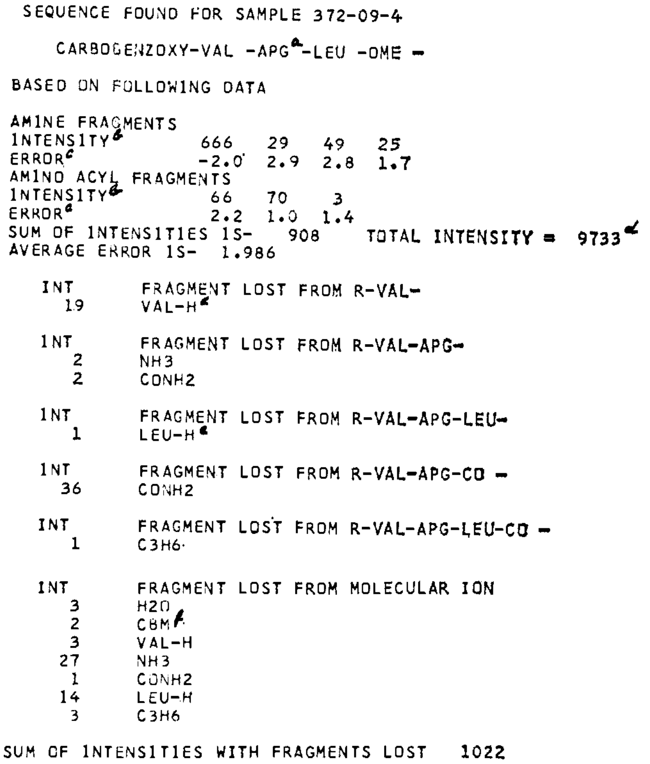
Oligopeptides containing two to five amino acids, such as Gly, Val, Ala, Leu, Ser, Met, S-Benzyl-Cys, Asp(NH_2), Pro, and Phe, have as yet been tested. Figure 1 shows a typical result produced by the computer, which had been provided with an automatically recorded high-resolution mass spectrum (density profile of a photographic plate), the type of N-terminal substituent, and the accurate masses of the "side chains" of the nineteen amino acids (HO-Pro, Orn, Asp, Glu, Glu(NH_2), Lys, His, Tyr, and Try, in addition to those listed above) to be considered for the sequence.



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SEQUENCE FOUND FOR SAMPLE 372-09-4

   CARBOGENZOXY-VAL -APG^a-LEU -OME -

BASED ON FOLLOWING DATA

AMINE FRAGMENTS
INTENSITY^b         666   29   49   25
ERROR^c            -2.0  2.9  2.8  1.7
AMINO ACYL FRAGMENTS
INTENSITY^b          66   70    3
ERROR^c             2.2  1.0  1.4
SUM OF INTENSITIES IS-    908     TOTAL INTENSITY =  9733^d
AVERAGE ERROR IS-  1.986

   INT        FRAGMENT LOST FROM R-VAL-
    19        VAL-H^e

   INT        FRAGMENT LOST FROM R-VAL-APG-
     2        NH3
     2        CONH2

   INT        FRAGMENT LOST FROM R-VAL-APG-LEU-
     1        LEU-H^e

   INT        FRAGMENT LOST FROM R-VAL-APG-CO -
    36        CONH2

   INT        FRAGMENT LOST FROM R-VAL-APG-LEU-CO -
     1        C3H6

   INT        FRAGMENT LOST FROM MOLECULAR ION
     3        H2O
     2        CBM^f
     3        VAL-H
    27        NH3
     1        CONH2
    14        LEU-H
     3        C3H6

SUM OF INTENSITIES WITH FRAGMENTS LOST   1022
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Figure 1. Reproduction of the result of a sequence analysis provided by the computer (explanatory footnotes added manually). (a) APG = asparaginyl; (b) in the order of A_1 through A_n, and B_1 through B_n, respectively; (c) difference between calculated and found mass, in millimass units; (d) above mass of R (163 for carbobenzoxy); (e) side chain of valine and leucine, respectively, minus one hydrogen transferred to peptide chain;[3] (f) benzylcarbamate.

In view of the small amount of material required (microgram quantities) and of the extreme speed (1–3 min of computer time) with which this objective and exhaustive interpretation is achieved, this approach shows considerable promise for the routine determination of the amino acid sequence of small peptides obtained upon partial hydrolysis of the oligopeptides resulting from the enzymatic cleavage of large polypeptides. It should also be useful in synthetic work, since the principle is independent of the end groups and additional protecting groups, the mass of which can be read in with the data.

