

A CATALYTIC ROLE OF Cu(II) FOR CONJUGATE ADDITION OF GRIGNARD REAGENTS. A COMPLETELY DIFFERENT BEHAVIOR FROM ORGANOCUPRATES.

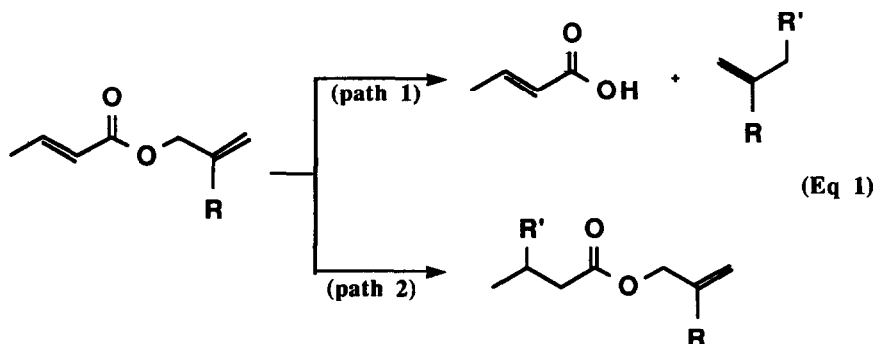
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Abstract: Different from lithium dialkylcuprates, Cu(II) catalyzed conjugate addition of Grignard reagents to allylic esters of α,β -unsaturated carboxylates has been effected in the presence of TMS-Cl, and the resulting allyl silyl keteneacetals further undergo rearrangement to afford 2-allyl 3-alkyl carboxylic acids in good yields.

In connection with our previous finding on an accelerating effect of TMS-Cl for addition of cuprates,¹⁾ we previously reported a role of Cu(II) species on the conjugate addition reaction of Grignard reagents.²⁾ Use of a catalytic amount of certain Cu(II) species greatly improved the reactivity to effect the addition to much less reactive α,β -unsaturated esters in excellent yields. In the present paper, we describe regioselective reactions of this catalytic system, e.g. Grignard reagents/TMS-Cl/cat. Cu(II), with bidentate electrophiles such as allyl esters of α,β -unsaturated carboxylates.

It has been well established lithium dialkylcuprates³⁾ react with allylic esters in S_N2' fashion to afford the corresponding alkenes.⁴⁾ Accordingly, two reaction pathways may be conceivable on treating the present system with allylic esters of α,β -unsaturated carboxylates: One is a S_N2' replacement similar with that of organocuprates (path 1). However, much higher reactivity of the Cu(II) catalytic system may effect a selective conjugate addition of Grignard reagents (path 2).



In order to shed light on the reactivity and reaction mode of the Cu(II) catalytic system, we initially undertook to compare the reaction type of the present system with that of lithium dialkylcuprates toward allylic crotonates. As expected from lower reactivity for conjugate addition, lithium dialkylcuprates preferentially reacted through S_N2' manner (path 1) to afford crotonic acid, whereas the catalytic Cu(II) system effected selective conjugate addition of Grignard reagents to the crotonates (path 2). Further, on heating, the silyl keteneacetals initially formed underwent Claisen rearrangement⁵⁾ to give the corresponding carboxylic acids in good

overall yields. Results are shown in Eq 2. Thus, the present catalytic reaction has allowed us a one-pot operation for a successive introduction of alkyl and allyl groups at 3- and 2-position, respectively.

