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Intramolecular Aromatic 1,5-Hydrogen Transfer in Free Radical Reactions III. Reactivity of Diaryl Ketones, Ethers, Thioethers, Sulfoxydes, and Sulfones. An Experimental and Theoretical Study

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ABSTRACT

Experiments show that free radical hydrogen shift is significant in the Pschorr cyclization of diphenyl ethers (X = O) and thioethers (X = S) and does not take place with sufoxides (X = SO) and sulfones (X = SO_2). DFT calculations of the product ratios, activation energies, rate constants for H-transfers, and ring-closings at the UB3PW91/6-31G(d,p) level are in excellent agreement with the experimental results reported here and elsewhere in the literature.

After a century of Pschorr chemistry, the free radical aromatic hydrogen shift was first clearly recognized in our attempt to use the Pschorr cyclization for the preparation of a substituted fluorenone.[1] It was unexpected to find that the chemistry of the benzophenone radical system is dominated by intramolecular hydrogen transfer as demonstrated by the dual products formed in Pschorr cyclization, the Sandmeyer reaction, and hydro-, hydroxy-, and iododediazoniation reactions.[2] The estimated rate of the hydrogen shift was 10^6–10^7 s^{-1}. Subsequently, we have shown that the rearrangement can be initiated by photolysis or by tin reduction of an iodobenzophenone and it can be terminated by reaction with aromatic solvents.[3] Molecular orbital calculations established the activation free energy for hydrogen transfer at 8.5 kcal and the estimated rate of the hydrogen shift was in good agreement with the experiments.[4]

Recently, several groups reported on the observation of analogous hydrogen migrations.[5] Notable among these is the elegant and detailed study of Hanson and his group,[6] confirming the hydrogen translocation rate at 1.2×10^6 s^{-1}.

Most of these studies were concentrated on the substituted benzophenone system. One could speculate that the conjugation and electronic effect of the carbonyl is essential to this rearrangement and therefore the all-aromatic hydrogen shift is limited to benzophenones.

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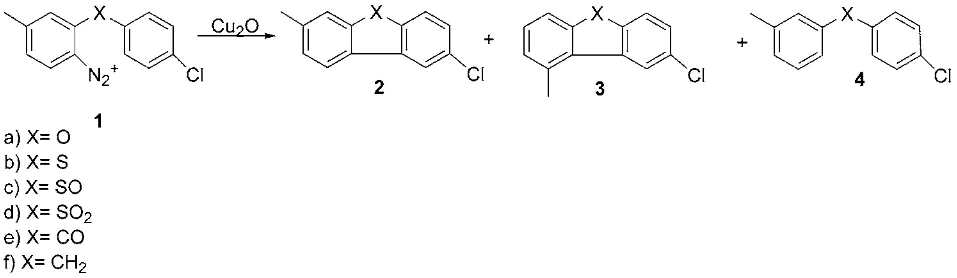
Scheme 1



In this paper we investigate the generality of this phenomenon, examining the role of the bridge between the two interacting aromatic systems. We report here the results of our experimental and theoretical study on the chemistry of diaryl ethers, -thioethers, -sulfoxides, and -sulfones, in comparison with benzophenones.

The copper-catalyzed Pschorr cylicization was used to evaluate the extent of free radical hydrogen migration operating in a system.[7] Since the reactions were carried out in water, the coating of the catalyst by the precipitating product prevented the completion of the reaction. When isopropyl alcohol or *tert*-butyl alcohol was used as a cosolvent, hydrogen transfer from the solvent became the dominant pathway, generating **4** as the major product. Addition of Celite to the solution of **1**[8] to physically adsorb the precipitating product resulted in complete reaction in a few hours.[9] As is summarized in Table 1, in the ether series a third of the product was generated by rearrangement (**3a**), while with the thioethers only 10% rearrangement (**3b**) was observed.

Pschorr cyclization with the corresponding sulfoxide **1c**[10] generated a mixture of sulfide (**2b**), sulfoxide (**2c**), and sulfone (**2d**), all derived from the direct ring closure product **2c** by a disproportionation process. Only direct ring closure to **2d** was observed in the reaction of diazo sulfone **1d.**[11] There was no indication of hydrogen shift in the last two systems. In all these reactions, about 25% reduction product **4a**, **4b**, **4c**, or **4d** accompanied the ring closure.

The diphenylmethane system (**1f**) was also tested but in this case no ring closure was observed and the dominant product was **4f**, probably the result of a favorable intramolecular hydrogen shift from the dibenzylic methylene group.

The mechanism of the hydrogen transfer and the various rate constants considered for the theoretical calculations are outlined in Scheme 2.

It is clear from Table 1 that the experimentally observed ratios of products **2a**, **3a** and **2b**, **3b** are in good agreement with the calculated ratios. Furthermore, in the case of sulfoxide **1c** and sulfone **1d**, where hydrogen transfer was not observed, calculations clearly favor rapid ring closure.

