CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201002092

# Competitive Pathways in the Reaction of Lithium Oxy-*ortho*-quinodimethanes and Fischer Alkoxy Alkynyl Carbene Complexes: Synthesis of Highly Functionalised Seven-Membered Benzocarbocycles

**Patricia García-García, Carlos Novillo, Manuel A. Fernández-Rodríguez, and Enrique Aguilar*[a]**

*Dedicated to our mentor, Professor J. Barluenga, on the occasion of his 70th birthday*

**Abstract:** Up to four different outcomes have been found for the reaction between 1-oxy-*ortho*-quinodimethanes (*o*QDMs) and alkoxy alkynyl Fischer carbene complexes (FCCs). The product formed depends on the structure of both reagents and on the reaction solvent. The pathways can be topologically classified as a [*4*C+*2*C], a [*3*(2C+O)+*3*C], and two different [*4*C+*3*C] processes and, in all these sequences, 1-oxy-*o*QDMs behave as enolates or as vinylogous enolates. The reaction of Choy and Yang's unsubstituted *o*QDM **1** with tungsten alkynyl FCCs is solvent controlled; thus, selective formation of benzocycloheptenones can be achieved in THF, whereas exclusive synthesis of benzocycloheptene ketals is reached in diethyl ether. On the other hand, THF is the solvent of choice to form benzocycloheptene ketals when an alkyl or aryl group is placed at position 1 of the oQDM in its reaction with tungsten carbene complexes; however, a pyranylidene carbene complex is formed when a chromium carbene complex is used. Alternatively, the presence of bulky alkoxy groups in the FCC component favours a Diels–Alder aromatisation sequence, which leads to 1-naphthyl FCCs. Furthermore, the isolation and the characterisation of several deuterated compounds by labelling experiments have provided some insight into the reaction pathways, and mechanisms consistent with those findings have been established and several reaction intermediates have been identified.

**Keywords:** carbenes · carbocycles · cycloaddition · solvent effects · tungsten

## Introduction

Even though we are now deeply submerged in an age of catalysis,[1] the role of Fischer carbene complexes (FCCs) as stoichiometric synthetic intermediates in organic chemistry remains a valuable tool,[2] because they provide a variety of reactivity patterns that are not amenable for alternative catalytic reagents. This fact is especially relevant in the case of alkoxy alkynyl FCCs of chromium and tungsten, which may also offer either similar or complementary modes of reactivity. In this sense, we have initiated an exploration of the reactivity of FCCs against *ortho*-quinodimethanes (*o*QDMs). These highly reactive intermediates can be generated in situ following different routes, with thermal ring opening of benzocyclobutenes being the most straightforward.[3] Although very high temperatures are usually required for the opening, this process is known to be favoured by the presence of electron-donating groups in the cyclobutene ring (Scheme 1),[3,4] thus allowing the formation of *o*QDMS under mild conditions compatible with FCCs. In this regard, we have first shown that the reaction of symmetric bis-trialkylsilyloxy *o*QDMs with alkoxy arylalkynyl FCCs follows a tandem [4+2]-cycloaddition–cyclopentannulation sequence leading to benzo[*b*]fluorene derivatives (Scheme 2).[5]

Moreover, Choy and Yang have reported that, for metalated benzocyclobuteneoxides, the ring opening takes place at temperatures as low as −25 °C and the resulting electron-rich dienes have been employed in Diels–Alder reactions with a variety of electron-deficient dienophiles.[4] Taking ad-

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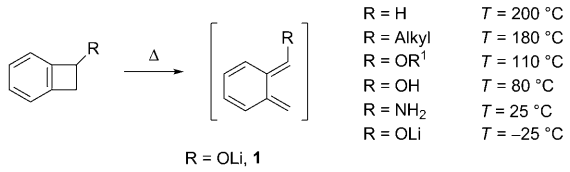
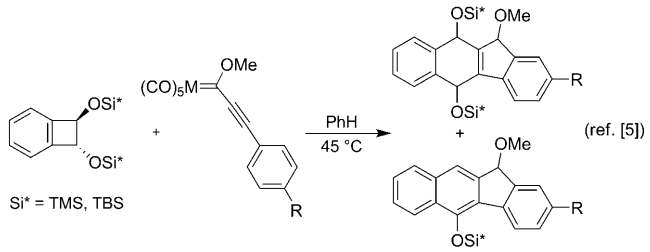
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201002092.

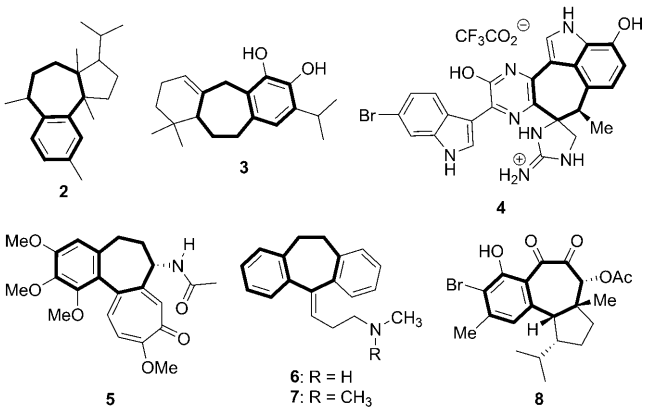



Scheme 1. Effect of the nature of the benzocyclobutene substituent in thermal *o*-QDM generation.

