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PAPER

Synthesis and thermal decomposition of *N*,*N*-dialkoxyamides†‡

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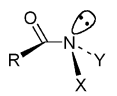
N,*N*-Dialkoxyamides **1c**, a virtually unstudied member of the new class of anomeric amides, amides bearing two electronegative atoms at nitrogen, have been synthesised in useful yields directly from hydroxamic esters using phenyliodine(III)bis(trifluoroacetate) (PIFA). Infrared carbonyl stretch frequencies and carbonyl ^{13}C NMR properties have been reported, which support strong inhibition of amide resonance in these amides. Their thermal decomposition reactions in mesitylene at 155 °C proceed by homolysis to form alkoxyamidyl and alkoxyl free radicals in preference to HERON rearrangements to esters. The reactions follow first-order kinetics and for a series of *N*,*N*-dimethoxy-4-substituted benzamides, activation energies of 125–135 kJ mol^{-1} have been determined together with weakly negative entropies of activation.

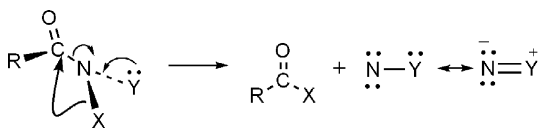
Introduction

Anomeric amides are defined as amides that are substituted at nitrogen with two electronegative atoms (**1a–f**).[1] This configuration at nitrogen radically alters the amide characteristics since the electronegative requirements of the heteroatoms are best satisfied if the nitrogen assumes sp^3 hybridisation in which the nitrogen lone pair becomes localised in a hybrid orbital with reduced p-character, resulting in significantly reduced amide resonance. In addition, such amides usually exhibit ground-state anomeric effects through the amide nitrogen, which influence their structure and reactivity; with a good leaving group at nitrogen (**1a** and **1b**) they can undergo S_N1 and S_N2 reactions at the amide nitrogen,[2–9] but with poor leaving groups (**1d**) and with **1b** in non-polar solvents they undergo the unusual HERON reaction in which anomeric destabilisation results in migration of one substituent from nitrogen to the carbonyl carbon with attendant formation of a stabilised nitrene (Scheme 1).[9–16]



1a X=Cl, Y=OR
1b X=OAcyl, Y=OR
1c X=Y=OR
1d X=NR_2, Y=OR
1e X=SR, Y=OR
1f X=Y=Halogen

Spectroscopic, theoretical and structural evidence has been presented for a range of such amides (**1a–f**). Notably, theoretical calculations predict a high degree of pyramidality at nitrogen (Winkler–Dunitz χ values[17,18] vary from 58.5° for **1b** to 31° for **1e**), long C–*N* bonds in the range of 1.405 Å for **1b** to 1.38 Å for **1e**, but relatively small twist angles (Winkler–Dunitz τ parameters typically less than 10°).§ [9,15,19–22] These predictions are borne out by structural data where this is available and by spectroscopic data.[1,9,15] While theoretical, spectroscopic and structural data for *ONCl*, *ONO*Ac, and *ONN* systems have been reported, the properties of dialkoxyamides **1c** are virtually unknown. Some spectroscopic properties of only a limited number have been reported to date[1,15] though we have recently obtained crystallographic data for two members of this class, which demonstrates, as predicted, a high degree of pyramidality at nitrogen and very long *N*–C bonds.¶ [23] Crystallographic data has been reported for urea analogues, *N*,*N*-dimethoxyurea and *N*,*N*-dimethoxy-*N*′-(4-nitrophenyl)urea,[24] which also possess highly pyramidal nitrogens and long *N*–*C* bonds but, on account of the competing α-amino group, are not representative of true anomeric amides.



Scheme 1

N,*N*-Dialkoxyamides **1c** can be synthesised by solvolysis of *N*-alkoxy-*N*-chloroamides **1a** in aqueous alcohol[1,11] or by the reaction of *N*,*N*-dialkoxyamines with acyl halides or isocyanates.[25] In this paper we report a new synthesis of these rare amides

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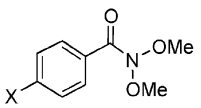
† Dedicated to the late Athel Beckwith FRS, a good friend and an outstanding chemist, who influenced in many positive ways the careers and lives all those who were drawn to him and his chemistry.

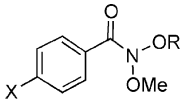
‡ Electronic supplementary information (ESI) available. See DOI: 10.1039/c1ob00008j

§ A χ value of 60° corresponds to a completely tetrahedral nitrogen and a τ value of 0° corresponds to alignment of the lone pair on nitrogen with the carbonyl carbon $2p_z$ orbital.

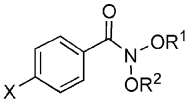
¶ *N*-Ethoxy-*N*-methoxy-4-nitrobenzamide (**3a**) and *N*-methoxy-*N*-(4-nitrobenzyloxy)benzamide (**3f**) have χ values of 58° and 56° and *N*–*C* bond lengths of 1.45 Å and 1.42 Å respectively.



2a X = H
2b X = Cl
2c X = Me
2d X = MeO



3a X= NO_2, R = Et
3b X= Cl, R = Bu
3c X= Br, R = Bu
3d X= NO_2, R = Bu
3e X= H, R = 4-$ClC_6H_4CH_2$
3f X=H, R = 4-$NO_2C_6H_4CH_2$
3g X=H, R = $C_6H_4CH_2$

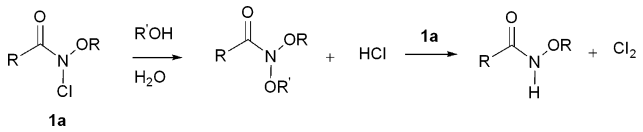


4a X= NO_2, R^1,R^2 = Et
4b X= H, R^1,R^2 = Bu
4c X= H, R^1 = Bu, R^2 = Bn

as well as their thermal decomposition reactions, which unlike other anomeric amides that undergo heterolytic HERON rearrangements, are radical in nature.

Results and Discussion

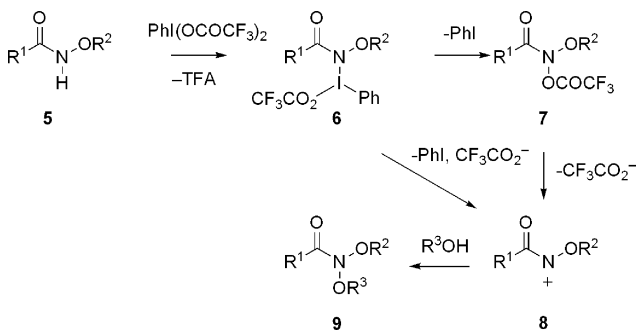
A limited number of *N*,*N*-dialkoxyamides have been synthesised by solvolysis of *N*-chlorohydroxamic esters in aqueous alcohols but only one experimental method has been reported in detail.[11] Aqueous methanolysis of *N*-chloro-*N*-methoxy-4-methylbenzamide afforded a 26% yield of *N*,*N*-dimethoxy-4-methylbenzamide **2c**. However, this method results in low yields since the reaction produces hydrochloric acid, which reacts with starting *N*-chloroamides producing hydroxamic esters and chlorine (Scheme 2).



1a

Scheme 2

Recently, hydroxamic esters themselves have been found to be oxidised to *N*-alkoxynitrenium ions by hypervalent iodine reagents,[26–31] which have been used in a variety of cyclisations onto aromatic rings and, very recently, onto alkenes.[26] We recently found that in the presence of alcohols, either as solvents or as reagents in acetonitrile, phenyliodine(III)bis(trifluoroacetate) (PIFA) reacts with a range of hydroxamic esters **5** giving *N*,*N*-dialkoxyamides **9** in synthetically useful yields and with short reaction times (Scheme 3). Presumably the intermediate is the *N*-(trifluoroacetoxyiodobenzene) derivative **6** or the *N*-trifluoroacetoxy compound **7**, formed through ligand coupling. Both **6** and **7** are themselves anomeric amides and in polar media



5 **6** **7** **8** **9**

Scheme 3

are sources of alkoxynitrenium ions **8**.[1,2,9,15] *N*,*N*-Dialkoxyamides **9** are generated by capture of the nitrenium ion by alcohol.

