DOI: 10.1002/ejoc.200700916

Synthesis and Rearrangement of Dewar Benzenes Into Biaryls: Experimental Evidence for Conrotatory Ring Opening

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Dedicated to Zbyněk Janoušek on the occasion of his 60th birthday

Keywords: Dewar benzene / Biaryls / Alkynes / Hammett / Rearrangement

Rearrangement of aryl-substituted Dewar benzenes into the corresponding biaryls may serve as an alternative pathway for synthesis of sterically hindered biaryls. The kinetic data obtained from thermal rearrangements of Dewar benzenes provide experimental evidence for the proposed orbital-symmetry-controlled electrocyclic ring opening.

Introduction

Syntheses and rearrangements of strained carbocyclic substances have been fertile ground for the discovery of new reactions and compounds.[1,2] One of these compounds that has attracted considerable synthetic and theoretical interest is Dewar benzene (DB) − a benzene valence isomer.[3] Syntheses of the first Dewar benzenes were performed in the 1960s by a clever choice of conventional reactions and/or UV irradiation of suitable precursors; they became the first isolated valence-bond isomers of benzene.[4] Facile isomerization of DBs into their more stable isomers − benzenes − can be achieved cleanly and quantitatively under thermal or photochemical conditions. Soon after these reports, a remarkable trimerization reaction of 2-butyne in the presence of $AlCl_3$ for the preparation of hexamethyl[2.2.0]bicyclohexa-2,5-diene (hexamethyl-DB) in reasonable yields was discovered.[5] This method also opened a simple pathway to other DB derivatives.[6–9] Although DBs are in many instances stable compounds, they have found interesting practical applications only recently, for example, in the synthesis of oligophenylene macrocycles,[10] as a supramolecular protecting group,[11] in the synthesis of ladderanes, and high-content DB polymers.[12]

During our studies on the Cu- and Ni-mediated reaction of zirconacyclopentadienes with *ortho*-substituted phenylpropynoates, we observed the formation of DBs as side products in relatively high yields.[13]

Results and Discussion

The above-mentioned results brought us to an idea of whether potentially atropoisomeric biaryls could be alternatively prepared with the use of Dewar benzenes followed by rearrangement. Because it was reported that alkynes react with $AlCl_3$ to give a stable "cyclobutadiene–$AlCl_3$ complex",[14] we decided to check its reactivity with substituted phenylpropynoates. Initially, the reactions were carried out with the complexes of 2-butyne (**1a**) or 3-hexyne (**1b**) with 2-methoxynaphthylpropynoate (**2a**; Scheme 1). Addition of a solution of **2a** in a mixture of dichloromethane and DMSO[15] into a preformed red solution of the cyclobutadiene complex proceeded in both cases uneventfully to give corresponding DB **3aa** and **3ba** in good isolated yields of 63 and 69%, respectively.

Both products were stable at room temperature. After recrystallization of **3aa** from MeOH, single-crystal X-ray analysis unambiguously confirmed its DB skeleton (Figure 1). Encouraged by these results, diastereoselective formation of DB was also attempted. Chiral (–)-menthyl 2-methoxynaphthylpropynoate (**2b**) was taken into the reaction with **1a** according to the above-mentioned method and corresponding DB **3ab** was isolated in 45% yield as a 1:1 diastereoisomeric mixture, which indicates that no diastereoselective discrimination took place. Both diastereoisomers were separated by preparative HPLC (unfortunately, attempts to determine the configuration of the separated diastereoisomers were unsuccessful; crystallization did not

