deuterioboration of *trans*-Δ^1-octalin.[3,20] Gas chromatography (diglycerol column at 150 °C) demonstrated that the four possible alcohols were formed in comparable yields; purification was therefore accomplished by preparative gas chromatography. The most rapidly eluted alcohol (16%, retention time 54 min) exhibited mp (54 °C), NMR and IR, and VPC retention time identical with those of authentic *trans,cis*-1-decalol. The second component (30%, retention time 76 min) was identified as *trans,cis*-2-decalol-*1α-d* (**2**-*1α-d*). It exhibited mp 52–53 °C (lit.[8] mp 53 °C), NMR and IR, and VPC retention time identical with those of the authentic unlabeled molecule (isolated from a commercial sample).[16] Since the alcohol did not exhibit a $M^{+\cdot}$ in its mass spectrum, the trimethylsilyl ether was prepared. It exhibited $M^{+\cdot}$ at *m/e* 227 ($C_{13}H_{25}DOSi$).

The third eluted alcohol (30%, retention time 60 min) exhibited physical and spectral characteristics[8,19] consistent with the expected *trans,trans*-1-decalol-*2β-d* structure. Finally, *trans,trans*-2-decalol-*1β-d* (24%, retention time 92 min) was obtained. It exhibited mp 75–76 °C (lit.[20] mp 75 °C), NMR and IR, and VPC retention time identical with those of the authentic unlabeled compound. The trimethylsilyl ether exhiited $M^{+\cdot}$ at *m/e* 227 ($C_{13}H_{25}DOSi$).

trans,cis*-2-Decalol-*1β-d (**2β,4aα,8aβ-decahydronaphthalenol-*1β-d***) was prepared from pure deuterated *trans,trans*-2-decalol by an oxidation–reduction sequence.[3,6] Jones oxidation of 0.075 g of the axial alcohol at 0 °C for 1 h followed by a rapid extractive workup and subvacuo removal of solvent gave 0.110 g of crude *trans*-2-decalone-*1β-d*. The crude ketone was immediately reduced with $LiAlH_4$ to produce a mixture of 2-decalols in which the equatorial alcohol was heavily predominant. Column chromatography gave 0.038 g of the pure *trans,cis*-2-decalol-*1β-d* whose melting point and spectra were identical with those of an authentic unlabeled sample. The mass spectrum of the corresponding trimethylsilyl ether exhibited $M^{+\cdot}$ at *m/e* 227 ($C_{13}H_{25}DOSi$).

trans,trans*-2-Decalol-*1α-d (**2α,4aα,8aβ-decahydronaphthalenol-*1α-d***). Treatment of the epoxide mixture (generated from the reaction of *trans*-Δ^1-octalin with *m*-chloroperbenzoic acid) with $LiAlD_4/AlCl_3$ generated a mixture of *trans,trans*-2-decalol-*1α-d* and *trans,cis*-1-decalol-*2β-d*.[3,6,20,22] Preparative gas chromatography (diglycerol column at 150 °C) generated a pure sample of the title alcohol whose physical and spectral characteristics were identical with those of authentic unlabeled compound. The corresponding trimethylsilyl ether exhibited $M^{+\cdot}$ at *m/e* 227 ($C_{13}H_{25}DOSi$).

trans,cis*-2-Decalol-*3α-d and ***-3β-d*** (**2β,4aα,8aβ-decahydronaphthalenol-*3α-d*** and ***-3β-d***) and ***trans,trans*-2-decalol-*3α-d*** and ***-3α-d*** (**2α,4aα,8aβ-decahydronaphthalenol-*3α-d*** and ***-3b-d***) were prepared by procedures strictly analogous to those used for formation of the 1-labeled alcohols, using *trans*-Δ^2-octalin (1,2,3,4,4aα,5,8,8aβ-octahydronaphthalene) as the starting material. However, the greater symmetry of the Δ^2-octalin greatly simplified the isolation of pure alcohol products. Deuterioboration of *trans*-Δ^2-octalin gave only *trans,cis*-1-decalol-*3α-d* and *trans,trans*-1-decalol-*3β-d*. These alcohols were readily separated by column chromatography. Similarly, the $LiAlD_4/AlCl_3$ opening of *trans*-decalin 2,3-epoxide gave essentially only *trans,trans*-2-decalol-*3α-d*.

