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Conformational Specificity in Photoinduced Intramolecular 1,7-Hydrogen Abstraction of Homonaphthoquinones with a Spiro-Linked Dibenzocycloheptene Ring

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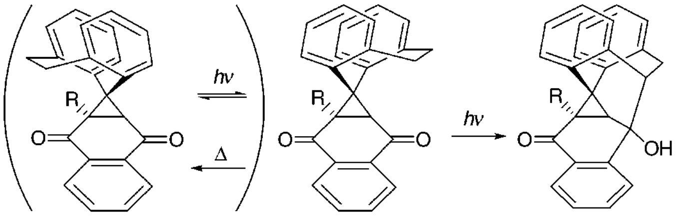
ABSTRACT



Irradiation of homonaphthoquinones with spiro-linked dibenzocycloheptene rings brings about the Norrish type II reaction to give polycyclic alcohols via a stereospecific 1,7-hydrogen abstraction of the less stable twist-boat conformer.

The intramolecular photochemical hydrogen abstraction reaction of carbonyl compounds, known as the Norrish type II reaction, is one of the most important primary photochemical processes, giving the corresponding cyclic alcohols via hydrogen abstraction of the excited triplet carbonyl oxygen followed by radical recombination.[1] Usually, such a 1,5-hydrogen abstraction occurs preferably via a quasi-six-membered ring transition state for the intramolecular reaction;[2] however, many examples of the skeletally far more remote hydrogen abstraction are also known.[3] Recently, photochemical hydrogen abstraction reactions in crystalline states have attracted much attention, especially those dealing with absolute asymmetric synthesis.[4] It is argued that the relative orientation of a carbonyl group and an abstracted hydrogen atom are important in view of molecular orbital considerations.[5] However, some caution is required in a

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(1) (a) Wagner, P. J.; Park, B.-S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker, Inc.: New York, 1991; Volume 11, Chapter 4, p 227. (b) Wagner, P. J. In *Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, 1995; Chapter 38, p 449.

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(3) (a) Descotes, G. L. In *Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, 1995; Chapter 41, p 501. See also recent papers: (b) Kerwin, S. M.; Heathcock, C. H. *J. Org. Chem.* **1992**, *57*, 4005. (c) Hasegawa, T.; Takahashi, K.; Aoyama, H.; Yoshioka, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3498. (d) Kraus, G. A.; Zhang, W.; Wu, Y. *Chem. Commun.* **1996**, 2439. (e) Leigh, W. L.; Lathioor, E. C.; St. Pierre, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 12339. (f) Hu, S.; Neckers, D. C. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1751. (g) Hu, S.; Neckers, D. *J. Org. Chem.* **1997**, *62*, 6820. (h) Mizuno, K.; Konishi, S.; Yoshimi, Y.; Sugimoto, A. *Chem. Commun.* **1998**, 1659. (i) Jung, M. E.; Johnson, T. W. *J. Org. Chem.* **1999**, *64*, 7651. (j) Giese, B.; Wettstein, P.; Stähelin, C.; Barbosa, F.; Neuburger, M.; Zehnder, M.; Wessig, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 2583.

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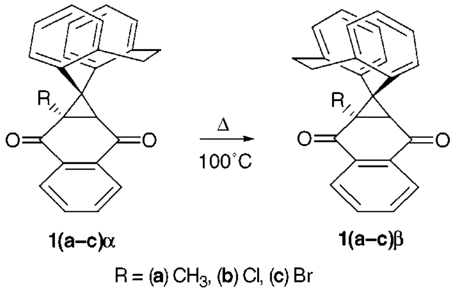
straightforward application of solid-state results to solution photochemistry due to an inevitable conformational change.

In our studies on homoquinone compounds, we have found that homoquinones bearing a spiro-linked dibenzocycloheptene ring have two isolable conformational isomers **1**α and **1**β at room temperature and that when heated (∼100 °C) the less stable **1**α isomerizes almost completely to **1**β via a conformational inversion of the twist-boat cycloheptene ring with a transition energy of 127 kJ mol^{-1} (**1a**α) (Scheme 1).[6]

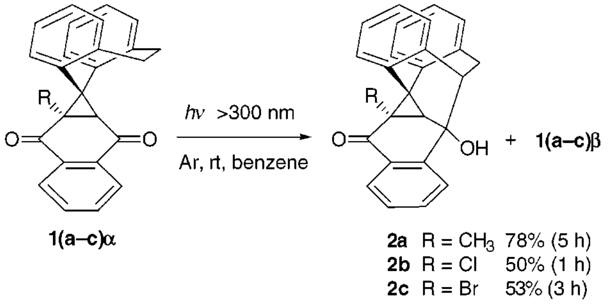
Scheme 1



Coupled with the X-ray crystal structure analysis of **1c**α and **1c**β,[7] this high-energy isomerization suggests that the conformational freedom of the spiro-linked dibenzocycloheptene ring is considerably restricted, forcing the ethano-bridging close to the facing carbonyl group. Therefore, we investigated the photoinduced hydrogen abstraction of these spirohomoquinones to identify the structural features governing the remote hydrogen abstraction.

