2-Pyridynitrene and 3-Pyridazylcarbene and Their Relationship via Ring-Expansion, Ring-Opening, Ring-contraction, and Fragmentation

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Photolysis of triazolo[1,5-b]pyridazine 8 isolated in Ar matrix generates diazomethylpyridazines 9Z and 9E and diazopentyynes 11Z and 11E as detected by IR spectroscopy. ESR spectroscopy detected the 3-pyridazylcarbene 10 as well as pent-2-en-3-ylidene 12 formed by loss of one and two molecules of N₂, respectively. Further photolysis caused rearrangement of the carbenes to 1,2-pentadien-4-yne 13 and 3-ethynylcyclopropene 14. Flash vacuum thermolysis (FVT) of 8 at 400–500 °C with Ar matrix isolation of the products yielded 13, 14, and 1,4-pentadiyne 15. At higher temperatures, glutacononitriles 27Z and 27E were formed as well together with minor amounts of 2- and 3-cyanopyrroles 28 and 29. Tetrazolo[1,5-a]pyridine/2-azidopyridine 22T/22A yields 2-pyridynitrene 19 as well as the novel open-chain cyanodienylnitrene 23 and the ring-expanded 1,3-diazacyclohepta-1,2,4,6-tetraene 21 on short wavelength photolysis. Nitrenes 19 and 23 were detected by ESR spectroscopy, and cumulene 21 by IR and UV spectroscopy. FVT of 22T/22A also affords 2-pyridynitrene 19 and diazacycloheptatetraene 21, as well as glutacononitriles 27Z,E and 2- and 3-cyanopyrroles 28 and 29. Photolysis of 21 above 300 nm yields the novel spiroazirene 25, identified by its matrix IR spectrum. The reaction pathways connecting the four carbenes (10Z,E and 12Z,E) and three nitrenes (19, 23EZ, and 23ZZ) in their open-shell singlet and triplet states are elucidated with the aid of theoretical calculations at DFT, CASSCF, and CASPT2 levels. Three possible mechanisms of ring-contraction in arylnitrenes are identified: (i) via ring-opening to dienylnitrenes, (ii) concerted ring-contraction, and (iii) via spiroazirenes 25, whereby (i) is the energetically most favorable.

Introduction

In recent papers we have demonstrated the occurrence of two types of ring-opening reactions of (hetero)aromatic nitrenes and carbenes, Type I and Type II (Scheme 1).

Type I ring-opening generates nitrile ylides exemplified by 3-pyridylcarbene, 3-pyridynitrene, and 2-pyrazinylnitrene/4-pyrimidynitrene. Pyridazynitrene 2, generated from tetrazolo[1,5-a]pyridazine/3-azidopyridazine 1T/1A, undergoes an analogous ring-opening to a diazonium ylide, viz. the diazo compound 3, under both thermal and photochemical conditions. Flash vacuum thermolysis (FVT) of 1 produced 3 and the products of N₂ elimination (Scheme 2). The same products were also obtained on matrix photolysis, and a weak signal ascribed to nitrene 2 was detected by ESR

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spectroscopy of Ar matrices. The formation of diazo compound 3 can be described as a Type I ring-opening reaction of the nitrene 2.

Type II ring-opening generates diradicals or vinylnitrenes (Scheme 1). The ring-opening of 2-pyridylnitrene is the subject of detailed discussion in this paper. Type II ring-openings in 2-quinoxalylnitrene and 1-isoquinolylnitrene have been reported previously.

Phenylnitrene 5a and 2-pyridylcarbene 7a can interconvert via 1-azacyclohepta-1,2,4,6-tetraene 6a (eq 1). 2-Pyridyl nitrene 5b and 7b undergos a degenerate interconversion with 1,3-diazacyclohepta-1,2,4,6-tetraene 6b, and 2-pyr aziynitrene 5c and 4-pyrimidylnitrene 7c interconvert via ring-expansion to 1,3,5-triazacycloheptatetraene 6c (eq 1).

These reactions motivated us to investigate the potential interconversion of 3-pyridazylcarbene 10 and 2-pyridynitrene 19. The results are described herein.

Results and Discussion

3-Pyridazylcarbene by Photolysis of Triazolo[1,5-b]-pyridazine. We first describe the formation of diazo compounds and carbenes (Scheme 3). Triazole 8 was prepared by oxidation of the hydrazone of 3-pyridazinecarboxaldehyde with active MnO2. The compound exists exclusively in the triazole form in the solid state at room temperature, and codeposition with Ar at 25 K also produced very largely the unchanged triazole (Figure S1 in the Supporting Information shows the IR and UV spectra), but a small amount of the diazo valence tautomer 9Z, E is formed on gentle FVT at 500 °C (see below). Photolysis of the matrix-isolated triazole 8 at 222 or 254 nm resulted in ring-opening to the diazo compound 9 with a UV maximum at ca. 460 nm and IR peaks at 2094 (vs), 1586 (m), 1446 (s), 1373 (w), 1222 (vw), 801 (w), and 671 (w) cm⁻¹ (Figure 1). Further photolysis resulted in increased intensity of an additional peak at 2097 cm⁻¹ as well as a smaller doublet at 2070-2075 cm⁻¹ accompanied by a C-H stretching band at 3321 cm⁻¹. The double peak at 2094 (2093-2079 cm⁻¹) is ascribed to the s-Z and s-E conformers of 9. The new peaks at 2070-2075 and 3321 cm⁻¹ indicate the presence of a second, acetylenic, diazo compound, viz. diazopentenynes 11Z and 11E (Figure 2). Good agreement with the calculated IR spectra (Figure 2) supports the assignments. Difference spectra show that, as 9 is photolyzed, 11 is formed (Scheme 3 and in the Supporting Information Figure S2).

