Mechanism of the Beckmann Rearrangement of Formaldehyde Oxime and Formaldehyde Hydrazone in the Gas Phase

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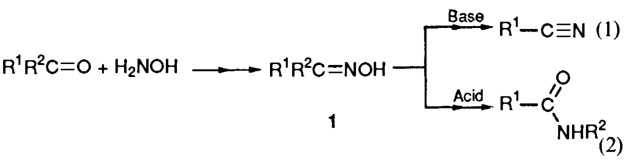
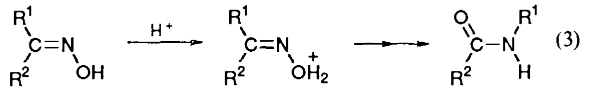
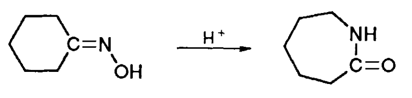
The potential energy surfaces corresponding to the Beckmann rearrangement of protonated formaldehyde oxime and formaldehyde hydrazone in the gas phase have been explored using *ab initio* molecular orbital calculations. Geometries of stationary points were optimized at the HF and MP2/6-31G(d,p) level while relative energies were estimated at the MP4SDTQ/6-311++G(d,p) level and corrected for zero-point energies. Both rearrangements are calculated to be concerted with a single transition structure connecting the protonated species and the product complex. In the transition structure, the 1,2-hydrogen shift from C to N is accompanied by a lengthening of the N–O (in oxime) or N–N (in hydrazone) distance, and the migrating hydrogen is in *trans* relative to the leaving group across the C=N bond. The transition structure in the hydrazone case is much closer to the final products than that in the oxime. This is also manifested by the energy barriers that amount to 44 and 189 kJ mol^{-1} for oxime and hydrazone, respectively. These results suggest that the Beckmann rearrangement of oxonium ion is a facile process, while that of hydrazonium ion is reachable under thermal conditions. The experimentally observed loss of HCN from hydrazonium ion can be better rationalized in terms of a Beckmann rearrangement than a 1,2-*cis*-elimination as recently proposed. The proton affinities at different sites in oxime and hydrazone are also evaluated.

In organic synthesis, oximes **1** are often involved as primary products in the chemical transformation of aldehydes and ketones. In the case of aldoximes (R^2 = H), when the methine hydrogen is activated by an electron-withdrawing substituent, *e.g.* R^1 = O–NH_2–C_6H_4, an aldoxime can, in the presence of a basic reactant, undergo a dehydration reaction giving the corresponding cyanide [eqn. (1)].[1] When treated by an acid, an aldoxime or a ketoxime ($R^2 \neq$ H) can also undergo a Beckmann rearrangement yielding an amide as the final product [eqn. (2)].[2] Both types of reactions are highly stereospecific. In the Beckmann rearrangement (designated hereafter as BR), the group *anti* to the hydroxy group always migrates from C to N. If the migrating group is chiral, its configuration is not changed during the migratory process [eqn. (3)]. While the kinetics of the base-catalysed dehydration of aldoximes is well studied,[1] little was known, until recently, about the mechanism of the acid-catalysed BR. Hunt and Rzepa[3] reported a preliminary study of the potential energy surface of the protonated formaldehyde oxime in which results obtained by different molecular orbital methods have been compared. According to this study, the semi-empirical PM3 and *ab initio* MP2 methods predict both concerted and stepwise pathways for the BR of formaldoxime whereas no concerted pathway exists at the MNDO, AM1 and HF/3-21G levels.[3]





In view of this method-dependency of the BRs potential energy surface, it is desirable to investigate it using more reliable levels of theory. In the present note, we report the results of such *ab initio* MO calculations on the BRs of formaldehyde oxime. To extend the scope of the problem we have also considered the formaldehyde hydrazonium cation (H_2C=N–NH_3^+) for which the existence in the gas phase has been recently established by an MS study[4] and a base-catalysed deamination similar to the dehydration of oxime [eqn. (1)] has also been observed.[5] The results reported in this paper are also to be used as a calibration for results on larger systems. The migratory aptitude of different substituents in the BR including the well established conversion of cyclohexanoxime into ε-caprolactam [eqn. (4)] will be examined in a future work.



