does not describe a simple titration. Linearizing analyses similar to that shown in Figure 2 indicate the presence of at least two transitions. Curve fits of the data according to titration processes involving either one or two independent pH-dependent transitions (with or without constraints[8]) are shown in Figure 3. Based on the sums of squares and pK_a values obtained (and further linearizing analyses), it appears that curve 2 gives the best fit.[9] Accordingly, the basic transition defined by $pK_a \simeq 6.5$[10,11] is assignable to the titration of the histidinyl 12 side chain itself. The low-pH transition, $pK_a \simeq 4.3$, may be due to at least one neighboring titrating group, which perturbs the His 12 imidazole chemical shift in ribonuclease-S', although the presence of a low-pH conformational transition (local or more general) cannot be ruled out. Based on earlier considerations from enzymic modification,[12] kinetics,[13] and ^{1}H nmr,[11] the acid transition may represent, at least in part, the titration of the β-carboxyl group of Asp 121. The two pK values obtained here are fairly consistent with those suggested previously.[11,14]

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Received March 18, 1974

Enthalpies of Transfer of Aromatic Molecules from the Vapor State to Polar and Nonpolar Solvents[1]

Sir:

A significant development in the understanding of reactivity and equilibria in solution has resulted in recent years from studies of the gaseous state.[2] These data, combined with measurements of the interactions of gaseous species with solvents, can provide insights into solution behavior and into the modification of intrinsic reactivity by solvation.[3] Similar measurements in appropriate systems can also contribute to an understanding of the intermolecular forces which become operative as gaseous molecules interact with solvents. This communication reports such data for the interactions of aromatic molecules with the polar solvents

(1) Presented in part at the Fourth Conference on Structure-Energy Relationships, San Juan, P. R., Jan 9–12, 1974.

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N,N-dimethylformamide and methanol and with the nonpolar solvents benzene and cyclohexane.

We have recently been interested in the extent to which the solvation of aromatic substituents changes upon transfer from methanol (MeOH) to N,N-dimethylformamide (DMF).[4,5] The observation was made that values of the enthalpy of transfer ($\Delta\Delta H_s$) of aromatic compounds are, within experimental error, additive functions of the substituent groups present, regardless of the relative positions of the groups on the aromatic ring.[6] Individual group $\Delta\Delta H_s$ values can be rationalized in terms of the greater dipole moment, hydrogen bond acceptor ability, and solvent-solvent association forces of DMF (relative to MeOH), and the resulting more exothermic dipole–dipole, dipole–induced dipole, and hydrogen bonding interactions with polar, polarizable, and hydrogen bond donating groups, respectively.

Comparison of $\Delta\Delta H_s$ values (MeOH → DMF) for aromatic and aliphatic compounds with available $\Delta\Delta G$ values[7] indicates that the latter are largely determined by the enthalpy contribution. Thus the enthalpy of transfer is a meaningful indication of the change in solvation that a molecule or group undergoes upon transfer from one solvent to another.

Enthalpies of solution (ΔH_s) for a number of aromatic compounds in the nonpolar solvent cyclohexane and in the nonpolar but highly polarizable solvent benzene have now been measured and are presented in Table I.

Table I. Enthalpies of Solution of Benzene Derivatives

Compound	c-C_6H_{12}	Benzene	MeOH	DMF
			$\Delta H_s{}^a$	
Benzene	0.94	0.00	0.36[b]	0.04[b]
Toluene	0.77	0.12	0.45[b]	0.16[b]
p-Xylene	0.86	0.25	0.59	0.39
Mesitylene	1.22	0.62	1.04[b]	0.83[b]
Cyclohexane	0.00	0.90	1.21	2.87
Perfluoro-(methylcyclohexane)	3.79	5.46	3.98	5.95
Fluorobenzene	1.10	0.02	0.03[b]	−0.35[b]
Chlorobenzene	0.90	0.03	0.17[b]	−0.25[b]
Bromobenzene	1.07	0.05	0.30[b]	−0.19[b]
Iodobenzene	1.31	0.20	0.51[b]	−0.40[b]
α,α,α-Trifluorotoluene	1.66	0.56	−0.05[b]	−0.01[b]
Acetophenone	3.14	0.36	1.20[b]	−0.14[b]
Nitrobenzene	2.85	0.56	1.00[b]	−0.19[b]
Ethyl benzoate	1.54	0.05	1.21[b]	0.27[b]
Aniline	4.22	1.25	−0.62[b]	−2.68[b]
m-Cresol	6.02	2.58	−1.55	−3.35

^{a} Calorimetric values ±0.05 kcal/mol. ^{b} Values from ref 5.

The enthalpies of solution were measured at concentrations of 10^{-4} to 10^{-3} M. No effect of concentration on ΔH_s was noted in this range. Values of ΔH_s and $\Delta\Delta H_s$ are thus essentially infinite dilution values.

