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

Haruyasu Asahara, Eiko Mochizuki, and Takumi Oshima[*]

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan.

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 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.

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 regioisomeric 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 ^{1}H and ^{13}C NMR spectra. The pentacyclic cage compound **5a**[7] 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]
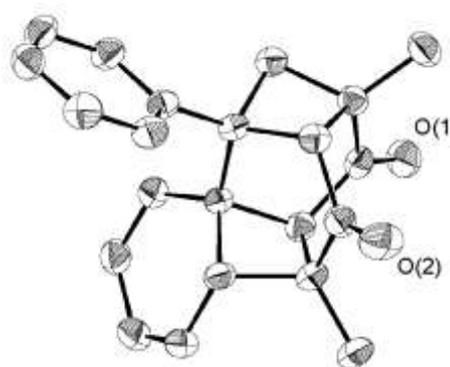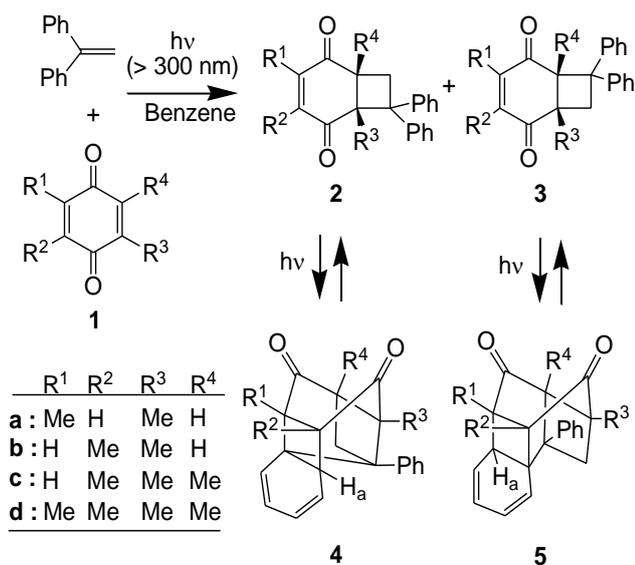

Figure 1. ORTEP drawing of **5a**. For clarity, hydrogen atoms are omitted.

Scheme 1

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

Entry	Compd.	Irradiation time (h)[c]	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 a NMR tube through a Pyrex filter.

[b] Based on quinone used.

[c] Irradiation time for complete consumption of quinones.

[d] Trace amount of unidentified products were detected in the ^{1}H 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 (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**.
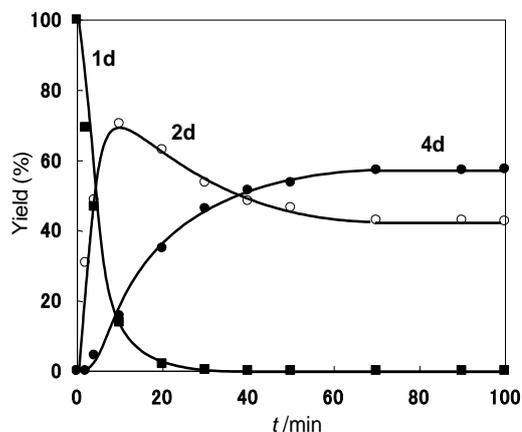
Figure 2. Time-dependent product ratios (%) of **2d** and **4d** in photochemical reaction of quinone **1d** with 1,1-diphenylethene (2 equiv) in benzene-d_6 irradiated in a NMR tube through a Pyrex filter.

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** (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**.

Entry	Compd.	Irradiation time (min)[a]	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 a NMR tube in benzene-d_6 through a Pyrex filter.

[b] Value in parenthesis was obtained in the photocycloreversion of **5a**.

