Mechanistic evidence for 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 π-aryl participated oxirane ring opening, whereas bis(*p*-tolyl)- and diphenyl-substituted homologues provided only the *ortho* products.

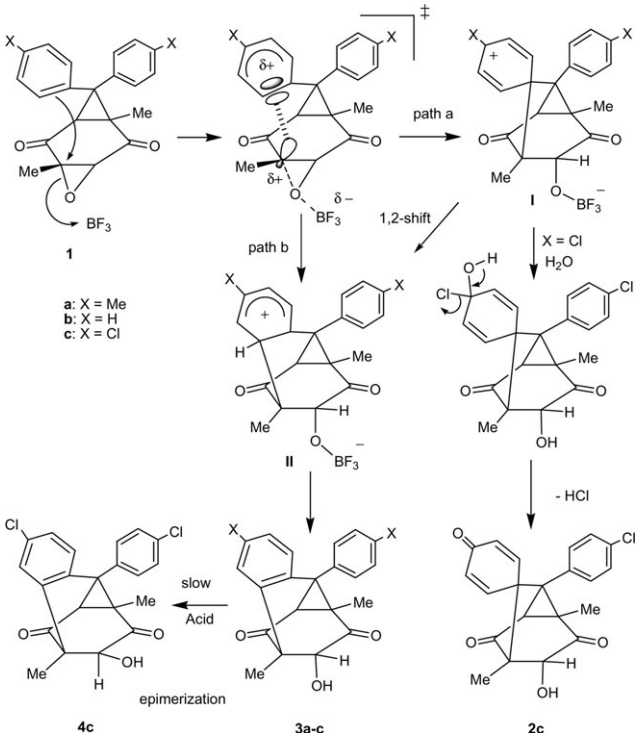
π-Aryl participation is one of the most important physicochemical phenomena which control the reactivity of substrates and govern the reaction mechanism.[1] Such effects are generally ascribed to (derived from) the through-space electronic stabilization of the transition states by the direct electronic donation (not by resonance) 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, 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 possible remote π-aryl participation provides a further useful insight into the mechanistic understanding of reactions involving through-space π-electronic interaction.

Very recently, we found that the BF_3-catalyzed ring-opening of diphenylhomobenzoquinone epoxide **1b** resulted in transannular S_E2-Ar displacement at the *ortho*-position to afford tricyclic diketo-alcohol **3b** (Scheme 1).[6] This reaction is of interest in that the endo-aromatic ring is likely to display remote π-aryl participation in the oxirane ring opening. Therefore, we felt that an appropriately *para*-substituted diphenylhomobenzoquinone epoxide **1** might allow provision of 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 reactions of *p*,*p*′-dimethyl-, unsubstituted, and *p*,*p*′-dichloro-substituted **1a–c** (0.02 mmol) were carried out in the presence of BF_3 (0.40 mmol) in $CDCl_3$ (0.62 ml) at room temperature.‡ The reaction proceeded with 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 consumed **1** (Scheme 1).

The structures of new compounds **2c**, **3a**, **3c**, and **4c** were deduced from their ^{1}H- and ^{13}C-NMR spectra and the structure of **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 by 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



Scheme 1 The dual pathway in the BF_3-catalyzed rearrangement of **1**.

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† Electronic supplementary information (ESI) available: Characterization data for the new substrates, **1a** and **1c**, and the products **3a**, **3c**, **4c**. Crystal data for **2c**. CCDC 666903. See DOI: 10.1039/b719663f

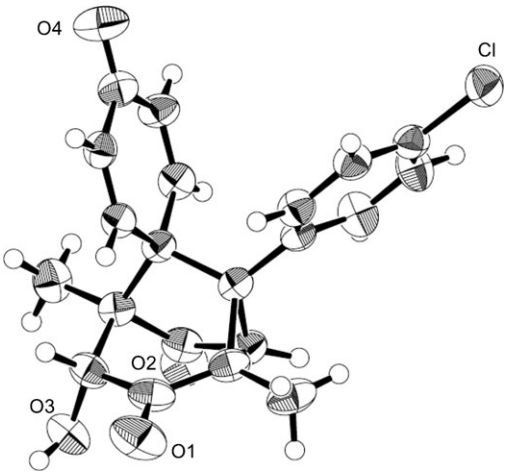

Fig. 1 ORTEP representation (50% ellipsoids) of the structure of **2c**.

