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Phototransposition Reactions of Methyl-Substituted Benzotrifluorides: Proof of the Role of Trifluoromethyl-Substituted Carbon

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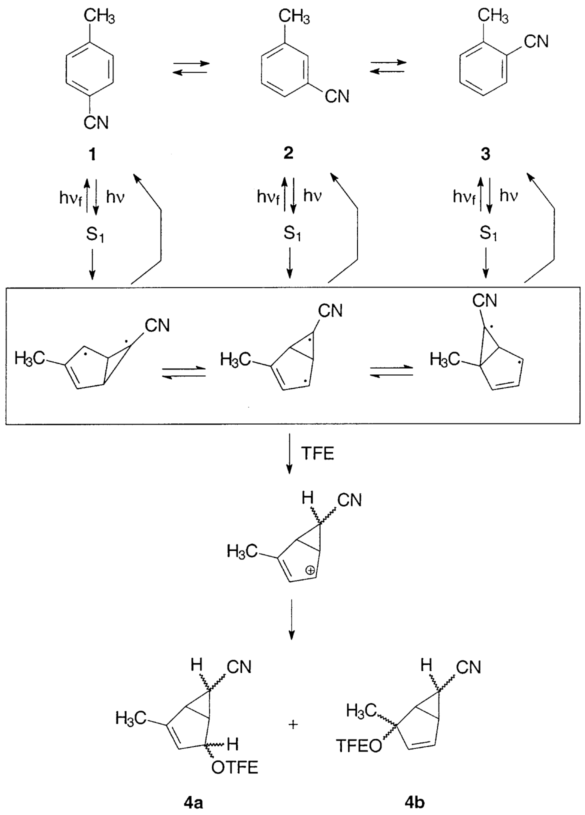
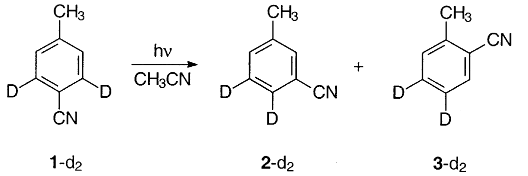
Abstract: Irradiation in acetonitrile of any one of the six isomers of dimethylbenzotrifluoride **8** resulted in efficient photoisomerization to the others. The dominant processes in these phototransposition reactions divides the isomers into two triads. The first consists of **8**-2,6 (2,6-dimethylbenzotrifluoride), **8**-2,3, and **8**-3,4; the second consists of **8**-3,5, **8**-2,4, and **8**-2,5. Moreover, irradiation of 2,6-dideuterio-4-methylbenzotrifluoride **5**-d_2 resulted in formation of 5,6-dideuterio-3-methylbenzotrifluoride **6**-d_2. These observations demonstrate that it is the trifluoromethyl-substituted carbon that is the migratory one in these reactions.

Recently, we have published a set of papers[1−4] on the phototransposition reactions of substituted benzenes and the photoaddition of 2,2,2-trifluoroethanol (TFE) to the same isomers. The three methylbenzonitriles **1** (para), **2** (meta), and **3** (ortho) were examined the most extensively.[1] The results are summarized in Scheme 1.

Irradiation in acetonitrile of either **1**, **2**, or **3** results in formation of the other two isomers, Scheme 1, although with quite different efficiencies (relative reactivity para/meta/ortho = 32:4:1). The mechanism proposed for these excited singlet-state reactions involved formation of bicyclo[3.1.0]hex-3-ene-2,6-diyl singlet biradicals/zwitterions, which allows the cyano-substituted carbon to migrate around the periphery of the other five carbons and collapse to any of the three isomers. The fact that the cyano-subsituted carbon was the critical one in these phototransposition reactions was demonstrated by two different experiments. First, as also shown in Scheme 1, irradiation of the para and meta isomers in TFE resulted in alcohol addition. The products formed, 6-cyanobicyclo-[3.1.0]hex-3-en-1-yl derivatives **4a** and **4b**, all resulted from protonation by TFE on the cyano-substituted carbon. Six of the eight possible regio- and stereoisomers were obtained, the missing ones being those with both the cyano and TFE groups endo. No phototransposition was observed in TFE. Second, irradiation of **1**-d_2, which has all the carbons labeled with a substitutent, resulted in **2**-d_2 and **3**-d_2, specifically labeled as in eq 1.[1] Other