Reactions were carried out either in solvent as nucleophile or, where higher alcohols were introduced, the hydroxamic ester was dissolved in acetonitrile and treated with PIFA in the presence of excess alcohol. Yields of *N*,*N*-dialkoxyamides **2**, **3a–f** and **4** produced by the PIFA method ranged between 40 and 96%.

N,*N*-Dialkoxybenzamides **2–4** are typical anomeric amides, exhibiting radically reduced amide resonance. The carbonyl stretch frequencies in the infrared (Table 1), while not as high as those of the analogous *N*-acyloxy-*N*-alkoxyamides (typically 1718–1742 cm^{-1}),[1,9,15] were mostly between 20–30 cm^{-1} higher than their parent hydroxamic esters. This is in accord with relative theoretical values for *N*,*N*-dimethoxyamides **10a** and **10b** and *N*,*N*-dimethylamides **11a** and **11b** computed at the B3LYP/6-31G(d) level;[15,19,22] scaled carbonyl stretch frequencies for **10b** and **11b** were computed to be 1740 and 1673 cm^{-1} respectively.[22] The amide nitrogens in **10a** and **10b** are also predicted to be highly pyramidal with average angles at nitrogen of 115° and 114° respectively and both have long *N*–*C*(*O*) bonds, 1.4 Å and 1.42 Å respectively.[15,19,22] Recent X-ray data confirm these predictions.[23] Consistent with the spectroscopic data, *N*,*N*-dialkoxyamides have very low amide isomerization barriers. Earlier NMR studies on *N*,*N*-dimethoxy-4-methylbenzamide (**2c**) showed that the methoxyl resonances were identical down to –90 °C. In addition the benzylic methylene protons of *N*-benzyloxy-*N*-methoxybenzamide (**3g**) remained isochronous down to the same temperature putting a limit of *ca* 32 $kJmol^{-1}$ on any isomerization process.[1]

10a R = H
10b R = Me

11a R = H
11b R = Me

^{13}C NMR carbonyl chemical shifts, reported here for the first time, are very similar to those of *N*-acyloxy-*N*-alkoxyamides (very close to 174 ppm and about 8 ppm higher than the precursor hydroxamic esters).[9,15] While in both anomeric amides the amide resonance interaction is greatly reduced, the carbonyl shifts are not ketonic and appear some 20 ppm upfield of aryl/alkyl ketones. The origin of this upfield shift from that of ketones, parallels that of esters, anhydrides and acid chlorides. The triad of electronegative atoms adjacent to the carbonyl in pyramidal *N*,*N*-dialkoxyamides and *N*-acyloxy-*N*-alkoxyamides destabilises the polar resonance form of their carbonyls relative to ketones. These carbonyls have greater double bond character resulting in higher electron density at carbon, higher field carbonyl chemical shifts and higher carbonyl vibrational frequencies. These observations are

Table 1 IR carbonyl stretch frequencies[a] and ^{13}C NMR chemical shifts[b] for *N*,*N*-dialkoxyamides ($R^1ON(OR^2)COR^3$) and their precursor hydroxamic esters ($R^1ONHCOR^3$)

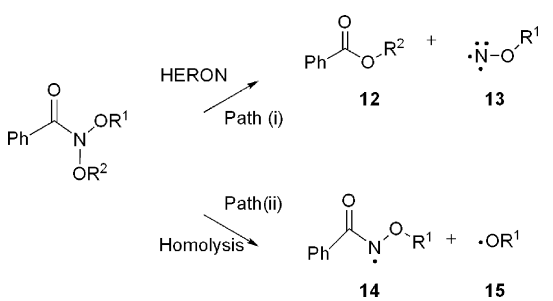
R^1	R^2	R^3	Amide ν/cm^{-1}	Hydroxamic ester ν/cm^{-1}	^{13}C NMR/ppm
Me	Me	Ph	1711	1683	174.3
Me	Me	4-ClC_6H_4	1712	1687	173.2
Me	Me	4-MeC_6H_4	1710	1685	174.3
Me	Me	4-$MeOC_6H_4$	1705	1687	173.8
Et	Me	4-$NO_2C_6H_4$	1708	1655[c](Me)	173.8
Bu	Me	4-ClC_6H_4	1713	1695 (Bu), 1687 (Me)	173.8
Bu	Me	4-BrC_6H_4	1702	1696 (Bu)	173.1
Bu	Me	4-$NO_2C_6H_4$	1717	1695 (Bu)	171.8
4-$ClC_6H_4CH_2$	Me	Ph	1702	1687 (4-$ClC_6H_4CH_2$)	174.0
4-$NO_2C_6H_4CH_2$	Me	Ph	1709	1691(4-$NO_2C_6H_4CH_2$)	174.3
Et	Et	4-$NO_2C_6H_4$	1704	1692	171.6
Bu	Bu	Ph	1703	1654	174.0
Bu	Bn	Ph	1710	1654 (Bu), 1678 (Bn)	174.1

[a] Solution state in $CHCl_3$ [b] $CDCl_3$. [c] Nujol or neat.

in line with those of Neovonen and coworkers, whose systematic study of ^{13}C NMR shift data for ester carbonyls showed that electron density is actually greater at such carbons; reactivity enhancement of ester carbonyls relative to ketones is actually due to destabilisation of the ground states of the esters by the electron-withdrawing substituents rather than positive polarisation at carbon.[32,33]

Anomeric amides bearing poor leaving groups have been found to undergo the HERON rearrangement. *N*-Alkoxy-*N*-aminoamides **1d** rearrange readily to alkyl esters and aminonitrenes in methanol, a process driven by a strong n_N–σ^*_{NO} anomeric destabilisation of the *N*–*O* bond.[9–15] *N*-Acyloxy-*N*-alkoxyamides **1b**, which undergo both acid-catalysed S_N1 and S_N2 reactions at nitrogen in polar solvents, also undergo the HERON rearrangement in toluene at 90 °C giving anhydrides and alkoxynitrenes.[9,14–16] While the alkoxyl oxygen is a weak anomeric donor when compared to nitrogen in **1d**, the driving force is stabilisation of the developing negative charge on the migrating carboxylate group in the transition state. However, in the case of thermolysis of **1b**, this reaction pathway is in competition with radical *N*–OAc dissociation to acyloxyl and *N*-alkoxyamidyl radicals.

Thermolysis studies have been carried out with a number of *N*,*N*-dialkoxyamides (**2a–d**, **3e**) and while these could in principle undergo a HERON reaction to esters **12** and alkoxynitrenes **13** (Scheme 4, path i), the products point to the primary process being homolysis of a nitrogen–oxygen bond to give an alkoxyamidyl radical **14** and an alkoxyl radical **15** (Scheme 4, path ii).



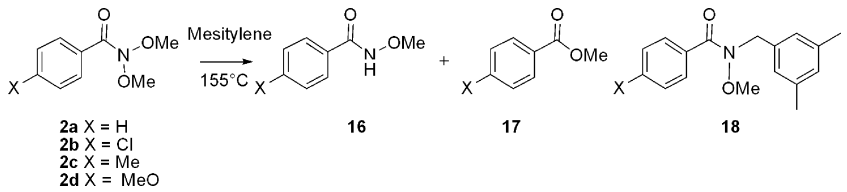
Scheme 4

Table 2 Percentage conversion of *N*,*N*-dimethoxybenzamides **2a–d** to hydroxamic esters **16**, methyl benzoates **17** and *N*-(3,5-dimethylbenzyl)-*N*-methoxybenzamides **18** in mesitylene at 155 °C