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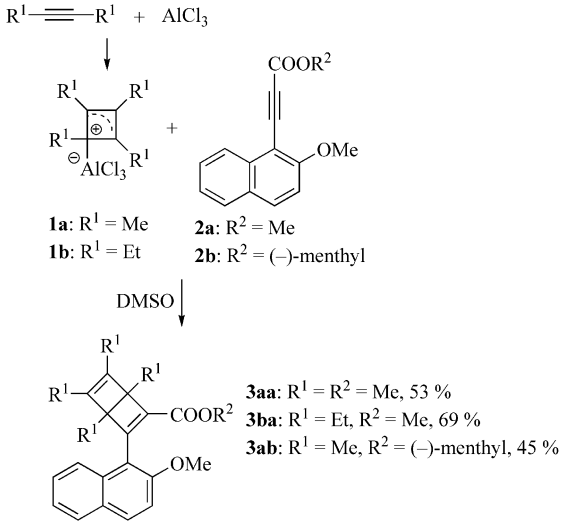


Scheme 1. Formation 2-methoxy-1-naphthyl-substituted Dewar benzenes **3**.

afford suitable crystals for X-ray analysis, and NMR spectroscopic analysis did not give any clear-cut data).

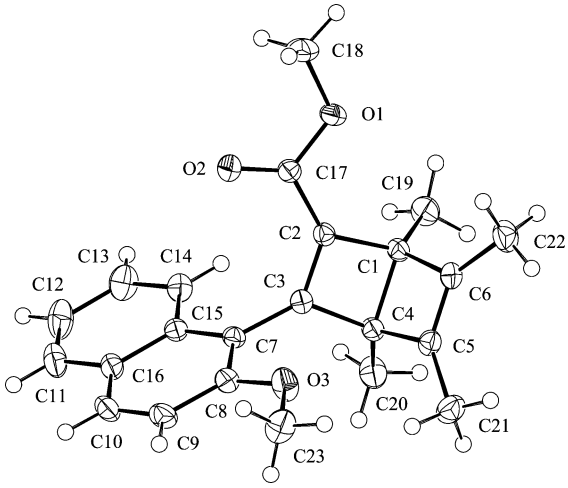
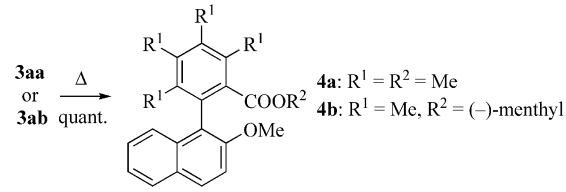


Figure 1. X-ray structure of **3aa**. Displacement parameters are shown at the 50% probability level.

With a set of DBs in hand, we decided to proceed with the rearrangement into the corresponding benzenes under thermal conditions (Scheme 2). Dewar benzene **3aa**, a solid and stable compound, was cleanly and quantitatively rearranged into corresponding benzene **4a** only after it was heated to its melting point (ca. >130 °C). Its structure was again unambiguously confirmed by single-crystal X-ray analysis (Figure 2). Also, enantiomerically pure diastereoisomer **3ab** was easily rearranged into corresponding biaryl **4b**; however, the stereochemical information introduced by the DB moiety was lost in the course of the reaction, which resulted in the formation of a 1:1 mixture of diastereoisomers. Whether this was caused by the formation of a highly distorted intermediate in which free rotation around the bond connecting the naphthyl moiety and the Dewar benzene backbone was allowed or by racemization of the formed arylnaphthalene remains, at the moment, unclear. Interestingly, attempts to rearrange DB **3aa** by transition-metal complexes, such as, $[IrCl(cod)]_2$, $[RhCl(CO)_2]_2$, $RhCl(PPh_3)_3$, and $PdCl_2(MeCN)_2$ (at 20 or 40 °C) did not take place, despite the fact that hexamethyl-DB could be rearranged into hexamethylbenzene at 20 °C.[16]



Scheme 2. Rearrangement of **3aa** and **3ab** into benzenes **4**.

