

Diastereoselective Cyclopropanation of Simple Alkenes by 2-Phenyl- and 2-Ferrocenylalkenyl Fischer Carbene Complexes of Chromium

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The cyclopropanation of olefins with heteroatom-stabilized pentacarbonyl complexes of the group 6 metals is found as one of the earliest and synthetically significant reactions reported in Fischer-type carbene complex chemistry.¹ The success of this formal [2 + 1] cycloaddition is highly dependent on the nature of the alkene and the intra- or intermolecular nature of the process.² The intermolecular reaction with electron-deficient olefins occurs smoothly.^{1a,b,3} Electron-rich olefins also produce useful amounts of substituted cyclopropanes when high pressures of carbon monoxide are used in order to avoid the corresponding olefin metathesis reaction.^{1c,4} However, the diastereoselectivity of these carbene transfer reactions is generally modest giving approximately equal amounts of *cis* and *trans* isomers; better diastereoselectivities have been obtained with alkenylcarbene complexes.^{3c,5} In sharp contrast, simple alkyl-substituted olefins fail to undergo intermolecular cyclopropanation with heteroatom-stabilized group 6 metal carbene complexes,⁶ although these unactivated alkenes can be easily cyclopropanated if the carbene transfer reaction is carried out in an intramolecular fashion.⁷ In this paper, we describe the first examples of the intermolecular cyclopropanation of simple alkenes with (*E*)-(3-ferrocenyl-1-methoxy-2-propenylidene)pentacarbonylchromium (1) and (*E*)-(1-methoxy-3-phenyl-2-propenylidene)pentacarbonylchromium (4).

(1) For the first examples with electron-deficient alkenes, see: (a) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1970**, *103*, 1273. (b) Dötz, K. H.; Fischer, E. O. *Chem. Ber.* **1972**, *105*, 1356. For those with electron-rich alkenes, see: (c) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1972**, *105*, 3966.

(2) For reviews, see: (a) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411. (b) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, pp 387–420. (c) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271.

(3) (a) Wienand, A.; Reissig, H.-U. *Organometallics* **1990**, *9*, 3133. (b) Harvey, D. F.; Brown, M. F. *Tetrahedron Lett.* **1990**, *31*, 2529. (c) Wienand, A.; Reissig, H.-U. *Chem. Ber.* **1991**, *124*, 957. (d) Herndon, J. W.; Tumer, S. U. *J. Org. Chem.* **1991**, *56*, 286.

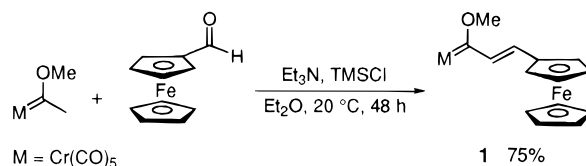
(4) (a) Wulff, W. D.; Yang, D. C.; Murray, C. K. *Pure Appl. Chem.* **1988**, *60*, 137. (b) Murray, C. K.; Yang, D. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1990**, *112*, 5660. (c) Barluenga, J.; Aznar, F.; Martín, A.; Vázquez, J. T. *J. Am. Chem. Soc.* **1995**, *117*, 9419.

(5) For a recent stereoselective cyclopropanation of an electron-poor alkene type (1-azadienes), see: (a) Barluenga, J.; Tomás, M.; López-Pelegrín, J. A.; Rubio, E. *J. Chem. Soc., Chem. Commun.* **1995**, 665. High stereoselectivity has been also observed in the cyclopropanation of simple 1,3-dienes^{5b,c} and electron-deficient 1,3-dienes:^{5c,d} (b) Harvey, D. F.; Lund, K. P. *J. Am. Chem. Soc.* **1991**, *113*, 8916. (c) Buchert, M.; Reissig, H.-U. *Chem. Ber.* **1992**, *125*, 2723. (d) Buchert, M.; Hoffmann, M.; Reissig, H.-U. *Chem. Ber.* **1995**, *128*, 605. (e) Herndon, J. W.; Tumer, S. U. *Tetrahedron Lett.* **1989**, *30*, 4771.