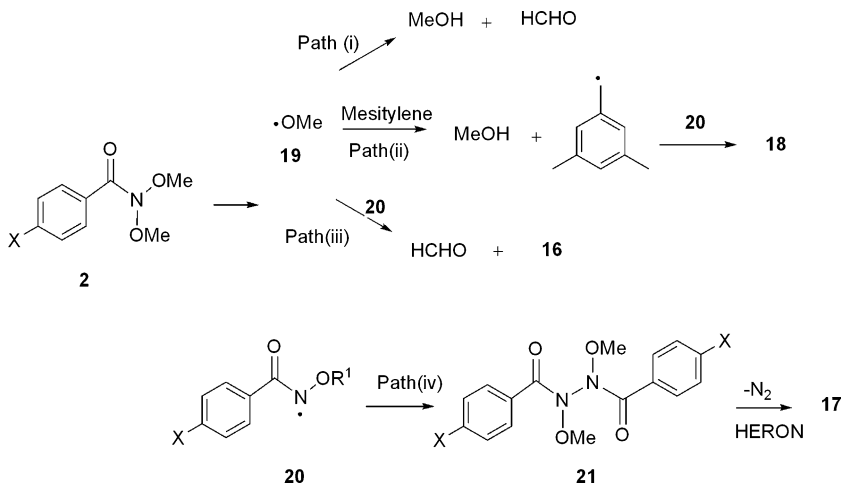
Dialkoxyamide (**2**)	Alkoxyamide (**16**)/%	Methyl benzoate(**17**)/%	Adduct (**18**)/%
2a	56	9	23
2b	66	15	11
2c	44	28	21
2d	25	37	22

The reactions have a higher temperature requirement than thermolysis of *N*-acyloxy-*N*-alkoxyamides (**1b**) and **2a–d** decomposed smoothly within 1.5–2.0 h in mesitylene at 155° C. The primary products in all cases were the corresponding hydroxamic esters **16**, methyl esters **17** and adducts *N*-(3,5-dimethylbenzyl)-*N*-methoxybenzamides **18** (Scheme 5). The adducts (**18**) were isolated chromatographically in a separate experiment and quantified together with **16** and **17** either by HPLC, or by NMR using diphenylethane as an internal standard after careful removal of mesitylene under reduced pressure. Yields from the four dialkoxyamides are presented in Table 2.

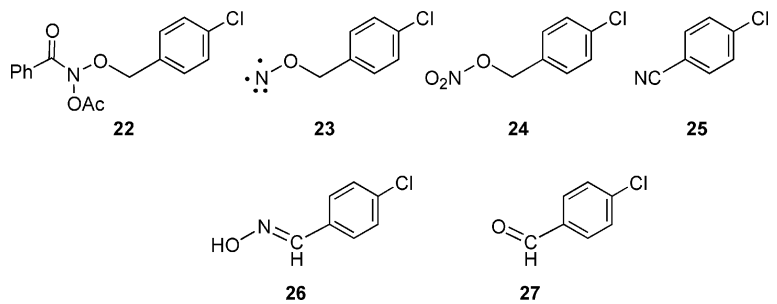
The significant amounts of mesitylene adduct **18** from these reactions, as well as the formation of hydroxamic esters **16**, is consistent with a homolysis reaction giving *N*-alkoxyamidyl and methoxyl radicals (Scheme 6). Methoxyl radicals **19** could disproportionate to methanol and formaldehyde, which would be undetectable under the conditions (Scheme 6, path i) or react with solvent generating methanol and 3,5-dimethylbenzyl radicals, which combine with alkoxyamidyl radicals **20** to generate **18** (Scheme 6, Path ii). However, on account of the high reactivity of alkoxyl radicals, hydrogen abstraction from mesitylene is much more likely than disproportionation. Solvent-cage transfer of a hydrogen to alkoxyamidyls **20** producing hydroxamic esters **16** and formaldehyde is also possible (Scheme 6, path iii). Though hydrogen abstraction from mesitylene by alkoxyamidyl radicals **20** leading to **16** cannot be precluded, it is considered less likely since in alkoxyamidyls such as **20**, the nitrogen-centred radical is captodative stabilised by the neighbouring oxygen and the carbonyl.[34–39] Relative to amidyl radicals, which are known to be electrophilic in nature and good hydrogen abstractors,[40–45] the high energy SOMO in alkoxyamidyls makes them electronically similar to nucleophilic



Scheme 5



Scheme 6



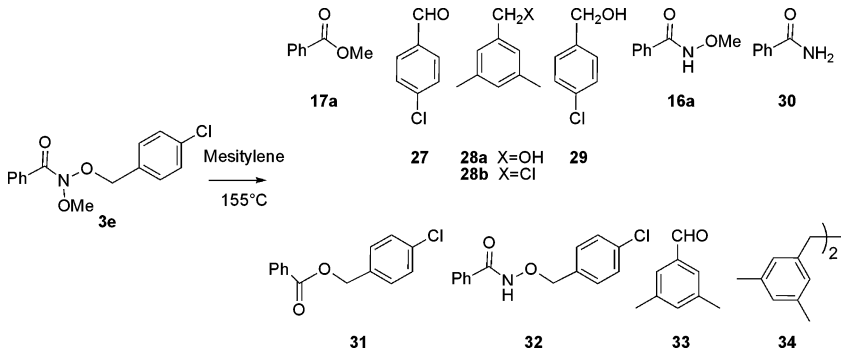
aminyl radicals, which are poor abstractors of hydrogen from carbon.[35,46]‖

Two mechanisms are possible for the formation of the esters **17**. Alkoxyamidyls generated under a variety of conditions are well known to dimerise to hydrazines, which decompose to esters.[35,36,38,47,49,50] Therefore **20** can dimerise to give the symmetrical hydrazines **21** and ultimately **17** (Scheme 6, path iv). We and others have more recently shown this decomposition to involve a double HERON rearrangement to two molecules of ester with liberation of nitrogen, as **21** are *NNO* anomeric amides.[1,9,11,12,14,15,21,51,52] That *N*-alkoxyamidyl radicals are sufficiently unreactive with the solvent and can therefore undergo dimerisation is evidenced by their interception of the secondary mesityl radicals giving **18**. A second direct route to the esters could be HERON rearrangement of *N*,*N*-dialkoxyamides themselves (Scheme 4, path i). This reaction would be less favourable than the corresponding rearrangement of *N*-alkoxy-*N*-aminoamides (**1d**) or *N*-acyloxy-*N*-alkoxyamides (**1b**) since the anomeric effect is weaker in this case.

Following a recent study on the thermal decomposition of *N*-acyloxy-*N*-alkoxyamides **1b**, which in toluene undergo a HERON reaction giving anhydrides and alkoxynitrenes,[16] a HERON rearrangement of *N*,*N*-dialkoxyamides would also be expected to generate alkoxynitrenes. These relatively rare nitrenes, which have a triplet ground state, have been shown to rearrange to oximes, dimerise to hyponitrites and react with oxygen to give nitrate esters.[53–55] In the thermal decomposition of *N*-acyloxy-*N*-alkoxyamides the identification of products derived from these processes confirmed the operation of a HERON reaction.[16] However, alkoxynitrenes identified in those studies contained either benzylic or long-chain alkyl groups and the likely volatile nature of products from similar reactions of methoxynitrene makes detection of a HERON pathway to esters more difficult in this case.

The fate of 4-chlorobenzyloxynitrene **23** from the thermal decomposition of *N*-acetoxy-*N*-(4-chlorobenzyloxy)benzamide **22** is known. The products 4-chlorobenzyl nitrate **24**, 4-chlorobenzonitrile **25** (formed under the conditions from 4-chlorobenzaldoxime **26**) and 4-chlorobenzaldehyde **27** were all detectable by MS and ^{1}H NMR. Thermolysis of the *N*-methoxy

‖ Intramolecular additions of alkoxyamidyls to alkenes at 110 °C in DMSO/dioxane has recently been reported,[47] but under the same conditions they do not undergo intramolecular allylic hydrogen abstraction or addition to a benzene substituent on the alkoxyl side chain, in support of our earlier findings on amidyl cyclisations in the biphenyl-2-carboxamide system.[35,48] This constitutes further evidence of their low electrophilicity.