[c] 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
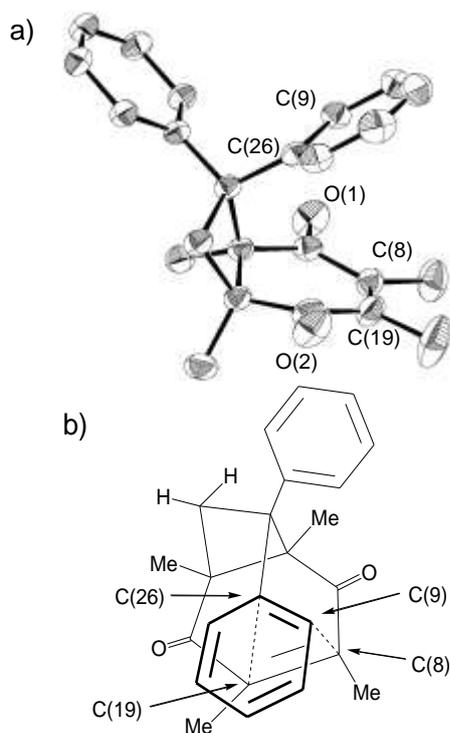

Figure 3. a) ORTEP drawing of **2d**. For clarity, hydrogen atoms are omitted, b) Schematic conformational representation of **2d** showing the favorable topological overlapping of *endo*-phenyl ring and quinone plane for [2+2] photocycloaddition.

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 **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 packered 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 3.46Å (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 **5c**, thus resulting in almost one-way transformation of **2c** to **5c** 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 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 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

References

1. (a) Jones, G.; Becker, W. G.; Chiang, S.-H. *J. Am. Chem. Soc*. **1983**, *105*, 1269; (b) Mehta, G.; Reddy, S. H. K. *Angew. Chem., Int. Ed*. **1993**, *32*, 1160; (c) Behr, J.; Braun, R.;

Grimme, S.; Kummer, M.; Martin, H.-D.; Mayer, B.; Rubin, M.B.; Ruck, C. Eur. *J. Org. Chem.* **1998**, 2339; (d)Laurenti, D.; Santelli-Rouvier, C.; Pèpe, G.; Santelli, M. *J. Org. Chem.* **2000**, *65*, 6418; (e) Koizumi, T,; Harada, K.; Asahara, H.; Mochizuki, E.; Kokubo, K.; Oshima, T. *J. Org. Chem.* **2005**, *70*, 8364.

2. (a) Nishimura, J.; Nakamura, Y.; Hayashida, Y.; Kudo, T. *Acc. Chem. Res.* **2000**, *33*. 679; (b) Faure, S.; Blanc, P.-L. S.; Piva, Olivier. *Tetrahedron Lett.* **1999**, *40*, 6001; (c) Vassilikogiannakis, G.; Hatzimarinaki, M.; Orfanopoulos, M. *J. Org. Chem.* **2000**, *65,* 8180; (d) Hoffmann, N. *Tetrahedron Lett.* **2002**, *58*, 7933.

3. (a) Mattay, J. *Tetahedron.* **1985**, *41*, 2405; (b)Yoshimi, Y.; Konishi, S.; Maeda, H.; Mizuno, K. *Tetrahedron Lett.* **2001**, *42,* 3475; (c) Maeda, H.; Waseda, S.; Mizuno, K. *Chem. Lett.* **2000**, 1238.

4. (a) Kokubo, K.; Nakajima, Y.; Iijima, K.; Yamaguchi, H.; Kawamoto, T.; Oshima, T. *J. Org. Chem.* **2000**, *65*, 3371; (b) Braun, M.; Christl, M.; Peters, E.M.; Peters, K. *J. Chem. Soc., Perkin Trans. 1.* **1999**, 2813; (c) Bosch, E.; Hubig, S.M.; Lindeman, S.V.; Kochi, J. K. *J. Org. Chem.* **1998**, *63*, 592; (d) Kokubo, K.; Masaki, T.; Oshima, T. *Org. Lett.* **2000**, *2*, 1979; (e) Kokubo, K.; Kawahara, K.; Takatani, T.; Moriwaki, H.; Kawamoto, T.; Oshima, T. *Org. Lett.* **2000**, *2*, 559.

