

Comparison of $\Delta G^\circ_{\text{Acid}}$ (gas phase) and kinetic acidities measured in methanolic sodium methoxide

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Received 21 July 1997; revised 14 December 1997; accepted 6 January 1978

ABSTRACT: Hydron exchange rates, k_{exc} ($\text{M}^{-1}\text{s}^{-1}$), using methanolic sodium methoxide were compared with $\Delta G^\circ_{\text{Acid}}$, (kcal mol^{-1}) (gas phase) for 9-phenylfluorene, $\text{C}_6\text{H}_5\text{CH}(\text{CF}_3)_2$, $m\text{-CF}_3\text{C}_6\text{H}_4\text{CH}(\text{CF}_3)_2$, $p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$, $m\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$, 3,5- $(\text{CF}_3)_2\text{C}_6\text{H}_3\text{CHClCF}_3$, fluorene and $\text{C}_6\text{F}_5\text{H}$. There is a good linear correlation for $p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$, $m\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$ and 3,5- $(\text{CF}_3)_2\text{C}_6\text{H}_3\text{CHClCF}_3$, with the others falling off the line. The fluorinated benzyl compounds and pentafluorobenzene have near-unity isotope effects and therefore differ from the fluorenyl compounds. Although the acidity and the exchange rates for three of the compounds [9-phenylfluorene, $\text{C}_6\text{H}_5\text{CH}(\text{CF}_3)_2$ and $p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$] are similar, the important proton-transfer step to form a hydrogen-bonded carbanion intermediate and the subsequent breaking of that weak bond to form a free carbanion in methanol differ significantly for the fluorenyl compound compared with the two fluorinated benzylic compounds. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: $\Delta G^\circ_{\text{Acid}}$ (gas phase); kinetic acidities; methanolic sodium methoxide

INTRODUCTION

Although relative $\text{p}K_{\text{a}}$ values for carbon acids in different organic solvents are an important contribution to the understanding of organic chemistry, they are not always able to predict relative rates of hydron transfer from a carbon acid to a base. For example, the methanolic sodium methoxide protodetrifitation of pentafluorobenzene-*t* (PFB-*t*)¹ is 15 times faster at 25 °C than that for 9-phenylfluorene-9-*t* (9-PhFl-9-*t*)², even though the $\text{p}K_{\text{a}}$ values (cyclohexylamine) for 9-PhFl (18.5) and PFB (25.8)³ predict that 9-PhFl-9-*t* should react much faster than PFB-*t*. Primary kinetic isotope effects (PKIE) differ for the two systems: at 25 °C, for 9-PhFl $k^{\text{D}}/k^{\text{T}} = 2.50$ and for PFB $k^{\text{D}}/k^{\text{T}} = 1.0$. The PKIE for PFB suggests extensive internal return,¹ and that hydron transfer occurs prior to the rate-limiting step. Scheme 1 featuring two carbanion intermediates, is our working model for these reactions. One carbanion is stabilized by a hydrogen bond, HB, while the other FC, has no contact stabilization by either solvent or the counter ion.⁴

A parameter $a = k_{-1}/k_2$ was defined as a measure of the amount of internal return for a reaction and can be

calculated if the rates of exchange for all three hydrogen isotopes are measured.⁵ Proton return from HB-*h*, k_{-1}^{H} , has a PKIE whereas the forward step, k_2^{H} , has a negligible PKIE. After the hydrogen bond is broken, bulk solvent molecules readily replace the newly formed methanol, $k_{\text{exc}} \gg k_{-2}^{\text{H}}$, in the best position to form HB-*d*, k_{-2}^{D} . Internal return is unimportant for the reactions of 9-PhFl-9-*t* ($a^{\text{T}} = 0.016$),⁵ negligible for 9-PhFl-9-*d* ($a^{\text{D}} = 0.050$) and plays a role for the reactivity of 9-PhFl-9-*h* ($a^{\text{H}} = 0.49$).

