give the corresponding sulfonyl chlorides which were subsequently hydrolyzed with water to sulfonic acids. Of the two possible routes, the one utilizing the benzyl mercaptan proved to be the most efficient with much higher yields.

The results described above are summarized in Scheme I.

Experimental Section

All melting points are uncorrected. The NMR spectra were recorded on a Varian Associates A-60 spectrometer.

CF_3CH_2OMs was prepared by the method described by Crossland and Servis:[11] 90% yield; bp 97–99 °C (35 mmHg); NMR (CD_3COCD_3) δ 3.24 (s, 3 H), 4.75 (q, 2 H, $J_{H,F}$ = 8.4 Hz).

CF_3CH_2OTs was prepared by the method described by Edgell and Parts:[12] 89% yield; bp 102–104 °C (0.8 mmHg); mp 40–41 °C; NMR (CD_3COCD_3) δ 6.6 (q, 4 H), 3.5 (q, 2 H), 1.5 (s, 3 H).

CF_3CH_2Br was prepared by the method described by Henne and Ruh:[14] 79% yield; bp 25.5–26 °C.

Reaction of CF_3CH_2Br with Na_2SO_3 in a Parr Pressure Reactor. A solution of 40 g (0.32 mol) of Na_2SO_3 dissolved in 200 mL of water and 48.6 g (0.3 mol) of CF_3CH_2Br was placed in a 1-L Parr pressure reactor and slowly heated with stirring. Usually at about 90 °C an exothermic process subsided, and the reactor was heated at 100 °C for 12–16 h. The reaction mixture was cooled, the unreacted bromide (if present) separated, the aqueous solution evaporated to dryness, and the solid residue extracted with hot EtOH. Evaporation of ethanol gave the crude sodium salt of $CF_3CH_2SO_3H$. The approximate yield is based on the amounts of crude sulfonate salt isolated. The IR spectra showed distinct absorptions at 1160 and 1060 cm^{-1} characteristic of sulfonic acid salts.

Preparation of 2,2,2-Trifluoroethyl Thiocyanate. A. From CF_3CH_2OMs. A solution of 145.8 g (1.8 mol) of NaSCN in 350 mL of DMF was brought to reflux and distilled through a 7-in. column packed with helices until the head temperature reached 152 °C. CF_3CH_2OMs (79.5 g, 0.45 mol) was added to the cooled solution. The reaction mixture was very slowly distilled, and the reaction boiling at 90–123 °C was collected over a period of 2.5–3 h. The distillate was taken up in 300 mL of CH_2Cl_2, washed several times with 100-mL aliquots of water and twice with brine, and dried over anhydrous $MgSO_4$. The solvent was evaporated and the residue vacuum distilled. The fraction boiling at 55–70 °C (30 mmHg) was collected. NMR (CD_3COCD_3) showed about 80% content of the thiocyanate [δ 3.45 (q, 2 H, $J_{H,F}$ = 10 Hz)]. The yield of the product corrected for impurities was 31.1 g (48%).

B. From CF_3CH_2OTs. In a similar experiment, 76.2 g (0.3 mol) of CF_3CH_2OTs, 97.2 g (1.2 mol) of NaSCN, and 200 mL of CH_2Cl_2 yielded 19.1 g (45%) of the thiocyanate, bp 57–72 °C (35 mmHg).

Oxidation of CF_3CH_2SCN with Nitric Acid. Concentrated nitric acid (182 mL, 2.77 mol) was placed in a three-necked flask supplied with mechanical stirrer, dropping funnel, thermometer, reflux condenser, and a nitrogen inlet tube. CF_3CH_2SCN was added (30 g, 0.21 mol) very slowly (over 4 h) at 80–90 °C. Nitrogen was continuously bubbled through the reaction mixture to remove the nitrogen oxides formed. The reaction mixture was then heated at 90–95 °C (steam bath) until the evolution of NO_2 ceased (about 12 h). It was then transferred to an evaporating dish and heated on a steam bath. The thick, oily residue was transferred into a distillation flask and vacuum distilled, yielding 17.2 g (50%) of $CF_3CH_2SO_3H$. The product is a colorless, hygroscopic solid: bp 108–110 °C (1.5 mmHg); mp 50–51 °C; neutralization equivalent 162 (calcd 164); NMR (D_2O) δ 3.85 (q, 2 H, $J_{H,F}$ = 10 Hz).

Reaction of CF_3CH_2OTs with Benzyl and *tert*-Butyl Mercaptan. In a three-necked flask fitted with mechanical stirrer, thermometer, reflux condenser, and dropping funnel were placed 16 g (0.20 mol) of 50% NaOH and 60 mL of DMF. The mixture was flushed well with N_2 and 24.8 g (0.20 mol) of benzyl mercaptan was added. When homogeneous, the warm solution was treated with 43.2 g (0.17 mol) of CF_3CH_2OTs at such a rate as to maintain the reaction temperature at 55–65 °C. The solution turned cloudy, and the stirring was continued until the temperature dropped to about 30 °C. The reaction mixture was quenched in 250 mL of water, the product was extracted with CH_2Cl_2, and the organic layer was washed with dilute NaOH and water and dried over anhydrous $MgSO_4$. The solvent was evaporated, and residue vacuum distilled to give 28.3 g (81%) of $CF_3CH_2SCH_2C_6H_5$: bp 45–46 °C (20 mmHg); NMR (CCl_4) δ 2.68 (q, 2 H, methylene, $J_{H,F}$ = 10 Hz), 3.61 (s, 2 H, benzyl), 7.14 (s, 5 H, aromatic).