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It should be stressed that the calculations were performed without any consideration of the solvent effect and correspond therefore mainly to the reactions which occurred in the gas phase. In addition, we considered only the first step of the transformation leading to the nitrilium ions. In the gas phase, these cations should be detectable. In aqueous solutions or in polar acidic solvents, reactions of these ions with OH^- giving finally amides should be the fast subsequent steps.

Calculations

Ab initio molecular orbital calculations were carried out using a local version of the Gaussian 90[6] set of programs. Structures of the stationary points considered were initially optimized at the Hartree–Fock (HF) level with the dp-polarized 6–31G(d,p) basis set and characterized by harmonic vibrational wavenumbers computed at this HF/6-31G(d,p) level making use of analytical force constants. The selected structures were then reoptimized at the second-order Møller–Plesset perturbation theory (MP2) level with the 6-31G(d,p) basis. Improved relative energies between stationary points were finally estimated from full fourth-order perturbation calculations (MP4SDTQ) using the sp-diffuse plus dp-polarized 6-311++G(d,p) basis set at MP2/6-31G(d,p)-optimized geometries. The zero-point energy

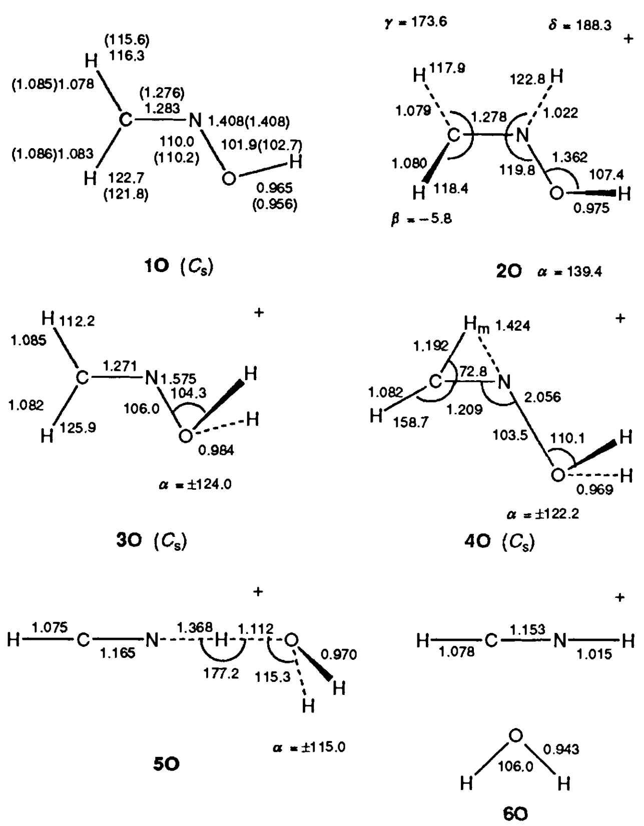

Fig. 1 MP2/6-31G(d,p)-optimized geometries of six stationary points related to the formaldoxime system. Values given in parentheses are the experimental data from ref. 7 for **1O**. The dihedral angles are: α = HONC, β and γ = HCNO and δ = HNCO.

corrections (ZPE) were estimated from HF/6-31G(d,p) vibrational wavenumbers. For the oxime system, a further estimate of the basis set dependency was also carried out at the MP2 level with the larger 6-311 + + G(2df,2p) basis.

Throughout this paper, bond lengths are given in ångströms, bond angles in degrees, total energies in hartrees,* zero-point and relative energies in kJ mol^{-1}. Unless otherwise noted, relative energies mentioned in the text refer to the MP4SDTQ/6-311 + + G(d,p)//MP2/6-31G(d,p) + ZPE level of theory.

Results and Discussion

Geometrical parameters optimized at the MP2/6-31G(d,p) level for the six stationary points involved in the BR of formaldehyde oxime are shown in Fig. 1 while the six points related to formaldehyde hydrazone are displayed in Fig. 2. In general, the number **1** refers to the neutral form, **2** to the imine-nitrogen protonated form, **3** to the oxygen or amine-nitrogen protonated form, **4** to the transition structure for the concerted BR, **5** to the product complex and finally **6** to the separated products. The letters **O** and **H** stand for oxime and hydrazone, respectively. Calculated total and zero-point vibrational energies are recorded in Table 1 while different relative energies are summarized in Table 2. Schematic energy profiles showing unimolecular rearrangements of both protonated forms **3** are displayed in Fig. 3.