Photolysis of *trans,trans*-2-Decalyl Phenylacetate and *trans,cis*-2-Decalyl Phenylacetate. Photolyses were conducted according to the general procedures of Yarchak, Dalton, and Saunders.[9] The phenylacetates were irradiated as thoroughly degassed 0.01 M solutions in hexane, using an eight-lamp Rayonet preparatory reactor equipped with Rayonet RPR 2537 Å lamps. The isomer distribution of the resulting alkenes was determined by gas chromatography on an Apiezon L column at 120 °C. The alkenes exhibited retention times and mass spectra identical with those of authentic samples of *trans*-Δ^1-octalin and *trans*-Δ^2-octalin. The relative proportions of the two alkenes were unchanged (within experimental error) as the amount of starting material consumed was varied from 5–50%.

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Registry No. **2**, 66964-89-4; **2**-d_4, 71912-19-1; **2**-*1α-d*, 71912-20-4; **2**-*1β-d*, 71912-21-5; **2**-*3α-d*, 71912-22-6; **2**-*3β-d*, 71962-38-4; **3**, 66964-88-3; **3**-d_4, 71912-23-7; **3**-*1α-d*, 71912-24-8; **3**-*1β-d*, 71912-25-9; **3**-*3α-d*, 71962-39-5; **3**-*3β-d*, 71962-40-8; **4**, 71912-26-0; **5**, 71912-27-1; *trans*-1-decalone, 21370-71-8; *trans,cis*-1-decalol, 2529-03-5; *trans*-Δ^1-octalin, 2001-49-2; *trans,cis*-2-decalol-*1α-d*, 71912-28-2; *trans,trans*-2-decalol-*1α-d*, 71912-29-3; *trans,trans*-1-decalol-*2β-d*, 71912-30-6; *trans,cis*-2-decalol-*1β-d*, 71912-31-7; *trans*-2-decalone-*1β-d*, 71912-32-8; *trans,cis*-2-decalol-*1β-d* trimethylsilyl ether, 71912-33-9; *trans,trans*-2-decalol-*1α-d*, 71912-34-0; *trans,trans*-2-decalol-*1α-d* trimethylsilyl ether, 71912-35-1; *trans,cis*-2-decalol-*3α-d*, 49644-48-6; *trans,cis*-2-decalol-*3β-d*, 71962-41-9; *trans,trans*-2-decalol-*3α-d*, 49644-47-5; *trans,trans*-2-decalol-*3β-d*, 49644-27-1; *trans*-Δ^2-octalin, 2001-50-5.

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Effects of Protonation and Hydrogen Bonding on Nitrogen-15 Chemical Shifts of Compounds Containing the >C=N̈- Group[1a]

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The effects of solvent changes from chloroform to trifluoroethanol to trifluoroacetic acid on the chemical shifts of nitrogen-15 resonances have been determined for fourteen imines, four oximes, and two pyridines. Upfield shifts were observed for all of the compounds in trifluoroethanol and trifluoroacetic acid, ranging from 8 to 28 ppm in the first and from 110 to 150 ppm in the second. These shift changes can be attributed to hydrogen bonding and protonation, respectively. The hydrogen-bonding shifts can be generally rationalized through consideration of the basicities of the nitrogens involved while the protonation shifts seem mostly influenced by the degree of substitution by phenyl groups, as expected from changes in the substantial contributions to the >C=N̈- type nitrogen shifts from the second-order paramagnetic effect.

Over the last 15 years, effects of protonation on ^{14}N and ^{15}N resonances have been investigated for various types of nitrogen compounds.[2-10] Whereas these effects are usually relatively small in the case of aliphatic amines,

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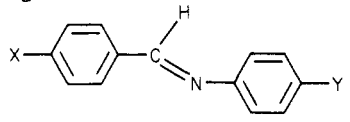
Table I. Effects of Hydrogen Bonding and Protonation on ^{15}N Chemical Shifts of *N*-Benzylideneanilines



X	Y	no.	solvent[a]	δ, upfield from ext DNO_3	Δδ[b]	$^1J_{N-H}$, Hz
CH_3O	H	1a	$CHCl_3$	56.4[c]	0.0	
			TFE	76.9	20.5	
			TFA	199.7	143.3	93.7
CH_3	H	1b	$CHCl_3$	51.9[c]	0.0	
			TFE	72.8	20.9	
			TFA	192.0	140.1	93.7
H	H	1c	$CHCl_3$	47.9[c]	0.0	
			TFE	67.8	19.9	
			TFA	187.4	139.5	94.6
O_2N	H	1d	$CHCl_3$	35.1[c]	0.0	
			TFE	48.8[d]	13.7	
			TFA	175.5	140.4	*e*
H	OCH_3	1e	$CHCl_3$	51.4[c]	0.0	
			TFE	71.0	19.6	
			TFA	192.0	140.6	90.2
H	NO_2	1f	$CHCl_3$	51.7[c]	0.0	
			TFE	*f*		
			TFA	193.6	141.9	*e*

