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Large primary kinetic isotope effects in the abstraction of hydrogen from organic compounds by a fluorinated radical in water †

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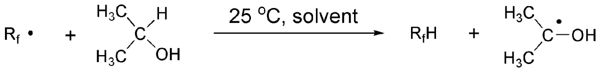
Isotope effects have been measured for the abstraction of hydrogen from a series of organic substrates by the perfluoro radical, $Na^+ \ ^-O_3SCF_2CF_2OCF_2CF_2^{\bullet}$, in water. Both primary and secondary deuterium isotope effects were measured, with the primary isotope effects ranging in value from 4.5 for isopropanol to 19.6 for acetic acid. The values for the α- and β-secondary deuterium isotope effects were 1.06 and 1.035, respectively. It was concluded that tunneling contributes significantly to the production of the observed, large primary kinetic isotope effects in these C–H abstraction reactions.

Introduction

Recently we have been engaged in a broad study involving the determination of rate constants of hydrogen abstraction from organic substrates by fluorinated radicals, $R_f^{\bullet}$, first in non-polar solvents,[1] such as 1,3-bis-trifluoromethylbenzene (BTB), and most recently in water.[2–4] The rate constants for abstraction of hydrogen from isopropanol in these two solvents are given below to exemplify, first the rather large rate constants of such processes, and secondly the modest rate-enhancing effect of the polar solvent, water.[1,3,4]

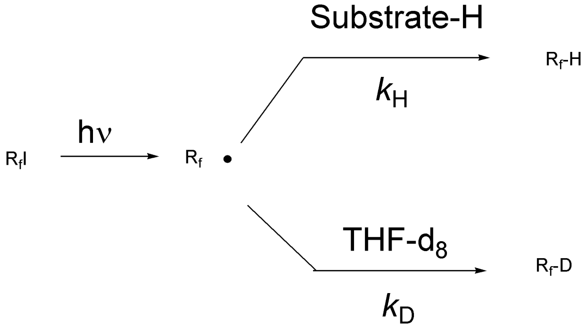


R_f •	Solvent	k_H
$CF_3CF_2CF_2CF_2$ •	BTB	1.6 (0.3) x $10^4 M^{-1}s^{-1}$
$Na^+ \ ^-O_3SCF_2CF_2OCF_2CF_2$ •	H_2O	4.8 (1.5) x $10^4 M^{-1}s^{-1}$

1

These absolute rate constants were determined by competition studies in which the $R_f^{\bullet}$ radical abstracted hydrogen from the substrate in competition with abstraction of a deuterium from a standard, carefully chosen deuterium transfer agent for which the rate constant for D-transfer had been determined.

The requirements for the deuterium transfer agent were stringent, requiring the agent to participate in creating a clean, radical chain process that gave high conversions and excellent mass balance: that is, high yields of the two products, with virtually no observable side products. The rate constant for D-transfer must also be of a magnitude that allowed a viable competition between H- and D-transfer to be observed. *t*-$BuMe_2SiD$, with a measured k_D of 1.5 (±0.3) × 10^5 M^{-1} s^{-1},[1] and THF-d_8, with a measured k_D of 4.2 (±1.2) × 10^3 M^{-1} s^{-1},[4] fulfilled these requirements admirably for the competition studies in BTB and H_2O, respectively, and they were therefore used as the D-transfer agents in these respective studies. These rate constants can be compared with their k_H values for the respective non-deuterated compounds: 4.9 × 10^5 M^{-1} s^{-1} for *t*-$BuMe_2SiH$ (in BTB) and 3.3 (±1.0) × 10^4 M^{-1} s^{-1} for THF (in H_2O),[1] which allowed the isotope effects (k_H/k_D) for H *versus* D abstraction from these two compounds to be calculated: 3.3 and 7.9, respectively – nothing overtly extraordinary. A similar isotope effect (k_H/k_D = 3.1) was observed for another silane, Et_3SiH, in another non-polar solvent, 1,1,2-trichloro-1,2,2-trifluoroethane,[5] whereas the isotope effect for THF *versus* THF-d_8 in BTB was 7.0 at 25 °C.[1]



However, particularly in the water study, many other prospective D-transfer agents were tested for possible use, including CD_3OD and CD_3COCD_3. During the course of such testing, both the H-transfer and the D-transfer rate constants were determined for these compounds, and the results were surprising in that unusually large isotope effects (k_H/k_D = 11.4 and 17.0, respectively) were observed for the progressively "slower" H-transfer agents. Of course, these two observed isotope effect values, as well as the earlier mentioned value for THF, derive from a combination of primary and secondary deuterium isotope effects, but it will be seen that the actual primary isotope effects, once corrected for the small secondary effects, remain quite large.