In general, the relative energies between stationary points are not particularly sensitive to the basis set. Incorporation of additional polarization functions, from the 6-311 + + G(d,p) to 6-311 + + G(2df,2p) set, induces a change of 8–9 kJ mol^{-1} on the proton affinity or energy barrier (at the MP2 level).

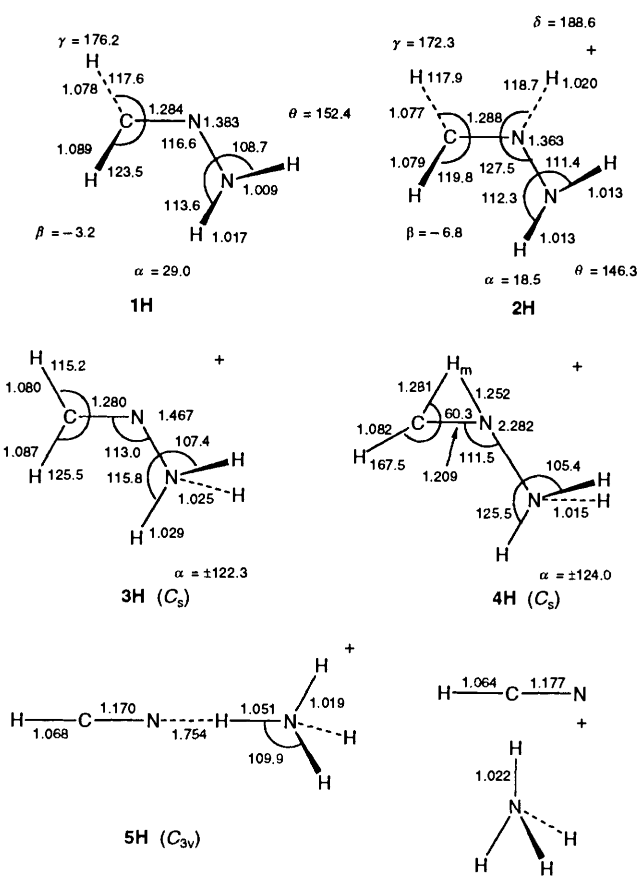

Fig. 2 MP2/6-31G(d,p)-optimized geometries of six stationary points related to the formaldehyde hydrazone system. The dihedral angles are α and θ = HNNC, β and γ = HCNN and δ = HNCH.

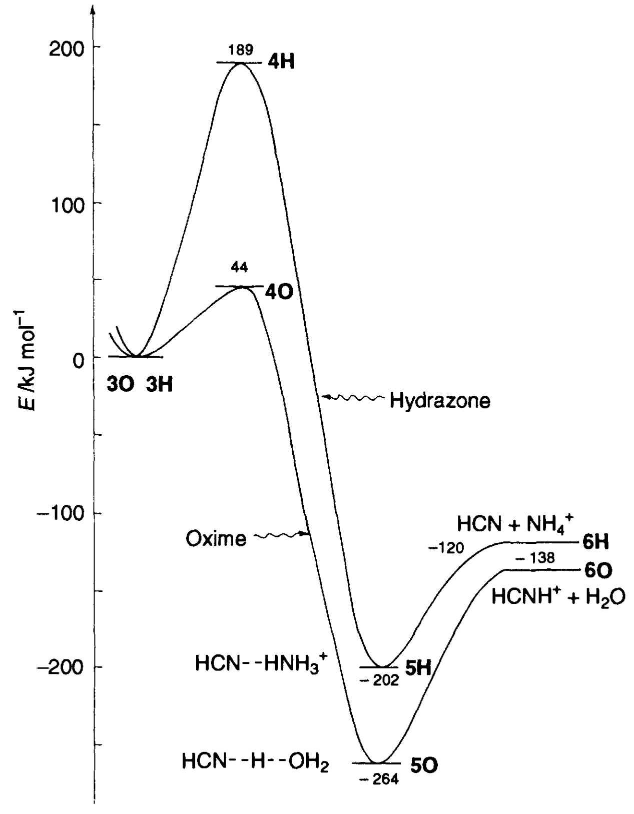

Fig. 3 Schematic energy profiles showing the BRs of both protonated formaldehyde oxime and formaldehyde hydrazone. Energies obtained from MP4/6 − 311 + + G(d,p) + ZPE calculations.

