J. Am. Chem. Soc. **1993,** *115,* 3362-3363

Carbometalation of Ketone Enolates with 1-Alkynes: An Alkylidenation Reaction of Silyl Enol Ethers Promoted by $SnCl_4$–Bu_3N Reagent

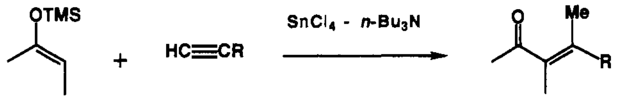
Masahiko Yamaguchi,* Akio Hayashi, and Masahiro Hirama

Department of Chemistry, Faculty of Science
Tohoku University, Aoba, Sendai 980, Japan

Received October 30, 1992

Carbometalation of enolate derivatives with alkynes is a straightforward method of synthesizing unsaturated carbonyl compounds. Only a quite limited number of metal enolates derived from simple carboxylic acid derivatives, however, have been known to possess this property.[1-3] Recently, we found an alkylidenation reaction of silyl enol ethers with 1-alkynes in the presence of $SnCl_4$ and Bu_3N. The transformation involves an interaction of *in situ* generated α-trichlorostannyl ketones with alkynylchlorotins and gives conjugated (*E*)-enones stereoselectively. This is the first intermolecular carbometalation of a ketone enolate derivative with 1-alkynes.[4,5] Use of silyl enol ethers as the enolate component, a variety of which are available,[6] and use of the readily available promoters are the practical aspects of this reaction.

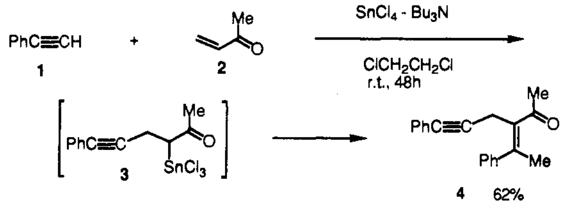
Scheme I



When 1.5 equiv of silyl enol ethers were treated with 1-alkynes (1 equiv) in the presence of $SnCl_4$ (2.5 equiv) and Bu_3N (1 equiv) under a refluxing acetonitrile–dichloroethane (4:1) condition, conjugated enones were obtained in high yields (Scheme I, Table I).[7] Use of the mixed solvent system gave better results than dichloroethane or acetonitrile alone. Several types of silyl enol ethers reacted with aliphatic and aromatic alkynes regioselectively at the internal carbon. As shown by the reactions of 4-phenyl-2-butanone silyl enol ethers (entries 8 and 9), silyl transposition did not take place. Notably, all these trisubstituted and tetrasubstituted enones possessed (*E*)-double bonds as determined by NOE studies. The stereochemistry of the products was not affected by that of the starting silyl enol ethers (entries 1–8). Thus, a stereoselective synthesis of tetraalkyl-substituted olefins is achieved with a concomitant carbon–carbon double bond formation from two distinct functionalities.[8]

The reaction proceeds via α-trichlorostannyl ketones. Transmetalation of silyl enol ethers and $SnCl_4$ to α-stannyl ketones has been reported.[9] Furthermore, the following experiment supports their intermediacy (Scheme II). When 3-buten-2-one (**2**) was treated with phenylacetylene (**1**) in the presence of $SnCl_4$ and Bu_3N, an (*E*)-enone (**4**) was obtained. Since 1-alkynes undergo 1,4-addition to conjugated enones with these reagents,[10] **4** must be formed by an interaction between an *in situ* generated α-stannyl ketone (**3**) and **1**.

Scheme II



1-Alkynes are activated as alkynylchlorotins. We have previously shown the formation of the organotin compounds in the reagent system of 1-alkyne–$SnCl_4$–Bu_3N.[10] A mixture of alkynyltributyltin and $SnCl_4$, an alternative system to generate the alkynylmetal, could also be used in the present alkylidenation reaction.[11] Disubstituted alkynes such as 1-phenyl-1-hexyne or (trimethylsilyl)phenylacetylene did not react.

