Aust. J. Chem. **2014**, *67*, 1344–1352 http://dx.doi.org/10.1071/CH14270

Full Paper

Studies of the Structure, Amidicity, and Reactivity of *N*-Chlorohydroxamic Esters and *N*-Chloro-β,βdialkylhydrazides: Anomeric Amides with Low Resonance Energies*

Stephen A. Glover, A,B Adam A. Rosser, A and Robert M. Spence

^AChemistry, School of Science and Technology, University of New England, Armidale, NSW 2351, Australia.

^BCorresponding author. Email: sglover@une.edu.au

Density functional calculations have been carried out to determine the properties of the title anomeric amides. At the B3LYP/6-31G(d) level, *N*-chloro-*N*-methoxyacetamide **8a** is computed to be strongly pyramidal at nitrogen with a long amide bond that is untwisted. *N*-Chloro-*N*-dimethylaminoacetamide **9a** is completely planar, but its amide bond is still much longer than that in *N*,*N*-dimethylacetamide **4**. This is a steric, rather than a resonance, effect. COSNAR and a *trans*-amidation method calculate low resonance energies for both model amides, which is attributed to the combined electronegativity of the heteroatoms at the amide nitrogen and the strong anomeric effect when there is a chlorine substituent on nitrogen. When M06 and ω B97X-D dispersion-corrected density functional methods are used with the expanded 6-311++G(d,p) basis set, the resonance energies of **8a** (-34 kJ mol⁻¹) and **9a** (-49 kJ mol⁻¹) are in line with the gross electronegativity of the substituent atoms. Unlike other anomeric amides, **8a** and **9a** are not predicted to undergo HERON reactivity.

Manuscript received: 29 April 2014. Manuscript accepted: 19 May 2014. Published online: 19 June 2014.

Introduction

Anomeric amides, an unusual class of amides highlighted in our research, bear two electronegative atoms on the amide nitrogen. Amides **1a–d** (Chart 1) all possess properties that are a response to the electron demand of the atoms X and Y.^[1–6] The substituent atoms at nitrogen induce localization of the nitrogen atom lone pair electrons in an sp³ hybrid orbital, which results in loss of resonance stabilization through both the increased 's' character, as well as the reduced basicity of the lone pair. Nonetheless, the lone pair still benefits from an, albeit weakened, resonance interaction with the carbonyl carbon as X-ray structural data for a variety of congeners show relatively little twist about the N–CO bond.^[6–9] In addition to crystal data, these altered properties are supported by experimental and spectroscopic data as well as theoretical studies.^[1-3,6-12]

The reduced resonance is evident in much higher than expected carbonyl stretch frequencies in their infrared spectra. For instance, *N*,*N*-dialkoxyamides **1b** (ONO systems), *N*-acyloxy-*N*-alkoxyamides **1c** (ONOAc systems), and *N*-alkoxy-*N*-aminoamides **1d** (NNO systems) exhibit solution-state amide carbonyl stretch frequencies in ranges of 1710–1720, 1718–1750⁻ and 1700–1744 cm⁻¹ respectively.^[1-3,9,13] Crystal structures demonstrated strong pyramidality at nitrogens of ONO and ONOAc systems with two oxygen atoms at nitrogen (Winkler–Dunitz^[14,15] pyramidality of $\chi = 56-58^{\circ}$ and $60-61^{\circ}$ respectively).



Chart 1.

^{*}This paper is dedicated to the memory of Professor Roger Brown, one of Australia's most notable physical organic chemists and a true gentleman.

The NNO amides studied to date are less pyramidal but nonetheless significantly puckered at nitrogen ($\chi = 47-48^{\circ}$).^[8] In all cases, the amide bonds are relatively untwisted but weakened resonance is evidenced by long N—CO bond lengths (ONO, 1.41–1.42 Å, ONOAc, 1.44 Å, NNO, 1.41 Å) when compared with typical amides (average 1.359 Å, median 1.353 Å),^[7] and very low barriers to amide isomerism. The barrier to rotation of several *N*,*N*-dialkoxyamides could not be observed by NMR down to -90° C.^[1] An n_Y— σ^*_{NX} anomeric stabilization is evident from alignment of a p-type lone pair on Y and the N–X σ^* orbital in crystal structures of all three systems.

Calculations employing the B3LYP/6–31G(d) level of theory have been found to reproduce the structural properties of anomeric amides as well as their reduced resonance energies.^[9–12,16] We recently demonstrated that the residual resonance energy (RE) in amides and lactams in general can be determined isodesmically^[17] and, using those methods, models *N*,*N*-dimethoxyacetamide **2** and *N*-methoxy-*N*-dimethylaminoacetamide **3** retain only 36 kJ mol⁻¹ and 51–52 kJ mol⁻¹ of resonance respectively, approximately 47 and 67% that of *N*,*N*-dimethylacetamide **4** (76 kJ mol⁻¹)^[9,18]

Anomeric amides **1b–d** have been shown to undergo the unusual HERON reaction,[†] which is illustrated in Fig. 1 and involves an anomerically driven migration of an electronegative atom from nitrogen to the carbonyl carbon with production of a stabilized nitrene.^[16,19–26] Initially discovered from spontaneous decomposition of *N*-alkoxy-*N*-aminoamides **1b**,^[2,21,22,24,27–30] it has subsequently been observed in the thermal decomposition of *N*-acyloxy-*N*-alkoxyamides **1c** at elevated temperatures.^[26] Acyclic *N*,*N*-dialkoxyamides instead undergo homolysis at elevated temperatures to alkoxyl and *N*-alkoxyamidyl radicals^[13] but several cyclic forms of *N*,*N*-dialkoxyamides **5a** and **5b** rearrange at room temperature in reactions under stereoelectronic control.^[16] Theoretical activation barriers from B3LYP/6–31G(d) calculations are in line with these observations. Computed barriers to rearrangement of methoxyl in **2** and **3a** are, respectively, 189 and 147 kJ mol^{-1.[16,18,19,22]} Model lactams **5c** and **5d** rearrange by ring opening and ring contraction respectively with computed barriers of 108 and 139 kJ mol^{-1.[16]}



