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Unusual Rearrangements of 2-Aroylimidoyl-2-phenylethylidene to 2,5-Disubstituted Oxazoles#

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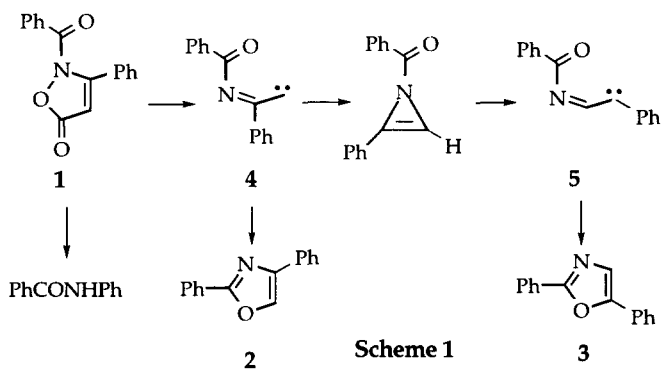
Absract: Flash vacuum pyrolysis of 2-aroyl-3-phenylisoxazol-5(2H)-ones leads to good yields of 2-aryl-4-phenyloxazoles, and smaller quantities of 2-aryl-5-phenyloxazoles and 5-aryl-2-phenyloxazoles. The mechanism of formation of the 2,5-disubstituted products has been investigated by ^{13}C and substituent labelling, and a non-statistical breakdown of a symmetrical intermediate is invoked to rationalise the product formation.

During a recent investigation[1,2] of the synthesis of oxazoles from N-acylisoxazol-5(2H)-ones by flash vacuum pyrolysis (FVP), it was noted that a number of by-products were obtained, particularly if the temperature was raised. In particular, when 2-benzoyl-3-phenylisoxazolone **1** was heated at 595°C, both benzanilide (15%) and 2,5-diphenyloxazole **3** (10%) were isolated in addition to the expected 2,4-diphenyloxazole **2** (60%) . The yield of 2,4-diphenyloxazole **2** was unusually low compared to the majority of similar examples reported and some effort was made to identify and rationalise the by-products. The origin of the benzanilide will be the subject of a separate study. Our initial explanation for the formation of the unexpected oxazole **3** involved a rearrangement of the carbene **4** to the more stable carbene **5** through an azirine intermediate, by analogy with rearrangements frequently postulated for carbenes generated from triazoles under photochemical [3] or thermal [4] conditions (Scheme 1).



Scheme 1

Dedicated to the memory of Derek H. R. Barton, who would have enjoyed the mechanistic problems contained in this communication.

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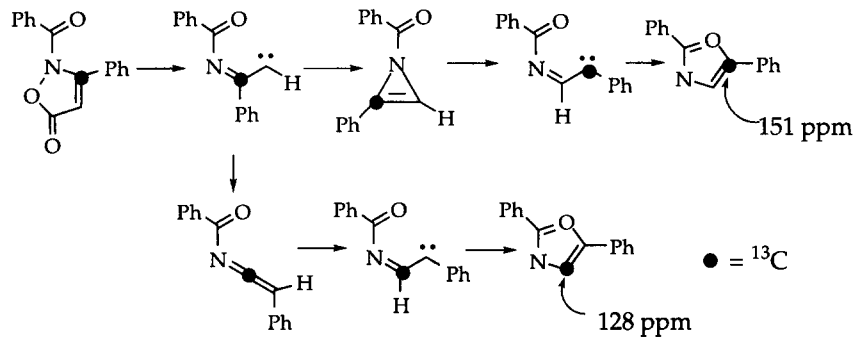
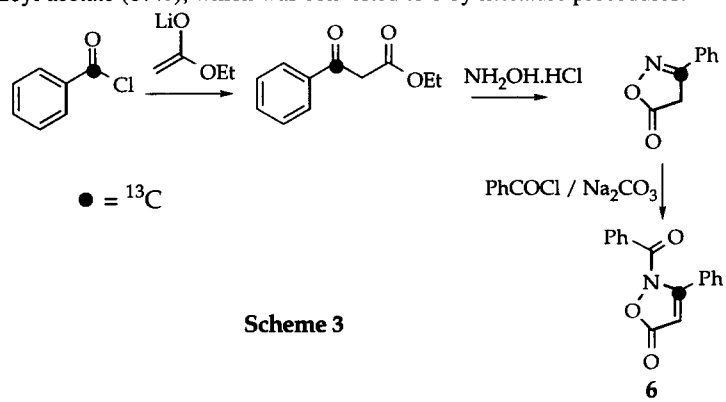
With few exceptions,[2,5] carbenes generated from isoxazolones have not undergone skeletal rearrangement, an observation which has been attributed to their low ground state energy compared to the same carbene generated from triazoles. In addition to the mechanism presented above, two other pathways for the generation of the 2,5-disubstituted oxazole appeared possible. The first was a thermal rearrangement of the first formed 2,4-diphenyloxazole. Although there are a small number of literature reports of photochemical isomerisation of oxazoles,[3,6] there are few concerning their thermal reactions, and no mechanism for this transformation has been proposed. The second possibility involved a Wolff rearrangement followed by a retro Wolff rearangement on the ketenimine.[3,7] We reasoned that these pathways could readily be distinguished by ^{13}C labelling (Scheme 2).



