Hindered ester formation by S_N2 azidation of *N*-acetoxy-*N*-alkoxyamides and *N*-alkoxy-*N*-chloroamides—novel application of HERON rearrangements

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Treatment of *N*-acetoxy-*N*-alkoxyamides or *N*-alkoxy-*N*-chloroamides with sodium azide in aqueous acetonitrile results in S_N2 displacement of chloride and the formation of reactive *N*-alkoxy-*N*-azidoamides. The reaction with *N*-acetoxy-*N*-benzyloxybenzamide has been studied kinetically (k_{294} = 2 L mol^{-1} s^{-1}) and azidation of *N*-formyloxy-*N*-methoxyformamide has been modeled computationally at the pBP/DN*//HF/6-31G* level of theory. The anomeric amides *N*-alkoxy-*N*-azidoamides decompose intramolecularly and spontaneously to esters and two equivalents of nitrogen. This extremely exothermic process facilitates the formation, in excellent yields, of highly hindered esters.

Introduction

N,*N*-Bisheteroatom-substituted amides constitute an unusual class of amides whose properties have recently been studied both experimentally and theoretically.[1–7] They are characterised, among other things, by an unusual degree of pyramidality at the amide nitrogens resulting in reduced conjugation between the nitrogen lone pair and the carbonyl π bond. Direct consequences of this are much lower amide isomerisation barriers and high carbonyl stretch frequencies in their infrared spectra (Fig. 1a). While these effects arise out of the additional electron

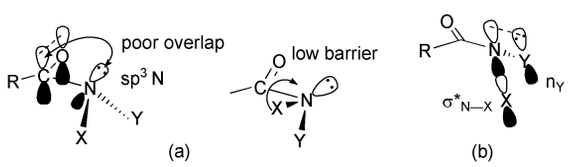
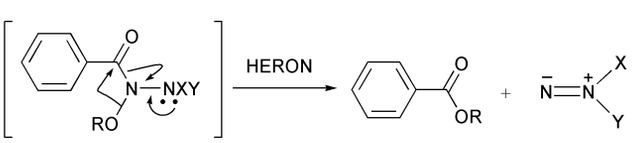


Fig. 1 (a) Pyramidalisation and (b) anomeric interactions in bisheteroatom-substituted amides.

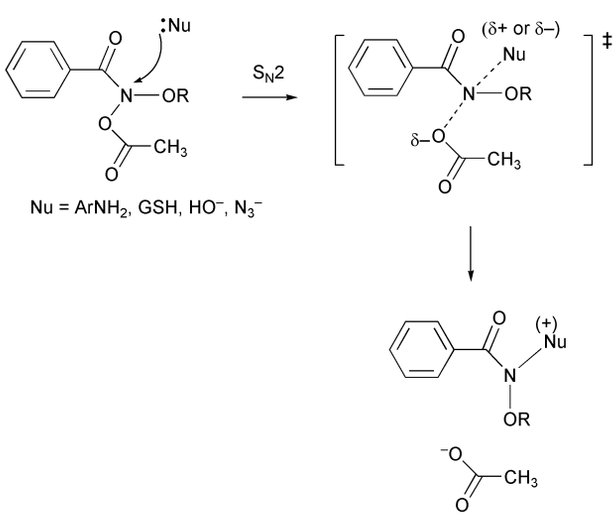
demand by two electronegative atoms, this geminal substitution pattern also facilitates unusual anomeric interactions through the amide nitrogen. A lone pair on one heteroatom can overlap with the neighbouring σ*-orbital between the second heteroatom and nitrogen (Fig. 1b). This is particularly effective where one heteroatom is more electronegative than the other, in which case it results in anomeric weakening of one of the bonds to nitrogen.[1,5] In *N*-alkoxy-*N*-aminoamides, such interactions have been found to result in the unusual HERON† rearrangement (Scheme 1).[3,7,8] Since alkoxides are poor leaving groups, the negative hyperconjugation results in a migration of the oxygen from nitrogen to carbon. HERON rearrangements have been found in the reactions of mutagenic *N*-acyloxy-*N*-alkoxyamides with aromatic amines[8,9] and in the thermal decomposition of *N*,*N*′-diacyl-*N*,*N*′-dialkoxy hydrazines.[3,6,10]



Scheme 1

† Heteroatom Rearrangements on Nitrogen.

Where the heteroatom is a part of a good leaving group, these amides undergo substitution reactions. We have reported both S_N1-type ($A_{Al}1$ acid-catalysed solvolysis) reactivity[11–13] and S_N2-type reactivity for one such class of compounds, the biologically active dioxo-substituted amides, *N*-acyloxy-*N*-alkoxyamides.[8,9,13] Aromatic amines and hydroxide ions have both been found to displace acetate or benzoate in a classical S_N2 reaction at nitrogen and recently we have also discovered that these mutagens react by an S_N2 process with the cellular conjugating agent, glutathione (Scheme 2).[14] S_N2 reactions with



Scheme 2

amines and glutathione have been modeled computationally and are characterised by a non-synchronous concerted process involving strong charge separation in the transition states which have long *N*–*O*Ac bonds and partial nitrenium ion character at the amide nitrogen.[15]

Recently we have also discovered that in aqueous-organic mixtures, both *N*-acyloxy-*N*-alkoxyamides as well as *N*-alkoxy-*N*-chloroamides undergo substitution reactions with azide.[16] Substitution of chloride or acetate leads to intermediate

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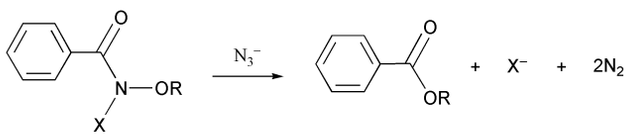
N-alkoxy-*N*-azidoamides which readily decompose to esters with the evolution of nitrogen (Scheme 3). The reaction involves a HERON-type reaction of a 1-acyl-1-alkoxydiazene intermediate. We now report on the kinetic and theoretical details of the formation and decomposition of *N*-alkoxy-*N*-azidoamides, the energetics and mechanism of which enable the synthesis of highly hindered esters that are unavailable by classical ester formation reactions.



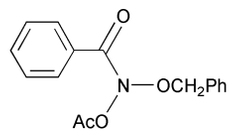
Scheme 3

Results and discussion

Azide trapping of carbocations and nitrenium ions in aqueous solution, a diffusion-controlled process, provides solvolysis rate constants in water, k_w, and a number of research groups have utilised this competition method for the evaluation of solvolysis rate constants for a variety of arylnitrenium ions.[17–23] In an attempt to determine the lifetimes of *N*-acyl-*N*-alkoxynitrenium ions in aqueous solution using similar methods, we found that *N*-acetoxy-*N*-butoxybenzamide **1a**, upon treatment with an aqueous-acidic solution of sodium azide afforded a near quantitative yield of butyl benzoate **3a**. The extremely rapid reaction was accompanied by liberation of two equivalents of nitrogen gas. A crossover experiment using *N*-acetoxy-*N*-ethoxy-*p*-toluamide **2a** and **1a** afforded exclusively the non-crossover esters, ethyl *p*-toluate **4a** and butyl benzoate **3a** (Scheme 4). *N*-Chlorohydroxamic esters reacted similarly and a crossover experiment with sodium azide and a mixture of *N*-benzyloxy-*N*-chlorobenzamide **1b** and *N*-chloro-*N*-ethoxy-*p*-nitrobenzamide **2b** in aqueous acetonitrile gave exclusively benzyl benzoate **3b** and ethyl *p*-nitrobenzoate **4b** as the only ester products (Scheme 4). Ester formation does not involve generation, in solution, of an acylating agent and alcohol since this would have resulted in mixed esters.

Kinetic results

N-Alkoxy-*N*-azidobenzamides **7** were postulated as unstable intermediates which decompose spontaneously to alkyl benzoate and nitrogen, and S_N1 and S_N2 limiting mechanisms for their formation are depicted in Scheme 5. The S_N1 reaction would involve rate limiting formation of an acylalkoxynitrenium ion **6** and the overall rate would be independent of the concentration of azide. When the reaction was carried out in aqueous acetonitrile in a closed system, progress of the reactions could be monitored dilatometrically but the reaction with *N*-alkoxy-*N*-chlorobenzamides **5a** as substrates was prohibitively fast, even at low temperatures and low concentrations of both reagents. However, the acetoxy derivatives **5b** reacted more slowly under the same conditions and a kinetic study of the reaction of sodium azide with *N*-acetoxy-*N*-benzyloxybenzamide **8** was possible.



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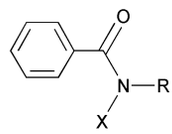


9

a: X=Cl, R=Bu
b: X=OCOPh, R=Benzyl

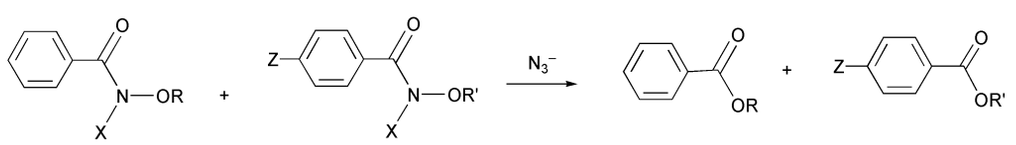
Two reactions of **8** and sodium azide were carried out in a 250 mL homogeneous acetonitrile–water solution at the initial, identical reagent concentrations of 0.0005 M and 0.0010 M, respectively. The volume of evolved nitrogen was measured dilatometrically at 750 mm. Since there is a proportionality between the concentrations, $[c]_t$, of **8** and azide and the remaining nitrogen in the reaction mixtures, $[c]_t$ was derived from the volumes of nitrogen liberated at time *t* and the total volume of nitrogen liberated upon completion of the reaction [eqn. (1)]:

$$\text{Reactant concentration } [c]_t = [N_2(\text{total}) - N_2(\text{evolved})] \times [c]_0/N_2(\text{total}) \quad (1)$$

With $[\mathbf{8}]_0 = [N_3^-]_0 = 1 \times 10^{-3}$ M and at 294.5 K, a plot of the reciprocal of concentrations ($1/[c]_t$) of **8** or azide *versus* time was linear with gradient equal to the rate constant, *k*, of 1.88 L mol^{-1} s^{-1} and $t_{1/2} = 4.9 \times 10^2$ s [Fig. 2(a)]. With starting concentrations of $[\mathbf{8}]_0 = [N_3^-]_0 = 5 \times 10^{-4}$ M a similar rate constant was obtained (Table 1) but $t_{1/2} = 1.06 \times 10^3$ s. ‡

Similar rate constants were obtained at this temperature for the reaction of **8** and azide under pseudo first order conditions,

‡ For bimolecular reactions with identical concentrations, $t_{½} = 1/[c]_0k$, thus halving the concentrations doubles $t_{½}$.