Infrared carbonyl stretch frequencies for a wide range of *N*-alkoxy-*N*-chloroamides range from 1718 to 1744 cm⁻¹ and are on average ~40 cm⁻¹ higher than their hydroxamic ester precursors.^[1,3] From a dynamic NMR study on *N*-benzyloxy-*N*-chlorobenzamide **7**, ΔG^{\ddagger} of 41.8 kJ mol⁻¹ for rotation about the O—N bond was determined but amide isomerism could not be detected and must have an even lower barrier.^[1] Corresponding computed isomerization barriers in *N*-chloro-*N*-methoxyforma-mide **8b** were 44.3 and 29.3 kJ mol⁻¹.^[10]

Anomeric destabilization of the N–X bond by a lone pair on Y plays a role in determining the ease of migration of X.^[1,3,19]

When Y is nitrogen, the high-energy amino lone pair results in a

strong n_N - σ^*_{NX} interaction and a weakening of the N–X bond in

accord with the much lower activation energy (E_A) for the

HERON reaction in NNO systems 1d relative to ONO systems

1b and 1c. However, computed migration transition states in all

HERON reactions demonstrate that residual RE is sacrificed, in

that the group X migrates in a plane orthogonal to the N-C(O)

plane, necessitating complete rotation of the nitrogen lone pair

away from conjugation and into that plane (Fig. 2). Clearly, this

loss of conjugation is a component of the overall activation

energy, and heteroatoms at nitrogen also impact on the HERON

activation barriers through their impact on the RE. The net

In contrast to ONCl systems, the structural and spectroscopic properties of NNCl systems **1e** are thus far unknown. The



Fig. 1. A generalized HERON reaction where X and Y are electronegative atoms.



Fig. 2. Theoretically derived transition state for the generalized HERON reaction of an XNY amide. (a) Perspective drawing; (b) Newman projection along the N–C bond.



[†]*He*teroatom *r*earrangements *on n*itrogen; first presented to the Second Heron Island Conference on Reactive Intermediates and Unusual Molecules, Heron Island, Australia, 1994.



 Table 1.
 B3LYP/6–31G(d) optimized geometries for N-chloro-N-methoxyacetamide 8a, N-chloro-N-dimethylaminoacetamide 9a, and N-chloro-N-methylaminoacetamide 10 together with data for 2 and 3a

	$\tau \left[^{\circ} ight]^{\mathrm{A}}$	$\chi \left[\circ \right]^{\mathrm{B}}$	$\theta [^{\circ}]^{C}$	N1—C1 [Å]	C1—O1 [Å]	N1—O2 or N1—N2 [Å]	N1—C1 [Å]	Twist [°] ^D
8a	-5.3	52.3	112.5	1.432	1.207	1.388	1.787	1
9a	0	0	120.0	1.396	1.212	1.351	1.820	0
10	-7.8	35.1	116.8	1.414	1.209	1.359	1.828	6
2 ^E	8.5	48.1	114.3	1.417	1.212	1.406 ^E	1.391 ^E	67/84
3a ^F	5.4	41.8	115.5	1.404	1.217	1.387 ^F	1.43 ^F	10

^AWinkler–Dunitz twist parameter.^[14,15]

^BWinkler–Dunitz pyramidality index.^[14,15]

^CAverage angle at nitrogen.

^DTwist of O2 (in 8a) or N2 (in 9a and 10) lone pair axes from the N—Cl bonds; a measure of anomeric alignment.

^EPreviously published data; N—O bonds in 2.^[9]

^FNew data; N—N (1.387 Å) and N—O (1.430 Å) in **3a**.^[18]

conformers of *N*-chloro-*N*-dimethylaminoformamide **9b** have been calculated at the B3LYP/6–31G(d) level as part of our initial investigations of anomeric amides and the nitrogen was predicted to be strongly pyramidal (average angle at the amide nitrogen of 112°) and to have a long N—C(O) bond (1.418 Å).^[10] However, to our knowledge no stable *N*-amino-*N*-chloroamides are known.

HERON reactions have not been observed for ONCl systems, which are thermally stable at room temperature. HERON reactions of NNCl systems would be expected to occur more readily than in ONCl systems and HERON has been implicated in at least one reaction between a hydrazide and *tert*-butyl hypochlorite (see below).

In this paper, we explore the theoretical properties of model ONCl system *N*-chloro-*N*-methoxyacetamide **8a**, and NNCl systems *N*-chloro-*N*-dimethylaminoacetamide **9a** and *N*-chloro-*N*-methylaminoacetamide **10** to establish their stability and REs as well as the potential for HERON reactivity in ONCl and NNCl systems.

Results and Discussion

The lowest-energy structures of *N*-chloro-*N*-methoxyacetamide **8a**, *N*-chloro-*N*-dimethylaminoacetamide **9a**, and *N*-chloro-*N*-methylaminoacetamide **10**, together with important geometrical parameters, are shown in Table 1.

The computed structure around nitrogen for **8a** closely matches the X-ray structure of **6** and the degree of pyramidality at nitrogen is akin to that computed for other anomeric amides with similar electron demand at nitrogen such as *N*,*N*-dimethoxyacetamide **2**, for which $\chi = 48^{\circ}$.^[9] The characteristic N—C(O) bond is longer than that for **2** (1.417 Å), which would imply even less amide character relative to **2**. From the twist angle, the anomeric alignment in **8a** is nearly optimal and indicates an $n_O - \sigma^*_{NCI}$ conformational stabilization in the ground state.

The theoretical structure of N-chloro-N-dimethylaminoacetamide **9a** is, at first inspection, quite anomalous in that the



Fig. 3. Space-filling models of (a) *N*-chloro-*N*-dimethylaminoacetamide **9a**; (b) *N*-chloro-*N*-methylaminoacetamide **10**.

amide nitrogen is completely sp² hybridized and it represents the first anomeric amide that is not predicted to become pyramidal in response to the electron demand of the heteroatoms. NNO systems are less pyramidal than ONO systems but in **3a**, the amide nitrogen is still computed to be quite pyramidal ($\chi = 42^{\circ}$) and the average angle at nitrogen in the formamide **3b** was predicted to be 116°.^[12,18] NNCl systems should exhibit appreciable pyramidality, even with the lower electronegativity of chlorine. However, although sp² hybridization shortens adjacent bonds, the N—C(O) bond in **9a** is in fact quite long when compared with *N*,*N*-dimethylacetamide **4** (1.378 Å at B3LYP/ 6-31G(d)) in which the amide nitrogen is similarly planar.^[17]

The driving force for the lack of pyramidality at the amide nitrogen in **9a** becomes clear on inspecting space-filling models of **9a** and of the B3LYP/6–31G(d) optimized structure of **10** (Fig. 3). Steric congestion in **9a**, which is relieved in the methylamino analogue **10**, enforces planarity in **9a**. The electronegativity of the –NHMe group in **10** would not be expected to differ greatly from –NMe₂ in **9a**, and on replacement of one methyl by sterically less-demanding hydrogen, the nitrogen becomes reasonably pyramidal ($\chi = 35^\circ$). The N—C(O) bond also lengthens in line with that of the methoxy analogue **8a**.

