Nitrenes, Carbenes, Diradicals, and Ylides. Interconversions of Reactive Intermediates

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CONSPECTUS

Rearrangements of aromatic and heteroaromatic nitrenes and carbenes can be initiated with either heat or light. The thermal reaction is typically induced by flash vacuum thermolysis, with isolation of the products at low temperatures. Photochemical experiments are conducted either under matrix isolation conditions or in solution at ambient temperature. These rearrangements are usually initiated by ring expansion of the nitrene or carbene to a seven-membered ring ketenimine, carbodiimide, or allene (that is, a cycloheptatetraene or an azacycloheptatetraene when a nitrogen is involved).

Type I ring opening ylidic

Type II ring opening diradicaloid or nitrenoid

Over the last few years, we have found that two types of ring opening take place as well. Type I is an ylidic ring opening that yields nitrile ylides or diazo compounds as transient intermediates. Type II ring opening produces either dienylnitrenes (for example, from 2-pyridylnitrenes) or 1,7-(1,5)-diradicals (such as those formed from 2-quinoxalinylnitrenes), depending on which of these species is better stabilized by resonance. In this Account, we describe our achievements in elucidating the nature of the ring-opened species and unraveling the connections between the various reactive intermediates.

Both of these ring-opening reactions are found, at least in some cases, to dominate the subsequent chemistry. Examples include the formation of ring-opened ketenimines and carbodiimides, as well as the ring contraction reactions that form five-membered ring nitriles (such as 2- and 3-cyanopyrroles from pyridylnitrenes, N-cyanoimidazoles from 2-pyrazinyl and 4-pyrimidinylnitrenes, N-cyanopyrazoles from 2-pyrimidinylnitrenes and 3-pyridazinylnitrenes, and so forth). The mechanisms of formation of the open-chain and ring-contraction products were unknown at the onset of this study. In the course of our investigation, several reactions with three or more consecutive reactive intermediates have been unraveled, such as nitrene, seven-membered cyclic carbodiimide, and open-chain nitrile ylide. It has been possible in some cases to observe them all and determine their interrelationships by means of a combination of matrix-isolation spectroscopy, photochemistry, flash vacuum thermolysis, and computational chemistry.

These studies have led to a deeper understanding of the nature of reactive intermediates and chemical reactivity. Moreover, the results indicate new directions for further exploration: ring-opening reactions of carbenes, nitrenes, and cyclic cumulenes can be expected in many other systems.
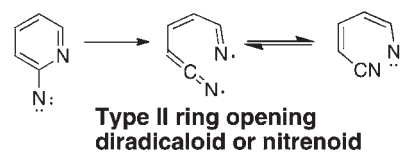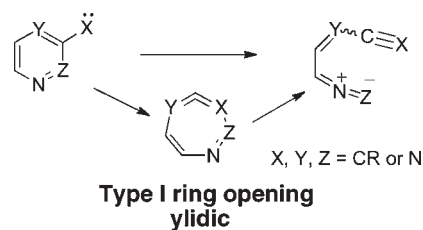
Introduction

The ring expansion of aromatic and heteroaromatic nitrenes and carbenes to seven-membered ring ketenimines, carbodiimides, and allenes, that is, (aza)cycloheptatetraenes, is well established. For example, phenylnitrene (**1**) and 2-pyridylcarbene (**3**) interconvert via 1-azacyclohepta-1,2,4,6-tetraene (**2**),[1,2] 2-pyridylnitrene (**4**) undergoes a degenerate rearrangement via the cyclic carbodiimide **5**,[3] and phenylcarbene **6** automerizes via cycloheptatetraene **7**, which effectively results in scrambling of all the carbon atoms except the quaternary C1

(Scheme 1).[4] All these reactions can take place thermally and photochemically, in the former case usually by flash vacuum thermolysis (FVT). The reactive intermediates can sometimes be observed directly by isolation of the FVT products in noble gas matrices, typically Ar, 10 K. The photolyses are carried out in noble gas matrices and sometimes in solution.

The seven-membered ring cumulene intermediates may themselves exist in "bond switch" isomeric forms, for example, **11a** (1700 cm^{-1}), **14** (1680 cm^{-1}), and **17** (1702 cm^{-1}), which are cyclic nitrile ylides.[5-7] They become important and

SCHEME 1. Nitrene and Carbene Rearrangements

* = ¹⁵N or ¹⁴N

* = ¹³C or ¹²C
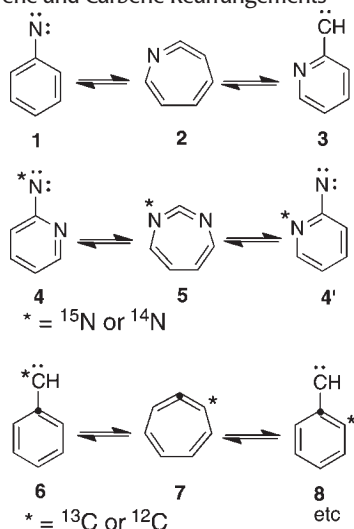
SCHEME 2. Formation of Cyclic Nitrile Ylides

9a X = CH
9b X = N

10a,b

11a

12

13

14

15

16

17
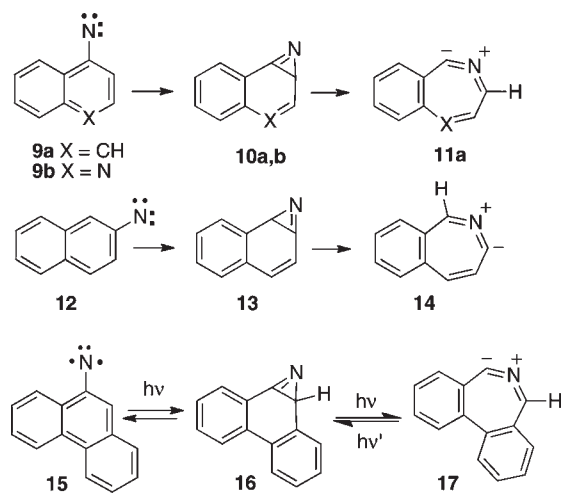
observable in the matrix photolyses of 1- and 2-naphthylnitrenes, **9a** and **12**, and 9-phenanthrylnitrene (**15**), where the "normal" cyclic cumulenes would be *o*-quinonoid. Here, the corresponding azirenes **10a** (1730 cm⁻¹), **10b** (1741 cm⁻¹), **13**, and **16** (1742 cm⁻¹) were also observed by IR spectroscopy (Scheme 2).[5–8]

While the reactions described so far may be regarded as typical, they are not universal. The ring expansions may be partly or completely superseded by ring-opening reactions, leading to ylides, diradicals, carbenes, or nitrenes, all of which may be observed directly by matrix isolation ESR or IR and UV–vis spectroscopies (Type I and Type II ring opening, Scheme 3).