Scheme III illustrates a proposed mechanism of a reaction for a diethyl ketone silyl enol ether (**5**) and **1**. It involves the carbometalation of an α-stannyl ketone (**6**) with an alkynyltin (**7**), the protonation of a dimetalated intermediate (**8**), and the double bond shift to an allylmetal species (**9**). Spectroscopic studies and further chemical transformations showed the formation of **9**. Quenching the reaction with D_2O gave monodeuterated α,β-enone **10** and β,γ-enone **11**, whereas an isomeric mixture of ((trimethylsilyl)oxy)butadienes **12** was obtained by treating with excess diethylzinc. A trace of the reaction by NMR also exhibited the first formed intermediate **8**[12] and its conversion to **9**. ^1H NMR (CD_2Cl_2, 600 MHz): δ 2.02 (3 H, t, $J = 1.1$ Hz, $CH_3C{=}$), 3.38 (2 H, q, $^5J(H\text{–}H) = 1.1$ Hz, $^2J(H\text{–}^{117}Sn) = 154$ Hz, $^2J(H\text{–}^{119}Sn) = 162$ Hz, $SnCH_2$). ^{13}C NMR (CD_2Cl_2, 150 MHz): δ 18.1 ($CH_3C{=}$), 45.9 ($^1J(^{13}C\text{–}^{117}Sn) = 733$ Hz, $^1J(^{13}C\text{–}^{119}Sn) = 767$ Hz, $SnCH_2$), 128.4 ($CH_2C{=}$), 155.7 ($CH_3C{=}$). Thus, the (*E*)-enone **10** is the product of direct protonation of

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[1] Rhenium enolates of an acetate, a propionate, and an acetamide were reported to react with 1-alkynes at the terminal carbon. Use of the noble metal enolate, however, does not seem to be convenient from the synthetic point of view: Stack, J. G.; Simpson, R. D.; Hollander, F. J.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1990**, *112*, 2716.

[2] α-Vinylacetonitriles were obtained from α-alkylphenylacetonitriles and certain 1-alkynes under phase-transfer conditions. A simple aliphatic 1-alkyne was reported not to react: Makosza, M. *Tetrahedron Lett.* **1966**, 5489. Makosza, M.; Czyzewski, J.; Jawdosiuk, M. *Org. Synth.* **1988**, *Collect. Vol. 6*, 940. Ehrhardt, H.; Mildenberger, H. *Liebigs Ann. Chem.* **1982**, 989.

[3] Zinc derivatives of malonates and cyanoacetates added to the internal carbon of 1-alkynes. The reaction, however, was not applied to ketone enolates: Seefelder, M. *Liebigs Ann. Chem.* **1962**, *652*, 107. Schulte, K. E.; Rücker, G.; Feldkamp, J. *Chem. Ber.* **1972**, *105*, 24. Bertrand, M. T.; Courtois, G.; Miginiac, L. *Tetrahedron Lett.* **1974**, 1945; *Ibid.* **1975**, 3147; *C. R. Acad. Sci. Paris, Sér. C* **1975**, *280*, 999. Several active methylene compounds were added to phenylacetylene in the presence of $HgSO_4$: Komarov, N. V.; Yurchenko, O. I.; Dybova, T. N. *J. Org. Chem. USSR* **1983**, *19*, 401.

[4] An intramolecular reaction of acetylenic silyl enol ethers in the presence of $HgCl_2$ is known: Drouin, J.; Boaventura, M.-A.; Conia, J.-M. *J. Am. Chem. Soc.* **1985**, *107*, 1726.

[5] Reactions of enolates with alkynes possessing strong electron-withdrawing groups are, of course, well-known. For examples of silyl enol ethers: Clark, R. D.; Untch, K. G. *J. Org. Chem.* **1979**, *44*, 248, 253. Kelly, T. R.; Ghoshal, M. *J. Am. Chem. Soc.* **1985**, *107*, 3879.

[6] Reviews: Poirier, J.-M. *Org. Prep. Proc. Int.* **1988**, *20*, 317. Brownbridge, P. *Synthesis* **1983**, 1 and 85.

