J. Org. Chem. 1993, 58, 2436–2441

Base-Induced Imine-Forming 1,2-Elimination Reactions in the Gas Phase

F. Matthias Bickelhaupt, Leo J. de Koning, and Nico M. M. Nibbering*

Instituut voor Massaspectrometrie, Universiteit van Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands

Received November 5, 1992

The gas-phase reactivity of CH_3NHOCH_3 (*N*,*O*-dimethylhydroxylamine, DHA) and NH_2OCH_3 (*O*-methylhydroxylamine, MHA) toward a series of anionic bases has been studied using the method of Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry. Both DHA and MHA undergo a competing proton abstraction from and nucleophilic substitution reaction on the nitrogen atom. The competition between these processes is governed by the strength of the base used. Unexpectedly, the nucleophilic attack on the nitrogen atom leading to the substitution of the methoxy group is found to be a relatively facile process. This is especially evident in the substitution reactions with *O*-methylhydroxylamine, NH_2OCH_3, where the formation of methoxide ions is much more efficient than in the highly inefficient substitution reactions of dimethyl ether, CH_3OCH_3. Apparently, substitution reactions on the nitrogen atom do not suffer from a very unfavorable activation barrier which is assumed to hamper nucleophilic substitution reactions on carbon atoms in the gas phase. This seems to be supported by high-level density-functional (DF) calculations which indicate that the nucleophilic substitution reactions on the nitrogen atom proceed via an entropically favored less tight, S_N1-like transition state. However, in the reactions of *N*,*O*-dimethylhydroxylamine, CH_3NHOCH_3, the proton abstraction and substitution processes unfavorably compete with a base-induced imine-forming 1,2-elimination. The efficiency of the imine-forming elimination reactions of CH_3NHOCH_3 can be compared favorably with the efficiency of base-induced alkene-forming 1,2-elimination reactions of corresponding simple ethers such as $CH_3CH_2OC_2H_5$.

Introduction

Base-induced alkene-forming 1,2-elimination reactions (eq 1) constitute one of the basic types of reaction in organic chemistry.[1] Since 1927, when Ingold[2,3] introduced the

$$B^- + HC^{\beta}R_2C^{\alpha}R_2L \rightarrow BH + CR_2{=}CR_2 + L^- \qquad (1)$$

concept of "base-promoted olefine-forming elimination reactions", many experimental investigations have been performed on this class of reactions in the condensed phase[4–13] as well as in the gas phase.[14–23] Considerable experience has been gathered concerning the parameters which determine the reaction rates, the product distribution, and the stereochemistry. The nature of base-induced alkene-forming 1,2-elimination reactions is now well understood and interpreted in terms of the concept of the variable transition state (VTS).[1,24] In this concept, reactions are classified according to the geometry of the transition state (TS), which is conceived as being located at one point in a continuous spectrum of mechanistic possibilities. The VTS theory comprises the Bunnet E2H-spectrum,[9,10] i.e., E1cb(-like), synchronous E2, and E1(-like) eliminations involving linear proton transfer, as well as the Winstein–Parker E2H-E2C-spectrum[11–13] in which bent proton transfer may occur with a certain degree of base/C$^{\alpha}$ covalent interaction. Furthermore, stereoelectronic arguments account for the preference of TS structures in which the base and the leaving group are anti- or syn-*periplanar*.[25–27]

In contrast, base-induced heteroalkene-forming 1,2-eliminations have received little attention both in condensed[28–33] and in gas-phase[34–36] mechanistic studies, although in synthetic organic chemistry they represent an important tool to introduce a π-bond between a carbon

---

(1) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*; Plenum Press: New York, 1984; Part A, Chapter 6.

(2) Hanhart, W.; Ingold, C. K. *J. Chem. Soc.* **1927**, 997.

(3) Hughes, E. D.; Ingold, C. K. *Trans. Faraday Soc.* **1941**, *37*, 657.

(4) Gandler, J. R. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1989; Vol. 2, Part I.

(5) Bartsch, R. A.; Závada, J. *Chem. Rev.* **1980**, *80*, 453.

(6) Saunders, W. H., Jr. *Acc. Chem. Res.* **1976**, *9*, 19.

(7) Bartsch, R. A. *Acc. Chem. Res.* **1975**, *8*, 239.

(8) Saunders, W. H., Jr.; Cockerill, A. F. *Mechanisms of Elimination Reactions*; Wiley: New York, 1973; Chapter 1.

(9) Bunnett, J. F. *Angew. Chem.* **1962**, *74*, 731.

(10) Bartsch, R. A., Bunnett, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 408.

(11) Parker, A. J.; Ruane, M.; Biale, G.; Winstein, S. *Tetrahedron Lett.* **1968**, 2113.

(12) Biale, G.; Cook, D.; Lloyd, D. J.; Parker, A. J.; Stevens, I. D. R.; Takahashi, J.; Winstein, S. *J. Am. Chem. Soc.* **1971**, *93*, 4735.

(13) McLennan, D. J. *Tetrahedron* **1975**, *31*, 2999.

(14) Koning, L. J. de; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 1715.

(15) Berkel, W. W. van; Koning, L. J. de; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 7602.

(16) Koning, L. J. de; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1988**, *110*, 2066.

(17) Ridge, D. P.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 637.

(18) Sullivan, S. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 1160.

(19) Sullivan, S. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 5017.

(20) Doorn, R. van; Jennings, K. R. *Org. Mass Spectrom.* **1981**, *16*, 397.

(21) DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, *103*, 5034.

(22) DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1982**, *104*, 6483.

