

Tin(IV) Chloride Catalyzed Addition of Methyl 2-Oxo-3-alkenoates
to Simple Alkenes

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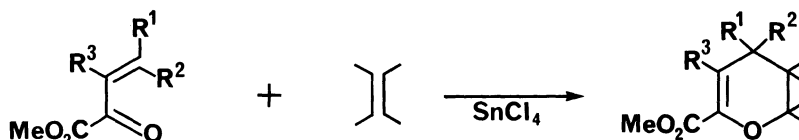
Tin(IV) chloride catalyzed inverse electron demand hetero-Diels-Alder reaction of substituted methyl 2-oxo-3-alkenoates with simple alkenes led to methyl 3,4-dihydro-2H-pyran-6-carboxylates in satisfactory yields. The addition proceeded stereospecifically through an *exo* transition state.

The inverse electron demand hetero-Diels-Alder reactions of 1-oxa-1,3-dienes with enol ethers have become a promising strategy in the synthesis of carbohydrates and related natural compounds,¹⁾ because the reaction can construct new C-C and C-O bonds with satisfactory regio- and stereoselectivities. However, the low reactivity of 1-oxa-1,3-dienes has restricted the choice of dienophiles. Thus in most cases, electron-rich dienophiles have been employed.²⁻⁷⁾ In selected instances, modification by means of introduction of an electron-withdrawing group or a hetero atom at 2 or 3 position of the 1-oxa-1,3-diene has been shown to enhance their reactivity.³⁻⁷⁾ Recently Boger and Robarge⁷⁾ have reported that methyl 4-methoxy- and 4-phenyl-2-oxo-3-butenates reacted with enol ethers and ketene acetals to afford corresponding methyl 3,4-dihydro-2H-pyran-6-carboxylates in good yields. Although some intramolecular hetero-Diels-Alder reactions⁸⁻¹⁰⁾ in which a 1-oxa-1,3-diene functionality cycloadds to an olefinic part of the molecule have been reported, only a few cycloadditions of 1-oxa-1,3-diene derivatives with simple alkenes have been documented,¹¹⁻¹³⁾ where the yields of the adducts were not satisfactory, and the stereochemistry of the addition was not fully clarified.

In the presence of tin(IV) chloride, methyl 4-substituted 2-oxo-3-alkenoates (**1a-c**) reacted with simple alkenes to give 2,4- and 2,3,4-alkyl substituted methyl 3,4-dihydro-2H-pyran-6-carboxylates (**2a-h**). The reaction did not take place without tin(IV) chloride [no reaction in toluene at 110 °C, or at room temperature under a pressure of 1.1 GPa], and titani-

um(IV) chloride was found to be less effective.¹⁴⁾

Complete regioselectivity of the reaction was observed (Table 1, **2a**, **b**, and **e-h**).¹⁵⁾ Stereochemistry of the adducts was determined by inspecting proton-proton coupling constants of their ¹H NMR spectra, and the C₂/C₄ trans configuration was deduced for the adducts (**2a**, **c**, and **e**) obtained from 1- and 3-hexenes. In addition, *trans*- and *cis*-3-hexenes gave *trans*- and *cis*-**2c**,¹⁵⁾ respectively, as a sole adduct.