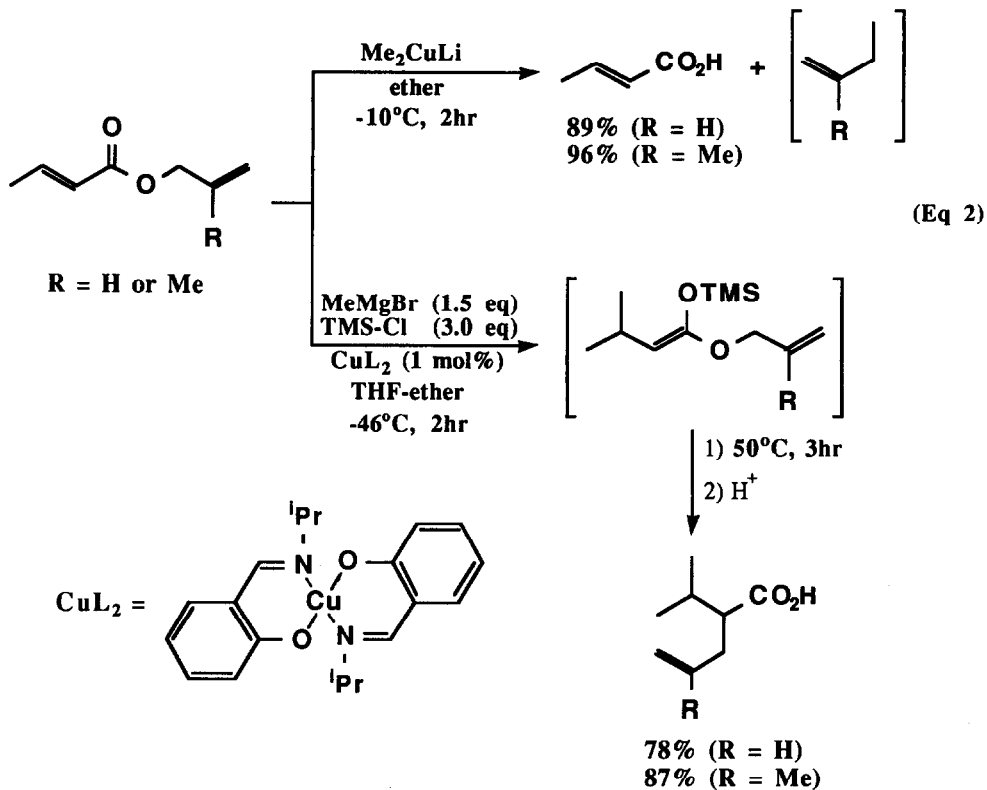
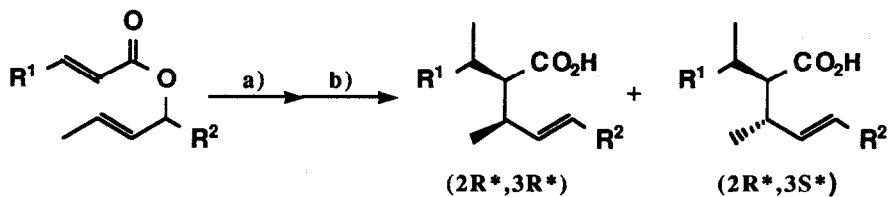


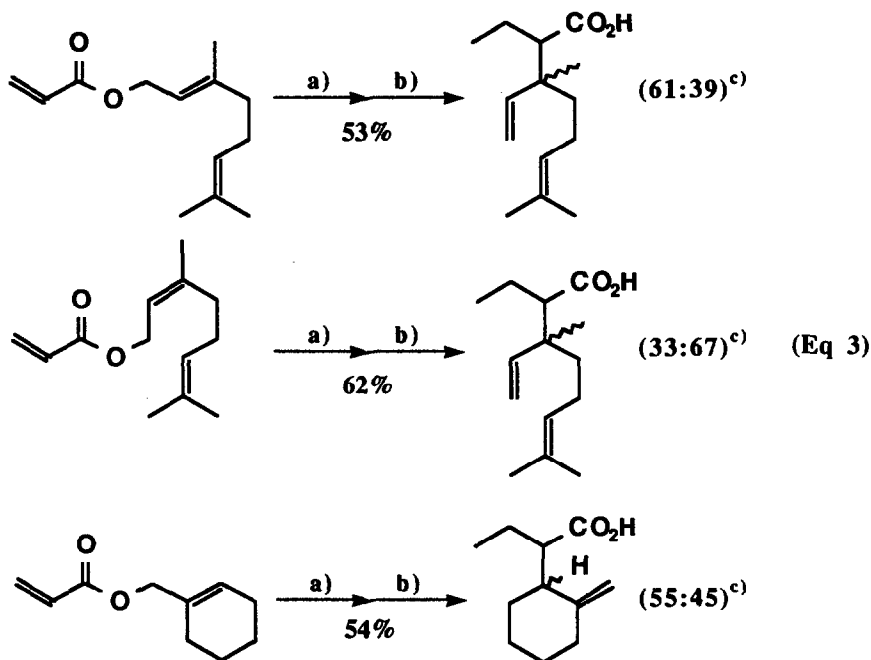
Table. Diastereoselectivity on Conjugate Addition and Claisen Rearrangement



