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Synthesis of Donor–Acceptor Alkynylcyclopropanes by Diastereoselective Cyclopropanation of Electron-Deficient Alkenes with Alkoxyalkynyl Fischer Carbene Complexes

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Dedicated to Prof. Dr. Gerald Pattenden on the occasion of his 65th birthday

Abstract: The reaction of electron-deficient alkenes with alkoxyalkynyl Fischer carbene complexes (FCCs) represents a straightforward route to a new type of captodative (donor–acceptor) alkynylcyclopropanes, which have been prepared in moderate to high yields and in a diastereoselective manner. Some studies regarding the employment of additives to facilitate the recovery of the metal moiety after the reaction are also described. Finally, the first example of a cyclopropanation reaction through employing Fischer carbene complexes under microwave irradiation is presented; this method proved to be an advantageous alternative to the thermal reaction.

Keywords: carbene ligands · carbenes · cyclopropanation · diastereoselectivity · microwave-accelerated reactions

Introduction

The cyclopropyl group is considered unique among carbocycles due to the special characteristics it exhibits.[1] In fact, cyclopropane derivatives are versatile building blocks in organic synthesis, due to both the ring strain as well as their facile interaction with electron-deficient centers, such as protons or alkenes. Among them, alkynylcyclopropanes, which are widely encountered throughout the chemical literature, act as substrates for numerous chemical transformations,[2] play important roles in biochemical processes, or display interesting pharmacological properties. Examples include callipeltoside A (which exhibits in vitro cytotoxic activity against NSCLC-N6 human bronchopulmonary non-small-cell lung carcinoma and P388 cells),[3] GT-2331 (Cipralisant, a potent and selective histamine H_3 receptor antagonist),[4] and efavirenz [Sustiva™, DMP 266, a non-nucleoside reverse transcriptase inhibitor of human immunodeficiency virus (HIV-1)].[5]

The direct alkynylcyclopropanation of alkenes has recently bloomed as a strategy for the preparation of alkynylcyclopropanes. Various approaches have been developed, such as the titanocene(II)-promoted reaction with 2-(alk-1-yn-1-yl)-1,3-dithianes;[6] the employment of alkynyl arsonium[7] or telluronium[8] ylides; the use of alkynyl carbenoids,[9] which are generated from diazo compounds in the presence of an Rh^{II} catalytic system; and the use of alkynylhalocarbenes,[10] generated either with KOH under phase-transfer catalysis or with *t*BuOK. However, a major drawback of these methodologies is that none of them offers a straightforward route to captodative (donor–acceptor) cyclopropanes.

Alternatively, the fact that Fischer carbene complexes (FCCs) offer easy access to cyclopropane derivatives was soon established after their discovery.[11] Thus, alkenes with various electronic properties have been treated with a wide range of Fischer carbene complexes to furnish the corresponding [2+1] cycloadducts.

Typically, the reaction between FCCs **1** and electron-deficient alkenes **2** requires quite energetic conditions with temperatures in the range 80–140 °C and sometimes the alkene also serves as the solvent (Scheme 1). Cyclopropanes **3** are thereby obtained in good yields, although as mixtures of diastereomers with the selectivity depending on the metal em-

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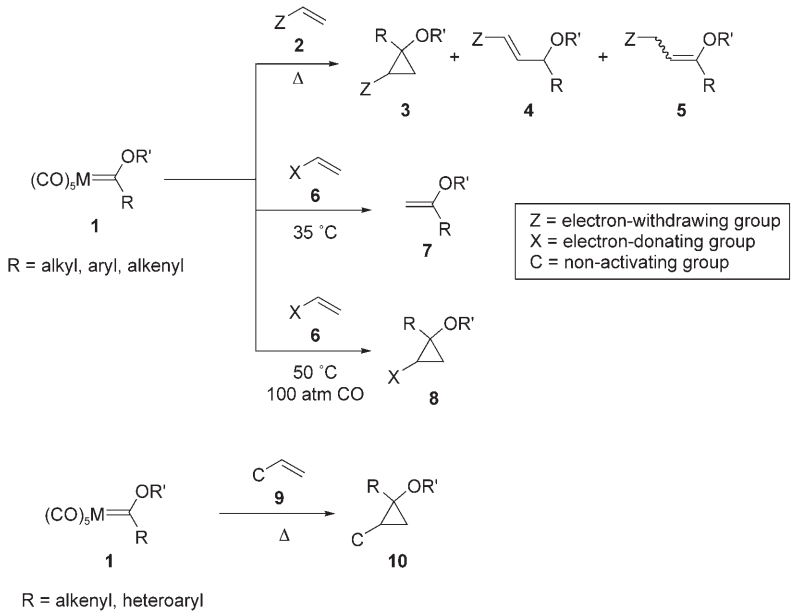


Scheme 1. Cyclopropanation reactions of Fischer alkoxy carbene complexes.

ployed. This indicates that the cyclopropanation takes place within the coordination sphere of the metal, ruling out the involvement of free carbene species. Occasionally, alkenes **4** and **5**, resulting from formal insertion into the alkene C–H bond and cyclopropane ring-opening, respectively, are obtained as secondary products.[12] Casey and Cesa proposed a mechanism to account for the observed results.[13] Recently, the cyclopropanation of electron-deficient alkenes **2** has been accomplished at room temperature by way of protocols that involve transmetalation to Ni[14] or Cu.[14a] All of these reactions represent easy routes to donor–acceptor cyclopropanes; these molecules should be valuable synthetic entities, since the electronic properties of their substituents guarantee ring activation and a high degree of versatility of the products after ring cleavage.[15]

On the other hand, the reaction of electron-rich alkenes **6** with alkoxy FCCs leads to the metathesis products **7**[16] instead of the cyclopropanes **8**, unless the reaction is performed under a high pressure of carbon monoxide,[13,17] also indicating that the cyclopropanation of electron-rich alkenes follows a different pathway.

Nonactivated alkenes **9** also undergo intramolecular cyclopropanation with FCCs[18] and, more recently, the corresponding intermolecular approach has been successfully achieved by the employment of alkenyl- or heteroarylcarbene complexes.[19]

However, the cyclopropanation of alkenes with alkynyl FCCs has hitherto remained largely elusive. Several experimental reports in this area have successively indicated that: 1) treatment of alkynyl FCCs with electron-rich alkenes leads to [2+2] cycloaddition,[20] 2) 1-hexene cannot be cyclopropanated with methoxy phenylethynyl chromium FCC **11a**,[19b] and 3) attempted transmetalation by using Cu^0 or Zn^0/CuCl is not viable for the cyclopropanation of methyl acrylate **2a**.[14a] Aumann was the first to propose a cyclopropanation as one of the steps in the mechanism of a cascade reaction (in which the alkynylcyclopropane was not isolated).[21] In fact, the only three examples in which the cyclopropane has been isolated have been reported from our laboratories and concerned reactions with especially reactive alkenes, namely fulvenes,[22] norbornene derivatives (in this case the cyclopropanes were obtained as minor products), and (*E*)-cyclooctene.[23]

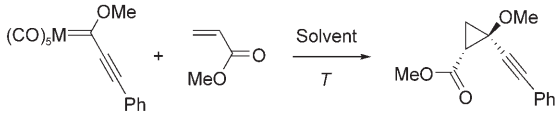
We report herein the reaction of electron-deficient alkenes with alkoxyalkynyl FCCs to produce captodative alkynylcyclopropanes. We also describe our studies regarding the employment of additives to facilitate the recovery of the metal moiety after the reaction. Finally, we present the first example of a cyclopropanation reaction employing Fischer carbene complexes under microwave irradiation, which proved to be an advantageous alternative to the thermal reaction.

Abstract in Spanish: *Se presenta un nuevo tipo de alquinilciclopropanos captodativos (dador-aceptor) que pueden ser obtenidos, con rendimientos de moderados a buenos y de forma altamente diastereoselectiva, mediante la reacción de complejos alcoxi alquinil carbeno de Fischer (FCCs) con olefinas electrónicamente deficientes. Además, en este manuscrito se incluyen los resultados de estudios dirigidos a la recuperación del fragmento metálico, una vez concluida la reacción. Finalmente, se describe el primer ejemplo de una reacción de ciclopropanación mediante irradiación microondas empleando FCCs; esta metodología supone una alternativa favorable a la correspondiente reacción térmica.*

Results and Discussion

Establishment of the cyclopropanation conditions: Fischer carbene complex **11a** and methyl acrylate **2a** were chosen to perform the initial set of experiments (Table 1) in order to determine the optimum reaction conditions. Temperature, number of equivalents of alkene, solvent, and the nature of the metal of the carbene complex were the variables considered. It was observed that the reaction requires temperatures higher than 80 °C to proceed; however, small differences were noted for temperatures ranging from 80 to 110 °C, with the best results being obtained at 90 °C (entries 1–3).

