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A CALORIMETRIC AND PMR STUDY OF THE INTERACTION BETWEEN HYDROGEN CHLORIDE AND DIMETHYLACETAMIDE, TETRAMETHYLUREA AND DIMETHYLSULPHOXIDE IN 1,2-DICHLOROETHANE

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Abstract—The interaction between HCl and dimethylacetamide (DMA), tetramethylurea (TMU) and dimethylsulphoxide (DMSO) in 1,2-dichloroethane solution has been studied. The enthalpies of formation of the 1:1 complexes have been determined and the equilibrium constants and enthalpy changes for the association of HCl to DMA·HCl and TMU·HCl to form the 1:2 complexes have been derived from calorimetric measurements.

The acidic proton chemical shifts in the 1:1 complexes were observed at considerably lower field than those reported for the protonated compounds.

The 1:1 complexes are described as strong, hydrogen bonded complexes in which HCl interacts at the O atom. In the 1:2 complexes the second HCl molecule is considered to associate at the N atom. Evidence of increased long range proton coupling and at the same time decreased rotational barrier about the N—C(O) bond in DMA·2HCl give support to this interpretation.

INTRODUCTION

THE system HCl–$SbCl_5$ functions as a strong Brönsted acid in the presence of proton accepting substances, D, and the two ionic complexes $[DH]^+SbCl_6^-$ and $[D_2H]^+$-$SbCl_6^-$ are formed in the solid state and in solution.[1,2] D represents weak organic bases such as ethers, ketons, amides, sulphides etc. The $[D_2H]^+$ cation contains two base molecules joined by a strong, probably symmetrical, H-bond. In a previous paper, enthalpies of formation and some PMR spectral parameter values were reported for the protonated hexachloroantimonate complexes of DMA, TMU, DMSO and EtOAc in 1,2-dichloroethane.[2]

To obtain information about the acidic properties of molecular HCl in the absence of $SbCl_5$, we have studied the interaction between HCl and DMA, TMU and DMSO in the same solvent. These systems could be studied conveniently by reaction calorimetry while the interaction with EtOAc and compounds of comparable base strength is too weak to make a quantitative study practicable.

Solid adducts of HCl of the composition 2D · HCl are known to exist in addition to the 1:1 adducts with *e.g.* acetamide,[3] methylacetamide[4] and urea.[5] The acetamide hemihydrochloride, $2CH_3CONH_2 \cdot HCl$, has been found to contain a hydrogen diacetamide cation with the hydrogen located midway between the two O atoms.[6] The 2:1 adducts may accordingly be described as salts with interaction at the O

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atoms and with complete proton transfer. Strong acids like $HClO_4$, and especially complex acids like $HF–SbF_5$ and $HF–PF_5$, give the same type of 2:1 salts of strongly, probably symmetrical H-bonded cations.[3, 7, 8]

The question of the preferred site of interaction in the solid D•HCl adducts of amides and ureas has not been definitely settled as there is, to our knowledge, no unambiguous determination of the molecular structure of such an adduct. NMR evidence for O-coordination in amide-protonating acid adducts in solution,[9] and the fact that protonation is at the carbonyl oxygen in the 1:1 HNO_3 salts of urea[10] and methylurea,[11] give support, however, to the interpretation that interaction is at oxygen also in the solid HCl adducts. The type of bonding in these adducts has not been established and it is questionable if they are best described as salts or as hydrogen bonded complexes.

RESULTS

Results of the calorimetric measurements of addition of HCl in 1,2-dichloroethane solution to a solution containing the electron pair donor compound, reaction 1, are summarized in column two of Table 1.

$$\mathrm{D(soln) + HCl(soln) \rightarrow D \cdot HCl(soln)} \qquad \Delta H_1 \qquad (1)$$

The concentration of HCl was 0·013 to 0·015 mol . l^{-1} in these experiments and the enthalpy changes were calculated per mole of HCl. The DMA concentration was varied between 0·025 to 0·30 mol . l^{-1} and no obvious trend was observed in the results of the eight experiments performed. Four experiments with TMU (0·13 to 0·19 mol . l^{-1}) and six with DMSO (0·21 to 0·43 mol . l^{-1}) gave the mean values shown in Table 1. The random errors, which are expressed as the single standard deviation of the means, are mostly due to variations in HCl concentration between the various ampoules.

