ORGANIC
LETTERS

1999
Vol. 1, No. 10
1635−1637

Ruthenium-Catalyzed Regioselective Codimerization of Enol Acylates with 2-Substituted-1,3-butadienes

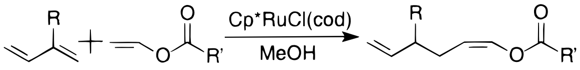
Mitsuhiko Fujiwhara,* Takenobu Nishikawa, and Yoji Hori

Central Research Laboratory, Takasago International Corporation,
1-4-11, Nishi-Yawata, Hiratsuka City, Kanagawa 254-0073, Japan

tic00309@nifty.ne.jp

Received September 2, 1999

ABSTRACT

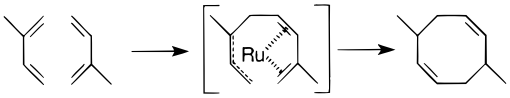


We have found a new ruthenium-catalyzed cooligomerization reaction of vinyl acylates with 2-substituted-1,3-butadienes, where very high yields as well as high regioselectivities were attained.

Ruthenium-catalyzed carbon−carbon bond-forming reactions have attracted a lot of attention recently.[1] Without mentioning the metatheses reported by Grubbs and others, those via ruthenacycle intermediates have been greatly advanced.[1] Especially, ruthenacyclopentenes, derived from alkynes and alkenes via coordination with the metal followed by oxidative ring formation, have been widely reported as intermediates. For example, simple reductive elimination of such ruthenacyclopentenes was shown to afford [2 + 2] cycloadducts,[2] while trapping them with CO was reported to give Pauson−Khand type products.[3] Acyclic products have also been obtained via β-hydride elimination pathway.[4] Moreover, some unusual reactivities, such as cyclopropanation[5] and [4 + 2] cycloaddition,[6] have been observed. Interestingly, none of these involves conjugated diene systems as their substrates.[7] Actually, since Mitsudo's pioneering work of the ruthenium-catalyzed coupling reaction using conjugated dienes,[8] only a few examples have appeared in this field. Among them, the Itoh group developed a novel dimerization reaction of butadiene derivatives, which proceeded via a ruthenacyclopentane analogous intermediate.[9] We found that the system could be applied to a reaction of conjugated dienes with simple α-olefins. The reaction, with proper combination of substrates, showed very high regioselectivities. Herein we wish to report a novel codimerization[10] reaction of enol acylates with 2-substituted-1,3-butadienes.

In our preliminary study, we found that Itoh's reaction (Scheme 1) was applicable in protic solvents, where no activation was required.[11] The same system was applied to the present codimerization reaction. Our first choice was the

Scheme 1. Dimerization of Isoprene



isoprene (**1a**) **2** **3**

---

(1) Naota, T.; Takaya, H.; Murahashi, S.-I. *Chem. Rev.* **1998**, *98*, 2599.

(2) (a) Mitsudo, T.-A.; Watanabe, Y. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 968. (b) Watanabe, Y.; Mitsudo, T.-A.; Kondo, T. *Catalysis* **1992**, *34*, 173. (c) Watanabe, Y.; Mitsudo, T.-A.; Tsuji, Y. *Synth. Org. Chem. Jpn.* **1988**, *46*, 789. (d) Mitsudo, T.-A.; Kokuryo, K.; Shinsugi, T.; Nakagawa, Y.; Watanabe, Y.; Takebami, Y. *J. Org. Chem.* **1979**, *44*, 4492. (e) Mitsudo, T.-A.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580.

(3) (a) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T.-A. *J. Am. Chem. Soc.* **1997**, *119*, 6187. (b) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762.

(4) (a) Trost, B. M.; Indolese, A. F.; Müller, T. J. J.; Treptow, B. *J. Am. Chem. Soc.* **1995**, *117*, 615. (b) Derien, S.; Jan, D.; Dixneuf, P. H. *Tetrahedron* **1996**, *52*, 5511.

