ORGANIC LETTERS

2004
Vol. 6, No. 22
4081−4084

Kinetic Evidence for Remote π-Aryl Participation in the BF_3-Catalyzed Rearrangement of [2 + 2] Photocycloadducts of Diarylhomobenzoquinones with Diphenylacetylene

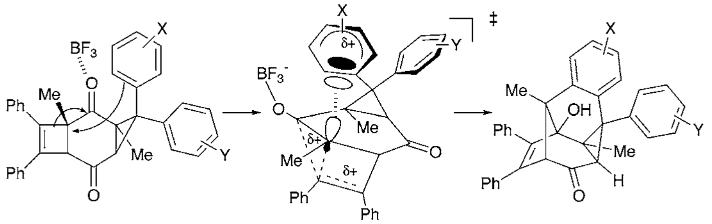
Takuya Koizumi, Kenji Harada, Eiko Mochizuki, Ken Kokubo, and Takumi Oshima*

Department of Materials Chemistry, Graduate School of Engineering, Osaka University, Toyonaka, Osaka 560-0043, Japan

oshima@ch.wani.osaka

Received September 6, 2004

ABSTRACT



The BF_3-catalyzed rearrangement of cyclobutene-fused *m*- and *p*-substituted diarylhomobenzoquinones exclusively gave the keto-alcohols via a Wagner–Meerwein vinyl-anion migration followed by the annulation of a δ-located *endo*-aryl group. The Hammett treatments for the *endo*/*exo* substituent effects, as well as the kinetic solvent effects, indicated that this reaction proceeds through the concerted S_N2-like mechanism involving a rate-determining *endo*-aryl-assisted transition state.

The π-aryl participation in the reaction center with neighboring aromatic rings is a well-documented phenomenon.[1] A large number of studies have been made for more than 5 decades, especially on the solvolyses (e.g., acetolysis) of β-arylalkyltosylates and brosylates from the kinetic[2] and stereochemical[3] points of view. By contrast, much less work has been done on the remote anchimeric assistance of aryl groups located in the γ-position or further away from the reaction site because of the entropical disadvantage.[4] However, these observations are of interest to organic chemists because a comprehensive understanding of the electronic factors that govern the through-space interactions plays a role in the elucidation of many mechanistic problems.

---

(1) (a) Lancelot, C. J.; Cram, D. J.; Schleyer, P. v. R. *Carbenium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience, New York, 1972; Vol. 3, Chapter 27, p 1347. (b) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*; Wiley: New York, 2001; Chapter 10, p 407. (c) Peeran, M.; Wilt, J. W.; Subramanian, R.; Crumrine, D. S. *J. Org. Chem.* **1993**, *58*, 202. (d) Kevil, D. N.; D'Souza, M. J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 257. (e) Fujio, M.; Goto, N.; Dairokuno, T.; Goto, M.; Saeki, Y.; Okusako, Y.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3072.

(2) (a) Fujio, M.; Funatsu, K.; Goto, M.; Mishima, M.; Tsuno, Y. *Tetrahedron* **1987**, *43*, 307. (b) Fujio, M.; Goto, M.; Mishima, M.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1121. (c) Okamura, M.; Hazama, K.; Ohta, M.; Kato, K.; Horiguchi, T.; Ohno, A. *Chem. Lett.* **1997**, *26*, 973.

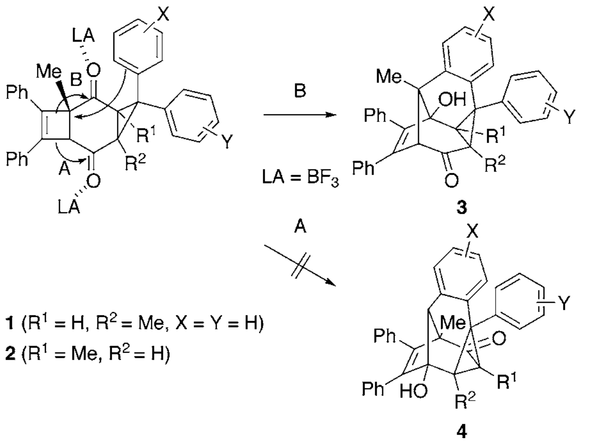
(3) (a) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2129, 2137. (b) Streitwieser, A., Jr.; Walsh, T. D.; Wolfe, J. R. *J. Am. Chem. Soc.* **1965**, *87*, 3686. (c) Cram, D. J.; Thompson, J. A. *J. Am. Chem. Soc.* **1967**, *89*, 6766. (d) Thompson, J. A.; Cram, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 1778.

