1 M NH_4OH or 1 M NaOH.

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Registry No. 1a, 58-96-8; **1b**, 65-46-3; **1c**, 951-77-9; **1d**·HCl, 69-74-9; **2a**, 2880-89-9; **2b**, 25130-29-4; **2c**, 32387-56-7; **2d**, 17676-65-2; **3a**, 58-61-7; **3b**, 5536-17-4; **3c**, 118-00-3; **4a**, 34408-14-5; **4b**·HCl, 77415-35-1; **4c**, 2104-68-9; **5**, 13089-44-6.

Sulfamides: Polar Aprotic Solvents Compatible with Grignard Reagents

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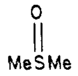
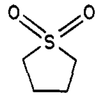
A polar aprotic solvent[2] has a reasonably high dielectric constant and a dipolar function with an exposed negative end but a buried positive end. As a result, it is an effective specific solvating agent for cations but not for anions. Anions in such solvents are less solvated and hence more reactive, often by many orders of magnitude, than in polar protic solvents. Polar aprotic solvents are used widely in physical chemical studies and in synthetic applications in which anion activity is important. Industrial uses for some of these solvents also are due to their considerable solubilities for certain gases and polymers and greater solubilities for aromatic than for aliphatic hydrocarbons.[3]

Polar aprotic solvents should be useful with organometallic compounds. For example, coordination by a polar aprotic solvent with the metal of a polar organometallic compound could increase the polarity of the carbon–metal bond. Unfortunately, polar organometallic compounds often react with these solvents. For example, Grignard reagents add to the carbonyl group of dimethylformamide to give aldehydes, reduce dimethyl sulfoxide (1), and abstract an α-hydrogen from sulfolane (2).[4]

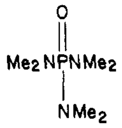


$\mathrm{Me}\overset{\mathrm{O}}{\overset{\|}{\mathrm{S}}}\mathrm{Me}$

1



2

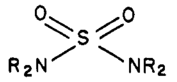


$\mathrm{Me_2N}\underset{\mathrm{NMe_2}}{\underset{|}{\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}}}\mathrm{NMe_2}$

3

Hexamethylphosphoramide (HMPA, 3) is the only polar aprotic solvent that has been used extensively with Grignard reagents.[5,6] Effects of HMPA used either as a solvent for organomagnesium compounds or as an additive to their solutions in other solvents are often large. However, even HMPA has limitations. Its stability is less than would be desirable. At temperatures well below ambient, organolithium compounds attack HMPA and are destroyed.[7] Even Grignard reagents are not completely stable in contact with HMPA.[8] Moreover, potential health hazards are associated with the use of HMPA.[9]

We thought that tetraalkylsulfamides (4) would be



4a, R = Me
b, R = Et

reasonable possibilities for use as polar aprotic solvents that could have considerable stability toward polar organometallic compounds.[10,11] The functional group, combining the sulfonyl and dialkylamino groups found in some commonly used polar aprotic solvents, would be expected to impart characteristic polar aprotic solvent properties, and it has been reported[12] that **4b** is hydrolyzed in aqueous base only with great difficulty.

Our observations with sulfamide **4b** are encouraging[13] and suggest that compounds with sulfamide functions may be useful as solvents for organometallic compounds and for other strongly basic and nucleophilic reagents. Solutions of ethylmagnesium bromide (90%), propylmagnesium bromide (80%), isopropylmagnesium chloride (87%), and phenylmagnesium bromide (40%) in **4b** were prepared directly from organic halides and magnesium at ambient temperature. The ethyl and propyl Grignard reagent solutions showed no signs of decomposition (^{1}H NMR observations) at ambient temperature during a 3-week period. A hexane solution (25%) of diethylzinc to which 2 equiv of **4b** was added also seemed to be stable. Even attack by an organolithium compound was not rapid. The half-life at ambient temperature of a 2.0 M hexane solution of butyllithium to which 2 equiv of **4b** was added was about 1 h. Presumably, stability would be even greater at lower temperature.

As solvents, sulfamides probably will resemble sulfolane rather than the more exciting HMPA. The effectiveness of polar aprotic solvents parallels roughly the chemical shifts of the ^{1}H NMR absorption of $CHCl_3$ at infinite dilution in the solvents (compared to the chemical shift

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[1] Undergraduate research participant.

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[13] Sulfamide **4a**, an obvious choice for study, is a solid (mp 73 °C) at ambient temperature and must be used with other solvents.