TABLE 1. THERMODYNAMIC QUANTITIES FOR THE FORMATION OF THE D•HCl AND D•2HCl COMPLEXES IN 1,2-DICHLOROETHANE

D	$-\Delta H_1$/kJ, mol^{-1}	K_2/l . mol^{-1}	$-\Delta H_2$/kJ . mol^{-1}
DMA	58·5 ± 0·5	10·2 ± 1·0	31·0 ± 1·0
TMU	58·5 ± 0·5	20·3 ± 2·0	32·5 ± 1·5
DMSO	44·9 ± 0·5	—	—

Results of calorimetric measurements of dissolving liquid DMA and TMU, respectively, in 1,2-dichloroethane solution containing a varying excess of HCl are indicated in Fig 1. The moderate variations in the concentrations of DMA (0·0100 to 0·0135 mol . l^{-1}) and TMU (0·0077–0·0093 mol . l^{-1}) influenced ΔH(app) only to a minor extent. The ΔH(app) values have been corrected for enthalpies of solution of the bases using the value of − 3·81 kJ . mol^{-1} for DMA and − 4·39 kJ . mol^{-1} for TMU.[12] The values have also been corrected for the evaporation of HCl caused by the escaping air bubble from the incompletely filled ampoules. The corrections were calculated using a value of − 15·0 kJ . mol^{-1} for the enthalpy of solution of HCl.[13] Calorimetric experiments of breaking ampoules containing known amounts of pure solvent verified the corrections. The found results were 0·55 ± 0·10 (calc. 0·52) and 0·74 ± 0·07 (calc. 0·81) joules per ml air space with HCl conc of 0·210 and 0·263 mol . l^{-1}, respectively. Due to this evaporation effect, the systems were not studied at HCl conc. higher than 0·24 mol . l^{-1}. The error in the individual ΔH(app) values is estimated to be 0·25 kJ . mol^{-1}.

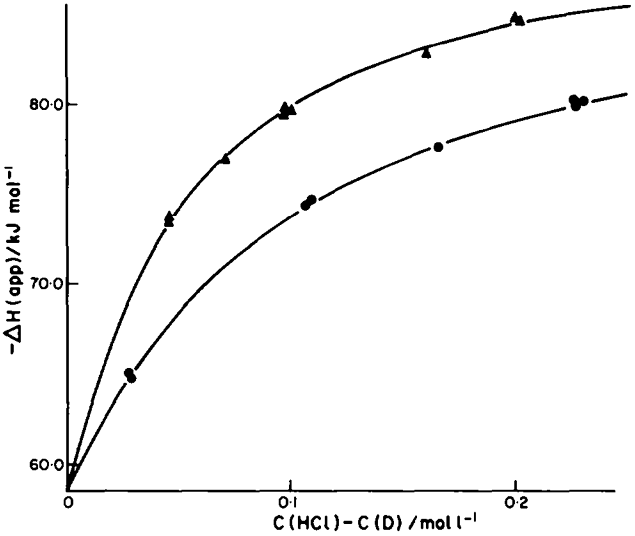

FIG 1. Apparent molar enthalpy changes for reaction 3 against excess HCl. c(HCl) and c(D) denote the initial concentrations of HCl and DMA or TMU. The continuous curves represent calculated values and ● experimentally determined values for DMA and ▲ for TMU.

The contamination of water is estimated to have been less than 0·001 mol . l^{-1} in these experiments. The influence of water is difficult to judge but we find it unlikely that the results could be seriously affected.

Under the conditions of the calorimetric experiments a second complex, D · 2HCl, is formed, reaction 2.

$$\mathrm{D \cdot HCl(soln) + HCl(soln) \rightarrow D \cdot 2HCl(soln)} \qquad \Delta H_2 \qquad (2)$$

The actual experiment can then be described by reaction 3.

$$\mathrm{D(soln)} + (1+\alpha)\mathrm{HCl(soln)} \rightarrow (1-\alpha)\mathrm{D \cdot HCl(soln)} + \alpha \mathrm{D \cdot 2HCl(soln)} \quad \Delta H(\mathrm{app}) \quad (3)$$

$$\Delta H(\mathrm{app}) = \Delta H_1 + \alpha \cdot \Delta H_2 \qquad (4)$$

The association constant for reaction 2 is defined by equation (5), where c(D) and c(HCl) denote the initial concentrations of donor and HCl, respectively.