[7] The following typifies the procedure: under an argon atmosphere, phenylacetylene (202 mg, 2.0 mmol) and Bu_3N (0.48 mL, 2.0 mmol) in CH_3CN (3 mL) was added to an CH_3CN (5 mL) solution of $SnCl_4$ (0.23 mL, 2.09 mmol) in flask A, and the mixture was stirred for 10 min at room temperature. A solution of $SnCl_4$ (0.35 mL, 3.0 mmol) and cycloheptanone trimethylsilyl enol ether (546 mg, 3.0 mmol) in $ClCH_2CH_2Cl$ (2 mL) was prepared in flask B and stirred for 15 min at room temperature. The contents of flask B were then transferred to flask A. The mixture was stirred at reflux for 1 h and poured over ice-cold saturated aqueous $NaHCO_3$. The enone (323 mg, 76%) was obtained by a standard workup.

[8] Recent syntheses of tetrasubstituted olefins involving stereospecific *syn*-addition to carbon–carbon triple bonds: Negishi, E.; Zhang, Y.; Cederbaum, F. E.; Webb, M. B. *J. Org. Chem.* **1986**, *51*, 4080. Piers, E.; Skerlj, R. T. *Ibid.* **1987**, *52*, 4421. Zweifel, G.; Leong, W. *J. Am. Chem. Soc.* **1987**, *109*, 6409. Examples involving stereoselective addition reaction to 1,3-dienes: Shibasaki, M.; Sodeoka, M. *Tetrahedron Lett.* **1985**, *26*, 3491. *Anti*-elimination of nitrosulfones was reported to give tetrasubstituted olefins stereospecifically. However, the precursor diastereomers need to be separated: Ono, N.; Kamimura, A.; Kaji, A. *J. Org. Chem.* **1987**, *52*, 5111.

[9] Nakamura, E.; Kuwajima, I. *Chem. Lett.* **1983**, 59.

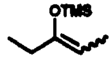
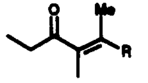
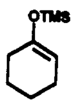
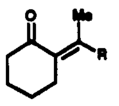
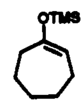
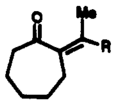
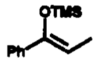
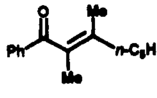
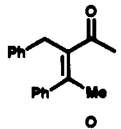
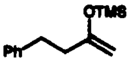
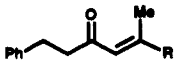
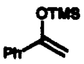
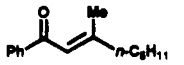
[10] Yamaguchi, M.; Hayashi, A.; Hirama, M. *Chem. Lett.* **1992**, 2479.

[11] Bis-stannylated **8** was detected by ^1H-NMR and ^{13}C-NMR spectroscopy of this reaction mixture. Furthermore, when the reaction was quenched with D_2O, a mixture of deuterated enones was obtained which contained (*E*)-6,6-dideuterio-4-methyl-5-phenyl-4-hexen-3-one. ^{13}C NMR ($CDCl_3$): δ 21.8 (quintet, $^1J(D\text{–}^{13}C) = 20$ Hz, $CHD_2C{=}$).

[12] ^1H NMR (CD_2Cl_2, 600 MHz): δ 1.61 (3 H, t, $J = 7.5$ Hz, CH_3CH), 4.36 (1 H, q, $J = 7.5$ Hz, CH_3CH). ^{13}C NMR (CD_2Cl_2, 150 MHz): δ 20.3 (CH_3CH), 52.1 ($^3J(^{13}C\text{–}^{117}Sn) = 84, 123$ Hz, $^3J(^{13}C\text{–}^{119}Sn) = 84, 129$ Hz, CH_3CH), 176.4 ($CHC{=}$). The presence of two $^{13}C\text{–}^{117}$ or $\text{–}^{119}Sn$ couplings suggests the formation of the bis-stannylated intermediate **8**.

