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Azirines. I. The Reaction of 2-Phenylazirine with Carbanions*[1]

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An attempt to prepare 2-phenylazirine by treating acetophenone dimethylhydrazone methiodide with methylsulfinyl carbanion gave 2, 4-diphenylpyrrole instead of 2-phenylazirine. The reaction of 2-phenylazirine with the carbanions derived from acetophenone, ethyl benzoylacetate, and benzyl cyanide gave the corresponding pyrrole derivatives by ring enlargement.

Although the formation of the azirine ring as an intermediate has been suggested in a number of reactions,[1] including the Neber and related rearrangements and aziridine ring formation, in only a few cases, have such intermediates actually been isolated. Thus, except for the long-neglected isolation of azirines by Neber,[2] this ring system has attracted only a little attention until recently, when study was initiated with a veiw toward synthesizing and isolating the azirines. The methods of preparing azirines may be classified into the base treatment of oxime tosylates[2,3] and dimethylhydrazone metihodides,[4] the reaction of ylides to nitriles[5] and nitrile oxides,[6] the photolysis[7] and pyrolysis[8] of vinyl azides, and the photolysis of

*1 This work has been partly reported in a preliminary form: S. Sato, H. Kato and M. Ohta, This Bullein, **40**, 1014 (1967).

*2 On leave of absence from the Kyorin Chemical Laboratory.

1) (a) P. E. Fanta, "Heterocyclic Compounds with Three and Four-membered Rings" Part I, ed. by A. Weissberger, Interscience Publishers, New York (1964), p. 562. (b) C. O'brien, *Chem. Revs.*, **64**, 81 (1964).

2) P. W. Neber and A. Burgard, *Ann.*, **493**, 281 (1932); **526**, 277 (1936).

3) D. J. Cram and J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953).

4) a) R. F. Parcell, *Chem. & Ind.* **1963**, 1396; b) D. F. Morrow and M. E. Butler, *J. Heterocyclic Chem.*, **1**, 53 (1964).

5) H. König, H. Metzger and K. Seelert, 100 *Jahre BASF*, **1965**, 49; *Chem. Abstr.*, **64**, 17409 (1966).

6) a) H. J. Bestmann and R. Kunstmann, *Angew. Chem.*, **78**, 1059 (1966); b) R. Huisgen and J. Wulff, *Tetrahedron Letters*, **1967**, 917.

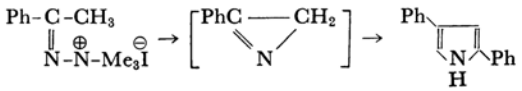
7) a) L. Horner, A. Christmann and A. Gross, *Chem. Ber.*, **96**, 399 (1963); b) G. R. Harvey and K. W. Ratts, *J. Org. Chem.*, **31**, 3907 (1966); c) A. Hassner and F. W. Fowler, *Tetrahedron Letters*, **1967**, 1545.

8) a) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962); b) C. S. Cleaver and C. G. Krespan, *J. Am. Chem. Soc.*, **87**, 3716 (1965); c) R. E. Banks and G. J. Moore, *J. Chem. Soc.*, **1966**, 2304.

an isoxazole.[9] The methods of preparation of such compounds, however, differ from case to case, and the applicability of these methods of preparation to other azirine derivatives is not known.

There have been only a few reports on the chemical properties of azirine as discrete species. The reactions so far described with azirines are: hydrogenation,[3,4b,7b] dimerization,[7a,8a,10] hydrolysis,[4a,6b,8b,10] photorearrangement,[9] and reaction with alkoxide,[4a] sodium hydrosulfide,[4b]: hydrogen fluoride,[8b] and amines.[9,11]