R^1	R^2	Yield(%)	$(2R^*,3R^*):(2R^*,3S^*)$
H	H	69	70:30
Me	H	84	69:31
H	Me	69	70:30
Me	Me	67	69:31

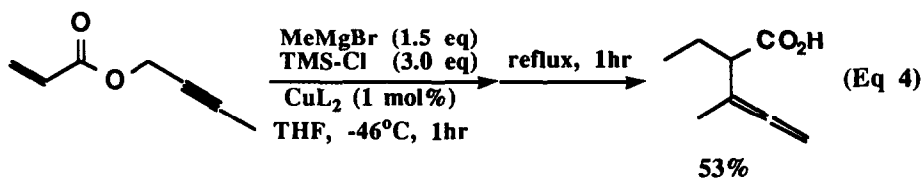
a,b) The reaction was performed under similar conditions cited in Eq 2.

Diastereoselectivity of the resulting carboxylic acids was also investigated by using 3-substituted allyl esters.⁵⁾ The reaction proceeded with moderate diastereoselection⁶⁾ (ca. 70:30) in every case (see the Table). Other examples illustrated in Eq 3 also indicated the selectivity is dependent on the allyl moieties of the ester. Relatively low stereoselection observed here may be attributable to the low (E)/(Z) selectivity of silyl keteneacetals formed under the present reaction conditions: Different from high (E) preference observed in the Cu(I) catalyzed conjugate addition of Grignard reagents to enals,^{1d)} almost 1:1 mixture of (E)- and (Z)-isomers was obtained in the reaction of methyl crotonate with octylmagnesium chloride.⁷⁾



a,b) The reaction was performed under similar conditions cited in Eq 2.
c) Relative configuration has not been determined.

The propargyl acrylate also underwent conjugate addition preferentially, not SN2' displacement,⁸⁾ to afford the corresponding 3,4-dienoic acid.⁹⁾



Thus, it has been made clear the present Cu(II) catalytic system exhibits not only much higher reactivity for conjugate addition, but also a complete different reaction mode from those of lithium dialkylcuprates. Such features seem to be very useful to improve or to compensate failure of synthetic transformations using

organocopper compounds. We are currently studying on wider synthetic applicability of the present system in more details.

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- 6) Relative configuration was determined by comparison with the authentic samples prepared by the procedure of Ireland. See ref 5.
- 7) Such low (E)/(Z) selectivity might be due to a relatively small difference of ground state stability between transoid and cisoid of unsaturated esters.¹⁰⁾
- 8) Propargyl esters are also known to undergo S_N2' substitution with lithium dialkylcuprates. See: Rona, P.; Crabbe, P. *J. Am. Chem. Soc.* **1968**, *90*, 4733; *ibid.* **1969**, *91*, 3289. Descoins, C.; Henrick, C. A.; Siddall, J. B. *Tetrahedron Lett.* **1972**, 3777.
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