(4) (a) Heck, R.; Winstein, S. *J. Am. Chem. Soc.* **1957**, *79*, 3105. (b) Muneyuki, R.; Tanida, H. *J. Am. Chem. Soc.* **1968**, *90*, 656. (c) Jackman, L. M.; Haddon, V. R. *J. Am. Chem. Soc.* **1974**, *96*, 5130. (d) Gates, M.; Frank, D. L.; von Felten, W. C. *J. Am. Chem. Soc.* **1974**, *96*, 5138. (e) Ando, T.; Yamawaki, J.; Saito, Y. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 219.

10.1021/ol0481986 CCC: $27.50

We have recently reported that the photocycloadduct **1** from 1,5-dimethyl-4,4-diphenylhomobenzoquinone and diphenyl acetylene[5] undergoes the Lewis acid catalyzed rearrangement to exclusively produce tricyclic keto-alcohol **3** (Scheme 1).[6]

Scheme 1



1 (R^1 = H, R^2 = Me, X = Y = H)
2 (R^1 = Me, R^2 = H)

	X	Y		X	Y
endo-**2a**:	*m*-MeO	H	**2f**:	H	H
exo-**2a**:	H	*m*-MeO	*endo*-**2g**:	*m*-Cl	H
endo-**2b**:	*p*-MeO	H	*exo*-**2g**:	H	*m*-Cl
exo-**2b**:	H	*p*-MeO	*endo*-**2h**:	*p*-Cl	H
endo-**2c**:	*m*-Me	H	*exo*-**2h**:	H	*p*-Cl
exo-**2c**:	H	*m*-Me	**2i**:	*p*-Cl	*p*-Cl
2d:	*p*-Me	*p*-Me	*endo*-**2j**:	*p*-CF$_3$	H
endo-**2e**:	*p*-Me	H	*exo*-**2j**:	H	*p*-CF$_3$
exo-**2e**:	H	*p*-Me			

This reaction formally proceeds through a Wagner–Meerwein vinyl-anion migration to the acid-activated upper carbonyl function (path B) and an intramolecular Friedel–Crafts alkylation of the *endo*-phenyl ring. Here, a mechanistic question arises as to whether the initial cyclobutene ring cleavage occurs via an S_N2-like mechanism with the *endo*-aryl π-participated transition state or via an unassisted stepwise displacement associated with the subsequent transannular cyclization.

We now wish to report unequivocal kinetic evidence for the remote (δ-located) π-aryl participation in the BF_3-catalyzed rearrangement of newly synthesized *m*- and *p*-substituted (*endo*-X/*exo*-Y) 1,3-dimethyl-4,4-diaryltricyclic-[5.2.0.0^{3,5}]non-8-ene-2,6-diones **2a**–**j** (R^1 = Me, R^2 = H). The X-ray crystal structure of unsubstituted **2f** revealed that the *endo*-phenyl ring adopts the suitable geometry for π-aryl participation, overhanging above the quinone plane (Figure 1).

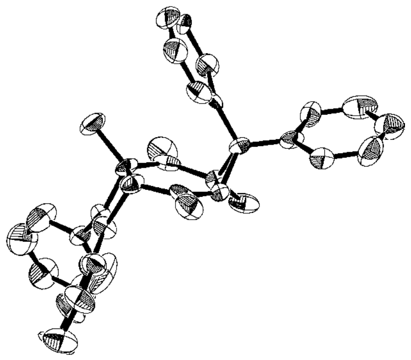


Figure 1. ORTEP drawing of unsubstituted **2f**. For clarity, hydrogen atoms were omitted.

As in **1**, the BF_3-catalyzed rearrangement of **2a**–**j** exclusively provided the stable tetracyclic keto-alcohols **3a**–**j** with no detectable amount of path A products **4** (Scheme 1).[7] This conveniently simplified the product analysis, as well as the kinetic treatment.[8] The structure of **3f** was deduced from ^1H and ^{13}C NMR spectra and confirmed by X-ray crystal analysis[9] (Supporting Information). The exclusive occurrence of the path B process is likely to support the cationic rearrangement involving a tertiary carbocation-like intermediate. However, an attempt to capture the plausible cationic intermediate by added methanol (20 equiv) for the reaction of **2f** failed and still gave only **3f**. Here, it should be noted that the PM3 calculation for BF_3 complexation of **2f** assumed that the more preferential binding occurs at the path A carbonyl by 3.2 kcal mol^{-1} ($\Delta\Delta H_f$) rather than at the path B carbonyl, i.e., $K_A > K_B$. Accordingly, the Curtin–Hammett principle[10] can be applied to the present case if the two complexes are in rapid equilibrium and the latter complex has the significantly larger rate constant for the cyclobutene ring cleavage, i.e., $k_B \gg k_A$.

