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

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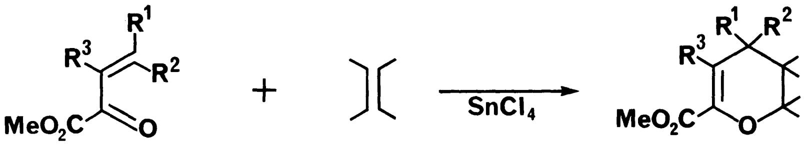
Tin(IV) chloride catalyzed inverse electron demand hetero-Diels-Alder reaction of substituted methyl 2-oxo-3-alkenoates with simple alkenes led to methyl 3,4-dihydro-2*H*-pyran-6-carboxylates in satisfactory yields. The addition proceeded stereospecifically through an exo transition state.

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-butenoates reacted with enol ethers and ketene acetals to afford corresponding methyl 3,4-dihydro-2*H*-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-2*H*-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 titanium(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 C_2/C_4 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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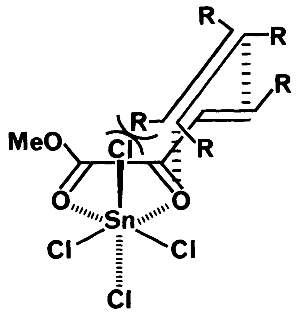
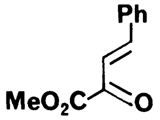
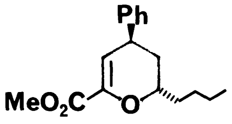
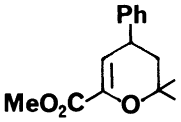
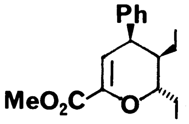
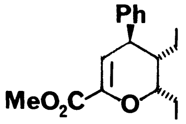
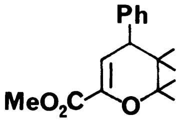
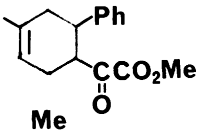
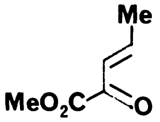
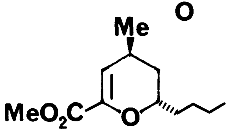
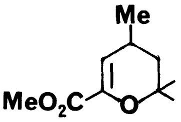
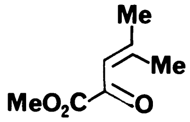
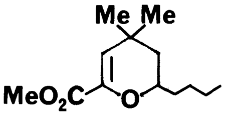
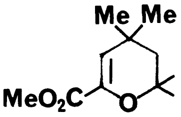
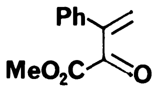
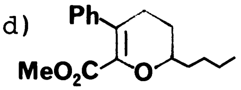
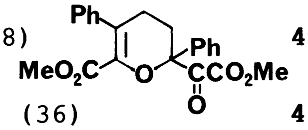
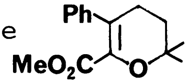
In the inverse electron demand hetero-Diels-Alder reactions of 1-oxa-1,3-diene derivatives with enol ethers, the kinetically controlled C_2/C_4 cis adducts are produced predominantly through an endo transition state.[3,5-7)] However, this is not observed in the present reactions. Thus we assume that 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-pentenenitrile 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-pentenenitrile.[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)
		trans-3-Hexene$^{c)}$		*trans*-**2c** (38)
		cis-3-Hexene$^{c)}$		*cis*-**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) 	**4** (52)
		2-Methylpropene	 **2j** (36)	**4** (41)

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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-2*H*-pyran derivatives with a rigorous C_2/C_4 trans configuration.

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14) Titanium(IV) chloride catalyed reactions of **1a** with alkenes showed high regio- and stereoselectivities as well, but the yields of the correresponding adducts were low (36-70%).
15) Satisfactory NMR, IR, and mass spectra were obtained for all new compounds listed in Table 1. Selected ^{1}H NMR data for assignment of stereochemistry of *trans*-**2c**; H_2 4.20-4.25 (1H, m, $J_{2,3}$=7.8 Hz), H_3 1.75-1.90 (1H, m, $J_{3,4}$=5.9 Hz), H_4 3.80 (1H, dd, $J_{4,5}$=3.4 Hz), and H_5 6.18 ppm (1H, dd); *cis*-**2c**; H_2 3.90-3.95 (1H, m, $J_{2,3}$=2.0 Hz), H_3 1.75-1.86 (1H, m, $J_{3,4}$=4.5 Hz), H_4 3.37 (1H, t, $J_{4,5}$=4.3 Hz), and H_5 6.08 ppm (1H, dd). We are indebted to Miss M. Nishinaka for microanalysis.
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