SYNTHESIS OF NITROGEN HETEROCYCLES BY MEANS OF NITRENES

I. FIVE-MEMBERED RINGS WITH ONE HETEROATOM (REVIEW)

V. P. Semenov, A. N. Studenikov,
and A. A. Potekhin

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The literature data on the synthesis of pyrroles, indoles, carbazoles, and other condensed systems containing a pyrrole ring and on their hydrogenated derivatives by means of nitrenes and potential precursors of the latter are correlated.

The publication of a monograph [1] and many reviews [2-11] devoted to the chemistry of nitrenes is a consequence of the constantly increasing interest in these sextet intermediate particles. Such interest is due not so much to the theoretical problems in the chemistry of nitrenes as to the prospects that the use of nitrenes in the synthesis of diverse nitrogen compounds (primarily heterocycles) has opened up. However, except for the reviews [3-6] in which primarily research by the authors on the synthesis of heterocycles through aryl- or carbonylnitrenes are systematized, the role of nitrenes in the synthesis of nitrogen heterocyclic systems has not been specially examined.

In the present review paper we attempted to treat the voluminous data in such a way as to demonstrate precisely this role of nitrenes. The foundation of the construction of the review was the type of monocyclic nitrogen-containing system formed with the participation of a nitrene and, within each division, the mechanism of the formation of the heterocyclic system. Some studies in which heterocycles were obtained from azides and other potential sources of nitrenes are also examined. This is, in our opinion, expedient, since it has by no means been proved in all cases that a nitrene does or does not participate in the reaction and since the same heterocycles can be formed from the same reagents but via different mechanisms — "nitrene" and "nonnitrene" — depending on the reaction conditions and the structure of the reagent–substrate pair [7]. It should be noted that the relationship between the "nitrene" (nonconcerted decomposition of the reagent) and "nonnitrene" (concerted decomposition of the reagent) mechanisms is on the whole similar to the problem of the relationship between mononuclear and binuclear nucleophilic substitution.

The methods for the generation of nitrenes and their stabilization pathways have been previously examined (for example, see [2, 7]). The most commonly used method is photolysis of azides, in which the nitrene is generated under mild conditions that exclude side or secondary reactions. Various nitrenes can also be obtained by thermal decomposition of azides. As a rule, the decomposition of the reagent to give the nitrene proceeds at no lower than 100°C. If the reagent reacts with the substrate at lower temperatures, the probability of reaction via the "nitrene" mechanism is low. A convenient method for the generation of arylnitrenes is deoxygenation of nitro- and nitrosoarenes by trivalent phosphorus compounds. The deoxygenation of nitroso compounds proceeds under milder conditions and the consumption of triethyl phosphite is much lower, but the inconvenience of the deoxygenation of nitro compounds is frequently compensated by their greater accessibility. Aminonitrenes, alkoxynitrenes, and some other nitrenes are formed by oxidation of the corresponding amino derivatives with, for example, lead tetraacetate. It is assumed that the resulting nitrenes exist in the singlet state [2, 7], except in the case of photosensitized photolysis of azides.

Despite the fact that it has been found possible to synthesize dozens of types of heterocyclic compounds by means of nitrenes, the transformations of the singlet nitrenes that constitute the basis of such syntheses can be divided into four principal groups: 1) intramolecular isomerization, rearrangement, or fragmentation of the nitrene, during which vinyl-

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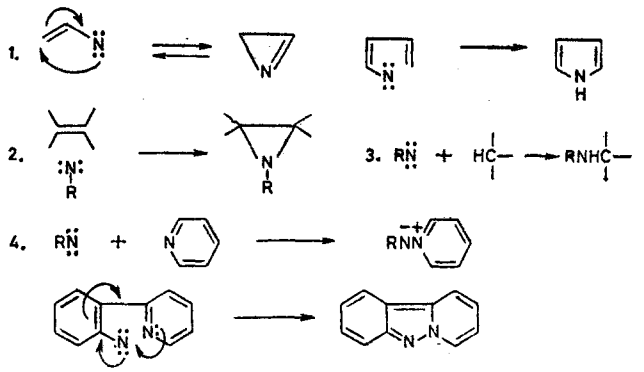
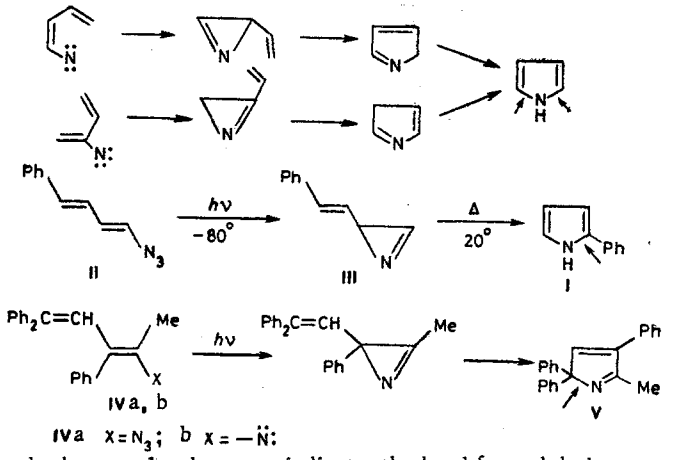
nitrene–azirine tautomerism and irreversible isomerization of 1,3-butadien-1-ylnitrenes to 1H-pyrrole derivatives are of greatest significance; 2) addition of the nitrene to a multiple bond, particularly the C=C bond, to give an aziridine; 3) incorporation of the nitrene in a C_{sp^3}–H bond; 4) reaction of the nitrene with the unshared electron pair of a heteroatom to give ylides or systems with rearranged multiple bonds.



