Reactions of 1-(2-alkoxyphenyl)alkaniminyl radicals

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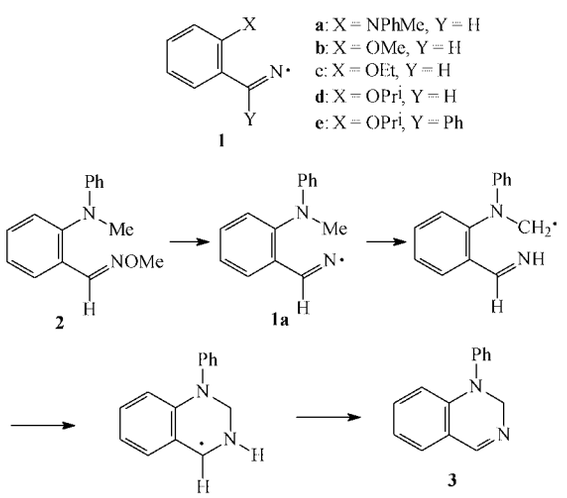
Genereration of the iminyls **1d** and **1e** by standard methods in the gas-phase by flash vacuum pyrolysis (FVP), or in solution, respectively, gives rise to 1,3-benzoxazines **18** and **22** by a mechanism which probably involves a 1,6-hydrogen atom translocation. Under FVP conditions, 2-cyanophenol **14** is a major product from 2-alkoxyphenylalkaniminyls **1b–d**; the dealkylation is an integral part of the reaction mechanism and not a subsequent reaction of 2-alkoxybenzonitriles, which themselves are only very minor products of the pyrolyses.

Introduction

We have previously examined the cyclisation reactions of iminyl radicals **1** bearing *ortho*-phenoxy,[1,2] anilino,[1,3] and thiophenoxy[4,5] substituents, generating the intermediates both in solution-phase[1,4] and in the gas-phase under flash vacuum pyrolysis (FVP) conditions.[2,3,5] In the reactions of the *N*-methylanilino intermediates, products were surprisingly obtained by mechanisms in which the iminyl had clearly interacted with the *N*-alkyl substituent rather than with the aromatic ring.[1,3] For example, gas-phase generation of the iminyl **1a** by FVP of the oxime ether **2** led to the dihydroquinazoline **3** and the mechanism shown in Scheme 1 was proposed to account for

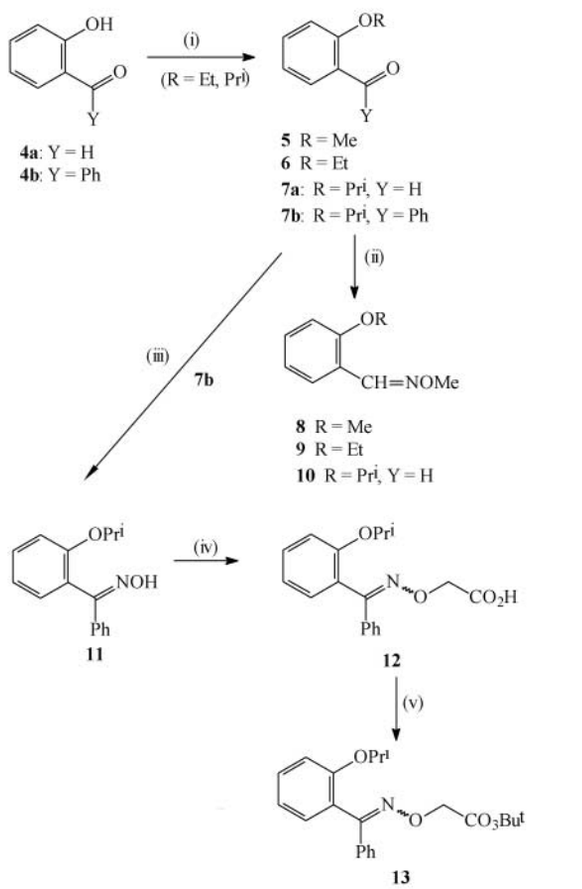


Scheme 1

the transformation.[3] In order to probe the generality of this unexpected behaviour, we have explored the interaction of iminyls **1b–e** with *ortho*-alkoxy substituents and report the results of both our solution-phase and gas-phase studies in this paper.

Results

For the gas-phase work, the oxime ether precursors **8–10** were made in standard fashion[6] by reaction of the appropriate 2-alkoxybenzaldehyde **5**, **6** and **7a** with *O*-methylhydroxylamine. If necessary the alkoxybenzaldehyde was first obtained from salicylaldehyde **4a** by treatment with the appropriate alkyl halide in DMF containing potassium carbonate (see Scheme 2



Scheme 2 *Reagents and conditions*: (i) RBr, K_2CO_3, DMF; (ii) $MeONH_2$·HCl, pyridine, EtOH; (iii) $HONH_2$·HCl, pyridine, EtOH; (iv) $ClCH_2CO_2H$; (v) Bu^tOOH, CDI.

and Experimental section). The solution-phase precursor **13** was made by analogous alkylation of ketone **4b** to the known alkoxy derivative **7b**, followed by reaction with hydroxylamine hydrochloride. Following a standard procedure,[7] the resulting

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oxime **11** was alkylated with chloroacetic acid to give compound **12**, which was finally transformed into perester **13** by reaction with *tert*-butyl hydroperoxide in the presence of 1,1′-carbonyldiimidazole (CDI) (Scheme 2).