In a similar fashion, 0.34 mol of 50% NaOH, 125 mL of DMF, 30.7 g of *tert*-butyl mercaptan, and 0.17 mol of CF_3CH_2OTs gave 16.2 g (55%) of *tert*-butyl 2,2,2-trifluoroethyl sulfide: bp 70–72 °C (100 mmHg); NMR (neat) δ 1.30 (s, 9 H, *tert*-butyl), 3.10 (q, 2 H, methylene, $J_{H,F}$ = 11 Hz).

Oxidation of Sulfides with Chlorine in Water. In a three-necked flask equipped with mechanical stirrer, thermometer, reflux condenser, and chlorine inlet tube were placed 0.12 mol of the preceding sulfide and 50 mL of water. The mixture was cooled in a dry ice–acetone bath. At 0 °C, with ice beginning to form on the walls, gaseous chlorine was added above the mixture, controlling the temperature from −5 to 0 °C generally, with −10 °C reached toward the end. Chlorine was introduced until saturation was obtained. The lower layer was mixed with 10 mL of CH_2Cl_2, drained, and chilled while being dried over anhydrous $MgSO_4$. Solvent was removed, and the residue distilled under reduced pressure to give $CF_3CH_2SO_2Cl$. (a) From benzyl 2,2,2-trifluoroethyl sulfide: yield 57%, bp 65–67 °C (45 mmHg); the product was contaminated with a small amount of benzyl chloride. (b) From *tert*-butyl 2,2,2-trifluoroethyl sulfide: yield 61%; bp 57–60 °C (40 mmHg);[11] the product was contaminated by unidentified admixtures which could not be removed by fractional distallation; NMR (neat) δ 4.37 (q, 2 H, $J_{H,F}$ = 9 Hz).

Hydrolysis of $CF_3CH_2SO_2Cl$ to Sulfonic Acid. $CF_3CH_2SO_2Cl$ (0.05 mol), or the appropriate amount of the sulfonyl chloride mixture with $C_6H_5CH_2Cl$, and 20 mL of water were refluxed with stirring for 10 h. After cooling, the solution was extracted twice with 10-mL aliquots of ether, the aqueous layer was evaporated, and then residue was vacuum distilled to give $CF_3CH_2SO_3H$: yield 83%; bp 90–93 °C (0.1 mmHg); neutralization equivalent 167 (calcd 164); NMR (D_2O) δ 3.87 (q, 2 H, $J_{H,F}$ = 10 Hz). Anal. Calcd for $C_8H_{10}O_3NF_3S$ (aniline derivative): C, 37.35; H, 3.89; F, 22.18; S, 12.45. Found: C, 37.13; H, 3.74; F, 22.05; S, 12.16.

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Registry No. 2,2,2-Trifluoroethyl thiocyanate, 33802-55-0; benzyl mercaptan sodium salt, 3492-64-6; *tert*-butyl mercaptan sodium salt, 29364-29-2; *tert*-butyl 2,2,2-trifluoroethyl sulfide, 77745-01-8; Na_2SO_3, 7757-83-7; CF_3CH_2Br, 421-06-7; $CF_3CH_2SO_3H\cdot Na$, 77745-02-9; NaSCN, 540-72-7; CF_3CH_2OMs, 25236-64-0; CF_3CH_2OTs, 433-06-7; $CF_3CH_2SO_3H$, 1827-97-0; $CF_3CH_2SCH_2C_6H_5$, 77745-03-0; $CF_3CH_2SO_2Cl$, 1648-99-3; $CF_3CH_2SO_3H$ aniline derivative, 77745-04-1.

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[14] Henne, A. L.; Ruh, R. P. *J. Am. Chem. Soc.* **1948**, *70*, 1025.

Hydrogen Bonding in Carbanions and Nitranions

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Evidence for hydrogen bonding in carbanions is provided by the strong influence that hydroxylic solvent components have on UV[1] and NMR[2] properties of carbanions and on

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[1] (a) Ford, W. T. *J. Am. Chem. Soc.* **1970**, *92*, 2857–2861. (b) Hogen-Esch, T. E. *Ibid.* **1973**, *95*, 639–641. (c) Hogen-Esch, T. E. *Adv. Phys. Org. Chem.* **1976**, *13*, 153–266. (d) Guthrie, R. D.; Cho, N. S. *J. Am. Chem. Soc.* **1975**, *97*, 2280–2281. (e) Guthrie, R. D.; Govindan, M. *Ibid.* **1979**, *101*, 5769–5773. (f) Guthrie, R. D.; Cho, N. S. *Ibid.* **1979**, *101*, 4698–4705.

