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The Affinities of Weak Nucleophiles for Incipient Methyl Cations

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The increasing use of powerful methylating agents, such as trimethyloxonium salts,[1] methyl fluorosulfonate ("magic methyl")[2] and methyl trifluoromethane sulfonate,[3] raises the question of the relative reactivities of these reagents as well as that of the relative affinities of various aprotic solvents for the incipient methyl cation. The answers to these questions are embodied in the equilibrium constants for the following equilibria, in which the methyl cation replaces the proton in the Lowry-Brønsted acid-base system.

$$A + BCH_3 \rightleftharpoons ACH_3^+ + B^-$$

$$A + BCH_3^+ \rightleftharpoons ACH_3^+ + B$$

We have determined equilibrium constants for a series of such equilibria so chosen as to permit the establishment of single scale of affinities over the range of systems investigated. The determinations were made on solutions of reactants in tetramethylene sulfone (sulfolane) a solvent of very low nucleophilicity.[4] The equilibrium concentrations of the species present in the equilibrium mixtures were determined by nmr spectroscopy and usually involved integration of the signals of the methyl protons and/or various types of aromatic protons. The concentrations of reactants were generally in range 0.1-0.5M but were adjusted within this range, depending on the equilibrium constant of the particular reaction, to provide the most sensitive determination of relative integrals. The results, together with the chemical shifts of the protons of the transferrable methyl groups, are recorded in the Table. With the exception of the last entry, the values were obtained by

Table 1

Chemical Shifts (δ) of Transferable Methyl Groups and Equilibrium Constants (30°) for the Reaction[a]

$$\overset{+}{A}CH_3 + [(CH_3)_2N]_3PO \overset{K}{\rightleftharpoons} A + [(CH_3)_2N]_3\overset{+}{P}OCH_3 \text{ (in Sulfolane)}$$

A	δ(ACH_3)	K
$[(CH_3)_2N]_3PO$ (HMPT)	3.91	(1.0)
$(CH_3)_2SO$ (DMSO)[b]	4.10	1.1
$(CH_3)_2NCHO$ (DMF)[c]	c	1.4
Ph_2S	3.77	3.45
2,4-Dimethoxybenzonitrile	4.11	5.5
Ph_2SO	4.30	5.75
p-Methoxybenzonitrile	4.18	10
p,p'-Denitrodiphenylsulfide	3.92	13
p-Toluonitrile	4.13	53
Benzonitrile	4.18	72
p-Fluorobenzonitrile	4.13	1.0×10^2
p-Chlorobenzonitrile	4.16	1.5×10^2
p-Bromobenzonitrile	4.12	1.6×10^2
p-Dicyanobenzene	4.23	3.1×10^2
p-Nitrobenzonitrile	4.22	1.1×10^3
FSO_3^-	4.35	2.2×10^3
$CF_3SO_3^-$	4.30	3.5×10^3
$(CH_3)_2O$	4.49	1.2×10^4
$(CH_3O)_3PO$ (TMP)	4.27	1.2×10^4
CH_3COOCH_3	4.52	1.3×10^5
Ph_2CO	4.98	5×10^7

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[a] Except for reactions involving FSO_3CH_3 and $(CH_3)_3O^+BF_4^-$, the counter anion was $CF_3SO_3^-$.

[b] No evidence for the S-methyl cation was observed; cf. S. G. Smith and S. Winstein, Tetrahedron, 1958, 3, 317.

[c] Under the reactions conditions and at equilibrium the cationic species were $(CH_3)_2NCH=\overset{+}{O}CH_3$ [δ, 4.38 (OCH_3); 7.64 (-CH=)], 80% and $(CH_3)_3\overset{+}{N}CHO$ [δ, 8.15 (-CH=) 20%; cf. ref. 2.

equilibrating pairs of substrates for which $0.1<K<10$. In cases for which K could be determined directly for A and B and indirectly from the systems A and C and B and C the values agreed within ± 10% and their averages are recorded in the Table. Although no quantitative measurements of rates at which the equilibria are established, it was noted that those reactions involving the last five entries in the Table were invariable complete within one to two hours.

Several practical conclusions can be drawn from these results. The common polar aprotic solvents HMPT, DMSO, and DMF are too nucleophilic to preserve the high reactivities of commercially available methylating agents such as methyl fluosulphonate, (magic methyl), methyl trifluoromethane sulphonate, and the trimethyl oxonium salts. On the other hand trimethyl phosphate is an extremely useful solvent and tetramethoxy phosphonium tetrafluoroborate[5] or hexafluoroantimonate are stable either in the solid state or in solution in trimethyl phosphate. These salts constitute cheap and efficient methylating agents for organic and inorganic substrates for which the use of a polar aprotic solvent is required or desirable.

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4. The methyl sulfolane cation can be prepared by treating anhydrous solutions of silver tetrafluoroborate or silver hexafluorantimonate in sulfolane with methyl iodide. The methyl protons of the cation absorbed at $\delta 4.45$. The solutions are unstable at room temperature decomposing the methyl fluoride and BF_3 (1 hr) and methyl fluoride and SbF_5 (24 hr).

5. L. V. Nesterov and R. I. Mutalapova, *Tetrahedron Letters*, 1968, **51**.