The DFT calculations used the B3PW91 hybrid functional. The details of the calculations are the same as described in our previous paper[4] except that the Gaussian 98 program was used. This method combines Becke's 3-parameter functional[12] with the nonlocal correlation provided by the Perdew−Wang expression.[13] According to recent reports,[14] only hybrid functionals can provide an accurate description for the systems with hydrogen bonds. Since the H···C interaction that occurs along the reaction path might bear some resemblance to an H-bonding interaction, we deemed

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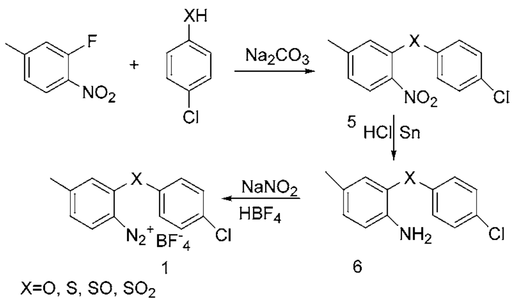
(7) The reactions were monitored and the product ratios were determined by liquid chromatography. The isolated products were identified by H^1 and ^{13}C NMR and mass spectometry.

(8) Standard synthetic methods were used to prepare the starting diazonium fluoroborates utilizing the following scheme:



(9) Typical experimental procedure for Pschorr cyclization is as follows: To a solution of 310 mg of diazonium fluoborate **1a** in 100 mL of 1 N sulfuric acid was added 1 g of Celite and the mixture was purged with nitrogen. Powdered cuprous oxide was then added and the mixture was stirred for several hours. After methylene chloride was added, the mixture was filtered, the layers were separated, the organic layer was dried, concentrated, and analyzed by liquid chromatography, and NMR Pure substrates were isolated by preparative TLC, utilizing silica gel plates.

(10) Sulfoxyde **1c** was prepared by the scheme shown in ref 8 except the nitrosufide **5** (X = S) was oxidixed to the corresponding sufoxyde **5** (X = SO) with Mg perphthalate in CH_2Cl_2, MeOH mixture.

(11) The sulfone **1d** was also prepared as shown in ref 8, but the nitrosufide intermediate **5** (X = S) was oxidized to the corresponding sufone **5** (X = SO_2) with *m*-chloro-perbenzoic acid in CH_2Cl_2.

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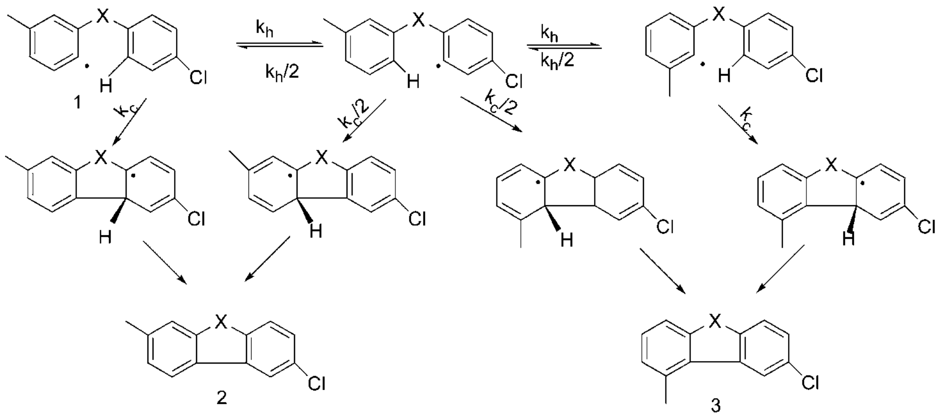
Scheme 2



it appropriate to use this type of functional.[15] B3PW91 eliminates the large spin contamination generally encountered with unrestricted Hartree−Fock (UHF) wave functions.[15] Stable structures were fully optimized and transition states located at the UB3PW91/6-31G(p,d) level with use of the GAUSSIAN 98 series of programs.[16] Standard integration grids were employed. We calculated the vibrational frequencies of all stationary points to characterize them and obtained the zero-point vibrational energies (ZPVE) and ΔH, ΔS, and ΔG values. These calculations used the harmonic oscillator, rigid rotor, and ideal gas approximations at room temperature (298.15 K) and 1 atm of pressure.

All calculations were performed on the parent system, which does not have methyl or chloro substituents.

The calculation of the rate constants and kinetic analyses depends on several assumptions. Specific rate constants, k, are calculated from the $\Delta G^{\ddagger}$ values, using the expression $(k_BT/h)\exp(-\Delta G^{\ddagger}/RT)$, which comes from absolute rate theory. In this expression, k_B is the Boltzmann constant, and h is Planck's constant. At 298 K $(k_BT/h) = 6.21 \times 10^{12}$. Since the TS values for H-transfer are planar (except for the sulfone, see below), there are ***two*** equivalent TS's for H-transfer, corresponding to transfer of an H-atom from either of the ortho positions of the ring. Since the TS for ring closure is *not* planar, there are ***four*** equivalent TS values for ring closure as C−C bond formation can be either above or below the ring at each of the two ortho positions. We multiplied the rate constants calculated as described above by the appropriate statistical factor (2 for H-transfer and 4 for ring closure) to obtain the values given in Table 1.