0022-3263/81/1946-3336$01.25/0

Table I. Effect of Cation and of Hydroxylic Solvents on UV Spectra of Anions

entry	conjugate anion[a]	solvent mixture	X_{ROH}	cation[b]	λ_{max},[c] nm (±1 nm)	$\Delta\lambda$
1	1	Me_2SO	0	Na^+	405	
2	1	Me_2SO	0	Me_4N^+	405	
3	1	Me_2SO-H_2O	0.40	Me_4N^+	399	6
4	1	Me_2SO-H_2O	0.52	Me_4N^+	398	7
5	1	Me_2SO-H_2O	0.71	Me_4N^+	389	16
6	1	Me_2SO-H_2O	0.71	Na^{+d}	387	18
7	1	Me_2SO-MeOH	0.40	Na^{+e}	397	8
8	1	Me_2SO-*t*-BuOH	0.40	Me_4N^+	400	5
9	2	Me_2SO	0	Me_4N^+	390	
10	2	Me_2SO-H_2O	0.48	Me_4N^{+d}	372	18
11	3	Me_2SO	0	Me_4N^+	375	0
12	3	Me_2SO-H_2O	0.29	Me_4N^{+d}	362	13
13	4	Me_2SO	0	Na^+	507	
14	4	Me_2SO	0	Me_4N^+	505	
15	4	Me_2SO-H_2O	0.71	Na^{+d}	499	8
16	4	Me_2SO-H_2O	0.71	Me_4N^{+d}	500	5
17	5	Me_2SO	0	Na^+	342	
18	5	Me_2SO	0	Me_4N^+	341	
19	6	Me_2SO	0	Me_4N^+	385	
20	6	Me_2SO-H_2O	0.52	Me_4N^{+d}	381	4

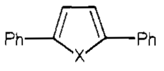
[a] The average substrate concentration was (2-5) × 10^{-5} M. [b] λ_{max} was unaffected by base concentration.[5] [c] Unless otherwise stated base concentration was 0.011 M. [d] Base concentration 0.22 M. [e] Base concentration 0.17 M.

ionization constants of carbon acids.[3] In a fundamental paper Hogen-Esch[1b,c] studied extensively the fluoradene anion in a variety of conditions. He observed that alcohols, either in bulk or as cosolvents in media of low polarity (such as THP), induce sizable blue shifts in the electronic spectrum of the carbanion, relative to the spectrum of the solvent-separated carbanion in THF. The same alcohols, however, have no appreciable effect either in good cation-coordinating solvents (THF) or in the presence of crown ethers. The absence of blue shifts in such cases was interpreted as a consequence of the disruption of the alcohol–cation association, promoted by the cation coordinating agents (THF or crown ether).

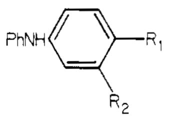
The investigation of H bonding in carbanions is inherently complex for two reasons: (i) most unfunctionalized[4] carbon acids have pK_a's too high to allow their conjugate anions to survive in media of high proton content; (ii) difficulties arise in separating the contributions to the hypsochromic shifts which are solely due to H-bonding processes and those which arise because of ion pairing of the carbanion. The second argument is particularly relevant in the light of Guthrie's results which show that fluoradene anion salts in methanol present cation-dependent electronic spectra.[1d-f]

We felt that a contribution in this field could be made by using a carbon acid of sufficiently low pK_a, provided it is possible to ascertain the nature (intimate or solvent separated) of the anionic species undergoing H bonding. This paper reports our results in circumventing these difficulties.

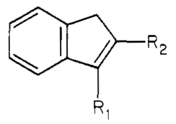
First, we selected 1,4-diphenylcyclopenta-1,3-diene (**1**) as a representative unfunctionalized carbon acid endowed with high acidity [pK_a = 15.38 (in Me_2SO-H_2O with an H_2O mole fraction X_{H_2O} = 0.60–0.77) relative to *p*-nitrodiphenylamine (pK_a = 15.67)].[5] Second, to prevent anion–cation pairing, we took advantage of the exceptionally high coordinating power of Me_2SO[6] toward Na^+ and monitored the effect of proton donors (H_2O, MeOH, *t*-BuOH) on the visible spectrum of the conjugate anion of **1** in Me_2SO-H_2O and Me_2SO–ROH mixtures. Third, to take account of Guthrie's results,[1d] we checked in different solvent mixtures the dependence of the spectra of the conjugate anion of **1** on the nature of the cation (Na^+ vs. Me_4N^+). Finally, to better evaluate the results obtained with the conjugate anion of **1**, we extended the above series of experiments to a number of anions derived from the carbon and nitrogen acids **2**–**6**.



1, X = CH_2
2, X = NH



3, R_1 = H; R_2 = Cl
4, R_1 = NO_2; R_2 = H



5, R_1 = H; R_2 = Ph
6, R_1 = Ph; R_2 = H

Cation and hydroxylic solvent effects on UV spectra of anions derived from compounds **1**–**6** are reported in the Table I. Examination of the data leads to the following conclusions. (i) Water in Me_2SO induces variable blue shifts, the size of which are strongly dependent on the nature of the anion: the shift observed for the conjugate anion of **1** is the largest within the series of carbanions considered. (ii) Both MeOH and *t*-BuOH in Me_2SO, under conditions where the mole fraction of ROH is comparable with that of water in Me_2SO (entries 3, 7, and 8), also act as proton donors and induce blue shifts on the conjugate anion of **1**. (iii) As expected, the UV properties of carbanions and nitranions, both in Me_2SO (compare entries 1 and 2, 13 and 14, and 17 and 18) and in Me_2SO-H_2O (compare entries 5 and 6 and entries 15 and 16), are insensitive to cation effects (Na^+ vs. Me_4N^+).