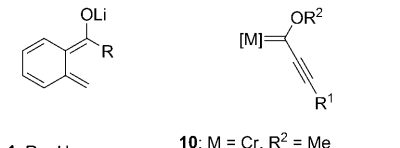



Scheme 2. Synthesis of benzo[*b*]fluorene derivatives by reaction of symmetric bis-trialkylsilyloxy *o*QDMs with alkoxy arylalkynyl FCCs. TMS = trimethylsilyl, TBS = *tert*-butyldimethylsilyl.

vantage of the ease of lithium benzocyclobuteneoxide ring opening at low temperature, we have recently reported that the reaction of alkoxy alkynyl FCCs with *o*QDM **1** leads to the preparation of highly functionalised seven-membered benzocarbocycles;[6] this transformation can be considered as a formal [*4*C+*3*C] process in terms of skeletal analysis.[7,8] Interestingly, the benzoheptacarbocycle skeleton, as a key structural element, is present in important synthetic intermediates and in various natural products and/or pharmacologically active compounds such as terpenes (i.e., (−)-presphaerene[9] (**2**), barbatusol[10] (**3**)), alkaloids (dragmacidin E (**4**)),[11] (−)-colchicine (**5**; an anti-tumour agent),[12] nortriptyline (**6**) and amitriptyline (**7**) (anti-depressant activity)[13] or hamigeran C (**8**; cytotoxic)[14] among others. Therefore,




we decided to carefully analyse such reactions and, in this manuscript, we present a full account regarding its scope and limitations. Thus, the reaction of *o*QDM **1** and 1-substituted *o*QDM **9** against alkoxy alkynyl FCCs of chromium **10** and tungsten **11** and **12**, has been explored, and we have found that up to four different reaction pathways may take place, depending on the structure of both reagents (*o*QDM and FCC) and on the reaction solvent. Such transformations can be classified as a [*4*C+*2*C], a [*3*(2C+O)+*3*C], and two different [*4*C+*3*C] processes, from a topological point of view. In addition, labelling experiments have also been performed to gain some insight into the reaction pathways; consequently, mechanisms accounting for the different transformations are proposed below, including a modification of our originally reported mechanism.[6]




**1**: R = H
**9**: R = Alkyl, aryl

**10**: M = Cr, $R^2$ = Me
**11**: M = W, $R^2$ = Me
**12**: M = W, $R^2$ = *i*Pr, menthyl

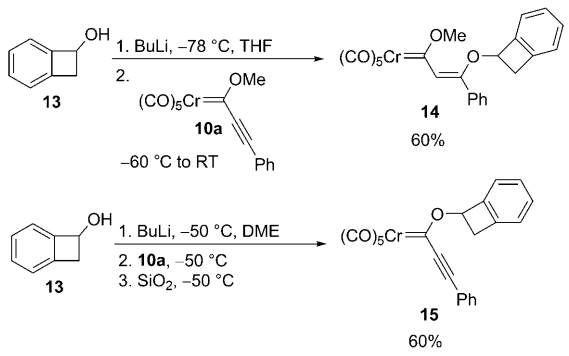
**Abstract in Spanish:** *Las reacciones entre 1-oxi-orto-quinodimetanos (oQDMs) y complejos alcoxi alquinil carbeno de Fischer (FCCs) pueden seguir cuatro posibles rutas diferentes, dependiendo de la estructura de los reactivos y del disolvente empleado. Topológicamente, estos procesos se pueden clasificar como [4C+2C], [3 (2C+O)+3C], y dos [4C+3C] diferentes y, en todas estas secuencias, los 1-oxi-oQDMs se comportan como enolatos o como enolatos vinílogos. Las reacciones entre el oQDM de Choy y Yang no-sustituido **1** y alquinil FCCs de volframio están controladas por el disolvente de las mismas; así, la formación de benzocicloheptenonas tiene lugar selectivamente en THF mientras que, en dietil éter, se obtienen benzocicloheptenoacetales de forma exclusiva. Por otra parte, cuando en la posición 1 del oQDM está situado un grupo alquilo o arilo, la reacción con complejos carbeno de volframio en THF permite obtener benzocicloheptenoacetales mientras que cuando se emplea un complejo carbeno de cromo se accede a un complejo piranilideno carbeno. Alternativamente, la presencia de grupos alcoxilo voluminosos en el FCC favorece una secuencia Diels–Alder aromatización que conduce a 1-naftil FCCs. Finalmente, experimentos de marcaje isotópico han conducido al aislamiento y a la caracterización de varios compuestos deuterados, proporcionando valiosa información acerca de los posibles mecanismos lo que, a su vez, ha permitido la identificación de varios intermedios y la propuesta de mecanismos de reacción consistentes con los hechos observados.*

## Results and Discussion

**Optimisation of the reaction conditions and scope of the reaction**: A set of preliminary experiments were carried out under conditions similar to those reported by Choy and Yang, which involved mixing the lithium benzocyclobutene-

oxide and the dienophile at low temperature, in different solvents. Thus, benzocyclobutenol **13** was deprotonated with *n*BuLi in THF at −78 °C; chromium FCC **10a** was added at −60 °C, and the reaction mixture was allowed to reach room temperature before silica gel was added. FCC **14** was isolated in 60 % yield, not surprisingly, as a result of alkoxide 1,4-addition to FCC **10a** (Scheme 3).[15] On the other hand,

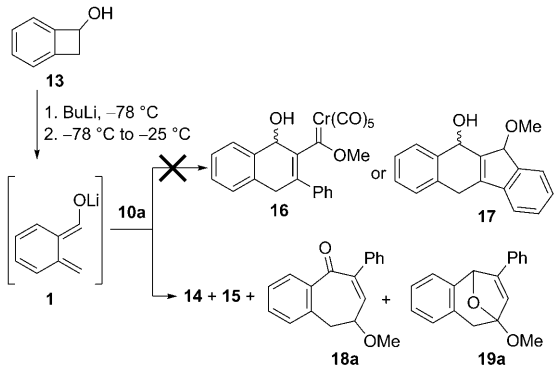



Scheme 3. Solvent-dependent addition of lithium benzocyclobuteneoxide to FCC **10a**. DME = 1,2-dimethoxyethane.