The photoreaction of methyl-substituted **1a**α (15 mM) was carried out at 20 °C under argon in benzene-d_6 by irradiation with a high-pressure mercury lamp through a Pyrex filter (>300 nm). The reaction cleanly proceeded to provide polycyclic alcohol **2a** (78% by NMR) as the sole product along with unreacted **1a**α (3%) and inverted **1a**β (19%) after 5 h (Scheme 2).[8] Similar irradiation of chloro- and bromo-substituted **1b**α and **1c**α resulted in the formation of polycyclic alcohols **2b** (50%, 1 h) and **2c** (51%, 3 h), respectively. The structure of **2** was deduced from the usual spectral analysis and also confirmed by X-ray crystallography for **2a**, indicating a 1,7-hydrogen abstraction[9] from the *endo*-benzylic methylene by the less substituted carbonyl group (Figure 1).

Scheme 2



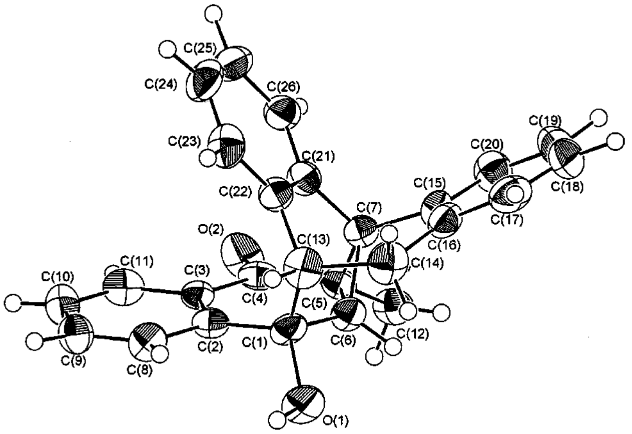


Figure 1. Crystal structure of cage product **2a**.

Figure 2a shows the time course of the photoreaction of the less stable **1a**α monitored by ^{1}H NMR using an internal