In both NNCl systems, the amino nitrogen lone pair axis lies very close to the plane containing the N—Cl bond, in support of an n_N — σ^*_{NCl} anomeric interaction.

Unequivocal support for reduced amidicity in both **8a** and **9a** can be derived from isodesmic calculations of the RE in each case. As in previous papers,^[9,16–18] we have established RE by two independent methods: carbonyl substitution nitrogen atom replacement (COSNAR)^[31,32] and a *trans*-amidation process.^[17]

$$\begin{array}{c} O \\ H_{3}C \\ 11 \\ 11 \\ 12 \\ \end{array} \begin{array}{c} \Delta E_{\underline{COSNAR}} \\ Y = OMe, NMe_{2} \\ H_{3}C \\ 13 \\ 13 \\ 14 \\ (1) \end{array} \begin{array}{c} O \\ Y \\ H_{3}C \\ 14 \\ (1) \\ \end{array} \right)$$

The COSNAR process, represented by Eqn 1, gives the energy stabilization when ketone **11** and amine **12**, in the same skeletal matrix, generate the amide **13** and hydrocarbon **14**. For *N*,*N*-dimethylacetamide **4**, the stabilization is -77.5 kJ mol⁻¹ and amidicity is given as a percentage of this value.^[17]

$$\begin{array}{c} \overset{O}{\underset{H_3C}{\overset{CH_3}{\longrightarrow}}}, \overset{Y}{\underset{H_3C}{\overset{H_3}{\longrightarrow}}}, \overset{Y}{\underset{H_3C}{\overset{V}{\longrightarrow}}}, \overset{\Delta E_{react}}{\underset{Y = OMe, NMe_2}{\overset{Me_2}{\longrightarrow}}}, \overset{O}{\underset{H_3C}{\overset{Y}{\longrightarrow}}}, \overset{Y}{\underset{H_3C}{\overset{V}{\longrightarrow}}}, \overset{CH_3}{\underset{H_3C}{\overset{H_3}{\longrightarrow}}}, \overset{CH_3}{\underset{H_3C}{\overset{H_3}{\overset{H_3}{\longrightarrow}}}, \overset{CH_3}{\underset{H_3C}{\overset{H_3}{\overset{H_3}{\longrightarrow}}}, \overset{CH_3}{\underset{H_3C}{\overset{H_3}{\overset{H_3}{\overset{H_3}{\longrightarrow}}}}, \overset{CH_3}{\underset{H_3C}{\overset{H_3}{\overset{H$$

The alternative method, which gives very similar REs but, in addition, sheds light on the effect of inductive substituents at nitrogen, first determines the change in stability of an amide relative to 4 through Eqn 2. However, electronegative substituents at nitrogen further destabilize the carbonyl of an amide through their β -inductive effect, and this can be determined isodesmically from Eqn 3 where the amides are fully twisted and are obtained as transition states by B3LYP/6–31G(d). As the total destabilization due to loss of RE is obtained as the difference between these two energies. In this approach, the maximum possible loss of resonance is $-76.0 \text{ kJ mol}^{-1}$ (determined from the destabilization in 1-aza-2-adamantanone, which, like Kirby's trimethylated derivative,^[33,34] is fully twisted^[17]) and the residual RE is given by Eqn 4.

Residual RE = $-76.0 + (\Delta E_{react} - \Delta E_{inductive}) \text{ kJ mol}^{-1}$ (4)

Based on B3LYP/6–31G(d) energies for all structures (Table S1 in the Supplementary Material), ΔE_{COSNAR} , ΔE_{react} , $\Delta E_{inductive}$, and REs have been computed for **8a**, **9a**, and **10** (Table 2). For *N*-chloro-*N*-methoxyacetamide **8a**, the COSNAR and *trans*-amidation REs are virtually identical and lower than that computed for *N*,*N*-dimethoxyacetamide **2** (36 kJ mol⁻¹), indicating only ~38 % retention of the level of resonance in *N*, *N*-dimethylacetamide **4**. The pyramidality is very similar in **2** ($\chi = 48^{\circ}$) and **8a**, but **8a** is less twisted than **2** ($\tau = 8.5$) (Table 1).

After incorporation of the β -inductive destabilizing effect of chlorine and nitrogen, the *trans*-amidation and COSNAR methods give very similar stabilization for each of **9a** and **10**.

Table 2. B3LYP/6-31G(d)-derived COSNAR and *trans*-amidation data for *N*-chloro-*N*-methoxyacetamide 8a, *N*-chloro-*N*-dimethylaminoacetamide 9a, and *N*-chloro-*N*-methylaminoacetamide 10 from Eqns 1–4 and acetyl chloride–methoxynitrene complex energies in Fig. 5

Structure	Energy $[kJ mol^{-1}]^{4}$
<i>N</i> -Chloro- <i>N</i> -methoxyacetamide 8a	
ΔE_{COSNAR} for $8a^{B}$	-29.60 [38%]
ΔE_{React} for $\mathbf{8a}^{\mathrm{C}}$	69.91
$\Delta E_{Inductive}$ for 8a ^D	23.41
RE for 8a ^E	-29.47 [39%]
N-Chloro-N-dimethylaminoacetamide 9a	
ΔE_{COSNAR} for 9a ^B	-28.73 [38%]
ΔE_{React} for 9a ^C	64.54
$\Delta E_{Inductive}$ for 9a ^D	17.60
RE for 9a ^E	-29.04 [37%]
N-Chloro-N-methylaminoacetamide 10	
ΔE_{COSNAR} for 10 ^B	-32.56 [42%]
ΔE_{React} for 10 ^C	66.57
$\Delta E_{Inductive}$ for 10 ^D	23.18
RE for 10 ^E	-32.58 [43 %]
Complex Fig. 5 anti $(i136 \text{ cm}^{-1})$	173.3 (166.3) ^F
Complex Fig. 5 syn ($i178 \text{ cm}^{-1}$)	$165.0(158.4)^{\rm F}$

^AAmidicities in square parentheses.