Scheme 2

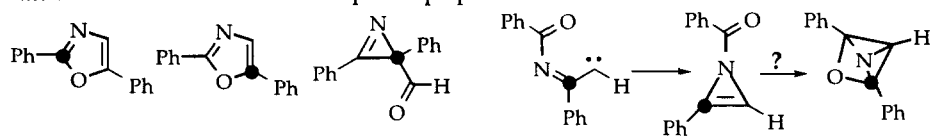
It was first determined that oxazole **2** was stable under the FVP conditions, and did not interconvert with isomer **3**. As the temperature was increased to 750°C, decomposition of **2** occurred, but again **3** was not among the products. Accordingly, the ^{13}C labelled material **6** was synthesised from benzoic acid(carboxy-^{13}C) as shown in Scheme 3, in which benzoyl chloride was reacted with the lithium enolate of ethyl acetate [8] to give ethyl (3-^{13}C-)benzoyl acetate (87%), which was converted to **6** by literature procedures.[9]



Scheme 3

6

Pyrolysis of 3-^{13}C-2-benzoyl-3-phenylisoxazolone **6** was carried out in the range 590°-750°C, but there was only a slight increase in the proportion of the "rearranged" oxazole **3** with increased temperature. The products from a 650°C pyrolysis were separated chromatographically, and the major product **2** was confirmed to be labelled only at C4, as expected from Scheme 1. Assignment of the label to C4 was not only on the basis of the enhanced carbon singlet at 142.2 ppm, but also by the expected splitting of the oxazole and phenyl resonances.The spectral data of the minor isomer **3** showed there was no enhanced signal at C4, ruling out the Wolff rearrangement pathway of Scheme 2. More importantly however, the oxazole was observed to be labelled at *two* positions, not only at C-5 in **3b** as anticipated in Scheme 2 (151.45ppm), but also at C-2 in **3a** (161.37 ppm). Furthermore, the pathway leading to the unexpected **3a** predominated by a factor of 3.2 to 1. Although Maeda and Kojima [6] reported the photochemical conversion of 2,5-diphenyloxazole to 2,4-diphenyloxazole in 4% yield , they further noted that the reverse reaction did not occur. We confirmed that pyrolysis of 4-^{13}C-2,4-diphenyloxazole did not produce any 2,5-diphenyloxazole (gc/ms analysis), and the recovered starting material remained labelled at C4 only. A very small amount of an isomeric compound was detectable in the pyrolysate by gc / ms, exhibiting a facile loss of CO under electron impact, and is tentatively assigned the structure **7** on the basis of its spectral properties.