These observations led to a more systematic examination of the primary and secondary kinetic isotope effects that derive from hydrogen transfer to the $Na^+ \ ^-O_3SCF_2CF_2OCF_2CF_2^{\bullet}$ radical, **1**, the results of which are given in Tables 1–3 below.

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† Electronic supplementary information (ESI) available: Tables of kinetic data and plots of kinetic data. See http://www.rsc.org/suppdata/ob/b4/b405075d/

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Table 1 Observed kinetic isotope effects for direct bimolecular competition between hydrogen and deuterium transfer from select organic compounds to the $Na^+ \, ^-O_3SCF_2CF_2OCF_2CF_2^\bullet$ radical, **1**, in water at 25 °C

H-Substrate	D-substrate	k_H/k_D [a] (observed)	$k_H/10^4\ M^{-1}\ s^{-1}$ [b, c]	$k_D/10^4\ M^{-1}\ s^{-1}$ [c]
$(CF_3)_2CHO^-Na^+$	$(CF_3)_2CDO^-Na^+$	5.9 (±0.4)	11 (±3)[6]	1.86 (±0.6)
Isopropanol	$(CD_3)_2CDOH$	5.8 (±0.1)	4.8 (±1.4)	0.83 (±0.25)
$(CD_3)_2CHOH$	THF-d_8	8.9 (±0.3)	3.7 (±1.1)	0.42 (±0.13)
THF	THF-d_8	7.9 (±0.4)	3.3 (±1.0)	0.42 (±0.13)
Ethanol	CD_3CD_2OH	8.8 (±0.2)	1.2 (±0.4)	0.14 (±0.04)
Ethanol	CH_3CD_2OH	8.11 (±0.12)	1.2 (±0.4)	0.15 (±0.04)
CH_3CHDOH		7.39 (±0.04)	—	—
Methanol	CD_3OH	11.4 (±0.4)	0.18 (±0.05)	0.016 (±0.005)
CHD_2OH		4.83 (±0.02)	—	—
Acetone	Acetone-d_6	17.0 (±0.4)	0.006 (±0.002)	0.00035
Acetic acid	CD_3CO_2H	22.2 (±0.7)	0.002 (±0.0006)	0.00009

[a] Errors in this column are standard deviations. [b] From reference 4, except where noted. [c] These LFP-derived absolute rate constants have an estimated error limit of 30%.[4]

Table 2 Data used to determine secondary deuterium isotope effects

H-Substrate	D-Substrate	k_H [a]	k_D [a]	k_H/k_D (secondary)	k_H/k_D (per D)
$(CH_3)_2CHOH$	$(CD_3)_2CHOH$	4.8	3.74	1.28	1.04[b] (β)
CH_3CD_2OH	CD_3CD_2OH	0.148	0.136	1.088	1.03[c] (β)
CH_3CHDOH		$k_H/k_D = 7.39$		1.07	1.07 (α)
CHD_2OH		$k_H/k_D = 4.83$		1.10	1.05

[a] Rates are all expressed as $k/10^4\ M^{-1}\ s^{-1}$, and are ±30%. [b] Obtained by taking the $^{6}\surd$ of 1.28. [c] obtained by taking the $^{3}\surd$ of 1.088.