FCC **15** was isolated, also in 60 % yield, when the whole deprotonation–FCC addition–$SiO_2$ quenching sequence was carried out at −50 °C in DME;[16] interestingly, FCC **15** is formed from 1,2-addition of alkoxide to the initial carbene complex, which has not been previously observed.[15] These results confirm that benzocyclobuteneoxide does not open to form *o*QDM **1** at or below −50 °C, and indicate that there is a remarkable solvent effect in the addition of the alkoxide to FCC **10a**.

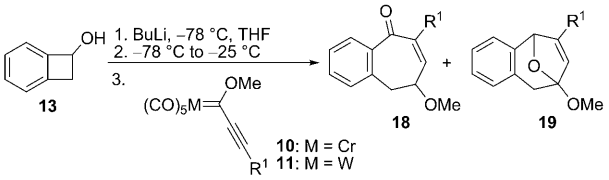
Considering these results, we performed a series of experiments at several temperatures and with different solvents, allowing the formation of the dienic system prior to addition of the alkynyl FCC. In one of the most promising tests, benzocyclobutenol **13** was deprotonated with *n*BuLi at −78 °C in THF and the reaction mixture was allowed to reach −25 °C to permit the formation of *o*QDM **1**; chromium FCC **10a** was added and the evolution of the reaction was monitored by TLC. However, instead of the expected [4+2] cycloaddition product **16** or benzo[*b*]fluorene **17** (see also Scheme 2), we isolated a mixture of two benzoheptacarbocycles **18a** and **19a** in low yield (Scheme 4 and Table 1, entry 1), among other low-yielding products (FCCs **14** and **15**).

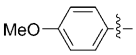
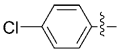
The identities of all new compounds were unequivocally ascertained by NMR spectroscopic experiments, including COSY, HSQC, HMBC and NOESY for selected compounds. For instance, correlations between the signal at $\delta$ = 4.27 ppm, which corresponds to the proton linked to the carbon atom with the methoxy group, and both $CH_2$ signals ($\delta$ = 3.22 and 3.44 ppm) and the olefin proton ($\delta$ = 6.82 ppm), were observed in the COSY spectrum of compound **18a**, which was crucial to establish the proposed structure. Moreover, long-range correlations in the HMBC spectrum, for example, between the carbonyl carbon ($\delta$ =




Scheme 4. Reaction of *o*-QDM **1** with FCC **10a**: unexpected outcome and formation of benzocycloheptene derivatives.

Table 1. Reaction of *o*QDM **1** with alkynyl carbene complexes **10** and **11** in THF.




| Entry[a] | FCC | Metal | $R^1$ | 18 | Yield [%][b] | 19 | Yield [%][b] |
|---|---|---|---|---|---|---|---|
| 1 | **10a** | Cr | Ph | **18a** | 8 | **19a** | 11 |
| 2 | **11a** | W | Ph | **18a** | 49 | **19a** | 16 |
| 3[c] | **11a** | W | Ph | **18a** | – | **19a** | 50 |
| 4 | **11b** | W |  | **18b** | 71 | **19b** | 14 |
| 5 | **11c** | W |  | **18c** | 67 | **19c** | 30 |
| 6 | **11d** | W |  | **18d** | 43 | **19d** | – |
| 7 | **11e** | W |  | **18e** | 52 | **19e** | 22 |
| 8 | **11f** | W |  | **18f** | 35 | **19f** | 22 |
| 9 | **11g** | W | *t*Bu | **18g** | 50[d] | **19g** | 5[d] |

[a] All the reactions were carried out on a 0.5 mmol scale of carbene complex (0.033 M) with 1.5 equiv of benzocyclobutenol (0.05 M). [b] Isolated yields based on the starting alkynyl carbene complexes. [c] Reaction performed in diethyl ether. [d] Products could not be separated; yield estimated by $^1$H NMR spectroscopic analysis (300 MHz) of a fraction enriched in **18g** after flash column chromatography.

195 ppm) and the olefin proton ($\delta$ = 6.82 ppm), were also in full agreement with the proposed structure. Furthermore, an X-ray structural elucidation for **19a** revealed that two planes, with a dihedral angle of 108.51°, contain all non-hydrogen atoms of the molecule except those of the methoxy group and the oxygen on the bridge.[17]

Taking into account that this is the first example in which oQDM (**1**) acts as a four-carbon synthon in a formal [4+3] cycloaddition, we decided to optimise the reaction conditions. To this end, we switched to the more stable tungsten FCC (**11a**) which, under similar reaction conditions, led to

an improved 65% isolated combined yield of both [4+3] cycloadducts **18a** and **19a** (Table 1, entry 2). Other solvents (hexane, 1,2-dimethoxyethane, toluene and dioxane) were examined, but they produced either low yielding mixtures of **18a** and **19a**, or no identifiable products. Interestingly, compound **19a** was the only adduct detected when the reaction was performed in diethyl ether (Table 1, entry 3). Such strong solvent effects[18] prompted us to consider the possibility of increasing the reaction yield by introducing additives or by varying the counterion; however, neither the addition of different coordinating reagents (pentamethyldiethylentriamine (PMDTA), [12]crown-4 ether or *N*,*N*′-dimethylpropyleneurea (DMPU)), nor the use of different bases (potassium hexamethyldisilazide (KHMDS), sodium hexamethyldisilazide (NaHMDS) or EtMgBr) or transmetallation strategies ($BuLi/ZnCl_2$), in either diethyl ether or THF, led to improved results.

