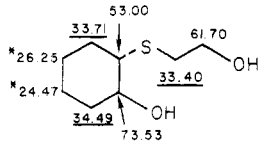
9.38; S, 18.60. Found (fraction 1): C, 62.51, H. 9.09; S. 18.32. Found (fraction 2): C, 62.59; H. 9.49; S, 18.41.

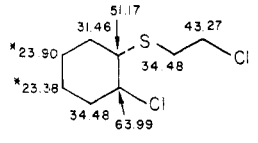
***trans*-1-Thiadecalin 1,1-dioxide (6).** *trans*-1-Thiadecalin (234 mg, 1.50 mmol) was dissolved in a solution of 7 mL of acetic acid and 4 mL of 30% hydrogen peroxide. The resulting solution was refluxed for 0.75 h, cooled to ambient temperature, neutralized with sodium bicarbonate, and finally extracted with methylene chloride (3 × 75 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to dryness (rotary evaporator) to afford 198 mg (70.2%) of a colorless crystalline solid. Purification using column chromatography (neutral alumina with hexanes, then hexanes–methylene chloride (1:1), and finally methylene chloride as eluents) gave 114 mg (41.0%) of thiadecalin sulfone **6**: mp 114.0–115.8 °C. Anal. Calcd for $C_9H_{16}SO_2$: C, 57.40; H, 8.58; S, 17.03. Found: C, 57.46; H, 8.79; S, 17.33.

***trans*-2-Hydroxycyclohexyl 2-Hydroxyethyl Sulfide.** Sodium (1.15 g, 0.050 mol) and 2-mercaptoethanol (39.0 g, 0.50 mol) were dissolved in absolute ethanol (150 mL) under a nitrogen atmosphere. Cyclohexene oxide (49.0 g, 0.50 mol) was added to the above solution dropwise (1.5 h), stirred at ambient temperature for 0.5 h, then refluxed overnight (approximately 20 h). The solution was allowed to cool to ambient temperature and diluted with 400 mL of water. The resulting mixture was extracted with ethyl ether (3 × 150 mL) and the ethereal solution was dried ($MgSO_4$) and filtered. The ether solvent was removed (rotary evaporator) to afford an oily residue which was distilled (bp 158–167 °C at 2.0–2.8 torr) to give 17.8 g of a white solid: mp 43–48 °C (lit.[25] mp 46 °C).



* and ___ are interchangeable

***trans*-2-Chlorocyclohexyl 2-Chloroethyl Sulfide.** A solution of *trans*-2-hydroxycyclohexyl 2-hydroxyethyl sulfide (8.8 g, 50 mmol) in 50 mL of ethyl ether was added to a solution containing thionyl chloride (9.0 mL, 14.6 g, 130 mmol) in 50 mL of dry ether over a period of 1 h. The solution was stirred at ambient temperature for 48 h. Removal of the ether solvent and excess thionyl chloride (rotary evaporator) followed by distillation at reduced pressure (2.6 torr) afforded a clear yellow liquid (8.8 g, 83%): bp 143 °C [lit.[26] mp 84–86 °C (0.2 torr)].



* are interchangeable

***trans*-1,4-Dithiadecalin (7).** 2-Chlorocyclohexyl 2-chloroethyl sulfide (3.3 g, 150 mmol) in 15 mL of ethanol was added to an ethanol–water (1:1) solution of sodium sulfide nonahydrate (7.2 g, 0.30 mol). The resulting solution was stirred for 2 h at 60 °C and poured over ice. The colorless solid which precipitated was collected by filtration and purified by sublimation (70 °C, 1.2 torr) and column chromatography (using alumina as solid support and cyclohexane and cyclohexane–methylene chloride (1:1) as eluents) to afford 720 mg (27%) of a crystalline solid: mp 72–75.5 °C [lit.[6] mp 77–78 °C].