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(8) **General Procedure for the Photoreaction of 1a−c and 3.** To a Pyrex tube containing **1a**α (54.6 mg, 0.15 mmol) under an argon atmosphere was added benzene (10 mL), and the tube was irradiated by a high-pressure Hg lamp at room temperature for 15 h. After removal of the solvent under reduced pressure, 1,1,1,2-tetrachloroethane was added as an internal standard for ^{1}H NMR analysis. The reaction mixture was column chromatographed on silica gel to give **2a** with a mixture of hexane and ethyl acetate as eluent. The products were purified by recrystallization from benzene/hexane. The reaction of **1a**α (5.5 mg, 0.015 mmol) in C_6D_6 (1 mL) was also conducted in a sealed NMR tube for the time course experiment. The structures of **2a**−**c** were confirmed as follows. **2a**: colorless prisms; mp 251−252 °C; ^{1}H NMR ($CDCl_3$) δ 7.69 (dd, 1H, $J = 7.9, 1.3$ Hz), 7.49 (dd, 1H, $J = 7.9, 1.3$ Hz), 7.37 (td, 1H, $J = 7.3, 1.6$ Hz), 7.24−7.20 (m, 1H), 7.10−6.96 (m, 5H), 6.80 (td, 1H, $J = 7.3, 1.3$ Hz), 6.73 (td, 1H, $J = 7.3, 1.3$ Hz), 6.65 (dd, 1H, $J = 7.3, 1.3$ Hz), 4.08 (d, 1H, $J = 17.8$ Hz), 3.47 (d, 1H, $J = 5.6$ Hz), 3.17 (dd, 1H, $J = 17.8, 5.6$ Hz), 2.67 (s, 1H), 2.37 (s, 1H), 1.85 (s, 3H); MS (EI) *m/z* 364 (M^+). Anal. Calcd for $C_{26}H_{20}O_2$: C, 85.69; H, 5.53. Found: C, 85.55; H, 5.75. **2b**: brown prisms; mp 263−265 °C; ^{1}H NMR ($CDCl_3$) δ 7.74 (dd, 1H, $J = 7.9, 1.3$ Hz), 7.52−7.38 (m, 3H), 7.13−7.04 (m, 5H), 6.85 (td, 1H, $J = 7.3, 1.3$ Hz), 6.77 (td, 1H, $J = 7.3, 1.3$ Hz), 6.65 (dd, 1H, $J = 7.3, 1.3$ Hz), 4.09 (d, 1H, $J = 18.1$ Hz), 3.47 (d, 1H, $J = 5.6$ Hz), 3.20 (dd, 1H, $J = 18.1, 5.6$ Hz), 2.96 (s, 1H), 2.85 (s, 1H); IR (KBr) 1671 cm^{-1} (C═O). Anal. Calcd for $C_{21}H_{17}O_2Cl$: C, 78.02; H, 4.45. Found: C, 78.29; H, 4.66. **2c**: orange prisms; mp 262−263 °C; ^{1}H NMR ($CDCl_3$) δ 7.74 (dd, 1H, $J = 7.9, 1.3$ Hz), 7.50 (td, 1H, $J = 7.3, 1.3$ Hz), 7.42 (td, 1H, $J = 7.3, 1.3$ Hz), 7.13−7.05 (m, 5H), 6.85 (td, 1H, $J = 7.3, 1.3$ Hz), 6.77 (td, 1H, $J = 7.3, 1.3$ Hz), 6.65 (dd, 1H, $J = 7.3, 1.3$ Hz), 4.08 (d, 1H, $J = 17.8$ Hz), 3.47 (d, 1H, $J = 5.6$ Hz), 3.19 (dd, 1H, $J = 17.8, 5.6$ Hz), 3.01 (s, 1H), 2.89 (s, 1H); IR (KBr) 1669 cm^{-1} (C═O). Anal. Calcd for $C_{21}H_{17}O_2Br$: C, 69.94; H, 3.99. Found: C, 69.97; H, 4.15. **Crystal data for 2a**: $C_{26}H_{20}O_2$, $M = 364.44$, orthorhombic, space group *Pbca*, $a = 14.793(8)$, $b = 18.317(9)$, and $c = 13.786(6)$ Å, $V = 3736(3)$ Å^3, $Z = 8$, $R = 0.077$ and $R_w = 0.070$ for 1672 reflections with $I > 1.5\sigma(I)$.

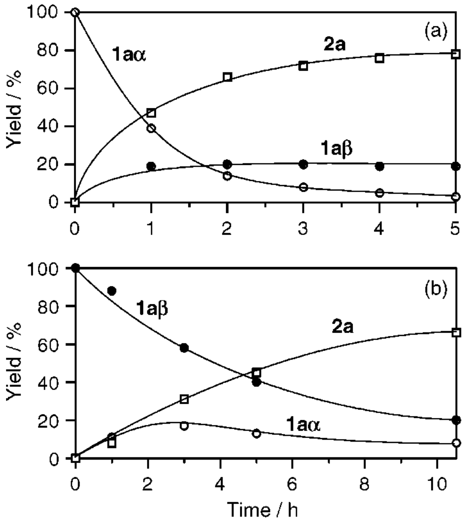
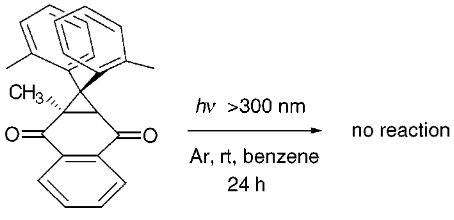


Figure 2. Time course study of the photoreaction of (a) **1a**α and (b) **1a**β.

standard. It was found that the rapid consumption of **1a**α was accompanied by the growing appearance of **2a** and an almost constant amount of inverted **1a**β (~20%). Also of interest is the fact that the reaction of more stable **1a**β produced the same **2a** in addition to the inverted conformer **1a**α, though the decay of **1a**β and the increment of **2a** were relatively slow and the inverted **1a**α gradually disappeared on progression of the reaction (Figure 2b). In both cases, the photoisomerization between **1a**α and **1a**β at a reaction temperature of 20 °C may be due to the cyclopropane ring cleavage enabling the fused cycloheptene ring to regain conformational freedom,[10] since the thermal isomerization requires high temperatures of ~100 °C and leads completely to the more stable **1a**β. Thus, the photoreaction of **1a**α and **1a**β results in the formation of **2a** via a Norrish Type II reaction associated with the 1,7-hydrogen abstraction of the less stable α-conformer as well as photoisomerization between the two conformers.