Scheme 1 accounts for the discrepancy between $\Delta\text{p}K_{\text{a}}$ and methoxide-catalyzed exchange rates for PFB and 9-PhFl and Fig. 1 gives pictorial representations. The $\text{p}K_{\text{a}}$ values come from energy differences between PFB and PFB^- vs 9-PhFl and 9-PhFl⁻, with exchange rates resulting from energy differences between PFB and the transition structure forming PFB^- vs one between 9-PhFl and the transition structure for forming 9-PhFl⁻ ... HOCH₃. The transition structure for hydron transfer from 9-PhFl to CH₃O⁻ is closer in energy to a localized hydrogen-bonded carbanion, 9-PhFl⁻ ... HOCH₃, than the π -delocalized species, 9-PhFl⁻.

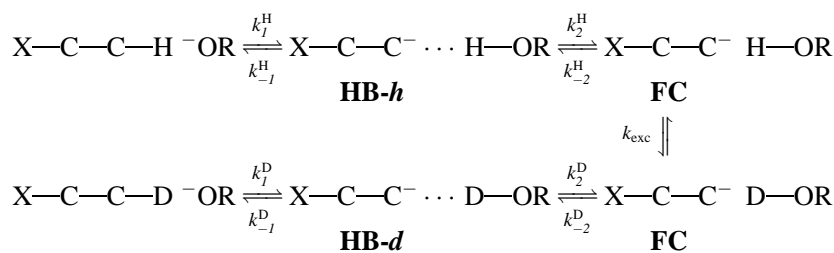
RESULTS AND DISCUSSION

Near-unity isotope effects for $\text{C}_6^i\text{H}_5\text{C-H}(\text{CF}_3)_2$ (**I**)⁶ and $p\text{-CF}_3\text{C}_6\text{H}_4\text{CTClCF}_3$ ($p\text{-CF}_3\text{-II}$)⁷ (Table 1) suggested energy diagrams similar to that for PFB (Fig. 1). Hydron

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Contract/grant sponsor: Petroleum Research Fund.

Contract/grant sponsor: Ministry of Education, Science, Sports and Culture, Japan.



Scheme 1.

transfer is not rate limiting and the free carbanions are at higher energy levels than the hydrogen-bonded intermediates. Although the protodetrifitation rates are similar for 9-PhFl-9-*t*, **I** and *p*-CF₃-**II**, the benzylic anions, [C₆H₅C(CF₃)₂]⁻ and [*p*-CF₃C₆H₄CClCF₃]⁻, behaved more like the localized PFB⁻ than the π -delocalized 9-PhFl⁻. The question arises regarding the p*K*_a of **I** and *p*-CF₃-**II** as to whether they are similar to PFB, 9-PhFl or neither. Equilibrium p*K*_a values for compounds with C—F bonds adjacent to a carbanion site cannot be measured in solution owing to the elimination of hydrogen fluoride. PFB⁻ loses fluoride ion readily in cyclohexylamine and requires an extrapolation back to the time of mixing to obtain an accurate value for the p*K*_a.³ Fortunately, an alternative is now available by measuring acidities in the gas phase. Even though the p*K*_a of **I** or *p*-CF₃-**II** cannot be obtained in solution, the gas-phase acidities, $\Delta G^\circ_{\text{Acid}}$, can be measured (Table 1).

Since $\Delta G^\circ_{\text{Acid}}$ values for **I** (335.3), 9-PhFl (335.6) and *p*-CF₃-**II** (337.4) are similar, new energy diagrams

similar to that for *p*-CF₃-**II** in Fig. 2 must be made. The exchange rate for 9-PhFl is faster than that for *p*-CF₃-**II** (Fig. 2 gap [Rate]). However, the proton transfer to form the hydrogen-bonded carbanion is much faster for *p*-CF₃-**II** (Fig. 2 gap [1]). Since the exchange reaction for *p*-CF₃-**II** has a near-unity isotope effect, the rate-limiting step is the formation of the free carbanion and the energy difference between internal return and the forward step is large (Fig. 2 gap [2]), while the forward step is slightly favored for 9-PhFl (Fig. 2 gap [3]). Although there is no experimental evidence that the hydrogen-bonded carbanion is lower in energy than the free carbanion for the reactions of *p*-CF₃-**II** (Fig. 2 gap [4]), preliminary PM3 calculations support this assignment.

