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TRIALKYLSILYL TRIFLATE PROMOTED CONJUGATE ADDITION OF ALKYNYLZINC COMPOUNDS TO α,β-ENONES

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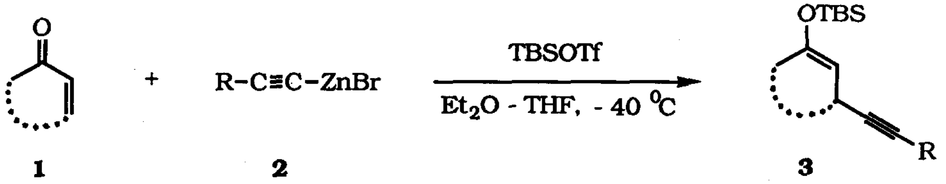
Summary: Trialkylsilyl triflate promotes conjugate addition of alkynylzinc compounds to α,β-enones to afford γ,δ-acetylenic silyl enol ethers.

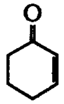
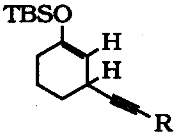
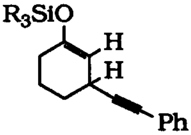
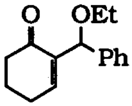
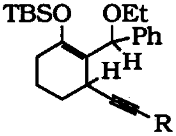
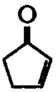
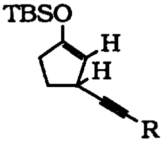
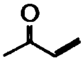
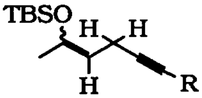
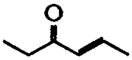
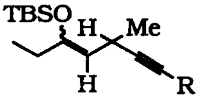
Conjugate addition of organometallics to α,β-enones is one of the most useful and reliable method for carbon-carbon bond formation.[1] Unlike facile 1,4- addition of alkyl and alkenyl groups with organocuprates[2] and organozinc compounds[3], conjugate alkynylation of α,β-enones is rather difficult to achieve.[4] Among several methods available,[5] nickel-catalyzed conjugate addition of organoaluminum acetylides to α,β-enones seems to be the most effective and reliable.[6] We wish to report that trialkylsilyl triflate[7] promotes conjugate addition of alkynylzinc compounds to α,β-enones to afford γ,δ-acetylenic silyl enol ethers.



Alkynylzinc compounds **2** did not react with α,β-enones **1** at room temperature. However, conjugate addition of the alkynylzinc compounds to α,β-enones proceeded cleanly and rapidly in the presence of t-butyldimethylsilyl triflate (TBSOTf) at -40 °C. Furthermore, other trialkylsilyl triflates such as trimethylsilyl triflate (TMSOTf) and triisopropylsilyl triflate (TIPSOTf) could be employed to effect the present reaction, although trimethylsilyl chloride turned out to be totally ineffective. Thus, the present method is based on (i) an initial strong complexation of carbonyl group by trialkylsilyl triflate[8] and (ii) preferential 1,4-addition of alkynyl group to α,β-enones. It is noteworthy that the reaction of alkynylzinc compounds with highly reactive trialkylsilyl triflates did not take place under the present conditions.

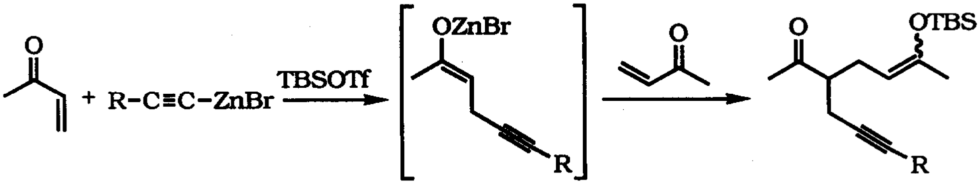
Table shows some of our experimental results and illustrates the efficiency and scope of the present method.[9] Several noteworthy features are apparent from the results. First, the method can be applied to both s-cis and s-trans enones. Second, the yields are

Table. Conjugate Addition of Alkynylzinc Bromides to α,β–Enones

α,β -Enones	Product		R	Yield(%) [a]
		**3a** :	Ph	96
		3b	n-Bu	79
		3c	Me_3Si	70
		**3d**	Me	77
		3e	i-Pr	74
		**3f**	Ph	92[b]
		**3g**	Ph	78
		3h	n-Bu	77
		**3i**	Ph	67[c,d]
		3j	n-Bu	60[c,e]
		**3k**	Ph	83[f]
		3l	Me_3Si	54[f]

[a] The yields refer to isolated products based on α,β–enones. ^{1}H-NMR spectral data of vinyl and/or allyl protons indicated in Table are shown in ref. 16. [b] a mixture of diastereoisomers(7 : 3). [c] a mixture of E : Z (2 : 1) isomer. [d] **5a** was isolated in 15 % yield. [e] **5b** was isolated in 16 % yield. [f] a mixture of E : Z (4 : 1) isomer.

