

New Synthesis of Pyrrolidine Derivatives *via* the Chromacyclobutanes generated from Enynes and Fischer Carbene Complexes

Miwako Mori* and Susumu Watanuki

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

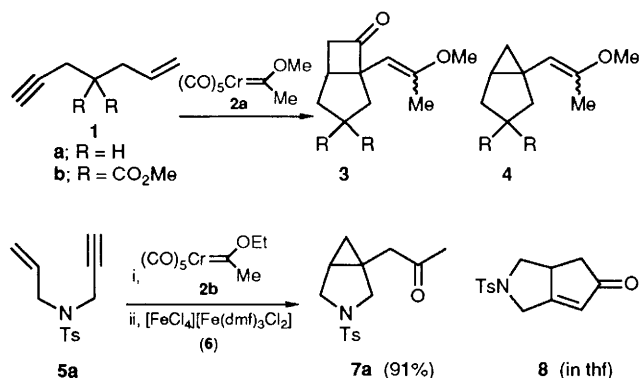
Pyrrolidine derivatives have been synthesized *via* chromacyclobutanes formed from the Fischer carbene complex **2b** and the aza-enyne **5a**; a mechanism is suggested on the basis of the products that are formed.

Recent studies of the reactivity of chromium carbene complexes with enynes have demonstrated their potential for ring construction of bicyclic carbon skeletons.¹ Wulff reported that treatment of enyne **1a** with the methylmethoxy carbene complex **2a** in MeCN gave the bicyclic cyclobutanone **3a** in 45% yield *via* the [2 + 2] alkene-ketene cycloaddition.^{1a} Hoyo reported that treatment of the enyne **1b** with **2a** afforded the bicyclic cyclopropane derivative **4b** in 69% yield by the reaction of the unactivated alkene and the chromium carbene complex.^{1c} These results show that the products of the reaction of such enynes with the Fischer carbene complexes depend on the substituents R. We now report the reaction of the enyne **5a** containing nitrogen in the chain with the Fischer carbene complex **2b**.

When an MeCN solution of **5a** and the pentacarbonyl-(ethoxyethylidene)chromium **2b** was warmed at 70 °C for 4 h and then treated with [FeCl₄][FeCl₂(dmf)₃]² **6** (dmf = dimethylformamide), the bicyclic cyclopropapyrrolidine de-

rivative **7a** was obtained in 91% yield.^{†‡} The yield of **7a** was not affected (84%) when the reaction was carried out in a similar manner under carbon monoxide (1 atm). When a tetrahydrofuran (thf) solution was used in place of MeCN, the bicyclic cyclopentenone derivative **8** was obtained in 18% yield along with **7a** (47% yield).§

Surprisingly, the reaction of compound (*E*)-**5b** (R = H) having a phenyl substituted double bond with **2b** gave the metathesis product **9³** in 53% yield as the main product along with **7b** (7% yield) and the cyclobutanone derivative **11b** (9% yield). These structures were determined by spectral data. NOE experiments on the ring junction proton H_a and the aromatic proton of compound **7b**, of H_b and the aromatic proton of compound **11b** suggested that the reaction proceeded stereoselectively. When the reaction of (*Z*)-**5b** with **2b** was carried out in a similar manner, we obtained only the metathesis products **9** and **9'** in 56% yield (**9**:**9'** = 7:1). Neither the cyclopropane derivative nor the cyclobutanone derivative was obtained in this case because of steric repulsion between the phenyl group and the five-membered ring in the transition state for the formation of the three- or four-membered ring.

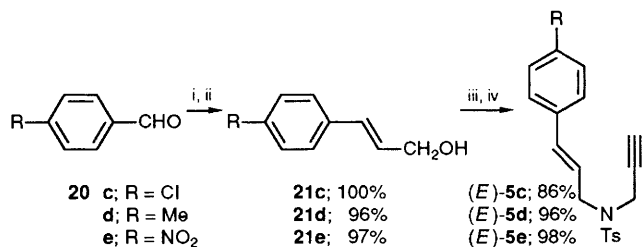
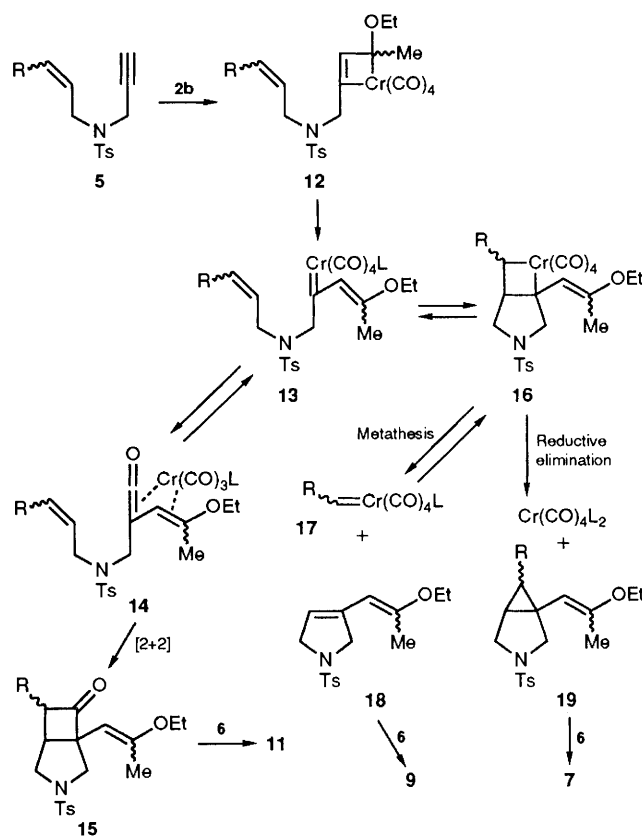
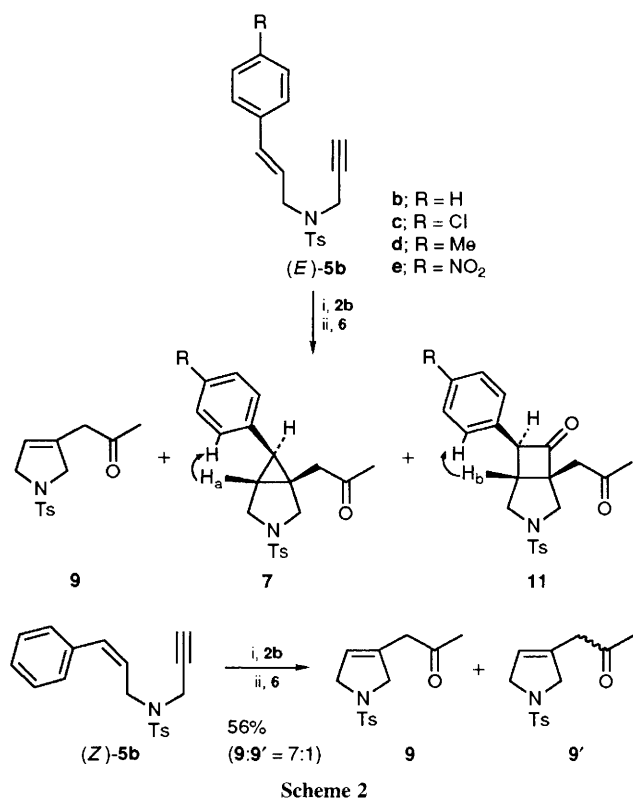


