with water there was obtained 0.10 g of a solid which was only partially soluble in *n*-hexane. A solution of the *n*-hexane-insoluble fraction in chloroform was filtered and on dilution of the filtrate with petroleum ether there was deposited 0.040 g of N-(*o*-hydroxybenzyl)benzamide (XIX), mp 144–145°, its identity being established by mixture melting point and infrared measurements.

Acetylation of Spiro[cyclohexane-1,2′-(3′,4′-dihydro)-2′H-1′,3′-benzoxazine] (XI). N-(*o*-Hydroxybenzyl)-N-(1′-cyclohexenyl)acetamide (XXI).—A mixture of 0.47 g of XI (2.3 mmoles) and 1.1 g of acetic anhydride (11 mmoles) in 10 ml of dry ether was allowed to stand at room temperature and then evaporated at reduced pressure. The residue was a colorless oil which did not crystallize on being scratched or cooled. The oil was mixed thoroughly with excess sodium carbonate solution and this mixture was extracted with three 10-ml portions of ether. The combined ether solutions were dried over magnesium sulfate and evaporated at reduced pressure to give 0.48 g of a colorless oil. The infrared spectrum (capillary film) of this oil showed broad absorption at 2600–3400 cm^{-1} (hydrogen-bonded phenolic OH), strong sharp absorption at 1775 cm^{-1} (ester C=O), and a broad strong peak at 1610–1660 cm^{-1} (tertiary amide C=O). The oil was taken up in warm aqueous ethanol and this solution was scratched and cooled to give 0.28 g of a crystalline solid, mp 76–112°. This solid was recrystallized, with considerable loss, twice from aqueous ethanol to give 0.064 g of XXI (11%): white platelets; mp 119–120°; ν_{max}^{KBr} 1590–1630 cm^{-1} (strong broad peak); τ 0.24 (singlet, 1 H, OH, vanished on deuterium exchange), 2.5–3.4 (multiplet, 4 H, aromatic protons), 4.59 (broad, 1 H, vinylic proton), 5.53 (singlet, 2 H, CH_2-N), and 7.6–8.7 (10–11 H, cyclohexene ring methylene protons and acetyl methyl protons with the latter as a sharp peak at τ 7.97 protruding from the methylene envelope). The product is insoluble in water and 10% aqueous sodium bicarbonate but soluble in 5% aqueous sodium hydroxide, from which it can be recovered unchanged by addition of dilute hydrochloric acid.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.52; H, 7.99; N, 5.86.

Improved yields of the same compound were obtained when the following procedure was employed. A 1.0-ml portion of acetic anhydride was added to a solution of 0.46 g of XI (2.3 mmoles) in 5 ml of dry pyridine. The solution was allowed to stand overnight at room temperature and evaporated at reduced pressure. A solution of the residual oil in 25 ml of ether was washed once with 25 ml of water and twice with 25-ml portions of saturated aqueous sodium bicarbonate, then dried over magnesium sulfate and evaporated at reduced pressure. The residue was 0.48 g of a colorless oil whose infrared spectrum (capillary film) showed two strong bands at 1770 and 1655 cm^{-1} and lacked phenolic hydroxyl or amide NH stretch absorption. Attempts to crystallize this oil by cooling, scratching, trituration with various solvents, or molecular distillation failed. This oil was dissolved in 3 ml of ethanol and 10 ml of 2.5% aqueous sodium hydroxide was added. The resultant emulsion was extracted with ether and the combined ether phases were washed with 5 ml of water and dried over magnesium sulfate. The aqueous phase and washings were combined and made acid with 1 *N* hydrochloric acid, producing an emulsion. Crystallization of the oil was induced by seeding the emulsion. The crystals were recrystallized from aqueous ethanol and 0.16 g of XXI (29%), mp 119–120°, was obtained. Evaporation of the ethanol extract obtained above and recrystallization of the residue from aqueous methanol gave a further 0.08 g of XXI (14%), mp 109–114° (impure).