^BFrom Eqn 1.

^CFrom Eqn 2.

^DFrom Eqn 3.

^EFrom Eqn 4.

 $^{\mathrm{F}}$ Relative to the energy of **8a**; ZPE and enthalpy-corrected values in parentheses.

The *N*-methylamino variant, **10**, has slightly greater resonance than that of **9a** and here the nitrogen is distinctly pyramidal $(\chi = 35^\circ; \text{Table 2})$. The computed structure of **9a** in which the nitrogen is completely sp² hybridized with zero twist clearly plays no role in promoting amide resonance, which must be reduced owing to localization of the amide nitrogen atom lone pair. Furthermore, resonance cannot account for the planarity in **9a**. B3LYP/6–31G(d) predicts the amide resonance in this NNCl system to be some 20 kJ mol⁻¹ lower than that computed for the NNO model **3a** (~50 kJ mol⁻¹).^[18] The combined Pauling electronegativities of oxygen with chlorine (6.5) and nitrogen with chlorine (6) are less than that of two oxygen atoms (7), yet the dampening of amide resonance at the B3LYP/6–31G(d) level of theory is similarly marked in the systems with lower overall electronegativity at nitrogen.

One possible contributor to this anomaly could be the enhanced anomeric effect in these systems. $n_{Y} - \sigma^*_{NX}$ anomeric interactions are favoured by Y atoms to the left and X atoms to the right of the p-block because the lone pair on Y, n_{Y} , and the N-X antibonding orbital, σ^*_{N-X} , become closer in energy, resulting in a stronger orbital interaction. Furthermore, σ^*_{NX} becomes lower proceeding down the halogen group (Fig. 4a).^[1,3,35,36] The anomeric interactions in **8a**, **9a**, and **10** (Fig. 4b) are likely to be stronger than those in 2 or **3a** on account of the lower-energy σ^*_{NC1} orbital when compared with σ^*_{NO} . The attendant charge separation and lengthening of the N-Cl bond in **8a**, **9a**, and **10** (Fig. 4c) when compared with a weaker $n_O - \sigma^*_{NO}$ interaction in **3** warrant a more rigorous methodology.

Although the geometries and energies of a diverse range of amides and lactams in general are adequately and cost-effectively dealt with at the B3LYP/6-31G(d) level,^[17] the



Fig. 4. (a) Energetics of anomeric effects; (b) anomeric overlap with an N—Cl bond; (c) polarization through $n_{Y}-\sigma^*_{NCl}$ anomeric interaction; Y is N and O.

Table 3.	Geometries of N-chloro-N-methoxyacetamide 8a, N-chloro-N-dimethylaminoacetamide 9a and N-chloro-N-methylaminoacetamide 10 at
	the B3LYP/6–311++G(d,p), M06/6–311++G(d,p), and ωB97X-D/6–311++G(d,p) levels of density functional theory (DFT)

	8a			9a			10		
	B3LYP	M06	ωB97X - D	B3LYP	M06	ωB97X - D	B3LYP	M06	ωB97X - D
N—Cl [Å]	1.783	1.746	1.743	1.821	1.776	1.764	1.821	1.775	1.760
N—O or N—N [Å]	1.385	1.368	1.372	1.349	1.347	1.354	1.357	1.352	1.361
N—CO [Å]	1.430	1.418	1.419	1.394	1.391	1.388	1.410	1.400	1.398
C—O [Å]	1.202	1.197	1.198	1.208	1.201	1.204	1.205	1.200	1.203
CONCl or CNNCl [°]	87.1	89.1	89.7	60/60	60/60	60/60	59/71	61/70	65/58
$\theta [\circ]^{A}$	113.0	114.1	113.7	120.0	120.0	120.0	117.43	118.3	118.4
$\chi [\circ]^{\mathrm{B}}$	50.73	47.3	48.6	0	0	0	31.6	25.6	25.1
$\tau [°]^{C}$	4.8	5.3	4.5	0	0	0	6.2	5.26	4.45

^AAverage angle at nitrogen.

^BWinkler–Dunitz pyramidality index.^[14,15]

^CWinkler–Dunitz twist parameter.^[14,15]

potential for partial charge separation described above would suggest that a density functional theory (DFT) method with dispersion corrections, together with a much-expanded basis set, with both extended polarization and with diffuse functions, might be more reliable. To test this, the structures, COSNAR REs, and amidicities of N-chloro-N-methoxyacetamide 8a, N-chloro-Ndimethylaminoacetamide 9a, and N-chloro-N-methylaminoacetamide 10 were computed at the B3LYP/6-311++G(d,p), M06/ 6–311++G(d,p), and ω B97X-D/6–311++G(d,p) levels of theory. Both the M06^[37] and ω B97X-D functionals^[38] are designed to correct empirically for dispersion.^[39] From Table 3, the geometries of the M06- and ω B97X-D-derived structures for 8a, 9a, and 10 were similar to those from B3LYP in most respects. All the bond lengths were slightly shorter than those obtained using B3LYP/6-311++G(d,p) and B3LYP/6-31G(d) methods but by all three methods, the nitrogens were predicted to be strongly pyramidal in 8a (χ close to 50°) while twist angles were small and nearly identical (τ close to 5°). Like B3LYP/ 6-31G(d), all three methods predicted 9a to be completely planar with zero twist (χ , $\tau = 0$) and for 10, all three methods predicted reasonably pyramidal nitrogens with limited twist. For all three anomeric amides, the N-C(O) bond lengths by B3LYP/ 6-311++G(d,p), M06/6-311++G(d,p), and ω B97X-D/ 6-311++G(d,p) methods were much longer than N,N-dimethylacetamide 4 at those levels (1.374, 1.372, and 1.369 Å respectively). Anomeric interactions were optimized in all cases as evidenced by CONCl dihedral angles close to 90° in 8a, and CNNCl dihedrals of 60° in **9a** and close to 60° in **10**.