The product ratios are calculated by using the following assumptions (see Scheme 2 for definitions of the rate constants):

(1) The meta-substituent does not affect the $\Delta G^{\ddagger}$ values for H-transfer or ring closure. Thus, all H-transfers have the same k_h. Due to statistics this is $k_h/2$ for each of the two ortho H's.

(2) The unrearranged and rearranged radicals ring-close exclusively to product **2** or **3**, respectively, with identical rate constants of k_c.

(3) The rearranged radical ring-closes with identical rate constants of $k_c/2$ to each of the products **2** and **3**.

(4) Once the ring is closed, it does not reopen. Thus the product ratio (**2**/**3**) is determined upon ring closure. There is no experimental evidence for this, but ring opening should be endoergonic.

(5) H-abstraction is not competitive with the H-transfer and ring closure. In the cases where this last assumption does not hold (see the experimental results), the abstraction is assumed to occur with equal facility from the unrearranged and rearranged radicals.

Table 1. Experimental and Calculated Product Ratios (**2**/**3**) and Calculated Activation Parameters (kcal/mol) and Rate Constants (s^{-1}) at 298 K

	ratio **2**:**3**		H-transfer			ring closure		
reacting system	exptl	calcd	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	k_h	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	k_c
ether (**1a**)	66:33	66:34	6.7	8.8	4.8×10^6	8.0	10.1	1.1×10^6
thioether (**1b**)	90:10	95:5	6.2	8.7	5.0×10^6	5.7	8.3	2.0×10^7
sulfoxide (**1c**)	no rearr	>99:<1	11.8	13.4	1.9×10^3	7.9	9.9	1.5×10^6
sulfone (**1d**)	no rearr	>99:<1	13.3	14.9	1.7×10^2	8.5	10.7	3.8×10^6
ketone (**1e**)	55:45[a]	55:45[b]	6.7	8.5	7.9×10^6	8.4	10.2	8.4×10^5
diphenylmethane (**1f**)	no rearr[c]	67:33	8.7	10.7	2.0×10^5	8.6	11.5	1.0×10^5

[a] See ref 2. [b] See ref 4. [c] No ring closure was observed.

By using these assumptions, the product fraction of **2** becomes $(k_c + k_h/2)/(k_c + k_h)$, where the numerator represents the sum of the rate constants for formation of **2** from unrearranged and rearranged radicals, while the denominator represents the sum of all reactions emanating from the original radical. This expression becomes $(1 + k_h/2k_c)/(1 + k_h/k_c)$ upon division of numerator and denominator by k_c. The calculated product ratios are collected with the rate constants in Table 1.

The calculated product ratios are in remarkably good agreement with the experimental observations. The calculated value for k_c for the benzophenone radical (8.4×10^5 L/s × mol) is in excellent agreement with our previous estimate and with the more precise value ($8.0 \pm 0.9 \times 10^5$ L/s × mol) reported by Hanson.[6] However, the corresponding values for k_h ($7.9 \times 10^6 \times$ and $1.2 \pm 0.2 \times 10^6$ L/s × mol) differ by a somewhat larger amount. Use of the Hanson's rate constants would lead to a predicted product ratio (**2e**/**3e**) of 70:30 rather than 55:45.

The three compounds for which H-transfer is predicted and observed all have similar activation energies for H-transfer (as does diphenylmethane for which there are no experimental data). On the other hand, the sulfone and sulfoxide both have significantly higher activation energies for this process. The higher barriers to H-transfer are likely due to a combination of two related factors: (1) the C−S−C angles in the ground states of these species are more acute than in the others, requiring a greater distortion to achieve a planar transition state for H-transfer. In fact, the TS for H-transfer in the sulfone is not planar. (2) The C−H···O interactions which favor the transition state of the benzophenone series preferentially stabilize the ground states of the sulfone and sulfoxide. The C−H···O distances calculated for these species are consistent with other calculated[17] and observed[18] C−H···O interactions.

The extent of H transfer depends on the ratio of the rates for H-transfer and ring closure. Since the rates for ring closure are much less sensitive to the structural variations studied here than those for H-transfer, this ratio is more sensitive to the H-transfer rate. H-transfer must occur through a planar (or nearly so) transition state. Those factors that stabilize such a structure such as C−H···O interactions and relatively unstrained C−X−C angles in the planar structure will favor H-transfer.

The conclusion of this paper is that free radical hydrogen shift takes place readily with aromatic ketones, ethers, and sufides and is expected to proceed with similar ease in other aromatic systems where the coplanarity required for the transition is not restrained. Therefore, we can expect that hydrogen transfer will participate in the free radical chemistry of a variety of aromatic systems.

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Supporting Information Available: Spectral data and structure correlation for relevant compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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