Different combinations and modifications of these principal types of transformations of nitrenes, which are frequently accompanied by multistep rearrangements of the intermediate reaction products, lead to a great diversity of heterocyclic systems that can be obtained by means of nitrenes.

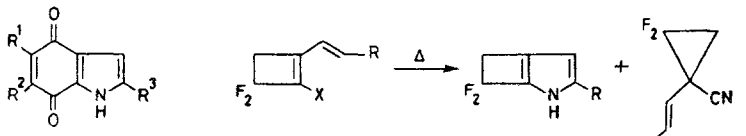
Pyrroles and Their Condensed Analogs

A large number of substituted pyrroles and their condensed derivatives have been synthesized through nitrenes. In the overwhelming majority of cases the pyrrole ring is formed as a result of rearrangement of 1,3-butadien-1-yl- and 1,3-butadien-2-ylnitrenes, the C=C bonds of which may be both olefinic and aromatic. If there is an olefinic bond adjacent to the sextet of the nitrogen atom in the nitrene, these nitrenes undergo cyclization to pyrroles through intermediate 1-azirines and 2H- or 3H-pyrroles; if there is an aromatic bond adjacent to this sextet, nitrenes of this type can be converted to 1H-indoles or carbazoles, with bypassing of the formation of 1-azirines.



Here and subsequently, the arrow indicates the bond formed during intramolecular cyclization.

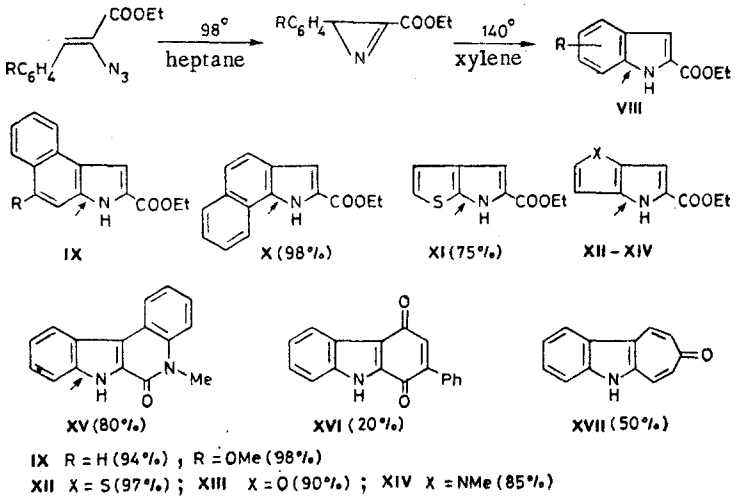
In fact, the thermal and photolytic decomposition of stereoisomeric 4-azido-1-phenyl-1,3-butadienes led to the formation of 2-phenylpyrrole (I) [12], and 3-styryl-1-azirine (III) was isolated as an intermediate under the conditions of low-temperature photolysis of trans,-trans isomer II. As one should have expected, 4,4-disubstituted butadienylnitrene IVb is converted to 2H-pyrrole V. Butadienylnitrenes that contain cycloolefinic bonds are isomerized to condensed analogs of pyrrole; for example, when o-azidovinylnaphthoquinones are heated in benzene, they are converted to benzindole-4,9-diones VI in 80-90% yields [13]. The strained cyclobutene bond in nitrene VIIb can also be included in the reaction under discussion, although ring contraction also takes place simultaneously [14].



VI VIIa,b 10% 72%

VI $R^1, R^2 = C_4H_4$ and Me; R^3 = Alk, Ph; VIIa X = N_3, b X = —N:, R = O(NCO)

Diene nitrenes in which one C=C bond is included in an aromatic system undergo isomerization to indole derivatives. The conversion of cis-ω-styrylnitrenes to indoles proceeds through the intermediate formation of 3-aryl-1-azirines, which can be isolated by photolysis or mild thermolysis of the corresponding azides [8, 15]. This method has made it possible to obtain 2-methylindole (86%) [16] and indole-2-carboxylic acid derivatives VIII (90-98%) [17, 18]. The cyclization of analogous nitrenes that contain heteroaromatic or cycloolefinic C=C bonds, as well as C=C bonds of polycondensed systems, has proved to be a convenient metho for the synthesis of diverse condensed pyrrole derivatives: benzo[e]- and benzo[g]indoles IX and X, furo[3,2-b]-, thieno[3,2-b]-, and thieno[2,3-b]pyrroles XI-XIII [18], and other compounds (XIV-XVII) [19-23]. It should be noted that the thermal decomposition of ω-styryl azides may proceed via a concerted mechanism with bypassing of the step involving the formation of nitrene [8]. Indoles are also formed by deoxygenation of ω-nitrostyrenes. For example, the reduction of ω-nitrostilbene with excess triethyl phosphite leads to 2-phenylindole (16%) [24].