Table 1. Optimization of the cyclopropanation conditions.[a]



11a, M = Cr
12, M = W

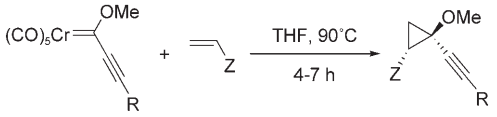
2a (*n* equiv)

13a

	Carbene	*n* equiv	Solvent	*T* [°C][b]	*d.r.*[c]	Yield [%][d]
1	**11a**	10	toluene	110	75:25	40
2	**11a**	10	toluene	RT–80	–	–
3	**11a**	10	toluene	90	75:25	42
4	**11a**	15	toluene	90	75:25	45
5	**11a**	15	–	90	58:42	40
6	**11a**	15	hexane	90	79:21	29
7	**11a**	15	CH_3CN	90	65:35	25
8	**11a**	15	DCE[e]	90	90:10	32
9	**11a**	15	THF	90	94:6	48
10	**12**	15	THF	90	–	–

[a] All of the experiments were carried out in sealed tubes due to the volatility of the alkene and, in some cases, of the solvent. [b] Bath temperature. [c] Diastereomeric ratio (*d.r.*) determined by ^{1}H NMR spectroscopy (300 MHz) of the crude reaction mixture. [d] Isolated yields of **13a** based on alkynylcarbenes **11a** (or **12**). [e] DCE = 1,2-dichloroethane.

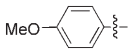
Table 2. Cyclopropanation of terminally monosubstituted alkenes.[a]



11

2

13

	11	R	**2**	Z	Product	*d.r.*[b]	Yield [%][c]
1	**11a**	Ph	**2a**	CO_2Me	**13a**	94:6	48
2	**11a**	Ph	**2b**	$CONMe_2$	**13b**	93:7	50
3	**11a**	Ph	**2c**	$PO(OEt)_2$	**13c**	91:9	30
4	**11a**	Ph	**2d**	CN	**13d**	>95:<5	51
5	**11b**		**2d**	CN	**13e**	>95:<5	48
6	**11c**		**2d**	CN	**13f**	>95:<5	69
7	**11d**		**2d**	CN	**13g**	>95:<5	49
8	**11e**	TMS	**2d**	CN	**13h**	>95:<5	70
9	**11f**	*t*Bu	**2d**	CN	**13i**	>95:<5	68
10	**11g**	*n*Bu	**2d**	CN	**13j**	>95:<5	45

[a] All of the experiments were carried out in THF at 90 °C (bath temperature) in sealed tubes using 0.5 mmol of the carbene and 15 equivalents of the alkene. [b] Diastereomeric ratio (*d.r.*) determined by ^{1}H NMR spectroscopy (300 MHz) of the crude reaction mixture. [c] Isolated yields based on alkynylcarbenes **11**.

Regarding the number of equivalents of the alkene, a considerable excess is required and slightly better results were achieved when 15 equivalents was employed instead of the initially used ten equivalents (entries 3 and 4); lesser amounts resulted in lower yields, while higher excesses did not have a beneficial effect. The polarity of the solvent plays a decisive role in the reaction: the use of highly polar solvents such as DMF or 1,2-dimethoxyethane (not listed in Table 1) led to carbene decomposition products; a decrease in both chemical yield and diastereoselectivity was observed when the reaction was performed neat (entry 5). However, the use of different solvents, such as hexane, acetonitrile, 1,2-dichloroethane, or THF, was found to lead to variable yields and selectivities (entries 6–9). Among the solvents tested, THF proved to be the best, giving cyclopropane **13a** in the highest yield and with the best diastereoselectivity (entry 9). Finally, the nature of the metal of the carbene also plays a decisive role as the tungsten carbene complex **12** decomposed instead of undergoing addition to the alkene **2a** (entry 10).

Scope of the reaction—cyclopropanation of terminally monosubstituted alkenes: Once the optimal reaction conditions had been established, several terminally monosubstituted electron-deficient alkenes were treated with different Fischer alkynylcarbene complexes **11** to evaluate the scope of the reaction. The results are collected in Table 2.

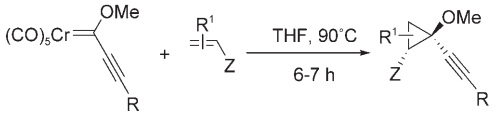
Entries 1–4 highlight the diversity of electron-withdrawing functional groups that can tolerate the reaction conditions. Thus, alkenes bearing ester, amide, phosphonate, and cyano groups are fully compatible and the corresponding cyclopropanes are obtained in moderate yields and with high diastereoselectivities. Acrylonitrile **2d** was selected as the most appropriate alkene to test the scope of the reaction with regard to the substitution pattern of the alkynylcarbene complexes, as it led to the best result (mainly in terms of diastereoselectivity). Thus, the nature of the substituent was examined and aryl- (entries 4–6), alkenyl- (entry 7), silyl- (entry 8), branched aliphatic- (entry 9), and linear aliphatic-substituted (entry 10) alkynyl FCCs proved to be suitable substrates for the cyclopropanation. However, in some cases excessive or prolonged heating led to opening of the cyclopropane ring and traces of the corresponding olefinic compounds were detected in the products.

On the other hand, other alkenes bearing a carbonyl group as an electron-withdrawing moiety, such as methyl vinyl ketone and acrolein, did not undergo cyclopropanation.

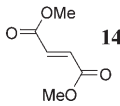
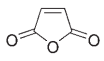
Scope of the reaction—cyclopropanation of di- and trisubstituted alkenes: Carbene complexes **11a** (which had been previously employed to optimize the reaction conditions) and **11f** (which led to high yields in the cyclopropanation of terminal alkenes) were chosen to test the behavior of several di- and trisubstituted alkenes. All of these reactions were carried out under the previously established optimum conditions and the results are listed in Table 3.

From these results, we can conclude that, first of all, the reaction is generally slower than when monosubstituted alkenes are used as substrates (6–7 h vs 4–7 h). Also, the cyclopropanation with carbene complex **11a** leads to lower yields than that with carbene complex **11f**, as was observed for methyl methacrylate **14a** and methyl crotonate **14b** (entries 1 and 3 vs 2 and 4); these results can be attributed to

Table 3. Cyclopropanation of di- and trisubstituted alkenes.[a]



11 14 15

	11	Alkene	15	*d.r.*[b]	Yield [%][c]
1	**11a**	 **14a**	**15a**	67:33	29
2	**11a**	 **14b**	**15b**	50:50	22
3	**11f**	**14a**	**15c**	67:33	86
4	**11f**	**14b**	**15d**	50:50	76
5	**11f**	 **14c**	**15e**	50:50	83
6	**11f**	 **14d**	**15f**	–	30[d]
7	**11f**	 **14e**	–	–	–

[a] All of the experiments were carried out in THF using 0.5 mmol of the carbene and 15 equivalents of the alkene, and required 6–7 h of heating at 90 °C (bath temperature) to reach completion. [b] Diastereomeric ratio (*d.r.*) determined by ^{1}H NMR spectroscopy (300 MHz) of the crude reaction mixture. [c] Isolated yields based on alkynyl carbenes **11**. [d] Product not isolated; the yield was estimated by ^{1}H NMR spectroscopy (300 MHz) of a mixture of cyclopropane **15f** and unreacted alkene.

the higher thermal stability of the latter carbene. In fact, **11f** is able to bring about the cyclopropanation of cyclic trisubstituted alkenes, such as methyl cyclopentanecarboxylate **14c**, in high yield (entry 5). Compounds **15** are typically obtained as a 1:1 mixture of diastereomers, except when the alkene is methyl methacrylate, which leads to a 2:1 diastereomeric ratio, the major diastereomer being the one having a *cis* relationship between the alkene ester group and the carbene alkynyl group. In all cases, the diastereomers are easily separated by column chromatography and they retain the stereochemistry of the starting alkene.

