A computational investigation of the structure of the novel anomeric amide *N*-azido-*N*-methoxyformamide and its concerted decomposition to methyl formate and nitrogen

Stephen A. Glover *[a] **and Arvi Rauk** [b]

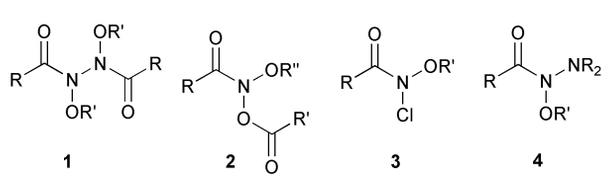
[a] *Division of Chemistry, School of Biological, Biomedical and Molecular Sciences, University of New England, Armidale 2351, New South Wales, Australia*
[b] *Department of Chemistry, University of Calgary, Calgary, AB, Canada T2N 1N4*

Received (in Cambridge, UK) 1st May 2002, Accepted 31st July 2002
First published as an Advance Article on the web 30th August 2002

Treatment of *N*-alkoxy-*N*-chloro- or *N*-acetoxyamides with sodium azide in aqueous acetonitrile results in S_N2 displacement of chlorine or acetate and the formation of reactive *N*-alkoxy-*N*-azidoamides which undergo a concerted decomposition to esters and nitrogen. The properties of the model *N*-azido-*N*-methoxyformamide have been computed at the B3LYP/6-31G* hybrid density functional level of theory. It is a typical anomeric amide in that the nitrogen is strongly sp^3 hybridised resulting in a low amide isomerisation barrier. It decomposes in a two-step process involving exothermic loss of N_2 to give 1-formyl-1-methoxydiazene which spontaneously undergoes a HERON decomposition to methyl formate and N_2. Overall, the process is highly exothermic (ΔG between −654 and −659 kJ mol^{-1}). The competitive one-step HERON process involving formation of methyl formate and tetrazene is kinetically unfavourable. Sterically hindered ester formation will be facilitated by both exothermicity and a transition state for ester formation which avoids a sterically crowded tetrahedral intermediate.

Introduction

Anomeric amides have been defined as the class of alkyl- or arylamides bearing two heteroatoms at the amide nitrogen.[1] The combined electron-withdrawing effect of two electronegative groups results in a strong deviation from the normal sp^2, to sp^3 hybridisation at nitrogen resulting in a nitrogen lone pair that is poorly conjugated with the amide carbonyl, and to radically altered amide properties. Both computed (AM1, B3LYP/6-31G*)[1–7] and experimental properties support these facts; anomeric amides have much higher carbonyl stretch frequencies in their infrared spectra (typically 1720–1740 cm^{-1}) and low barriers to isomerisation about the *N*—*CO* bond. *N*,*N*′-Diacyl-*N*,*N*′-dialkoxyhydrazines **1**, which are strongly anomeric *NNO* systems, have an amide isomerisation barrier of only 50 kJ mol^{-1}.[7] An X-ray structure of *N*,*N*′-bis(4-chlorobenzoyl)-*N*,*N*′-diethoxyhydrazine **1a** was strongly pyramidal at the nitrogen atoms and recently, we have obtained X-ray data for the anomeric *ONO* system, *N*-benzoyloxy-*N*-(4-*tert*-butylbenzyloxy)benzamide **2a** which possesses one of the most pyramidal amide nitrogens yet observed (average angle at nitrogen of only 108°).[8]



As is the case for carbon, there is now ample evidence for anomeric effects through the amide nitrogen in bisheteroatom-substituted amides (Fig. 1). Where *X* is more electron-withdrawing than *Y*, this negative hyperconjugation can result in a significantly weakened *N*—*X* bond; computed, ground state structures generally favour a conformation about the

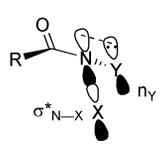
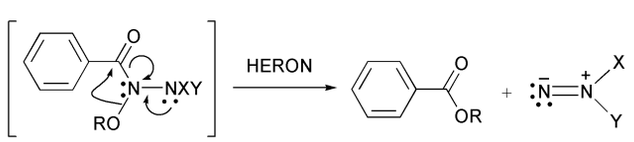


Fig. 1 Anomeric interactions in bisheteroatom-substituted amides.

N—*Y* bond which facilitates an n_Y—σ^*_{NX} overlap leading to longer than normal *N*—*X* bonds. Because of this the *N*,*N*′-diacyl-*N*,*N*′-dialkoxyhydrazines **1** exhibit restricted rotation about the *N*—*N* bonds and have large *N*—*N* isomerisation barriers in the region of $\Delta G^{\ddagger}$ = 65–73 kJ mol^{-1}.[7] For the same reason, the mutagenic *N*-acyloxy-*N*-alkoxyamides **2** have weak acyloxy oxygen—nitrogen bonds and undergo facile S_N2 reactions at nitrogen which may account for their biological activity[9] in that they react at nucleophilic guanine-N7 and adenine-N3 in plasmid DNA.[10] Chemically, they have also been shown to undergo bimolecular S_N2 reactions with hydroxide,[11] aromatic amines,[12,13] glutathione[14] and, as reported in the previous paper, with azide.[15] S_N2 reaction with glutathione results in a reactive *N*-alkoxy-*N*-thioalkylamide intermediate, itself an anomeric amide, which reacts with a second glutathione molecule at sulfur to give *N*-alkoxyamide and the oxidised disulfide form of glutathione.[13,14] The reaction with aromatic amines yields *N*-amino-*N*-alkoxyamide intermediates **4** which are unstable. These too are anomeric amides but they undergo the novel HERON rearrangement to give esters and 1,1-substituted diazene (Scheme 1).[12] This reaction has a firm theoretical basis as do the properties of *N*-amino-*N*-alkoxyamides.[1,3–7]



Scheme 1

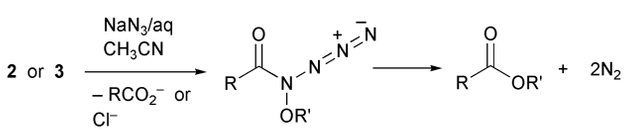
 DOI: 10.1039/b204232k

Table 1 B3LYP/6-31G* absolute and relative energies, free energies (298 K), and entropies (298 K) of *N*-azido-*N*-methoxyformamide **7**, and related transition states