Registry No.—Va, 10358-86-8; Vb, 14723-37-6; Vc, 10358-87-9; Vd, 13293-96-4; Ve, 10358-88-0; Vf, 10358-89-1; Vg, 3946-40-5; VIa, 14680-09-2; VIb, 14680-10-5; VIc, 14680-11-6; VId, 14680-12-7; VIe, 14680-13-8; VII, 14680-14-9; VIII, 14680-15-0; IX, 14746-04-4; X, 14723-39-8; XI, 14783-46-1; XII, 14746-05-5; XIII, 14723-40-1; XIV, 14746-06-6; XVI, 14680-16-1; XVII, 12125-64-3; XVIII, 14680-17-2; XIX, 14680-18-3; XX, 14680-19-4; XXI, 14723-41-2; N-(3α-hydroxy-5α-androstan-17-ylidene)-*o*-hydroxybenzylamine, 14723-42-3; N-(3α-hydroxy-5α-androstan-17-ylidene)benzylamine, 14723-43-4.

Ring–Chain Tautomerism of Derivatives of *o*-Hydroxybenzylamine with Aldehydes and Ketones. The Nuclear Magnetic Resonance Spectra of Immonium Ions[1]

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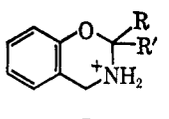
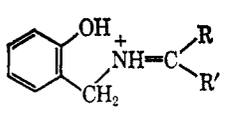
The condensation products (2-substituted 3,4-dihydro-2H-1,3-benzoxazines or the corresponding imines) of *o*-hydroxybenzylamine with several aliphatic and aromatic carbonyl compounds form immonium ions when dissolved in trifluoroacetic acid, no evidence for the cyclic tautomers being detected. The nuclear magnetic resonance spectra of these and other immonium ions are presented. The cyclic protonated 3,4-dihydro-2H-1,3-benzoxazine tautomer is preferred for ions derived from the products formed by reaction of chloral or formaldehyde with *o*-hydroxybenzylamine. 3,4-Dihydro-2H-1,3-benzoxazonium ion is generated by dissolving either 1,3,5-tris(*o*-hydroxybenzyl)hexahydro-*s*-triazine or 3,3′-methylenebis(3,4-dihydro-2H-1,3-benzoxazine) in trifluoroacetic acid; in the latter case a ternary immonium ion is also formed.

We have previously shown[4] that the condensation products of *o*-hydroxybenzylamine with aldehydes and ketones are 2-substituted 3,4-dihydro-2H-1,3-benzoxazines or Schiff bases, or mixtures of these, and that in certain cases a rapid tautomeric equilibrium exists between the two forms. A similar type of tautomerism is also possible for the protonated derivatives of these compounds. *A priori*, it is impossible to predict whether a given derivative, when protonated, will exist



I



II

as a protonated benzoxazine (I), an immonium ion (II), or a mixture of these. There has been no systematic study of this type of tautomeric equilibrium. Hydrochloride salts of tetrahydro-1,3-oxazines,[5] oxazolidines,[6]

(1) Taken from the Ph.D. Thesis of A. F. M., Vanderbilt University, Jan 1967.

(2) Shell predoctoral fellow, 1964–1965; Department of Chemistry, Queen Mary College, Mile End Road, London, England.

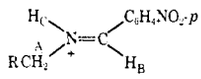
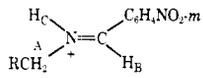
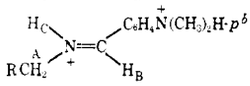
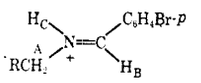
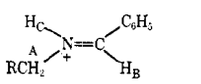
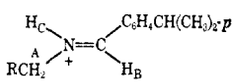
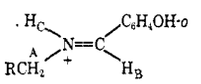
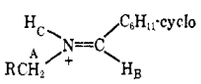
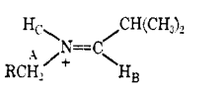
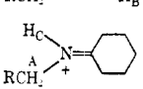
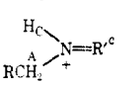
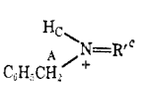
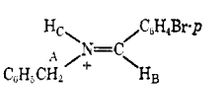
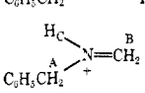
(3) To whom inquiries should be sent.

(4) A. F. McDonagh and H. E. Smith, *J. Org. Chem.*, **33**, 1 (1968).