The REs of *N*,*N*-dimethylacetamide **4**, used as calibration for the amidicities of **8a**, **9a**, and **10**, necessitated computation of ΔE_{COSNAR} (from Eqn 1) by the three different DFT methods for *N*,*N*-dimethylacetamide **4** along with **8a**, **9a** and **10**. The REs

Table 4. COSNAR energies (from Eqn 1) and amidicities for *N*-chloro-*N*-methoxyacetamide 8a, *N*-chloro-*N*-dimethylaminoacetamide 9a, *N*chloro-*N*-methylaminoacetamide 10, and *N*,*N*-dimethylacetamide 4 obtained at B3LYP/6–311++G(d,p), M06/6–311++G(d,p), and ω B97X-D/6–311++G(d,p) levels of density functional theory (DFT)

	DALLE		DARK D
DFT method	B3LYP	M06	ωB97X-D
ΔE_{COSNAR} 8a [kJ mol ⁻¹]	-27.2	-34.4	-33.9
ΔE_{COSNAR} 9a [kJ mol ⁻¹]	-28.6	-48.7	-48.5
ΔE_{COSNAR} 10 [kJ mol ⁻¹]	-29.4	-46.0	-45.0
ΔE_{COSNAR} 4 [kJ mol ⁻¹]	-75.9	-75.9	-77.1
Amidicity 8a [%]	35.8	45.4	44.0
Amidicity 9a [%]	37.7	64.2	62.9
Amidicity 10 [%]	38.8	60.6	58.4

from ΔE_{COSNAR} for 4 (Table 4) are very similar and almost the same as the B3LYP/6–31G(d) value $(-77.5 \text{ kJ mol}^{-1})$.^[17] Dispersion contributions are clearly unimportant in the treatment of this N,N-dialkylamide. However, the values for 8a, where the DFT incorporated dispersion corrections, are \sim 7 kJ mol⁻¹ higher than the B3LYP/6-311++G(d,p) value, which suggests an improvement when dispersion is taken into account. Nonetheless, N-chloro-N-methoxyacetamide 8a still retains only \sim 45% of the resonance in 4. This discrepancy between B3LYP and dispersion-corrected DFT methods is measurably greater for N-chloro-N-dimethylaminoacetamide 9a and N-chloro-N-methylaminoacetamide 10, where resonance is computed to be $\sim 60\%$ that of N,N-dimethylacetamide 4 and substantially higher than that predicted from B3LYP/ 6-311++G(d,p), which was identical to the B3LYP/6-31G(d) value (29 kJ mol⁻¹). Furthermore, the RE parity for **8a** and **9a** at



Fig. 5. Methoxynitrene-acetyl chloride complexes from 8a with oxygens (a) anti, and (b) syn relative to the N-C-Cl plane.

B3LYP is no longer observed with M06 and ω 97X-D, which predicted nearly identical REs that are significantly higher than those for **8a** and in line with the lower overall electronegativity of nitrogen and chlorine. **10** has slightly less resonance than the dimethyl analogue **9a** but the results again show that the planarity in **9a** is a steric rather than an electronic factor. These results would indicate the necessity for inclusion of dispersion corrections in treatments of molecules where anomeric interactions are likely to have a pronounced influence.

The REs of ONCl and NNCl systems are still low when compared with normal amides, and because this energy is sacrificed in HERON reactions, both systems might be susceptible to HERON rearrangements. However, the overall E_A for HERON reactions has not only a component equivalent to the RE but also a rearrangement component, E_{rearr} , which, if substantial, can be rate-limiting.^[18]

Many *N*-alkoxy-*N*-chloroamides **1a** have been synthesized in our laboratory as precursors to *N*-alkoxynitrenium ions^[40–42] and a wide range of biologically active mutagens, *N*-acyloxy-*N*-alkoxyamides **1c**.^[1–3,23,27,43–53] Despite their very low REs, to date HERON reactions of **1a** have not been observed. The HERON reaction of *N*-chloro-*N*-aminoamides **1e** could be inferred from the quantitative conversion of β , β -dimethylbenzhydrazide **16** to 1,1-dibenzoyl-2,2-dimethylhydrazine **20** on treatment with *tert*-butyl hypochlorite according to Scheme 1. The intermediate **17** could undergo HERON reaction to form benzoyl chloride **19** and 1,1-dimethyldiazene **21**. Alternatively, elimination of chloride could give **18**. Both **18** and **19** could be responsible for *N*,*N*-bisacyl substitution in **20** by rapid reaction with unreacted hydrazide.

Both **8a** and **9a** could also undergo elimination reactions to form respectively the *N*-acetyl-*N*-methoxynitrenium ion **22a** and *N*-acetyl-*N*-dimethylaminonitrenium ion **22b** (Scheme 2). Both processes would be driven by the anomeric effect at the amide nitrogen, which, as outlined, is strongly favoured with geminal chlorine. B3LYP/6–31G(d) calculations shed some light on these experimental possibilities.

A HERON transition state search with 8a using geometries similar to that in Fig. 2 generates two structures with oxygens syn and anti (Fig. 5), each with one imaginary frequency, and their energies relative to the ground state including thermal correction are given in Table 2. The structures exhibit very long N-C(O) and N-Cl bonds, and a short Cl-CO separation that is not much greater than the length of the Cl-CO bond in acetyl chloride optimized at the same level (1.835 Å). The lowest energy difference relative to ground state 8a is 158 kJ mol^{-1} , which places these just below the energy of the products, acetyl chloride and methoxynitrene, and each structure can best be regarded as a complex between the two. Gas-phase separated acetyl chloride and methoxynitrene are higher than ground state **8a** by 168 kJ mol^{-1} . They do not represent HERON transition states, as from either structure a small contraction of the N-Cl separation resulted in a different complex between chloride and N-acetyl-N-methoxynitrenium ion 22a. This is clear from analysis of charge separation and geometry in Fig. 6a where the chlorine bond is long, is orthogonal to the N-C(O) plane, and bears a charge of -0.3 as opposed to its +0.1 charge in the

Fig. 6. (a) Optimized structure from contraction of the N—Cl bond in Fig. 6a; (b) structure of **22b** from HERON transition state search on **9a**.

ground-state structure **8a**. The complexes do not lie on a HERON reaction coordinate. In the gas phase, the enforced adoption of a typical HERON transition-state geometry, similar to that in Fig. 2, results in collapse to acetyl chloride and methoxynitrene. ONCl systems would not be expected to undergo HERON reactions in accord with the experimental findings. In solution, particularly, ONCl systems would be expected to dissociate to nitrenium and chloride ions according to Scheme 2.