1

a: X=OAc, R=Bu
b: X=Cl, R=benzyl

2

a: X=OAc, R'=Et, Z=Me
b: X=Cl, R'=Et, Z=NO_2

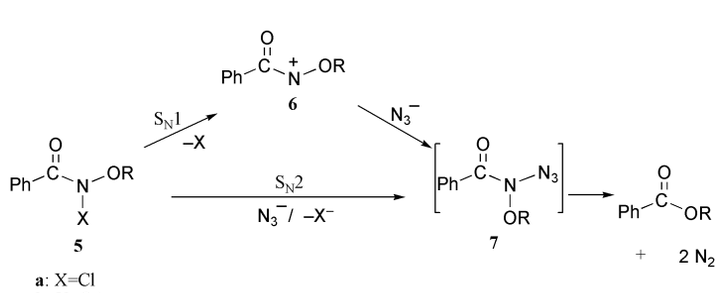
3

a: R=Bu
b: R=benzyl

4

a: R'=Et, Z=Me
b: R'=Et, Z=NO_2

Scheme 4



5

a: X=Cl
b: X=OAc

6

7

Scheme 5

Table 1 Rate constants at 294.5 K for the reaction sodium azide and *N*-acetoxy-*N*-benzyloxybenzamide in acetonitrile–water

Experiment	[Azide]/10^{-4} M	[Acetoxy]/10^{-4} M	k/L mol^{-1} s^{-1}	Calc. method[a]
1	5.0	5.0	1.91	(1)
2	10.0	10.0	1.88	(1)
3	50.0	5.0	1.81	(2)
4	5.0	50.0	2.08	(3)

[a] k calculated according to eqns. (1)–(3).

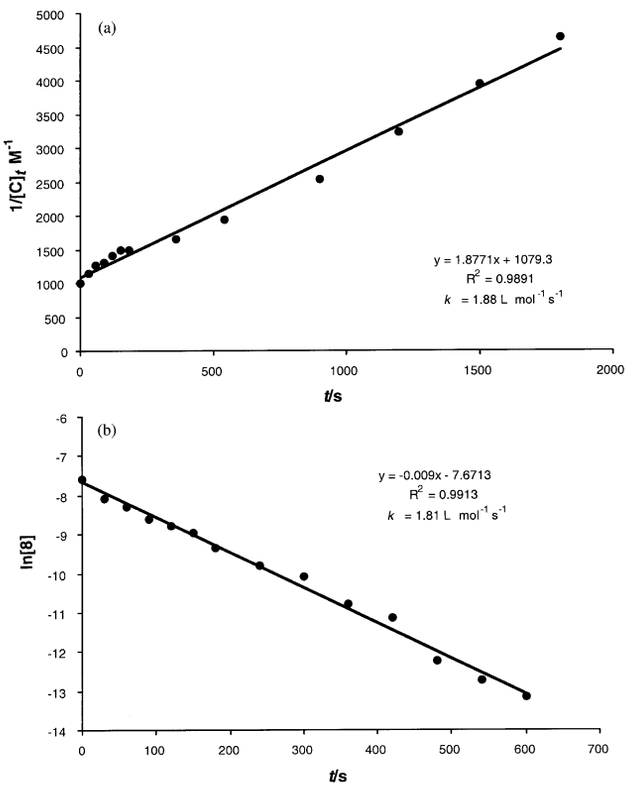


Fig. 2 (a) Second order plot for the reaction of *N*-acetoxy-*N*-benzyloxybenzamide **8** with sodium azide in acetonitrile–water (3 : 1, 250 mL) at 294.5 K. $[\mathbf{8}]_0 = [N_3^-]_0 = 1 \times 10^{-3}$ M; (b) Pseudo first order plot for the reaction of **8** (5×10^{-4} M) and N_3^-(5×10^{-3} M) in acetonitrile–water (3 : 1, 250 mL) at 294.5 K.

both with a ten-fold excess of azide or a ten-fold excess of acetoxy compound. A plot of the natural logarithm of the concentrations of acetoxy compound ($[\mathbf{8}]_0 = 5 \times 10^{-4}$ M, $[N_3^-]_0 = 5 \times 10^{-3}$ M) *versus* time [eqn. (2)] was linear (Fig. 2(b)).

$$\ln[\mathbf{8}] = \ln[\mathbf{8}]_0 - k[N_3^-] \times t \quad (2)$$

$$\ln[N_3^-] = \ln[N_3^-]_0 - k[\mathbf{8}] \times t \quad (3)$$

The second order rate constant, k, calculated from the gradient of the line of best fit was 1.81 L mol^{-1} s^{-1} with $t_{½} = 69$ s. With a ten-fold excess of mutagen and reverse concentrations, the value was similar with a $t_{½} = 60$ s (Table 1).

The reaction of **8** and azide is therefore dependent upon first order concentrations of both reagents. Since *N*-alkoxy-*N*-chlorobenzamides solvolyse relatively slowly under aqueous organic conditions,[6,24] their facile reaction in the presence of sodium azide must also follow bimolecular kinetics.

The *N*-alkoxy-*N*-azidoamide intermediates from these reactions, though readily generated, are clearly unstable. However, since non-crossover products were obtained from mixtures of *N*-acetoxy and *N*-chloro precursors, ester formation from the *N*-alkoxy-*N*-azidoamides must be an intramolecular process.

Recent calculations on the energetics of S_N2 reactions at nitrogen confirm the role of the *N*-alkoxy group in these reactions. The gas-phase activation energy for the S_N2 reaction of ammonia with *N*-formyloxy-*N*-methylformamide (148.65 kJ mol^{-1}) is double that of the reaction of ammonia with *N*-formyloxy-*N*-methoxyformamide (72.37 kJ mol^{-1}).[15] Interestingly, neither *N*-butyl-*N*-chlorobenzamide **9a** nor *N*-benzoyloxy-*N*-benzylbenzamide **9b** reacted with azide in the same manner. Upon reaction in acetonitrile–water parent hydroxamic ester was formed indicating alternative reaction pathways. Destablisation of the *N–Cl* or *N–OAc* bond through negative hyperconjugation facilitates attack at nitrogen by azide with the displacement of chloride or acetate. The sp^3 nature of the amide nitrogen in **5a** and **5b** also facilitates this process. **9a** and **9b**, on the other hand should be closer to sp^2 hybridised at the amide nitrogen and exhibit substantially more lone pair conjugation with the carbonyl. The ease of S_N2 reactions at such nitrogens might therefore be compared to the energetically unfavourable bimolecular substitution at vinylic carbons.

Theoretical properties

The S_N2 reaction of azide has been modelled theoretically at the pBP/DN*//HF/6-31G* level by the reaction of azide with *N*-formyloxy-*N*-methoxyformamide **10** (Scheme 6). In the gas phase the transition state is preceded by an ion–molecule complex (Fig. 3a) which is at a minimum on the reaction coordinate and in which the azide anion is 3.7 Å from the amide nitrogen, and approaching the axis of the formyloxy–nitrogen (N1–O9) bond. The early nature of this interaction is demonstrated by the largely unchanged geometry of the amide molecule. The average angle at nitrogen of 109.7°, which reflects a characteristically high degree of pyramidality at N1, and the N1–O9 bond length of 1.383 Å are similar to those computed for the ground state structure for **10** (109.8° and 1.376 Å). Energies and thermodynamic values are given in Tables 2 and 3. Including zero point energies, the reaction is computed to be exothermic in the gas phase at 0 K ($\Delta E = -58.5$ kJ mol^{-1}) but the transition state, while at a saddle-point, is lower in energy than the ion–molecule complex ($E_A = -18.4$ kJ mol^{-1}) in accord with the expected stabilisation due to charge delocalisation; the charge on azide (−1) is shared by both the azide (−0.76) and the formate group (−0.62) in the transition state. Decreased solvent stabilization of the transition state relative to the intermediate complex should be important and inclusion of AM1 solvation energies resulted in a small positive E_A. At 298 K, and including enthalpy and entropy terms, $\Delta H^‡$ is computed to be −18.7 kJ mol^{-1} but, in accord with the associative transition state, $\Delta S^‡$ is −14.5 J K^{-1} mol^{-1} and $\Delta G^‡$ is computed to be −14.3 kJ mol^{-1} without solvation effects. By comparison, at the HF/6-31G* level of theory, ΔG and $\Delta G^‡$ are computed to be −86.4 and 125.5 kJ mol^{-1} respectively.

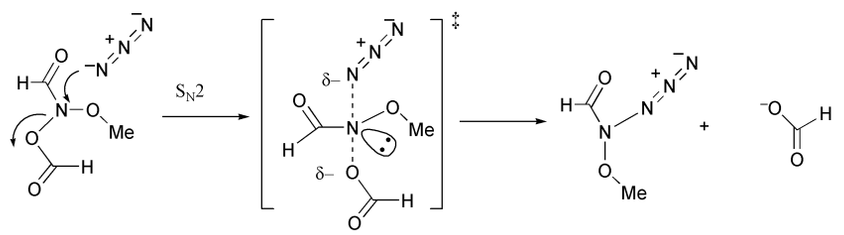
The computed energetics suggest a facile S_N2 reaction in agreement with the experimental findings. Rate constants for the reaction of *N*-acyloxy-*N*-alkoxyamides with aromatic amines or glutathione are slower by two to three orders of magnitude.[8,14]

In the computed transition state **11** (Fig. 4a) the azide and formyloxy groups are approaching collinearity (N2–N1–O9 = 158.6°) and the S_N2 displacement is predicted to be concerted but non-synchronous. The increase in negative charge of the

Table 2 pBP/DN*//HF/6-31G* and HF/6-31G* energies[a], enthalpies, entropies for reactants, gas-phase complexes, transition states and products[b] and AM1 solvation energies for the reaction of azide with *N*-formyloxy-*N*-methoxyformamide (**10**) and *N*-formyloxy-*N*-methylformamide (**14**).

	ZPE/kJ mol^{-1}	E_{elec}/au	H/kJ mol^{-1}	S/J K^{-1} mol^{-1}	E_{solv}/kJ mol^{-1}
HCON(OCHO)OMe **10**	233.0	−473.05455	246.0	316.1	−34.0
	(261.5)	(−470.2843)	(284.7)	(380.8)	
N_3^-	28.0	−164.31803	34.9	213.5	−314.9
	(32.6)	(−163.26100)	(39.2)	(211.5)	
[**10**–N_3]$^-$ complex	264.2	−637.39671	284.5	390.0	−293.7
	(299.4)	(−633.57434)	(331.1)	(487.4)	
T.s. **11**	256.7	−637.40085	276.7	375.5	−254.7
	(291.1)	(−633.52633)	(322.4)	(461.9)	
HCON(N_3)OMe **12**	204.7	−448.09735	219.2	324.8	−43.8
	(230.7)	(−445.39062)	(251.2)	(371.2)	
HCO_2^- **13**	53.7	−189.29648	61.6	244.8	−320.3
	(59.0)	(−188.18263)	(66.7)	(243.9)	
HCON(OCHO)Me (**14**)	233.0	−397.86254	236.4	307.4	−41.7
	(252.3)	(−395.49629)	(271.0)	(352.5)	
[**14**–N_3]$^-$ complex	254.9	−562.20473	272.0	357.8	−303.1
	(287.8)	(−558.7831)	(317.0)	(464.4)	
T.s **15**	246.7	−562.17967	265.0	360.4	−246.8
	(279.3)	(−558.70577)	(305.0)	(411.8)	

[a] HF/6-31G* values in parentheses. [b] *N*-Azido-*N*-methylformamide **16** was unstable at the HF/6-31G* level of theory decomposing to N_2 and 1-formyl-1-methyldiazene.



