description, though four electron pairs, rather than three, participate in the process.

(3) The very high regioselectivity usually depicted by these cycloadditions appears to obey electronic reasons, i.e., to the conjugative or hyperconjugative stabilization of the transition state leading to the observed regioisomer by the olefin substituent.

(4) The striking diastereoselectivity of this reaction is well reproduced by the calculations, and it is seen to obey the minimization of steric interactions between the substituents of the ketene and olefin partners in the transition state.

(5) The calculated substituent effects on reaction rates, regioselectivities, and stereoselectivities are in good agreement with the available experimental results.

Acknowledgment. The calculations were performed with the IBM 3090 computer at the "Centre d'Informàtica de la Universitat de Barcelona". Financial support from the CICYT (Grant PB86-510) is gratefully acknowledged. We are indebted to Dr. Josep M. Bofill for making available to us the program for TCSCF calculations. We also thank Prof. Santiago Olivella and Dr. Antoni Riera for helpful discussions.

Supplementary Material Available: Cartesian coordinates of the optimized molecular structures (67 pages). Ordering information is given on any current masthead page.

Heats of Reaction for Nucleophilic and Electrophilic Displacement Reactions in Solution

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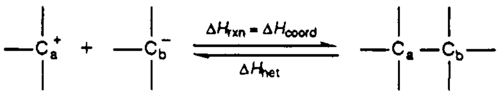
Measured heats of displacement, ΔH_{dis}, in sulfolane/3-methylsulfolane solution at 25 °C, are reported for the attack of carbenium ions and various anions on neutral compounds, most of whose heats of heterolysis, ΔH_{het}, have been published previously. Some new ΔH_{het} values are derived from measured heats of reaction of resonance-stabilized carbenium ions with inorganic anions. In most cases there is good agreement between the measured ΔH_{dis} and that calculated by the First Law from the combined ΔH_{het}s. However, large discrepancies are found for other cases, and these are shown to be due to formation of a variety of products, presumably because of extreme steric hindrance to direct displacement at the original bonding site.

Introduction

Nucleophilic and electrophilic displacements encompass a major domain of mechanistic study.[1] Historically, they have been approached primarily in terms of kinetics with relatively little consideration of the overall thermodynamics of such processes. Against this background, results reported here are, to the best of our knowledge, the first thermochemical data available for the heats of nucleophilic displacement of one base by another, or electrophilic displacement of one carbenium ion by another from neutral compounds.

Scheme I



$$-C_a^+ + -C_b^- \underset{\Delta H_{het}}{\overset{\Delta H_{rxn} = \Delta H_{coord}}{\rightleftharpoons}} -C_a-C_b-$$

$$-\Delta H_{coord} = -\Delta H_{rxn} = \Delta H_{het}$$

Recently we became engaged in an extensive investigation of direct reactions between carbenium ions with a wide variety of anionic bases. The kinetics, thermodynamics, and electrochemistry for such systems, including the energetics of bond cleavage to form ions or radicals, were reported.[2-6] Heats of reaction (rxn) for the coordination (coord) of carbenium ions with carbanions to form neutral species led to an extensive tabulation[7-11] of heterolysis (het) energies (Scheme I) and these values were correlated with remarkably high precision to the pK_as of the conjugate acids[12] of the carbanions and the pK_{R^+}s of the carbenium ions.[13] With this information in hand it is reasonable to predict that highly reactive anions which form a strong bond (high ΔH_{het}) with a given carbenium ion should displace more stable anions which form less endothermic bonds. Exactly the same reasoning applies to displacement reactions by carbenium ions. By means of the First Law, the heats of displacement should be accurately predictable as the difference between the heats of heterolysis of the bond being broken and the bond being made. This article describes the application of this simple proposal to displacement reactions.

Until this point, our research has been limited to resonance-stabilized organic anions. However, extensive kinetic studies of carbenium ions with inorganic anions in predominantly aqueous solution by Ritchie and others[14,15]

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(1) (a) Lowry, T. H.; Richardson, K. S. *Mechanisms and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987. (b) March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley & Sons: New York, 1985. (c) Harris, J. M.; McManus, S. P., Eds. *Nucleophilicity*; Advances in Chemistry Series; American Chemical Society: Washington, DC, 1987.

(2) Arnett, E. M.; Troughton, E. B. *Tetrahedron Lett.* **1983**, *24*, 3299.

(3) Arnett, E. M.; Troughton, E. B.; McPhail, A.; Molter, K. E. *J. Am. Chem. Soc.* **1983**, *105*, 6172.