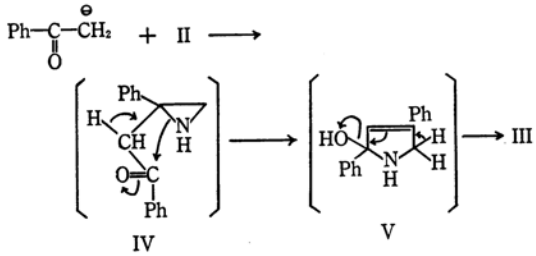
In an attempt to find out a general method of preparing azirine by the treatment of dimethylhydrazone methiodides with a base,[4] acetophenone dimethylhydrazone methiodide (I) was treated with methylsulfinyl carbanion in dimethylsulfoxide (DMSO). No 2-phenylazirine (II) or its hydrolysis product was isolated, but instead a compound with a composition of $C_{16}H_{13}N$ was obtained. The infrared, ultraviolet, and NMR spectra of this compound suggest that it is an aromatic compound with an NH group; it was identified as 2, 4-diphenylpyrrole (III) by its melting point and by its conversion to the corresponding 5-nitroso derivative by nitrous acid.



I II III

Although the mechanism of the formation of III is not yet clear, it might be possible to consider 2-phenylazirine as an intermediate. This consideration led us to examine the reaction of 2-phenylazirine with carbanions.

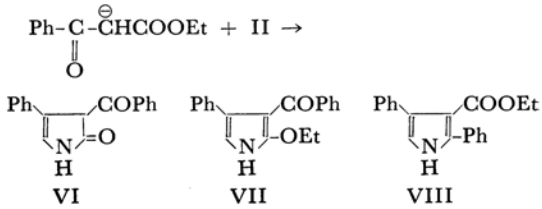
When 2-phenylazirine (II) was treated with acetophenone in the presence of methylsulfinyl carbanion, 2, 4-diphenylpyrrole[12] was obtained in 73% yield. This reaction may be explained by considering the attack of the phenacyl anion on the C–N double bond of phenylazirine to give the intermediate (IV), followed by the stages of ring expansion and dehydration (Chart 1) to give III.



IV V

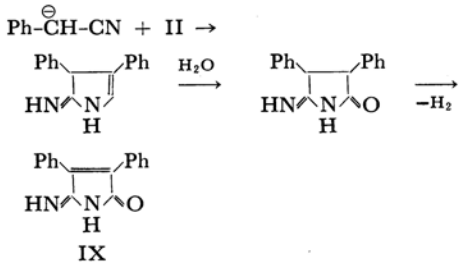
Chart 1

The reaction of 2-phenylazirine with ethyl benzoylacetate seemed to be of interest because, if the reaction proceeds *via* an analogous route, three structures, VI—VIII, are possible for the reaction product. The product actually isolated in 51% yield was found to be 3-benzoyl-4-phenyl-2-oxopyrroline (VI). This assignment was based on the infrared absorptions at 3230 cm^{-1} for the NH group, at 1690 cm^{-1} for the lactam carbonyl group, and at 1640 cm^{-1} for the benzoyl carbonyl group. The position of the double bond in VI is only tentative.



VI VII VIII

The reaction of 2-phenylazirine with benzyl cyanide under the same reaction conditions gave, after treatment with water, a compound with a composition of $C_{16}H_{12}N_2O$ instead of the expected 3, 4-diphenyl-2-aminopyrrole. The infrared spectrum of this compound exhibits bands at 3300 cm^{-1} for the NH group, at 1700 cm^{-1} for the lactam carbonyl, and at 1660 cm^{-1} for the C=N double bond. These spectral data suggest that this compound is 3, 4-diphenyl-2-oxo-5-iminopyrroline (IX); it was indeed identified as such by comparison with an authentic sample of IX,[13] kindly supplied by Dr. Banfield. It was probably formed by the addition of a molecule of water to 2-amino-3, 4-diphenylpyrrole, followed by dehydrogenation.



IX

The reaction of 2-phenylazirine with such more acidic compounds as dibenzoylmethane, barbituric acid, and rhodanine did not give the condensation products; only the 2, 5-diphenylpyrazine resulting from the dimerization of 2-phenylazirine was isolated.

Experimental

The melting points were measured on a micro hot stage and have not been corrected. The infrared spectra were taken on KBr tablets. All the reactions were carried out under an atmosphere of nitrogen with the careful exclusion of moisture.