(23) Bierbaum, V. M.; Filley, J.; DePuy, C. H.; Jarrold, M. F.; Bowers, M. T. *J. Am. Chem. Soc.* **1985**, *107*, 2818.

(24) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; Chapter 7.

(25) Bach, R. D.; Badger, R. C.; Lang, T. J. *J. Am. Chem. Soc.* **1979**, *101*, 2845.

(26) Minato, T.; Yamabe, S. *J. Am. Chem. Soc.* **1985**, *107*, 4621.

(27) Minato, T.; Yamabe, S. *J. Am. Chem. Soc.* **1988**, *110*, 4586.

(28) Dayagi, S.; Degani, Y. In *The Chemistry of Carbon–Nitrogen Double Bonds*; Patai, S., Ed.; Wiley: London, 1970; pp 121–124.

(29) Cockerill, A. F.; Harrison, R. G. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: London, 1977; Supplement A, Part 1, Chapter 4.

0022-3263/93/1958-2436$04.00/0

and a heteroatom or between two heteroatoms.[28–33] As an exception, the base-induced *imine*-forming 1,2-elimination reaction (eq 2) has been investigated extensively in the condensed phase during the past decade.[37–43] Extensive

$$B^- + HC^{\beta}R_2N^{\alpha}RL \rightarrow BH + CR_2{=}NR + L^- \qquad (2)$$

studies have been performed on base-induced imine-forming 1,2-eliminations of *N*-chloroamines in the condensed phase.[43] These studies provide convincing evidence that these imine-forming 1,2-elimination reactions are of E2 type. For example, alkoxide-induced imine-forming 1,2-elimination reactions of *N*-chloro-*N*-methylbenzylamines exhibit overall second-order kinetics. Hammett studies indicate that the electron density increases at the β-carbon in going to the transition state (TS). Furthermore, stretching of the C^{β}–H and N^{α}–L bonds in the activated complex is revealed by a considerable primary kinetic H/D isotope and a large leaving group element effect, respectively.[37,38]

However, there are some significant differences between imine- and alkene-forming 1,2-elimination reactions. In the former, a C–N π-bond is formed which is ca. 10 kcal/mol[24,44] stronger than the C–C π-bond which results from the latter. Furthermore, the N–L single bond which has to be broken is about 31 kcal/mol (L = Cl)[24,44] weaker than the C–L single bond. As a result, base-induced imine-forming 1,2-eliminations are considerably more exothermic and have a lower activation enthalpy ($\Delta H^{\ddagger}$) than their alkene-forming analogues (the $\Delta S^{\ddagger}$ values are comparable).[43] Consequently, the reaction rate constants for the imine-forming eliminations of *N*-chloroamines are found to be a factor of about 10^4 higher than the alkene-forming eliminations of the corresponding chloroalkanes.[37,43]

On the basis of the results from Hammett studies it is suggested that the E2 transition state is shifted from E1cb-like for alkene-forming eliminations toward a more central E2 for analogous imine-forming eliminations.

In the present study the feasibility of gas-phase base-induced imine-forming 1,2-eliminations in comparison with competing substitution processes has been explored. To this end the reactivity of *N,O*-dimethylhydroxylamine (DHA) and *O*-methylhydroxylamine (MHA) toward a series of anionic bases has been studied as a function of the strength of the base, under the low-pressure conditions of a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer where association of solvent molecules and/or counter ions is avoided.[45,46] This experimental study is supplemented with quantum chemical calculations using a high-level density-functional (DF) method.[47–52]

Table I. Primary Product Anion Distributions (%) and Overall Second-Order Rate Constants, $k(B^-)$ (10^{-9} cm^3 s^{-1} molecule^{-1}), for Reactions of B^- with *N,O*-Dimethylhydroxylamine (DHA)

		product anion distribn[a]			
B^-	$k(B^-)$	$(DHA - H)^-$	CH_3O^-	$[CH_3O^-, HB]$	$CH_2{=}N^-$
NH_2^-	2.9 ± 0.4[b]	11	56		33
$C_6H_5^-$	*c*	17	49		34
OH^-	3.9 ± 1.4[b]	9	72		19
CH_3O^-	*c*		100		
$C_2H_5O^-$	*c*		100		
F^-	*c*		96	4	
CN^-	0.0				
Cl^-	0.0				

[a] See eq 3a–f. [b] Deviation from average over two independent experiments. [c] Rate constant determination complicated (see Experimental Section).

Experimental Section

The experiments were performed with a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer constructed at the University of Amsterdam and equipped with a 1.4-T electromagnet and a cubic inch cell (De Koning and Nibbering,[14] and references cited therein). The segmented fourier transform (SEFT) procedure[53] was employed to obtain relative ion abundances with an accuracy of better than ±1%. General operating and experimental procedures have been described previously.[14]

The temperature in the cell was around 333 K as measured by a thermocouple on the trapping plate opposite the filament. The total pressure in the different experiments was normally kept below 10^{-4} Pa with a background pressure lower than 5×10^{-7} Pa. The pressure was measured with an ionization gauge placed in a side arm of the main pumping line.

The ionization gauge was calibrated for methane by fitting our rate constant for the reaction $CH_4^{\bullet+} + CH_4 \rightarrow CH_5^+ + CH_3^{\bullet}$ to the average literature value of $(1.11 \pm 0.04) \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}.[54] Absolute pressures were obtained by correction for the sensitivities R_x of the ionization gauge for gases x relative to methane, using the relationship $R_x = 0.36\alpha + 0.30$ of Bartmess and Georgiadis[55] and polarizabilities α from Miller.[56] The determination of overall second-order rate constants $k(B^-)$ for the reactions of B^- with the substrate was complicated by the formation of CN^-, probably due to proton abstraction from traces of HCN, which are considered to result from pyrolysis of nitrogen-containing compounds on the hot filament. This complication can lead to an overestimation of the determined overall rate constants. Therefore, rate constants could be determined only for relatively efficient reactions (Tables I and III).