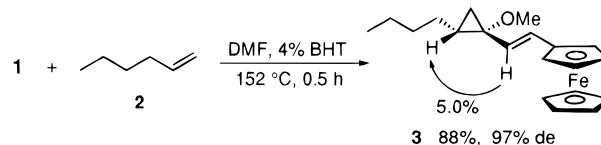
(6) This intermolecular reaction with nonheteroatom-stabilized group 6 metal carbene complexes is known: (a) Casey, C. P.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 7808. (b) Casey, C. P.; Tuinstra, H. E.; Saeman, M. C. *J. Am. Chem. Soc.* **1976**, *98*, 608. (c) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. J.; Jones, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 7282. (d) Harvey, D. F.; Brown, M. F. *J. Am. Chem. Soc.* **1990**, *112*, 7806. (e) Harvey, D. F.; Brown, M. F. *Tetrahedron Lett.* **1991**, *32*, 5223. (f) Fischer, H.; Hofmann, J. *Chem. Ber.* **1991**, *124*, 981. See also: (g) Rudler, H.; Audouin, M.; Parlier, A.; Martín-Vaca, B.; Goumont, R.; Durand-Réville, T.; Vaissermann, J. *J. Am. Chem. Soc.* **1996**, *118*, 12045.

(7) (a) Toledano, C. A.; Rudler, H.; Daran, J.-C.; Jeannin, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 574. (b) Casey, C. P.; Vollendorfer, N. W.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 3754. (c) Casey, C. P.; Hornung, N. L.; Kosar, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 4908. (d) Söderberg, B. C.; Hegedus, L. S. *Organometallics* **1990**, *9*, 3113. (e) Barluenga, J.; Montserrat, J. M.; Flórez, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1068.

Scheme 1



Scheme 2



mium (1) and (*E*)-(1-methoxy-3-phenyl-2-propenylidene)pentacarbonylchromium (4).

Chromium carbene complex 1, in which the carbene ligand contains a ferrocenyl group attached at the β carbon to the carbene carbon atom, was prepared following a previously reported method⁸ as shown in Scheme 1. The *trans* configuration of the carbon–carbon double bond was verified by ¹H NMR ($J = 15.0$ Hz, vinyl protons). This (2-ferrocenylvinyl)-carbene complex 1,⁹ which was isolated as an air-stable dark violet solid, represents a novel heterobinuclear organometallic compound consisting of conjugated donor–acceptor systems. Complexes of these characteristics are attractive synthetic goals due to their physical and chemical properties.¹⁰

Scheme 2 shows the preliminary experiment of our study. Treatment of carbene complex 1 with a 20-fold molar excess of 1-hexene¹¹ and a catalytic amount of 2, 6-di-*tert*-butyl-4-methylphenol (BHT)¹² in dimethylformamide (DMF)¹³ at reflux for 0.5 h led, after chromatographic purification, to (*Z*)-vinylcyclopropane 3¹⁴ with very high diastereoselectivity and good chemical yield.¹⁵ When this reaction was refluxed for a longer period of time (2.5 h), a slightly lower diastereoselectivity (90% de) was observed. The stereochemistry of the major isomer was determined by a difference NOE experiment (Scheme 2; the arrow stands for the observed NOE enhancement). Additionally, we have found that alkenylcarbene complex 4, bearing a phenyl substituent instead of the ferrocenyl group, afforded also, although with lower chemical yield and

(8) Aumann, R.; Heinen, H. *Chem. Ber.* **1987**, *120*, 537.

(9) Ferrocenylcarbene complexes of Cr, W, and Mn have been previously described: (a) Connor, J. A.; Lloyd, J. P. *J. Chem. Soc., Dalton Trans.* **1972**, 1470. Cyclopropanation of dimethyl fumarate with the Cr derivative has been reported: (b) Connor, J. A.; Lloyd, J. P. *J. Chem. Soc., Perkin Trans. 1* **1973**, 17.