Scheme 1 Ts = *p*-MeC₆H₄SO₂

[†] All new compounds were characterized by ¹H NMR, IR and mass spectroscopy and high-resolution mass spectrometry.

[‡] Katz has reported that the reaction of a metal carbene complex with an enyne afforded the cyclopropane derivative. The conditions involved absorbing the carbene complex on silica gel and using no solvent.^{1b}

[§] The mechanism for the formation of compound **8** is not clear. Possibly, reductive cyclization of the enyne **5a** by a low-valent chromium complex followed by insertion of carbon monoxide would occur to give **8**. When the reaction of **5a** with Cr(CO)₆ in thf was carried out, a small amount of **8** was obtained.



Scheme 3 Reagents and conditions: i, Ph₃P=CHCO₂Et; ii, Bu^t₂AlH; iii, PPh₃-CBr₄; iv, T₅NHCH₂C≡CH

It is interesting that the enyne having an unsubstituted alkene unit afforded the cyclopropane derivative **7** whereas the metathesis product **9** was obtained from the enyne having a phenyl substituted double bond. If the formation of the metathesis product **18** or the cyclopropane derivative **19** was determined by electronic factors involving the double bond the substituent on the aromatic ring should affect the reaction.[¶] To study this compound (*E*)-**5c**, **-5d** and **-5e** were prepared as shown in Scheme 3 and their reactions with **2b** were carried out in a similar manner.

As shown in Table 1, the metathesis pathway was accelerated by the *para*-methyl group on the aromatic ring and compound **9** was obtained in 62% yield. In this case, the reductive elimination product **7d** from the chromacycle **16** was not observed. The reaction of compound (*E*)-**5c** having an electron-withdrawing group on the aromatic ring with **2b** led to an increase in the ratio of the reductive elimination product **7c** to the metathesis product **9** (3:1). It is interesting that compound (*E*)-**5e** have a *para*-nitrophenyl group on the double bond afforded the cyclopropane derivative **7e** as the

Table 1 Effect of the substituent on the aryl group of the double bond^a

| Run | Starting material | R | Yield (%) | | | |
|----------------|-------------------------|-----------------|-----------|----------|-----------|------------|
| | | | 9 | 7 | 11 | 9:7 |
| 1 | (<i>E</i>)- 5b | H | 53 | 7 | 9 | 7.7: 1 |
| 2 ^b | (<i>E</i>)- 5b | H | 29 | 5 | 6 | 6: 1 |
| 3 | (<i>E</i>)- 5c | Cl | 46 | 18 | 8 | 3: 1 |
| 4 | (<i>E</i>)- 5d | Me | 62 | — | 6 | 1: 0 |
| 5 | (<i>E</i>)- 5e | NO ₂ | 4 | 75 | — | 1:19 |

^a All reactions were carried out in MeCN at 70 °C for 4 h. ^b The reaction was carried out under carbon monoxide.

main product. The fact that the unsubstituted alkene **5a** (R = H) and compound **5e** having a *para*-nitrophenyl group on the double bond afforded the cyclopropanes may be explained as follows (Scheme 4).

Since [2 + 2] cycloadditions are controlled by HOMO-LUMO interactions, the cycloaddition in this instance should be retarded by lack of activation of the double bond. Thus, compounds **5a** and **5e** would afford only the chromacycles **16a** and **16e** which would give the cyclopropanes **7a** and **7e** in good yields because of the instability of the alkylidene carbene complexes **17a** and **17e**. On the other hand, the electron-donating groups on the double bond would favour the metathesis process because of the stabilization of the alkylidene carbene complex **17** generated from the chromacycle **16**.

In conclusion, the reaction pathway of the enyne **5** and the Fischer carbene complex **2b** was dramatically affected by the substituents on the double bond; in particular the compound

[¶] Hoye has reported that the reaction of an enyne having a methyl group on the double bond with the Fischer carbene complex afforded the metathesis product in 30% yield.^{1c}

having a *p*-tolyl substituted double bond gave only the metathesis product **18** from the chromacycle **16**.

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