(5) (a) H. Piotrowska and T. Urbanski, *Bull. Acad. Polon. Sci., Classe III*, **3**, 389 (1955); *Chem. Abstr.*, **50**, 13935 (1956); (b) T. Urbanski and H. Piotrowska, *Roczniki Chem.*, **31**, 553 (1957); *Chem. Abstr.*, **52**, 5414 (1958); (c) Z. Horii, T. Inoi, S.-W. Kim, Y. Tamura, A. Suzuki, and H. Matsumoto, *Chem. Pharm. Bull.* (Tokyo), **13**, 1151 (1965); *Chem. Abstr.*, **64**, 5078 (1966).

(6) R. V. Heinzelmann, H. G. Kolloff, and J. H. Hunter, *J. Am. Chem. Soc.*, **70**, 1386 (1948); J. S. Pierce, C. D. Lunsford, R. W. Raiford, Jr., J. L. Rush, and D. W. Riley, *ibid.*, **73**, 2595 (1951).

TABLE I
NMR[a] SPECTRA OF IMMONIUM IONS IN TRIFLUOROACETIC ACID

Ion	Structure (R = C_6H_4OH-*o*)	H_A τ	H_A Multiplicity	J_{AC}	H_B τ	H_B Multiplicity	J_{BC}
1		4.64	Singlet		0.78	Broad hump	
2		4.67	Singlet		0.73	Broad hump	
3		4.69	Broad singlet		0.89	Broad doublet	10
4		4.80	Doublet	5	1.11	Doublet	17
5		4.79	Doublet	5	1.10	Doublet	18
6		4.83	Doublet	6	1.19	Doublet	18
7		4.90	Doublet	5	1.36	Doublet	17
8		5.00	Doublet	5	1.67	Quartet	18
9		4.95	Doublet	5	1.56	Quartet	18
10		5.01	Doublet	6			
11		5.15	Doublet	5			
12		5.11	Doublet	6			
13		4.83	Doublet	5	1.20	Doublet	17
14		4.84	Broad singlet		1.81	Broad singlet	

[a] Concentration 0.5–0.7 *M*; chemical shifts in τ units with tetramethylsilane as internal standard (τ 10); coupling constants in cycles per second. [b] The $\overset{+}{N}(CH_3)_2H$ signal is a sharp singlet at τ 6.42. [c] R′ = 5α-androstan-3α-ol-17-ylidene.

and a naphthoxazine[7] have been reported. Witkop and Beiler[8] have studied some condensation products of *o*-aminobenzyl alcohol with substituted benzaldehydes both as the free bases and their hydrochloride salts. They found that, of two compounds having the dihydro-3,1-benzoxazine structure in chloroform solution, one remains cyclic and the other tautomerizes when they are converted into their hydrochloride salts. N-Salicylidene-*o*-aminobenzyl alcohol, however, has an open-chain structure whether protonated or not.[8]

In order to investigate this type of tautomerism further, we have examined the nuclear magnetic resonance (nmr) spectra of a number of Schiff bases and dihydro-1,3-benzoxazines derived from *o*-hydroxybenzylamine in trifluoroacetic acid (TFA) solution. The results are of additional interest because of the data they provide on the nmr spectra of immonium ions.

(7) W. J. Burke and R. J. Reynolds, *J. Am. Chem. Soc.*, **76**, 1291 (1954).
(8) B. Witkop and T. W. Beiler, *ibid.*, **76**, 5589 (1954).

Results and Discussion

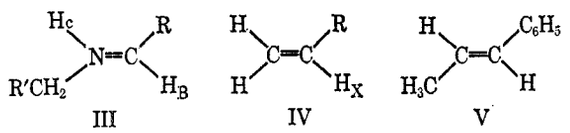
The nmr spectra (Table I) of eight Schiff bases of *o*-hydroxybenzylamine[4] (Table I, **1–7** and **11**) and three 3,4-dihydro-2H-1,3-benzoxazines[4] (Table I, **8–10**) show that in TFA these compounds exist as open-chain immonium ions (II). Included in Table I for comparison are spectral parameters for two Schiff bases of benzylamine in TFA (Table I, **12** and **13**).

For most of the ions, exchange of the immonium proton with the solvent is sufficiently slow for spin–spin coupling between this proton and its vicinal neighbors to be observed. In most cases the methylene protons adjacent to the nitrogen appear as a doublet at about τ 5 with a coupling constant of about 5 cps. In the aldimmonium structures the methine proton signal occurs between τ 0.7–1.8 with a coupling constant to the $\overset{+}{N}H$ proton of about 18 cps. The size of this coupling constant indicates that these structures are immon-

ium ions rather than adducts of the imines with TFA. The $\overset{+}{N}H$ proton resonance is not directly observable in any of the spectra. However, in several cases integration of the spectrum revealed that it is probably concealed under the aromatic ring poton multiplet at about τ 2.8.