VIII

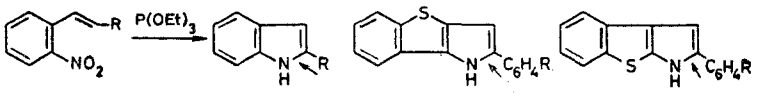
IX X (98%) XI (75%) XII - XIV

XV (80%) XVI (20%) XVII (50%)

IX R = H (94%), R = OMe (98%)

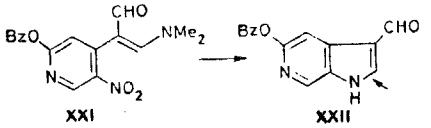
XII X = S (97%); XIII X = O (90%); XIV X = NMe (85%)

o-Styrylnitrenes and their heteroanalogs constitute another type of 1,3-butadien-1-ylnitrenes that are also capable of cyclization to indoles. Nitrenes of this type are usually obtained by deoxygenation of o-nitrostyrenes. The reduction of o-nitrostilbene with triethyl phosphite gives 2-phenylindole in 58% (from the trans isomer) and 85% (from the cis isomer) yields: 2-alkyl- (50-60%), 2-benzoyl- (16%), and 2-carbethoxyindole (20%) (XVIII) were similarly obtained [24-27]. Benzothieno[2,3-b]- and benzothieno[3,2-b]pyrrole derivatives XIX and XX were obtained in 65-80% yields with a large excess of triethyl phosphite in the deoxygenation of heteroaromatic nitro compounds [28].

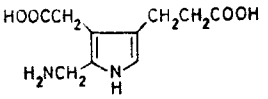


XVIII XX XIX

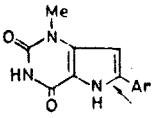
The cyclization of nitropyridine XXI to pyridopyrrole XXII was used for the synthesis of porphobilinogen XXIII [29]; pyrrole [3,2-d]pyrimidine derivatives XXIV were similarly synthesized in 40-60% yields [30].



XXI XXII

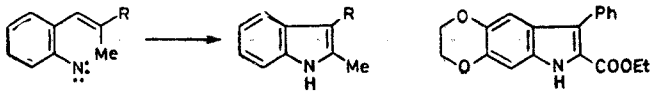


XXIII



XXIV

When there are two substituents in the ω position of o-styrylnitrene XXV, the reaction may proceed with rearrangement of the intermediate 2,2-disubstituted 2H-indoles to 2,3-disubstituted indoles XXVI and XXVII [31, 32]. o-Styrylnitrenes XXVIII with an exocyclic C=C bond undergo cyclization to condensed analogs of indoles XXIX [31]. Pseudorutecarpine and other indole derivatives were obtained by cyclization of analogous nitrenes [32-36].

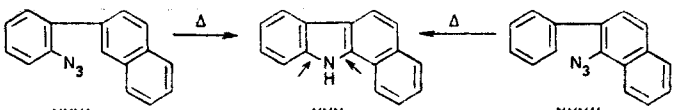


XXV* XXVI XXVII (75%)

XXVIII* XXIX

XXVI R = Me, Ph (21-33%); XXIX X = CH_2 (15%), CH_2CH_2 (35%)

The cyclization of 1,3-butadien-1-ylnitrenes in which both C=C bonds are included in an aromatic system (o-biphenylylnitrenes or their analogs) has been investigated most extensively [1-3]. Unsubstituted carbazole can be obtained in 70-80% yield by thermolysis or photolysis of o-azidobiphenyl [37-40], by treatment of o-nitroso- [37, 41-43] and o-nitrodiphenyls [44] with triethyl phosphite, and by photolysis of o-isocyanatobiphenyl [45]. Unsymmetrical carbazoles can be obtained by two methods [46]. For example, benzo[b]carbazole XXX is formed by thermolysis of azides XXXI and XXXII [47]; α-(o-nitrophenyl)naphthalene undergoes cyclization in the presence of triethyl phosphite to benzo[d]carbazole [24].

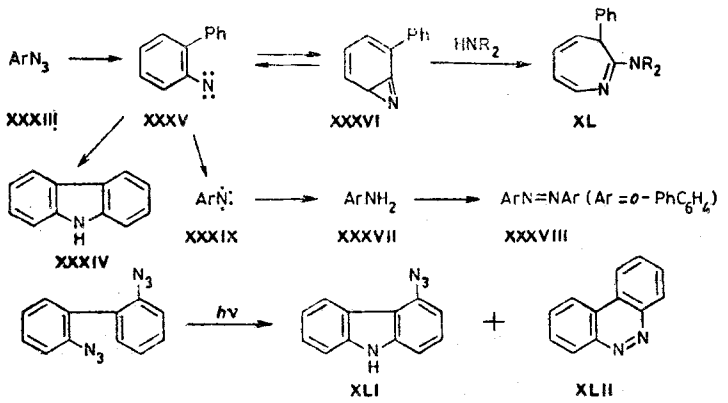


XXXI XXX XXXII

4'-R-Biphenylylnitrenes, obtained by similar methods, undergo isomerization to 2-R-carbazoles (R = CH_3, CH_3O, HO, Br), and 2'-R-biphenylylnitrenes to 4-R-carbazoles R = CH_3 Cl, Br) in 50-100% yields [24, 43, 44, 47-49]. Some 2'-R-2-azidobiphenyls (R = OH, CN, N_3) are not converted to carbazoles because of reactions via other pathways [47, 49-51]. It is preferable to obtain 3-R-carbazoles (R = Br, NO_2) from 5-R-2-azidobiphenyls [52], since the cyclization of 3'-R-biphenylylnitrenes proceeds ambiguously to give a mixture of 1-R- and 3-R-carbazoles [46, 53]. Various polysubstituted carbazoles can be obtained in high yields in the case of correct selection of the structure of the diphenyl derivative and the method for the generation of the nitrene [52, 54]. The latter may be of substantial value in for example, the synthesis of nitrocarbazoles, which are preferably obtained by deoxygenation of nitroso nitro derivatives or thermolysis (but not photolysis) of nitroazidobiphenyls [52].