Values of ΔH_s from Table I and previous values[5] have been combined with enthalpies of evaporation

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Table II. Aromatic Group Enthalpies of Transfer from Vapor to Solvents[a]

Compound (substituent)	Group polarizability[b]	Group molar volume[c]	ΔΔH			
			v → c-C$_6$H$_{12}$[d]	v → Bz[d]	v → MeOH[d]	v → DMF[d]
Benzene			(−7.15)	(−8.09)	(−7.73)	(−8.05)
Me	4.9	17.5	−1.16	−0.87	−0.90	−0.87
1,4-Me$_2$	4.9	17.5	−1.06	−0.90	−0.90	−0.87
1,3,5-Me$_3$	4.9		−0.99	−0.88	−0.86	−0.82
c-C$_6$H$_{12}$			(−7.91)	(−7.01)	(−6.70)	(−6.04)
c-C$_6$F$_{11}$CF$_3$			(−3.9)	(−2.2)	(−3.7)	(−1.7)
F	0	5.0	−0.24	−0.38	−0.73	−0.75
Cl	5.0	12.9	−2.12	−2.05	−2.27	−2.37
Br	7.2	16.2	−2.65	−2.73	−2.84	−2.97
I	13.1	23.0	−3.39	−3.56	−3.61	−4.16
CF$_3$	4.6	34.1	−0.17	−0.33	−1.30	−0.94
COCH$_3$	10.3	28.0	−2.90	−4.74	−4.26	−5.24
NO$_2$	6.7	13.5	−3.19	−4.54	−4.46	−5.29
COOEt	16.4	53.9	−5.41	−5.96	−5.16	−5.74
NH$_2$	4.4	23.0	−1.60	−3.63	−5.86	−7.60
OH	1.6[e]		+0.07	−2.72	−6.92	−8.69

[a] Values in kcal/mol. Estimated accuracy ±0.1–0.2 kcal/mol. [b] Values calculated from Lorenz–Lorentz equation. Polarizability $C_6H_5X − C_6H_6$. [c] Group molar volume (in ml) $= MV(C_6H_5X) − MV(C_6H_6)$. [d] Based on ΔH_v values from R. R. Dreisbach, Advan. Chem. Ser., No. 15 (1955). Values in parentheses are for entire molecules; others are those of individual groups. [e] Calculated from polarizability of m-cresol − toluene.

(ΔH_v) to give enthalpies of transfer for the compounds from the vapor state to solutions in DMF, MeOH, benzene, and cyclohexane, using the relationship $\Delta\Delta H(\text{vap} \to S) = \Delta H_s(S) − \Delta H_v$. Since the transfer values from vapor to solution are at least approximately additive (see results for −CH$_3$, Table II), it is possible to discuss $\Delta\Delta H(\text{vap} \to S)$ in terms of group contributions, where $\Delta\Delta H(X) = \Delta\Delta H(C_6H_5X) − \Delta\Delta H(C_6H_6)$. Group $\Delta\Delta H_s$ values, along with values for the molecules benzene, cyclohexane, and perfluoro-(methylcyclohexane) are given in Table II.

The quantity $\Delta\Delta H(\text{vap} \to S)$ is usually taken as equal to the enthalpy of solvation, although it also includes a term for the "hole" energy in that solvent. Solvation enthalpies of neutral molecules are small compared with those of typical ions, but $\Delta\Delta H_s(S_1 \to S_2)$ may be comparable. In the transfer of the reaction of a benzene derivative with an ion from one solvent to another, rate changes may result from changes in solvation of both reacting species, as well as that of the transition state.

A number of interesting conclusions regarding the solvation of functional groups can be drawn from the data in Table II. (I) A principle solvation interaction for hydrocarbon molecules and groups as solutes is dispersion interactions. These are comparable for solute benzene and cyclohexane. Dipole–induced dipole forces cause a more exothermic interaction of solute benzene with DMF than with cyclohexane. The less polarizable solute cyclohexane has a less exothermic interaction with DMF, reflecting the rather large solvent–solvent forces and "hole" energy in this solvent. This effect is still more pronounced in the case of perfluoro(methylcyclohexane). (II) The enthalpies of solvation of polar and nonpolar substituents in the nonpolar solvent cyclohexane roughly parallel the group polarizabilities and must, therefore, result largely from dispersion interactions. (III) Substituents with large dipole moments (−COCH$_3$, −NO$_2$) interact more strongly with the polarizable or polar solvents, benzene, MeOH, and DMF, than with cyclohexane. (IV) The hydrogen bond donor groups OH and NH$_2$ undergo large increases in solvation upon transfer

from cyclohexane to solvents of greater polarity and basicity. Nearly half of the solvation enthalpy of m-cresol in DMF results from the interactions of solvent with the hydroxyl group.

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Received February 28, 1974

Edge Participation by a β-Cyclobutene Ring in a 7-Norbornenyl System

Sir:

Edge participation by a cyclobutene ring at an incipient carbonium ion has been demonstrated in the 7-norbornyl system.[1,2] Product studies indicate an intermediate trishomocyclopropenyl type cation. However, because of degenerate rearrangements of the intermediate species, conclusive evidence about the nature of the developing carbonium ion could not be given.[1,2] In a previous communication we described the capability of a methoxy group attached to the cationic center to cancel neighboring group participation and consequently suppress rearrangement of the cation.[3] We now wish to report the generation and direct observation of the 9-ethoxy-endo-tricyclo[4.2.1.0^{2,5}]-nona-3,7-dien-9-yl carbonium ion, III (Figure 1).

9-Ethoxy-9-chloro-endo-tricyclo[4.2.1.0^{2,5}]nona-3,7-diene, prepared from diethoxy compound I[4] and PCl$_5$ or SOCl$_2$, was dissolved in liquid SO$_2$ at −60° and observed by nmr. The downfield shift of the methylene protons of the ethoxy group (δ 5.11) indicates a posi-

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