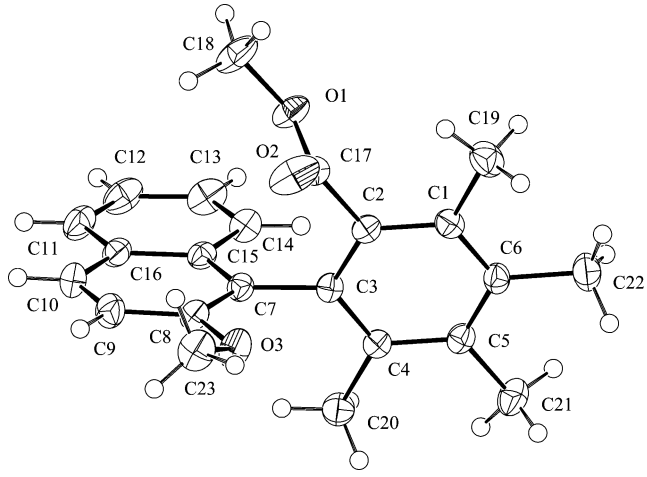
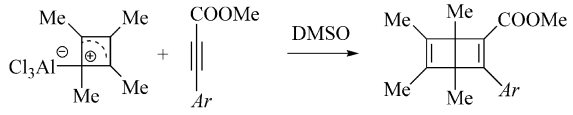


Figure 2. X-ray structure of **4a**. Displacement parameters are shown at the 50% probability level.

Next, our attention shifted to the reaction of the cyclobutadiene complex with *ortho*- and *para*-substituted phenylpropynoates. We assumed that the synthesis of a series of DBs with variously substituted benzene rings attached, followed by a study of substituent effects on their rearrangement could provide further insight into its reaction mechanism. The reaction was carried out under the above-mentioned conditions and the obtained results are presented in Table 1. In all cases, the reaction proceeded uneventfully and corresponding DBs **5a**–**l** were isolated in a broad range of yields (9–70%).

The rearrangements of *para*-phenyl-substituted DBs **5a**–**g** were carried out in DMSO at 135 °C in an NMR device to monitor the course of the reaction and to collect reliable data for calculation of rate constants. The results presented in Table 2 clearly show that the rate constants strongly depend on the nature of the substituent in the *para* position. The difference in the rate constants for DB with a strongly electron-donating substituent (OMe) and a strongly electron-accepting substituent (CN) is 6.5-fold. This indicates that electronic effects exerted by the *para* substituents are translated across the π system of the conjugated C–C bonds to the Dewar ring backbone and influence its stability. Quite importantly, a Hammett-type correlation with a good

Table 1. Formation of Dewar benzenes.

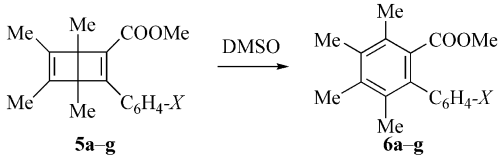


1a **5**

Propynoate *Ar*	Dewar benzene **5**	Isolated yield [%]
4-$MeOC_6H_4$	**5a**	49
4-MeC_6H_4	**5b**	53
C_6H_5	**5c**	70
4-ClC_6H_4	**5d**	50
4-$MeOOCC_6H_4$	**5e**	39
4-$CF_3C_6H_4$	**5f**	27
4-CNC_6H_4	**5g**	51
2-$MeOC_6H_4$	**5h**	50
2-MeC_6H_4	**5i**	70
2-ClC_6H_4	**5j**	37
2-$MeOOCC_6H_4$	**5k**	9
2-$CF_3C_6H_4$	**5l**	18

fit (R^2 = 0.987) was obtained between $\ln k_{exp}$ and the σ_p substituent constants with a slope of 1.79, which indicates a strong dependence on electronic effects (Figure 3).

Table 2. Rearrangement of Dewar benzenes **5** into benzenes **6**.



