Energetics of P, S, and N Ylide Formation and Reaction in Solution

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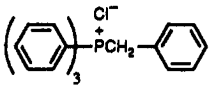
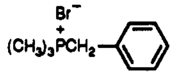
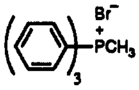
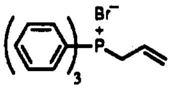
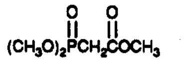
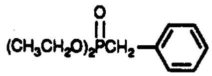
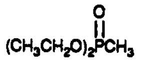
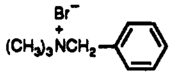
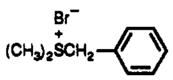
Summary: Calorimetric heats of deprotonation for several carbon acid precursors of P, S, and N ylides are reported in DMSO at 25 °C. The ylide obtained from benzyltrimethylammonium bromide undergoes the Sommelet–Hauser rearrangement immediately after its formation so that the heat and rate of rearrangement, as well as the heat of formation of the ylide, can all be derived from a single thermogram.

Since their discovery by Wittig,[1] carbanions stabilized by adjacent fifth or sixth group onium ions have developed as valuable reactive intermediates. Although overshadowed by the utility of phosphonium ylides for the Wittig and Horner–Emmons olefination reactions;[2] the Stevens and Sommelet–Hauser types of rearrangement of nitrogen and sulfur ylides are also noteworthy.[3] For example, Tanaka et al. have recently reported a strong sensitivity of *N,N*-dimethyl(substituted benzyl)ammonium N-alkylides to partitioning between the Sommelet–Hauser and the Stevens rearrangement products based on solvent polarity.[4] Despite the obvious value and relevance of quantitative evaluations of their thermodynamic stabilities/reactivities, no data exist which allow exact comparisons of many phosphorus, sulfur, and nitrogen ylides.[5] Rapid rearrangement of ammonium salts often precludes the usual type of equilibration study with strong bases used to establish pK_{HA}s.[5] However, we have found that rapid injection solution calorimetry permits determination of the heats of generating ylides whose half-lives are greater than ~5 min at room temperature.

Table I lists the heats of deprotonation, ΔH_{dep}, by the two strongly basic systems shown at 25 °C for a carefully chosen series of phosphonium, sulfonium, and ammonium salts and phosphonates. Such values are exactly equivalent to the heats of conversion of the carbon acid precursors to the ylides under the same conditions. Most of the heat of deprotonation[6] measurements employed a Tronac 450 isoperibol solution calorimeter with a motor-driven syringe to titrate the ylide precursor into the alkali DMSYL solution at a slow, steady rate.[6,7] Usually there was an immediate evolution of heat followed by return of the thermogram to a straight baseline. An unusual opportunity was provided by the case of benzyltrimethylammonium bromide where the first exotherm was followed by a gradual secondary evolution of heat (Figure 1). To take advantage of this observation the rapidly rearranging benzyltrimethylammonium bromide was added by the rapid injection of 0.5-mL increments of the 0.1–0.25 M solution of the onium salt from a thermostated 5-mL syringe into a hundred-fold excess of the base in the thermostated 50-mL Dewar calorimeter vessel.

Table I. Heats of Formation of Phosphonium, Sulfonium, and Ammonium Ylides at 25 °C in DMSO and Aggregation State of Phosphonium Ylides and Phosphonates in THF