Scheme 6

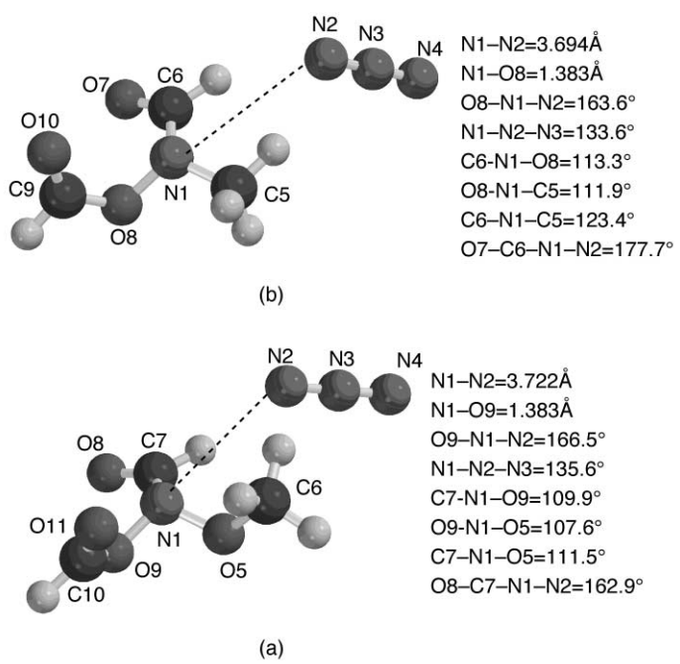


Fig. 3 HF/6-31G* geometries of azide complexes with (a) *N*-formyloxy-*N*-methoxyformamide (**10**); (b) *N*-formyloxy-*N*-methylformamide (**14**).

formate group [$\Delta q_{formate} = -0.65$] is larger than the decrease in negative charge over the azide group [$\Delta q_{azide} = +0.24$] which is indicative of more N1–O9 bond stretching than N2–N1 bond formation. In this respect the transition state is similar to that reported for the corresponding reactions of ammonia or methanethiol with the same mutagen model.[15] However, the transition states for those reactions, involving neutral nucleophiles, exhibited significant charge separation as opposed to the charge delocalisation in the azide reaction transition state. Near coplanarity of O8–C7–N1–O5–C6 indicates that the lone pair on N1 is completely out of conjugation with the carbonyl at the transition state and both the C7 and O5 p-orbitals are aligned with the partial bonds between N1 and the incoming azide and departing formate.

The reaction of azide with *N*-formyloxy-*N*-methylformamide (**14**) (Scheme 7) likewise involves an intermediate ion–molecule

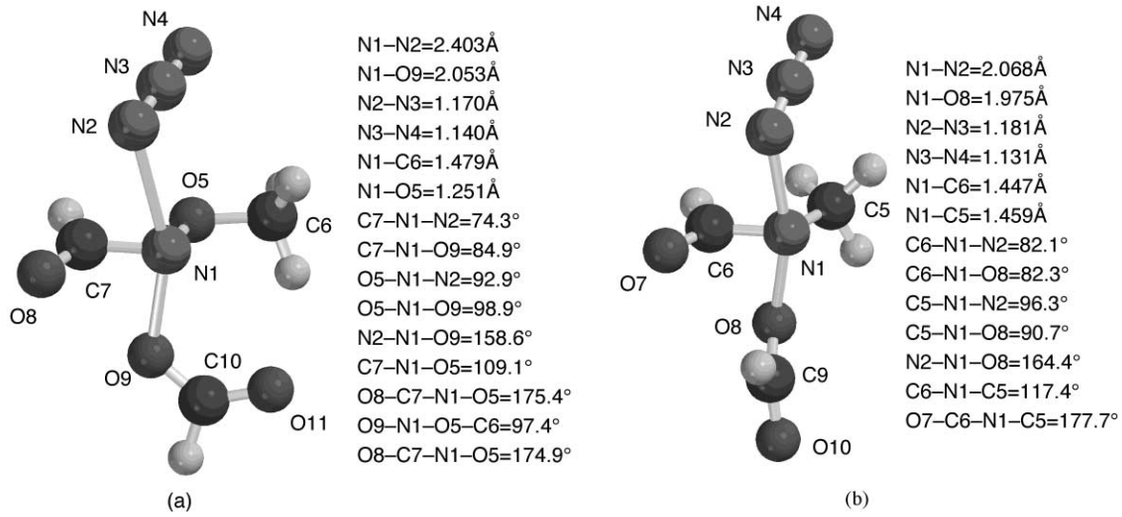
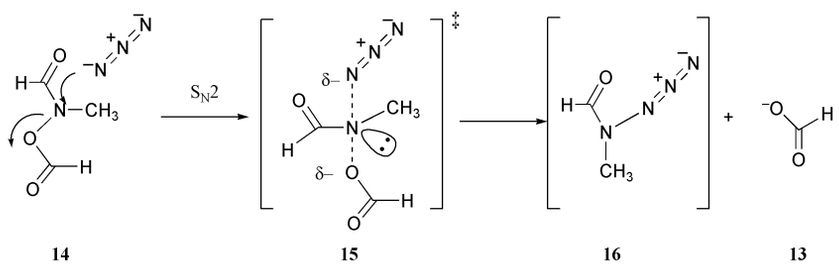


Fig. 4 HF/6-31G* transition state geometries for the reaction of azide anion with (a) *N*-formyloxy-*N*-methoxyformamide and (b) *N*-formyloxy-*N*-methylformamide.



Scheme 7

complex (Fig. 3b) but activation energies and $\Delta G^{\ddagger}$ are computed to be significantly greater than those for the reaction of azide with (**10**) at both the pBP/DN*//HF/6-31G* and HF/6-31G* levels of theory (Table 3). This could be attributable, in part, to a stronger N1–O8 bond (no anomeric destabilisation) as well as to a loss in amide resonance in this case, since lone pair resonance with the carbonyl is also lost in the transition state (Fig. 4(b)). Computational results therefore predict that a similar reaction with **14** would be much less favourable than the reaction of azide with **10** which is in accord with the failure of **9a** and **9b** to react.

N-Alkoxy-*N*-azidoamides constitute a special class of *NNO* anomeric amides in which anomeric overlap could be n_N–σ^*_{NO}.[1] However, while one resonance form [Fig. 5(b)]

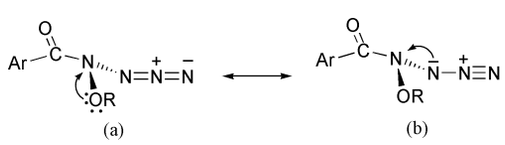


Fig. 5 Anomeric effects in *N*-azido-*N*-alkoxyamides.

generates anionic nitrogen adjacent to the amide nitrogen, the strongly electron-withdrawing effect of the quaternary ammonium centre [Fig. 5(a)] could both reduce the donor capacity of this nitrogen, as well as result in a reverse n_O–σ^*_{NN} anomeric effect through a lowering of the *C(O)N–N* σ* orbital energy.

N-Azido-*N*-methoxyformamide is predicted to be a stable point on the energy surface. At the pBP/DN*//HF/6-31G* level the *E*- form is computed to be 5 kJ mol^{-1} lower in energy than the *Z*-form and its geometry is illustrated in Fig. 6(a). Like other *anomeric* amides,[1,2,4,5] it has a strongly pyramidal amide nitrogen and Newman projections in Fig. 6(b) and Fig. 6(c) indicate only one anomeric alignment, namely that between the p-type lone pair on the alkoxy oxygen and the N–N σ*orbital. This

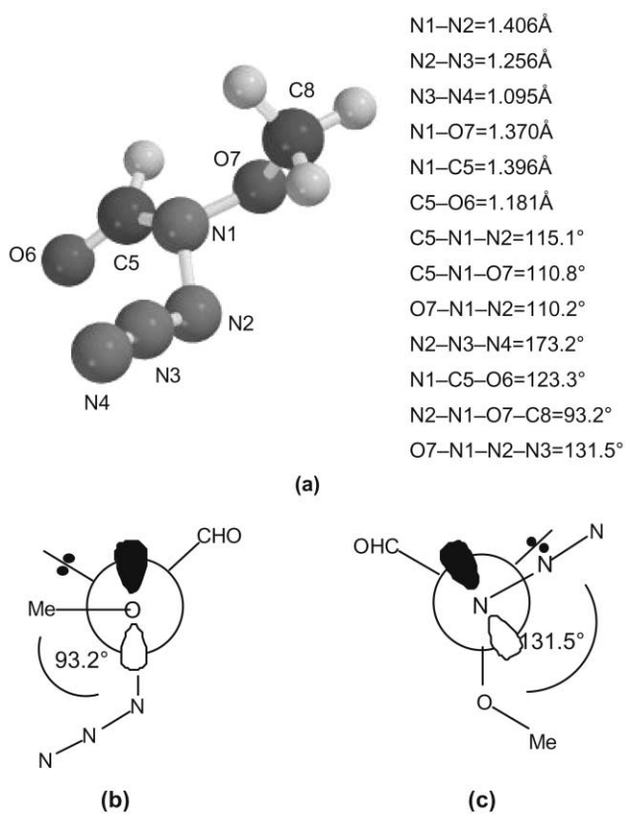


Fig. 6 HF/6-31G* optimised geometry for (a) (*E*)-*N*-azido-*N*-methoxyformamide; (b) Newman projection along the *O7–N1* bond; (c) Newman projection along the *N2–N1* bond.

geometry is similar to that described in the accompanying paper where a full analysis of the energetics of ground state reactants, products, and reactivity of *N*-azido-*N*-methoxy-

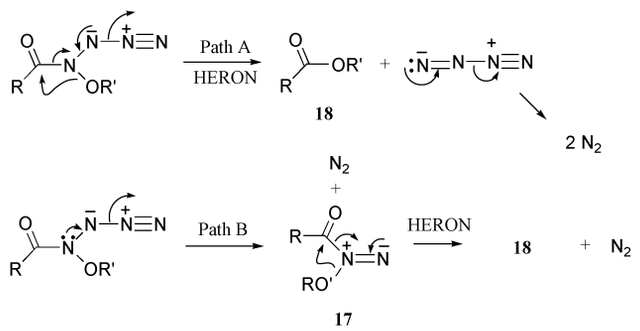
Table 3 pBP/DN*//HF/6-31G* and HF/6-31G derived activation[a] and reaction energies, enthalpies, entropies and free energies for the reactions of azide with *N*-formyloxy-*N*-methoxyformamide (**10**) and *N*-formyloxy-*N*-methylformamide(**14**) (HF/6-31G* values in parentheses).

