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Synthesis of Cyclopent-2-enones through Stepwise [3 + 2] Cycloaddition of Simple Silyl Enol Ethers and Alk-1-ynes

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Treatment of silvl enol ethers and alk-1-ynes with $SnCl_4$ -Bu₃N reagent followed by DBU, leads to cyclopent-2-enones, through [3 + 2] cycloaddition reactions; the initial carbon-carbon bond formation is carbometallation of alkynes, and the second step is a base-promoted intramolecular alkylation which reductively eliminates tin species (DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene).

[3 + 2] Cycloaddition of enolate derivatives with carboncarbon multiple bonds is an attractive method to construct cyclopentanone nuclei. During our investigations on activation of alk-1-ynes with SnCl₄-Bu₃N reagent,¹ we found a novel stepwise [3 + 2] cycloaddition of silvl enol ethers 1 and alk-1-ynes 2. This cyclopent-2-enone synthesis involves carbometallation of alkynes and subsequent intramolecular alkylation which reductively eliminates the tin species. When compared with related cycloaddition reactions using oxyallyl cations,²⁻⁴ the following synthetic aspects are characteristic; (i) This reaction employs simple silvl enol ethers instead of α -haloenolates for the three-carbon unit. (ii) Aliphatic and aromatic alk-1-ynes are used for the two-carbon unit, while the conventional reactions were conducted with olefins possessing cation-stabilizing groups, e.g styrenes, enamines, or dienes.

Silyl enol ethers 1 and alk-1-ynes 2 were treated with $SnCl_4$ and Bu_3N in refluxing MeCN for 1 h; DBU was then added, and refluxing continued for 30 min. As shown in Table 1,

 Table 1 [3 + 2] Cycloaddition reaction of silyl enol ethers and alk-1-ynes



^a Mixtures of (*E*)- and (*Z*)-isomers were used. ^b All the products gave satisfactory ¹H NMR, ¹³C NMR, IR and MS spectra and elemental analysis either by combustion or high resolution MS. ^c Isolated yields are shown.

cyclopent-2-enones 4 were obtained in good yields from the reaction of several alk-1-ynes and silyl enol ethers derived from methylene ketones.[†] A simple synthesis of bicyclo[9,2,1]tetradecenone derivatives is notable. Using Me₃CN as the solvent and the stepwise addition of the reagents gave good results. Higher yields are attained with triethylsilyl or *tert*-butyldimethylsilyl enol ethers compared with trimethylsilyl derivatives, which formed a substantial amount of enones 5 and other byproducts.

Previous studies have revealed that (Z)-allyltin **3** is formed from **1** and **2** in the presence of $SnCl_4$ and Bu_3N .¹ Accordingly, **4** must be the cyclization product of **3**, and the overall process can be envisaged as a stepwise [3 + 2] cycloaddition. The added amine is essential for the second carbon–carbon bond formation; the effects of other amine additives studied are shown in Table 2. Hindered and non-nucleophilic amines such as DBU, 1,8-bis(dimethylamino)naphthalene, Bu₃N, or 2,6di(*tert*-butyl)-4-methylpyridine are effective. It appears that basicity is not an important factor. Using chiral amines, (–)-brucine or (R)-N-(1-phenylethyl)pyrrolidine, lead to racemic cyclopentenones. Inorganic salts such as LiCl or KF also show some activity. It may be reasonable to assume that

OSiEt ₃ Me → PhCΞCH SnCl ₄ -Bu ₃ N	additive Me
Additive	Yield (%)
None	5
DBU	70
1,8-Bis(dimethylamino)naphthalene	56
Bu ₃ N	66
Pr ⁱ ₂ NH	61
(-)-Brucine	39
(R)-N-(1-Phenylethyl)pyrrolidine	58
N, N, N', N'-Tetramethylethylenediamine	5
Pyridine	11
2,6-Di(<i>tert</i> -butyl)-4-methylpyridine	$53(11)^{a}$
Bu ₃ P	12
Hexamethylphosphoramide	20
Me ₂ SO	14
LiCi	10
KF	26

^{*a*} Yield of a byproduct, 5-acetyl-2,5-dimethyl-3-phenylcyclopent-2enone, formed by acylation of the product with acetonitrile.

[†] Typical procedure: Under an argon atmosphere, 1 ($R^1 = Et$, $R^2 = Et$) (343 mg, 1.5 mmol) in MeCN (1.5 ml) was added to a MeCN (1.5 ml) solution of SnCl₄ (0.18 ml, 1.5 mmol) at room temp. After stirring for 15 min at room temp. 2 ($R^3 = Ph$) (102 mg, 1.0 mmol) in Me₃CN (1 ml) and Bu₃N (0.05 ml, 0.2 mmol) were added successively, and the mixture was stirred for 1 h under reflux. DBU (0.19 ml, 1.3 mmol) was then added, and refluxing was continued for 30 min. The mixture was poured on a saturated cooled NaHCO₃ (aq) and filtered. Organic materials were extracted with ethyl acetate, washed with KHSO₄ (aq) and brine, dried, concentrated, and chromatographed over alumina giving 4 ($R^1 = Et$, $R^2 = Et$, $R^3 = Ph$) (159 mg, 74%).

Table 2 Effects of additives



these additives promote enolization of 3, and intramolecular alkylation gives the cyclization products 4, where SnCl₃ functions as a leaving group^{5,6} liberating Sn¹¹ species.⁷ This reductive elimination redeems the use of the simple enolates in the present [3 + 2] cycloaddition instead of α -haloenolates. Takeda et al. have reported related reductive alkylation reactions with allyltins under Lewis acidic conditions,5 whereas here the alkylation is under basic conditions.

The following substituent effects on this cyclization reaction disclose some properties of the reductive leaving group. (i) Cyclopentenone was not obtained from silyl enol ether 1 (R¹ = H, R^2 = PhCH₂) and 2 (R^3 = Ph). Since 3 (R^1 = H, R^2 = PhCH₂, $R^3 = Ph$) is formed in a high yield by the carbometallation reaction,1 the unfavourable result is attributable to inefficiency at the cyclization process. The unsusceptibility of the methyl ketone to cyclization compared with methylene ketones is pertinent to the reactivity of the corresponding enolates.8 (ii) The reaction proceeds with aliphatic alkynes as well as aromatic alkynes, and β -substituents R³ of 3 do not have much effect on the cyclization. (iii) Allyltin 3 ($R^1 = PhCH_2$, $R^2 = H$, $R^3 = Ph$ or $n-C_5H_{11}$) generated from silvl enol ether 1 ($R^1 = PhCH_2, R^2 = H$) gives 4 ($R^1 = PhCH_2, R^2 = H, R^3 = Ph$ or $n-C_5H_{11}$) in low yields. Serious decomposition of 3 takes place on the base treatment. Removal of the γ -substituent R² inhibits the cyclization. The substituent effects (ii) and (iii) suggest some similarity of this reductive alkylation to nucleophilic substitution reactions of allyl halides.9,10

In summary, a stepwise [3 + 2] cycloaddition reaction of simple silvl enol ethers and alk-1-ynes gives cyclopent-2enones; the SnCl₃ group functions as a reductive leaving group in the base-promoted enolate alkylation reaction.

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