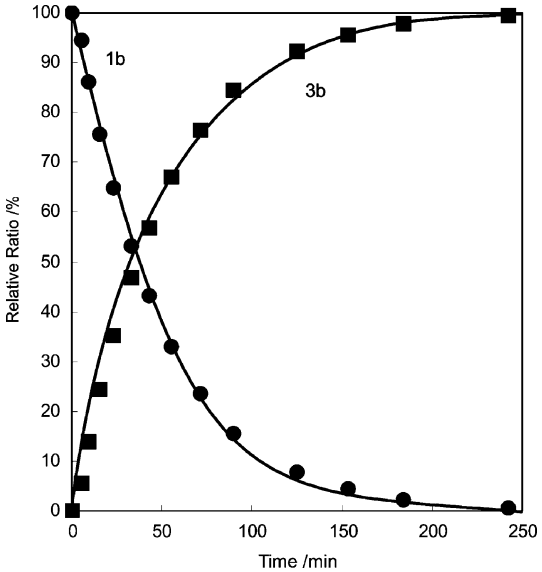

Fig. 2 A representative time course of the $MeSO_3H$ ([300 mM])-catalyzed rearrangement of **1b** into **3b** in $CDCl_3$ (650 μl) at 30 °C.

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 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 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 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 participating aromatic nucleus as well as on the breaking oxirane carbon atom.[10] In such a S_N2-like transition state, it is conceivable that orbital interaction between the HOMO of the π-electron donating aromatic group and the Walsh-type LUMO of the 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 forward in order to explain the *syn*-stereochemistry 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-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 the *p*-Cl substituent as exhibiting an electron-donating resonance effect as well as a 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 facilitate such a reaction more efficiently than the *p*-chlorophenyl group. However, even if formed, such *ipso* σ-complexes of **1a** and **1b** would inevitably be transformed into the *ortho* σ-complex *via* a facile 1,2-shift because of the lack of leaving ability of the *p*-Me group (and of the *p*-H atom). As a result, the lability of the *ipso* intermediate I of **1c** toward residual water plays a decisive 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

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

Solvent	$E_T(30)$	$10^3\ k_2{}^a/M^{-1}\ s^{-1}$	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
Chlorobenzene	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 ([300 mM]).

in the present reactions will provide a useful insight into the understanding of Lewis acid-induced rearrangements of polycyclic epoxides.

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Notes and references

‡ *Representative procedure for acid-catalyzed rearrangement*: To a solution of **1c** (0.02 mmol, 7.75 mg) in 0.62 ml of $CDCl_3$ was added $BF_3{\cdot}OEt_2$ (0.40 mmol, 50.2 μl). After standing for the requisite time at room temperature, the reaction mixture was quenched by water (5 ml) and extracted with $CHCl_3$ (5 ml × 3). The combined organic extracts were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residual mixture was submitted for ^{1}H NMR analysis to determine the 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. Pure **4c** was obtained on treatment of **3c** with a few drops of Et_3N in $CDCl_3$ (0.6 ml) for 24 h. The conversions of **1a**, **1b**, and **1c** were 100% (for 0.5 h), >99% (4 h), and 82% (20 h), respectively.

§ Compound **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}, 14 930 reflections measured, 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 residual water in the solvents employed, we investigated the kinetic solvent effects by using water-persistent $MeSO_3H$. The decay of **1b** was monitored using ^{1}H NMR spectroscopy for $CDCl_3$ and by HPLC for other solvents.

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