***α,β-trans*-1,4-Dithiadecalin 1-Oxides (8α,8β).** Hydrogen peroxide (30%, 0.6 mL, 5 mmol) in 15 mL of acetic acid was added slowly to a solution containing *trans*-1, 4-dithiadecalin (1.74 g, 10.0 mmol) in acetic acid (25 mL). The solution was stirred overnight (20 h), diluted with water (50 mL) to precipitate unreacted starting material, filtered, and finally neutralized with saturated sodium bicarbonate (solution). The resulting mixture was extracted with methylene chloride (3 × 50 mL) and dried ($MgSO_4$), and the solvent was removed (rotary evaporator) to give a colorless solid. Purification by column chromatography (alumina, cyclohexane, cyclohexane–methylene chloride (1:1), methylene chloride, and methylene chloride–ethyl acetate (3:1) solvents) gave 100 mg of a crystalline material as fraction 1, later identified as 8β (mp 113.0–114.0 °C); 58 mg of crystalline material as fraction 2 (mp 88–100 °C); 124 mg of colorless solid as fraction 3, later identified as 8α (mp 120.2–121.5 °C). Anal. Calcd for $C_8H_{14}SO$: C, 50.49; H, 7.41; S, 33.69. Found (fraction 1): C, 50.62; H, 7.40; S, 33.40. Found (fraction 3): C, 50.64; H, 7.61; S, 33.45.

***trans*-1,4-Dithiadecalin 1,1-Dioxide (9).** A mixture of the two dithiadecalin sulfoxides 8α and 8β (95 mg, 0.50 mmol) was suspended in a solution containing magnesium sulfate (150 mg) in 20 mL of water. An aqueous solution of potassium permanganate (53 mg, 0.33 mmol) was added slowly to the suspension and the resulting mixture was stirred for 2 h. The reaction mixture was treated with excess sodium bisulfite to dissolve the manganese dioxide. The clear aqueous solution was extracted with methylene chloride (3 × 25 mL). The methylene chloride solution was dried ($MgSO_4$) and concentrated to dryness (rotary evaporator) to give 81 mg (79%) of a crystalline solid. This material was purified by column chromatography (alumina, cyclohexane, cyclohexane–methylene chloride (1:1), methylene chloride, and methylene chloride–ethyl acetate (5:1) solvents) to give 49 mg (48%) of analytically pure material: mp 138–142 °C. Anal. Calcd for $C_8H_{14}S_2O_2$: C, 46.57; H, 6.84; S, 31.08. Found: C, 46.49; H, 6.81; S, 30.91.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Graduate Fellowship Program sponsored by the National Science Foundation (Grant No. SP-178-21239) for a fellowship to R.P.R. We thank Dr. David L. Harris for recording numerous ^{13}C NMR spectra related to this research. Purchase of the NMR instrument was made possible by NSF Instrument Grants GU-2059, 2059-Amendment I, and GP-37602 and by NIH Grant 5S05RR07072.

Registry No. 1, 62015-71-8; 2α, 62057-86-7; 2β, 62015-75-2; 3, 62015-76-3; 4, 54340-73-7; 5α, 67530-09-0; 5β, 67530-10-3; 6, 71989-44-1; 7, 16291-03-5; 8α, 71989-45-2; 8β, 72028-92-3; 9, 71989-46-3; *trans*-2-hydroxycyclohexyl 2-hydroxyethyl sulfide, 71989-47-4; 2-mercaptoethanol, 60-24-2; cyclohexene oxide, 286-20-4; *trans*-2-chlorocyclohexyl 2-chloroethyl sulfide, 71989-48-5.

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(26) R. C. Fuson, C. C. Price, R. A. Bauman, O. H. Bullitt, W. R. Hatchard, and E. W. Maynert, *J. Org. Chem.*, 11, 469 (1946).

A Spectrophotometric Probe for Studying Solvent-Sorting Effects

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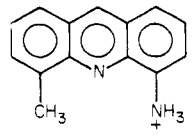
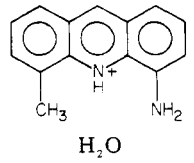
Over three decades ago Craig discovered an exception to the rule that aminoacridines in dilute acid protonate at the ring nitrogen.[1] Protonation of 4-amino-5-methylacridine in acidic *ethanol* occurs on the primary amino group (although in *water* the ring nitrogen remains the more basic atom):



C_2H_5OH



H_2O

(1) Craig, D. P. *J. Chem. Soc.* **1946**, 534. Note that this article uses a numbering system which has now been replaced.