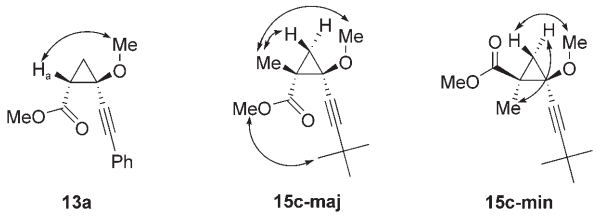
The reaction was also tested with some 1,2-disubstituted alkenes bearing two electron-withdrawing groups, namely methyl fumarate **14d** and maleic anhydride **14e**. Cyclopropanation of methyl fumarate occurred with carbene complex **11f** (entry 6), although the product could not be completely separated from the unreacted alkene and the yield was estimated by ^{1}H NMR spectroscopy (300 MHz). On the other hand, cyclopropanation of maleic anhydride could not be achieved and instead the carbene complex decomposed; this result was somehow expected as it is already known that electron-deficient alkenes that cannot adopt an s-*trans* conformation, such as maleic anhydride, are unable to undergo cyclopropanation with alkyl FCCs.[12h]

β,β-Disubstituted electron-deficient alkenes, electron-rich alkenes such as ethyl vinyl ether, and non-activated alkenes such as cyclooctene, cyclopentene, styrene, isoprene, and hexene, among others, were also checked under the optimized conditions, but they did not undergo cyclopropanation.

Structural assignment: The atom connectivity as well as the relative stereochemistry of cyclopropanes **13** and **15** was established by 1D NMR (^{1}H and ^{13}C NMR) and 2D NMR (COSY, HMBC, HSQC, NOESY) studies; in fact, the NOESY experiments were the main tool for the assignment of the relative stereochemistry of cyclopropanes **13**.

Thus, a cross-peak signal in the NOESY spectrum between the hydrogen atom at $\delta = 2.18$ ppm (H_a), in a position α to the ester group, and the methoxy group, which initially belonged to the carbene complex, is observed for the major diastereomer of cyclopropane **13a**; this result indicates a *cis* relationship between the other two substituents of the cyclopropane ring, that is, the acetylene moiety and the ester group.

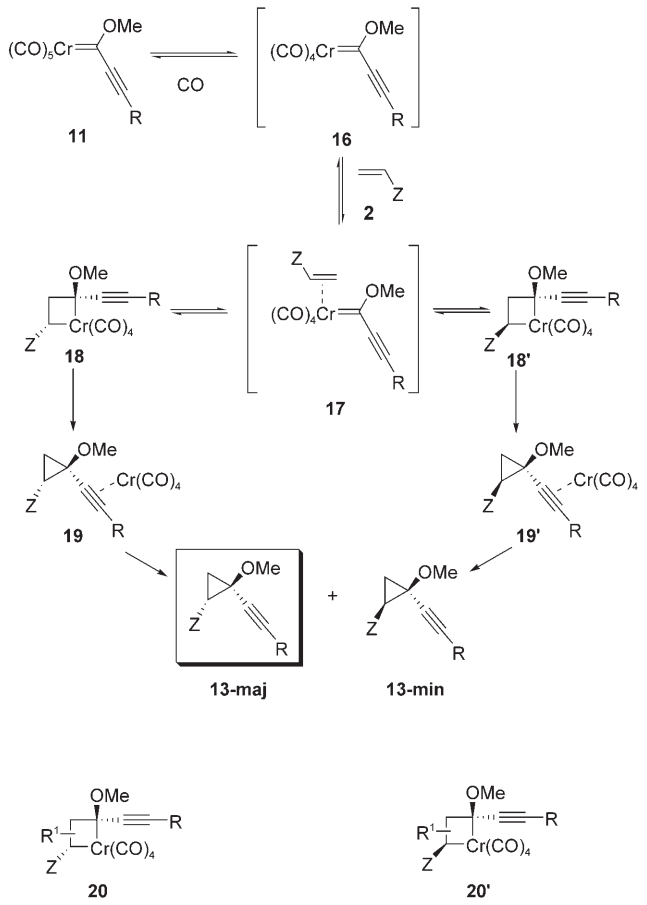
The same assignment protocol was also applied for cyclopropane derivatives **15** obtained from di- and trisubstituted alkenes. For instance, in the case of **15c**, from the presence in the NOESY spectrum of two cross-peak signals (the first between the ester and *tert*-butyl groups and the second between the methoxy and methyl groups), the relative stereochemistry of the major diastereomer may be proposed to be that indicated in the structure depicted as **15c-maj** in Figure 1. As expected, these cross-peak signals were absent in the spectrum of the minor diastereomer **15c-min**, which helped to confirm the proposed assignment of the relative configuration of the two diastereomers; for **15c-min**, the only cross-peak signals observed were those involving the methylene group, which are not relevant to the stereochemical aspects.



13a 15c-maj 15c-min

Figure 1. Relative configuration of alkynylcyclopropanes: NOESY cross-peak signals observed.

Mechanistic proposal: The results obtained can be rationalized in terms of Casey's proposed mechanism.[13] Thus, as a thermal reaction, the first step will be the dissociation of a carbonyl ligand from the coordination sphere of the chromium to form the coordinatively unsaturated species **16** (Scheme 2). This intermediate will be stabilized by coordination to **2** to form a η^2-alkenecarbene complex **17**, which may evolve towards two possible diastereomeric metallacyclobutanes **18** and **18′** by alkene insertion (the other possible regioisomers would give rise to the same cyclopropanation



Scheme 2. Proposed mechanism for the cyclopropanation of electron-deficient alkenes **2** (or **14**).

products). Finally, reductive elimination of the metal fragment followed by metal decoordination from **19** and **19′** leads to the formation of cyclopropanes **13**.

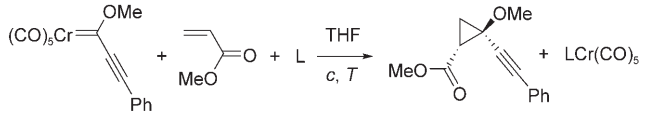
The high levels of diastereoselection observed in the cyclopropanation reaction may be attributed to the relative steric interactions between the two carbene substituents (the methoxy group and the alkynyl group) and the alkene Z-group in the formation of metallacyclobutanes **18** and **18′**.

This model may also explain the low diastereoselectivities observed when di- or trisubstituted alkenes **14** were employed. Thus, for methyl methacrylate **14a**, the geminal substitution causes a decrease in the difference in energy between the diastereomeric metallacyclobutanes **20** and **20′**. For *trans*-di- or trisubstituted alkenes, the formation of an almost equimolecular amount of the two diastereomers may be due to low regioselectivity in the formation of metallacyclobutanes **20** and **20′**.

Recovery of the metallic moiety after the reaction: The requirement for a stoichiometric amount of the metal is considered to be the main drawback of the chemistry of Fischer carbene complexes. In this sense, the recovery and reutilization of the metallic fragment might allow the FCCs to be considered as more environmentally friendly reagents. We tested several alternatives with a view to recovering the highest possible amount of the metallic portion from the reaction medium.[24] However, initial attempts involving the bubbling of CO through the mixture once the reaction was complete resulted only in minimal recovery of $[Cr(CO)_6]$.

A new strategy was then adopted: different reagents (L) capable of metal complexation were added to the reaction mixture. These reactions were carried out employing alkynyl carbene **11a** and methyl acrylate **2a** under the optimal conditions as previously described, but variables such as concentration, number of equivalents of ligand, and, occasionally, temperature were considered. The reactions were complete within 1 h or 4 h depending on the temperature, and the yields and diastereoselectivities are listed in Table 4.

Table 4. Recovery of the metallic fragment.[a]



11a **2a** (*n* equiv) **13a**

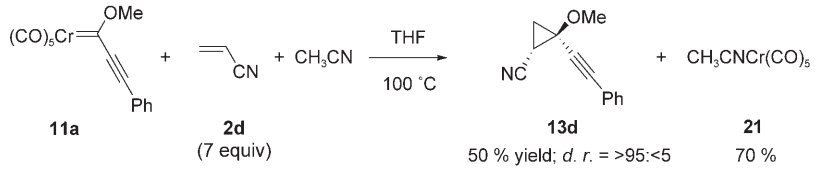
	L	*n* equiv	*c* [M]	*T* [°C][b]	*d.r.*[c]	**13a**[d]	$[LCr(CO)_5]$[d]
1	CH_3CN	3	0.034	90	75:25	41	55
2	CH_3CN	3	0.034	100	70:30	38	72
3	CH_3CN	3	0.017	90	89:11	46	45
4	CH_3CN	6	0.017	100	86:14	45	78
5	pyridine	3	0.034	100	75:25	22	70
6	Ph_3P	3	0.034	90	94:6	40	85
7	DMAP	3	0.050	90	–	–	–

[a] All of the experiments were carried out in sealed tubes. [b] Bath temperature. [c] Diastereomeric ratio (*d.r.*) determined by ^1H NMR spectroscopy (300 MHz) of the crude reaction mixture. [d] Yield [%]: isolated yields based on alkynylcarbene complex **11a**.

