Chemistry of 5-oxodihydroisoxazoles. Part 18.[1] Synthesis of oxazoles by the photolysis and pyrolysis of 2-acyl-5-oxo-2,5-dihydroisoxazoles

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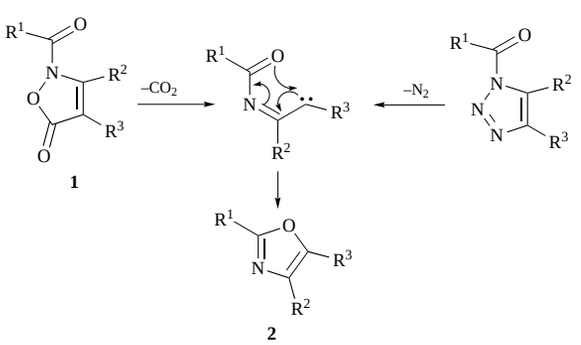
***N*-Acylisoxazol-5-ones lose carbon dioxide under photochemical and thermal conditions affording iminocarbenes which undergo intramolecular cyclisation through the oxygen of the acyl group to give oxazoles. Under photochemical conditions those acylisoxazolones with electron withdrawing groups at C-4 usually give high yields of oxazoles, while those with electron donating groups at C-4 give only poor yields: the reverse is observed under thermal conditions.**

Introduction

There is still no general synthesis of oxazoles that is satisfactory for the preparation of all substituted analogues.[2] The two earliest methods involve the reaction of amides with α-halo ketones,[3] or the dehydration of α-acylaminocarbonyl compounds.[4] However, these reactions are limited in their scope and are often low yielding. The most general and widely used method is still that developed by Cornforth and Cornforth,[5] and the method reported by Yokoyama *et al.*[6] is essentially a variant of this procedure. The growing number of marine derived natural products containing the oxazole,[7] bis-oxazole,[8] tris-oxazole[9] or alkylaminooxazole[10] system has revived interest in the development of new synthetic procedures for this ring system. Most recent methods have utilised a biosynthetic modelled approach, involving oxidation[11–13] of a peptide-derived oxazoline, although the capture of rhodium carbenoids by nitriles has also been developed as a good oxazole synthesis.[14,15]

We have previously pointed out the similarity in the photochemical or thermal loss of nitrogen and carbon dioxide from triazoles and isoxazol-5-ones respectively[16] (Scheme 1), and



Scheme 1

have pyrolysed[17] or photolysed[18] the latter to produce a variety of heterocycles including imidazoles and pyrimidines. Extrapolation of this mechanism suggests *N*-acylated isoxazolones would give oxazoles (Scheme 1), although the photolysis[19] and thermolysis[20,21] of *N*-acyltriazoles appear to lead mainly to diradicals,[22–25] giving rather poor support for this hope. However, Williams[26] has recently reported a new procedure for the thermal conversion of a number of acyltriazoles to oxazoles in good yields, although the procedure appears to be capable of variation only in the substituent at C-2.

In our accompanying paper[1] we report our study of the *N*-acylation of isoxazol-5(2*H*)-ones: herein we elaborate our preliminary report[27] on the photolytic and pyrolytic conversion of these species into oxazoles.

Discussion

Photolysis

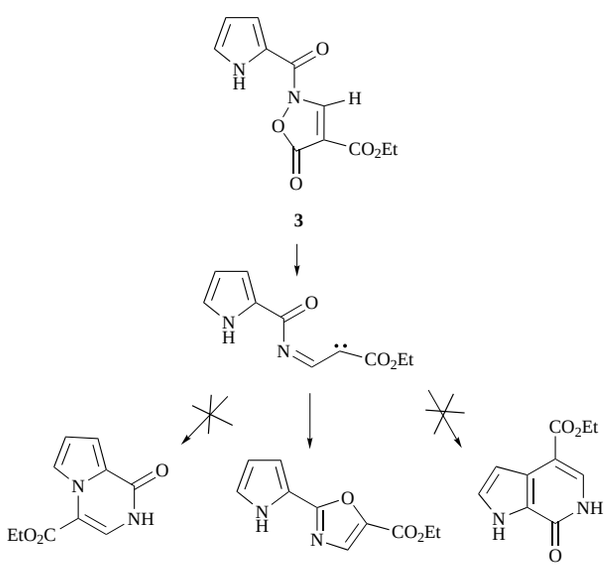
The photolysis or pyrolysis of *N*-acylisoxazolones gave oxazoles in yields that were generally superior to those obtained from the corresponding acyltriazoles where corresponding data was available, as shown in Table 1. Photolyses of *N*-acylisoxazol-5(2*H*)-ones were carried out at 254 and 300 nm, in a variety of solvents. While formation of oxazoles was fast in acetonitrile at 254 nm, the cleanest products were formed in acetone at 300 nm, and these conditions have been most widely used in this work. *N*-Acylisoxazolones with an ester group at C-4 were efficiently photolysed to the corresponding oxazoles, many of which had not previously been prepared. Both 2-alkyl- and 2-aryl-oxazoles were readily prepared although the synthesis of the corresponding 4-nitrophenyl analogue was unsuccessful, presumably because of predominant light-absorption by this group. The photolysis of the (pyrrol-2-ylcarbonyl)isoxazolone **3** shows the selectivity of the cyclisation, as the intermediate iminocarbene could conceivably be captured by the nitrogen of the pyrrole to give a pyrazine, or by C-3 of the pyrrole to give a pyridone derivative (Scheme 2). In fact, the oxazole **4** was the only product isolated and was identified by its spectral properties.

The success of the photolysis of derivatives with an ester group at C-3 depended on the nature of the *N*-acyl group. The *N*-acetyl derivative did not react at 300 nm, but photolysed rapidly at 254 nm to give the oxazole in 40% yield (80% based on consumed starting material): longer photolysis led to decomposition of the oxazole, and the benzoyl derivative gave similar results. Likewise, the photolysis of acylated 3-phenyl- and 3-methyl-isoxazolones gave dramatically reduced yields of the corresponding oxazoles which were accompanied by fragmentation products, including amides and nitriles. The photolysis of acylated benzisoxazolones at either 254 or 300 nm gave no identifiable products. The presence of halogen atoms at C-4 also decreased the synthetic value of photolysis. Thus the benzoylated isoxazolone **5** gave the expected oxazole **6**, accompanied by numerous by-products, of which only the isomeric oxazole **7** was identified (Scheme 3). Oxazole **7** probably arises by rearrangement of the intermediate iminocarbene, presumably *via* the 1*H*-azirine intermediate (Scheme 4). This rearrangement of iminocarbenes has previously been reported to occur in

Table 1 Synthesis of oxazoles **2** from 2-acylisoxazol-5(2*H*)-ones **1**

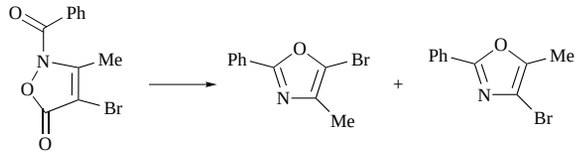
R^1	R^2	R^3	Yield (%)[a]
Me	H	CO_2Et	A 10; C 65
Pr^i	H	CO_2Et	B 81
$PhCH_2$	H	CO_2Et	C 88
$PhCH_2CH_2$	H	CO_2Et	C 72
Ph	H	CO_2Et	C 70
2-ClC_6H_4	H	CO_2Et	C 79
4-ClC_6H_4	H	CO_2Et	C 77
2-$MeOC_6H_4$	H	CO_2Et	C 79
4-$MeOC_6H_4$	H	CO_2Et	C 80
Pyrrol-2-yl	H	CO_2Et	B 30; C 30
Ph	Me	CO_2Et	C 30
Me	CO_2Et	Me	A 95; B 40
Ph	CO_2Et	Me	A 95; B 40; C 35
2,5-Me_2-oxazol-4-yl	CO_2Et	Me	A 45; C 61
2,5-Ph_2-oxazol-4-yl	CO_2Et	Me	A 32; C 26
$CHCl_2$	CO_2Et	Me	A 18
CO_2Me	CO_2Et	Me	A 56
CO_2Et	CO_2Et	Me	A 50
2-[6-(Oxazol-2-yl)-pyridin-2-yl]	CO_2Et	Me	E
4-CO_2Et-5-Me-oxazol-2-yl	CO_2Et	Me	A 8
Phth-CH_2 D[a]	CO_2Et	Me	B 80; C 90
Me	Ph	H	A 95; C 29
Ph	Ph	H	A 60; C 24
Me	benzo		A 95; B, C 0
Ph	benzo		A 95; B, C 0
Ph	Me	H	A 95; C 24
Ph	Me	Br	F 15
Me	Me	H	A 95
Ph	H	H	A 80
Me	Ph	Ph	A 95
Ph	Ph	Ph	A 70
CF_3	Ph	H	A 50
MeO	CO_2Et	Me	A 66
EtO	CO_2Et	Me	A 31
PhO	CO_2Et	Me	A 64