0022-3263/80/1945-0183$01.00/0

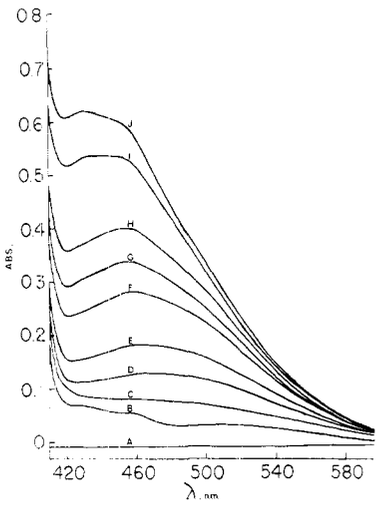


Figure 1. Spectra of 1.10×10^{-3} M 4-amino-5-methylacridine in ethanol–water mixtures containing 0.20 N HCl with plot A being the baseline (ethanol vs. ethanol). The mole fractions of water in the mixtures are: B, 0.00; C, 0.52; D, 0.76; E, 0.83; F, 0.88; G, 0.91; H, 0.93; I, 0.97; J, 1.00.

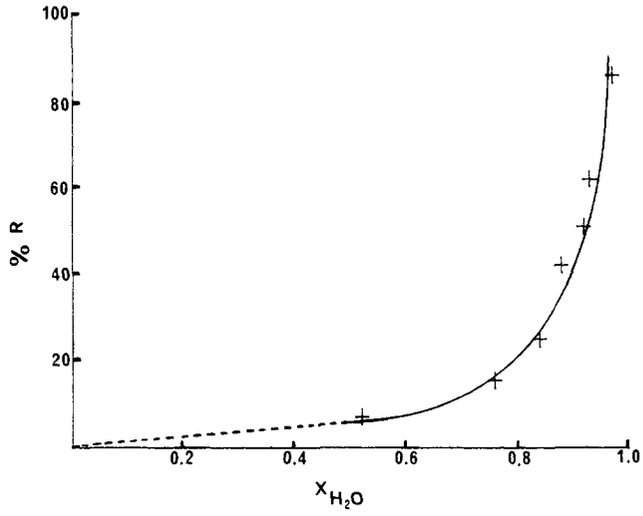


Figure 2. The percentage of ring-protonated 4-amino-5-methylacridine as a function of the mole fraction of water. Data are based on the spectra in Figure 1.

Spectral evidence for the anomalous behavior in ethanol is convincing. 4-Amino-5-methylacridine in ethanolic HCl has a UV spectrum similar to that of unprotonated acridine. On the other hand, 4-amino-5-methylacridine in aqueous HCl displays an absorption band near 460 nm characteristic of the ring-protonated 4-aminoacridinium ion. The primary amino group of 4-aminoacridines protonates preferentially in ethanol only when the methyl is present in the 5-position. Most likely, therefore, the 5-methyl substituent sterically impedes ethanol solvation of the ring NH^+, thus favoring reaction at the more exposed 4-amino group. In water, protonation of the ring nitrogen and solvation of the resulting cation can take place despite the methyl group.

It occurred to us that the work of Craig offered a potentially useful means for studying solvation in binary solvent mixtures. Small additions of water to ethanolic solutions of 4-amino-5-methylacridine could conceivably induce protonation at the ring nitrogen if the probe is able to "sort out" water molecules; such specific solvation would manifest itself by large spectral changes near 460 nm. Although solvent sorting is an old concept (having been discussed by Debye,[2] Scatchard,[3] Hyne,[4] and many others), the behavior of solutes in solvent mixtures is far from understood. In fact, Langford and Tong[5] recently referred to mixed solvents as "a kineticist's troubled waters".

We were initially concerned that possible association of 4-amino-5-methylacridine (AMA) would complicate the interpretation of solvent-induced spectral changes. (Acridine orange and related dyes in water are well-known to form dimers which absorb at lower wavelength and with less intensity than monomer.)[6,7] Fortunately, dimerization was not a serious problem with 4-amino-5-methylacridine under our experimental conditions. Thus, Beer's law is obeyed for 4.95×10^{-5} to 9.90×10^{-4} M AMA in 100% water and for 4.60×10^{-5} to 1.04×10^{-3} M AMA in 10% ethanol–90% water (λ 460 nm; 0.01 M HCl). Consistent with this apparent lack of dimerization, Albert and Goldacre[8] mention no complications in their potentiometric and spectrophotometric pK_a determinations of over 100 substituted acridines (including AMA) in water and in 50% ethanol–50% water. Moreover, the presence of ethanol or other cosolvent in water is known to suppress dimerization of acridine orange; its association constant is lowered 40-fold by adding only 15% ethanol to an aqueous solution.[9]