[a] Solute concentrations were 20 mol % in $CHCl_3$, 10 mol % in TFE, and 9 mol % in TFA. [b] $\Delta\delta = \delta_{solvent} - \delta_{CHCl_3}$. [c] From ref 12. [d] Estimated value; compound not sufficiently soluble at 28 °C, observed shift was 44.8 ppm at 55 °C. [e] Only one signal, identical with that of the decoupled spectrum, was present in the undecoupled spectrum. [f] Solubility less than 1 mol %.

resulting in shifts of only a few ppm,[2,4,8] they are striking for unsaturated compounds such as pyridine, quinoline, diphenylketimine, azobenzene, and acetoxime, where upfield shifts, often greater than 100 ppm, are observed.[2-6] These large upfield shifts have been attributed variously to decreases in bond order and increases in electron density by Witanowski and co-workers[5] and to decreases in the magnetic anisotropy of the nonbonded electron pair of unsaturated nitrogens and changes in the second-order paramagnetic contributions to the nitrogen shifts by Gil and Murrell[10] and by Lambert and co-workers.[2] Methanol also produces sizable (about 10 to 20 ppm) upfield solvent shifts of the ^{15}N resonances of pyridine[3,6] and various imines,[7,11] in contrast to its very small effect on the nitrogen resonances of most aliphatic amines.[8] These upfield shifts have been attributed to hydrogen bonding, and it has been suggested that the same factors are responsible for both the hydrogen-bonding and protonation shifts.[6,11]

In the present research, the ^{15}N and ^{13}C chemical shifts have been determined for fourteen imines (of three types: ArC(R′)=NAr, ArC(R′)=NR, and RC(R′)=NAr), four oximes, and two pyridines, each in chloroform, 2,2,2-trifluoroethanol, and trifluoroacetic acid. The results for the nitrogen resonances are discussed here, while those for the carbon resonances are given in a subsequent paper.

Experimental Section

The ^{15}N spectra were obtained with a Bruker WH-180 spectrometer operating at 18.25 MHz in the FT mode and capable of accommodating 25-mm sample tubes. Except for when trifluoroacetic acid was the solvent, unfavorable NOE (nuclear Overhauser effects) and long relaxation times angle) the order of 50 s at 28 °C for imines[12]) combined to make taking the spectra a slow process. With pulse gating so that the decoupler was on during the acquisition time only [55-μs (70° flip angle), pulse widths and 50-s pulse delays], spectra with good signal to noise (S/N) ratios required 1–1.5 h and 4–5 h for 20 and 10 mol % solutions, respectively. The sample temperatures under these conditions were 28 °C. It was much easier to obtain spectra for trifluoroacetic acid solutions because there was a large favorable NOE and shorter relaxation times. With this solvent, a 55-μs pulse, 15-s delays, and continuous decoupling, spectra with excellent S/N ratios could be obtained in less than 30 min for 9 mol % solutions. For proton-coupled spectra, gating so that the decoupler was off only during acquisition was used to take advantage of the favorable NOE. Because, without cooling, complete proton-decoupling power heated the sample up to 50 °C, the samples were cooled to 28 ± 4 °C. The data length for all measurements was 16K points, giving a resolution of 0.9 Hz/point for a spectral width of 7000 Hz. A 5-mm coaxial DNO_3 (1 M) in D_2O capillary was used to provide both the reference and the field-frequency lock signal. The reported shifts are uncorrected for bulk-magnetic susceptibilities.

Pyridine, 2,6-dimethylpyridine, acetaldoxime, and cyclohexanone oxime were commercial materials. The other compounds were prepared from the corresponding carbonyl compounds and amines according to published procedures[13] and

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(7) R. O. Duthaler and J. D. Roberts, *J. Am. Chem. Soc.*, **100**, 3882–9 (1978).

(8) R. O. Duthaler and J. D. Roberts, *J. Am. Chem. Soc.*, **100**, 3889–95 (1978).

(9) R. O. Duthaler and J. D. Roberts, *J. Magn. Reson.*, **34**, 129–139 (1979).

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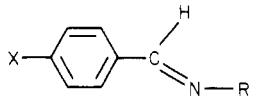
(12) R. E. Botto, unpublished research.