[a] (A) Flash vacuum pyrolysis, 490–600 °C; (B) photolysis, 254 nm, CH_3CN, silica; (C) photolysis, 300 nm, acetone or CH_3CN, Pyrex; (D) phthalimidomethyl; (E) refer to Experimental section; (F) photolysis, 300 nm, 1,4-dioxane, pyrex.

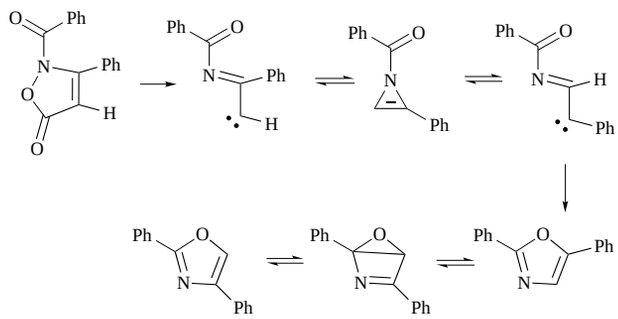


Scheme 2

the photolysis of 1,2,3-triazoles,[28] but is the first example in which an isomerised oxazole has been isolated from photolysis of our isoxazolone. None of the photolysis reactions gave rise to products involving hydrogen abstraction, suggesting that the intermediate is a singlet iminocarbene and not a triplet diradical. This is supported by the observation that the presence



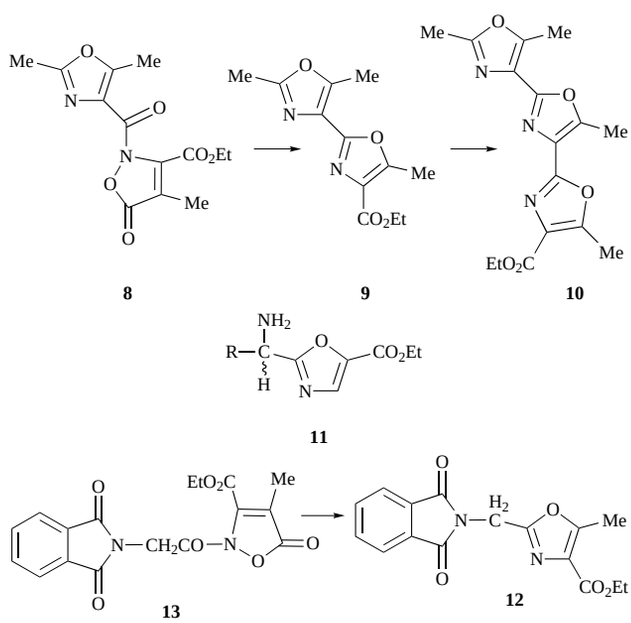
Scheme 3



Scheme 4

of the triplet quenchers or sensitisers, 9-methylanthracene and benzophenone, had no effect on the photolysis yields.

Due to increased interest in natural products which contain an oxazole or polyoxazole moiety, we investigated the application of this method to the synthesis of oxazoles of this type. The photolysis of (2-oxazolecarbonyl)isoxazolone **8** gave the



bis-oxazole **9** in 61% yield. Following its hydrolysis and conversion to the acid chloride, the bis-oxazole could be used to acylate a further isoxazolone, leading to the synthesis of the tris-oxazole **10** (10% overall).

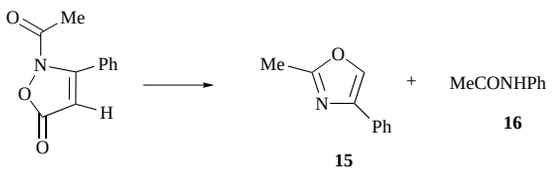
A common feature of the peptide derived cyclic polyoxazoles is the 2-aminoalkyl-5-carboxyoxazole unit similar to **11**. We found that a precursor to this—oxazole **12**—could be prepared in high yield by the photolysis of the appropriate isoxazolone **13** at 300 nm.

Pyrolysis

Pyrolysis of *N*-acylisoxazol-5(2*H*)-ones generally gave poor results when carried out in a Dowtherm reactor at 250–300 °C or under vacuum in the condensed phase. Flash vacuum pyrolysis using a 30 cm silica tube filled with silica beads at 500 °C gave the best results. In contrast to the observations with photolysis, those *N*-acylisoxazolones unsubstituted at C-4

and/or with electron withdrawing groups at C-3, which included benzisoxazolones, were found to give oxazoles in good yields except with involatile or thermally unstable compounds as shown in Table 1. In most cases these isoxazolones had either failed to rearrange under photochemical conditions or gave poor yields.

Pyrolysis at higher temperatures than 500 °C led to formation of side products. When **14** was pyrolysed at 700 °C, 20% of acetanilide **16** was formed in addition to the oxazole **15**, but none could be detected at 500 °C (Scheme 5). Small amounts of

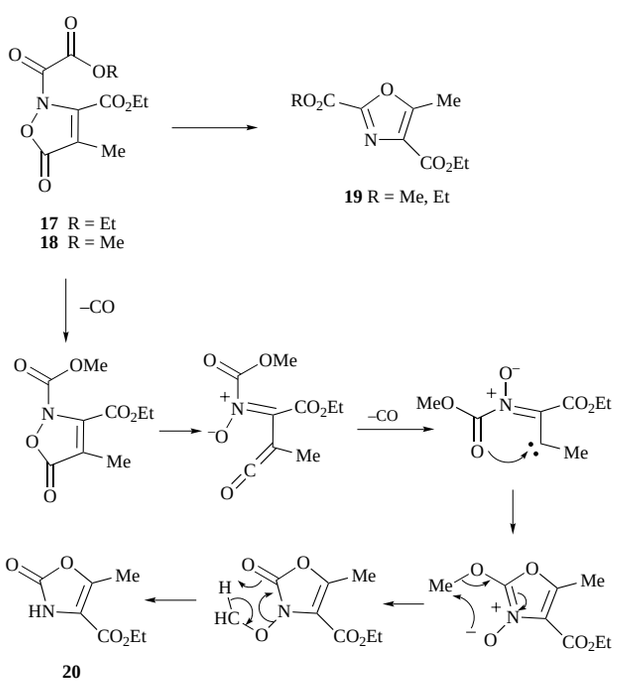


14 **15** **16**

Scheme 5

the isomeric oxazoles were produced in some cases, particularly when higher temperatures were used, but it is not certain whether they were derived from the rearrangement of the *N*-acylcarbene or isomerisation of the oxazole (Scheme 4).