SCHEME 1. Proposed Mechanism for the Phototransposition in Acetonitrile and the Photoaddition in TFE of the Methybenzonitriles





(1)

deuterated isomers would be obtained if carbons other than the cyano-substituted one were involved in the rearrangement. Because these reactions are providing fundamental information about changes in charge distribution and geometry that occur on excitation of substituted benzenes to S_1, we completed a survey of other substitutents.[4] In general, electron-withdrawing groups are required to make the phototransposition efficient. The methylbenzotrifluorides **5**, **6,** and **7** are particularly interesting for two reasons. First, all three reach a photostationary state composition of ortho/meta/para = 7:32:61 that is essentially the reverse of that of the methylbenzonitriles (ortho/meta/para = 77:20:3).[1] Second, they reach this photostationary state about 10 times faster than 4-methylbenzonitrile. We inferred from these results that, by analogy to the nitrile substi-

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[1] MacLeod, P. J.; Pincock, A. L.; Pincock, J. A.; Thompson, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 6443−6450.

[2] Foster, J.; Pincock, A. L.; Pincock, J. A.; Thompson, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 13354−13361.

[3] Foster, J.; Pincock, A. L.; Pincock, J. A.; Rifai, S.; Thompson, K. A. *Can. J. Chem.* **2000**, *78*, 1019−1029.

[4] Howell, N.; Pincock, J. A.; Stefanova, R. *J. Org. Chem.* **2000**, *65*, 6173−6178.

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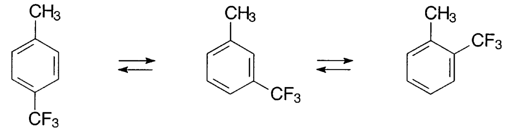
TABLE 1. Photolysis of Dimethylbenzotrifluorides 8 in Acetonitrile

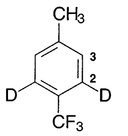
isomer	time for 10% conversion (min)	major products and their ratio at low conversion	leakage
8-2,6	80	**8**-2,3/**8**-3,4 = 10	**8**-2,5 = 8%
8-2,3	20	**8**-3,4/**8**-2,6 > 100	
8-3,4	665	**8**-2,3/**8**-2,6 > 100	**8**-3,5 = 8%
8-3,5	130	**8**-2,4/**8**-2,5 = 12	**8**-3,4 = 6%
8-2,4	30	**8**-3,5/**8**-2,5 = 1.6	**8**-2,3 = 18%
8-2,5	500	**8**-2,4/**8**-3.5 > 50	

tuted cases, that the trifluoromethyl-substituted carbon is the migratory one. However, although the two groups are both electron withdrawing ($\sigma = 0.66$ [4-CN]; $\sigma = 0.54$ [4-CF_3]), the former has a conjugative effect that the latter does not.

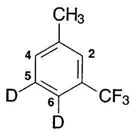


5 **6** **7**

To prove whether the one carbon is critical for the rearrangement of the methylbenzotrifluorides as in the mechanism proposed in Scheme 1 for the methylbenzonitriles, we now report the results of two different experimental tests. The first used the six isomeric dimethylbenzotrifluorides **8** and the second, deuterated 4-methylbenzotrifluoride **5**-d_2.



5-d2



6-d2

Photochemistry of the Six Isomers of Dimethylbenzotrifluoride 8 in Acetonitrile. The six compounds were synthesized from the corresponding bromides by a method described previously[5] for **8**-2,6; MS, ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and HRMS are given in the Supporting Information. Irradiation of each of the isomers in acetonitrile using a low-pressure Hg lamp (254 nm) resulted in conversion to the other isomers as followed by GC/FID. The results are summarized in Table 1, and a typical conversion plot is shown in Figure 1.

From the results in Table 1, the isomers react with different efficiencies, the time for 10% conversion of the starting material varying from 20 min (**8**-2,3) to 500 min (**8**-2,5). Moreover, as Figure 1 indicates, the major products for each of the substrates divide the six compounds into two triads, Scheme 2. One traid consists of **8**-2,6, **8**-2,3, and **8**-3,4; the other of **8**-3,5, **8**-2,4, and **8**-2,5.