---

(30) *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M., Scherer, O. J., Eds.; Georg Thieme Verlag: Stuttgart, 1990; in particular Chapter D.4 (Appel, R.), Chapter D.8 (Niecke, E.), and Chapter D.9 (Yoshifuji, M.).

(31) Cullis, C. F.; Fish, A. In *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Wiley: London, 1966; pp 142–143.

(32) Kice, J. L.; Kopczyk-Subotkowska, L. *J. Org. Chem.* **1990**, *55*, 1523 and references cited therein.

(33) Davy, M. B.; Douglas, K. T.; Loran, J. S.; Steltner, A.; Williams, A. *J. Am. Chem. Soc.* **1977**, *99*, 1196 and references cited therein.

(34) Thomas, D. A.; Bloor, J. E.; Bartmess, J. E. *J. Am. Soc. Mass Spectrom.* **1990**, *1*, 295.

(35) Grabowski, J. J.; Zhang, L. *J. Am. Chem. Soc.* **1989**, *111*, 1193.

(36) Noest, A. J.; Nibbering, N. M. M. *Adv. Mass Spectrom.* **1980**, *8A*, 227.

(37) Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1979**, *101*, 3587.

(38) Cho, B. R.; Yoon, Y. C.; Bartsch, R. A. *J. Org. Chem.* **1985**, *50*, 4943.

(39) Cho, B. R.; Namgoong, S. K.; Kim, T. R. *J. Org. Chem.* **1986**, *51*, 1320.

(40) Cho, B. R.; Maeng, J. H.; Yoon, J. C.; Kim, T. R. *J. Org. Chem.* **1987**, *52*, 4752.

(41) Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1989**, *111*, 2252.

(42) Cho, B. R.; Suh, Y. W. *J. Org. Chem.* **1989**, *54*, 2855.

(43) Hoffman, R. V.; Bartsch, R. A.; Cho, B. R. *Acc. Chem. Res.* **1989**, *22*, 211 and references cited therein.

(44) Waser, J.; Trueblood, K. N.; Knobler, C. M. *Chem One*; McGraw-Hill: New York, 1976.

(45) Nibbering, N. M. M. *Adv. Phys. Org. Chem.* **1988**, *24*, 1.

(46) Nibbering, N. M. M. *Acc. Chem. Res.* **1990**, *23*, 279.

(47) Slater, J. C. *Quantum Theory of Molecules and Solids*; McGraw-Hill: New York, 1974; Vol. 4.

(48) Parr, R. G.; Yang, W. *Density-Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.

(49) Baerends, E. J.; Ellis, D. E.; Ros, P. *Chem. Phys.* **1973**, *2*, 41.

(50) Boerrigter, P. M.; Velde, G. te; Baerends, E. J. *Int. J. Quantum Chem.* **1988**, *33*, 87.

(51) Baerends, E. J.; Ros, P. *Chem. Phys.* **1975**, *8*, 412.

(52) Baerends, E. J.; Ros, P. *Int. J. Quantum Chem. Quantum Chem. Symp.* **1978**, *S12*, 169.

(53) Koning, L. J. de; Kort, C. W. F.; Pinkse, F. A.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Processes* **1989**, *95*, 71.

(54) Huntress, W. T., Jr.; Laudenslager, J. B.; Pinizzotto, R. F., Jr. *Int. J. Mass Spectrom. Ion Physics* **1974**, *13*, 331.

(55) Bartmess, J. E.; Georgiadis, R. M. *Vacuum* **1983**, *33*, 149.

(56) Miller, K. J. *J. Am. Chem. Soc.* **1990**, *112*, 8533.

