Thermal Rearrangements of 3,5-Diphenylisoxazole

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Flash pyrolysis of 3,5-diphenylisoxazole at 960 °C yields 2,5-diphenyloxazole, 2-phenylindole, and benzamide as major products. 2,3-Diphenyl-2*H*-azirsu and fluorene were minor products. A similar experiment with 3,5-diphenyl[3,5-$^{13}C_2$]isoxazole produces 2,5-diphenyl[2,5-$^{13}C_2$]oxazole, 2-phenyl[2-^{13}C]indole, 2,3-diphenyl-2*H*-[^{13}C]azirine, and [9-^{13}C]fluorene. The thermal, photochemical, and electron-impact behaviour of 3,5-diphenylisoxazole are seen to be related.

3,5-DIPHENYLISOXAZOLE (I) undergoes photochemical transformation into 2,5-diphenyloxazole (III) through the intermediacy of the benzoylazirine (II).[1] It has been suggested [2-4] that the electron-impact-induced fragmentation of isoxazoles may be rationalised in terms of decomposition of radical cations corresponding to (II). For example, the 3,5-diphenylisoxazole molecular ion is thought to rearrange to the radical ion from (II), which then eliminates carbon monoxide to produce

charged 2,3-diphenyl-2*H*-azirine (IV). This in turn loses acetylene to yield either the fluorene or phenalene ion radical.[5]

It has been recently reported [6] that 4-acylisoxazoles can be converted thermally into 4-acyloxazoles. This suggests the possibility of thermal, photochemical, and electron-impact behaviour of isoxazoles being analogous. We were therefore interested to determine whether the thermal behaviour of 3,5-diphenylisoxazole is similar to the electron-impact and photochemical behaviour.

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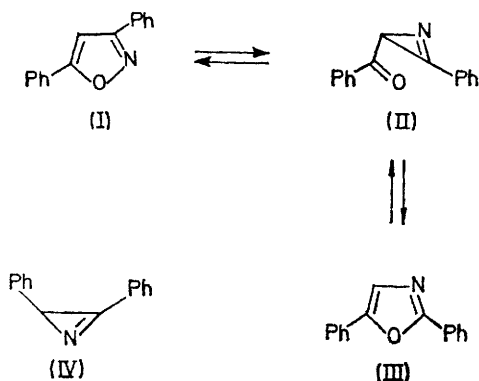
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This paper describes results obtained from flash pyrolysis experiments.

RESULTS AND DISCUSSION

Flash pyrolysis of 3,5-diphenylisoxazole (5 g) at 960 °C gave, on average, 2.8 g of pyrolysate. Components were separated by column chromatography on alumina, and were identified by comparison with authentic compounds. The initial fractions from the column contained benzonitrile, fluorene, and a variety of other hydrocarbons. These were identified by their g.l.c. retention times and also by g.l.c.–mass spectrometry. Fluorene was isolated by preparative g.l.c. Later products from the alumina column were 2,3-diphenyl-2H-azirine (IV), 2-phenylindole (V), 2,5-diphenyloxazole (III), and benzamide. Averaged yields of products from these reactions are shown in Table 1. Flash-pyrolytic reactions were carried out with certain of the products to ascertain their stability under the reaction conditions. The results are summarised in Table 1.

The results show that under the high-temperature conditions (i) 2,5-diphenyloxazole is much more stable than 3,5-diphenylisoxazole; (ii) 2-phenylindole is formed mainly from 2,3-diphenyl-2H-azirine (as has been previously demonstrated[7]); † (iii) fluorene is produced from 2,3-diphenyl-2H-azirine and to a lesser extent from 2-phenylindole; and (iv) fluorene and phenalene are not interconvertible—an observation of importance for comparison with the electron-impact study.[5]

