

Gas Phase Chemistry of Dipole Stabilized Carbanions Derived from *N,N*-Dimethylthioformamide and *N,N*-Dimethyl-*N*-nitrosamine

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The gas phase chemistry of the formal dipole stabilized carbanions derived from *N,N*-dimethylthioformamide (DMTF) and *N,N*-dimethyl-*N*-nitrosamine (DMNA) has been investigated with the use of Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry. The $\Delta G_{\text{acid}}^{\circ}$ values for the various positions in DMTF are reported to be 1561 ± 8 kJ/mol, which means that the two methyl groups are close in acidity to each other. In the case of DMNA, it is concluded that the two methyl groups are different with respect to gas phase acidity; the acidity of the most acidic methyl group is measured to be $\Delta G_{\text{acid}}^{\circ} = 1567 \pm 8$ kJ/mol. These results are compared with those previously obtained for the formal dipole stabilized carbanions derived from methyl formate and *N,N*-dimethylformamide.

Knowledge of the structure, stability and reactivity of free carbanions in the gas phase is not only of theoretical importance, but can also increase the understanding of reactions involving organometallic compounds which are frequently used in synthesis. The gas phase acidity of various acids has been measured during the last decade with the use of methods such as Ion Cyclotron Resonance (ICR),^{1,2} Flowing Afterglow (FA)³ and High Pressure Mass Spectrometry (HPMS).⁴ Recently, reports have appeared on the gas phase chemistry of α -heteroatom carbanions,^{5,6} homoenolate anions,⁷⁻⁹ and dipole stabilized carbanions derived from methyl formate (MF) and *N,N*-dimethylformamide (DMF).¹⁰⁻¹³ MF and DMF were selected for study partly because recent *ab initio* calculations have indicated that the primary carbanions derived from these compounds and *N*-methylformamide prefer the *anti* over the *syn* geometry.¹⁴ Lithiation of *tert*-amides, however, proceeds *syn* to the oxygen atom.¹⁴⁻¹⁶ This has been explained by association between the lithium atom and the carbonyl oxygen atom.¹⁴⁻¹⁶ In the gas phase, it is observed that the $[M-H]^{-}$ ion from $\text{DCON}(\text{CH}_3)_2$ exchanges two hydrogen atoms for deuterium atoms relatively fast with ND_3 , whereafter the exchange process becomes slower.¹⁰ This result indicates that the two methyl groups in DMF have a different gas phase acidity, but whether the *anti* or the *syn* methyl group is the more acidic cannot be concluded.

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This report is concerned with the formal dipole stabilized carbanions derived from *N,N*-dimethylthioformamide (DMTF) and *N,N*-dimethyl-*N*-nitrosamine (DMNA). These compounds were chosen in order to compare the gas phase acidity of methyl groups bonded to various polar functional groups. Furthermore, it is possible to generate from both compounds carbanions which may adopt the *anti* or the *syn* geometry. The experiments have been performed with the use of Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry.¹⁷⁻¹⁹

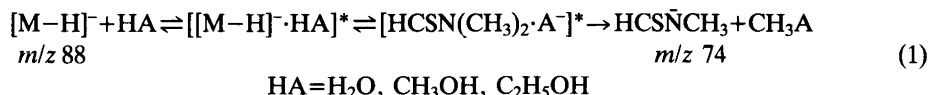
EXPERIMENTAL

The experiments were performed with a home-made FT-ICR instrument. The basic hardware,²⁰ software,²¹ and the general operation procedure²²⁻²⁴ have been described previously. The total pressure was kept in the range 0.5 to 1.0·10⁻⁴ Pa. The ratio of the partial pressures of DMTF or DMNA, NH₃ or N₂O and HA (conjugate acid of the anion of interest) was generally 0.5-1:1:0.5-1. The primary reactant ions NH₂⁻, HO⁻ and O⁻ were generated by dissociative resonance capture of electrons (electron energy in brackets) by NH₃ (5 eV), H₂O (6 eV, HO⁻ is formed via H⁻) and N₂O (1.2 eV).

