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Highly Functionalized Bicyclo[2.2.2]octenone-Fused [60]Fullerenes from Masked *o*-Benzoquinones and C_{60}

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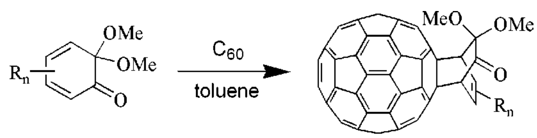
ABSTRACT



The Diels–Alder reactions of masked *o*-benzoquinones (MOBs) with [60]fullerene, affording novel and highly functionalized bicyclo[2.2.2]-octenone-fused [60]fullerene derivatives, are described.

Since the discovery[1] and macroscale preparation[2] of C_{60}, numerous reactions have been developed to explore the potentially rich and diverse chemistry of this new and spherical allotrope of carbon.[3] Although a number of protocols have been devised, cycloaddition reactions[4] proved to be one of the most outstanding and expeditious methods for the functionalization of [60]fullerene. The [4 + 2] cycloaddition is of special significance in this context.[4,5] C_{60} with a low-lying LUMO[6] behaves as a good dienophile, reacting with a large variety of dienes, particularly with electron-rich dienes, to afford selectively the adducts on 6,6-ring junctions. In some cases these cycloadducts undergo a facile retro-Diels−Alder reaction as a result of their low thermodynamic stability.[3a,7] However, cycloreversion could be prevented by stabilizing the cycloadducts through incorporation of the formed double bond into an aromatic ring, as in the cases of *o*-quinonedimethanes[8] and isobenzofuran,[9] by the extrusion of CO,[7a] or by converting the double bond into a single bond, as in the cases of Danishefsky's diene,[6b] 2-silyloxy-1,3-butadienes,[10] and 4-hydroxytropones.[11a]

Recently, electron-deficient dienes such as tropones,[11] 1,3-dienes bearing an electron-withdrawing group,[10b,12] and 2-pyrone[13] were employed in the Diels−Alder reactions of electron-poor polyolefin C_{60}, and the cycloadducts were found to be quite stable. In this communication we report

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the Diels–Alder reactions of masked *o*-benzoquinones (MOBs), which are known as electron-deficient dienes, with C_{60} to obtain novel and highly functionalized bicyclo[2.2.2]-octenone-fused [60]fullerenes.

Masked *o*-benzoquinones, a class of cyclohexa-2,4-dienones, can be easily generated in situ by the oxidation of readily available 2-methoxyphenols with hypervalent iodine reagents such as diacetoxyiodobenzene (DAIB) and bis(trifluoroacetoxy)iodobenzene in MeOH. Over the past 10 years we have been investigating the inter-[14−17] and intramolecular[14,18] Diels–Alder reactions of MOBs, and their synthetic potential[19] has been explored. Despite the fact that MOBs are electron-deficient, they readily undergo Diels–Alder cycloadditions with both electron-poor[16] and electron-rich[20] dienophiles. It occurred to us that if MOBs, being electron-deficient dienes, participate in the [4 + 2] cycloaddition with [60]fullerene, easy access to stable bicyclo[2.2.2]-octenone-fused [60]fullerenes could be achieved. Therefore, work was carried out in this direction.

Unlike other cyclohexa-2,4-dienones, MOBs are highly reactive and readily undergo dimerization,[16,21] leaving less room for their isolation (Figure 1). To circumvent this obstacle, the Diels–Alder reactions could be carried out by slowly generating MOBs in the presence of a dienophile. However, owing to the solubilty problems associated with C_{60} under the reaction conditions for the in situ generation of MOBs, it was not possible to perform the cycloaddition as mentioned above. Alternatively, toluene solutions of unstable MOBs, which are generated in MeOH at 0 °C, can be used for the cycloaddition step. The reactive MOB **1a** was first generated, and its toluene solution[22a] was used for the [4 + 2] cycloaddition with C_{60} at three different temperatures. While the reactions performed at 30 and 60 °C produced the desired cycloadduct **3a** in poor yields together with a dimer of **1a**, the reaction carried out at 110 °C resulted in the exclusive formation of dimer of **1a**. In contrast to **1a**, MOBs **1b** and **1c** exhibited improved reactivity toward C_{60} at 110 °C and afforded the adducts **3b** and **3c** in acceptable yields.

