

Thermal Rearrangements of 2,3-Diphenyl-2*H*-azirine

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Heating 2,3-diphenyl-2*H*-azirine in a sealed tube at 250 °C for 3 h yields 2-phenylindole, 2,3,4,5-tetraphenylpyrrole, 2,4,5-triphenylimidazole, and 1-benzyl-2,4,5-triphenylimidazole as major products, with tetraphenylpyrazine, tetraphenylpyrimidine, pentaphenylpyridine, benzonitrile, benzamide, and stilbene being produced in smaller yield. In an attempt to elucidate the reaction pathways, it was shown that benzonitrile is not an intermediate, that the reaction between tetraphenylpyrrole and phenylcarbene yields pentaphenylpyridine, and that a similar reaction with 2,4,5-triphenylimidazole produces 1-benzyl-2,4,5-triphenylimidazole, tetraphenylpyrazine, and tetraphenylpyrimidine.

We have published a preliminary account¹ of the thermal behaviour of 2,3-diphenyl-2*H*-azirine² (1) in a sealed system, in which we showed how g.l.c. treatment of this material at 220 °C produced 2-phenylindole (in 60% yield) by an intramolecular nitrene insertion process, a reaction analogous to the conversion³ of 2-phenyl-2*H*-azirine and 2-methyl-3-phenyl-2*H*-azirine into indole and 2-methylindole, respectively. The photoreactions of the azirine (1) have been studied by several groups. Irradiation in benzene yields 2,4,5-triphenylimidazole⁴ and tetraphenylpyrazine.⁵ Irradiation in cyclohexane produces the two diastereoisomeric 1,3-diazabicyclo[3.1.0]hex-3-enes (3), which on further irradiation give tetraphenylpyrazine and on treatment with base produce tetraphenylpyrimidine.⁶ We now consider the thermal reaction in more detail; we advance mechanistic proposals to rationalise the complex rearrangement processes, and consider the possible intermediacy of the compounds (3) [produced by the

† During this work a similar sequence was published by Padwa.⁶

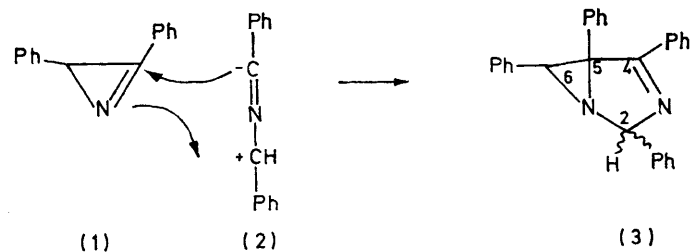
¹ J. H. Bowie and B. Nussey, *Chem. Comm.*, 1970, 1565.

² F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, 1967, **89**, 2077.

³ K. Isomura, S. Kobayashi, and H. Taniguchi, *Tetrahedron Letters*, 1968, 3499.

reaction between (1) and its ring-opened nitrile ylide form (2)].

The products obtained from heating the azirine (1) at 100, 250, and 470 °C for 3 h are listed in Table 1. All



products are known compounds, except tetraphenylpyrimidine, which was prepared by the reaction between benzimidine and 2,3-diphenylacrylophenone followed by aerial oxidation.† The products were purified by column chromatography over silica acid. At 100 °C 92% of the starting material was recovered, and at 470 °C the major product was 2-phenylindole (75%).

⁴ H. Giezendanner, M. Märky, B. Jackson, H. J. Hanson, and H. Schmid, *Helv. Chim. Acta*, 1972, **55**, 745.

⁵ A. Hassner and L. A. Levy, *J. Amer. Chem. Soc.*, 1965, **87**, 4203.

⁶ A. Padwa, S. Clough, M. Dharan, J. Smolanoff, and S. I. Wetmore, *J. Amer. Chem. Soc.*, 1972, **94**, 1395.