9) E. F. Ullmann and B. Singh, *J. Am. Chem. Soc.*, **88**, 1844 (1966).
10) G. Smolinsky, *ibid.*, **83**, 4483 (1961).
11) G. Smolinsky and B. I. Feuer, *J. Org. Chem.*, **31**, 1423, (1966).
12) M. A. Rogers, *J. Chem. Soc.*, **1943**, 590.
13) J. E. Banfield, *ibid.*, **1960**, 2108.

2-Phenylazirine (II). This was prepared by the photolysis of α-azidostyrene following the procedure of Horner.[7a]

2, 4-Diphenylpyrrole (III). a) A solution of 10 g (0.033 mol) of acetophenone dimethylhydrazone methiodide in 20 m*l* of DMSO was added to a solution of methylsulfinyl carbanion, prepared from 1.6 g (0.033 mol) of 50% sodium hydride and 40 m*l* of DMSO. A vigorous evolution of trimethylamine was observed. The mixture was then stirred for one hour at room temperature and poured into water; the pale yellow crystals which then immediately separated out were collected. Recrystallization from methanol gave 2.5 g of 2, 4-diphenylpyrrole as pale yellow leaflets melting at 179.5—180.5°C; reported mp 178—179°C.[12] (Found: C, 87.32; H, 5.89; N, 6.66%). IR: 3450 cm^{-1} UV: λ_{max}^{EtOH} mμ 237, 249, 288, 306. 5-Nitroso derivative, (picrate) mp 188—189°C (decomp.). Reported mp 188°C (decomp.).[12]

b) To a solution of 2.4 g (0.02 mol) of acetophenone and 0.8 g (0.017 mol) of 50% sodium hydride in 25 m*l* of DMSO, 2.3 g (0.02 mol) of II was added, after which the mixture was stirred for five hours at room temperature. It was then poured into water, and the pale yellow crystals (3 g, mp 178—179°C) which immediately separated out were collected and recrystallized from methanol to give 2, 4-diphenylpyrrole, which was identical with the sample previously obtained. Mp 178—179°C (Found: C, 87.28; H, 6.09; N, 6.63%).

3-Benzoyl-4-phenyl-2-oxopyrroline (VI). Into a solution of methylsulfinyl carbanion, prepared from 0.8 g (0.017 mol) of 50% sodium hydride and 25 m*l* of DMSO, 3.8 g (0.02 mol) of ethyl benzoylacetate and then 2.3 g (0.02 mol) of II were added. The mixture was stirred for seven hours at room temperature and then poured into water; the resulting blue solution was acidified with hydrochloric acid to give 2.1 g of pale brown crystals. Recrystallization from ethanol gave 1.5 g of 3-benzoyl-4-phenyl-2-oxopyrroline as colorless crystals melting at 188—189°C.
IR: 3230, 1690; 1640 cm^{-1}.

Found: C, 75.97; H, 5.22; N, 5.25%. Calcd for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57%.

3, 4-Diphenyl-2-oxo-5-iminopyrroline (IX). Into a solution of methylsulfinyl carbanion, prepared from 0.8 g (0.017 mol) of 50% sodium hydride and 25 m*l* of DMSO, 2.3 g (0.02 mol) of benzyl cyanide and then 2.3 g (0.02 mol) of II were added. The mixture was stirred for one hour at room temperature and then poured into water; the resulting reddish borwn paste was solidified by washing it with ether. The recrystallization of the solid from ethanol afforded 1.3 g of 3, 4-diphenyl-2-oxo-5-iminopyrroline as pale yellow needles melting at 255—256°C (decomp.). Reported mp 244—249°C (decomp.)*3 IR: 3300,1700, 1660 cm^{-1}. UV: λ_{max}^{EtOH} mμ (ε) 225.5 (14600), 250 (12400), 274 (15000), 330 (5200). Its infrared and ultraviolet absorption spectra were identical with those of an authentic sample.[13] (Found: C, 76.95; H, 4.84; N, 11.38%.)

We are indebted to Dr. J. E. Banfield for kindly sending us the sample of IX.

*3 Although the melting point of this substance does not agree nicely with the reported value, the melting point and mixed melting point depend on crystal size, degree of compacting and technique of melting point measurement, and are practically no diagnostic value for this type of compounds.[14]

14) J. E. Banfield, Private communication.