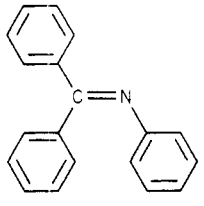
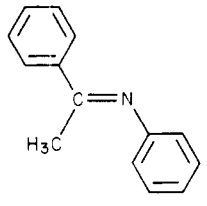
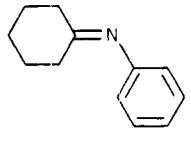
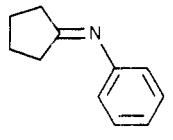
Table II. Effects of Hydrogen Bonding and Protonation on ^{15}N Chemical Shifts of *N*-Benzylidenealkylamines



X	R	no.	solvent[a]	δ, upfield from ext DNO_3	Δδ[b]	$^1J_{N-H}$, Hz
CH_3O	C_6H_{11}	2a	$CHCl_3$	38.5[c]	0.0	
			TFE	66.3	27.8	
			TFA	189.3	150.8	91.0
O_2N	C_6H_{11}	2b	$CHCl_3$	14.7[c]	0.0	
			TFE	38.5	23.8	
			TFA	164.1	149.4	92.0
H	$CH(CH_3)_2$	2c	$CHCl_3$	28.5[c]	0.0	
			TFE	55.6	27.1	
			TFA	176.8	148.3	92.4
H	$CH_2CH(CH_3)_2$	2d	$CHCl_3$	43.0[c]	0.0	
			TFE	71.0	28.0	
			TFA	192.1	149.1	89.1

[a] Solute concentrations were as follows: **2a** and **2b**, 20 mol %; **2c** and **2d**, 36 mol % in $CHCl_3$; all compounds 10 mol % in TFE and 9 mol % in TFA. [b] $\Delta\delta = \delta_{solvent} - \delta_{CHCl_3}$. [c] From ref 12.

Table III. Effects of Hydrogen Bonding and Protonation on ^{15}N Chemical Shifts of Ketimines

compd	no.	solvent[a]	δ, upfield from ext DNO_3	Δδ[b]	$^1J_{N-H}$, Hz
	3a	$CHCl_3$	46.1	0.0	
		TFE	[c]		
		TFA	192.0	145.9	92.0
	3b	$CHCl_3$	44.5	0.0	
		TFE	64.3	19.8	
		TFA	183.6	139.1	92.0
	3c	$CHCl_3$	58.9	0.0	
		TFE	81.3	22.4	
		TFA	177.9	119.0	92.0
	3d	$CHCl_3$	60.5	0.0	
		TFE	82.3	21.8	
		TFA	180.8	120.3	95.4

[a] Solute concentrations were 20 mol % in $CHCl_3$, 10 mol % in TFE, and 9 mol % in TFA. [b] $\Delta\delta = \delta_{solvent} - \delta_{CHCl_3}$. [c] Not sufficiently soluble to obtain a spectrum.

purified by recrystallization from 95% ethanol or by reduced-pressure distillation. The purity and identity were confirmed by melting and boiling points and ^1H and ^{13}C spectra. The alkylideneanilines oxidized very readily and therefore were handled and stored under nitrogen. The solvents were dried over molecular sieves.

Ultraviolet spectra were obtained with a Beckman Model 25 spectrometer, using a 1-cm path length and ca. 10^{-4} M solute concentrations.

Results and Discussion

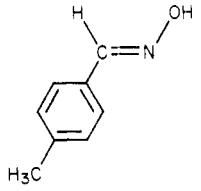
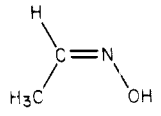
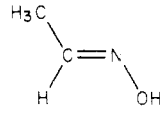
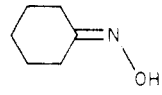
A. Some General Considerations. Chemical shifts in chloroform, 2,2,2-trifluoroethanol (TFE), and trifluoroacetic acid (TFA) are summarized in Tables I–V. The imines are divided in the tables into three groups on the basis of common structural features. The ^{15}N shifts of the oximes,[14] pyridines,[6] and the first two groups of imines[11] in chloroform solution have already been reported.

The dependence of the ^{15}N resonances of the imines in Tables I and II and of the oximes in Table IV on both substituents and structure has already been discussed in detail.[11,14] Therefore, we will comment only briefly on the data in Table III. The effect of substituting the vinylic hydrogen in benzylideneaniline, **1c**, by either a phenyl or a methyl group (giving **3a** and **3b**, respectively) is small and, perhaps surprisingly, results in deshielding. The more or less analogous substitution of the α hydrogen of pyridine

(13) R. W. Layer, *Chem. Rev.*, **63**, 489–510 (1963).

(14) R. E. Botto, P. W. Westerman, and J. D. Roberts, *Org. Magn. Reson.*, **11**, 510–5 (1978).