Spectra were obtained from solutions of 1.1×10^{-3} M AMA in various ethanol–water mixtures containing 0.20 M HCl (Figure 1). At this level of HCl, the AMA is totally monoprotonated (pK_a = 3.22 in 50% ethanol–50% water[8]) but not diprotonated. Our attention focused on the >460-nm region where AMA in absolute ethanol displays tailing from a large absorbance rising up sharply below 420 nm. As the solvent is made increasingly aqueous, a broad peak emerges in the 440–480-nm range. Appearance of this peak is presumed to reflect conversion of AMA protonated at the 4-amino group (A) into AMA protonated at the ring nitrogen (R). An unexpected behavior is readily apparent from Figure 1. Protonation at the 4-amino group persists even with large amounts of water in the ethanol. For example, when the mole fraction of water (X_{H_2O}) is 0.52, the absorbance at 460 nm exceeds that in absolute ethanol by only 0.03 unit. Effective solvent sorting of water from ethanol to form the generally more stable ring NH^+ is seen, therefore, *not* to occur. On the other hand, relatively little ethanol is required to transform R in pure water into A. For example, substantial amounts of A clearly exist along with R at X_{H_2O} = 0.91. Thus, ethanol induces a protonic shift to the 4-amino group even when the solvent is overwhelmingly aqueous.

The spectra in Figure 1 are influenced not only by the relative levels of A and R but also by shifts to lower wavelengths as the solvent becomes more aqueous. Owing to this complication, it is not possible to calculate A/R ratios from "vertical" absorbance readings at a particular wavelength (such readings give ratios which are wavelength dependent). A crude attempt to quantitate the situation was carried out by measuring absorbances along straight lines with negative slopes of 0.12 absorbance unit per 10 nm. By correcting for spectral shifts in this manner, we secured A/R ratios which are independent of the wave-

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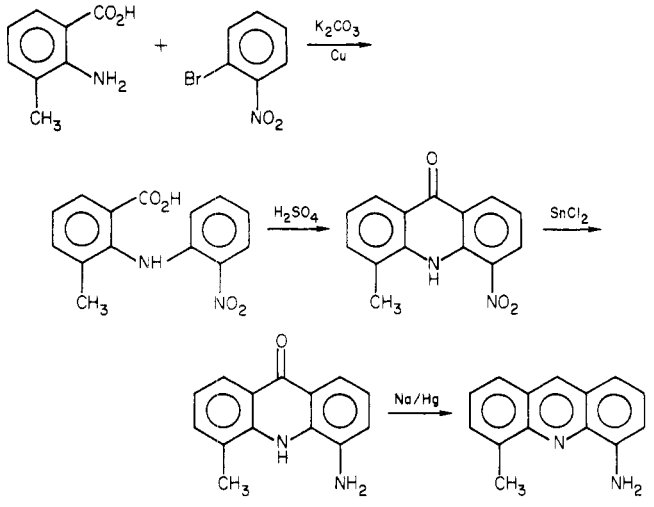
Scheme I



length from 470 to 520 nm. A plot of % R vs. X_{H_2O} is given in Figure 2. Despite the uncertainty in the % R values, Figure 2 depicts clearly the ability of the probe to sort ethanol from water but not water from ethanol.[10]

Since AMA has a large hydrocarbon region, we can reasonably postulate that ethanol molecules preferentially solvate the probe in ethanol–water mixtures. Even the ammonium ion moiety should be specifically solvated by ethanol which, according to Franks and Ives,[11] is more basic (a better electron-pair donor) than water. Consequently, adding 0.1–0.8 mol fraction of water to ethanol hardly affects the solvent shell surrounding the AMA, and the 4-amino group remains the favored protonation site. In 100% water, however, the acridine protonates on the ring nitrogen because steric effects related to the 5-methyl group play no role here. As small amounts of ethanol are added to water, the solvation shell of AMA rapidly becomes rich in ethanol, thereby inducing a proton shift from the ring nitrogen to the 4-amino group nitrogen.