No transition state could be found for the HERON reaction of **9a**. All approximations to transition states similar to that in Fig. 2 resulted in a complex between chloride and *N*-acetyl-*N*-dimethylaminonitrenium ion **22b**. An exemplary structure is shown in Fig. 6b. Here, too, the chlorine is orthogonal to the N—C(O) plane and bears substantial negative charge relative to the ground state structure of **9a** where chlorine bears +0.2 charge. Strong anomeric destabilization of the N—Cl bond coupled with formation of a strongly resonance-stabilized nitrenium ion would favour this reaction over a HERON, particularly in solution. The most probable route to 1,1-dibenzoyl-2,2-dimethylhydrazine **20** in Scheme 1 is pathway (ii).

Conclusion

N-Chloro-*N*-methoxyacetamide is computed to have the typical properties of anomeric amides, namely a strongly pyramidal nitrogen and long N-C(O) bond as well as correct orbital alignment for an $n_0 - \sigma^*_{NCl}$ interaction. N-chloro-N-dimethylaminoacetamide 9a has a most unusual structure, being planar at nitrogen, yet with reduced resonance with the carbonyl. The planarity is not borne out of a requirement to optimize the resonance interaction, but rather it derives from steric inhibition to pyramidalization at nitrogen because in 10, where steric compression is relaxed, the nitrogen becomes puckered as expected. The combination of nitrogen with chlorine at the amide nitrogen results in similarly low REs whether the nitrogen is planar or not and this must be attributed to the electronic influence of the electronegative atoms. Although at the B3LYP/6-31G(d) level, the RE in these NNCl systems, with total electronegativity at nitrogen less than in the ONCl model 8a, is approximately the same as that calculated for 8a, with DFT methods that incorporate dispersion corrections such as M06 and $\omega B97X$ -D and an expanded 6-311++G(d,p) basis set, the NNCl model has greater resonance than the ONCl model, which in turn has slightly more intrinsic resonance than computed at B3LYP/6-31G(d). The difference probably lies in the very much better treatment of the

anomeric delocalization into the low-lying N—Cl σ^* orbital in **8a** and particularly in **9a**. With higher-energy σ^*_{NO} orbitals, such as in **2** and **3**, the B3LYP/6–31G(d) method probably performs adequately. However, the origin of resonance dampening in anomeric amides warrants further theoretical investigation.

Although the structures of ONCl and NNCl systems are likely to possess lowered REs, a component of activation energies for HERON reactions, neither *N*-chloro-*N*-methoxyacetamide nor *N*-chloro-*N*-dimethylaminoacetamide will rearrange concertedly to acetyl chloride and nitrenes. Instead, they are predicted to undergo preferential elimination of chloride, which would suggest that ONCl and NNCl systems would produce stabilized nitrenium ions, particularly in polar solvents.

Experimental

Materials and Methods

Melting points were determined on a Reichert microscopic hot stage and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1725X Fourier-transform (FT) instrument. 300 MHz ¹H NMR spectra were recorded on a Bruker AC-300P FT spectrometer with a 5-mm probe operating at 300.13 MHz.

Computational Methods

Energies and geometries for fully optimized ground states of models of all structures in Tables 1-4 and associated structures utilized in Eqns 1-3, as well as complexes depicted in Figs 5 and 6, were computed by DFT based on Becke's three-parameter functional B3LYP,^[54,55] the dispersion-corrected functionals M06 of Zhao and Truhlar^[37] and ω B97X-D of Chai and Head-Gordon^[38] with split-valence basis sets^[56,57] at the B3LYP/6– 31G(d), B3LYP/6-311++G(d,p), M06/6-311++G(d,p), and ω B97X-D/6-311++G(d,p) levels using *MacSpartan 10*^[58] and Gaussian $03.^{[59]}$ B3LYP/6–31G(d) has been shown to perform well in determinations of structure and properties of a wide range of amides, lactams, and anomeric amides.^[9,10,12,16-19,22] Energies of model structures in isodesmic Eqns 1, 2, and 3 were computed without ZPE and thermal corrections because these largely cancel. For 8a and the complexes (Fig. 5a, b) ZPE and vibrational corrections required full frequency calculations. The complexes possessed one imaginary frequency. Lowest-energy twisted amides used in Eqn 3 were obtained by transition state searches starting with twisted forms. The most stable twisted forms of N,N-dimethylacetamide 4, N-chloro-Nmethoxyacetamide 8a, N-chloro-N-dimethylaminoacetamide 9a, and N-chloro-N-methylaminoacetamide 10 had the lone

pairs respectively *anti*, *syn*, *anti*, and *syn* to the carbonyl. In the cases of **8a** and **10**, these conformations needed to be constrained to keep the lone pair in the N—C(O) plane. In addition, optimized structures of the corresponding amines **12** (Y = OMe and NHMe) used in Eqn 3 were not global minima but were obtained with the lone pair and 2-methyl *anti* for consistent steric impact. Geometries for all structures computed at B3LYP/ $6-31G^*$ level are provided as Supplementary Material.

β , β -Dimethylbenzydrazide **16**

An ice-cold solution of benzoyl chloride (10 g, 71 mmol) in diethyl ether (60 mL)was added dropwise to a stirred solution of 1,1-dimethylhydrazine (7.0 g, 119 mmol) in diethyl ether (30 mL). After 1 h, the solution was washed with 10 % sodium hydroxide (40 mL) and water. The ether layer was separated, dried over sodium sulfate, and concentrated to a light-yellow solid. Crystallization from benzene/petroleum spirit afforded **16** (7.2 g, 63 %). Mp 102–104°C (lit. mp 106–107°C^[60]). v_{max} (CHCl₃)/cm⁻¹ 3350 (br), 1690. $\delta_{\rm H}$ (CDCl₃, 300 MHz) 2.8 (s, 6H), 7.2–7.4 (m, 3H), 7.7–8.0 (d, 2H).