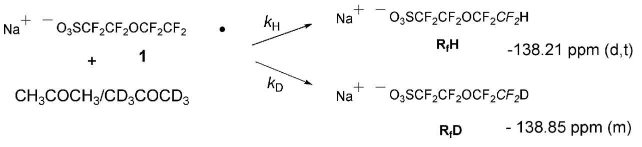
Table 3 Primary isotope effects (after correction for α- and β-deuterium isotope effects)

Substrate	k_H [a]	k_D [a]	k_H/k_D (uncorr)	Corrections	k_H/k_D (primary)
$(CF_3)_2CHO^-Na^+$	11[6]	1.86	5.9	none	**5.9**
Isopropanol	4.8[4]	0.83	5.8	6β (1.28)	**4.5**
THF	3.3[4]	0.42	7.9	1α,2β (1.14)	**6.9**
Ethanol	1.2[4]	0.136[b]	8.8	1α,3β (1.17)	**7.5**
Ethanol	1.2[4]	0.148[c]	8.1	1α (1.07)	**7.6**
Methanol	0.18[4]	0.016	11	2α (1.10)	**10.0**
Acetone	0.006[4]	0.00035	17	2α (1.12)	**15.2**
Acetic acid	0.002[4]	0.00009	22	2α (1.12)	**19.6**

[a] All these LFP-derived absolute rate constants have an estimated error of 30%.[4] [b] CD_3CD_2OH as k_D substrate. [c] CH_3CD_2OH as k_D substrate.

Results

All of the isotope effects (k_H/k_D), both primary and secondary, were obtained *via* simple, direct competition experiments involving the photolysis of $Na+^-O_3SCF_2CF_2OCF_2CF_2I$ in the presence of mixtures of the respective protiated and deuterated substrates, varying relative concentrations in order to establish the linearity (pseudo first order nature) of the concentration dependence of the substrates towards proton/deuteron transfer. The conversions were 100%, with the mass balance of products always being ~90%. The linear relationship between the ratio of R_fH/R_fD products and the ratio of protiated and deuterated products defined the value of the isotope effect (k_H/k_D). The derivation of both relative and absolute rate constants from such data has been discussed in detail in earlier papers.[1,4] A typical plot of data for the reaction of **1** with CH_3COCH_3/CD_3COCD_3 mixtures is provided in Fig. 1.



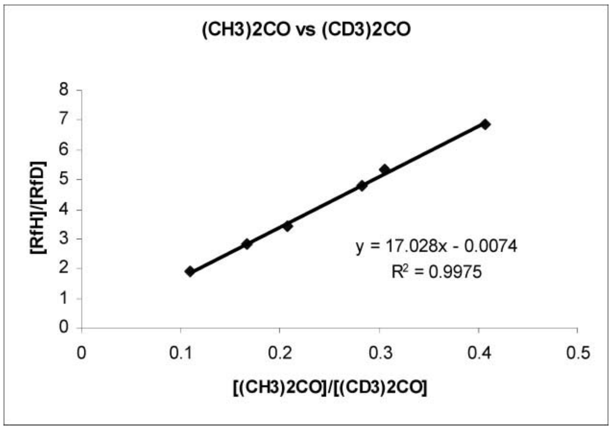


Fig. 1 Plot of $[R_fH]/[R_fD]$ *vs.* $[(CH_3)_2CO]/[(CD_3)_2CO]$.

The "observed" kinetic isotope effects given in column 3 of Table 1 in all cases except the first derive from a combination of primary and secondary kinetic deuterium isotope effects, the latter being either α- or β- in nature (or in the case of CD_3CD_2OH, both α- and β). The absolute values of the k_H rate constants were known from previous work.[4] Therefore, knowledge of the k_H/k_D values in Table 1 allows determination of the values for k_D for the given deuterated compound.

Secondary isotope effects

Because of the multiple deuterium substitution that is present in THF-d_8, CD_3CD_2OH, CH_3CD_2OH, CD_3OH, acetone-d_6 and CD_3CO_2H, it is necessary to have some measure of expected α- and β-*secondary* deuterium isotope effects in order to be able to calculate the actual *primary* isotope effects for these substrates. For example, in the case of CD_3CD_2OH, when the rate constant, k_D, for α-deuterium abstraction is measured, the remaining α-deuterium and the three β-deuteriums give rise to secondary isotope effects that lower the rate constant compared to what it would have been had only hydrogens remained in the radical product, as depicted in Fig. 2.

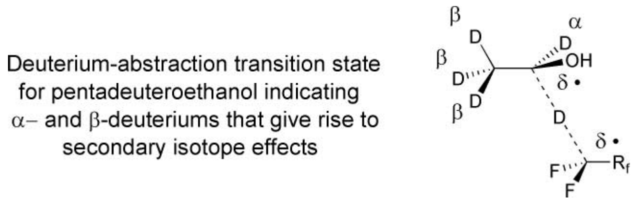


Fig. 2 Depiction of transition state for D-abstraction from pentadeuteroethanol.

