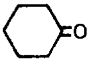
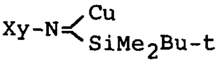
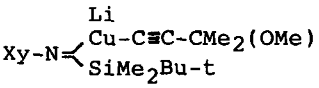
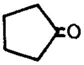
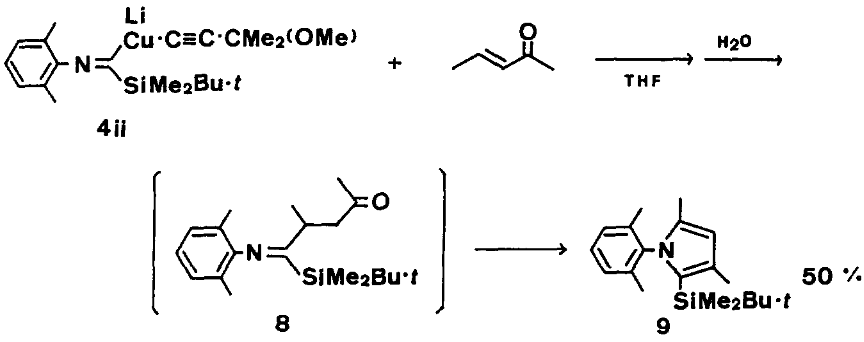


Table.

Run	5	4a)	Additive	Product	Yield(%)
1		 $\mathrm{Xy\text{-}N{=}}{<}^{\mathrm{Cu}}_{\mathrm{SiMe_2Bu\text{-}t}}$ 4i	$BF_3 \cdot OEt_2$	6i	30
2		4i	Me_3SiCl-HMPA	7i (R^3=Me)	46
3		 $\mathrm{Xy\text{-}N{=}}{<}^{\overset{\mathrm{Li}}{\mathrm{Cu\text{-}C{\equiv}C\text{-}CMe_2(OMe)}}}_{\mathrm{SiMe_2Bu\text{-}t}}$ 4ii	—	6i	83
4		4ii	Me_3SiCl-Et_3N	7i (R^3=Me)	75
5		4ii	t-$BuMe_2SiCl$-HMPA	7ii (R^3=t-Bu)	68
6		4i	$BF_3 \cdot OEt_2$	6ii	56
7		4ii	—	6ii	30
8	MeCH=CHCOMe	4ii	t-$BuMe_2SiCl$-HMPA	7ii (R^3=t-Bu)	74
9	MeCH=CHCHO	4ii	t-$BuMe_2SiCl$-Et_3N	7iv (R^3=t-Bu)	70
10	CH_2=CHCHO	4ii	t-$BuMe_2SiCl$-Et_3N	7v (R^3=t-Bu)	70

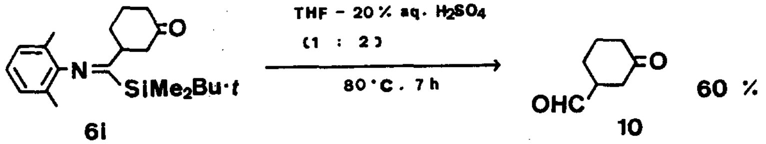
a) The organocopper reagents (4i and 4ii) were prepared in situ by addition of a THF-dimethylsulfide (1:1) solution of copper(I) bromide dimethylsulfide (1.0 equiv) and a THF solution of copper(I) acetylide[4)] (1.1 equiv), respectively, to a THF solution of 2 at -78°C, and stirring the mixture at the same temperature. Xy- = 2,6-xylyl.

The conjugate additions of [(2,6-xylylimino)(trialkylsilyl)methyl]copper reagents (**4**) with some other α,β-unsaturated carbonyl compounds are shown in Runs 6-10. The reaction of 2-cyclopentenone with organocopper reagents (**4**) was still unsatisfactory. With the mixed cuprate (**4ii**) in the presence of chlorotrialkylsilane, 2-cyclopentenone gave the corresponding silyl enol ether of the conjugate addition product in low yield. On the other hand, acyclic α,β-unsaturated ketones and aldehydes including acrolein furnished good yields of the corresponding conjugate addition products with the mixed cuprate (**4ii**) in the presence of chlorotrialkylsilane (Runs 8-10). Of interest is that the similar treatment of organocopper (**4ii**) with acyclic α,β-unsaturated carbonyl compounds in the absence of chlorotrialkylsilane resulted in the formation of pyrrole derivative **9**, as exemplified with 3-penten-2-one. The formation of **9** may have arisen from cyclization of the conjugate addition product (**8**) after aqueous workup.



Typical experimental procedure for the synthesis of the conjugate addition product (**5**) is as follows: To a stirred THF solution (0.5 ml) of 3-methoxy-3-methylbut-1-yne (125 mg, 1.27 mmol) was added a hexane solution of n-butyllithium (0.92 ml, 1.28 mmol) at 0°C under nitrogen. The resulting pale yellow solution was added to a suspension of copper(I) iodide in THF (0.5 ml) at 0°C to give dark brown solution, which was then transfered to a THF solution of [(2,6-xylylimino)(tert-butyldimethylsilyl)methyl]lithium prepared from **1** (473 mg, 1.15 mmol) as previously reported,2b) at -78°C. After stirring for 40 min, 2-cyclohexenone (77 mg, 0.80 mmol) was added at that temperature, and the mixture was warmed to room temperature over about 3 h. Extractive workup with ether and subsequent TLC on silica gel gave 6i (228 mg, 83%). Analytical sample was prepared by Kugelrohr distillation; b.p. 200°C (pot temperature, 0.4 mmHg). IR (neat) 1716, 1612, 1592 cm^{-1}; ^{1}H NMR (CDCl$_3$, cyclohexane as an internal standard) δ -0.31∿0.36 (6H, br), 1.00 (9H, s), 1.19∿3.05 (9H, br), 1.99 (3H, s), 2.00 (3H, s), 6.70∿7.05 (3H, br); MS m/z 343 (M$^+$), 246 (M - 3-oxocyclohexyl). Anal. (%) Calcd for $C_{21}H_{33}NOSi$: C, 73.41; H, 9.68; N, 4.08. Found: C, 73.20; H, 9.59; N, 4.03.

The 1,4-addition product (6i) thus obtained was hydrolyzed to γ-oxo-aldehyde (10) by treatment with aqueous sulfuric acid.[5)]



Extensions of the present methodology are now in progress in our laboratory.

References and Notes.

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(b) Y. Ito, T. Matsuura, and M. Murakami, J. Am. Chem. Soc., in press.

3) 3: bp 160°C (pot temperature by Kugelrohr distillation, 0.1 mmHg). IR (neat) 1668, 1596 cm^{-1}. ^{1}H NMR ($CDCl_3$, cyclohexane as an internal standard) δ 0.11 (6H, s), 0.87 (9H, s), 1.70∿2.24 (6H, br), 2.07 (6H, s), 5.70∿6.26 (2H, br), 6.75∿7.10 (3H, br), 7.59 (1H, s). MS m/z 343 (M^+), 286 (M - t-Bu), 211.

4) E. J. Corey, D. Floyd, and B. H. Lipshutz, J. Org. Chem., 43, 3418 (1978).

5) All attempts to hydrolyze 6 to the corresponding γ-oxoacylsilane have so far failed.

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