Scheme 7

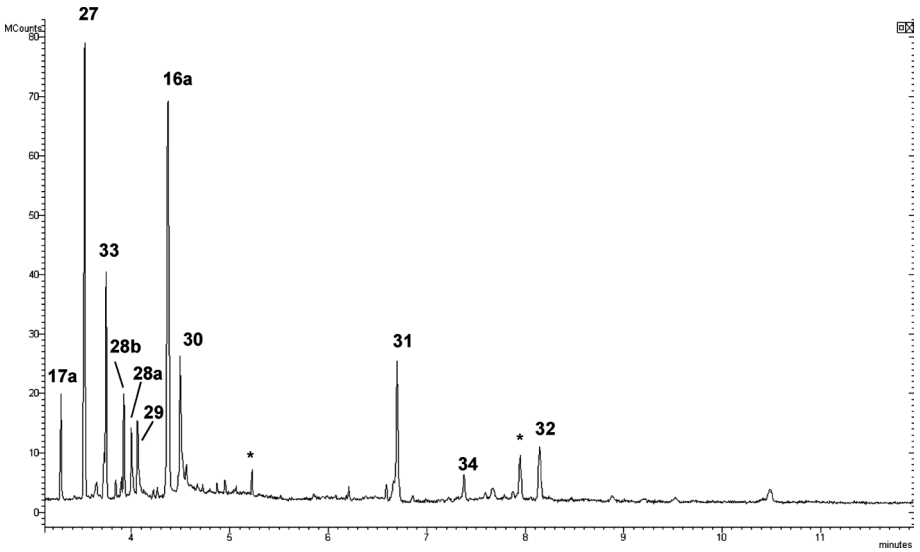
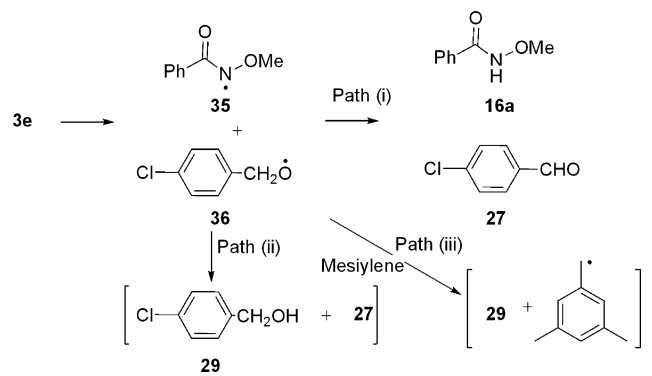


Fig. 1 GC-MS trace of the reaction mixture from thermal decomposition of *N*-(4-chlorobenzyloxy)-*N*-methoxybenzamide **3e** at 155 °C in mesitylene. Numbers correspond to structures in Scheme 7; * denotes minor, unidentified products.

analogue of **22**, **3e**, in mesitylene at 155 °C afforded a complex reaction mixture (Scheme 7) that was analysed by GC-MS. The chromatographic trace is shown in Fig. 1 together with assignment of the major products. Mass spectral fragmentation patterns for these are presented in Table 5.

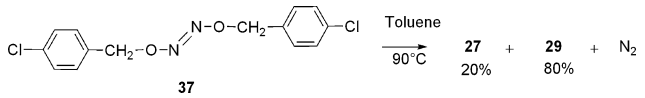
Qualitatively the two possible esters from the decomposition, methyl benzoate **17a** at retention time (r.t.) 3.3 min. and 4-chlorobenzyl benzoate **31** at r.t. 6.7 min. are relatively minor products. The major products, present in similar amounts, are 4-chlorobenzaldeyde **27** and *N*-methoxybenzamide **16a** at r.t. 3.5 and 4.4 respectively. This, together with the fact that *N*-(4-chlorobenzyloxy)benzamide **32** is also a very minor product, indicates that the major decomposition pathway is homolysis of the bond between nitrogen and the 4-chlorobenzyloxyl group giving *N*-methoxybenzamidyl radical **35** and 4-chlorobenzyloxyl radical **36** (Scheme 8). It also supports hydrogen transfer from the 4-chlorobenzyloxyl radical **36** to **35** giving the *N*-methoxybenzamide (**16a**) and 4-chlorobenzaldehyde (**27**) (Scheme 8, path (i)). 4-Chlorobenzyl alcohol **29**, which would be produced by disproportionation or hydrogen abstraction from mesitylene (Scheme 8, pathways (ii) and (iii)) is clearly a minor component since it is present in low yield (at the retention time of 4.1 min). Lending further support to this is the fact that we recently



Scheme 8

showed that 4-chlorobenzyloxyl radicals **36**, generated independently upon thermal decomposition of the hyponitrite, 1,2-bis(4-chlorobenzyloxy)diazene (**37**) in toluene, gave mainly alcohol and only a limited quantity of 4-chlorobenzaldehyde (Scheme 9),[16] which must be generated by an alternative process from **36**.

Several minor solvent-derived oxidation products were detected in the form of mesitaldehyde **33**, 3,5-dimethylbenzyl alcohol **28a**,



Scheme 9

3,5-dimethylbenzyl chloride **28b**, and 1,2-di(3,5-dimethylphenyl) ethane **34**, presumably all derived from hydrogen abstraction from solvent. While the source of alcohol and aldehyde is most likely reaction with molecular oxygen, the origin of **28b** and of benzamide **30** is unknown. A number of minor components could not be identified.

The absence of 4-chlorobenzyl nitrate **24**, 4-chlorobenzonitrile **25** or 4-chlorobenzaldoxime **26**, whose ions were not present anywhere in the chromatogram, suggests that the HERON rearrangement of methoxyl that would lead to methyl benzoate (**17a**) and 4-chlorobenzyloxynitrene (**23**) is not a significant pathway. The reverse HERON reaction that would lead to 4-chlorobenzyl benzoate and methoxynitrene cannot be excluded on this evidence but formation of the esters by dimerisation of alkoxyamidyls and double HERON decomposition suggests this as the most likely route to esters **17a** and **31**, and the most likely route for formation of **17** from **2**.

Table 2 indicates a clear trend in the yields of hydroxamic ester **16** and ester **17**, which are related; low yields of methyl ester correlate with high yields of hydroxamic ester and *vice versa*. This is consistent with both products being formed from methoxybenzamidyl radicals. The yields suggest that, relative to hydrogen and chlorine, *para*-methyl and *para*-methoxyl groups disfavour hydrogen transfer leading to a greater degree of dimerisation. A similar electronic effect has recently been reported in the competition between intramolecular 1,5-*exo* cyclisation and dimerisation of alkoxyamidyl **39** generated by oxidation of the hydroxamic ester **38** with *o*-iodoxybenzoic acid (IBX) (Scheme 10). Whereas the acetamide **38a** typically gave an 83% conversion to isoxazolidine **40a** and ester **41a** (through the hydrazine) in the ratio 70 : 30, the *p*-methoxybenzamide **38b** afforded only a trace of cyclic material, the major product being the ester **41b** (40%). A 4-methoxyphenacyl group would further raise the energy of the SOMO and disfavour hydrogen transfer in our reactions and the 5-*exo*-cyclisation of **39b**.**

Table 3 Arrhenius parameters and rate constants at 373 K for thermal decomposition of *N*,*N*-dimethoxybenzamides (**2a–d**)

Amide	ln A	E_A/kJmol^{-1}	$\Delta S^{\ddagger}$/J K^{-1}mol^{-1}	$10^6 k^{373}$/dm^{3}mol^{-1}s^{-1}
2a	27.68	125.3 ± 1.7	–23.3 ± 4.1	2.96
2b	28.404	126.5 ± 7.6	–17.1 ± 18.6	4.24
2c	29.632	132.5 ± 1.5	–6.9 ± 3.6	2.12
2d	30.310	134.4 ± 6.0	–1.2 ± 14.6	2.24

Table 4 Rate constants for the thermal decomposition of *N*,*N*-dialkoxyamides **2a–d** in mesitylene

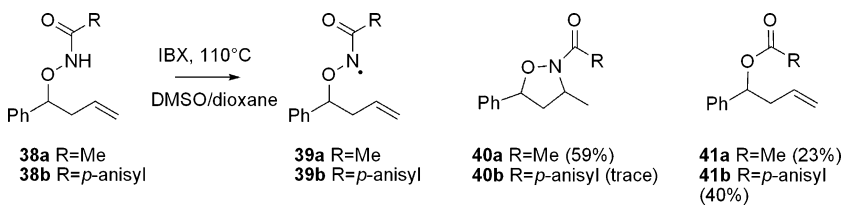
2a		**2b**		**2c**		**2d**	
T/K	10^5 k/s^{-1}	T/K	10^5 k/s^{-1}	T/K	10^5 k/s^{-1}	T/K	10^5 k/s^{-1}
391	1.95 ± 0.03	388	2.22 ± 0.07	401	4.18 ± 0.18	399	3.79 ± 0.19
401	4.74 ± 0.06	398	4.59 ± 0.06	412.5	12.4 ± 0.99	404	6.11 ± 0.16
409	10.25 ± 0.4	408	13.76 ± 0.31	417	19.8 ± 0.53	407	8.71 ± 0.29
419	25.57 ± 0.37	417	38.54 ± 0.44	424	35.9 ± 0.61	413	13.62 ± 0.16
426	46.71 ± 3.1	429	78.90 ± 2.20	427	46.6 ± 0.72	418	24.99 ± 0.27

The thermal decomposition of **2a–d** in mesitylene was monitored by HPLC and shown to be a first order process. From rate studies at different temperatures Arrhenius activation parameters were obtained (Table 3).