3a **3b** **7** **4** **9** **8**

Scheme 4

The formation of the major isotopomer **3a** is difficult to rationalise. One possibility involves the formation of the tricyclic intermediate **8**, which would require a [2+2] intramolecular cycloaddition within the 1H-azirene **9**, which would be expected as a minor pathway from the carbene **4** (Scheme 4) . The closely related carbocyclic species tricyclo[1.1.1.0^{4,5}]pentane has been known for some time,[10] and formally antiaromatic systems such as **9** are well documented.[3,4,11] However, concerted rearrangement of **4** to **8** can also be imagined. Hartree-Fock *ab initio* geometry optimisations, in conjunction with the density functional (B3LYP) single point energy calculations using the 6-31G(d) basis set ,[12,13] suggest that the nitrogen in **4** is more electron rich than the carbonyl O, favouring formation of **9**. While the ground state of **4** is predicted to be 2.1kcal.mol^{-1} higher in energy than **8**, the azirine **9** is considerably more stable (ΔE **4** to **9**, - 24.3 kcal.mol^{-1}). This difference is such that vibrationally excited states would need to be involved, and this pathway would be expected to be most significant at higher temperatures. While the proposed intermediate **8** accounts for the

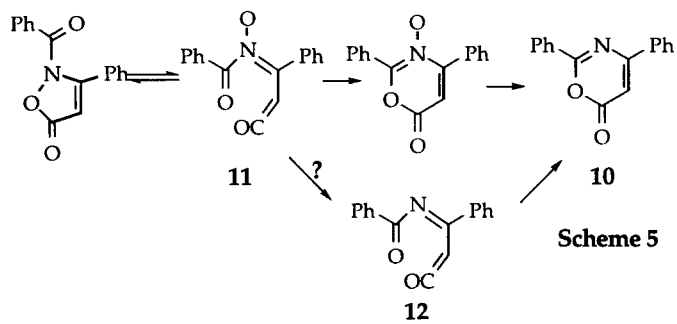
formation of **3a** and **3b**, its symmetry does not accord with the observed product ratio, favouring **3a** over **3b** by a factor of 3.2:1. Classical transition state theory requires the products to arise by two different pathways, with different activation barriers.

When the pyrolysis of 2-benzoyl-3-^{13}C-3-phenylisoxazol-5(2H)-one **6** was repeated at 750°C, there was a small increase in the proportion of 2,5-diphenyloxazole relative to 2,4-diphenyloxazole, but the isotope distribution within the 2,5-diphenyloxazole was unchanged from that observed at 650°C. Such a maintenance of isotope distribution is inconsistent with the occurrence of two reaction pathways. Recent developments in molecular dynamics theory,[14-15] as detailed by Carpenter, provide a different interpretation. Provided that a significant fraction of the reacting population remains in the the vicinity of the transition structure for an exceptionally short time, of the order of several molecular vibrations, and possesses an unsymmetrical distribution of rotational and vibrational energies which influences the nature of orbital overlap, it is said to traverse the potential energy surface in a ballistic trajectory. Compound **8** may be a high energy transition structure, and the short life time portion of the population reacts in a trajectory that produces exclusively 2-^{13}C-2,5-diphenyloxazole **3a**.

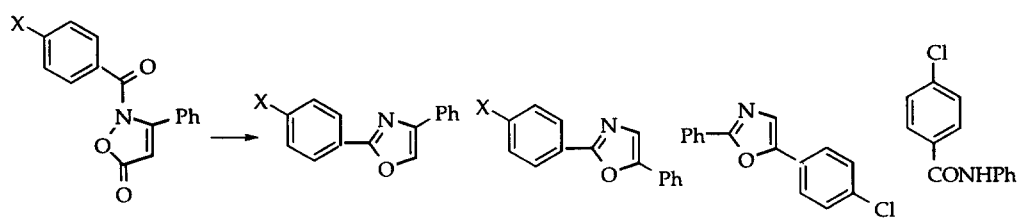
A further consequence of this model is that dramatic changes in the reaction temperature are predicted to have little or no effect on the product ratio. Carpenter [14,15] has recently pointed out that such reactions can be diverted from ballistic trajectories by intermolecular collisions, which would allow randomisation of vibrational and rotational motion to produce the statistical product distribution expected from classical theory. In the current work it was not possible to significantly vary the collision rate by increasing the pressure, and hence pyrolysis was carried out in the condensed phase as a melt. After 15 minutes at 200°C, the pyrolysate from **6** was analysed by gc/ms and ^{13}C nmr spectroscopy. The oxazoles **2** and **3** were shown to be present in addition to 4-^{13}C-2,4-diphenyl-1,3-oxazine-6-one, **10**. Most importantly, the oxazole **3** was totally in the form **3b**. It appears that the melt strategy diverted the reaction through a low energy pathway, probably leading to **2** and **3** from the ground state carbenes as shown in Scheme 1. The relative energy of the azirene **9** is predicted to be only 1.7 kcal.mol-1 lower than that of the rearranged carbene **5**, which leads to **3**.