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* 1 $E_h \approx 4.359\,75 \times 10^{-18}$ J.

Table 1 Total[a] and zero-point energies of the stationary points considered

Structure		HF/ 6–31G(d,p)[b]	MP2/ 6–31G(d,p)[c]	MP2/ 6–311 + G(d,p)[d]	MP4SDTQ/ 6–311 + + G(d,p)[d]	MP2/ 6–311 + + G(2df,2p)[d]	ZPE[e]	$\nu_i f$/cm^{-1}
H_2C=NOH	**1O**	–168.850 75	–169.348 16	–169.420 36	–169.462 65	–169.510 12	115	
H_2C=NH–OH^+	**2O**	–169.184 31	–169.671 42	–169.735 45	–169.779 75	–169.824 76	149	
H_2C=N–OH_2^+	**3O**	–169.147 10	–169.637 69	–169.701 03	–169.748 13	–169.787 40	143	
HC(H)–N–OH_2^+	**4O**	–169.116 72	–169.606 89	169.676 88	–169.723 17	–169.759 86	121	760i
HCNH ··· OH_2^+	**5O**	–169.237 49	–169.739 53	–169.807 75	–169.844 86	–169.891 09	133	
$HCNH^+$	**6O**	–93.165 30	–93.457 30	–93.481 09	–93.507 24	–93.526 11	72	
OH_2		–76.023 62	–76.222 45	–76.274 91	–76.287 25	–76.314 93	55	
H_2C=N–NH_2	**1H**	–149.040 08	–149.528 98	–149.582 23	–149.628 25	—	146	
H_2C=NH–NH_2^+	**2H**	–149.391 67	–149.875 59	–149.919 40	–149.967 80	—	182	
H_2C=N–NH_3^+	**3H**	–149.385 56	–149.870 64	–149.914 54	–149.963 67	—	183	
HC(H)NNH_3^+	**4H**	–149.292 90	–149.783 05	–149.831 83	–149.880 34	—	153	836i
HCN ··· HNH_3^+	**5H**	–149.455 69	–149.947 85	–149.992 61	–150.036 75	—	173	
HCN	**6H**	–92.877 14	–93.174 37	–93.203 16	–93.226 85	—	42	
HNH_3^+		–56.545 53	–56.737 65	–56.755 66	–56.776 64	—	125	

[a] Based on MP2/6–31G(d,p)-geometries unless otherwise noted. [b] Based on HF/6–31G(d,p)-geometries. [c] Using full sets of MOs. [d] Core orbitals are frozen. [e] Zero-point energies obtained from HF/6–31G(d,p) vibrational wavenumbers and scaled by 0.9. [f] Imaginary vibrational wavenumbers of transition structures.

Table 2 Calculated energetic parameters related to the Beckmann rearrangement of formaldehyde oxime and formaldehyde hydrazone (kJ mol^{-1})

Parameter[a]		HF/ 6–31G(d,p)	MP2(F)/ 6–31G(d,p)	MP2/ 6–311 + G(d,p)	MP4SDTQ/ 6–311 + + G(d,p)	MP2/ 6–311 + + G(2df,2p)	MP4 + ZPE[c]
Proton affinity H_2C=NOH	at O	778	760	737	750	728	722
	at N_{im}[b]	876	849	827	833	826	799
H_2C=NNH_2	at N_{am}[b]	907	897	872	881	—	844
	at N_{im}[b]	923	910	885	892	—	856
Energy barrier for BR	Oxime	80	81	64	66	72	44
[$\Delta E^\dagger = E(\mathbf{4}) - E(\mathbf{3})$]	Hydrazone	243	230	217	219	—	189
Reaction energy	Oxime	–237	–267	–280	–254	–272	–264
[ΔE_r = E(**5**) – E(**3**)]	Hydrazone	–184	–203	–205	–192	—	–202
Complexation energy	Oxime	128	157	136	132	131	126
[ΔE_c = E(**6**) – E(**5**)]	Hydrazone	87	94	89	88	—	82

[a] Using total energies given in Table 1. [b] N_{im} = imine nitrogen; N_{am} = amine nitrogen. [c] Including MP4/6–311 + + G(d,p) energies and ZPEs.

