Ruthenium-Catalyzed Reactions of Acyclic α,β-Enones with Olefins and Their Reaction Mechanisms

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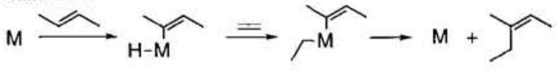
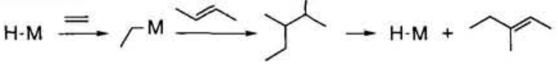
The reaction of 4,4-dimethyl-5-phenyl-4-peneten-3-one with styrene (**2**) using $Ru(H)_2(CO)(PPh_3)_3$ as the catalyst gave the stereochemically retained product. In the case of 2,2-dimethyl-4-hexen-3-one, the stereochemically inverted branched product was obtained. These results are consistent with two different reaction pathways operating, *i.e.* one involving a direct C-H bond cleavage and the other, a pathway involving hydrometallation.

A priori, several mechanisms can be envisaged for transition metal-catalyzed olefin to olefin coupling reactions.[1-6] Among these, Mechanisms 1-3, shown below, represent the most likely ones; (1) a direct C-H bond cleavage (Mechanism 1); [2-4] (2) hydrometallation (Mechanism 2);[5] (3) cyclometallation (Mechanism 3).[6] In these Mechanisms 1-3, all the addition and elimination steps take place in *syn* manner. It is normally very difficult to distinguish between these.[7] For example, deuterium labeling experiments would be inconclusive, since for all 3 Mechanisms, the position of C-D cleavage and the position of the C-D bond formed in the product are identical. The stereochemistry of the reaction also suffers from ambiguities arising from isomerization. As a result, very few (if any) reports exist, to our knowledge, which clearly point to any of these mechanisms as the most probable one. We have devised a catalytic system which permits evidence to be obtained relative to the mechanism for this reaction. We wish to report herein that the reaction of acyclic α,β-enones with olefins in the presence of a ruthenium-catalyst gives olefin/olefin coupling products which are formed *via* different mechanisms, depending on the substrates employed.

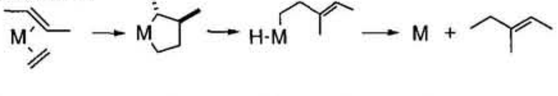
Mechanism 1



Mechanism 2

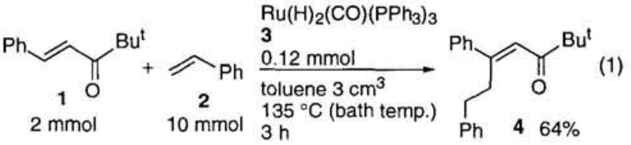


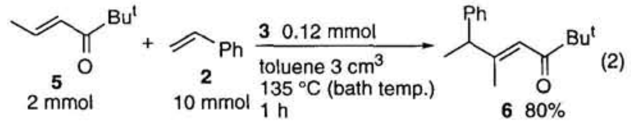
Mechanism 3



The characteristic features of Mechanisms 1-3 are as follows: for Mechanism 1, the stereochemistry around the double bond in the product is retained, while for Mechanisms 2 and 3, it is inverted.

The reaction of 4,4-dimethyl-5-phenyl-4-peneten-3-one (**1**) with styrene (**2**) using $Ru(H)_2(CO)(PPh_3)_3$ (**3**) as the catalyst, was carried out under reaction conditions shown in Eq. 1 to give the linear product **4** in 64% isolated yield as the exclusive product (Eq. 1). In this case, the stereochemistry around the double bond was completely retained. In contrast, the reaction of 2,2-dimethyl-4-hexen-3-one (**5**) with **2** under identical reaction conditions gave the branched product **6** in 80% yield as the sole product (Eq. 2). In this case, the stereochemistry around the double bond in **6** is completely opposite to that of **4**.



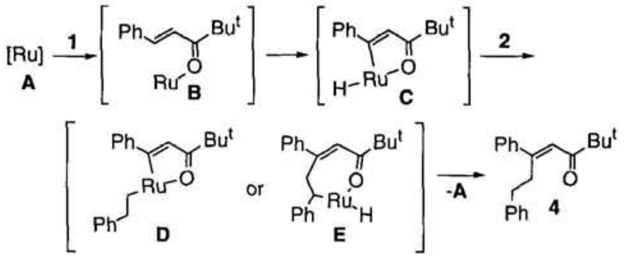


These results suggest that two different reaction pathways appear to be operative for these two reactions. The exclusive formation of **4** can be explained by the direct C-H bond cleavage pathway, *i.e.*, Mechanism 1. In contrast, the completely reversed stereochemistry around the double bond in **6** suggests that the reaction proceeded either via Mechanism 2 or Mechanism 3. We prefer Mechanism 2 because for the following three reasons: 1) The exclusive formation of the branched isomer **6** can be explained by assuming a π-benzyllic intermediate which is formed by hydroruthenation of styrene (*vide infra*).[8] 2) The large steric repulsion between the phenyl and methyl groups on the ruthenacyclopentane in the course of Mechanism 3 would be expected to disfavor the formation of the metallacycle.[9] 3) Even if a ruthenacycle is formed, the β-hydride elimination from the metallacycle would be predicted to be a difficult process.[10]

One can argue that both **4** and **6** might have been formed just because these are more stable stereo-isomers. This is not the case. A control experiment using a mixture of isolated *E*- and *Z*-isomers of **4** revealed that the *Z*-**4** isomer does not isomerize to *E*-**4**.[11]