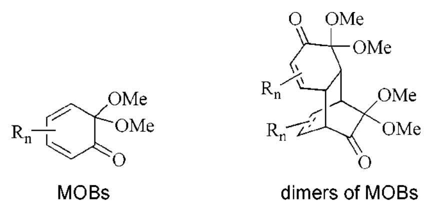
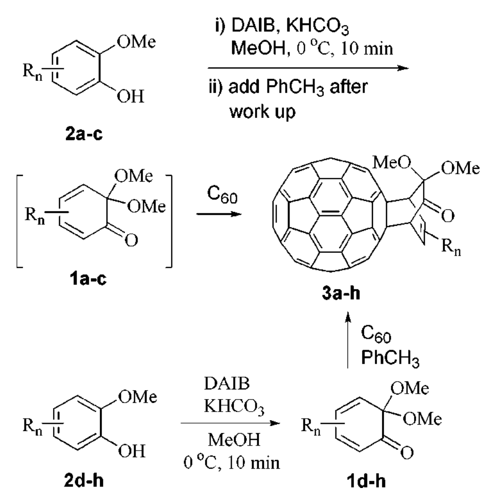


Figure 1. Structures of MOBs and their dimers.

To broaden the scope of these reactions, we have prepared a series of stable MOBs **1d–j**. Thus, MOBs **1d–j** were produced at 0 °C in MeOH by the oxidation of the corresponding 2-methoxyphenols **2d–j** in the presence of DAIB and were isolated in very good to excellent yields.[23] The Diels–Alder reactions of MOBs **1d–h** were carried out at different temperatures in toluene to furnish cycloadducts **3d–h**[22b] (Scheme 1), and the results are summarized in Table 1.

Scheme 1



The gross structures of adducts **3a–h** were established from their IR, UV–vis, ^{1}H (600 MHz) and ^{13}C NMR (150 MHz), DEPT, and low- and high-resolution FAB-MS spectral analyses. The cycloadducts **3a–h** exhibit IR absorption at ca. 526 cm^{-1} and a weak band in UV–vis spectra at ca. 432 nm, indicating the characteristic features of dihydrofullerenes.[7a,24] In the ^{13}C NMR spectra, the fullerene bridgehead

