

pK_a Measurements in Tetrahydrofuran

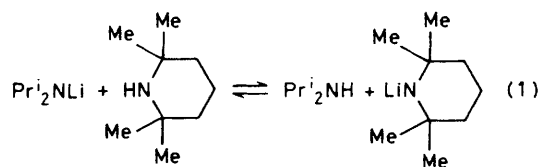
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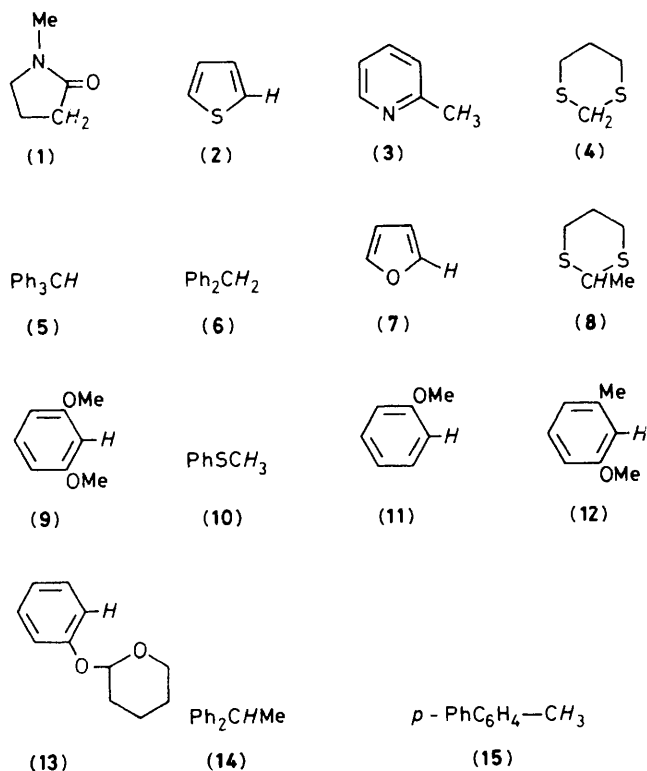
The relative acidities of fifteen weakly acidic hydrocarbons have been measured in tetrahydrofuran using ¹³C n.m.r. spectroscopy.

The development of an acidity scale for weak carbon acids has been a continuously evolving area of research. The MSAD scale was assembled by Cram¹ from the works of many chemists, mainly McEwen, Streitwieser, Applequist, and Dessy, and covered a range in pK_a values from 18.5 to 45 in a variety of solvents. Streitwieser subsequently extended and refined his pK_a measurements in cyclohexylamine (CHA) which he termed 'ion-pair acidity' measurements² to indicate the nature of species in solution. A new scale has been established by Bordwell. In pure dimethyl sulphoxide (DMSO) equilibrium measurements by indicator methods, in conjunction with extrapolations of Hammett plots and substituent effects, provided pK_a values up to and including methane (pK_a = 55).³ Other important methods for measuring pK_a values include the electrochemical method of Breslow⁴ and heats of deprotonation as used by Arnett and Venkatasubramanian.⁵ In general, agreement between pK_a values for the same acid in different solvents has been quite good although significant solvent effects have been encountered.⁶ At present there are few data available pertaining to tetrahydrofuran

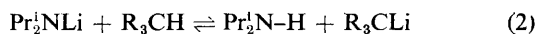
(THF), in spite of its widespread use as a solvent for carbanion reactions. We describe here a simple direct method of measurement of relative acidities of weak carbon acids in THF. Our measurements cover a range of 7 pK units, allowing assignment of values for pK_a of up to 40.



We recently described the determination of *K* for the equilibrium (1) using ¹³C n.m.r. spectroscopy.⁷ Owing to unusually slow Li–H interchange the concentrations of all four species in equilibrium (1) were measured directly to provide *K* and thereby a ΔpK_a of 1.6 between the amines diisopropylamine (DIPA) and tetramethylpiperidine (TMP).



We find that the same approach[†] provides *K* for equilibria of the type shown in (2) where, again, Li-H interchange is slow



on the n.m.r. time-scale. By using both lithium di-isopropylamide (LDA) and lithium tetramethylpiperide (LTMP) with various carbon acids we have measured the relative acidities of acids having $\text{p}K_{\text{a}}$ values from 2.5 units lower than that of DIPA to 2.5 units greater than that of TMP. Table 1 summarizes our $\text{p}K_{\text{a}}$ measurements (in acidity per hydrogen).

The data in Table 1 show that, in THF, some $\text{p}K_{\text{a}}$ values are unusually low, others surprisingly high. For example thiophene is completely metallated by LDA[‡] while *p*-methylbiphenyl, which has a similar $\text{p}K_{\text{a}}$ in CHA, is not at all metallated by the stronger base, LTMP. The results for (6) and (10) also reveal appreciable differences in $\text{p}K_{\text{a}}$ values in THF vs. DMSO. Of practical significance is the fact that furan is more than 90% metallated by LTMP suggesting these conditions to be suitable when functionality precludes the use of alkyl-lithiums.