It was obvious in our early work on FVT reactions that ring opening of nitrenes could take place; for example,

SCHEME 3. Type I and Type II Ring Opening

X, Y, Z = CR or N

Type I ring opening
ylidic

**Type II ring opening**
diradicaloid or nitrenoid
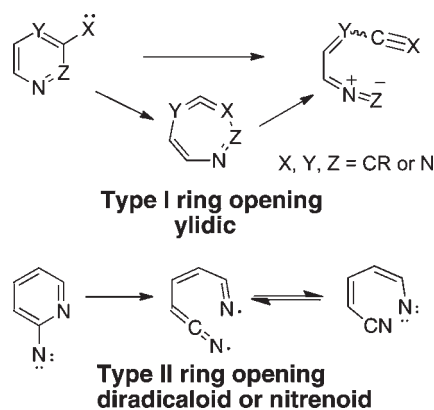
glutacononitriles are minor byproducts from pyridylnitrenes[3] (see Scheme 14), and ring opening to diazo compounds takes place on generation of 3-pyridazylnitrenes (see Scheme 13). It occurred to us that analogous ring opening of, for example, 3-pyridylnitrenes and 2-pyrazinylnitrenes would lead to nitrile ylides (see Schemes 4–7), which might be detectable spectroscopically, and these species could be the sources of the isolated open-chain products. This led to a long series of experiments aimed at elucidating the nature of the ring-opened species and unraveling the interrelationships between the various reactive intermediates.

Type I Ring Opening to Nitrile Ylides

Not only do 2-pyridylcarbene (**3**) and phenylnitrene (**1**) interconvert via 1-azacycloheptatetraene (**2**); the 2-, 3-, and 4-pyridylcarbenes, **3**, **19**, and **20**, all undergo thermal and photochemical rearrangement to phenylnitrene **1** (Scheme 4).[2] Because nitrenes are generally of lower energy than the isomeric carbenes,[9,10] phenylnitrene is the thermodynamic sink of all these intermediates. The zwitterionic seven-membered ring species **22** had been postulated as the link between 4- and 3-pyridylcarbenes **20** and **19**,[2] but the ylidic ring opening conjecture (Scheme 3) suggested to us that the nitrile ylide **21** might be involved instead,[11] and this turned out to be the case. Compound **21** absorbs strongly at 1930 cm⁻¹ in the matrix IR spectrum, and the same species is also formed on matrix photolysis of 4-diazomethylpyridine, the precursor of 4-pyridylcarbene **20** (Scheme 4). Further photolysis of ylide **21** led to a new species identified as the isocyanovinylallene **23**, formed by a 1,7-H shift. It is likely that both the carbene **19** and the cyclic allene **18** can undergo the ring opening to nitrile ylide **21**, and calculations indicate that the activation barriers for these two processes are nearly identical.[11]

SCHEME 4. The 1930 cm^{-1} Nitrile Ylide **21** from Pyridylcarbenes
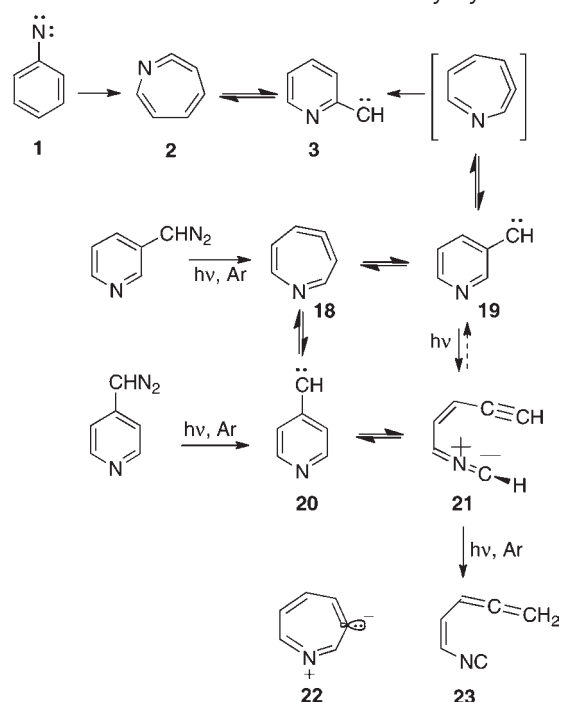
**SCHEME 5.** The Nitrile Ylide from 3-Pyridylnitrene
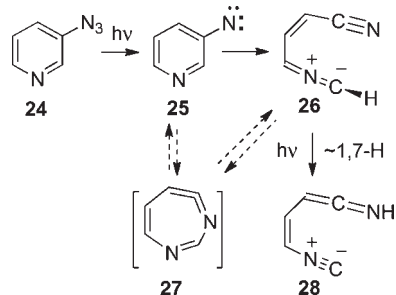
3-Pyridylnitrene **25** underwent analogous ring opening to the directly observed cyanovinylnitrile ylide **26** (1961, 2212 cm^{-1}), which on further photolysis underwent the 1,7-H shift to isocyanovinylketenimine **28** (Scheme 5).[11]

Again, it is possible that ring opening may take place in either the nitrene **25** or the unobserved cyclic ketenimine **27**, and calculations indicate that both paths are energetically feasible.

Clear evidence for the nitrile ylide **30** derived from 3-quinolylnitrene **29** was obtained by matrix photolysis of 3-azidoquinoline.[12] The nitrene was generated at 305–310 nm and characterized by ESR, IR, and UV spectroscopies. The nitrene was stable to photolysis at wavelengths above 600 nm, but at 395 nm, it underwent rapid ring opening to the nitrile ylide **30**, which was characterized by its IR and UV spectra. Further photolysis afforded a mixture of the *Z* and *E*

SCHEME 6. 3-Quinolylnitrene
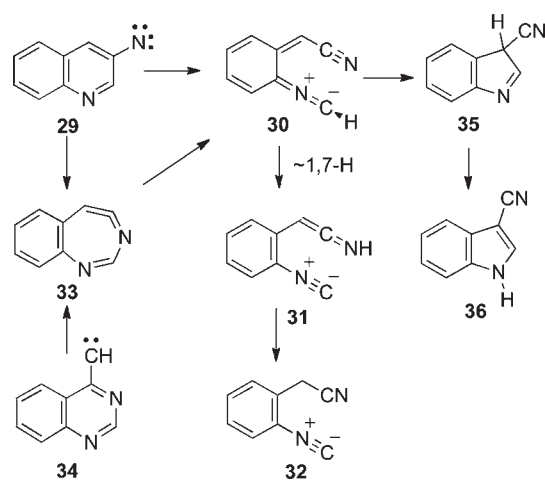
isomers of *o*-isocyanophenylketenimine **31** and eventually *o*-isocyanophenylacetonitrile **32** (Scheme 6). A low barrier for the 1,7-H shift **30** → **31** is indicated by DFT calculations at the B3LYP/6-31G* level. The ring opening to the ylide may also take place in the seven-membered ring ketenimine **33** (Scheme 6), and DFT calculations indicate that the two paths **29** → **30** and **33** → **30** are nearly isoergic (activation barriers ca. 20 kcal/mol relative to the open-shell singlet nitrene). A weak absorption at 1910 cm^{-1} suggested the presence of the ketenimine **33**. This intermediate can also be generated by ring expansion of the isomeric carbene **34** (Scheme 6), which affords the same products as the nitrene on photolysis and thermolysis. FVT of the precursors of the nitrene **29** as well as the carbene **34** afforded the ring contraction product 3-cyanoindole **36** in high yield, and it is postulated that this is the result of cyclization of the ylide **30** to the 3*H*-indole **35** (Scheme 6). The calculated energy barrier for this process is only 5 kcal/mol.[12] Further evidence for ring opening of the seven-membered ring species will be given below.

