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Sulfamides and Sulfonamides as Polar Aprotic Solvents[1]

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Five tetraalkylsulfamides, one *N,N*-dialkylsulfonamide, two sulfurous diamides, and one sulfinamide were investigated for potential use as polar aprotic solvents that would be compatible with strongly basic and nucleophilic reagents. The values of Taft β and π^* measured for these compounds indicated that all possess significant polar aprotic solvent character. Their stabilities toward ethylmagnesium bromide, diethylzinc, methyllithium, and butyllithium were determined. Tetraethylsulfamide ($Et_2NSO_2NEt_2$) and *N,N*-diethyltrimethylmethanesulfonamide ($Me_3CSO_2NEt_2$) were the most stable of the solvents, showing no evidence of decomposition with the magnesium or zinc compounds and an appreciable lifetime with methyllithium.

Polar aprotic solvents[2] have reasonably high dielectric constants, and their molecules possess a dipolar function with an exposed negative end but a buried positive end. As a result, these solvents are effective at separating ions and are effective specific solvating agents for cations but not for anions. In such solvents, anions are less solvated and hence more reactive, often by orders of magnitude, than in polar protic solvents such as water or alcohols.

Although a number of polar aprotic solvents having excellent solvent properties are available, lack of stability often limits their use. Reactions with basic and nucleophilic reagents are a particular limitation, although thermal stability[3] also can be a problem. Polar aprotic solvents could be useful with organometallic compounds, for example, by increasing the carbon–metal bond polarity. Unfortunately, polar organometallic compounds often react with these solvents. Grignard reagents, for example, add to the multiple bonds of acetonitrile, acetone, and dimethylformamide; reduce dimethyl sulfoxide; and abstract an α-hydrogen from sulfolane.[4]

Hexamethylphosphoramide (HMPA) is the only polar aprotic solvent to be used extensively with organomagnesium compounds.[5] Effects of HMPA used either as a solvent for organomagnesium compounds or as an additive to their solutions in other solvents are often large. As examples, HMPA accelerates addition of an allylic organomagnesium compound to aryl-substituted alkenes,[6] addition of Grignard reagents to carbon monoxide,[7] metalation by organomagnesium compounds of acidic hydrocarbons,[8,9] and polymerization by Grignard reagent catalysts of some vinyl monomers.[10] HMPA alters the position of the Schlenk equilibrium and greatly slows the rate at which it is established,[11] affects the electrochemical behavior of organomagnesium compounds,[12] and changes the ultraviolet spectra of Grignard reagents such as benzyl and diphenylmethyl from those characteristic of relatively covalent compounds to those characteristic of carbanions.[8]

Even HMPA has less stability than would be desirable. Organolithium compounds attack HMPA and are destroyed, even at below-ambient temperatures.[13] Sodium hydride has been shown to attack HMPA.[14] Even Grignard reagents are not completely stable in contact with HMPA.[15] Another serious limitation is the potential

(1) Most of this work is taken from the Ph.D. Dissertation of J. Farkas, The Pennsylvania State University, 1985.

(2) For reviews of the behavior of polar aprotic solvents see: Parker, A. J. *Q. Rev. Chem. Soc.* **1962**, *16*, 163; *Adv. Phys. Org. Chem.* **1967**, *5*, 173; *Chem. Rev.* **1969**, *69*, 1. Ritchie, C. D. In *Solute–Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1969; Chapter 4. Amis, E. S.; Hinton, J. F. *Solvent Effects on Chemical Phenomena*; Academic: New York, 1973; Vol. 1, Chapter 5.

(3) Sulfolane, for example, decomposes significantly at 240 °C, a temperature well below its boiling point (285 °C) [*Sulfolane*, Bulletin 524, Phillips Petroleum Company].

(4) Nützel, K. *Methoden Org. Chem. (Houben-Weyl), 4th Ed.* **1973**, *13* (Part 2a), 47.

(5) For reviews of the use of HMPA, see: Normant, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1046; *Russ. Chem. Rev. (Engl. Transl.)* **1970**, *39*, 457.

(6) Luteri, G. F.; Ford, W. T. *J. Org. Chem.* **1977**, *42*, 820.

(7) Sprangers, W. J. J. M.; Louw, R. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1895.

(8) Ebel, H. F.; Wagner, B. O. *Chem. Ber.* **1971**, *104*, 320.

(9) Tomoi, M.; Kakiuchi, H. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3233.

(10) Tomoi, M.; Kakiuchi, H. *Polym. J. (Tokyo)* **1973**, *5*, 195; *Chem. Abstr.* **1974**, *80*, 133910. Tomoi, M.; Onozawa, T.; Seki, K.; Kakiuchi, H. *Polym. J. (Tokyo)* **1975**, *7*, 372; *Chem. Abstr.* **1975**, *83*, 132038.

(11) Evans, D. F.; Fazakerley, G. V. *J. Chem. Soc. A* **1971**, 184. Ducom, J. *Bull. Soc. Chim. Fr.* **1971**, 3518.

