The Ruthenium-Catalyzed Addition of β C–H Bonds in Aldehydes to Olefins

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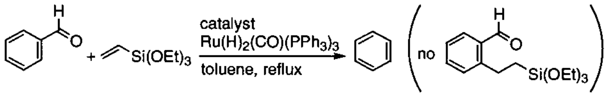
The addition of a β C–H bond to the formyl group of aldehydes to olefins took place with the aid of $Ru(H)_2(CO)(PPh_3)_3$ as a catalyst. Several olefins can be used in the catalytic reaction of conjugate enals. The presence of a sterically hindered substituent at the *ortho* position of benzaldehyde and the presence of an electron donating substituent appear to be important factor in accomplishing the desired coupling reaction.

We recently reported on a series of "chelation-assisted" ruthenium-catalyzed reactions which enable the direct addition of aromatic C–H bonds, which are positioned *ortho* to ketones[1] or esters,[2] to olefins. In these reactions, the coordination of the oxygen atom of the carbonyl groups relative to the ruthenium represents a critical factor in C–H bond cleavage.[1–4] In due course, we attempted a similar C–H/olefin coupling using benzaldehyde in the presence of ruthenium complexes as catalysts. We were, however, surprised to observe that no addition reaction took place and that the majority of the starting material had been decarbonylated to benzene (eq 1). To effect the catalytic addition of the *ortho* C–H bond of an aromatic aldehyde to olefins, the usual reactions such as decarbonylation[5] and hydroacylation[6] (of olefins) must be suppressed. In this paper, we describe our successful attempts on these problems, in which clean C–H/olefin coupling for aldehydes has been observed.



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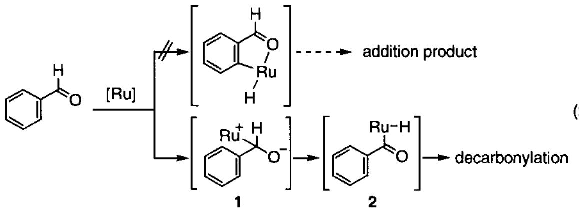


(2)

We concluded that the failure to achieve catalytic addition in our earlier attempts was due to the followings: with respect to the aldehyde carbon, which is less crowded than those of aromatic ketones or esters, the ruthenium center can undergo nucleophilic attack to easily give intermediate **1** (eq 2). Hydrogen migration onto the ruthenium (**1** to **2**) then initiates the conventional course of decarbonylation. To prevent the attack of the ruthenium on the aldehyde carbon, two methods were devised, one steric and the other electronic in nature. In the former case, the presence of a sterically hindered substituent adjacent to the formyl group would be expected to suppress the approach of a metal to the formyl group (Figure 1). In the latter case, a heteroatom would be expected to decrease the electrophilicity of the formyl group via the donation of the lone-pair of electrons of the heteroatom (Figure 2). The heteroatom on the β carbon may increase the contribution of resonance form **B** (Figure 2) in which the formyl group would not be predicted to be attacked by the metals. Moreover, the presence of such a heteroatom would increase the ability of the aldehyde oxygen to coordinate to the catalytic center, thus enhancing the course of the coupling reaction.

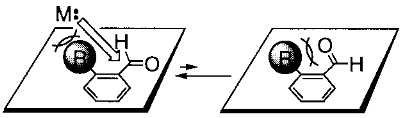


Figure 1.

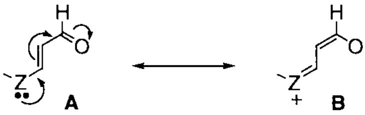
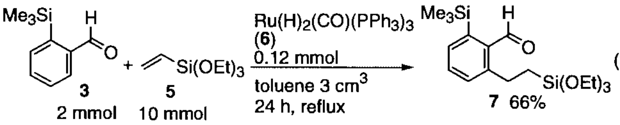


Figure 2.

The first strategy for suppressing the decarbonylation of aldehydes (Figure 1) was examined using *o*-trimethylsilylbenzaldehyde (**3**) and 2,4-di-*tert*-butylbenzaldehyde (**4**), which contain a sterically hindered group at a position *ortho* to the formyl group (eq 3 and 4). The reactions of the aldehydes **3** and **4** with triethoxyvinylsilane (**5**) in the presence of $Ru(H)_2(CO)(PPh_3)_3$ (**6**) as the catalyst resulted in the *ortho* addition products **7** and **8** in 66% and 69% yields, respectively.[7] These results were in contrast to the reaction of benzaldehyde with **5**, in which a decarbonylation to give benzene was observed (eq 1). This distinct change in the course of the reaction appears to be caused from the anticipated steric effect of the substituent as shown in Figure 1.



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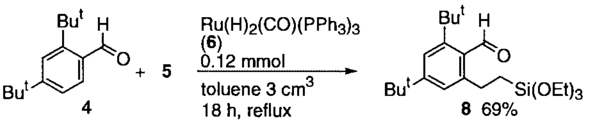
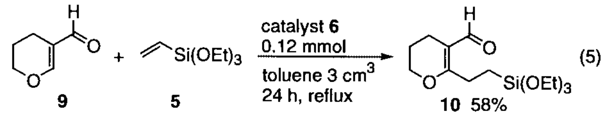


(4)

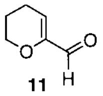
We then studied the reaction according to the second strategy on the basis of which is an electronic effect (Figure 2). The reaction of 5,6-dihydro-4*H*-pyran-3-carbaldehyde (**9**), which contains a heteroatom at the carbon β to the carbonyl group, with **5** gave the addition product **10** in 58% yield (eq 5) with no detectable decarbonylation product being formed. It is noteworthy that an olefinic C–H bond in the conjugate enal **9** can add to the C–C double bond and that the formyl group remained intact in the coupling product.

