J. Am. Chem. Soc. **1995**, *117*, 5425–5426

Intramolecular Aromatic 1,5-Hydrogen Transfer in Free Radical Reactions. 1. Unprecedented Rearrangements in Pschorr Cyclization, Sandmeyer, and Hydro-, Hydroxy-, and Iododediazoniation Reactions

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Received February 13, 1995

Radical-induced hydrogen migration is very common when the migrating hydrogen originates from an aliphatic carbon or from a heteroatom. Normally, the initially formed less stable radical rearranges to a more stable one.[1,2] On the other hand, rearrangements where the migrating hydrogen originates from an aromatic carbon have not been generally recognized.[3] It is commonly assumed that aromatic hydrogens cannot be abstracted by radicals. In fact, benzene is an often used solvent in free radical reactions, because it is a poor hydrogen donor.

In this paper we report that the chemistry of benzophenone radicals, generated from the corresponding diazonium salts, is dominated by very rapid 1,5-hydrogen transfer leading to a partial equilibrium between the radicals. The results are summarized in Table 1, following the rationale depicted in Scheme 1.

Pschorr cyclization[4] of **1a**,[5] initiated by cuprous ions,[4a] ultraviolet light,[6] or cathodic reduction,[7] produced two isomeric fluorenones **2a** and **3a** in nearly equal amounts[8] (entries 1–3). The most obvious explanation is that the initially formed radical **A** rearranged to radicals **B** and **C** by 1,5-hydrogen transfers and that the products were derived from these three radicals.

The origin of the migrating hydrogen was clearly shown by the photolysis of pentadeuterio diazonium salt **7** in water. Rearrangement in this case was minimized by the deuterium isotope effect, yielding fluorenones **8** and **9** in a 96:4 ratio. The structure of **9**, however, unequivocally established that deuterium migration took place from ring B to ring A. In addition to **9**, tetradeuteriofluorenone **10**, derivable from a pentadeuterio analog of radical **C**, was also detected.[9] A crossover experiment, utilizing a 9:1 mixture of **7** and **1a**, showed no indication of intermolecular label distribution. These results strongly support the intramolecular 1,5-hydrogen transfer mechanism, as depicted in Scheme 1.

Table 1. Reaction of Diazonium Salts

entry	substance	reactn	products	ratio[8]
1	**1a**	$h\nu$, H_2O	**2a:3a**	55:45
2	**1a**	Cu_2O, 0.1 N H_2SO_4	**2a:3a**	55:45
3	**1a**	Hg anode, 0.1 N H_2SO_4	**2a:3a**	55:45
4	**7**	$h\nu$, H_2O	**8:9:10**	96:4:trace[9]
5	**1a**	$h\nu$, CH_3OH	**4a**	
6	**1a**	$h\nu$, CD_3OD	**4b:5b:6b**	50:50:trace[9]
7	**1a**	Cu_2O, CD_3OD	**4b:5b**	50:50[9]
8	**1b**	$h\nu$, H_2O	**2b:3b**	55:45
9	**1c**	$h\nu$, CD_3OD	**4c:5c**	50:50[9]
10	**1a**	CuCl, CH_3CN	**4d:5d**	76:24[11]
11	**1a**	CuCN, CH_3CN	**4g:5g:6g**	73:22:5[11]
12	**1a**	KI + I_2, acetone	**4e:5e:6e**	64:30:6[11]
13	**1a**	KI + I_2, H_2O	**4e**	
14	**1a**	Cu_2O + $Cu(NO_2)_2$, H_2O	**4f:5f**	80:20[11]
15	**11a**	$h\nu$, H_2O	**13a**	
16	**11b**	$h\nu$, H_2O	**13b**	

There are numerous reactions of diazonium salts based on atom transfer to the initially formed radical.[4] The most common of these is the hydrodediazoniation reaction where hydrogen is transferred to the radical. Photodecomposition of diazonium fluoroborate **1a** in methanol yielded benzophenone **4a** as the main product, while in CD_3OD, deuterated benzophenones **4b, 5b**, and **6b** were generated (entries 5 and 6). This attests that intramolecular hydrogen transfer can effectively compete with hydrogen or deuterium abstraction from the solvent.

Another popular atom transfer is the Sandmeyer reaction,[10] using cuprous salts to initiate the reaction. Hydrogen migration also took place with **1a** under Sandmeyer conditions, generating the isomeric chloro compounds **4d** and **5d**[11] (entry 10) and cyano benzophenones **4g, 5g**, and **6g** (entry 11).