Considering that, at this point, we had already developed conditions that allowed for the selective formation of two differently functionalised benzoheptacarbocycles, we then expanded the scope of the transformations by examining the nature of the substituents of the carbene complex. Thus, carbene complexes **11b–g** were treated with **1** in THF to obtain moderate to good yields of benzocycloheptenones **18** (Table 1, entries 4–9); the transformation was usually accompanied by the formation of small amounts of benzocycloheptene ketals **19**, which could usually be separated by flash column chromatography. The best yields were achieved when $R^1$ was a *para*-substituted aromatic group (Table 1, entries 4 and 5), although the reaction also took place selectively for *ortho*-substituted aryl, alkenyl and alkyl substituted alkynyl FCCs **11d–g** (Table 1, entries 6–9).

On the other hand, benzocycloheptene ketals **19** were obtained as unique products when carbene complexes **11** were treated with **1** in diethyl ether (Table 2), as expected (see also Table 1, entry 3). This reaction was much slower and usually required somewhat higher temperatures (room temperature or diethyl ether reflux temperature; Table 2, entries 5 and 9). Again, *para*-substituted aryl alkynyl carbene complexes gave the best yields (Table 2, entries 2 and 3). These reaction conditions tolerated *ortho*-substituted aryl (Table 2, entry 4), alkenyl (entries 5 and 6), alkyl (entries 7 and 8) and silyl (entry 9) groups as substituents in the alkynyl FCC. We also observed that the yield may be improved by performing the reaction at a higher concentration and with a larger excess of benzocyclobutenol (Table 2, entry 1 vs. Table 1, entry 3).

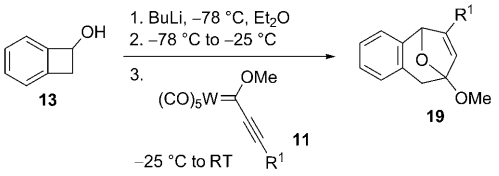
**Reaction with 1-substituted *o*QDMs**: We then expanded the scope of the reaction by analysing the reactivity of 1-substituted *o*QDMs **9**. In principle, these intermediates may be accessed by direct addition of alkyl or aryl lithium compounds to benzocyclobutenone **20** followed by ring opening of the formed benzocyclobuteneoxide **21** (Scheme 5).

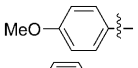
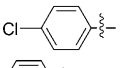
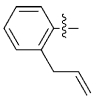
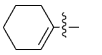
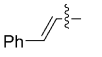
Initially, *n*BuLi was used as the nucleophile to react with benzocyclobutenone. Thus, when *n*BuLi was added to a solution of benzocyclobutenone in diethyl ether at −35°C, followed by addition of FCC **11a**[19] and warming of the reaction mixture to room temperature, ketal **22a** was obtained as the major product, albeit in a modest 22% yield. The yield could be slightly improved by performing the reaction in THF (Table 3, entry 2). It should be noted that, in the case of substituted *o*QDMs **9**, the formation of benzocycloheptenes **18**, which are obtained as major compounds when the reaction with *o*QDM **1** was performed in THF, is not possible (see mechanism below).

Attempts to optimise the reaction conditions were carried out by varying factors such as the temperatures of the reaction and during addition, the solvents, the additives (hexamethylphosphoric triamide (HMPA), [12]crown-4, DMPU or PMDTA), and the metal-ion exchange (Na, K, Zn or Cu). However, further improvement in the reaction yield was not observed under any of the conditions.

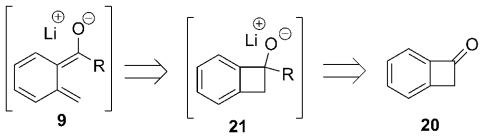
By employing the best conditions found, the reaction was also extended to FCC **11b** (Table 3, entry 3) and to the secondary alkyl lithium reagent *sec*BuLi (Table 3, entry 4) with

Table 2. Reaction of *o*QDM **1** with tungsten alkynyl carbene complexes **11** in $Et_2O$.




| Entry[a] | FCC | $R^1$ | 19 | Yield [%][b] |
|---|---|---|---|---|
| 1[c] | **11a** | Ph | **19a** | 70 |
| 2 | **11b** |  | **19b** | 56 |
| 3 | **11c** |  | **19c** | 86 |
| 4 | **11d** |  | **19d** | 51 |
| 5 | **11e** |  | **19e** | 55[d] |
| 6 | **11h** |  | **19h** | 33[e] |
| 7 | **11g** | *t*Bu | **19g** | 50 |
| 8 | **11i** | *n*Bu | **19i** | 25 |
| 9 | **11j** | TMS | **19j** | 38[d] |

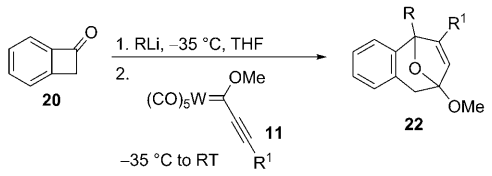
[a] All the reactions were carried out on a 0.5 mmol scale of carbene complex (0.033 M) with 1.5 equiv of benzocyclobutenol (0.05 M), unless otherwise stated. [b] Isolated yields based on the starting alkynyl carbene complexes **4**. [c] Reaction carried out with 5 equiv of benzocyclobutenol (0.33 M). [d] It was necessary to heat the reaction to reflux to make it proceed. [e] Reaction was carried out with 3 equiv of benzocyclobutenol (see the Supporting Information).