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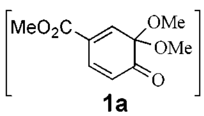
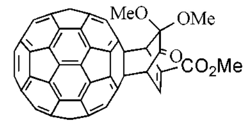
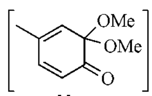
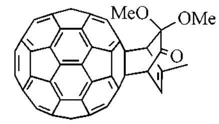
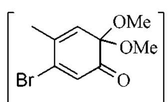
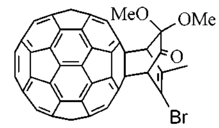
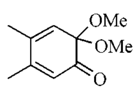
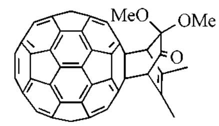
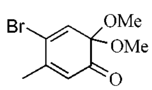
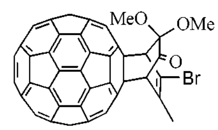
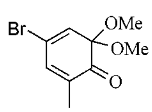
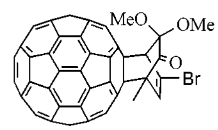
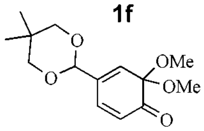
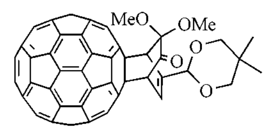
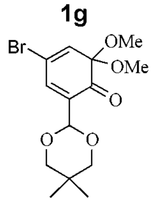
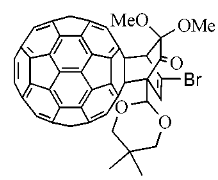
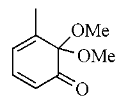
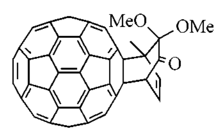
(21) Andersson, G.; Berntsson, P. *Acta Chem. Scand. B* **1975**, *29*, 948.
(22) **General Procedure.** (a) To a suspension of DAIB (3.3 equiv) and $KHCO_3$ (7 equiv) in MeOH (3 mL) was added a solution of phenols **2a–c** (3 equiv) in MeOH (2 mL) in one portion at 0 °C under nitrogen. After 5 min of stirring, the reaction mixture was diluted with CH_2Cl_2, washed with brine, and dried over anhydrous $MgSO_4$. The thus obtained solution was further diluted with toluene (10 mL), C_{60} (1 equiv., 50 mg, 0.069 mM) was added, and the low boiling solvents were removed under reduced pressure. Then the reaction was continued as mentioned in Table 1. After the reaction was complete, the reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography with toluene as an eluent to furnish the pure cycloadducts **3a–c**. (b) A solution of MOBs **1d–j** (1.2 equiv) and C_{60} (1 equiv, 50 mg, 0.069 mM) in toluene (1,2-dichlorobenzene for the reactions at 180 °C) (10 mL) was stirred at the appropriate temperature over a period of time (Table 1). The solvent was removed under reduced pressure at room temperature [removal of toluene at above room temperature provided monoadducts **3d–h** in low yields as a result of (further) formation of bisadducts with unreacted MOBs under high concentrations!], and the residue was purified as in the case of **3a–c** to afford pure adducts **3d–h**.
(23) For the synthesis of MOBs **1e** and **1f**, see: Lai, C.-H.; Shen, Y.-L.; Liao C.-C. *Synlett* **1997**, 1351. Synthesis of other stable MOBs will be published elsewhere.
(24) (a) Taylor, R.; Walton, D. R. M. *Nature* **1993**, *363*, 685. (b) Hirsch, A.; Grösser, T.; Skiebe, A.; Soi, A. *Chem. Ber.* **1993**, *126*, 1061. (c) Isaacs, L.; Wehrsig, A.; Diderich, F. *Helv. Chim. Acta* **1993**, *76*, 1231.

Table 1. Bicyclo[2.2.2]octenone-Fused [60]Fullerene Derivatives **3** from the Diels−Alder Reactions of MOBs **1** and C_{60}

entry	MOB	reaction conditions[b]	cycloadduct		yield[c] (%)
1	 **1a**	30 °C/ 8 h		**3a**	8
2		60 °C/ 6 h			15
3		110 °C/ 3 h			0
4	 **1b**	30 °C/ 36 h		**3b**	44
5		60 °C/ 12 h			52
6		110 °C/ 6 h			62
7	 **1c**	30 °C/ 48 h		**3c**	21
8		60 °C/ 24 h			34
9		110 °C/ 12 h			43
10	 **1d**	30 °C/ 72 h		**3d**	69
11		60 °C/ 24 h			54
12		110 °C/ 12 h			37[d]
13	 **1e**	30 °C/ 72 h		**3e**	54
14		60 °C/ 6 h			42[d]
15		110 °C/ 3 h			0[d]
16	 **1f**	30 °C/ 72 h		**3f**	62
17		60 °C/ 24 h			58[d]
18		110 °C/ 12 h			32[d]
19	 **1g**	30 °C/ 96 h		**3g**	42
20		60 °C/ 72 h			53[d]
21		110 °C/ 18 h			62[d]
22	 **1h**	30 °C/ 96 h		**3h**	53
23		60 °C/ 72 h			56[d]
24		110 °C/ 36 h			76[d]
25	 **1i**	60 °C/ 72 h		**3i**	0
26		110 °C/ 72 h			0[e]
27		180 °C/ 48 h[f]			trace[e,g]

[a] All reactions were carried out with MOBs (3 equiv for **1a**−**c** or 1.2 equiv for **1d**−**i**) and C_{60} (1 equiv) in toluene unless otherwise specified; also see ref 22. [b] Temperature refers to oil bath. [c] Yields of pure and isolated adducts are based on consumed C_{60}. [d] Bisadducts were also obtained. [e] Part of MOB was aromatized. [f] Reaction was performed in 1,2-dichlorobenzene. [g] Observed in ^{1}H NMR spectrum of the crude reaction mixture.