FVP of the oxime ether **8** at 650 °C (*ca*. 0.01 Torr) gave a complex pyrolysate, the ^{1}H NMR spectrum of which showed a surprising lack of significant resonances due to methoxy groups. The presence of an aldehyde signal at δ_H 9.89 was shown to be due to salicylaldehyde **4a** (*ca*. 24%) by comparison of the ^{13}C NMR spectrum of the pyrolysate with literature data.[8] Dry-flash chromatography of the mixture gave only one clean product which was identified as 2-cyanophenol **14** (46%) by comparison of its spectrum with that of an authentic sample (see Experimental section). All the major peaks in the aromatic region of the ^{13}C NMR spectrum of the crude pyrolysate are accounted for by products **4a** and **14** (Scheme 3). However, a significant product which gave rise to a CH_2 signal at δ_C 74.04 but which was not associated with any other peaks of comparable intensity, remains unidentified; it may be derived from methoxyl radicals, formed as co-products in the generation of the iminyl.

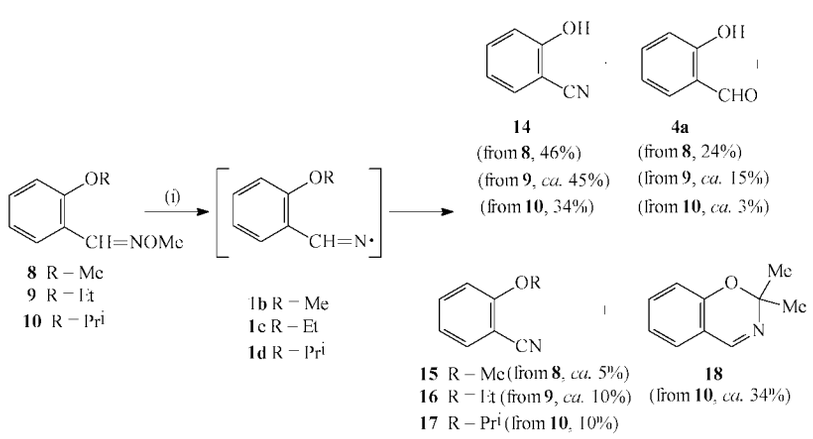
Nitriles are well-known decomposition products of iminyl radicals, but, significantly, only a trace of 2-methoxybenzonitrile **15** (*ca*. 5%) could be detected in the crude pyrolysate from **8**. Methoxy groups are also known to degrade to phenols under FVP conditions, but generally at higher temperatures than we have employed for iminyl generation.[9] Indeed, control pyrolyses of authentic **15** showed little evidence of dealkylation at temperatures up to 750 °C and even at 850 °C *ca*. 30% of the starting material remained. These results demonstrate that the dealkylation process observed in the pyrolysis of **8** which gives rise to 2-cyanophenol **14** is an integral part of the mechanism and not merely a secondary decomposition.

Pyrolysis of the ethoxy compound **9** under the same conditions as those used for the methoxy analogue **8** also gave rise to 2-cyanophenol **14** and salicylaldehyde **4a** in a *ca*. 3 : 1 ratio as the major products (Scheme 3). The assignment was clear from the ^{13}C NMR spectrum of the pyrolysate, by analogy with the previous results (see Experimental section), and no further analysis was carried out. Once again, compounds containing alkyl groups (including the presence of a small amount of 2-ethoxybenzonitrile **16**) accounted for only a small proportion of the products; the unidentified signal (δ_C 73.97) found in the pyrolysis of **8** was again present.

In contrast, the ^{1}H NMR spectrum of the pyrolysate obtained by FVP of the isopropoxy compound **10** at 650 °C was quite different in character. Only a small aldehyde peak was present which was assumed to be due to **4a** (*ca*. 3%) by analogy with the previous results. Instead, significant singlets at δ_H 8.08 and 1.53 (ratio 1 : 6) were observed; this product was apparently unstable in chloroform solution. In addition, it could not be isolated by dry-flash chromatography under our standard conditions, which provided only 2-cyanophenol **14** (34%) and 2-isopropoxybenzonitrile **17** (10%). The latter product has been reported only once in the literature[10] and so an authentic sample was synthesised and its full characterisation is reported in the Experimental section. In particular, the base peak in its electron impact mass spectrum appears at *m*/*z* 119 due to loss of propene from the molecular ion, presumably by a McLafferty-type rearrangement involving the aromatic ring.

GC-MS analysis of the pyrolysate confirmed the presence of **4a** (*m*/*z* 132), **14** (*m*/*z* 119) and **17** (*m*/*z* 161) and revealed one other major peak which had its molecular ion at *m*/*z* 161, corresponding to loss of a hydrogen atom from the iminyl **1d**. This behaviour is reminiscent of the dihydroquinazoline formation (Scheme 1) and a similar mechanism would give rise to the 1,3-benzoxazine **18**. The imine and *C*-dimethyl groups of this structure would conveniently explain the signals at δ_H 8.08 and 1.53 respectively in the NMR spectrum of the crude pyrolysate; in particular, the known[11] 2,2-diaryl derivatives **19**–**21** (in which the 2,2-substituents might be expected to have a deshielding effect on the adjacent imine position) show imine signals in the range δ_H 8.35–8.41. In addition, the base peak of the mass spectrum was formed by a loss of 15 Da (= CH_3) from the molecular ion, which would be expected from a structure such as **18**.

The constitution of the 1,3-benzoxazine **18** was proved, as a 1 : 1 mixture with 2-cyanophenol **14** in the crude pyrolysate, by the following sequence of NMR experiments. These were carried out in [$^2H_6$]acetone solvent, in which seven of the eight aromatic resonances were clearly resolved. Comparison with a spectrum of **14** allowed the identification of the four aromatic protons of **18** as those at δ_H 7.42 (t), 7.33 (d), 7.00 (t) and 6.79 (d) and this assignment was confirmed by a COSY experiment. The imine proton at δ_H 8.08 was related *via* a NOESY experiment to the benzenoid doublet proton at δ_H 7.33, which was itself adjacent to the triplet at δ_H 7.00. Other NOESY correlations allowed the assignments shown in Fig. 1a which were extended into the ^{13}C dimension by a ^{1}H–^{13}C HMQC experiment whose results are shown in Fig. 1b. The ^{13}C NMR spectrum also showed the presence of a quaternary signal at δ_C 92.24 comparable with the data for C2 of the known 1,3-benzoxazines **19**–**21** (δ_C 94.10–94.33).[11] Final confirmation of the structure **18** was derived from an HMBC experiment tailored to show longer-range proton–carbon correlations than those revealed by the HMQC. The key correlations (Fig. 1c) showed that the imine proton at δ_H 8.08 was coupled not only to carbon atoms in the benzene ring, but also, crucially, to the quaternary carbon at δ_C 92.24. This quaternary signal also correlated with the methyl protons at δ_H 1.53. The linking of the substructures shown in Fig. 1c was therefore established. Finally, after this sequence of NMR experiments had been carried out, it was observed that the intensity of the methyl singlet in the ^{1}H NMR spectrum had diminished relative to the