K. Biemann, C. Cone, B. R. Webster

Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts

Received March 25, 1966

Enthalpies of Transfer from Water to Dimethyl Sulfoxide for Some Ions and Molecules[1,2]

Sir:

Large changes in the rates of certain reactions have been noted as a result of changing the medium from a hydroxylic to a dipolar aprotic solvent.[3-7] Although the other activation parameters need not parallel the free energy of activation (see below), the relative enthalpies of solvation for typical molecules and ions should be important to an eventual understanding of these medium effects.[8] We present here some preliminary results which furnish strong support for the frequently cited notion of a large difference between cation and anion solvation in the two kinds of systems.[7]

In Table I are presented calorimetric partial molal heats of solution, $\Delta\bar{H}_s$ (defined below), for a few selected nonelectrolytes and salts in water and dimethyl sulfoxide (DMSO) and the derived enthalpy of transfer ($\delta\Delta\bar{H}_s$) for each compound from water to DMSO. The nonelectrolytes give (by this criterion) remarkably perfect solutions in DMSO, the values for all twelve compounds lying between -1.32 and $+1.30$ kcal/mole. The hydrogen-bonding solutes chloroform, water, and methanol show an exothermic interaction whereas the steady endothermic trend for the larger alcohols probably reflects the increasing heat of vaporization which must be supplied to separate their molecules. In the alcohol series, there is a gradual increase in the enthalpies of transfer. This seems to be evidence for a progressive increase in exothermic "structure making"[9] around the larger molecules in water.

The results for the salts are better interpreted by calculating single ion enthalpies of transfer. It is customary to compare cations with each other through salts of a common anion and to construct a similar, but separate, scale for anions. If we make the special assumption that the tetraphenylarsonium cation and the tetraphenylboride anion have equal enthalpies of transfer, it is possible to put anions and cations on a common scale. This is a reasonable assumption since the main difference between the two ions is the sign of their respective charges which lie buried within similar large organic envelopes.[10] These single ion enthalpies of transfer, listed in Table II, bring out the difference in the solvating abilities of water and DMSO. The large negative heats of transfer for the small metal cations indicate that DMSO is the better solvating medium for these ions. Wu and Friedman have recently arrived at an opposite conclusion for another dipolar

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[1] Solvent Effects in Organic Chemistry. IX. Previous paper is E. M. Arnett and G. Mach, *J. Am. Chem. Soc.*, **88**, 1177 (1966).

[2] Supported by National Science Foundation Grant GP-2014.

[3] C. A. Kingsbury, *J. Am. Chem. Soc.*, **87**, 5409 (1965).

[4] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965 (see index for references to DMSO).

[5] H. E. Zaugg and A. D. Schaefer, *J. Am. Chem. Soc.*, **87**, 1857 (1965); **83**, 837 (1961).

[6] R. Gompper, *Angew. Chem. Intern. Ed. Engl.*, **3**, 560 (1964).

[7] A. J. Parker, *Quart. Rev.*, (London), 163 (1962).

[8] I. P. Evans and A. J. Parker, *Tetrahedron Letters*, 163 (1966).

[9] For key references see previous papers in this series, especially (a) E. M. Arnett and D. R. McKelvey, *Record Chem. Progr.*, **26**, 185 (1965); (b) E. M. Arnett, W. G. Bentrude, J. J. Burke, and P. McC. Duggleby, *J. Am. Chem. Soc.*, **87**, 1541 (1965).

[10] E. Grunwald, G. Baughman, and G. Kohnstam, *ibid.*, **82**, 5801 (1960). Tables I and II indicate that the comparison of $\delta\Delta\bar{H}_s$ for these ions with tetraphenylmethane would be neither grossly in error nor completely exact.

Table I. Heats of Solution in DMSO and H_2O[a]

Nonelectrolytes	$\Delta\bar{H}_s$, DMSO	$\Delta\bar{H}_s$, H_2O	$\delta\Delta\bar{H}_s$, DMSO-H_2O
Benzene	0.65 ± 0.03	0.72[b]	−0.07
Toluene	0.89 ± 0.03	0.77[b]	0.12
Isopropylbenzene	1.30 ± 0.04	1.06[c]	0.24
Carbon tetrachloride	0.00 ± 0.03		
Chloroform	−1.32 ± 0.09		
Acetone	0.37 ± 0.03	−2.37 ± 0.04	2.74
Water	−1.28 ± 0.03	0.00	−1.28
Methanol	−0.34 ± 0.03	−1.74 ± 0.05	1.40
Ethanol	0.28 ± 0.02	−2.45 ± 0.05	2.73
1-Propanol	0.61 ± 0.04	−2.48 ± 0.05	3.09
1-Butanol	0.99 ± 0.03	−2.16 ± 0.03	3.15
2-Methyl-2-propanol	1.21 ± 0.04	−4.10 ± 0.04	5.31
Electrolytes[d]			
NaI	−11.53 ± 0.13	−1.86 ± 0.04	−9.67
KI	−6.15 ± 0.11	4.85 ± 0.03	−11.36
CsI	−2.84 ± 0.08	7.46 ± 0.05	−10.30
$NaB(C_6H_5)_4$	−14.23 ± 0.14	−4.77 ± 0.10	−9.46
$(C_6H_5)_4AsI$	3.44 ± 0.05	8.28 ± 0.09	−4.84
Et_4NI	4.86 ± 0.10	6.83 ± 0.12	−1.97
Et_4NBr	3.27 ± 0.07	1.38 ± 0.08	1.89
Et_4NCl	2.42 ± 0.05	−3.02 ± 0.07	5.44