quaternary sp^3 carbon atoms appeared at ca. δ 66 and 69 (**3a**−**e** and **3g**) or ca. δ 68 and 72 (**3f** and **3h**), which indicates the closed transannular bond, confirming the 6−6 ring junction on the C_{60} cage.[7a,25] Of the 58 sp^2 carbons of the fullerene framework that are diastereotopic in nature owing to the introduction of chiral centers in the fused bicyclo[2.2.2]octenone system, ^{13}C NMR spectra of **3a**−**h** showed only 49−56 peaks in the region δ 135−156 because of overlap of the rest of the signals. In the mass spectra, the parent ions of the cycloadducts are clearly observed, although the major peak in each spectrum is at *m*/*z* 720 corresponding to C_{60}^+. In addition, the bicyclo[2.2.2]octenone system also showed characteristic signals at ca. δ 200 for carbonyl and ca. δ 97 for quaternary carbon with *gem* dimethoxy groups in ^{13}C NMR for the adducts **3a**−**h**.

From Table 1, it is clear that the yields of the cycloadducts depend on the nature of MOBs and the reaction conditions employed. The ^{1}H NMR (400 MHz) spectra of the crude samples revealed the compositon of the compounds formed during the reaction. In the cases of more reactive MOBs **1a−c**, which are unstable, large amounts of dimers were obtained along with fullerene derivatives; however, no unreacted MOBs were noticed. It is worth mentioning that MOB **1a**, which exhibited very good reactivity with many other dienophiles,[14−17] failed to produce **3a** in good yields in the cycloaddition with C_{60}. This diminished reactivity of **1a** appears to be due to electronic reasons. The stable MOBs **1d−f** produced the Diels−Alder cycloadducts **3d−f** in higher yields at 30 °C. The reactions of **1d−f** at higher temperatures resulted in lowering the yields of **3d−f** and increasing the yields of bisadducts of C_{60} as a result of the enhanced Diels−Alder reactivity of **1d−f**. The stable MOBs **1g** and **1h** require higher temperatures in order to furnish the adducts **3g** and **3h**, respectively, in high yields, presumably because of the bulky ketal group. While MOB **1d** produced noticeable amounts of dimer at low temperatures, MOBs **1e−h** did not dimerize under the reaction conditions.

MOB **1i**, having substitution at position 5, did not participate in the Diels−Alder reaction with C_{60} in toluene. However, the ^{1}H NMR (400 MHz) analysis of the crude reaction mixture from the reaction in 1,2-dichlorobenzene at 180 °C showed signals corresponding to the cycloadduct **3i**. The MOB **1j** (R_n = 5-CO_2Me) did not give the Diels−Alder adduct even at 180 °C, presumably because of steric and electronic factors. These results illustrate that 5-substituted MOBs are more stable and exhibit less Diels−Alder reactivity toward less reactive/bulky dienophiles. Our findings are in accordance with Andersson's observations on the Diels−Alder reactions of 5-methoxy-MOB.[26]

Initially it was assumed that the low yields observed in some reactions might be due to the cycloreversion of the adducts **3**. To verify this assumption, cycloadduct **3e** was taken in toluene and 1,2-dichlorobenzene and stirred at 110 and 180 °C, respectively, for 24 h. However, **3e** was found to be unchanged, and neither the dimer of MOB nor bisadduct/higher adducts were observed, indicating that no retro-Diels−Alder reaction had taken place.

In conclusion, we have shown that masked *o*-benzoquinones, which are reactive cyclohexa-2,4-dienones, undergo Diels−Alder cycloadditions with [60]fullerene to produce hitherto unknown, stable, and highly functionalized bicyclo[2.2.2]octenone derivatives. In light of the mild conditions and considerable generality, these reactions are certainly noteworthy. Because of their high functionality, compounds **3** will allow easy access to other derivatives. Such further derivatization is underway in our laboratory.

Acknowledgment. Financial support from the National Science Council (NSC) of the Republic of China is sincerely acknowledged. R.K.P. thanks NSC for a postdoctoral fellowship.

Supporting Information Available: ^{1}H and ^{13}C NMR and DEPT spectra for compounds **3a−h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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