(5) Kikuchi, H.; Uno, M.; Takahashi, S. *Chem. Lett.* **1997**, 1273.

(6) Trost, B. M.; Imi, K.; Indolese, A. F. *J. Am. Chem. Soc.* **1993**, *115*, 8831.

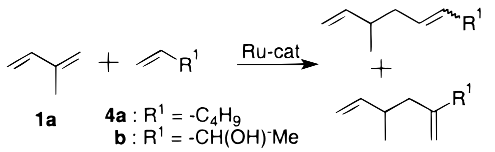
(7) Quite recently, Dixneuf et al. reported a Ru-catalyzed coupling reaction. The reaction was reported to yield conjugated diene system. Paih, J. L.; Derien, S.; Dixneuf, P. H. *Chem. Commun.* **1999**, 1437.

(8) Mitsudo, T.-A.; Nakagawa, Y.; Watanabe, K.; Hori, Y.; Misawa, H.; Watanabe, H.; Watanabe, Y.*J. Org. Chem.* **1985**, *50*, 565.

10.1021/ol991004f CCC: $18.00

coupling of isoprene (**1a**) with 1-hexene (**4a**). The reaction proceeded smoothly to afford a mixture of codimers as we expected. The selectivity was, however, quite poor. (Selectivity of the major isomer was 55%.) Trial to improve the selectivity by using 3-buten-2-ol (**4b**) by means of chelation control did not work either, giving only comparable results (60% selectivity, Scheme 2).[12]

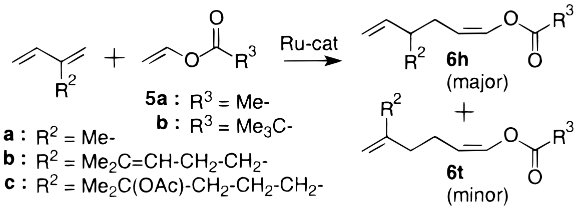
Scheme 2. Cross Coupling Reaction of α-Olefins with Isoprene



Then enol compounds were tested to change the electron density. Though ethyl vinyl ether gave unfruitful results (84% selectivity), use of vinyl acetate (**5a**) dramatically changed the selectivity, affording a codimer in 95% regioselectivity. Typically, isoprene (**1a**) and vinyl acetate (**5a**) in methanol were heated at 100 °C for 14 h in the presence of catalyst [Cp*RuCl(cod) (**7a**),[13] 0.7 mol %] to afford 4-methyl- and 5-methyl-(*Z*)-1,5-hexadienyl acetate (**6h** and **6t**,[14] respectively, in a ratio of 95:5) in 95% yield.[15]

In the same manner, other conjugated dienes [myrcene (**1b**), myrcenyl acetate (**1c**)] as well as another enol acylate [vinyl pivalate (**5b**)] were subjected to the same reaction as summarized in Table 1. All of the combinations were shown to be compatible and gave products in moderate to good yields with high regioselectivities.