Rates of decomposition at 373 K are similar, although formation of methoxybenzamidyls from **2c** and **2d** would appear to have looser transition states requiring higher activation energies than those for decomposition of **2a** and **2b**.

Interestingly, considering that the major decomposition pathway is a homolytic process the $\Delta S^{\ddagger}$ are slightly negative. Thermal decomposition of diacyl peroxides and dialkyl peroxides require a similar E_A to those found for *N*,*N*-dialkoxyamides but their $\Delta S^{\ddagger}$ are appreciably more positive (typically around +40 JK^{-1}mol^{-1}).[56] We attribute this in part to conjugation in alkoxyamidyl radicals. ESR hyperfine coupling constants, A_N, for alkoxyamidyls are

** B3LYP/6-31G(d) SOMO energies of benzamidyls **20a–d** are computed to be –6.78, –6.66, –6.58 and –6.2 eV respectively.



Scheme 10

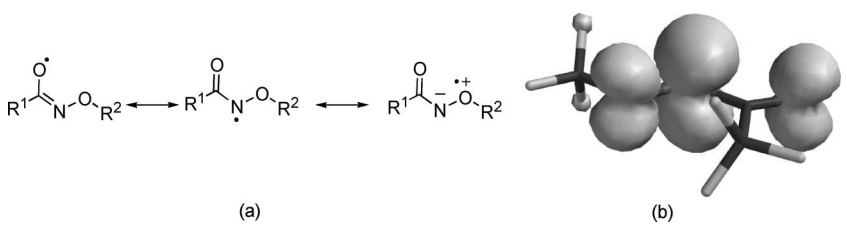


Fig. 2 (a) Resonance-stabilisation in *N*-alkoxyamidyl radicals; (b) spin density in *N*-methoxyacetamidyl radical calculated at B3LYP/6-31G(d) level of theory.

Table 5 GC-MS Retention times and fragmentation patterns for products from decomposition of *N*-(4-chlorobenzyloxy)-*N*-methoxybenzamide (**3e**) in mesitylene at 155 °C

Product	Retention time/min	Parent and fragment ions
Methyl benzoate **17a**	3.3	136 ($M^{+\bullet}$, 40%), 105 (100, M-(OCH_3), 77 (32), 51 (20).
4-Chlorobenzaldehyde **27**	3.5	140 and 142 ($M^{+\bullet}$, 100 and 38%), 139 (92, M-H), 111 (53, M-CHO), 75 (30, M-[CHO, HCl]).
3,5-Dimethylbenzaldehyde **33**	3.7	134 ($M^{+\bullet}$, 100%), 133 (75, M-H), 105 (48, M-CHO), 91 (17, M-[CHO, CH_2]), 77 (16).
3,5-Dimethylbenzyl chloride **28b**	3.9	154 and 156 ($M^{+\bullet}$, 30 and 10%), 119 (100, M-Cl), 91 (15, M-[Cl, 2 × CH_2]), 77 (8).
3,5-Dimethylbenzyl alcohol **28a**	4.0	136 ($M^{+\bullet}$, 100%), 121 (58, M-CH_3), 107 (33, M-[CH_3,CH_2]), 105 (25, M-CH_3O), 93 (54, M-C_3H_7), 91 (60, M-[CH_3O,CH_2]), 77 (23).
4-Chlorobenzyl alcohol **29**	4.1	142 and 144 ($M^{+\bullet}$, 70 and 23%), 141(10, M-H), 125 (12, M-OH), 107 (100, M-Cl), 89 (15, C_7H_6), 79 (86, C_6H_7), 77 (80, C_6H_5).
N-Methoxybenzamide **16a**.	4.4	151 ($M^{+\bullet}$, 100%), 105 (99, M-NHOMe), 91 (24, C_7H_6), 77 (98, C_6H_5), 51 (85).
Benzamide **30**	4.5	121, ($M^{+\bullet}$,100%), 105 (95, M-NH_2), 77 (70, C_6H_5), 51 (30).
4-Chlorobenzyl benzoate **31**	6.7	246 and 248($M^{+\bullet}$, 46 and 16%), 125 (95, M-$PhCO_2$), 105 (100, M-$OCH_2C_6H_4Cl$), 89 (30, M-[$PhCO_2$, HCl]), 77 (58, C_6H_5), 51.
1,2-Di(3,5-dimethylphenyl)ethane **34**	7.4	238, ($M^{+\bullet}$, 25%), 119 (12, M-C_9H_{11}), 105 (100, $C_8H_9^+$), 91 (8), 77 (24).
N-(4-Chlorobenzyloxy)benzamide **32**	8.2	261 and 263($M^{+\bullet}$, 9% and 3%), 125 and 127(100 and 33, M-PhCONO), 89 (8, M-[PhCONO, HCl]).

1.04 mT[35,37–39] as opposed to about 1.48 mT for amidyls,[34,57,58] and alkoxyamidyls are not only resonance-stabilised by the carbonyl, they are strongly delocalised onto the alkoxyl oxygen (Fig. 2a), a main source of their stabilisation and the reduced A_N value. Fig. 2b shows the spin density distribution in *N*-methoxyacetamidyl radical calculated at B3LYP/6-31G(d). The resonance forms in Fig. 2a and spin density distribution in Fig. 2b indicate that stabilisation of alkoxyamidyls involves pi overlap between nitrogen, the carbonyl and alkoxyl oxygen p-orbitals, which would be expected to result in some restricted rotation about both the *N–C* and *N–O* bonds and impose additional constraints in the transition state for homolysis.

Conclusion

N,*N*-Dialkoxyamides can be synthesised directly from hydroxamic esters using phenyliodine(III)bis(trifluoroacetate). Their IR and ^{1}H NMR spectroscopic properties are similar to those of other anomeric amides and are further evidence of diminished amide resonance when two electronegative atoms are present on nitrogen. Thermal decomposition of *N*,*N*-dialkoxyamides proceeds by homolysis of a nitrogen—oxygen bond generating alkoxyl and alkoxyamidyl free radicals. No evidence could be found for a HERON rearrangement process; esters, which are a significant product, are more than likely formed from dimerisation of alkoxyamidyl radicals to hydrazines that are known to produce esters by HERON rearrangements. The decompositions follow unimolecular kinetics and E_A's are in a similar range to those of other alkoxyl radical sources.

Apart from this study, the chemistry of *N*,*N*-dialkoxyamides is virtually unexplored. The new synthetic procedure outlined in this paper should make possible further investigation of this unusual class of anomeric amides. We will shortly present the first X-ray structures of two members of this class and studies of their properties as free radical initiators as well as their solvolytic behaviour at various pH's are underway in our laboratories.

Experimental

Materials and methods

Infrared spectra were recorded on a Perkin–Elmer1600 series fourier-transform (FT)-IR spectrophotometer as solutions in chloroform. Mass spectra were recorded on a Varian 1200L Quadrupole mass spectrometer coupled to a Varian CP-3800 gas chromatograph; the column used was a FactorFour Capillary Column, VF-5ms, 30m x 0.25mm, 0.25μm. Samples were injected into the column at 100 °C which was held for 2 min. before increasing by 40 °C per minute until the maximum temperature of 250 °C, which was maintained until the end of each run. The injector was 523 K and the sample was subjected to a capillary voltage of 70 eV. TOF ESI accurate mass determinations were obtained from the Mass Spectral Unit of the Australian National University. Nuclear magnetic resonance spectra were recorded in $CDCl_3$ on a Bruker Avance 300P FT NMR spectrometer with a 5-mm 1H inverse/BroadBand probe with a z-gradient, operating at 300.13 MHz (^{1}H), 75.46 MHz (^{13}C). Kinetic runs and yield analysis were performed on a Millipore-Waters system HPLC using an automatic gradient controller, Waters 501 and 510 pumps and a U6K injector. A C18 reverse phase radial-pak column was eluted with acetonitrile/water mixtures and the detector used was a 481 lambda-max LC spectrophotometer (set at 254 nm) linked to a 740 data module.