Acetonitrile was the first choice as L due to its capacity for metal coordination. Its addition as a metal-complexing ligand strongly affects the diastereoselectivity of the reaction; this result is not at all surprising, because when it was employed as a solvent a low diastereoselectivity was obtained (Table 1, entry 7). To minimize the loss of selectivity, the reaction was performed under more dilute conditions, which led to an increase in the diastereoselectivity (Table 4, entries 3 and 4 vs 1 and 2). On the other hand, the temperature of the reaction has an effect on the amount of metallic complex that is recovered; this fact can be attributed to partial decomposition of the complex because of the lengthy reactions (Table 4, entries 2 and 4 vs 1 and 3). Finally, an increment in the number of equivalents of acetonitrile allowed the recovery of higher amounts of metal without a significant decrease in the stereoselectivity of the reaction.

Interestingly, cyclopropane **13d** and metal complex **21** were obtained in yields of 50% and 70%, respectively, when acrylonitrile was employed as an electron-deficient alkene in the presence of three equivalents of acetonitrile; the diastereoselectivity of the reaction was maintained

(Scheme 3). Although the concentration of acetonitrile was lower than that of acrylonitrile, the former showed more affinity for the metal as no evidence of metal species complexed by acrylonitrile was found.



Scheme 3. Reaction with acrylonitrile in the presence of acetonitrile.

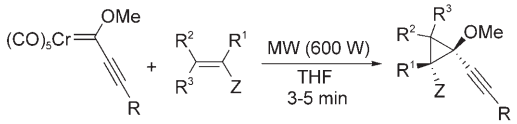
Other complexing reagents such as pyridine and triphenylphosphine were also tested. Cyclopropane formation decreased when pyridine was used, as only a 22% yield of **13a** with moderate diastereoselectivity (75:25) was isolated (Table 4, entry 5). However, the employment of triphenylphosphine proved to be especially beneficial as cyclopropane **13a** was obtained in 40% yield with identical diastereoselectivity to that achieved when the reaction was performed in the absence of triphenylphosphine, while the metal complex was recovered in high yield (Table 4, entry 6; cf. Table 2, entry 1). On the other hand, the addition of DMAP[25] inhibited the cyclopropanation and led to a mixture of unidentified products.

Microwave-accelerated cyclopropanation of electron-deficient alkenes: Since the first application of microwave (MW) irradiation in organic synthesis, such techniques have shown an overwhelming ability to facilitate organic reactions, mainly by accelerating them, enhancing their chemical yields, increasing the purity of the products, and, occasionally, leading to a change in the diastereoselective composition of the products.[26] Moreover, they currently constitute a cornerstone of the so-called "green" chemistry due to the excellent results achieved in solvent-free reactions or when solid-supported reagents are used.[27] However, even though a large number of chemical reactions have been tested under MW conditions, microwave-promoted cyclopropanations have hitherto been restricted to the formation of bicyclic cyclopropane derivatives from allylic esters of malonic acid[28] and to the reaction of ethyl diazoacetate with alkenes in the presence of catalytic amounts of copper(II) acetylacetonate.[29] We decided to test this option as an alternative to conventional heating in cyclopropanation reactions with Fischer carbene complexes.[30]

The microwave power was calibrated with reference to previously reported procedures,[31] and an initial set of reactions was performed with carbene complex **11a** and methyl acrylate **2a** in sealed tubes.[32] As a result, we found the best reaction conditions to be a power of 600 W, THF as solvent, and a 0.05 M carbene concentration.

We then proceeded to examine the scope of microwave activation for the cyclopropanation of other alkoxyalkynyl FCCs and electron-deficient alkenes. The results are listed in Table 5. Although the yields and selectivities are slightly lower, they are not, in general, significantly different from the results obtained under classical heating, with the big advantage that the reaction times have been considerably shortened (compare Table 5 with the corresponding results listed in Tables 2 and 3). However, it was found that a nonactivated alkene such as cyclopentene **9a** could not be cyclopropanated by alkynyl FCC **11a** under microwave irradiation.

Table 5. Microwave-accelerated cyclopropanations of alkoxy alkynyl FCCs **11** with electron-deficient alkenes **2** (or **14**).[a]



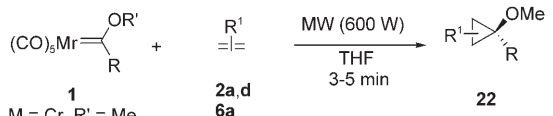
11 **2** (or **14**) **13** (or **15**)

	Carbene	Alkene	t [min]	Product	$d.r.$[b]	Yield [%][c]
1	**11a**	**2a**	3	**13a**	90:10	51
2	**11a**	**2d**	3	**13d**	>95:<5	28
3	**11a**	**14a**	3	**15a**	80:20	25
4	**11a**	**14b**	4	**15b**	–[d]	20
5	**11d**	**2d**	3	**13g**	80:20	42
6	**11f**	**2d**	3	**13i**	>95:<5	63
7	**11f**	**2a**	5	**13k**	92:8	49

[a] All of the experiments were carried out in sealed tubes. [b] Diastereomeric ratio ($d.r.$) determined by ^{1}H NMR spectroscopy (300 MHz) of the crude reaction mixture. [c] Isolated yields based on alkynylcarbenes **11**. [d] Not determined.

Several experiments were also run to check if FCCs **1** (R′=Me) that do not bear an alkynyl group can perform the cyclopropanation of different kinds of alkenes. To this end, alkenyl FCCs **1a**,**b**, aryl FCC **1c**, and alkyl FCC **1d** were treated under microwave conditions with electron-deficient alkenes, such as methyl acrylate **2a** and acrylonitrile **2d** to lead, in less than 5 min, to the corresponding cyclopropanes **22** (Table 6, entries 1, 3, 5, 6, and 8). Alkenyl FCC **1a** was found to be able to perform the cyclopropanation of cyclopentene **9a** (entry 2), while electron-rich dihydrofuran **6a** was reactive towards alkenyl FCC **1b** and aryl FCC **1c** under microwave conditions (entries 4 and 7); in general, these results are in agreement with those obtained under thermal conditions at 80°C. However, the cyclopropanation of an acyclic electron-rich alkene, such as ethyl vinyl ether, could not be accomplished, not even with alkenyl FCC **1b**. From all of these results, we can readily conclude that if the thermal reaction takes place, then the cyclopropanation can be accelerated by MW irradiation, although a definitive rule cannot be established in terms of yields and diastereoselectivity.

Table 6. Microwave-accelerated cyclopropanations.[a]



1
M = Cr, R' = Me

2a,**d**
6a
9a

22

	1	R	Alkene	Product	*d.r.*[b]	Yield [%][c]
1	**1a**		**2a**	**22a**	75:25	79
2	**1a**		 **9a**	**22b**	>95:5	82
3	**1b**		**2d**	**22c**	50:50	55
4	**1b**		 **6a**	**22d**	89:11	65
5	**1c**	Ph	**2a**	**22e**	50:50	97
6	**1c**	Ph	**2d**	**22f**	n.d.	58
7	**1c**	Ph	**6a**	**22g**	71:29	46
8	**1d**	Bu	**2a**	**22h**	52:48	40

[a] All of the experiments were carried out in sealed tubes. [b] Diastereomeric ratio (*d.r.*) determined by ^{1}H NMR spectroscopy (300 MHz) of the crude reaction mixture. [c] Isolated yields based on FCCs **1**.

Conclusion

In summary, we have established experimental conditions to accomplish the thermal cyclopropanation of electron-deficient alkenes by treating a wide range of alkoxyalkynyl Fischer carbene complexes (FCCs). In this way, we have obtained a type of donor–acceptor alkynylcyclopropane that has not been prepared previously. The procedure is highly diastereoselective for monosubstituted alkenes and gives high yields for the cyclopropanation of 1,1-di-, 1,2-di-, and trisubstituted alkenes with the *tert*-butyl-derived FCC **11f**. The stereochemical outcome of the process can be rationalized according to Casey's proposed mechanism, and the employment of triphenylphosphine as an additive allows the recovery of up to 85% of the metal fragment without compromising either the yield or the diastereoselectivity of the reaction. Finally, the cyclopropanation of various types of alkenes can be performed in a few minutes with a wide variety of FCCs, not only alkynyl-derived FCCs, by subjecting the mixtures to microwave irradiation in a domestic oven. The microwave-accelerated reactions were found to give similar yields and diastereoselectivities as the conventional thermally promoted reactions. Work is currently in progress to explore the synthetic utility of these new captodative alkynylcyclopropanes, mainly through their participation in transition-metal-catalyzed cycloaddition reactions.[2]

