The Journal of
Organic
Chemistry

VOLUME 58, NUMBER 21 OCTOBER 8, 1993

Communications

Stereoselection in the Chromium-Mediated Intramolecular [2 + 2] Cycloadditions of Vinyl Ketenes and Alkenes

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Received June 22, 1993[•]

Summary: The first study of the relative diastereoselectivity of the intramolecular [2 + 2] cycloadditions of alkenes and vinyl ketenes generated from the reactions of carbene complexes with chiral enynes is reported.

Since the initial reports on the reactions of enynes with Fischer carbene complexes in 1985,[1,2] these reactions have been found to produce a number of products including cyclopropanes of the type 4 and cyclobutanones of the type 6.[3] All studies subsequent to the initial report have been focused on the cyclopropane products of the type 4 which result from the intramolecular transfer of the carbene ligand to the alkene in intermediate 3. An alternate outcome of this reaction involves the migratory insertion of a CO ligand into the carbene ligand to generate the vinyl ketene complex 5 and then a formal [2 + 2] cycloaddition of the ketene and alkene to give the cyclobutanone 6.[1a,4] This reaction is related to the intramolecular [2 + 2] cycloaddition of the metal free ketene with a tethered alkene, a reaction of established synthetic utility[5,6] due to the importance of cyclobutanones as synthetic intermediates.[7] We report that the reaction of Fischer carbene complexes with chiral enynes gives cyclobutanones 6 with high diastereoinduction and evidence that indicates that both the rates and the diastereoselectivity of the [2 + 2] cycloaddition step are greater for the metal-mediated process.

The results of the reactions of the methyl substituted Fischer carbene complexes 1 with several 1,6-heptenynes are summarized in Table I. The primary products of these reactions are the bicyclo[3.2.0]heptanones 9 with the angular enol ether function, and in those reactions with chiral enynes they are obtained as a mixture of four diastereomers. The isolated yields of 9 as a mixture of isomers are given in entries c, d, and f, and in one case the stereochemical assignment was made for each of the four

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[•] Abstract published in *Advance ACS Abstracts,* September 1, 1993.

(1) (a) Wulff, W. D.; Kaesler, R. W. *Organometallics* **1985**, *4*, 1461. (b) Katz, T. J.; Sivavec, T. M., *J. Am. Chem. Soc.* **1985**, *107*, 737.

(2) For reviews on the chemistry of Fischer carbene complexes, see: (a) Dötz, K. H. In *Organometallics in Organic Synthesis: Aspects of a Modern Interdisciplinary Field*; tom Dieck, H., de Meijere, A., Eds.; Springer: Berlin, 1988. (b) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 5, pp 1065–1113.

(3) (a) Korkowski, P. F.; Hoye, T. R.; Rydberg, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 2676. (b) Sivavec, T. M.; Katz, T. J.; Chiang, M. Y.; Yang, G. X.-Q. *Organometallics* **1989**, *8*, 1620. (c) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1989**, *8*, 2070. (d) Hoye, T. R.; Rehberg, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 2841. (e) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1990**, *9*, 3014. (f) Katz, T. J.; Yang, G. X.-Q. *Tetrahedron Lett.* **1991**, *32*, 5895. (g) Harvey, D. F.; Lund, K. P. *J. Am. Chem. Soc.* **1991**, *113*, 5066. (h) Harvey, D. F.; Lund, K. P.; Neil, D. A. *Tetrahedron Lett.* **1991**, *32*, 6311. (i) Hoye, T. R.; Suriano, J. A. *Organometallics* **1992**, *11*, 2044. (j) Harvey, D. F.; Brown, M. F. *J. Org. Chem.* **1992**, *57*, 5559. (k) Harvey, D. F.; Lund, K. P.; Neil, D. A. *J. Am. Chem. Soc.* **1992**, 114, 8424. (l) Mori, M.; Watanuki, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1082.

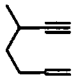
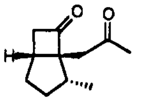
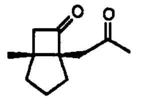
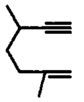
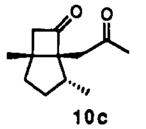
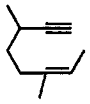
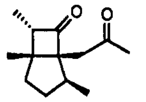
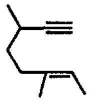
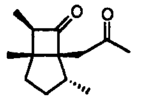
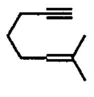
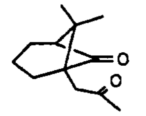
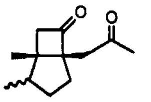
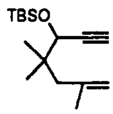
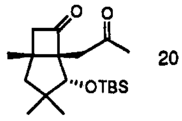
(4) For examples of [2 + 2] cycloadditions of alknenes with photogenerated ketenes from Fischer carbene complexes, see: Hegedus, L. S.; Bates, R. W.; Soderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923.