A preliminary investigation has been made of the tolerance to the pyrolytic reaction conditions of acyl groups substituted by other than aryl or alkyl groups. While oxamides such as **17** and **18** were readily available, their potential to undergo decarbonylation before loss of carbon dioxide and oxazole formation was of interest. In the event, the ethyl ester **17** underwent rearrangement to give oxazole **19** without side reactions. Pyrolysis of the methyl ester **18** gave not only the expected oxazole **19**, but also a small amount of the oxazolone **20**, whose origin is suggested to arise from a Meisenheimer rearrangement[29] (Scheme 6) following a double decarbonyl-



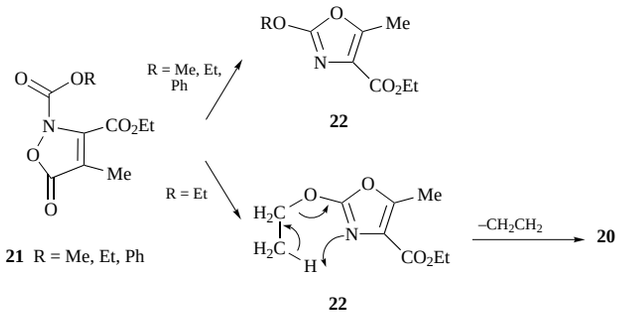
17 R = Et
18 R = Me

19 R = Me, Et

20

Scheme 6

ation. This unexpected rearrangement encouraged us to investigate *N*-alkoxycarbonylisoxazolones like **21** in the hope of observing similar rearrangements and it was found that pyrolysis of the methyl and phenyl carbamates gave only the corresponding oxazoles **22**. However, the ethyl carbamate gave a mixture of both the expected oxazole and the oxazolone **20** observed above, but in this instance we believe that **20** is not derived from a Meisenheimer rearrangement but by ethylene elimination from the first formed oxazole **22** (R = Et) (Scheme 7).



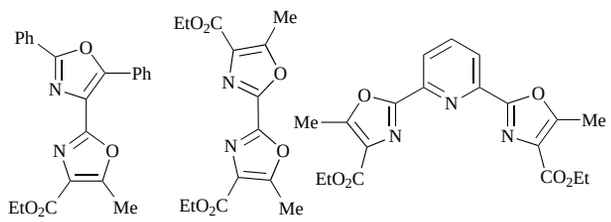
21 R = Me, Et, Ph

22

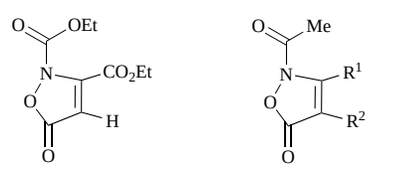
20

22

Scheme 7



23 **24** **25**



26

27 R^1 = CO_2Et, R^2 = H
28 R^1 = Me, R^2 = CO_2Et

The polyoxazoles **23**–**25** were prepared from the respective isoxazolones. While the yields were low (8–32%) the procedure has the advantage of being a two step process.

Surprisingly, 2-ethoxycarbonylisoxazolone **26**, while formally very similar to **21** above, decomposed to unidentifiable material, because of its low volatility. Finally, 2-acetylisoxazolones such as **27** and **28** lost ketene as the major thermolytic pathway: fortunately this was not a major problem in their photolytic reactions.

In summary, oxazoles are available by a new route from the decarboxylation of 2-acylisoxazol-5(2*H*)-ones. Photolysis of the latter proceeds best when electron withdrawing groups are present at C-4, whereas flash vacuum pyrolysis is the method of choice for all other substitution patterns.

Experimental

General experimental procedures have been described previously.[1] NMR spectra were determined in $CDCl_3$ using $SiMe_4$ as an internal reference on a Varian Gemini 300 MHz spectrometer. Coupling constants *J* are given in Hz. Light petroleum refers to the fraction boiling in the range 40–60 °C. Photolyses were conducted in a Rayonet photochemical reactor using either 300 or 254 nm tubes as stated. Flash vacuum pyrolyses involved either direct injection or sublimation into a Thermolyne Pyrolyser tube furnace, 30 cm long, packed with silica beads. Furnace temperature, sublimation temperature, pressure and time required for completion are shown in parentheses. Unless otherwise stated, acylisoxazolones were prepared by the method of Prager *et al.*[1]

Ethyl 2-methyloxazole-5-carboxylate 2 (R^1 = Me, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, benzene–acetone, 1:9, 15 h) of ethyl 2-

acetyl-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave an oil which was distilled at 55 °C/0.02 mmHg (lit.,[30] 75–80 °C/0.15 mmHg) as a colourless oil (101 mg, 65%) (Found: M^+, 155.0557. Calc. for $C_7H_9NO_3$: *M*, 155.0582); δ_H 1.38 (3 H, t, *J* 7), 2.56 (3 H, s), 4.38 (2 H, q, *J* 7) and 7.65 (1 H, s); δ_C 14.2, 14.2, 61.3, 134.0, 142.5, 157.7 and 164.7; ν_{max}/cm^{-1} 1733, 1589 and 1545; *m/z* 155 (M, 50%), 127 (80), 110 (43) and 82 (100).

Flash vacuum pyrolysis of the above isoxazolone (200 mg) (540 °C, 120 °C, 0.05 mmHg, 60 min) gave a mixture of the above oxazole (16 mg, 10%) and ethyl cyanoacetate (102 mg, 90%), whose identities were confirmed by GC–MS.

Ethyl 2-isopropyloxazole-5-carboxylate 2 (R^1 = Pr^i, R^2 = H, R^3 = CO_2Et)

Photolysis (254 nm. acetonitrile, 2 h) of ethyl 2-(2-methylpropionyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a product which was distilled to give a *colourless oil* (131 mg, 81%), bp 40 °C/0.05 mmHg (Found: C, 58.9; H, 7.3; N, 7.7%; M^+, 183.0896. $C_9H_{13}NO_3$ requires C, 59.0; H, 7.2; N, 7.7%; *M*, 183.0895); δ_H 1.37 (3 H, t, *J* 7), 1.40 (6 H, d, *J* 7), 3.20 (1 H, septet, *J* 7), 4.40 (2 H, q, *J* 7) and 7.70 (1 H, s); ν_{max}/cm^{-1} 1724, 1599 and 1537; *m/z* 183 (M, 24%), 168 (8), 155 (12), 138 (6) and 110 (100).

Ethyl 2-benzyloxazole-5-carboxylate 2 (R^1 = Bn, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone, 3 h) of ethyl 5-oxo-2-phenylacetyl-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a *colourless oil*, bp 90 °C/0.1 mmHg (148 mg, 88%) (Found: C, 67.8; H, 6.0; N, 5.9. $C_{13}H_{13}NO_3$ requires C, 67.5; H, 5.7; N, 6.1%); δ_H 1.37 (3 H, t, *J* 7), 4.19 (2 H, s), 4.37 (2 H, q, *J* 7), 7.22–7.39 (5 H, m) and 7.68 (1 H, s); δ_C 14.3, 34.8, 61.5, 127.5, 128.7, 128.9, 134.0, 134.3, 142.8, 157.8 and 164.4; ν_{max}/cm^{-1} 1728, 1590 and 1533; *m/z* 231 (M, 61%), 203 (10), 186 (6), 158 (71), 130 (9), 118 (7), 103 (9) and 91 (100).

Ethyl 2-phenyloxazole-5-carboxylate 2 (R^1 = Ph, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone, 3 h) of ethyl 2-benzoyl-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave an oil which was crystallised from diethyl ether–light petroleum as white needles (150 mg, 90%), mp 58–60 °C (lit.,[30] 56 °C) (Found: M^+, 217.0737. Calc. for $C_{12}H_{11}NO_3$: *M*, 217.0739); δ_H 1.42 (3 H, t, *J* 7), 4.42 (2 H, q, *J* 7), 7.45–7.58 (3 H, m), 7.85 (1 H, s) and 8.12–8.18 (2 H, m); δ_C 14.3, 61.5, 126.4, 127.3, 129.0, 131.7, 135.3, 142.4, 157.9 and 164.2; ν_{max}/cm^{-1} 1708, 1574 and 1528; *m/z* 217 (M, 58%), 189 (14), 172 (10), 144 (84), 122 (47), 116 (64) and 105 (100).

Ethyl 2-(2-chlorophenyl)oxazole-5-carboxylate 2 (R^1 = 2-ClC_6H_4, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone) of ethyl 2-(2-chlorobenzoyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a crude product which was distilled to afford a *colourless oil* (134 mg, 79%), bp 100 °C/0.05 mmHg (Found: C, 57.5; H, 4.1; N, 5.3%; M^+, 251.0329. $C_{12}H_{10}ClNO_3$ requires C, 57.3; H, 4.0; N, 5.6%; *M*, 251.0349); δ_H 1.41 (3 H, t, *J* 7), 4.45 (2 H, q, *J* 7), 7.32–7.67 (3 H, m), 7.93 (1 H, s) and 7.93–8.20 (1 H, m); ν_{max}/cm^{-1} 1733, 1583, 1528; *m/z* 251 (M, 59%), 178 (100) and 123 (24).