(4) Troughton, E. B.; Molter, K. E.; Arnett, E. M. *J. Am. Chem. Soc.* **1984**, *106*, 6726.

(5) Arnett, E. M.; Molter, K. E. *J. Phys. Chem.* **1986**, *90*, 471.

(6) Arnett, E. M.; Molter, K. E. *Acc. Chem. Res.* **1985**, *18*, 339.

(7) Arnett, E. M.; Chawla, B.; Molter, K. E.; Amarnath, K.; Healy, M. *J. Am. Chem. Soc.* **1985**, *107*, 5288.

(8) Arnett, E. M.; Chawla, B.; Amarnath, K.; Whitesell, L. G., Jr. *Fuel Energy* **1987**, *1*, 17.

(9) Arnett, E. M.; Whitesell, L. G., Jr.; Amarnath, K.; Cheng, J.-P.; Marchot, E. *Die Macromolekular Chemie*; Macromolecular Symposium (Munich, 1987) **1988**, *13/14*, 21-31.

(10) Arnett, E. M.; Harvey, N. G.; Amarnath, K.; Cheng, J.-P. *J. Am. Chem. Soc.* **1989**, *111*, 4143.

(11) Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1990**, *112*, 344.

(12) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456 and private communications.

(13) Bethell, D.; Gold, V. In *Carbonium Ions*; Academic Press: New York, 1967.

(14) Ritchie, C. D. *Can. J. Chem.* **1986**, *64*, 2239.

(15) McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1989**, *111*, 2929.