1,1-Dibenzoyl-2,2-dimethylhydrazine 20

To dry benzene (60 mL) was added β,β-dimethylbenzhydrazide (1 g, 3.7 mmol) and the reaction vessel shielded from light. *tert*-Butyl hypochlorite (0.66 g, 2.46 mmol) in benzene was added dropwise. After standing for 12 h, the solution was concentrated to afford a near-quantitative yield of 1,1-dibenzoyl-2,2-dimethylhydrazine (0.87 g). Crystallization from ethanol afforded colourless crystals. Mp 154.5°C (lit. mp 152–153°^[60]). v_{max} (CHCl₃)/cm⁻¹ 1700. δ_{H} (CDCl₃, 300 MHz) 3.0 (s, 6H), 7.3–7.8 (m, 10H). *m/z* (EI) 268 (10), 105 (100) 77(54) and 51 (10%). Anal. calc. for C₁₆H₁₆N₂O: C 71.84, H, 6.01, N 10.43. Found: C 71.63, H, 6.21, N 10.39%.

Supplementary Material

The following material is available on the Journal's website:

- Table S1. Full version of Table 2 incorporating B3LYP/ 6-31G(d) energies for N-chloro-N-methoxyacetamide 8a, N-chloro-N-dimethylaminoacetamide 9a, and N-chloro-Nmethylaminoacetamide 10, for relevant COSNAR and *trans*amidation structures in Eqns 1–3 and for complexes in Fig. 5.
- Table S2. Full version of Table 4 incorporating DFT energies and COSNAR data for *N*-chloro-*N*-methoxyacetamide 8a, *N*-chloro-*N*-dimethylaminoacetamide 9a, *N*-chloro-*N*-methylaminoacetamide 10, and *N*,*N*-dimethylacetamide 4 at B3LYP, M06 and ωB97X-D with the 6-311++G(d,p) basis set.
- 3. Geometries (*xyz* format) of all ground-state structures and complexes in Table 2
- 4. Complete ref. [59].

References

- S. A. Glover, *Tetrahedron* 1998, 54, 7229. doi:10.1016/S0040-4020 (98)00197-5
- S. A. Glover, in Advances in Physical Organic Chemistry (Ed. J. Richard) 2008, Vol. 42, pp. 35–123 (Elsevier: London).
- [3] S. A. Glover, in *The Chemistry of Hydroxylamines, Oximes and Hydroxamic Acids, Part 2* (Eds Z. Rappoport, J. F. Liebman) 2009, pp. 839–923 (Wiley: Chichester).
- [4] V. G. Shtamburg, O. V. Shishkin, R. I. Zubatyuk, S. V. Kravchenko, A. V. Tsygankov, A. V. Mazepa, E. A. Klots, R. G. Kostyanovsky, *Mendeleev Commun.* 2006, 16, 323. doi:10.1070/MC2006V016N06 ABEH002382

- [5] V. G. Shtamburg, O. V. Shishkin, R. I. Zubatyuk, S. V. Kravchenko, A. V. Tsygankov, V. V. Shtamburg, V. B. Distanov, R. G. Kostyanovsky, *Mendeleev Commun.* 2007, 17, 178. doi:10.1016/J.MENCOM. 2007.05.016
- [6] V. G. Shtamburg, A. T. Tsygankov, O. V. Shishkin, R. I. Zubatyuk, B. V. Uspensky, V. V. Shtamburg, A. V. Mazepa, R. G. Kostyanovsky, *Mendeleev Commun.* 2012, 22, 164. doi:10.1016/J.MENCOM.2012. 05.019
- [7] A.-M. E. Gillson, S. A. Glover, D. J. Tucker, P. Turner, Org. Biomol. Chem. 2003, 1, 3430. doi:10.1039/B306098P
- [8] S. A. Glover, G. Mo, A. Rauk, D. Tucker, P. Turner, J. Chem. Soc., Perkin Trans. 2 1999, 2053. doi:10.1039/A9045751
- [9] S. A. Glover, J. M. White, A. A. Rosser, K. M. Digianantonio, J. Org. Chem. 2011, 76, 9757. doi:10.1021/JO201856U
- [10] A. Rauk, S. A. Glover, J. Org. Chem. 1996, 61, 2337. doi:10.1021/ JO9521817
- [11] S. A. Glover, A. Rauk, J. Chem. Soc., Perkin Trans. 2 2002, 1740. doi:10.1039/B204232K
- [12] S. A. Glover, A. Rauk, J. Org. Chem. 1999, 64, 2340. doi:10.1021/ JO982048P
- [13] K. M. Digianantonio, S. A. Glover, J. P. Johns, A. A. Rosser, Org. Biomol. Chem. 2011, 9, 4116. doi:10.1039/C1OB00008J
- [14] F. K. Winkler, J. D. Dunitz, J. Mol. Biol. 1971, 59, 169. doi:10.1016/ 0022-2836(71)90419-0
- [15] J. D. Dunitz, X-Ray Analysis and Structure of Organic Molecules 1979 (Cornell University Press: London).
- [16] S. A. Glover, A. A. Rosser, A. Taherpour, B. W. Greatrex, Aust. J. Chem. 2014, 67, 507. doi:10.1071/CH13557
- [17] S. A. Glover, A. A. Rosser, J. Org. Chem. 2012, 77, 5492. doi:10.1021/ JO300347K
- [18] S. A. Glover, A. A. Rosser, J. Phys. Org. Chem. 2014. doi:10.1002/ POC.3322
- [19] S. A. Glover, A. Rauk, J. M. Buccigross, J. J. Campbell, G. P. Hammond, G. Mo, L. E. Andrews, A.-M. E. Gillson, *Can. J. Chem.* 2005, *83*, 1492. doi:10.1139/V05-150
- [20] J. M. Buccigross, S. A. Glover, J. Chem. Soc., Perkin Trans. 2 1995, 595. doi:10.1039/P29950000595
- [21] J. M. Buccigross, S. A. Glover, G. P. Hammond, Aust. J. Chem. 1995, 48, 353.
- [22] S. A. Glover, G. Mo, A. Rauk, *Tetrahedron* 1999, 55, 3413. doi:10.1016/S0040-4020(98)01151-X
- [23] S. A. Glover, G. Mo, J. Chem. Soc., Perkin Trans. 2 2002, 1728. doi:10.1039/B111250N
- [24] J. J. Campbell, S. A. Glover, J. Chem. Res. (M) 1999, 8, 2075.
- [25] S. A. Glover, in *Merck Index Fourteenth Edition* (Ed. M. J. O'Neil) 2006, p. ONR-43 (Merck & Co., Inc.: Whitehouse Station, NJ).
- [26] J. P. Johns, A. van Losenoord, C. Mary, P. Garcia, D. S. Pankhurst, A. A. Rosser, S. A. Glover, *Aust. J. Chem.* 2010, 63, 1717. doi:10.1071/ CH10350
- [27] K. L. Cavanagh, S. A. Glover, H. L. Price, R. R. Schumacher, Aust. J. Chem. 2009, 62, 700. doi:10.1071/CH09166
- [28] M. V. De Almeida, D. H. R. Barton, I. Bytheway, J. A. Ferriera, M. B. Hall, W. Liu, D. K. Taylor, L. Thomson, *J. Am. Chem. Soc.* 1995, *117*, 4870. doi:10.1021/JA00122A018
- [29] L. M. Thomson, M. B. Hall, J. Phys. Chem. A 2000, 104, 6247. doi:10.1021/JP000623Z
- [30] N. Zhang, R. Yang, D. Zhang-Negrerie, Y. Du, K. Zhao, J. Org. Chem. 2013, 78, 8705. doi:10.1021/JO401435V
- [31] A. Greenberg, D. T. Moore, T. D. DuBois, J. Am. Chem. Soc. 1996, 118, 8658. doi:10.1021/JA960294H
- [32] A. Greenberg, in *The Amide Linkage. Structural Significance in Chemistry, Biochemistry and Materials Science* (Eds A. Greenberg, C. M. Breneman, J. F. Liebman) 2003, pp. 47–83 (John Wiley & Sons, Inc.: New York, NY).
- [33] A. J. Kirby, I. V. Komarov, P. D. Wothers, N. Feeder, Angew. Chem. Int. Ed. 1998, 37, 785. doi:10.1002/(SICI)1521-3773(19980403) 37:6<785::AID-ANIE785>3.0.CO;2-J