Ethyl 2-(4-chlorophenyl)oxazole-5-carboxylate 2 (R^1 = 4-ClC_6H_4, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone) of ethyl 2-(4-chlorobenzoyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a crude product which was distilled to afford a pale yellow oil, bp 110 °C/0.05 mmHg, and solidified on cooling to form a *white solid* (131 mg, 77%), mp 76–78 °C (Found: C, 57.6; H, 4.1; N, 5.4%; M^+, 251.0349. $C_{12}H_{10}ClNO_3$ requires C, 57.3; H, 4.0; N, 5.6%; *M*, 251.0349); δ_H 1.42 (3 H, t, *J* 7), 4.42 (2 H, q, *J* 7), 7.45 (2 H, d, *J* 9), 7.83 (1 H, s) and 8.08 (2 H, d, *J* 9); δ_C 14.3, 61.6, 124.9, 128.5, 129.4, 135.3, 138.5, 142,5, 157.8 and 163.3; ν_{max}/cm^{-1} 1724, 1599 and 1468; *m/z* 251 (M, 92%), 178 (100) and 139 (40).

Ethyl 2-(2-methoxyphenyl)oxazole-5-carboxylate 2 (R^1 = 2-$MeOC_6H_4$, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone) of ethyl 2-(2-methoxybenzoyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a crude product which was distilled as a colourless oil (134 mg, 79%), bp 102 °C/0.1 mmHg, and solidified on cooling to form a *white solid*, mp 51–53 °C (Found: C, 63.2; H, 5.3; N, 5.7%; M^+, 247.0847. $C_{13}H_{13}NO_4$ requires C, 63.15; H, 5.3; N, 5.7%; M, 247.0844); δ_H 1.42 (3 H, t, *J* 7), 3.97 (3 H, s), 4.43 (2 H, q, *J* 7), 6.91–7.37 (2 H, m), 7.52 (1 H, dt, *J* 8, 2), 7.95 (1 H, s) and 8.10 (1 H, dd, *J* 8, 2); δ_C 14.4, 56.1, 61.4, 112.1, 115.4, 120.7, 130.9, 133.0, 135.2, 141.8, 158.1, 158.2 and 162.5; ν_{max}/cm^{-1} 1717, 1604, 1580, 1521 and 1491; *m/z* 247 (M, 60%), 218 (10), 174 (86), 146 (100), 133 (12) and 118 (58).

Ethyl 2-(4-methoxyphenyl)oxazole-5-carboxylate 2 (R^1 = 4-$MeOC_6H_4$, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone) of ethyl 2-(4-methoxybenzoyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a crude product which was recrystallized from benzene–light petroleum as a *white solid*, mp 69–70 °C (136 mg, 80%) (Found: C, 63.1; H, 5.2; N, 5.4%; M^+, 247.0847. $C_{13}H_{13}NO_4$ requires C, 63.2; H, 5.3; N, 5.7%; *M*, 247.0844); δ_H 1.40 (3 H, t, *J* 7), 3.88 (3 H, s), 4.42 (2 H, q, *J* 7), 7.01 (2 H, d, *J* 9), 7.84 (1 H, s) and 8.13 (2 H, d, *J* 9); ν_{max}/cm^{-1} 1716, 1605 and 1483; *m/z* 247 (M, 41%), 174 (55), 152 (36), 146 (60), 135 (72) and 105 (100).

Ethyl 2-(2-phenylethyl)oxazole-5-carboxylate 2 (R^1 = $PhCH_2CH_2$, R^2 = H, R^3 = CO_2Et)

Photolysis (300 nm, acetone) of ethyl 5-oxo-2-(3-phenylpropionyl)-2,5-dihydroisoxazole-4-carboxylate (200 mg) gave a crude product which was subjected to silica radial chromatography (diethyl ether–light petroleum, 1:4) affording the title compound (122 mg, 72%) as a *pale yellow oil* (Found: M^+, 245.1049. $C_{14}H_{15}NO_3$ requires *M*, 245.1052); δ_H 1.38 (3 H, t, *J* 7.14), 3.14 (3 H, s), 4.38 (2 H, q, *J* 7.14), 7.15–7.35 (5 H, m) and 7.65 (1 H, s); δ_C 14.3, 30.2, 32.8, 61.4, 126.6, 128.3, 128.6, 134.1, 139.8, 142.4, 157.8 and 167.3; ν_{max}/cm^{-1} 1733, 1589 and 1538; *m/z* 245 (M, 32%), 216 (3), 172 (9), 144 (9) and 131 (3).

Reactions of 2-benzoyl-3-methylisoxazol-5(2*H*)-one 1 (R^1 = Ph, R^2 = Me, R^3 = H)

The isoxazolone (1.8 g, 8.8 mmol) was irradiated in dichloromethane (800 ml) for 5 h at 300 nm. Radial silica chromatography (diethyl ether–light petroleum, 3:7) separated the mixture into three components. Fraction 1 was identified as 4-methyl-2-phenyloxazole (0.28 g, 27%) by direct comparison with an authentic sample prepared by the method of Lewy[31] (Found: M^+, 159.0630. Calc. for $C_{10}H_9NO$: *M*, 159.0684); δ_H 2.22 (3 H, d, *J* 1.25), 7.28–7.44 (4 H, m) and 7.99–8.02 (2 H, m); δ_C 11.5, 126.1, 127.5, 128.6, 130.1, 134.2, 137.5 and 161.3; ν_{max}/cm^{-1} 1603 and 1550; *m/z* 159 (M, 100%), 130 (50), 104 (32), 90 (83), 77 (39) and 51 (25). Fraction 2 (0.17 g, 12%) was identified as unreacted starting material. Fraction 3 (0.12 g, 14%) was identified as benzamide.

Flash vacuum pyrolysis (595 °C, 135 °C, 0.05 mmHg, 40 min) of the isoxazolone (100 mg) gave 4-methyl-2-phenyloxazole (74 mg, 95%), isolated as a pale yellow oil, and identical with the sample prepared above.

Photolysis of 2-benzoyl-4-bromo-3-methylisoxazol-5(2*H*)-one 1 (R^1 = Ph, R^2 = Me, R^3 = Br)

The isoxazolone **5** (0.5 g, 1.78 mmol) was irradiated in 1,4-dioxane (200 ml) at 300 nm for 5 h. Separation by silica gel column chromatography (diethyl ether–light petroleum, 15:85)

gave 5-*bromo*-4-*methyl*-2-*phenyloxazole* **6** (0.07 g, 16%) as the first fraction. The identity was confirmed by direct comparison with an authentic sample, prepared by bromination of the 4-methyl-2-phenyloxazole isolated above (Found: M^+, 238.9798; 236.9815. $C_{10}H_8BrNO$ requires *M*, 238.9770; 236.9790); δ_H 2.57 (3 H, s), 7.31–7.64 (3 H, m) and 8.08 (2 H, dd, *J* 8, 2); $\nu_{max}(CDCl_3)/cm^{-1}$ 1678 and 1574; *m/z* 239 (M, 18%), 237 (M^+, 20), 211 (33), 209 (39), 170 (41), 168 (41), 130 (100) and 104 (48). The remainder of the material was subjected to reversed phase HPLC (H_2O–CH_3CN, 1:4) and GC–MS analysis: 4-bromo-5-methyl-2-phenyloxazole **7** (*ca*. 8%) was isolated and identified by direct comparison with an authentic sample prepared by bromination of the oxazole.[32]

2-Methyl-4-phenyloxazole 15

Photolysis (300 nm, acetone, 4 h) of 2-acetyl-3-phenylisoxazol-5(2*H*)-one **14** (1 g, 4.93 mmol) gave two products which were separated by silica gel radial chromatography (diethyl ether–light petroleum, 3:7). The first was identified as the title compound **15** (0.23 g, 29%). The second fraction was identified as benzonitrile (0.06 g, 11%).