4-Pyrimidinylnitrenes and 2-Pyrazinylnitrenes

2-Pyrazinylnitrenes (e.g., **37**) and 4-pyrimidinylnitrenes (e.g., **39**) interconvert on both thermolysis and photolysis and therefore usually give rise to the same products in identical yields. The nitrenes are generated from the corresponding tetrazolo[1,5-*a*]pyrazines or tetrazolo[1,5-*c*]pyrimidines via valence isomerization to the 2-azidopyrazines and 4-azido-pyrimidines. Matrix isolation of the azides is usually achieved by mild FVT of the tetrazoloazines below their decomposition temperatures, for example, at 200 °C. Both triplet nitrenes have been characterized by ESR spectroscopy

(**37**, $D/(hc) = 1.014$, $E/(hc) = 0.000$ cm^{-1}; **39**, $D/(hc) = 1.1937$, $E/(hc) = 0.0012$ cm^{-1}).[7,13] Matrix photolysis with $\lambda > 260$ nm gave rise to an intermediate absorbing at 1973 and 840 cm^{-1} in the IR spectrum, but this was rapidly replaced by 1-cyanoimidazole, **43** (2268 cm^{-1}), and isocyanovinylcarbodiimide, **44** (2118, 2135 cm^{-1}) (Scheme 7).[14]

The transient intermediate absorbing at 1973 and 840 cm^{-1} could be either the seven-membered ring carbodiimide **41** or the open-chain nitrile ylide **42** (Scheme 7), which have very similar calculated IR spectra at the B3LYP/6-31G* level. The calculated energetics of the reactions indicate that the nitrile ylide **42** is of lower energy, and the barriers for its conversion to the products, **43** by cyclization and **44** by the 1,7-H shift, are very low, so low that they can take place even in matrices at cryogenic temperatures (Scheme 7).

SCHEME 7. 4-Pyrimidinylnitrene and 2-Pyrazinylnitrene[a]
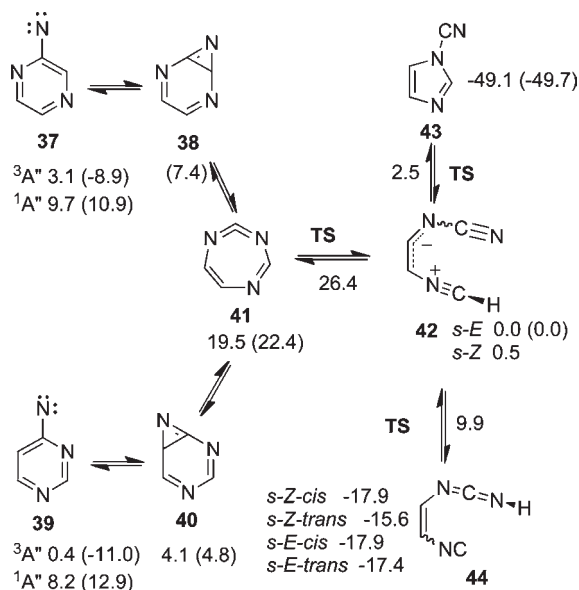
[a]G3(MP2) energies (CASPT2/6-31G*+ZPE values in parentheses) in kcal/mol.

FVT of tetrazolopyrazines and tetrazolopyrimidines affords 1-cyanoimidazoles in virtually quantitative yields (e.g., **48** and **52**, Scheme 8). Using ^{15}N-labeling, it was shown that the nitrene-N in the pyrazinylnitrene **45** ends up in the cyano group of **48**, but in the pyrimidinylnitrene **49**, it becomes a ring-nitrogen atom in **52** in agreement with these reactions taking place via the nitrile ylides **47** and **51** (Scheme 8).[15]

In summary, there is no doubt that 2-pyrazinylnitrenes and 4-pyrimidinylnitrenes undergo ring opening to nitrile ylides (**42**, **47**, **51**) via the seven-membered ring carbodiimides (**41**, **46**, **50**). It remains a possibility that 2-pyrazinylnitrene **45** may also undergo direct ring opening to **47**. More detailed information is obtainable from the benzo derivatives, that is, the quinoxalines and quinazolines described below, where both the cyclic carbodiimides and the nitrile ylides become observable.

## 2-Quinoxalinylnitrenes and 4-Quinazolinylnitrenes

Mild FVT of the isomeric tetrazoles **53T** and **61T** results in partial ring opening to the azides **53A** and **61A** (Scheme 9). FVT at 450–500 °C afforded two products, **58** and **60**, in nearly quantitative isolated yield (ratio ca. 55:45) (Scheme 9). Matrix photolysis permitted the observation of the triplet nitrenes **54** and **62** by ESR spectroscopy ($D/(hc) = 0.955$ and 0.995; $E/(hc) = 0.0033$ and 0.0040 cm^{-1}, respectively).[16]

The two nitrenes were also observed by matrix IR and UV–vis spectroscopy. Long-wavelength photolysis (>610 m) caused the rapid disappearance of the ESR, IR, and UV–vis spectra assigned to the nitrenes, while a new species absorbing strongly at 2005 cm^{-1} was formed rapidly. All the IR bands belonging to this species were identical in the two photolyses and agreed well with the calculated spectrum of the cyclic carbodiimide **55** at the B3LYP/6-31G** level. Continued photolysis caused disappearance of **55** and formation of

SCHEME 8. Results of ^{15}N-Labeling of Pyrazinyl- and Pyrimidinylnitrenes

* = [15]N or [14]N
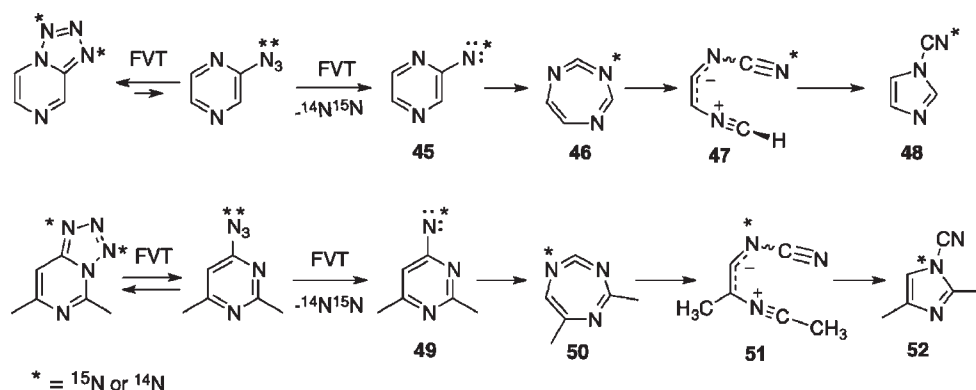
SCHEME 9. 2-Quinoxalinylnitrene and 4-Quinazolinylnitrene