Scheme 3 *Reagents and conditions*: (i) FVP (650 °C, *ca*. 0.01 Torr).

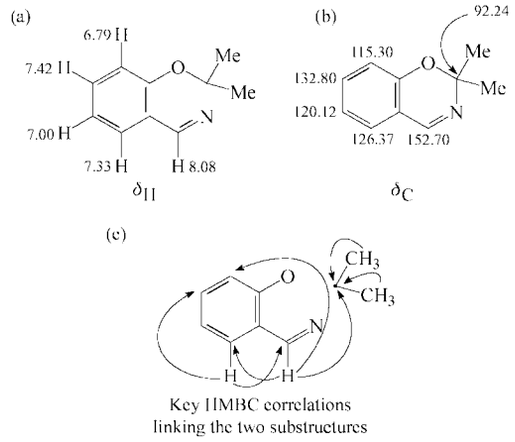
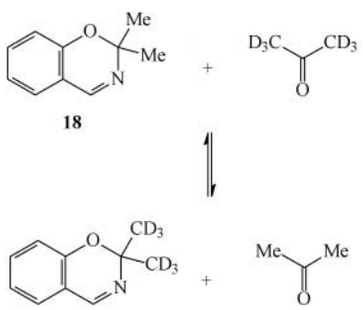
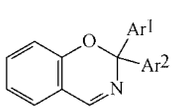


Fig. 1 NMR spectroscopic parameters of the 1,3-benzoxazine **18**.

other resonances and that a new singlet had appeared adjacent to the deuteriated acetone solvent multiplet. This behaviour can be readily explained by exchange with solvent of the ketone sub-unit of the aminal moiety, and the result lends further support to the proposed structure (Scheme 4).



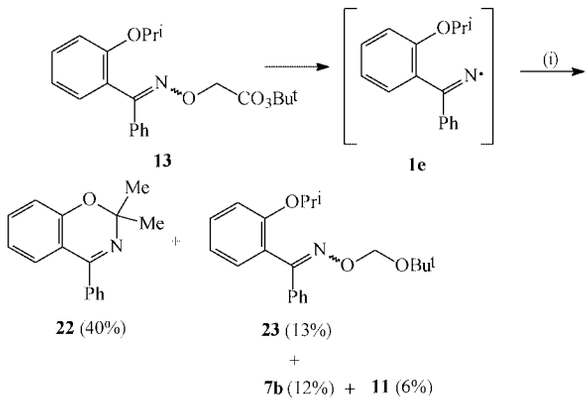
Scheme 4



19 Ar^1 = Ph; Ar^2 = *m*-MeC_6H_4
20 Ar^1 = Ar^2 = *m*-MeC_6H_4
21 Ar^1 = Ar^2 = *p*-MeC_6H_4

In order to probe this heterocyclisation reaction further, the iminyl **1e** was generated in solution, using conditions under which it was hoped that both the degradation to 2-cyanophenol and fragmentation to nitrile **17** should not compete. When perester **13** was decomposed in boiling bromobenzene, a mixture of four products was obtained, consisting of one major component (see below) together with the ketone **7b** (12%), the oxime **11** (6%) and the oxime ether **23** (13%) as minor components (Scheme 5). The structure of compound **23**, expected on the basis of our previous results,[1,4] was clearly confirmed by its ^{1}H NMR spectrum, which showed the characteristic signals of the isopropyl group (a doublet and a septuplet at δ_H 1.05 and 4.41, respectively), the *tert*-butyl group (a singlet at δ_H 1.20), and, above all, the O–CH_2–O moiety (a singlet at δ_H 5.34).

The main reaction product, obtained in an unusually high yield (40%) for this kind of reaction, was the 1,3-benzoxazine **22**. This was by far the main product both before and after chromatographic separation, as proved by GC-MS analysis of the crude reaction mixture. Unlike the 4-unsubstituted analogue **18**, compound **22** was stable during chromatography and also when kept in chloroform solution for many hours. The structure of **22** was established by the similarity of its spectroscopic characteristics with those of **18**. In particular, the

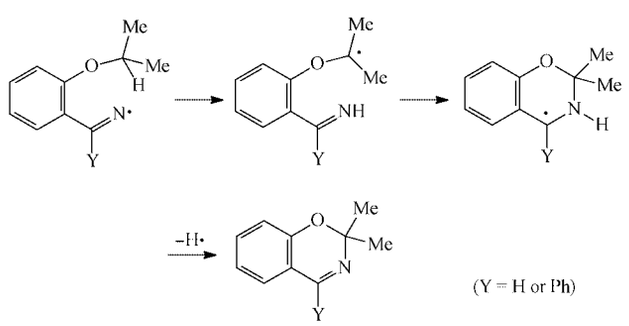


Scheme 5 *Reagents and conditions*: (i) bromobenzene, 156 °C.

^{13}C NMR spectrum of **22** showed aliphatic (δ_C 91.35) and iminic (δ_C 162.36) quaternary signals perfectly compatible with the data reported for **18** and **19**–**21**. Moreover, a signal at δ_H 1.66 is conveniently explained by the *C*-dimethyl group and the base peak of the mass spectrum was formed by a loss of 15 Da from the molecular ion, as found for **18**.

