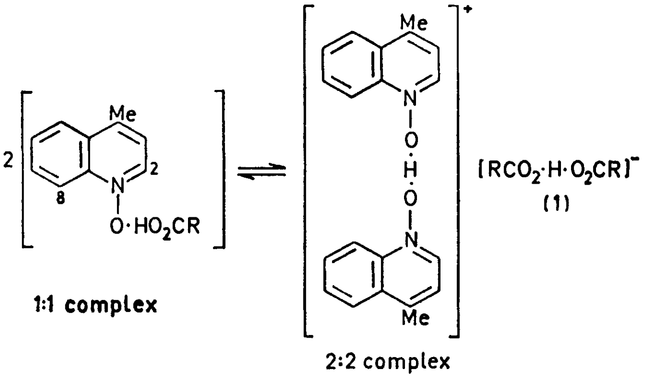
Hydrogen Bonding in Complexes of Heterocyclic *N*-Oxides with Halogenoacetic Acids. Part IV.[1] Osmometric and Nuclear Magnetic Resonance Study of Lepidine *N*-Oxide Complexes with Trifluoroacetic and Monochloroacetic Acids in Toluene at 27 °C

By **Z. Dega-Szafran** Institute of Organic Chemistry, Polish Academy of Sciences, Poznań, Poland
E. Grech, Institute of Engineering Chemistry and Physical Chemistry, Technical University, Szczecin, Poland
M. Szafran,* Institute of Chemistry, A. Mickiewicz University Poznan, Poland

N.m.r. spectra and average molecular weights of lepidine *N*-oxide complexes with trifluoroacetic and monochloroacetic acids have been measured in toluene at 27 °C. The results indicate that the following equilibrium is required to interpret the experimental results: $2(B{\cdot}HO_2CR) \rightleftharpoons (B{\cdot}H{\cdot}B)^+(RCO_2{\cdot}H{\cdot}O_2CR)^-$. The molecular weights are employed to calculate the H-bond shift. Concentration-dependence of the 8-H and 2-H ring resonance of complexes and free base is discussed.

IN previous Parts[1,2] we reported i.r. and n.m.r. spectra and vapour pressure osmometric (v.p.o.) measurements of average molecular weights of lepidine (4-methylquinoline) *N*-oxide complexes with halogenoacetic acids. From these studies it was shown that the interaction of *N*-oxide with acid in complexes in benzene, toluene, chloroform, and methylene dichloride as solvents is described by equation (1).



(1)

R=CF$_3$,CCl$_3$,CHCl$_2$ or CH$_2$Cl

In the present investigation the relationship between the n.m.r. properties and v.p.o. data has been studied in an attempt to obtain more specific information about the equilibrium involved and the nature of 1 : 1 and 2 : 2 complex species. It is assumed that the 2 : 2 complex forms ion pairs in the solvent used.

EXPERIMENTAL

The molecular weights were measured with a Hewlett–Packard vapour pressure osmometer, model 302B, calibrated with benzil in toluene at 27 ± 0·002 °C over a wide range of concentration in toluene. Toluene and benzil were purified as before.[1] Output microvoltages quoted are averages of 16 readings, usually on two separate solutions; reproducibility of V was $\pm 2\%$.

All n.m.r. spectra were measured at 80 MHz on a Tesla BS 487 A spectrometer in toluene at 27 ± 1 °C. Spectra were calibrated with respect to internal tetramethylsilane. Chemical shifts quoted are averages of at least six determinations, usually on two separate solutions. The chemical-shift measurements of ring protons were usually reproducible to within ±1 Hz. The complexes show a single 'average' resonance at very low field. Hereafter this resonance will be called an H-bond shift. The H-bond shift measurements were usually reproducible to within ±5 Hz.

RESULTS AND DISCUSSION

The procedure for determining the calibration constant (K), solute molecular weight (M), number of moles of 1 : 1 complexes in solution (m), and equilibrium constant (K_{21}) was the same as previously.[1] Equations (2)—(5) were used, where V is the measured resistance difference

$$\frac{V}{C} = \frac{K}{M} \tag{2}$$

$$K = M\,\frac{V}{C} = MA_1 + A_2C \tag{3}$$

$$m = \frac{2M_1x}{M} - x \tag{4}$$

$$K_{21} = \frac{{}^xM_2}{({}^xM_1)^2} = \frac{(x - m)(2s + x + m)}{4m^2} \tag{5}$$

(μV), A_1 and A_2 are constants, obtained by use of a least-squares procedure, x is the total number of moles of all forms of complex, s is the total number of moles of solvent, M_1 and M_2 are molecular weights of 1 : 1 and 2 : 2 complexes, respectively, and ${}^xM_1$ and ${}^xM_2$ are mole fractions of 1 : 1 and 2 : 2 complexes in solution.