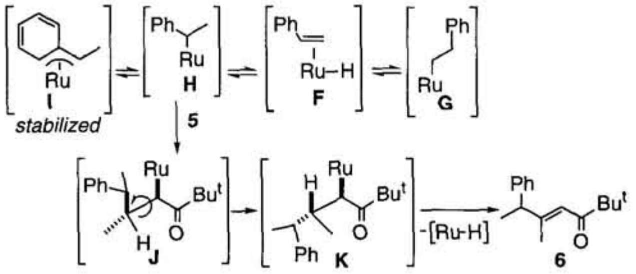
An outline of the plausible reaction mechanism for the reaction described in Eq. 1 is shown in Scheme 1. The chelation-assisted insertion of the ruthenium into the C-H bond gives **C**. Hydrometallation or carbometallation (less likely) of **2** would result in the formation of **D** or **E**, respectively. Reductive elimination from **D** or **E** provides **4**, regenerating the catalytically active species **A**. The stereochemisty around the double bond is retained in each step.

A plausible mechanism for the reaction of Eq. 2 is shown in Scheme 2. The catalytic reaction appears to be initiated by the *syn* addition of the ruthenium-hydride to an olefin (**F** → **G** or **F** → **H**).[12] The preferential formation of the branched isomer can be explained by the formation of a benzyllic π-ruthenium complex **I**.[8] The addition of **H** to **5** in a *syn* fashion[13] gives adduct **J**. Since β-hydride elimination requires a metal oriented *syn* to the hydrogen, a C-C bond rotation is required to give **K** having the



Scheme 1. Pathway for the Formation of **4**.

desired conformation (**J** → **K**). The stereochemisty around the double bond is reversed to *E* in the *syn* β-hydride elimination step (**K** → **6**).[12]



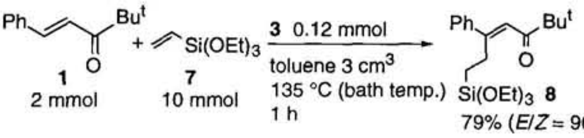
Scheme 2. Pathway for the Formation of **6**.

We suggest that the differences in reactivities of **1** vis-à-vis **5** arise as the result of a difference in the conformational rigidities of the enone moieties with respect to the *s*-cis form. A higher conjugation due to the *s*-cis phenyl group in **1** appears to contribute to conformational rigidity, compared to **5**. This conformational rigidity in **1** would be expected to facilitate the formation of carbonyl-coordinated metallacycle. Moreover, the bulky intermediate **H** can react only with an enone which contains a small substituent, such as **5**, but not with **1**.

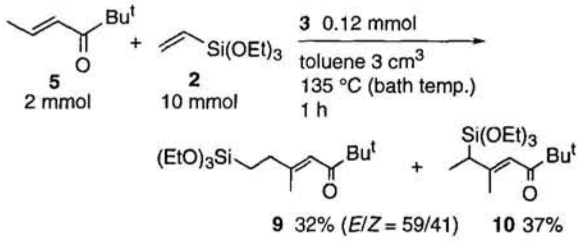
When the olefinic C-H/olefin coupling reactions were conducted using triethoxyvinylsilane (**7**), similar stereoselectivities were observed. In the case of the reaction of **1** with **7**, the coupling product **8** was obtained in a good yield and with high stereoselectivity (*E*/*Z* = 96/4) (Eq. 3). The ratio of *E* to *Z* was not changed for the conversion of **1**. Therefore, it appears likely that the *E*-isomer is formed through Mechanism 1. The reaction of **5** with **7** gave three isomeric products (**9** and **10**) in 69% total yield (Eq. 4). Two of these isomers were stereoisomers, *i.e.*, ***E*-9** (the stereochemically reversed product) and ***Z*-9** (the retention product). The other product **10** was stereochemically pure and corresponded to adduct **6**, both being formed *via* Mechanism 2. The ratio of ***E*-9** to ***Z*-9** was nearly constant (ca. *E*/*Z* = 60/40) throughout the reaction (5-60 minutes). Whether this is due to thermodynamic equilibrium or to two independent courses with different mechanisms is not clear at present. Again, the opposite stereochemical outcome for the production of **8** and **10** indicates the existence of two different reaction courses, namely, Mechanisms 1 and 2, respectively.

In summary, in the ruthenium-catalyzed reaction of acyclic α,β-enones with olefins, two different reaction mechanisms apparently operate. The reaction pathway strongly depends on the substrate employed.

Supporting Information Available (4 pages) including spectral data of new compounds are available on request to the author by telefax (+81-6-879-7396).



(3)



(4)

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11 No double bond isomerization of the coupling product to the thermally stable isomer, i.e., isomerization of *Z*-**4** to *E*-**4**, during the catalytic reaction was confirmed by the following control experiment. The reaction of the enone **1** with *p*-methylstyrene was carried out in the presence of a *E*/*Z* mixture of **4** (*E*/*Z* = 36/64), which had been prepared by photo isomerization of *E*-**4**. After 1 h, **1** was completely consumed, and then the reaction mixture was further heated for additional 3 h (4 h totally). The ^{1}H NMR spectrum of the mixture of **4** recovered and the similar product derived from *p*-methylstyrene indicated that the *E*/*Z* ratio of **4** did not change. This result suggests that the thermal or catalytic double bond isomerization of the products is not important for the present C-H/olefin coupling reaction.

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