Most of the chemicals used were commercially available. The inlet and the vacuum system of the FT-ICR instrument were fluxed 3 times with CD₃OD before the deuterium content of this sample was measured to be 83 % *d*₄ and 17 % *d*₃ by EI (*p*(CD₃OD)=8·10⁻⁶ Pa, electron energy=12 eV, trapping time²²⁻²⁴=10 ms). The DCSN(CH₃)₂ sample (DMTF-*d*₁) was prepared by reaction between ((CH₃)₂CH)₂NLi and DMTF followed by quenching with D₂O.²⁵ The product was purified with preparative GC (column OV 17, temperature 160 °C) and the position of the deuterium was checked by NMR. The label content was measured to be 89 % *d*₁ by field ionization (Varian MAT 711 double focusing mass spectrometer) and FT-ICR mass spectrometry.

RESULTS

N,N-Dimethylthioformamide (DMTF). The NH₂⁻, HO⁻ and CH₃O⁻ ions react with DMTF exclusively through proton abstraction, whereas C₂H₅O⁻ reacts by proton abstraction and hydride ion transfer.²⁶ Proton transfer is reversible in the RO⁻-ROH-DMTF systems (R=CH₃, C₂H₅). The unspecified gas phase acidity of DMTF is measured to be 1561±8 kJ/mol (the temperature of the system is assumed to be 298 K) relative to CH₃OH ($\Delta G_{\text{acid}}^{\circ}$ =1568±3 kJ/mol)²⁷ and C₂H₅OH ($\Delta G_{\text{acid}}^{\circ}$ =1555±3 kJ/mol).^{27a} The determination of the gas phase acidity is disturbed to some extent by the formation of a HCSN⁻CH₃ ion. This ion is not a primary product, but formed as shown in eqn. (1).²⁸ Part of the [M-H]⁻ ion does



not react to form the *m/z* 74 ion in the NH₂⁻-NH₃-DMTF (≤20 % unreactive ions) and in the HO⁻-H₂O-DMTF (≤14 % unreactive ions) system. The amount of unreactive ions is negligible in the CH₃O⁻-CH₃OH-DMTF system (≤2 % unreactive ions). These results indicate that proton abstraction from DMTF may result in an ion mixture, but at present no conclusions can be reached regarding the possible structures of the unreactive ions.

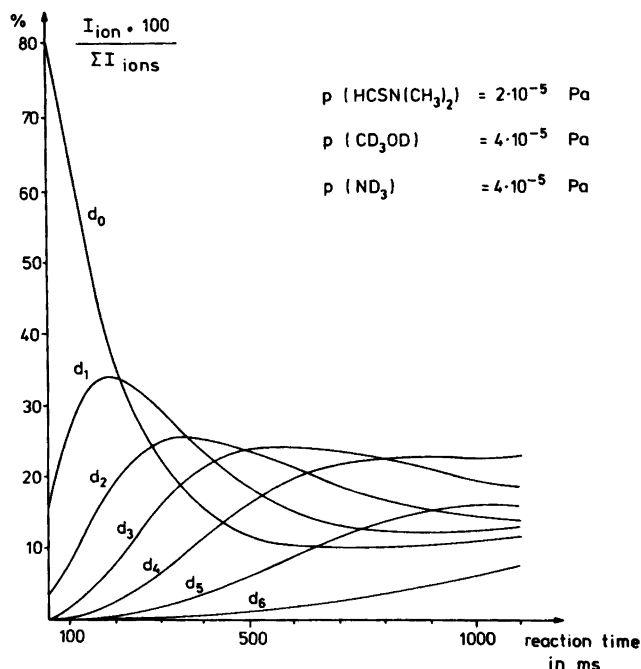


Fig. 1. The hydrogen-deuterium exchange reaction of the $[\text{M}-\text{H}]^-$ ion from DMTF with CD_3OD followed as a function of reaction time. d_0 refers to the $[\text{M}-\text{H}]^-$ ions and d_1 to those $[\text{M}-\text{H}]^-$ ions which have exchanged one hydrogen atom for a deuterium atom, etc. The slight increase in the relative abundance of the $[\text{M}-\text{H}]^-$ (d_0) ions at a reaction time of about 1000 ms is caused by the fact that $\leq 2\%$ of these ions do not react as shown in eqn. (1). The experimental parameters were as follows: magnetic field strength=1.4 Tesla; electron energy=5 eV; emission current=600 nA; recording of m/z 50–300.