Structure	Energy/hartree	ZPVE/ kJ mol^{-1}	Imaginary frequency *vi*/cm^{-1}	ΔE/kJ mol^{-1} [a]	Free energy/ hartree	S/J K^{-1} mol^{-1}	ΔG/kJ mol^{-1}
$(E)_{exo}$-**7**	−447.89855	210.3		0	−447.85243	380.7	0
$(E)_{endo}$-**7**	−447.89805	209.7		0.7 [b]	−447.85208	380.3	0.9 [b]
$(Z)_{exo}$-**7**	−447.89719	209.9		3.2 [b]	−447.85123	381.2	3.2 [b]
$(Z)_{endo}$-**7**	−447.89571	209.3		6.5 [b]	−447.85069	388.8	4.6 [b]
7-R_{exo}-ts	−447.88005	206.1	76*i*	44.4 [b]	−447.83501	372.5	45.7 [b]
7-R_{endo}-ts	−447.87801	206.4	213*i*	50.1 [b]	−447.83239	367.8	52.6 [b]
7-N_2-$(E)_{exo}$-ts	−447.88335	202.5	674*i*	32.1 [b]	−447.84028	382.3	31.9 [b]
7-N_2-$(E)_{endo}$-ts	−447.88708	202.6	680*i*	22.4 [b]	−447.84413	384.2	21.8 [b]
7-N_2-$(Z)_{exo}$-ts	−447.88358	202.9	663*i*	31.9 [b]	−447.84065	385.1	30.9 [b]
7-N_2-$(Z)_{endo}$-ts	−447.88643	203.0	664*i*	24.3 [b]	−447.84363	386.2	23.1 [b]
7-HERON-ts	−447.95607	194.1	183*i*	−155.3 [b]	−447.92304	463.0	−185.4 [b]
7-$Azide_{anti}$-ts	−447.82700	203	273*i*	180.5 [b]	−447.78354	380.1	180.8 [b]
7-$Azide_{syn}$-ts	−447.82818	203.2	278*i*	177.7 [b]	−447.78487	382.8	177.4 [b]
(*E*)-**17**	−338.43635	181.1		0	−338.39849	343.6	0
(*Z*)-**17**	−338.43311	181.8		9.2 [c]	−338.39482	341.4	9.6 [c]
17-HERON-ts	−338.43068	178.2	181*i*	12.0 [c]	−338.39291	330.1	14.6 [c]
Methyl formate **14**	−229.06301	164.1		−574.9 [b d] −398.1 [c e]	−229.02737	284.7	−653.5 [b d] −435.4 [c e]
Formyl azide **12**	−278.1137	85			−278.10877	289.3	
Methoxynitrene **13**	−169.71944	111.9		158.4 [b f]	−169.70174	262.6	110.0 [b f]
N_2	−109.52413	14.7			−109.53698	191.6	

[a] Includes zero point vibrational energy correction. [b] Energies relative to $(E)_{exo}$-**7**. [c] Energies relative to (*E*)-**17**. [d] ΔE or ΔG for the reaction $(E)_{exo}$-**7** ⟶ methyl formate **14** + $2N_2$. [e] ΔE or ΔG for the reaction (*E*)-**17** ⟶ methyl formate **14** + N_2. [f] ΔE or ΔG for the reaction $(E)_{exo}$-**7** ⟶ formyl azide **12** + methoxynitrene **13**.

In the previous paper, we outlined the synthesis of esters, including highly hindered esters, by the reaction of *N*-acyloxy-*N*-alkoxyamides **2** or *N*-alkoxy-*N*-chloroamides **3** with sodium azide in aqueous-organic mixtures (Scheme 2).[15] The reaction is



Scheme 2

bimolecular resulting in the formation of *N*-alkoxy-*N*-azidoamide intermediates **5**. In these, the azido group results in an electron-withdrawing *N*-substituent which, together with the electronegative alkoxy oxygen atom, results in a strong, combined electron withdrawal from the amide nitrogen. By analogy with other, similar systems, the resultant amide should be strongly pyramidal at nitrogen.[1,4,6,7] *N*-Alkoxy-*N*-azidoamides **5** are, however, unstable intermediates and decompose by a concerted process to esters **6** and molecular nitrogen. Not only is this an intramolecular reaction, it proceeds exothermically and in high yield. Ester formation from conventional bimolecular reactions of alcohols and carboxylic acids by Fischer esterification or by reaction of acyl halides and alcohols do not proceed well when both the carboxylic acid and alcohol reactants are bulky. Both require the formation of a tetrahedral intermediate which is destabilised by steric compression.[16–18] Hydroxamic esters, on account of the incorporation of an additional heavy atom, are quite easily formed, either from salts of hydroxamic acids[2,5,11,12,15,19–22] or from acid chlorides and alkoxyamines,[15,23] even when the amide and alkyl groups are bulky. For similar reasons the formation of either *N*-acyloxy- (**2**) or a *N*-chloro-*N*-alkoxyamides (**3**) can also be achieved with bulky acyl and alkoxy groups.[1,11,12,15,19–21,24–26] The reaction of these with azide, and subsequent decomposition of *N*-alkoxy-*N*-azidoamides, thus provides a new and important route to sterically hindered esters.

In this paper, we report on the theoretical properties of the model reactive intermediate *N*-azido-*N*-methoxyformamide **7**, as well as upon the mechanism of its decomposition to methyl formate and nitrogen.

Results and discussion

Ground state structures of *N*-azido-*N*-methoxyformamide 7

B3LYP/6-31G* calculations on the ground state *N*-azido-*N*-methoxyformamide **7** found four minima characterised by the disposition of the carbonyl and alkoxy oxygens as (*E*) and (*Z*) to one another and the conformation of the azido group (*exo* and *endo* to the pyramid defined by O8, C2 and N4). Absolute and relative energies, zero point vibrational energies, and free energies and entropies at 298 K, are given in Table 1. Geometries and selected structural parameters are shown in Fig. 2.