The kinetic runs were carried out in $CDCl_3$ at 30 °C. The decay of **2** was followed by HPLC (naphthalene as an internal standard) or by ^1H NMR (TMS as an internal standard). The observed pseudo-first-order rate constants k_{obs} were divided by the concentration of BF_3 to provide the second-order rate constants k. The values for k and the relative rate constants k_{rel} compared to **2f** are collected in Table 1.

As easily noticed, for both the *endo*- and *exo*-isomer series, the rates increased with increasing electron-donating ability of the substituents, irrespective of *m*- or *p*-positions. The

---

(5) Kokubo, K.; Yamaguchi, H.; Kawamoto, T.; Oshima, T. *J. Am. Chem. Soc.* **2002**, *124*, 8912.

(6) (a) Kokubo, K.; Koizumi, T.; Yamaguchi, H.; Oshima, T. *Tetrahedron Lett.* **2001**, *42*, 5025. (b) Koizumi, T.; Mochizuki, E.; Kokubo, K.; Oshima, T. *J. Org. Chem.* **2004**, *69*, 4577.

(7) **General Procedure.** To a solution of **2f** (0.02 mmol) in chloroform-*d* (0.67 mL) was added $BF_3 \cdot OEt_2$ (0.06 mmol), and the solution was allowed to stand for 70 h at 25 °C to give quantitatively **3f**. The pure **3f** was obtained after washing with water (2 × 1 mL) and then recrystallization from benzene–pentane.

(8) The stereochemistry of *endo*/*exo* **2a**,**b**,**c**,**e**,**g**,**h**, and **j** was deduced from their kinetic behaviors. Thus, we tentatively assigned that the more reactive isomers **2a**,**b**,**c**, and **e** are *endo* and the less reactive isomers **2g**,**h**, and **j** are *endo*, respectively. An attempt to assign the stereochemistry of **2** by NMR failed because of the complexity due to the *meta*/*para*-substitution as well as the possible conformation-dependent anisotropy of aromatic nuclei (Supporting Information).

(9) The structures of other products of **3** (involving the *endo*/*exo* mixtures) were deduced by comparing their diagnostic ^1H NMR signals of the two methyl and one methine protons with those of the parent **3f**.

(10) For the Curtin–Hammett principle, see: (a) Seman, J. I. *Chem. Rev.* **1983**, *83*, 83. (b) Seeman, J. I. *J. Chem. Educ.* **1986**, *63*, 42.

Table 1. Rate Constants for BF_3-Catalyzed Rearrangements of **2a**−**j** in $CDCl_3$ at 30 °C

		substituent			
run	compound	X	Y	k^a (10^3, M^{-1} s^{-1})	k_{rel}
1	*endo*-**2a**	*m*-MeO	H	27.6	22
2	*endo*-**2b**	*p*-MeO	H	21.1	17
3	*endo*-**2c**	*m*-Me	H	7.03	5.6
4	**2d**	*p*-Me	*p*-Me	6.60	5.3
5	*endo*-**2e**	*p*-Me	H	6.13	4.9
6	**2f**	H	H	1.25	1.0
7	*endo*-**2g**	*m*-Cl	H	0.0973	0.078
8	*endo*-**2h**	*p*-Cl	H	0.0218	0.017
9	**2i**	*p*-Cl	*p*-Cl	0.0181	0.015
10	*endo*-**2j**	*p*-CF_3	H	0.00497	0.0040
11	*exo*-**2a**	H	*m*-MeO	0.736	0.59
12	*exo*-**2b**	H	*p*-MeO	4.05	3.2
13	*exo*-**2c**	H	*m*-Me	0.860	0.70
14	*exo*-**2e**	H	*p*-Me	1.47	1.2
15	*exo*-**2g**	H	*m*-Cl	0.415	0.33
16	*exo*-**2h**	H	*p*-Cl	0.484	0.39
17	*exo*-**2j**	H	*p*-CF_3	0.379	0.30

[a] The second-order rate constants *k* were obtained by dividing the pseudo-first-order rate constants k_{obs} by the concentration of BF_3.