$$K_2 = \alpha/(1-\alpha)\,\{c(\mathrm{HCl}) - (1+\alpha)c(\mathrm{D})\} \qquad (5)$$

Combination of Eqns (4) and (5) gives the relation

$$(\Delta H_2)^2 - \Delta H_2\{\Delta H(\text{app}) - \Delta H_1\}\{c(\text{HCl}) + K_2^{-1}\}/\{c(\text{HCl}) - c(\text{D})\} \\ + \{\Delta H(\text{app}) - \Delta H_1\}^2 . c(\text{D})/c(\text{HCl}) - c(\text{D}) = 0 \qquad (6)$$

For the evaluation of the values of K_2 and ΔH_2 the error sum

$$\Sigma\delta^2 = \sum_{i=1}^{k} \{(\Delta H(\text{app})_i - \Delta H_1) - (\Delta H(\text{app})_i - \Delta H)_{\text{calc}}\}^2 \qquad (7)$$

was calculated from eight measured values of ΔH(app) with DMA and nine with TMU for an array of K_2 and ΔH_2 values. The sets of values of the parameters which minimize function (7) are shown in the third and fourth columns of Table 1. The given error limits were estimated from analysis of $\Sigma\delta^2$ as a function of the parameter values. A Univac 1108 computer was used for the calculations.

The continuous curves in Fig. 1 represent $-\Delta H$(app) as a function of HCl concentration calculated for a DMA concentration of 0·0117 mol.l^{-1} and a TMU concentration of 0·0085 mol.l^{-1}, using the parameter values shown in Table 1. The agreement between calculated and experimentally determined values is good.

The following $-\Delta H$(app) values were found from experiments on the DMSO–HCl system: 48·7 kJ.mol^{-1} for c(D) 0·018 and c(HCl) 0·12 mol.l^{-1} and 53·1 kJ.mol^{-1} for c(D) 0·012 and c(HCl) 0·21 mol.l^{-1}. The ΔH values have been corrected for enthalpies of solution of DMSO ($-$1·45 kJ.mol^{-1})^2 and vaporization of HCl. The increase in the measured $-\Delta H$ values with increasing HCl concentration is lower in this system than in the DMA and TMU systems. A $-\Delta H$(app) value of 40·0 kK.mol^{-1} was found for c(D) 0·011 and c(HCl) 0·042 mol.l^{-1}. This value, being 4·9 kJ.mol^{-1} lower than the $-\Delta H$ value found for the formation of DMSO·HCl, indicates that the association constant is not large enough to give complete conversion to the 1:1 complex under these conditions.

NMR. In spectra recorded at -20°C of solutions containing 0·3 to 1·1 mol.l^{-1} of DMA and 0·3 mol.l^{-1} of HCl (7 samples), a low field peak ascribed to the acidic proton was observed at δ 16·1 ± 0·1. Somewhat varying chemical shift values and peak widths were observed for the different samples and the scatter was increased at 37°C. There was no obvious correlation between the results and the composition of the samples. At 37°C the acidic proton was observed at δ 15·4 ± 0·2.

The exchange was rapid between complexed and excess DMA and the resulting spectra showed only one peak from the aminomethyl groups. The chemical shift values shown in Table 2 of the acetyl and aminomethyl protons in the DMA·HCl complex were calculated under the assumption that the 1:1 complex is the only complex formed in solutions containing DMA in excess.

In spectra recorded at 37°C of HCl solutions containing TMU and DMSO in excess the acidic proton was observed at δ 14·0 and δ 12·8, respectively. The peak in the TMU spectrum was fairly broad but became narrow at -20°C (δ 14·1). The chemical shift of the acidic proton in the DMSO solution moved to higher field in standing of the sample, but the peak remained narrow and of seemingly the same intensity. Indications of slow secondary reactions were also observed in the reaction calorimetric experiments.

The spectrum of DMA in 1,2-dichloroethane solution containing excess HCl (c(DMA) 0·44 and c(HCl) 1·25 mol.l^{-1}) shown in Fig 2 is interpreted as a quartet centered at δ 3·26, arising from the dimethylamino group and a septet at δ 2·62 from the acetylmethyl group. The structure of the latter signal, which is due to the long range coupling to the aminomethyl protons, proves the magnetic equivalence of the two aminomethyl groups. The long range coupling constant, $^5J_{H-H}$, was observed to be 0·6 Hz. A narrow peak of the acidic proton (δ 8·9) was also observed in the above mentioned spectrum. Due to rapid exchange, the shift is averaged over the various acidic species in the solution. The chemical shift values for DMA in the 1:2 complex shown in Table 2, were derived using the K_2 value given in Table 1 to calculate the composition of the solution.

