

# Thermally Equilibrated Two Conformers of 10,11-Dihydro-5*H*-dibenzo[*a,d*]cycloheptene Spiro-linked Homobenzoquinone Epoxide

HARUYASU ASAHARA, TAKUYA KOIZUMI, EIKO MOCHIZUKI AND TAKUMI OSHIMA

*Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1, Yamada-oka, Suita, Osaka 565-0871, Japan*

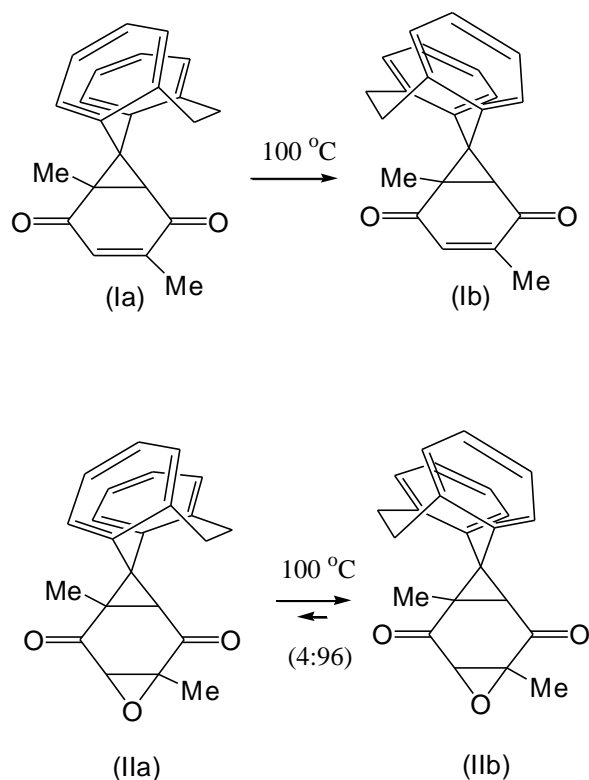
Correspondence e-mail: [oshima@chem.eng.osaka-u.ac.jp](mailto:oshima@chem.eng.osaka-u.ac.jp)

The crystal structures of the thermally equilibrated two conformational isomers of the title epoxide, spiro[10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene-5,8'-1',5'-dimethyl-4'-oxa-tricyclo[5.1.0.0<sup>3',5'</sup>]octane-2',6'-dione] (C<sub>23</sub>H<sub>20</sub>O<sub>3</sub>), have been determined by X-ray diffraction. The tricyclicdione skeleton takes the *anti*-structure of oxirane and cyclopropane rings with respect to the conjunct quinone frame. The major isomer (IIb) has a fairly twisted boat form of the spiro-linked 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene ring folding opposite to the adjoining cyclopropane CH<sub>3</sub>-substituent, whereas the minor isomer (IIa) has almost ideal twist-boat form of the seven-membered ring inversely folding to the side of relevant CH<sub>3</sub> group. The conformational structures of these isomers have been compared with those of the corresponding isomers of unepoxidized homobenzoquinone.