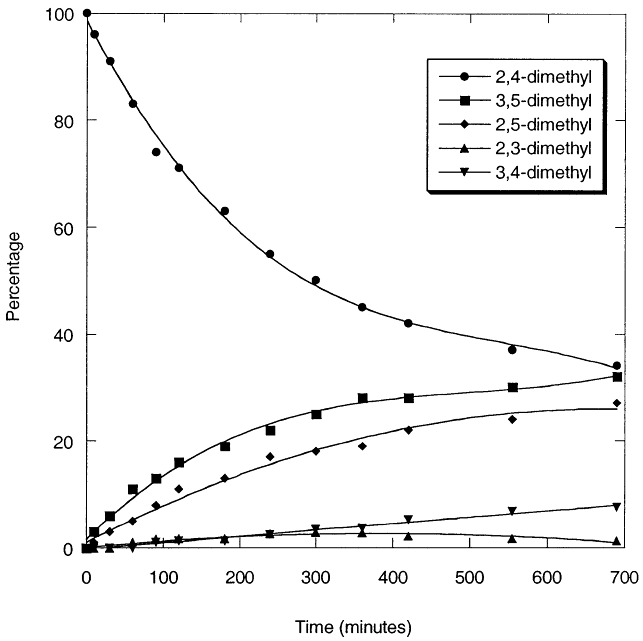
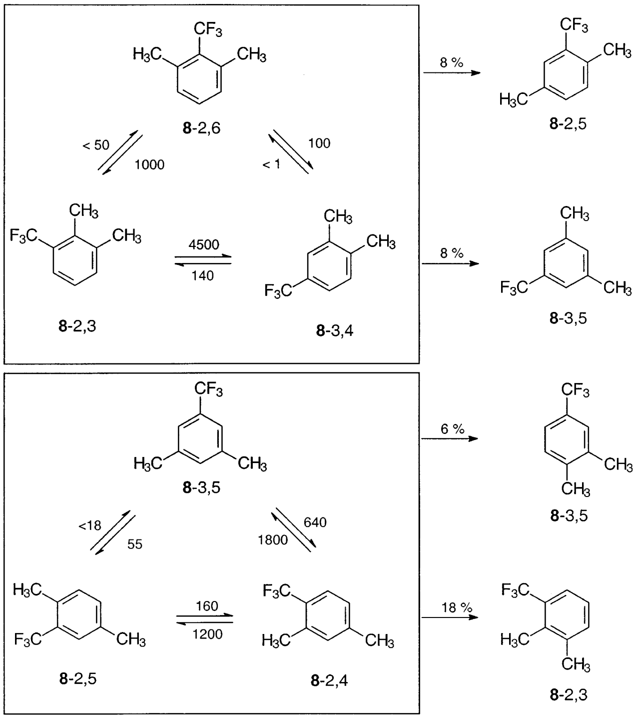


FIGURE 1. Phototransposition of 2,4-dimethylbenzonitrile in acetonitrile.

SCHEME 2. Phototransposition Reactions of the Six Isomeric Dimethylbenzonitriles 8 in Acetonitrile[a]



[a] Relative efficiencies for each process are given by the reaction arrow.

By measuring yields at very low conversion (<5%), product ratios for each of the isomers could be obtained (Table 1). For some cases, only lower limits for these values could be estimated because overlapping peaks in the GC traces prevented the reliable quantitation of the very small peaks growing in beside the very large ones. Using these product ratios and the times for 10% conversion of each substrate, the relative efficiency of the twelve possible conversions were estimated, arbitrarily scaled to 4500 for the fastest process, conversion of **8**-2,3 to **8**-3,4. These values are shown over each reaction arrow in

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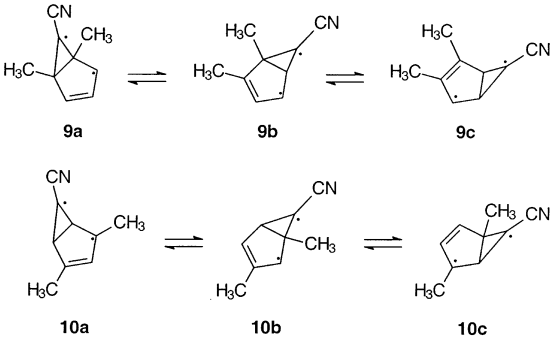
[5] Van der Boom, M.; Ben-David, Y.; Milstein, D. *J. Am. Chem. Soc.* **1999**, *121,* 6652−6656.