acid	ΔH_{deprot}[a] by DMSYL⁻ Li⁺ in DMSO (kcal/mol)	ΔH_{deprot}[a] by DMSYL⁻ K⁺ in DMSO (kcal/mol)	aggregation no.[b] using LiHMDS in THF
	−24.56 ± 0.9 −23.68 ± 0.2	−21.85 ± 0.3 −21.89 ± 0.6	insoluble
	−16.89 ± 0.2 −17.02 ± 0.4	−15.23 ± 0.3 −16.59 ± 0.4	1.1 ± 0.1
	−14.39 ± 0.3 −15.02 ± 0.4	−13.01 ± 0.2 −13.33 ± 0.3	1.1 ± 0.1
	−25.40 ± 0.4 −25.74 ± 0.3	precipitate	1.4 ± 0.3
 $(CH_3O)_2P(O)CH_2C(O)OCH_3$	−28.78 ± 0.1 −27.47 ± 0.3	−26.86 ± 0.6 −26.68 ± 0.5	1.7 ± 0.1
	−13.50 ± 0.5 −13.12 ± 0.3	−15.46 ± 0.5 −14.13 ± 0.4	2.0 ± 0.2
 $(CH_3CH_2O)_2P(O)CH_3$	−1.45 ± 0.2 −1.25 ± 0.2	precipitate	1.0 ± 0.1
	−8.95 ± 0.3 −9.10 ± 0.3	−9.96 ± 0.7	
	−32.73 ± 0.3 −33.8 ± 2.0	−35.7 ± 0.9	

[a] Heats of deprotonation correspond to heats of formation of the ylides under these reaction conditions. [b] Solution aggregation states of the ylides in THF were determined using vapor-pressure osmometry.

This could be related directly through ^1H and ^{13}C NMR, UV, and mass spectra to the Sommelet–Hauser rearrangement of the ylide to form *N,N*-dimethyl-2-methylbenzylamine,[8] and a unimolecular rate constant could be

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[1] (a) Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44. (b) Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *28*, 1318.

[2] (a) Vedejs, E.; Fleck, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 5861. (b) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (c) Schmidbaur, H.; Jeong, J.; Schier, A.; Graf, W.; Wilkinson, D. L.; Muller, G. *New J. Chem.* **1989**, *13*, 341. (d) Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1988**, *110*, 3948. (e) Schlosser, M.; Oi, R.; Schaub, B. *Phosphorus Sulfur* **1983**, *18*, 171. (f) Becker K. B. *Tetrahedron* **1980**, *36*, 1717.

[3] (a) Pine, S. H. In *Organic Reactions*; Dauben, W. G., Ed.; John Wiley and Sons: New York, 1970; Vol. 18, pp 404–464. (b) Pine, S. H. *J. Chem. Educ.* **1971**, *48*, 99. (c) Wittig, G. *J. O. Organomet. Chem.* **1975**, *100*, 279. (d) Ollis, W. D.; Rey, M.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans 1* **1983**, 1009. (e) Ollis, W. D.; Rey, M.; Sutherland, I. O. *J. Chem. Soc., Chem. Commun.* **1975**, 543. (f) Klein, K. P.; Hauser, C. R. *J. Org. Chem.* **1966**, *31*, 4276. (g) Stevens, T. S.; Watts, W. E. *Selected Molecular Rearrangements*; Van Nostrand Reinhold: London, 1973; pp 81–88.

[4] Tanaka, T.; Shirai, N.; Sugimari, J.; Sato, Y. *J. Org. Chem.* **1992**, *57*, 5034.

[5] Professor F. G. Bordwell has provided us with a preprint of an extensive study of pK_{HA}s for the deprotonation of ammonium and phosphonium salts to give ylides in DMSO at 25 °C under equilibration conditions.

[6] Arnett, E. M.; Moe, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 7068–7288.

[7] Eatough, B. J.; Christensen, J. J.; Izatt, R. M. *Experiments in Thermometric Titrimetry and Titration Calorimetry, rev. ed.*; Brigham Young University Press: Salt Lake City, UT, 1974.

[8] Note that the Sommelet–Hauser product is also reported to be formed exclusively in DMSO with Li⁺DMSYL⁻ and Na⁺DMSYL⁻; see ref 3f.