Scheme 5. Retrosynthetic route to 1-substitued *o*-quinodimethides **9**.

Table 3. Reaction of *o*QDM **9** with alkynyl carbene complexes **11**.

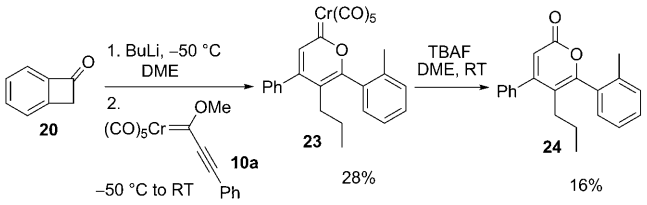



| Entry[a] | FCC | $R^1$ | R | 22 | Yield [%][b] |
|---|---|---|---|---|---|
| 1[c] | **11a** | Ph | *n*Bu | **22a** | 22 |
| 2 | **11a** | Ph | *n*Bu | **22a** | 32 |
| 3 | **11b** | MeO– | *n*Bu | **22b** | 35 |
| 4 | **11a** | Ph | *sec*Bu | **22c** | 31[d] |
| 5 | **11a** | Ph | *t*Bu | **22d** | 11 |
| 6 | **11a** | Ph | Me | **22e** | 11 |
| 7 | **11a** | Ph | Ph | **22f** | 21 |

[a] All the reactions were carried out on a 1.0 mmol scale of carbene complex (0.05 M) with 1.1 equiv of benzocyclobutenone (0.055 M) and 1.1 equiv of organolithium reagent. [b] Isolated yields based on the starting alkynyl carbene complexes. [c] Reaction performed in diethyl ether. [d] Isolated as a 1:1 mixture of diastereoisomers.

similar yields. However, a decrease in yield was observed when *t*BuLi (Table 3, entry 5), MeLi (entry 6) or PhLi (entry 7) were used.

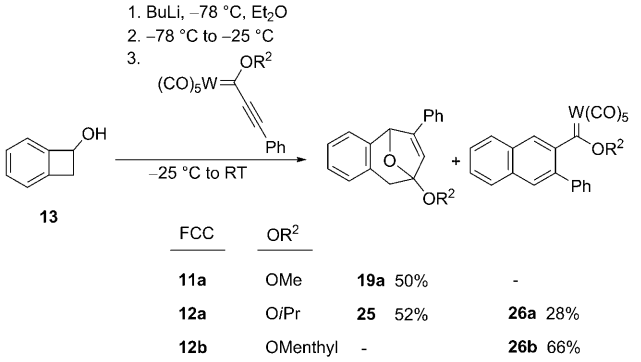
In contrast, instead of a seven-membered carbocycle, pyranylidene FCC **23** was isolated as the major product[20] when chromium FCC **10a** was employed. The best yield in this case was obtained by using DME as solvent and by adding the reagents at −50 °C (Scheme 6). The structure of




Scheme 6. Synthesis and oxidation of pyranylidene FCC **23**.

pyranylidene carbene complex **23** was determined by NMR spectroscopic analysis. Moreover, the oxidation of FCC **23** to its analogous ester **24** by air, with tetrabutylammonium fluoride (TBAF) in DME,[21] allowed complete confirmation of the proposed structure (Scheme 6). Topologically, this transformation can be classified as a [*3*(2C+O)+*3*C] cycloaddition.

**Reaction with bulky FCCs**: The reactivity of *o*QDM **1** toward FCCs with bulky alkoxy groups was then assessed. Thus, *o*QDM **1** was generated from benzocyclobutenol **13** following the usual procedure, and isopropoxy-derived tungsten alkynyl FCC **12a** was added at −25 °C. Once the carbene complex was consumed, and the usual workup and purification was followed, a mixture of benzocycloheptene ketal **25** and naphthyl FCC **26a**, coming from a formal Diels–Alder cycloaddition (topologically, [*4*C+*2*C]), was isolated in a combined 80% yield (Scheme 7). Moreover, when the even more sterically hindered menthyloxy-derived




Scheme 7. Influence of steric hindrance at the carbene carbon. Synthesis of naphthyl FCCs **26**.