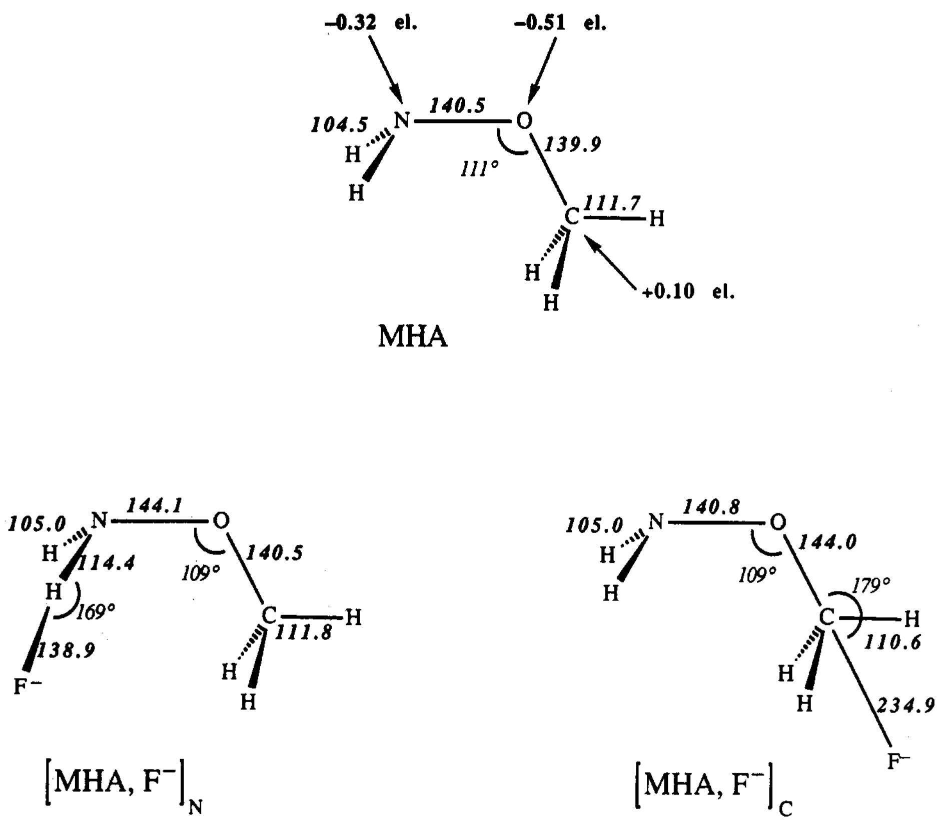


Figure 1. Calculated minimum energy structures (pm) of *O*-methylhydroxylamine (MHA) and its complexes with F^- and gross Mulliken atom charges (electrons) for MHA.

NH_2^- was generated via dissociative resonant capture of electrons with a kinetic energy of 5 eV by NH_3. $C_6H_5^-$ was produced via proton abstraction from benzene by NH_2^-. OH^- was generated via dissociative resonant capture of electrons with a kinetic energy of 6 eV by H_2O (OH^- is formed via H^-). CH_3O^- was generated via reaction of NH_2^- with *N,O*-dimethylhydroxylamine or via reaction of OH^- with *O*-methylhydroxylamine and was selected as the ^{13}C isotopomer (*m/z* 32) in order to distinguish the reactant from the product methoxide. $C_2H_5O^-$ was formed via proton abstraction from ethanol by OH^-. F^- was generated via dissociative resonant capture of electrons with a kinetic energy of 6 eV by CF_4. Cl^- was made in a S_N2 substitution of NH_2^- and CH_3Cl. Finally, CN^- was obtained by proton abstraction from HCN (contamination, vide supra).

Chemicals. Gaseous *O*-methylhydroxylamine was generated from its hydrochloric salt by treating it with an excess of grained sodium hydroxide under high vacuum in the inlet system of the FT-ICR. *N,O*-Dimethylhydroxylamine (DHA) and the hydrochloric salt of *O*-methylhydroxylamine (MHA·HCl) were a gift from Professor F. Bickelhaupt of the Scheikundig Laboratorium, Vrije Universiteit, Amsterdam. All other chemicals were commercially available. GC analysis (Reoplex, 60 °C) of the DHA sample indicated that the purity was better than 98%. MS analysis (MAT 90, Finnigan MAT, Bremen, Germany) indicated that the MHA·HCl was free from methanol, while no significant amount of methanol was detected in the gaseous MHA sample which was introduced to the FT-ICR cell as described above.

Theory

Quantum chemical calculations were performed using a high-level density-functional (DF) method, as implemented in the Amsterdam density-functional (ADF) program system.[47-52] The MOs were expanded in a large set of Slater type orbitals (STOs). The basis is of double-ζ quality (two STOs per nl shell). A polarization function was added on each atom: 2p on H, 3d on N, O, and F. Geometries were optimized with the simple $X\alpha$ exchange-correlation potential[47] using gradient techniques.[57] The energy data reported for stable structures have been obtained in the optimum geometry with more sophisticated density-functionals (DF) for exchange and correlation. Exchange is described with Slater's $\rho^{1/3}$ potential ($X\alpha$ with $\alpha = {}^2/_3$), with a nonlocal correction due to Becke.[58-60] According to the suggestion by Stoll et al.,[61] only correlation between electrons of different spin is introduced, for which electron gas data (in the Vosko–Wilk–Nusair[62] parametrization) are used.

It has been noticed before that the complexation energy of fluorine-containing anion/molecule complexes depends very critically on the quality of the basis set.[63] Therefore, after the geometries were optimized with the double-ζ basis, DFT calculations for the anion/molecule complexes $[MHA, F^-]_N$ and $[MHA, F^-]_C$ (vide infra) and their fragments MHA and F^- were performed with an extra large triple-ζ basis augmented with two polarization functions on each atom (3d and 4f on F, N, O, C; 2p and 3d on H). However, the gross Mulliken population analysis[64] (see charges in Figure 1 and Table VI) has been performed using the smaller double-ζ basis set to avoid problems associated with the application of this method in the case of very large basis sets containing diffuse functions.[65]

Considerable experience shows that with the DF approach interaction energies in systems involving main

---

(57) Versluis, L.; Ziegler, T. *J. Chem. Phys.* **1988**, *88*, 322.

(58) Becke, A. D. *Int. J. Quantum. Chem.* **1983**, *23*, 1915.

(59) Becke, A. D. *J. Chem. Phys.* **1986**, *85*, 7184.

(60) Ziegler, T.; Tschinke, V.; Becke, A. *Polyhedron* **1987**, *6*, 685.

(61) Stoll, H.; Golka, E.; Preus, H. *Theor. Chim. Acta* **1980**, *55*, 29.

(62) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200.

(63) Bickelhaupt, F. M.; Koning, L. J. de; Nibbering, N. M. M.; Baerends, E. J. *J. Phys. Org. Chem.* **1992**, *5*, 179.

(64) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.

(65) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735.