No hydrogen–deuterium exchange is observed in the ND_2^- – ND_3 –DMTF system, but all 6 hydrogen atoms in the $[\text{M}-\text{H}]^-$ ions are exchanged in the presence of D_2O or CD_3OD . The results in Fig. 1 show that all hydrogen atoms can be exchanged with the same apparent rate. Furthermore, CH_3O^- reacts with DMTF- d_1 to produce $\approx 89\%$ $[\text{M}-\text{H}]^-$ and $\approx 11\%$ $[\text{M}-\text{D}]^-$ ions, whereas $\text{C}_2\text{H}_5\text{O}^-$ reacts to form $\approx 73\%$ $[\text{M}-\text{H}]^-$ and $\approx 27\%$ $[\text{M}-\text{D}]^-$ ions. The combined results indicate that the various positions in DMTF are close in acidity to each other and that the ΔG_{acid}^0 values are 1561 ± 8 kJ/mol. It can here be mentioned that lithiation of DMTF results exclusively in $\text{LiCSN}(\text{CH}_3)_2$ (see Experimental).²⁵

The results in Fig. 1 and the acidity measurements indicate that proton abstraction from DMTF can lead to a primary carbanion. This is supported by the observation that reaction between the $[\text{M}-\text{H}]^-$ ion from DMTF or DMTF- d_1 and CF_2O , proceeds nearly exclusively through loss of two HF molecules from the collision complex, a reaction which has been observed for a number of primary carbanions.^{29,5,6,10}

N,N-Dimethyl-*N*-nitrosamine (DMNA): Proton transfer is the sole reaction channel observed in the anion (NH_2^- , HO^- , CH_3O^-)–DMNA systems. This process is reversible in the $\text{CH}_3\text{O}^-/\text{CH}_3\text{OH}/\text{DMNA}$ system and the unspecified gas phase acidity of DMNA is measured to be 1567 ± 8 kJ/mol relative to CH_3OH .²⁷ The $[\text{M}-\text{H}]^-$ ion exchanges all 5 hydrogen atoms for deuterium atoms with the same apparent rate in the presence of D_2O .

