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<td>Oshima, Takumi, Asahara, Haruyasu, Koizumi, Taku, Miyamoto, Saki</td>
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Mechanistic evidence for the remote π-aryl participation in acid-catalyzed ring opening of homobenzoquinone epoxides

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The acid-induced reaction of bis(p-chlorophenyl)homobenzoquinone epoxide gave the dual ipso/ortho intramolecular Si2-Ar products associated with the π-aryl participated oxirane ring opening, whereas bis(p-toly1)- and diphenyl-substituted homologues provided only the ortho products.

The π-aryl participation is one of the most important physicochemical phenomena which control the reactivity of substrates and govern the reaction mechanism. Such effects are generally ascribed to (derived from) the through-space electronic stabilization of the transition states by the direct electronic donation (not by resonance) of π-electrons from the aryl groups to the incipient carbocation center. For instance a large number of studies have been made of the π-aryl assisted solvolyses of β-aryltsulfoxides and brosylates from the kinetic and stereochemical point of view. By contrast, a little is known for the remote anchimeric assistance of aryl groups located in the carbon linkage far away from the reaction site. Thus, the elucidation of the possible remote π-aryl participation provides a further useful insight into the mechanistic understanding of the reactions involving the through-space π-electronic interaction.

Very recently, we found that the BF3-catalyzed ring-opening of diphenylhomobenzoquinone epoxide 1b resulted in the transannular Si2-Ar displacement at o-position to afford tricyclic diketo-alcohol 3b (Scheme 1). This reaction becomes of interest in that the endo-aromatic ring is likely to display the remote π-aryl participation in oxirane ring opening. Therefore, we felt that an appropriately p-substituted diphenylhomobenzoquinone epoxide 1 might allow to provide a possible ipso-product from the π-aryl participated transition state. Herein, we wish to report the mechanistic evidence for the very rare π-aryl-assisted oxirane ring opening in the BF3-catalyzed reaction of bis(p-chlorophenyl)homobenzoquinone epoxide 1c.

The acid-induced reaction of p,p’-dimethyl-, unsubstituted, and p,p’-dichloro-substituted 1a-c (0.02 mmol) was carried out in the presence of BF3 (0.40 mmol) in CDCl3 (0.62 ml) at ordinary temperature. The reaction proceeded in a regioselective oxirane ring-opening at the Me substituted C-O bond and on treatment with water gave the common o-phenylene bridged tricyclic diketo-alcohols 3a-c (for 3c (20%), as a mixture of its epimer 4c (25%)) and 2,5-cyclohexadien-4-one spiro-linked tricyclic diketo-alcohol 2c (47%) for only the chloro-substituted 1c in almost quantitative total yields based on the consumed 1 (Scheme 1).

![Scheme 1](image-url)

Scheme 1 A dual pathway in BF3-catalyzed rearrangement of 1.

Fig. 1 ORTEP representation (50% ellipsoids) of the structure 2c.

The structures of new compounds 2c, 3a, 3c, and 4c were...
deduced from their $^1$H- and $^{13}$C-NMR spectra and the $2c$ was also confirmed by the X-ray crystal analysis (Fig. 1). 

As shown in Scheme 1, the formation of $2c$ and $3a-c$ can be rationalized by the occurrence of the competitive ipso- and ortho-Si2-Ar reaction via aryl bridged benzenonium ions, i.e., $\sigma$-complexes I and II (path a and path b), respectively. Although the ortho-bound intermediate II easily undergoes a rearomatization to afford $3a-c$ via a proton migration, the formation of compound $2c$ can be explained by the capture of the ipso-bound intermediate I with some water followed by the loss of HCl. Thus, the isolation of both the $2c$ and $3c$ can be taken as a strong evidence for the intervention of two $\sigma$-complexes, I and II. These schematic considerations prompted us to further examine the following mechanistic questions about the transition state leading to these $\sigma$-complexes$^7$ as well as the marked substituent effects on the product distributions.

1) Which can better explain the initial oxirane ring-opening, a concerted Si2-like pathway involving a $\pi$-aryl-assisted transition state or a stepwise Si1-like pathway generating a tertiary carbocation intermediate?