The experimental $(k^{\text{D}}/k^{\text{T}})_{\text{Obs}}^{\text{MeOH}} = 1.34$ and $(k^{\text{H}}/k^{\text{T}})_{\text{Obs}}^{\text{MeOH}} = 1.77$ measured for the reactions of triphenylmethane (TPM) at 97.9 °C result in values of $a^{\text{H}} = 6.6$, $a^{\text{D}} = 1.3$ and $a^{\text{T}} = 0.68$,⁵ whereas those for 9-methylfluorene (9-MeFl) at 45 °C ($a^{\text{H}} = 0.55$, $a^{\text{D}} = 0.068$ and $a^{\text{T}} = 0.024$) are similar to those for 9-PhFl.² When

Table 1. $\Delta G^\circ_{\text{Acid}}$ and exchange rates in methanolic sodium methoxide

Compound	$\Delta G^\circ_{\text{Acid}}$ (gas phase) (kcal mol ⁻¹)	<i>k</i> (25 °C) (M ⁻¹ s ⁻¹)	Isotope effects
<i>m</i> -CF ₃ C ₆ H ₄ CT(CF ₃) ₂	326.8	4.70 × 10 ⁻¹	
3,5-(CF ₃) ₂ C ₆ H ₃ CDClCF ₃	332.4	7.51 × 10 ⁻²	
C ₆ H ₅ CD(CF ₃) ₂	335.3	2.13 × 10 ^{-3a}	$k^{\text{D}}/k^{\text{T}} = 1.02$
C ₆ H ₅ CT(CF ₃) ₂		2.09 × 10 ^{-3a}	
C ₆ H ₅ CT(CF ₃) ₂ [MeOD]		5.49 × 10 ^{-3a}	$k^{\text{H}}/k^{\text{T}} = 1.12$
C ₆ H ₅ CH(CF ₃) ₂ [MeOD]		6.14 × 10 ^{-3a}	$k^{\text{OD}}/k^{\text{OH}} = 2.63$
9-Phenylfluorene-9- <i>d</i>	335.6 ^b	4.28 × 10 ^{-3c}	$k^{\text{D}}/k^{\text{T}} = 2.46$
9-Phenylfluorene-9- <i>t</i>		1.73 × 10 ^{-3c}	
9-Phenylfluorene-9- <i>t</i> (MeOD)		3.15 × 10 ^{-3c}	$k^{\text{H}}/k^{\text{T}} = 15.9$
9-Phenylfluorene (MeOD)		5.01 × 10 ^{-2c}	$k^{\text{OD}}/k^{\text{OH}} = 1.81$
<i>p</i> -CF ₃ C ₆ H ₄ CDClCF ₃	337.4	8.58 × 10 ⁻⁴	$k^{\text{D}}/k^{\text{T}} = 1.08$
<i>p</i> -CF ₃ C ₆ H ₄ CTClCF ₃		7.91 × 10 ^{-4d}	
<i>p</i> -CF ₃ C ₆ H ₄ CTClCF ₃ (MeOD)		2.06 × 10 ^{-3d}	$k^{\text{OD}}/k^{\text{OH}} = 2.56$
<i>m</i> -CF ₃ C ₆ H ₄ CDClCF ₃	340.1	1.04 × 10 ⁻⁴	$k^{\text{D}}/k^{\text{T}} = 1.02$
<i>m</i> -CF ₃ C ₆ H ₄ CTClCF ₃		1.02 × 10 ⁻⁴	
<i>m</i> -CF ₃ C ₆ H ₄ CTClCF ₃		2.61 × 10 ⁻⁴	$k^{\text{OD}}/k^{\text{OH}} = 2.56$
Fluorene-9- <i>t</i>	343.9 ^b	3.14 × 10 ^{-5a}	
C ₆ F ₅ T	349.2	2.57 × 10 ^{-2e}	$k^{\text{D}}/k^{\text{T}} = 1.0^e$
C ₆ F ₅ H (MeOD)		6.53 × 10 ⁻²	

^a Data from Ref. 6.