(12) Chevrot, C.; Kham, K.; Perichon, J.; Fauvarque, J. F. *J. Organomet. Chem.* **1978**, *161*, 139.

(13) Bowers, K. W.; Giese, R. W.; Grimshaw, J.; House, H. O.; Kolodny, N. H.; Kronberger, K.; Roe, D. K. *J. Am. Chem. Soc.* **1970**, *92*, 2783. Kaiser, E. M.; Petty, J. D.; Solter, L. E. *J. Organomet. Chem.* **1973**, *61*, C1. Abatjoglou, A. G.; Eliel, E. L. *J. Org. Chem.* **1974**, *39*, 3042. Magnus, P.; Roy, G. *Synthesis* **1980**, 575.

(14) Proni, A.; Roggero, A.; Mazzei, A.; Bruzzone, M. *Inorg. Chim. Acta* **1977**, *21*, 47.

(15) Fraenkel, G.; Ellis, S. H.; Dix, D. T. *J. Am. Chem. Soc.* **1965**, *87*, 1406. Unpublished work in our laboratory.

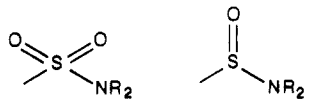
0022-3263/87/1952-0479$01.50/0

health hazard associated with its use.[16]

It has also been mentioned that tetramethylurea is not attacked by Grignard reagents,[17] though its use with organomagnesium compounds apparently has been limited.[18,19] Cyclic ureas (lacking α-hydrogens) also have been found to be compatible with relatively strong bases,[20] though it has been noted[21] that addition of a hexane solution of butyllithium to a solution of tetrahydrofuran and *N,N'*-(dimethylpropylene)urea (1,3-dimethyl-2-oxo-hexahydropyrimidine) leads to a rapid reaction at −78 °C.

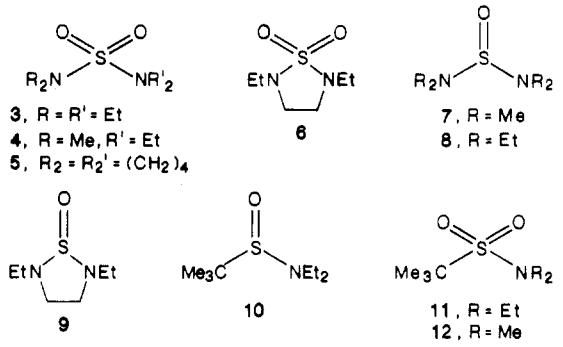
Clearly a need remains for new polar aprotic solvents that are particularly stable toward polar organometallic compounds as well as toward other strongly basic and nucleophilic reagents. To be useful as a solvent (though not necessarily as an additive to other solvents), a compound must be a liquid at the temperature at which it will be used. For it to be relatively volatile also will often facilitate its handling. Finally, it is desirable to use compounds that are potentially available at relatively low cost.

We thought that compounds containing the functional grouping **1** would be good possibilities. This grouping,



1 **2**

combining the sulfonyl and dialkylamino groups found in commonly used polar aprotic solvents, should impart characteristic polar aprotic solvent properties. We decided to study both sulfamides (e.g., **3**) and sulfonamides (e.g., **11**), choosing examples, of course, that because of appropriate substitution with alkyl groups lack hydrogens α to the sulfur. *N,N*-Dialkylsulfonamides are known to be particularly stable toward nucleophilic and basic reagents.[22] The only report that we have found of attack by an organomagnesium compound on an N,N-disubstituted sulfonamide involved reactants subjected to prolonged heating at 130–135 °C.[23,24] Even cleavage by complex aluminum hydrides is difficult.[23,25] Tetraalkylsulfamides also are known to be stable toward nucleophilic and basic reagents. It has been reported, for example, that **3** is hydrolyzed in aqueous base only with great difficulty.[26]



3, R = R' = Et
4, R = Me, R' = Et
5, $R_2 = R_2' = (CH_2)_4$

6

7, R = Me
8, R = Et

9

10

11, R = Et
12, R = Me

A preliminary study showed *N,N,N',N'*-tetraethylsulfamide (TES, **3**) to be a promising solvent.[27] Grignard reagents could be prepared directly in this solvent by the usual reaction of an organic halide with magnesium metal, and the resulting solutions were stable for weeks at ambient temperature. This solvent has since become available commercially.[28]

This paper describes further studies relating to the use as solvents of four sulfamides (**3–6**) and one sulfonamide (**11**). By analogy to comparisons[29] between sulfoxides and sulfones, compounds containing functional group **2** should be more effective polar aprotic solvents than those containing functional group **1**. Although we recognized that, unfortunately, they would react far more rapidly with nucleophiles and bases,[30] three sulfurous diamides (**7–9**) and one sulfinamide (**10**) related to the sulfamides and the sulfonamide were included in the study.

