Conformational Analysis in Reversible Intramolecular [2+2] Photocycloaddition of Diphenylbicyclo[4.2.0]oct-3-ene-2,5-diones

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Abstract—Irradiation of diphenylbicyclo[4.2.0]oct-3-ene-2,5-diones bearing variously substituted Me groups resulted in the reversible intramolecular [2+2] cycloaddition between the excited enedione C=C double bond and the facing endo-phenyl ring to exclusively give pentacyclotetradeca-10,12-diene-2,7-diones. The equilibrated product ratios were much dependent on the substitution pattern of the Me-groups as well as the irradiated wavelength. The regiochemistry of these photoadditions was elucidated on the basis of the restricted conformation of the starting enediones. © 2015 Elsevier Science. All rights reserved

Intramolecular photochemical [2+2] cycloaddition is one of the most sophisticated methods for the synthesis of strained polycyclic cage compounds.1 A variety of starting molecules bearing the incorporated several π-bond functionaries have been reported to exhibit these fascinating processes.2 In these photocycloadditions, the geometrical and topological arrangements of the relevant two 2π-components play a crucial role in an efficient cycloaddition of the conformatonally restricted substrates.3 In particular, quinones and their derivatives have attracted the continuous attention in view of the conjugated ring system as well as the suitable structural design of the reacting sites.4 Accordingly, a number of studies have been made on their intramolecular photocycloadditions.5

We now wish to report that the photoreaction of variously methyl-substituted 1,4-benzoquinones with 1,1-diphenylethene resulted in the reversible intramolecular [2+2] cycloaddition of the primary 1:1 photoadducts to afford the pentacyclic diones only via the 1,2-addition of endo-phenyl ring.

Irradiation of quinones 1a-d (30 mM) and 2 equiv. amount of 1,1-diphenylethene in benzene under the argon atmosphere with a high-pressure Hg lamp through a Pyrex filter (λ > 300 nm) provided the regiosomeric mixture of the primary 1:1 photoadducts 2 and 3 along with the respective secondary intramolecular [2+2] cycloadducts 4 and 5 in almost quantitative total yield (Scheme 1 and Table 1).6 The structures of these products were deduced from their 1H and 13C NMR spectra. The pentacyclic cage compound 5a7 was also confirmed by the X-ray crystal analysis (Figure 1).8 It is clearly demonstrated that the cage compound 5a includes the diagonal connection of the two cyclobutane rings.9

Keywords: photocycloaddition; quinone; cage compound; photocycloreversion; conformational analysis;

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Figure 1. ORTEP drawing of 5a. For clarity, hydrogen atoms are omitted.
Scheme 1

Table 1. Product Distributions in Photoreaction of Quinones 1a-d with 1,1-Diphenylethene.1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compd.</th>
<th>Irradiation time (h)</th>
<th>Irradiation time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>1a'</td>
<td>4</td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>1b'</td>
<td>6</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>1</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>1</td>
<td></td>
<td>43</td>
</tr>
</tbody>
</table>

* Carried out in benzene-d6, in a NMR tube through a Pyrex filter.

† Irradiation time for complete consumption of quinones.

‡ Trace amount of unidentified products were detected in the 1H NMR spectra of the reaction mixture.

In conformity with this distinctive structure, all cage compounds obtained exhibited no diagnostic NOE effects between the inwardly directed allyl proton (H4) of fused cyclohexadiene and the inside methylene proton of the original cyclobutane ring.

The polycyclic products 4 and 5 are considered to be formed via a very rare intramolecular [2+2] photocycloaddition between the excited enedione C=O double bond with the facing endo-phenyl ring at the 1,2-position.10 Mechanistically, as in the case of usual [2+2] photocycloaddition of enones,11 these reactions seem to involve a triplet 1,4-biradical intermediate derived from the spin-inverted excited triplet state of the primary 1:1 adducts, 2 and 3.

Figure 2. Time-dependent product ratios (%) of 2d and 4d in photochemical reaction of quinone 1d with 1,1-diphenylethene (2 equiv) in benzene-d6, irradiated in a NMR tube through a Pyrex filter.

Interestingly, the prolonged irradiation established the photochemical equilibrations between the primary and the secondary photocycloadducts under the complete consumption of the starting quinones as represented for the case of quinone 1d (Figure 2). This finding apparently indicates the occurrence of [2+2] cycloreversion of the cage compounds (Scheme 1).

Table 2. Photostationary Equilibrated Product Ratios (%) of 4 and 5 in Reversible Photocycloaddition of 2 and 3.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compd.</th>
<th>Irradiation time (min)*</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>2a</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>3a</td>
<td>60</td>
<td>43(44)</td>
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<tr>
<td>3</td>
<td>2b</td>
<td>60</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>3b</td>
<td>60</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>2c</td>
<td>60</td>
<td>90(&gt;99)</td>
</tr>
<tr>
<td>6</td>
<td>2d(3d)</td>
<td>100</td>
<td>70</td>
</tr>
</tbody>
</table>

* Irradiated in a NMR tube in benzene-d6, through a Pyrex filter.

† Value in parenthesis was obtained in the photocycloaddition of 5a.

