# 4,3 ADDITIONS TO α,β-UNSATURATED KETONES VIA η^2 C=C BINDING TO A RUTHENIUM COMPLEX.

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Abstract: The $[Cp^*Ru(CO)_2]^+$ fragment ($Cp^* = \eta^5$-C_5Me_5) binds α,β-unsaturated ketones in an η^2-C=C fashion. The resulting complex is subject to attack by H$^-$ at the 4-position, leaving the ruthenium bound to the substrate at the 3-position. The Ru-C bond, formed in this way, can be cleaved to give a variety of 4,3-addition products.

Nucleophilic 1,4 or 1,2-addition to α,β unsaturated carbonyl compounds is an important reaction in natural product synthesis. In particular, reagents which give 1,4-addition of hydride to enones continue to be of interest.[1,2] Here we show how binding the enone to a Lewis acid metal fragment, $[Cp^*Ru(CO)_2]^+$ ($Cp^* = \eta^5$-C_5Me_5), not only shows selectivity for attack at the 4-position by $Na[H_3B(CN)]$,[3] but also leaves a reactive Ru-C bond which can lead to subsequent functionalization of the enone at the 3-position, to give overall 4,3-addition (Eq. 1).

$$ (1) $$
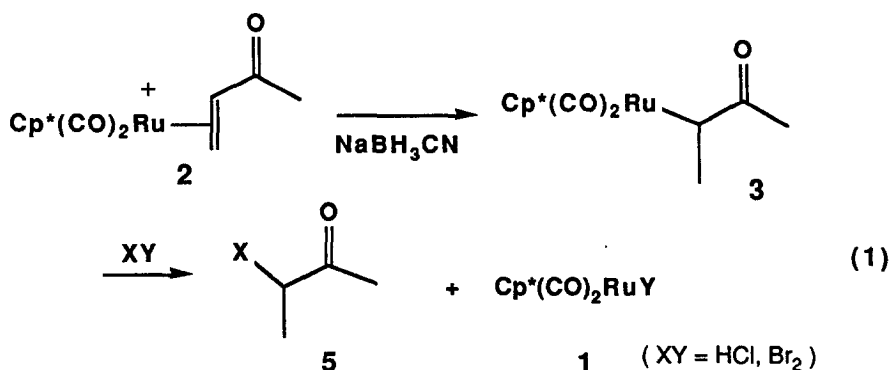
$\eta^1(O)$, $\eta^2(C=C)$ and η^4-bonding modes are all known for enone complexes.[4] We find that the [CpRu(CO)(PPh$_3$)]$^+$ fragment binds a variety of enones, but only monosubstituted ones bind in an η^2-C=C fashion, others bind η^1 *via* the oxygen. We believe that the greater steric bulk of the ligand when bound η^2 *via* the C=C group leads to the adoption of the alternate η^1 binding mode for bulky metal fragments. This suggested to us that, of the common Lewis acid fragments, [Cp*Ru(CO)$_2$]$^{+}$, might most consistently bind *via* the C=C group.

The required intermediates can easily be generated by the addition of Ag[SbF$_6$] to a CH$_2$Cl$_2$ solution of [Cp*Ru(CO)$_2$Cl][5] and enone in the dark. The resulting enone complex **2** reacts over a few seconds at 0°C with Na[H$_3$B(CN)] in methanol to afford the intermediate ruthenium alkyls (**3**) as shown in Eq. 1. The ruthenium carbon bond can now be cleaved with HCl , CuBr$_2$ [6] or pyridinium tribromide to afford the [Cp*Ru(CO)$_2$X] (X = halide) and the 4,3-addition product in modest yields; the saturated ketone is formed as a significant by-product in most cases (Table 1).

We describe in detail the conversion of ethyl vinyl ketone to 3-pentanone. To [Cp*Ru(CO)$_2$Cl] (100mg, 0.305 mmol) in CH$_2$Cl$_2$(10mL), is added ethylvinyl ketone (26μL., 0.34 mmol) followed by Ag[SbF$_6$] (105mg, 0.305 mmol) in the dark under argon. The mixture is allowed to stir for 30 minutes and then filtered over Celite to remove silver salts. The colorless solution is then reduced to ca. 5 mL *in vacuo*. To the enone complex, which need not be purified, is added dry methanol (10mL), and the solution cooled in an ice bath. Sodium cyanoborohydride (0.305mmol, 19mg) is added and the solution warmed to room temperature and the solvent removed *in vacuo*. Ether (15mL) is added and the resulting yellow solution is separated from the salts by filtration over Celite. Hydrogen chloride gas is then bubbled through the ether solution for two minutes to give 3-pentanone in 68% yield by G.C.(determined with toluene standard) and [Cp*Ru(CO)$_2$Cl] (47% yield after recryst.).