In order to determine the values of the secondary isotope effects, four additional competition studies were carried out. These were (a) the intermolecular competition between $(CD_3)_2CHOH$ and THF-d_8, (b) the intermolecular competition between CH_3CD_2OH and CH_3CH_2OH; and *intra*molecular competitions using (c) CH_3CHDOH and (d) CHD_2OH. The data obtained from these experiments are contained in Tables 1 and 2.

The first two experiments allowed independent determinations of the β-secondary deuterium isotope effect, the values of which were calculated to be 1.28 and 1.088, for isopropanol and ethanol respectively, or 1.04 and 1.03 per deuterium in each case (using sixth route and cube root of the overall isotope effects, respectively).

The results from the intramolecular competition experiments using CH_3CHDOH and CHD_2OH allowed two determinations of the value of the α-secondary deuterium isotope effect. The isotope effect for the CH_3CHDOH system can be calculated from the raw R_fH/R_fD integral as follows:

$$\frac{(\mathrm{CF_2H\ integral})}{(\mathrm{CF_2D\ integral})} = \frac{k_H(\mathrm{EtOH}) \times k_D/k_H(\alpha\text{-secondary})}{k_D(\mathrm{CH_3CD_2OH}) \times k_H/k_D(\alpha\text{-secondary})}$$

$$7.39 = \frac{12 \times [k_D/k_H(\alpha\text{-secondary})]^2}{1.5} \qquad \text{Thus, } k_H/k_D = 1.05$$

However, a 500 MHz ^{1}NMR spectrum of the synthesized CH_3CHDOH indicated that it contained a 1% diethyl ether contaminant (4% integral of its CH_2 groups *versus* 100% integral for the CHD of the deuteroethanol). This small amount of contaminant will have a small, but not negligible impact upon the $(CF_2H)/(CF_2D)$ integral ratio, which when taken into account yields *a corrected value of 1.07* for the α-secondary deuterium isotope effect for the ethanol system.[7]

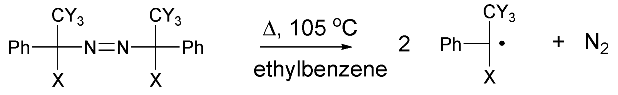
The value of the isotope effect in the methanol system can likewise be calculated as shown below:

$$\frac{(\mathrm{CF_2H\ integral})}{(\mathrm{CF_2D\ integral})} = \frac{1/3 \times k_H(\mathrm{CH_3OH}) \times k_D/k_H(\alpha\text{-secondary})^2}{2/3 \times k_D(\mathrm{CD_3OH}) \times k_H/k_D(\alpha\text{-secondary})}$$

$$4.83 = \frac{.33 \times 0.18 \times [k_D/k_H(\alpha\text{-secondary})]^3}{.667 \times 0.016}$$

Thus, $(k_D/k_H)^3 = 0.863$ and k_H/k_D (per deuterium) = 1.05

Although the absolute rate constants of Table 1 are not reliable more than ±30%, the data obtained in our competition experiments have standard deviations generally in the 3–4% range, which allows the values for the secondary isotope effects to be credible. The relatively small β-effects are consistent with the limited data that have been previously reported for radical-forming reactions.[8,9] For example, in studies of the deazetation of deuterium labeled azo compounds, Seltzer and coworkers found that β-secondary deuterium isotope effects, which derive largely from hyperconjugative interaction of the isotopically-labeled site with the incipient β-radical site, were generally much smaller for radical-forming reactions than for carbocation-forming reactions. In contrast, α-secondary deuterium isotope effects, which can be understood as deriving from a change in hybridization at the radical-forming carbon atom, have been found to be of similar magnitude to those deriving from carbocation-forming reactions.[10] Thus the average of our two observed α-secondary deuterium isotope effects, k_H/k_D = 1.06, is somewhat smaller than might have been expected based on the limited data available in the literature for radical-forming processes. However, the faster, exothermic hydrogen abstraction reactions of our study should have much earlier transition states than the endothermic dissociative reactions studied by Seltzer, a fact consistent with the smaller α-secondary deuterium isotope effect that we have observed.