2) Why does the $p$-chloro-substituted $1c$ provide the dual ipso/ortho conjunct products in contrast to the $p, p'$-dimethyl-substituted $1a$ and the unsubstituted $1b$?

As to the first question, the kinetic solvent effects provide a useful mechanistic information on the transition state. Namely, the more polar solvent will stabilize the polar transition state and largely accelerate the rate like in the Si1 reactions. $^8$ We have measured the rate constants for the MeSO$_3$H-catalyzed oxirane ring-opening of the parent unsubstituted epoxide $1b$ by monitoring its first-order decay in various less basic solvents (Fig. 2). $^9$ This reaction also gave the same tricyclic diketo-alcohol $3b$ in almost quantitative yield as the BF$_3$-catalyzed reaction. The observed rate constants in a wide range of solvents at 30°C are summarized along with the solvent polarity parameter $E_{T}(30)^{10}$ (Table 1). The total variation of $k_2$ amounts to only a factor of 3 over a wide range of solvent polarities investigated. The very poor kinetic solvent effects strongly support a concerted mechanism involving a less polar transition state. This observation is consistent with the appearance of the transition state in which the charge is highly dispersed on the $\pi$-aryl participated aromatic nucleus as well as on the breaking oxirane carbon atom. $^{10}$ In such a Si2-like transition state, it is conceived that the orbital interaction between the HOMO of the $\pi$-electron donating aromatic group and the Walsh-type LUMO of oxirane ring$^{11}$ plays a crucial role in the cleavage of the relevant C-O bond as depicted in Scheme 1. The aryl participation in the ring opening of oxiranes is scarcely reported but has been put forwarded in order to explain the syn-stereochimistry in the acid-induced ring opening of a particular case of oxiranes bearing aryl groups directly or indirectly linked to the epoxide ring such as stilbene oxides$^{12}$ and spiro-linked 2-phenyl-1,2-epoxides$^{13}$ or 1-benzyl-1,2-epoxides$^{14}$ in which the well-documented phenonium ion intermediates are invoked.

The second question can be easily solved by considering the characteristic electronic properties of $p$-Cl substituent as exhibiting the electron-donating resonance effect as well as the good leaving ability which would stabilize the adjoining positive center of I and then enhance the release of HCl (Scheme 1). As to the ipso-attack, the $p$-tolyl and phenyl groups would rather facilitate such a reaction more efficiently than the $p$-chlorophenyl group. However, even if formed, such ipso $\sigma$-complexes of $1a$ and $1b$ would be inevitably transformed into the ortho $\sigma$-complex via a facile 1,2-shift because of the lack of the leaving ability of $p$-Me group (and of $p$-H atom). As a result, the lability of ipso intermediate I of $1c$ toward residual water play a desiccisive role in the present product partitioning steps from the common transition state (Scheme 1).

In summary, we have succeeded in isolating both the ipso- and ortho-Si2-Ar products in the acid-catalyzed reaction of bis($p$-chlorophenyl)-substituted homobenzoquinone epoxide $1c$. The present dual pathway for $1c$ as well as the kinetic solvent effects is likely to prove that the acid-catalyzed ring-opening of diarylhomobenzoquinone epoxides $1$ occurs via a concerted manner involving a very rare remote ($\delta$-located) $\pi$-aryl participated transition state. The information obtained in the present reactions will provide a

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Table 1 Rate constants for MeSO$_3$H-catalyzed ring-opening of epoxide $1b$ in various solvents at 30 °C

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$E_{T}(30)$</th>
<th>$k^a$ (10$^3$, M$^{-1}$s$^{-1}$)</th>
<th>$k_{rel}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2-Dichloroethane</td>
<td>41.3</td>
<td>1.15</td>
<td>3.0</td>
</tr>
<tr>
<td>Dichloromethane</td>
<td>40.7</td>
<td>1.17</td>
<td>3.1</td>
</tr>
<tr>
<td>Chloroform-$d$</td>
<td>39.0</td>
<td>0.979</td>
<td>2.6</td>
</tr>
<tr>
<td>$o$-Dichlorobenzene</td>
<td>38.0</td>
<td>0.280</td>
<td>0.73</td>
</tr>
<tr>
<td>Fluorobenzene</td>
<td>37.0</td>
<td>0.380</td>
<td>0.99</td>
</tr>
<tr>
<td>Chlorobenzene</td>
<td>36.8</td>
<td>0.297</td>
<td>0.77</td>
</tr>
<tr>
<td>Benzene</td>
<td>34.3</td>
<td>0.384</td>
<td>1.0</td>
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$^4$ The second-order rate constants $k_2$ were obtained by dividing the pseudo-first-order rate constants $k_{obs}$, by the catalyst concentration ([30 mM]).