[a] We wish to thank Mr. F. M. Jones for his assistance in obtaining these measurements. Heats expressed in kcal/mole. Errors are expressed as confidence limits at the 95% level on six to twenty separate measurements on different batches of carefully dried and purified materials. [b] R. L. Bohon and W. F. Claussen, *J. Am. Chem. Soc.*, **73**, 1571 (1951). [c] D. N. Glew and R. E. Robertson, *J. Phys. Chem.*, **60**, 335 (1956). [d] Alkali chlorides and bromides are too insoluble in DMSO to permit direct measurement.

Table II. Single Ion Enthalpies of Transfer from Water to DMSO[a]

Ion	$\delta\Delta\bar{H}_s$	Ion	$\delta\Delta\bar{H}_s$
K^+	−8.84[b]	$(C_6H_5)_4As^+$	−2.32
Cs^+	−7.78	$(C_6H_5)_4B^-$	−2.31
Na^+	−7.15	Et_4N^+	0.55
I^-	−2.52	Br^-	1.34
		Cl^-	4.89

[a] For the purpose of placing anions and cations on the same scale, it has been assumed that $\delta\Delta\bar{H}_s((C_6H_5)_4B^-) = \delta\Delta\bar{H}_s((C_6H_5)_4As^+)$. [b] Heats expressed in kcal/mole.

aprotic solvent by a different criterion.[11] The positive heats of transfer for chloride and bromide ions indicate that water is the better solvating medium for small anions. Furthermore, the heats of transfer for the halide ions become rapidly more exothermic in the order $Cl^- < Br^- < I^-$, with I^- actually having an exothermic heat of transfer.

It is important that *these results should not be applied to* rate or equilibrium differences between these two solvents. A dramatic demonstration of the disparity that may arise between $\delta\Delta\bar{H}_s$ and the corresponding free energy of transfer is supplied by benzene. This compound is nearly insoluble in water but completely miscible with DMSO. Therefore, $\delta\Delta\bar{G}_s$ must be enormous although $\delta\Delta\bar{H}_s$ is negligible. In all likelihood this reflects the peculiar position of water among hydroxylic solvents in its interactions with nonelectrolytes. The correspondence between $\delta\Delta\bar{H}_s$ and $\delta\Delta\bar{G}_s$ should be better for transfer of small ions.[12] Our data should be of value for analyzing the effect of medium change on energies of activation between these solvents, but we know of no kinetic study to date to which they may be applied.

Our results may be compared with two recent studies of enthalpies of transfer from water to propylene carbonate[11] and to formamide.[13] Comparison of their data for NaI, KI, and $NaB(C_6H_5)_4$ with ours indicates that the abilities of these three dipolar aprotic solvents to solvate small cations decreases in the order DMSO > formamide > propylene carbonate.

All measurements were carried out at 25.0 ± 0.5° as described earlier.[9b] At the concentrations employed in this study (approximately 5×10^{-3} *M*), the heats of solution were found to be independent of concentration within experimental error for all compounds except tetraphenylarsonium iodide. The heats of solution for this compound in water and DMSO were found to be highly dependent upon concentration. It was therefore necessary to make measurements at various concentrations (0.5×10^{-3} *M* to 2.5×10^{-3} *M*) and extrapolate by least squares to zero concentration.

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(11) Y. C. Wu and H. L. Friedman, *J. Phys. Chem.*, **70**, 501 (1966).

(12) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd ed, Butterworths, London, 1959, p 70.

(13) G. Somsen and J. Coops, *Rec. Trav. Chim.*, **84**, 985 (1965).

Edward M. Arnett, Donald R. McKelvey
Department of Chemistry, University of Pittsburgh
and Mellon Institute, Pittsburgh, Pennsylvania 15213

Received March 18, 1966

Carbonyl Neighboring Group Participation *via* Enolization

Sir:

The role of the ketonic carbonyl group in solvolysis reactions has been the topic of a recent report.[1] In this recent discussion, carbonyl participation *via* enolization was not considered to be an important factor. We wish to report evidence for the overwhelming role of enol neighboring group participation in the solvolysis of *anti*-7-hydroxynorbornan-2-one *p*-toluenesulfonate (**1**).

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(1) D. J. Pasto and M. P. Serve, *J. Am. Chem. Soc.*, **87**, 1515 (1965).