Although peripheral to the main issue of this communication, the origin of the oxazine **10** merits comment. We envisage it to arise from the nitronoketene isomer **11** of the isoxazolone (Scheme 5),[16] although the nature of the reduction of the N-oxide is not understood. We have noted a similar reaction pathway on another occasion.[17] Mc Nab[18] has recently reported that the cyclisation of N-acylimidoylketenes under FVP conditions gives 1,3-oxazines in high yields, and it may be that the reduction of the nitrone to the species **12** in the condensed phase is the important step in this pathway.

Support for the general rearrangement pathways observed above was obtained from the products of FVP of the chlorinated and methoxylated analogues **13** and **14**. The pyrolysis products of **13** at 500°C were analysed by gc/ms, and then isolated and characterised. The products isolated were the expected 2,4-disubstituted oxazole **15** and the isomeric 2,5-disubstituted oxazoles **16** and **17**. The fourth product was the chlorobenzanilide **18** (Scheme 6). As observed with the ^{13}C labelled materials, only the 2,5-disubstituted oxazoles had undergone scrambling. The isoxazolone **14** gave only a single product, the expected 2,4-disubstituted oxazole **19**. While we have favoured a pathway for the thermal rearrangements involving unimolecular reactions leading to tricyclic intermediates similar to **8**, it was possible that the reactions were a consequence of the presence of acidic sites on the silica packing used in our FVP experiments. However, when **13** was subjected to FVP at 550°C in an empty silica tube, the same three oxazoles as above were obtained; the major product was **15** (95%) , with essentially equal amounts (ca 2%) of the rearranged oxazoles, **16** and **17**. The difference in product ratio is the expected outcome of an effectively lower pyrolysis temperature. In addition, independent pyrolysis of **16** at 500°C resulted in no change; in particular, there was no formation of **17**.

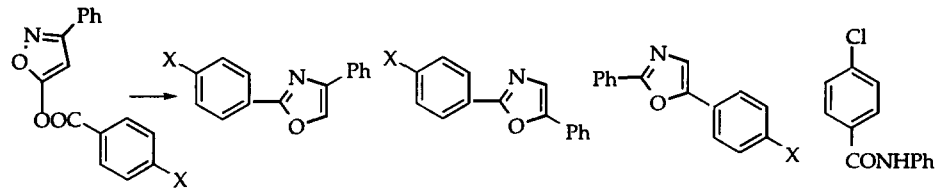


Scheme 5



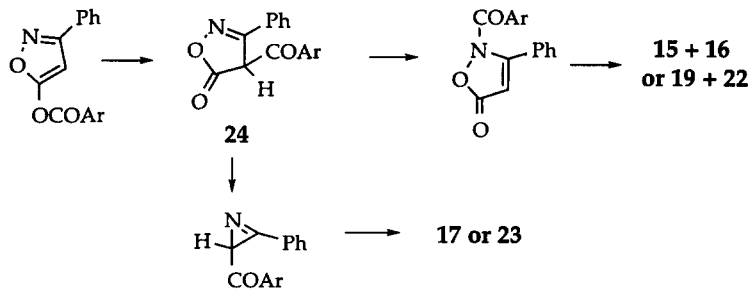
Scheme 6

In the preparation of the N-acylated materials **13** and **14**, considerable amounts of the O-acylated isoxazoles **20** and **21** were obtained.[9] In the hope that FVP of these compounds would involve prior O- to N-acyl group transfer (Scheme 8), each was subjected to FVP at 500°C. The results were surprising (Scheme 7). Isoxazole **20** gave the products **15-18**, and in this instance, the methoxylated isoxazole also gave the rearranged isomeric 2,5-disubstituted oxazoles **22** and **23**. However, since the "unrearranged" oxazoles **15** and **19** were not the major products in these experiments, it is clear that the O-aroylisoxazoles do not undergo complete isomeristion to the N-aroylisoxazolones before loss of CO_2. It is tempting to suggest that the observed products arise partly from decomposition of the N-acylisoxazolone, and partly from the decomposition of the presumed intermediate, the 4-acyl derivative **24** (Scheme 8).