At 250 °C, an average of 84% (by weight) of products was obtained, but there was considerable variation in the product ratios, especially of 2-phenylindole and tetraphenylpyrrole, even though identical conditions were used for the four determinations. It is difficult to

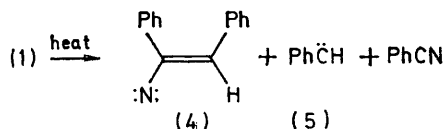
TABLE 1

Products (%) from pyrolysis of the azirine (1) at various temperatures for 3 h

Product	100 °C	250 °C †				470 °C
		1	2	3	4	
2,3-Diphenyl-2H-azirine	91.5					
2-Phenylindole		0.8	44.5	Trace	Trace	75.4
2,4,5-Triphenylimidazole		46.2	14.8	31.5	28.8	
1-Benzyl-2,4,5-triphenylimidazole		Trace	11.9	18.4	24.8	
Tetraphenylpyrrole	6.1	35.5	Trace	27.4	16.5	
Tetraphenylpyrazine	2.4	5.9	8.0	9.5	14.7	2.0
Tetraphenylpyrimidine		4.1	Trace	5.4	Trace	
Pentaphenylpyridine		2.6		0.8	Trace	
Benzamide			5.9	2.3	10.0	
Benzonitrile	Trace					
Stilbene					5.3	
Tar						13.8

† The values listed here are percentages of total product recovered. The average total product for four pyrolyses was 84% by weight of starting material.

rationalise this variation but it may be relevant that 2-phenylindole is produced by an intramolecular process^{1,3} whereas tetraphenylpyrrole must be formed by an intermolecular process (see later). The thermal stability of azirines has been studied by several groups^{1,3,7-9} and it seems that the formation of products may be explained in terms of carbene or nitrene intermediates. If this is so, then the different product ratios obtained may be likened to a similar situation for methylene reactions,¹⁰ and explained in terms of the high reactivity of the intermediates, their excess energy, the small energies of activation of the reactions, and the formation of products containing sufficient energy to undergo further reactions.



* Similar reactions have been observed with the related 1,3-diazabicyclohexanes.^{25,26}

⁷ W. Bauer and K. Hafner, *Angew. Chem. Internat. Edn.*, 1969, **8**, 772.

⁸ D. J. Anderson, T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *Chem. Comm.*, 1971, 1518.

⁹ T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *Chem. Comm.*, 1971, 1519.

¹⁰ H. M. Frey in 'Carbene Chemistry,' ed. W. Kirmse, Academic Press, New York, 1964.

¹¹ C. L. Arcus, R. E. Marks, and M. M. Coombs, *J. Chem. Soc.*, 1957, 4064.

¹² W. H. Saunders and E. A. Caress, *J. Amer. Chem. Soc.*, 1964, **86**, 861.

¹³ H. Hemetsberger, D. Knittel, and H. Weidmann, *Monatsh.*, 1970, **101**, 161.

¹⁴ T. L. Gilchrist, C. W. Rees, and E. Stanton, *J. Chem. Soc. (C)*, 1971, 3036.

¹⁵ O. Fisher and O. Heiler, *Ber.*, 1893, **26**, 378.

The initial products from heating 2,3-diphenyl-2H-azirine should be the nitrene (4),^{1,3,8,9,11-14} phenylcarbene (5),^{8,9} and benzonitrile.^{8,9} To test whether any of the products are obtained from benzonitrile, the reaction was carried out at 250 °C in the presence of 2,4,6-trideuteriobenzonitrile. The latter was recovered unchanged and mass spectral analysis showed that none of the rearrangement products contained deuterium.