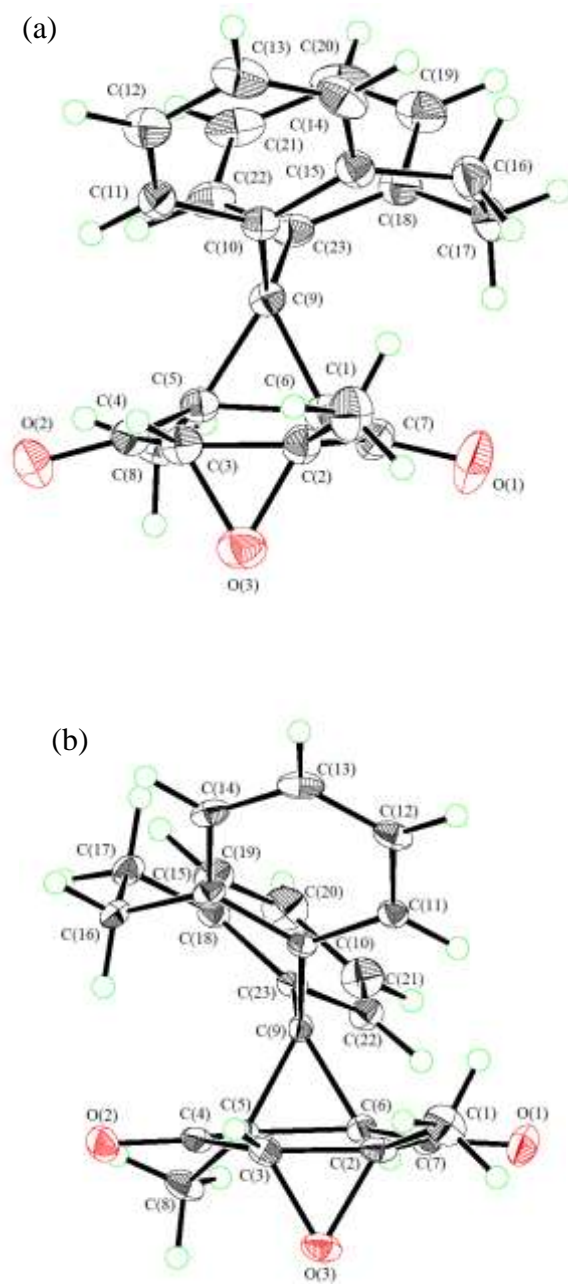
## Comment

Recently, 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene and its derivatives have received considerable pharmacological attention in view of a suitable subunit for drug-receptor concave-convex interaction (Burger, 1983). In our previous paper, we have reported that the reaction of 5-diazo-10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene and 2,5-dimethyl-1,4-benzoquinone gave the corresponding spirohomobenzoquinone (Ia) via the conformationally locked nitrogen release of the primary adduct pyrazolines (Oshima & Nagai, 1994). The compound (Ia) was found to turn out to be the more stable conformer (Ib) at 100 °C by way of a complete one-way conformational inversion of the spiro-linked 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene moiety (Oshima, Fujii, Takatani, Kokubo & Kawamoto, 1999). We have also found that the epoxidation of these conformers (Ia) and (Ib) proceeded without any conformational inversion to give the corresponding epoxides (IIa) and (IIb), respectively, but that the thermal equilibration was attained at 100 °C in CDCl<sub>3</sub> in preference of (IIb) (96%) (Asahara, Koizumi & Oshima, unpublished results).

In this paper, we describe the conformational details of these two isomers, (IIa) and (IIb), as determined by X-ray crystallography in comparison with the parent unepoxidized two conformers Ia and Ib.



As shown in Fig. 1(a), The ORTEP drawing of (IIa) revealed that the dibenzo-fused cycloheptene ring adopts a fairly twisted boat conformation folding opposite to the cyclopropane CH<sub>3</sub>-substituent in analogy with (Ia), but the dihedral angle ( $\theta = 33.1^\circ$ ) of the  $-\text{CH}_2-\text{CH}_2-$  bridge and the intramolecular bond angle ( $\omega = 108.9^\circ$ ) centered at the spiro-carbon are slightly larger than those of the corresponding (Ia) ( $27.3$  and  $107.8^\circ$ ) (Table 1). For comparison, we also listed the reference crystalline values of  $\theta$  and  $\omega$  ( $57.9$  and  $114.6^\circ$ ) for the least strained pristine 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene (III) (Reboul & Cristau, 1981) together with the differential dihedral angles ( $\Delta\theta = \theta_c - \theta_x$ ), in which  $\theta_c$  and  $\theta_x$  are the angles for (III) and the given conformer, respectively. On the other hand, as shown in Fig. 1(b), the conformationally inverted (IIb) takes a more highly twisted boat conformation with  $\theta = 63.6^\circ$  and  $\omega = 113^\circ$  as compared with the corresponding (Ib) ( $55.5$  and  $111.3^\circ$ ). It was also found that the  $\omega$  is well correlated with the  $\theta$  probably because of the constrained dibenzo-fusion; i.e.,  $\omega = 0.133\theta + 104$  ( $n = 4$ ,  $R = 0.99$ ).



**Figure 1**

Molecular structures of (a) isomer (IIa) and (b) isomer (IIb), with the atomic numbering scheme. Displacement ellipsoids are plotted at the (35)% probability level. H atoms are drawn as spheres of arbitrary radii.

**Table 1**

Conformational parameters of the 10,11-dihydro-5*H*-dibenzo [*a,d*]cycloheptene rings of crystalline (Ia), (Ib), (IIa), (IIb) as well as the reference (III).