Although hypsochromic shifts of the anions are observed only in the presence of the protic cosolvent, it is not straightforward to ascribe their origin to hydrogen bonding

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[2] Kerber, R. C.; Porter, A. *J. Am. Chem. Soc.* **1969**, *91*, 366–371.

[3] (a) Ritchie, C. D.; Uschold, R. E. *J. Am. Chem. Soc.* **1967**, *89*, 1721–1725, 2752–2753; **1968**, *90*, 2821–2824. (b) Steiner, E. C.; Starkey, J. D. *Ibid.* **1967**, *89*, 2751–2752. (c) Kohlthoff, I. M.; Chantooni, M. K.; Bhowmik, S. *Ibid.* **1968**, *90*, 23–28. (d) Clare, B. W.; Cook, D.; Ko, E. C. F.; Mac, Y. C.; Parker, A. J. *Ibid.* **1966**, *88*, 1911–1916. (e) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *Ibid.* **1975**, *97*, 7006–7014.

[4] No functionalities containing heteroatoms and stabilizing the carbanion should be present in the carbon acid: in the conjugate anions, in fact (e.g., enolates, nitronates, etc.), H bonding at the heteroatom site can overlap and hide other processes occurring at the carbanion carbon.

[5] Greifenstein, L. G.; Pagani, G. A.; Nienhuis, R.; Lambert, J. J., submitted for publication.

[6] Hogen-Esch, T. E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307–324.

processes only. In fact, the variation of the medium on going from pure Me_2SO to Me_2SO–ROH mixtures necessarily produces the simultaneous variation of a number of parameters and properties. Thus, (i) the extent of association of cation with the anion may be varied, (ii) the polarity of the solvent is different, and (iii) the hydrogen bonding ability of the medium is greatly enhanced. Although in principle a variation of each one of the above factors might be responsible on its own for the observed hypsochromic shifts, we will show that only hydrogen bonding processes can reasonably account for the observed blue shifts.

(i) Despite the fact that Me_2SO solvates Na^+ ion better than water and Me_4N^+ less strongly than water[7] in the Me_2SO–H_2O mixture, the blue shifts are cation independent. Thus, carbanions are unpaired entities,[8] both in Me_2SO and Me_2SO–H_2O, and, consequently, blue shifts cannot be ascribed to different ion pairing in the pure and mixed solvent, respectively. This conclusion should be extended also to nitranions: although these species are known to form contact ion pairs more strongly than the corresponding carbanions,[9] in Me_2SO and HMPA they are certainly present as solvent-separated ions pairs.[9,10]

(ii) Changing solvent polarity would have some effect on the relative energies of ground and electronically exited states. The fact, however, that the spectra of the unpaired fluoradene anion in solvents of high dielectric constants [Me_2SO ($\epsilon = 46$) and HMPA ($\epsilon = 30$)] are identical with those in solvents of low dielectric constants such as THF ($\epsilon = 7.4$) and DME ($\epsilon = 7.15$)[1b] is a clear indication that solvent polarity plays a minor role on exitation energies of delocalized unpaired carbanions. Thus the hypsochromic shifts observed on going from pure Me_2SO to Me_2SO–ROH mixtures cannot be ascribed to variations of the solvent polarity. In fact, the blue shifts are observed both when the dielectric constant of pure Me_2SO ($\epsilon = 46$) is increased by addition of water ($\epsilon = 78.4$; Me_2SO–H_2O; $\epsilon > 46$[11]) and when it is decreased by addition of alcohols (MeOH, $\epsilon = 32.6$; *t*-BuOH, $\epsilon = 11$).

The foregoing analysis indicates that hypsochromic shifts of the carbanions and nitranions in Me_2SO–ROH mixtures are solely due to interaction of these species with the proton donor. To elucidate both the nature of the species responsible for the observed blue shifts and the factor(s) which dominate the variable (from substrate to substrate) hypsochromic shifts, we have further studied the effect of increasing the water content of Me_2SO on the λ_{max} both of the anion of **1** and of 3-chlorodiphenylamine (**3**). Owing to the high pK_a of **3** ($pK_a = 20.73$[12] in Me_2SO–H_2O with $X_{H_2O} = 0.12$–0.22), the maximum water content in which the nitranion can still be observed falls to $X_{H_2O} = 0.30$. The trends for the carbanion and the nitranion are compared in Figure 1. It is noted that for the carbanion the blue shift is linearly related to the water mole fraction with an abrupt increase in slope at about $X_{H_2O} = 0.5$. The blue shift of the nitranion of **3** is also linearly related to X_{H_2O} with a slope comparable with that presented by the carbanion at $X_{H_2O} > 0.5$. Since the change in slope occurs at the point of the solvent composition corresponding to $Me_2SO \cdot H_2O$, it is plausible that in the range of X_{H_2O} between 0 and 0.5 water is better coordinated by Me_2SO than by the carbanion.