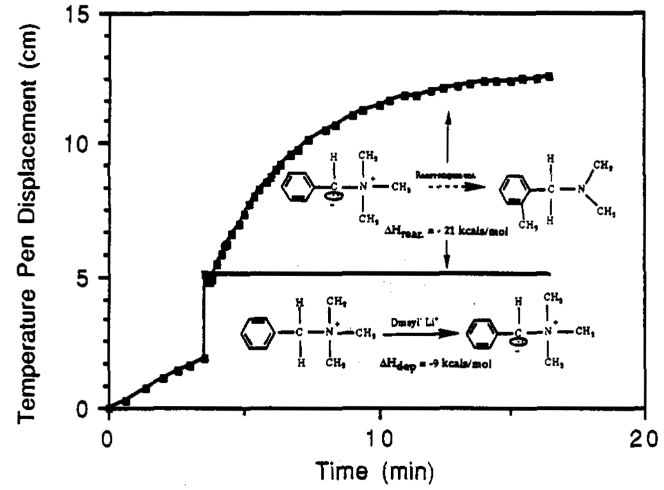

Figure 1. Thermogram for deprotonation and rearrangement of benzyltrimethylammonium bromide by lithium DMSYL in DMSO at 25 °C.

derived from both the UV spectral change and from the curved thermogram. Careful NMR examination of the other deprotonation products confirmed the formation of ylides that were stable over the course of an hour.

Thus, for this special case, the heat and rate of rearrangement as well as the heat of ylide formation could be inferred from the thermogram alone: $\Delta H_{rgt} = -21.0 \pm 0.9$ kcal/mol in Li$^+$ DMSYL; $\Delta H_{rgt} = -19.4 \pm 1$ kcal/mol in K$^+$ DMSYL.

The data in Table I indicate a high sensitivity of ΔH_{dep} to the structures of the ylides and their precursors. The most exothermic reactions in the phosphorus series can be generally rationalized in terms of factors which would stabilize the ylide either through their influence on the polar P=C double bond or the carbanionic carbon. The order of ΔH_{dep}s for the N, P, and S benzyl dimethyl onium ions is in the order proposed by others[3c,9] based on other types of considerations. However, it is important to recall that all measurements, be they thermodynamic or kinetic, necessarily reflect stability factors in the initial state as well as the product. We are unaware of any data that would allow comparison of the relative stabilities of analogous ammonium, phosphonium, and sulfonium salts so that the contribution from that source could be factored out and thus reveal the relative stabilities of the ylides themselves.

One would not expect there to be a significant cation effect on ΔH_{dep} in DMSO. However, alkali salts, especially lithium ones, are well-known for their effect on Wittig and Horner–Emmons reactions. Comparison of ΔH_{dep}s using Li$^+$ vs K$^+$ in DMSO show differences that are barely outside experimental error and are too erratic to justify interpretation at this time.

The role of aggregation is widely recognized in the behavior of other organolithiums.[11] Although ylides are formally neutral, electrostatic interaction of the carbanionic center with the lithium ion might be significant in some cases. Also it is reasonable that zwitterions might aggregate (± ∓) in low polarity solvents. However, the data in the third column do not imply that aggregation is important for these systems. We are pursuing these and related matters.

Procedures for purifying DMSO and preparing its alkali salts were modifications of those established by Bordwell et al.[12] DMSO was predried over 4-Å molecular sieves for a minimum of 2 days and transferred in an argon-filled glovebox to a 2-L round-bottom flask. Approximately 10 mg of triphenylmethane was added as an indicator. A rubber septum was placed over the 10/30 round-bottom flask joint, and the flask was removed from the glovebox. *n*-Butyllithium (2.1 M in hexane) was added by a gas-tight syringe until the dark red color of triphenylmethide anion was maintained, at which point an additional 15 mL of the *n*-butyllithium solution in hexane was added. The DMSO was doubly distilled under a vacuum of 10^{-2} Torr, the first and last 25 vol % being discarded from both distillations, and was stored in an argon-filled glovebox with a three-way stopcock on the round-bottom flask. Karl Fisher titration after each distillation always showed less than 70 ppm residual water.

DMSYL-Li$^+$ was prepared as a 1.0 M solution by adding the appropriate amount of *n*-butyllithium (Johnson and Mathews 2.10 M in hexane) via gas-tight syringe to a three-neck flask containing doubly-distilled DMSO and was stirred magnetically under vacuum (10^{-2} Torr) for 45 min to remove any *n*-butane and *n*-hexane from the DMSYL-Li$^+$ solution.