20, X = Cl **15**, X = Cl; 14% **16**, X = Cl; 16% **17**, X = Cl; 9% **18**; 38%
21, X = OMe **19**, X = OMe; 28% **22**, X = OMe; 24% **23**, X = OMe; 24%

Scheme 7



Scheme 8

In conclusion, while it is clearly a general phenomenon that the minor pathway for the thermal decomposition of 2-aroyl-3-phenylisoxazolones involves formation of 2,5-disubstituted oxazoles in which the aryl groups become scrambled, the mechanism of the process is less clear and merits further investigation.

EXPERIMENTAL

Proton (^1H) and Carbon (^{13}C) nuclear magnetic resonance (nmr) spectra were recorded using a Varian Gemini Spectrometer, at 300 MHz and 75.5 MHz respectively, in deuteriochloroform ($CDCl_3$), unless otherwise stated. Infrared spectra were recorded on a Perkin Elmer 1600 FTIR spectrometer; solids were

analysed as nujol mulls, and liquids as films . High resolution mass spectra were recorded on a Kratos MS25RF spectrometer. Melting points were determined on a Reichert hot-stage apparatus and remain uncorrected. Radial chromatography was performed with silica gel 60 PF 254 coated glass rotors using a Chromatotron (model 7924T). Gc / ms analysis was performed on a Varian Saturn 4D instrument, using a 5% phenylmethyl polysiloxane column (30 m, 0.25 mm ID, 0.25 mm thickness). Molecular modelling calculations were carried out using Spartan interfaced to Gaussian 94, Revision D.4,[12] on a IRIX64 Silicon Graphics Indigo workstation. *Ab initio* ground state geometries were calculated with Hartree-Fock methods using the 3-21G basis set and *ab initio* ground state single point energies using the 6-31G(d) (B3LYP) basis set. Flash vacuum pyrolysis was carried out by slowly subliming the substrate through a silica tube (400 mm x 25 mm, packed with silica chips and heated to the quoted temperature) under reduced pressure (0.01 mmHg). The products were collected in a liquid nitrogen cold trap, and analysed by gc / ms, followed by chromatographic isolation. Microanalyses were performed by Chemical and Micro Analytical Services, Melbourne.

Ethyl Benzoyl-(3-^{13}C) acetate

Benzoic-(*carboxy-*^{13}C) acid (1.0 g, 8.12 mmol) was converted to the acid chloride (95%) with thionyl chloride, and then to ethyl benzoyl-(3-^{13}C) acetate (87%) by the procedure of Rathke.[8]

3-^{13}C-3-Phenylisoxazol-5(4H)-one

Ethyl benzoyl-(3-^{13}C) acetate (734 mg, 3.80 mmol) and hydroxylamine hydrochloride (800 mg, 11.5 mmol) were heated in water (4 ml) at 100°C for 5 min. Ethanol (4.5 ml) was added and heating continued for 30 min. The mixture was cooled and filtered to provide the desired product (402 mg, 66%) as large colourless needles, mp. 145-148°C (lit .[19] mp. 150-152°C). ^{1}H NMR δ : 3.81 (d, J 5.4 Hz, 2H); 7. 50 (m, 3H); 7.68(m, 2H). ^{13}C NMR δ : 34.0 (d, J 41.7 Hz, CH_2); 126.6 (d, J 2.3 Hz, CH) ; 127.6 (d, J 62.8 Hz, C) ; 129.2 (d, J 4.7 Hz, CH); 132.2, CH ; 163.1, C3* ; 174.7, CO. HRMS Calc. for $C_8{}^{13}CH_7NO_2$ 162.0510, found 162.0507 .