(10) For a recent paper, see: (a) Fischer, H.; Leroux, F.; Roth, G.; Stumpf, R. *Organometallics* **1996**, *15*, 3723 and references cited therein. See also: (b) Togni, A.; Rihs, G. *Organometallics* **1993**, *12*, 3368. (c) Wong, W.-Y.; Wong, W.-T.; Cheung, K.-K. *J. Chem. Soc., Dalton Trans.* **1995**, 1379. (d) Sato, M.; Mogi, E.; Katada, M. *Organometallics* **1995**, *14*, 4837. (e) Behrens, U.; Brussaard, H.; Hagenau, U.; Heck, J.; Hendrickx, E.; Körnich, J.; van der Linden, J. G. M.; Persoons, A.; Spek, A. L.; Veldman, N.; Voss, B.; Wong, H. *Chem. Eur. J.* **1996**, *2*, 98.

(11) With a lower amount of alkene (5–10 equiv), we observed both lower chemical yields and lower stereoselectivities. With an excess of alkene (2–3 equiv), an unidentified mixture of products was obtained.

(12) When this reaction was conducted in the absence of BHT, compound 3 was obtained in 75% yield. This additive has been used in order to prevent polymerization of the alkene.

(13) When this reaction was carried out in refluxing acetonitrile, the chemical yield was significantly lower (50%), and even worse when it was run in THF at reflux (20%).

(14) The structure of 3 was assigned on the basis of ¹H and ¹³C NMR spectra including 2D HMQC and HMBC experiments.

(15) Vinylcyclopropanes are recognized to have high synthetic potential: (a) Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 971. (b) Tang, Y.; Huang, Y.-Z.; Dai, L.-X.; Chi, Z.-F.; Shi, L.-P. *J. Org. Chem.* **1996**, *61*, 5762.

(16) Under similar reaction conditions alkyl-, alkynyl-, and arylcarbene complexes of chromium led to unidentified polymeric materials.

Scheme 3

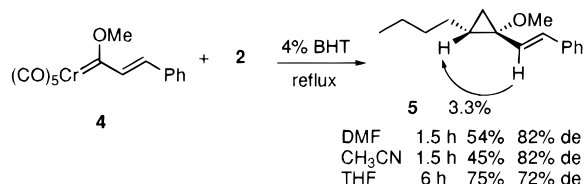


Table 1. Cyclopropanation Reactions of Carbene Complex **1** with Electronically Neutral Alkenes^a

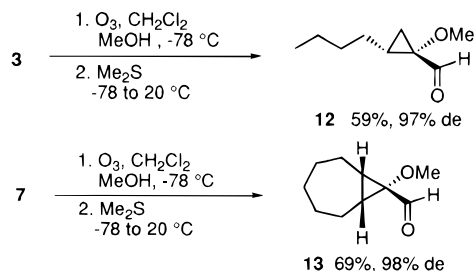
entry	alkene ^b	product ^c	yield (%) ^d	de (%) ^e
1			6 40 ^f	89 ^g
2			7 61	83
3			8 65	90 ^g
4			9 45	- ^h
5			10 44	82
6			11 62	- ^g

^a Reactions were carried out in DMF at reflux for 25–35 min in the presence of 4 mol % of BHT. ^b 20 equiv of alkene were used. ^c Only the major diastereoisomer is shown. Fc = ferrocenyl. ^d Isolated yield based on carbene complex **1**. ^e Determined by ¹H NMR at 300 MHz; integration of MeO signal. ^f 40 equiv of cyclohexene were used. ^g Reaction refluxed for 2–2.5 h. ^h A 1:1 mixture of diastereoisomers was formed.

lower diastereoselectivity, the corresponding vinylcyclopropane **5** when was treated with 1-hexene as shown in Scheme 3.¹⁶