	E_A+ZPE/ kJ mol^{-1}	$E_A+\Delta E^{\ddagger}_{solv}$/ kJ mol^{-1}	$\Delta H^{\ddagger}$[b]/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ J K^{-1} mol^{-1}	$\Delta G^{\ddagger}$/ kJ mol^{-1}	ΔE/ kJ mol^{-1}	$\Delta E+\Delta E_{solv}$/ kJ mol^{-1}	ΔH[c]/ kJ mol^{-1}	ΔS/ J K^{-1} mol^{-1}	ΔG/ kJ mol^{-1}
N_3^- +	−18.4	20.6	−18.7	−14.5	−14.3	−58.5	−73.7	−56.1	40.0	−68.0
HCON(OCHO)OMe(**10**)	(118.2)	(157.3)	(117.8)	(−25.5)	(125.5)	(−77.9)	(−93.1)	(−79.6)	(22.9)	(−86.4)
N_3^- +	57.8	114.1	59.1	2.5	58.3			[d]	[d]	[d]
HCON(OCHO)Me (**14**)	(195.2)	(251.5)	(191.6)	(−52.5)	(207.3)					
Difference[e]	76.2	93.4	77.7	17.0	72.6					
	(77.0)	(94.2)	(73.9)	(−27.0)	(81.9)					

[a] Relative to ion–molecule complexes [**10**–N_3]$^-$ and [**14**–N_3]$^-$. [b] $\Delta H^{\ddagger} = [E_{elec}+H]^{\ddagger} - \Sigma[E_{elec}+H]_{complex}$. [c] $\Delta H = [E_{elec}+H]_{products} - \Sigma[E_{elec}+H]_{reactants}$. [d] *N*-Azido-*N*-methylformamide **16** was unstable at the HF/6-31G* level of theory decomposing to N_2 and 1-formyl-1-methyldiazene. [e] Difference between properties for reaction of azide with **14** and azide with **10**.

formamide **11**, at B3LYP/6-31G* hybrid density functional level of theory, is given.[25]

By analogy with concerted decompositions of *N*-alkoxy-*N*-aminoamides or *N*,*N*′-diacyl-*N*,*N*′-dialkoxyhydrazines,[3,6,8] ester formation could occur by a normal HERON process (Scheme 8, pathway A). However, with *N*-alkoxy-*N*-azido-



Scheme 8

amides an alternative process is possible; initial loss of nitrogen followed by a HERON reaction of the intermediate 1,1-disubstituted diazene **17** would lead to the same products (Scheme 8, Path B). **17** is also formed as intermediate from the three-centre rearrangement of *N*,*N*′-diacyl-*N*,*N*′-dialkoxyhydrazines.

Becke3LYP/6-31G* calculations on these and other possible reaction pathways of **12** show that path B, which proceeds in two steps is computed to be the lowest energy process and, significantly, the overall transformation of **11** into two molecules of nitrogen and ester is computed to be exothermic by 584 kJ mol^{-1}.[25] Such favourable energetics should facilitate the formation of high energy esters. The driving force for the formation of **17** and the subsequent HERON rearrangement to esters (Scheme 8, Path B) is derived from the liberation of two molecules of N_2 and should facilitate coupling of sterically hindered alkoxy and acyl substituents.

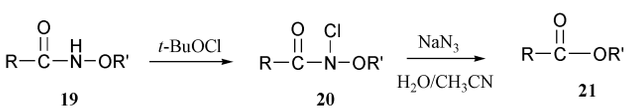
Synthesis of sterically hindered esters

In classical Fischer esterification reactions, bulky groups on either the carboxylic acid or the alcohol slow down the reaction considerably.[26–28] The tetrahedral intermediate in these reactions imparts significant steric compression at the acyl carbon when either the acyl side chain of the acid or the alkyl group of the alcohol, or both of these are bulky or have branching adjacent to the carboxylic acid and hydroxy functionality. Similarly, there are impediments in hindered ester formation from alcohols and acid chlorides. There is therefore continued interest in new methods to activate the carboxy group toward facile esterification. Parish and coworkers have presented a simple method for the esterification of hindered carboxylic acids involving the reaction of trifluoroacetic anhydride with alcohol.[29] However, because of the strongly acidic reaction conditions, the esterification could not be achieved in some cases, especially those involving aliphatic tertiary alcohols. Kaiser and coworkers reported a synthesis in which alcohols were converted into their lithium alkoxide salts with *n*-butyllithium and then heated briefly with an appropriate acid chloride.[30] This method is restricted to acid chlorides without labile α-hydrogen atoms, and to those halides whose corresponding ketenes (intermediates in the reaction) are not volatile or do not readily dimerise. The method of Rossi and coworkers involving two-step reactions by means of potassium alkoxides is only applicable to the preparation of benzoate esters of appropriate tertiary alcohols but not demonstrated for other cases.[31] Silver cyanide was employed by Takimoto and coworkers in the preparation of sterically hindered esters from the corresponding acid chlorides and alcohols.[32] This method is excellent and complementary to the methods developed previously when

considering the high yields and the speed of the reaction, but it is not suitable for some other cases under mild conditions. The efficient synthesis of macrocyclic lactones and esters by the activation of thiol esters with metal salts such as Hg^{II}, Cu^{I}, Cu^{II}, and Ag^{I} in the presence of alcohols has been reported by Masamune and coworkers.[33] However, the reaction depends largely on the nature of the thiol esters and metal salts employed. Kim and coworkers introduced a synthesis of sterically hindered esters by the reaction of *S*-2-pyridyl thioates and 2-pyridyl esters with alcohols in the presence of cupric bromide.[34] More recently Barton and coworkers have demonstrated that decomposition of *N,N′*-diacyl-*N,N′*-dialkoxyhydrazines could be fashioned as a synthesis of highly hindered esters.[10] However, the generation of considerable amounts of the corresponding acids in the course of formation of highly hindered esters, offsets the advantages in this method.

In contrast to carboxylic ester formation, we have found that bulky substituents present little barrier to the synthesis of hydroxamic esters, either by reaction of acid chlorides with alkoxyamines or by alkylation of sodium salts of hydroxamic acids. The additional heavy atom between the acyl and alkoxy side chains reduces the influence of steric effects. Similarly, *N*-chlorination of hydroxamic esters with *tert*-butyl hypochlorite is not impeded by sterically demanding groups in the hydroxamic ester. We envisaged that treatment of *N*-alkoxy-*N*-chloroamides with sodium azide would therefore provide an energetically favourable route to sterically hindered esters.

tert-Butyl hydroxamates (**19a**–**c**) were prepared through the treatment of *O*-(*tert*-butyl) hydroxylamine hydrochloride with the appropriate acid chloride in the presence of pyridine, in anhydrous conditions at 0 °C.[10] Other hydroxamic esters (**19d**–**i**) have been prepared previously by condensation of alkyl halides and potassium benzohydroxamates. Treatment of **19a**–**i** with a three molar excess of *tert*-butyl hypochlorite in anhydrous DCM in the dark at room temperature for 3–12 hours (at 0 °C in the cases of **19b** and **19c**), followed by removal of the solvent under reduced pressure (room temperature) afforded the appropriate *N*-chlorohydroxamates **20a**–**i** as yellow oils (Scheme 9).



19 **20** **21**

a; R=Ph, R'=Bu^t
b; R= R'=Bu^t
c; R= 1-adamantyl, R'=Bu^t
d; R=Bu^t, R'= cyclohexyl
e; R=Ph, R'=$(CH_3)_2CH$
f; R=Ph, R'=$PhCH_2$
g; R=CH_3, R'=$PhCH_2$
h; R=*p*-$NO_2C_6H_4$, R'=Et
i; R=Ph, R'=Et

Scheme 9

N-*tert*-Butoxy-*N*-chloro-2,2-dimethylpropanamide **20b** and *N*-*tert*-butoxy-*N*-chloroadamantane-1-carboxamide **20c** were unstable at room temperature in the dark and partially decomposed in the course of the chlorination reaction. *N*-Chlorination of **19b** and **19c** was however successfully effected below 0 °C. The chlorides were formed cleanly in high yields and were characterised by IR (high carbonyl frequencies: 1715–1740 cm^{-1})[1] and ^1H NMR. These chlorides were used directly in subsequent reactions.

The reaction of *N*-*tert*-butoxy-*N*-chloroamides **20a**–**i** with excess sodium azide in aqueous acetonitrile (H_2O–CH_3CN = 1 : 3) proceeded rapidly and was essentially complete within a few minutes (Scheme 9). Nitrogen gas evolved during the course of the reaction was measured by dilatometry and nearly two equivalents were evolved in each case. Extraction of the mixtures with DCM afforded, after drying and concentration, the corresponding *tert*-butyl carboxylic esters. The reaction has the advantage that it is easy to perform and, in most cases, the products are readily isolated from the reaction mixtures by extraction with organic solvents.

Table 4 Ester (RCOOR′) formation from the reaction of alkyl *N*-alkoxy-*N*-chloroamides (RCONClOR′) with sodium azide in aqueous acetonitrile

Ester	R	R′	Isolated crude yield (%)
21a	Ph	$(CH_3)_3C$	87
21b	$(CH_3)_3C$	$(CH_3)_3C$	30[a]
21c	1-Adamantyl	$(CH_3)_3C$	82[b]
21d	$(CH_3)_3C$	Cyclohexyl	97
21e	Ph	$(CH_3)_2CH$	92
21f	Ph	$PhCH_2$	93
21g	CH_3	$PhCH_2$	92
21h	*p*-$NO_2C_6H_4$	Et	94
21i	Ph	Et	94

[a] GLC analysis; reaction accompanied by formation of pivalic acid 29%. [b] Traces of adamantanecarboxylic acid were also detected.

Sterically crowded esters formed by this process and their yields are summarised in Table 4. *tert*-Butyl pivalate **21b** and to a lesser extent, *tert*-butyl adamantane-1-carboxylate **21c** were accompanied by formation of some of their parent carboxylic acid. Since the esters were stable under the reaction conditions, acid formation is most likely derived from the *N*-chloro precursor prior to azide reaction.