A large number of papers have been devoted to the study of the mechanism of the photolytic and thermal decomposition of 2-azidodiphenyls XXXIII to carbazoles XXXIV [37, 38, 40, 46, 55-60]. Nitrene XXXV—benzazirine XXXVI tautomeric equilibrium precedes the formation of the carbazole. Whereas the isomerization of the nitrene to the azirine is a reversible process, the cyclization of the nitrene to the carbazole is an irreversible process [55]. The side products in this reaction are the corresponding anilines XXXVII and azo compounds XXXVIII, which are usually regarded as products of transformations of triplet nitrenes XXXIX.

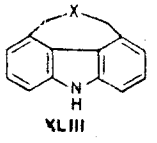
*Obtained by deoxygenation of the nitro compounds with triethyl phosphite.



The yields of carbazoles decrease in the presence of bases, since azirines XXXVI tie up the base irreversibly and undergo rearrangement to 3H-azepines XL [37]. The yields of carbazoles decrease in the presence of triplet sensitizers and increase in the presence of singlet sensitizers [38, 51, 57]. A sharp decrease in the photolysis temperature leads to an increase in the yields of the azo compounds, since the rate of cyclization of singlet nitrenes to carbazoles depends on the temperature to a greater degree than the rate of the singlet–triplet transition [40, 50, 51]. Thus in the irradiation of 2,2'-diazidobiphenyl, carbazole XLI is formed in 65% yield at 290°K, 10% carbazole and 55% benzo[c]cinnoline XLII are formed at 201°K, and only cinnoline XLII (98%) is formed in the solid matrix at 77°K [51].

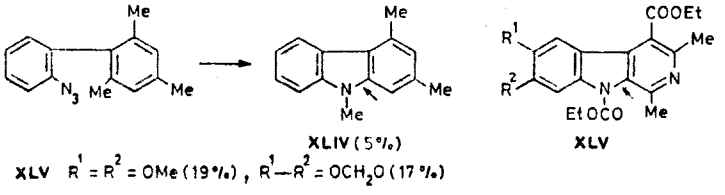
The mechanism of cyclization of nitrenes to carbazoles has not been established unambiguously. It has been shown that under the conditions of photochemical decomposition of azides triplet nitrene XXXIX is hardly the only or principal carbazole precursor [56]. However, under the conditions of thermolysis [60] or pulse photolysis [59] of o-azidobiphenyls the initally formed singlet nitrene is rapidly converted to a triplet nitrene, which is slowly (via the kinetically-controlled step) cyclized to a diradical and subsequently to the carbazole. A study of the cyclization of 2-nitrobiphenyl to carbazole showed that triethyl phosphite and triphenylphosphine have approximately identical reactivities, whereas phosphoru trichloride is not a cyclizing agent, and the rate of cyclization of o-nitro- and o-nitroso-diaryls is determined by the rate of formation of biphenylnitrene precursors [24, 41, 43, 61]

Whereas the deoxygenation of 2-nitro-2',6-dimethylbiphenyl with triphenylphosphine gives only 12% 4,5-dimethylcarbazole, possibly because of the difficulty involved in the formation of a coplanar structure in the transition state, nitrobiphenyls with a bridge in the 2',6 position undergo deoxygenation to carbazoles XLIII in higher yields (40-80%) [62].



X :	$C(COOEt)_2$	NMe	NCH_2Ph	O	S	SO_2	S—S
Yield, %:	78	50	77	71	45	30	18

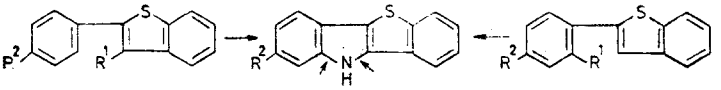
If both ortho positions in the second ring of the biphenylylnitrene are substituted, carbazoles either are not formed, or 9-R-carbazole rearrangement products XLIV and XLV (in no more than 20% yields) are formed [49, 58, 63, 64]; it is assumed that in this case triplet nitrenes precede the formation of carbazoles.



XLV $R^1 = R^2 = OMe$ (19%), $R^1—R^2 = OCH_2O$ (17%)

The cyclizations of heteroanalogs of o-biphenylnitrenes are of considerable interest. Benzothieno[3,2-b]indoles [65] were obtained by thermolysis of azides XLVII and XLVIII and by deoxygenation of nitro compounds XLIX and L [65, 66]. Similarly, heating a 1% solution of 2-(o-azidophenyl)thiophene in decalin at 180°C leads to another sulfur-containing carbazol

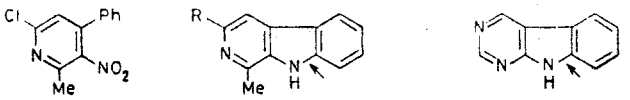
analog — thieno[3,2-b]indole (95%) [67].



XLVII, XLIX XLVI (30-65%) XLVIII, L

XLVII, XLVIII $R^1=N_3, R^2=H$; XLIX $R^1=NO_2, R^2=H, Me, Cl, Br$; L $R^1=NO_2, R^2=H$

An aza analog of carbazole — δ-carboline (65%) — was obtained by heating 3-azido-2-phenylpyridine in decalin at 160°C [68], and deoxygenation of 3-nitro-4-phenylpyridine LI with triethyl phosphite gave 3-chloro-β-carboline LII (15%), which was subsequently reduced to harman LIII [69]. Irradiation of 4-azido-5-phenylpyrimidine in trifluoroacetic acid gives pyrimido[4,5-b]indole LIV (91%) [70].