The reactions with other simple alkyl-substituted alkenes were carried out with the most selective (2-ferrocenylalkenyl)carbene complex **1**, and the results are summarized in Table 1. Cyclic olefins like cyclohexene, cycloheptene, and norbornene provided the corresponding bicyclic or tricyclic vinylcyclopropane containing products **6–8**, again with good diastereoselectivity and reasonable yields (entries 1–3). For cyclohexene, a larger excess of this alkene (40 equiv) was needed in order to obtain the cyclopropanation product **6**. Unconjugated dienes with either structurally equivalent or nonequivalent double bonds afforded exclusively the corresponding monocyclopropanated adducts (entries 4 and 5). Thus, the reaction of 4-vinylcyclohexene with **1** occurred regio- and stereoselectively at the exocyclic double bond producing compound **9** as a 1:1 mixture of diastereoisomers (entry 4). This nearly equimolecular mixture is due to the presence of a stereogenic carbon atom in the starting diene. The relative configuration of vinylcyclopropanes **6–10** was likewise ascertained on the basis of NOE studies (see the Supporting Information). The major diastereoisomer in each of these transformations is that in which the

Scheme 4



2-phenylvinyl or the 2-ferrocenylvinyl group is *cis*-positioned with respect to the vicinal cyclopropane methine proton. This stereoselectivity may be likely explained by a mechanism presumably similar to that initially proposed by Harvey and Lund^{5b,17} for the cyclopropanation of simple 1,3-dienes, but in which steric interactions between the phenyl or the bulkier ferrocenyl group and the olefin alkyl chain would significantly disfavor the formation of the corresponding minor isomer. In addition, the thermal reaction of carbene complex **1** with a conjugated enyne showed that in this case the Dötz benzannulation reaction,¹⁸ which finally provided the phenol derivative **11**, is highly favored over the cyclopropanation process (entry 6).¹⁹

The ferrocenyl group was removed by oxidative cleavage of the vinyl portion with ozone.²⁰ Thus, as shown in Scheme 4, ozonolysis of vinylcyclopropanes **3** and **7**, each as a single isomer,²¹ gave the corresponding cyclopropanecarbaldehydes **12** and **13** with high diastereomeric purities.²²

In summary, the results described herein demonstrate for the first time that alkoxy-stabilized vinylcarbene complexes of chromium, containing a phenyl or the strongly electron-donating ferrocenyl group attached in a conjugated fashion, are able to cyclopropanate electron neutral alkenes in an intermolecular manner. Furthermore, these quite fast [2 + 1] cycloaddition reactions occur with high diastereoselectivity, and from the initial adducts the ferrocenyl group is readily removed by ozonolysis.^{23,24}

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Supporting Information Available: Experimental procedures, analytical and spectral data for compounds **1**, **3**, **5–13**, and chart of NOE enhancements for compounds **6–10** (7 pages). See any current masthead page for ordering and Internet access instructions.

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(17) For a similar mechanistic rationale applied by Reissig for the reactions of electron-deficient 1,3-dienes, see: ref 5c and d. See also ref 7d.

(18) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.

(19) This preference has precedents. For example, see: Reissig, H.-U. In *Organometallics in Organic Synthesis*; Werner, H., Erker, G., Eds.; Springer: Berlin, 1989; Vol. 2, pp 311–322.

(20) (a) Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807. (b) Hanessian, S.; Andreotti, D.; Gomsyan, A. *J. Am. Chem. Soc.* **1995**, *117*, 10393.

(21) In each case, the major diastereoisomer was previously separated by column chromatography.

(22) This treatment would additionally generate ferrocenecarbaldehyde, originally used in the synthesis of carbene complex **1**, which potentially could be recovered from the reaction mixture.

(23) Work is in progress to study the scope of this remarkable result and to replace the ferrocenyl substituent for a η^5 -cyclopentadienyl metal group from which the metal fragment could be removed without the cleavage of carbon–carbon bonds.

(24) This ferrocenyl-containing carbene complex (**1**) is also able to react with electron-deficient olefins and dienes. These results will be reported separately.