2-Benzoyl-3-^{13}C-3-phenylisoxazol-5(2H)-one 6

The 3-^{13}C-3-phenylisoxazol-5(4H)-one (350 mg, 2.16 mmol) was benzoylated as described in the literature, [9] to give 35% of the title compound, mp 160°C (lit. 158-160°C), in addition to unreacted starting material (132 mg, 32%). ^{13}C NMR δ : 96.9 (d, J 71 Hz, C4); 127.9 (d, J 2.9 Hz, CH); 128.2, C ; 128.6,

CH ; 128.8 (d, J 4.9 Hz, CH) ; 130.5, CH ; 130.8, C ; 131.7, CH ; 134.0, CH ; 163.4, C3* ; 164.4, CO ; 166.9, CO. HRMS Calc. for $C_{15}{}^{13}CH_{11}NO_3$ 266.0772, found 266.0763.

Pyrolysis of 2-Benzoyl-3-^{13}C-3-phenylisoxazol-5(2H)-one

(i) 2-Benzoyl-3-^{13}C-3-phenylisoxazol-5(2H)-one (67 mg, 0.25 mmol) was pyrolysed (650°C, 100°C, 0.1 mmHg) as described above. Analysis by gc / ms confirmed the product (54.7 mg) to contain only 3 significant components : N-phenylbenzamide, ^{13}C enriched 2,4-diphenyloxazole and ^{13}C enriched 2,5-diphenyloxazole . The mixture was separated by radial chromatography, affording 4-^{13}C-2,4-diphenyloxazole, mp 101°C (24 mg, 43%), and a mixture of 2-^{13}C-2,5-diphenyloxazole and 5-^{13}C-2,5-diphenyloxazole, mp 70-72°C (4 mg, 7%), present in a ratio of 3:1, and N-phenylbenzamide, mp 157°C (8%).

4-^{13}C-2,4-diphenyloxazole : ^{13}C NMR δ : 125.8 (d, J 2.3 Hz, CH) ; 126.6, CH ; 127.6 (d, J 3.9 Hz, C); 128.2 (d, J 1.1 Hz, CH) ; 128.9 (d, J 4.6 Hz, CH) ; 128.9, CH ; 142.2, C4* ; 162.1, C2. IR ν_{max} (neat): 1551, 1483 ,1445, 1336, 1122, 1067, 928 cm^{-1}. HRMS Calc. for $C_{14}{}^{13}CH_{11}NO$ 222.0874, found 222.0871.

2-^{13}C-2,5-diphenyloxazole and 5-^{13}C-2,5-diphenyloxazole: ^{13}C NMR δ: 123.5 (d, J 3.5 Hz, CH) ; 124.3, CH ; 126.4 (d, J 2.1 Hz, CH) ; 127.6, C ; 128.1, C ; 128.6, CH ; 129.0, CH ; 129.0 (d, J 5.1 Hz, CH) ; 129.1, CH ; 130.5, CH ; 151.4, C5* ; 161.4, C2*. Doublets around 127.6 and 128.1 were not detectable above baseline noise. HRMS Calc. for $C_{14}{}^{13}CH_{11}NO$ 222.0874, found 222.0874.

(ii) Isoxazolone **6** (22 mg, 0.08 mmol) was pyrolysed (750°C,100°C, 0.1 mmHg) as above and led to an increase in the ratio of 2,5-diphenyloxazole to 2,4-diphenyloxazole compared to that observed at 650°C . ^{13}C nmr analysis of the crude pyrolysate (13 mg) showed the distribution of the ^{13}C label within the 2,5-diphenyloxazole to be identical to that observed at 650°C.

iii) Isoxazolone **6** (49 mg, 0.18 mmol) was heated neat at 200° for 15 minutes under nitrogen. Gc / ms analysis of the product (49 mg) indicated the presence of both 2,4-diphenyloxazole and 2,5-diphenyloxazole, but the major product was 4-^{13}C-2,4-diphenyl-1,3-oxazin-6-one. ^{13}C nmr analysis showed the isotope label to be absent from carbon 2 of the 2,5-diphenyloxazole. Radial chromatography afforded the oxazinone as a pale brown crystalline solid (5.0 mg, 11%), the bulk of the material being unidentified.