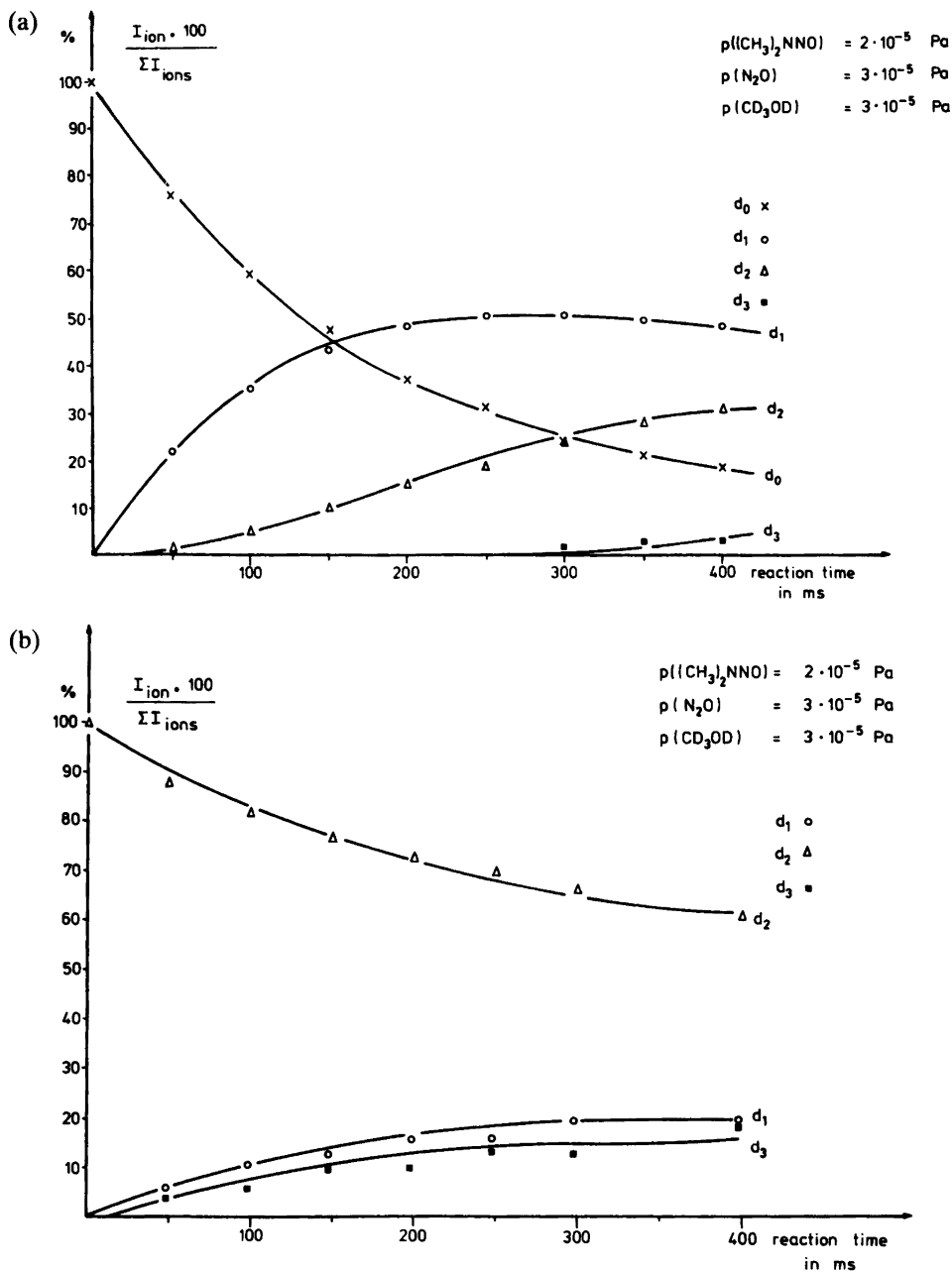


Fig. 2. The hydrogen–deuterium exchange reaction between the conjugate base of DMNA and CD_3OD followed as a function of reaction time. The experiments were performed by first isolating CD_3O^- (see Refs. 21–24), and then allowing this ion to react with DMNA for 300 ms. Subsequently, the d_0 ion (m/z 73, see Fig. 2a) or the d_2 ion (m/z 75, see Fig. 2b) was isolated and allowed to react with CD_3OD under conditions where the CD_3O^- ion was ejected continuously from the cell during the reaction period. The experimental parameters were as follows: magnetic field strength=1.4 Tesla; electron energy=1.2 eV; emission current=400 nA; recording of m/z 50–300.

The same result has previously been obtained in our laboratory with the use of drift-cell ICR.³⁰ The FT-ICR method, however, permits the reactions to be followed as a function of time more accurately. The conjugate base of DMNA reacts with CD₃OD partly by exchange and partly by formation of CD₃O⁻. The relative abundances of the ions observed, therefore, remain constant after a certain time (about 500 ms) with the values being: 42 % (CD₃O⁻, *m/z* 34), 22 % (*d*₀, *m/z* 73), 21 % (*d*₁, *m/z* 74), 13 % (*d*₂, *m/z* 75) and 2 % (*d*₃, *m/z* 76). No significant changes in this distribution are observed when the partial pressures of CD₃OD and DMNA are varied with a factor of 2. The regeneration of CD₃O⁻ disturbs the investigation of the exchange reaction, and in order to observe the exchange more clearly, the CD₃O⁻ ions were ejected continuously from the cell during the reaction time. The results are shown in Fig. 2.