3,5-Diphenyl[3,5-$^{13}C_2$]isoxazole was required to aid the elucidation of the reaction sequence in the flash pyrolysis reaction, and was prepared by the following method. Methyl-lithium with [α-^{13}C]benzoic acid (^{13}C 62.1%) gave labelled acetophenone, which with ethyl benzoate–sodamide gave labelled dibenzoylmethane. Reaction

with hydroxylamine gave 3,5-diphenyl[3,5-$^{13}C_2$]isoxazole [^{13}C(3) 31.0%; ^{13}C(5) 31.0%]. The incorporation of label into the products obtained by pyrolysis of

TABLE 1

Products from flash pyrolysis experiments *†

	% Product from pyrolysate of			
Product	3,5-diphenyl-isoxazole (I)	2,5-diphenyl-oxazole (III)	2,3-diphenyl-2H-azirine (IV)	2-phenyl-indole (V)
Mass (%) of recovered pyrolysate	56	82	42	90
Benzonitrile				
Naphthalene				
Diphenyl				
Diphenylmethane	3.4 ‡	2.9 ‡	15.0 ‡	6.0 ‡
Fluorene				
Phenalene				
Stilbene				
Phenanthrene				
Benzyl cyanide				
2,3-Diphenyl-2H-azirine	2.0		5.0	
2-Phenylindole	25.4	9.0	70.0	75.0
2,5-Diphenyl-oxazole	29.0	55.3		
Benzamide	11.0	20.0		

* Fluorene and diphenylmethane were recovered unchanged under the reaction conditions (960 °C and 10⁻¹ Torr). † Phenalene yields diphenyl and diphenylmethane as major products. No fluorene is produced. ‡ Product ratios were not obtained for these fractions, except for fluorene, which comprised ca. 40% of the fractions from (I), (III), and (IV), and 20% from (V). Phenanthrene is the second most abundant hydrocarbon from (I) but is a minor component in the other systems. Benzonitrile and benzyl cyanide are major components of the fraction from (IV).

labelled isoxazole was measured by mass spectrometry, and the positions of ^{13}C enrichment were determined by ^{13}C n.m.r. spectroscopy. Results are recorded in Table 2. Insufficient 2,3-diphenyl-2H-azirine was available for the ^{13}C n.m.r. spectrum to be measured.

TABLE 2

Flash pyrolysis of 3,5-diphenyl[3,5-$^{13}C_2$]isoxazole

| Product	% Incorporation of original label *	Positions labelled †
3,5-Diphenyloxazole	100	C-2 (50%), C-5 (50%)
2,3-Diphenyl-2H-azirine	49	
2-Phenylindole	51	C-2 (90%), C-3 (10%)
Fluorene	28	C-9 (100%)
Phenalene	28	
Phenanthrene	74	
Benzonitrile	50	
Benzamide	50	

* From mass spectrometry; ±2%. † From ^{13}C n.m.r.; ±5%.

The results obtained from the product and labelling studies may be rationalised as illustrated in the Scheme. Positions containing major enrichment of ^{13}C are marked with an asterisk. The main product, 2,5-diphenyl-oxazole (VIII), is probably produced by rearrangement

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† Since this manuscript was submitted, it has been reported[8] that thermolysis of 2-phenylindole at 800 °C and 10⁻³ Torr yields a mixture of 1-, 2-, and 3-phenylindole. In our work we found only 2-phenylindole and no isomeric indoles. 3-Phenylindole is the only other isomer which might be expected in reasonable amount. As the isomerisation of 2-phenylindole is controlled closely by temperature and by the amount of packing in the reaction tube,[8] perhaps the lack of isomerisation in this case is a result of a shorter contact time of the reactant. No 1- or 3-phenylindole was detected by g.l.c.–mass spectrometry, and the homogeneity of the 2-phenylindole product is evidenced particularly by its ^{13}C n.m.r. spectrum (see Experimental section).