^b Data from Ref. 9.

^c Data from Ref. 2.

^d Data from Ref. 7.

^e Data from Ref. 1.

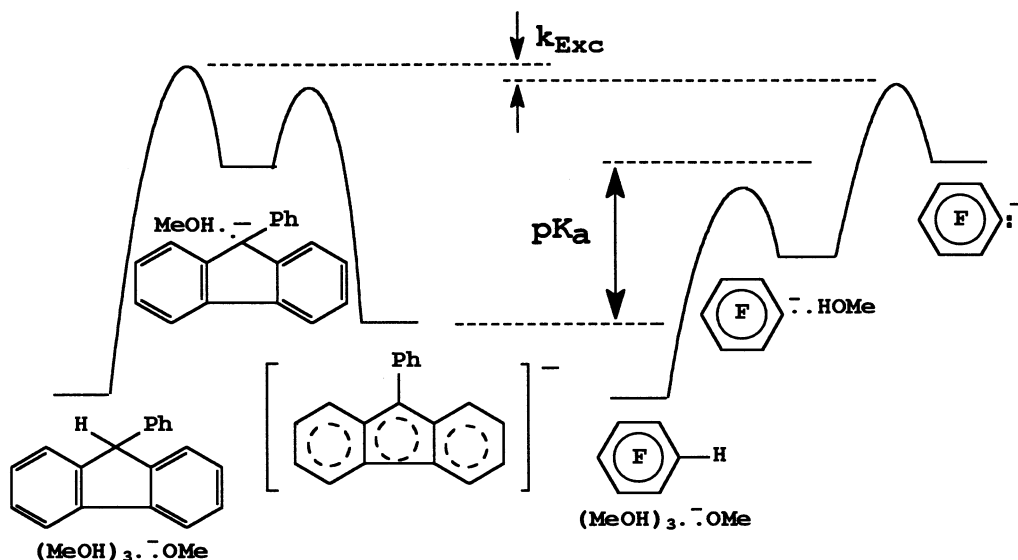


Figure 1. Possible energy diagrams for the reactions of 9-phenylfluorene and pentafluorobenzene with methoxide

corrected for internal return, values for k_1^H/k_1^T and k_1^D/k_1^T are calculated and found to 'differ little considering the 13 pK_a unit difference in acidity for these hydrocarbons.'⁸ The isotope effects associated with the reactions of **I** and p -CF₃-**II** are too small to allow the accuracy needed to calculate internal-return parameters; however, they would both be greater than those calculated for TPM. This is probably due to much greater steric factors for TPM. An estimate can be made of the proton-transfer step for p -CF₃-**II** by comparing it with the dehydrochlorination rate of p -CF₃C₆H₄CHClCF₂Cl, which is 2×10^3 faster at 25°C.⁷

A plot of $\log k$ ($M^{-1}s^{-1}$) vs ΔG°_{Acid} ($kcal\ mol^{-1}$) for fluorene,⁹ 9-PhFl,⁸ **I** and p -CF₃-**II** gives a good linear correlation. According to that line, PFB-*t* reacts 10 000 times faster than predicted by its ΔG°_{Acid} value. The linear relationship breaks down when other derivatives of **I** or **II** are added. The first was m -CF₃-**II**, which is slower by only a factor of 2, and this is reasonable; however, the addition of a second m -trifluoromethyl, 3,5-(CF₃)₂-**II**, results in a rate that is 10 times faster than predicted by $\Delta G^\circ_{Acid} = 332.4\ kcal\ mol^{-1}$. m -CF₃-**I** is four times faster than predicted. There is now a good linear correlation for the three points, m -CF₃-**II**, p -CF₃-**II** and 3,5-(CF₃)₂-**II**.