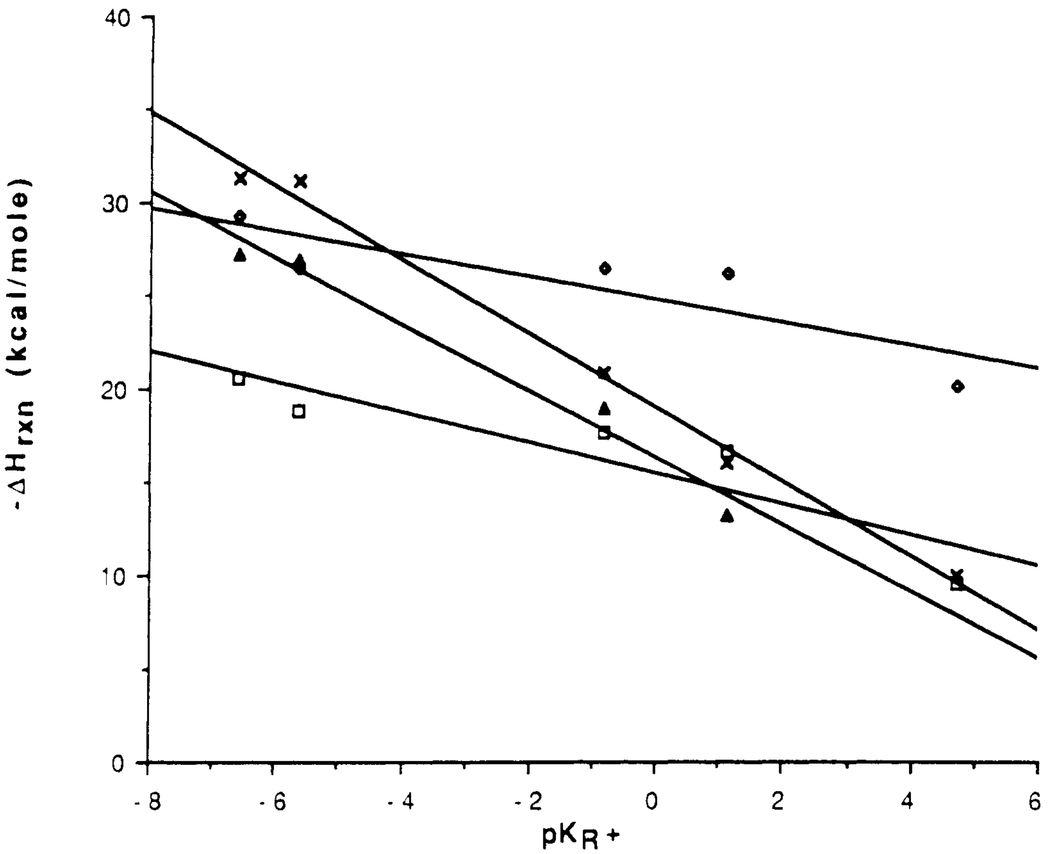

Figure 1. Plot of ΔH_{rxn} in sulfolane/3-methylsulfolane at 25 °C against pK_{R^+} of the cations. (□) Azide: $\Delta H_{rxn} = 15.46 - 0.82pK_{R^+}$; corr = 0.91. (×) Methylthioglycolate: $\Delta H_{rxn} = 18.98 - 1.98pK_{R^+}$; corr = 1.00. (◆) Thiophenolate: $\Delta H_{rxn} = 24.78 - 0.61pK_{R^+}$; corr = 0.86. (▲) Nitrite: $\Delta H_{rxn} = 16.23 - 1.79pK_{R^+}$; corr = 0.99.

have prompted us to include some inorganic salts in our study of the thermochemistry of bond formation and displacement.

Experimental Section

Calorimetry. Heats of displacement (ΔH_{dis}) were measured using a Tronac 450 titration calorimeter which was configured with two motor-driven burets. Its operation has been described elsewhere.[16] All the solutions were prepared in an argon-filled dry box and protected from air when placed in the calorimeter by maintaining an argon atmosphere over the solutions. The following exemplifies the procedure for measuring the heat of displacement reactions and is typical for all types of displacements measured.

A solution of potassium 4-nitrothiophenoxide in sulfolane–5% 3-methylsulfolane (19.7 mg in 30 mL of solvent, 0.12 mM) was placed in the calorimeter dewar. Trityl tetrafluoroborate (0.1702 g in 5 mL of solvent, 0.1031 M) was added to the anion solution in the dewar via one of the motor-driven burets until all of the anion had reacted (approximately 0.99 mL of the trityl solution). The heat of reaction of the carbenium ion with the anion agreed well in each case with previously reported values.[9] The displacing anion, potassium 4-fluorophenoxide (0.0492 g in 5 mL of solvent, 0.0655 M) was then titrated with the other motor-driven buret into the solution inside the dewar containing the coordinated product of trityl cation and 4-nitrothiophenoxide. The heat of displacement was calculated from the observed heat change by standard procedures.[8] Each reported ΔH_{dis} is the average of two to six enthalpy measurements with the same solution of coordinated product. Reproducibility of the ΔH_{dis} was verified by using different carbocation and anion solutions prepared on different days.

Heats of Reaction with Inorganic Anions. Most inorganic salts are not soluble in sulfolane–3-methylsulfolane (5%). However, the potassium salts (e.g., K^+Cl^-) dissolved readily on stirring with 1:1 molar ratio of 18-crown-6 overnight. Similarly for sodium salts (e.g., $NaNO_2$) dibenzo-18-crown-6 was used. The anion solutions were then titrated against the cation as described earlier.[8]

HPLC Analysis. HPLC analysis of the various products was made on a Varian 5000 liquid chromatograph using a solvent mixture of 55% THF and 45% H_2O and an Alltech C18 5μ 4.6 mm × 25 cm reversed-phase column; 10-μL injections were made at 350 atm, and the peaks were detected at 250 nm at 25 °C.

The displacement reactions for analysis were carried out on a microscale inside an argon-filled dry box, and the product samples were quenched with previously degassed demineralized water before HPLC analysis.

Results and Discussion

Table I gives the heats of heterolysis ($-\Delta H_{rxn}$) for the compound formed by reaction of some inorganic anions with five cations. Table II compares the measured versus calculated ΔH_{dis} values for a series of displacements by different types of carbenium ions and anions in the solvent of choice, sulfolane/3-methylsulfolane (5%) at 25 °C. For the majority of cation and anion displacements, there is good agreement, within experimental error, between measured and calculated values. However, some discrepancies can be seen. Each data set was repeated at least three times with three different batches of materials (especially in the cases of the greatest discrepancies) over the course of a year. Therefore, the discrepancies cannot be assigned simply to experimental error. Since they also cannot be due to a failure of the First Law, the products were examined carefully to see whether they were different for the displacement reactions from those produced by the direct cation/anion combinations. In cases where nucleophilic or electrophilic attack by a bulky cation or anion is taking place on a very congested bonding site, it is

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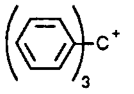
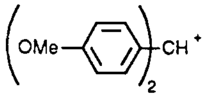
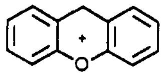
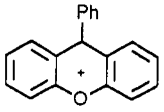
[16] Arnett, E. M.; Chawla, B. *J. Am. Chem. Soc.* **1978**, *100*, 217.