of the benzoylazirine (VII), although (VII) is not detected in the pyrolysate.* 2,3-Diphenyl-2H-azirine (IX) may be formed by elimination of carbon monoxide from (VII) but there is no evidence to preclude direct formation from (VI). The azirine (IX) yields 2-phenylindole by nitrene insertion into a C–H bond.[7,9] Some scrambling of ^{13}C label in (IX) may account for the indole (X)
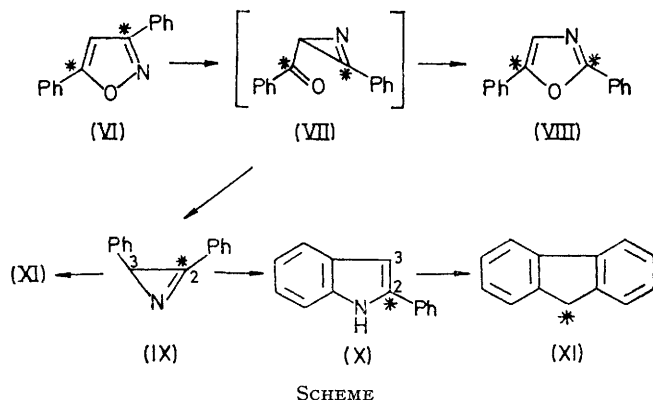
SCHEME

having the C-2 : C-3 label ratio 9 : 1. Scrambling of the label between C-2 and C-3 in (IX) can be accomplished by 1,2-shifts of the hydrogen atom on the azirine ring, and it is perhaps surprising that more pronounced scrambling is not observed. On the other hand, a small amount of 2-phenylindole originates from 2,5-diphenyloxazole, and as the mechanism of this reaction is not known, it may be that this process accounts for the minor labelling at C-3 of (X). Fluorene (XI) is formed from the azirine (IX) by loss of hydrogen cyanide, an elimination which involves each azirine ring carbon atom equally. This reaction is analogous to that proposed for the electron-impact decomposition.[10] Formation of fluorene from 2-phenylindole results in elimination of half the label at C-2.

The formation of certain other products is also of interest. Benzonitrile comes from 3,5-diphenylisoxazole, 2,5-diphenyloxazole, and 2,3-diphenyl-2H-azirine, and perhaps also from the benzoylazirine (II). Benzamide is produced mainly from 2,5-diphenyloxazole (see Table

1). Phenanthrene appears to originate directly from 3,5-diphenylisoxazole, and is obtained with 75% retention of the original ^{13}C label from the pyrolysis of (VI). This can only mean that the loss of CHNO involves equal loss of each of the three original isoxazole ring carbon atoms. The production of phenalene is of particular interest for comparison with our mass spectral studies; unfortunately, it is a very minor product, and its genesis in the thermal reaction is not understood.

Our results illustrate that the thermal, photochemical, and electron-impact behaviour of 3,5-diphenylisoxazole resemble each other closely. There have been many correlations reported between thermal and electron-impact reactions (e.g. refs. 11—20), and between electron-impact and photochemical reactions (e.g. refs. 21—25), but this is the first report of a direct correspondence amongst all three processes for a heterocyclic system whose decomposition proceeds via complex rearrangement of the ring system.

EXPERIMENTAL

Products were identified by m.p., mixed m.p., and i.r. and mass spectra, or in the case of benzonitrile and hydrocarbons (except fluorene) by g.l.c.–mass spectrometry. Mass spectra were determined with a Hitachi–Perkin-Elmer RMU 7D spectrometer operating at 70 eV, with samples introduced at 100 °C through the all-glass inlet system. G.l.c. experiments were carried out with an A.E.I. MS 30 instrument operating at 20 eV,† equipped with a Perkin-Elmer F11 gas chromatograph. A 10 ft × 1/8 in steel column maintained at 165 °C and packed with 10% Carbowax 20 M on Chromosorb W was used, with helium as carrier gas at a flow rate of 30 cm³ min⁻¹. [13]C N.m.r. spectra were recorded with a Bruker HX 90 E spectrometer, operating at 22.625 MHz (pulse Fourier transform; 8 K data points; 1 500 scans). Both [1]H-decoupled and off-resonance [1]H-decoupled spectra were obtained. Chemical shifts are quoted relative to Me₄Si. [²H]Chloroform was used as solvent.