- [34] A. J. Kirby, I. V. Komarov, N. Feeder, J. Chem. Soc., Perkin Trans. 2 2001, 522. doi:10.1039/B008270H
- [35] N. D. Epiotis, W. R. Cherry, S. Shaik, Y. L. Yates, F. Bernardi, *Structural Theory of Organic Chemistry*, 1977 (Springer-Verlag: Berlin).
- [36] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds* 1994 (John Wiley & Sons, Inc.: New York, NY).
- [37] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* 2008, 120, 215. doi:10.1007/S00214-007-0310-X
- [38] J.-D. Chai, M. Head-Gordon, Phys. Chem. Chem. Phys. 2008, 10, 6615. doi:10.1039/B810189B
- [39] S. Grimme, WIREs Comput. Mol. Sci. 2011, 1, 211. doi:10.1002/ WCMS.30
- [40] S. A. Glover, A. Goosen, C. W. McCleland, J. L. Schoonraad, J. Chem. Soc., Perkin Trans. 1 1984, 2255. doi:10.1039/P19840002255
- [41] S. A. Glover, A. Goosen, C. W. McCleland, J. L. Schoonraad, *Tetrahedron* 1987, 43, 2577. doi:10.1016/S0040-4020(01)81665-3
- [42] S. A. Glover, C. A. Rowbottom, A. P. Scott, J. L. Schoonraad, *Tetrahedron* 1990, 46, 7247. doi:10.1016/S0040-4020(01)87905-9
- [43] R. G. Gerdes, S. A. Glover, J. F. Ten Have, C. A. Rowbottom, *Tetrahedron Lett.* **1989**, *30*, 2649. doi:10.1016/S0040-4039(00) 99089-0
- [44] J. J. Campbell, S. A. Glover, C. A. Rowbottom, *Tetrahedron Lett.* 1990, 31, 5377. doi:10.1016/S0040-4039(00)98076-6
- [45] J. J. Campbell, S. A. Glover, G. P. Hammond, C. A. Rowbottom, J. Chem. Soc., Perkin Trans. 2 1991, 2067. doi:10.1039/ P29910002067
- [46] A. M. Bonin, S. A. Glover, G. P. Hammond, J. Chem. Soc., Perkin Trans. 2 1994, 1173. doi:10.1039/P29940001173

- [47] S. A. Glover, G. P. Hammond, A. M. Bonin, J. Org. Chem. 1998, 63, 9684. doi:10.1021/JO980863Z
- [48] J. J. Campbell, S. A. Glover, J. Chem. Res. (S) 1999, 8, 474. doi:10.1039/A9035551
- [49] A. M. Bonin, T. M. Banks, J. J. Campbell, S. A. Glover, G. P. Hammond, A. S. Prakash, C. A. Rowbottom, *Mutat. Res.* 2001, 494, 115. doi:10.1016/S1383-5718(01)00189-9
- [50] L. E. Andrews, T. M. Banks, A. M. Bonin, S. F. Clay, A.-M. E. Gillson, S. A. Glover, *Aust. J. Chem.* **2004**, *57*, 377. doi:10.1071/CH03276
- [51] T. M. Banks, A. M. Bonin, S. A. Glover, A. S. Prakash, Org. Biomol. Chem. 2003, 1, 2238. doi:10.1039/B301618H
- [52] L. E. Andrews, A. M. Bonin, L. E. Fransson, A.-M. E. Gillson, S. A. Glover, *Mutat. Res.* 2006, 605, 51. doi:10.1016/J.MRGENTOX. 2006.02.003
- [53] S. A. Glover, R. R. Schumacher, A. M. Bonin, L. E. Fransson, *Mutat. Res.* 2011, 722, 32. doi:10.1016/J.MRGENTOX.2011.02.007
- [54] A. D. Becke, J. Chem. Phys. 1993, 98, 5648. doi:10.1063/1.464913
- [55] P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, J. Phys. Chem. 1994, 98, 11623. doi:10.1021/J100096A001
- [56] R. Ditchfield, W. J. Hehre, J. A. Pople, J. Chem. Phys. 1971, 54, 724. doi:10.1063/1.1674902
- [57] W. J. Hehre, L. Radom, P. R. Schleyer, J. A. Pople, *Ab Initio Molecular Orbital Theory* 1986 (John Wiley & Sons: New York, NY).
- [58] Spartan10 for Macintosh 2010. 1.1.0 2010 (Wavefunction Inc.: Irvine, CA).
- [59] M. J. Frisch et al., Gaussian 03, Revision E.01 2005 (Gaussian, Inc.: Wallingford, CT).
- [60] R. L. Hinman, J. Am. Chem. Soc. 1956, 78, 1645. doi:10.1021/ JA01589A040