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Michael Reactions Promoted by η^1-*O*-Enolatoruthenium(II) Complexes Derived from Ru(cod)(cot), Diphosphine, and Dimethyl Malonate

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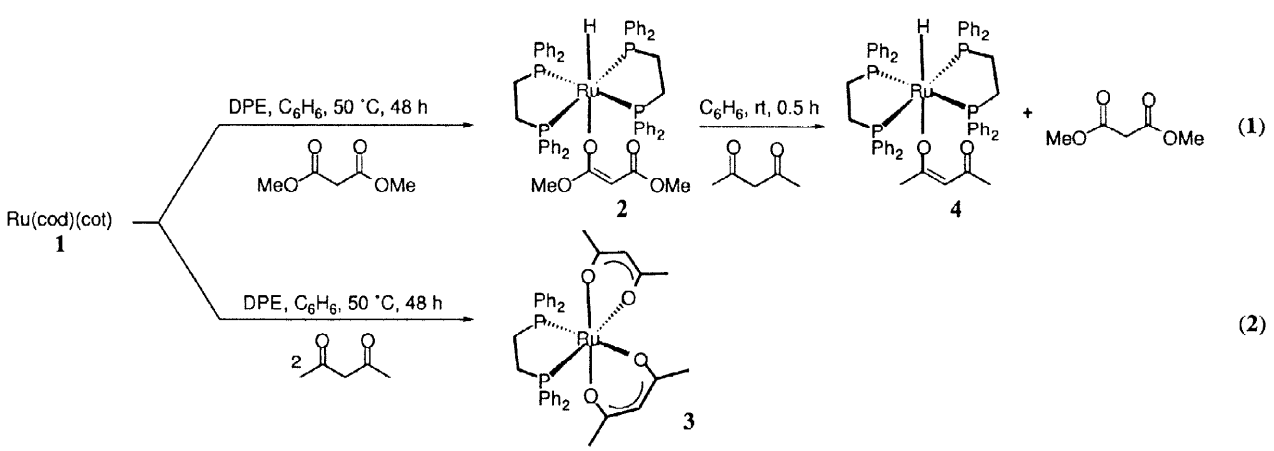
Abstract: The Michael reaction of 1,3-dicarbonyls with α,β-unsaturated esters and nitriles has been carried out very efficiently, under mild and neutral conditions, in the presence of a catalytic amount of *trans*-hydrido(η^1-*O*-enolato) ruthenium(II) complex (**2**), which is prepared from the reaction of Ru(cod)(cot) (**1**) (cod = cycloocta-1,5-diene; cot = cycloocta-1,3,5-triene) with dimethyl malonate in the presence of 1,2-bis(diphenylphosphino)ethane (dpe).

Keywords: Ruthenium and Compounds; Catalysts; Complexes; Phosphines.

A recent attractive application of catalytic active-C-H bond activation is in the preparation of aldol and Michael reaction adducts,[1,2] since both reactions constitute a powerful synthetic strategy for the construction of C-C bonds and, in turn, is attracting more interest in synthetic organic chemistry because of its potential applications.[3,4] We previously isolated zwitterionic active intermediates[1a] in Murahashi's[1b] selective ruthenium-catalyzed aldol and Michael reactions of nitriles via α-C-H bond activation of nitriles. In this system, 1,3-dicarbonyls remained unreacted without Lewis base because of little nucleophilicity of the chelated enolates. Herein, a new strategy for the catalytic α–C-H bond activation of 1,3-diketones by creating monodentate enolato ruthenium(II) complexes, under neutral and mild conditions, and their application in the Michael reaction is described.

The reaction of complex **1**[5] with dimethyl malonate in the presence of two equiv of dpe afforded the corresponding *trans*-hydrido(η^1-*O*-enolato) ruthenium(II) complex (**2**)[6] in 21% yield after recrystallization (eq 1), whereas the reaction with acetylacetone (acacH) gave Ru(dpe)(acac)$_2$ (**3**)[7] in 12% yield after recrystallization (eq 2). The coordination mode of the enolato ligand in **2** is deduced to be monodentate by the carbonyl oxygen while that in **3** is bidentate by the two carbonyl oxygens, based on the spectroscopic