Flash vacuum pyrolysis (350 mg) (595 °C, 100 °C, 0.05 mmHg, 30 min) gave the oxazole **15**, bp 80 °C/0.1 mmHg (lit.,[33] 241 °C/760 mmHg), as a straw coloured oil (260 mg, 95%), identical with a sample prepared by the method of Lewy[33] (Found: M^+, 159.0689. Calc. for $C_{10}H_9NO$: *M*, 159.0684); δ_H 2.49 (3 H, s), 7.27 (1 H, t, *J* 7), 7.37 (2 H, t, *J* 7), 7.69 (2 H, d, *J* 7) and 7.78 (1 H, s); δ_C 13.9, 125.3, 127.8, 128.6, 131.1, 133.1, 140.7 and 161.8; ν_{max}/cm^{-1} 1594 and 1276; *m/z* 159 (M, 97%), 131 (58), 117 (38), 103 (35), 90 (100), 77 (23), 63 (42) and 51 (31). A white solid (3 mg, 2%) isolated from the pyrolysis tube was identified as *N*-phenylacetamide **16** by direct comparison with an authentic sample.

2,4-Diphenyloxazole

Photolysis (300 nm, acetone, 4 h) of 2-benzoyl-3-phenylisoxazol-5(2*H*)-one (0.5 g, 1.89 mmol) gave the title compound which was purified by radial chromatography (diethyl ether–light petroleum, 2:3) and recrystallised from benzene–light petroleum as white crystals (100 mg, 24%), mp 101 °C.

Flash vacuum pyrolysis (150 mg) (595 °C, 155 °C, 0.05 mmHg, 60 min) gave a solid which was separated by radial chromatography (dichloromethane–light petroleum, 35:65) to give three fractions. The first fraction was recrystallised from dichloromethane–light petroleum to give colourless needles of 2,4-diphenyloxazole (75 mg, 60%), mp 101–102 °C (lit.,[33] mp 102–103 °C) (Found: M^+, 221.0844. Calc. for $C_{15}H_{11}NO$: *M*, 221.0841); δ_H 7.52–7.56 (1 H, m), 7.42–7.51 (5 H, m), 7.82–7.86 (2 H, m), 7.97 (1 H, s) and 8.12–8.16 (2 H, m); δ_C 125.6, 126.5, 127.5, 128.1, 128.1, 128.8, 130.4, 131.1, 133.4, 142.0 and 161.9; ν_{max}/cm^{-1} 1553 and 1339; *m/z* 221 (M, 100%), 193 (73), 165 (12), 90 (53), 89 (54), 63 (23) and 51 (15). The second fraction, a white solid, mp 72–73 °C (lit.,[34] 73 °C), was identified as 2,5-diphenyloxazole (13 mg, 10%) by comparison with an authentic sample[34] (Found: M^+, 221.0844. Calc. for $C_{15}H_{11}NO$: M, 221.0841); δ_H 7.32–7.53 (7 H, m), 7.72 (2 H, m) and 8.13 (2 H, m); δ_C 123.4, 124.1, 126.2, 127.4, 128.0, 128.4, 128.8, 128.9, 130.3, 151.2 and 161.1; *m/z* 221 (M^+, 76%), 193 (7), 165 (30), 122 (39), 105 (100), 77 (97) and 51 (52). The third fraction was identified as *N*-phenylbenzamide (17 mg, 15%), mp 156–158 °C.

Ethyl 5-methyl-2-phenyloxazole-4-carboxylate 2 (R^1 = Ph, R^2 = CO_2Et, R^3 = Me)

Photolysis (254 nm, acetonitrile, 30 min) of ethyl 2-benzoyl-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate (200 mg, 0.73 mmol) gave an oil which was chromatographed (dichloromethane–light petroleum, 7:3) to give one major fraction. A second chromatogram (diethyl ether–light petroleum, 1:4), gave the title compound as a colourless oil (67 mg, 40%) (lit.,[35] bp 95 °C/0.05 mmHg) (Found: M^+, 231.0895. Calc. for $C_{13}H_{13}NO_3$: *M*, 231.0905); δ_H 1.38 (3 H, t, *J* 7), 2.66 (3 H, s), 4.39 (2 H, q, *J* 7), 7.42 (3 H, m) and 8.03 (2 H, m); δ_C 12.1, 14.3, 60.9, 126.4, 126.4, 128.6, 128.6, 130.6, 156.0, 159.5 and 162.3; ν_{max}/cm^{-1} 1716 and 1615; *m/z* 231 (M, 100%), 203 (31), 186 (10), 158 (29), 130 (90), 104 (71), 77 (49) and 51 (22).

Flash vacuum pyrolysis (170 mg) (540 °C, 155 °C, 0.05 mmHg, 60 min) gave the oxazole as a straw coloured oil (129 mg, 90%) which was spectroscopically pure.

Ethyl 2,5-dimethyloxazole-4-carboxylate 2 (R^1 = R^3 = Me, R^2 = CO_2Et)

Photolysis (254 nm, acetonitrile, 90 min) of ethyl 2-acetyl-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate (210 mg) gave a product which was chromatographed (dichloromethane–light petroleum, 9:1) to give two fractions which were identified as unreacted starting material (84 mg, 40%) and ethyl 2,5-dimethyloxazole-4-carboxylate (67 mg, 40%) by comparison with authentic samples.[4]

Ethyl 4-methyl-2-phenyloxazole-5-carboxylate 2 (R^1 = Ph, R^2 = Me, R^3 = CO_2Et)

Photolysis (300 nm, acetonitrile, 45 min) of ethyl 2-acetyl-3-methyl-5-oxo-2,5-dihydroisoxazole-4-carboxylate (300 mg) gave a product which was subjected to radial chromatography (diethyl ether–light petroleum, 15:85) to give two fractions. The first fraction was an oil which slowly solidified, mp 44–45 °C and was identified as the title compound (88 mg, 35%)[36] (Found: M^+, 231.0905. Calc. for $C_{13}H_{13}NO_3$: *M*, 231.0895); δ_H 1.43 (3 H, t, *J* 7), 2.56 (3 H, s), 4.42 (2 H, q, *J* 7), 7.50 (3 H, m) and 8.13 (2 H, dd, *J* 7, 2); δ_C 13.5, 14.4, 61.1, 126.4, 127.2, 128.9, 131.5, 137.1, 147.1, 158.9 and 162.2; ν_{max}/cm^{-1} 1716, 1610 and 1543; *m/z* 231 (M, 100%), 203 (30), 158 (29), 130 (90), 104 (71) and 77 (49). The second fraction contained a 1:1 mixture of two compounds which could not be separated or identified.

A mixture of benzamide (200 mg, 1.65 mmol) and ethyl α-chloroacetoacetate (270 mg, 1.65 mmol) was heated at 140 °C for 2 h. The product was purified by radial chromatography (diethyl ether–light petroleum, 15:85) to give the title compound (76 mg, 20%) as a straw coloured oil. The spectral data were identical with those reported above.

Ethyl 2-(pyrrol-2-yl)oxazole-5-carboxylate 4

Photolysis (300 nm, acetonitrile, 1.5 h) of ethyl 5-oxo-2-(pyrrol-2-ylcarbonyl)-2,5-dihydroisoxazole-4-carboxylate **3** (240 mg) gave a product which was purified by radial chromatography (diethyl ether–light petroleum, 1:1) to give two fractions. The first fraction was recrystallised from ethanol–water to give the *title compound* (59 mg, 30%), mp 136–138 °C (Found: M^+, 206.0701. $C_{10}H_{10}N_2O_3$ requires *M*, 206.0692); δ_H 1.40 (3 H, t, *J* 7), 4.40 (2 H, q, *J* 7), 6.34 (1 H, m), 7.00 (2 H, m), 7.76 (1 H, s) and 10.04 (1 H, NH, br s); δ_C 14.3, 61.4, 111.0, 113.1, 119.3, 122.9, 134.9, 140.8, 157.9 and 159.2; ν_{max}/cm^{-1} 3201, 1713, 1611 and 1585; *m/z* 206 (M, 100%), 178 (21), 133 (39), 105 (47), 94 (11) and 78 (19). The second fraction (96 mg, 40%) was identified as unreacted starting material.