Experimental Section

General considerations: All reactions involving air-sensitive compounds were carried out under an N_2 atmosphere (99.99%). All glassware was oven-dried (120°C), evacuated, and purged with nitrogen. All common reagents and solvents were obtained from commercial suppliers and were used without any further purification unless otherwise indicated. Fischer carbene complexes **1**, **11**, and **12** were prepared according to described procedures.[33] Solvents were dried by standard methods. Hexane and ethyl acetate were distilled before use. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized under ultraviolet light and/or by staining with a Ce/Mo reagent, anisaldehyde or phosphomolybdic acid solution and subsequent heating. R_f values refer to silica gel. Flash column chromatography was carried out on silica gel 60, 230–240 mesh. Routine NMR measurements were made on Bruker AC-300 or DPX-300 spectrometers. For ^{1}H NMR, the splitting pattern abbreviations are: s, singlet; brs, broad singlet; d, doublet; t, triplet; at, apparent triplet; dd, doublet of doublets; q, quartet; m, multiplet. For ^{13}C NMR, multiplicities were determined by DEPT, and the abbreviations used are: q, CH_3; t, CH_2; d, CH; s, quaternary carbons, except in the case of compound **13c** (see below). NOESY experiments were carried out on a Bruker AMX-400 spectrometer. Standard pulse sequences were employed for the DEPT experiments. FT-IR spectra were recorded on a Mattson 3000 FT-IR spectrometer. High-resolution mass spectra (HRMS) were obtained with a Finnigan MAT 95 mass spectrometer; low-resolution mass spectra were obtained with a Hewlett-Packard 5880A spectrometer. In both cases, electron impact (70 eV) or fast atom bombardment (FAB) techniques were employed. Elemental analyses were carried out with a Perkin–Elmer 240B microanalyzer.

Cyclopropanation of electron-deficient alkenes with Fischer alkynyl carbene complexes 11—general procedure: A solution of the appropriate carbene complex **11** (0.5 mmol) and the requisite electron-deficient alkene **2** (or **14**) (7.5 mmol, 15 equiv) in dry THF (10 mL) under an inert atmosphere was warmed at 90°C in a sealed tube until the starting carbene complex was completely consumed (4–7 h). Silica gel (0.5 g) was then added to the reaction mixture and the solvents were removed under vacuum. The residue was purified by flash column chromatography employing mixtures of hexane/EtOAc (20:1 to 3:1) as eluents. Captodative cyclopropanes **13** (or **15**) were isolated with high diastereoselectivities when monosubstituted alkenes **2** were employed, but with low to moderate diastereoselectivities from di- and trisubstituted alkenes **14**.

Microwave-promoted cyclopropanation of electron-deficient alkenes with Fischer alkynyl carbene complexes—general procedure: A solution of the appropriate carbene complex **11** (0.5 mmol) and the requisite electron-deficient alkene **2** (or **14**) (10 mmol, 20 equiv) in dry THF (10 mL) under an inert atmosphere in a sealed tube was placed in a domestic microwave oven at 600 W until the starting carbene complex was completely consumed (3–4 min), as indicated by a color change in the reaction vessel and further confirmed by TLC monitoring. The solvents were then removed under vacuum, and the residue was redissolved in hexane and exposed to light in an open-air vessel to induce decomplexation of the metal species present. The resulting suspension was filtered through Celite, silica gel (0.5 g) was added, and the solvents were removed under vacuum. The residue was purified by flash column chromatography, employing mixtures of hexane/EtOAc (20:1 to 3:1) as eluents, to give captodative cyclopropanes **13** (or **15**) in the yields and diastereoselectivities indicated in Table 5.

Methyl (1*R,2*R**)-2-methoxy-2-phenylethynylcyclopropanecarboxylate (13a-maj)**: Colorless oil; major diastereomer from a 94:6 mixture; yield 48% (combined yield for the two diastereomers); R_f=0.30 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=7.44–7.41 (m, 2H), 7.30–7.25 (m, 3H), 3.73 (s, 3H), 3.49 (s, 3H), 2.18 (at, ^3J(H,H)=7.5, 9.1 Hz, 1H), 1.79 (at, ^3J(H,H)=7.5 Hz, ^2J(H,H)=6.0 Hz, 1H), 1.61 ppm (dd, ^3J(H,H)=9.1 Hz, ^2J(H,H)=6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ=169.6 (s), 131.7 (d, 2×CH), 128.4 (d), 128.2 (d, 2×CH), 122.3 (s), 86.2 (s), 83.4 (s), 59.2 (s), 56.0 (q), 52.0 (d), 29.6 (d), 22.1 ppm (t); FT-IR (neat): $\tilde{\nu}$=1734 cm^{-1}; MS (FAB): *m*/*z* (%): 231 (10) $[M+1]^+$, 221 (53), 207 (100), 191 (36), 171 (42); HRMS (FAB): *m*/*z* calcd for $C_{14}H_{15}O_3$ $[M+1]^+$: 231.1021; found: 231.1030; elemental analysis calcd (%) for $C_{14}H_{14}O_3$ (230.26): C 73.03, H 6.13; found: C 73.18, H 6.17.

Methyl (1*S,2*R**)-2-methoxy-2-phenylethynylcyclopropanecarboxylate (13a-min)**: Colorless oil; minor diastereomer from a 94:6 mixture; yield

48% (combined yield for the two diastereomers); $R_f = 0.30$ (hexane/EtOAc, 5:1); spectroscopic data retrieved from an enriched mixture; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.45$–7.42 (m, 2H), 7.33–7.29 (m, 3H), 3.76 (s, 3H), 3.44 (s, 3H), 2.24 (at, $^3J(H,H) = 5.7$, 7.4 Hz, 1H), 1.94 (at, $^3J(H,H) = 7.4$ Hz, $^2J(H,H) = 8.0$ Hz, 1H), 1.53 ppm (dd, $^3J(H,H) = 5.7$ Hz, $^2J(H,H) = 8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 168.7$ (s), 131.7 (d, 2×CH), 128.6 (d), 128.3 (d, 2×CH), 122.0 (s), 86.4 (s), 83.9 (s), 58.1 (s), 56.3 (q), 52.2 (d), 29.8 (d), 21.3 ppm (t); FT-IR (neat): $\tilde{\nu} = 1738$ cm^{-1}.

(1*R,2*R**)-2-Methoxy-*N*,*N*-dimethyl-2-phenylethynylcyclopropanecarboxamide (13b)**: Colorless oil; major diastereomer from a 93:7 mixture; yield 50% (combined yield for the two diastereomers); $R_f = 0.25$ (hexane/EtOAc, 1:2); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.39$–7.17 (m, 5H), 3.42 (s, 3H), 3.13 (s, 3H), 2.92 (s, 3H), 2.25 (at, $^3J(H,H) = 7.2$, 9.4 Hz, 1H), 1.71 (at, $^3J(H,H) = 7.2$ Hz, $^2J(H,H) = 5.4$ Hz, 1H), 1.37 ppm (dd, $^3J(H,H) = 9.4$ Hz, $^2J(H,H) = 5.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 167.1$ (s), 131.3 (d, 2×CH), 128.0 (d), 127.8 (d, 2×CH), 122.1 (s), 85.2 (s), 83.9 (s), 57.6 (s), 55.3 (q), 37.0 (q), 35.3 (q), 30.1 (d), 19.6 ppm (t); FT-IR (neat): $\tilde{\nu} = 1645$ cm^{-1}; MS (FAB): *m*/*z* (%): 244 (100) $[M+1]^+$, 243 (55) $[M]^+$, 207 (11), 199 (11), 171 (15); HRMS (FAB): *m*/*z* calcd for $C_{15}H_{18}NO_2$ $[M+1]^+$: 244.1338; found: 244.1332; elemental analysis calcd (%) for $C_{15}H_{17}NO_2$ (243.13): C 74.05, H 7.04, N 5.76; found: C 73.94, H 7.09, N 5.87.

Diethyl (1*R,2*S**)-2-methoxy-2-phenylethynylcyclopropanephosphonate (13c)**: Yellow oil; yield 30% (combined yield for the two diastereomers); $R_f = 0.30$ (hexane/EtOAc, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.49$–7.42 (m, 2H), 7.31–7.25 (m, 3H), 4.24–4.05 (m, 4H), 3.46 (s, 3H), 1.65–1.54 (m, 2H), 1.48–1.40 (m, 1H), 1.32–1.25 ppm (m, 6H); for this compound, the abbreviations regarding the carbon multiplicity refer to the P–C coupling; the number of hydrogen atoms linked to a determined carbon atom is indicated after the multiplicity due to P–C coupling: ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 131.5$ (s, 2×CH), 128.3 (s, CH), 128.1 (s, 2×CH), 122.4 (s, C), 86.4 (s, C), 84.4 (d, $^3J(C,P) = 4.0$ Hz, C), 62.2 (d, $^2J(C,P) = 5.8$ Hz, CH_2), 61.8 (d, $^2J(C,P) = 5.8$ Hz, CH_2), 55.9 (d, $^2J(C,P) = 4.7$ Hz, C), 55.8 (s, CH_3), 21.6 (d, $^1J(C,P) = 191.0$ Hz, CH), 20.7 (d, $^2J(C,P) = 5.8$ Hz, CH_2), 16.4 (d, $^3J(C,P) = 2.4$ Hz, CH_3), 16.3 ppm (d, $^3J(C,P) = 1.7$ Hz, CH_3); ^{13}P NMR ($CDCl_3$, 121.49 MHz, 25°C, H_3PO_4): $\delta = 23.55$ ppm; FT-IR (neat): $\tilde{\nu} = 1491$, 1443 cm^{-1}; MS (FAB): *m*/*z* (%): 309 (100) $[M+1]^+$, 308 (25) $[M]^+$, 221 (29), 171 (44); HRMS (FAB): *m*/*z* calcd for $C_{16}H_{22}O_4P$ $[M+1]^+$: 309.1256; found: 309.1256.