Synthesis of *N*-alkoxybenzamides

Hydroxamic esters *N*-methoxy-4-methylbenzamide,[11] *N*-ethoxy-4-nitrobenzamide,[12] *N*-butoxybenzamide, *N*-butoxy-4-chlorobenzamide, *N*-butoxy-4-bromobenzamide, *N*-butoxy-4-nitrobenzamide,[2] *N*-(4-chlorobenzyloxy)benzamide and *N*-(4-nitrobenzyloxy)benzamide[2] have been reported previously.

General synthesis of *N*-methoxybenzamides[59]

Potassium benzohydroxamates[60] were stirred overnight with MeI (1.8 equivalents) and Na_2CO_3 (1.2 equivalents) in 50% aqueous methanol (240 cm^3). The mixtures were refluxed for 2 h and the methanol removed under reduced pressure. The resulting aqueous mixture was acidified with dilute HCl and extracted with dichloromethane, which was dried over anhydrous Na_2CO_3 and concentrated under reduced pressure. The crude product was purified by crystallisation or chromatography.

N-Methoxybenzamide

Potassium benzohydroxamate (8.06 g, 0.50 mmol) was reacted with MeI (12.57 g, 0.09 mmol) and Na_2CO_3 (7.59 g, 0.058 mol). Work-up afforded an oil which was purified by flash chromatography. *N*-Methoxybenzamide (3.58 g, 47%) was a low-melting solid, mp 60 °C (from benzene) (lit.,[59] 63.5–64.5 °C); ν_{max} ($CHCl_3$)/cm^{-1} 1683 (C═O)); δ_H(300 MHz; $CDCl_3$) 3.81 (3 H, s, NH-OCH3), 7.38 (2 H, t, *m*-Ar-H), 7.48 (1 H, t, *p*-Ar-H), 7.75 (2 H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 64.24 (q, NHOCH3), 127.10 (2 × d, *m*-Ar), 128.50 (2 × d, *o*-Ar), 131.73 (s, *i*-Ar) 131.91 (d, *p*-Ar), 166.39 (s, *C*═O).

N-Methoxy-4-methoxybenzamide

Potassium *p*-methoxybenzohydroxamate (10.26 g, 0.05 mol) was reacted with MeI (12.57 g, 0.09 mol) and Na_2CO_3 (7.59 g, 0.058 mol). The title compound was obtained as an almost pure solid (3.34 g, 37%). Recrystallisation gave pure *N*-methoxy-4-methoxybenzamide, mp 101 °C(from ethyl acetate/cyclohexane) (lit.,[61] 100–102.5 °C); ν_{max}($CHCl_3$)/cm^{-1} 1687 (C═O); δ_H(300 MHz; $CDCl_3$) 3.801 (3H, s, NH-OCH3), 3.804 (3H, s, Ar-OCH3) 6.84 (2H, d, *m*-Ar-H), 7.75 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 55.24 (q, Ar-OCH3) 64.09 (q, NHOCH3), 113.64 (2 × d, *m*-Ar), 123.89 (s, *i*-Ar), 128.97 (2 × d, *o*-Ar), 162.40 (s, *p*-Ar), 166.09 (s, C═O).

N-Methoxy-4-chlorobenzamide

Potassium *p*-chlorobenzohydroxamate (9.28 g, 0.05 mol) was reacted with MeI (12.57 g, 0.09 mol) and Na_2CO_3 (7.59 g, 0.058 mol). The solid obtained after extraction into dichloromethane was almost pure. Recrystallisation gave pure *N*-methoxy-4-chlorobenzamide (4.28 g, 46%), mp 105 °C(from ethyl acetate-cyclohexane) (lit.,[61] 106–108 °C); ν_{max}($CHCl_3$)/cm^{-1} 1687 (C═O); δ_H(300 MHz; $CDCl_3$) 3.85 (3H, s, NH-OCH3), 7.36 (2H, d, *m*-Ar-H), 7.67 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 64.22 (q, NHOCH3), 128.55 (2 × d, *m*-Ar), 128.80 (2 × d, *o*-Ar), 129.95 (s, *i*-Ar), 138.22 (s, *p*-Ar), 173.02 (s, C═O).

Synthesis of *N*,*N*-dialkoxyamides

***N*,*N*-Dimethoxybenzamide 2a.** *N*-Methoxybenzamide (0.645 g, 4.27 mmol) was dissolved in methanol (10 cm^3). PIFA (2.754 g, 6.4 mmol) was added and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.504 g, 65%) as a yellow oil. νmax($CHCl_3$)/cm^{-1} 1711; δ_H(300 MHz; $CDCl_3$) 3.81 (6H, s, N(OCH3)2), 7.43 (2H, t, *m*-Ar-H), 7.53 (1H, t, *p*-Ar-H), 7.79 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 60.48 (2 × q), 128.2 (2 × d), 129.2 (2 × d), 132.4 (s) 132.6 (d), 174.3 (s). *m*/*z* (ESI) 204.0637 ([M+ Na^+]. $C_9H_{11}NO_3Na$ requires 204.0637).

***N*,*N*-Dimethoxy-4-chlorobenzamide 2b.** *N*-Methoxy-4-chlorobenzamide (0.2695 g, 1.45 mmol) was dissolved in methanol (10 cm^3). PIFA (0.935 g, 2.18 mmol) was added and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.157 g, 50%) as a yellow oil. ν_{max}($CHCl_3$)/cm^{-1} 1712; δ_H(300 MHz; $CDCl_3$) 3.79 (6H, s, N(OCH3)2), 7.39 (2H, d, *m*-Ar-H), 7.73 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 60.49 (2 × q), 128.5 (2 × d), 130.6 (2 × d), 130.7 (s) 138.9 (s), 173.2 (s). *m*/*z* (ESI) 216.0426 and 218.0395 ([M+ H^+]. $C_9H_{11}NO_3{}^{35}Cl$ requires 216.0427 and $C_9H_{11}NO_3{}^{37}Cl$ requires 216.0398).

***N*,*N*-Dimethoxy-4-methylbenzamide 2c.** *N*-Methoxy-4-methylbenzamide (0.275 g, 1.67 mmol) was dissolved in methanol (10 cm^3). PIFA (1.08 g, 2.51 mmol) was added and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.17 g, 43%) as a yellow oil. ν_{max}($CHCl_3$)/cm^{-1} 1710; δ_H(300 MHz; $CDCl_3$) 2.40 (3H, s, Ar-CH3), 3.80 (6H, s, N(OCH3)2, 7.22 (2H, d, *m*-Ar-H), 7.70 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 21.61 (q) 60.29 (2 × q), 128.9 (2 × d), 129.4 (2 × d), 137.5 (s), 143.3 (s), 174.3 (s). *m*/*z* (ESI) 196.0970 ([M+ H^+]. $C_{10}H_{14}NO_3$ requires 196.0974).

***N*,*N*-Dimethoxy-4-methoxybenzamide 2d.** *N*-Methoxy-4-methoxybenzamide (0.329 g, 1.82 mmol) was dissolved in methanol (10 cm^3). PIFA (1.17 g, 2.73 mmol) was added and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.184 g, 0.87 mmol, 48%) as a yellow oil. ν_{max}($CHCl_3$)/cm^{-1} 1705; δ_H(300 MHz; $CDCl_3$) 3.79 (6H, s, N(OCH3)2), 3.85 (3H, s, Ar-OCH3), 6.91 (2H, d, *m*-Ar-H), 7.82 (2H, d, *o*-Ar-H); δ_C(75 MHz; $CDCl_3$) 55.46 (q) 60.13 (2 × q), 113.5 (2 × d), 124.2 (s), 131.7 (2 × d), 163.2 (s), 173.8 (s). *m*/*z* (ESI) 212.0923 ([M+H^+]. $C_{10}H_{14}NO_4$ requires 212.0239).