Table IV. Effects of Hydrogen Bonding and Protonation on ^{15}N Chemical Shifts of Oximes

compd	no.	solvent[a]	δ, upfield from ext DNO_3	$\Delta\delta$[b]
	4a	$CHCl_3$	20.1[c]	0.0
		TFE	29.3	9.2
		TFA	153.6	133.5
	4b[d]	$CHCl_3$	24.1[e]	0.0
		TFE	33.3	9.2
		TFA	135.0	110.9
	4c	$CHCl_3$	28.4[e]	0.0
		TFE	36.1	7.7
		TFA	135.0	106.6
	4d	$CHCl_3$	46.1[e]	0.0
		TFE	54.5	8.4
		TFA	135.0	112.0

[a] Solute concentrations were as follows: 20 mol % for 4a, 36 mol % for 4b and 4c, and 25 mol % for 4d in $CHCl_3$; 10 mol % for 4a and 4c and 25 mol % for 4d in TFE; 9 mol % for all compounds in TFA. [b] $\Delta\delta = \delta_{solvent} - \delta_{CHCl_3}$. [c] From ref 7. [d] Mixture of 4b and 4c consisting mostly of 4b. [e] From ref 15.

by a methyl group produces a small degree of shielding. A larger shift effect results when the phenyl ring of **3b** is replaced by a saturated alkyl group (**3c** and **3d**). This change is similar to, but larger than, that observed for C_β[15] when the phenyl ring of an α-alkylstyrene is replaced by an alkyl group.[15]

Tables I–V show that TFE produces moderate and TFA very large upfield shifts of nitrogen resonances compared to those in chloroform[16] and that the magnitude of the shifts depends on structure, although the differences are sometimes small. The effects for pyridines are of the same order of magnitude as those for other compounds even though the pyridine nitrogen is part of an aromatic system. The much larger ^{15}N shifts in TFA compared to TFE suggest different interactions between the nitrogen compounds and these solvents—protonation with TFA and hydrogen bonding with TFE.

The ^{15}N resonances in TFA were all sharp and strong, with a large favorable NOE produced on proton decoupling. For several compounds, well-resolved doublets were found in proton-coupled ^{15}N spectra, which arise from the nonexchanging protonated species. The one-bond coupling constants derived from the proton-coupled spectra (Tables I–V) range from 89 to 96 Hz, indicating a substantial degree of sp^2 character. Corresponding coupling constants of about 92 Hz have been reported for some of the imines (**1b**, **1c**, **1d**, and **1f**) in $HFSO_3$.[17] Where no coupling was observed, the coupled resonances were identical with those in the decoupled spectra because of fast proton exchange.

Oximes, for which no coupling was observed in TFA, are expected to be the weakest bases because of the inductive effect of the hydroxyl group. Although two sites are available for protonation in oximes, the position, intensity, and sharpness of the signals indicate that the bulk of the oxime molecules exits in TFA solution protonated on nitrogen.

Apart from the oximes, only two other compounds showed no proton coupling in TFA, the imines **1d** and **1f**. This is not suprising–one would expect the nitro groups to decrease the basicity of the imine nitrogens by either delocalization, induction, or both. It is not clear whether **1d** and **1f** are essentially completely protonated in TFA and undergo fast proton exchange through equilibration with the counterion or are substantially less than completely protonated and are equilibrated by proton transfer between the free base and the conjugate acid. Analogy for either possibility can be cited, but we favor the former on the basis that the protonation shifts of **1d** and **1f** are comparable to those of the other imines shown in Table I. Because the protonated imine **2b** exhibits coupling in spite of the nitro substituent, clearly, group 2 imines are much stronger bases than those of group 1—a result expected for an alkyl vs. aryl group on the nitrogen.

To best compare and interpret the effects of hydrogen bonding and protonation in terms of differences in structure, one should use the ^{15}N shifts at infinite dilution. At higher concentrations, the observed shifts may be influenced by changes in the degree of intermolecular association or by incomplete hydrogen-bond formation between solvent and solute. In practice, however, infinite dilution may already be well approximated at concentrations as high as 10 mol % in TFA, but it is less clear to what extent this is true in TFE, particularly for the oximes.[18] Increasing the concentration from 10 to 20 mol % in TFE resulted in a definite decrease in the observed δ—about 2 ppm for **1a**, **1c**, and **2a** and 1 ppm for **2d** and **2c**. Similar changes were also observed for ^{13}C shifts, but decreasing the concentration below 10 mol % (to as low as 2 mol %) did not seem to result in further decreases in the ^{13}C shifts. Measurement of ^{15}N resonances at the natural-abundance level below 10 mol % was not practicable because of the long times necessary to obtain spectra.

The effects of temperature on ^{15}N shifts were determined for **1a** and **1c** at 20 mol % concentration in TFE; going from 28 to 55 °C resulted in a 4-ppm decrease in δ. The direction of the changes is consistent with an increase in the proportion of unhydrogen-bonded solute molecules or a change in the total number of solvent molecules involved in hydrogen bonding to a given solute molecule.