Interestingly, the reaction of enal **11** with **5** did not proceed, although the corresponding ketone analogue **12** exhibited



(5)

a high reactivity in the ruthenium-catalyzed olefinic C–H/olefin coupling as well as enone **13**.[1b] In the reaction of 1-cyclohexenecarbaldehyde (**14**), decarbonylation to cyclohexene was the predominant reaction. These results suggest that the presence of the oxygen atom on the β carbon is important in accomplishing the desired coupling reaction.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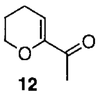
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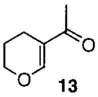
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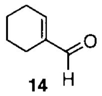
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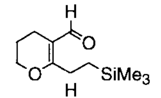
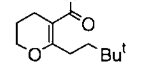
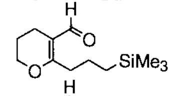
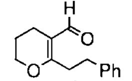
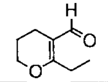
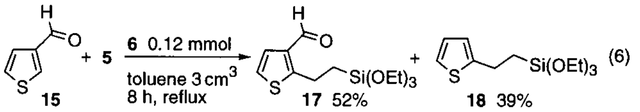
Reactions of **9** with several olefins were also examined (Table 1). The reaction of **9** with trimethylvinylsilane gave the corresponding product in 77% yield (Entry 1). A sterically hindered olefin, i.e., *tert*-butylethylene, can also be used (Entry 2). The reaction with allyltrimethylsilane took place smoothly to give the expected product in good yield (Entry 3). In the case of the reaction with styrene, the coupling product was obtained in quantitative yield, in the form of a mixture of linear and branch products in a ratio of 75 : 25 (Entry 4). The ethylation of **9** using ethylene proceeded in good yield (Entry 5).

Table 1. Reaction of aldehyde **9** with various olefins[a]

Entry	Aldehyde	Olefin	Product	Yield[b]/%
1	**9**			77%
2				46%
3				65%
4[c]				quant. (n:i = 75:25)
5[d]		=		78%

[a]Reaction conditions: aldehyde (2 mmol), olefin (10 mmol), toluene (3 cm^3), in a screw-capped vial, at 115 °C (oil bath temperature), for 24 h. [b]GC yield. [c]Reaction was carried out in refluxing toluene (oil bath temperature, 135 °C). [d]Reaction with ethylene (7 atm, 14 mmol) was carried out in an autoclave at 115 °C.

These observations described above motivated us to further investigate this type of reaction. Five-membered heteroaromatic aldehydes, e.g., 3-thiophenecarboxaldehyde (**15**) and 1-methylindole-3-carboxaldehyde (**16**), were also applicable to the present catalytic reaction (eq 6 and 7). In these cases, the product selectivities were not high and a mixture of the C–H/olefin coupling product and the decarbonylation product was obtained in both cases. The formation of decarbonylation products **18** and **20** are the predicted products from **17** and **19**, respectively because the reactions of thiophene and *N*-methylindole with **5** did not give detectable amounts of coupling products such as **18** and **20** at all, and the reaction of **17** with **5** under the same conditions of eq 6 gave the decarbonylation product **18** in high yield. The reaction of **16** with ethylene under the same reaction conditions as used in Entry 5 of Table 1 gave the addition product in quantitative yield.



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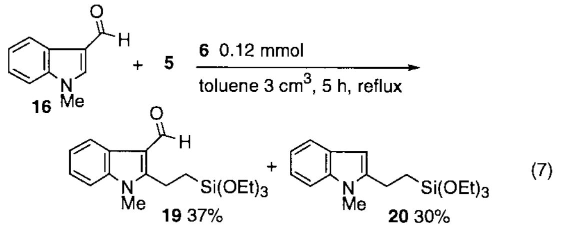
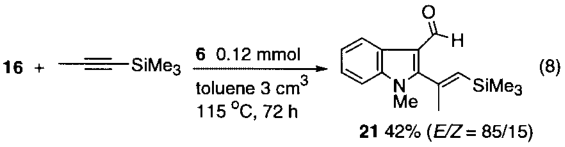


(7)

In place of an olefin, acetylenes were used for the reactions described below. The reaction of aldehyde **16** with 1-(trimethylsilyl)-1-propyne provided the vinylation product **21** in 42% yield as a mixture of stereoisomers (eq 8).



(8)

This paper outlines our results concerning the ruthenium-catalyzed reaction of aldehydes with olefins, which gave addition products. Two unique effects of the substituents in attaining the desired C–H/olefin coupling have been mentioned. One is the use of a steric effect and the other one, electronic effects. Further studies on the applications of these unique effects of substituents on the chelation-assisted C–H/olefin coupling are currently in progress.

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References and Notes

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7 Supporting Information (6 pages) including a typical experimental procedure and spectral data of new compounds are available on request to the author by FAX (+81-6-6879-7396).