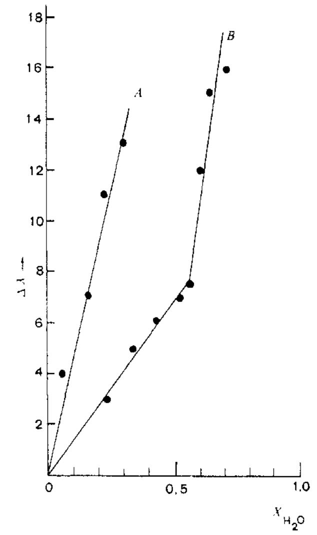

Figure 1. Variation of $\Delta\lambda_{max}$ ($\lambda_{Me_2SO} - \lambda_{Me_2SO-H_2O}$) vs. X_{H_2O} (water mole fraction in the solvent mixture): line A, *N*-phenyl-*N*-(3-chlorophenyl) nitranion; line B, 1,3-diphenylcyclopentadienide anion.

The behavior of the carbanion of **1** is analogous to that observed for *p*-nitrothiophenoxide in dimethylacetamide–water mixtures:[13] comparatively large amounts of water are needed to produce appreciable shifts which become large only when the mole fraction of water exceeds 0.5. Several equilibria, besides the hydrolytic ones, can be envisaged to take place in solution according to eq 1–5.

$$Me_2SO + H_2O \rightleftarrows Me_2SO \cdot H_2O \qquad (1)$$

$$Me_2SO \cdot H_2O + H_2O \rightleftarrows Me_2SO \cdot 2H_2O \qquad (2)$$

$$A^- + H_2O \rightleftarrows A^- \cdot H_2O \qquad (3)$$

$$A^- + Me_2SO \rightleftarrows A^- \cdot Me_2SO \qquad (4)$$

$$A^- + Me_2SO \cdot nH_2O \rightleftarrows [A \cdot Me_2SO \cdot (H_2O)_n]^- \qquad (5)$$

If eq 4 does not play any role, then the sudden increase above $X = 0.5$ is explained by assuming that eq 3 competes much more favorably with eq 2 than with eq 1. If instead eq 4 plays an important role or, in other words, if the carbanion is more efficiently solvated by Me_2SO than by the proton donor, then hydrogen bonding of the carbanion will be effective only when the interaction of A^- with Me_2SO is disrupted, that is, when Me_2SO is captured by water as in eq 1. At this point A^- can interact either with water directly or with $Me_2SO \cdot nH_2O$ (where $n = 1$ or 2) according to eq 5: in this latter case, Me_2SO would participate in the H-bonding process. A consideration of the relevant data as well as Ritchie's observations[14] suggests that the ineffectiveness of the carbanion in competing with Me_2SO for hydrogen bonding to water molecules in mixtures of low water content is attributable to the fact that large delocalized anions[14] (and polarizable anions[7]) can be

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(7) Arnett, E. M.; McKelvey, D. R. *J. Am. Chem. Soc.* **1966**, *88*, 2598–2599.

(8) Experiments of T_1 relaxation times for a number of ^{13}C carbon atoms in (1,3-diphenylcyclopentadienyl)potassium (0.3 M in Me_2SO)[5] supported for the anionic species an average molecular weight of about 440, which roughly corresponds either to an average of 1.7 ion pair units or to an average of 2.3 solvating molecules of Me_2SO per unit of anion. Since concentration is the most important factor in aggregation, once other conditions are kept constant (substrate, solvent, temperature, etc.) it can be safely anticipated that, if the first hypothesis were true, ion pairing should vanish upon reducing the anion concentration in the UV cuvette by a factor of 10^4 relative to the NMR experiment.

(9) Vos, H. W.; Blom, H. H.; Velthorst, N. H.; Macbean, C. *J. Chem. Soc., Perkin Trans. 2* **1972**, 635–639.

(10) Bradamante, S.; Marchesini, A.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 568–571.

(11) Wolford, R. K. *J. Phys. Chem.* **1964**, *68*, 3392–3398.

(12) Dolman, D.; Stewart, R. *Can. J. Chem.* **1967**, *45*, 911–924.

(13) Parker, A. D.; Brody, D. *J. Chem. Soc.* **1963**, 4061–4068.

(14) Coetzee, J. F.; Ritchie, C. D. "Solute-Solvent Interactions"; Marcel Dekker: New York, 1961; pp 225, 231–243.

more efficiently solvated by dipolar aprotic than by protic solvents. The line for the carbanion in Figure 1 corresponds to a titration of the $Me_2SO\cdot$ carbanion species with water. In mixtures of low water content the carbanion would be solvated by protic aggregates of composition intermediate between Me_2SO and $Me_2SO\cdot H_2O$, while in mixtures of high water content it would be solvated by a solvent cage of composition intermediate between $Me_2SO\cdot H_2O$ and $Me_2SO\cdot 2H_2O$: within each range, therefore, the variation of λ is continuous.

For the nitranion of **3** the situation is different: as a poorly delocalized species,[3e] this anion should be quite amenable to hydrogen bonding and compete favorably with Me_2SO as an acceptor.