‡ Value in parenthesis was attained by irradiation of 2c through a filter (>350nm).
To more explicitly know the Me-substituent effects on the photostationary product ratios of cage compounds / bicyclic diones, we have performed the photoequilibration by using the isolated bicyclic diones. As expected, NMR monitoring of the reactions showed the apparent equilibration within 100 min at the photostationary state for all cases tested (Table 2). We also noted that the irradiation of cage compound led to the identical photoequilibrium as exemplified for 5a (entry 2). A perusal of Table 2 indicates that the relative ratios (%) of cage compounds tended to increase for the bicyclic diones in which the ipso-carbon of endo-phenyl ring combines to the unsubstituted alkenoic carbon atom (entries 2, 3 and 5), but decrease for the bicyclic diones in which the ipso-carbon needs to bind to the Me-substituted alkenoic carbon (entries 1 and 4). However, the tetramethyl-substituted 2d(=3d)12 provided an unexpected intrinsically large amount of cage compound probably because of rather enhanced steric congestion around original cyclobutane ring (entry 6). Thus, the lower ratios of cage compounds can be explained in terms of the more enhanced steric congestion between the ipso-carbon of phenyl ring and the substituted Me group.

Why does the present intramolecular photoreaction bring about the diagonal [2+2] cycloaddition of endo-phenyl ring? To answer the question, we first made of the conformational analysis of the representative 2d on the basis of its X-ray crystal structure (Figure 3a). The whole structure of 2d13 was found to be considerably twisted in such a way that the endo-phenyl ring is inwardly located over the quinone plane. Namely, the cyclobutane ring of 2d adopts a packed conformation and the endo-phenyl ring considerably overhangs the quinone frame (Figure 3b). The spatial distances (broken lines) between the relevant carbon atoms are 3.45 (C(19)-C(26)) and 3.46 Å (C(9)-C(8)), respectively. These values are sufficient for the effective photochemical [2+2] cycloaddition.14

Furthermore, the p-orbital axis of the aromatic ipso-carbon is allowed to favorably overlap with that of the underlying alkenoic carbon atom. These conformational preference would lead to the diagonal conjunction of two cyclobutane rings.

To obtain some information on the photoreversibility in the present intramolecular [2+2] cycloaddition of bicyclic diones, we have measured the absorption spectra of 2c and 4c in acetonitrile. It was found that both the 2c and 4c have the comparable absorptions in the range of 300-340 nm which are responsible for cycloaddition and cycloreversion. However, 2c apparently showed the larger absorption band over 340 nm as compared with 4c, thus resulting in almost one-way transformation of 2c to 4c on longer-wavelength irradiation (>350 nm) (Table 2, entry 5).

As to the photochemical cycloreversion of cyclobutane ring, the conformations of the adjoining π-bond substituents play a role in the efficient bond cleavage.15 In the case of 4 and 5, it is likely that the fused cyclohexadiene ring and the two vicinal carbonyl groups are responsible for the regioselective bond fission on account of the favorable excited π-electron donating conjugation with the antibonding orbital (π*) of the cleaved cyclobutane ring.

In summary, the primary [2+2] photocycloadducts of variously Me-substituted 1,4-benzoquinones with 1,1-diphenylethene underwent the reversible intramolecular [2+2] photocycloaddition to provide pentacyclotetradeca-10,12-diene-2,7-diones. The cage skeleton was characterized by very rare diagonal conjunction of two facing cyclobutane rings. The geometrical features of these reactions were interpreted in terms of the conformational preference which allowed the proximity of the relevant 2π components.

**Supplementary data**

Details experimental procedure and 1H and 13C NMR spectra of the synthesized compounds 2-5 as well as UV spectra of compounds 2c and 4c. Supplementary data associated with this article can be found, in the online version.

**References**


6. We could not find any appreciable CT absorption due to the quinone-ethene complexation over practical 330 nm in view of the essential superimposition of UV spectrum of 1a (10 mM in benzene; λ_{abs} = 350 nm (ε = 134), λ_{max} = 427 (25.3) and 443 (25.7)), and λ_{abs} = 470 (15.6)) in the absence and the presence of 10 equivalent of ethene. This implies that the possible CT complex plays a less important role in the present [2+2] photocycloaddition.

7. 5a: 1H NMR (270 MHz, CDCl3) δ 1.27 (s, 3H), 1.30 (s, 3H), 2.56 (d, 1H, J = 10.7), 2.66 (d, 1H, J = 10.7), 3.04 (m, 1H), 3.31 (s, 1H), 3.63 (s, 1H), 5.56-5.61 (m, 1H), 5.72-5.76 (m, 1H), 5.82-5.88 (m, 1H), 5.84-5.98 (m, 1H), 7.05-7.09 (m, 2H), 7.22-7.29 (m, 1H), 7.33-7.38 (m, 1H); 13C NMR (270MHz, CDCl3) δ 12.6, 18.3, 41.2, 44.6, 47.3, 53.1, 57.6, 57.8, 64.6, 122.8, 123.3, 124.6, 125.4, 126.3, 126.6, 128.4, 142.4, 207.5, 208.9.

8. Crystallographic data for the compound 5a have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 615011. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-363033 or e-mail: deposit@ccdc.cam.ac.uk).

9. Recently, Xu et al. reported that the irradiation of chloranil with variously p-substituted 1,1-diphenylethenes gave the pentacyclic cage compounds with orthogonally connected two cyclobutane rings in markedly contrast to our pentacyclic cage compounds; see J. Org. Chem. 2000, 65, 30.