

Regioselective Allenylation of Carbonyl Compounds with Propargylic Organometallics

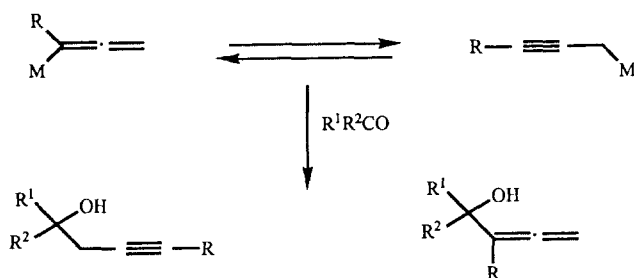
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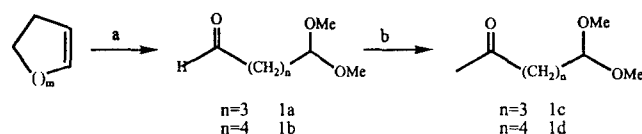
Regioselective synthesis of α -hydroxyallenes has great synthetic value, because they are used for the extension of carbon chain and the conversion of functionality (Patai, 1980; Okamura *et al.*, 1982; Zweifel, 1983; Marshall, 1990; Cha., 1992; Mayers *et al.*, 1993). Also, natural products such as antibiotics and pheromones have allenic linkage (Landor *et al.*, 1971). Their utility in organic synthesis has been limited due to the difficulties in controlling the regioselectivity of the reactions. The ambident anions, propargylic and allenic anions, may be equilibrated in solution (Patai, 1978), therefore in the condensation with aldehydes or ketones, two products, propargylic and allenic alcohols, can be formed (Scheme 1).



Scheme 1.

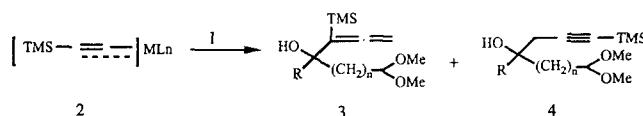
With the aim of elaboration to improve the regioselectivity for α -allenic alcohols, a variety of organometallics and solvents were investigated. We report herein the results of our research.

By the conventional method (Claus *et al.*, 1985), aldehyde **1a** and **1b** were prepared from ozonolysis of cyclopentene and cyclohexene, the **1c** and **1d** were synthesized in two steps (MeLi and PCC) from **1a** and



a) O_3 , MeOH ; p-TsOH ; $NaHCO_3$, DMS b) MeLi ; PCC

Scheme 2.



Scheme 3.

1b (Scheme 2).

The lithio ion generated from tert-butyllithium and 1-(trimethylsilyl) propyne at $-78^\circ C$ was treated with proper organometallics (titanium tetraisopropoxide, diethyl aluminum chloride) to afford metalated propargylic compounds **2**, which were reacted with aldehydes and ketones to give α -hydroxy allenes regioselectively.

A typical procedure for the reaction of **1** with **2** is as follows; To a stirred solution of metalated propargylic compounds **2** (1.71 mmol) at $-78^\circ C$ was slowly added dimethoxy carbonyl compounds **1** (1.14 mmol) in dry ether or THF (1 ml) under nitrogen atmosphere. The reaction mixture was stirred for 1-2 hr at $-78^\circ C$ and quenched with cold sat. ammonium chloride (5 ml). The mixture was poured into cold water (10 ml). The aqueous layer was extracted with ether (3×10 ml), and then the combined organic solution was dried over anhydrous $MgSO_4$ and concentrated. The products **3** and **4** were isolated by column chromatography. Compounds **3** and **4** were identified with IR, 1H -NMR, respectively.

Generally, the regioselectivity is dependent on the kind of metal ion. The lithium reagent showed the lowest regioselectivity (Table I) in a variety of metal ion investigated. The titanium and aluminum reagents exhibited excellent regioselectivity (Table II, III). A bulky size of the organometallic compounds probably

Table I. The regioselectivity of the reaction of lithiated anion with aldehyde or ketone

Entry	Solvent	3/4 Ratio	Yield (%)
1.	Ether	45 : 55	58
2.	Ether	33 : 64	53
3.	Ether	43 : 57	66

*This material was purchased from Janssen Chimica Co..

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Table II. The regioselectivity of the reaction of titanated anion with aldehyde or ketone

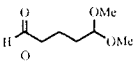
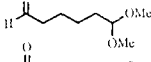
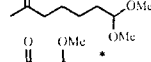
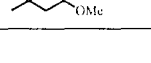
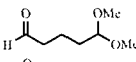
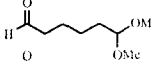
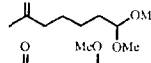
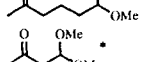
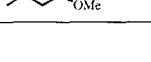
Entry	Solvent	3/4 Ratio	Yield (%)
1. 	Ether/THF	97 : 3/97 : 3	59/63
2. 	Ether/THF	99 : 1/97 : 3	40/67
3. 	Ether	43 : 57/94 : 6	70
4. 	Ether	80 : 20	65

Table III. The regioselectivity of the reaction of aluminated anion with aldehyde or ketone

Entry	Solvent	3/4 Ratio	Yield (%)
1. 	Ether/THF	84 : 16/94 : 6	58/66
2. 	Ether/THF	95 : 5/95 : 5	60/72
3. 	Ether/THF	95 : 5/92 : 8	55/82
4. 	THF	94 : 6	69
5. 	Ether/THF	97 : 3/93 : 7	62/73

enhances the formation of allenes (Noyori *et al.*, 1990). In most cases, THF was a superior solvent to ether in yield (Table II, III). This method is practically useful for selective allenylation of ketones and aldehydes.

ACKNOWLEDGEMENT

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