The *entgegen* forms are slightly more stable than the *zusammen* configurations. All showed considerable degree of pyramidalisation at nitrogen and average angles (in <>) are significantly below the ideal 120° for simple amides and similar to those calculated at the same level of theory for **8**(*NNO*, <116°>), **9**(*ONO*,<114°>), **10**(*ONCl*, <113°>) and **11**(*NNCl*, <112°>) anomeric formamides.[4,6] The azide groups were slightly bent in all cases with short terminal *N5—N6* bonds, intermediate length *N4—N5* and long *N3—N4* bonds. The *N—CO* bond lengths in all four structures are longer than that computed for formamide (1.362 Å),[4] *N*-chloroformamide (1.382 Å)[4] and *N*-methoxyformamide (1.380 Å)[4] but similar to those of **9**(1.396 Å), **10**(1.410 Å) and **11**(1.418 Å) systems reflecting a much lower degree of conjugation between the amide nitrogen lone pair and the carbonyl.

This reduced conjugation is reflected in smaller amide rotational barriers in *N*-azido-*N*-methoxyformamide **7**. Two rotation transition states, **7**-R_{exo}-ts and **7**-R_{endo}-ts (depending

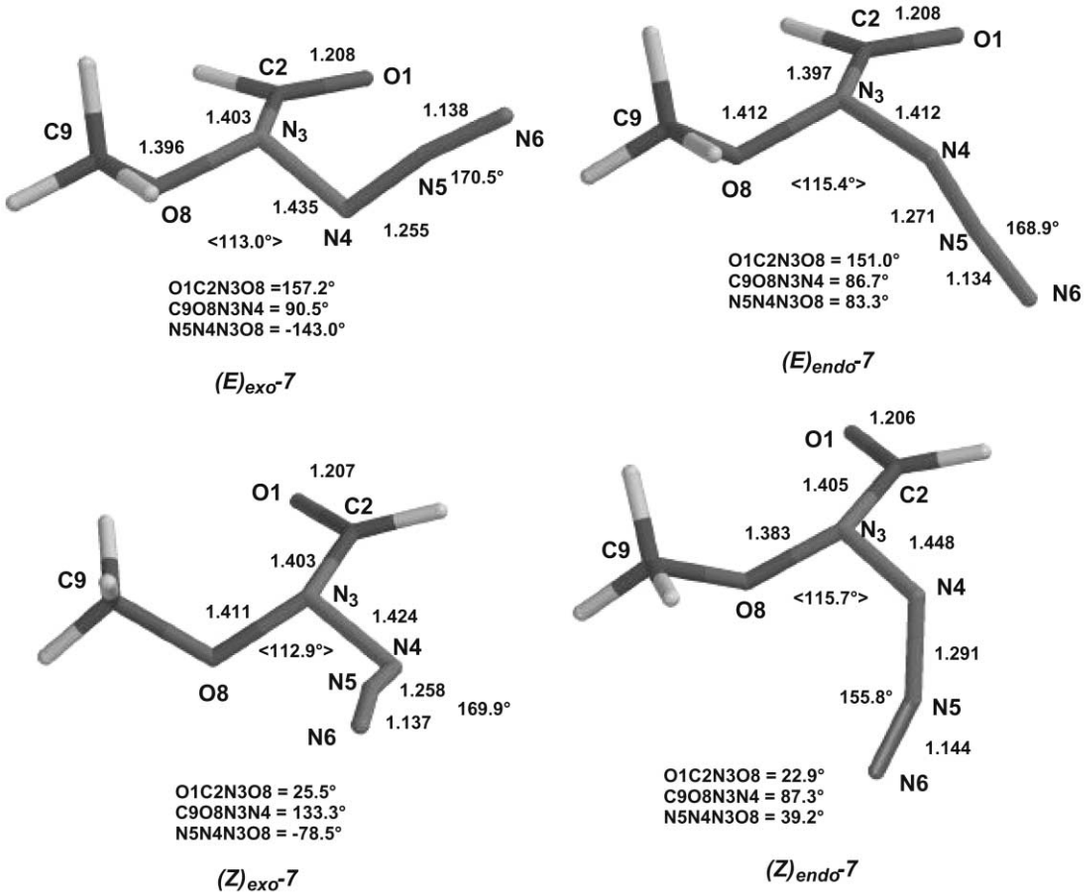
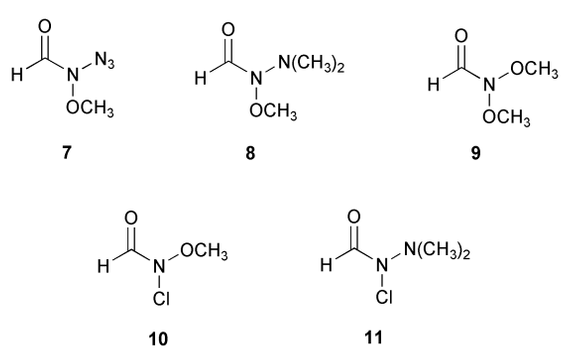


Fig. 2 B3LYP/6-31G* lowest energy structures for *N*-azido-*N*-methoxyformamide **7**; bond lengths in Å; average angle at nitrogen in <>.



upon the orientation of the carbonyl relative to the pyramid at nitrogen) were located which are 45.7 and 52.6 kJ mol^{-1} higher in energy (ΔG) than the lowest ground state structure (Fig. 3). Both have nearly linear azide groups which are *endo* to the pyramid at nitrogen. The lowest barrier is considerably reduced relative to those known for simple amides and *N*-alkylamides which are in the range 90–100 kJ mol^{-1} [27] and is similar to those calculated previously for anomeric systems **9**–**11** (30–50 kJ mol^{-1}).[4,6] It is also lower than that computed for the *NNO* system, *N,N*-dimethylamino-*N*-methoxyformamide **8** (53 kJ mol^{-1}).[6] Clearly the positive charge at the central nitrogen of the azide group, *N5*, results in a more strongly electron-withdrawing effect than is the case for the amino substituent in **8**, resulting in both a more pyramidal nitrogen and greater loss in amide conjugation. Not surprisingly, the rotational transition states are more strongly pyramidal at nitrogen and have longer *N—CO* bonds on account of the complete loss of conjugation between the nitrogen lone pair and the carbonyl at these twisted geometries.