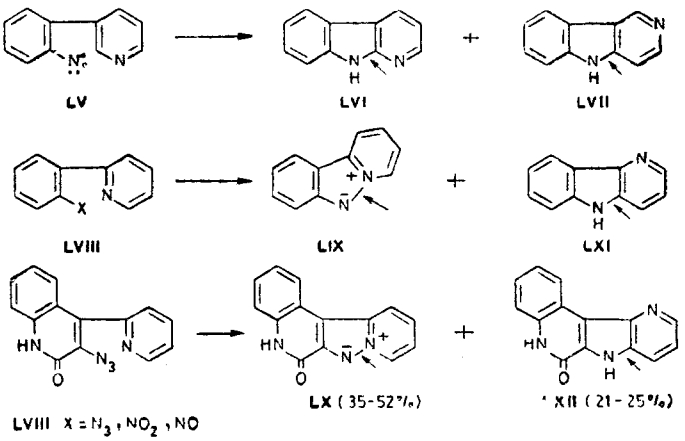


LI LII, LIII LIV

LI $\xrightarrow{P(OEt)_3}$ LII $\xrightarrow{LiAlH_4}$ LIII

LII R = Cl ; LIII R = H

In contrast to phenylpyridylnitrenes, the cyclization of o-(3-pyridyl)phenylnitrenes LV proceeds ambiguously to give a mixture of α- and γ-carbolines LVI and LVII; the percentage of α isomer in the mixture (70-82%) depends on the method of generation of the nitrene [43, 67]. 2-[o-Azido(nitro-, nitroso)phenyl]pyridines LVIII are cyclized in most cases at the more nucleophilic nitrogen atom to give pyrido[1,2-b]indazoles LIX (90-100%) [44, 71]. In individual cases the formation of δ-carbolines LXI and LXII in a ratio of 2:1 was noted in addition to the formation of pyridoindazoles LIX and LX [71, 72]. It is assumed [72] that δ-carbolines are formed with the participation of singlet nitrenes, whereas the pyridoindazoles are the final result of [3 + 2]-cycloaddition of the azido group to the pyridine ring.



LV LVI LVII

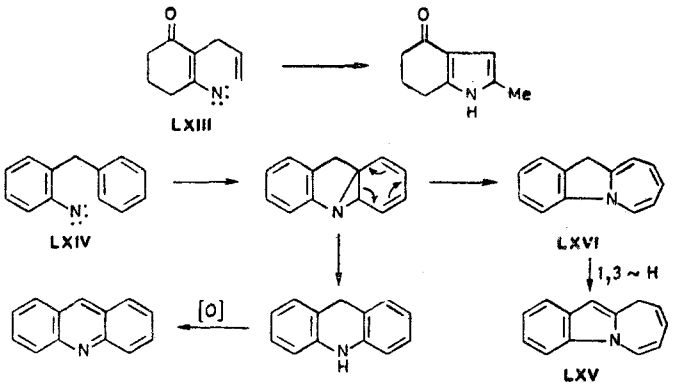
LVIII LIX LXI

LX (35-52%) XII (21-25%)

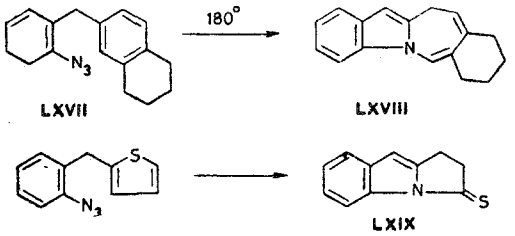
LVIII X = N_3, NO_2, NO

Information that carbazole (in 20% yield) can be obtained from o-diphenylhydroxylamine in the presence of phosphorus pentachloride [73] and from o-diphenylhydrazine in alcoholic hydrogen bromide solution [10] is also of some interest; both of these reactions scarcely include the intermediate formation of a biphenylylnitrene, since the formation of nitrenes in strongly acidic media is unlikely.

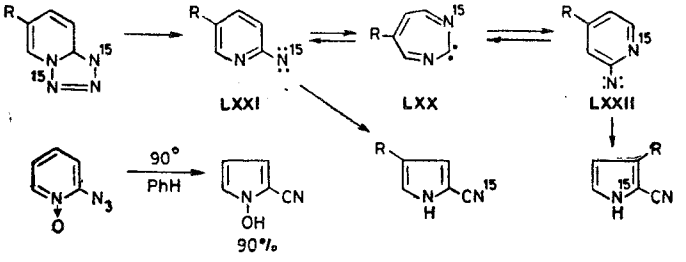
Not only conjugated diene nitrenes but also unconjugated 1,4-pentadienylnitrenes are inclined to form a pyrrole ring [74]. It is natural that the cyclization of nitrenes of the LXIII type to pyrrole derivatives is accompanied by rearrangement. Most study has been devoted to the rearrangement of o-benzylphenylnitrenes LXIV, which can be converted to azepinoindoles LXV or to a mixture of acridans and acridines [2-4].



Most authors assume that intramolecular addition of the nitrene to the remote C=C bond occurs in the first step, after which the intermediate aziridine (which was isolated in [33]) undergoes opening of the $C_{(2)}$—$C_{(3)}$ bond and is coverted to 11H-azepino[1,2-a]indole LXVI [75], which usually is subsequently isomerized to 10H isomer LXV [76]. Thus 10H-azepinoindole LXVIII (70%) and small amounts of the 11H isomer are formed when azide LXVII is heated [77]. As yet, it is difficult to formulate the mechanism of the conversion of o-benzylphenylnitrenes to azepinoindoles and acridans. Whereas azide LXVII is converted to azepinoindole LXVIII, under the same conditions 1- and 2-(o-azidobenzyl)naphthalenes give a mixture of the corresponding acridans and acridines [77].