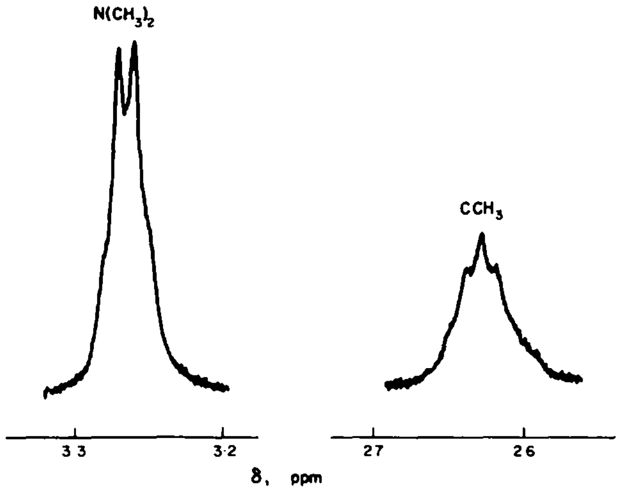

Fig 2. 60 MHz PMR spectrum of DMA • 2HCl in equilibrium with a small amount DMA • HCl in 1,2-dichloroethane at 37°C. The chemical shift parameter is expressed in δ (ppm) relative internal TMS.

Table 2. Chemical shifts and coupling constants in DMA and its proton acid adducts in 1,2-dichloroethane at 37°C. The chemical shifts were measured relative that of the solvent and recaltulated to δ in ppm relative internal TMS

	CCH_3	$N(CH_3)_2$ mean value	$^5J_{H-H}$/Hz
DMA	1·98	2·90	unresolved
DMA • HCl	2·50	3·10	0·6
DMA • 2HCl	2·64	3·32	0·6
$[DMAH]^+SbCl_6^-$[a]	2·78	3·44	~0·3(cis); 1·0(trans)
$[(DMA)_2H]^+SbCl_6^-$[a]	2·41	3·25	not observed

[a] From ref. 2.

PMR spectra at 37°C of DMA in the same solvent show two peaks, somewhat broadened but without resolved long range coupling, from the Me_2N group and one peak from the Me—C group.

DISCUSSION

There are pronounced differences between the complexes formed in the D–HCl and D–HCl–$SbCl_5$ systems in solution, although analogous adducts are apparently formed in the solid state. We have found no evidence for the existence of a 2DMA · HCl complex in 1,2-dichloroethane solution, neither from calorimetric nor from NMR experiments. The TMU and DMSO systems have been less thoroughly studied but it is judged unlikely that strong 2D · HCl complexes are formed in solution.

The formation of the DMA · HCl and TMU · HCl complexes are quite exothermal but far less than for the corresponding $[DH]^+SbCl_6^-$ complexes. The association constants are large enough ($> \sim 10^3$ l/mol) to give complete conversion to the HCl complexes under the conditions of the calorimetric experiments. The interaction of DMSO with HCl as well as with HCl–$SbCl_5$ is weaker than that of DMA and TMU.[2]

The acidic proton chemical shifts are observed at a considerably lower field in the D · HCl complexes than in the protonated compounds in strongly acidic media or in the $[DH]^+SbCl_6^-$ complexes, Table 3. As can be seen from the table, the D · <u>H</u>Cl proton shifts are in fact closer to the low field shifts in the strongly H-bonded cations in the $[D_2H]^+SbCl_6^-$ complexes. Interaction is considered to take place at the oxygen atom in the D · HCl complexes as well as in the $[DH]^+$ and $[D_2H]^+$ complexes.