Two additional degrees of conformational freedom are available to **7**, namely rotation of the azide group about *N3–N4*, and rotation of the methoxy group about *N3–O8*. Due to the anomeric interactions, the orientations of both of these groups are quasi-perpendicular to the average *C2–N4–O8* plane, and two diastereomeric transition structures exist for each process, corresponding to rotation of the relevant group approximately through 90° in either direction. Rotation of the azide group interconverts $(E)_{exo}$-**7** with $(E)_{endo}$-**7**, and $(Z)_{exo}$-**7** with $(Z)_{endo}$-**7**. The former process is hindered by free energy barriers of 15.1 and 17.3 kJ mol^{-1} (ΔE = 11.0 and 13.6 kJ mol^{-1}). We have not examined the latter. Rotation of the methoxy group is accompanied by inversion of the *N3* pyramid, and interconverts each conformer of **7** with its enantiomeric form. In $(E)_{exo}$-**7**, the methoxy group rotation is hindered by free energy barriers of 32.0 and 45.2 kJ mol^{-1} (ΔE = 29.6 and 43.1 kJ mol^{-1}). We have not located the transition structures for the other three conformations of **7** (Fig. 2). In summary, conformational interconversions in **7** are expected to be subject to the following approximate minimum free energy barriers: azide rotation, 15 kJ mol^{-1}; methoxy rotation, 30 kJ mol^{-1}; acyl rotation, 45 kJ mol^{-1}.

Anomeric interactions and HERON reactions

The lowest energy *entgegen* isomer, $(E)_{exo}$-**7**, displays a single anomeric stabilisation from an n_O—σ^*_{NN} overlap (*C9–O8–N3–N4* dihedral nearly 90°) which results in a short *N—O* bond of 1.396 Å and an unusually long *N3—N4* bond (1.435 Å) when compared to **8** in which the anomeric effect is strongest in the reverse direction (n_N—σ^*_{NO}) and which results in *N—N* and *N—O* bond lengths of 1.386 Å and 1.424 Å respectively. In the $(E)_{endo}$-**7** form, mutual n_O—σ^*_{NN} and n_N—σ_{NO} anomeric overlaps appear to be operative (both *C9–O8–N3–N4* and *N5–N4–N3–O8* approaching 90°). The $(Z)_{exo}$-**7** and $(Z)_{endo}$-**7** geometries appear to facilitate n_N—σ^*_{NO} and n_O—σ^*_{NN} overlaps respectively.

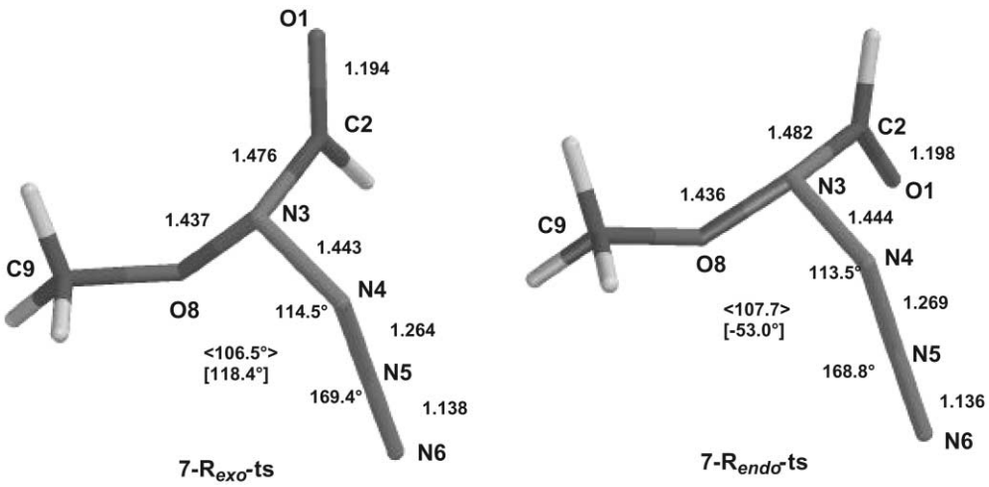
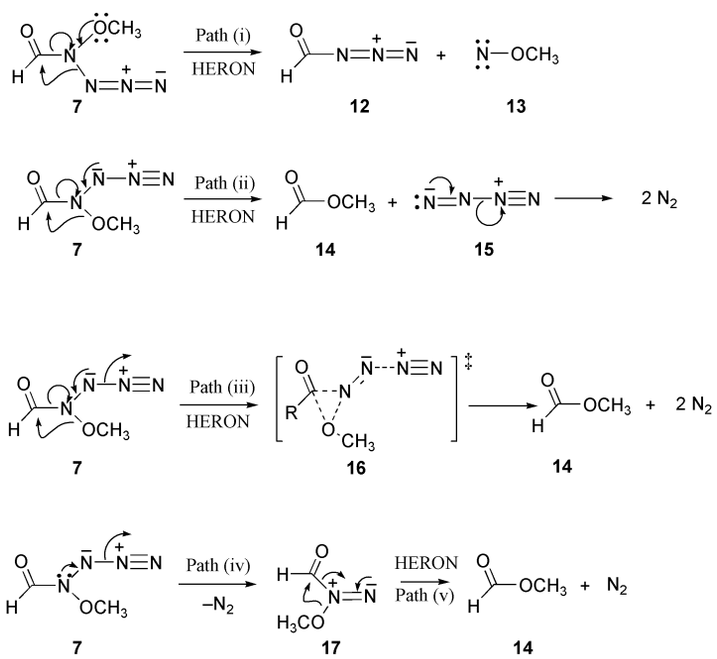


Fig. 3 B3LYP/6-31G* acyl rotation transition states for **7**, O1 *exo* and *endo* to the N3 pyramid; bond lengths in Å; average angle at nitrogen in <> and *OCNO* dihedral angles in [].