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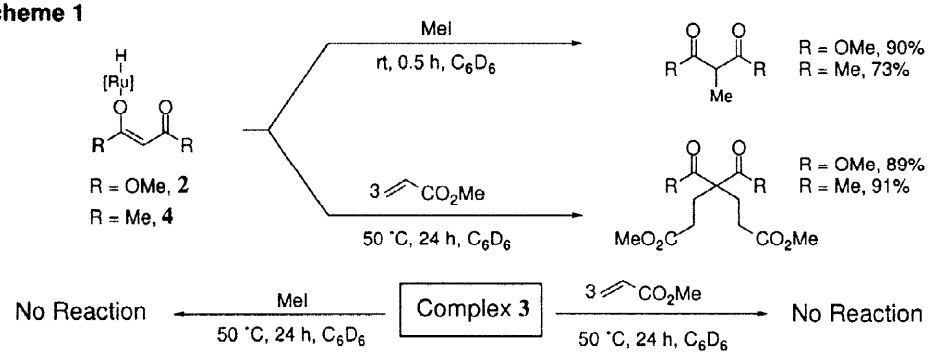
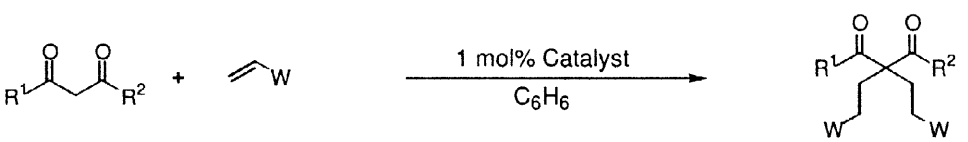
data. Interestingly, complex **2** smoothly facilitated the enolate exchange reaction with acetylacetone giving an analogous *trans*-hydrido(η^1-*O*-enolato) ruthenium(II) complex (**4**)[8] (82% yield) where the acac ligand binds to Ru in a monodentate fashion (eq 1). Intrigued by these results, and with our interests in investigating the synthetic utility of transition-metal complexes in organic synthesis, we conducted a series of preliminary experiments which indicated that enolato ligands in **2** and **4** could be alkylated with electrophiles such as MeI and methyl acrylate quantitatively , whereas complex **3** showed no reactivity. The progress of the reactions were monitored by NMR in benzene-d_6 (Scheme 1).

Scheme 1



Encouraged by our preliminary stoichiometric results, we set out to explore the catalytic behavior of complexes **2** and **4** in the promotion of the Michael addition of 1,3-dicarbonyls to excess Michael acceptors.[9] All the Michael adducts were characterized by NMR, IR, mass spectroscopy, and in some cases compared to authentic samples prepared from literature methods.[10] Representative results are illustrated in Table 1.

Table 1. Ru(II)-Catalyzed Michael Reaction of 1,3-Dicarbonyls with α,β-Unsaturated Esters and Nitriles. [a]



Entry	Catalyst	R^1	R^2	W	Temp. (°C)	Time (h)	Yield (%)[b]
1	**2**	OMe	OMe	CO_2Me	50	48	89
2	**2**	Me	Me	CN	50	96	70
3	**2**	OMe	OMe	CN	25 (50)	48	24 (5)
4	**3**	Me	Me	CN	50	48	0[c]
5	**3**	Me	Me	CO_2Me	50	48	0[c]
6	**4**	Me	Me	CO_2Me	70	96	62
7	**2**	Me	Me	CO_2Me	70	96	60

a. Catalyst (0.010 mmol), Michael donor (1.0 mmol), and Michael acceptor (2.5 mmol) in benzene (5 mL).
b. Yield based on Michael donor. c. No reaction.

It is noteworthy that the Michael adducts do not undergo neither retro-Michael reaction nor undesired transformations. Under similar reaction conditions and in the absence of diphosphine or complex **1**, the Michael adduct was not detected or a complex mixture resulted, respectively. Thus, complex **2** catalyzed the

reactions of methyl acrylate with dimethyl malonate (Entry 1) and acetylacetone (Entry 7) in 89 and 60% yields, respectively. Moreover, an important feature of this procedure, is the chemoselectivity observed in the presence of different active methylene compounds. For example, the complex **2**-catalyzed reaction of methyl acrylate (2 equiv) with an equimolar mixture of dimethyl malonate (pK_a = 13)[11] and acetylacetone (pK_a = 9)[11] gave the acetylacetone Michael adduct (67%) exclusively, while 20 mol% NaOMe in THF or 10 mol% PEt_3 in benzene provided a mixture of acetylacetone:dimethyl malonate Michael adducts.[12] Complex **2** catalyzed the conjugate addition of acetylacetone to acrylonitrile (Entry 2, 70%), while with dimethyl malonate the reaction was sluggish (Entry 3, 5%). A chelated enolate from acacH **3** has little activity toward Michael reactions, while monodentate one **4** acts as active catalyst (Entries 4-6). This fact shows the importance of monohapto coordination mode of enolates for the catalytic activity.

A possible mechanism for the complex **2**-catalyzed Michael reaction is outlined in Figure 1. The active α-C-H bond of dimethyl malonate oxidatively adds to a Ru(0) complex, which results from the reaction of **1** with 2 equiv of dpe, to generate the active catalytic species **2**. Conjugate addition of complex **2** to the Michael acceptor, forms **A** followed by a 1,3-proton transfer to generate the less basic species **B**. Species **B** adds to another Michael acceptor giving species **C**, which then abstracts a proton from dimethyl malonate giving the Michael adduct and the active catalytic species **2** to continue the catalytic cycle.