***N*-Ethoxy-*N*-methoxy-4-nitrobenzamide 3a.** *N*-Ethoxy-4-nitrobenzamide (0.216 g, 1.00 mmol) was dissolved in methanol (10 cm^3). PIFA (0.64 g, 1.50 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$ (aq), extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.139 g, 58%) as a pale yellow solid, which crystallised as prisms mp 45–47 °C (from ethyl acetate/hexane by solvent displacement); ν_{max}($CHCl_3$)/cm^{-1} 1708.2; δ_H(300 MHz; $CDCl_3$) 1.25 (3H, t), 3.79 (3H, s), 4.12 (2H,q), 7.93 (2H, d), 8.27 (2H,d); δ_C(75 MHz; $CDCl_3$) 13.52 (q), 60.57 (q), 69.95 (t), 123.30 (2 × d), 130.06 (2 × d), 138.36 (s), 149.83 (s), 173.83 (s); *m*/*z* (ESI) 263.0644 [M+Na^+]. $C_{10}H_{12}N_2O_5Na$ requires 263.0644)

***N*-Butoxy-*N*-methoxy-4-chlorobenzamide 3b.** *N*-Butoxy-4-chlorobenzamide (0.192 g, 0.842 mmol) was dissolved in methanol (10 cm^3). PIFA (0.54 g, 1.26 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$ (aq), extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.085 g, 44%) as a pale yellow oil. ν_{max}($CHCl_3$)/cm^{-1} 1713.0; δ_H(300 MHz; $CDCl_3$) 0.89 (3H, t),

1.37 (2H, sx), 1.61 (2H, qn), 3.77 (3H, s), 4.01 (2H,t), 7.40 (2H, d), 7.76 (2H,d); δ_C(75 MHz; $CDCl_3$) 13.67 (q), 19.08 (t), 30.16 (t), 60.12 (q), 73.33 (t), 128.39 (2 × d), 130.67 (2 × d), 130.94 (s), 138.36 (s), 173.83 (s); *m/z* (ESI) 258.0895 and 260.0869 ([M+H$^+$]. $C_{12}H_{17}NO_6{}^{35}Cl$ requires 258.0897 and $C_{12}H_{17}NO_6{}^{37}Cl$ requires 260.0867).

***N*-Butoxy-*N*-methoxy-4-bromobenzamide 3c.** *N*-Butoxy-4-bromobenzamide (0.207 g, 0.761 mmol) was dissolved in methanol (10 cm^3). PIFA (0.491 g, 1.14 mmol) was added and the mixture stirred for 5 min. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound as a yellow oil (0.113 g, 49%). $\nu_{max}(CHCl_3)$/cm^{-1} 1702.1;δ_H(300 MHz; $CDCl_3$) 0.89 (3H, t), 1.34 (2H, sx), 1.61 (2H, qn), 3.77 (3H, s), 4.01 (2H, t), 7.57 (2H, d), 7.68 (2H,d); δ_C(75 MHz; $CDCl_3$) 13.69 (q), 19.10 (t), 30.17 (t), 60.17 (q), 73.39 (t), 127.22 (s), 130.79 (2 × d), 131.29 (2 × d), 131.40 (s), 173.11 (s), one signal obscured; *m/z* (ESI) 324.0211 and 326.0191 ([M+Na$^+$]. $C_{12}H_{16}NO_3{}^{79}BrNa$ requires 324.0211 and $C_{12}H_{16}NO_3{}^{81}BrNa$ requires 326.0191).

***N*-Butoxy-*N*-methoxy-4-nitrobenzamide 3d.** *N*-Butoxy-4-nitrobenzamide (0.160 g, 0.670 mmol) was dissolved in 10 cm^3 of methanol. PIFA (0.430 g, 1.00 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with saturated $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane afforded the title compound as a pale yellow oil. Yield: 30%; $\nu_{max}(CHCl_3)$/cm^{-1} 1716.7 (C═O); δ_H(300 MHz; $CDCl_3$) 0.86 (3H, t) 1.33 (2H, sx) 1.61 (2H, p) 3.80 (3H, s) 4.02 (2H, t) 7.93 (2H, d) 8.26 (2H, d); δ_C(75 MHz; $CDCl_3$) 13.64 (q) 19.05 (t), 30.09 (t), 60.60 (q), 73.90 (t), 123.25 (2 × d), 123.50 (s),130.04 (2 × d), 130.68 (s), 149.80 (s), 171.75 (s); *m/z* (ESI) 291.0956 ([M+Na$^+$]. $C_{12}H_{16}N_2O_5Na$ requires 291.0957).

***N*-(4-Chlorobenzyloxy)-*N*-methoxybenzamide 3e.** *N*-4-Chlorobenzyloxybenzamide (0.20 g, 0.76 mmol) was dissolved in methanol (10 cm^3). PIFA (0.493 g, 1.15 mmol) was added and the mixture was stirred for 1 h. The solution was quenched with 10% $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.123 g, 55%) as a yellow oil. $\nu_{max}(CHCl_3)$/cm^{-1} 1702.1; δ_H(300 MHz; $CDCl_3$) 3.77 (3H, s), 4.96 (2H, s), 7.27 (4H, q), 7.41 (2H, t), 7.52 (1H, t), 7.76 (2H, d); δ_C(75 MHz; $CDCl_3$) 60.3 (q), 74.3 (t), 128.2 (2 × d), 128.7 (s), 129.2 (2 × d), 130.5 (2 × d), 132.4 (s), 132.5 (d), 133.6, 134.6, 174.2 (s). *m/z* (ESI) 314.0560 and 316.0530 ([M + Na$^+$]. $C_{15}H_{14}NO_3{}^{35}ClNa$ requires 314.0560 and $C_{15}H_{14}NO_3{}^{37}ClNa$ requires 316.0530).

***N*-Methoxy-*N*-(4-nitrobenzyloxy)benzamide 3f.** *N*-(4-Nitrobenzyloxy)benzamide (0.114 g, 0.419 mmol) was dissolved in methanol (10 cm^3). PIFA (0.270 g, 0.629 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with 10% $NaHCO_3$ (aq), extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Centrifugal chromatography in 10% ethyl acetate/hexane and concentration *in vacuo* gave the title compound (0.073 g, 58%) as a pale yellow oil. $\nu_{max}(CHCl_3)$/cm^{-1} 1709.4; δ_H(300 MHz; $CDCl_3$) 3.77 (3H, s), 5.11 (2H, s), 7.41–7.54 (5H, m), 7.78 (2H,d), 8.19 (2H,d); δ_C(75 MHz; $CDCl_3$) 60.38 (q), 73.79 (t), 123.65 (2 × d), 128.28 (2 × d), 129.26 (4 × d), 132.04 (s), 132.80 (d), 142.60 (s), 147.93 (s), 174.33 (s) one signal obscured; *m/z* (ESI) 303.0981 ([M+H$^+$]. $C_{15}H_{15}N_2O_5$ requires 303.0981).

***N*,*N*-Diethoxy-4-nitrobenzamide 4a.** *N*-Ethoxy-4-nitrobenzamide (0.152 g, 0.722 mmol) was dissolved in 10 cm^3 of methanol. PIFA (0.53 g, 1.23 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with saturated $NaHCO_3$, extracted with dichloromethane which was washed with brine, and dried over anhydrous $MgSO_4$ and concentrated to give an oil. Centrifugal chromatography in 10% ethyl acetate/hexane afforded the title compound as a pale yellow oil. Yield: 62%; $\nu_{max}(CHCl_3)$/cm^{-1} 1704.2 (C═O); δ_H(300 MHz; $CDCl_3$) 1.24 (6H, t) 4.11 (4H, q) 7.94 (2H, d) 8.28 (2H, d); δ_C(75 MHz; $CDCl_3$) 13.49 (2 × q), 69.63 (2 × t), 123.19 (2 × d), 130.01 (2 × d), 138.55 (s), 149.67 (s), 171.58 (s); *m/z* (ESI) 277.0800 ([M+Na$^+$]. $C_{11}H_{14}N_2O_5Na$ requires 277.0800).