Scheme 3

In principle, two HERON reactions are possible in *N*-azido-*N*-alkoxyamides; an *N* to *C* migration of the alkoxy group giving ester and azidonitrene and an *N* to *C* migration of the azido group to give an acyl azide and alkoxynitrene. These are illustrated for *N*-azido-*N*-methoxyformamide **7** in Scheme 3. Migration of azide (Scheme 3, path(i)) leads to stable formyl azide **12** and methoxynitrene **13** but is highly endothermic and would not lead to ester formation. Methoxy migration, (Scheme 3, Path (ii)), while enabling the intramolecular formation of methyl formate **14**, is not directly feasible since azidonitrene **15** is not stable, decomposing spontaneously and with zero energy of activation to two molecules of nitrogen. The overall reaction would be highly favourable though, being exothermic by 575 kJ mol^{-1} with $\Delta G = -653.5$ kJ mol^{-1}. Thus, while energetically highly favourable, the formation of esters from the reaction of sodium azide and *N*-acetoxy-*N*-alkoxyamides or *N*-alkoxy-*N*-chloroamides, as outlined in the previous paper, can not be attributed to a straightforward HERON process initiated by an n_N—σ^*_{NO} interaction. A loss of nitrogen in concert with methoxy migration (*via* transition state **16** is however feasible (Scheme 3, Path (iii)). Alternatively, a two-step process involving sequential loss of nitrogen (Scheme 3, Path (iv)) followed by a HERON rearrangement of 1-formyloxy-1-methoxydiazene **17** (Scheme 3, Path (v)) could occur.

Fig. 4 illustrates fully optimised transition states for the expulsion of nitrogen from each of the ground state conformations of *N*-azido-*N*-methoxyformamide **7** (Scheme 3, Path (iv)). The absolute energies and activation energies relative to the lowest ground state structure, $(E)_{exo}$-**7**, are given in Table 1 and the lowest free energy barrier for loss of N_2 from the lowest ground state, $(E)_{exo}$-**7**, would be only 22 kJ mol^{-1}. N_2 loss will thus be a facile process competing favourably with conformational changes involving acyl and methoxy group rotations. In all four transition states (**7**-N_2-$(E)_{exo}$-ts, *etc.*), the *N4—N5* bond is stretched to *ca.* 1.5 Å while both the *N3—N4* and *N5—N6* bonds are significantly shorter than they are in the ground state structures. These shortened bond lengths, together with the average angles at *N3*, which are close to 120° in all four transition states, indicate progress along the reaction coordinate towards 1-formyl-1-methoxydiazene **17** and nitrogen. Conversion of conformers of ground state *N*-azido-*N*-methoxyformamide **7** to 1-formyl-1-methoxydiazene **17** and nitrogen (Scheme 3, Path (iv)) is however exothermic by $\Delta E = 177$–183 kJ mol^{-1} and $\Delta G = 218$–223 kJ mol^{-1}, and in accord with the Hammond postulate, correlates with the low $\Delta E^{\ddagger}$. Addition-

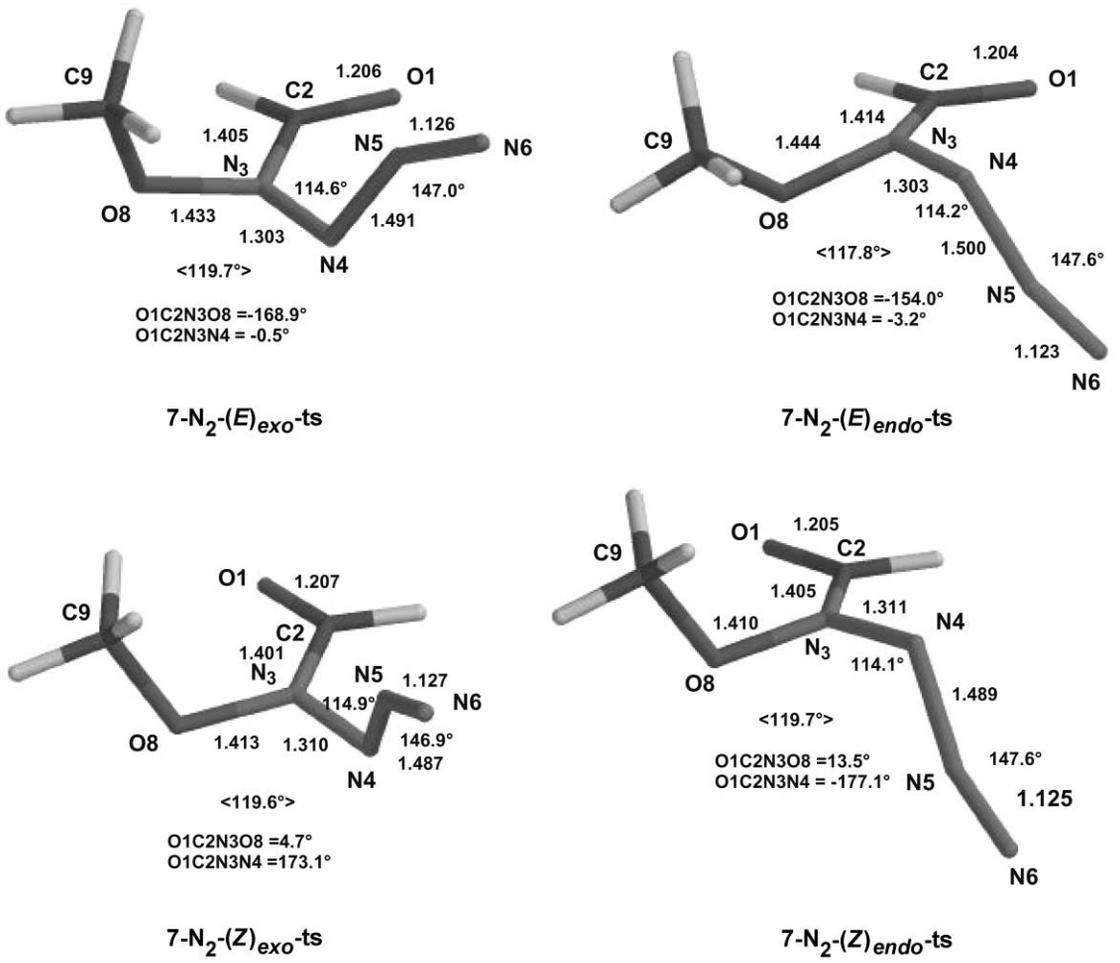


Fig. 4 B3LYP/6-31G* nitrogen expulsion transition states from ground state structures of *N*-azido-*N*-methoxyformamide **7**; bond lengths in Å; average angle at nitrogen in <>.