Preparations of **3–12** were routine and are described in the Experimental Section. Careful examination of the ^{1}H NMR spectra of concentrated solutions showed the samples of each of these compounds to be free of detectable amounts of other components. Only **5** and **10** are new compounds. Compound **12** proved to be a solid with a melting point (87–88 °C) high for routine use as a solvent

Table I. Half-Lives of Organometallic Compounds in Solutions[a] Containing the Polar Aprotic Solvent at 25 ± 2 °C

solvent	half-life		
	BuLi[b]	CH_3Li[c]	EtMgBr[d,e]
3	15 min	16 h	∞
4	<5 min	1 h	∞
5	<5 min	<5 min	∞
6	<5 min	<5 min	∞
7	<5 min	<5 min	<5 min[f]
8	<5 min	<5 min	1.5 h
9	<5 min	<5 min	<5 min
10	<5 min	<5 min	72 h
11	<5 min	14 h	∞

[a] The solution of the organometallic compound (1 mmol) was added to the polar aprotic solvent. [b] Hexane solution (1.3 M). [c] Diethyl ether solution (1.8 M). [d] Diethyl ether solution (2.1 M). [e] Solutions which showed no significant loss of organometallic compound after 5 days are labeled ∞. [f] When the sample of **7** was cooled in an ice bath prior to adding the EtMgBr solution to ensure that the heat of mixing did not lead to the decomposition, the resulting solution after being warmed to 25 °C still at the first observation had no remaining Grignard reagent.

(16) Sittig, M. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*, 2nd ed.; Noyes Publications: Park Ridge, NJ, 1985; p 496. Sax, N. I. *Dangerous Properties of Industrial Materials*, 6th ed.; Van Nostrand Reinhold: New York, 1979; p 1522. Schmutz, J. F. *Chem. Eng. News* **1978**, *56*(3), 37. Spencer, H. *Chem. Ind. (London)* **1979**, 728.

(17) Lüttringhaus, A.; Dirksen, H. W.; *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 260.

(18) We have found only one reference [Brodzki, D.; Wakselman, C.; Wartski, L. *Bull. Soc. Chim. Fr.* **1972**, 1429] to its use as a solvent for organomagnesium compounds, and that was for methyl reagents, which are known to be relatively unreactive.

(19) For reviews of tetraalkylureas as solvents, see: ref 17. Barker, B. J.; Rosenfarb, J.; Caruso, J. A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 503.

(20) For example: Sakurai, H.; Kondo, F. *J. Organomet. Chem.* **1975**, *92*, C46; **1976**, *117*, 149. Reference 21. Seebach, D.; Henning, R.; Mukhopadhyay, T. *Chem. Ber.* **1982**, *115*, 1705. Eyer, M.; Seebach, D. *J. Am. Chem. Soc.* **1985**, *107*, 3601. Tests for mutagenic and chromosome-damaging activity of *N,N'*-dimethylpropyleneurea are reported to be negative: *Chimia* **1985**, *39*, 147. Seebach, D. *Chem. Br.* **1985**, *21*, 632.

(21) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385.

(22) For a review of the cleavage of sulfonamides, see: Searles, S.; Nukina, S. *Chem. Rev.* **1959**, *59*, 1077.

(23) Klamann, D. *Monatsh. Chem.* **1953**, *84*, 651.

(24) For a specific instance where most of the amide was recovered after treatment with a Grignard reagent using stringent conditions, see: Gilman, H.; Vernon, C. C. *Recl. Trav. Chim. Pays-Bas* **1929**, *48*, 745.

(25) Gold, E. H.; Babad, E. *J. Org. Chem.* **1972**, *37*, 2208.

(26) Yamaguchi, H.; Nakano, K. *Kenkyu Hokoku - Hiroshima Daigaku Kogakubu* **1972**, *21*, 23; *Chem. Abstr.* **1973**, *79*, 65420. Also see: Spillane, W. J.; Barry, J. A.; Heaphy, W. A.; Scott, F. L. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1974**, *29*, 702.

(27) Richey, H. G., Jr.; Smith, R. D.; King, B. A.; Kester, T. C.; Squiller, E. P. *J. Org. Chem.* **1981**, *46*, 2823.

(28) Fluka Chemical Corp. and Aldrich Chemical Co.

(29) For example, see: Arnett, E. M.; Mitchell, E. J.; Murty, T. S. S. R. *J. Am. Chem. Soc.* **1974**, *96*, 3875.

(30) For reactions of sulfurous diamides with nucleophiles, see: Fischer, E. *Methoden Org. Chem. (Houben-Weyl), 4th Ed.* **1985**, *E11*, 530. While sulfonamides are resistant to basic hydrolysis [Anderson, K. K. *Compr. Org. Chem.* **1979**, *3*, Chapter 11.19], sulfinamides hydrolyze readily in aqueous base and react with nucleophiles at sulfur [Anderson, K. K. *Compr. Org. Chem.* **1979**, *3*, Chapter 11.18].