DMSYL-K$^+$ was prepared in a similar manner only the KH, freed from mineral oil by washing with *n*-hexane, was weighed into a three-neck round-bottom flask and DMSO added via a gas-tight syringe.

Calorimetry. The onium salts were prepared as 0.1–0.25 M solutions in DMSO in an Ar-filled glovebox. The onium salt titrants were transferred to a 2.5-mL Gilmont titration syringe attached to the Tronac 450 microcalorimeter, and 5 mL of the 1.0M DMSYL-Li$^+$ or DMSYL-K$^+$ base was pipetted into a 50-mL calorimeter Dewar in the glovebox and 40 mL of the doubly distilled DMSO added. The Dewar was attached to the Tronac 450, and the titrant and titrate containers were submerged in the thermostated bath at 25 °C.

The ΔH_{dep}s of the onium salts are reported as the averages of at least five titrant additions into the titrate, the experimental error being reported as one standard deviation from the five measurements. Batch-to-batch errors can be assessed from the duplicate values listed for each compound in Table I.

For the benzyltrimethylammonium bromide, 0.1–0.25 M solutions in DMSO were drawn into a 5-mL (0.1-mL

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(9) (a) Ammon, H. L; Wheeler, G. L.; Watts, P. H., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 6158. (b) Albright, T. A.; Gordon, M. D.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1976**, *98*, 6249. (c) Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1965**, *87*, 5603. (d) Jemison, R. W.; Mageswaran, S.; Ollis, W. D.; Sutherland, I. O.; Thebtaranonth, Y. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1154. (e) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

(10) (a) Thompson, S. K.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 3386. (b) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823. (c) Ward, W. J.; McEwen, W. E. *J. Org. Chem.* **1990**, *55*, 493. (d) Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1988**, *2*, 238. (e) Schlosser, M.; Schaub, B.; de Oliveira-Neto, J.; Jeganathan, S. *Chimia* **1986**, *40*, 244. (f) Reitz, A. B.; Nortey, S. O.; Jordan, A. D., Jr.; Mutter, M. S.; Maryanoff, B. E. *J. Org. Chem.* **1986**, *51*, 3302. (g) Allen, D. W. *J Chem. Res.* **1980**, 384.

(11) Some recent key references to the large and scattered literature on lithium aggregates are: (a) Bernstein, M. P.; Romesberg, F. E.; Fuller, D. J.; Harrison, A. T.; Collum, D. B.; Liu, Q.-Y.; Willard, P. G. *J. Am. Chem. Soc.* **1992**, *114*, 5100. (b) Nichols, M. A.; McPhail, A. T.; Arnett, E. M. *J. Am. Chem. Soc.* **1991**, *113*, 6222. (c) Williard, P. G. In *Comprehensive Organic Synthesis*; Pergamon: New York, in press. (d) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624. (e) Schleyer, P. von R. *Pure Appl. Chem.* **1984**, *56*, 151. (f) Klumpp, G. W. *Recl. Trav. Chim. Pays Bas.* **1986**, *105*, 1.

(12) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Dracker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006.

graduated) gas-tight syringe, in the glovebox, attached to the Tronac 450 and submerged in the thermostated water bath at 25 °C. Increments (0.5 mL) of the titrant were injected quickly into the excess base.

UV Spectroscopy. One mL of a 0.5 M DMSYL-Li^+ solution was placed in a 2.0-mL quartz UV cell in the glovebox. The cell was stoppered with a rubber septum, and 0.5 mL of a 0.155 M benzyltrimethylammonium bromide solution (in DMSO) was added through the septum by a 1-mL gas-tight syringe. A broad absorbance peak at 530 nm was observed due to the formation of the benzyltrimethylammonium ylide. The disappearance of this UV absorption peak was monitored as a function of time, the cell being inverted and shaken between absorption measurements. The decrease in the ylide absorption peak was due to the rearrangement of the ylide to the Sommelet–Hauser product. The first-order rate constant derived from these spectrophotometric data was $(1.54 \pm 0.3) \times 10^{-3}\ s^{-1}$ compared to $(1.12 \pm 0.6) \times 10^{-3}\ s^{-1}$ from the calorimetric data.

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