B. Protonation Shifts in Trifluoroacetic Acid. It will be seen from Tables I–V that, for a given structural type, the changes in ^{15}N chemical shifts of the C=N nitrogen on protonation have distinctive values.[18] However, within a particular group, they are only to a slight degree influenced by substituents as diverse as the nitro and methoxy groups at the 4-positions of any phenyl rings which are present. This kind of insensitivity has been subsequently shown to be true for a larger number of protonated *N*-benzylidenecyclohexylamines (**2a** and **2b**).[19]

(15) Cf., J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972, p 71.

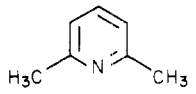
(16) The choice of chloroform as the "standard" solvent was dictated by the practical requirement of having sufficient solubility to take the spectra in reasonable accumulation times. Because chloroform is well-known to be a hydrogen-bonding solvent, albeit by no means as effective as TFE,[6] the hydrogen-bonding shifts produced by TFE taken relative to chloroform as standard will, in fact, be several parts per million too small. However, because the TFE shifts are large, this will not make any serious errors in qualitative interpretations.

(17) T. Axenrod and H. J. Wieder, "Nitrogen NMR", M. Witanowski and G. A. Webb, Eds., Plenum, London, 1973. p 280.

(18) Because oximes appear to be substantially self-associated in chloroform solution by hydrogen bonding of one oxime molecule to another, the chloroform shifts are probably several parts per million more upfield than they would be at infinite dilution.[14]

(19) R. E. Botto and J. D. Roberts, *J. Org. Chem.*, **44**, 140-1 (1979).

Table V. Effects of Hydrogen Bonding and Protonation on ^{15}N Chemical Shifts of Pyridines

compd	no.	solvent[a]	δ, upfield from ext. DNO_3	$\Delta\delta$[b]	$^1J_{^{15}N-H}$, Hz
	5a	$CHCl_3$	63.0	0	
		TFE	86.1[c]	23.1	
		TFA	178.6	115.6	96.3
	5b	$CHCl_3$	64.7	0	
		TFE	88.3	23.6	
		TFA	177.0	122.3	96.3

[a] Solute concentration was 14.5 mol %. [b] $\Delta\delta = \delta_{solvent} - \delta_{CHCl_3}$. [c] From ref 6.

The protonation shifts are largest when there are one or two phenyl groups on the carbon of the C=N group (**1a–f**, **2a–d**, **3a,b**, **4a**), much less large for the imines with the only phenyl group attached to the nitrogen (**3c,d**) and for the pyridines (**5a,b**), and smallest for the alkyl-substituted oximes (**4b–d**).[18] Extended conjugation produced by having both C and N of the C=N carrying phenyl groups (**1a–f**, **3b**) gives, perhaps unexpectedly, somewhat smaller protonation shifts than those cases having phenyl on C and alkyl on N (**2a–d**). The protonation shifts are consistent with predictions based on consideration of changes in the second-order paramagnetic effect, except for the differences between **1a–f** and **3b** vs. **2a–d**. The determining factor should be the energies of the various electronic transitions, because mixing of excited-state wave functions into the ground-state wave function is expected to make important contributions to the nuclear screening. The characteristic large paramagnetic shifts of the >C=N– nitrogens are usually presumed to correspond to the n → π* optical transitions.[2,6,10,11,19-22] This is because protonation in effect converts these transitions to much higher energy σ → π* transitions, a change which accounts nicely for the large diamagnetic shifts observed on protontion. Increased conjugation is expected to decrease the n → π* energies and result in larger protonation shifts, as reflected by the general trend noted here. However, comparison with actual energy values is difficult because the n → π* transitions for the substances studied here are difficult to identify, often being obscured by the much more intense π → π* transitions. The ultraviolet spectra of **1c**, **2d**, and **3c** (Figure 1) are not much help in making an a priori decision concerning these compounds. If one were to follow Jaffé and co-workers[23] and accept their estimate of 360 nm for the maximum wavelength of the n → π* transition of **1c**, then the order of protonation shifts expected is **1c** > **2d** > **3c**, while the actual order is **2d** > **1c** > **3c**. But Jaffeé's assignment is not certain; there is no clear indication as to the position of $\lambda_{n\rightarrow\pi^*}$ of **2d**,[24] and there is no conclusive evidence that the n → π* energy of **1c** *is* lower than that of **2d**. But, even accepting that it is, other factors could also contribute: there will be changes in electron density accompanying protonation; the excited-state contributions may not correspond to specific optical transitions; furthermore, one should keep in mind that chemical