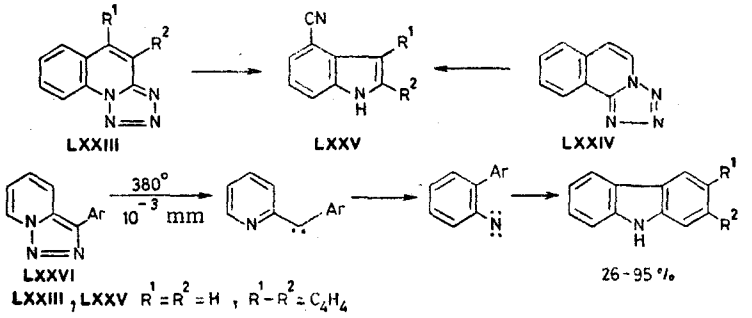
o-(4-R-Benzyl)phenyl azides undergo cyclization to 8R-10H-azepinoindoles (R = OMe, 48%), whereas the isomeric o-(2-R-benzyl)phenyl azides (R = Me, MeO) undergo cyclization to 10-R-10H-azepinoindoles (26-28%), and 6-R-azepinoindoles are not formed [78, 79]. The thermolysis of o-azidobenzylmesitylene leads to a mixture of isomeric 6H- (41%), 8H- (13%), and 10H-6,-8,10-trimethylazepinoindoles (20%) [79]. The thermal decomposition of 2-(o-azidobenzyl)-thiophene proceeds via a different mechanism and leads to the formation of indole LXIX [80, 81].



Another general method for the preparation of pyrrole derivatives is the rearrangement of pyridylnitrenes to cyanopyrroles. 2-Cyanopyrroles were obtained as a result of ring contraction of 2-pyridyl- [82], 3-pyridyl- [83], and 1-oxide-2-pyridylnitrenes [84]. The mechanism of this reaction may include a tautomeric equilibrium between the intermediate diazepinocarbene LXX and two isomeric pyridylnitrenes LXXI and LXXII [82].

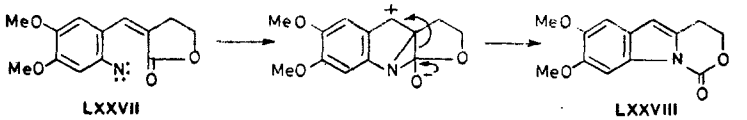
4-Methyl- and 5-methyl-2-pyridylnitrenes, obtained by pyrolysis of tetrazolo[1,5-a]-pyridines (at 500°C and 0.05 mm), are converted to 3-methyl- and 4-methyl-2-cyannopyrroles in up to 45% yields [85]. 4-Cyanoindole LXXV was obtained by gas-phase pyrolysis of tetrazolo[1,5-a]quinoline and phenanthridine LXXIII, as well as tetrazolo[5,1-a]isoquinoline LXXIV [86]. The basis of these transformations is the rearrangement of 2-quinolyl- and 1-isoquinolylnitrenes to the same o-cyanostyrylnitrene [87, 88]. The analogous 3-isoquinolyl-

nitrene and benzo[g]quinolylnitrene are converted to 1-cyanoisoindole (100%) and 2-cyanobenz-[e]indole (10%) [88]. It was shown that pyridocarbenes may exist in equilibrium with phenylnitrenes. Thus under the conditions of gas-phase pyrolysis pyridotriazoles LXXVI are converted to carbazoles [89, 90].



Other examples of the formation of a pyrrole ring from azides and different potential sources of nitrenes are less characteristic. Thus the addition of ethoxycarbonylnitrene to thiophene and 2,5-dimethylthiophene terminated with the formation of 1-carbethoxypyrrole (21%) and its 2,5-dimethyl derivative (18%). The analogous addition of carbethoxynitrene to pyrrole gave 14% 2-amino-1-carbethoxypyrrole [91]. 2,5-Diphenylpyrrole (32%) was obtained by rearrangement of acetophenone dimethylhydrazone methiodide in the presence of sodium isopropoxide [92] and by thermal decomposition of α-styryl azide [93]. In the latter case, however, the reaction begins with **[3 + 2]-cycloaddition** of the azido group to the C=C bond of another vinyl azide molecule, after which the intermediate triazoline is converted to 5-azido-5-phenyl-1-pyrroline and subsequently to 2,5-diphenylpyrrole.

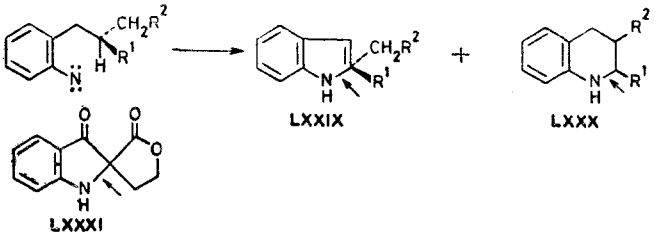
Examples of "unexpected" cyclizations of some types of arylnitrenes to carbazoles are known. In the presence of compounds of the trimethyl phosphite type, o-phenoxyphenylnitrene undergoes cyclization to a carbazole rather than to a phenoxazine as a result of cleavage of the Ph–O bond by the organophosphorus reagent and splitting out of trimethyl phosphate [94]. Carbazole (mixed with tetrahydrocarbazole) is formed in the dehydration of 2-phenylcyclohexanone oxime and from the O-3,5-dinitrobenzoyl derivative of this oxime [95], as well as in the reaction of o-nitrocyclohexylbenzene with ferric oxalate [10, 96]. A new method for the synthesis of benzo[α]carbazole (37%) or 5,6-dihydrobenzo[α]carbazole (38%) consists in deoxygenation of 1-(o-nitrobenzyl)-1,2-dihydroisoquinoline derivatives with triethyl phosphite [97, 98]. 4-Carbonyl-1,3-butadien-1-ylnitrene LXXVII is converted to oxazinoindole LXXVIII as a result of intramolecular **2,3-addition** of the sextet nitrogen atom to the conjugated system of C=C–C=O bonds and cleavage of the C–C bond in the intermediate aziridine **[33-35,** 99].



