

Conformational analysis in the reversible intramolecular [2+2] photocycloaddition of diphenylbicyclo[4.2.0]oct-3-ene-2,5-diones

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Abstract—An 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 pentacycletetradeca-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.

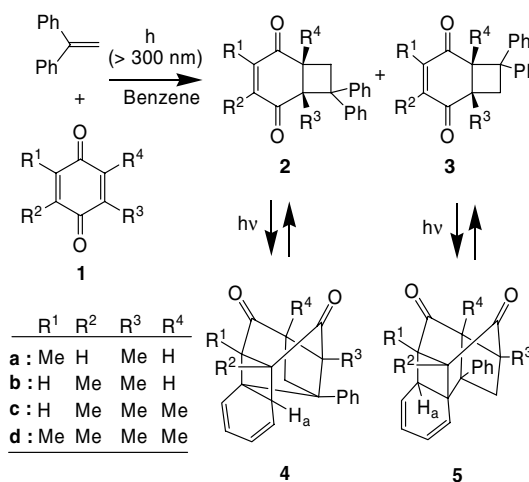
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Intramolecular photochemical [2+2] cycloaddition is one of the most sophisticated methods for the synthesis of strained polycyclic cage compounds.¹ A variety of starting molecules bearing the incorporated several π -bond functionalities have been reported 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 conformationally 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.

The irradiation of quinones **1a–d** (30 mM) and 2 equiv amount of 1,1-diphenylethene in benzene under an

argon atmosphere with a high-pressure Hg lamp through a Pyrex filter ($\lambda > 300$ nm) provided the regioisomeric mixture of the primary 1:1 photoadducts **2** and **3** along with the respective secondary intramolecular [2+2] cycloadducts **4** and **5** in an 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 **5a**⁷ was also confirmed by X-ray crystal analysis (Fig. 1).⁸ It is clearly demonstrated that cage compound **5a** includes the diagonal connection of the two cyclobutane rings.⁹



Scheme 1.

Keywords: Photocycloaddition; Quinone; Cage compound; Photocycloreversion; Conformational analysis.

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Table 1. Product distributions in photoreaction of quinones **1a–d** with 1,1-diphenylethene^a

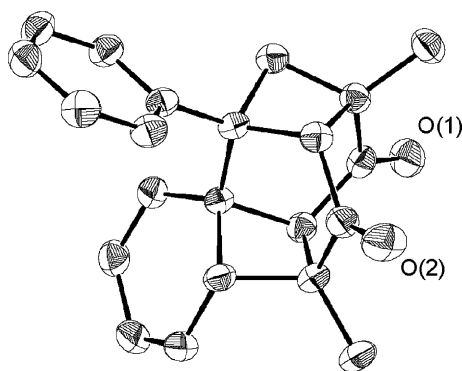
Entry	Compound	Irradiation time ^c (h)	Yield ^b (%)			
			2	3	4	5
1	1a ^d	4	60	20	5	14
2	1b ^d	6	30	26	35	8
3	1c	1	14	34	42	10
4	1d	1	43	—	57	—

^a Carried out in benzene-*d*₆ in an NMR tube through a Pyrex filter.

^b Based on quinone used.

^c Irradiation time for complete consumption of quinones.

^d Trace amounts of unidentified products were detected in the ¹H NMR spectra of the reaction mixture.

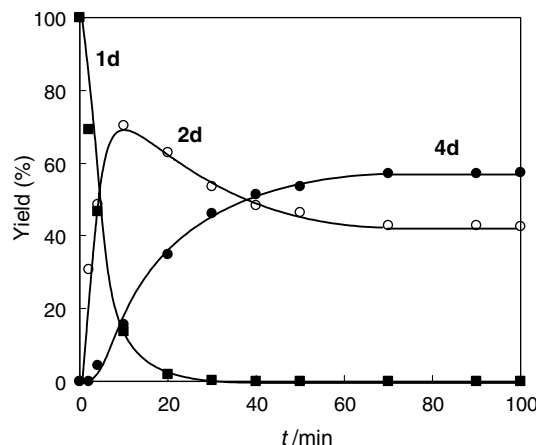
**Figure 1.** ORTEP drawing of **5a**. For clarity, hydrogen atoms are omitted.

In conformity with this distinctive structure, all cage compounds obtained exhibited no diagnostic NOE effects between the inwardly directed allyl proton (H_a) 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] photoreaction between the excited enedione C=C 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**.

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

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, the NMR monitoring of the reactions showed the apparent equilibration within 100 min at the photo-

**Figure 2.** Time-dependent product ratios (%) of **2d** and **4d** in the photochemical reaction of quinone **1d** with 1,1-diphenylethene (2 equiv) in benzene-*d*₆ irradiated in an NMR tube through a Pyrex filter.**Table 2.** Photostationary equilibrated product ratios (%) of **4** and **5** in reversible photocycloaddition of **2** and **3**

Entry	Compound	Irradiation time ^a (min)	Yield (%)	
			4	5
1	2a	100	10	—
2	3a	60	—	43 (44) ^b
3	2b	60	67	—
4	3b	60	—	31
5	2c	60	90 (>99) ^c	—
6	2d (=3d)	100	70	—

^a Irradiated in an NMR tube in benzene-*d*₆ through a Pyrex filter.