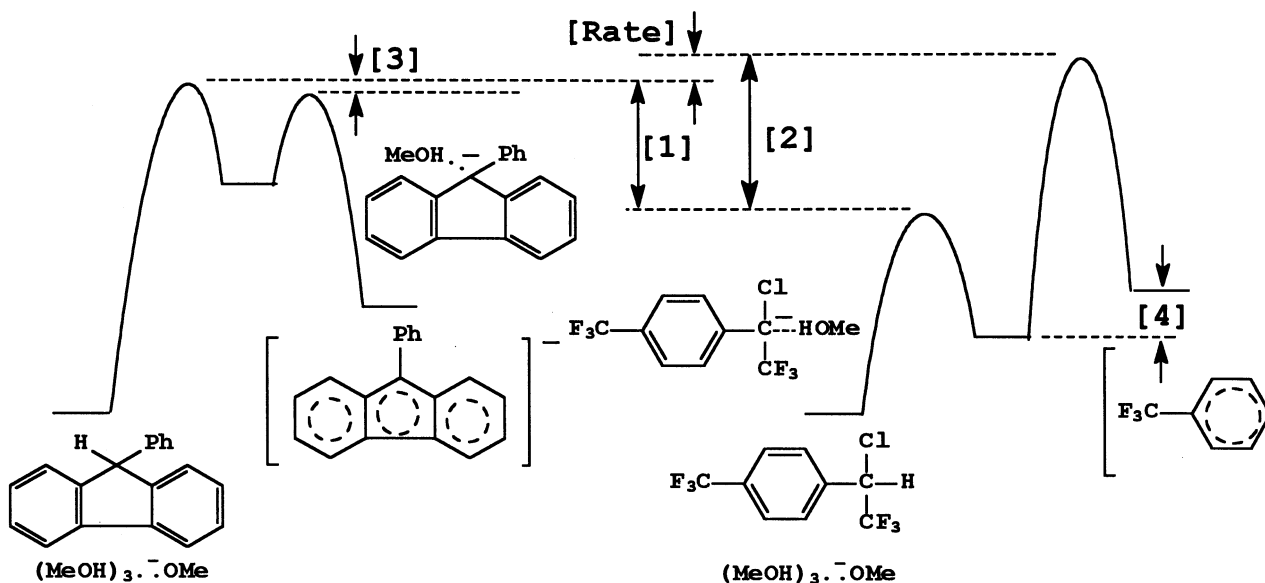
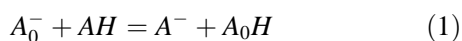


Figure 2. Possible energy diagrams for the reactions of 9-phenylfluorene and p -CF₃C₆H₄CHClCF₃ with methoxide

In conclusion, although the acidities of 9-PhFl and *p*-CF₃-II are similar, the important proton-transfer step to form a hydrogen-bonded carbanion and the subsequent breaking of that weak bond to form a free carbanion in methanol differ greatly. Studies are continuing to investigate these reactions.

EXPERIMENTAL

Gas-phase measurements. Gas-phase acidity measurements were performed on an Extrel FTMS 2001 Fourier transform mass spectrometer. Most of the experimental techniques used for the measurements of the equilibrium constants of the reversible proton-transfer reaction (1) are the same as those described previously.¹⁰ Only significant changes and additional procedures will be given here.