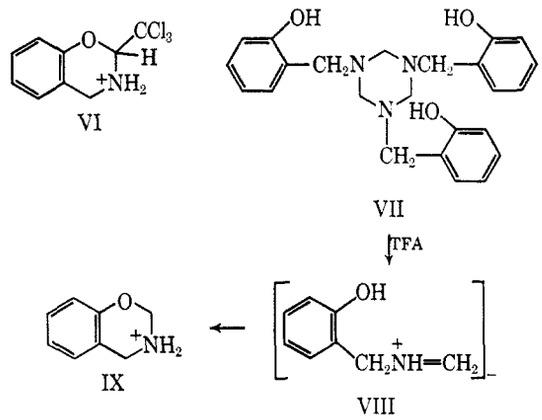
In the spectra of two of the immonium ions (Table I, **1** and **2**) the methylene and azomethine proton signals are singlets. In these ions the strongly electron-withdrawing nitro substituents so reduce the basicity of the nitrogen atom that exchange of the immonium proton is sufficiently rapid to cause collapse of the $CH_2\overset{+}{N}H=$ and $\overset{+}{N}H=CH$ spin–spin doublets. The spectrum of N-(*p*-dimethylaminobenzylidene)-*o*-hydroxybenzylamine in TFA (Table I, **3**) shows a broad singlet from the methylene protons, a broad partially coalesced doublet from the methine proton, and a sharp singlet for the *p*-dimethylamino methyl protons. Therefore, the immonium proton is exchanging rapidly, though not so rapidly as in the case of the nitro-substituted cations (Table I, **1** and **2**), which shows that there is an electron-withdrawing substituent in the benzylidene aromatic ring. Since the *p*-dimethylamino group is strongly electron donating, whereas *p*-ammonium groups are electron withdrawing, it is concluded that both the imino and the dimethylamino nitrogen atoms become protonated in TFA. Coupling of the dimethylammonium methyl protons with the adjacent ammonium proton is not observed because of the rapid exchange of the latter with the solvent. The Hammett *para* substituent constant for the dimethylammonium group does not appear to have been measured;[9] the nmr spectra of the ions numbered **1**, **2**, and **3** in Table I, considered together, indicate that it has a value in this system somewhat smaller than the substituent constants for *m*- and *p*-nitro groups.

Immonium ions are isoelectronic with the corresponding olefins. There are certain similarities between the nmr spectra of the aldimmonium ions in Table I and the spectra of some structurally related olefins. For those ions in Table I with the general structure III the J_{BC} coupling constant is about 18 cps, regardless of whether R is an alkyl or aryl group. However, the chemical shift of H_B is quite sensitive to the nature of R. Similarly in monosubstituted ethylenes (IV) the *trans* proton coupling constant is about 17 cps irrespective of whether the substituent R is phenyl or an alkyl group, but the chemical shift of the α proton (H_X) varies according to the nature of R.[10] The *trans* proton coupling constant in *trans*-β-methylstyrene (V) is 15.6 cps;[11] a comparison between the size of the coupling constant in V and the coupling constants in the aldimmonium ions in Table I indicates that, as expected, the latter have the *trans* configuration.



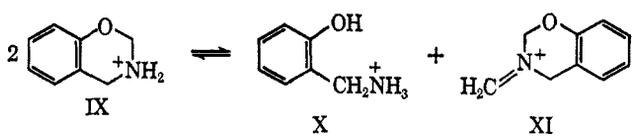
III IV V

In two instances a protonated benzoxazine structure is preferred to the open-chain tautomer. One example is the chloral-*o*-hydroxybenzylamine derivative VI discussed in our previous paper,[4] and the other is the 3,4-dihydro-2H-1,3-benzoxazonium ion (IX). The nmr