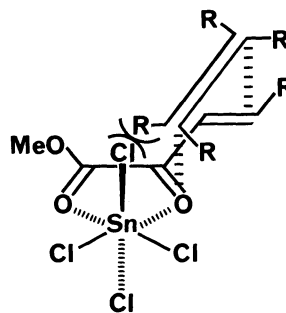


1a	R ¹ =Ph,	R ² =H,	R ³ =H
b	Me	H	H
c	Me	Me	H
d	H	H	Ph

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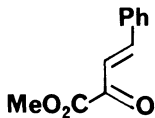
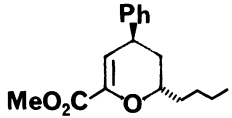
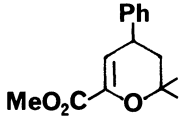
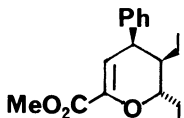
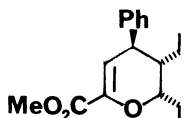
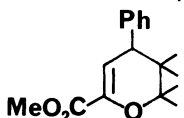
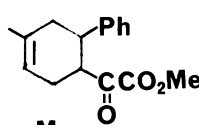
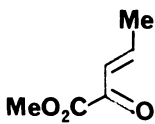
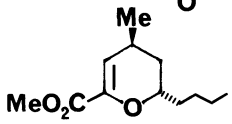
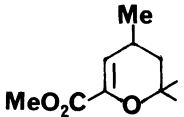
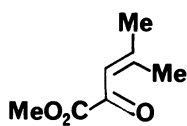
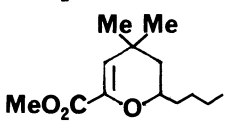
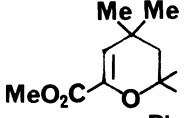
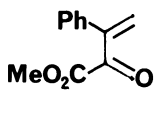
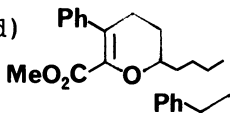
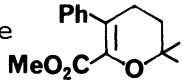
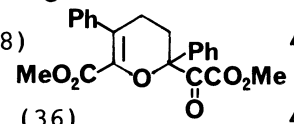
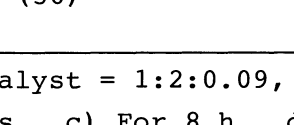
In the inverse electron demand hetero-Diels-Alder reactions of 1-oxa-1,3-diene derivatives with enol ethers, the kinetically controlled C₂/C₄ *cis* adducts are produced predominantly through an endo transition state.^{3,5-7)} However, this is not observed in the present reactions. Thus we assume that the addition proceeded through an *exo* transition state, in which the incoming alkene molecule possessed the *exo* orientation because of steric interference induced by the co-ordinated tin(IV) chloride catalyst. Similar stereoselection (enhancement of an *exo* adduct formation) caused by Lewis acids chelation was reported for the ene reactions of methyl glyoxylate with 2-butenes.¹⁶⁾

Although the aluminum chloride catalyzed reaction of 2-oxo-3-pentenitrile with 4-methyl-1,3-pentadiene was reported to give a corresponding dihydropyran derivative,¹³⁾ the reaction of **1a** with 2-methyl-1,3-butadiene afforded a carbocyclic Diels-Alder adduct (**3**), and no dihydropyran derivative was isolated. In addition, both methyl 2,5-



diphenyl-2-methoxalyl-3,4-dihydro-2*H*-pyran-6-carboxylate (**4**, a cyclic dimer of **1d**, as a major product) and a normal adduct (**2i** or **j**) were obtained in the reaction of methyl 3-phenyl-2-oxo-3-butenoate (**1d**) with alkenes. A related easy dimerization was observed for 3-methyl-2-oxa-3-pentenitrile.¹⁷⁾

Table 1. Tin(IV) chloride catalyzed cycloaddition of methyl 2-oxo-3-alkenoates with simple alkenes^{a)}

2-Oxo-3-alkenoate	Alkene	Products and yields ^{b)} / %
 1a	1-Hexene	 2a (63)
	2-Methylpropene	 2b (84)
	<i>trans</i> -3-Hexene ^{c)}	 <i>trans</i> - 2c (38)
	<i>cis</i> -3-Hexene ^{c)}	 <i>cis</i> - 2c (10)
	2,3-Dimethyl-2-butene	 2d (96)
	2-Methyl-1,3-butadiene	 3 (76)
 1b	1-Hexene	 2e (22)
	2-Methylpropene	 2f (74)
 1c	1-Hexene ^{d)}	 2g (30)
	2-Methylpropene	 2h (78)
 1d	1-Hexene ^{d)}	 2i (38)
	2-Methylpropene	 2j (36)
		 4 (52)
		 4 (41)

a) Reaction conditions: molar ratio of 1:alkene:catalyst = 1:2:0.09, in dichloromethane at 0 °C for 3 h. b) Isolated yields. c) For 8 h. d) With 1.73 equivalents of tin(IV) chloride at room temperature.

In conclusion, the tin(IV) chloride catalyzed cycloaddition of 1-oxa-1,3-dienes with alkenes provided 3,4-dihydro-2H-pyran derivatives with a rigorous C₂/C₄ trans configuration.

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- 14) Titanium(IV) chloride catalyzed reactions of **1a** with alkenes showed high regio- and stereoselectivities as well, but the yields of the corresponding adducts were low (36-70%).
- 15) Satisfactory NMR, IR, and mass spectra were obtained for all new compounds listed in Table 1. Selected ¹H NMR data for assignment of stereochemistry of *trans*-**2c**; H₂ 4.20-4.25 (1H, m, J_{2,3}=7.8 Hz), H₃ 1.75-1.90 (1H, m, J_{3,4}=5.9 Hz), H₄ 3.80 (1H, dd, J_{4,5}=3.4 Hz), and H₅ 6.18 ppm (1H, dd); *cis*-**2c**; H₂ 3.90-3.95 (1H, m, J_{2,3}=2.0 Hz), H₃ 1.75-1.86 (1H, m, J_{3,4}=4.5 Hz), H₄ 3.37 (1H, t, J_{4,5}=4.3 Hz), and H₅ 6.08 ppm (1H, dd). We are indebted to Miss M. Nishinaka for microanalysis.
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