Table 1. Results of Codimerization



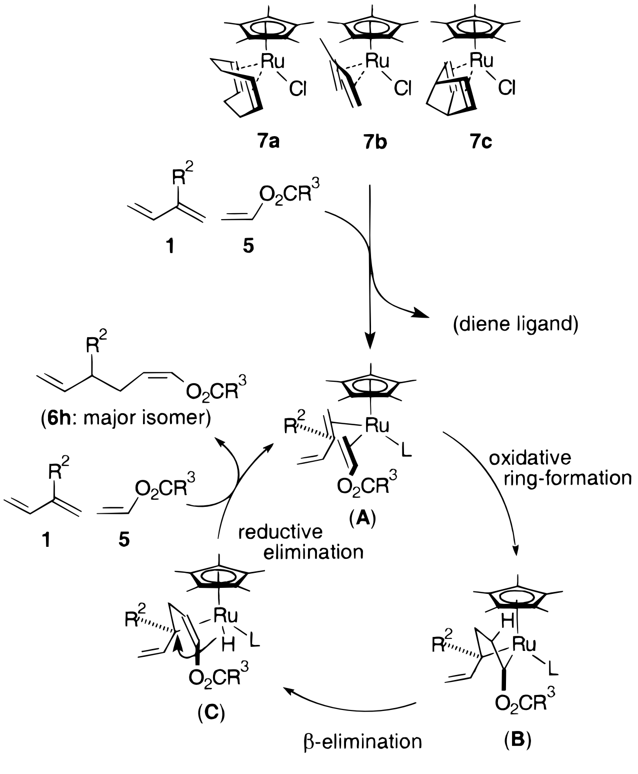
diene	vinyl acylate	catalyst[a]	time (h)	yield[b] (%)	selectivity (**6h**/**6t**)[14]
1a	**5a**	**7a**	14	95	96/4
1a	**5b**	**7b**	12	84	95/5
1b	**5a**	**7a**	14	83	96/4
1b	**5b**	**7c**	15	41	94/6
1c	**5a**	**7c**	15	50	95/5

[a] **7a**: Cp*RuCl(cod). **7b**: Cp*RuCl(isoprene). **7c**: Cp*RuCl(nbd).[13] [b] Yields are calculated on the basis of the less charged starting materials.

The present codimerization reaction has two characteristic features. One is the thermodynamically unfavorable *Z* selectivity, and the other is the unprecedentedly high regioselectivity. Actually, ruthenium-catalyzed codimerization so far reported has shown *E*-selectivity; i.e., Trost's results showed *E*-selectivity.[4a] The present unusual *Z*-selectivity may be attributed to the steric hindrance of the ruthenium complex, as was deduced by Itoh et al.[9] On the other hand, the reason for the high regioselectivity is still obscure. The electronic effect must play an important role, since a change in the electronic environment of the α-olefin moiety affected the regioselectivity significantly. A similar phenomenon was discussed by Dixneuf et al. in the cross coupling of alkynes with alkenes,[4b] which would support our hypothesis. Moreover, a similar high selectivity of isoprene was reported in the nickel-catalyzed reaction quite recently, in which the electronic effect was the explanation for the selectivity.[16]

With these, we propose a plausible reaction mechanism as depicted in Scheme 3. Though there are other possibilities, such as sp^2 C−H activation of enol acylates, the simple ruthenacycle route seems reasonable. The catalytic cycle shows the analogy of Itoh's reaction.[9a] The *Z*-selectivity may be realized by the configurational limitation in the intermediate B, and the regioselectivity might be explained by the

Scheme 3. Plausible Reaction Mechanism



---

(9) (a) Itoh, K.; Masuda, K.; Fukahori, T.; Nakano, K.; Aoki, K.; Nagashima, H. *Organometallics* **1994**, *13*, 1020. (b) Yamamoto, Y.; Ohkoshi, N.; Kameda, M.; Itoh, K. *J. Org. Chem*. **1999**, *64*, 2178.

(10) The term "cooligomerization" was used in place of cross-coupling, because the reaction is analogous to copolymerization.

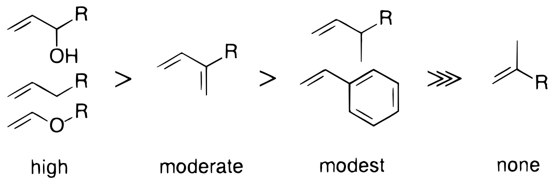
(11) Fujiwhara, M.; Miura, T.; Nishikawa, T.; Hori, Y. Japanese Patent Application H11-194185.

(12) It should be noted that the regioselectivity with regard to the isoprene moiety was reasonably high.

coordination direction of olefins in A governed by electronic factor. The ligand (L) may be Cl, solvent, or even the intramolecular coordination of either free double bond to construct a π-allyl complex equivalent or acyl group. It should be noted, however, that the reductive elimination did not occur to construct a trisubstituted olefin. This indicates that allylic migration did not occur in the intermediate C.