In these experiments, the exchange of those *d*₀ to *d*₂ ions which are not lost due to reactions with CD₃OD giving CD₃O⁻ is observed. It can be seen that the *d*₀ ion exchanges two hydrogen atoms relatively fast (Fig. 2a). In the case of the *d*₂ ion (Fig. 2b) some *d*₃ can be observed, but the amount formed is less than the amount of *d*₁ formed by back exchange with CD₃OH present in the system (see Experimental).

In terms of structure, the results indicate that proton abstraction from DMNA can result in a primary carbanion. Support for this can be found, for example, in the reaction of the [M-H]⁻ ion with N₂O which proceeds through loss of H₂O from the collision complex. This reaction has been observed for several primary carbanions.^{29,31,5,6,10}

DISCUSSION

The general structure of formal dipole stabilized carbanions is shown in eqn. (2) and the extent of dipole stabilization within this simplified picture is determined by the significance of the resonance form shown.¹³



Y=NR, O, S

Z=N=O, C=O, C=S

For the neutral molecules, the importance of this charge separation is reflected in the dipole moment, and the energy barrier towards rotation around the bond between the heteroatom and the functional group. The relevant data for MF, DMF, DMTF and DMNA are collected in Table 1 together with the obtained gas phase acidities.

In principle, the acidities given for DMF, DMNA and DMTF can refer either to one, or to both methyl groups. Previously, it has been concluded on the basis of hydrogen-deuterium exchange reactions, that the two methyl groups of DMF have different gas phase acidities.¹⁰ The results shown in Fig. 2 can be taken to mean that this is also true for DMNA, whereas the results in Fig. 1 indicate that the two methyl groups in DMTF are close to each other in acidity. These statements are based upon the assumption that the methyl groups retain their geometrical relationship with respect to the functional group during the exchange (see Scheme 1 and Table I) and that internal rotation in the ions is slow, relative to the time the ions are trapped in the cell of the instrument. The mechanism of the exchange

Table 1.

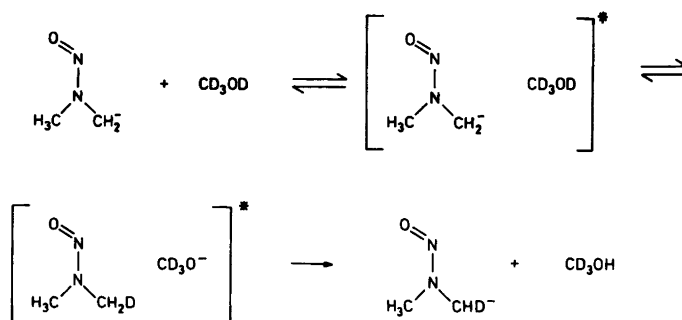
Compound	$\Delta H_{\text{acid}}^{\circ}/\text{kJ mol}^{-1}$	μ_{D}/D	$\Delta G_{\text{internal rotation}}^{\ddagger}/\text{kJ mol}^{-1}$
HCO_2CH_3	(MF) 1665 ± 16^a	1.77^c	50^f
$\text{HCON}(\text{CH}_3)\text{CH}_3$	(DMF) 1635 ± 16^a	3.82^d	81^g
$\text{CH}_3(\text{CH}_3)\text{NNO}$	(DMNA) 1660 ± 8^b	4.01^d	88^h
$\text{HCSN}(\text{CH}_3)\text{CH}_3$	(DMTF) 1594 ± 8^b	4.74^e	101^i

^a Taken from Ref. 11. ^b Estimated using $\Delta G_{\text{acid}}^{\circ}$ values given in the text and taking only symmetry changes into account (see also Ref. 1). ^c For the gas phase. Taken from Ref. 32. ^d In benzene. Taken from Ref. 32. ^e In benzene. Taken from Ref. 33. ^f For the gas phase. Taken from Ref. 34. ^g For the gas phase. Taken from Ref. 35. ^h For the gas phase. Taken from Ref. 36. ⁱ In ortho-dichlorobenzene. Taken from Ref. 37. The value for the gas phase may be somewhat lower, see note g for the case of DMF.

reaction is shown in Scheme 1 for the *anti* form of the $[\text{M}-\text{H}]^-$ ion from DMNA.