(5) Snider, B. B. *Chem. Rev.* **1988**, *88*, 793.

(6) For citations to the recent literature, see: (a) Chen, L. Y.; Ghosez, L. *Tetrahedron Asymmetry* **1991**, *2*, 1181. (b) Xu, S. L.; Xia, H. J.; Moore, H. W. *J. Org. Chem.* **1991**, *56*, 6094. (c) Baeckstrom, P.; Li, L.; Polec, I.; Unelius, C. R.; Wimalasiri, W. R. *J. Org. Chem.* **1991**, *56*, 3358. (d) Snider, B. B.; Allentoff, A. J. *J. Org. Chem.* **1991**, *56*, 321.

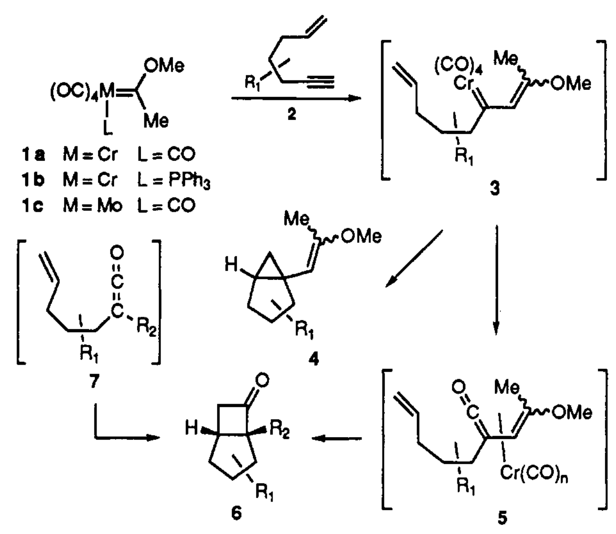
(7) Bellus, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797.

Table I. Reactions of Enyne 8 with Carbene Complex 1[a]

entry	enyne	% yield 9	% yield 10[b]	major diastereomer of 10	selectivity
a			33	 **10a**	11.0 : 1
b			50	 **10b**	
c		83[c]	69 49 60 25	 **10c**	11.3 : 1 **1a**, CH_3CN 4.9 : 1 **1a**, acetone 6.4 : 1 **1b**, CH_3CN 5.8 : 1 **1c**, CH_3CN
d		39[d]	39	 **10d**	1 : >10
e			64	 **10e**	>11 : 1
f		73[e]	69[f]	 **10f**	
g			67	 **10g**	2 : 1[g]
h			73	 **10h**	20 : 1[h]

[a] Unless otherwise specified all reactions were carried out in acetonitrile at 0.005–0.01 M in complex **1a** with 1.5 equiv of alkyne at 70 °C for 3–4 h. [b] Overall yield from complex **1** in each case after workup with aqueous HOAC. [c] Reference 8a. [d] Reference 8b. [e] 2.35: 1.0 mixture of *E* and *Z* isomers. [f] Reference 9. [g] Stereochemistry not determined. [h] Stereochemistry assigned on the basis of **10c**.

Scheme I



diastereomers (entry c).[8] It was found most convenient, however, to remove the stereochemistry of the enol ether function in **9** by including an acid hydrolysis in the workup which gave the diketones as a more simplified mixture of only two diastereomers of which only the structure of the major diastereomer is shown. Chiral centers at the position α to the alkyne lead to diastereoselection of from ~90% for **10a**, **10c**, **10d**, and **10e** to 95% for the siloxy derivative **10h**. For the enyne **8g** with a chiral center α to the alkene the stereoselection was only 2:1 in the cyclobutanone **10g** and the stereochemistry was not assigned. In the case of the enyne **8f** the cyclobutanone **10f** was obtained in good yield that resulted from a crossed [2 + 2] cycloaddition.[9] The stereochemistry of the major diketone **10c** from the reaction of the enyne **8c** was shown to be that where the methyl on the tertiary carbon is trans to the quaternary methyl substituent by an X-ray analysis of **13**.[10] Interestingly, the stereochemistry of methyl group on the tertiary carbon in **10d** (but not **10e**) is reversed from that of **10c**.[10]