(though not precluding its use in combination with other solvents).[31] Water could be removed easily from these compounds. For example, the concentration of water in **3** saturated with water (0.8 M) was reduced to 8×10^{-3} M by the usual distillation at reduced pressure. If the distillation was from CaH_2, then the water concentration was instead reduced to less than 3×10^{-3} M. Letting the solvent stand or reflux over CaH_2 prior to distillation results in a further reduction of water concentration.

Only **7**, **9**, and **10**, compounds with sulfoxide groups and not too many carbons, were found to be miscible with water at 25 °C. The solubilities of the other compounds in water at 25 ± 1 °C were as follows: **3** (15 mg/mL), **4** (25), **5** (75), **6** (94), **8** (10), and **11** (37). The solubilities of water in the compounds at 25 ± 1 °C were as follows: **3** (3 mg/mL), **4** (11), **5** (10), **6** (46), **8** (19), and **11** (7). Compounds **3**–**11** all were miscible with toluene. All of these but **5** and **6** also were miscible with hexane, but **5** and **6** dissolved to the extent of somewhat less than 10 mg/mL of hexane. It was observed that copper(II) bromide was very soluble in **8** but only moderately soluble in **3**. Zinc chloride and potassium iodide were only slightly soluble in either solvent.

Lifetimes of several polar organometallic compounds in the presence of **3**–**11** are recorded in Table I. As anticipated, the ethyl Grignard reagent is stable in the presence of the sulfamides and the sulfonamide. As also expected, sulfurous diamides are attacked, though the tetraethyl compound (**8**) significantly less rapidly than either its tetramethyl homologue (**7**) or a corresponding cyclic compound (**9**). Attack on the sulfinamide (**10**) is surprisingly slow, though obviously very much faster than on the corresponding sulfonamide (**11**). In similar experiments with **3**–**11** using a solution (25% w/w in hexane) of diethylzinc, a much less reactive compound than the Grignard reagent, the amount of zinc compound had not diminished after 5 days.

Butyllithium has a lifetime longer than the minimum observation time only in the presence of sulfamide **3**. Methyllithium, however, which generally is a less reactive organolithium compound, has its longest lifetime with **3** but also has significant lifetimes with **4** and **11**. These results suggest that sulfamides and sulfonamides generally are considerably more stable toward organolithium compounds than are HMPA[13] or ureas[21] and presumably also might be more stable toward other reactive, polar organometallic compounds. Since **3** and **11** seem generally to be the most stable, and of these **3** is more readily obtained in substantial quantities, **3** probably would be the usual choice for use with polar organometallic compounds.

To verify that Grignard reagents could be prepared and would function reasonably in one of these solvents, a solution of propylmagnesium chloride was prepared (94% yield) in a normal fashion with **3** as the solvent, and then portions of the resulting solution were allowed to react with two ketones. A reaction with 0.5 equiv of diisopropyl ketone furnished after hydrolysis a 57% yield of the normal addition product (diisopropylpropylmethanol), 27% of the usual reduction product (diisopropylmethanol), and 13% of the ketone (presumably material that had undergone metalation). A similar reaction with 2-cyclohexen-1-one furnished 72% of the 1,2-addition product (1-propyl-2-cyclohexen-1-ol), 10% of the 1,4-addition product (3-propylcyclohexanone), and 4% of recovered ketone.

(31) This compound has been previously reported but not the fact that it is a solid [Kopinke, F. D.; Kröckel, W.; Pritzkow, W.; Mateew, K.; Radeglia, R. *J. Prakt. Chem.* **1979**, *321*, 107].

Table II. Taft β and π^* Values for Various Solvents[a]

solvent	π^*	β
3	0.67	0.52
4	0.69	0.48
5	0.75	0.51
6	0.69	0.47
7	0.75	0.61
8	0.56	0.63
9	0.58	0.67
10	0.56	0.74
11	0.65	0.59
dimethyl sulfoxide	1.00	0.76
dimethylformamide	0.88	0.69
hexamethylphosphoramide	0.87	1.05
tetramethylurea	0.83	0.80
acetonitrile	0.75	0.31
acetone	0.71	0.48
ethanol	0.54	(0.77)
diethyl ether	0.27	0.47
hexane	−0.08	0.00

[a] The values for compounds other than **3**–**11** are taken from ref 33. The parentheses indicate a relatively less certain value.

To assess the "polar aprotic character" of **3**–**11**, their Taft π^* and β values were determined.[32] The values are recorded in Table II along with those of a representative group of other solvents.[33] The π^* parameter is related to polarity and polarizability of a solvent, and hence its ability to stabilize a charge or a dipole by virtue of its dielectric effect.[34,35] Of the various procedures that have been used to determine π^* values, we chose one involving ^{13}C NMR spectra of trifluoromethylbenzene.[36] The polarity of a solvent is related to the degree to which the absorption of the para carbon is deshielded relative to that of the meta carbon in that solvent. Since the π^* values were determined only in a single manner for each solvent, small differences in the values should not be considered significant. It is evident, however, that sulfurous diamides have somewhat lower values than the corresponding sulfamides (compare **3** with **8** and **6** with **9**). Similarly, the sulfinamide (**10**) has a somewhat lower value than the corresponding sulfonamide (**11**). As a group these solvents have significant π^* values, somewhat lower than those of Me_2SO, dimethylformamide, or HMPA, but comparable to those of acetonitrile and acetone and considerably higher than those of ethanol or diethyl ether.