Tables 1 and 2 and Figure 1 collect the data for the complexes of lepidine *N*-oxide with trifluoroacetic and monochloroacetic acids. The values obtained for molecular weights are higher in comparison with the values for 1 : 1 complexes. This is certainly caused by the presence of the 2 : 2 complexes in solution.

The shift observed for the H-bond protons and ring protons at several concentrations are shown in Figures 2—6. The spin–spin coupling constants of the ring protons are influenced by complex formation as follows: lepidine *N*-oxide J_{23} 6·5 Hz, J_{78} 8·0 Hz; complexes with trifluoroacetic acid $J_{23} = 6{\cdot}3$ Hz, $J_{78} = 9{\cdot}7$ Hz; and monochloroacetic acid $J_{23} = 6{\cdot}0$ Hz, $J_{78} = 9{\cdot}3$ Hz.

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[1] Part III, M. Szafran, E. Grech, and Z. Dega-Szafran, *Bull. Acad. polon. Sci. ser. sci. chim.*, 1971, **19**, 643.

[2] M. Szafran and Z. Dega-Szafran, *Roczniki Chem.*, 1970, **44**, 793, M. Szafran and M. D. Rozwadowska, *ibid.*, p. 1465.

TABLE 1

Summary of v.p.o. results and calculated H-bond chemical shifts for the lepidine *N*-oxide complex with trifluoroacetic acid in toluene at 27 °C

$\frac{x}{\text{mol kg}^{-1}}$	$\frac{C}{\text{g kg}^{-1}}$	$\frac{V}{\mu\text{V}}$	$\frac{V/C}{\mu\text{V kg g}^{-1}}$	M	$M - M_1$	% of 2 : 2 complex	$\frac{m}{\text{mol kg}^{-1}}$	K_{21}	δ_{calc}*/Hz
0·0466	12·73	352·7	27·70	311·38	38·16	14	0·0352	50·38	1178
0·0699	19·11	498·4	26·08	327·71	54·49	20	0·0467	58·21	1223
0·0931	25·44	638·1	25·08	337·66	64·44	23	0·0576	58·62	1248
0·1171	31·99	778·0	24·32	344·88	71·66	26	0·0684	56·87	1266
0·1406	38·42	897·4	23·36	355·66	82·44	30	0·0754	62·57	1291
0·1633	44·62	1032	23·13	355·87	82·65	31	0·0874	54·87	1292
0·2106	57·55	1280	22·24	362·94	89·72	33	0·1062	51·32	1308
0·2321	63·41	1357	21·40	373·82	100·60	37	0·1072	59·93	1330
0·2875	78·54	1603	20·41	382·81	109·59	40	0·1229	60·25	1347
0·3508	95·84	1888	19·70	385·75	112·53	41	0·1461	53·34	1353
0·4055	110·79	2061	18·60	398·65	125·43	46	0·1504	62·80	1377
0·4661	127·35	2266	17·79	405·31	132·05	48	0·1622	64·52	1389
0·5192	141·84	2416	17·03	412·90	138·01	51	0·1679	69·99	1401
0·5851	159·86	2598	16·25	419·04	145·82	54	0·1779	72·22	1411
0·6448	176·18	2705	15·35	430·48	157·26	58	0·1736	88·15	1429
0·7033	192·15	2844	14·80	433·15	159·94	59	0·1838	86·80	1433
0·7554	206·38	2943	14·26	437·25	164·03	60	0·1885	90·42	1440
0·8161	222·95	3063	13·74	438·91	165·69	61	0·1999	87·14	1442

* From equation (6) with $\delta_{1:1} = 1051$ and $\delta_{2:2} = 1569$ Hz.

TABLE 2

Summary of v.p.o. results and calculated H-bond chemical shifts for the lepidine *N*-oxide complex with monochloroacetic acid in toluene at 27 °C