Lithiation of dialkyl-*N*-nitrosamines is known to proceed *syn* to the oxygen atom and for *N*-nitrosopiperidines the *syn*-axial form of the organometallic compound is generated.^{38,39} Furthermore, the *syn*-axial hydrogen atom in a conformationally rigid *N*-nitrosamine has been observed to undergo hydrogen-deuterium exchange in $(\text{CH}_3)_3\text{COD}$ containing *tert*-butoxide with a much larger rate constant than the other hydrogen atoms attached to the carbon atoms bonded to the NNO function.⁴⁰ These observations have been rationalized by an overlap between the carbanionic lone-pair and an orbital on the oxygen atom of the NO function in the HOMO of the ion with *syn* geometry.⁴⁰ The same type of interaction could occur in the formal dipole stabilized carbanions derived from MF and DMF. However, as previously mentioned, ab initio calculations indicate that the ions are more stable in the *anti* geometry where destabilizing electrostatic interactions between the carbanionic lone-pair, and the partial negative charge on the oxygen atom are minimal.¹⁴ The present experimental results indicate that the gas phase acidities of the two methyl groups in DMNA are different, but it cannot be concluded whether the *syn* or the *anti* methyl group is the more acidic.

The data in Table 1 show that the methyl group in MF is the least acidic and that the most acidic methyl group in DMNA is ≈ 35 kJ/mol more acidic than the most acidic methyl group in DMF. In the case of DMTF the methyl groups are roughly 40 kJ/mol more acidic than the most acidic methyl group in DMF. This trend in gas phase acidity follows the dipole moments of the neutral molecules (see μ_{D} column in Table 1), although DMNA is more acidic than expected on the basis of this simple relationship. The enhanced acidity of dialkyl-*N*-nitrosamines compared to that of *tert*-amides is also observed in solution and



Scheme 1.

reflected in the facile hydrogen–deuterium exchange of DMNA in D₂O containing sodium deuterioxide.⁴¹ The gas phase acidity of an acid, HA, is given by eqn. (3). For the four

$$\Delta H_{\text{acid}}^{\circ}(\text{HA}) = D(\text{A}-\text{H}) - \text{EA}(\text{A}^{\cdot}) + \text{IP}(\text{H}^{\cdot}) \quad (3)$$

compounds of interest, no data on the relevant bond dissociation energies, D(C–H), are available. It is, therefore, not possible to estimate the extent to which the observed gas phase acidities are determined by changes in the D(C–H) energies and/or the electron affinities, EA, of the radicals corresponding to the formal dipole stabilized carbanions.

The higher acidity of DMNA compared to that of the methyl groups in DMF might be caused by changes in the EA values of the corresponding radicals. If this is true, then it would imply that the NO function exerts a larger stabilizing effect on the carbanion than the CO group. The lack of data on the appropriate D(C–H) energies, however, renders any conclusion regarding this stabilizing effect too uncertain.

For CH₃Y systems where the heteroatoms Y are from the same column of the periodic system, it has been concluded that the gas phase acidity is mainly determined by the EA of the [•]CH₂Y radicals.^{5,6} The observed increase in acidity when going from DMF to DMTF will be caused by an extra stabilizing effect of the sulphur atom in the anion from DMTF, if it is assumed that no significant changes in the D(C–H) energies occur. In the *anti* form of the carbanion, the larger polarizability of sulphur compared to that of oxygen may increase the charge separation [eqn. (2)] and thereby stabilize the system more effectively. In the *syn* form of the carbanion from DMTF a dipole may be induced on the sulphur atom, thus decreasing the electrostatic repulsion between the carbanionic lone-pair and the sulfur atom. In conclusion, the larger polarizability of sulphur may cause the methyl groups in DMTF to be more acidic than the ones in DMF and may account for the observation that the two methyl groups in DMTF are nearly equally acidic in the gas phase.

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