Photolysis of the isoxazolone **3** (100 mg) in acetone at 300 nm for 2 h gave the oxazole **4** (25 mg, 30%).

Ethyl 2-(2,5-dimethyloxazol-4-yl)-5-methyloxazole-4-carboxylate 9

Pyrolysis (500 °C, 140 °C, 5×10^{-5} mm) of a 4:1 mixture (270 mg) of *N*- and *O*-acylated derivatives from the reaction of ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate with 2,5-dimethyloxazole-4-carbonyl chloride and the usual work up gave the *title compound* **9** (83 mg, 45%), mp 81–83 °C (Found: M^+, 250.0935. $C_{12}H_{14}N_2O_4$ requires *M*, 250.0954); δ_H 1.40 (3 H, t, *J* 7.12), 2.48 (3 H, s), 2.67 (3 H, s), 2.69 (3 H, s) and 4.39 (2 H, q, *J* 7.12); δ_C 11.7, 12.1, 13.7, 14.3, 60.9, 124.4, 128.5, 150.2,

154.1, 155.5, 160.2 and 162.4; ν_{max}/cm^{-1} 1721, 1652 and 1618; *m/z* 250 (M, 100%), 222 (5), 204 (48), 176 (55), 149 (3), 135 (9), 124 (97) and 97 (8).

Photolysis of the above mixture (145 mg) for 25 min in acetonitrile at 300 nm gave the above oxazole (60 mg, 61%) after radial chromatography (dichloromethane–light petroleum, gradient). The isomeric *ethyl* 2-(2,5-*dimethyloxazol*-4-*yl*)-4-*methyloxazole*-5-*carboxylate* (5 mg, 5%) was also obtained (Found: $M^+ - C_2H_5O$, 205.0637. $C_{10}H_9N_2O_3$ requires *M*, 205.0613); δ_H 1.32 (3 H, t, *J* 7.16), 2.41 (3 H, s), 2.43 (3 H, s), 2.58 (3 H, s) and 4.33 (2 H, q, *J* 7.16); δ_C 11.6, 13.7, 14.1, 22.3, 61.8, 124.9, 128.2, 131.1, 154.1, 158.6, 159.5 and 163.1; *m/z* 251 (M + 1, 66%), 241 (5), 223 (3), 205 (61), 176 (3), 149 (1), 135 (3), 124 (100) and 96 (6).

Ethyl 2-[2-(2,5-dimethyloxazol-4-yl)-5-methyloxazol-4-yl]-5-methyloxazole-4-carboxylate 10

Pyrolysis (590 °C; 100–200 °C gradient 15 °C per 15 min, 10^{-4} mm) of the product (120 mg) obtained from acylation of ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate with the acid chloride derived from hydrolysis of the above ester **9**, resulted in substantial decomposition. After 2 h only a small amount (18 mg) of material had proceeded through the furnace: the remainder had not sublimed. The residue in the sublimation flask was pre-adsorbed onto alumina and eluted with diethyl ether to give a yellow solid, which was triturated with cold diethyl ether and recrystallised from dichloromethane–light petroleum to give the *title compound* as pale yellow needles (10 mg, 9%), mp 162–165 °C (Found: M^+, 331.1142. $C_{16}H_{17}N_3O_5$ requires *M*, 331.1168); δ_H 1.41 (3 H, t, *J* 7.14), 2.49 (3 H, s), 2.70 (3 H, s), 2.71 (3 H, s), 2.77 (3 H, s) and 4.40 (2 H, q, *J* 7.14); δ_C 11.7, 11.9, 12.2, 13.7, 14.4, 160.7, 128.6, 155.81, 154.1, 124.5, 150.1, 154.9, 125.6, 150.1 and 162.4; *m/z* 331 (M, 66%), 285 (7), 257 (45), 205 (14), 187 (4) and 123 (9). The volatile material consisted of numerous unidentified products.

Ethyl 5-methyl-2-(phthalimidomethyl)oxazole-4-carboxylate 12

Photolysis (300 nm, acetonitrile, 2 h) of isoxazolone **13** (310 mg) gave a product which was eluted through a short plug of silica (dichloromethane) and then recrystallised from ethanol–water to give colourless needles (245 mg, 90%) of the *title compound*, mp 166–167 °C (Found: M^+, 314.0888. $C_{16}H_{14}N_2O_5$ requires *M*, 314.0902); δ_H 1.33 (3 H, t, *J* 7), 2.54 (3 H, s), 4.32 (2 H, q, *J* 7), 4.95 (2 H, s), 7.74 (2 H, dd, *J* 5.5, 2.9) and 7.87 (2 H, dd, *J* 5.5, 2.9); δ_C 12.02, 14.27, 34.51, 60.94, 123.67, 127.93, 131.94, 134.32, 156.10, 156.8, 161.9 and 167.1; ν_{max}/cm^{-1} 1716 and 1417; *m/z* 314 (M, 97%), 268 (14), 240 (17), 197 (79), 160 (100), 104 (24), 76 (24) and 43 (50).

Photolysis of **13** (160 mg) at 254 nm for 1 h afforded the title compound (156 mg) in 80% yield.

2-Phenylbenzoxazole

Pyrolysis (595 °C, 150 °C, 0.05 mmHg, 90 min) of *N*-benzoylbenzisoxazolone (200 mg) gave a crude product which was passed through a short plug of silica and recrystallised from ethanol to give the title compound (147 mg, 90%) as white needles, mp 103–105 °C (lit.,[37] mp 102–104 °C) (Found: M^+, 195.0690. Calc. for $C_{13}H_9NO$: *M*, 195.0684); δ_H 7.31–7.35 (2 H, m), 7.48–7.50 (3 H, m), 7.53–7.57 (1 H, m), 7.77–7.81 (1 H, m) and 8.24–8.27 (2 H, m); δ_C 110.5, 119.9, 124.4, 125.0, 127.0, 127.5, 128.8, 131.4, 142.0, 150.6 and 162.9; ν_{max}/cm^{-1} 1618 and 1552; *m/z* 195 (M, 100%), 167 (13), 98 (5), 92 (7), 77 (10), 64 (18) and 63 (21).

2,4-Dimethyloxazole

Pyrolysis (595 °C, 100 °C, 0.05 mmHg, 15 min) of 2-acetyl-3-methylisoxazol-5(2*H*)-one (150 mg) gave the title compound (98 mg, 95%) as an oil, identical with the sample obtained in very poor yield by the method of Oesterreich;[38] δ_H 1.99 (3 H, d, *J* 1.25), 2.29 (3 H, s) and 7.13 (1 H, q, *J* 1.25); δ_C 10.9, 13.4, 133.7, 136.4 and 161.0.

2-Phenyloxazole[39]

Pyrolysis (590 °C, 100 °C, 0.05 mmHg, 30 min) of 2-benzoylisoxazol-5(2*H*)-one (400 mg) gave the title compound as a colourless oil (246 mg, 80%) (Found: M^+, 145.0523. Calc. for C_9H_7NO: *M*, 145.0527); δ_H 7.26 (1 H, d, *J* 0.8), 7.46 (3 H, m), 7.71 (1 H, d, *J* 0.8) and 8.06 (2 H, m); δ_C 126.3, 127.3, 128.2, 128.8, 130.4, 138.6 and 162.0; *m/z* 145 (M, 100%), 122 (42), 117 (53), 105 (55), 90 (92), 77 (51) and 51 (46).

2-Methyl-4,5-diphenyloxazole[40]

Pyrolysis (540 °C, 155 °C, 0.05 mmHg, 60 min) of 2-acetyl-3,4-diphenylisoxazol-5(2*H*)-one (300 mg) gave the title compound (240 mg, 95%), bp 150 °C/1 mmHg, as a straw coloured oil (Found: M^+, 235.1006. Calc. for $C_{16}H_{13}NO$: *M*, 235.0997); δ_H 2.51 (3 H, s), 7.27–7.37 (6 H, m) and 7.55–7.67 (4 H, m); δ_C 13.8, 126.3, 127.7, 127.9, 128.3, 128.4, 128.5, 130.4, 132.1, 135.1, 145.3 and 160.0; ν_{max}/cm^{-1} 1724, 1604 and 1594; *m/z* 235 (M, 67%), 207 (31), 206 (34), 165 (85), 105 (70), 77 (100), 51 (80) and 43 (60).