The formation of certain products is easily rationalised. An intramolecular cyclisation of the nitrene (4) will generate 2-phenylindole. There are many examples of nitrene insertions into aromatic C-H bonds,^{3,13,15-19} and the mechanism for the formation of 2-phenylindole is similar to that proposed^{20,21} to account for the production of an indole from *o*-nitrostyrene. Tetraphenylpyrrole may be produced by a 1,3-dipolar addition of the nitrene (4) to itself, a mechanism similar to that suggested for the conversion of α -styryl azide into 2,5-diphenylpyrrole.^{22,23}

No direct evidence is available to explain the formation of 2,4,5-triphenylimidazole, 1-benzyl-2,4,5-triphenylimidazole, tetraphenylpyrazine, tetraphenylpyrimidine, and pentaphenylpyridine. It is however relevant to compare the photochemical (see before) and thermal behaviour of the azirine (1). Although the intermediates (3) were not isolated in the thermal reaction, they could be produced by the reaction between species (1) and (2), and their intermediacy rationalises the formation of several products. The thermal formation of tetraphenylpyrazine (analogous to the dimerisation of 2-phenyl-2H-azirine to 3,6-dihydro-2,5-diphenylpyrazine²⁴) could be effected by two mechanisms. Formation of the diazohexatriene (6) from (3) (*cf.* ref. 6) followed by cyclisation,* or dimerisation of the nitrene (4) could produce 2,3,4,5-tetraphenyldihydropyrazine, which upon oxidation during isolation could yield tetraphenylpyrazine. The intermediates (3) could also eliminate phenylcarbene to produce 2,4,5-triphenylimidazole and undergo a proton transfer from C-2 to C-6 to produce either 1-benzyl-2,4,5-triphenylimidazole (cleavage of the 5,6-bond) or tetraphenylpyrimidine (cleavage of the 1,5-bond).

The formation of pentaphenylpyridine may be rationalised in terms of a phenylcarbene intermediate. Insertion of phenylcarbene into a double bond of

¹⁶ H. McCombie, H. A. Scarborough, and W. A. Waters, *J. Chem. Soc.*, 1928, 353.

¹⁷ J. S. Swenton, *Tetrahedron Letters*, 1967, 2855.

¹⁸ G. Smolinsky and C. A. Pryde, *J. Org. Chem.*, 1968, **33**, 2411.

¹⁹ P. A. S. Smith in 'Nitrenes,' ed. W. Lwowski, Interscience, New York, 1970, p. 130, and references therein.

²⁰ R. J. Sundberg, *J. Org. Chem.*, 1965, **30**, 3604.

²¹ R. J. Sundberg and T. Yamazaki, *J. Org. Chem.*, 1967, **32**, 290.

²² J. H. Boyer, W. E. Krueger, and R. Mohler, *Tetrahedron Letters*, 1968, 5979.

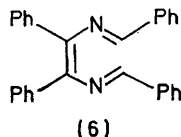
²³ F. P. Woerner and H. Rumlinger, *Chem. Ber.*, 1970, **103**, 1908.

²⁴ L. Horner, A. Christmann, and A. Gross, *Chem. Ber.*, 1963, **96**, 399.

²⁵ A. Padwa, S. Clough, and E. Glazer, *J. Amer. Chem. Soc.*, 1970, **92**, 1778.

²⁶ A. Padwa and E. Glazer, *Chem. Comm.*, 1971, 838; T. Dominh and A. M. Trozzolo, *J. Amer. Chem. Soc.*, 1970, **92**, 6997.

tetraphenylpyrrole should produce pentaphenylpyridine. Carbene insertions into aromatic systems have been observed previously;²⁷⁻³² in particular, the Reimer-Tiemann reaction between phenylchlorocarbene and



pyrrole yields 3-phenylpyridine.³³ To test this possibility, the lithium salt of tetraphenylpyrrole was treated with phenylchlorocarbene (from benzylidene chloride) to give pentaphenylpyridine in 60% yield. Tetraphenylethylene and hexaphenylethane are produced as by-products of this reaction, presumably by displacement reactions at organometallic sites rather than by carbene additions (*cf.* refs. 34-36). The formation of pentaphenylpyridine demonstrates the possibility of a carbene insertion reaction, but this reaction is not directly comparable with the thermal intermediates or conditions.