SCHEME 10. Reactions of Substituted Quinoxalinylnitrenes
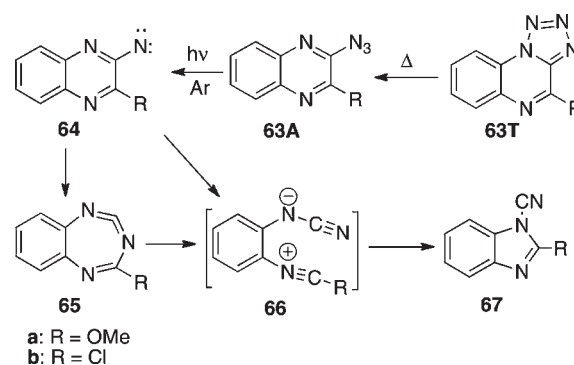

a: R = OMe
b: R = Cl
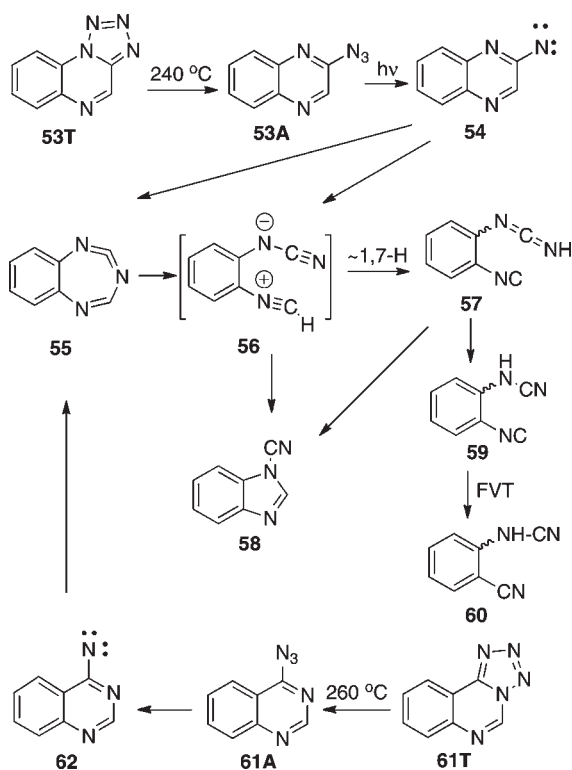
the two end products **57** and **58** (Scheme 9). Due to its partly *o*-quinonoid nature, the open-chain nitrile ylide **56** is higher in energy than **55** by a calculated 22.4 kcal/mol, and it was not observed. This is reasonable because it has only a small calculated barrier toward isomerization to the open-chain carbodiimide **57** (4.5 kcal/mol).[16]

The methoxy- and chloro-substituted quinoxalinylnitrenes **64** (Scheme 10) were generated in an effort to suppress the 1,7-H shifts of the type **56** → **57**. Matrix photolysis of the azides **63A** at 308 nm allowed the characterization of both nitrenes by IR and UV spectroscopy. Photolysis in the visible absorption bands of the nitrenes caused their disappearance and formation of the seven-membered ring carbodiimides **65**, characterized by very strong absorptions in the IR spectra (**65a**, 2000 cm^{-1}; **65b**, 2005 cm^{-1}). Here, the energies of the seven-membered ring carbodiimides are calculated to lie significantly below the unobserved nitrile ylides **66** (e.g., 29 kcal/mol for **65b**). FVT of **63Tb** at 450–550 °C caused formation of 2-chloro-1-cyanobenzimidazole **67b** as the only identifiable product. The nitrile ylide **66b** has a calculated barrier of only 9.6 kcal/mol toward cyclization to **67b**.[16]

In summary, the cyclic carbodiimides **65** are protected by relatively high energy barriers from further rearrangement in low-temperature matrices, but under FVT conditions

1-cyanobenzimidazoles **67** can form via readily accessible transition states. We postulate that ring contraction takes place via ring opening to the unobserved nitrile ylides **66** (Scheme 10).

The rapid 1,7-H shifts in the formonitrile ylides **56** makes their direct observation difficult. The substituted nitrile ylides **66** cannot undergo the 1,7-H shifts easily, but they can still cyclize rapidly to either **65** or **67** via low activation barriers. Introduction of a phenyl group on the ylidic function makes these species longer-lived and makes it possible to selectively form and destroy them as described below.[16]

A mixture of the nitrene **68** ($\lambda_{max} = 548$ and 735 nm) and the ylide **70** ($\lambda_{max} = 536$ nm) is generated by matrix photolysis at 308 nm. The UV−vis and IR spectra of nitrene and ylide are in good agreement with the calculated transitions at the (TD)B3LYP/6-31G** level. Subsequent irradiation of the matrix at $\lambda > 610$ nm caused disappearance of the nitrene and formation of the cyclic carbodiimide **69**, absorbing strongly at 2008 cm^{-1} in the IR. Further irradiation of the same matrix at $\lambda > 395$ nm for 2 min caused disappearance of the absorptions assigned to ylide **70** and, again, the cyclic carbodiimide **69** was clearly formed. This allowed the IR bands at 2281, 2141, and 2119 cm^{-1} to be assigned to the ylide **70**, which can exist in at least two *s-E* and *s-Z* conformations **70Z** and **70E** (Scheme 11). Calculated energies of ground and transition state structures at the B3LYP/6-31G** level are summarized in Scheme 11. It is seen that the phenyl substitution has stabilized the ylide **70** significantly, so that it is now only ca. 14 kcal/mol higher in energy than the cyclic carbodiimide **69**. The barrier between them is small (ca. 18 kcal/mol from the carbodiimide side). The *s-E* ylide **70E** can cyclize via a very low barrier (ca. 8 kcal/mol) to the 1-cyanobenzimidazole **71**.

Both singlet nitrenes **68** and **72** undergo ring expansion to the cyclic carbodiimide **69** very easily (ca. 9−10 kcal/mol

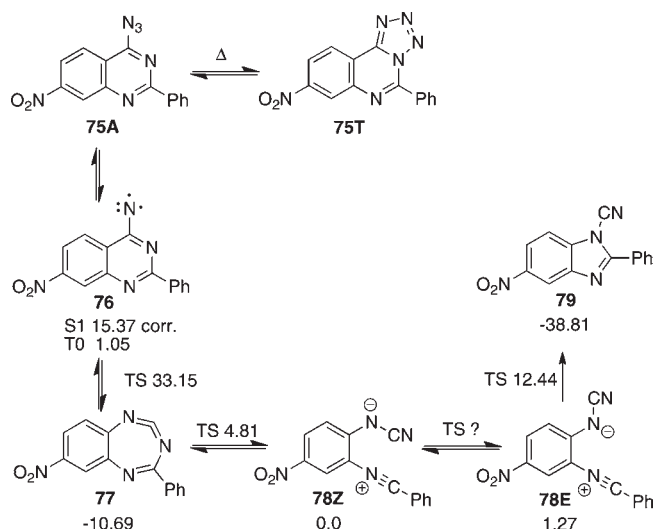**SCHEME 11.** The Phenyl-Substituted Quinoxalinyl- and Quinazolinylnitrenes[a]
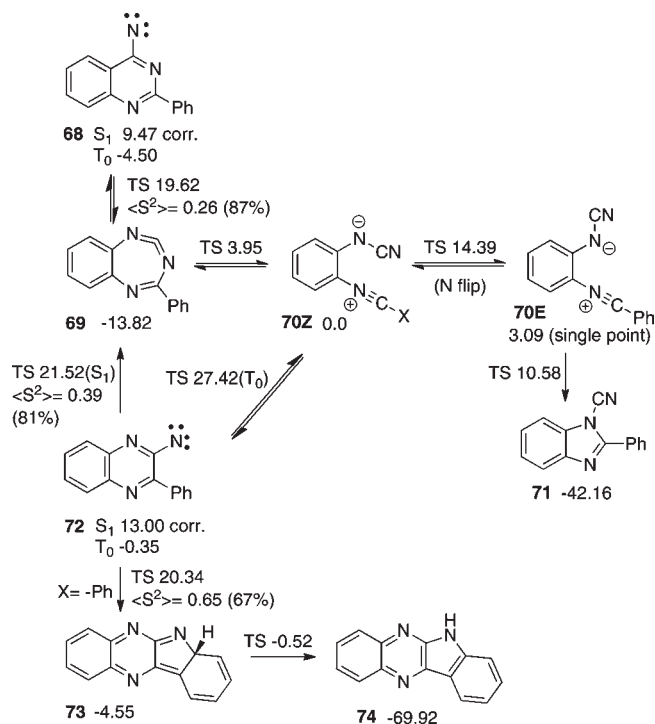
[a]Relative energies of ground and transition state structures in kcal/mol calculated at the B3LYP/6-31G** level.