Discussion

For synthetic purposes, the most useful results from this study are the novel gas- and solution-phase cyclisation reactions to form the benzoxazines **18** and **22**. As mentioned above, the most likely mechanism of their formation involves a 1,6-hydrogen atom shift, followed by cyclisation and consolidation by loss of a hydrogen atom (Scheme 6). The 1,6-hydrogen atom

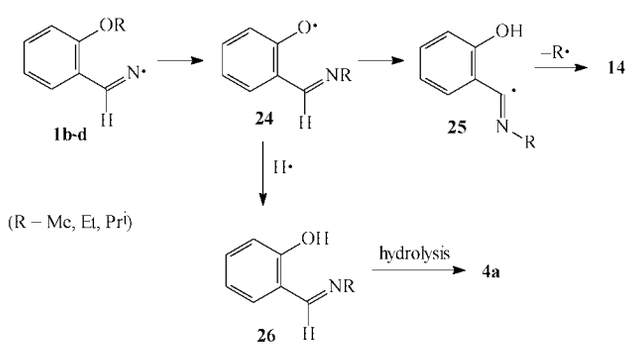


Scheme 6

shift, although still rather uncommon, has been observed[12] under a variety of conditions, including FVP experiments,[3,12k] and with many sorts of carbon- or heteroatom-centred radicals. Even theoretical studies have been carried out,[12f,g,j] showing that 1,6-H shifts have activation barriers comparable[12f] or only slightly higher[12g] than those of the more usually encountered 1,5-H translocations. Literature references include carbon-to-carbon,[12a–g] carbon-to-oxygen,[12h–k] oxygen-to-carbon,[12l] carbon-to-sulfur,[12m] and carbon-to-nitrogen[3,12n,o] migrations. In particular, only two examples have been reported to date concerning the intermediacy of nitrogen-centred radicals: one deals with the aminium radical ions involved in the Hofmann–Löffler reaction[12n] and the other with the sulfonamidyl radicals produced during the oxidative chlorination of alkanesulfonamides with the sodium persulfate–copper(II) chloride system.[12o] To our knowledge, our reactions—including that previously reported[3]—are the first examples of 1,6-hydrogen atom shifts towards an iminyl radical. Although we have not explored the synthetic potential of iminyl cyclisations as a route to the 1,3-benzoxazine system, compounds **18** and **22** are, respectively, the first 4-unsubstituted benzoxazine containing only alkyl substituents and the first 2,2-disubstituted 4-aryl derivative.

The absence of the corresponding benzoxazines in the gas-phase pyrolyses of the methoxy and ethoxy compounds **8** and **9** may be due to rapid hydrolysis of the ring system in solution. In agreement with this interpretation, the level of salicylaldehyde **4a**, the ultimate hydrolysis product of the benzoxazines, is particularly high in these two reactions.

The other major products of the gas-phase reactions are the nitriles **14** and **15**–**17**. It is well known[13] that iminyls can give rise to nitriles by an α-cleavage mechanism and so the formation of the low levels of alkoxynitriles **15**–**17** is not unexpected. However, the large amounts of 2-cyanophenol **14** as a major product in all three pyrolyses cannot be explained in this way. In particular, control experiments showed that 2-methoxybenzonitrile **15** did not undergo dealkylation to 2-cyanophenol **14** under the conditions of the original pyrolysis. As one possible mechanism, we suggest that the iminyls **1b**–**d** can undergo a 1,5-alkyl shift under the FVP conditions to generate the phenoxyls **24**. We have previously observed[2] that such phenoxyls with an adjacent aldimine function can provide nitriles by rearrangement to imidoyls **25** followed by α-cleavage (Scheme 7). Alternatively, hydrogen capture—a well known



Scheme 7

reaction of phenoxyls[2]—leads to the imines **26** which may provide an alternative source of salicylaldehyde **4a** by hydrolysis (Scheme 7).

Conclusions

In conclusion, the work described in this paper has demonstrated for the first time that iminyl radicals can interact with *ortho*-alkoxy substituents under both gas- and solution-phase conditions. The cyclisation to the benzoxazines **18** and **22** has established the principle of a new route to these unusual heterocycles, particularly under solution-phase conditions where other reactions of the iminyl do not interfere. In the gas-phase, these 'other reactions' include a surprisingly mild dealkylation process, which may take place by an unusual alkyl group transfer mechanism.

Experimental

^{1}H and ^{13}C NMR spectra are recorded at 250 (or 200) and 63 (or 50) MHz respectively for solutions in [^{2}H]chloroform unless otherwise stated. Coupling constants are quoted in Hz; ^{13}C NMR signals refer to CH resonances unless otherwise stated. The ^{1}H–^{13}C HMQC and HMBC experiments were performed using a Bruker DPX 360 NMR spectrometer, operating at 360.13 MHz for ^{1}H acquisitions, using the INV4GP and INV4GPLPLRND sequences respectively, as provided by Bruker Spectrospin. Mass spectra were obtained under electron impact conditions unless otherwise stated. IR spectra were recorded in chloroform solution on a Perkin-Elmer Spectrum RX I FT-IR spectrophotometer. Column chromatography was carried out on silica (H) using a hexane–ethyl acetate gradient as eluent unless otherwise stated. When elemental analyses—or high resolution mass spectra—were not performed, the purity of the compounds was confirmed by the absence of any significant extraneous peak in the ^{1}H NMR spectra and/or by GC-MS analysis.