All equilibrium measurements were performed at a 3.0 T magnetic field strength using a cubic (2 × 2 × 2 in) trapped analyzer cell. The typical operating pressures were 10⁻⁶–10⁻⁷ Torr. The proton-transfer reactions were initiated by a pulsed electron beam (electron energy *ca* 0.3 eV, uncorrected, with a pulse width of 5 ms) through the cell containing *ca* 10⁻⁷ Torr of methyl nitrite used to generate methoxide ions. The mass spectra and time plots were acquired and processed in the Fourier transform mode. Depending on the pressure of the neutrals, the proton transfer equilibrium was achieved within 5–10 s of initiation of the reaction (depending on the pressure of the neutrals), and the equilibrium constant *K* for reaction (1) was evaluated using the expression $K = [A^-][A_0H]/[A_0^-][AH]$. The relative abundances of A⁻ and A₀⁻ ions were determined from the relative intensities in the ion cyclotron resonance (ICR) mass spectra after equilibrium was attained. The pressures of the neutral reactants were measured by means of a Bayard–Alpert-type ionization gauge with appropriate correction factors being applied to the gauge readings for the different ionization cross-sections of various compounds.¹¹ The sample inlet system and the ICR chamber were kept at 50 °C. Literature $\Delta G^{\circ}_{\text{Acid}}$ values for the reference compounds are⁹ *m*-trifluoromethylbenzoic acid 325.3, *m*-nitrophenol 327.4, malononitrile 328.2, *m*-cyanophenol 328.9, *m*-trifluoromethylphenol 332.5, *p*-trifluoromethylbenzyl nitrile 332.9, benzoic acid 333.0, *p*-trifluoromethylaniline 346.1, *m*-trifluoromethylaniline 349.70 and nitromethane 349.7.

Kinetic Measurements. Protodetrutiation kinetics have been described previously.⁶ Protodeuteriation kinetics made use of a Hewlett-Packard model 5890 Series II gas chromatograph with a model 5972 mass-selective detector using an electron beam energy of 70 eV. Since there is some separation of the protio- and deuterio-compounds, the entire GC peak was sampled. Calculations were made using the parent peak and also the largest signal which resulted from the loss of a trifluoromethyl group to form the benzylic carbocation. No P-1 peaks were observed for the fluorinated compounds. The concentration of sodium methoxide was corrected for the temperature of each kinetic run.

Acknowledgements

H.F.K. thanks the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support, and M.M. gratefully acknowledges support by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan.

REFERENCES

1. A. Streitwieser, Jr, J. A. Hudson and F. Mares. *J. Am. Chem. Soc.* **90**, 648–651 (1968).
2. A. Streitwieser, Jr, W. B. Hollyhead, A. H. Pudjaatmake, P. H. Owens, T. L. Kruger, P. A. Rubenstein, R. A. MacQuarrie, M. L. Brokaw, W. K. C. Chu and H. M. Niemeier. *J. Am. Chem. Soc.* **93**, 5088–5096 (1971).
3. A. Streitwieser, Jr, P. J. Scannon and N. H. Neimeyer. *J. Am. Chem. Soc.* **94**, 7936–7937 (1972).
4. H. F. Koch. in *Comprehensive Carbanion Chemistry, Part C*, edited by E. Bunzel and T. Durst, pp. 321–360. Elsevier, Amsterdam (1987).
5. A. Streitwieser, Jr, W. B. Hollyhead, G. Sonnichsen, A. H. Pudjaatmake, C. J. Chang and T. L. Kruger. *J. Am. Chem. Soc.* **93**, 5096–5102 (1971).
6. H. F. Koch, D. B. Dahlberg, G. Lodder, K. S. Root, N. A. Touchette, R. L. Solsky, R. M. Zuck, L. J. Wagner, N. H. Koch and M. A. Kuzemko. *J. Am. Chem. Soc.* **105**, 2394–2398 (1983).
7. H. F. Koch, G. Lodder, J. G. Koch, D. J. Bogdan, G. H. Brown, C. A. Carlson, A. B. Dean, R. Hage, P. Han, J. C. P. Hopman, L. A. James, P. M. Knape, E. C. Roos, M. L. Sardina, R. A. Sawyer, B. O. Scott, C. A. Testa and S. D. Wickham. *J. Am. Chem. Soc.* **119**, 9965–9974 (1997).
8. Ref. 5, p. 5099.
9. S. G. Lias, J. E. Bartmess, J. F. Leibman, J. L. Holmes, R. D. Levin and G. W. Mallard. *J. Phys. Chem. Ref. Data* **17**, Suppl. 1 (1988).
10. M. Fujio, R. T. McIver, Jr and R. W. Taft. *J. Am. Chem. Soc.* **103**, 4017–4029 (1981).
11. J. J. Miller. *J. Am. Chem. Soc.* **112**, 8533–8542 (1990).