In order to approach the thermal conditions more closely, phenylcarbene (from phenyldiazomethane) was heated under reflux for 2 h with tetraphenylpyrrole dissolved in a suspension of copper in cyclohexane.* Small yields of pentaphenylpyridine (3%) and stilbene (5%) were obtained and starting material (90%) was recovered unchanged.

The insertion of phenylcarbene into 2,4,5-triphenylimidazole could in principle produce three of the thermal products, namely 1-benzyl-2,4,5-triphenylimidazole, tetraphenylpyrazine, and tetraphenylpyrimidine, by insertion into the N-H bond, the C=N bond, and a C=C bond, respectively. When 2,4,5-triphenylimidazole (300 mg) was treated with phenylcarbene the following products were obtained: stilbene (200 mg), starting material (100 mg), 1-benzyl-2,4,5-triphenylimidazole (105 mg), tetraphenylpyrazine (40 mg), and tetraphenylpyrimidine (15 mg). The ratio of the last three products (7 : 3 : 1) shows that the reactivity of the various bonds is NH > C=N > C=C. When this procedure was applied to 2,3-diphenyl-2H-azirine only traces of tetraphenyl-

pyrrole, tetraphenylpyrazine, and tetraphenylpyrimidine were obtained. The major product was 1-azido-1,2,3-triphenylpropene, produced by the reaction between the azirine (1) and phenyldiazomethane.³⁹

Finally, because Crow and Wentrup⁴⁰ have demonstrated that pyrazine will thermally rearrange to pyrimidine, we subjected tetraphenylpyrazine, tetraphenylpyrimidine, 2,3,4,5-tetraphenylpyrrole, 2,4,5-triphenylimidazole, and 2-phenylindole to control thermal reactions. Unchanged starting material was recovered in all cases.

In summary, it is possible that tetraphenylpyrrole and 2-phenylindole are produced by nitrene insertion reactions, that 2,4,5-triphenylimidazole is formed from a reactive intermediate [perhaps (3)], that 1-benzyl-2,4,5-triphenylimidazole, tetraphenylpyrazine, and tetraphenylpyrimidine are formed by insertion of phenylcarbene into 2,4,5-triphenylimidazole, but may also be produced from (3), and that pentaphenylpyridine is formed from the reaction between tetraphenylpyrrole and phenylcarbene.

EXPERIMENTAL

Products were identified by m.p., mixed m.p., and i.r. and mass spectra. M.p.s were determined on a Kofler hot-stage apparatus. Mass spectra were measured with an Hitachi-Perkin-Elmer RMU 7D spectrometer operating at 70 eV, with samples being introduced at 200° through the all-glass inlet system. Light petroleum refers to the fraction of b.p. 40-60°.

Authentic benzonitrile, benzamide, stilbene, and 2-phenylindole were purified commercial samples. The following compounds were prepared by reported procedures: 2,3-diphenyl-2H-azirine,² 2,4,5-triphenylimidazole,⁴¹ 1-benzyl-2,4,5-triphenylimidazole,⁴² 2,3,4,5-tetraphenylpyrrole,⁴³ tetraphenylpyrazine,⁴⁴ and pentaphenylpyridine.⁴⁵

2,4,5,6-Tetraphenylpyrimidine.—This was made by a modification of the method of Anker and Cook.⁴⁶ A mixture of 2,3-diphenylacrylophenone⁴⁷ (284 mg) and benzamide⁴⁸ (122 mg) in ethanol (25 cm³) and aqueous sodium hydroxide (10%; 20 cm³) was stirred at 20 °C for 4 days. The solution was diluted with an excess of glacial acetic acid and set aside for 1 week. The precipitate (382 mg, 98%) crystallised from ethanol as needles, m.p. 195-196° (lit.,⁴⁹ 199°) (Found: C, 87.5; H, 5.3. Calc. for C₂₈H₂₀N₂: C, 87.5; H, 5.25%).