2-Methoxybenzaldehyde *O*-methyloxime 8

A solution of 2-methoxybenzaldehyde **5** (1.13 g, 8.3 mmol) and *O*-methylhydroxylamine hydrochloride (1.40 g, 16.8 mmol) in ethanol (35 cm^3) containing pyridine (1.34 g, 14.7 mmol) was heated under reflux for 1 h. The reaction mixture was allowed to cool and concentrated under reduced pressure. The residue was treated with dilute hydrochloric acid [HCl (5 drops) in water (150 cm^3)] and extracted with ether (3 × 70 cm^3) to remove remaining traces of pyridine. The organic extracts were combined, dried ($MgSO_4$) and concentrated to give the crude oxime ether as a yellow oil. Distillation gave a single isomer of **8** as a clear liquid (1.11 g, 81%), bp 72–76 °C (1.5 Torr) [lit.,[14] 125–127 °C (16 Torr)], δ_H 8.45 (1H, s), 7.78 (1H, dd, ^3J 7.7 and ^4J 0.7), 7.33 (1H, m), 6.91–6.86 (2H, m), 3.96 (3H, s) and 3.83 (3H, s); δ_C 157.38 (quat.), 144.67, 130.94, 126.23, 120.61, 110.88, 61.74 (CH_3) and 55.39 (CH_3) (one quaternary signal overlapping) (spectra consistent with literature data[15]); *m*/*z* 165 (M$^+$, 33%), 119 (100), 91 (85) and 77 (54).

2-Ethoxybenzaldehyde 6

Salicylaldehyde **4a** (7.52 g, 59.7 mmol) was added to a suspension of potassium carbonate (16.52 g, 120 mmol) in DMF (100 cm^3). Bromoethane (6.71 g, 61 mmol) was then added dropwise and the solution was stirred at room temperature for 21 h. Water (100 cm^3) was added and the mixture was extracted with ether (3 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the crude aldehyde. This was distilled to give pure **6** as a clear liquid (7.89 g, 88%), bp 58–60 °C (0.5 Torr) [lit.,[8] 137 °C (24 Torr)], δ_H 10.48 (1H, s), 7.80 (1H, m), 7.49 (1H, m), 7.01–6.92 (2H, m), 4.16–4.07 (2H, q, ^3J 7.0) and 1.45 (3H, t, ^3J 7.0); δ_C 189.80, 161.19 (quat.), 135.74, 128.02, 124.61 (quat.), 120.29, 112.29, 63.93 (CH_2) and 14.49 (CH_3) (spectra consistent with literature data[8]); *m*/*z* 150 (M$^+$, 44%), 121 (100), 104 (16) and 76 (12).

2-Ethoxybenzaldehyde *O*-methyloxime 9

A solution of 2-ethoxybenzaldehyde **6** (1.53 g, 10.2 mmol) and *O*-methylhydroxylamine hydrochloride (1.74 g, 20.7 mmol) in ethanol (50 cm^3) containing pyridine (1.64 g, 20.7 mmol) was heated under reflux for 1 h. Following the standard work up (described for **8** above) the crude oxime ether was distilled to give a single isomer of *2-ethoxybenzaldehyde O-methyloxime* **9** as a clear liquid (1.60 g, 87%), bp 86–88 °C (0.8 Torr) (Found: M$^+$, 179.0947. $C_{10}H_{13}NO$ requires *M*, 179.0946); δ_H 8.53 (1H, s), 7.84 (1H, dd, ^3J 7.8 and ^4J 1.7), 7.35 (1H, m), 6.99–6.89 (2H, m), 4.11–4.06 (2H, q, ^3J 7.0), 4.01 (3H, s) and 1.45 (3H, t, ^3J 7.0); δ_C 157.41 (quat.), 145.35, 131.44, 126.71, 121.28 (quat.), 121.06, 112.48, 64.41 (CH_2), 62.25 (CH_3) and 15.17 (CH_3); *m*/*z* 179 (M$^+$, 13%), 150 (32), 133 (40), 121 (100), 91 (21) and 77 (14).

2-Isopropoxybenzaldehyde 7a

Salicylaldehyde **4a** (7.54 g, 61.8 mmol) was added to a suspension of potassium carbonate (17.01 g, 123 mmol) in DMF (100 cm^3). 2-Bromopropane (7.52 g, 61 mmol) was then added dropwise and the solution was stirred at room temperature for 21 h. Water (100 cm^3) was added and the mixture was extracted with ether (3 × 100 cm^3). The combined organic extracts were washed with dilute sodium hydroxide solution (2 M, 3 × 50 cm^3), to remove unreacted salicylaldehyde, and the organic layer was dried ($MgSO_4$) and concentrated to give the crude

aldehyde. This was distilled to give pure **7a** as a clear liquid (2.66 g, 27%), bp 52–54 °C (0.4 Torr) [lit.,[16] 83 °C (1.8 Torr)]; δ_H 10.47 (1H, s), 7.80 (1H, dd, ^3J 7.9 and ^4J 1.8), 7.50 (1H, m), 6.99–6.93 (2H, m), 4.66 (1H, sept, ^3J 6.1) and 1.38 (6H, d, ^3J 6.1); δ_C 190.05, 160.44 (quat.), 135.62, 128.09, 125.50 (quat.), 120.21, 113.81, 70.59 and 21.81 (CH_3) (spectra consistent with literature data[16]); *m*/*z* 164 (M^+, 38%), 121 (100), 104 (24), 93 (13) and 74 (33).

2-Isopropoxybenzaldehyde *O*-methyloxime 10

A solution of 2-isopropoxybenzaldehyde **7a** (1.62 g, 9.8 mmol) and *O*-methylhydroxylamine hydrochloride (1.67 g, 19.9 mmol) in ethanol (50 cm^3) containing pyridine (1.60 g, 20.2 mmol) was heated under reflux for 1 h. Following the standard work up (described for **8** above) the crude oxime ether was distilled to give a single isomer of *2-isopropoxybenzaldehyde O-methyloxime* **10** as a clear liquid (1.70 g, 90%), bp 90–92 °C (0.9 Torr) (Found: M^+, 193.1101. $C_{11}H_{15}NO$ requires *M*, 193.1102); δ_H 8.47 (1H, s), 7.79 (1H, dd, ^3J 7.7 and ^4J 1.8), 7.28 (1H, m), 6.94–6.86 (2H, m), 4.55 (1H, sept, ^3J 6.2), 3.96 (3H, s) and 1.32 (6H, d, ^3J 6.2); δ_C 155.84 (quat.), 144.98, 130.79, 126.23, 121.61 (quat.), 120.47, 113.69, 70.66 (CH), 61.69 (O-CH_3) and 21.91 (CH_3); *m*/*z* 193 (M^+, 23%), 151 (41), 119 (100) and 91 (72).