2,4,5-Triphenyloxazole

Pyrolysis (540 °C, 165 °C, 0.05 mmHg, 90 min) of 2-benzoyl-3,4-diphenylisoxazol-5(2*H*)-one (280 mg) gave a solid (171 mg, 70%), mp 109–111 °C (lit.,[41] mp 116 °C) which was identified by comparison with an authentic sample (Found: M^+, 297.1158. Calc. for $C_{21}H_{15}NO$: *M*, 297.1153); δ_H 7.35–7.57 (9 H, m), 7.77–7.78 (4 H, m) and 8.20 (2 H, m); δ_C 126.5, 126.6, 127.4, 128.2, 128.2, 128.6, 128.6, 128.7, 128.8, 129.0, 130.4, 132.5, 136.7, 145.5 and 160.1; ν_{max}/cm^{-1} 769 and 694; *m/z* 297 (M, 100%), 269 (14) and 165 (55).

2-Trifluoromethyl-4-phenyloxazole

Pyrolysis (590 °C, 100 °C, 0.05 mmHg, 60 min) of 3-phenyl-2-trifluoroacetylisoxazol-5(2*H*)-one (170 mg) appeared to decompose the material and after 1 h no more material distilled into the furnace. The oily *title product* (70 mg, 50%) was isolated from the cold trap and solidified on standing, mp 46–48 °C (Found: M^+, 213.0401. $C_{10}H_6F_3NO$ requires *M*, 213.0401); δ_H 7.39–7.78 (5 H, m) and 8.03 (1 H, s); δ_C 113.5 (q, *J* 177, CF_3), 125.8, 129.0, 129.1, 132.2, 136.6, 142.0 and 150.8; ν_{max}/cm^{-1} 1380 and 1245; *m/z* 213 (M, 100%), 185 (16), 103 (15), 90 (57) and 63 (26).

Pyrolysis of 3-phenyl-2-(pyrrol-2-ylcarbonyl)isoxazol-5(2*H*)-one 1 (R^1 = pyrrol-2-yl, R^2 = Ph, R^3 = H)

Pyrolysis of the reactant (200 mg) (540 °C, 150 °C, 0.05 mmHg, 1h) appeared to decompose the sample rapidly and only a small amount of material (*ca.* 10–20 mg) sublimed into the furnace. The product collected was *N*-phenylpyrrole-2-carboxamide (15 mg, 10%), mp 152–154 °C (lit.,[42] 153–154 °C); δ_H 6.48 (1 H, t, *J* 3.5), 7.21–7.41 (6 H, m) and 7.72 (1 H, dd, *J* 3.2, 1.6); ν_{max}/cm^{-1} 3118, 1698 and 1557; *m/z* 186 (M, 100%), 158 (11), 130 (22), 93 (46) and 64 (30).

Ethyl 2-dichloromethyl-5-methyloxazole-4-carboxylate 2 (R^1 = $CHCl_2$, R^2 = CO_2Et, R^3 = Me)

Pyrolysis (490 °C, 150 °C, 0.1 mmHg) of ethyl 2-dichloromethyl-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate (217 mg) gave a crude product which was subjected to radial chromatography (diethyl ether–light petroleum, 1:3) affording the *title compound* (33 mg, 18%) as a pale yellow oil (Found: M^+, 236.9960; 238.9938. $C_8H_9Cl_2NO_3$ requires *M*, 236.9959; 238.9930); δ_H 1.40 (3 H, t, *J* 7.14), 2.71 (3 H, s), 4.40 (2 H, q, *J* 7.14) and 6.71 (1 H, s); δ_C 12.2, 14.3, 59.9, 61.3, 127.9, 156.1, 158.3 and 161.4; ν_{max}/cm^{-1} 1722 and 1614; *m/z* 237 (M, 45%), 209 (16), 202 (100), 191 (66), 174 (46), 165 (24) and 156 (34).

Diethyl 5-methyloxazole-2,4-dicarboxylate 19 (R = Et)
Pyrolysis (490 °C, 150 °C, 0.1 mmHg) of a 9:1 mixture (240 mg) of the *N*- and *O*-acylated products from ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate and ethyl oxalyl chloride gave a pale yellow oil which was subjected to silica radial chromatography (diethyl ether–light petroleum, 1:4) to give two products. The first was the title compound (90 mg, 50% based on *N*-acylated reactant) obtained as a *white solid*, mp 63–65 °C (bp 120 °C/0.1 mmHg) (Found: C, 53.2; H, 6.0; N, 6.3%; M^+, 227.0798. $C_{10}H_{13}NO_5$ requires C, 52.9; H, 5.8; N, 6.2%; *M*, 227.0794); δ_H 1.40 (3 H, t, *J* 7.14), 1.43 (3 H, t, *J* 7.14), 2.74 (3 H, s), 4.41 (2 H, q, *J* 7.14) and 4.48 (2 H, q, *J* 7.14); δ_C 12.3, 14.1, 14.3, 61.3, 62.9, 129.5, 150.1, 155.3, 159.1 and 161.3; ν_{max}/cm^{-1} 1734, 1718, 1595 and 1550; *m/z* 227 (M, 44%), 199 (14), 182 (25), 171 (20), 155 (21), 143 21), 127 (16) and 109 (33).

The second fraction was an oil, identified by its spectral properties as *diethyl* 4-*methyloxazole*-2,5-*dicarboxylate* (7 mg, 4%); δ_H 1.436 (3 H, t, *J* 7.14), 1.440 (3 H, t, *J* 7.14), 2.51 (3 H, s), 4.46 (2 H, q, *J* 7.14) and 4.47 (2 H, q, *J* 7.14); ν_{max}/cm^{-1} 1738, 1732 and 1615; *m/z* 227 (M, 3%), 182 (30), 171 (14), 154 (20), 143 (10), 125 (31), 110 (25) and 99 (23).

Ethyl 2-methoxycarbonyl-5-methyloxazole-4-carboxylate 19 (R = Me)
Pyrolysis (490 °C, 150 °C, 0.01 mmHg) of a 9:1 mixture (309 mg) of *N*- and *O*-acyl derivatives from ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate and methyl oxalyl chloride gave an oil which was subjected to silica radial chromatography (dichloromethane–light petroleum, gradient) to give two fractions. The first was the *title compound* (106 mg, 46% based on *N*-acylated reactant) obtained as a transparent solid after distillation, mp 92–94 °C (bp 140–150 °C/0.2 mmHg) (Found: C, 50.7; H, 5.1; N, 6.2. $C_9H_{11}NO_5$ requires C, 50.7; H, 5.2; N, 6.6%); δ_H 1.41 (3 H, t, *J* 7.14), 2.75 (3 H, s), 4.01 (3 H, s) and 4.42 (2 H, q, *J* 7.14); δ_C 12.2, 14.1, 53.1, 61.2, 129.4, 149.6, 155.5, 159.1 and 161.1; ν_{max}/cm^{-1} 1745, 1707 and 1598; *m/z* 213 (M, 21%), 185 (7), 167 (34), 141 (11) and 129 (4).

The second fraction was characterised as ethyl 5-methyl-2-oxo-2,3-dihydrooxazole-4-carboxylate **20** (6 mg, 3% based on *N*-acylated reactant) obtained as a *white solid*, mp 116–120 °C after recrystallisation from dichloromethane–light petroleum (Found: M^+, 171.0532. $C_7H_9NO_4$ requires *M*, 171.0532); δ_H 1.36 (3 H, t, *J* 7.13), 2.40 (3 H, s), 4.34 (2 H, q, *J* 7.13) and 8.4 (1 H, br s); δ_C 12.0, 14.3, 61.6, 114.2, 146.6, 153.1 and 158.9; *m/z* 171 (M, 22%), 143 (24), 125 (45), 113 (3), 83 (18) and 69 (100).