To obtain further insight into the conformationally specific hydrogen abstraction, we conducted a comparison reaction for formally ethano-bridge severed di-*o*-tolyl-substituted homoquinone **3** (Scheme 3).[11] The nonbridged aromatic rings are expected to rotate in such a way that the two *o*-methyl substituents are located in the opposite directions. As a matter of fact, the X-ray structure of **3** revealed the conformation just as depicted in Scheme 3, although the ^{1}H NMR spectrum showed a 93:7 conformational equilibration with another inverted conformer in $CDCl_3$. Despite the presence of a corresponding abstractable hydrogen atom, **3** remained essentially intact even after a 24 h irradiation.

Scheme 3



3

As a prospective criterion of carbonyl hydrogen abstraction, Scheffer proposed some geometrical parameters for orientational requirements of intramolecular hydrogen transfer in the crystalline state.[5] The parameters involve the O···H distance d, the C−H···O angle θ, the C=O···H angle Δ, and the dihedral angle ω that the O···H vector makes with respect to the mean plane of the carbonyl group (see Table 1). As summarized in Table 1, we obtained these parameters for the *endo*- (H_a) and *exo*-hydrogen (H_b) of the ground states of **1a**α and **1a**β by semiempirical calculations[12,13] and applied them to our solution photochemistry.[14] The solid-state parameters obtained from the X-ray structures of **1c**α, **1c**β, and **3** are also shown in Table 1 as well as the Scheffer's "ideal" value. Due to the dibenzocycloheptene ring, three or two possible thermally equilibrating conformations exist for each of the α- and β-conformers: TB_{ax}, the twist-boat form with axial H_a and equatorial H_b; TB_{eq}, the twist-boat form with equatorial H_a and axial H_b; B, the boat form with both the axial H_a and H_b. As the Norrish type II reaction allows a somewhat looser transition state with distance d as long as 3.10 Å,[15] all the hydrogens of **1a**, **1c**, and **3** listed in Table 1 would be the candidates for hydrogen abstraction. However, the shorter d for the TB_{ax} H_a hydrogen

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(9) For example: (a) Carless, H. A. J.; Fekarurhobo, G. K. *Tetrahedron Lett.* **1984**, *25*, 5943. (b) Aoyama, H.; Arata, Y.; Omote, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 1381. (c) Zhou, B.; Wagner, P. J. *J. Am. Chem. Soc.* **1989**, *111*, 6796. (d) Sauers, R. R.; Huang, S.-Y. *Tetrahedron Lett.* **1990**, *31*, 5709.

(10) Unfortunately, at present, the position of photochemical equilibration was not determined due to the preferential photocyclization of α-conformer.

(11) The compound **3** was identified as follows. **2-Methyl-2,3-di(2-tolyl)-methano-2,3-dihydronaphthoquinone (3)**: colorless prisms; mp 185−186 °C; 93:7 mixture of conformational isomers for ^{1}H NMR ($CDCl_3$) δ 7.95 (dd, 1H, J = 7.6, 1.3 Hz), 7.71 (dd, 1H, J = 7.6, 1.3 Hz), 7.64 (dd, 1H, J = 7.6, 1.3 Hz), 7.47 (td, 1H, J = 7.6, 1.3 Hz), 7.37 (td, 1H, J = 7.6, 1.3 Hz), 7.25−7.09 (m, 3H), 6.73 (dd, 2H, J = 4.9, 1.3 Hz), 6.64−6.60 (m, 2H), 3.43 (s, 1H), 2.87 (s, 1H, minor), 2.71 (s, 3H, minor), 2.41 (s, 3H, minor), 2.34 (s, 3H), 2.22 (s, 3H), 1.68 (s, 3H, minor), 1.32 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 196.4, 193.4, 139.2, 138.8, 135.3, 133.5, 133.2, 133.0, 132.8, 132.5, 132.5, 131.6, 131.4, 127.7, 127.2, 126.0, 125.4, 124.7, 124.0, 52.9, 44.8, 41.1, 21.8, 21.1, 17.1; IR (KBr) 3064, 2975, 1673, 1594, 1327, 1302, 763, 724 cm^{-1}. Anal. Calcd for $C_{26}H_{22}O_2$: C, 85.22; H, 6.05. Found: C, 85.17; H, 6.12. **Crystal data for 3**: $C_{26}H_{22}O_2$, M = 366.45, monoclinic, space group $P21/a$, a = 16.537(5), b = 25.150(5), and c = 9.356(4) Å, β = 99.68(3)°, V = 3836(2) Å^3, Z = 8, R = 0.062 and R_w = 0.064 for 4895 reflections with $I > 2.00\sigma(I)$.