$\frac{x}{\text{mol kg}^{-1}}$	$\frac{C}{\text{g kg}^{-1}}$	$\frac{V}{\mu\text{V}}$	$\frac{V/C}{\mu\text{V kg g}^{-1}}$	M	$M - M_1$	% of 2 : 2 complex	$\frac{m}{\text{mol kg}^{-1}}$	K_{21}	δ_{calc}*/Hz
0·0117	2·96	100·6	33·98	257·39	3·70	1	0·0113	14·36	959
0·0467	11·84	385·0	32·53	265·49	11·80	5	0·0425	13·11	983
0·0700	17·76	563·5	31·73	269·88	16·19	7	0·0616	12·18	998
0·0932	23·64	731·7	30·95	274·34	20·65	8	0·0792	12·22	1007
0·1165	29·56	894·4	30·26	278·18	24·49	10	0·0960	12·22	1018
0·1401	35·54	1057	29·75	280·47	26·78	10	0·1133	11·55	1023
0·2094	53·13	1484	27·93	290·93	37·26	15	0·1557	12·24	1049
0·2333	59·18	1617	27·32	294·73	41·04	16	0·1684	12·65	1057
0·3496	88·68	2200	24·81	309·88	56·19	22	0·2227	14·24	1090
0·4075	103·37	2456	23·76	315·62	61·93	25	0·2475	14·61	1102
0·4658	118·16	2674	22·63	323·64	69·95	28	0·2645	16·14	1117
0·5246	133·09	2857	21·47	332·55	78·86	32	0·2759	18·81	1134
0·5823	147·71	3013	20·40	341·11	87·45	34	0·2838	20·91	1150
0·6415	162·74	3190	19·60	345·60	91·91	36	0·3002	21·88	1156
0·6982	177·12	3332	18·81	350·61	96·92	38	0·3121	22·51	1164
0·7578	192·25	3512	18·27	350·83	97·16	38	0·3381	20·93	1165
0·8155	206·87	3670	17·74	351·13	97·44	38	0·3629	19·66	1165

* From equation (6) with $\delta_{1:1} = 949$ and $\delta_{2:2} = 1339$ Hz.

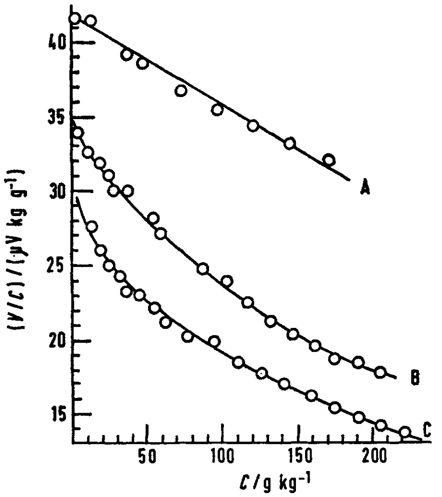

FIGURE 1 Plots of V/C against C for A, benzil; B, lepidine *N*-oxide,$HO_2C{\cdot}CH_2Cl$; and C, lepidine *N*-oxide,$HO_2C{\cdot}CF_3$ at 27 °C in toluene. For curve A, $V/C = 41{\cdot}7749 - 0{\cdot}0587C$

The resonance attributed to H-bond protons have a marked concentration-dependence. This behaviour is that expected from a system in which protons are present in various molecular species which are in rapid equilibrium. The concentration-dependence reflects changes in the relative amounts of these molecular species. Huggins, Pimentel, and Shoolery[3] have shown that such a system can be studied advantageously by the n.m.r. technique. In the case where two species, 1 : 1 and 2 : 2 complexes, are in equilibrium, the observed shift of δ of H-bond protons is given by the expression[4] (6), where $\delta_{1:1}$ and $\delta_{2:2}$ are the characteristic shifts for

$$\delta = \frac{m}{x}\,\delta_{1:1} + \frac{x - m}{x}\,\delta_{2:2} \qquad (6)$$

1 : 1 and 2 : 2 complexes, m the number of moles of complexes in the 1 : 1 form, and x the total number of

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[3] C. M. Huggins, G. C. Pimentel, and J. N. Schoolery, *J. Phys. Chem.*, 1956, **60**, 1311.

[4] J. C. Davis, jun., and K. S. Pitzer, *J. Phys. Chem.*, 1960, **64**, 886.

moles of complexes used to make up the solution. Since m is known from v.p.o. data, it can be substituted in equation (6) along with the measured δ for that solution. The unknown quantities $\delta_{1:1}$ and $\delta_{2:2}$ can then be obtained by solving any such equations for two different complex solutions simultaneously. Unfortunately, there are some differences in concentrations used in v.p.o. and n.m.r. measurements. Nevertheless we have solved 60 pairs of such equations. The average values of $\delta_{1:1}$ and $\delta_{2:2}$ are in Table 3. Next the average