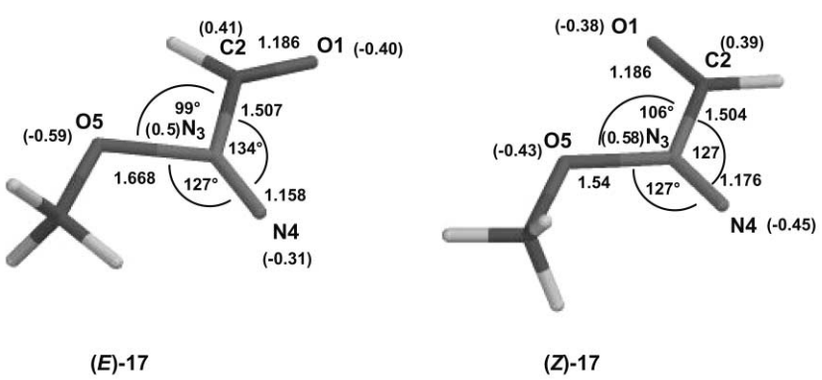


Fig. 5 B3LYP/6-31G* ground state structures for (*E*)- and (*Z*)-1-formyl-1-methoxydiazene; electrostatic charges in parentheses; bond lengths in Å.

ally, structures in Fig. 4 show only modest shortening of the *N3—N4* (*e.g.* −0.132 Å for $(E)_{exo}$-**7** to **7**-N_2-$(E)_{exo}$-ts), and elongation of the *N4—N5* bond (*e.g.* +0.236 Å for $(E)_{exo}$-**7** to **7**-N_2-$(E)_{exo}$-ts) in accordance with an early, rather than a late transition state.

The product from this nitrogen expulsion, 1-formyl-1-methoxydiazene **17**, exists as two planar conformers, (*Z*)-**17** and (*E*)-**17**, depending upon the orientation of the formyl group. Only the (*Z*) orientation of the methoxy group is stable in each. Ground state structures and energies are presented in Fig. 5 and Table 1 respectively. Both structures are characterised by short *N—N* bonds and long *N—C(O)* and *N—O* bonds. The much larger *C2–N3–N4* angle for the (*E*) form (134°) can be attributed to dipole–dipole repulsion; both the *C—O* and *N—N* bonds are polarised in the same direction. Electrostatic charges computed at the 6-31G* level (Fig. 5) are in accordance with the zwitterionic rather than the aminonitrene form of the 1,1-substituted diazene.

Rearrangement of the lowest energy conformation of 1-formyl-1-methoxydiazene, (*E*)-**17**, to methyl formate **14** and nitrogen (Scheme 3, Path (v)) is exothermic by $\Delta G = -435$ kJ mol^{-1} ($\Delta E = -398$ kJ mol^{-1}). The reaction has a precedent in the decomposition of *N*,*N*′-diacyl-*N*,*N*′-dialkoxyhydrazines which produce the same intermediate after the first HERON reaction,[2,5] and the process can itself be regarded as a HERON reaction. The nitrogen extrusion proceeds with a low activation barrier of only $\Delta G^{\ddagger} = 14.6$ kJ mol^{-1} and the transition state (**17**-HERON-ts, Fig. 6(a)) reflects its early nature relative to that computed previously for the slightly exothermic HERON rearrangement of *N*-dimethylamino-*N*-methoxyformamide (**8**-HERON-ts, Fig. 6(b)).[5] The *N3–O5* bond is shorter than the *C2–O5* bond and, whereas in transition state Fig. 6(b) the

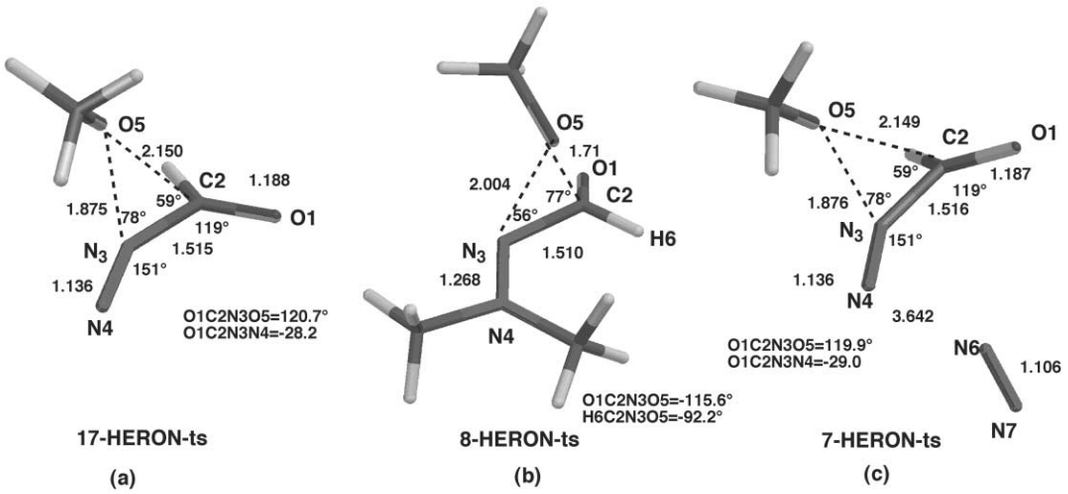


Fig. 6 B3LYP/6-31G* HERON transition states: (a) rearrangement of **17** to methyl formate **14** and nitrogen; (b) rearrangement of *N*-dimethylamine-*N*-methoxyformamide **8**; (c) rearrangement directly from **7**; bond lengths in Å.

