

A Novel [2 + 2 + 1]/[2 + 1] Tandem Cycloaddition Reaction of Fischer Alkynyl Carbenes with Strained Bicyclic Olefins

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The remarkable variety and extraordinary richness of the chemistry displayed by α,β -unsaturated Fischer carbene complexes have prompted de Meijere to term them as "chemical multitools".¹ A wide array of cycloadducts can be prepared in high yield by appropriate selection of the carbene complexes counterparts and the reaction variables. In this regard, alkenyl carbene complexes are suitable reagents for the cyclopropanation of olefins,² and, more recently, we have found that alkynyl carbene complexes are capable of doing so with olefins bearing special modes of reactivity such as fulvenes,³ this one being the only example reported so far of alkene cyclopropanation with Fischer alkynyl carbene complexes.⁴

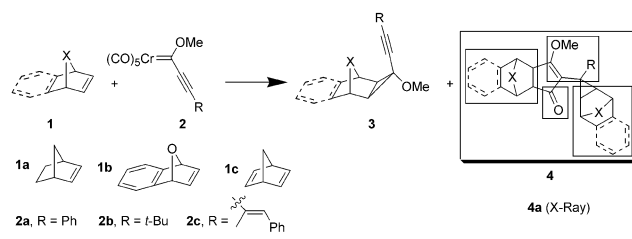
On the other hand, multicomponent reactions (M-CRs)⁵ are becoming increasingly popular as they are extremely valuable tools to produce chemical libraries and represent an important approach to diversity-oriented organic syntheses, by introducing multiple points of diversity.⁶ In this report, we present the results obtained when treating strained bicyclic olefins such as norbornene derivatives with alkynyl Fischer carbene complexes. In this reaction, four simple components are converted into a complex structure in a single operation by the creation of five new σ C–C bonds that leads to the concomitant formation of two new rings: cyclopentenone and cyclopropane moieties.

We initially studied the reaction of methoxyphenylethynyl chromium carbene **2a** with an excess of norbornene (10 equiv) (method A) in refluxing toluene for 30 min, which resulted in the isolation of compound **4a** in 43% yield as a 3:1 mixture of diastereomers. The structure of **4a** was tentatively proposed by NMR (COSY, HMQC, HMBC, NOESY) and confirmed by X-ray diffraction of the major diastereomer, which crystallized separately. The cyclopropyl derivatives **3a** were isolated as minor products (12% yield) in a 3:1 diastereomeric ratio.

After screening several reaction conditions, we found slow addition of the carbene complex to the bicyclic olefin in refluxing toluene to be the most suitable conditions regarding yield. Also, the performance of the reaction under CO atmosphere (method B) diminished and some times totally prevented the direct cyclopropanation as a side reaction.

A close examination of the structure of compound **4a** shows several interesting features: first, it has incorporated two units of norbornene, one molecule of carbene complex **2a** and a CO moiety; second, five σ C–C new bonds have been formed, and two rings have been created; third, the alkynyl carbene complex reacts in an unprecedented manner through the carbene carbon and both acetylenic carbons and allows the incorporation of a carbonyl ligand into the cyclopentenone ring; and, finally, it represents a

Table 1. [2 + 2 + 1]/[2 + 1] Cycloaddition Reactions with Bicyclic Olefins



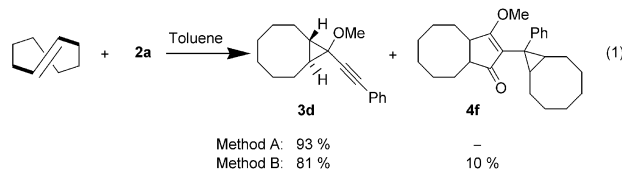
| entry | 1 | 2 | 3 | yield (%) ^a | dr ^b | 4 | yield (%) ^a | dr ^b |
|----------------|-----------|-----------|-----------|------------------------|-----------------|------------------------|------------------------|-----------------|
| 1 ^c | 1a | 2a | 3a | 12 | 3:1 | 4a | 43 | 3:1 |
| 2 ^d | 1a | 2a | 3a | 4 | 4:1 | 4a | 75 | 3:1 |
| 3 ^d | 1a | 2b | 3b | 26 | 4:1 | 4b | 53 | 1:1 |
| 4 ^d | 1a | 2c | 3c | 16 | 2:1 | 4c | 58 | 3:1 |
| 5 ^d | 1b | 2a | | | | 4d ^e | 66 | |
| 6 ^f | 1c | 2a | | | | 4e | 65 ^g | 3:1 |