Table I. Heats of Heterolysis ($-\Delta H_{rxn}$, kcal/mol) for Inorganic Anions with Cations in Sulfolane (95%)/3-Methylsulfolane (5%) at 25 °C

		cations (pK_{R^+})				
		trityl	DPM	Xa	9PhXa	Trop
						
anions[a]	pK_a[b] (in DMSO)	(−6.6)	(−5.65)	(−0.85)	(1.1)	(4.7)
azide (NaN_3)	7.9	20.56 ± 0.87	18.88 ± 0.30	17.71 ± 0.57	16.55 ± 0.23	9.58 ± 0.11
thiophenolate ($C_6H_5S^-K^+$)	10.3	29.25 ± 0.63	26.47 ± 1.22	26.43 ± 0.38	26.11 ± 0.35	20.17 ± 0.11
sulfite (Na_2SO_3)	–	22.34 ± 0.30	–	–	–	–
$K^{+-}SCH_2COOMe$	13.0	31.30 ± 1.00	31.11 ± 1.81	20.85 ± 1.04	16.06 ± 1.06	10.03 ± 1.40
cyanide (NaCN)	12.9	32.38 ± 0.76	32.87 ± 1.20	34.00 ± 0.36	33.11 ± 0.59	31.57 ± 0.70
acetate (NaOAc)	11.6	20.57 ± 1.32	–	15.44 ± 0.43	8.90 ± 0.62	–
carbonate (K_2CO_3)	–	22.28 ± 0.49	–	–	–	–
nitrite	–	27.16 ± 0.69	26.93 ± 1.27	19.04 ± 0.27	13.23 ± 0.37	–
hydroxide	–	–	–	27.04 ± 1.57[c]	–	–
phenoxide	–	–	41.18 ± 1.20	31.53 ± 2.21[c]	23.53 ± 0.55	–
chloride	–	12.44 ± 0.21	–	5.69 ± 0.81[c]	–	–
methoxide	–	–	–	–	–	–

[a] Anions were dissolved in sulfolane mixture using 1:1 mol ratio of 18-crown-6 (for K^+ salts, e.g., KCl) and dibenzo-18-crown-6 (for Na^+ ions, e.g., $NaNO_2$). [b] pK_a values are taken from ref 18. [c] Values are the average of one set of runs.