³⁷ R. W. Murray, A. M. Trozzolo, E. Wasserman, and W. A. Yager, *J. Amer. Chem. Soc.*, 1962, **84**, 3213.

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³⁹ J. H. Bowie, B. Nussey, and A. D. Ward, *Austral. J. Chem.*, in the press.

⁴⁰ W. D. Crow and C. Wentrup, *Tetrahedron Letters*, 1968, 3115.

⁴¹ H. Brederick, R. Gomper, and D. Hayer, *Chem. Ber.*, 1956, **92**, 338.

⁴² F. R. Japp and W. B. Davidson, *J. Chem. Soc.*, 1895, 35.

⁴³ D. Davidson, *J. Org. Chem.*, 1938, **3**, 364.

⁴⁴ C. F. Winans and H. Adkins, *J. Amer. Chem. Soc.*, 1933, **55**, 2051.

⁴⁵ E. Knoevenagel and R. Wassgerber, *Ber.*, 1893, **26**, 440.

⁴⁶ R. M. Anker and R. H. Cook, *J. Chem. Soc.*, 1941, 323.

⁴⁷ J. Thiele and P. Ruggi, *Annalen*, 1912, **393**, 71.

⁴⁸ A. R. Ronzio and J. B. Ekeley, *Org. Synth. Coll. Vol. I*, 1944, p. 6.

⁴⁹ G. Rio, A. Ranjon, and O. Pouchot, *Compt. rend.*, 1966, **263**, 634.

* Copper-catalysed reactions of this type are thought²⁷⁻²⁹ to involve complexed singlet carbenes. It is not clear whether the reactive species in the pyrolysis is singlet or triplet phenylcarbene, but it is known from e.s.r. studies^{37,38} that phenylcarbene has a triplet ground state.

²⁷ C. P. Gutsche, G. L. Bachman, and R. T. Coffey, *Tetrahedron*, 1962, **18**, 617.

²⁸ G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, 1964, **86**, 4042.

²⁹ G. L. Closs and J. J. Loyle, *J. Amer. Chem. Soc.*, 1965, **87**, 4270.

³⁰ G. L. Closs and G. M. Schwartz, *J. Org. Chem.*, 1961, **26**, 2609.

³¹ E. A. Lalancette and R. E. Benson, *J. Amer. Chem. Soc.*, 1963, **85**, 2853.

³² T. J. Katz and P. J. Garrett, *J. Amer. Chem. Soc.*, 1963, **85**, 2852.

³³ E. R. Alexander, A. R. Herrick, and T. M. Roder, *J. Amer. Chem. Soc.*, 1950, **72**, 2760.

³⁴ C. Engler and H. Bethge, *Ber.*, 1874, **7**, 1125.

³⁵ W. Löb, *Ber.*, 1903, **36**, 3059.

³⁶ H. Staundinger and O. Kupfer, *Ber.*, 1911, **44**, 2194.

General Procedure for Thermal Reactions.—2,3-Diphenyl-2H-azirine (2.0 g) was sealed in a stainless steel bomb (103 cm³) and heated for 3 h in an oven pre-equilibrated at the required temperature (Table 1). The cooled products dissolved in diethyl ether (100 cm³) were added to silicic acid (Mallinkrodt greater mesh; 10 g), the ether was removed *in vacuo*, and the dried material was applied to a column of silicic acid (120 × 3 cm) prepared in light petroleum. The column was eluted with mixtures of light petroleum (LP), ether (E), and methanol (M) of increasing polarity and fractions of 50 cm³ were collected. Each fraction was evaporated *in vacuo* and the residue crystallised from either methanol or glacial acetic acid. The product ratios are listed in Table 1. The compounds were eluted in the order given in Table 2.