The effect of charge delocalization on the size of the hypsochromic shifts is further illustrated by the following examples. It can be seen (compare entries 4 and 10) that the nitranion derived from 2,5-diphenylpyrrole (**2**; an aza analogue of **1**) is comparatively *more* sensitive to water than the carbanion of **1** while the 3-phenylindenyl anion, an extensively delocalized anion in which substantial negative charge is present not only in the five-membered ring but also in the annelated benzene ring, is *less* sensitive than the anion of **1** (compare entries 4 and 20). On the same grounds one may interpret the considerable difference in sensitivity of the two nitranions derived from *p*-nitrodiphenylamine (**4**) and 3-chlorodiphenylamine (**3**) (compare entries 12 and 16).

The above analysis of factors influencing anion sensitivity contributes to an understanding of the different results obtained for the three different substrates fluoradene, 9-phenylfluorene, and 1,4-diphenylcyclopentadiene. Hogen-Esch[1b] found that for solvent-separated fluoradene ion pairs in THF–alcohol mixtures, the spectra are neither broadened nor shifted relative to those in THF. Analogously, Ford[1a] found that methanol fails to change the visible spectra of 9-phenylfluorenyl anion in THF. We observe instead that for the 1,3-diphenylcyclopentadienyl anion in Me_2SO–ROH mixtures, the spectra are blue shifted relative to those in Me_2SO. In the case of Ford's experiments it must be conceded that failure to observe any change in the electronic spectra can be ascribed to the extremely low concentration of the proton donor, so that, as Ford noted,[1a] most or all of the methanol associates with methoxide or THF rather than the cation or anion. We believe this is only a concomitant factor in preventing the observation of blue shifts: furthermore, this explanation does not hold for the Hogen-Esch experiments. It is quite evident from our results that benzoannelation onto a cyclopentadienyl ring to form the indenyl ring drastically decreases the effect of the proton donor (from 7 to 4 nm on going from **1** to **6**). If this trend continues on going from an indenyl structure to a fluorenyl one and further to a fluoradenyl arrangement, a rapid falloff to zero of the hypsochromic shift must be anticipated. This is indeed what Ford and Hogen-Esch found. We believe that data reported here are strong evidence that the absence of blue shifts (and thus of very weak H bonding, if any) in the fluoradene unpaired anion in THF is due to the extreme delocalization of the carbanion, much more than in 1,3-diphenylcyclopentadienyl anion.[15]

It should be noted finally that the relatively high uncertainties of the measures of the blue shifts do not allow a firm quantitative relationship of the size of the shifts with parameters of solvent polarity and H-bonding acidity as measured by Taft's π and α scales.[18]

In conclusion, we have shown that delocalized and unfunctionalized carbanions can hydrogen bond not only as the reported "free ions" in pure alcohols but also as solvent-separated ion pairs in a medium of high dissociating power and cation coordinating ability such as dimethyl sulfoxide.

Experimental Section

Materials. 3-Chlorodiphenylamine and 4-nitrodiphenylamine were commercial products (Aldrich). 1,4-Diphenylcyclopenta-1,3-diene,[5,19] 2,5-diphenylpyrrole,[20] 3-phenylindene,[21] and 2-phenylindene,[22] were prepared according to known procedures.

Solvents. Me_2SO was distilled from CaH_2 under vacuum (after 2 h at 70 °C under N_2) and stored under N_2 in a flask equipped with serum caps. Water, methanol, and *tert*-butyl alcohol were distilled and stored under N_2 in flasks fitted with serum caps to allow transfer by syringe. All solutions were transferred by syringe under a slight N_2 pressure. Oxygen contamination was scrupulously avoided in every flask or container that was going to be filled with solvents or solutions destined for the UV cuvette and spectrophotometric determination. UV cuvettes also were fitted with serum caps. Usually a cycle of five vacuum evacuations (to at least 10^{-2} torr) and five fillings with ultrapure N_2 was performed before transfer into empty receivers. Weight rather than volumetric determinations were done. Thus molarities of solutes in samples obtained upon mixing weighed amounts of solutions were obtained by transforming weight determinations of Me_2SO and Me_2SO–H_2O mixtures into volumetric data from the interpolated density of the solvent in question and the known graphic relationship of density vs. X_{H_2O} in Me_2SO–H_2O mixtures.[11]

Procedures. Me_2SO solutions of known concentration (ca. 10^{-3}–10^{-4} M) in the acidic neutral substrate were prepared in a volumetric flask by weighing in known amounts of substrate and of anhydrous Me_2SO. The anions were prepared directly in the cuvette to be submitted to UV determination by mixing a weighed amount (ca. 1 mL) of Me_2SO solution of the compound and a weighed amount (ca. 1 mL) of a solution of the base of known titer. The nature and the composition of the added base solution determined the final composition (cation and solvent mixture) of the sample to be submitted to UV determination. Six cases of different cation/solvent composition were used: (a) sodium dimsyl in Me_2SO, (b) Me_4NOH in Me_2SO, (c) NaOH in Me_2SO–H_2O, (d) Me_4NOH in Me_2SO–H_2O, (e) NaOMe in Me_2SO–MeOH, (f) Me_4NOH in Me_2SO–*t*-BuOH.