$$\mathrm{Ph{-}C(CY_3)(X){-}N{=}N{-}C(CY_3)(X){-}Ph} \xrightarrow[\text{ethylbenzene}]{\Delta,\ 105\ ^{\circ}\mathrm{C}} 2\ \mathrm{Ph{-}\dot{C}(CY_3)(X)} + \mathrm{N_2}$$

α-isotope effect: X =D, Y = H, k_H/k_D = 1.13 per d

β-isotope effect: X = H, Y = D, k_H/k_D = 1.02 per d

Primary isotope effects

With both the α- and the β-secondary isotope effects now in hand, it becomes possible to convert the observed isotope effects in Table 1 to the pure primary deuterium isotope effects for each of the substrates. For isopropanol, ethanol, and methanol the specific values of the secondary isotope effects that were determined have been used, whereas for the THF, acetone and acetic acid calculations, the per-deuterium value of 1.06 for the α- and 1.035 for the β-secondary isotope effects were used. The calculated primary isotope effects are given in Table 3.

Discussion

The values of the isotope effects for the latter three substrates are considerably larger than what are generally considered to be the theoretical limits for semiclassical H/D primary isotope effects. It can be seen that the values exhibit a correlation with the absolute rate constants for H-transfer, which vary over a considerable range, with acetic acid being approximately 3000 times less reactive than isopropanol (per hydrogen, 9000 times!). The absolute rate constants themselves correlate with the C–H BDE's of the respective substrates.

These isotope effects appear to be real. The reactions are clean, and good linear correlations with concentrations are observed. One possible trivial explanation for the data might have been that H-transfer from the solvent water could have become increasingly competitive with H-transfer from the less reactive substrates. However, the competition experiments for acetone were run in both H_2O and D_2O, with the observed k_H/k_D in D_2O being 18.5 ± 0.7, which indicates that H-transfer from solvent water cannot be competitive with H-transfer from the substrates under the conditions of the study.

Tunneling must be considered as a possible contributing factor to such large isotope effects that are certainly outside of the generally accepted semiclassical limits for hydrogen transfer isotope effects, where one assumes that the zero-point-energy difference associated with carbon–hydrogen stretching in the substrate is completely lost in the transition state.[11,12] Isotope effects moderately larger than the ~6.9 limit at 25 °C can be accommodated by allowing weakening of bending modes, but when such large values as those found in Table 1 are observed, one is almost compelled to invoke tunneling.[12] Therefore, as a classical probe of tunneling, a temperature dependence study was carried out for the acetone reaction, although the range of temperatures that could be examined was limited severely by the fact that water was the solvent. Thus the values determined for k_H/k_D at 24, 56, and 80 °C were 16.6 (±0.7), 12.6 (±0.1), and 10.2 (±0.5), respectively. An Arrhenius plot of this data (Fig. 3) indicates a linear correlation between $\ln(k_H/k_D)$ and $1/T$, with $E_a(D) - E_a(H) = 1.8$ kcal mol^{-1} and $A_H/A_D = 0.80$.

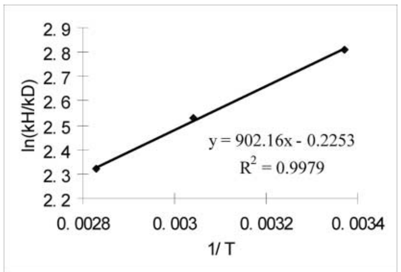


Fig. 3 Plot of $\ln(k_H/k_D)$ for reaction of $R_f^{\bullet}$ radical, **1**, with acetone *vs.* $1/T$.