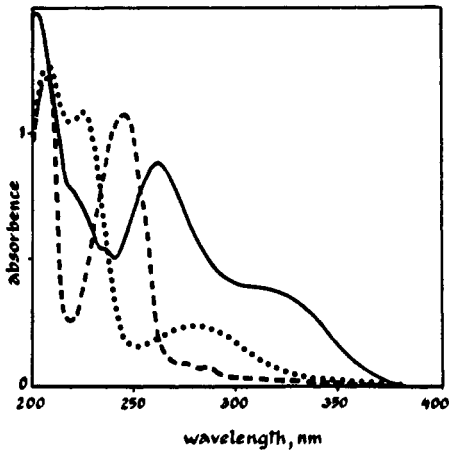


Figure 1. Ultraviolet spectra of imines in cyclohexane: —, *N*-benzylideneaniline (**1c**); ---, *N*-benzylideneisobutylamine (**2d**); ···, *N*-cyclohexylideneaniline (**3c**).

shifts measured in solutions where the molecules are tumbling rapidly are averages of very sizable shift anisotropies. Consequently, if we predict a shift difference based on a supposed contribution to some one particular anisotropy, it may not be possible to ignore the effect of this contribution on the other shift anisotropies the molecule possesses. With the compounds we have studied, the protonation shifts are all large and are all in the right direction. It may well be unwarranted to indulge in the "fine tuning" required to account for the relatively small differences with particular substituent groups when the basic structural variations are as large as they are.

C. Hydrogen-Bonding Shifts in 2,2,2-Trifluoroethanol. The situation with regard to the hydrogen-bonding shifts produced by a change of solvent from chloroform to trifluoroethanol is somewhat different from that noted for trifluoroacetic acid. In theory, if one could find a super hydrogen-bonding solvent for imines, but one which would not donate a proton to achieve actual protonation, it seems possible that something approaching full protonation shifts would be produced, modified, of course, to some extent by the presence and character of the group carrying the proton which forms the hydrogen bond. In practice, one finds that hydrogen-bonding power parallels acidity, and as it increases, a point is reached where actual protonation begins to set in. The onset of protonation in competition with hydrogen bonding has been shown to occur for imidazole with acetic acid in chloroform as solvent by infrared spectroscopy.[25] The ^{13}C chemical shifts of several imines in acetic acid as solvent also indicate partial protonation, the extent of which depends on the imine's basicity.[26] With trifluoroethanol, imidazole seems to be predominantly, if not exclusively, hydrogen bonded;[25]

(20) K. A. K. Ebraheem, G. A. Webb, and M. Witanowski, *Org. Magn. Reson.*, **11**, 27–30 (1978).
(21) J. Mason, W. von Bronswijk, and J. E. Vinter, *J. Chem. Soc., Perkin Trans. 2*, 469–73 (1977).
(22) See J. A. Pople, *J. Chem. Phys.*, **37**, 60–6 (1962), for a discussion of the importance of the n → π* energies in determining the shieldings of carbonyl groups.
(23) H. H. Jaffé, S. J. Yah, and R. W. Gardner, *J. Mol. Spectrosc.*, **2**, 120–36 (1958).
(24) Whether the small shoulders in the spectrum of **2d** correspond to the n → π* transition is questionable: R. Bonnet in "The Chemistry of the Carbon–Nitrogen Double Bond", S. Patai, Ed., Interscience, New York, 1970, Chapter 4, Section I.
(25) I. S. Schuster and J. D. Roberts, *J. Org. Chem.*, **44**, 2658 (1979).
(26) M. Allen and J. D. Roberts, to be submitted for publication.

this also appears to be the case for the imines. The ^{15}N hydrogen-bonding shifts of the various nitrogen compounds studied here are unlike the protonation shifts in that they reflect, to at least some degree, the different basicities of the nitrogens in the various groups of compounds. Thus, we see from the data that the smallest hydrogen-bonding shifts occur for the oximes and the largest for group 2 amines—the weakest and strongest bases, respectively. Within the oximes (Table IV), hydrogen-bonding effects for the aliphatic and aromatic ones are comparable, which is not the case for protonation. The imines **3c** and **3d** and the pyridines **5a** and **5b** have slightly larger hydrogen-bonding shifts than any of the group 1 imines, although their protonation shifts are considerably smaller. But group 1 imines, even those without the nitro substituent, appear to be slightly weaker bases. Within groups 1 and 2, the 4-nitrophenylimines **1d** and **2b** have smaller hydrogen bonding shifts than those of the corresponding methoxyimines **1a** and **2a**. Following the earlier suggestion that, analogous to protonation, the upfield hydrogen-bonding shifts also result from changes in the second-order paramagnetic effect,[6,11] one observes that the relative magnitudes of these shifts largely reflect differences in hydrogen-bond enthalpies. This seems reasonable, because the increases in the $n \rightarrow \pi^*$ transition energies that result from hydrogen bonding and that presumably are responsible for the upfield shifts should be largely dependent on the strength of the hydrogen bond. The epitome of this kind of behavior is exhibited by azobenzene which has only a very small ^{15}N solvent shift in methanol but a protonation shift of about 155 ppm.[2,6] Azobenzene is a rather weak base, and its nitrogens are not hydrogen bonded effectively by a weakly acidic hydroxylic solvent such as methanol, but when protonated by a strong enough acid, the resonances of these nitrogens shift far upfield.