(1*S,2*R**)-2-Methoxy-2-phenylethynylcyclopropanecarbonitrile (13d)**: Colorless oil; yield 51%; $R_f = 0.34$ (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.45$–7.30 (m, 5H), 3.65 (s, 3H), 1.90 (dd, $^3J(H,H) = 6.8$, 9.7 Hz, 1H), 1.74 (at, $^3J(H,H) = 6.8$ Hz, $^2J(H,H) = 6.3$ Hz, 1H), 1.63 ppm (dd, $^3J(H,H) = 9.7$ Hz, $^2J(H,H) = 6.3$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 131.7$ (d, 2×CH), 129.0 (d), 128.3 (d, 2×CH), 121.2 (s), 117.5 (s), 85.5 (s), 83.5 (s), 56.2 (q + s), 22.6 (t), 13.4 ppm (d); FT-IR (neat): $\tilde{\nu} = 2241$ cm^{-1}; MS (FAB): *m*/*z* (%): 198 (100) $[M+1]^+$, 197 (32) $[M]^+$, 168 (31), 154 (17); HRMS (FAB): *m*/*z* calcd for $C_{13}H_{12}NO$ $[M+1]^+$: 198.0919; found: 198.0926; elemental analysis calcd (%) for $C_{13}H_{11}NO$ (197.23): C 79.16, H 5.62, N 7.10; found: C 79.28, H 5.66, N 7.25.

(1*S,2*R**)-2-Methoxy-2-(4-methoxyphenylethynyl)cyclopropanecarbonitrile (13e)**: Colorless oil; yield 48%; $R_f = 0.26$ (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.38$ (d, $^3J(H,H) = 8.6$ Hz, 2H), 6.86 (d, $^3J(H,H) = 8.6$ Hz, 2H), 3.82 (s, 3H), 3.64 (s, 3H), 1.89 (dd, $^3J(H,H) = 6.8$, 9.8 Hz, 1H), 1.73 (at, $^3J(H,H) = 6.8$ Hz, $^2J(H,H) = 6.2$ Hz, 1H), 1.63 ppm (dd, $^3J(H,H) = 9.8$ Hz, $^2J(H,H) = 6.2$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 160.1$ (s), 133.3 (d, 2×CH), 117.5 (s), 113.9 (d, 2×CH), 113.2 (s), 85.6 (s), 82.3 (s), 56.3 (s), 56.1 (q), 55.2 (q), 22.6 (t), 13.4 ppm (d); FT-IR (neat): $\tilde{\nu} = 2240$ cm^{-1}; MS (FAB): *m*/*z* (%): 228 (100) $[M+1]^+$, 198 (46), 155 (16); HRMS (FAB): *m*/*z* calcd for $C_{14}H_{14}NO_2$ $[M+1]^+$: 228.1025; found: 228.1029; elemental analysis calcd (%) for $C_{14}H_{13}NO_2$ (227.26): C 73.99, H 5.77, N 6.16; found: C 73.85, H 5.70, N 6.21.

(1*S,2*R**)-2-Ferrocenylethynyl-2-methoxycyclopropanecarbonitrile (13f)**: Brown oil; yield 69%; $R_f = 0.26$ (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 4.44$ (m, 2H), 4.25 (m, 2H), 4.22 (s, 5H), 3.65 (s, 3H), 1.86 (dd, $^3J(H,H) = 6.7$, 9.6 Hz, 1H), 1.72 (at, $^3J(H,H) = 6.7$ Hz, $^2J(H,H) = 6.1$ Hz, 1H), 1.61 ppm (dd, $^3J(H,H) = 9.6$ Hz, $^2J(H,H) = 6.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 117.5$ (s), 85.0 (s), 79.9 (s), 71.64 (d), 71.59 (d), 69.9 (d, 5×CH), 69.0 (d, 2×CH), 62.7 (s), 56.4 (s), 56.0 (q), 22.6 (t), 13.4 ppm (d); FT-IR (neat): $\tilde{\nu} = 2236$, 2181 cm^{-1}; MS (FAB): *m*/*z* (%): 305 (100) $[M]^+$, 210 (10); HRMS (FAB): *m*/*z* calcd for $C_{17}H_{15}FeNO$ $[M+1]^+$: 306.0581; found: 306.0568.

(1*S,2*R**)-2-Methoxy-2-(phenylbut-3-en-1-yl)cyclopropanecarbonitrile (13g)**: Yellow oil; yield 49%; $R_f = 0.16$ (hexane/EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.49$–7.32 (m, 5H), 7.02 (d, $^3J(H,H) = 16.3$ Hz, 1H), 6.17 (d, $^3J(H,H) = 16.3$ Hz, 1H), 3.64 (s, 3H), 1.88 (dd, $^3J(H,H) = 7.0$, 9.9 Hz, 1H), 1.74 (at, $^3J(H,H) = 7.0$ Hz, $^2J(H,H) = 6.0$ Hz, 1H), 1.62 ppm (dd, $^3J(H,H) = 9.9$ Hz, $^2J(H,H) = 6.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 143.1$ (d), 135.4 (s), 129.0 (d), 128.6 (d, 2×CH), 126.2 (d, 2×CH), 117.4 (s), 106.0 (d), 85.6 (s), 84.8 (s), 56.3 (s), 56.1 (q), 22.5 (t), 13.4 ppm (d); FT-IR (neat): $\tilde{\nu} = 2241$, 2177 cm^{-1}; MS (FAB): *m*/*z* (%): 224 (100) $[M+1]^+$, 194 (25), 165 (16); HRMS (FAB): *m*/*z* calcd for $C_{15}H_{14}NO$ $[M+1]^+$: 224.1075; found: 224.1067.

(1*S,2*R**)-2-Methoxy-2-(trimethylsilylethynyl)cyclopropanecarbonitrile (13h)**: Colorless oil; yield 70%; $R_f = 0.37$ (hexane/EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 3.53$ (s, 3H), 1.78 (dd, $^3J(H,H) = 7.1$, 10.1 Hz, 1H), 1.60 (at, $^3J(H,H) = 7.1$ Hz, $^2J(H,H) = 6.3$ Hz, 1H), 1.52 (dd, $^3J(H,H) = 10.1$ Hz, $^2J(H,H) = 6.3$ Hz, 1H), 0.15 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 117.2$ (s), 99.3 (s), 91.4 (s), 55.9 (s + q), 22.4 (t), 13.2 (d), −0.5 ppm (q, 3×CH_3); FT-IR (neat): $\tilde{\nu} = 2242$, 2176 cm^{-1}; MS (FAB): *m*/*z* (%): 194 (100) $[M+1]^+$, 178 (38), 166 (48), 156 (51); HRMS (FAB): *m*/*z* calcd for $C_{10}H_{16}NOSi$ $[M+1]^+$: 194.1001; found: 194.1006.

(1*S,2*R**)-2-(3,3-Dimethylbut-1-ynyl)-2-methoxycyclopropanecarbonitrile (13i)**: Colorless liquid; yield 68%; $R_f = 0.40$ (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 3.51$ (s, 3H), 1.70 (dd, $^3J(H,H) = 6.8$, 9.8 Hz, 1H), 1.57 (at, $^3J(H,H) = 6.8$ Hz, $^2J(H,H) = 6.0$ Hz, 1H), 1.46 (dd, $^3J(H,H) = 9.8$ Hz, $^2J(H,H) = 6.0$ Hz, 1H), 1.20 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 117.6$ (s), 94.8 (s), 73.2 (s), 55.8 (s), 55.5 (q), 30.4 (q, 3×CH_3), 27.2 (s), 22.3 (t), 12.9 ppm (d); FT-IR (neat): $\tilde{\nu} = 2240$ cm^{-1}; HRMS (FAB): *m*/*z* calcd for $C_{11}H_{16}NO$ $[M+1]^+$: 178.1232; found: 178.1227; elemental analysis calcd (%) for $C_{11}H_{15}NO$ (177.24): C 74.54, H 8.53, N 7.90; found: C 74.60, H 8.56, N 7.85.