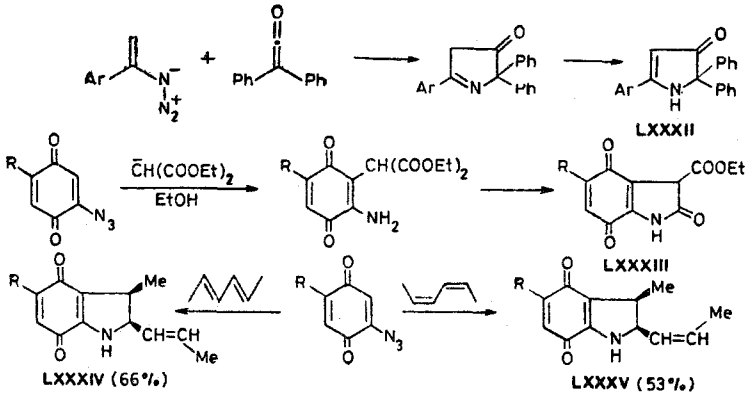
Indigo (85%) was obtained by thermolysis of o-aminophenacyl azide at 210°C; it is assumed that its precursor is 2-amino-1-hydroxyindole [100].

Pyrrolines and Their Analogs

It has been found that the most accessible compounds are 2-pyrroline derivatives, particularly indolines, the principal method for the synthesis of which is intramolecular C–H incorporation of o-alkylarylnitrenes. The incorporation proceeds regioselectively to give indolines LXXIX (40-80%) rather than tetrahydroquinolines LXXX [49, 101-103]. **Stereospecificity of the** incorporation with retention of the configuration of the asymmetric carbon atom, in the C–H bond of which a nitrene is incorporated, is also observed [103].



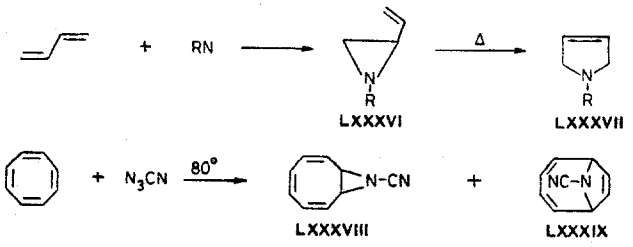
In contrast to the cyclization of 1,3-butadienylnitrenes to pyrrole derivatives, the structures and yields of side products in the isomerization of o-alkylarylnitrenes depend substantially on the conditions under which the nitrene is generated. This can be explained by the fact that only singlet nitrenes participate in the formation of the pyrroline ring, whereas reactions involving detachment of a hydrogen atom to give o-alkyl- and o-alkenylanilines are characteristic for triplet nitrenes, and the rate of C–H incorporation of single nitrenes and the rate of their singlet–triplet conversion are comparable. The decisive factor that determines the yields of pyrroline derivatives is dilution by an inert solvent and elimination of increased local concentrations of the reagents. Thus the yields of indolines are higher in the gas-phase pyrolysis of azides [101, 102] than in the case of decomposition in the condensed phase [49, 101] or deoxygenation of nitro compounds [96, 104, 105]; the more reactive nitroalkylbenzenes frequently form dihydroindoles in lower yields than o-nitroalkylbenzenes. This reaction has also been used for the synthesis of indolinone spiro derivative LXXXI [34, 35].



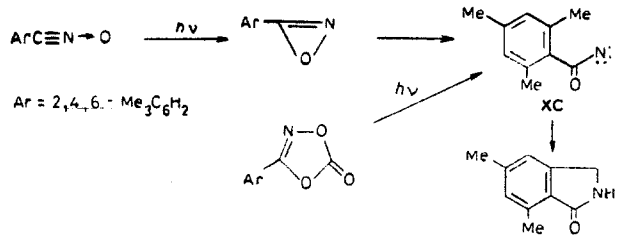
Other types of reactions in which nitrenes participate in the formation of a 2-pyrroline ring have also been described; for example, 2-phenylpyrroline is formed by thermolysis of 1-azido-1-phenylcyclobutane [106]. 2,5-Diaryl-2-pyrrolin-4-ones LXXXII are formed in good yields (45-50%) by the addition of α-styryl azides to the C=C bond of diphenylketene at 20°C, but the formation of nitrenes is excluded in this case [107]. The formation of 2-carbethoxy-2,4,7-indoletrione LXXXIII (77%) from o-azidoquinone and sodiomalonic ester also proceeds without the participation of nitrenes [108]. Irradiation of solutions of o-azidoquinones in the presence of aliphatic or alicyclic 1,3-dienes (λ_{max} 360 nm) leads to 2-vinyl-2,3-dihydro-4,7-indolediones LXXXIV and LXXXV and their condensed derivatives in high yields [109]. This reaction regiospecifically gives only 2-phenylindoles and proceeds only at the least substituted diene C=C bond; the reaction is stereospecific, since cis-2,3-disubstituted indoles are always formed, regardless of the configuration of the corresponding C=C bond in the starting diene, while the orientation of the substituents attached to the C=C bond is retained. The authors explain the results obtained by nonsynchronous cycloaddition of the photoexcited azido group to the diene C = C bond.