The structure of formaldehyde oxime **1O** has been the subject of a number of previous studies [7,8] and thus warrants no further comment. We only note that the MP2/6-31G(d,p) geometry for **1O** compares quite well with the experimental data [7] determined using microwave spectrometry (Fig. 1). For its part, formaldehyde hydrazone **1H** exhibits a strongly pyramidal amino moiety even at the MP2 level. The C=N distances in both N-substituted imines **1O** and **1H** are similar to that in the parent H_2C=NH species (1.282 Å).

Each of the two neutral forms **1** possesses two distinct protonation sites, namely O and N in the oxime and amine-nitrogen (N_{am}) and imine-nitrogen (N_{im}) in the hydrazone. We have considered both protonated forms **2** and **3**. Because the proton affinity of ammonia is much larger than that of water, the N-protonated form **2O** is expected to lie lower in energy than its O-protonated isomer **3O**. Our best estimate in fact places **2O** about 77 kJ mol^{-1} below **3O**. In the case of formaldehyde hydrazone, the protonation at N_{im} remains favoured, by 12 kJ mol^{-1}, over that at N_{am}. The latter value is somewhat larger than a recent value of 3 kJ mol^{-1} derived from CISD/6-31G(d,p) calculations.[4] The N_{im}-proton affinity in hydrazone is also larger (47 kJ mol^{-1}) than that in oxime, both values are however smaller than the N-proton affinity in H_2C=NH (865 kJ mol^{-1} at the same level). This indicates that the N_{im} atom becomes less basic by interacting with a hydroxy or amino group. It is however important to note that the N_{im}-protonated species **2** are involved only indirectly in the BR. The latter species can either give the corresponding neutral back *via* a pre-equilibrium or rearrange to their isomers **3** by a 1,2-hydrogen shift. The latter process requires a substantial activation energy[4] of $\geq$200 kJ mol^{-1} and thus the **2**→**3** interconversion cannot occur simultaneously. Although the protonated species **3** is less stable, if formed by protonation, it can undergo further rearrangement and thus displaces the equilibrium in its favour.

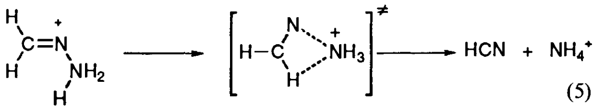
As far as the geometries of protonated species are concerned, it is worth noting the non-planarity of **2O** in which the hydrogen of the OH group lies completely out of the molecular plane. The pyramidal character of the amino group in hydrazone is also carried over into the protonated species **2H**. While the C=N distance is not significantly changed upon protonation, the N–O and N–N distances are appreciably stretched, in particular the N–O in **3O** (0.167 Å). The latter bond is calculated to be quite long (1.575 Å)—it is even longer than the N–N bond in the hydrazonium counterpart **3H** (1.467 Å). However, because the structure H_2C=N^+ does not exist as a local minimum on the $(CH_2N)^+$ potential energy surface, **3O** cannot be viewed as a strong complex between H_2CN^+ and H_2O.