The comparable yields indicate that sterically hindered esters are formed with similar ease relative to less hindered esters. The HERON-type reaction of 1,1-disubstituted diazenes, which proceeds through a three-centered transition state involving extrusion of a stable nitrogen molecule, is not only extremely exothermic, its concerted nature can avoid the limiting formation of a tetrahedral intermediate since the *CO–N* bond is broken as the *O–CO* bond is formed. Theoretical modelling of these reactions and the unusual properties of *N*-alkoxy-*N*-azidoamides forms the basis of the accompanying publication.[25]

Experimental

Melting points were determined on a Reichert Microscopic Hot-Stage and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1725X Fourier-transform instrument. 300 MHz ^1H and 75 MHz ^{13}C NMR spectra were recorded on a Bruker AC-300P FT spectrometer or a Bruker Avance 300 FT spectrometer. Deuterated chloroform ($CDCl_3$) was commercially obtained from Aldrich. All routine samples for structural analysis were run at 300 K in $CDCl_3$, with tetramethylsilane (0.1%) or $CHCl_3$ as an internal standard. Chemical shifts are reported in ppm downfield of TMS. Abbreviations used to indicate spectral multiplicity are: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). GLC analyses were performed on a Shimadzu Gas Chromatograph (GC-8A) instrument. Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with 0.2 mm of silica gel 60 F_{254} (Merck). Preparative plate chromatography was carried out centrifugally on a Harrison 7924T Research Chromatotron. Mass spectral data were obtained on a Kratos MS902 spectrometer from the Mass Spectrometry Unit, School of Chemistry, the University of Sydney. Microanalyses were performed at the Microanalytical Unit, Research School of Chemistry, Australian National University.

Computational methods

Molecular orbital calculations were executed with MACSPARTAN PRO and SPARTAN 5 molecular modelling software.[35] Geometries were optimised at the HF/6-31G* level of theory.

Energies were obtained from single point density functional calculations from non-local density calculations using the BP86 functional of Becke and Perdew[36,37] in which the non-local corrections are introduced perturbatively (pBP method). The numerical polarisation basis set, DN*, which is comprised of atomic solutions supplemented by d-type functions on heavy atoms, was used throughout.[35,38] Frequency calculations at the HF/6-31G* level were carried out to verify stationary points as minima (all positive force constants) and transition states (one negative force constant) and HF/6-31G* and pBP/DN* frequency calculations with force constant analysis were used to determine zero point vibrational energies (*ZPE*) at 0 K and enthalpy (*H*) and entropy (*S*) thermodynamic quantities at 298.15 K and 1 atmosphere. Aqueous solvation energies were estimated semiempirically for HF/6-31G* optimised geometries using the SM2 method of Cramer and Truhlar within Spartan 5.[39] Group charges ($q_{formate}$ and q_{azide}) were derived from the sum of electrostatic charges computed at the HF/6-31G* level of theory and changes in group charges (Δq) were determined from the difference between total electrostatic charge on azide and formate in the transition state and that on the same group in the ground state of azide and *N*-formyloxy-*N*-methoxyformamide (**10**).

The synthesis of *N*-acetoxy-*N*-butoxybenzamide (**1a**),[11,40] *N*-benzyloxy-*N*-chlorobenzamide (**1b**),[11,12] *N*-acetoxy-*N*-benzyloxybenzamide (**8**),[11,12] *N*-chloro-*N*-isopropoxybenzamide (**20e**),[11] ethyl *p*-methylbenzohydroxamate,[3] ethyl *p*-nitrobenzohydroxamate,[3] benzyl acetohydroxamate[3] and *N*-chloro-*N*-ethoxybenzamide (**20i**)[11] have been described previously.

Synthesis of *tert*-butyl hydroxamates[10]

***tert*-Butyl benzohydroxamate 19a.** To a stirred solution of *O*-(*tert*-butyl)hydroxylamine hydrochloride (1.00 g, 0.008 mol) in dry pyridine (10 mL) at 0 °C was added, dropwise, a chilled solution of benzoyl chloride (1.12 g, 0.008 mol) in anhydrous THF. The reaction mixture was stirred overnight at room temperature, and filtered and concentrated under reduced pressure with gentle heating. The residue was dissolved in DCM (50 mL) which was washed with 10% Na_2CO_3 (50 mL), water (100 mL), dried with anhydrous sodium carbonate, and concentrated to give the crude title compound. Recrystallisation from diethyl ether gave pure *tert*-butyl benzohydroxamate as colourless crystals (0.54 g, 35%), mp 132 °C (Lit.[41] mp 134–135 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3382 (NH) and 1684 (C=O); $\delta_H(CDCl_3)$ 1.35 (9H, s, CH_3), 7.42 (2H, t, *m*-ArH), 7.51 (1H, t, *p*-ArH), 7.75 (2H, d, J_{AB} = 8 Hz, *o*-ArH), 8.42 (1H, br, NH); $\delta_C(CDCl_3)$ 26.40 (q, CH_3), 82.40 (s, $CCH_3)_3$), 127.10 (d, *m*-C), 128.60 (d, *o*-C), 131.80 (d, *p*–C), 132.60 (s, *ipso*-C), 167.90 (s, CO).

***tert*-Butyl 2,2-dimethylpropanohydroxamate 19b.** To a stirred solution of *O*-(*tert*-butyl)hydroxylamine hydrochloride (1.00 g, 0.008 mol) in dry pyridine (10 mL) at 0 °C was added, dropwise, a chilled solution of pivaloyl chloride (1.54 g, 0.013 mol) in anhydrous THF. The reaction mixture was stirred overnight at room temperature, filtered and concentrated under reduced pressure with gentle heating. The residue was dissolved in DCM (50 mL) which was washed with 10% Na_2CO_3 (50 mL), water (100 mL), dried with anhydrous sodium carbonate and concentrated to give the crude title compound. Recrystallisation from benzene gave pure *tert*-butyl 2,2-dimethylpropanohydroxamate as colourless needles (0.30 g, 22%), mp 84–95 °C (Found: C, 61.83%; H, 11.10%; N, 8.10%. $C_9H_{19}O_2N$ requires C, 62.39%; H, 11.05%; N, 8.08%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3416 (NH), 1690 (C=O); $\delta_H(CDCl_3)$ 1.24 (9H, s, CH_3–C–C(O)–), 1.27 (9H, s, CH_3–C–O–), 7.81 (1H, br, NH); $\delta_C(CDCl_3)$ 26.30 (q, CH_3), 27.40 (q, CH_3), 38.30 (s, $(CH_3)_3\underline{C}$–CO–), 81.90 (s, –O–$\underline{C}(CH_3)_3$), 177.30 (s, CO); *m*/*z* 173 (M^+, 3%), 85 (pivaloyl, 11), 57 (*tert*-butyl, 100).

***tert*-Butyl adamantane-1-carbohydroxamate 19c.** To a stirred solution of *O*-(*tert*-butyl)hydroxylamine hydrochloride (1.00 g, 0.008 mol) in dry pyridine (10 mL) at 0 °C was added, dropwise, a chilled solution of adamantane-1-carbonyl chloride (2.59 g, 0.013 mol) in anhydrous THF. The reaction mixture was stirred overnight at room temperature, filtered and concentrated under reduced pressure with gentle heating. The residue was dissolved in DCM (50 mL) which was washed with 10% Na_2CO_3 (50 mL), water (200 mL), dried with anhydrous sodium carbonate and concentrated to give the crude title compound. Recrystallisation from benzene gave pure *tert*-butyl adamantane-1-carbohydroxamate as colourless crystals (1.56 g, 78%), mp 164–166 °C (Found: C, 72.23%; H, 9.52%; N, 5.57%. $C_{15}H_{25}O_2N$ requires C, 71.67%; H, 10.02%; N, 5.57%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3413 (NH) and 1682 (C=O); ν_{max}(Nujol)/cm^{-1} 3260 (NH), 1655 (C=O), 1187, 1013, 930, 860 and 810; $\delta_H(CDCl_3)$ 1.27 (9H, s, CH_3), 1.71–1.78 (6H, m, CH–CH_2–CH), 1.90–1.92 (6H, m, CH–CH_2–C), 2.01–2.12 (3H, m, CH), 7.76 (1H, br, NH); $\delta_C(CDCl_3)$ 26.30 (q, CH_3), 28.00 (t, CH_2), 36.50 (t, CH_2), 39.10 (d, CH), 40.50 (s, *C*–CO), 81.80 (s, –O–$C(CH_3)_3$), 176.60 (s, CO). The product was consistent spectroscopically (IR, ^1H, ^{13}C NMR) with the oil reported for the same compound by Barton and coworkers.[10]

Synthesis of cyclohexyl 2,2-dimethylpropanohydroxamate[42]

A solution of potassium trimethylacetohydroxamate (64.95 g, 0.42 mol),[43] cyclohexyl bromide (68.22 g, 0.42 mol), sodium carbonate (21 g), methanol (200 mL) and water (150 mL) was stirred for 24 hours then refluxed for 2 hours. Removal of methanol under reduced pressure, acidification and extraction with DCM afforded the crude cyclohexyl 2,2-dimethylpropanohydroxamate upon concentration (10.75 g, 13%). Recrystallisation from benzene gave pure cyclohexyl 2,2-dimethylpropanohydroxamate as colourless crystals, mp 159–160 °C (Found: C, 65.51%; H, 10.19%; N, 7.07%. $C_{11}H_{21}O_2N$ requires C, 66.30%; H, 10.62%; N, 7.03%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3433 (NH) and 1686 (C=O); $\delta_H(CDCl_3)$ 1.22 (9H, s, CH_3), 1.20–1.98 (10H, m, CH_2), 3.82–3.88 (1H, m, CH), 8.16 (1H, br, NH); $\delta_C(CDCl_3)$ 23.70 (q, CH_3), 25.60 (t, CH_2), 27.30 (t, CH_2), 30.60 (t, CH_2), 38.10 (s, $C(CH_3)_3$–), 83.00 (d, CH), 176.40 (s, CO); *m*/*z* 199 (M^+, 10%), 83 (cyclohexyl, 48), 57 (*tert*-butyl, 100).

General synthesis of *N*-chlorohydroxamates[11]

A solution of the appropriate hydroxamate and excess *tert*-butyl hypochlorite[44] in DCM was stirred in the dark under anhydrous condition for 3–5 hours. The solvent and excess *tert*-butyl hypochlorite were removed under reduced pressure at room temperature to give the *N*-chlorohydroxamate in near quantitative yields, as a yellow oil. Since these are generally thermally unstable as well as light sensitive, they were characterised by ^1H NMR and IR spectroscopy. Relative to precursor hydroxamic esters, protons β- and γ- to the alkoxy oxygen undergo a downfield shift in their ^1H NMR spectrum. As anomeric amides, the carbonyls of *N*-alkoxy-*N*-chloroamides appear between 40 and 60 wave numbers higher in frequency than the corresponding hydroxamic esters.[1]

***N*-*tert*-Butoxy-*N*-chlorobenzamide 20a.** *tert*-Butyl benzohydroxamate (0.0510 g, 2.59×10^{-4} mol) and *tert*-butyl hypochlorite (2.05 g, 1.89×10^{-2} mol) gave the title compound as a yellow oil in a good yield (0.058 g, 98%). $\nu_{max}(CDCl_3)/cm^{-1}$ 1723 (C=O); $\delta_H(CDCl_3)$ 1.40 (9H, s, CH_3), 7.46 (2H, t, *m*-ArH), 7.56 (1H, t, *p*-ArH), 7.84 (2H, d, *o*-ArH); $\delta_C(CDCl_3)$ 26.70 (q, CH_3), 78.10 (s, $C(CH_3)_3$), 118.70 (d, *m*–C), 128.20 (d, *o*–C), 129.50 (d, *p*–C), 132.60 (s, *ipso*-C), CO not present.