^a Isolated yield based on the starting carbene complex. ^b Diastereomeric ratio estimated by ¹H NMR (300 MHz) of the isolated products. ^c Method A: **1** (10 equiv), **2** (1 equiv), toluene, reflux. ^d Method B: Slow addition of **2** (1 equiv) to **1** (10 equiv) in refluxing toluene under CO atmosphere. ^e Obtained as a mixture of three diastereomers in a 56:20:24 ratio. ^f Method C: Slow addition of **2** (1 equiv) to **1** (10 equiv) and BHT (4%) in refluxing toluene with N₂ bubbling. ^g Polymerized norbornadiene of undetermined molecular weight was also isolated.

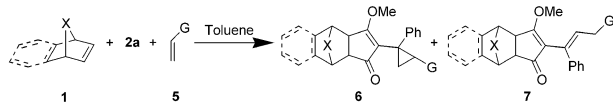
densely functionalized compound which should be amenable to further transformation.

The reaction tolerates different patterns of alkyne substitution in the Fischer carbene complex, as carbenes **2b** and **c** were found to yield the same kind of cycloadducts (Table 1, entries 3–5).

With norbornene being an alkene that exhibits a large strain energy, we decided to test these reaction conditions in other strained olefins such as (*E*)-cyclooctene. However, the reaction of **2a** with (*E*)-cyclooctene following method A conditions resulted in the direct cyclopropanation of the double bond, while 8% of the four-component cycloadduct **4f** was obtained under method B reaction conditions (eq 1). These results point out that, in addition to the ring strain, steric hindrance seems to play an important role and may be required for the reaction to proceed in acceptable yields. In fact, the reaction also takes place with bicyclic alkenes **1b** and **c** (Table 1, entries 6–7) which, as norbornene, are strained and sterically hindered.

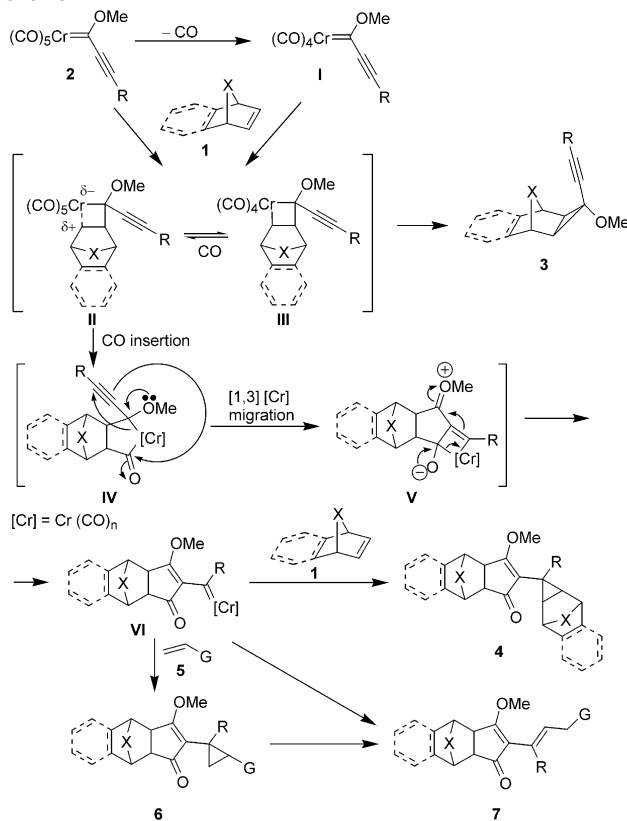


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Table 2. [2 + 2 + 1]/[2 + 1] Cycloaddition Reactions Involving Four Different Components


