Mechanistic evidence for the remote π-aryl participation in acid-catalyzed ring opening of homobenzoquinone epoxides

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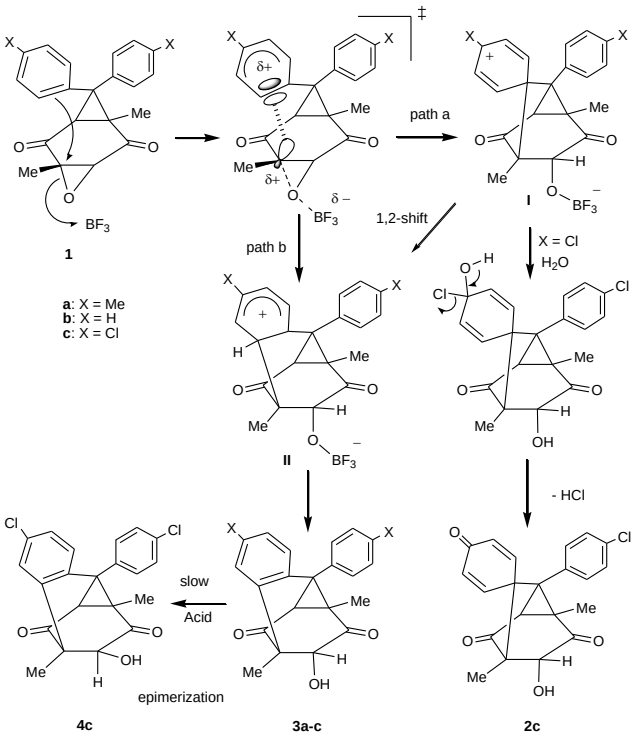
The acid-induced reaction of bis(*p*-chlorophenyl)-homobenzoquinone epoxide gave the dual *ipso*/*ortho* intramolecular S_E2-Ar products associated with the π-aryl participated oxirane ring opening, whereas bis(*p*-tolyl)- and diphenyl-substituted homologues provided only the *ortho* products.

The π-aryl participation is one of the most important physicochemical phenomena which control the reactivity of substrates and govern the reaction mechanism.[1] Such effects are generally ascribed to (derived from) the through-space electronic stabilization of the transition states by the direct electronic donation (not by resonace) of π-electrons from the aryl groups to the incipient carbocation center.[2] For instance a large number of studies have been made of the π-aryl assisted solvolyses of β-aryltosylates and brosylates from the kinetic[3] and stereochemical[4] 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.[5] 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 BF_3-catalyzed ring-opening of diphenylhomobenzoquinone epoxide **1b** resulted in the transannular S_E2-Ar displacement at *o*-position to afford tricyclic diketo-alcohol **3b** (Scheme 1).[6] 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 BF_3-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 BF_3 (0.40 mmol) in $CDCl_3$ (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 A dual pathway in BF_3-catalyzed rearrangement of **1**.

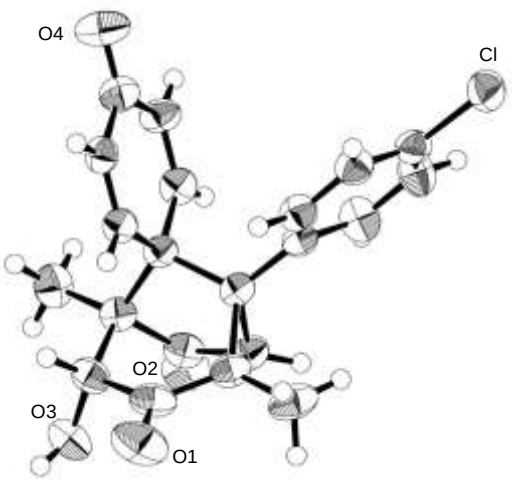


Fig. 1 ORTEP representation (50% ellipsoids) of the structure **2c**.