Since the reactions of enynes with the carbene complexes **1** were all carried out in acetonitrile the question is raised whether the metal unit is displaced from the vinyl ketene complex **5** (Scheme I) and thus whether the [2 + 2] cycloaddition occurs via the free vinyl ketene.[11] Evidence that the metal is coordinated to the vinyl ketene during the cycloaddition can be taken from the fact that the stereoselectivity of the formation of **10c** is dependent on the nature of the metal (11.3:1 for Cr, 5.8:1 for Mo, entry c) and the nature of the metal ligands (11.3:1 for $(CO)_5$, 6.4:1 for $(CO)_4PPh_3$, entry c). Further evidence for the presence of the metal during the cycloaddition comes from a comparison of the rates and the stereoselectivity of the formation of **10c** and **10d** obtained from the reaction of a carbene complex **1a** and from the free vinyl ketene **7** generated from the electrocyclic ring-opening of the cyclobutenones **11c** and **11d**.[12,14,17] The carbene complex **1a** gives **10c** as a 11.3:1 mixture of isomers (entry c) whereas the free vinyl ketene gives **10c** as a 4.3:1 mixture of isomers,

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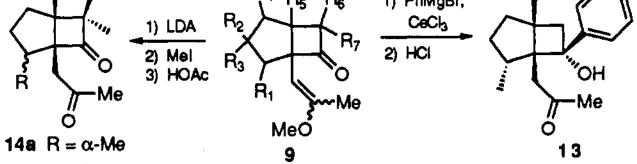
[8] (a) Compound **9c** was isolated in 83% total yield as a 72.4:19.5: 6.7:1.4 mixture of four diastereomers that were identified as **9c**-*E*α, **9c**-*Z*α, **9c**-*E*β, and **9c**-*Z*β, respectively (*E* and *Z* refers to the enol ether stereochemisty and α refers to the isomer with the two methyl groups on the 5-membered ring trans). (b) This reaction also produces a lactone product in 27% yield and a cyclobutenone product in 6% yield.

[9] The structure of **10f** was confirmed by ^{13}C labeling experiments (see supplementary material).

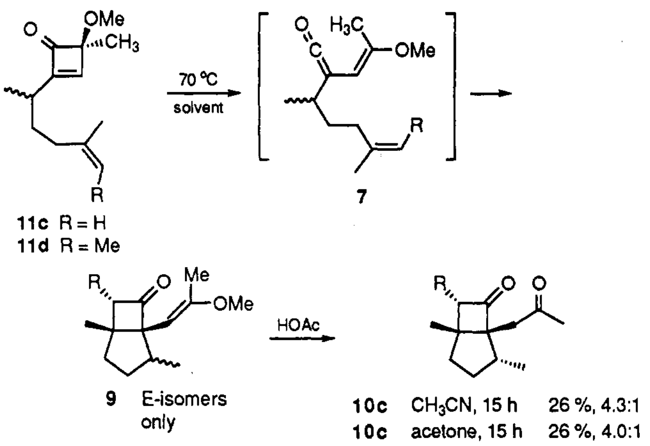
[10] Addition of phenyl Grignard to the ketone of the mixture of isomers of **9c** and hydrolysis produced the ketone alcohol **13** (59%) as the major isomer which provided suitable crystals for X-ray analysis. Exhaustive methylation of the mixtures of isomers of **9c**, **9d**, and **9e** and subsequent hydrolysis in each case produced a mixture of **14a** and **14b** for which **14a** is the major isomer from **9c** and **9e** but not from **9d**.



14a R = α-Me
14b R = β-Me
9
13

[11] (a) Chan, K. S.; Peterson, G. A.; Brandvold, T. A.; Faron, K. L.; Challener, C. A.; Hyldahl, C.; Wulff, W. D. *J. Organomet. Chem.* 1987, *334*, 9. (b) McCallum, J. S.; Kunng, F. A.; Gilbertson, S. R.; Wulff, W. D. *Organometallics* 1988, *7*, 2346.