The sodium dimsyl solution in Me_2SO was prepared by adding, under stirring, a weighed amount of Me_2SO to a weighed amount of dry sodamide, in turn obtained by evaporating at 25 °C under vacuum (0.1 mm) a suspension in toluene (50% w/w, Fluka AG). NH_3 was degassed from the solution for a few minutes under vacuum at 20 °C.

The tetramethylammonium hydroxide solution in Me_2SO was prepared by mixing in a volumetric flask a weighed amount of $Me_4NOH\cdot 5H_2O$ and a weighed amount of Me_2SO.

The tetramethylammonium hydroxide solution in Me_2SO–H_2O and sodium hydroxide solution in Me_2SO–H_2O were prepared by mixing in a volumetric flask a weighed amount of $Me_4NOH\cdot 5H_2O$ or of NaOH and a weighed amount of a stock Me_2SO–H_2O mixture, which in turn was prepared by mixing under N_2 appropriate weighed amounts of Me_2SO and water. The water mole

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[15] One referee suggests that the very high acidity of **1** indicates a very important delocalization of charge that may very well be more significant than that in 9-phenylfluorene. Theoretical calculations[16] indicate, however, that in indenyl anion almost 40% of the π electron density is withdrawn from the five-membered ring and dispersed in the anellated benzene ring. Evidence for extensive delocalization of charge including the benzene rings of indenyl and fluorenyl anions is further provided both by ^1H and ^{13}C NMR spectra.[17]

(16) Pugmire, R. J.; Robins, M. J.; Grant, D. M.; Robins, R. K. *J. Am. Chem. Soc.* **1971**, *93*, 1887–1893.

(17) (a) Grutzner, J. B.; Lanlor, J. M.; Jackman, L. M. *J. Am. Chem. Soc.* **1972**, *94*, 2306. (b) Edlund, U. *Org. Magn. Reson.* **1979**, *12*, 661–666.

(18) Taft, R. W.; Kamlet, M. J. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1723–1729.

(19) Drake, N. L.; Adams, J. R. *J. Chem. Soc.* **1939**, *61*, 1326–1329.

(20) Kapf, S.; Paal, C. *Chem. Ber.* **1888**, *21*, 3053–3063.

(21) Galton, S. A.; Kalafer, M.; Beringer, F. M. *J. Org. Chem.* **1970**, *35*, 1–6.

(22) Dubois, J. E.; Hegarty, A. F. *J. Chem. Soc. B* **1969**, 638–643.

fraction (X_{H_2O}) in the stock mixture was predetermined so that the final desired X_{H_2O} in the cuvette solution to be submitted to UV determination was obtained upon mixing ca. 1 mL of Me_2SO with ca. 1 mL of the stock Me_2SO-H_2O mixture.

The sodium methoxide solution in Me_2SO was prepared by mixing in a volumetric flask a known aliquot of a stock methanolic sodium methoxide solution with a weighed amount of anhydrous Me_2SO in such proportions to obtain, after mixing in the cuvette with the Me_2SO solution of the acidic compound, both the desired X_{MeOH} and the desired base concentration. The stock methanolic sodium methoxide solution was prepared at 0 °C from a small weighed amount of clean sodium metal and a weighed amount of CH_3OH.

The tetramethylammonium hydroxide solution in Me_2SO-t-BuOH was prepared by mixing in a volumetric flask a weighed amount of $Me_4NOH{\cdot}5H_2O$ with weighed amounts of Me_2SO and t-BuOH under conditions quite similar to those described in the preceding paragraph.

UV and visible spectra were recorded as described elsewhere[5] by use of Beckman DB-GT instrument: the cell compartment was thermostated at 25 ± 0.1 °C.

Registry No. 1, 4982-34-7; **2**, 838-40-4; **3**, 101-17-7; **4**, 836-30-6; **5**, 4505-48-0; **6**, 1961-97-3.

A New Amine Catalyzed Synthesis of 2-Substituted 2,3-Dihydro-4*H*-1,3-benzoxazin-4-ones

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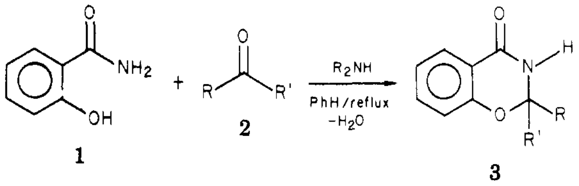
2-Alkyl-, 2,2-dialkyl-, 2-aryl-, and 2-alkyl-2-aryl-2,3-dihydro-4*H*-1,3-benzoxazin-4-ones (**3**, see Table I)[1] are conceptually important because of their similarity in structure to the medicinally interesting benzopyran-4-ones.[2] To date the only method for synthesis of the 2,3-dihydro-4*H*-1,3-benzoxazin-4-one nucleus relies on the acid-catalyzed condensation between suitably substituted salicylamides and aldehydes or ketones.[3]

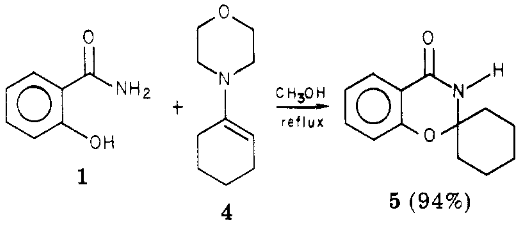
During the course of a recent synthesis we required the construction of the dihydrobenzoxazin-4-one system on a somewhat complex salicylamide. Not entirely to our surprise, we found that under various acidic reaction conditions the reaction either completely failed or proceeded in only moderate (not synthetically useful) yield. In light of this problem, we began to search for alternate methods (i.e., nonacidic) to synthesize 2,3-dihydro-4*H*-1,3-benzoxazin-4-ones. In order to compare an alternate method with existing literature examples (acid catalyzed) we chose salicylamide as our substrate. Our findings are summarized below and in Table I.