Kinetic studies of many solvolyses in ethanol–water mixtures show distinct minima in ΔH^* at 0.8–0.9 mol fraction of water.[12,13] Partial molal heats of solution for a wide variety of compounds in ethanol–water mixtures give endothermic maxima also in the 0.8–0.9 region.[14] These extrema have been attributed to the fact that 0.1–0.2 mol fraction of ethanol in water actually *increases* solvent structuredness;[11] the trend reverses with additional ethanol. Figure 2 does not manifest these changes in solvent structure, probably because they affect both sides of the prototropic equilibrium equally. If this is true, then AMA offers a useful means for detecting specific solvation without the attendant complexities and uncertainties associated with "structure-making" and "structure-breaking" effects.

Experimental Section

4-Amino-5-methylacridine. This compound was prepared according to Scheme I following known procedures closely. In the first step, 3-methylanthranilic acid (Research Organic/Inorganic Chemical Corp.) and 1-bromo-2-nitrobenzene (Aldrich), active copper powder,[15] potassium carbonate, and cyclohexanol were heated to 175 °C as described by Albert and Goldacre.[8] Cyclization mediated by concentrated sulfuric acid produced 4-nitro-5-methylacridone.[8] Since a direct reduction of the acridone to the final product[8] failed in our hands, we carried out the transformation in two steps. The nitro group was initially reduced to the amino group with stannous chloride dihydrate in concentrated hydrochloric acid.[16] The crude product in 90% ethanol/10% water was then treated with sodium amalgam (City Chemical Corp.) and sodium bicarbonate to give 4-amino-5-methylacridine.[8] After repeated crystallizations from heptane, the compound melted at 110–111 °C (lit.[8] mp 111 °C) and gave a satisfactory elemental analysis. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 80.56; H, 5.98; N, 13.46.

Procedure. An appropriate volume of 4-amino-5-methylacridine in absolute ethanol (0.001 to 0.10 M) was added with the aid of a micropipet to a volumetric flask partially filled with a particular ethanol–water mixture. The desired acidity was attained by adding a small quantity of 1.0 or 2.0 N aqueous HCl, and the flask was then filled to the mark with the same ethanol–water mixture. Since the acridine appeared sensitive to light, solutions were protected by aluminum foil and used immediately after preparation. Most spectra were traced using 1.10×10^{-3} M 4-amino-5-methylacridine solutions thermostated at 25.0 °C in a Cary 14 spectrophotometer.

Acknowledgment. This work was supported by grants from the National Science Foundation and the National Institutes of Health.

Registry No. 4-Amino-5-methylacridine, 3408-00-2; 3-methylanthranilic acid, 4389-45-1; 1-bromo-2-nitrobenzene, 577-19-5.

(10) The latter behavior would have been indicated in Figure 2 by a convex curve rising steeply at low X_{H_2O} values.
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Ring Expansion of 3-Methoxy-6-vinyl-7,8,9,10-tetrahydro-6(5*H*)-benzocyclooctenol

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Relatively few effective routes[1] to benzo-substituted medium-sized rings are available and fewer still have been applied to systems with substituents on the benzo group. In an earlier paper,[2] we described a reaction sequence which resulted in ring expansion of benzosuberone (**1a**) to a ten-membered ring system **4a**. We were particularly interested in oxygen functionality at the 3-position of benzosuberone because it relates to our synthetic work and because it could provide some mechanistic information.

By use of earlier procedures,[3] benzosuberone (**1a**) was nitrated[4] and converted to the 3-hydroxy derivative **1c** which was methylated with dimethyl sulfate to give **1b**. Trimethylsilyl cyanide (Me_3SiCN) was added to **1b** by using the 18-crown-6 complex of potassium cyanide as a catalyst.[5] This step sometimes gave low conversion to product but normally gave good yields if freshly distilled Me_3SiCN and freshly prepared catalyst were used. The reduction to the amino alcohol followed by treatment with nitrous acid proceeded smoothly to **2b**. The addition of

(1) For some alternative routes, see ref 8 of ref 2.
(2) Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050.
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(4) Ring expansion of the nitro compound was not successful.
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