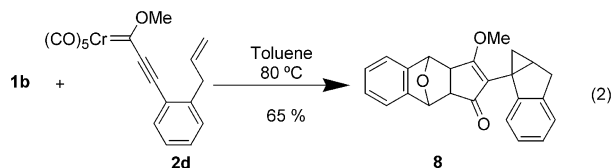
| entry ^a | 1 | 5 | G | 6 | yield (%) ^b | dr ^c | 7 | yield (%) ^b |
|--------------------|----|----|---|----|------------------------|-----------------|----|------------------------|
| 1 | 1a | 5a | OEt | 6a | 13 | 4:1 | 7a | 28 ^d |
| 2 | 1b | 5a | OEt | 6b | 12 | 3:1 | 7b | 68 |
| 3 | 1a | 5b | <i>n</i> -C ₄ H ₉ | 6c | 17 ^e | 1:1 | 7c | 39 ^e |

^a The reactions were performed at 80 °C in a sealed tube. ^b Isolated yield based on the starting carbene complex. ^c Diastereomeric ratio estimated by ¹H NMR (300 MHz) of the isolated products. ^d Compound 4a (11%, 3:1 ratio) was also isolated. ^e Compounds 6c and 7c could not be separated; the yield was estimated by NMR from a 56% combined isolated yield; a 4% yield of direct cyclopropanation product 3a was also isolated.

Scheme 1

To check if the carbene moiety was able to selectively discriminate between two different olefins, carbene **2a** was treated with bicyclic olefins **1a** or **1b** in the presence of an excess of terminal olefins **5**, producing cyclopropanes **6** and conjugated dienes **7** which were isolated in moderate to good combined yields. Compounds **6** are the result of the cyclopropanation of **5** with a nonstabilized carbene complex and were obtained as a mixture of diastereomers, while only one diastereomer was detected for **7**, which came from a cyclopropane rearrangement of **6** (Table 2).⁷ These results proved that carbene complex **2a** can effectively discriminate between two olefins: a strained bicyclic alkene **1** which forms a cyclopentenone ring and a terminal alkene **5** that is cyclopropanated.

An intramolecular version of this reaction could be achieved by carrying out the reaction between bicyclic olefin **1b** (5 equiv) and alkynyl carbene **2d**, bearing an allylic moiety, at 80 °C. Under these conditions, cycloadduct **8**, which was formed by an intramolecular cyclopropanation, was isolated in a 65% yield as a 1.5:1 diastereomeric mixture (eq 2).



With all of these results in hand, we propose the mechanism depicted in Scheme 1. An initial CO ligand removal from carbene complexes **2** can occur, thus generating a tetracarbonyl species **I**; bicyclic olefins **1** will probably add to **2** or **I** in a 1,2-fashion or by a [2 + 2]-cycloaddition leading to the dipolar addition product **II** or metallacyclobutane **III**, respectively, which may be in equilibrium. Intermediate **III** may evolve to the formation of cyclopropanes **3**, this pathway being enhanced in the absence of CO; however, when the reaction is carried out in the presence of CO, an alternative route is highly preferred. A CO insertion should then take place followed by a 1,3-metal migration⁸ to form a nonstabilized carbene species **VI**,⁹ which in fact bears a captodative moiety and will account for the formation of compounds **4**, **6**, and **7** in the final steps.

In summary, Fischer alkynyl carbenes react in an unprecedented manner with strained and hindered olefins, yielding products that incorporate up to four different components (two of them may be identical) by the formation of five σ C–C bonds. On the other hand, the reaction with strained olefins, such as (*E*)-cyclooctene, resulted in the high yield formation of the corresponding cyclopropane derivative, which opens the door to a previously undisclosed reactivity with alkynyl carbenes.

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Supporting Information Available: Experimental procedures and characterization data for the new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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