Table II. Reaction Enthalpies (ΔH_r, kcal/mol) for Reactions of B^- with *N,O*-Dimethylhydroxylamine (DHA)[a]

B^-	$PA(B^-)$[b]	ΔH_r					
		PT[c]	$S_N2(N)$[c]	$S_N2(C)$[c]	1,2-E[c]	1,2-E_{solv}[c]	1,2-E/PT[c]
NH_2^-	403.7	−18	−29	−19	−45	−55	−37
$C_6H_5^-$	400.8	−15	−59	−29	−42	−52	−34
OH^-	390.8	−5	−4	−2	−32	−56	−24
CH_3O^-	380.5	6	0	3	−22	−51	−14
$C_2H_5O^-$	377.4	9		6	−19	−39	−11
F^-	371.4	15		14	−13	−43	−5
CN^-	351.1	35		13	7	−9	15
Cl^-	333.4	53	48	48	25	11	33

[a] Calculated using data of Lias et al.[73] and Benson.[74] For formaldimine, $CH_2{=}NH$, we have used the revised heat of formation of 17 kcal/mol determined in our group[75] and accordingly adjusted heat of formation of 40 kcal/mol for the imide $CH_2{=}N^-$: $\Delta H_f(CH_2{=}N^-) = \Delta H_f(CH_2{=}NH)^{73} + PA(CH_2{=}N^-)^{75} - \Delta H_f(H^+)$.[73] Thermochemical data for $(DHA - H)^-$, CH_3NHO^-, and NH_2F have been determined in this work (see Table V). [b] The gas-phase proton affinity (PA) is defined as the enthalpy change associated with the reaction $BH \rightarrow B^- + H^+$ (see ref 73). [c] See eq 3a–f.

group elements and/or metals can be calculated with an accuracy of better than 5 kcal/mol.[57,63,66–72]

Thermochemistry. The proton affinity (PA) of NH_2O^- (Table V) has been obtained by anchoring the calculated energy difference ΔE for the reaction $NH_2OH + F^- \rightarrow NH_2O^- + HF$ to the literature value for the proton affinity of F^-,[73] using the relation $PA(NH_2O^-) = PA(F^-) + \Delta E + \Delta ZPE$ and assuming that $\Delta ZPE \approx 0$ for the proton transfer. The proton affinity of CH_3NHO^- has been estimated using the relation $PA(CH_3NHO^-) = PA(NH_2O^-) + [PA(CH_3NHO^-) - PA(NH_2O^-)]$ and assuming that $[PA(CH_3NHO^-) - PA(NH_2O^-)] \approx [PA(C_2H_5O^-) - PA(CH_3O^-)]$, where the PA values for methoxide and ethoxide have been obtained from the literature.[73] The heat of formation (ΔH_f) of NH_2F (Table V) has been obtained by anchoring the calculated energy difference ΔE for the reaction $F^- + NH_2OCH_3 \rightarrow NH_2F + CH_3O^-$ to the literature values for the heats of formation of F^- and NH_2OCH_3,[73] using the relation $\Delta H_f(NH_2F) = \Delta H_f(F^-) + \Delta H_f(NH_2OCH_3) - \Delta H_f(CH_3O^-) + \Delta E + \Delta ZPE$ and assuming that $\Delta ZPE \approx 0$ for the substitution reaction.

Results

The experimental results and thermochemical data are summarized in Tables I–V. Tables I and III show the primary product anion distribution for the reactions of B^- with *N,O*-dimethylhydroxylamine (DHA) and *O*-methylhydroxylamine (MHA), respectively. The corresponding thermicities for a number of conceivable processes (eq 3a–f) are listed in Tables II and IV, respectively. The results of the quantum chemical DF calculations are shown in Tables V and VI and in Figure 1.

Table III. Primary Product Anion Distributions (%) and Overall Second-Order Rate Constants, $k(B^-)$ (10^{-9} cm^3 s^{-1} $molecule^{-1}$), for Reactions of B^- with *O*-Methylhydroxylamine (MHA)

B^-	$k(B^-)$	product anion distribn[a]	
		$(MHA - H)^-$	CH_3O^-
NH_2^-	1.7	49	51
$C_6H_5^-$	*b*	30	70
OH^-	1.3	45	55
CH_3O^-	*b*		100
$C_2H_5O^-$	0.0		
F^-	*b*		100

[a] See eq 3a–c. [b] Rate constant determination complicated (see Experimental Section).

Table IV. Reaction Enthalpies (ΔH_r, kcal/mol) for Reactions of B^- with *O*-Methylhydroxylamine (MHA)[a]

B^-	PA	ΔH_r			
		PT[b]	$S_N2(N)$[b]	$S_N2(C)$[b]	1,1-E[c]
NH_2^-	403.7	−18	−31	−17	25
$C_6H_5^-$	400.8	−15	−61	−27	28
OH^-	390.8	−5	−5	0	38
CH_3O^-	380.5	6	0	5	48
$C_2H_5O^-$	377.4	9	3	8	51
F^-	371.4	15	5	16	57

[a] Calculated using data of Lias et al.[73] and Benson.[74] Thermochemical data for $(MHA - H)^-$, NH_2O^-, and NH_2F have been determined in this work (see Table V). [b] See eq 3a–c. [c] See eq 4.

Table V. Selected Proton Affinities (PA, kcal/mol) and Heats of Formation (ΔH_f, kcal,mol) Obtained from Proton Transfer Bracketing Experiments and DFT Calculations

system	quantity	value	method
$(DHA - H)^-$	PA	386 ± 5	experimental bracketing[a]
$(MHA - H)^-$	PA	386 ± 5	experimental bracketing[a]
NH_2O^-	PA	385	DFT[b]
CH_3NHO^-	PA	382	estimated[b]
NH_2F	ΔH_f	−27	DFT[b]

[a] PA bracketed between PA of OH^- and CH_3O^- (see Tables I and III). [b] See theoretical section.