(1*S,2*R**)-2-(Hex-1-ynyl)-2-methoxycyclopropanecarbonitrile (13j)**: Colorless oil; yield 45%; $R_f = 0.27$ (hexane/EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 3.57$ (s, 3H), 2.24 (t, $^3J(H,H) = 6.9$ Hz, 2H), 1.74 (dd, $^3J(H,H) = 6.7$, 9.8 Hz, 1H), 1.63 (at, $^3J(H,H) = 6.7$ Hz, $^2J(H,H) = 5.9$ Hz, 1H), 1.56–1.37 (m, 5H), 0.93 ppm (t, $^3J(H,H) = 7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 117.7$ (s), 86.9 (s), 74.8 (s), 56.1 (s), 55.8 (q), 30.3 (t), 22.4 (t), 21.8 (t), 18.2 (t), 13.5 (q), 13.0 ppm (d); FT-IR (neat): $\tilde{\nu} = 2241$ cm^{-1}; MS (EI): *m*/*z* (%): 177 (100) $[M]^+$, 148 (51), 135 (85), 95 (53); HRMS (EI): *m*/*z* calcd for $C_{11}H_{15}NO$: 177.1154; found: 177.1155; elemental analysis calcd (%) for $C_{11}H_{15}NO$ (177.24): C 74.54, H 8.53, N 7.90; found: C 74.58, H 8.55, N 7.92.

Methyl 2-(3,3-dimethylbut-1-ynyl)-2-methoxycyclopropanecarboxylate (13k): Colorless oil; yield 49% (combined yield for the two diastereomers), 44% (yield of the major diastereomer); $R_f = 0.25$ (hexane/EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 3.71$ (s, 3H), 3.40 (s, 3H), 2.05 (dd, $^3J(H,H) = 7.3$, 9.4 Hz, 1H), 1.63 (dd, $^3J(H,H) = 7.3$ Hz, $^2J(H,H) = 5.8$ Hz, 1H), 1.47 (dd, $^3J(H,H) = 9.4$ Hz, $^2J(H,H) = 5.8$ Hz, 1H), 1.22 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 169.3$ (s), 95.2 (s), 72.5 (s), 58.8 (s), 55.4 (q), 51.7 (q), 30.7 (q, 3×CH_3), 29.3 (d), 27.4 (s), 21.6 (t), 13.7 ppm (q); elemental analysis calcd (%) for $C_{12}H_{18}O_3$ (210.27): C 68.54, H 8.63; found: C 68.72, H 8.59.

Methyl (1*R,2*S**)-2-methoxy-1-methyl-2-phenylethynylcyclopropanecarboxylate (15a-maj)**: Colorless oil; major diastereomer from a 2:1 mixture; yield 29% (combined yield for the two diastereomers); $R_f = 0.44$ (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.45$–7.41 (m, 2H), 7.35–7.31 (m, 3H), 3.75 (s, 3H), 3.54 (s, 3H), 2.01 (d, $^2J(H,H) = 5.8$ Hz, 1H), 1.53 (s, 3H), 1.20 ppm (d, $^2J(H,H) = 5.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): $\delta = 172.0$ (s), 131.6 (d, 2×CH), 128.3 (d), 128.2 (d, 2×CH), 122.5 (s), 85.5 (s), 84.5 (s), 60.9 (s), 56.1 (q), 52.1 (q), 34.5 (s), 26.6 (t), 14.0 ppm (q); FT-IR (neat): $\tilde{\nu} = 1729$ cm^{-1}; MS (EI):

m/*z* (%): 244 (12) $[M]^+$, 197 (19), 185 (100), 153 (28), 129 (67); HRMS (EI): *m*/*z* calcd for $C_{15}H_{16}O_3$: 244.1094; found: 244.1096.

Methyl (1*R,2*S**)-2-methoxy-1-methyl-2-phenylethynylcyclopropanecarboxylate (15a-min)**: Colorless oil; minor diastereomer from a 2:1 mixture; yield 29% (combined yield for the two diastereomers); R_f = 0.37 (hexane/EtOAc, 5:1); spectroscopic data retrieved from an enriched mixture; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 7.49–7.30 (m, 5H), 3.77 (s, 3H), 3.44 (s, 3H), 2.10 (d, ^2J(H,H) = 6.0 Hz, 1H), 1.54 (s, 3H), 1.11 ppm (d, ^2J(H,H) = 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 170.9 (s), 131.7 (d, 2×CH), 128.5 (d), 128.2 (d, 2×CH), 122.3 (s), 86.7 (s), 84.4 (s), 62.3 (s), 56.0 (q), 52.3 (q), 33.1 (s), 26.5 (t), 18.1 ppm (q).

Methyl 2-methoxy-3-methyl-2-phenylethynylcyclopropanecarboxylate (15b): Colorless oil; a 1:1 mixture of nonseparated diastereomers: combined yield 22%; R_f = 0.34 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 7.62–7.26 (m, 10H), 3.80 (s, 3H), 3.73 (s, 3H), 3.53 (s, 3H), 3.43 (s, 3H), 2.22–2.12 (m, 1H), 2.10–2.03 (m, 1H), 1.85 (d, ^3J(H,H) = 7.1 Hz, 1H), 1.78 (d, ^3J(H,H) = 7.2 Hz, 1H), 1.31–1.27 ppm (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 169.9 (s), 169.0 (s), 131.8 (d, 2×CH), 131.6 (d, 2×CH), 128.6 (d), 128.3 (d, 2×CH), 128.2 (d), 128.0 (d, 2×CH), 122.2 (s), 86.4 (s, 2×C), 84.2 (s, 2×C), 64.1 (s), 62.3 (s), 56.4 (q), 56.2 (q), 52.1 (q), 51.8 (q), 36.4 (d), 35.5 (d), 29.4 (d), 27.1 (d), 13.8 (q), 10.6 ppm (q).

Methyl (1*R,2*S**)-2-(3,3-dimethylbut-1-ynyl)-2-methoxy-1-methylcyclopropanecarboxylate (15c-maj)**: Colorless oil; major diastereomer from a 2:1 mixture; yield 85% (combined yield for the two diastereomers); R_f = 0.20 (hexane/EtOAc, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.69 (s, 3H), 3.40 (s, 3H), 1.80 (d, ^2J(H,H) = 5.8 Hz, 1H), 1.42 (s, 3H), 1.20 (s, 9H), 1.00 ppm (d, ^2J(H,H) = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 172.1 (s), 94.5 (s), 73.5 (s), 60.4 (s), 55.5 (q), 51.7 (q), 33.8 (s), 30.8 (q, 3×CH_3), 27.3 (s), 26.0 (t), 13.9 ppm (q); FT-IR (neat): $\tilde{\nu}$ = 1728 cm^{-1}; HRMS (FAB): *m*/*z* calcd for $C_{13}H_{21}O_3$ $[M+1]^+$: 225.1491; found: 225.1493; elemental analysis calcd (%) for $C_{13}H_{20}O_3$ (224.30): C 64.66, H 6.63; found: C 64.72, H 6.57.

Methyl (1*S,2*S**)-2-(3,3-dimethylbut-1-ynyl)-2-methoxy-1-methylcyclopropanecarboxylate (15c-min)**: Colorless oil; minor diastereomer from a 2:1 mixture; yield 85% (combined yield for the two diastereomers); R_f = 0.10 (hexane/EtOAc, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.72 (s, 3H), 3.32 (s, 3H), 1.95 (d, ^2J(H,H) = 5.8 Hz, 1H), 1.42 (s, 3H), 1.25 (s, 9H), 0.91 ppm (d, ^2J(H,H) = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 171.3 (s), 96.1 (s), 73.5 (s), 62.0 (s), 55.5 (q), 52.2 (q), 32.2 (s), 30.9 (q, 3×CH_3), 27.5 (s), 26.3 (t), 18.0 ppm (q); FT-IR (neat): $\tilde{\nu}$ = 1737 cm^{-1}; HRMS (FAB): *m*/*z* calcd for $C_{13}H_{21}O_3$ $[M+1]^+$: 225.1491; found: 225.1493.