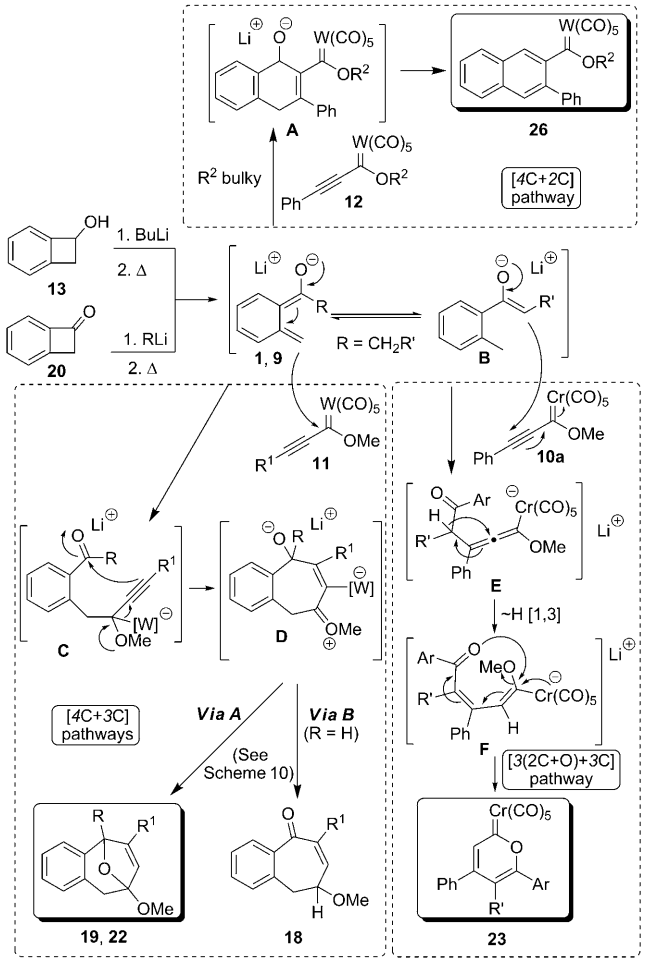
FCC **12b** was used, naphthyl FCC **26b** was formed exclusively and in good yield.

These results demonstrate how fine-tuning of the steric hindrance of the alkoxy group allows the outcome of the reaction of lithium oxy-*ortho*-quinodimethanes and Fischer alkoxyalkynyl carbene complexes to be controlled.

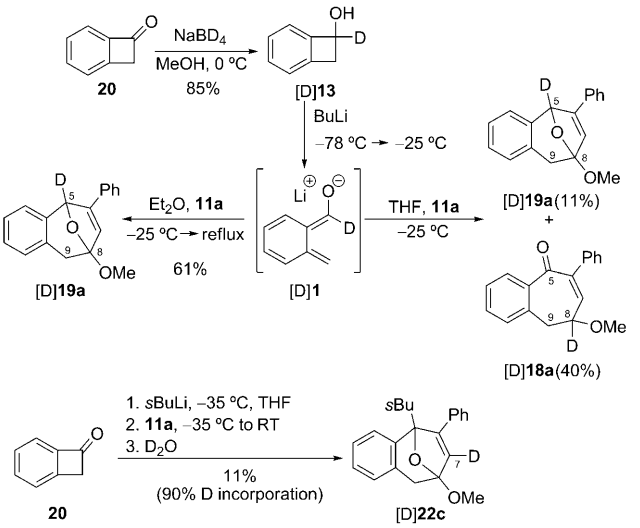
**Reaction mechanism**: The different reaction pathways depicted above can be rationalised from a mechanistic point of view. The *o*QDM (**1** or **9**), initially formed by deprotonation of benzocyclobutenol **13** or by addition of RLi to benzocyclobutenone **20**, can behave in distinct fashions depending on the characteristics of both the *o*QDM and the FCC (Scheme 8). The [4+2] cycloaddition-derived product, generally observed in the reaction of *o*QDMs with dienophiles, is only formed when a FCC with a bulky $R^2$ group is used. In this case, the carbene carbon is sterically blocked and remains untouched during the reaction. Otherwise, the addition of the *o*QDM to the carbene carbon is preferred, finally leading to seven-membered benzoheptacarbocycles **18**, **19** or **22** (see below). On the other hand, when $R=CH_2R'$ tautomerisation of the *o*QDM to enolate **B** is possible. In this case the reaction can then proceed through **B**, and the substituted enolate adds to the triple bond of the carbene complex, which is less hindered than the carbene carbon, to generate allenoate intermediate **E**. The evolution of **E** through a 1,3-H shift to **F**, followed by cyclisation, leads to pyranylidene FCC **23**.

Moreover, the mechanism of the most synthetically useful transformation of those described above, the formation of seven-membered benzoheptacarbocycles, has been studied in detail. To this end, regiospecifically deuterated benzocyclobutenol ([D]**13**) was synthesised, through reduction of benzocyclobutenone **20** with sodium borodeuteride, and used as a precursor of *o*QDM [D]**1**, under standard conditions. The obtained results, depicted in Scheme 9, show that conducting the reaction at reflux temperature in $Et_2O$ led to the formation of deuterated benzocycloheptene ketal [D]**19a** in 61% yield. In contrast, by conducting the reaction in THF, a mixture of both deuterated benzoheptacarbocycles [D]**18a** and [D]**19a** was obtained in slightly lower yields