2-Isopropoxybenzonitrile 17

2-Cyanophenol (200 mg, 1.7 mmol), followed by 2-bromopropane (207 mg, 1.7 mmol), was added to a suspension of potassium carbonate (340 mg, 3.4 mmol) in DMF (3 cm^3) and the solution was stirred overnight. Water (6 cm^3) was added and the mixture was extracted with ether (3 × 6 cm^3). The combined organic extracts were washed with water (6 cm^3) and the organic layer was dried ($MgSO_4$) and concentrated to give the crude nitrile **17**, bp 146–149 °C (15 Torr) [lit.,[10] 137–138 °C (13 Torr)] (Found: M^+ 161.0841. $C_{10}H_{11}NO$ requires *M* 161.0841); δ_H 7.53–7.44 (2H, m), 6.97–6.90 (2H, m), 4.63 (1H, sept, ^3J 6.1) and 1.38 (6H, d, ^3J 6.1); δ_C 159.74 (quat.), 133.97, 133.73, 120.28, 116.60 (quat.), 113.48, 102.75 (quat.), 71.59 and 21.66 (CH_3); *m*/*z* 161 (M^+, 9%), 119 (100), 91 (47), 64 (18) and 63 (17).

Pyrolysis experiments

Precursors were sublimed or distilled under vacuum through the furnace tube which was held at the stated temperature. Conditions are quoted in the following manner: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, products (most abundant first). Products were trapped in liquid nitrogen. The work up of the pyrolyses involved the dissolution of the pyrolysate in dichloromethane and then separation by dry flash chromatography over silica using hexane–ethyl acetate mixtures as eluent.

Pyrolysis of 2-methoxybenzaldehyde *O*-methyloxime 8

FVP of 2-methoxybenzaldehyde *O*-methyloxime **8** (0.365 g, 2.2 mmol), 30–70 °C, 650 °C, 3 × 10^{-2} Torr, 20 min: dry-flash chromatography gave 2-cyanophenol **14** (0.115 g, 46%), mp 82–83 °C, mixed mp 89–91 °C (lit.,[8] 94 °C); δ_H 7.50–7.41 (2H, m), 7.00–6.92 (2H, m) and 5.62 (1H, br s); δ_C 158.72 (quat.), 134.66, 132.85, 120.65, 116.50 and 99.21 (one quaternary not apparent) (spectra consistent with literature data[8]); *m*/*z* 119 (M^+, 75%), 91 (85), 64 (100) and 39 (7). In addition, salicylaldehyde **4a** (0.062 g, 24%), δ_H 9.89, was obtained, whose presence was unambiguously confirmed from the ^{13}C NMR spectrum of crude pyrolysate, δ_C 196.54, 161.57 (quat.), 136.91, 133.64, 120.63 (quat.), 119.75 and 117.49 (spectra consistent with literature data[8]): the presence of a trace of 2-methoxybenzonitrile **15** (*ca*. 5%) was inferred from the methoxy group signal at δ_H 3.92 in the spectrum of the crude pyrolysate [δ_H (authentic sample) 3.92].

2-Methoxybenzonitrile 15—control pyrolyses

FVP of 2-methoxybenzonitrile **15** (75 mg, 0.56 mmol), 80–90 °C, 650 °C, 10^{-2} Torr, 15 min: the NMR spectrum of the pyrolysate showed complete recovery of starting material. A repeat pyrolysis at a furnace temperature of 750 °C showed *ca*. 10% decomposition and at 850 °C *ca*. 70% decomposition was observed.

Pyrolysis of 2-ethoxybenzaldehyde *O*-methyloxime 9

FVP of 2-ethoxybenzaldehyde *O*-methyloxime **9** (0.169 g, 0.9 mmol), 50–80 °C, 650 °C, 3 × 10^{-2} Torr, 20 min (all products identified from ^{13}C NMR spectra of crude pyrolysate; absolute yields estimated by comparison with previous pyrolyses): 2-cyanophenol **14** (*ca*. 45%); δ_C 159.73 (quat.), 134.29, 132.87, 119.79, 117.04 (quat.), 116.59 and 99.74; salicylaldehyde **4a** (*ca*. 15%); δ_C 196.54, 136.91, 134.29, 120.38, 117.48 (2 quaternaries not apparent). No further separation was carried out (spectra consistent with those listed above). In addition, the presence of 2-ethoxybenzonitrile **16** (*ca*. 10%) was inferred from ethoxy group signals at δ_H 1.47 and 4.14, and at δ_C 14.40 and 64.49 in the spectrum of the crude pyrolysate, which correspond closely to those of literature data.[8]