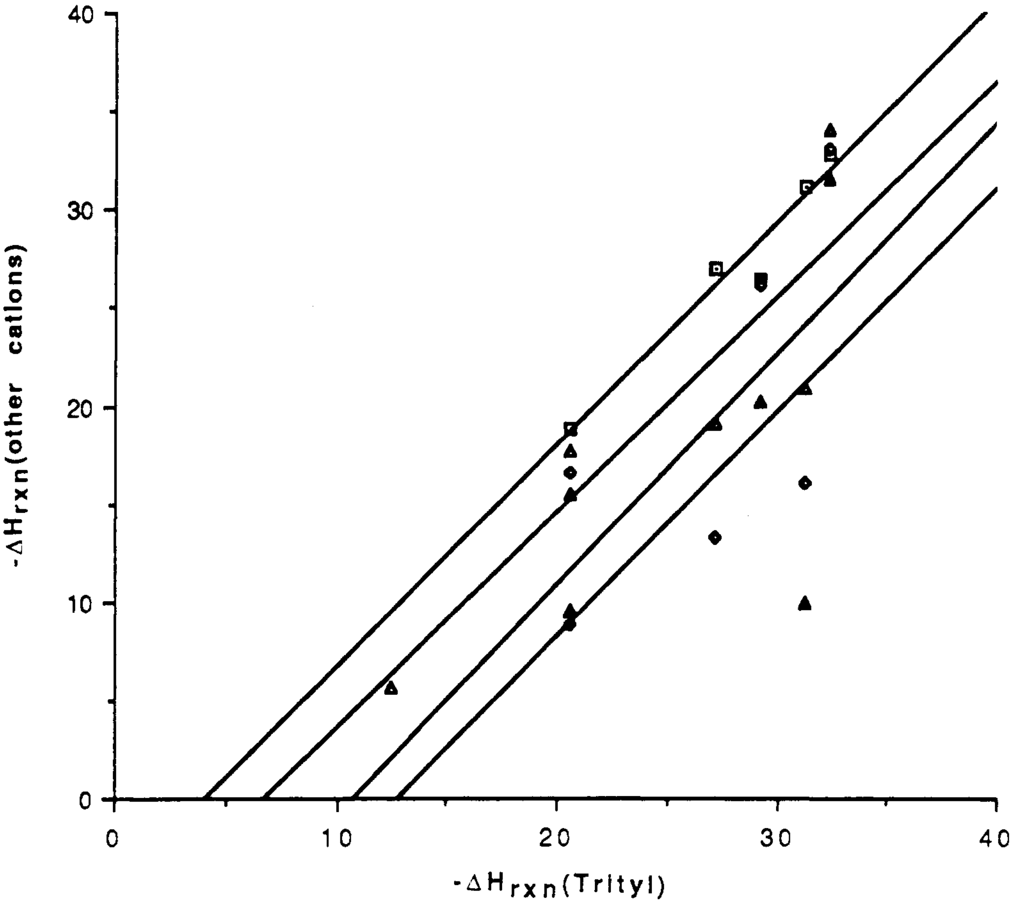


Figure 2. Comparison of heats of reaction (kcal/mol) of five carbenium ions with anions in Table I. (□) $-\Delta H_{rxn}$(DPM) = −4.51 − 1.13ΔH_{rxn}(trityl); R = 0.98. (△) $-\Delta H_{rxn}$(Xa) = −7.31 − 1.10ΔH_{rxn}(trityl); R = 0.90. (◆) $-\Delta H_{rxn}$(9-PhXa) = −12.61 − 1.18ΔH_{rxn}(trityl); R = 0.68. (▲) $-\Delta H_{rxn}$(Trop) = −14.57 − 1.14ΔH_{rxn}(trityl); R = 0.59.

reasonable that attack could occur instead at a more remote position to produce an isomer of the expected product. Since steric hindrance also favors electron-transfer processes,[17] it is also possible that a mechanism change produced free radicals and a less selective reaction.

However, it must be emphasized that all of the reactions reported here were instantaneous on the time scale of titration. None of the thermograms was curved.

Full HPLC analyses of the products of the displacement reactions have been made. Generally, in those cases where there is a good agreement between the experimentally measured and calculated heats of displacement values, there is an exact, point to point correspondence between

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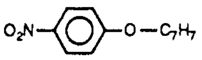
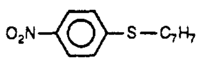
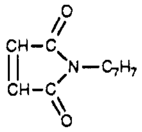
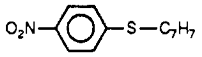
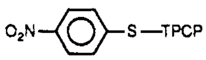
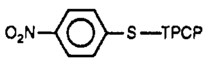
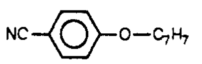
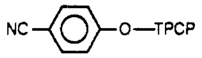
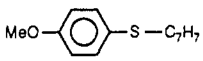
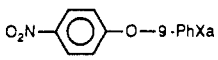
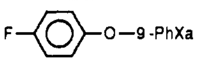
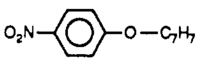
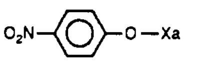
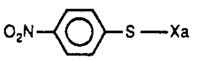
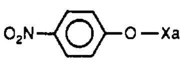
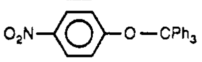
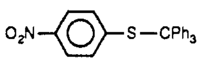
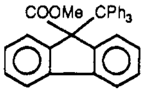
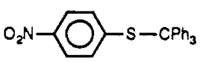
[17] Bordwell, F. G.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 1052.

Table II. Heats of Displacement Measured at 25 °C in Sulfolane/3-Methylsulfolane (5%)