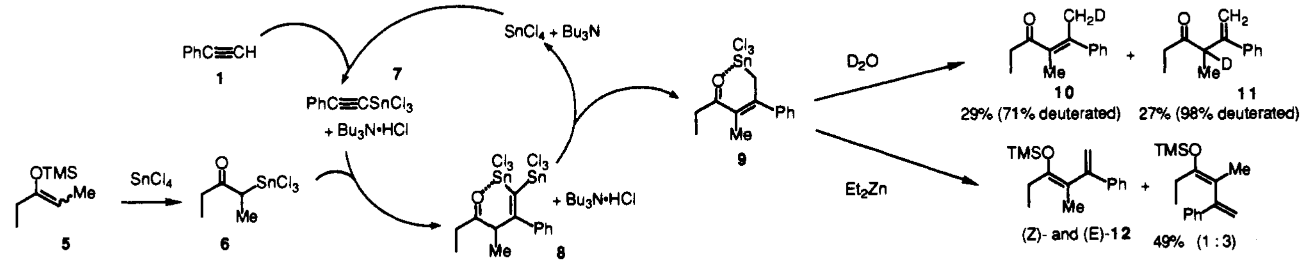
0002-7863/93/1515-3362$04.00/0

Table I. Carbon-Carbon Bond Formation Reaction of Silyl Enol Ethers and 1-Alkynes Promoted by $SnCl_4$ and Bu_3N

entry	silyl enol ether	R	product	yield/%[a]	(*E*):(*Z*)[b]
1[c]		Ph		85[d]	20:1
2[c]		*n*-C_5H_{11}		75	>20:1
3		Ph		63	>20:1
4		$PhCH_2CH_2$		58	18:1
5		Ph		76	>20:1
6		*n*-C_5H_{11}		77	>20:1
7[e]		*n*-C_5H_{11}		72	20:1
8[f]		Ph		64[g]	>20:1
9		Ph		63	>20:1
10		*m*-$MeOC_6H_4$		71	20:1
11		*n*-C_5H_{11}		70	19:1
12		*n*-C_5H_{11}		68	>20:1

[a] Isolated yields are shown. Satisfactory spectroscopic data (^1H NMR, ^{13}C NMR, IR, and MS) as well as elemental analysis either by HRMS or combustion were obtained. A very small amount (<20:1) of the β:γ-isomer was detected by ^1H NMR unless otherwise noted. [b] Determined by ^1H NMR. Authentic (*Z*)-isomers were obtained by the photochemical or thermal isomerization of the above products. [c] A mixture of (*E*)- and (*Z*)-isomers (1:1.9) was used. [d] The ratio of the α:β- and β:γ-isomer was 18:1. [e] (*Z*)-Isomer was used. [f] A mixture of (*Z*)-, (*E*)-4-phenyl-2-((trimethylsilyl)oxy)-2-butene, and 4-phenyl-2-((trimethylsilyl)oxy)-1-butene (65:22:13) was used. [g] A 7:1 mixture of this compound and the product of the reaction of entry 9.

Scheme III



(*Z*)-allylmetal **9**.[13] It should also be noted that this mechanism involves a catalytic activation of the alkyne **1**. In accordance with the proposal, a reaction of **1**, **5**, $SnCl_4$, and Bu_3N in a molar ratio of 1:1.5:1.5:0.2 gave the product in 75% yield. A catalytic amount of the amine efficiently promoted the reaction.

In summary, silyl enol ethers reacted with 1-alkynes in the presence of $SnCl_4$ and Bu_3N, giving conjugated (*E*)-enones stereoselectively. Alkynyltins are shown to be highly reactive toward the carbometalation with α-stannyl ketones. Studies are now under way on the novel chemical properties of these carbon-carbon triple bonds.

Acknowledgment. This work was supported by grants from the Ministry of Education, Science and Culture, Japan (Nos. 01649515 and 04554018).

Supplementary Material Available: Structures, experimental details, and spectroscopic data for the compounds discussed in this work (7 pages). Ordering information is given on any current masthead page.

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[13] A NOE was observed between phenyl protons and vinylic methyl protons of **9**.