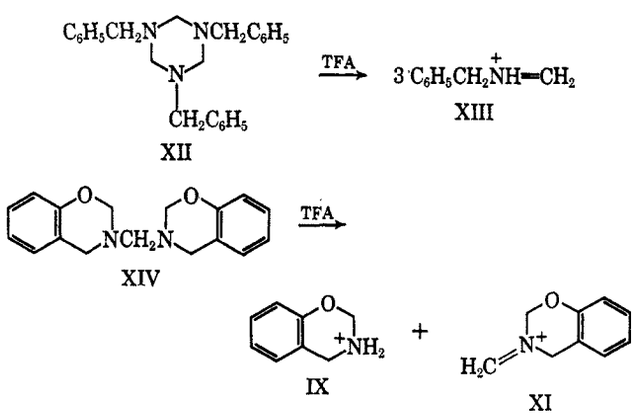
VI VII VIII IX

spectrum of a solution of 1,3,5-tris(*o*-hydroxybenzyl)-hexahydro-*s*-triazine (VII) in TFA shows (Figure 1, upper spectrum), in addition to aromatic proton signals, predominant absorption at τ 4.70 (broad singlet), 5.30 (unresolved triplet), and about 1.8 (very broad band). These peaks are assigned, respectively, to the OCH_2N, $ArCH_2N$, and $\overset{+}{N}H_2$ protons of the ion IX. Exchange of the $\overset{+}{N}H_2$ protons is sufficiently slow for their detection, but too rapid for complete splitting of the methylene signals to be observed. The nmr spectrum (Figure 1, upper spectrum) also reveals the presence of *o*-hydroxybenzylammonium (X) and 3-methylene-3,4-dihydro-2H-1,3-benzoxazonium (XI) ions in low concentration, the mole ratio of IX to XI being about 20:1. The presence of these ions could be explained on the basis of the following equilibrium.



IX X XI

However, they probably arise from traces of 3,3′-methylenebis(3,4-dihydro-2H-1,3-benzoxazine) (XIV) (see below) and *o*-hydroxybenzylamine present as impurities in the starting material. The spectrum of the *s*-triazine VII in TFA is not consistent with the open-chain immonium structure VIII, although this must be an intermediate in the formation of the protonated dihydrobenzoxazine IX. This is affirmed by comparison



XII XIII XIV IX XI

(9) G. B. Barlin and D. D. Perrin, *Quart. Rev.* (London), **20**, 75 (1966).
(10) C. N. Banwell and N. Sheppard, *Mol. Phys.*, **3**, 351 (1960).
(11) R. W. Fessenden and J. S. Waugh, *J. Chem. Phys.*, **30**, 944 (1959).