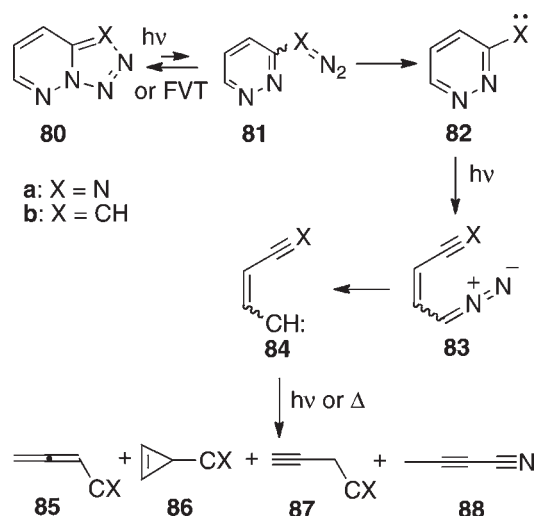**SCHEME 12.** 7-Nitro-2-phenyl-4-quinazolinylnitrene

77 has now decreased further to ca. 11 kcal/mol. The activation barrier between the two is ca. 14 kcal/mol from the carbodiimide side and 5 kcal/mol from the ylide side. The barrier for cyclization of the ylide **78E** to 1-cyanobenzimidazole **79** has increased to ca. 11 kcal/mol.

In conclusion, the seven-membered ring carbodiimides (**55**, **65**, **69**, and **77**) are formed readily by photolysis of all the nitrenes (**54**, **62**, **64**, **68**, **72**, and **76**). The products of subsequent photolyses are postulated to form via ring opening of the seven-membered ring carbodiimides to nitrile ylides (**56**, **66**, **70**, and **78**). Both the nitrile ylide **70** and the seven-membered ring carbodiimide **69** were finally observed and well characterized in the 2-phenyl-4-quinazolinylnitrene/3-phenyl-2-quinoxalinylnitrene series (Scheme 11), and in the case of 7-nitro-2-phenyl-4-quinazolinylnitrene **76**, a reversible photochemical interconversion of the cyclic carbodiimide **77** and the nitrile ylide **78** was achieved (Scheme 12).

Type I Ring Opening to Diazo Compounds. 3-Pyridazinylcarbenes and 3-Pyridazinylnitrenes

Type I ring opening of 3-pyridazinylnitrenes **82a** and 3-pyridazinylcarbenes **82b** leads to diazo compounds **83** (Schemes 13). Tetrazolopyridazine **80a** undergoes a very small degree of ring opening to the azide **81a** (2145, 2118 cm^{-1}) on gentle FVT at 250 °C. Deposition of this mixture of tetrazole and azide in an Ar matrix and subsequent photolysis at 222, 254, or 308 nm caused formation of the nitrene **82a** as revealed by ESR spectroscopy ($D/(hc) = 1.006$; $E/(hc) = 0.003$ cm^{-1}).[18] In the IR spectrum, two conformers of diazo compound **83a** were observed at 2086 and 2072 cm^{-1} within the first few minutes of

barriers). On FVT, the indoloquinoxaline **74** is obtained in 8% yield from **72** but not from **68**. The cyclization of the singlet nitrene **72** to the "isocarbazole"-type[17] intermediate **73** (Scheme 11) also has a very low calculated barrier (ca. 7 kcal/mol).

Conclusive evidence for the ylide, the seven-membered cyclic carbodiimide, and their interconversion was obtained in the 7-nitro-2-phenyl-4-quinazolinylnitrene series (Scheme 12).

Photolysis of nitrene **76** (Scheme 12) in its visible absorption band at $\lambda > 695$ nm converted it to the seven-membered ring carbodiimide **77** (λ_{max} 340 nm; ν'_{max} 2013 cm^{-1}). Further photolysis of the latter at 308 nm caused ring opening to the nitrile ylide **78** (λ_{max} 479−540 nm). Two isomers of this ylide, **78Z** and **78E**, were observed in the IR and UV−vis spectra, and they were destroyed selectively on irradiation at $\lambda > 550$ and $\lambda > 495$ nm, respectively, when they both reverted to the cyclic carbodiimide **77**. It was possible to cycle several times between the ylides and the seven-membered ring, but eventually a small amount of 1-cyanobenzimidazole **79** was also formed. This compound is formed in quantitative yield on FVT of **75** at 400−500 °C.[16]

The calculated energies (Scheme 12) indicate that the difference between the nitrile ylide **78Z** and the cyclic carbodiimide

SCHEME 13. 3-Pyridazinylnitrene and 3-Pyridazinylcarbene

SCHEME 14. 2-Pyridylnitrene

irradiation. The diazo compounds disappeared on further irradiation, giving rise to the two cyanovinylcarbenes **84a**, which were also detected by ESR ($D/(hc) = 0.389$; $E/(hc) = 0.021$ cm^{-1}). A 1,3,4-triazacycloheptatetraene was not observed.
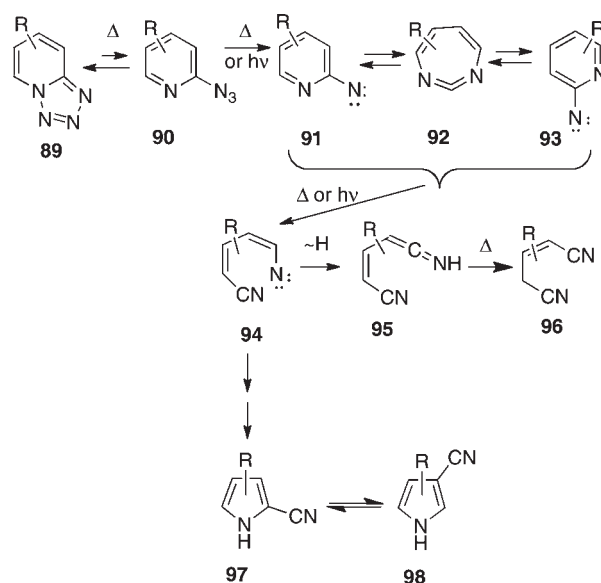
Continued matrix photolysis or FVT of **80a** at 305−380 °C yields cyanoallene **85a** and 3-cyanocyclopropene **86a**, which, particularly in the higher temperature regime, rearrange partially to propargyl cyanide **87a** and tetrolonitrile **88**; these four products were isolated in a combined yield of 99% in the FVT reaction (Scheme 13).[19]

Similar matrix photolysis of triazolopyridazine **80b** at 222 nm or FVT at 500 °C gave rise to the *s-Z* and *s-E* conformers or diazo compound **81b**. Photolysis of these at 308 nm in the ESR spectrometer afforded carbenes **82b** ($D/(hc) = 0.5440$; $E/(hc) = 0.0254$ cm^{-1})[7] and two conformers of **84b** ($D/(hc) = 0.3360$ and 0.389; $E/(hc) = 0.0208$ and 0.021 cm^{-1}). The diazo compound **83b** was detected by IR spectroscopy. Both matrix photolysis and FVT gave rise to 1,2,4-pentadienyne **85b**, 3-ethynylcyclopropene **86b**, and 1,4-pentanediyne **87b**. The calculated activation energy for loss of N$_2$ from diazo compound **83b** is 41 kcal/mol, and the barriers for isomerization of carbene **84b** to **85b** and **86b** are only 5.12 and 2.43 kcal/mol, respectively (B3LYP/6-31G*) (Scheme 19). A further rearrangement of 3-pyridazinylcarbene **82b** to 2-pyridylnitrene will be described below (Scheme 16).[20]