As shown in entry 12, the iododediazoniation reaction[12] in acetone produced three isomeric iodobenzophenones **4e, 5e**, and **6e.**[11] In contrast to this, the same reaction when carried out in water, at various concentrations, produced only the unrearranged iodo compound **4e** (entry 13).

The presence of **6b, 6e,** and **6g** clearly shows the existence of radical **C** and indicates that there is a partial equilibration between radicals **A**, **B**, and **C**.

The copper-catalyzed phenol synthesis, introduced by Cohen,[13] also yielded two isomeric phenols, **4f** and **5f** (entry 14). In addition, other aqueous reactions of **1a** produced the same mixture of phenols as byproducts.

As expected, the mode of radical generation had no effect on hydrogen transfer, as various initiation methods produced similar mixtures (entries 1–3). Similarly, the methyl and bromine substituents of **1a** did not alter the course of the reaction because **1b** and **1c** reacted similarly (entries 8 and 9). On the other hand, ring substituents which stabilize intermediate **12** accelerated the ring closure, thereby minimizing the hydrogen migration. Thus, photolysis of **11a** and **11b** yielded predominantly the direct cyclization product **13** (entries 15 and 16, Scheme 3).

The iododediazoniation reaction offered an opportunity to clock the rate constant of the 1,5-hydrogen shift.[14] We observed that the ratio of products **4e** and **5e** is inversely proportional to the iodine concentration. Since at low iodine concentration the hydrogen shift competes effectively with the diffusion-controlled iodination, it must be an equally rapid transformation. From

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[1] Beckwith, A. L.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, p 251.

[2] For a recent example, see: Curran, D. P.; Somayajulu, K. V.; Yu, H. *Tetrahedron Lett.* **1992**, *33*, 2295.

[3] (a) "Intramolecular chain transfer" (i.e., aromatic 1,5-hydrogen shift) was first observed by DeTar during the low-yield conversion of a diazonium salt (similar to **1d**) to two isomeric chlorobenzophenones in CCl_4 and NaOH. DeTar, D. F.; Relyea, D. J. *J. Am. Chem. Soc.* **1956**, *78*, 4302. (b) 1,5-Hydrogen transfer was reported in the high-temperature gas phase reaction of diaryl ether radicals. Cadogan, J. I. G.; Hutchinson, H. S.; McNab, H. *Tetrahedron* **1992**, *48*, 7747.

[4] (a) For review, see: Abramovitch, R. A. *Adv. Free Radical Chem.* Heyden and Sons: London, 1967; Vol. 2, p 87. (b) For a review on radical reactions of arenediazonium ions, see: Galli, C. *Chem. Rev.* **1988**, *88*, 765.

[5] Aminobenzophenones were prepared by a modified procedure of Sugasawa: (a) Saskura, K ; Terui, Y.; Sugasawa, T. *Chem. Pharm. Bull.* **1985**, *33*, 1836. (b) Douglas, A. W.; Abramson, N. L.; Houpis, I. N.; Karady, S.; Molina, A.; Xavier, L. C.; Yasuda, N. *Tetrahedron Lett.* **1994**, 35, 6807.

[6] Kyba, E. P.; Liu S.; Chockalingam, K.; Reddy, B. R. *J. Org. Chem.* **1988**, *53*, 3513. Pyrex equipment was used without photosensitizer.

[7] Gadallah, F. F.; Cantu A. A.; Elofson, R. M. *J. Org. Chem.* **1973**, *38*, 2386.

[8] The ratios of isomeric products were determined by HPLC assay.

[9] Estimation was based on ^{13}C intensities of normal vs. isotopically shifted signals.

[10] Kochi, J. K. *J. Am. Chem. Soc.* **1957**, *79*, 2942.

[11] Determined by GC/MS, using total ion integration. Fragmentation patterns were as expected.

[12] Abeywickrema, A. N.; Beckwith, A. J. *J. Org. Chem.* **1987**, *52*, 2568.

[13] Cohen, T.; Dietz, A. G.; Miser, J. R. *J. Org. Chem.* **1977**, *42*, 2053.