In the various reactions of B^- ($B^- = NH_2^-$, $C_6H_5^-$, OH^-, MeO^-, EtO^-, F^-, CN^-, and Cl^-) with DHA, the competing formation of four types of primary product anions is observed, namely $(DHA - H)^-$, CH_3O^-, $[CH_3O^-, HB]$, and $CH_2{=}N^-$ (Table I). The relatively weak bases CN^- and Cl^- appear to be unreactive toward DHA. This can be ascribed to the relatively unfavorable reaction enthalpy of the conceivable reactions listed in Table II. For all other reaction systems, CH_3O^- appears to be the dominant product anion.

In the reactions of B^- ($B^- = NH_2^-$, $C_6H_5^-$, OH^-, MeO^-, EtO^-, and F^-) with MHA the competing formation of two types of primary product anions is observed, namely $(MHA - H)^-$ and CH_3O^- (Table III). The efficiency of the reactions involving MHA is significantly lower than for

---

(66) Bickelhaupt, F. M.; Fokkens, R. H.; Koning, L. J. de; Nibbering, N. M. M.; Baerends, E. J.; Goede, S. J.; Bickelhaupt, F. *Int. J. Mass Spectrom. Ion Processes* **1991**, *103*, 157.

(67) Bickelhaupt, F. M.; Nibbering, N. M. M.; Wezenbeek, E. M. van; Baerends, E. J. *J. Phys. Chem.* **1992**, *96*, 4864.

(68) Ziegler, T.; Tschinke, V.; Ursenbach, C. *J. Am. Chem. Soc.* **1987**, *109*, 4825.

(69) Ziegler, T.; Tschinke, V.; Versluis, L.; Baerends, E. J. *Polyhedron* **1988**, *7*, 1625.

(70) Fan, L.; Ziegler, T. *J. Chem. Phys.* **1990**, *92*, 3645.

(71) Ziegler, T.; Rauk, A. *Theor. Chim. Acta* **1977**, *46*, 1.

(72) Ziegler, T. *Chem. Rev.* **1991**, *91*, 651.

(73) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. No. 1.

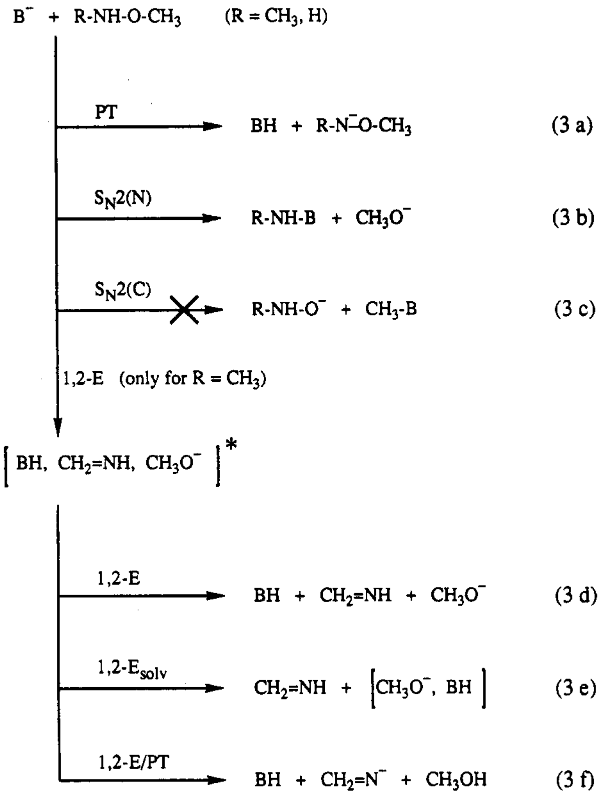
(74) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

(75) Peerboom, R. A. L.; Ingemann, S.; Nibbering, N. M. M.; Liebman, J. F. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1825.

Table VI. Complexation Energies $\Delta E_{\text{complex}}$ (kcal/mol) and Gross Mulliken Charges Q (electrons) which the Fragments Acquire in the Complexes of *O*-Methylhydroxylamine (MHA) and Fluoride Obtained from DFT Calculations[a]

system	$\Delta E_{\text{complex}}$	Q(F⁻)	Q(MHA)
$[\text{MHA}, F^-]_N$	−22.1	−0.68	−0.32
$[\text{MHA}, F^-]_C$	−11.4	−0.75	−0.25

[a] See Figure 1 for calculated minimum energy structures.



the reactions involving DHA. This trend continues for the reaction of $C_2H_5O^-$ with MHA, where no product anion was formed at all. However, for all other bases CH_3O^- appears to be the most abundant product anion as in the reactions with DHA.

Discussion

The Formation of (DHA − H)⁻ and (MHA − H)⁻. The formation of (DHA − H)⁻ and (MHA − H)⁻ is considered to proceed via a proton abstraction from DHA and MHA at the nitrogen atom, leading to $(CH_3)(CH_3O)N^-$ and CH_3ONH^-, respectively (eq 3a). This proton transfer (PT) is observed in the reactions of the stronger bases (PA ≥ 390.8 kcal/mol) NH_2^-, $C_6H_5^-$, and OH^- but not for the weaker bases (PA ≤ 380.5 kcal/mol) MeO⁻, EtO⁻, F⁻, CN⁻, and Cl⁻ (Tables I and III). Assuming that entropy changes associated with the studied proton transfers are small, the proton affinity (PA) of both $(CH_3)(CH_3O)N^-$ and CH_3ONH^- is bracketed between the proton affinities of hydroxide (PA = 390.8 kcal/mol) and methoxide (PA = 380.5 kcal/mol) and, hence, amounts to 386 ± 5 kcal/mol (Table V).