Compound	$\theta^a$ ( $\Delta\theta$ ) <sup>b</sup>	$\omega^c$
Ia	27.3 (30.6)	107.8
Ib	55.5 (2.4)	111.3
IIa	33.1 (24.8)	108.9
IIb	63.6 (-5.7)	113.0
III	57.9 (0)	114.6

<sup>a</sup> Dihedral angles (°) of  $-\text{CH}_2\text{CH}_2-$  bridge. <sup>b</sup> Values in parentheses are the differential dihedral angles  $\Delta\theta (= \theta_c - \theta_x)$ , where  $\theta_c$  and  $\theta_x$  are the angles (°) for the reference (III) and the given conformer, respectively. <sup>c</sup> C-C-C bond angles (°) centered at the spiro-carbon.

Assuming that the  $\Delta\theta$  is a measure of the strain energy of the spiro-linked seven-membered ring, it seems that the stability difference between the epoxides (IIa) and (IIb) is smaller than that between (Ia) and (Ib). This thermodynamical consideration is consistent with the observation that the conformers (IIa) and (IIb) were equilibrated in preference of the latter (96%), though the parent (Ia) exhibited the one-way isomerization to (Ib).

A perusal of the X-ray structure of (IIa) indicates that the several atoms of the dibenzo-fused seven-membered ring occupy the crowded positions almost touching the underlying quinone component as represented by the very short spatial distances; i.e., C(8)···H(20) (2.72 Å), O(1)···H(16) (2.75), and O(1)···H(14) (2.87). These unfavorable non-bonding interactions may be taken as a driving force for the conformational isomerization. However, such a van der Waals contact was also observed for the stable (IIb), in particular, between the ethano-bridge hydrogen atom H(14) and the facing carbonyl oxygen atom O(2) [2.44 Å], appreciably raising the strain energy of (IIb).

With respect to the structure of quinone frame, (IIb) is specially characterized by the almost planar plane as represented by the dihedral angles of 177.8 and -176.1° for the bond linkages of O(2)-C(4)-C(3)-C(2) and O(1)-C(7)-C(2)-C(3), respectively, whereas the others conformers (Ia), (Ib) as well as (IIa) adopt rather slightly folded (12~22°) boat conformations as indicated by the corresponding angles of 157.7 and -163.5° for (Ia), 164.0 and -168.2° for (Ib), and 164.3 and -163.8° for (IIa), respectively. Further

interest is that the carbon atoms of oxirane rings of (IIa) and (IIb) are almost planar as represented by the angles of 355° or more when we add three angles made by the substituents of oxirane and another carbon center. Such a geometrical planarity of oxirane carbon is commonly known for the most of oxirane derivatives compiled in the Cambridge Structural Database (Oki, Toyofuku, Sakaue, Hirose, Asakura, Morita & Toyota, 2003).

## Experimental

Samples of (IIa) and (IIb) were synthesized by epoxidation of the parent (Ia) and (Ib), respectively, and were recrystallized from a mixture of pentane and *t*-butyl methyl ether (10:1). Compound (IIa): <sup>1</sup>H (CDCl<sub>3</sub>); δ 0.77 (3H, s), 1.60 (3H, s), 2.44 (1H, s), 2.73–2.97 (2H, m), 3.00 (1H, s), 3.30–3.40 (1H, m), 4.08–4.17(1H, m), 6.95–6.99(2H, m), 7.00–7.26 (6H, m); <sup>13</sup>C (CDCl<sub>3</sub>); δ 13.4, 18.5, 29.8, 31.6, 38.0, 44.9, 48.1, 59.7, 60.6, 125.8, 126.3, 126.5, 126.9, 128.1, 128.1, 130.2, 132.2, 134.9, 138.6, 139.2, 140.4, 197.4, 201.0. Compound (IIb): <sup>1</sup>H (CDCl<sub>3</sub>); δ 1.21 (3H, s), 1.34 (3H, s), 2.71–2.95 (2H, m), 2.73 (1H, s), 2.97 (1H, s), 3.41–3.67 (2H, m), 7.0–7.37 (8H, m); <sup>13</sup>C (CDCl<sub>3</sub>); δ 14.6, 16.3, 30.3, 32.2, 7.9, 39.5, 48.8, 60.1, 61.0, 126.1, 126.2, 126.8, 127.2, 128.2, 128.7, 130.2, 131.7, 135.5, 136.9, 138.4, 141.0, 199.0, 199.4.

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