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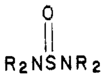
in cyclohexane) and the infrared stretching frequency of the C–H bond of PhC≡CH in the solvents (compared to the frequency in CCl_4).[14] The values for **4b** of −0.70 ppm and $-55\ cm^{-1}$ are much closer to those for sulfolane (−0.68 ppm and $-47\ cm^{-1}$) than to those for HMPA (−2.03 ppm and $-153\ cm^{-1}$) or even dimethyl sulfoxide (−1.34 ppm and $-110\ cm^{-1}$). With respect to its E_T value, a parameter[15] related more to general solvent polarity than to specific solvating ability, **4b** (41.8 kcal/mol) is similar to sulfolane (44.0 kcal/mol). The dipole moment of **4a** (4.38 D)[16] is also similar to that of sulfolane (4.69 D).[17]

By analogy to comparisons[18] between sulfoxides and sulfones, sulfurous diamides (**5**) should have more polar aprotic solvent character than do sulfamides. However, they would be expected to be considerably less stable toward nucleophilic and basic reagents. We found that a 2.5 M tetrahydrofuran solution of methylmagnesium chloride to which 1 equiv of **5a** was added had a half-life of about 2 h at ambient temperature.



$$R_2N\overset{\overset{\displaystyle O}{\|}}{S}NR_2$$

5a, R = Me

One problem with (or virtue of) the use of sulfamides as solvents is their low water solubility. Unlike many polar aprotic solvents, **4a** and **4b** cannot be removed easily from typical organic materials by a few washes with water. As a result, applications that require separation of the solvent from other relatively water-insoluble compounds would necessitate distillation, chromatography, or repeated extraction with water. Of course, for some applications, low water solubility could be advantageous. There is also the possibility of constructing related molecules having greater water solubility.

Experimental Section

Tetraethylsulfamide (4b). The following procedure proved to be convenient.[19] A solution of sulfuryl chloride (76.6 mL, 0.946 mol) in pentane (100 mL) was added dropwise to a stirred solution of diethylamine (392 mL, 3.78 mol) in pentane (400 mL) that was cooled in an ice bath. After the addition was complete, the reaction mixture was allowed to warm to ambient temperature. Additional diethylamine (100 mL) was added, and the mixture was refluxed for 6 h. The reaction mixture was filtered, and most of the pentane was removed from the filtrate at reduced pressure. The remaining filtrate was washed repeatedly with small portions of water and then distilled to give **4b**, bp 95–102 °C (1 torr). A Karl Fischer titration showed the water content to be less than 10^{-3} M.

Other Materials. Tetramethylsulfurous diamide (**5a**) was synthesized by using a procedure already reported.[20] The Grignard reagents were prepared by using freshly distilled organic halides and magnesium turnings (Johnson Matthey Chemicals, "Puratronic"). Solutions of diethylzinc, butyllithium, and methylmagnesium chloride were commercial samples (Alfa Products). The 4-(2,4,6-triphenylpyridinium)-2,6-diphenylphenoxide used to determine the E_T value was donated by Charles deBrosse (The Pennsylvania State University).

Preparation of Grignard Reagents in Tetraethylsulfamide (4b). Reactions were carried out in a standard-taper, three-necked, round-bottomed flask containing a magnetic stirring bar and fitted with a pressure-equalizing dropping funnel and a condenser having a gas-inlet tube at the top. Magnesium (0.53 g, 22 mmol) was added to the apparatus, and then the apparatus was heated gently with a heat gun while nitrogen flowed rapidly through it. During the course of a reaction, a slightly positive pressure of nitrogen was maintained in the closed reaction system. After the apparatus had cooled, the organic halide (20 mmol) and **4b** (20 mL) were added to the flask, and then the reaction mixture was stirred for 12 h. In the reaction with bromobenzene, a small amount of 1,2-dibromoethane was also added; in the absence of this additive, the Grignard reagent did not form appreciably.

Concentrations of Grignard reagents were determined by hydrolysis of aliquots followed by titration of the resulting base. Two preparations of ethylmagnesium bromide gave essentially identical yields, as did three preparations of propylmagnesium bromide. Essentially the same concentrations of one ethylmagnesium bromide and one propylmagnesium bromide preparation were found when a double-titration procedure[21] was used.

Acknowledgment. We are grateful to the National Science Foundation for support of this research and for aiding in the purchase of the NMR spectrometers that were used. We thank Charles DeBrosse for helpful suggestions.

Registry No. 4b, 2832-49-7.

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One-Step Conversions of Esters to 2-Imidazolines, Benzimidazoles, and Benzothiazoles by Aluminum Organic Reagents

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Aluminum organic reagents play an increasingly important role in effecting simple chemical transformations. Several examples, recently published, include conversions of esters to thioesters,[1] ketene thioacetals,[2] and amides,[3] of esters to nitriles,[4] and of epoxides to amino alcohols.[5]

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