We have found that the condensation between salicylamide (**1**) and aldehydes or ketones (**2**, see Table I) can also be catalyzed by secondary amines[4] (pyrrolidine, morpholine, etc). The reactions are best carried out in refluxing benzene or toluene with 10 mol% amine catalyst. Water is removed from the reaction with the aid of a Dean–Stark trap. In many cases the product of the reaction (**3**, see Table I) crystallizes directly from the reaction mixture upon cooling. Filtration of the reaction mixture then gives pure product. Noteworthy is the fact that this new amine-catalyzed reaction generally results in higher yields of the 2,3-dihydro-4*H*-1,3-benzoxazin-4-ones than does the previous acid-catalyzed reaction. An exception to this seems to arise when alkyl aldehydes are used (see Table I, entry 17). For example, the use of acetaldehyde failed to give any of the desired product. The only ketones that failed to undergo reaction, or that gave low yields, were either sterically congested (entry 9), capable of forming stable products with the amine catalyst (entry 11), or involved volatile substrates[5] (entry 1).



(1)

It is also interesting that enamines, such as **4**, can also be used as substrates in this reaction and provide the product in a slightly higher yield than that obtained in the catalytic process. N-Substituted salicylamides (i.e., *N*-aryl) fail to undergo reaction with both aldehydes and ketones. The use of an optically active amine catalyst leads to only trace amounts of optical induction.



(2)

An excellent alternative to the previous acid-catalyzed synthesis of 2,3-dihydro-4*H*-1,3-benzoxazin-4-ones is now available. It very nicely complements the existing methodology since in many cases higher yields are obtained by utilizing an amine rather than an acid catalyst.

Experimental Section

All analytical data, except for NMR spectra, were obtained by the Physical and Analytical Chemistry Department of The Upjohn Company. NMR spectra were obtained at 60 MHz in chloroform-*d* solutions containing tetramethylsilane as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 197 spectrophotometer in $CHCl_3$ solution or as mulls. Thin-layer chromatography (TLC) was conducted by using Merck glass plates precoated with silica gel 60 F-254. The TLC plates were visualized by UV light or iodine. All solvents were reagent grade distilled in glass (Burdick and Jackson).

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(1) J. Finkelstein and E. Chiang, *J. Med. Chem.*, 11, 1038 (1968).

(2) G. P. Ellis, "Chromenes, Chromanones and Chromones", John Wiley and Sons, New York, 1967, pp 345–348, 613, 668, 715, 791, 823, 881, 912, 985, 1063.

(3) A. W. Titherley, *J. Chem. Soc.*, **91**, 1425 (1907); C. A. Keane and W. W. S. Nicholls, *ibid.*, 266 (1907); E. Glaser and S. Frisch, *Arch. Pharm.*, **266**, 103 (1928); H. P. Kaufmann, *ibid.*, **265**, 266 (1927); W. L. Hicks, *J. Chem. Soc.*, **97**, 1032 (1910); V. Moucka and C. Royl, *Chem. Ber.*, **59**, 756 (1926); A. W. Titherley and E. C. Hughes, *J. Chem. Soc.*, **97**, 1368 (1910); *ibid.*, **99**, 23 (1911); N. W. Hirwe and K. N. Rana, *Chem. Abstr.*, **34**, 2819 (1940); K. N. Rana, *J. Indian Chem. Soc.*, **19**, 299 (1942); H. O. Fischer, G. Dangschat, and H. Slettiner, *Chem. Ber.*, **65**, 1032 (1932); D. T. Mowry, W. H Yanko, and E. L. Ringwald, *J. Am. Chem. Soc.*, **69**, 2358 (1947); B. W. Horrom and H. E. Zaugg, *ibid.*, **72**, 721 (1950); J. L. Irvine and C. Piantadosi, *Synthesis*, 568 (1972); T. Kametani, T. Higa, C. V. Loc, M. Ihara, and K. Fukumoto, *Heterocycles*, **6**, 255 (1977); M. Covello, F. DeSimone, and E. Abignete, *Ann. Chim.* (*Rome*), **59**, 367 (1969).

(4) For a similar reaction that results in the synthesis of 2-substituted-4*H*-chromanones see H. J. Kabee, *Synthesis*, 886 (1978).

(5) The low yield resulting from the reaction with acetone appeared to be due to the low boiling point of acetone and perhaps the inability to separate the water from the acetone efficiently. A number of drying agents (K_2CO_3, alumina, $MgSO_4$, $CaCl_2$) were employed but yields were not dramatically improved. The use of 3-Å molecular sieves did afford the acetone adduct in 50% after heating at reflux in a 1:1 mixture of benzene/acetone for 4 days.