Pyrolysis of 2-isopropoxybenzaldehyde *O*-methyloxime 10

FVP of 2-isopropoxybenzaldehyde *O*-methyloxime **10** (0.450 g, 2.3 mmol), 60–90 °C, 650 °C, 3 × 10^{-2} Torr, 30 min: 2-cyanophenol **14** (0.155 g, 34%), mp 84–86 °C, mixed mp 91 °C (lit.,[8] 94 °C); δ_H 7.48–7.41 (2H, m) and 6.98–6.92 (2H, m) (OH signal not apparent); δ_C 160.33 (quat.), 134.39, 132.84, 119.40, 117.22 (quat.), 116.68 and 99.30 (quat.) (spectra consistent with literature data[8]); *m*/*z* 119 (M^+, 58%), 91 (100), 64 (35) and 38 (21): 2,2-dimethyl-2*H*-1,3-benzoxazine **18** (*ca*. 0.125 g, 34%) (^1H and ^{13}C NMR spectra obtained as a 1 : 1 mixture with **14** at 360 and 90 MHz respectively in [$^2H_6$]acetone); δ_H 8.08 (1H, s), 7.42 (1H, ddd, $^3J_1$ 7.4, $^3J_2$ 8.2 and ^4J 1.7), 7.33 (1H, dd, ^3J 7.3 and ^4J 1.7), 7.00 (1H, overlapping m), 6.79 (1H, d, ^3J 8.2) and 1.53 (6H, s); δ_C 152.70, 132.80, 126.37, 120.12, 115.30, 92.24 (quat.) and 25.98 (CH_3) (2 aromatic quaternaries not assigned); *m*/*z* (GC-MS) 161 (M^+, 46%), 146 (100), 120 (43), 91 (23) and 77 (22); 2-isopropoxybenzonitrile **17** (0.041 g, 10%) δ_H 7.57–7.45 (2H, m), 6.98–6.91 (2H, m), 4.64 (1H, m) and 1.39 (6H, d, ^3J 6.1); δ_C 159.80 (quat.), 133.97, 133.82, 120.32, 116.70 (quat.), 113.53, 102.84 (quat.), 71.67 and 21.72 (CH_3); *m*/*z* (GC-MS) 161 (M^+, 9%), 119 (100), 91 (31) and 64 (8) (spectra compatible with those of the authentic sample reported above); a trace of salicylaldehyde **4a** (*ca*. 3%) was identified by the presence of its aldehyde signal (δ_H 9.88) in the ^1H NMR spectrum of the crude pyrolysate.

(2-Isopropoxyphenyl)(phenyl)methanone oxime 11

According to a standard procedure,[17] a solution of (2-isopropoxyphenyl)(phenyl)methanone (**7b**)[18] (7.68 g, 32 mmol) and hydroxylamine hydrochloride (6.62 g, 96 mmol) in a mixture of ethanol (80 cm^3) and pyridine (8 cm^3) was heated under reflux overnight under mechanical stirring. Most of the solvent was evaporated and the resulting mixture was poured into ice–water and extracted with diethyl ether. The organic phase was dried, the solvent was removed and the residue chromatographed (light petroleum–diethyl ether gradients) to give the title compound **11** (7.34 g, 90%) as a 4 : 1 mixture of geometric isomers, mp 108–110 °C (lit.,[19] 111 °C); δ_H 9.06 (1H, br s, OH, both isomers), 7.60–7.20 (m, Ar-H, both isomers), 7.04 (1H, ddd, $^3J_1$, $^3J_2$ 7.3 and $^4J_3$ 1.0, Ar-H, major isomer), 6.99 (1H, br d, ^3J 8.7, Ar-H, major isomer), 6.93 (1H, ddd, $^3J_1$, $^3J_2$ 7.3 and $^4J_3$ 1.2, Ar-H, minor isomer), 6.82 (1H, br d, ^3J 8.0, Ar-H, minor isomer), 4.45 (1H, sept, ^3J 6.2, CH, major isomer), 4.33 (1H, sept, ^3J 5.9, CH, minor isomer), 1.10 (6H, d, ^3J 6.2, Me, major isomer), and 0.92 (6H, d, ^3J 5.9, Me, minor isomer).

2-{[(2-Isopropoxyphenyl)(phenyl)methylidene]aminooxy}acetic acid 12

According to the reported procedure,[20] a mixture of oxime **11** (7.15 g, 28 mmol), chloroacetic acid (4.25 g, 45 mmol) and sodium hydroxide (3.36 g, 84 mmol) in water (25 cm^3)–ethanol (15 cm^3) was heated under reflux overnight. Then it was poured into ice–water and neutralised with conc. hydrochloric acid. The mixture was extracted with dichloromethane, the organic phase was dried, the solvent removed and the residue chromatographed (light petroleum–diethyl ether gradients) to give the *title compound* **12** (5.82 g, 66%) as a practically pure single isomer, mp 137–138 °C (from light petroleum–benzene) (Found: C, 69.3; H, 6.0; N, 4.45. $C_{18}H_{19}NO_4$ requires C, 69.0; H, 6.1; N, 4.5%. Found: M^+ 313.1318. $C_{18}H_{19}NO_4$ requires *M*, 313.1314); ν_{max}/cm^{-1} 3286, 1769, 1487, 1447, 1349 and 1325; δ_H 9.70 (1H, br s, OH), 7.55–7.27 (6H, m, Ar-H), 7.18–7.09 (3H, m, Ar-H), 4.74 (2H, s, CH_2), 4.56 (1H, sept, ^3J 6.0, CH), and 1.22 (6H, d, ^3J 6.0, Me); δ_C 172.48 (quat.), 155.18 (quat.), 135.20 (quat.), 131.30 (quat.), 130.72, 129.86, 129.01, 128.13, 128.00, 125.03 (quat.), 122.72, 117.23, 75.51 (CH), 71.98 (CH_2), and 22.75 (CH_3); *m*/*z* 313 (M^+, 12%), 271 (12), 238 (33), 196 (66), 195 (100), 167 (54) and 77 (47).