Scheme 2. This very large range of reactivities means that the less reactive compounds would likely be considered to be unreactive unless one were specifically looking for phototranspositions.

The fact that the major photochemical process is conversion within the triads shown in Scheme 2 indicates that the mechanism does indeed proceed through two triads of bicyclic diradicals that are trifluoromethyl-substituted at C6. One triad **9a**−**c** allows interconversion of **8**-2,6, **8**-2,3, and **8**-3,4; the other, **10a**−**c**, allows interconversion of **8**-3,5, **8**-2,5, and **8**-2,4. The same mechanistic proposal has been advanced by us previously for the dimethylbenzonitriles[4] where the cyano-substituted carbon is at C6 (as in Scheme 1 for the monomethylbenzonitriles) and in the gas-phase phototransposition reactions of the dimethylpyridines where the nitrogen of the pyridine served the role of the migratory atom.[6]



Because of the symmetry of the intermediate/transition state for the migration of two of the intermediates, namely **9c** and **10c**, some phototranspositions will be invisible. For instance, both **8**-3,4 and **8**-2,5 can undergo transposition reactions that switch a trifluoromethyl-substituted carbon with a neighboring hydrogen-subsituted carbon in a process that does not result in formation of a new isomer. Therefore, the efficiency of reactivity for the two compounds could be greatly underestimated.

As indicated in Table 1, "leakage" occurs from one triad to the other. This is shown graphically in Figure 1 where formation of **8**-2,3 from **8**-2,4 occurs with a yield of 18% at low conversion. This is the highest yield of the leakage process, the others being under 10%. Because **8**-2,3 is the most reactive isomer of the set of six, it very rapidly undergoes its own photochemistry so that **8**-3,4 is formed. These leakage pathways, shown in Scheme 2, all involve phototransposition of a methyl-substituted carbon. This is not unexpected because the substrates **8** can be regarded as trifluoromethyl-substituted xylenes and historically, the xylenes were among the first substrates where phototranspositions were observed.[7] In fact, this discovery lead to the proposal that substituted benzvalenes were important intermediates in aromatic phototransposition reactions and eventually to the photochemical preparations of benzvalene from benzene itself.[8] The low efficiency of the leakage processes indicates that the quantum yield of phototransposition for the methylbenzotrifluorides is 5−10 times more efficient than that reported for *m*-xylene (0.01).[9]

We have examined the phototransposition reactions of the xylenes in acetonitrile as solvent[3] in more detail than previous reports.[7,9] The relative reactivity of the three isomers is 1:1.4:0.3 for ortho/meta/para and the primary product ratios are meta/para = 11:1 for ortho, ortho/para = 6.0:1 for meta and meta/ortho > 25:1 for para. Thus the most reactive isomer is the meta one with the ortho one reacting somewhat more slowly. Therefore, as expected and indicated in Scheme 2, three of the leakage processes involve reaction of a meta xylene isomer, i.e., **8**-2,6, **8**-3,5, and **8**-2,4; the fourth involves reaction of an ortho xylene derivative, namely **8**-3,4.

The efficiency of these reactions must be determined by two quite different factors. The first is how efficiently the excited-state undergoes the required geometric changes to convert it to the bicyclic diradicals **9** and **10**. If the barrier for this process is high, then other nonproductive excited-state processes (fluorescence, internal conversion, intersystem crossing) likely dominate. The second required step is migration of the trifluoromethyl-substituted carbon around the periphery of the other five allowing interconversion of the three isomeric intermediates in the two sets **9** and **10**. If the barrier to the latter steps is high then, even if the intermediates **9** and **10** are formed, no reaction will be observed. The process will just be one mode of internal conversion. With the limited evidence available, determining whether one or the other of these two possibilities is the more important one is not posssible. However, a tentative proposal is possible on the basis of the results for photolysis of the isomers of **8** in TFE.