Scheme II



10c	CH_3CN, 15 h	26 %, 4.3:1
10c	acetone, 15 h	26 %, 4.0:1
10d	CH_3CN, 10 h	—
10d	CH_3CN, 4 d	<4 %

and furthermore the stereoselectivity of the reaction is solvent dependent from the carbene complex but not from the free vinyl ketene.[13] The diketone **10d** is obtained in 39% yield from the reaction of carbene complex **1a** in 4 hours at 70 °C. Under exactly the same conditions the free vinyl ketene **12d** gives no detectable amount of **10d** after 10 hours and only trace amounts of **10d** after 4 days. With the reasonable assumption that **11c** and **11d** undergo electocyclic ring-opening to **7** with similar rates, it can be concluded that the intramolecular [2 + 2] cycloaddition of **7d** is slower than **7c** (thermolysis of **11c** is complete in 15 h) and also slower than the metal complexed **7c** generated from the reaction of **1a** with **8d**. The conformations of **7c** and **5c** shown in Figure 1are drawn to depict likely close contacts in the coordinated and free ketenes as the olefin begins to approach the ketene in a perpendicular fashion. The stereoselectivity of the [2 + 2] cycloaddition of the free vinyl ketene **7c** is likely the result of the lower energy of the conformation of **7c** shown relative to that of its epimer at C-4. The increased stereoselectivity in the formation of **10c** from the chromium coordinated vinyl ketene would be expected from a consideration of the conformer **5c** since the methyl group at C-4 would have additional close contacts with the metal and its ligands in the C-4 epimer of **5c** that would not be present in the C-4 epimer of the conformer **7c** of the free ketene. Why the metal unit in **5c** would be preferred (or preferentially react from) on the lower face of the vinyl ketene can not be probed with the present experiments.

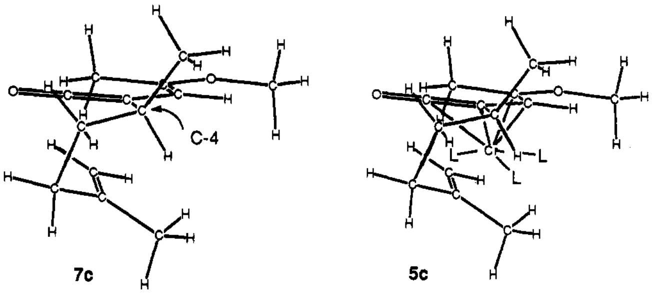


Figure 1.

Although a large number of ketene metal complexes have been isolated and characterized,[15] there is only one example of a [2 + 2] cycloaddition of an alkene with a coordinated ketene. In this intermolecular example, the [2 + 2] cycloaddition of cyclopentadiene with a manganese complex of diphenylketene is slower for the coordinated ketene than for the free ketene.[16] This is in contrast with the data above which suggest that the rate for the [2 + 2] cycloaddition of the metal coordinated ketene **7d** is greater than that for the free ketene. A possible explanation for this which remains to be experimentally verified is that the manganese complex undergoes cycloaddition with an anti approach of the alkene to the coordinated ketene and the reaction of the present chromium complex proceeds via a syn approach of the alkene perhaps through an alkene complex.

This work should prompt experiments to further explore the mechanistic issues associated with the reactions of carbene complexes with enynes and the consideration of synthetic strategies created by the ready access to the bicycloheptanones described herein.

Acknowledgment. This work was supported by a grant from the National Institutes of Health (PHS-CA 32974). Some of the mass spectral data were obtained at the Midwest Center for Mass Spectrometry with partial support by the National Science Foundation, Biology Division (Grant No. DIR 9017262). The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program.

Supplementary Material Available: Experimental procedures and spectral data for compounds **8a–8h, 9c, 10a–10h,** and **13** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(12) (a) The synthesis of **11d** was accomplished with a strategy similar to that described for **11c**,[12b] and the details will be reported in a full account of this work. (b) Challener, C. A.; Wulff, W. D.; Anderson, B. A.; Chamberlin, S.; Faron, K. L.; Kim, O. K.; Murray, C. K.; Xu, Y. C.; Yang, D. C.; Darling, S. D. *J. Am. Chem. Soc.* **1993**, *115*, 1359.

(13) The electrocyclic ring opening of **11c** gives exclusively the *E*-isomer of **12c** as expected[17] which cyclizes to a 4.3:1 mixture of **10c**. The stereoselectivity of the formation of only the *E*-isomers of **9c** from the carbene complex **1a** is 10.8:1.[8]

(14) Mayr, H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 500.

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(16) Herrman, W. A.; *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 335.

(17) (a) Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T., *J. Org. Chem.* **1988**, *53*, 2482. (b) Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Patil, S.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 975. (c) Houk, K. N.; Spellmeyer, D. C.; Jefford, C. W.; Rimbault, C. G.; Wang, Y.; Miller, R. D. *J. Org. Chem.* **1988**, *53*, 2127.