***tert*-Butyl 2-{[(2-isopropoxyphenyl)(phenyl)methylidene]aminooxy}peracetate 13**

According to the reported procedure,[21] the iminoxyacetic acid **12** (5.82 g, 18.6 mmol) was added at room temperature and under nitrogen to a stirred solution of CDI (3.01 g, 18.6 mmol) in anhydrous THF (70 cm^3). After 1 h, a solution of *tert*-butyl hydroperoxide (4.31 g, 33.5 mmol) in light petroleum (30 cm^3) was added dropwise at 0 °C and the mixture was kept at 0–5 °C for 4 h. *tert*-Butyl hydroperoxide (Aldrich) was used as a 70 wt% solution in water, previously dried by extraction with cold light petroleum. The mixture was poured into ice–water and extracted with cold diethyl ether. The organic phase was washed twice with cold water and dried. After removal of the solvent the residue was chromatographed (light petroleum–diethyl ether gradients) to give the *title perester* **13** (5.62 g, 78%) as a thick oil which was a 5 : 1 mixture of geometric isomers;[22] ν_{max}/cm^{-1} 3000, 1792, 1598, 1486, 1451, 1368, 1246 and 1089; δ_H (300 MHz) 7.52–7.24 (m, Ar-H, both isomers), 7.02 (1H, ddd, $^3J_1$, $^3J_2$ 7.4 and $^4J_3$ 1.0, Ar-H, major isomer), 6.98–6.92 (1H + 1H, br d, ^3J 8.2, Ar-H, major isomer, overlapped with ddd, $^3J_1$, $^3J_2$ 7.5 and $^4J_3$ 1.0, Ar-H, minor isomer), 6.81 (1H, br d, ^3J 8.2, Ar-H, minor isomer), 4.81 (2H, s, CH_2, minor isomer), 4.76 (2H, s, CH_2, major isomer), 4.43 (1H, sept, ^3J 6.0, *CH*Me_2, major isomer), 4.33 (1H, sept, ^3J 6.0, *CH*Me_2, minor isomer), 1.32 (9H, s, *tert*-Bu, both isomers), 1.06 (6H, d, ^3J 6.0, CH*Me*$_2$, major isomer), and 0.88 (6H, d, ^3J 6.0, CH*Me*$_2$, minor isomer); *m*/*z* 385 (M^+, <1%), 341 (4), 311 (3), 255 (6), 238 (90), 237 (49), 236 (39), 223 (100), 222 (95), 196 (87), 195 (97), 181 (35), 167 (40), 152 (36), 77 (63) and 57 (98).

CAUTION: since hydroperoxides and peresters are potentially hazardous compounds, they must be handled with due care; avoid exposure to strong heat or light, mechanical shock, oxidizable organic materials, or transition metal ions. No particular difficulties were experienced in handling of the new perester synthesised in this work using the procedure described above. Even its column chromatography did not give any problem; however, we advise that the separation should be carried out with extreme care, evaporating the solvent under reduced pressure with a water bath kept below 20 °C.

Decomposition of perester 13

A solution of the perester **13** (5.62 g, 14.6 mmol) in bromobenzene (50 cm^3) was added dropwise over a period of 1 h to boiling bromobenzene (700 cm^3). After one additional hour at reflux, the solution was cooled, the solvent was evaporated and the residue chromatographed (light petroleum–diethyl ether gradients) to give, in order of elution, *2,2-dimethyl-4-phenyl-2H-1,3-benzoxazine* **22** (1.38 g, 40%), as a thick oil that slowly crystallises in square prisms, mp 82–83 °C (from light petroleum) (Found: C, 90.3; H, 6.3; N, 5.8. $C_{16}H_{15}NO$ requires C, 90.0; H, 6.4; N, 5.9%. Found: M^+ 237.1162. $C_{16}H_{15}NO$ requires *M*, 237.1154); ν_{max}/cm^{-1} 2985 and 1614; δ_H (300 MHz) 7.57–7.53 (2H, m, Ar-H), 7.47–7.42 (3H, m, Ar-H), 7.36 (1H, ddd, $^3J_1$ 9.0, $^3J_2$ 7.3 and $^4J_3$ 1.7, Ar-H), 7.18 (1H, dd, $^3J_1$ 7.5 and $^4J_2$ 1.5, Ar-H), 6.95–6.80 (2H, m, Ar-H), and 1.66 (6H, s, Me); δ_C (75 MHz) 162.36 (quat.), 155.77 (quat.), 137.80 (quat.), 134.11, 130.21, 129.37, 128.97, 128.46, 121.22, 117.72, 117.56 (quat.), 91.35 (quat.) and 27.61 (CH_3); *m*/*z* 237 (M^+, 16%), 236 (27), 222 (100), 153 (15), 152 (34), 77 (28) and 76 (39); *(2-isopropoxyphenyl)(phenyl)methanone O-(tert-butoxymethyl)oxime* **23** (0.62 g, 13%) as a single geometric isomer, oil (Found: C, 74.1; H, 8.2; N, 4.15. $C_{21}H_{27}NO_3$ requires C, 73.9; H, 8.0; N, 4.1%); ν_{max}/cm^{-1} 2976, 1598, 1486, 1450, 1243, 1119, 1012 and 961; δ_H (300 MHz) 7.54–7.47 (2H, m, Ar-H), 7.36–7.21 (4H, m, Ar-H), 7.19 (1H, dd, $^3J_1$ 7.5 and $^4J_2$ 1.8, Ar-H), 6.98 (1H, dd, $^3J_1$ 7.4 and $^4J_2$ 0.8, Ar-H), 6.93 (1H, br d, ^3J 8.5, Ar-H), 5.34 (2H, s, CH_2), 4.41 (1H, sept, ^3J 6.0, C*H*Me_2), 1.20 (9H, s, *tert*-Bu), and 1.05 (6H, d, ^3J 6.0, CH*Me*$_2$); δ_C (75 MHz) 156.42 (quat.), 155.34 (quat.), 136.94 (quat.), 130.86, 130.28, 129.45, 128.50, 127.70, 125.05 (quat.), 120.59, 114.47, 93.38 (CH_2), 75.32 (quat.), 71.03, 29.35 (CH_3), and 22.47 (CH_3); *m*/*z* 315 (M^+ − 86, 1%), 238 (29), 223 (34), 196 (43), 195 (66), 167 (33), 77 (62) and 57 (100); ketone **7b** (0.42 g, 12%); oxime **11** (0.22 g, 6%).

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