4-^{13}C-2,4-diphenyl-1,3-oxazin-6-one : ^{1}H NMR δ : 6.63 (d, J 1.5 Hz, 1H); 7.56 (bm, 6H); 8.13 (m, 2H); 8.38 (d, J 7.5 Hz, 2H). ^{13}C NMR δ: 162.0. No other signals were identifiable. IR ν_{max} (neat): 1750, 1605, 1572 cm^{-1}. Mass Spectrum m/z : 251 (M+1, 3%), 250 (8), 223 (8), 222 (49), 166 (25), 165 (21), 123 (10),

122 (13), 121 (27), 116 (13), 106 (36), 105 (58), 90 (19), 77(100), 62 (17), 51 (44). HRMS Calc. for $C_{15}{}^{13}CH_{11}NO_2$ 250.0823, found 250.0818.

Pyrolysis of 4-^{13}C-2,4-Diphenyloxazole

4-^{13}C-2,4-Diphenyloxazole (17.6 mg, 0.085 mmol) was pyrolysed (650°C, 80°C, 0.1 mmHg) as described above. The product (17.5 mg) was found to contain unchanged 4-^{13}C-2,4-diphenyloxazole and a trace amount of a more volatile compound of the same mass, tentatively assigned as 2,3-diphenyl-2H-azirine-2-carbaldehyde.The prominant mass spectral breakdown was M-28.

Reaction of 3-Phenylisoxazol-5(4H)one with Benzoyl Chlorides

(i) The isoxazolone (1.5 g) was stirred at 0°C with 4-chlorobenzoyl chloride (4ml) in 10% aqueous Na_2CO_3 (100 ml) for 30 min, with addition of further acid chloride (0.5 ml) at 10 min intervals. The resulting mixture was extracted with dichloromethane, and the extract dried and evaporated. The solid residue was separated into its components by flash chromatography (CH_2Cl_2), yieding two products.

The first was 2-(4-chlorobenzoyl)-3-phenyl-isoxazol-5(2H)-one **13** (2.9 g, 65%), mp 126°C (light petroleum). ^{1}H NMR δ : 5.75 (s, 1H); 7.4-7.8 (m, 9H). ^{13}C NMR δ : 97.1, 127.8, 128.1, 128.8, 129.0, 129.1, 131.7, 131.8, 140.6, 163.3, 163.8, 166.6. IR ν_{max}: 1775, 1700 cm^{-1}. HRMS Calc. for $C_{16}H_{10}ClNO_3$ 299.0349, found 299.0352.

The second product was identified as 5-(4-chlorobenzoyloxy)-3-phenylisoxazole **20** (580 mg, 13%), mp 137°C (light petroleum). ^{1}H NMR δ: 6.50 (s, 1H); 7.4-8.2 (m, 9H). ^{13}C NMR δ: 85.9, 125.6, 126.7, 129.0, 129.1, 129.5, 130.5, 132.1, 142.8, 159.6, 164.3, 165.5. IR ν_{max}: 1760 cm^{-1}. Anal. Calcd. for $C_{16}H_{10}ClNO_3$: C, 64.1 ; H, 3.4 ; N, 4.7 . Found: C, 64.05 ; H, 3.25 ; N, 4.7 .

When the isoxazolone and the acid chloride were heated in the absence of solvent at 100°C for 18h under nitrogen, **13** could be isolated in 17% yield, and **20** in 41% yield.

(ii) The use of 4-methoxybenzoyl chloride under the same conditions as above gave 2-(4-methoxybenzoyl)-3-phenylisoxazol-5(2H)-one **14** (38%) , mp 137°C (light petroleum). Anal. for $C_{17}H_{13}NO_4$, calc. C, 69.1; H, 4.4; N, 4.7%; found C, 68.9; H, 4.4; N, 4.7%. ^{1}H NMR δ : 3.90 (s, 3H); 5.72, (s, 1H); 6.9-8.1 (m, 9H). ^{13}C NMR δ : 55.5, 96.2, 113.9, 122.6, 127.7, 128.4, 128.6, 131.4, 133.0, 163.6, 164.2, 163.3, 167.1. IR ν_{max}: 1775, 1700 cm^{-1}. HRMS Calc. for $C_{17}H_{13}ClNO_4$ 295.0845, found 295.0836.