Taft β values are determined in a number of ways, all really measuring hydrogen bond acceptor ability, however.[37] This parameter also is related to the ability of solvent molecules to specifically solvate cationic species,[38] the feature often of greatest interest in the application of a polar aprotic solvent. We determined the β values using the ^{19}F NMR method,[39] which assigns the donor ability of a solvent on the basis of its ability to participate in hydrogen bond formation with *p*-fluorophenol. The strength

(32) For a review of π^* and β, see: Kamlet, M. J.; Abboud, J. L. M.; Taft, R. W. *Prog. Phys. Org. Chem.* **1981**, *13*, 485.

(33) For a listing of π^* and β values for many solvents, see: Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877.

(34) Kamlet, M. J.; Abboud, J. L.; Taft, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 6027. Kamlet, M. J.; Hall, T. N.; Boykin, J.; Taft, R. W. *J. Org. Chem.* **1979**, *44*, 2599.

(35) For a summary of other measures of solvent polarity and their relation to π^* and β, see: ref 32. Reichardt, C. In *Molecular Interactions*; Ratajczak, H., Orville-Thomas, W. J., Eds.; Wiley: Chichester, 1982; Vol. 3, Chapter 5.

(36) Chawla, B.; Pollack, S. K.; Lebrilla, C. B.; Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 6924. Also see ref 32.

(37) Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1976**, *98*, 377. Taft, R. W.; Gramstad, T.; Kamlet, M. J. *J. Org. Chem.* **1982**, *47*, 4557.

(38) Taft, R. W.; Pienta, N. J.; Kamlet, M. J.; Arnett, E. M. *J. Org. Chem.* **1981**, *46*, 661.

(39) Gurka, D.; Taft, R. W. *J. Am. Chem. Soc.* **1969**, *91*, 4794.

of the hydrogen bond is established by the upfield shift of the ^{19}F NMR absorption of *p*-fluorophenol relative to the absorption of *p*-fluoroanisole in the same medium. Again, the values were determined in only one manner, and small differences should not be considered significant.

The finding of significantly higher β values for the sulfurous diamides (0.61–0.67) and the sulfinamide (0.74) than for the corresponding sulfamides (0.47–0.52) and sulfonamide (0.59) was expected. Ability to hydrogen bond to phenols is known to be greater for sulfoxides than for sulfones,[29,40] and greater for sulfinamides than for sulfonamides.[40] The β values of compounds in the sulfinyl group series decrease in the order sulfoxides (0.76–0.83 for four sulfoxides having only alkyl carbons)[33] > the sulfinamide (0.74) > the sulfurous diamides (0.61–0.67), though the differences are relatively small. Other studies generally have shown that sulfoxides and sulfinamides are quite similar in ability to hydrogen bond to phenols.[40,41] In the sulfonyl group series, there apparently is no literature β value for a sulfone; we find a slightly greater β value for the sulfonamide (0.59) than for the sulfamides (0.47–0.52). Other studies have shown sulfones and sulfonamides to be quite similar in ability to hydrogen bond to phenols.[40] Introduction of a dialkylamino group in place of an alkyl group in these sulfur compounds does not profoundly reduce donor ability. The β values for sulfamides and the sulfonamide, though less than for HMPA or even dimethyl sulfoxide, dimethylformamide, or tetramethylurea, nevertheless are significantly higher than the values, for example, for acetonitrile or acetone.

The usefulness of a compound as a polar aprotic solvent will depend to some degree on the properties approximated both by β and by π^*. Those parameters for the sulfamides and the sulfonamide do not place them quite with solvents such as dimethyl sulfoxide or even dimethylformamide. Nevertheless, to a considerable degree, the sulfur containing solvents possess the features of good polar aprotic solvents. They should find use where particularly great stability toward basic and nucleophilic reagents (or relatively low water solubility) are important.

Experimental Section

^1H NMR chemical shifts are reported in ppm (δ) downfield from internal Me_4Si. Absorptions are reported using the following notations: s, singlet; t, triplet; q, quartet; m, a more complex multiplet. Gas chromatographic analyses were performed with an instrument with a flame ionization detector, helium as the carrier gas, and the following column: 3% SP-2100 on Supelcoport (100–120 mesh), 2 mm i.d. × 10 ft (glass tubing). Microanalyses were performed by Midwest Microlab, Ltd.

***N,N,N',N'*-Tetraethylsulfamide (3).** This compound was prepared (67% yield) as previously reported:[27] bp 85–88 °C (0.5 torr) [lit.[27] bp 95–102 °C (1 torr)]; d^{25} 1.037; ^1H NMR (CCl_4) δ 1.17 (t, 3, J = 7.1 Hz, CH_3), 3.22 (q, 2, J = 7.1 Hz, CH_2).