TABLE 3. CHEMICAL SHIFTS OF THE ACIDIC PROTON IN SOME PROTONATED COMPOUNDS AND PROTON ACID ADDUCTS

	δ/ppm	acid system or solvent	T/°C	Lit. ref.
$MeNH(H)COH^+$	10·5	HSO_3F	−85	14
$Me_2N(H)COH^+$	10·0	HSO_3F	−80	15
$DMAH^+$	9·8	HSO_3F	−79	15
$DMSOH^{+a}$	6·8	HSO_3F-SbF_3-SO_2ClF	−80	16
$MeNH(H)CO \cdot HCl$	15·9	sulpholane	room temp.	9
$Me_2N(H)CO \cdot HCl$	13·9	2-nitropropane	room temp.	9
DMA · HCl	15·4	$C_2H_4Cl_2$	37	this work
TMU · HCl	14·0	$C_2H_4Cl_2$	37	this work
DMSO · HCl	12·8	$C_2H_4Cl_2$	37	this work
$[DMAH]^+SbCl_6^-$	9·4	$C_2H_4Cl_2$	37	2
$[TMUH]^+SbCl_6^-$	7·7	$C_2H_4Cl_2$	37	2
$[(DMA)_2H]^+SbCl_6^-$	18·7	$C_2H_4Cl_2$	37	2
$[(TMU)_2H]^+SbCl_6^-$	16·2	$C_2H_4Cl_2$	37	2
$[(DMSO)_2H]^+SbCl_6^-$	14·6	$C_2H_4Cl_2$	37	2

[a] Interpreted as sulphur protonation by the original authors.

From the results of the calorimetric experiments it is concluded that DMA · 2HCl and TMU·2HCl complexes are formed in solutions containing excess of HCl. Also in the DMSO–HCl system secondary, although seemingly weaker, interactions were observed. The obvious second site of interaction in DMA and TMU is the N atom. In a recent paper it was concluded that medium effects associated with cation hydration cause a changeover from O-protonation of amides in anhydrous acid media to N-protonation in largely acid media.[17] Such a changeover indicates that the difference between the "intrinsic" basicities of the O and N atoms cannot be too large. PMR spectra show that in DMA·2HCl there is increased long range proton coupling and at the same time decreased rotational barrier about the N—C(O) bond compared to unbound DMA.

Interaction of the second HCl molecule at the amino group will increase the tetrahedral character of nitrogen and thereby counteract the strengthening of the conjugation resulting from O-co-ordination of the first HCl and make possible the rapid rotation about the amide bond. Other models of the 1:2 complex in which the second HCl molecule interacts at the O atom or associates at the first HCl would lead to strengthened (or unchanged) resonance interaction with the free pair of electrons on nitrogen in the amide group and are therefore not consistent with the observed onset of free rotation of the amino group.

The formation of the quite stable 1:2 complexes in 1,2-dichloroethane solution containing only modest excess of HCl is different from the behaviour of the protonated bases. Aliphatic amides and ureas have pK_{BH^+} values of about zero[18] but still in 100% sulphuric acid ($H_0 = -11{\cdot}0$) amides[19] and urea[20] have been found to be monoprotonated and tetraethylurea diprotonated to only 10%.[21]

The low field shifts of the acidic proton in the 1:1 complexes and the formation of the 1:2 complexes of DMA and TMU make us believe that the HCl complexes in 1,2-dichloroethane solution are best described as hydrogen bonded complexes. The weak solvating properties of the solvent will counteract charge separation and make the formation of ion pairs less favourable. The formation of 1:2 complexes is not hampered in this case by electrostatic repulsion as in the formation of diprotonated cations.

The enthalpy changes are, within the experimental errors, equal for DMA and TMU for the formation of both the 1:1 and 1:2 complexes, revealing a striking similarity between the basic properties of not only the carbonyl groups but also of the amino groups in DMA and TMU. It is suggestive to compare the equilibrium constants for the formation of the 1:2 complexes. In the association of the second HCl molecule there is one coordination site in DMA while there are two equivalent N atoms for HCl to choose between in TMU. In the dissociation process, the two complexes are comparable and accordingly the difference between the observed K_2 values should include the statistical factor 2, see *e.g.* ref. 22. The found K_2(TMU)/K_2(DMA) ratio of 2 may thus be of statistical origin.

EXPERIMENTAL

Materials and *Apparatus* and *measurements* see applicable parts of *Experimental* in ref. 2.

Units of measurements. The results of the calorimetric experiments are expressed in terms of absolute joules and refer to the isothermal process at 25°C.

The chemical shift values were determined relative that of the solvent with the usual side band technique. The values were recalculated to δ values relative internal TMS using a δ value of 3·76 for 1,2-dichloroethane.

The value was determined from a solution of TMS in 1,2-dichloroethane and it is assumed that the chemical shift of the solvent did not vary with the composition of the samples.

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