5a–g **6a–g**

Dewar benzene	*X*	Benzene **6**	k [s^{-1}] at 135.1 °C
5a	OMe	**6a**	0.44×10^{-4}
5b	Me	**6b**	0.63×10^{-4}
5c	H	**6c**	0.71×10^{-4}
5d	Cl	**6d**	1.03×10^{-4}
5e	COOMe	**6e**	1.70×10^{-4}
5f	CF_3	**6f**	1.72×10^{-4}
5g	CN	**6g**	2.86×10^{-4}

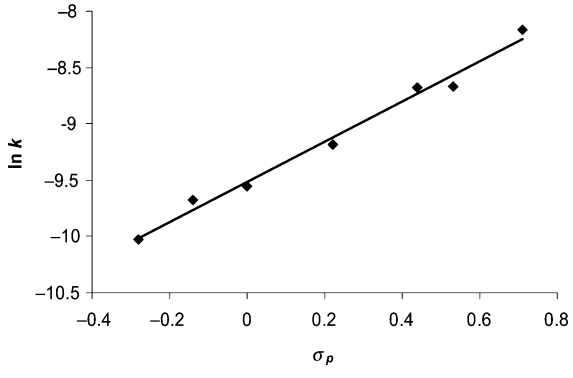


Figure 3. Correlation of *para*-σ Hammett constants with ln of rearrangement rate constants k.

As it has been proposed that electrocyclic ring opening of DB benzene is controlled by orbital symmetry, it is reasonable to assume that the substituent effects on the course of the reaction could be similar to those affecting the electrocyclic ring opening of cyclobutenes. It has been shown that substituents attached to the double bond of the cyclobutene ring affect the reaction rate depending on its electronic properties.[17] Thus electron-donating substituents increase the activation energy and thus decrease the reaction rate, whereas electron-accepting substituents exert the opposite effect. In this regard, the results presented in Table 2 follow the same trend: electron-donating substituents such as Me and MeO decrease the reaction rate of the rearrangement, whereas electron-accepting substituents increase it (with respect to **5c**, which was used as a standard).

The reaction mechanism of the rearrangement of DB into benzene has for a long time been a target of many studies and has led to the universal assumption that electrocyclic ring opening of DB must follow an orbital symmetry-forbidden disrotatory path. However, contrary to this assumption, recent calculations indicate that conrotatory opening of DB to intermediate *cis*,*cis*,*trans*-cyclohexatriene, which then rearranges into benzene, proceeds through a slightly *lower* energy transition state than direct disrotatory opening. Thus, despite formidable ring constraints and the formation of an extraordinarily strained intermediate, orbital symmetry control triumphs in a case long maintained as a paradigm for a symmetry-forbidden reaction.[18]

In this paper,[18] two modes of electrocyclic ring opening of DB into benzene were studied: the commonly accepted C_{2v} transition state for the disrotatory pathway was found to be a second-order saddle point. Instead, a C_s true transition state, positioned 3.7 kcal mol^{-1} below the C_{2v} saddle point, was identified, as expected for the thermally allowed conrotatory electrocyclic ring opening of DB. Later, the disrotatory and conrotatory pathway were studied at the CASSCF(10,10) level.[19]

True transition states (with one imaginary frequency) were found for both modes of the ring-opening reaction; the conrotatory transition state was 6.6 kcal mol^{-1} below the disrotatory transition state. Furthermore, an IRC calculation showed that the conrotatory transition state connects DB directly with benzene without passing through the *cis*,*cis*,*trans*-cyclohexa-1,3,5-triene. In another work,[20] it was found that the potential energy surface of hexamethyl-DB is slightly different from that of DB. The ring opening of hexamethyl-DB leads to the strained *trans* conformation of hexamethylbenzene.

To shed further light on the reaction mechanism of the rearrangement, calculations were carried out by using the Gaussian 03 software package and DFT calculations were performed by using the Becke3LYP functional with the 6-311+G(d,p) basis set. A conrotatory transition state was found for all derivatives. The relative energies for the calculated structures and the free energies are listed in Table 3. The calculated free energies of activation can be compared with the experimentally obtained value of $\Delta G^{\#}$ from the Eyring equation $\Delta G^{\#} = RT[23.76 - \ln(k/T)]$. The calculated free energies of activation are slightly lower than the experimental (up to 0.9 kcal mol^{-1}) but the change in the experimental free energy depending on the substituent in the *para*

position is very well reproduced by the theoretical calculations. The correlation between the calculated and experimental free energies of activation is shown in Figure 4.