The present reaction is applicable to a variety of vinyl acylates and 2-substituted-1,3-butadiene derivatives, but the importance of steric factor should be emphasized. The reactivity of α-olefins, not limited to vinyl acylates, is summarized in Table 2. For this study, isoprene was employed as the 2-substituted-1,3-butadiene derivative, and the ratio of isoprene to α-olefin employed was ca. 1:1. The judgment was made by comparing the amount of a mixture of codimers and dimethylcyclooctadiene (homodimer of isoprene) in the products. As is easily recognized, the 3,4-olifinic portion of isoprene can be regarded as an α-olefin, and the codimerization of isoprene as a diene with isoprene as an α-olefin (i.e., homodimerization) should be competitive with the intended codimerization. Thus the α-olefinic nature of isoprene was thought to be a standard for judging the reactivity of several α-olefins.

Table 2. Reactivity of α-Olefins



run	α-olefin[a]	codimer/homodimer
1	1-hexene	11
2	3-buten-2-ol	14
3	ethyl vinyl ether	8.5
4	vinyl acetate	19
5[b]	3-methyl-1-butene	6.8
6	styrene	1.2

[a] Ca. 1 equiv of α-olefin was used except for run 5. [b] 5 equiv of α-olefin was used. Due to its volatility (bp 20 °C), it was difficult to charge the same proportion with the other cases.

When 1-hexene, 3-buten-2-ol, ethyl vinyl ether, or vinyl acetate was employed as the α-olefin, the ratio of co-/homodimer was ca. 10. This apparently indicated that they reacted with isoprene much faster than the reaction of isoprene alone. So their reactivity was assigned to be "high". The products, codimers, also have α-olefinic portions, i.e., 3-methyl-1,2-olefin, and the reaction of the co-dimers as α-olefins with isoprene (i.e., over-reaction) should be possible. To our delight, only 3% of over-reacted products was detected, and thus the reactivity of the 3-substituted-1,2-olefin was assigned to be "modest". To confirm this, isoprene was reacted with 5 equiv of 3-methyl-1-butene. Even in such an extreme condition, the ratio of codimer to homodimer was lower than that for the former case (7.6). Styrene showed comparable selectivity, though the reactivity was not high with regard to the catalyst turn over number. (TON = ca. 3 for styrene. Typical isoprene dimerization showed a TON of ca. 200.) Steric hindrance was supposed to be the reason for the modest reactivity. The reactivity was completely lost when more than two subutituents were present on the double bond. This also implied the importance of steric effect.

Next, the importance of 2-substitution of 1,3-butadiene should be explained. When the simple 1,3-butadiene was used, the product was a less hindered α-olefin, whose reactivity could be classified as "high", and thus the reaction went out of control. Therefore, the combination of vinyl acylate as the α-olefin and a 2-substituted-1,3-butadinene as the diene was crucial for the selectivity.

In conclusion, we have found a novel codimerization reaction catalyzed by ruthenium complexes. The reaction gave codimers in good to high yields (41−95%) with high regioselectivity(∼95%). Some efforts to utilize the codimers (**6**) are now underway.

Acknowledgment. We thank Drs. H. Tsuruta, H. Kumobayashi, T. Hagiwara, and T. Miura for their useful discussion.

OL991004F

---

(13) Cp* = pentamethylcyclopentadienyl; cod = cyclooctadiene; nbd = norbornadiene.

(14) Charactors "h" and "t" came from the terms "head" and "tail". Conventionally, in the isoprene chemistry, these terms have been used to represent the C1 position and the C4 position, respectively.

(15) ^{1}H NMR (200 MHz, CDCl$_3$): 1.01 (3H, d, J = 6.6 Hz), 2.14 (3H, s), 2.0−2.4 (3H, m), 4.8−5.1 (3H, m), 5.74 (1H, ddd, J = 6.8, 10.2, 17.2 Hz), 7.08 (1H, dm, J = 6.6 Hz: this indicates the Z configuration).

(16) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 397.