substrate[a]	displacing cation or anion[b]	heats of displacement ΔH_{dis}, kcal/mol	
		measured	calculated
	xanthylium	9.63 ± 2.24	9.44 ± 0.71
	trityl	9.65 ± 0.39	8.39 ± 0.43
	trityl	6.56 ± 1.46	7.17 ± 0.79
	xanthylium	7.63 ± 0.30	6.77 ± 0.40
	trityl	8.85 ± 0.41	8.90 ± 0.39
	xanthylium	7.57 ± 0.55	7.22 ± 0.40
	xanthylium	9.63 ± 0.49	10.1 ± 0.5
	xanthylium	8.33 ± 0.26	9.02 ± 0.46
	xanthylium	9.67 ± 0.50	8.06 ± 0.79
	trityl	9.71 ± 0.71	16.0 ± 0.4
	trityl	9.72 ± 0.63	14.4 ± 0.7
	trityl	14.2 ± 2.4	20.4 ± 0.8
	4-fluorophenoxide	8.81 ± 2.1	10.0 ± 0.6
	4-fluorophenoxide	7.02 ± 1.88	8.00 ± 0.68
	phenoxide	10.7 ± 1.1	9.07 ± 0.65
	4-fluorophenoxide	8.02 ± 1.39	7.30 ± 0.81
	4-fluorophenoxide	8.61 ± 0.46	14.8 ± 0.8
	4-fluorophenoxide	4.22 ± 0.46	12.0 ± 0.8
	4-carbomethoxyphenoxide	5.78 ± 0.38	12.3 ± 3.1
C_7H_7-N_3	trityl	11.61 ± 0.86	10.98 ± 0.88
C_7H_7-SCH_2COOMe	9-PhXa	5.36 ± 1.49	6.03 ± 1.76
C_7H_7-SCH_2COOMe	Xa	9.64 ± 0.19	10.82 ± 1.74
Xa-NO_2	trityl	9.75 ± 0.55	8.12 ± 0.74
9-PhXa-NO_2	trityl	9.79 ± 1.22	13.63 ± 0.54
C_7H_7-SCH_2COOMe	trityl	15.84 ± 1.2	21.27 ± 1.72

[a] C_7H_7 = tropylium, TPCP = triphenylcyclopropenylium, 9-PhXa = 9-phenylxanthylium, Xa = xanthylium, CPh_3 = trityl. [b] Counterion = tetrafluoroborate for cations; counterion = potassium for anions.

the HPLC trace of the presumed covalent product and the salt formed by the displacement reaction. For those systems where there is an anomaly or discrepancy between the measured and calculated heats of displacement values, the HPLC trace has additional peaks demonstrating the presence of a variety of products. These are most likely due to attack on the covalent reactant at several positions on the neutral substrates to give isomeric products. This clearly establishes the fact that these reactions are not clean and can lead to several other products in addition to that from displacement.

The heats of heterolysis in Table I are simply the heats of reaction (ΔH_{rxn}) of the cation–anion reaction with the sign changed. In previous reports of reactions of carbenium ions with resonance-stabilized organic anions we have found fairly good correlations between ΔH_{het} and the pK_{R^+} of the cation.[11] Thus, the affinity of the cation for a water molecule is proportional to its affinity for carbanions. Figure 1 gives rough confirmation of such a relationship for small inorganic anions. However, only scatter diagrams were obtained from plots of $-\Delta H_{het}$ versus the logarithms of the corresponding rates of reaction as represented by Ritchie and McClelland.[14,15,18] Correlation between log k_{rate} and the logs of the equilibrium constants is poor in water also. Hence there is no reason to involve solvation effects in the present case.[19]

Table I shows some puzzling trends. Although ΔH_{het}s generally decrease reading from left to right across Table I (as the carbenium ion becomes more stable), the rates of decrease are very dependent on the nature of the anion. Thus, cyanide values scarcely vary outside of experimental error between 34.00 ± 0.36 and 31.57 ± 0.07 while thioglycolate values cover a 20 kcal/mol range. We are unable to provide a simple, satisfactory rationalization for these large effects but believe that they are real in view of their reproducibility and the fact that the reactions are clean. It is quite possible that the site of attack on the cations varies for the different anions, but we have no evidence for this proposal. Figure 2 suggests that a rough pattern lies behind these erratic results. Here the heats of reaction of the other four carbenium ions with the anions in Table I are plotted against the corresponding heats of reaction of trityl cation. Four nearly parallel lines have been generated by the computer, but the low correlation coefficients for 9-phenylxanthylium and tropylium indicate that the significance of these correlation lines is marginal at best. Figure 2 is reminiscent of Ritchie's well known N_+ correlation for the correlations of rates of attack by many nucleophiles, including some of these anions on a series of resonance-stabilized carbenium ions in aqueous solution. Although the Hammond Postulate relates rates to heats of reaction, its relevance to the present case is only vague at best.

Conclusion

The majority of these displacements on large congested molecular systems are clean processes whose heats of reaction are predicted from the relatively unencumbered coordination reactions of free carbenium ions and carbanions in this polar solvent system. In all of the cases where anomalous heats of displacement were found, multiple products were generated. Although there is no completely consistent pattern to the results, the anomalous cases appear to be correlated with extreme steric crowding at the primary displacement center.

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