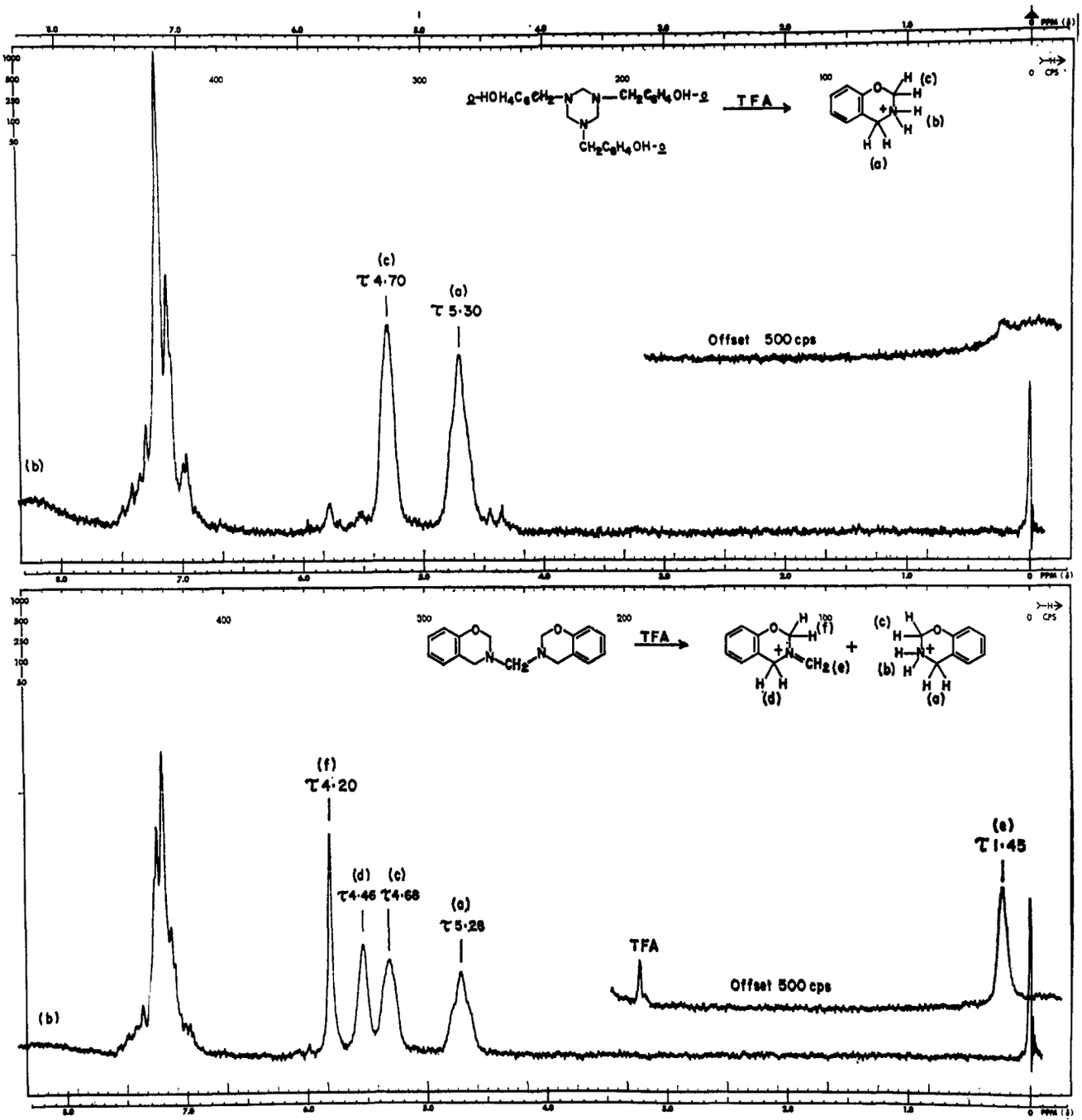


Figure 1.—Nmr spectra of 3,4-dihydro-2H-1,3-benzazonium ion (IX) (upper) and 3,4-dihydro-2H-1,3-benzoxazonium (IX) and 3-methylene-3,4-dihydro-2H-1,3-benzoxazonium (XI) ions (lower) in trifluoroacetic acid.

with the spectrum of N-benzyl-N-methyleneimmonium ion (XIII) (Table I, **14**), which was generated by dissolving 1,3,5-tribenzylhexahydro-*s*-triazine (XII) in TFA. It is noted in passing that the immonium ion XIII is believed to be the active intermediate in the Sommelet reaction,[12] and similar ions are also postulated as intermediates in several types of reductive aminations.[13]

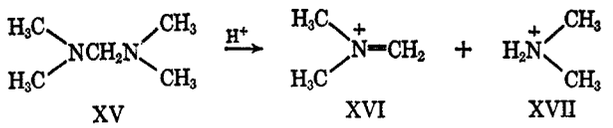
The protonated dihydrobenzoxazine IX can also be generated from the methylenebisdihydrobenzoxazine XIV.[4] The spectrum (Figure 1, lower spectrum) of a solution of the latter in TFA shows aromatic proton signals, a broad absorption band centered at about τ 1.8, and five other peaks of equal intensity at τ 1.45, 4.20, 4.46, 4.68, and 5.28. Three of these, at τ 1.8, 4.68, and 5.28, are characteristic of the protonated dihydro-1,3-benzoxazine IX already discussed. The remaining three are then readily accounted for on the basis of structure XI, with the low-field signal (τ 1.45) owing to the exocyclic methylene group. Thus the amine XIV dissociates in TFA to give the protonated benzoxazine IX and the ternary immonium ion XI. No evidence was found for protonated forms of the amine XIV. Skell and de Luis[14] have found that a similar fragmentation occurs when other methylenebisamines are dissolved

(12) (a) M. Sommelet, *Compt. Rend.*, **157**, 852 (1913); (b) S. J. Angyal, D. R. Penman, and G. P. Warwick, *J. Chem. Soc.*, 1742 (1953).

(13) (a) P. J. McLaughlin and E. C. Wagner, *J. Am. Chem. Soc.*, **66**, 251 (1944); (b) E. Staple and E. C. Wagner, *J. Org. Chem.*, **14**, 559 (1949).