consistently high for β-monosubstituted α,β-enones. However, reaction with β-unsubstituted enones like methyl vinyl ketone afforded a byproduct **5**[10] to some extent, which would be formed by further conjugate addition of the enolate **4**, derived from conjugate addition of alkynylzinc compound to methyl vinyl ketone.[11] Furthermore, the present method is unsuccessful with β-disubstituted enones, yielding a mixture of 1,2- and 1,4-addition product along with the starting material as a major product. Thus, reaction of isophorone with PhC≡C–ZnBr and TBSOTf gave 60% of the starting material along with 1,2- and 1,4-addition product in 15% and 14% yield, respectively. Third, conjugate addition products **3** bearing silyl enol ether group can be further α-functionalized.[12] Finally, optimal yields of conjugate addition products are obtained with 1.25 equiv of alkynylzinc bromides and 1.25 equiv of TBSOTf for each mole of α,β-enones.[13] The use of ether and tetrahydrofuran as mixed solvent seems to be beneficial for optimal yields.[14]



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5a : R= Ph
5b : R= n-Bu

A typical procedure is illustrated as follows. To a stirred solution of acetylene (2.5 mmol) in ether (5 mL) at -40 °C were added successively n-butyllithium (2.5 mmol) and zinc bromide (2.5 mL, 1.0M in THF)[15] and the reaction mixture was stirred at room temperature for 10 min. To a solution of alkynylzinc compound at -40 °C were added successively α,β-enone (2.0 mmol) and TBSOTf (2.5 mmol). After being stirred at -40 °C for 10 min, addition of saturated $NaHCO_3$ (5 mL) was then followed by dilution with ether (40 mL). The organic layer was washed with brine and dried. Removal of solvent and purification on silica gel gave the γ,δ-acetylenic silyl enol ether.[17]

References and Notes

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9. TBSOTf rather than TMSOTf was normally used due to better stability of the products.
10. Spectral data for **5a**: ^{1}H-NMR($CDCl_3$) δ 0.20(s, 6H), 1.00(s, 9H), 1.90(s, 3H), 2.27(s, 3H), 2.20-2.90(m, 3H), 2.62(s, 2H), 4.52(t, J=8 Hz, 1H), 7.32(s, 5H). ; IR(film) 1713, 2215 cm^{-1}, Mass (m/e) 356.
11. The use of 2 equiv of methyl vinyl ketone gave 36% of **5** along with 30% of conjugate addition product **3**. Apparently, **5** was not produced from **3** because no change was observed when additional 1 equiv of methyl vinyl ketone was further added to the reaction mixture. However, the exact structure of the intermediate species is unclear at this time.
12. Rasmussen, J. K. *Synthesis* **1977**, 91. Brownbridge, P. *Ibid.* **1983**, 1, 85. Magnus, P.; Mugrage, B. *J. Am. Chem. Soc.* **1990**, *112*, 462.
13. Alkynylzinc compounds were prepared by treatment of lithium acetylides with 1.0 equiv of zinc bromide in THF. Thus, it is belived that the solution consists of an equimolar mixture of alkynylzinc bromide and lithium bromide. Wilkinson, G.; Stone, F. G. A.; Abel, E. W. *Comprehensive Organometallic Chemistry* ; Vol. 2. p 825, Pergamon Press: **1982.**
14. Conjugate addition of $PhC{\equiv}C{-}ZnBr$ to 2-cyclohexen-1-one in THF gave the product in 85% yield. When the same reaction was carried out in ether, the yield was drastically decreased to 40%, apparently due to the insolubility of alkynylzinc bromide in ether.
15. Brown, D. S.; Ley, S. V. *Tetrahedron Lett.* **1983**, *29*, 4869.
16. ^{1}H-NMR spectra were taken in $CDCl_3$ and chemical shifts are expressed in ppm. **3a**: 4.84(d, J=3.7 Hz, 1H), 3.36-3.48(m, 1H). **3b**: 4.75(d, J=3.5 Hz, 1H), 2.95-3.12(m, 1H). **3c**: 4.79(d, J=3.6 Hz, 1H), 2.99-3.15(m, 1H). **3d**: 4.83(d, J=3.7 Hz, 1H), 3.36-3.49(m, 1H). **3e**: 4.82(d, J=3.7 Hz, 1H), 3.36-3.48(m, 1H). **3f**: 5.94(s, 0.7H), 5.91(s, 0.3H), 3.10-3.15(broad s, 1H). **3g**: 4.72(d, J=3.4 Hz, 1H), 3.68-3.80(m, 1H). **3h**: 4.65(d, J=3.3 Hz, 1H), 3.25-3.45(m, 1H). **3i**: 4.85(t, J=7.3 Hz, 0.66H), 4.65(t, J=8.0 Hz, 0.34H), 3.24(d, J=8.0 Hz, 0.7H), 3.14(d, J=7.3 Hz, 1.3H). **3j**: 4.76(t, J=7.2 Hz, 0.65H), 4.57(t, J=8.0 Hz, 0.35H), 2.65-2.90(m, 2H). **3k**: 4.72(d, J=19.4 Hz, 0.8H), 4.62(d, J=8.0 Hz, 0.2H), 3.37-3.52(m, 1H). **3l**: 4.65(d, J=20 Hz, 0.8H), 4.51(d, J=8.1 Hz, 0.2H), 3.00-3.31(m, 1H).
17. We gratefully acknowledge financial support from KOSEF and OCRC.

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