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*-S_E2-Ar reaction via aryl bridged benzenonium ions, i.e., σ-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 σ-complexes, I and II. These schematic considerations prompted us to further examine the following mechanistic questions about the transition state leading to these σ-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 S_N2-like pathway involving a π-aryl-assisted transition state or a stepwise S_N1-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 S_N1 reactions.[8] We have measured the rate constants for the $MeSO_3H$-catalyzed oxirane ring-opening of the parent unsubstituted epoxide **1b** by monitoring its first-order decay in various less basic solvents (Fig. 2). ¶ This reaction also gave the same tricyclic diketo-alcohol **3b** in almost quantitative yield as the BF_3-catalyzed reaction. The observed

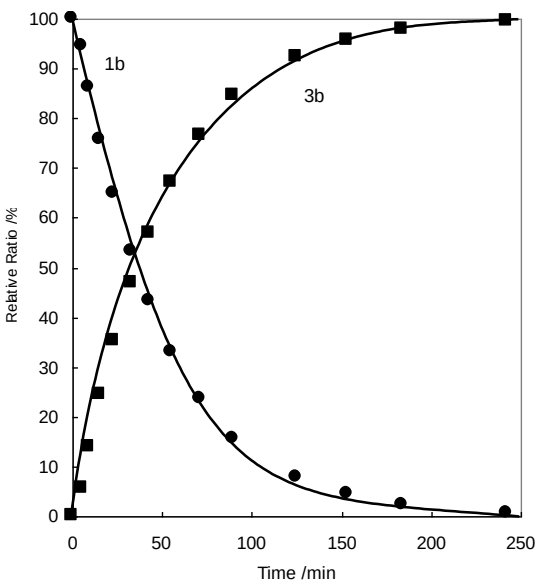


Fig. 2 A representative time course of the $MeSO_3H$ ([30 mM])-catalyzed rearrangement of **1b** into **3b** in $CDCl_3$ (650 μl) at 30°C.

Table 1 Rate constants for $MeSO_3H$-catalyzed ring-opening of epoxide **1b** in various solvents at 30 °C

Solvent	$E_T(30)$	k_2[a] (10^3, $M^{-1}s^{-1}$)	k_{rel}
1,2-Dichloroethane	41.3	1.15	3.0
Dichloromethane	40.7	1.17	3.1
Chloroform-*d*	39.0	0.979	2.6
o-Dichlorobenzene	38.0	0.280	0.73
Fluorobenzene	37.0	0.380	0.99
Chlorobenezene	36.8	0.297	0.77
Benzene	34.3	0.384	1.0

[a] 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]).

rate constants in a wide range of solvents at 30°C are summarized along with the solvent polarity parameter $E_T(30)$[9] (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 π-aryl participated aromatic nucleus as well as on the breaking oxirane carbon atom.[10] In such a S_N2-like transition state, it is conceived that the orbital interaction between the HOMO of the π-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*-stereochemistry in the acid-induced ring opening of a particular case of oxiranes bearing aryl groups directry or indirectry linked to the epoxide ring such as stilbene oxides[12] and spiro-linked 2-phenyl-1,2-epoxide[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* σ-complexes of **1a** and **1b** would be inevitably transformed into the *ortho* σ-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 desicisive 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*-S_E2-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 (δ-located) π-aryl participated transition state. The information obtained in the present reactions will provide a

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useful insight into the understanding of Lewis acid-induced rearrangements of polycyclic epoxides.

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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 rearrangemen*t: To a solution of **1c** (0.02 mmol, 7.75mg) in 0.62 ml of $CDCl_3$ was added $BF_3{\cdot}OEt_2$ (0.40 mmol, 50.2 μl). After standing for requisite time at ordinary temperature, the reaction mixture was quenched by water (5 ml) and extracted with $CHCl_3$ (5 ml × 3). The combined organic exrtracts were dried over anhydrous $MgSO_4$ and evapolated under reduced pressure. The residual mixture was submitted for ^{1}H 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 Et_3N in $CDCl_3$ (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 206.5-207 °C, colorless prisms (from hexane-chloroform). ^{1}H NMR ($CDCl_3$, 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). ^{13}C NMR ($CDCl_3$, 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: $C_{21}H_{17}O_4Cl$, M = 368.82, monoclinic, a =11.4880(7), b = 12.5251(10), c = 13.3085(6) Å, β = 114.312(1) °, V = 1745.1(2) Å^3, T = 23.0 °C, space group $P2_1/n$ (#14), Z = 4, μ(MoKα) = 2.43 cm^{-1}, 14930 reflections mesured, 3986 were unique (R_{int} = 0.070), $R1[I > 2.0\sigma(I)]$ = 0.0901, w$R2$ (all data) = 0.2083. CCDC 666903.

¶ Since BF_3 is very sensitive to the residual water in the solvents employed, we investigated the kinetic solvent effects by using water-persistent $MeSO_3H$. The decay of **1b** was monitored by ^{1}H NMR for $CDCl_3$ and by HPLC for other solvents.

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