We now turn to the BR of the protonated species **3**. As mentioned above, Hunt and Rzepa[3] reported that both concerted and stepwise pathways exist for the BR of **3O** at the MP2 level of theory. We can here confirm the existence of a concerted pathway, but we were unable to identify a stepwise reaction path. Unfortunately no detailed information on a possible intermediate has been given in ref. 3. The concerted BRs of the formaldehyde oxime **3O** and formaldehyde hydrazone **3H** cations occur through the transition structures **4O** and **4H**, respectively. In each of the two transition structures, the migration of the hydrogen atom H_m from carbon to nitrogen is accompanied by a significant lengthening of the N–O or N–N distance. From a geometrical point of view, the transition structure for hydrazone ion **4H** is closer to the product structure than that for oxime ion **4O**. In fact, the ratio of the distances N–O(**4O**)/N–O(**3O**) = 1.305 is much smaller than the ratio N–N(**4H**)/N–N(**3H**) = 1.556. While the new bond N–H_m in **4O** is not formed yet, its formation in **4H** is well advanced. In both cases, the transition structure possesses a C_s symmetry in which the migrating atom H_m and the leaving group (H_2O or NH_3) are situated in a *trans* configuration. This is consistent with experimental observation for the BRs in solution.

The late transition state found for the hydrazone ion is consistent with the calculated energy barriers. As seen in Fig. 3, the classical energy barrier for the BR of the hydrazone ion is far larger than that for the oxime ion, namely 189 *versus* 44 kJ mol^{-1}. These barriers suggest that the water molecule is a much better leaving group than the ammonia.

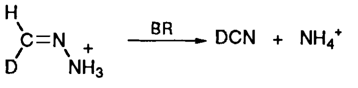
In the oxime, as well as in the hydrazone system, the reaction product is a complex between two fragments. In **5O** which is the common complex of the systems $HCNH^+ + H_2O$ and $HCN + H_3O^+$, the proton lies between the nitrogen and oxygen atoms. In **5H** which is the common complex of the systems $HCNH^+ + NH_3$ and $HCN + NH_4^+$, the ion NH_4^+ is formed due to the large difference between both proton affinities of HCN and NH_3. Both **5O** and **5H** complexes correspond thus to single-well hydrogen bond potentials. Nevertheless, it should be stressed that these type of product complex do not exist when hydrogen is replaced by bulkier groups and is therefore not quite relevant to the BR.

Van Garderen and coworkers[4] recently reported a theoretical and mass spectrometric study of the $(CH_5N_2)^+$ ions. It has been shown that metastable formaldehyde hydrazone cations **3H** dissociate to $HCN + NH_4^+$. The small kinetic energy release (KER) accompanying this reaction is rather consistent with the formation of the ion–dipole complex **5H**. Nevertheless, these authors[4] proposed a different pathway for the loss of HCN [eqn. (5)] which is in fact a 1,2-*cis*-elimination of NH_4^+ from **3H**. Such a mechanism is not uncommon[9] but it is associated with a substantial energy barrier of 251 kJ mol^{-1} as calculated at the CISD/6–31G(d,p) level.[4] Although the latter value cannot be directly compared with our results, it is clear that the BR *via* the route **3H**→**4H**→**5H**→**6H** involving a barrier height of 189 kJ mol^{-1} (Fig. 3) provides a lower-energy and thereby more competitive alternative for the formation of HCN from **3H** than the route seen in eqn (5). These two possible routes can be distinguished either by isotopic labelling experiments [eqn. (6)] or by experiments using C-substituted substances [eqn. (7)].



(5)

3H



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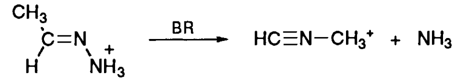

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In conclusion, the *ab initio* calculations at different levels of theory reported in the present paper suggest that the Beckmann rearrangement is a concerted reaction in which the O-protonated formaldehyde oxime or N_{am}-protonated formaldehyde hydrazone is connected to the products (or product complex) by a single transition structure. In the latter, the migrating atom and the leaving group are situated in a *trans* configuration with respect to the C=N bond, in agreement with experiment. The energy barriers for the Beckmann rearrangement are calculated to be 44 and 189 kJ mol^{-1} for the protonated formaldehyde oxime and formaldehyde hydrazone, respectively. Thus, this process is relatively facile for oxime and also reachable for hydrazone in thermal reaction conditions. In both cases, the protonation at the imine-nitrogen is favoured but the resulting protonated form is not directly involved in the process under consideration. Finally, the loss of H–C≡N from metastable formaldehyde hydrazone cations observed in an MS study can better be rationalized in terms of a Beckmann rearrangement than a 1,2-*cis*-elimination as recently proposed.[4]

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