Registry No. **1a**, 836-41-9; **1b**, 2362-77-8; **1c**, 538-51-2; **1d**, 785-80-8; **1e**, 783-08-4; **1f**, 785-81-9; **2a**, 56644-00-9; **2b**, 42974-61-8; **2c**, 6852-56-8; **2d**, 6852-57-9; **3a**, 574-45-8; **3b**, 1749-19-5; **3c**, 1132-38-3; **3d**, 13683-42-6; **4a**, 3717-15-5; **4b**, 5775-72-4; **4c**, 5780-37-0; **4d**, 100-64-1; **5a**, 110-86-1; **5b**, 108-48-5.

Kinetics of the Reaction of Some Tryptophan Derivatives with the Osmium Tetraoxide–Pyridine Reagent

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A series of indole derivatives related to tryptophan reacted with the osmium tetraoxide–pyridine reagent to form bis(pyridine)osmate esters by addition to the 2,3-position of the indole ring. 1-Methyl-α-*N*-acetyl-DL-tryptophan formed a pair of easily separable diastereomeric esters. A study of the kinetics of these reactions showed the expected first-order dependence on osmium tetraoxide and on the indole component. The dependence on pyridine, however, varied with the structure of the indole. Those 3-indolyl derivatives with a three- or four-carbon side chain terminating in a carboxyl group showed an apparent pyridine dependence close to first order. Other indole derivatives approached the normal second-order dependence. We postulate intramolecular carboxylate catalysis to account for these findings. An interesting consequence of the variation in pyridine dependence is that at low pyridine concentrations, a substrate with first-order dependence on pyridine is kinetically favored. At high pyridine concentrations this kinetic selectivity can be inverted to favor the substrate with a square dependence on pyridine.

Osmium tetraoxide is a common tissue fixative and staining reagent. Although it has been used for more than 100 years,[1] the chemistry of its reactions with tissue components is still poorly known. In particular, whereas the reactions with unsaturated fatty acids[2] and nucleic acid components[3] have been investigated fairly thoroughly, the reactions with amino acid residues of proteins have received little attention. Bahr showed in 1954 that certain of the amino acids, including tryptophan, reacted rapidly with osmium tetraoxide.[4]

Hake showed that cysteine was oxidized to cysteic acid and methionine to methionine sulfone.[5] At high temperatures all amino acids are oxidatively deaminated.[6] Ockenden and Schofield[7] showed that several *N*-substituted indoles reacted with the osmium tetraoxide–pyridine reagent to give osmate esters which could be hydrolyzed to the corresponding 2,3-glycols. Indoles which lacked N substitution did not give isolable glycols. Maupin-Szamier and Pollard's interesting study of the reaction of actin with osmium tetraoxide showed reaction of cysteine, methionine, and lysine residues.[8] Since these authors analyzed the reacted protein following acid-catalyzed hydrolysis, tryptophan reactivity could not be studied. Nielson and Griffith[9] have published a valuable study of the reactivity of a variety of blocked amino acid derivatives with osmium tetraoxide. Complexes were isolated from derivatives of histidine, methionine, and cysteine. A blocked tryptophan derivative proved intractable in the sense that isolation of the osmate ester was not successful–but clearly reaction had taken place.

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(2) E. D. Korn, *J. Cell Biol.*, **34**, 627–38 (1967).
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(4) G. F. Bahr, *Exp. Cell Res.*, **7**, 457–79 (1954).
(5) T. Hake, *Lab. Invest.*, **14**, 470–4 (1208–12) (1965).
(6) J. Nyilasi and P. Orsős, *Acta Chim. Acad. Sci. Hung.*, **75**, 405–10 (1973).
(7) D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 612–8 (1953).
(8) P. Maupin-Szamier and T. D. Pollard, *J. Cell Biol.*, **77**, 837–52 (1978).
(9) A. J. Nielson and W. P. Griffith, *J. Chem. Soc., Dalton Trans.*, 1084–8 (1979).

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