The Formation of CH₃O⁻. The formation of methoxide in the reactions of B⁻ with MHA can be associated with a nucleophilic substitution on the nitrogen atom (S_N2(N), eq 3b). The possibility of a 1,1-elimination (1,1-E; eq 4) leading to the formation of the highly energetic nitrene NH (ΔH_f = 90 kcal/mol)[73] can be excluded as this process is very endothermic for all bases used (Table IV). However,

$$B^- + NH_2OCH_3 \xrightarrow{1,1\text{-}E} \!\!\!\!\!\!\!\times\;\; BH + |\underline{\dot{N}}H + CH_3O^- \qquad (4)$$

the formation of methoxide in the reactions of B⁻ with DHA may proceed via both S_N2(N) (eq 3b) and a base-induced imine-forming 1,2-elimination (1,2-E, eq 3d). The S_N2(N) reaction of DHA is expected to be less efficient than the S_N2(N) reaction of MHA due to the steric shielding of the nitrogen center by the methyl substituent. Nonetheless, both the proportion of the reactions resulting in methoxide ions and the overall reaction rate constants, k(B⁻), are significantly larger for the reactions with DHA than for the corresponding reactions with MHA (Tables I and III), implying that the formation of methoxide ions is much more efficient in the reactions with DHA. This leads to the conclusion that the formation of methoxide anions in the reactions with DHA dominantly (if not exclusively) proceeds via an 1,2-E process (eq 3d) which is considered to be much more efficient than the competing S_N2(N) process (eq 3b). One arrives at an upper limit of 20% and 15% for the proportion of methoxide ions which are formed via a S_N2(N) substitution in the reactions DHA with NH_2^- and OH^-, respectively, if it is assumed that the branching ratios of the proton transfer (PT) and the S_N2(N) substitution are similar for DHA and MHA.

An interesting question that remains is why the nucleophilic substitution on the nitrogen atom resulting in methoxide ions (S_N2(N), eq 3b) is not in competition with the nucleophilic substitution on the carbon atom of the methoxy group (S_N2(C), eq 3c), which is anticipated to result in the formation of unobserved CH_3NHO^- and NH_2O^- ions in the reactions with DHA and MHA, respectively. At first sight one might expect that nucleophilic substitution on the more electronegative nitrogen ($Q_{N \text{ in MHA}}$ = −0.32 electrons) would be less effective than nucleophilic substitution on carbon ($Q_{C \text{ in MHA}}$ = +0.10 electrons; Figure 1). From the results in Tables II and IV it appears that the observed S_N2(N) process always is favored energetically over the corresponding S_N2(C) process. In general, an increase of the exothermicity of a reaction leads to a decrease of the activation barrier.[24] This effect may partly compensate for the effect of the electron distribution which shields the nitrogen center from nucleophilic attack. Theoretical calculations[26] show that gas-phase S_N2(C) reactions are hampered by a tight transition state (TS) which can be considered as an "entropy bottleneck". As a result, S_N2(C) reactions very unfavorably compete with less exothermic 1,2-E processes.[14,21] The apparent prevalence of S_N2(N) over S_N2(C) may have the same origin. The average homolytic bond strength of the N–O single bond (43 kcal/mol) is nearly two times smaller than that of the C–O single bond (84 kcal/mol).[44] Furthermore, the DF theoretical investigation (Figure 1) shows that the N–O bond (140.5 pm) in MHA is slightly longer than the C–O bond (139.9 pm).

The relatively large N–O bond distance is probably the result of the mutual repulsion between the nitrogen and oxygen atoms which both have a lone pair in the same plane (Figure 2). This contrasts to the situation for the slightly positively charged methoxy carbon in MHA which has no lone pair.

The above considerations may lead to the conclusion that the S_N2(N) substitution proceeds via a TS in which N–O bond rupture is more advanced than C–O bond rupture in the TS of the S_N2(C) substitution. This implies

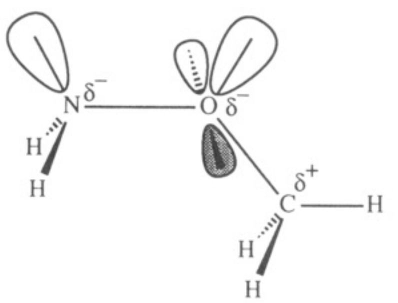


Figure 2. Schematic representation of lone pair orbitals in *O*-methylhydroxylamine (MHA).

that relative to $S_N2(C)$, $S_N2(N)$ proceeds via a less tight, S_N1-like TS associated with a higher density of states and, thus, a more favorable activation entropy. Further support for this hypothesis comes from the DF calculations on the anion/molecule complexes of MHA and F^- (Table VI, Figure 1).