***N,N*-Diethyl-*N',N'*-dimethylsulfamide (4).** A solution of dimethylsulfamoyl chloride (75 mL, 0.69 mol) in hexane (100 mL) was added dropwise over a period of 1 h to a stirred solution of diethylamine (144 mL, 1.4 mol) in hexane (300 mL) that was cooled in an ice bath. After the addition was complete, the ice bath was removed. The reaction mixture spontaneously warmed sufficiently to reflux. When refluxing ceased, the mixture was filtered and most of the hexane was removed under reduced pressure. The remainder was washed with water (four 25-mL portions) and then distilled to give 4 (88 g, 0.49 mol, 70%): bp 60–65 °C (0.2 torr) [lit.[42] bp 229 °C with partial decomposition]; d^{25} 1.091; ^1H NMR ($CDCl_3$) δ 1.20 (t, 3, J = 7.1 Hz, CH_3C), 2.78 (s, 3, CH_3N), 3.28 (q, 2, J = 7.1 Hz, CH_2).

Dipyrrolidinesulfamide (5). A solution of sulfuryl chloride (60 mL, 0.75 mol) in pentane (100 mL) was added dropwise over a period of 2 h to a stirred solution of pyrrolidine (250 mL, 3.0 mol) in pentane (400 mL) that was cooled to −30 °C. After addition was complete, the reaction mixture was allowed to warm to ambient temperature. Additional pyrrolidine (45 mL, 0.54 mol) was added rapidly, and the mixture was refluxed for 5 h. The reaction mixture was filtered, and most of the pentane was removed under reduced pressure. The filtrate was washed with water (four 25-mL portions) and then distilled to give 5 (90 g, 0.44 mol, 59%): bp 114–118 °C (0.1 torr); d^{25} 1.207. The distillate solidified to a solid: mp 25–26 °C; d^{25} 1.207; ^1H NMR ($CDCl_3$) δ 1.87 (m, 1, CH_2CH_2N), 3.26 (m, 1, CH_2N). Anal. Calcd for $C_8H_{16}N_2O_2S$: C, 47.03; H, 7.89; N, 13.71; S, 15.66. Found: C, 46.72; H, 7.99; N, 13.49; S, 15.16.

2,5-Diethyl-1,1-dioxo-1,2,5-thiadiazolidine (6). This compound was prepared using a procedure modified from one previously reported.[43] A solution of sulfuryl chloride (69 mL, 0.86 mol) in diethyl ether (200 mL) was added dropwise over a period of 2 h to a stirred solution of *N,N'*-diethylethylenediamine (123 mL, 0.86 mol) and triethylamine (263 mL, 1.9 mol) in diethyl ether (600 mL) that was cooled to −30 °C. After addition was complete, the reaction mixture was allowed to warm to ambient temperature and then refluxed for 5 h. The reaction mixture was filtered and most of the ether removed under reduced pressure. The filtrate was washed with water (four 25-mL portions) and then distilled to give 6 (31 g, 0.17 mol, 20%; a significant amount of high boiling residue remained in the pot): bp 92–97 °C (0.05 torr) [lit.[43] bp 96 °C (0.05 torr)]; d^{25} 1.170; ^1H NMR ($CDCl_3$) δ 1.26 (t, 3, J = 7.2 Hz, CH_3), 3.09 (q, 2, J = 7.3 Hz, CH_2CH_3), 3.30 (s, 2, CH_2CH_2).

***N,N,N',N'*-Tetramethylsulfurous Diamide (7).** This compound was prepared as already described[44] except that the temperature of the reaction mixture was maintained at −30 °C. Distillation gave 7 (69%): bp 45–50 °C (0.05 torr) [lit.[44] bp 63–65 °C (4 torr)]; mp 31 °C [lit.[45] mp 30–30.5 °C]; ^1H NMR (CCl_4) δ 2.55 (s).

***N,N,N',N'*-Tetraethylsulfurous Diamide (8).**[46] A solution of thionyl chloride (50 mL, 0.69 mol) in pentane (100 mL) was added dropwise over 2 h to a stirred solution of diethylamine (289 mL, 2.8 mol) in pentane (500 mL) that was cooled to −30 °C. After addition was complete, the mixture was allowed to warm to ambient temperature. Additional diethylamine (50 mL, 0.48 mol) was added rapidly, and the mixture was refluxed for 1 h. The reaction mixture was filtered, and most of the pentane was removed under reduced pressure. The remaining filtrate was washed with water (four 25-mL portions) and distilled to give 8 (83 g, 0.43 mol, 62%): bp 68–72 °C (0.3 torr) [lit.[47] bp 118 °C (27–28 torr)]; d^{25} 0.970 [lit.[47] d^{15} 0.985]; ^1H NMR (CCl_4) δ 1.10 (t, 3, J = 7.0 Hz, CH_3), 2.95 (q, 2, J = 7.0 Hz, CH_2).