Type II Ring Opening to Nitrenes/Diradicals. 2-Pyridylnitrenes, Quinolyl- and Isoquinolylnitrenes, and 9-Phenanthridinylnitrene

Type II ring opening (Scheme 3) usually occurs when a Type I ring opening is not possible on structural grounds. Consequently, open-chain diradical- or nitrene-type intermediates are formed instead, and Type II ring opening tends to have higher activation barriers. Type II ring opening is often a minor side reaction in FVT of tetrazolopyridines **89**, giving 0−10% yields of mixtures of *Z*- and *E*-glutacononitriles **96** accompanying the main products, 2- and 3-pyrrolecarbonitriles **97** and **98** (small amounts of 2-aminopyridines are also formed) (Scheme 14).[9,21] The nitrene−nitrene interconversion **91**−**92**−**93** is much faster than the formation of the subsequent products. Therefore, nitrogen scrambling (and substituent scrambling) is seen in the products, and that was how the nitrene−nitrene interconversion was originally demonstrated.[3a] The cyclic carbodiimides **92** are readily observed on Ar matrix photolysis of tetrazolo/azidopyridines at 254 nm, formed in nearly quantitative yields and typically absorbing in the range 1980−2020 cm^{-1}. Under matrix conditions, open-chain ketenimines **95** can be observed as byproduct of continued photolysis in many cases.[22,23] The parent cyanovinylketenimine absorbs at 3311, 2222, and 2042 cm^{-1}. Further photolysis of the unsubstituted carbodiimide **99** affords a new species with prominent IR bands at 1688, 1207, and 1077 cm^{-1}, which are assigned to the spiro-azirene **101** (Scheme 15) on the basis of excellent agreement with the calculated IR spectrum.[20] *NH*-Ketenimines readily tautomerize to nitriles, so **95** is assumed to be the precursor of glutacononitriles **96** isolated in the FVT reactions.[20,21] Both the vinylnitrene **94** (unsubstituted) and the 2-pyridylnitrenes **91** have been detected by ESR spectroscopy in Ar matrices.[20,21]

The photochemical and thermal (600 °C) reactions of pyridazylcarbene **82b** was described in Scheme 13. Very remarkably, FVT at higher temperatures, 700−800 °C, gives,

in addition to the products described in Scheme 13, low yields of the products expected from 2-pyridylnitrene, namely, **96**, **97**, and **98** (Scheme 16). Energy calculations at the B3LYP/6-31G* level support the feasibility of this rearrangement. The relative energies indicated in Scheme 16 suggest that the cyclization of carbene **82b** to the unobserved cyclopropene **102** requires a very modest energy barrier, and its rearrangement to the seven-membered ring **103** is strongly exothermic. The further isomerization of **103** to diazirene **104** requires a barrier of ca. 13 kcal/mol. The ring opening of **104** to 2-pyridylnitrene **105** has a very small barrier, and the formation of the triplet ground state ($^3A''$) of **105** is exothermic by ca. 34 kcal/mol. Open-shell singlet arylnitrenes are usually 18−20 kcal/mol higher in energy than the triplets;[10] we calculate a S−T splitting of 19.7 (CASPT2) or 16.2 (B3LYP) kcal/mol for 2-pyridylnitrene **105** (Scheme 16). Thus, the overall reaction, **82b** ($^1A'$) → **105** ($^1A''$) is exothermic by about 40 kcal/mol on the singlet energy surface.[20]

There are three potential pathways for the ring contraction to cyanopyrroles (Scheme 16): (i) ring closure of the vinylnitrene **94ZZ** to 2*H*-2-cyanopyrrole **107**; (ii) concerted ring contraction of 2-pyridylnitrene (**105** → **107**), and (iii) rearrangement of the spiro-azirene **101**.[20] Ring contraction of 2-pyridylnitrenes to *N*-cyanopyrroles has never been observed, and such reactions have been ruled out by ^{15}N and substituent labeling.[20] In contrast, 2-pyrazinyl- and 4-pyrimidinylnitrenes and their benzo derivatives readily undergo ring contraction to *N*-cyanoimidazoles and *N*-cyanobenzimidazoles (Schemes 7−12). As described above, this takes place via the ring-opened nitrile ylides, a path not possible for 2-pyridylnitrenes.

2-Quinolyl- and 1-isoquinolylnitrenes **110** and **108** interconvert via the seven-membered ring carbodiimide **109** (Scheme 17).[24] The nitrenes have been detected by

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**SCHEME 15.** Rearrangement of 1,3-Diazacycloheptatetraene

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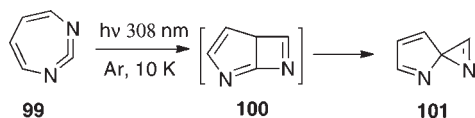
SCHEME 16. 3-Pyridazinylcarbene−2-Pyridylnitrene Rearrangement[a]
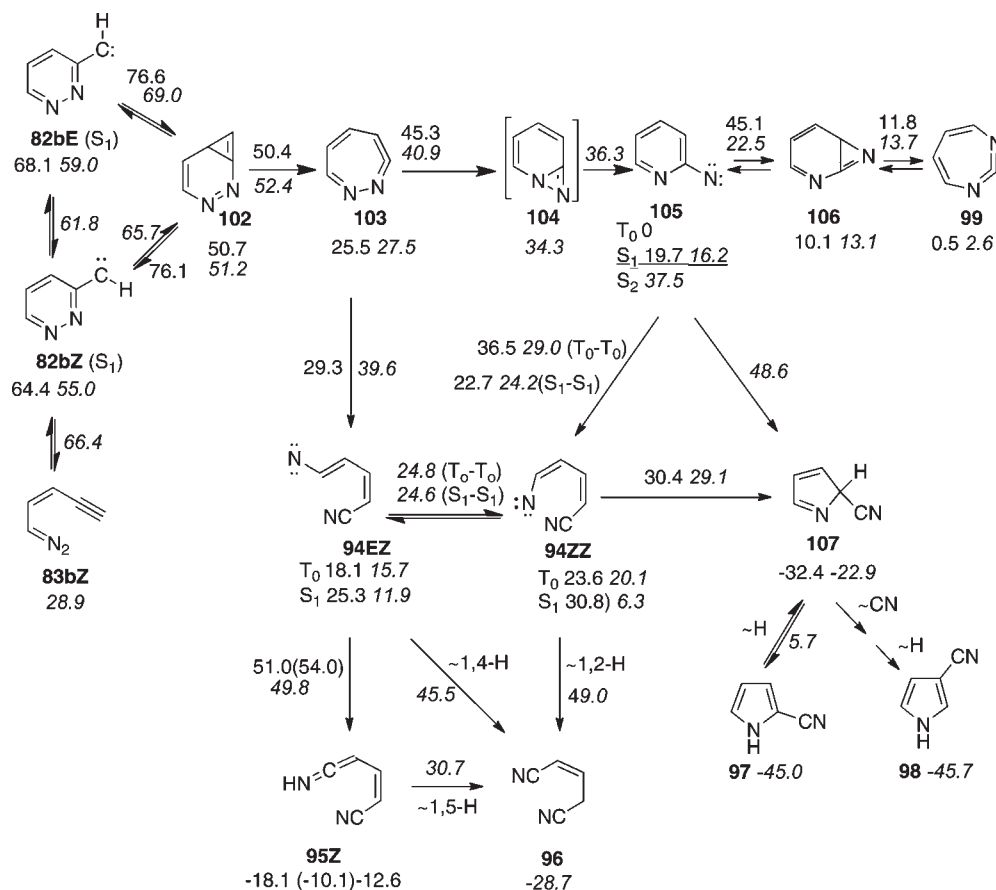
[a]Calculated energies in Arabic numbers at the CASPT2 level and in italics at the (U)B3LYP/6-31G* level (kcal/mol relative to triplet 2-pyridylnitrene **105**). A QCISD(T)/6-31G* single point calculation yielded a value for TS(**102** → **103**) 1.3 kcal/mol above **102**.