The formation of a 3-pyrroline ring should be expected in the case of 1,4-cycloaddition of nitrenes to 1,3-dienic hydrocarbons. Examples of reactions of this sort have been presented in reviews [1, 2, 5]. However, there is no assurance that 3-pyrrolines are the direct result of [1 + 4]-cycloaddition of nitrenes to conjugated dienes [2, 91, 110]. In fact, in a number of cases it has been possible to demonstrate the intermediate formation of 2-vinylaziridines LXXXVI, the thermal expansion of the ring of which [for example, under conditions of gas–liquid chromatography (GLC) at 100°C] led to 3-pyrrolines LXXXVII [111]. A mixture of aziridine LXXXVIII and pyrroline LXXXIX (10%) is formed in the thermal decomposition of

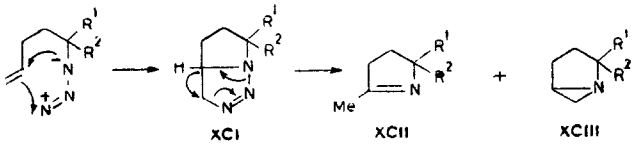
cyanogen azide in cyclooctatetranene; it was shown that the pyrroline is not the result of isomerization of the aziridine, and it was assumed that the aziridine is formed by a singlet nitrene and that the pyrroline is formed by a triplet nitrene [112, 113].



Intramolecular C—H incorporation of aroylnitrenes XC can serve as another method for the synthesis of **compounds that** contain a 3-pyrroline ring [114, 115].

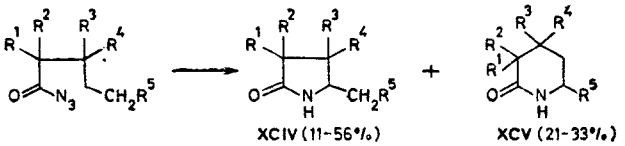


The formation of 1-pyrrolines is possible in the decomposition of cyclobutyl azides [14] or 5-azidoalkenes [5]; in the latter case intermediate triazoline XCI undergoes decomposition to give a mixture of XCII and XCIII (50-70%) **containing primarily** cyclic imine XCII [116].



Pyrrolidines

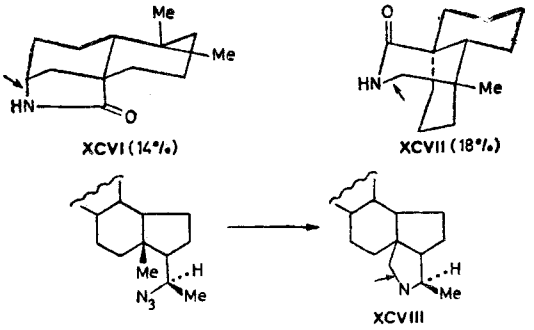
The pyrrolidine ring can be constructed as a result of intramolecular incorporation of nitrenes obtained by photolysis of alkyl or **alkanoyl** azides [1, 5, 11]. Piperidines, as well as nitrene isomerization products — alkylimines or alkyl isocyanates — are also formed simultaneously [117-119]. The yields of pyrrolidine itself and its 2-substituted derivatives are low (20-30%) [117, 120]. It is possible that the cyclization of alkylnitrenes to pyrrolidines proceeds through a step involving detachment of a hydrogen atom by a triplet nitrene [120]. It was initially assumed that in the photolysis of alkanoyl azides 2-pyrrolidones XCIV are formed by a triplet nitrene and that 2-piperidinones XCV are formed by a singlet nitrene [121], but later both lactams were considered to be products of C—H incorporation of singlet carbonylnitrenes [122]. The synthetic aspect of this reaction for monocyclic lactams XCIV is apparent from the data in [122]. Photolysis of ethyl δ-azidovalerate and subsequent hydrolysis give proline (15%) [120, 123], while photolysis of azides of terpene acids gives the corresponding polycyclic lactams [5, 119].



R^1, R^2, R^3, R^4 = H or Me, R^5 = H, Me, Pr

Whereas the ratio between the γ- and δ-lactams for acyclic azides is determined primarily by the relative reactivities of the primary, secondary, and tertiary C—H bonds with respect to incorporation of carbonylnitrenes [124], in the case of polycyclic carbonylazides it is determined primarily by the stereochemical requirements [5]. For example, 1,1-dimethyl-trans-decalin-10-carboxylic acid azide is converted to γ-lactam XCVI as a result of incorpo-

ration in the $C_{(6)}$—H bond, whereas the azide of the analogous cis-decalincarboxylic acid is converted to δ-lactam XCVII as a result of incorporation in the methyl group [125-127]. This reaction has frequently been used for the synthesis of podocarpic acid derivatives [114, 119] and for the determination of the configurations of triterpene derivatives [5] and some alkaloids; it has been found to be possible to accomplish the elegant synthesis of the steroid alkaloid conessine (XCVIII) by means of this reaction [120, 123].



Another general method for the construction of the pyrrolidine ring is intramolecular addition of unsaturated nitrenes to a remote C=C bond with subsequent opening of the aziridine ring [5, 128]. The 1-carbethoxypyrrolidine ring was constructed by intermolecular addition of carbethoxynitrene to a substituted cyclobutene with subsequent hydrogenation of the reaction products [129]. The ability of vinyl azides to undergo conversion to 1-azirines can be used for the synthesis of 2-pyrrolidines if the reaction is carried out in the presence of ethyl benzoylacetate [130].

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