***N*-*tert*-Butoxy-*N*-chloro-2,2-dimethylpropanamide 20b.** *tert*-Butyl 2,2-dimethylpropanohydroxamate (0.130 g, 7.50×10^{-4} mol) and *tert*-butyl hypochlorite (4.50 g, 0.041 mol) gave the title compound as a yellow oil in a good yield (0.156 g, 100%).

$\nu_{max}(CDCl_3)/cm^{-1}$ 1732 (C=O); $\delta_H(CDCl_3)$ 1.36 (9H, s, CH_3–C–C(O)–), 1.39 (9H, s, CH_3–C–O–); $\delta_C(CDCl_3)$ 26.88 (q, CH_3), 28.01 (q, CH_3), 41.17 (s, $(CH_3)_3C$–CO–), 84.70 (s, –O–$C(CH_3)_3$), CO not present. This *N*-chloro derivative was unstable at room temperature and upon standing for some time in the dark converted back to **19b**.

***N*-*tert*-Butoxy-*N*-chloroadamantane-1-carboxamide 20c.** *tert*-Butyl adamantane-1-carbohydroxamate (0.13 g, 5.17×10^{-4} mol) and *tert*-butyl hypochlorite (3.10 g, 0.029 mol) in dry DCM (50 mL) were stirred at 0 °C in an ice bath in the dark for 5 hours. Removal of solvent on a rotary evaporator *in vacuo* provided the title compound as a yellow oil in a good yield (0.15 g, 100%). $\nu_{max}(CHCl_3)/cm^{-1}$ 1740 (C=O); $\delta_H(CDCl_3)$ 1.38 (9H, s), 1.71–1.76 (6H, m, CH–C$\underline{H}_2$–CH), 2.05–2.10 (3H and 6H, m, C$\underline{H}$, CH–C$\underline{H}_2$–C); $\delta_C(CDCl_3)$ 26.90 (q, CH_3), 28.10 (t, CH_2), 36.40 (t, CH_2), 39.10 (d, CH), 43.80 (s, $\underline{C}$–CO), 84.60 (s, –O–$\underline{C}(CH_3)_3$), 186.10 (s, CO). Upon standing at room temperature, *N*-*tert*-butoxy-*N*-chloroadamantane-1-carboxamide converted back to its N–H parent precursor **19c** and in aqueous solution, it reverted to adamantane-1-carboxylic acid.

***N*-Chloro-*N*-cyclohexyloxy-2,2-dimethylpropanamide 20d.** Cyclohexyl 2,2-dimethylpropanohydroxamate (1.06 g, 5.32×10^{-2} mol) and *tert*-butyl hypochlorite (4.65 g, 4.28×10^{-2} mol) gave *N*-chloro-*N*-cyclohexyloxy-2,2-dimethylpropanamide (1.22 g, 98%) as a yellow oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 1715 (C=O); $\delta_H(CDCl_3)$ 1.32 (9H, s, CH_3), 1.20–2.14 (10H, m, CH_2), 4.11–4.20 (1H, m, CH); $\delta_C(CDCl_3)$ 24.00 (q, CH_3), 25.40 (t, CH_2), 27.40 (t, CH_2), 30.60 (t, CH_2), 41.40 (s, $C(CH_3)_3$–), 83.00 (d, CH), 183.70 (s, CO).

***N*-Chloro-*N*-ethoxy-*p*-nitrobenzamide 2b.** Ethyl *p*-nitrobenzohydroxamate (0.25 g, 1.19×10^{-3} mol) and *tert*-butyl hypochlorite (1.94 g, 0.018 mol) gave *N*-chloro-*N*-ethoxy-*p*-nitrobenzamide (0.27 g, 93%) as a yellow oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 1723 (C=O); $\delta_H(CDCl_3)$ 1.26 (3H, t, CH_3), 4.21 (2H, q, CH_2), 7.93 (2H, d, J_{AB} = 8 Hz, *o*-ArH), 8.32 (2H, d, J_{AB} = 9 Hz, *m*-ArH); $\delta_C(CDCl_3)$ 12.80 (q, CH_2CH_3), 71.00 (t, CH_2CH_3), 123.50 (d, *m*-C), 130.20 (d, *o*-C), 137.20 (s, *ipso*-C), 150.00 (s, *p*-C), 171.90 (s, CO).

***N*-Benzyloxy-*N*-chloroacetamide 20g.** Benzyl acetohydroxamate (0.45 g, 2.70×10^{-3} mol) and *tert*-butyl hypochlorite (1.00 g, 9.21×10^{-3} mol) gave *N*-benzyloxy-*N*-chloroacetamide (0.54 g, 99%) as a yellow oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 1729 (C=O); $\delta_H(CDCl_3)$ 2.13 (3H, s, CH_3), 5.03 (2H, s, CH_2), 7.30–7.52 (5H, m, ArH); $\delta_C(CDCl_3)$ 21.60 (q, CH_3), 77.30 (t, CH_2), 128.50 (d, *p*-C), 129.90 (d, *o*-C), 133.60 (d, *m*-C), 149.10 (s, *ipso*-C), 175.40 (s, CO).

Synthesis of *N*-acetoxy-*N*-ethoxy-*p*-toluamide 2a

Ethyl *p*-toluohydroxamate (0.22 g, 1.23×10^{-3} mol) and *tert*-butyl hypochlorite (0.53 g, 4.9×10^{-3} mol) reacted according to the standard procedure in DCM (25 mL) afforded *N*-chloro-*N*-ethoxy-*p*-toluamide. ν_{max}(neat)/cm^{-1}1719 (C=O); $\delta_H(CDCl_3)$ 1.28 (3H, t, CH_3), 2.43 (3H, s, CH_3), 4.18 (2H, q, CH_2), 7.26 (2H, d, *m*-H), 7.72 (2H, d, *o*-H). The *N*-chloro-*N*-ethoxy-*p*-toluamide was stirred overnight in dry acetone (20 mL) with sodium acetate (0.58 g, 7.0×10^{-3} mol). After filtration, the solution was concentrated under reduced pressure to give *N*-acetoxy-*N*-ethoxy-*p*-toluamide as a pale yellow oil (0.17 g, 60%) which was a single component by both TLC and ^{1}H NMR. ν_{max}(neat)/cm^{-1} 1791 (C=O), 1721 (C=O); $\delta_H(CDCl_3)$ 1.34 (3H, t, CH_3), 2.12 (3H, s, $COCH_3$), 2.42 (3H, s, $ArCH_3$), 4.5 (2H, q, CH_2), 7.43 (2H, d, ArH), 7.70 (2H, d, ArH); $\delta_C(CDCl_3)$ 13.5 (q, CH_3), 18.7 (q, CH_3), 21.50 (q, CH_3), 71.00 (t, CH_2), 128.70 (s, *ipso*-C), 129.00 (d), 129.10 (d), 143.60 (s, *p*-C), 168.10 (s, amide CO), 174.10 (s, ester CO).

Ester formation from *N*-chlorohydroxamic esters

***tert*-Butyl benzoate 21a.** To a solution of *N*-*tert*-butoxy-*N*-chlorobenzamide (0.058 g, 2.55×10^{-4} mol) in CH_3CN (5 mL) was added a solution of sodium azide (0.20 g, 3.08×10^{-3} mol) in CH_3CN–water (1 : 1, 20 mL). A pale pink colour was formed immediately. The reaction mixture was stirred at room temperature for 2 hours during which nitrogen (9.7 mL, 85%) was collected. The reaction solution was extracted with DCM (50 mL) which was dried and concentrated to give *tert*-butyl benzoate as a yellow oil (0.04 g, 87%) which was consistent, spectroscopically, with previously reported data. [30,31,34] $\nu_{max}(CHCl_3)/cm^{-1}$ 1707 (C=O); $\delta_H(CDCl_3)$ 1.62 (9H, s, CH_3), 7.44 (2H, t, *m*-ArH), 7.54 (1H, t, *p*-ArH), 8.01 (2H, d, J_{AB} = 7 Hz, *o*-ArH); $\delta_C(CDCl_3)$ 27.90 (q, CH_3), 80.90 (s, $C(CH_3)_3$), 128.10 (d, *m*-C), 129.40 (d, *o*-C), 132.10 (d, *p*-C), 132.40 (s, *ipso*-C), 165.80 (s, CO).

***tert*-Butyl 2,2-dimethylpropanoate 21b.** Reaction 1: *N*-*tert*-butoxy-*N*-chloro-2,2-dimethylpropanamide was prepared from 2,2-dimethylpropanohydroxamate (0.18 g, 1.04×10^{-3} mol) and *tert*-butyl hypochlorite as described previously. Treatment with a solution of sodium azide (0.09 g, 2.14×10^{-3} mol) in CH_3CN–water (1 : 1, 1.2 mL) led to an immediate evolution of nitrogen and development of a pink colouration. The CH_3CN was separated and made up to 2.5 mL in a volumetric flask and analysed by GLC. *tert*-Butyl 2,2-dimethylpropanoate (30%) and pivalic acid (29%) were detected by comparison with standard solutions of authentic materials.

Reaction 2: to *N*-*tert*-butoxy-*N*-chloro-2,2-dimethylpropanamide (0.156 g, 7.50×10^{-4} mol) was added a solution of sodium azide (0.07 g, 1.08×10^{-3} mol) in CD_3CN (0.50 g)–D_2O (0.50 g). Nitrogen gas was evolved immediately after which the solution was dried with anhydrous sodium carbonate. NMR analysis of the d_3-acetonitrile layer indicated the presence of ester. Removal of CD_3CN by distillation at 60 °C on an BÜCHI GKR-50 distillation apparatus afforded *tert*-butyl 2,2-dimethylpropanoate as the major component with minor quantities of decomposition products. $\nu_{max}(CDCl_3)/cm^{-1}$ 1714 (C=O); $\delta_H(CDCl_3)$ 1.15 (9H, s, CH_3–C–C(O)–), 1.44 (9H, s, CH_3–C–O–);[30] $\delta_C(CDCl_3)$ 28.03 (q, CH_3), 29.68 (q, CH_3), 38.60 (s, $(CH_3)_3C$–CO–), 79.30 (s, –O–$C(CH_3)_3$), CO not present; *m*/*z* 173 (M^+, <1%), 85 (pivaloyl, 20), 57 (*tert*-butyl, 100).