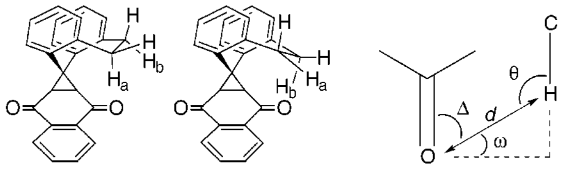
(12) Calculations using the PM3 method were performed with the CS MOPAC Pro program (version 4.0) using CS Chem3D Pro software, CambridgeSoft Co.

(13) Since the hydrogen abstraction is generally known to occur from the excited triplet state in the case of carbonyl compounds, geometrical parameters for the lowest triplet states were also calculated. However, the structural relaxation for the excited state is so small that the triplet structure essentially resembles the ground state (within a deviation of ±0.02 Å for d, and ±0.6° for other angles).

(14) For a recent paper in which the semiempirical calculation is also applied to the geometrical parameters for the Norrish type II reaction, see: Griesbeck, A. G.; Henz, A.; Kramer, W.; Wamser, P. *Tetrahedron Lett.* **1998**, *39*, 1549 and ref 8d.

(15) Sauers, R. R.; Scimone, A.; Shams, H. *J. Org. Chem.* **1988**, *53*, 6084.

Table 1. Geometrical Parameters for Hydrogen Abstraction



1α/β (TB$_{ax}$) 1α/β (TB$_{eq}$)

compd			d/Å	θ/deg	Δ/deg	ω/deg
1aα[a]	(TB$_{ax}$)	H$_a$	2.51	168.6	74.2	65.8
	(TB$_{eq}$)[b]	H$_a$	2.94	108.0	110.4	57.0
		H$_b$	2.68	130.6	90.5	10.5
1aβ[a]	(TB$_{ax}$)[b]	H$_a$	2.41	141.5	91.9	37.3
	(TB$_{eq}$)	H$_a$	3.19	103.0	113.5	50.4
		H$_b$	2.89	129.7	91.0	9.6
1cα[c]	(TB$_{eq}$)	H$_a$	2.84	127.8	82.9	80.0
1cβ[c]	(B)	H$_a$	2.64	139.9	88.6	75.0
3[c]		H$_a$[d]	2.60	141.1	86.4	56.0
ideal			≤2.7	180	90−120	0

[a] Calculated by the MOPAC PM3 method for possible conformations (TB$_{ax}$, twist-boat with axial H$_a$; TB$_{eq}$, twist-boat with equatorial H$_a$; B, boat). The data for H$_b$ of TB$_{ax}$ of **1a**α and **1a**β are omitted because of the longer $d > 4$ Å. [b] The more stable conformer in each of the α- and β-forms. [c] From the X-ray crystal structure data. [d] The nearest *o*-methyl hydrogen to the carbonyl oxygen.

of both **1a**α (d = 2.51 Å) and **1a**β (2.41 Å) is expected to be more favored for the hydrogen abstraction. Such a prerequisite geometry with a relative stability is important for the present hydrogen abstraction and is virtually derived from the spiro-linkage to the homoquinone frame.[6] The photoresistance of **3** may be ascribed to the increased flexibility as judged by the probable geometrical parameters.

Then, why does **1a**β not give a corresponding H-abstracted product? The geometrical parameters alone cannot explain the present negative result. The most conceivable reason for the quantum inefficiency in the β-conformer reaction is reversion of the initially formed biradical to ground state starting material. Additionally, it is noticed that the calculated heat of formation of **2a** (184.5 kJ mol^{-1}) is somewhat smaller than that of the expected product (196.2 kJ mol^{-1}) from **1a**β, although **1a**α (144.6 kJ mol^{-1}) is presumed to be less stable than **1a**β (134.1 kJ mol^{-1}). The larger energy difference of ca. 62 kJ mol^{-1} between **1a**β and its expected cyclic alcohol may be one of the reasons for such exclusive deactivation of the **1a**β biradical.

To conclude, we have found that irradiation of homonaphthoquinones bearing a spiro-linked dibenzocycloheptene ring smoothly brought about a conformationally specific 1,7-hydrogen abstraction to give the polycyclic alcohols only from the less stable conformational isomer. Comparable di-*o*-tolylhomoquinone did not react due to the loss of the conformational rigidity. Thus, these results indicate that the present 1,7-hydrogen abstraction requires the proper spatial orientation of the relevant hydrogen atom toward the excited carbonyl oxygen as well as sufficient conformational lifetime.

Supporting Information Available: Crystallographic data for the compounds studied. This material is available free of charge via the Internet at http://pubs.acs.org.

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