The second product was identified as 5-(4-methoxybenzoyloxy)-3-phenylisoxazole **21** (20%), mp 121°C (light petroleum). Anal. for $C_{17}H_{13}NO_4$, calc. C, 69.1; H, 4.4; N, 4.7%; found C, 69.0; H, 4.3; N,

4.6%. ^{1}H NMR δ: 3.90 (s, 3H); 6.52 (s, 1H); 6.9-8.25 (m, 9H).^{13}C NMR δ : 55.6, 85.6, 114.3, 119.2, 126.3, 129.0, 129.3, 130.3, 133.1, 160.0, 164.2, 165.1, 166.0. ν_{max}: 1760 cm^{-1}. HRMS Calc. for $C_{17}H_{13}ClNO_4$ 295.0845, found 295.0850.

Pyrolysis of 2-Aroyl-3-phenylisoxazol-5(2H)ones

(i) Compound **13** was subjected to FVP (500°C, 150°C, 0.01mm Hg), and the pyrolysate (90%) was analysed by gc / ms, yielding 2-(4-chlorophenyl)-4-phenyloxazole **15**, (68%), 2-(4-chlorophenyl)-5-phenyloxazole **16** (7%), 5-(4-chlorophenyl)-2-phenyloxazole **17** (9%), and N-phenyl-4-chlorobenzamide **18** (7%). Traces of two further components, neither being an oxazole, were observed. The identity and yields were confirmed by flash chromatographic isolation of **15-18**, and comparison of spectral data with those of authentic samples.

(ii) Compound **14** was pyrolysed at 500°C as above to give an 84% isolated yield of 2-(4-methoxyphenyl)-4-phenyloxazole **19**.

Synthesis of Oxazoles

i) 2-(4-Chlorophenyl)-4-phenyloxazole **15** was prepared [20] by heating a mixture of phenacyl bromide (1.0 g, 5 mmol) and 4-chlorobenzamide (2.0 g, 12.5 mmol) at 140°C for 3h. Recrystallisation from light petroleum gave 1.0 g (78%), mp 142°C. ^{1}H NMR δ : 7.3-8.1 (m, 10H). ^{13}C NMR δ : 125.7, 126.0, 127.9, 128.3, 128.9, 129.1, 131.0, 133.7, 136.6, 142.3, 161.1. HRMS Calc. for $C_{15}H_{10}ClNO_4$ 255.0451, found 255.0450.

(ii) 2-(4-Chlorophenyl)-5-phenyloxazole **16**, mp 115-116°C [21] was prepared by Gabriel's method.[22] ^{13}C NMR δ : 123.5, 124.2, 125.9, 127.5, 127.8, 128.6, 128.9, 129.1, 136.4, 151.5, 160.2.

(iii) 5-(4-Chlorophenyl)-2-phenyloxazole **17**, mp 100-102°C [23] (hexane), was prepared as above.[22] ^{13}C NMR δ : 123.8, 125.3, 126.3, 126.4, 127.2, 128.8, 129.1, 130.4, 134.1, 150.2, 161.3.

(iii) 2-(4-Methoxyphenyl)-4-phenyloxazole **19** was prepared by a modified procedure of Maeda. [6] A well ground mixture of phenacyl bromide 0.6 g, 3 mmol) and 4-methoxybenzamide (1.5 g, 10 mmol) was heated at 140°C for 1h. The product (1.6 g, 80%), mp 99°C, was purified by flash chromatography (CH_2Cl_2). ^{1}H NMR δ : 3.80 (s, 3H); 6.7-8.1 (m, 9H); 7.80 (s, 1H). ^{13}C NMR δ : 55.1, 114.1, 120.3, 125.6. 128.0, 128.2, 128.7, 131.3, 132.9, 141.8, 161.4, 162.0.

(iv) 2-(4-Methoxyphenyl)-5-phenyloxazole **22,** mp 99°C, [24] was prepared by Gabriel's method. [22] ^{13}C NMR δ : 55.1, 114.1, 120.1, 123.1, 123.9, 127.8, 128.1, 150.6, 161.2, 161.3.

(v) 5-(4-Methoxyphenyl)-2-phenyloxazole **23** was prepared by the procedure of Gabriel ,[22] mp 85°C.[24] ^{13}C NMR δ : 55.4, 114.6, 121.1, 122.1, 125.9, 126.3, 127.8, 129.0, 130.3, 151.6, 160.1, 160.8.

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