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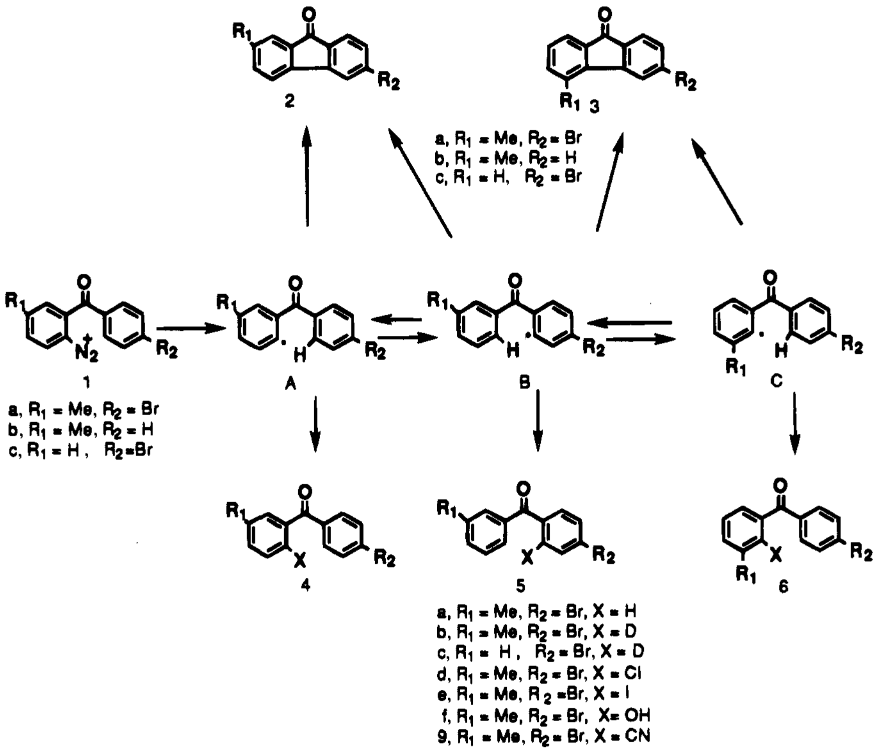
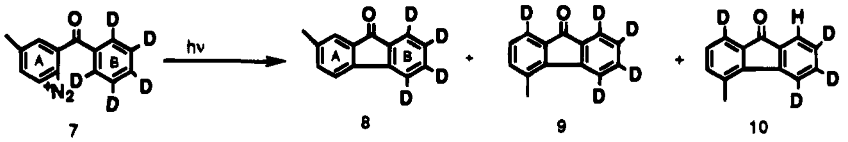
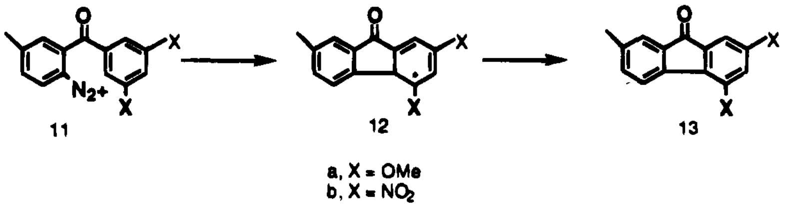
Scheme 1



Scheme 2



Scheme 3



the ratio of **4e**/**5e**, using the method and iodination rate constant of Abeywickrema and Beckwith,[12] we estimate the rate constant for the 1,5-hydrogen migration k_r to be 10^6-10^7 s^{-1}.

We suspect that the all-aromatic 1,5-hydrogen transfer is a general phenomenon which plays a part in many aromatic radical transformations. It is surprising that, after a century of diazonium chemistry, this simple rearrangement has not been recognized. Future research will reveal the significance of this, in other free radical reactions.

Acknowledgment. We thank Professor J. K. Kochi for his encouragement and many useful suggestions. We are also grateful to Drs. J. Y. Chung, R. J. Cvetovitch, G. H. Ho, W. Leonard, and N. Yasuda of Process Research for stimulating discussions, Mrs. D. Zink for exact mass measurements, and Dr. M. Baum for NMR studies.

Supplementary Material Available: Experimental procedures including ^{13}C NMR chemical shift assignments (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(14) The steady-state expression of k_r/k_I = (5e) × (I_2)/(4e) and the absolute rate constant $k_I = 5 \times 10^9$ M^{-1} s^{-1} (iodination of analogously generated aryl radical in acetone at 20 °C)[12] were used. Since iodination is a diffusion-controlled reaction, the actual concentration of I_2 should be lower than theory and therefore the calculated rate constant should be considered as an upper limit.