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Fig. 2 A representative time course of the MeSO$_3$H ([30 mM])-catalyzed rearrangement of $1b$ into $3b$ in CDCl$_3$ (650 μl) at 30°C.
useful insight into the understanding of Lewis acid-induced rearrangements of polycyclic epoxides.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Characterization data for the new substrates, 1a and 1c, and the products, 3a, 3c, 4c. See DOI: 10.1039/b000000x/

‡ Representative procedure for acid-catalyzed rearrangement: To a solution of 1c (0.02 mmol, 7.75mg) in 0.62 ml of CDCl3 was added BF3·OEt2 (0.40 mmol, 50.2 μl). After standing for requisite time at ordinary temperature, the reaction mixture was quenched with water (5 ml) and extracted with CHCl3 (5 ml × 3). The combined organic extracts were dried over anhydrous MgSO4 and evaporated under reduced pressure.

The residual mixture was submitted for 1H NMR measurement for the determination of conversion of 1c as well as the yields of 2c and 3c(4c). The reaction mixture was then purified by column chromatography on silica gel to successively afford 2c and 3c as a mixture with 4c with hexane-benzene as eluent. The pure 4c was obtained on treatment of 3c with a few drops of Et3N in CDCl3 (0.6 ml) for 24h. The conversions of 1a, 1b, and 1c were 100% (for 0.5h), >99 (4h), and 82 (20h), respectively.

§ The compound of 2c has the following analytical data: mp 206.5–208.5 °C, colorless prisms (from hexane-chloroform), 1H NMR (CDCl3, 270 MHz, ppm): δ 1.00 (s, 3H), 1.08 (s, 3H), 2.75 (s, 1H), 2.93 (s, 1H), 4.00 (s, 1H), 6.17 (dd, J = 1.81, 10.4 Hz, 1H), 6.52 (dd, J = 1.81, 10.2 Hz, 1H), 6.54 (dd, J = 3.13, 10.4 Hz, 1H), 6.82 (dd, J = 3.13, 10.2 Hz, 1H), 7.00–7.10 (m, 2H), 7.25–7.26 (m, 2H). 13C NMR (CDCl3, 75 MHz, ppm): δ 10.9, 14.8, 29.8, 43.1, 46.0, 52.8, 56.0, 75.4, 128.9, 129.7, 130.5, 131.3, 134.4, 135.3, 142.7, 147.5, 184.0, 203.0, 204.0. IR (KBr): 3417, 2925, 1745, 1664, 1261, 1091, 801 cm⁻¹.

Crystal data. 2c: C₂₁H₂₂O₂Cl₂, M = 368.82, monoclinic, a = 11.4880(7), b = 12.3259(10), c = 13.3085(6) Å, β = 114.3121(9)°, V = 1745.12(2) Å³, T = 23.0 °C, space group P2₁/n (No. 14), Z = 4, μ(MoKα) = 2.43 cm⁻¹, 14930 reflections measured, 3986 were unique (R(int) = 0.070), R1(I) < 2σ(I) = 0.0901, wR2(all data) = 0.2083. CCDC 666903.

¶ Since BF3 is very sensitive to the residual water in the solvents employed, we investigated the kinetic solvent effects by using water-persistent MeSO-H. The decay of 1b was monitored by 1H NMR for CDCl3, and by HPLC for other solvents.


10 We have previously reported a similar type of less polar transition state in the acid-catalyzed intramolecular S2,2Ar reaction of cyclobutene-fused diarylhomobenzoquinones, see K. Koizumi, K. Harada, E. Mochizuki, K. Kokubo and T. Oshima, Org. Lett., 2004, 6, 4081.