dependency of *k* on *endo*-X is much higher than on *exo*-Y. Thus, the *endo*-*m*-MeO-**2a** brought about ca. 5600-fold faster rearrangement than the *endo*-*p*-CF_3-**2j** (runs 1 and 10). In sharp contrast, the *exo*-*p*-MeO-**2b** provided only ca. 11-fold acceleration compared with the *exo*-*p*-CF_3-**2j** (runs 12 and 17). It was also recognized that the *endo*/*exo*-disubstituted *p*,*p*-$(Me)_2$-**2d** and *p*,*p*-$(Cl)_2$-**2i** gave a rate constant comparable to that of the corresponding *endo*-monosubstituted *p*-Me-**2e** and *p*-Cl-**2h** (runs 4 and 5, 8 and 9), respectively. These clear *endo*-substituent effects can be taken as a decisive criterion for π-participation in the rate-determining step.[11]

Of particular interest is that the maximam rate constant was unusually attained by *endo*-*m*-MeO-**2a** rather than *endo*-*p*-MeO-**2b**. Though not large, similar reversed substituent effects were also found in a couple of *endo*-*m*/*p*-Me-substituted **2c** and **2e** (runs 3 and 5) and *endo*-*m*/*p*-Cl substituted **2g** and **2h** (runs 7 and 8), respectively. By contrast, the corresponding couples of *exo*-isomers showed the usual substituent effects as found for the *m*/*p*-MeO-, *m*/*p*-Me-, and *m*/*p*-Cl-substituted compounds (runs 11−16). These findings strongly indicate that the participation of *endo*-aryl group occurs both at the *ipso*-position and the *ortho*-position (*para*-position with respect to the *m*-substituted X).

Keeping this in mind, we attempted to correlate the log k_{rel}^{endo} with the combination of σ^{ipso} (σ_p^+ for *p*-X and σ_m for *m*-X) for *ipso*-participation and σ^{ortho} (σ_m for *p*-X and σ_p^+ for the *m*-X) for the *ortho*-participation, respectively. Thus, a sufficient regression was obtained (eq 1 and Figure 2) and revealed somewhat larger *ortho*-participation by judging from the percent contribution of σ^{ortho} (52%).[12]

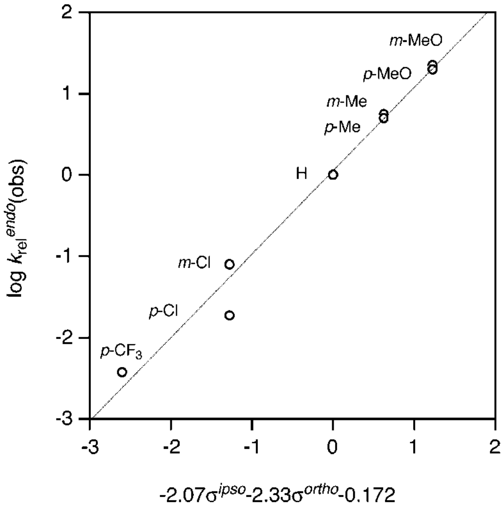


Figure 2. Plots of the observed log k_{rel}^{endo}(obs) vs the calculated log k_{rel}^{endo}(calc) according to the eq 1 for BF_3-catalyzed rearrangements of *endo*-isomers of **2a**−**c**,**e**,**g**,**h**,**j** and the unsabstituted **2f** in $CDCl_3$ at 30 °C.

On the other hand, the *exo*-isomers gave a fairly good Yukawa−Tsuno equation (eq 2).[13] The poor substituent effects for *exo*-isomers with a large *r* value of 0.90 is suggestive of the stabilization of the acid-activated carbonyl carbon by the long-range resonance contribution through the intervened cyclopropane ring.

$$\log k_{rel}^{endo} = -2.07\sigma^{ipso} - 2.33\sigma^{ortho} - 0.172 \quad (n = 8, R = 0.99) \quad (1)$$

$$\log k_{rel}^{exo} = -0.795(\sigma^0 + 0.904\Delta\,\bar{\sigma}_R^{+}) \ (n = 8, R = 0.97) \quad (2)$$

Mechanistically, the present kinetic substituent effects strongly insists that both the *ipso*- and *ortho*-carbons play a special role in the S_N2-like transition state as shown in Scheme 2. Such a transition state straightforwardly leads to the *ortho*-attacked arenium ion I and then to **3** by a rearomatization. Compared to the common S_E2-Ar reaction where the rate constants are typically correlated with σ^+ in the large and negative ρ values ranging between −3 to −13,[14] the rather low and negative ρ with σ^+_p and σ_m for the present reaction may be explained in terms of the highly charge-dispersed transition state. The crucial role of the π-aryl participation was firmly manifested by the fact that the displacement of *endo*-phenyl group of **2f** by a methyl group