Flash pyrolysis experiments were carried out at 960 °C and 0.1 mmHg in an all-silica apparatus. Samples were sublimed at 300 °C into a silica tube (packed with 5 mm lengths of 6 mm silica tubing) contained in an electric furnace (type 70T, Hevi-Duty Heating Equipment Co.). The pyrolysate was collected in traps maintained at −80 °C. Light petroleum refers to the fraction of b.p. 55—61°.

* The benzoylazirine (VII) is relatively unstable even at room temperature, and rearranges to (VIII).[1]

† The incorporations of ^{13}C into fluorene, phenalene, and phenanthrene were measured at 12 eV, because of the presence of M − 1 peaks at energies above this value.

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Naphthalene, biphenyl, diphenylmethane, fluorene, biphenylene, stilbene, phenanthrene, benzonitrile, benzyl cyanide, benzamide, and 2,5-diphenyloxazole were purified commercial products. 3,5-Diphenylisoxazole,[26] 2,3-diphenyl-2H-azirine,[27] 2-phenylindole,[28] and phenalene [29] were prepared by reported procedures.

Flash Pyrolysis of 3,5-*Diphenylisoxazole*.—3,5-Diphenylisoxazole (5 g) was subjected to flash pyrolysis under conditions described above. The pyrolysate (2.8 g) was applied to an alumina column (24 × 1.5 in) and eluted with light petroleum–diethyl ether mixtures. Elution with light petroleum alone gave the benzonitrile–hydrocarbon fraction; light petroleum–ether (95 : 5) eluted 2,3-diphenyl-2H-azirine; light petroleum–ether (90 : 10) eluted 2,5-diphenyloxazole; light petroleum–ether (80 : 20) eluted 2-phenylindole; and ether eluted benzamide. Yields are shown in Table 1. Fluorene was isolated from the hydrocarbon fraction by preparative g.l.c. [Aerograph Autoprep A-700 fitted with an alumina column (10 ft × 0.25 in) packed with SE 30 (20%) on Chromosorb A; N_2 as carrier gas]. Fluorene and other products were identified by m.p., mixed m.p., and i.r. and mass spectrometry. Components of the hydrocarbon fraction were identified by g.l.c.–mass spectrometry (see above for experimental conditions). [Retention times (min) were: benzonitrile (1.8), naphthalene (9.0), biphenyl (20.0), diphenylmethane (22.0), stilbene (29.6), fluorene (63.2), phenalene (77.2), and phenanthrene (84.1).]

Flash pyrolyses of other compounds indicated in Table 1 were carried out in a similar manner.

3,5-*Diphenyl*[3,5-[13]C$_2$]*isoxazole*.—The reaction [30] between [α-^{13}C] benzoic acid ([13]C 61.2%) and methyl-lithium yielded [2-^{13}C]acetophenone (80% yield). When treated with ethyl benzoate and sodamide this gave 1,3-diphenyl[1-^{13}C]-propane-1,3-dione ([13]C 61.2%; 75% yield). The dione was converted into 3,5-diphenyl[3,5-[13]C$_2$]isoxazole (C-3 [13]C 30.6%; C-5 [13]C 30.6%) by treatment with hydroxylamine.[31] The yield was quantitative.

Pyrolysis of 3,5-*Diphenyl* [3,5-[13]C$_2$]*isoxazole*.—The pyrolysis was carried out on 1 g of material as described above. Incorporations of label into products are listed in Table 2 (converted to % for easy comparison). The ^{13}C spectra follow (data for enriched positions are italicised; see also Table 2): fluorene, δ_C 143.52, 142.01, 127.01, 125.28, 120.21, and *37.12* (C-9); 2,5-diphenyloxazole, *161.0* (C-2), *151.3* (C-5), 130.4, 128.8, 128.4, 128.1, 126.4, 214.2, and 123.6; 2-phenylindole, *137.90* (C-2), 136.88, 132.45, 129.27, 129.05, 127.70, 125.17, 122.37, 120.26, 110.93, and *100.03* (C-3).

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