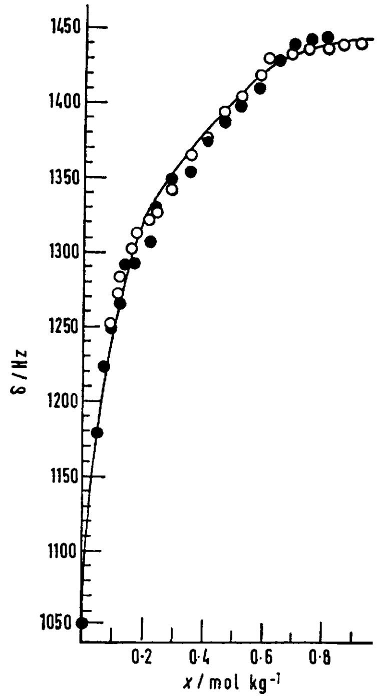


FIGURE 2 H-Bond shift in lepidine N-oxide,$HO_2C{\cdot}CF_3$ as a function of concentration; ○, observed; ●, calculated

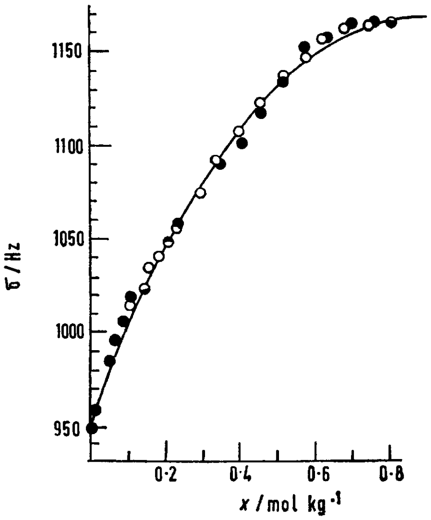


FIGURE 3 H-Bond shift in lepidine N-oxide,$HO_2C{\cdot}CH_2Cl$ as a function of concentration; ○ observed; ●, calculated

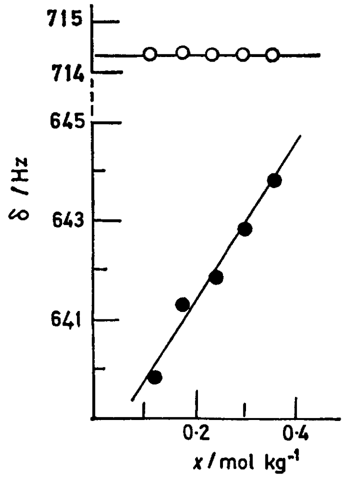


FIGURE 4 The ring proton shifts of lepidine N-oxide as a function of concentration; ○, proton 8; ●, proton 2. From the graph σ_2 = 638·09 + 15·95x

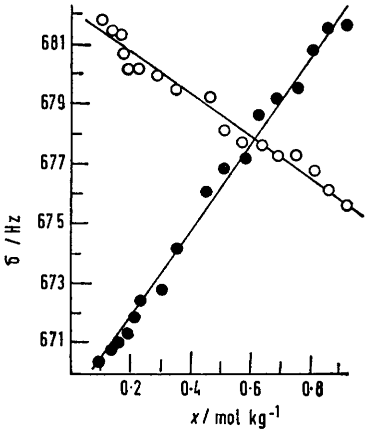


FIGURE 5 The ring proton shifts of lepidine N-oxide,$HO_2C{\cdot}CF_3$ as a function of concentration; ○, proton 8; δ_8 = 682·11 − 6·93x; ●, proton 2; δ_2 = 668·99 + 14·38x

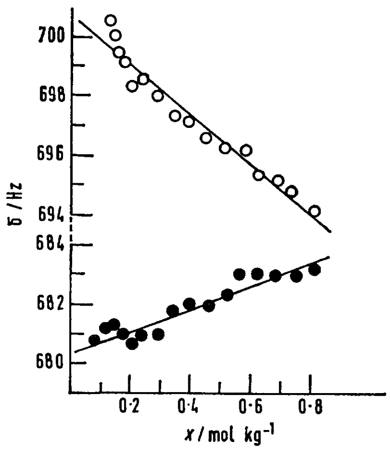


FIGURE 6 The ring proton shifts of lepidine N-oxide,$HO_2C{\cdot}CH_2Cl$ as a function of concentration; ○, proton 8; δ_8 = 700·74 − 8·32x; ●, proton 2; δ_2 = 680·35 + 3·79x

values $\delta_{1:1}$ and $\delta_{2:2}$, and equation (6) were used to calculate δ values for each solution used in v.p.o. measurements. The results are in Tables 1 and 2. In Figures 2 and 3 observed and calculated values of δ are compared. It seems that the calculations employed offer very satisfactory correlations with the observed shifts.