---

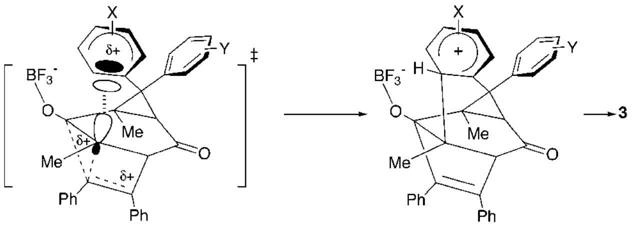
(11) (a) Muneyuki, R.; Tanida, H. *J. Am. Chem. Soc.* **1968**, *90*, 656. (b) Rachon, J.; Goedken, V.; Walborsky, H. M. *J. Org. Chem.* **1889**, *54*, 1006.

(12) Snedecor, G. W.; Cochran, W. G. *Statistical Methods*, 6th ed.; Iowa State University Press: Ames, 1967.

(13) Tsuno, Y.; Fujio, M. *Advances in Physical Organic Chemistry*; Bethell, D., Ed.; Academic Press: London, 1999; Vol 32, p 267.

(14) Isaacs, N. S. *Physical Organic Chemistry*; Longman Science & Technical: Essex, 1995; Chapter 10, p 473.

Scheme 2



I

Table 2. Rate Constants for BF_3-Catalyzed Rearrangements of **2f** in Various Solvents at 30 °C

solvent	E_T	k^a (10^3, M^{-1} s^{-1})	k_{rel}
1,2-dichloroethane	41.3	33.1	36
dichloromethane	40.7	19.7	21
chloroform-*d*	39.0	1.25	1.3
o-dichlorobenzene	38.0	8.54	9.2
fluorobenzene	37.0	2.67	2.8
chlorobenzene	36.8	1.84	2.0
benzene	34.3	0.930	1.0

[a] The k_2 were obtained by dividing the pseudo first-order rate constants k_{obs} by the concentration of BF_3.

resulted in the quantitative recovery of the **2f** even in 40 h reaction with or without 20 equiv of CH_3OH.

To gain further insight into the mechanistic features of the present rearrangement, we investigated the solvent effects on the rate of the reaction of parent **2f** in various less basic nonpolar and polar solvents. The obtained k_2, which was apt to moderately increase with the solvent polarity, was collected together with the polarity parameter[15] E_T (Table 2). The logarithmic rate constants, log k_2, were well-correlated by E_T except for only chloroform (eq 3). The solvent dependency certainly suggests the intervention of at least a polar transition state. However, despite the wide range of variation in solvent polarity [1,2-dichloroethane (E_T = 41.3) and benzene (34.3)], the rate acceleration amounts to only a factor of 36. The small solvent effects obviously reflect the delocalization of incipient carbocationic charge by participation of the *endo*-aromatic ring at the transition state. Incidentally, the significant lower deviation of chloroform from the regression line may be due, no doubt, to the intrinsic acidic nature of this solvent,[16] by which the possible hydrogen bonding to the carbonyl function of **2f** would somewhat impede the BF_3 complexation.

$$\log k_2 = 0.227E_T - 10.9\ (r = 0.97,\ n = 6) \qquad (3)$$

In conclusion, the most likely interpretation based on the present *endo*/*exo* kinetic substituent and solvent effect analyses is that the BF_3-catalyzed rearrangement of **2** proceeds via a rate-determining remote aryl-assisted transition state that leads to the 1,2-vinyl migration and the phenylene annulation.

Acknowledgment. We gratefully appreciate financial support by General Sekiyu Research & Development Assistance Foundation. This work was also supported by a Grant-in-Aid for Science Research on Priority Areas (no. 10650849) from the Ministry of Education, Culture, Sports, Science and Technology of Japanese Government.

Supporting Information Available: Spectral data of **2a−j** and **3f** and crystallographic data of **2f** and **3f**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0481986

---

(15) Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319.

(16) Gutmann et al. proposed the acceptor number *AN* as expressing the acidic properties of solvents based on the solvent-dependent ^{31}P NMR chemical shifts of triethylphosphine oxide. The acidity of chloroform (*AN* = 23.1) is stronger than 1,2-dichloroethane (16.7) and dichloromethane (20.4), being related to the hydrogen bonding interaction with the oxygen atom. See: (a) Gutmann, V. *Electrochem. Acta* **1976**, *21*, 661. (b) Parker, A. J.; Mayer, U.; Schmid, R.; Gutmann, V. *J. Org. Chem.* **1978**, *43*, 1843.