As Kreevoy has indicated,[13] there is probably no unambiguous way to demonstrate tunneling for reactions carried out around 300 K.[14] However, he and others contend that, even in this temperature range, values of $E_a(D) - E_a(H) > 1.20$ kcal mol^{-1} will generally signal tunneling, as will values of $A_H/A_D < 1.0$ for hydrogen transfer between massive, polyatomic donors and acceptors.[11–13] Although our Arrhenius data must be considered suspect because of the small temperature range and the small number of data points, nevertheless the data *are* consistent with these criteria for the involvement of tunneling in the H-transfer process. Moreover, Truhlar has analyzed kinetic data for the related reaction of $CF_3^{\bullet}$ with CD_3H within the context of his calculations of the kinetic isotope effect for this reaction,[15] and he finds tunneling *must* be included in the calculation in order to attain agreement with the experimental data.[16] Similarly, Roberto-Neto has analyzed isotope effect data for the reaction of $Cl^{\bullet}$ with ethane,[17] Michelsen[18] and Hewitt[19] have similarly analyzed such data for the reaction of $Cl^{\bullet}$ with methane, and Osman has examined the reaction of $HO^{\bullet}$ with isopropanol,[20] all concluding that tunneling effects make a significant contribution to the H-transfer rate constants in these reactions.

Carbon–hydrogen abstractions by alkyl radicals, and even more so by perfluoroalkyl radicals, should involve relatively sterically hindered transition states. It is recognized that such sterically-constrained transition states for hydrogen abstraction can lead to a steep rise in potential energy upon close approach of the reactants to each other, resulting in a high and thin potential barrier that can lead to large tunneling contributions.[12,21,22]

Taking all of this into account, in the absence of a plausible alternative explanation, we conclude that tunneling is probably a significant factor in producing the large kinetic isotope effects that are observed in our C–H abstraction reactions of perfluoroalkyl radical **1** in water.

Experimental

All deuterated compounds were purchased in >98% purity from Isotech, Inc, except CH_3CHDOH and $(CD_3)_2CHOH$, which were synthesized by reduction of acetaldehyde by $LiAlD_4$, and reduction of acetone-d$_6$ by $LiAlH_4$, respectively.

General procedure for competition kinetic studies

The kinetics were carried out in a manner similar to the earlier studies in BTB, and the analysis of the data was also analogous.[1]

The kinetic studies were run in pyrex NMR tubes containing a sealed capillary tube ($CFCl_3$ in C_6D_6) as the internal standard. For each kinetic study, a group of samples were prepared at the same time. The NMR tubes were capped with rubber septa, and wrapped with Teflon tape before chemicals were added. The radical precursor, $Na^+ \ {}^-O_3SCF_2CF_2OCF_2CF_2I$,[2] was used as a stock solution (17.8% by weight) and added to the NMR tubes with a micro-syringe. Quantities of the protiated and deuterated substrates were added with syringes and weighed on the balance. The samples were degassed by 3 cycles of freeze–pump–thaw. After ^{19}F NMR spectra were taken, they were irradiated using a RPR-204 Rayonet photochemical reactor. The ^{19}F NMR spectrum was taken again after 24 hours. The acquisition time of NMR was at least 15 minutes to assure accurate integration. The ratios of products were obtained directly from the ratios of integration of the CF_2H and CF_2D signals. The conversion and yield were obtained by comparison of the integration of the CF_2I peak in the starting material and the (CF_2H+CF_2D) peaks in the products relative to the internal standard.

Procedure for measurement of the intramolecular isotope effects of CH_3CHDOH and CHD_2OH

The CH_3CHDOH was prepared by a literature procedure,[23] and, after purification, it was analyzed by ^1H NMR. No significant undeuterated ethanol could be detected (<1%), but a 1% impurity of diethyl ether was detected (4% integral for its CH_2 groups *versus* the 100% due to the CHD group of CH_3CHDOH). The small impact of this impurity on the measured $[CF_2H]/[CF_2D]$ ratio was corrected for in the calculation of the α-secondary isotope effect. The CHD_2OH was purchased from Isotech, Inc.

For both CH_3CHDOH and CHD_2OH, two repetitive kinetic studies were run in pyrex NMR tubes containing a sealed capillary tube ($CFCl_3$ in C_6D_6) as the internal standard, capped with rubber septa, and wrapped with Teflon tape before the chemicals were added.