^b The value in parentheses was obtained in the photocycloreversion of **5a**.

^c The value in parentheses was attained by the irradiation of **2c** through a filter (>350 nm).

stationary state for all cases tested (Table 2). We also noted that the irradiation of the 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 with 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 the rather enhanced steric congestion around the 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 representative **2d** on the

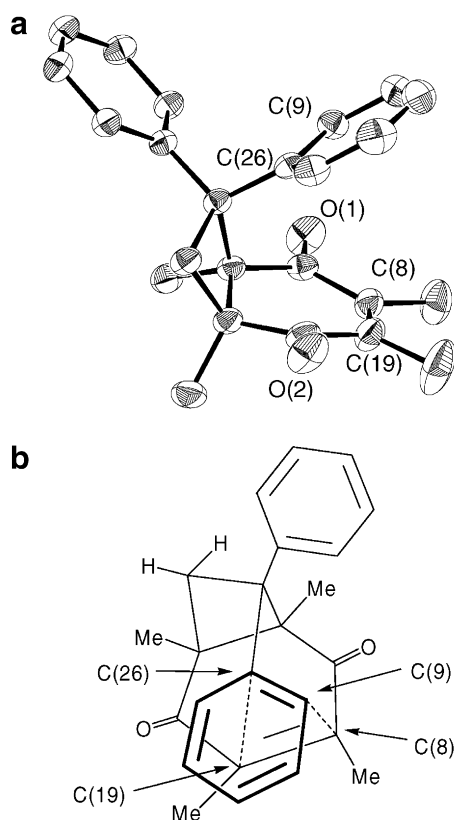


Figure 3. (a) ORTEP drawing of **2d**. For clarity, hydrogen atoms are omitted and (b) schematic conformational representation of **2d** showing the favorable topological overlapping of *endo*-phenyl ring and quinone plane for [2+2] photocycloaddition.

basis of its X-ray crystal structure (Fig. 3a). The whole structure of **2d**¹³ 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 (Fig. 3b). The spatial distances (broken lines) between the relevant carbon atoms are 3.45 Å (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 overlap favorably with that of the underlying alkenoic carbon atom. This conformational preference would lead to the diagonal conjunction of the 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 **2c** and **4c** have 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 **5c**, thus resulting in almost a one-way transformation of **2c** to **5c** on a longer-wavelength irradiation (>350 nm) (Table 2, entry 5).

As to the photochemical cycloreversion of the cyclobutane ring, the conformations of the adjoining π -bond substituents play a role in 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 anti-bonding orbital (σ^*) 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 pentacyclopentadeca-10,12-diene-2,7-diones. The cage skeleton was characterized by a very rare diagonal conjunction of the 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 of the experimental procedure and ¹H and ¹³C NMR spectra of the synthesized compounds **2–5** as well as UV spectra of compounds **2c** and **4c** are given. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.09.013.

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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; $\lambda_{\text{shol}} = 350$ nm ($\epsilon = 134$), $\lambda_{\text{max}} = 427$ (25.3) and 443 (25.7), and $\lambda_{\text{shol}} = 470$ (15.6)) in the absence and the presence of 10 equiv of ethene. This implies that the possible CT complex plays a less important role in the present [2+2] photocycloaddition.
7. Compound **5a**: ^1H NMR (270 MHz, CDCl_3) 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); ^{13}C NMR (270 MHz, CDCl_3) δ 12.6, 18.3, 41.2, 44.6, 46.4, 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 compound **5a** have been deposited with the Cambridge Crystallographic Data Centre as Supplementary publication number CCDC 615010. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 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-diphenylethene gave the pentacyclic cage compounds with orthogonally connected two cyclobutane rings in marked contrast to our pentacyclic cage compounds; see *J. Org. Chem.* **2000**, 65, 30.
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12. Compound **2d**: ^1H NMR (270 MHz, CDCl_3) δ 1.20 (s, 3H), 1.43 (s, 3H), 1.64 (d, 3H, $J = 1.07$), 1.72 (d, 3H, $J = 1.07$), 2.71 (d, 1H, $J = 12.0$), 3.73 (d, 1H, $J = 12.0$), 6.98–7.15 (m, 4H), 7.20–7.34 (m, 6H); ^{13}C NMR (270 MHz, CDCl_3) δ 13.0, 13.0, 18.3, 21.8, 39.9, 47.9, 58.3, 58.4, 125.9, 126.2, 126.9, 127.5, 128.0, 141.8, 145.7, 145.9, 146.8, 200.2, 203.1.
13. Crystallographic data for compound **2d** 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 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
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