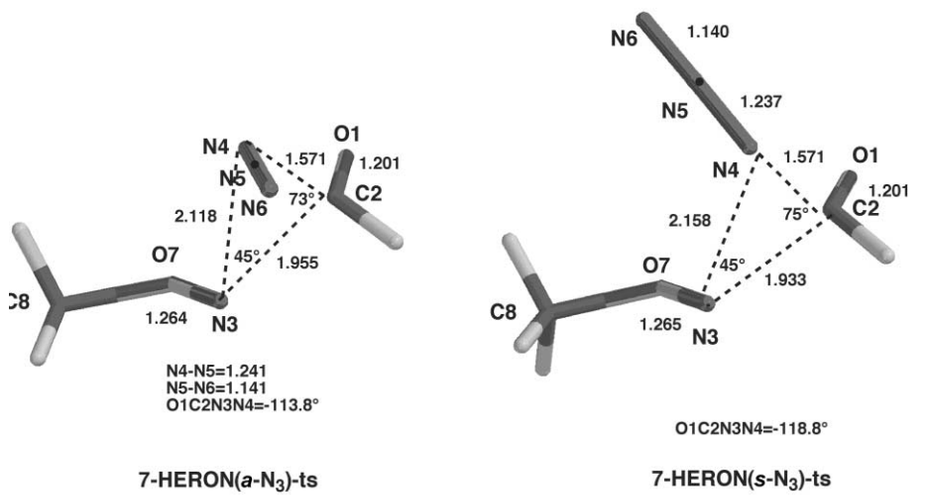


Fig. 7 B3LYP/6-31G* transition states for a HERON migration of the azide group in 1-formyl-1-methoxydiazene **7**; bond lengths in Å.

formyl group is fully rotated to receive the *O5*-oxygen electrons and this oxygen is perpendicular to the *N4–N3–C2–H6* plane, the migrating oxygen in Fig. 6(a) is offset and the formyl group is much less rotated.

Overall, the formation of methyl formate and two molecules of nitrogen by the sequential steps depicted in Scheme 3, pathways (iv) and (v) would appear to be highly favourable with a rate-determining $\Delta G^{\ddagger}$ of only 22 kJ mol^{-1}.

The concerted decomposition (Scheme 3, Path (iii)) would benefit from the simultaneous formation of methyl formate and two molecules of nitrogen. However, in an attempt to model the HERON migration of the methoxy group in the $(E)_{exo}$-**7** ground state, no transition state could be achieved without prior loss of nitrogen according to (Scheme 3, Path (iv)). By artificially freezing *N–N* distances to those in $(E)_{exo}$-**7**, a "transition state" for migration of methoxy was located, but with an $\Delta E^{\ddagger}$ of 110 kJ mol^{-1}. Expulsion of nitrogen from this structure occurred spontaneously upon relaxation of the constraints. The result was the transition state, **7**-HERON-ts, illustrated in Fig. 6(c). Its energy was some 166 kJ mol^{-1} lower than the $(E)_{exo}$-**7** ground state (Table 1). In fact, **7**-HERON-ts is equivalent to **17**-HERON-ts with a spectator N_2, as is evident from comparison of the structures in Fig. 6(a) and Fig. 6(c). Clearly, neither the concerted decomposition (Scheme 3, pathway (iii)) nor the HERON migration to methyl formate and azidonitrene (Scheme 3, pathway (ii)) will be competitive with the two-step process.

The alternate HERON migration of the azido group in **7** leading to formyl azide **12** and methoxynitrene **13** (Scheme 3, Path (i)) was also investigated although, experimentally, we have no evidence for acyl azide formation in the reaction of *N*-acyloxy-*N*-alkoxyamides **2** and *N*-alkoxy-*N*-chloroamides **4** with sodium azide. The overall reaction is computed to be extremely endothermic with a high $\Delta G^{\ddagger}$ relative to $(E)_{exo}$-**7** (Table 1). Two transition states, **7**-HERON(s-N_3)-ts and **7**-HERON(a-N_3)-ts, were located differing only in the conformation of the azide group which is either *syn* or *anti* to the acyl and alkoxy oxygen atoms (Fig. 7). They were derived from $(Z)_{exo}$-**7** and $(Z)_{endo}$-**7** conformations respectively. Transition states for similar migrations from the $(E)_{exo}$-**7** and $(E)_{endo}$-**7** conformations were not located. Both transition states resembled products; the *N4–C2* bonds were well developed and both the *N3—N4* and *C2—N3* bonds were extremely long. The methoxynitrene character is well developed in that the *O7—N3* bond (1.264 Å and 1.265 Å) is only marginally longer than that of the ground state methoxynitrene **13** (1.24 Å). Structures and energies of the products, methyl formate **14**, formyl azide **12** and methoxynitrene **13** are illustrated in Fig. 8 and Table 1 respectively.

The overall energetics of decomposition of *N*-azido-*N*-methoxyformamide **7** to methyl formate and nitrogen is computed by B3LYP/6-31G* calculations to be exothermic by $\Delta G = -654 - -659$ kJ mol^{-1}. This degree of exothermicity would, in itself, provide an excellent driving force for the synthesis of sterically hindered esters. However, it plays another role. The transition state for ester formation from 1-formyl-1-alkoxyformamide (Fig. 6(a)) is early along the reaction coordinate, indicating little bond formation between the

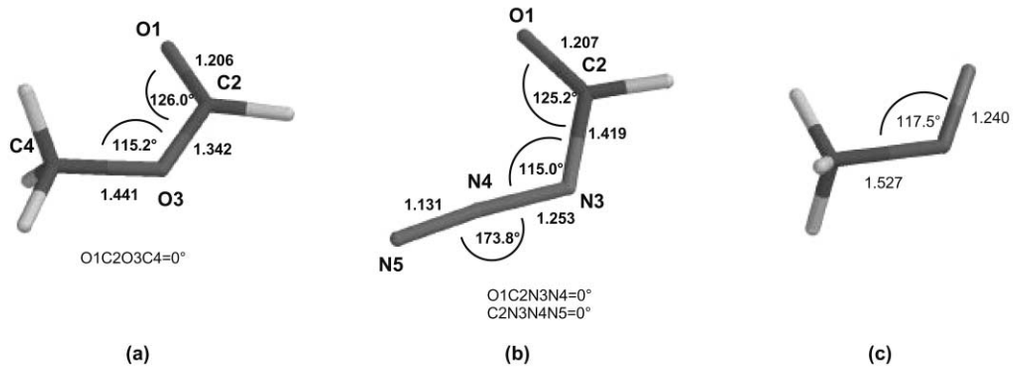


Fig. 8 B3LYP/6-31G* ground state structures for (a) methyl formate **14** (b) formyl azide **12** and (c) methoxynitrene **13**.