5. (a) Barborak, J. C.; Watts, L.; Pettit, R. *J. Am. Chem.Soc.* **1966**, *88*, 1328; (b) Fessner, W.-D.; Rodriguez, M. *Angew. Chem., Int. Ed.* **1991**, *30*, 1020; (c) Nair, M. S.; Sudhir, U.; Joly, S.; Rath, N. P.; *Tetrahedron.* **1999**, *55*, 7653; (d) Wladislow, B.; Marzorati, L.; Campos, I. P. A.; Viertler, H. *J. Chem. Soc., Perkin Trans. 2.* **1992**, *2*, 475; (e) Iwamoto, H.; Takuwa, A.; Hamada, K.; Fujiwara, R. *J. Chem. Soc., Perkin Trans. 1.* **1999**, 575; (f) Appel, W. K.; Greenhough, T. J.; Scheffer, J. R.; Trotter, J.; Walsh, L. *J. Am. Chem. Soc.* **1980**, *102*, 1158; (g) Appel, W. K.; Greenhough, T. J.; Scheffer, J. R.; Trotter, J.; Walsh, L. *J. Am.Chem.Soc.* **1980**, *102*, 1160.

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; $\lambda_{shol} = 350$ nm ($\varepsilon = 134$), $\lambda_{max} = 427$ (25.3) and 443 (25.7), and $\lambda_{shol} = 470$ (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**: ^{1}H 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 (270MHz, 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 the 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(0)-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 markedly contrast to our pentacyclic cage compounds; see *J. Org. Chem.* **2000**, *65*, 30.

10. (a) Crimmins, M. T.; Pace, J. M.; Nantermet, P. G.; Kim-Meade, A. S.; Thomas, J. B.; Watterson, S. H.; Wagman, A. S. *J. Am. Chem. Soc.* **2000**, *122*, 8453; (b) Ferrer, L. O.; Margaretha, P. *Chem. Commun.* **2001**, 481; (c) Chen, C.; Chang, V.; Cai, X.; Duesler, E.; Mariano, P. S. *J. Am. Chem. Soc.* **2001**, *123*, 6433.

11. (a) Wagner, P. J.; *Tetrahedron Lett.* **2002**, *43*, 3569; (b) Kokubo, K.; Yamaguchi, H.; Kawamoto, T,.; Oshima, T. *J. Am. Chem.Soc.* **2002**, *124*, 8912; (c) Hei, X.-M.; Song, Q.-H.; Li, X.-B.; Tang, W.-J.; Wang, H.-B.; Guo, Q.-X. *J. Org. Chem.* **2005**, *70*, 2522; (d) Chen, C.; Chang, V.; Cai, X.; Duesler, E.; Mariano, S. P. *J. Am. Chem. Soc.* **2001**, *123*, 6433; (e) Aoyama, H.; Arata, Y.; Omote, Y. *J. Chem. Soc. Commun.* **1990**, 736.

12. **2d**: ^{1}H 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 (270MHz, 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 the 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(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

14. Kohmoto, S.; Ono, Y.; Masu, H.; Yamaguchi, K.; Kishikawa, K.; Yamamoto, M. *Org. Lett.* **2001**, *3*, 4153.

15. (a) Miranda, M. A.; Izquierdo, M. A. *Chem. Comm.* **2002**, 364; (b) Okada, K.; Hisamitsu, K.; Mukai, T. *Tetrahedron Lett.* **1981**, *22*, 1251; (c) Masnovi, J. M.; Kochi, K. *J. Am. Chem.Soc.* **1985**, *107*, 6781; (d) Yonezawa, N.; Yamashita, T.; Kanoe, T.; Saigo, K.; Hasegawa, M. *Ind. Eng. Chem. Prod. Res.* **1985**, *24*, 593.