TABLE 3

Calculated H-bond shifts for 1 : 1 and 2 : 2 forms of lepidine *N*-oxide complexes with trifluoroacetic and monochloroacetic acids

Complex	$\delta_{1:1}$/Hz	$\delta_{2:2}$/Hz
Lepidine *N*-oxide,HO_2CCF_3	1051	1569
Lepidine *N*-oxide,HO_2CCH_2Cl	949	1339

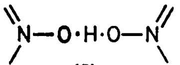
It is widely accepted that the position of a proton resonance signal is shifted toward lower applied fields when the hydrogen atom takes part in a hydrogen bond.[5] The magnitude of the shift can be taken as a qualitative measure of hydrogen-bond strength.[5] The largest downfield shift has been found in maleate monocation.[6] One would expect that the proton resonance shift in potassium hydrogen maleate [6] ($\delta = -15{\cdot}40$ in dimethyl sulphoxide referred to external water; the equivalent of this is 1648 Hz from tetramethylsilane at 80 MHz) should be very close to the 'lower limit' for $O \cdots H \cdots O$ hydrogen bonds. Accordingly, the hydrogen bonds in a 2 : 2 complex of lepidine *N*-oxide with trifluoroacetic acid should be comparable in strength with that of the maleate monoanion. The slightly smaller shift in the investigated complex as compared with maleate monoanion (in sodium hydrogen maleate the observed shift is lower, $\delta = -15{\cdot}03$) may indicate that these hydrogen bonds (both or only one) are not symmetrical. Further, it is expected that the hydrogen bonds in anion and cation are not equivalent. This agrees with some *X*-ray data. According to Speakman the $O \cdots H \cdots O$ distances in potassium hydrogen bistrifluoroacetate [7] and semihydrobromide of 2-picoline *N*-oxide [8] are 2·435 and 2·5 Å, respectively.

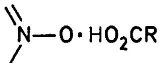
The calculated shift for the 2 : 2 complex of lepidine *N*-oxide with monochloroacetic acid is much lower than that for the complex with trifluoroacetic acid. It is expected that the shift of cation is the same for both complexes and the observed lowering is caused by anion. I.r. studies [9] have shown that CH_2ClCO_2 groups in potassium hydrogen bismonochloroacetate are not equivalent.

The difference between $\delta_{1:1}$ values of investigated complexes seems to be consistent with the pK_a data of the acids.

The further point of interest is the examination of the ring protons shift. In Figures 4—6 concentration-dependences of the 2- and 8-ring proton shifts are shown for free base and complexes. The effect of concentration on the shift in the case of lepidine *N*-oxide is marked for the 2-ring proton (Figure 4). Similar results for pyridine *N*-oxide in benzene [10] have been interpreted as due to the 1 : 1 benzene–pyridine *N*-oxide complex. Since the chemical shift of the 8-ring proton of lepidine *N*-oxide is not affected by concentration, toluene then interacts with the pyridine ring (but not with the benzene ring) by specific solute–solvent interaction.[11]

It appears likely that in the case of lepidine *N*-oxide complexes with halogenoacetic acids toluene interacts with the pyridine ring. In another words, the observed variations of shift of the 8-ring proton in the complexes are affected by the H-bond. As can be seen from Figures 4—6 the signal of the 8-ring proton is shifted to higher fields with increasing of H-bond strength. As was shown above the H-bond in the 2 : 2 complexes (I) is stronger than in 1 : 1 complexes (II). With increasing concentration an increasing percentage of 2 : 2 complex and further upfield shift of the signal of the 8-ring proton is observed. The difference in slope between the investigated complexes (Figures 5 and 6) can be explained very easily by difference in strength of the H-bond.


(I)


(II)

Comparison of the data for the 2-ring proton in these compounds shows any trend reasonably predicted on the basis of an H-bond effect. Evidently there must be some other compensating effect(s).

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[5] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Resonance Spectroscopy,' Pergamon Press, Oxford, 1967.

[6] S. Forsen, *J. Chem. Phys.*, 1959 **31**, 852.

[7] L. Goldič and J. C. Speakman, *J. Chem. Soc.*, 1965, 2530.

[8] H. H. Mills and J. C. Speakman, *Proc. Chem. Soc.*, 1963, 216.

[9] Z. Dega-Szafran, *Bull. Acad. polon. Sci. ser. sci. chim.*, 1968, **16**, 115.

[10] H. H. Perkampus and U. Krüger, *Z. phys. Chem.* (*Frankfurt*), 1967, **55**, 202.

[11] J. Ronayne and D. H. Williams, in 'Annual Review of NMR Spectroscopy,' vol. 2, ed. E. F. Mooney, Academic Press, New York, 1969.