The α-bromoketones are obtained by the addition of CuBr$_2$ (0.6 mmol) to the ether solution of **3**. CuBr is removed by filtration and ether removed from the solution *in vacuo* to give **5** (X = Br), isolated by extraction with pentane, and [Cp*Ru(CO)$_2$Br] (1).[7] The α-bromoketones can also be obtained by adding a CH$_2$Cl$_2$ solution of pyridinium tribromide (0.3mmol) to the ether solution of **3** in a dry ice/acetone bath and allowing the mixture to stir for thirty minutes. The solution is extracted with saturated sodium bisulfite, brine, dried over magnesium sulfate, filtered and the solvent removed *in vacuo*. Compound **5** and **1** are isolated as before.

TABLE 1

Enone	Reagent	5 (X=H)	5 (X=Br)	Cp*Ru(CO)₂Y
ethylvinylketone(**4a**)	HCl	68% [a]		47% [c]
2-cyclopentenone(**4b**)	HCl	50% [a]		45% [c]
Chalcone (**4c**)	HCl	42% [b]		
4a	CuBr₂	17.8% [b]	11% [b]	
4c	CuBr₂	7% [b]	7% [b]	
4c	CuBr₂/NBu₄Br	10% [b]	20% [b]	
3-octene-2-one(**4d**)	[pyH]Br₃		37% [b,d]	51% [c]
4c	[pyH]Br₃	29%	e	

a.) Overall yield determined by GC with an internal standard. b.) Overall yield determined by NMR ($CHBr_3$ internal standard, 10 sec. pulse delay). c.) isolated yield after recrystallization. d.) no 1-bromo-2-octanone was formed. e.) The ruthenium alkyl (**3**) does not appear to react with [pyH]Br₃ under these conditions. The ketone is likely formed during workup with sat'd sodium bisulfite sol'n.

The identity of the intermediate ruthenium species **2** was determined by isolation of **2** (92%) from the CH_2Cl_2 solution with ether. Microanalytical and ^{1}H NMR evidence supports the proposed formulation. {^{1}H NMR (250MHz, CD_2Cl_2): 4.07 (m, 2H); 3.16 (dd, 1H, J_{gem} = 2.6Hz, J_{cis} = 5.2Hz), 2.73 (m, 2H); 2.05 (s, 15H);1.01 (br. t, 3H) IR (CD_2Cl_2): 2088, 2077; 2052, 2041cm^{-1} ν(MCO) (there appear to be two enone conformers in solution, which may have the s-cis and s-trans configurations), 1648,1630 cm^{-1}, ν(org. CO) }. In particular, η^1-(O) bound complexes can be distinguished from η^2-C=C bound species by proton NMR. The olefin-bound species have a 2-4 ppm upfield coordination shift of the vinyl (=C$\underline{H}$) resonances, while oxygen-bound species have a negligable vinyl coordination shift. The intermediate alkyl, **3**, was not sufficiently stable for microanalysis, but ^{1}H and ^{13}C NMR evidence, as well as the formation of the α-bromoketone cleavage product, supports the proposed formulation.{^{1}H NMR (250MHz, $CDCl_3$) 2.3-2.1 (m,3H), 1.88 (s,15H); 1.40 (d, 3H, J = 6.5Hz), 1.06 (t, 3H, J = 7.2 Hz); ^{13}C NMR 213.6; 203.7; 202.0; 99.6; 33.5; 27.8; 21.7; 15.0; 9.7 ppm; IR (neat, NaCl plates): 2006,1950 cm^{-1} ν(MCO), 1745 ν(CO), no ν(OH).}

We are currently investigating the addition of other nucleophiles[8] and other methods of ruthenium carbon bond cleavage.

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7.   a) $CuBr_2$ has been shown to give α-bromoketones from ketones in refluxing chloroform/ethylacetate mixture.[7b] In order to prove the α-bromoketones (**5**) were coming from **3** and not the ketone, we attempted to prepare the 2-bromo-3-pentanone from $CuBr_2$ and 3-pentanone in ether at room temperature. Neither Cu(I)Br nor the α-bromoketone were formed. b) Bauer, D. P.; Macomber, R. S., *J. Org. Chem.,* 1975, **40,**1990.

8.   We have also observed carbon-carbon bond formation in the addition of 1-phenyl-1-(trimethylsilyloxy)ethylene to give the expected diketone after cleavage with HCl.