Table 3. Calculated relative energies (referenced to biaryl derivatives, $E_{rel} = 0$), energies of activation in vacuo and in DMSO, dipole moments and calculated and experimental free energies of activation for the rearrangement of Dewar benzene derivatives.[a]

DB	E_{Rel} DB	E_{Rel} TS	$\Delta E^{\#}$[b]	$\Delta\mu^{\#}$	$\Delta E^{\#}$[c]	$\Delta G^{\#}$[c]	$\Delta G^{\#}$ exp.
6a	54.28	87.44	33.17	0.85	32.29	31.89	32.28
6b	54.95	87.66	32.71	1.20	31.89	31.57	32.00
6c	55.39	87.77	32.38	0.90	31.42	31.03	31.90
6d	55.24	87.59	32.35	0.13	31.04	30.74	31.60
6e	55.73	87.47	31.74	–1.32	30.50	30.27	31.19
6f	55.83	87.34	31.72	–0.26	30.35	30.37	31.18
6g	55.64	87.34	31.70	–0.42	30.02	29.83	30.77

[a] All energies in kcal mol^{-1}, dipole moments in Debye. [b] In vacuum. [c] In DMSO.

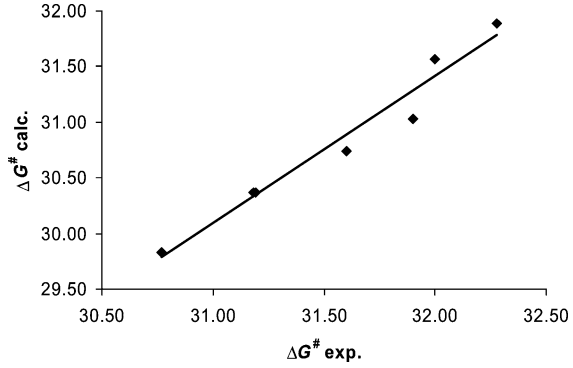


Figure 4. Correlation between calculated and experimental free energies of activation of Dewar benzene derivatives rearrangement.

Conclusions

The obtained results could be summarized into the following points. Firstly, the aryl-substituted DBs and their easy thermal rearrangement into the corresponding benzenes may serve as an alternative pathway for synthesis of sterically hindered biaryls. Secondly, the data obtained from thermal rearrangements of DBs provide further experimental evidence for the proposed orbital-symmetry-controlled electrocyclic ring opening. Thirdly, the theoretical calculations concerning the transition states and the thermochemical data are in good agreement with values obtained from the experimental measurements, and they support the proposed conrotatory Dewar benzene ring opening.

Experimental Section

A Typical Procedure for the Preparation of Dewar Benzenes: A solution of 2-butyne (196 μL, 2.5 mmol) was added to a stirred suspension of powdered anhydrous $AlCl_3$ (166 mg, 1.25 mmol) in dry dichloromethane (3 mL) at –10 °C. To the resulting complex was added the substituted arylpropynoate (1.25 mmol) at –15 °C. After stirring for 1 h at –15 °C, DMSO (450 μL) was added. The mixture was poured onto crushed ice and extracted with hexane (3 × 10 mL). The combined organic layer was dried with $MgSO_4$. The solvent was evaporated, and column chromatography afforded the desired products.

Supporting Information (see footnote on the first page of this article): Experimental details, kinetic measurements, and spectral and crystallographic data.

Acknowledgments

This project was supported by the Centre for New Antivirals and Antineoplastics (project No. 1M0508) and a project from the Ministry of Education of the Czech Republic (MSM0021620857).

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Received: September 27, 2007
Published Online: November 12, 2007