SCHEME 17. 1-Isoquinolylnitrene and 2-Quinolylnitrene

SCHEME 18. 9-Phenanthridinylnitrene


* = [15]N or [14]N
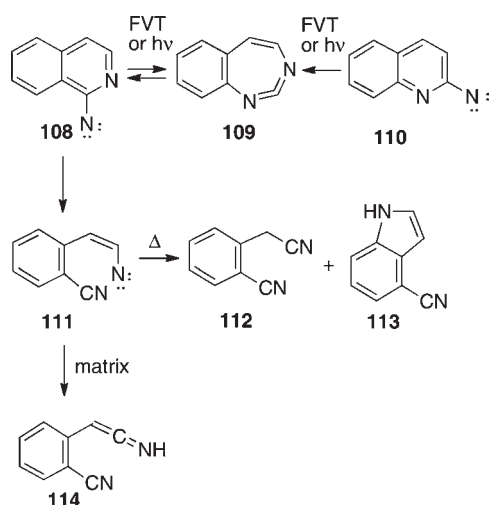
ESR,[13,18] and the ring expanded carbodiimide has been detected by IR spectroscopy under both FVT and photolysis conditions.[24] Under FVT conditions, both **108** and **110** afford the nitriles **112** and **113** as end products. Matrix photolysis affords the *NH*-ketenimine **114**. These three products are readily explained in terms of initial ring opening of isoquinolylnitrene to the vinylnitrene **111** (Scheme 17).[24]

[15]N-labeling demonstrated analogous ring opening in 9-phenanthridinylnitrene **115**, causing the formation of nitrogen-scrambled products **121** and **122** *after* the equilibration of the nitrenes via the seven-membered ring carbodiimide **116** (2010 cm^{-1}, neat). The latter is stable as a solid until ca. $-40\,°C$, when it dimerizes to the diazete derivative **118**.[3b] These results imply the biphenylylnitrene **119** as an intermediate en route to 4-cyanocarbazole **121**. The exact origin of 9-cyanocarbazole **122** is more difficult to determine: it may be formed in concerted reactions of either **115**/**117** or **116**, or quite likely via the diradical **120** (Scheme 18).[3b,15,25]

2-Pyrimidinylnitrenes and 2-Quinazolinylnitrenes

Clear evidence for the diradicaloid (nitrenoid) ring opening of nitrenes was achieved in the 2-pyrimidinyl- and 2-quinoxalinyl-nitrene systems.[18] Early work demonstrated the formation of 1-cyanopyrazole **126** and ketenimine **127** on FVT of tetrazolo-[1,5-*a*]pyrimidine/2-azidopyrimidine **123T**/**123A** above 320 °C (Scheme 19).[27] Ketenimine **127** and the ring-opened nitrene **125** are observable by matrix IR and ESR spectroscopy, respectively. 2-Pyrimidinylnitrenes **124** can also be observed directly by ESR spectroscopy under both FVT and photolysis conditions (e.g., **124a** $D/(hc) = 1.217$; $E/(hc) = 0.0052$ cm^{-1})[13] and by IR spectroscopy[26] on photolysis at 254 nm.
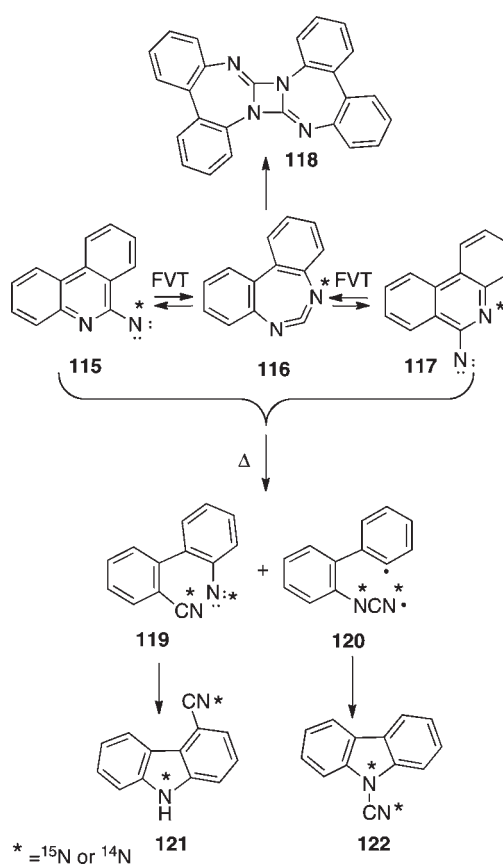
The fascinating 2-quinazolinylnitrene **129** was generated as indicated in Scheme 20.[18] Ar matrix photolysis of **128a** produced three triplet species, the major one being 2-quinazolinylnitrene **129a**, identified by IR, UV, and ESR spectroscopies ($D/(hc) = 1.1465$; $E/(hc) = 0.0064$ cm^{-1}). The second species formed more slowly and was a short-lived diradical, identified as **132Ra** by ESR spectroscopy ($D/(hc) = 0.1187$; $E/(hc) = 0.0026$ cm^{-1}); it corresponds to a Type II ring opening of nitrene **129a** or carbodiimide **130a**. Both reactions are computationally feasible. Diradical **132a** reacted already at 15 K to produce the end products of photolysis, **134a** and **135**. The calculated barrier for the cyclization **132a** → **134a** was only 1−2 kcal/mol. In compound **132**, the diradical form will have higher weight than the nitrene **132N**, the latter being *o*-quinoidal. The third, minor, triplet species observed by ESR was another arylnitrene ($D/(hc) = 0.9587$; $E/(hc) < 0.0008$ cm^{-1}), assigned as the phenylnitrene **136a**, formed in an alternate Type II ring opening of **129a** (Scheme 20).