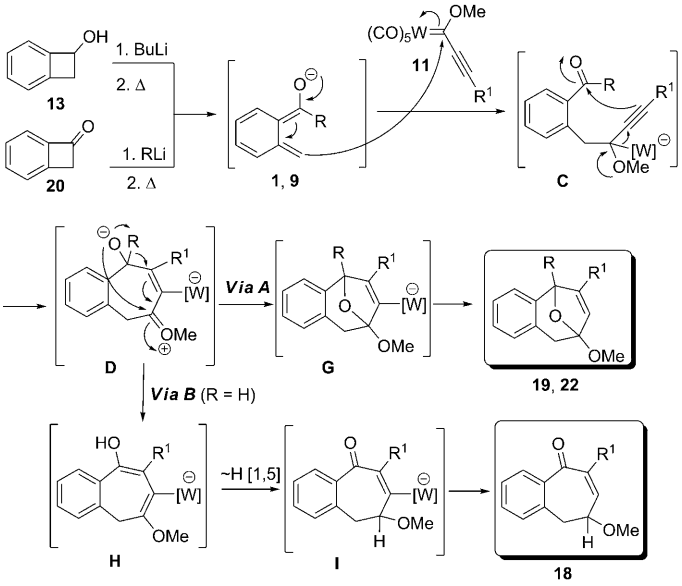
  




Scheme 8. Mechanistic pathways for the reaction of *o*QDMs with FCCs.




Scheme 9. Labelling experiments.




Scheme 10. Proposed mechanism for the formation of seven-membered benzocarbocycles **18**, **19** and **22** ($Li^+$ in intermediates **1**,**9** and **C**–**I** has been omitted for clarity).

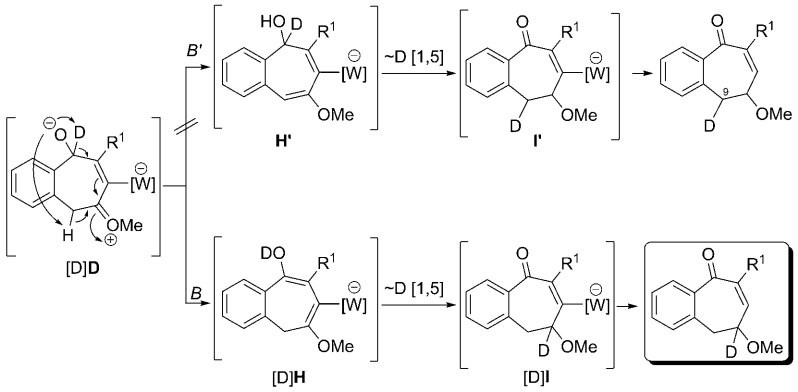
than in the non-deuterated, analogous process. In both cases, benzocycloheptene ketal [D]**19a** was quantitatively deuterated in position 5, whereas [D]**18a** was deuterated, also quantitatively, in position 8.

Further mechanistic evidence was obtained when *sec*BuLi was added to benzocyclobutenone, followed by the addition of tungsten FCC **11a** under the optimised reaction conditions and the final quenching was performed with deuterium oxide (Scheme 9). Under these conditions, an 11% yield of benzocycloheptene ketal [D]**22c** was isolated that had 90% deuterium incorporation at position 7, indicating the presence of the metal at this position prior to hydrolysis.

These observations are consistent with a common mechanism (Scheme 10). We propose that, after the initial deprotonation of benzocyclobutenol **13** at −78°C (or alkyl lithium addition to benzocyclobutenone **20**), the resulting lithium benzocyclobuteneoxide opens to give **1** (or **9**) upon warming to −25°C. Subsequently, *o*QDM **1** (or **9**) behaves as a vinylogous enolate, rather than a 1,3-diene, and nucleophilic attack[22,23] on the carbene carbon of **11** would take place to form intermediate **C**. A 1,2-metal migration,[23] promoted by the methoxy group, would cause ring closure to form intermediate **D**. The evolution of **D** could follow two different routes: in the first one (via **A**, Scheme 10) an intramolecular nucleophilic attack would produce metalated benzocycloheptene ketal **G**, which would account for the formation of **19** (or **22**). On the other hand, evolution according to via **B** mechanistic pathway (Scheme 10) may involve the formation of intermediate **H** through an intramolecular acid–base interchange; a subsequent 1,5-hydrogen-migration would give metalated intermediate **I**. Final protonation leads to the isolated compounds **18**.

To account for the formation of compounds **18**, in our previous communication we suggested that an intramolecular acid–base reaction involving the hydrogen atoms of the $CH_2$ moiety (Scheme 11, via B′) would generate a metalated intermediate **H′**, which, via a 1,5-deuterium shift and keto–enol tautomerisation, would lead to **I′** and finally to **18**




Scheme 11. Initially proposed mechanism and the corrected mechanism for the formation of seven-membered benzocarbocycles **18**.

through a 1,5-hydrogen shift and keto–enol tautomerisation. However, if this was the operating mechanism, deuterium incorporation should have been found at position 9 instead of in position 8 as observed in benzocycloheptene ketal [D]**18a**, and this was not the case. Moreover, the presence of the metal fragment in position 7 at the end of the reaction, prior to hydrolysis, was confirmed by trapping a type-**G** intermediate with deuterium, leading to [D]**22c** (Scheme 9).

## Conclusion

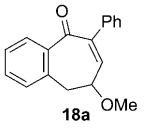
The reaction between 1-oxy-*o*QDMs and alkoxy alkynyl FCCs may result in up to four different reaction outcomes, depending on the structure of both reagents and on the reaction solvent. The reactions can be topologically classified as a [*4*C+*2*C], a [*3*(2C+O)+*3*C], and two different [*4*C+*3*C] processes; in all these sequences, the 1-oxy-*o*QDMs behave either as enolates or as vinylogous enolates. The reaction of Choy and Yang's *o*QDM **1** with tungsten alkynyl FCCs is solvent controlled; thus, new direct routes to different types of seven-membered functionalised benzocarbocycles have been established (selective formation of benzocycloheptenones can be achieved in THF and exclusive synthesis of benzocycloheptene ketals is accomplished in diethyl ether). Moreover, THF is the solvent of choice to form benzocycloheptene ketals when an alkyl or aryl group is present at position 1 of the oQDM in its reaction with tungsten carbene complexes; however, pyranylidene carbene complexes are formed when chromium carbene complexes are used. On the other hand, the presence of bulky alkoxy groups in the FCC component favours an alternative Diels–Alder pathway.