The $\text{p}K_{\text{a}}$ values of the acids listed in Table 1 have been assigned with reference to 2-methyl-1,3-dithiane (8). We assign this acid a $\text{p}K_{\text{a}}$ of 37.8, the same value as reported by Streitwieser and Guibe.⁹ The choice of (8), though arbitrary, was made to place the acids studied in as close overall agreement with the CHA scale as possible (selection of this reference

[†] The relative concentrations of the four species are determined from peak heights after equilibration. The differential effects of relaxation times were minimized by using a small pulse angle and a 1 s pulse delay (use of a 2 s pulse delay caused no change in peak intensity ratios). Differential Overhauser effects, or other factors, are removed by using a correction factor for the α - or β -carbons of the lithiated vs. free amine (as determined by partial lithiation of the amine in the presence of a small amount of naphthalene, as internal standard). Our resultant values for *K* are thought to be accurate to $\pm 25\%$ leading to a maximum error of ± 0.1 units for each reported $\text{p}K$ value.

[‡] Metallation of 2-bromothiophene was reported to occur at position 5 but the yield of silylation product was not given.⁸

Table 1. $\text{p}K_{\text{a}}$ Values of weak organic acids.

Compound	THF	DMSO	CHA
(1)	<33.8		
(2)	<33.3	35 ^a	38.2 ^b
(3)	34.5		
(4)	34.8		31.9 ^{b,c}
(5)	34.6	30.6	31.5
(6)	35.9	32.1	33.4
(7)	35.9		38.1 ^d
(8)	37.8 ^e		37.8 ^{b,c}
(9)	37.8		
(10)	38.3	43 ^f	
(11)	38.4		
(12)	38.7		
(13)	39.1		
(14)	39.4		>35 ^e
(15)	>40.2		39.0 ^b

^a Ref. 10. ^b Ref. 9. ^c Ref. 11. ^d Estimated from data in ref. 12.

^e Chosen as standard. ^f Estimated from data in ref. 13. ^g Ref. 14.

leads to $\text{p}K_{\text{a}}$ values of 35.7 and 37.3 for DIPA and TMP, respectively).

We are currently extending our measurements to include other common weak organic acids and additional structurally hindered amines with the aim of enlarging the range of accessible $\text{p}K_{\text{a}}$ values. It should be kept in mind that the data obtained in THF, though of immediate utility to carbanion chemistry, probably describe 'ion-pair' or 'ion aggregate' acidities.[§] Until the solvation and association of these lithiated hydrocarbons is well understood, the interpretation of structural effects on $\text{p}K_{\text{a}}$ must be made with caution.

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References

- D. J. Cram, 'Fundamentals of Carbanion Chemistry,' Academic Press, New York, 1965, p. 19.
- D. W. Boerth and A. Streitwieser, Jr., *J. Am. Chem. Soc.*, 1981, **103**, 6443, and references therein; for a recent review see A. Streitwieser, Jr., 'Equilibrium Carbon Acidities in Solution,' in 'Comprehensive Carbanion Chemistry,' part 1, eds. E. Bunel and T. Durst, Elsevier-North Holland, 1980.
- F. G. Bordwell, G. E. Drucker, and H. E. Fried, *J. Org. Chem.*, 1981, **46**, 632, and references therein.
- B. Jaun, J. Schwarz, and R. Breslow, *J. Am. Chem. Soc.*, 1980, **102**, 5741, and references therein.
- E. M. Arnett and K. G. Venkatasubramanian, *Tetrahedron Lett.*, 1981, 987.
- W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum, and N. R. Vanier, *J. Am. Chem. Soc.*, 1975, **97**, 7006.
- R. R. Fraser, A. Baignée, M. Bresse, and K. Hata, *Tetrahedron Lett.*, 1982, 4195.
- G. M. Davies and P. S. Davies, *Tetrahedron Lett.*, 1972, 3507.
- A. Streitwieser, Jr., and F. Guibé, *J. Am. Chem. Soc.*, 1978, **100**, 4532.
- F. G. Bordwell, J. C. Branca, D. L. Hughes, and W. N. Olmstead, *J. Org. Chem.*, 1980, **45**, 3305.
- A. Streitwieser, Jr., and S. P. Ewing, *J. Am. Chem. Soc.*, 1975, **97**, 190.
- A. Streitwieser, Jr., and P. J. Scannon, *J. Am. Chem. Soc.*, 1973, **95**, 6273.
- F. G. Bordwell, J. E. Bares, J. E. Bartmess, G. E. Drucker, J. Gerhold, G. J. McCallum, M. Van der Puy, N. R. Vanier, and W. S. Matthews, *J. Org. Chem.*, 1977, **42**, 326.
- A. Streitwieser, Jr., J. R. Murdoch, G. Häfelinger, and C. J. Chang, *J. Am. Chem. Soc.*, 1973, **95**, 4248.

[§] Experiments at 0.1 M concentration revealed no change in *K* in comparison with measurements on 0.5 M solutions.