Only a very weak IR band at 1990 cm^{-1} was observable for the assumed cyclic carbodiimide **130a**. However, the phenyl derivative **130b** was very easily identified by matrix IR spectroscopy (2006 cm^{-1}) in the photolysis of nitrene

SCHEME 19. 2-Pyrimidinylnitrenes

a: R = R' = H
b: R = R' = CH$_3$

SCHEME 20. 2-Quinazolinylnitrenes


a: R = H
b: R = Ph
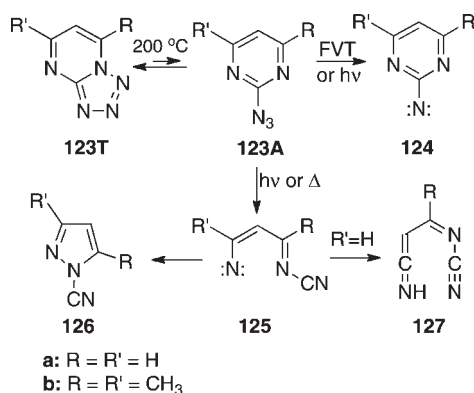
129b or its precursor azide at 310 nm (Scheme 20). In this case, the diradical **132b** was not observed, either because its cyclization to the end product **134** was too fast or because the reversible ring opening to diazo compund **131** (observed at 2120 and 2142 cm^{-1}) took precedence. Thus, photolysis of **130b** at 310 nm produced **131**, and the reaction was reversed at $\lambda > 475$ nm. Both of the latter compounds disappeared slowly, due to formation of the end product **134b** (also the end product of FVT, where it was isolated in 63% yield[27]) as well as to N$_2$ loss from **131**, which generated a diphenylcarbene, assigned as **133** ($D/(hc) = 0.4053$; $E/(hc) = 0.0192$ cm^{-1}). Finally, a second nitrene was also present in the matrix, and this is assigned as the alternate Type II ring-opening product, the phenylnitrene **136b** ($D/(hc) = 1.0163$; $E/(hc) < 0.001$ cm^{-1}).[18]

It should be noted that ring-opening reactions of the seven-membered ring carbodiimides or ketenimines derived from *s*-triazinylnitrenes, 2-pyrimidinylnitrenes and pyridine-2,6-dinitrenes have been reported by Chapyshev.[28] Ring opening of *p*- and *m*-phenylenedinitrenes and 1,5-naphthalenedinitrene or the corresponding ketenimines have been reported by Tomioka et al.,[29,30] and Sander et al. reported ring opening of 3-dehydrophenylnitrenes.[31]

Conclusion and Outlook

Two types of ring opening of (hetero)arylnitrenes and -carbenes have been identified. The most facile ring opening (Type I) takes place when there is a *meta* relationship between a ring nitrogen atom and a carbene or nitrene substituent, and it leads to the formation of nitrile ylides. This is the case for 3-pyridylcarbene and 3-pyridylnitrene (Schemes 4 and 5), 3-quinolylnitrene (Scheme 6), and 2-pyrazinylnitrenes and 2-quinoxalinylnitrene (Scheme 7). Here it must be kept in mind that both the nitrenes (carbenes) and the seven-membered ring-expanded cumulene intermediates may undergo
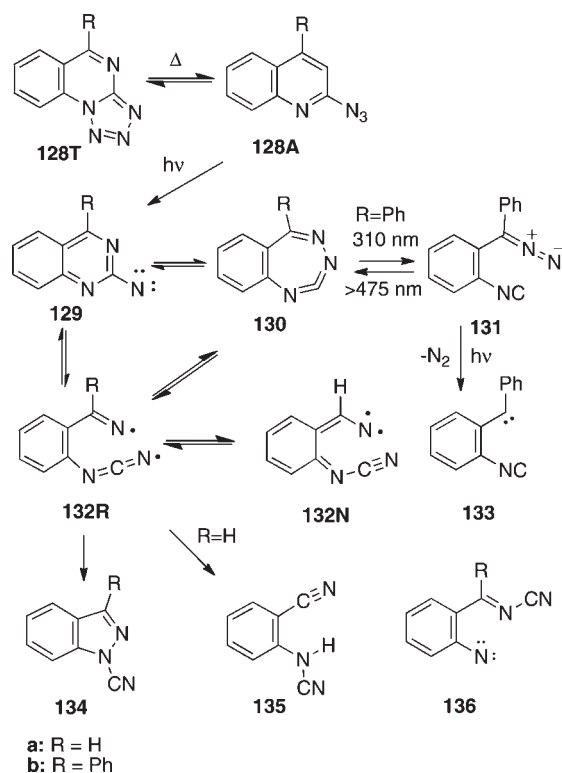
the ring-opening reaction (Scheme 3). Indeed, a photochemically reversible ring opening—ring closure interconverting the cyclic carbodiimide and the open-chain nitrile ylide was established in the case of the quinazolinylnitrenes (Schemes 11 and 12). The other, energetically less favorable Type II ring opening can take place when no such *meta* relationship exists, and it leads to the formation of 1,5- or 1,7-diradicals, nitrenes, or carbenes. This type of ring opening has been demonstrated for 2-pyridylnitrenes and 2-quinazolinylnitrenes by ESR spectroscopy (Schemes 16 and 20). In some cases, the ring-opening reactions take precedence to the extent of almost completely hiding the traditional ring expansion to the cyclic cumulenes (this is the case for the unsubstituted 3-quinolylnitrene **29** and 2-quinazolinylnitrene **129a**). Nevertheless, hetarylnitrenes, carbenes, nitrile ylides, diradicals, and ring-opened nitrenes have all been identified by direct observation, although in many cases it is impossible to observe all the reactive intermediates directly in the same system. The ring-opening reactions appear to be ubiquitous.

The ring-opened intermediates appear in many cases to be the direct precursors of the five-membered ring nitriles, which are often the thermodynamically highly favorable end products of both photolysis and thermolysis of (hetero)arylnitrenes, but concerted ring contractions of the nitrenes may also sometimes take place (e.g., Scheme 16).

Indeed, there may be a plethora of mechanisms of ring contraction.[20]

Ring-opening reactions of carbenes, nitrenes, and cyclic cumulenes can be expected in many other systems. For example, both 1- and 2-naphthylnitrenes or their ring-expanded cumulene equivalents appear to undergo several ring-opening reactions on extended photolysis.[6] 4-Pyridylnitrene and the isomeric 2-pyridazinylcarbene, as well as the benzo derivatives 4-quinolylnitrene and 2-quinoxalinylcarbene, undergo ring expansion to cyclic seven-membered ring ketenimines absorbing at $1872-1909$ cm^{-1}, but they also rearrange in part to species absorbing in the $1985-2100$ cm^{-1} region due to ring opening to nitrile ylides, which isomerize further to open-chain ketenimines. 2-Quinoxalinylcarbene undergoes substantial ring opening to a substituted phenylnitrene as well. Not only a carbene[13] but also prominent ESR signals due to two diradicals as well as a second nitrene are observed when 2-quinolylnitrene is generated by matrix photolysis. Generation of 9-phenanthridinylnitrene **115** (unlabeled) by matrix photolysis likewise gives rise to a carbene as well as a diradical (probably **120**) and a second nitrene (most probably **119**).

BIOGRAPHICAL INFORMATION

Curt Wentrup was born in Denmark, where he studied under Professor K. A. Jensen (University of Copenhagen), receiving a *cand. scient.* degree (1966) followed by a Ph.D. at the Australian National University, Canberra (1969, with W. D. Crow), and a D.Sc. from the University of Copenhagen (1976). He started his academic career at the University of Lausanne, Switzerland (1969–1976), initially as a postdoctoral fellow with Professor Hans Dahn, and was Professor of Organic Chemistry at the University of Marburg, Germany (1976–1985), before being appointed to the Chair of Organic Chemistry at The University of Queensland. He is a Fellow of the Australian Academy of Science. His research interests are in mechanistic and synthetic chemistry of reactive intermediates and unusual molecules. Other major research themes are the chemistry of iminopropadienones and -thiones, R—N=C=C=C=X, and the characterization and rearrangement of pseudohalides of the types RX—N=C=Y and RY—CNX.

FOOTNOTES

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