migrating methoxy group and the acyl carbon. The *C2–N3* bond is virtually intact at the transition state and analysis of the intrinsic reaction coordinate indicates that bonding to the acyl carbon occurs after the transition state complex and *in concert* with the acyl carbon–nitrogen bond cleavage. This obviates the need to bond both the alkoxy and the amide nitrogen to the carbonyl in a tetrahedral intermediate. Hence, formation of sterically hindered esters by the HERON rearrangement in 1-acyl-1-alkoxydiazenes is not impeded by the steric constraints imposed through intermediacy of tetrahedral intermediates such as play a role in Fischer esterification.

Computational methods

All structures were fully optimised at the B3LYP/6-31G* level of theory using procedures implemented in Gaussian 94 and Gaussian 98.[28]

Harmonic frequency analysis was performed to provide zero point energy corrections to the relative energies and to verify the nature of each stationary point as a minimum (all real frequencies) or as a transition state structure (exactly one imaginary frequency). Thermal corrections, as reported by the Gaussian programs, were applied to all species. All internal motions were treated as vibrations for the purpose of obtaining enthalpy corrections, free energies, and entropies at 298 K within the harmonic oscillator/rigid rotator approximation.[29]

Acknowledgements

The authors gratefully acknowledge financial support from the Australian Research Council and Natural Sciences and Engineering Research Council of Canada

References

1 S. A. Glover, *Tetrahedron*, 1998, **54**, 7229 Tetrahedron Report 455.
2 J. M. Buccigross, S. A. Glover and G. P. Hammond, *Aust. J. Chem.*, 1995, **48**, 353.
3 J. M. Buccigross and S. A. Glover, *J. Chem. Soc., Perkin Trans. 2*, 1995, 595.
4 S. A. Glover and A. Rauk, *J. Org. Chem.*, 1996, **61**, 2337.
5 S. A. Glover, G. Mo and A. Rauk, *Tetrahedron*, 1999, **55**, 3413.
6 S. Glover and A. Rauk, *J. Org. Chem.*, 1999, **64**, 2340.
7 S. A. Glover, G. Mo, A. Rauk, D. Tucker and P. Turner, *J. Chem. Soc., Perkin Trans. 2*, 1999, 2053.
8 A. Gillson, S. A. Glover, and P. Turner 2002 Recent unpublished results.
9 T. M. Banks, A. M. Bonin, J. J. Campbell, S. A. Glover, G. A. Hammond, A. S. Prakash and C. A. Rowbottom, *Mutat. Res.*, 2001, **494**, 115.
10 T. M. Banks, S. A. Glover, and A. S. Prakash, unpublished results.
11 A. M. Bonin, S. A. Glover and G. P. Hammond, *J. Org. Chem.*, 1998, **63**, 9684.
12 J. J. Campbell and S. A. Glover, *J. Chem. Res. (S)*, 1999, **8**, 474 (*J. Chem. Res. (M)*, 2075–2096).
13 S. A. Glover, *Arkivok*, 2001 (http://www.arkat-usa.org/ark/journal/Volume2/Part3/Tee/OT-308C/OT-308.htm).
14 M. Adams S. A. Glover D. J. Tucker, unpublished results.
15 Preceding paper: S. A. Glover and G. Mo, *J. Chem. Soc., Perkin Trans. 2*, 2002, DOI: 10.1039/b111250n.
16 I. O. Sutherland, in *Comprehensive Organic Chemistry*, ed. I. O. Sutherland, Pergamon Press, Oxford, 1979, p. 871.
17 J. Mulzer, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, Pergamon Press, Oxford, 1991, p. 323.
18 J. Mulzer, in *Comprehensive Organic Functional Group Transformations*, ed. C. J. Moody, Pergamon, Oxford, 1995, p. 121.
19 A. M. Bonin, S. A. Glover and G. P. Hammond, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1173.
20 J. J. Campbell, S. A. Glover, G. P. Hammond and C. A. Rowbottom, *J. Chem. Soc., Perkin Trans. 2*, 1991, 2067.
21 J. J. Campbell, S. A. Glover and C. A. Rowbottom, *Tetrahedron Lett.*, 1990, **31**, 5377.
22 J. H. Cooley, W. D. Bills and J. R. Throckmorton, *J. Org. Chem.*, 1960, **25**, 1734.
23 M. V. De Almeida, D. H. R. Barton, I. Bytheway, J. A. Ferriera, M. B. Hall, W. Liu, D. K. Taylor and L. Thomson, *J. Am. Chem. Soc.*, 1995, **117**, 4870.
24 S. A. Glover, C. A. Rowbottom, A. P. Scott and J. L. Schoonraad, *Tetrahedron*, 1990, **46**, 7247.
25 S. A. Glover, A. Goosen, C. W. McCleland and J. L. Schoonraad, *Tetrahedron*, 1987, **43**, 2577.
26 S. A. Glover, A. Goosen, C. W. McCleland and J. L. Schoonraad, *J. Chem. Soc., Perkin Trans. 2*, 1984, 2255.
27 L. M. Jackman and F. A. Cotton, *Dynamic Nuclear Magnetic Resonance Spectroscopy*, Academic Press, New York, 1975.
28 (*a*) M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. A. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrewski, J. V. Oritz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, in *Gaussian 94, (SGI-Revision B.3)*, Pittsburgh, PA, 1995; (*b*) M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, *Gaussian, Inc.*, Pittsburgh PA, 2001.
29 D. A. McQuarrie, *Statistical Thermodynamics*, Harper & Row, New York, NY, 1973.