Ethyl 2-methoxy-5-methyloxazole-4-carboxylate 22 (R = Me)
Isoxazolone **21** (R = Me) (190 mg) was subjected to flash vacuum pyrolysis (490 °C, 150 °C, 0.1 mmHg). The crude product, collected in both the exit tube and the cold trap, was subjected to radial chromatography (diethyl ether–light petroleum, 1:3) affording the *title compound* (101 mg, 66%) as a colourless oil (Found: M^+, 185.0688. $C_8H_{11}NO_4$ requires *M*, 185.0688); δ_H 1.38 (3 H, t, *J* 7.13), 2.53 (3 H, s), 4.11 (3 H, s) and 4.38 (2 H, q, *J* 7.13); δ_C 11.7, 14.2, 59.3, 60.8, 126.4, 151.4, 160.4 and 162.4; ν_{max}/cm^{-1} 1732, 1651 and 1615; *m/z* 185 (M, 33%), 157 (9), 139 (61), 125 (26), 111 (13) and 84 (6).

A trace of ethyl 2-methoxy-4-methyloxazole-5-carboxylate (<1%) was also obtained.

Ethyl 2-ethoxy-5-methyloxazole-4-carboxylate 22 (R = Et)
Isoxazolone **21** (R = Et) (220 mg) was subjected to flash vacuum pyrolysis (490 °C, 150 °C, 0.1 mmHg). Material collected in the cold trap was subjected to radial chromatography (diethyl ether–light petroleum, 2:3) affording the title compound (56 mg, 31%) as a *colourless oil* (Found: M^+, 199.0847. $C_9H_{13}NO_4$ requires *M*, 199.0845); δ_H 1.37 (3 H, t, *J* 7.2), 1.42 (3 H, t, *J* 6.98), 2.52 (3 H, s), 4.37 (2 H, q, *J* 7.2) and 4.50 (2 H, q, *J* 6.98); δ_C 11.7, 14.2, 14.3, 60.8, 67.8, 126.4, 151.1, 152.6 and 162.6; ν_{max}/cm^{-1} 1732, 1713, 1644 and 1606; *m/z* 199 (M, 23%), 171 (30), 154 (12), 143 (14), 125 (100) and 97 (9).

The second fraction was *ethyl* 2-*ethoxy*-4-*methyloxazole*-5-*carboxylate* (13 mg, 7%). (Found: M^+, 199.0848. $C_9H_{13}NO_4$ requires *M*, 199.0845); δ_H 1.33 (3 H, t, *J* 7.05), 1.39 (3 H, t, *J* 6.98), 2.47 (3 H, s), 4.14 (2 H, q, *J* 7.05) and 4.25 (2 H, q, *J* 6.98).

The material collected in the exit tube was passed through a silica plug (methanol–ethyl acetate) affording ethyl 5-methyl-2-oxo-2,3-dihydrooxazole-4-carboxylate **20** (76 mg, 49%) as a white solid, identical with that characterised previously.

Ethyl 5-methyl-2-phenoxyoxazole-4-carboxylate 22 (R = Ph)
Isoxazolone (115 mg) **21** (R = Ph) was subjected to flash vacuum pyrolysis (490 °C, 150–200 °C, 0.1 mmHg). The crude material, collected from both the exit tube and the cold trap, was subjected to radial chromatography (diethyl ether–light petroleum, 2:3) affording the *title compound* (62 mg, 64%) as a colourless oil (Found: M^+, 247.0842. $C_{13}H_{13}NO_4$ requires *M*, 247.0845); δ_H 1.36 (3 H, t, *J* 7.13), 2.58 (3 H, s), 4.34 (2 H, q, *J* 7.13), 7.19–7.26 (1 H, m) and 7.31–7.43 (4 H, m); δ_C 11.7, 14.1, 60.8, 119.2, 125.7, 126.6, 129.8, 151.9, 153.2, 157.5 and 162.2; ν_{max}/cm^{-1} 1732, 1634, 1581 and 1493; *m/z* 247 (M, 31%), 201 (10), 126 (8), 104 (12) and 94 (100).

Ethyl 2-(2,5-diphenyloxazol-4-yl)-5-methyloxazole-4-carboxylate 23
Pyrolysis (490 °C, 280 °C, 0.1 mmHg) of a 76:24 mixture (185 mg) of the *N*- and *O*-acylated products derived from the reaction of ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate with 2,5-diphenyloxazole-4-carbonyl chloride and the usual work up gave the *title compound* (40 mg, 32%), mp 136–139 °C (Found: C, 70.7; H, 4.8; N, 7.4%; M^+, 374.1262. $C_{22}H_{18}N_2O_4$ requires C, 70.6; H, 4.9; N, 7.5%; *M*, 374.1267); δ_H 1.43 (3 H, t, *J* 7.14), 2.75 (3 H, s), 4.41 (2 H, q, *J* 7.14), 7.4–7.6 (6 H, m), 8.1–8.2 (2 H, m) and 8.3–8.4 (2 H, m); δ_C 12.2, 14.3, 60.9, 124.9, 126.4, 126.8, 127.1, 127.4, 128.6, 128.7, 128.8, 129.8, 131.0, 150.4, 153.8, 156.4, 160.3 and 162.2; ν_{max} 1772, 1712, 1652 and 1627; *m/z* 374 (M, 4%), 221 (9), 178 (20), 167 (14), 149 (24), 131 (5), 122 (37) and 105 (100).

Photolysis of the above mixture (135 mg) for 25 min in benzene at 300 nm gave the oxazole (24 mg) in 26% yield after radial chromatography (dichloromethane–light petroleum, gradient): the isomeric oxazole was obtained in trace amounts.

4,4′-Bis(ethoxycarbonyl)-5,5′-dimethyl-2,2′-bi(oxazole) 24
Pyrolysis (540 °C, 250 °C, 0.01 mmHg) of *N*,*N*′-bis(3-ethoxycarbonyl-4-methyl-5-oxo-2,5-dihydoisoxazol-2-yl)oxamide (230 mg) resulted in the material decomposing: only a small amount of solid material was collected in the exit tube. This material was passed through a silica plug (diethyl ether) and the residue triturated with cold diethyl ether to give the title compound as a white solid (16 mg, 8%), mp 208–209 °C (Found: M^+, 308.0998. $C_{14}H_{16}N_2O_6$ requires *M*, 308.1008); δ_H 1.41 (6 H, t, *J* 7.14), 2.74 (6 H, s) and 4.43 (4 H, q, *J* 7.14); δ_C 12.3, 14.4, 61.4, 129.4, 148.3, 158.3 and 161.5; ν_{max}/cm^{-1} 1717, 1607 and 1501; *m/z* 308 (M, 60%), 262 (46), 235 (26), 183 (62), 164 (9) and 155 (34).

2,6-Bis(4-ethoxycarbonyl-5-methyloxazol-2-yl)pyridine 25
Injection flash vacuum pyrolysis (thin bore needle) (490 °C, 0.01 mmHg) of a 8:1:1 mixture of bis-*N*-, bis-*O*- and *N*,*O*-acylated compounds (111 mg) from ethyl 4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate and pyridine-2,6-dicarbonyl chloride, dissolved in chlorobenzene (0.5 ml) gave a product (79 mg) which decomposed substantially on chromatography. Use of a short plug of silica treated with triethylamine allowed the isolation of pale yellow crystals, mp 197–199 °C (dichloromethane–light petroleum), but an analytically pure sample could not be obtained, δ_H 1.44 (6 H, t, *J* 7.14), 2.80 (6 H, s), 4.45 (4 H, q, *J* 7.14), 7.98 (1 H, dd, *J* 8.6, 7.65) and 8.34 (2 H, d, *J* 8.6); δ_C 12.5,

14.4, 61.3, 123.7, 129.4, 138.2, 145.6, 158.0 and 162.1; ν_{max}/cm^{-1} 1715, 1609, 1592 and 1551; *m/z* 385 (M, 100%), 341 (4), 259 (13), 232 (94), 204 (12), 186 (28) and 149 (10).

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