(14) (a) P. S. Skell and J. de Luis, unpublished results quoted by N. C. Deno in *Progr. Phys. Org. Chem.*, **2**, 183 (1964); *Chem. Eng. News*, **42**, 88, Oct 5 (1964); (b) J. de Luis, *Dissertation Abstr.*, **25**, 6227 (1965).

in sulfuric acid. Thus N,N,N′,N′-tetramethylmethylenediamine (XV) dissociates into N,N-dimethyl-N-methyleneimmonium (XVI) and dimethylammonium (XVII) ions. However, it was found that the con-



XV XVI XVII

centration of sulfuric acid is critical. In dilute solutions the hydrated form of the ternary ion XVI predominates, whereas in 96% sulfuric acid the original diamine is stable in its diprotonated form. We have found that only the ions XVI and XVII are detectable in a TFA solution of the diamine XV. For the ternary immonium ion XVI in TFA the methylene protons are a singlet at τ 1.97 and the methyl protons a singlet at τ 6.13. However, dilution of the solution with water caused a decrease in the intensity of the peaks at τ 1.97 and 6.13 and the appearance of a doublet at about τ 5.3, indicating the formation of the diprotonated form of the diamine XV. This behavior was not investigated further.

Conclusions

The direction of ring–chain tautomerism exhibited by the condensation products of *o*-hydroxybenzylamine with aldehydes and ketones in a strongly acidic medium can be considered to be dictated by the electrophilicity of the azomethine carbon atom of the open-chain tautomer. The presence of an alkyl group (R or R′ in II) on this atom is sufficient to so reduce its electrophilicity that cyclic tautomers do not occur. But when the substituents are hydrogen or the strongly electron-withdrawing trichloromethyl groups, then the azomethine carbon is a strong enough electrophile to attack the proximal phenolic oxygen and thereby effect ring closure to I. Another influence obtains for the derivatives of aromatic aldehydes. In these cases stabilization of the open-chain tautomer by conjugation appears to be of dominating importance.

The results also demonstrate the utility of TFA as a solvent for the generation and study of immonium ions and suggest the use of this solvent for the characterization of imine groups.

Experimental Section

Nmr spectra were obtained with a Varian Associates A-60 spectrometer operating at 60 Mcps.[15] The trifluoroacetic acid used was Eastman White Label grade "referenced" with 1% of tetramethylsilane. Solutions in TFA were prepared by adding the acid to a known weight of sample in an nmr tube until the volume of the solution was 0.5 ml; the spectra were then run immediately in open tubes. The preparation and physical properties of all but two of the compounds whose spectra in TFA were studies have been described in a previous paper.[4]

N-(*p*-Bromobenzylidene)benzylamine had mp 43–44° (from ethanol) (lit.[16] mp 43°).

1,3,5-Tribenzylhexahydro-*s*-triazine (XII).—To 3.0 g of benzylamine was added 1 *N* hydrochloric acid solution until the solution was acid to litmus. To this solution was added 7.0 g of USP formalin, followed by addition of 5% aqueous sodium hydroxide until the mixture was basic. The mixture was extracted with 75 ml of ether and the extract was washed with saturated aqueous sodium chloride and dried over potassium hydroxide. The viscous oil which remained after evaporation of the ether was dissolved in ethanol. This solution was filtered, diluted with water, and cooled to −12°. The crystals which formed (1.9 g, mp 47–49°) were recrystallized from aqueous ethanol to give 1.4 g of XII (42%): mp 49–50°; nmr ($CDCl_3$) τ 2.75 (5 H), 6.37 (2 H), and 6.60 (2 H) (lit.[12b] mp 50°).

Registry No.—**1**, 12126-02-2; **2**, 12126-03-3; **3**, 12126-07-7; **4**, 12126-01-1; **5**, 12126-04-4; **6**, 12126-08-8; **7**, 12126-05-5; **8**, 12126-06-6; **9**, 12125-98-3; **10**, 12125-99-4; **11**, 12126-10-2; **12**, 12126-09-9; **13**, 12126-00-0; **14**, 12125-96-1; IX, 12126-97-2; XI, 14760-76-0; XII, 2547-66-2.

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(16) C. W. Shoppee, *J. Chem. Soc.*, 1225 (1931).