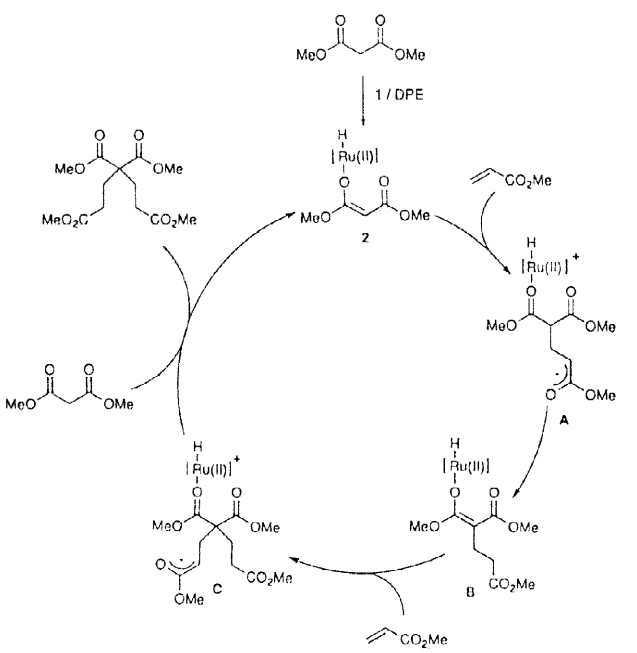


Figure 1. Possible Mechanism for the Ruthenium-Catalyzed Michael Reaction of Active Methylene Groups.

In summary, we have demonstrated the synthetic utility of *trans*-hydrido(η^1-*O*-enolato) ruthenium(II) complex **2**, formed from **1**, dpe, and dimethyl malonate, in the catalytic Michael reaction of 1,3-dicarbonyls with Michael acceptors. Efforts are underway to explore further this catalytic system for utilities in organic synthesis and the reaction mechanism.

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6. Data for **2**: Yield 21% (yellow crystals from THF/hexane); mp 164-166 °C; ^{1}H NMR (300 MHz, $C_6D_5CD_3$, -50 °C) δ -21.01 (qui, J_{PH} = 19.2 Hz, 1H, Ru-H), 1.33 (s, 3H, OMe), 1.81 (br, 2H, CH_2 (dpe)), 2.35 (br, 4H, CH_2 (dpe)), 3.96 (s, 1H, CH), 4.05 (s, 3H, OMe), 4.05 (br, 2H, CH_2 (dpe)), 6.48-7.47 (m, 40H, Ph (dpe)); ^{31}P{^{1}H} NMR (122 MHz, $C_6D_5CD_3$, -50 °C) δ 58.36, 60.80 AA'BB' system (ddd, J_{PP} = 269.0, -55.0, 30.0 Hz); FT-IR (KBr, cm^{-1}): 1989 (w, Ru-H), 1673 (vs, C=O). Anal. Calcd for $C_{57}H_{56}O_4P_4Ru$: C, 66.47; H, 5.48. Found: C, 67.24; H, 5.33.
7. Data for **3**: Yield 12% (orange crystals from THF/hexane); mp 164 °C; ^{1}H NMR (300 MHz, C_6D_6) δ 1.47 (s, 6H, CH_3), 1.92 (s, 6H, CH_3), 2.29 (m, 2H, CH_2 (dpe)), 2.56 (m, 2H, CH_2 (dpe)), 5.01 (s, 2H, CH), 6.88-8.22 (m, 20H, Ph (dpe)); ^{31}P{^{1}H} NMR (122 MHz, C_6D_6) δ 82.10 (s); FT-IR (KBr, cm^{-1}): 1570 (vs, C=O). Anal. Calcd for $C_{36}H_{38}O_4P_2Ru$: C, 61.97; H, 5.49. Found: C, 62.44; H, 5.59.
8. Data for **4**: Yield 82% (yellow crystals from benzene/hexane); mp 150-151 °C; ^{1}H NMR (300 MHz, CD_2Cl_2) δ -21.65 (qui, J_{PH} = 20.1 Hz, 1H, Ru-H), 0.82 (s, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.18 (br, 4H, CH_2 (dpe)), 2.88 (br, 4H, CH_2 (dpe)), 3.55 (s, 1H, CH), 6.92-7.29 (m, 40H, Ph (dpe)); ^{31}P{^{1}H} NMR (122 MHz, CD_2Cl_2) δ 68.60 (s); FT-IR (KBr, cm^{-1}): 1604 (s, C=O). Anal. Calcd for $C_{57}H_{56}O_2P_4Ru$: C, 68.60; H, 5.66. Found: C, 68.15; H, 5.41.
9. The following is a typical procedure: Under a nitrogen atmosphere, 1 mol% complex **2** (0.010 mmol) was dissolved in anhydrous benzene (5 mL), charged with dimethyl malonate (1.0 mmol), methyl acrylate (2.5 mmol), and stirred at 50 °C for 48 h. After the solvent was evaporated *in vacuo*, the crude solid product was washed with *n*-hexane (3 x 5 mL) followed by cannulation of the solvent to give a semi-pure product which was recrystallized from a mixture of benzene and *n*-hexane to provide the Michael adduct in 89% isolated yield.
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12. NaOMe in THF (50 °C, 24 h) provided a 28:72 mixture and PEt_3 in benzene (rt, 4 h) gave a 86:14 mixture of acetylacetone:dimethyl malonate Michael adducts, respectively.