Reaction 3: *N*-*tert*-butoxy-*N*-chloro-2,2-dimethylpropanamide (0.042 g, 2.03×10^{-4} mol) was reacted with sodium azide (0.10 g, 1.54×10^{-3} mol) in CH_3CN–water (3 : 1, 50 mL) to give N_2 (8.85 mL, 98%) by dilatometry.

***tert*-Butyl adamantane-1-carboxylate 21c.** To a solution of *N*-*tert*-butoxy-*N*-chloroadamantane-1-carboxamide (0.15 g, 5.17×10^{-4} mol) in CH_3CN (5 mL) was added a solution of sodium azide (0.25 g, 3.85×10^{-3} mol) in CH_3CN–water (1 : 1, 10 mL) with immediate evolution of nitrogen (21.2 mL, 92%) and development of a pink colouration. The reaction solution was extracted with DCM (50 mL) which was dried and concentrated to give a crude product as a pale yellow oil (0.10 g, 82%). Centrifugal chromatography (EtOAc–hexane, 5% : 95%) afforded *tert*-butyl adamantane-1-carboxylate as a colourless oil which was consistent, spectroscopically, with previously reported data.[34] $\nu_{max}(CHCl_3)/cm^{-1}$ 1708 (C=O); $\delta_H(CDCl_3)$ 1.44 (9H, s, CH_3), 1.68–1.74 (6H, m, CH–CH_2–CH), 1.85–1.90 (6H, m, CH–CH_2–C), 2.00–2.22 (3H, m, CH); $\delta_C(CDCl_3)$ 28.00 (q, CH_3), 28.10 (t, CH_2), 36.60 (t, CH_2), 38.90 (d, CH), 41.10 (s, *C*–CO), 79.30 (s, –O–$C(CH_3)_3$), 177.10 (s, CO).

Cyclohexyl 2,2-dimethylpropanoate 21d. To a solution of *N*-chloro-*N*-cyclohexyloxy-2,2-dimethylpropanamide (0.93 g, 3.98×10^{-3} mol) in CH_3CN (50 mL) was added a solution of sodium azide (1.20 g, 0.019 mol) in CH_3CN–water (3 : 1, 100 mL). The reaction mixture was stirred at room temperature for

5 min, extracted with DCM (100 mL) which was dried and concentrated to give cyclohexyl 2,2-dimethylpropanoate as a pale yellow oil (0.71 g, 97%) which was consistent, spectroscopically, with previously reported data;[34] $\nu_{max}(CHCl_3)/cm^{-1}$ 1714 (C=O); $\delta_H(CDCl_3)$ 1.20 (9H, s, CH_3), 1.20–1.79 (10H, m, CH_2), 4.67–4.71 (1H, m, CH); $\delta_C(CDCl_3)$ 23.30 (q, CH_3), 25.40 (t, CH_2), 27.10 (t, CH_2), 31.30 (t, CH_2), 38.60 (s, $C(CH_3)_3$–), 71.70 (d, CH), 177.80 (s, CO). In addition 0.042 g (1.80×10^{-4} mol) of *N*-chloro-*N*-cyclohexyloxy-2,2-dimethylpropanamide reacted with sodium azide (0.10 g, 1.54×10^{-3} mol) in CH_3CN–water (3 : 1, 50 mL) to give N_2 (7.55 mL, 94%) by dilatometry.

Isopropyl benzoate 21e. To a solution of *N*-isopropoxy-*N*-chlorobenzamide (0.92 g, 4.31×10^{-3} mol) in CH_3CN (50 mL) was added a solution of sodium azide (1.10 g, 0.017 mol) in CH_3CN–water (3 : 1, 100 mL). The reaction mixture was stirred at room temperature for 5 min, extracted with DCM (100 mL) which was dried and concentrated to give isopropyl benzoate as a pale yellow oil (0.65 g, 92%) which was identical to authentic material; $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 (C=O); $\delta_H(CDCl_3)$ 1.39 (6H, d, CH_3), 5.28 (1H, septet, CH), 7.44 (2H, t, *m*-ArH), 7.56 (1H, t, *p*-ArH), 8.06 (2H, d, $J_{AB} = 8$ Hz, *o*-ArH);[31] $\delta_C(CDCl_3)$ 21.90 (q, CH_3), 68.30 (d, CH), 128.20 (d, *m*-C), 129.50 (d, *o*-C), 131.00 (d, *p*-C), 132.60 (s, *ipso*-C), 166.10 (s, CO). In addition 0.039 g (1.83×10^{-4} mol) of *N*-isopropoxy-*N*-chlorobenzamide reacted with sodium azide (0.10 g, 1.54×10^{-3} mol) in CH_3CN–water (3 : 1, 50 mL) and gave N_2 (7.60 mL, 93%) by dilatometry.

Benzyl benzoate 21f. To a solution of *N*-benzyloxy-*N*-chlorobenzamide (0.28 g, 1.07×10^{-3} mol) in CH_3CN (50 mL) was added a solution of sodium azide (0.70 g, 0.011 mol) in CH_3CN–water (1 : 1, 100 mL). The reaction mixture was then stirred at room temperature for 5 min, extracted with DCM (100 mL) which was dried and concentrated under reduced pressure to give benzyl benzoate as a pale yellow oil (0.21 g, 93%) which was identical to authentic material; $\nu_{max}(CHCl_3)/cm^{-1}$ 1716 (C=O); $\delta_H(CDCl_3)$ 5.40 (2H, s, CH_2), 7.28–7.58 (8H, m, ArH), 8.11 (2H, d, *o*-ArH–CO–); $\delta_C(CDCl_3)$ 66.70 (t, CH_2), 128.20 (s, *ipso*-C), 128.30 (d, *p′*-C), 128.40 (d, *m′*-C), 128.60 (d, *o′*-C), 129.70 (d, *m*-C), 130.20 (d, *o*-C), 133.00 (d, *p*-C), 136.20 (s, *ipso′*-C), 166.40 (s, CO). In addition N_2 (43.50 mL, 91%) was collected by dilatometry.

Benzyl acetate 21g. To a solution of *N*-benzyloxy-*N*-chloroacetamide (0.45 g, 2.25×10^{-3} mol) in CH_3CN (50 mL) was added a solution of sodium azide (1.50 g, 2.31×10^{-2} mol) in CH_3CN–water (1 : 1, 100 mL). The reaction mixture was then stirred at room temperature for 5 min, and extracted with DCM (50 mL) which was dried with anhydrous sodium carbonate, and concentrated to give benzyl acetate as a pale yellow oil (0.31 g, 92%) identical to authentic material. $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (C=O); $\delta_H(CDCl_3)$ 2.13 (3H, s, CH_3), 5.13 (2H, s, CH_2), 7.28–7.45 (5H, m, ArH); $\delta_C(CDCl_3)$ 20.90 (q, CH_3), 66.30 (t, CH_2), 128.40 (d, *p*-C), 128.70 (d, *o*-C), 136.10 (d, *m*-C), 148.90 (s, *ipso*-C), 170.80 (s, CO). In addition 0.042 g (2.10×10^{-4} mol) of *N*-benzyloxy-*N*-chloroacetamide reacted with sodium azide (0.15 g, 2.31×10^{-3} mol) in CH_3CN–water (1 : 1, 50 mL) gave N_2 (8.30 mL, 88%) by dilatometry.

Ethyl *p*-nitrobenzoate 21h. To a solution of *N*-ethoxy-*N*-chloro-*p*-nitrobenzamide (0.19 g, 7.77×10^{-4} mol) in CH_3CN (50 mL) was added a solution of sodium azide (0.50 g, 7.69×10^{-3} mol) in CH_3CN–water (3 : 1, 100 mL). The reaction mixture was stirred at room temperature for 5 min and extracted with DCM (50 mL) which was dried with anhydrous sodium carbonate and concentrated to give ethyl *p*-nitrobenzoate as a pale yellow oil (0.14 g, 94%) identical to authentic material. $\nu_{max}(CHCl_3)/cm^{-1}$ 1723 (C=O); $\delta_H(CDCl_3)$ 1.44 (3H, t, CH_3), 4.45 (2H, q, CH_2), 8.22 (2H, d, $J_{AB} = 8$ Hz, *o*-ArH), 8.30 (2H, d, $J_{AB} = 8$ Hz, *m*-ArH); $\delta_C(CDCl_3)$ 14.10 (q, $CH_2\underline{C}H_3$), 61.90 (t, $\underline{C}H_2CH_3$), 123.40 (d, *m*-C), 130.60 (d, *o*-C), 135.80 (s, *ipso*-C), 150.40 (s, *p*-C), 164.60 (s, CO). In addition 0.040 g (1.64×10^{-4} mol) of *N*-ethoxy-*N*-chloro-*p*-nitrobenzamide reacted with sodium azide (0.10 g, 1.54×10^{-3} mol) in CH_3CN–water (3 : 1, 50 mL) in a dilatometric apparatus evolved N_2 (6.90 mL, 94%).

Ethyl benzoate 21i. To a solution of *N*-ethoxy-*N*-chlorobenzamide (0.58 g, 2.91×10^{-3} mol) in CH_3CN (50 mL) was added a solution of sodium azide (1.80 g, 0.028 mol) in CH_3CN–water (3 : 1, 100 mL). The reaction mixture was stirred at room temperature for 5 min and extracted with DCM (50 mL) which was dried with anhydrous sodium carbonate and concentrated to give ethyl benzoate as a yellow oil (0.41 g, 94%) identical to authentic ester. $\nu_{max}(CHCl_3)/cm^{-1}$ 1713 (C=O); $\delta_H(CDCl_3)$ 1.41 (3H, t, CH_3), 4.40 (2H, q, CH_2), 7.45 (2H, t, *m*-ArH–), 7.56 (1H, t, *p*-ArH), 8.07 (2H, d, $J_{AB} = 8$ Hz, *o*-ArH); $\delta_C(CDCl_3)$ 14.30 (q, CH_2CH_3), 60.90 (t, CH_2CH_3), 128.00 (d, *m*-C), 129.50 (d, *o*-C), 130.50 (d, *p*-C), 132.80 (s, *ipso*-C), 166.60 (s, CO). In addition 0.040 g (2.00×10^{-4} mol) of *N*-ethoxy-*N*-chlorobenzamide reacted with sodium azide (0.13 g, 2.00×10^{-3} mol) in CH_3CN–water (3 : 1, 20 mL) and gave N_2 (8.52 mL, 95%) by dilatometry.

Ester crossover experiments

Experiment with 1a and 2a. A solution of *N*-acetoxy-*N*-butoxybenzamide (0.5 g, 2×10^{-3} mol) and *N*-acetoxy-*N*-ethoxy-*p*-toluamide (0.45 g, 2×10^{-3} mol) was reacted with sodium azide (1.0 g, 0.015 mol) in 50 mL acetonitrile–water. Once evolution of nitrogen had subsided, the acetonitrile was removed under reduced pressure and the mixture was extracted with chloroform (100 mL) which was separated, dried and concentrated to an oil. NMR analysis using an internal standard indicated the presence of butyl benzoate and ethyl *p*-toluate in near quantitative yield.