Association of MHA (calculated dipole moment of 2.623 D) and F^- can lead to the formation of two different anion/molecule complexes in which the base is bonded to the amino or to the methyl group of MHA, i.e., $[MHA, F^-]_N$ and $[MHA, F^-]_C$, respectively (Figure 1). In $[MHA, F^-]_C$ the fluoride anion is bound by ca. 11.4 kcal/mol to the "backside" of the methyl group of MHA and thus has an appropriate configuration for an $S_N2(C)$ substitution. The complexation is accompanied by a charge transfer of −0.25 electrons from F^- to MHA and a lengthening of the C–O bond by 4.1 to 144.0 pm. The amino-bonded complex $[MHA, F^-]_N$ appears to be considerably more stable than the methyl-bonded complex $[MHA, F^-]_C$ (Table VI). In $[MHA, F^-]_N$ the fluoride anion is bound by 22.1 kcal/mol to MHA which now has acquired a charge of −0.32 electrons. In contrast to the situation for $[MHA, F^-]_C$, the fluoride anion in $[MHA, F^-]_N$ is hydrogen bonded to one of the N–H bonds of MHA. This N–H bond has been extended by about 10 pm from 104.5 in the free MHA to 114.4 pm, while the F–H bond length amounts to 138.9 pm. In fact, no stable conformation for a "backside" $S_N2(N)$ attack could be found. Nevertheless, the formation of $[MHA, F^-]_N$ is accompanied by a significant lengthening of the weak N–O bond in MHA by 3.6 to 144.1 pm. This suggests that in the $S_N2(N)$ TS the N–B bond formation lags behind N–O bond breaking more than the C–B bond formation lags behind the C–O bond breaking in the $S_N2(C)$ TS. Furthermore, the DF calculations show that upon formation of the reaction complex only a slight deviation (6° at $d(FC) = 281$ pm) from the F^- approach coaxial with the CO axis results in a collapse of the reaction complex to $[MHA, F^-]_N$ rather than to $[MHA, F^-]_C$. Although this cannot directly be related to the relative energies of the transition states for $S_N2(N)$ and $S_N2(C)$, it suggests that F^- is captured in the vicinity of nitrogen and thus is predisposed for attack at this center. Summarizing, association of MHA and F^- preferentially leads to the formation of the more stable $[MHA, F^-]_N$ reaction complex leading to $S_N2(N)$ substitution with a relatively loose, S_N1-like TS.

The Formation of $[CH_3O^-, HB]$. The formation of the HB-solvated methoxide, i.e., the $[CH_3O^-, HB]$ anion/molecule complex, in the reaction between B^- and DHA can unambiguously be associated with a mechanistic pathway in which a base-induced imine-forming 1,2-elimination (1,2-E) takes place followed by evaporation of formaldimine, $CH_2{=}NH$, from the product complex $[BH, CH_2{=}NH, CH_3O^-]^*$ (1,2-E_{solv}, eq 3e). The formation of HB-solvated methoxide is observed only for the reaction induced by F^-, probably because the reaction enthalpy gained in the 1,2-E process of F^- ($\Delta H_{1,2\text{-}E}(F^-) = -13$ kcal/mol, see Table II) is the lowest for the reaction systems studied and may be insufficient to fuel the very endothermic desolvation of the methoxide anion from HB ($\Delta H_{complex} = -30$ kcal/mol[73] for $[CH_3O^-, HF]$). It may be supposed that formation of CH_3O^- and $[CH_3O^-, HF]$ proceed via two stereochemically distinct elimination mechanisms, i.e., anti- and syn-1,2-E, respectively, as has been suggested for analogous gas-phase base-induced alkene-forming 1,2-elimination reactions of simple ethers[14] and thioethers.[15]

The Formation of $CH_2{=}N^-$. The formation of the imide ion $CH_2{=}N^-$ in the reactions between B^- and DHA can be associated with a mechanism that initiates with a 1,2-E reaction step. As discussed above, this results in the formation of the $[BH, CH_2{=}NH, CH_3O^-]^*$ product complex. Prior to the dissociation of this intermediate reaction complex a proton is transferred from formaldimine to methoxide leading to the formation of $CH_2{=}N^-$ (1,2-E/PT, eq 3f). The PT step, which is about 8 kcal/mol[73] endothermic, has to be fueled by the reaction enthalpy gained in the preceding 1,2-E reaction step. If the 1,2-E reaction step becomes less exothermic, the reaction enthalpy gained may be insufficient for the overall 1,2-E/PT process to occur (Table II). In agreement with this, the formation of $CH_2{=}N^-$ is observed only in the reactions induced by the three strongest bases, i.e., NH_2^-, $C_6H_5^-$, and OH^- (Table I).

Conclusion

It appears that base-induced imine-forming 1,2-elimination reactions can be very efficient in the gas phase, as has been found for the reactions of *N*,*O*-dimethylhydroxylamine, CH_3NHOCH_3, with anionic bases. The efficiency of the imine-forming elimination reactions of CH_3NHOCH_3 can be compared favorably with the efficiency of base-induced alkene-forming 1,2-elimination reactions of corresponding simple ethers such as diethyl ether, $CH_3CH_2OC_2H_5$.[14]

Unexpectedly, nucleophilic attack on the nitrogen atom leading to the substitution of the methoxy group is found to be a relatively facile process. This is especially evident in the substitution reactions of anionic bases with *O*-methylhydroxylamine, NH_2OCH_3, where the formation of methoxide anions is much more efficient than in the corresponding highly inefficient substitution reactions with dimethyl ether, CH_3OCH_3.[21] Apparently, substitution reactions on a nitrogen atom do not suffer from a very unfavorable activation entropy which is assumed to hamper nucleophilic substitution reactions on a carbon atom in the gas phase. This seems to be supported by high-level density-functional (DF) calculations which indicate that the nucleophilic substitution reactions on the nitrogen atom proceed via an entropically favored less tight, S_N1-like transition state.

Acknowledgment. The authors thank the Netherlands Organization for Scientic Research (NCF/SON/NWO) for financial support. We gratefully acknowledge Professor E. J. Baerends for helpful discussions and Dr. B. L. M. van Baar for the analysis of the *O*-methylhydroxylamine samples.