2,5-Diethyl-1-oxo-1,2,5-thiadiazolidine (9). This compound was prepared in a manner similar to one already described.[43,48] A solution of thionyl chloride (31 mL, 0.43 mol) in diethyl ether (100 mL) was added dropwise over a period of 2 h to a solution of *N,N'*-diethylethylenediamine (62 mL, 0.43 mol) and triethylamine (132 mL, 0.95 mol) in diethyl ether (500 mL) that was cooled to −30 °C. After addition was complete, the reaction mixture was allowed to warm to ambient temperature and then heated at reflux temperature for 5 h. The mixture was filtered, and most of the diethyl ether was removed under reduced pressure. The filtrate was washed with water (four 25-mL portions) and then distilled to give 9 (27 g, 0.17 mol, 39%; a significant amount of high boiling residue remained in the pot): bp 72–75 °C (0.1 torr) [lit.[43] bp 88 °C (1 torr)]; d^{25} 1.088; ^1H NMR ($CDCl_3$) δ 1.27

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***N,N*-Diethyltrimethylmethanesulfinamide (10).** The procedure was adapted from one already described.[49] *tert*-Butylmagnesium chloride was prepared by the dropwise addition over 10 h of a solution of freshly distilled *tert*-butyl chloride (193 mL, 1.8 mol) in diethyl ether (400 mL) to a stirred mixture of magnesium turnings (60.8 g, 2.5 mol) in diethyl ether (450 mL) followed by an additional 16 h of stirring. Diethyl ether was distilled from sodium benzophenone ketyl prior to use. Excess sulfur dioxide was bubbled for 6 h into the Grignard reagent solution which was cooled in an ice bath. The resulting solution was poured into a cold solution of ammonium chloride (300 g) in water (900 mL). The mixture was stirred for 30 min, and then the ether layer was separated, dried ($CaCl_2$), and evaporated to give trimethylmethanesulfinic acid (101 g, 0.83 mol, 46%): ^{1}H NMR (CCl_4) δ 1.28 (s, 9, CH_3), 9.40 (s, 1, OH).

A solution of thionyl chloride (73 mL, 1.0 mol) in diethyl ether (100 mL) was added over 1 h to a stirred solution of the crude sulfinic acid (101 g, 0.83 mol) in diethyl ether (150 mL). After the addition was complete, most of the diethyl ether was evaporated, and the residue was distilled to give trimethylmethanesulfinyl chloride (59 g, 0.42 mol, 51%): bp 35–40 °C (0.1 torr) [lit.[50] bp 62 °C (15 torr)]; ^{1}H NMR (CCl_4) δ 1.40 (s).

A solution of the sulfinyl chloride (59 g, 0.42 mol) in pentane (100 mL) was added over a period of 1 h to a stirred solution of diethylamine (95 mL, 0.92 mol) in pentane (250 mL) that was cooled in an ice bath. The mixture was filtered, and most of the pentane was removed under reduced pressure. The filtrate was washed with water (four 25-mL portions) and then distilled to give **10** (57 g, 0.32 mol, 76%): bp 65–69 °C (0.1 torr); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 6, J = 7.1 Hz, CH_3CH_2), 1.23 (s, 9, $(CH_3)_3C$), 3.05 (m, 2, CHH), 3.23 (m, 2, CHH) [each multiplet in this spectrum (taken at 200 MHz) consists of six peaks, equally spaced at 7.1–7.2 Hz intervals, presumably part of an ABX_3 pattern with $J_{AX} = J_{BX} = 1/2\ J_{AB}$]. Anal. Calcd for $C_8H_{19}NOS$: C, 54.19; H, 10.80; N, 7.90; S, 18.08. Found: C, 53.98; H, 10.87; N, 7.45; S, 17.69.

***N,N*-Diethyltrimethylmethanesulfonamide (11).**[51] A solution of potassium permanganate (71.5 g, 0.45 mol) in acetone (300 mL) was added slowly to a stirred solution of **10** (19.9 g, 0.11 mol) in acetone (50 mL). Then the reaction mixture was heated at reflux temperature for 5 h, during which time the progress of the reaction was monitored by gas chromatography (120 °C, retention times relative to decane of 3.9 for **10** and 4.7 for **11**). The mixture was cooled to ambient temperature and filtered. Most of the acetone was removed under reduced pressure, and the residue was dissolved in a small amount of pentane, washed with water (four 25-mL portions), and distilled to give **11** (15 g, 0.08 mol, 73%): bp 84–86 °C (0.5 torr) [lit.[52] bp 66 °C (0.3 torr)]; d^{25} 1.023; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, 6, J = 7.1 Hz, CH_3CH_2), 1.42 (s, 9, $(CH_3)_3C$), 3.42 (q, 4, J = 7.1 Hz, CH_2).