Labelling experiments have provided insights into the reaction pathways; the isolation and characterisation of several deuterated compounds have led to the identification of reaction intermediates and to mechanisms consistent with those findings.

## Experimental Section

**General synthesis of benzocycloheptenones 18**: *n*BuLi (1.6 M in hexane, 1.6 equiv) was added to a solution of benzocyclobutenol (1.5 equiv) in anhydrous THF (15 mL) at −78 °C. After 30 min, the temperature was raised to −25 °C and, after a further 10–15 min (red solution observed), the corresponding tungsten FCC **11** (1 equiv, 0.5 mmol) was added in portions. The mixture was stirred until complete disappearance of the carbene complex was observed by TLC. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography; the corresponding benzocycloheptenone **18** was isolated in the yield reported in Table 1.

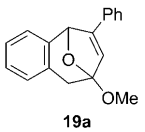
**Compound 18a**: Yield: 49%; yellow oil; $R_f$=0.24 (hexane/AcOEt, 5:1); $^1$H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.81 (d, $^3J$(H,H)=7.7 Hz, 1H), 7.53–7.34 (m, 7H), 7.30 (d, $^3J$(H,H)=7.7 Hz, 1H), 6.82 (m, 1H), 4.27 (m, 1H), 3.49 (s, 3H), 3.44 (m, 1H), 3.22 ppm (app. d, $^2J$(H,H)=14.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz, 25 °C): $\delta$=195.1 (s), 142.7 (d), 142.4 (s), 140.1 (s), 139.0 (s), 135.0 (s), 132.0 (d), 129.8 (d), 129.4 (d), 128.4 (d, 2 CH), 127.9 (d, 2 CH), 127.7 (d), 127. 0 (d), 77.2 (d), 56.5 (q), 39.2 ppm (t); FTIR (film): $\tilde{\nu}$= 1772, 1975, 1597 cm$^{-1}$; MS (FAB): *m*/*z* (%): 265 (100) [$M^+$+H], 233 (35), 205 (36); HRMS (FAB): *m*/*z* calcd for $C_{11}H_{17}O_2$: 265.1229 [$M^+$+H]; found: 265.1224; elemental analysis calcd (%) for $C_{11}H_{19}O_2$ (264.32): C 81.79, H 6.10; found: C 81.75, H 6.08.



**18a**

**General synthesis of benzocycloheptene ketals 19**: *n*BuLi (1.6 M in hexane, 1.6 equiv) was added to a solution of benzocyclobutenol (1.5 equiv) in anhydrous diethyl ether (15 mL) at −78 °C. After 30 min, the temperature was raised to −25 °C and, after 10–15 min, carbene complex **11** (1 equiv, 0.5 mmol) was added in portions. The mixture was stirred until complete disappearance of the carbene complex was observed by TLC. The solvent was removed under reduced pressure and the residue was purified by flash chromatography; the corresponding benzocycloheptene ketal **19** was isolated in the yield reported in Table 2.

**Compound 19a**: Yield: 50%; yellow solid; $R_f$=0.27 (hexane/AcOEt, 5:1); $^1$H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.58–7.10 (m, 9H), 6.24 (s, 1H), 5.88 (s, 1H), 3.59 (s, 3H), 3.29 (d, $^2J$(H,H)=19.8 Hz, 1H), 2.93 ppm (d, $^2J$(H,H)=19.8 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz, 25 °C): $\delta$=151.8 (s), 137.8 (s), 134.1 (s), 131.2 (s), 130.0 (d), 128.7 (d), 128.6 (d, 2 CH), 127.1 (d), 126.2 (d, 2 CH), 125.3 (d), 123.8 (d), 121.3 (d), 110.9 (s), 80.4 (d), 51.2 (q), 35.4 ppm (t); FTIR (film): $\tilde{\nu}$=1190, 1009 cm$^{-1}$; m.p. 110–112 °C; MS (FAB): *m*/*z* (%): 265 (39) [$M^+$+H], 257 (74), 205 (100), 202 (80), 195 (99); HRMS (FAB): *m*/*z* calcd for $C_{11}H_{17}O_2$: 265.1229 [$M^+$+H]; found: 265.1231; elemental analysis calcd (%) for $C_{11}H_{19}O_2$ (264.32): C 81.79, H 6.10; found C 81.74, H 6.09.



**19a**

## Acknowledgements

We are deeply grateful to Professor Barluenga for his constant support and for fruitful discussions. We thank Dr. Facundo Andina for his help with the X-ray structure of **19a**. We also appreciate the financial support

received from the Ministerio de Ciencia y Tecnología (Spain) (grants CTQ2004-08077-C02-01 and CTQ2007-61048, predoctoral fellowships to P.G.-G. and C.N., and a Juan de la Cierva postdoctoral contract to M.A.F.-R.) and Principado de Asturias (project IB08-088).

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Received: July 22, 2010
Published online: November 5, 2010

  