TABLE 2
Thermal reaction products

Compound	Eluant	M.p. (°C)	Mixed m.p. (°C)
Stilbene	LP	123—124	123—125
2,4,5,6-Tetraphenylpyrrole	LP-E (85 : 15)	214—215	211—215
2-Phenylindole	LP-E (80 : 20)	187—188	186—189
Tetraphenylpyrazine	LP-E (70 : 30)	248—251	245—251
Tetraphenylpyrimidine	LP-E (70 : 30)	195—197	194—197
Pentaphenylpyridine	LP-E (50 : 50)	247—249	244—249
1-Benzyl-2,4,5-triphenylimidazole	LP-E (25 : 75)	164—166	163—166
2,4,5-Triphenylimidazole	E	279—280	276—280
Benzamide	E-M (95 : 5)	129—130	127—130

Pentaphenylpyridine from 2,3,4,5-Tetraphenylpyrrole.—

(a) *From phenylchlorocarbene.* To a solution of tetraphenylpyrrol-1-yl-lithium obtained from tetraphenylpyrrole (3.5 g) and phenyl-lithium [from lithium (0.9 g) and bromobenzene (10.6 g) in diethyl ether (35 cm³)] was added benzylidene chloride (10.6 g) in dry diethyl ether (20 cm³) under nitrogen. The mixture was stirred at 20 °C for 1 week. The lithium salts were filtered off and the solvent was removed *in vacuo* to leave an oil which was chromatographed over silicic acid (120 × 3 cm), with light petroleum—

diethyl ether (LP-E) as eluant. Elution with LP-E (95 : 5) gave tetraphenylethylene (0.075 g, 2%), m.p. 225—227 (lit.,⁵⁰ 227°), with LP-E (90 : 10) gave hexaphenylethane (0.19 g, 4.4%), m.p. 145—146° (lit.,⁵¹ 145—147°), and LP-E (60 : 40) gave pentaphenylpyridine, which crystallised from ethanol as needles (2.53 g, 59%), m.p. 244—249°.

The reaction was repeated in the absence of 2,3,4,5-tetraphenylpyrrole; chromatography yielded tetraphenylethylene (1.44 g, 37.5%), hexaphenylethane (1.95 g, 40.5%), and benzylidene chloride (7.98 g).

(b) *From phenylcarbene.* Benzaldehyde azine^{52,53} (20 g) in hydrazine hydrate (70 cm³) was heated under reflux for 15 h. The solution was cooled, and the two layers separated. The crude benzylidenehydrazine (*cf.* ref. 54) was used without purification (distillation or chromatography results in disproportionation).

Phenyldiazomethane (2.2 g) (prepared from benzylidenehydrazine by the method of Mohrbacher and Cromwell⁵⁵) in cyclohexane (150 cm³) was added slowly under nitrogen to a stirred suspension of copper powder and 2,3,4,5-tetraphenylpyrrole (1.0 g) in cyclohexane (150 cm³) heated under reflux. Heating was continued for 2 h, the solvent was removed *in vacuo*, and the residue was chromatographed over silicic acid (120 × 3 cm), with LP-E as eluant [see (a)]. The isolated products were stilbene (100 mg), 2,3,4,5-tetraphenylpyrrole (905 mg), and pentaphenylpyridine (50 mg).

Reaction of 2,4,5-Triphenylimidazole with Phenylcarbene.—The reaction and chromatographic separation were as for 2,3,4,5-tetraphenylpyrrole. The products were eluted as described for the thermal reactions. 2,4,5-Triphenylimidazole (0.30 g) in cyclohexane (150 cm³) and phenyldiazomethane (2.2 g) yielded stilbene (205 mg), 2,4,5-triphenylimidazole (100 mg), 1-benzyl-2,4,5-triphenylimidazole (105 mg), 2,3,5,6-tetraphenylpyrazine (40 mg), and 2,4,5,6-tetraphenylpyrimidine (15 mg).

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