***N,N*-Dimethyltrimethylmethanesulfonamide (12).** *N,N*-Diethyltrimethylmethanesulfinamide was prepared in the same manner as **10** except that dimethylamine was used instead of diethylamine: ^{1}H NMR (CCl_4) δ 1.10 (s, 3, $(CH_3)_3C$), 2.60 (s, 2, CH_3N). Without being further purified, the sulfinamide was used to prepare **12** by use of the same procedure used for **11**. After the solvent was removed, the solid residue was recrystallized from pentane to give **12** (12% yield based on *tert*-butyl chloride): mp[31] 87–88 °C; ^{1}H NMR (CCl_4) δ 1.46 (s, 3, $(CH_3)_3C$), 3.04 (s, 2, CH_3N).

Determination of Solubilities and Water Content. After water and the solvent had been shaken thoroughly together and the layers separated, solubility of water in the solvent was determined by a Karl Fisher titration carried out by an amperometric method using a Fisher model 391 K-F titrimeter and a Karl Fisher reagent (Fisher Scientific) that has been described.[53] The solubility of the solvent in water was determined by comparing peak areas due to the solvent and acetone hydrogens in the ^{1}H NMR spectrum of the aqueous layer after a known amount of acetone had been added. After hexane and the solvent had been shaken together and the layers separated, the solubility in hexane was determined by comparing peak areas in the ^{1}H NMR spectrum of the hexane layer due to the hydrogens of the solvent and of a known amount of added benzene.

Stability Studies. A sample was prepared by adding the solution of organometallic compound (1 mmol) and benzene (30 μL) to a stirred sample (3 mmol) of the solvent being tested. Commercial solutions (Morton Thiokol, Inc., Alfa Products) of diethylzinc (25% w/w in hexane), butyllithium (1.3 M in hexane), and methyllithium (1.8 M in diethyl ether) were used. The solution of ethylmagnesium bromide in diethyl ether was prepared in a conventional way and its concentration (2.1 M) determined by hydrolysis of aliquots followed by addition of a standard HCl solution and back titration with a standard NaOH solution to a bromothymol blue endpoint. A sample of a solution was transferred to an NMR tube which was then sealed. Disappearance (if any) of an organometallic compound was determined by monitoring in ^{1}H NMR spectra the reduction in area of the absorption of its α-hydrogens relative to the absorption of the benzene hydrogens.[54]

Determination of Taft π^*. The values were calculated from the equation[36] $C_p - C_m = 2.80 + 0.48\ \pi^*$ where C_p is the downfield shift of the ^{13}C NMR absorption of the para carbon of trifluoromethylbenzene relative to the absorption of benzene and C_m is the corresponding shift for the absorption of the meta carbon. The ^{13}C NMR spectra were recorded at 25 MHz; a capillary containing D_2O was placed into the NMR tube to provide a deuterium lock. The experimental values determined from solutions of trifluoromethylbenzene and benzene in the various solvents were as follows: CCl_4 (C_p = 3.21; C_m = 0.31), dimethylsulfoxide (4.15, 0.88), **3** (3.95, 0.83), **4** (3.95, 0.82), **5** (4.04, 0.88), **6** (3.95, 0.82), **7** (4.00, 0.84), **8** (3.86, 0.79), **9** (3.99, 0.91), **10** (3.94, 0.87), **11** (3.90, 0.79). The values of $C_p - C_m$ for CCl_4 and dimethylsulfoxide both were within 0.03 of those that have been reported.[36]

Determination of Taft β. The values were calculated from the equation[37] $\beta = \Delta/(2.80)(1.365)$ where Δ is the limiting upfield shift of the ^{19}F NMR absorption of *p*-fluorophenol relative to the absorption of *p*-fluoroanisole. The CCl_4 solutions that were prepared had 0.01 M concentrations of *p*-fluorophenol and *p*-fluoroanisole and a 0.4 M concentration of the solvent being tested. The ^{19}F NMR spectra were recorded at 93.6 MHz; a capillary containing D_2O was placed in the NMR tube to provide a deuterium lock. A trial run with dimethyl sulfoxide gave a Δ value of 2.71, within 0.03 of the value previously reported.[39] The following experimental values of Δ were determined: **3** (1.98), **4** (1.85), **5** (1.95), **6** (1.81), **7** (2.35), **8** (2.40), **9** (2.58), **10** (2.84), **11** (2.24).

Reactions of Propylmagnesium Bromide. A solution of freshly distilled propyl bromide (9.08 mL, 0.10 mol) in **3** (100 mL) was added to magnesium turnings (2.67 g, 0.11 mol) and the mixture stirred for 16 h. The yield of the Grignard reagent was determined to be 94% by hydrolysis of aliquots followed by addition of a standard HCl solution and back titration with a standard NaOH solution to a bromothymol blue endpoint. A sample of a solution of the ketone (5.0 mL, 0.43 M, 2.15 mmol) was added dropwise to a stirred solution of Grignard reagent (5.0 mL, 0.86 M, 4.3 mmol). After 3 h, the reaction was quenched with a saturated aqueous solution of ammonium chloride (5 mL). The ammonium chloride solution was washed with diethyl ether, and the combined organic layers were subjected to GC analysis.

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