***N*,*N*-Dibutoxybenzamide 4b.** *N*-Butoxybenzamide (0.380 g, 1.97 mmol) was dissolved in 5.0 cm^3 of 1-butanol. PIFA (1.27 g, 2.95 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with saturated $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Removal of solvent afforded the title compound as a pure yellow oil. Yield: 96%. $\nu_{max}(CHCl_3)$/cm^{-1} 1703.1 (C═O); δ_H(300 MHz; $CDCl_3$) 0.87 (3H, t) 1.35 (4H, sx) 1.56 (4H, p) 4.01 (4H, t) 7.40 (2H, t) 7.48 (1H, t) 7.77 (2H, d); δ_C(75 MHz; $CDCl_3$) 13.7 (2 × q), 19.1 (2 × t), 30.2 (2 × t) 73.0 (2 × t), 127.9 (2 × d), 129.2(2 × d), 132.1(d) 132.7 (s) 174.0 (s); *m/z* (ESI) 288.1575 ([M+Na$^+$]. $C_{15}H_{23}NO_3Na$ requires 288.1576).

***N*-Benzyloxy-*N*-butoxybenzamide 4c.** *N*-Butoxybenzamide (0.107 g, 0.554 mmol) and benzyl alcohol (0.141 g, 1.30 mmol) were dissolved in 5.0 cm^3 of acetonitrile. PIFA (0.36 g, 0.837 mmol) was added in one portion and the mixture was stirred for 5 min. The solution was quenched with saturated $NaHCO_3$, extracted with dichloromethane, washed with brine, and dried over anhydrous $MgSO_4$. Purification by centrifugal chromatography with 10% ethyl acetate/hexane afforded the title compound as a yellow oil. Yield: 29%. $\nu_{max}(CHCl_3)$/cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.88 (3H, t) 1.33 (2H, sx) 1.60 (2H, p) 4.02 (2H, t) 4.98 (2H, s) 7.25–7.31 (5H, m) 7.42 (2H, t) 7.51 (1H, t) 7.77 (2H, d); δ_C(75 MHz; $CDCl_3$) 13.7 (q), 19.1 (t), 30.1 (t), 73.2 (t), 75.0 (t), 128.0 (2 × d), 128.4 (2 × d), 128.6 (d), 129.2 (4 × d), 132.2 (d), 132.7 (s), 135.1 (s), 174.1 (s); *m/z* (ESI) 322.1419 ([M+Na$^+$]. $C_{18}H_{21}NO_3Na$ requires 322.1419).

Decomposition of *N*,*N*-dimethoxybenzamides 2a–d. *N*,*N*-Dimethoxybenzamide (0.1 g) and diphenyl (0.02 g) (internal standard) were placed in a 10 cm^3 two-neck pear-shaped flask. Mesitylene (5 cm^3), pre-heated to the appropriate temperature, was added and the flask submerged in a constant temperature oil bath. The reaction was carried out under an atmosphere of N2. The mixture was allowed to heat to constant temperature and aliquot's were taken at regular intervals. The consumption of *N*,*N*-dimethoxybenzamide was monitored by *hplc* using the peak ratio of dimethoxybenzamide to diphenyl. Rate constants at different temperatures are presented in Table 4.

Product analysis

The products of decomposition of *N*,*N*-dimethoxybenzamide **2a**, *N*,*N*-dimethoxy-4-chlorobenzamide and *N*,*N*-dimethoxy-4-methoxybenzamide **2d** were separated by centrifugal chromatography with the aim of characterising adducts **18a**, **18b** and **18d**. The formation of **18c** from *N*,*N*-dimethoxy-4-methylbenzamide **2c** has been described previously.[11]

N-(3,5-Dimethylbenzyl)-*N*-methoxybenzamide **18a**; ν_{max}(CH-Cl_3)/cm^{-1} 1646 cm –1 (C═O); δ_H(300 MHz; $CDCl_3$) 2.32 (6H, s, ArCH3), 3.48 (3H, s, OCH3), 4.85 2H, s, CH2), 6.94 (1H, s, *p*′-Ar), 7.00 (2H, s, *o*′-Ar), 7.69 (2H, d *o*-Ar) 7.39, 7.41 (3H, *m*, *p*-Ar); δ_C(75 MHz; $CDCl_3$) 21.26 (q, Ar-CH3), 50.00 (t, CH2), 61.87 (q, NOCH3), 125.95 (2 × d, *o*′-Ar), 129.39 (d, *p*′-Ar) 136.09 (s, *i*′-Ar), 138.16 (s, *m*′-Ar), 127.99 and 128.16 (2 × d, *o*,*m*-Ar), 130.57 (d, *p*-Ar), 134.15 (s, *i*-Ar), 169.64 (s, C═O).

N-(3,5-Dimethylbenzyl)-*N*-methoxy-4-chlorobenzamide **18b**; ν_{max}($CHCl_3$)/cm^{-1} 1639.4 cm –1 (C═O); δ_H(300 MHz; $CDCl_3$) 2.31 (6H, s, $ArCH_3$), 3.45 (3H, s, OCH_3), 4.84 (2H, s, CH_2), 6.94 (1H, s, *p*′-Ar), 6.98 (2H, s, *o*′-Ar), 7.37 (2H, d, *m*-Ar), 7.68 (2H, d, *o*-Ar); δ_C(75 MHz; $CDCl_3$) 21.31 (q, Ar-CH3), 49.94 (t, CH2), 62.01(q, NOCH3), 126.06 (2 × d, *o*′-Ar), 128.30 (d, *o*-Ar), 129.54 (d, *p*′-Ar), 129.95 (d, *m*-Ar), 132.02 (s, *i*-Ar), 135.95 (s, *i*′-Ar), 136.82 (s, *p*-Ar), 138.29 (s, *m*′-Ar), 168.38 (s, C═O); *m*/*z* (ESI) 326.0925 ([M+Na^+]. $C_{17}H_{18}NO_2{}^{23}Na^{35}Cl$ requires 326.0924) .

N - (3,5 - Dimethylbenzyl) - *N* - methoxy - 4 - methoxybenzamide **18d**; ν_{max}($CHCl_3$)/cm^{-1} 1634 (C═O); δ_H(300 MHz; $CDCl_3$) 2.31 (6H, s, Ar-CH3), 3.49 (3H, s, NOCH3), 3.83 (3H, s, Ar-OCH3), 4.85 (2H, s, CH2), 6.89 (2H, d, *m*-Ar), 6.93 (1H, s, *p*′-Ar), 7.00 (2H, s, *o*′-Ar), 7.77 (2H, d, *o*-Ar); δ_C(75 MHz; $CDCl_3$) 21.21 (q, Ar-CH3), 50.195 (t, CH2), 55.22 (q, Ar-OCH3), 61.67 (q, N-OCH3), 113.21 (d, *m*-Ar), 125.89 (2 × d, *o*′-Ar), 129.28 (d, *p*′-Ar), 130.56 (d, *o*-Ar), 136.26 (s, *m*′-Ar), 138.07 (s, *i*′-Ar), 161.51 (s, *p*-Ar), 168.96 (s, C═O), one overlapping signal (s, *i*-Ar).

Yield Analysis of *N*,*N*-dimethoxybenzamides

N,*N*-Dimethoxybenzamide (0.025 g) was decomposed in mesitylene at 155 °C under the same conditions as those used for the kinetic analysis. Decompositions were complete between 1.5 to 2 h. External standards for each of the corresponding *N*-methoxybenzamide (**16**), methyl benzoate (**17**) and *N*-(3,5-dimethylbenzyl)-*N*-methoxybenzamide (**18**) to be analysed were prepared. The reaction mixture was made up to 10 cm^3 in a volumetric flask and analysed by *hplc*.

Decomposition of *N*-(4-Chlorobenzyloxy)-*N*-methoxybenzamide 3e

N-(4-Chlorobenzyloxy)-*N*-methoxybenzamide (0.025 g, 0.086 mmol) was decomposed in mesitylene at 155 °C under the same conditions as those used for dimethoxybenzamides **2**. After complete consumption of starting material, the product mixture was analysed by GC-MS. Retention times correspond to Fig. 1 and characteristic fragmentations for each major product are presented in Table 5.

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