Experiment with 1b and 2b. A solution of *N*-ethoxy-*N*-chloro-*p*-nitrobenzamide (0.65 g, 2.66×10^{-3} mol) and *N*-benzyloxy-*N*-chlorobenzamide (0.67 g, 2.56×10^{-3} mol) was treated with a solution of sodium azide (1.05 g, 0.016 mol) in 50 mL acetonitrile–water (3 : 1). The reaction was complete within a minute and the mixture was extracted with DCM (100 mL). Removal of solvent under reduced pressure provided a crude mixture which by ^1H NMR analysis contained ethyl *p*-nitrobenzoate and benzyl benzoate and a complete lack of the crossover esters, ethyl benzoate and benzyl *p*-nitrobenzoate. Separation of the crude mixture by centrifugal chromatography (5% EtOAc–95% hexane) gave ethyl *p*-nitrobenzoate as a colourless solid (0.43 g, 83%) and benzyl benzoate as a colourless oil (0.41 g, 76%), both consistent, spectroscopically, with authentic samples.

Rate studies. An appropriate quantity of sodium azide in water was added rapidly by syringe to a solution of the required amount of *N*-acetoxy-*N*-benzyloxybenzamide (**8**) in acetonitrile–water such that the final volume was 250 mL and final solvent composition of acetonitrile–water was 3 : 1. The closed system was attached to a dilatometry apparatus and the volume of evolved nitrogen was monitored throughout the reaction at atmospheric pressure (Tables 5–8).

Preparation of *N*-butyl-*N*-chlorobenzamide 9a

Treatment of *N*-butylbenzamide (2.24 g, 1.3×10^{-2} mol) in DCM (100 mL) with *tert*-butyl hypochlorite (4.12 g, 3.8×10^{-2} mol) gave a 2 : 1 mixture (3.4 g) of *N*-butyl-*N*-chlorobenzamide and *N*-butylbenzamide (by ^1H NMR). Purification by centrifugal chromatography (10% EtOAc–hexane) afforded pure title compound (1.33 g, 48%) which was analysed for positive chlorine iodometrically (Found: Cl, 16.6%. $C_{11}H_{14}ClNO$ requires Cl, 16.75%); $\delta_H(CDCl_3)$ 0.90 (3H, t, CH_3), 1.31 (2H, sextet, CH_2), 1.75 (2H, quintet, CH_2), 3.71 (2H, t, OCH_2), 7.28–7.53 (5H, m, ArH).

Table 5 Data for reaction of *N*-acetoxy-*N*-benzyloxybenzohydroxamate **8** (5×10^{-4} M) and sodium azide (5×10^{-4} M) in acetonitrile–water (3 : 1) (250 mL) at 21.5 °C

Time/s	N_2(lib.)/mL [a]	N_2(rem.)/mL [b]	N_2(rem.)/N_2 (total)	$[c]_t/10^{-4}$M [c]	$\frac{1}{[c]}/10^3$ M^{-1}
0	0.00	4.61	1.00	5.00	2.00
15	0.16	4.45	0.97	4.83	2.07
25	0.22	4.39	0.95	4.76	2.10
60	0.42	4.19	0.91	4.54	2.20
90	0.60	4.01	0.87	4.35	2.30
120	0.77	3.84	0.83	4.16	2.40
150	0.88	3.73	0.81	4.05	2.47
240	1.06	3.55	0.77	3.85	2.60
360	1.32	3.29	0.71	3.57	2.80
480	1.54	3.07	0.67	3.33	3.00
600	1.73	2.88	0.63	3.12	3.20
900	2.12	2.49	0.54	2.70	3.70
1200	2.38	2.23	0.48	2.42	4.13
1500	2.65	1.96	0.43	2.13	4.70
1800	2.82	1.79	0.39	1.94	5.15
2400	3.21	1.40	0.30	1.52	6.59
3000	3.49	1.12	0.24	1.21	8.23

[a] Nitrogen liberated at time *t*. [b] Nitrogen remaining in the reaction mixtures at time *t*. [c] Concentrations [*c*] of **8** and N_3^- at time *t*.

Table 6 Data for reaction of *N*-acetoxy-*N*-benzyloxybenzohydroxamate **8** (1×10^{-3} M) and sodium azide (1×10^{-3} M) in acetonitrile–water (3 : 1) (250 mL) at 21.5 °C

Time/s	N_2(lib.)/mL [a]	N_2(rem.)/mL [b]	N_2(rem.)/N_2 (total)	$[c]_t/10^{-4}$ M [c]	$\frac{1}{[c]_t}/10^3$ M^{-1}
0	0.00	8.95	1.00	10.00	1.00
30	1.17	7.78	0.87	8.69	1.15
55	1.85	7.10	0.79	7.93	1.26
90	2.08	6.87	0.77	7.68	1.30
120	2.56	6.39	0.71	7.14	1.40
150	2.90	6.05	0.68	6.76	1.48
180	2.98	5.97	0.67	6.67	1.50
360	3.53	5.42	0.61	6.06	1.65
540	4.34	4.61	0.52	5.15	1.94
900	5.42	3.53	0.39	3.94	2.54
1200	6.18	2.77	0.31	3.09	3.23
1500	6.68	2.27	0.25	2.54	3.94
1800	7.02	1.93	0.22	2.16	4.64

[a] Nitrogen liberated at time *t*. [b] Nitrogen remaining in the reaction mixtures at time *t*. [c] Concentrations [*c*] of **8** and N_3^- at time *t*.

Table 7 Data for reaction of *N*-acetoxy-*N*-benzyloxybenzohydroxamate **8** (5×10^{-4} M) with sodium azide (5×10^{-3} M) in acetonitrile–water (3 : 1) (250 mL) at 21.5 °C

Time/s	N_2(lib.)/mL [a]	N_2(rem.)/mL [b]	N_2(rem.)/N_2 (total)	[**8**]/10^{-5} M	ln[**8**]
0	0.00	5.13	1.00	50.00	−7.60
30	1.95	3.18	0.62	31.00	−8.08
60	2.52	2.61	0.51	25.40	−8.28
90	3.25	1.88	0.37	18.30	−8.61
120	3.55	1.58	0.31	15.40	−8.78
150	3.83	1.30	0.25	12.70	−8.97
180	4.25	0.88	0.17	8.58	−9.36
240	4.56	0.57	0.11	5.56	−9.80
300	4.70	0.43	0.08	4.19	−10.08
360	4.92	0.21	0.04	2.05	−10.80
420	4.98	0.15	0.03	1.46	−11.13
480	5.08	0.05	0.01	0.49	−12.23
540	5.10	0.03	0.01	0.29	−12.74
600	5.11	0.02	0.00	0.19	−13.15

[a] Nitrogen liberated at time *t*. [b] Nitrogen remaining in the reaction mixtures at time *t*.

Preparation of *N*-benzoyloxy-*N*-benzylbenzamide 9b [45]

Benzoyl peroxide (3.33 g, 0.014 mol) in DCM (50 mL) was added dropwise to a mixture of benzylamine (1.34 g, 0.013 mol) and sodium carbonate (1.99 g) in DCM (50 mL) in an ice bath and the reaction mixture was stirred for a further 2 hours at room temperature. Progress of the reaction was monitored by TLC. Inorganic materials were removed by filtration and the filtrate was treated dropwise with a pre-chilled solution of benzoyl chloride (1.76 g, 0.013 mol) and triethylamine (1.27 g) in DCM (50 mL) at 0 °C. The reaction mixture was stirred for a further one hour after which it was washed with 10% aqueous sodium carbonate, dilute HCl, dried with anhydrous sodium carbonate and concentrated to give the crude product. Purification by centrifugal chromatography (2% EtOAc–98% hexane) afforded the title compound as colourless crystals (1.55 g, 37%), mp 95 °C (Found: C, 76.14%; H, 5.22%; N, 4.47%. $C_{21}H_{17}O_3N$ requires C, 76.12%; H, 5.17%; N, 4.23%); $\nu_{max}(CHCl_3)/cm^{-1}$

Table 8 Data for reaction of *N*-acetoxy-*N*-benzyloxybenzohydroxamate **8** (5×10^{-3} M) with sodium azide (5×10^{-4} M) in acetonitrile–water (3 : 1) (250 mL) at 21.5 °C

Time/s	N_2(lib.)/mL[a]	N_2(rem.)/mL[b]	N_2(rem.)/N_2 (total)	$[N_3^-]/10^{-5}$ M	$\ln[N_3^-]$
0	0.00	4.94	1.00	50.00	−7.60
10	0.56	4.38	0.89	44.30	−7.72
45	1.82	3.12	0.63	31.60	−8.06
60	2.37	2.57	0.52	26.00	−8.25
90	2.88	2.06	0.42	20.90	−8.48
120	3.45	1.49	0.30	15.10	−8.80
150	3.95	0.99	0.20	10.00	−9.21
180	4.35	0.59	0.12	5.97	−9.73
240	4.68	0.26	0.05	2.63	−10.55
300	4.80	0.14	0.03	1.42	−11.16
360	4.81	0.13	0.03	1.32	−11.24
420	4.88	0.06	0.01	0.61	−12.01
480	4.91	0.03	0.01	0.30	−12.71
540	4.92	0.02	0.00	0.20	−13.11
600	4.93	0.01	0.00	0.10	−13.80

[a] Nitrogen liberated at time *t*. [b] Nitrogen remaining in the reaction mixtures at time *t*.

1764 and 1668 (C=O); $\delta_H(CDCl_3)$ 5.12 (2H, s, CH_2), 7.33–7.42 (10H, m, ArH), 7.58 (1H, t, *p*-ArH–COO–), 7.69 (2H, d, $J_{AB} = 8$ Hz, *o*-ArH–CON-), 7.84 (2H, d, $J_{AB} = 8$ Hz, *o*-ArH–COO–); $\delta_C(CDCl_3)$ 53.50 (t, CH_2), 126.90 (s), 127.90 (d), 128.40 (d), 128.60 (d), 128.70 (d), 129.80 (s), 130.20 (d), 131.00 (d), 133.40 (d), 133.60 (d, *p*-C–CO), 134.10 (d, *p*-C–CO), 135.20 (s, *ipso*-C–CH_2O–), 164.30 (s, CO), 170.70 (s, CO); *m*/*z* 210 ($M - 121^+$, 9%), 105 (benzoyl, 100), 77 (phenyl, 25).

Reaction of 9a and 9b with sodium azide

Treatment of *N*-butyl-*N*-chlorobenzamide **9a** with sodium azide in aqueous acetonitrile, at rt or under reflux afforded parent *N*-butylbenzamide as the sole product. Similarly, *N*-benzoyloxy-*N*-benzylbenzamide **9b** reverted to *N*-benzylbenzamide.

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