Methyl (1*R,2*R**,3*R**)-2-(3,3-dimethylbut-1-ynyl)-2-methoxy-3-methylcyclopropanecarboxylate (15d; first diastereomer)**: Colorless oil; one of the diastereomers from a 1:1 mixture; yield 76% (combined yield for the two diastereomers); R_f = 0.22 (hexane/EtOAc, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.70 (s, 3H), 3.44 (s, 3H), 1.91 (quintet, ^3J(H,H) = 6.3 Hz, 1H), 1.64 (d, ^3J(H,H) = 6.3 Hz, 1H), 1.22 (s, 9H), 1.22 ppm (d, ^3J(H,H) = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 170.0 (s), 94.9 (s), 73.3 (s), 62.0 (s), 55.7 (q), 51.6 (q), 35.3 (d), 30.8 (q, 3×CH_3), 28.7 (d), 27.4 (s), 10.5 ppm (q); FT-IR (neat): $\tilde{\nu}$ = 1729 cm^{-1} (data from the mixture of the two diastereomers); HRMS (FAB): *m*/*z* calcd for $C_{13}H_{21}O_3$ $[M+1]^+$: 225.1491; found: 225.1496 (data from the mixture of the two diastereomers).

Methyl (1*S,2*R**,3*S**)-2-(3,3-dimethylbut-1-ynyl)-2-methoxy-3-methylcyclopropanecarboxylate (15d; second diastereomer)**: Colorless oil; one of the diastereomers from a 1:1 mixture; yield 76% (combined yield for the two diastereomers); R_f = 0.13 (hexane/EtOAc, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.72 (s, 3H), 3.33 (s, 3H), 2.03 (quintet, ^3J(H,H) = 6.3 Hz, 1H), 1.63 (d, ^3J(H,H) = 6.3 Hz, 1H), 1.24 (s, 9H), 1.19 ppm (d, ^3J(H,H) = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 169.3 (s), 95.6 (s), 73.3 (s), 64.0 (s), 55.6 (q), 51.9 (q), 36.0 (d), 30.9 (q, 3×CH_3), 27.5 (s), 26.6 (d), 13.7 ppm (q); FT-IR (neat): $\tilde{\nu}$ = 1729 cm^{-1} (data from the mixture of the two diastereomers); HRMS (FAB): *m*/*z* calcd for $C_{13}H_{21}O_3$ $[M+1]^+$: 225.1491; found: 225.1496 (data from the mixture of the two diastereomers); elemental analysis calcd (%) for $C_{13}H_{20}O_3$ (224.30): C 64.66, H 6.63; found: C 64.60, H 6.59.

Methyl (1*R,5*R**,6*S**)-6-(3,3-dimethylbut-1-ynyl)-6-methoxybicyclo-[3.1.0]hexanecarboxylate (15e; first diastereomer)**: Colorless oil; one of the diastereomers from a 1:1 mixture; yield 83% (combined yield for the two diastereomers); R_f = 0.53 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.68 (s, 3H), 3.44 (s, 3H), 2.27–2.16 (m, 2H), 2.12–1.86 (m, 3H), 1.83–1.62 (m, 2H), 1.21 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 171.9 (s), 94.2 (s), 73.6 (s), 64.6 (s), 55.5 (q), 51.5 (q), 46.0 (s), 38.9 (d), 30.8 (q, 3×CH_3), 27.9 (t), 27.3 (s), 25.9 (t), 25.7 ppm (t); FT-IR (neat): $\tilde{\nu}$ = 1726 cm^{-1}; MS (EI): *m*/*z* (%): 250 (<5) $[M]^+$, 235 (68), 191 (100), 175 (29), 91 (37); HRMS (EI): *m*/*z* calcd for $C_{15}H_{22}O_3$: 250.1563; found: 250.1569; elemental analysis calcd (%) for $C_{15}H_{22}O_3$ (250.33): C 71.97, H 8.86; found: C 71.91, H 8.93.

Methyl (1*S,5*S**,6*S**)-6-(3,3-dimethylbut-1-ynyl)-6-methoxybicyclo-[3.1.0]hexanecarboxylate (15e; second diastereomer)**: Colorless oil; one of the diastereomers from a 1:1 mixture; yield 83% (combined yield for the two diastereomers); R_f = 0.40 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.73 (s, 3H), 3.31 (s, 3H), 2.30 (d, ^3J(H,H) = 5.4 Hz, 1H), 2.25–2.17 (m, 1H), 2.13–1.98 (m, 2H), 1.87–1.69 (m, 3H), 1.26 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 171.0 (s), 99.1 (s), 70.8 (s), 66.8 (s), 55.4 (q), 52.0 (q), 45.1 (s), 37.9 (d), 30.8 (q, 3×CH_3), 29.0 (t), 27.7 (s), 26.2 (t), 25.3 ppm (t); FT-IR (neat): $\tilde{\nu}$ = 1735 cm^{-1}; MS (EI): *m*/*z* (%): 250 (<5) $[M]^+$, 235 (67), 191 (100), 175 (27), 91 (29); HRMS (EI): *m*/*z* calcd for $C_{15}H_{22}O_3$: 250.1563; found: 250.1565; elemental analysis calcd (%) for $C_{15}H_{22}O_3$ (250.33): C 71.97, H 8.86; found: C 72.02, H 8.90.

Dimethyl (1*R,2*R**)-3-(3′,3′-dimethylbut-1-ynyl)-3-methoxy-1,2-cyclopropanedicarboxylate (15f)**: Colorless oil; product not isolated; yield 30% [estimated by ^{1}H NMR (300 MHz) of a mixture with the unreacted alkene]; R_f = 0.12 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 3.73 (s, 3H), 3.71 (s, 3H), 3.38 (s, 3H), 2.76 (d, ^3J(H,H) = 7.3 Hz, 1H), 2.70 (d, ^3J(H,H) = 7.3 Hz, 1H), 1.19 ppm (s, 9H).

Microwave-promoted cyclopropanation of alkenes with Fischer carbene complexes 1—general procedure: A solution of the appropriate carbene complex **1** (0.5 mmol) and the requisite alkene **2a**,**d**, **6a** or **9a** (10 mmol, 20 equiv) in dry THF (10 mL) under an inert atmosphere in a sealed tube was placed in a domestic microwave oven at 600 W until the starting carbene complex was completely consumed (3–4 min). The solvents were then removed under vacuum, and the residue was redissolved in hexane and exposed to light in an open-air vessel to induce decomplexation of the metal species present. The resulting suspension was filtered through Celite, silica gel (0.5 g) was added, and the solvents were removed under vacuum. The residue was purified by flash column chromatography, employing mixtures of hexane/EtOAc (20:1 to 3:1) as eluents, to give captodative cyclopropanes **22** in the yields and diastereoselectivities indicated in Table 6. Cyclopropanes **22a**,[12g] **22b**,[18b] **22c**,[12g,34] **22e**,**f**,[12h,34] and **22h**[35] have been reported previously.

6-[(*E*)-2-(Furan-2-yl)vinyl]-6-methoxy-2-oxa-bicyclo[3.1.0]hexane (22d): Yellow oil; yield 65% (combined yield for the two diastereomers); data for the major diastereomer: R_f = 0.33 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 7.29 (br s, 1H), 6.33 (m, 1H), 6.19 (d, ^3J(H,H) = 16.0 Hz, 1H), 6.15 (d, ^3J(H,H) = 3.4 Hz, 1H), 5.75 (d, ^3J(H,H) = 16.0 Hz, 1H), 4.20–4.11 (m, 1H), 3.95–3.86 (m, 2H), 3.46 (s, 3H), 2.23–2.13 (m, 2H), 1.85–1.79 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 152.5 (s), 141.5 (d), 126.5 (d), 115.3 (d), 111.2 (d), 107.1 (d), 72.6 (t), 68.7 (s), 68.1 (d), 56.2 (d), 30.5 (d), 25.6 ppm (t); elemental analysis calcd (%) for $C_{12}H_{14}O_3$ (206.24): C 69.88, H 6.84; found: C 70.12, H 6.99.

6-Methoxy-6-phenyl-2-oxa-bicyclo[3.1.0]hexane (22g): Colorless oil; yield 46% (combined yield for the two diastereomers); the diastereomers could not be separated; R_f = 0.32 (hexane/EtOAc, 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ = 7.57–7.43 (m, 2H), 7.37–7.26 (m, 4H), 7.24–7.18 (m, 4H), 4.29–4.11 (m, 6H), 3.46 (s, 3H, maj), 3.10 (s, 3H, min), 2.33–2.26 (m, 4H), 2.16–2.04 (m, 1H), 1.97–1.91 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C): δ = 139.7 (s, 2×C), 131.2 (d), 128.3 (d, 2×CH), 128.2 (d, 2×CH), 126.7 (d), 125.4 (d, 4×CH), 73.0 (t, maj), 70.7 (t, min), 69.5 (s, 2×C), 67.3 (d, maj), 65.9 (d, min), 55.9 (q, maj), 53.4 (q, min), 31.8 (d, maj), 29.1 (d, min), 26.5 (t, min), 26.1 ppm (t, maj).

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