In the typical case for CH_3CHDOH, the IR_fSO_3Na in water was used as a stock solution (17.8% by weight) and added to the NMR tubes with a micro-syringe. Then, 80 μL of monodeuteroethanol (14.3×10^{-4} moles) was added to each tube. The samples were then degassed by three freeze–pump–thaw cycles. After ^{19}F NMR spectra of the two samples were taken, the samples were irradiated using a RPR-204 Rayonet photochemical reactor. The ^{19}F NMR spectrum of each sample was taken again after 24 hours. The NMR acquisition time was at least 15 minutes to assure accurate integration. The product ratios were obtained, as usual, from the ratios of integration of the CF_2H and CF_2D signals, with multiple integrations being carried out for each. The conversion and yield were obtained from the integration of the CF_2I peak in the starting material *versus* those of the $(CF_2H + CF_2D)$ peaks in the products relative to the internal standard.

For CH_3CHDOH, the average of the raw CF_2H/CF_2D ratios was 7.39 (±0.04).

For CHD_2OH, the average of the raw CF_2H/CF_2D ratios was 4.83 (±0.02).

Tables of kinetic data and plots of kinetic data for all kinetic experiments are available in the ESI.†

Acknowledgements

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References

1 A. B. Shtarev, F. Tian, W. R. Dolbier, Jr. and B. E. Smart, *J. Am. Chem. Soc.*, 1999, **121**, 7335.

2 L. Zhang, W. R. Dolbier, Jr., B. Sheeller and K. U. Ingold, *J. Am. Chem. Soc.*, 2002, **124**, 6362.

3 L. Zhang, The Addition and Hydrogen Abstraction Reactions of a Fluorinated Radical in Aqueous Solution, Ph. D. Dissertation, University of Florida, Gainesville, 2001.

4 L. Zhang, J. Cradlebaugh, G. Litwinienko, B. E. Smart, K. U. Ingold and W. R. Dolbier, Jr., *Org. Biomol. Chem.*, 2004, **2**, 689.

5 W. R. Dolbier, Jr. and X. X. Rong, *J. Fluorine Chem.*, 1995, **72**, 235.

6 J. Cradlebaugh, L. Zhang, G. R. Shelton, G. Litwinienko, B. E. Smart, K. U. Ingold and W. R. Dolbier, Jr., *Org. Biomol. Chem.*, 2004, DOI: 10.1039/b405075d (preceding paper).

7 The method used for calculation of the "corrected" value of the isotope effect can be found in the ESI †.

8 S. Seltzer and E. J. Hamilton, Jr., *J. Am. Chem. Soc.*, 1966, **88**, 3775.

9 A. Tsolis, P. P. Hunt, J. K. Kochi and S. Seltzer, *J. Am. Chem. Soc.*, 1976, **98**, 992.

10 S. Seltzer and S. G. Mylonakis, *J. Am. Chem. Soc.*, 1967, **89**, 6584.

11 R. P. Bell, *The Tunnel Effect in Chemistry*, Chapman and Hall, London, 1980.

12 L. Melander and W. H. Saunders, Jr., *Reaction Rates of Isotopic Molecules*, John Wiley and Sons, New York, 1980.

13 Y. Kim and M. M. Kreevoy, *J. Am. Chem. Soc.*, 1992, **114**, 7116.

14 K. U. Ingold, *Pure Appl. Chem.*, 1984, **56**, 1767.

15 Y. P. Liu, D. H. Lu, A. Gonzalez-Lafont, D. G. Truhlar and B. C. Garrett, *J. Am. Chem. Soc.*, 1993, **115**, 7806.

16 T. E. Sharp and H. S. Johnston, *J. Chem. Phys.*, 1962, **37**, 1541.

17 O. Roberto-Neto and F. B. C. Machado, *Theor. Chem. Acc.*, 2001, **107**, 15.

18 H. A. Michelsen and W. R. Simpson, *J. Phys. Chem. A*, 2001, **105**, 1476.

19 G. D. Boone, F. Agyin, D. J. Robichaud, F.-M. Tao and S. A. Hewitt, *J. Phys. Chem. A*, 2001, **105**, 1456.

20 N. Luo, D. C. Kombo and R. Osman, *J. Phys. Chem. A*, 1997, **101**, 926.

21 E. S. Lewis and L. H. Funderburk, *J. Am. Chem. Soc.*, 1967, **89**, 2322.

22 H. Wilson, J. D. Caldwell and E. S. Lewis, *J. Org. Chem.*, 1973, **38**, 564.

23 A. J. Gellman, M. T. Buelow, S. C. Street and T. H. Morton, *J. Phys. Chem. A*, 2000, **104**, 2476.