All six of the isomers react in TFE to give products that clearly result from alcohol addition (GC/MS, molecular ion $m/z = 274$). No phototranspositions were observed. All gave complex mixtures, with **8**-2,3 being typical with four major products accounting for around 65% of the yield and more than a dozen others constituting the rest. Presumably, these addition products are similar to those shown in Scheme 1 for the methylbenzonitriles but we were unable to characterize them further. Even simply evaporating the solvent gave samples whose ^{1}H NMR spectra showed no assignable signals but rather broad bands extending over ranges of δ 1−3 and δ 4.5−4.0 suggesting oligomers or polymers. We had previously observed the same difficulties characterizing TFE addition products for the three monomethylbenzotrifluorides and trifluoromethylbenzene itself.[3]

However, the photoreactions in TFE did provide evidence on their relative reactivity. As in the phototransposition reactions, the least reactive isomers were again **8**-3,4 and **8**-2,5. This suggests that formation of the bicyclic diradical intermediates **9** or **10** is slow in both solvents. After this formation, they either isomerize (acetonitrile) or are trapped (TFE).

The Photochemistry of 4-Methylbenzotrifluoride-d_2 (5-d_2). This compound was synthesized starting from

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(6) Pavlik, J. W.; Kebede, N.; Thompson, M.; Day, A. C.; Barltrop, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5666−5673.

(7) Wiltzbach, K. E.; Kaplan, L. *J. Am. Chem. Soc.* **1964**, *86*, 2307−2308.

(8) Wilzbach, K. E.; Ritscher, J. S.; Kaplan, L. *J. Am. Chem. Soc.* **1967**, *89*, 1031−1032.

(9) Anderson, D. *J. Phys. Chem.* **1970**, *74*, 1686−1690.

4-methylanilinium hydrochloride, exchanging the protons ortho to the ammonium group with D_2O as described previously,[1] followed by diazotization and conversion to the iodide with KI and finally conversion of the iodide to a CF_3 group. As with the deuterated 4-methylbenzonitrile studied previously,[1] all the chemically distinct carbons are now labeled and their positions can be tracked during phototranposition. The analytical method used is ^{13}C NMR of those aromatic ring carbons which are proton (hydrogen or deuterium) substituted. Those with deuterium give very weak signals with the normal pulse delay (1 s) acquisition because of their long relaxation times. For instance, 4-methylbenzotrifluoride **5** gives two strong signals at δ 130.8 and 126.2, the latter being assigned to C2 by the coupling (3.7 Hz) to the CF_3 group. In **5**-d_2, this signal is essentially invisible appearing as a very weak triplet at δ 125.9.

On irradiation in acetonitrile, **5**-d_2 (para) is converted to 3-methylbenzotrifluoride **6**-d_2 (meta) by phototranposition. The meta isomer **6** has four proton-substituted carbons appearing at δ 134.1, $J < 1$ Hz (C4), 130.2, $J = 2.3$ Hz (C5), 126.7, $J = 3.7$ Hz (C2) and 123.3, $J = 3.7$ Hz (C6). These assignments are also made on the basis of coupling constants with the fluorines of the CF_3 group and by distinguishing C2 from C6 by simulation using the ACD program.[10] The **6**-d_2 produced in the mixture by phototransposition[11] has visible carbons at δ 134.3 (C4) and 126.6 (C2), as expected. A very weak signal could be observed for C6 at δ 123.3 with an intensity ratio of C2:C6 > 10:1; in the fully protonated sample this intensity ratio is ~1:1. Unfortunately, the region of the spectrum for the signal corresponding to C5 was obscured by other signals and a noisy baseline. However, **6**-d_2 most probably is principally the isomer with the deuterium distribution shown. Therefore, **5** is converted to **6** by migration of the CF_3-substituted carbon.

We are in the process of doing high level MO calculations to probe the potential energy surfaces for these phototransposition reactions. The knowledge that the CF_3-substituted carbon is the migratory one is necessary for this approach that may help to explain why the order of reactivity (ortho/meta/para) is reversed on going from a CN to CF_3 group.

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Supporting Information Available: The Experimental Section including spectral data for the five synthesized isomers of dimethylbenzotrifluoride **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0205715

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(10) Advanced Chemistry Development, Inc., 90 Adelaide Street West, Toronto, ON M5H 3V9, Canada.

(11) The deuterium distribution in the ortho isomer **7** could not be obtained because it reaches a yield of only 7% at complete photoequilibration.