Photolysis of an Ar matrix of triazolopyridazine 8 in the ESR spectrometer gave rise to three sets of carbene signals (Figure 3), which are ascribed to pyridazylcarbene 10 and the s-E and s-Z conformers of pentenyliodine, 12E and 12Z, on the basis of their zero field splitting (ZFS) parameters. After 45 s of photolysis at 308 nm only 10 and one conformer of 12
were detectable (Figure S3, SI). After 60 s at 308 nm all three species were obtained (Figure 3). Only one conformer of 10 was detected at all times. The spectra become more intense but also more complicated at longer photolysis times with small amounts of other, unidentified triplet species being formed (see below). ZFS parameters for 10: \( \frac{D}{hc} = 0.5440 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0254 \text{ cm}^{-1} \). This \( D \) value fits the correlation with calculated natural spin densities on the carbene carbon in aryl- and heteroarylcarbenes.\(^{10}\) Vinylcarbenes have significantly smaller \( D \) values. ZFS parameters for 12E: \( \frac{D}{hc} = 0.3360 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0208 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0619 \); 12Z: \( \frac{D}{hc} = 0.3798 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0162 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0427 \). For comparison, the ZFS parameters for the parent vinylcarbene in MTHF solution at 6 K are the following:\(^{11}\) (s-E)-vinylcarbene: \( \frac{D}{hc} = 0.4093 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0224 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0547 \); (s-Z)-vinylcarbene: \( \frac{D}{hc} = 0.4578 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0193 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0422 \). The lower \( D \) values for 12Z,E are


\(^{11}\) Hutton, R. S.; Marion, M. L.; Roth, H. D.; Wasserman, E. J. Am. Chem. Soc. 1974, 96, 4680.

FIGURE 1. (a) UV difference spectrum of 3-pyridazylidizomethane 9 (major conformer at 2094 cm\(^{-1}\)) in Ar matrix, obtained by photolysis of 8 in Ar matrix at 254 nm for 1 min (200 mA, 50 W low-pressure Hg lamp). (b) The corresponding IR spectrum. (For the matrix UV and IR spectra of 8, see Figure S1 in the Supporting Information)

(12E) were detectable (Figure S3, SI). After 60 s at 308 nm all three species were obtained (Figure 3). Only one conformer of 10 was detected at all times. The spectra become more intense but also more complicated at longer photolysis times with small amounts of other, unidentified triplet species being formed (see below). ZFS parameters for 10: \( \frac{D}{hc} = 0.5440 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0254 \text{ cm}^{-1} \). This \( D \) value fits the correlation with calculated natural spin densities on the carbene carbon in aryl- and heteroarylcarbenes.\(^{10}\) Vinylcarbenes have significantly smaller \( D \) values. ZFS parameters for 12E: \( \frac{D}{hc} = 0.3360 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0208 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0619 \); 12Z: \( \frac{D}{hc} = 0.3798 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0162 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0427 \). For comparison, the ZFS parameters for the parent vinylcarbene in MTHF solution at 6 K are the following:\(^{11}\) (s-E)-vinylcarbene: \( \frac{D}{hc} = 0.4093 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0224 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0547 \); (s-Z)-vinylcarbene: \( \frac{D}{hc} = 0.4578 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0193 \text{ cm}^{-1} \); \( \frac{E}{D} = 0.0422 \). The lower \( D \) values for 12Z,E are


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FIGURE 2. IR spectrum of triazolopyridazine 8 in Ar matrix after photolysis at 254 nm for 2 min, showing peaks of diazo compounds 9 and 11 (9Z, 9E and 11Z, 11E). (a) Calculated spectrum of diazo compound 9E. (b) Calculated spectrum of diazo compound 9Z; (c) photolysis at 254 nm, 2 min (the negative peaks are the spectrum of 8 before photolysis). (d) Calculated spectrum of diazo compound 11Z. (e) Calculated spectrum of diazo compound 11E. The shoulders indicating the presence of the s-Z and s-E geometrical isomers of 9 and 11 are shown in the inset. All calculations are at the B3LYP/6-311G** level, with wavenumbers scaled by a factor of 0.967.

FIGURE 3. ESR spectrum showing three carbenes after photolysis of 8 at 308 nm for 60 s. 10: \( \frac{D}{hc} = 0.5440 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0254 \text{ cm}^{-1} \); \( Z_1 = 2330 \text{ G} \); \( Z_2 = 5128 \text{ G} \); \( Y_2 = 6188 \text{ G} \); \( Z_2 = 9243 \text{ G} \). 12: \( \frac{D}{hc} = 0.3360 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0208 \text{ cm}^{-1} \); \( X_2 = 4550 \text{ G} \); \( Y_2 = 5341 \text{ G} \). Z-12: \( \frac{D}{hc} = 0.3798 \text{ cm}^{-1} \); \( \frac{E}{hc} = 0.0162 \text{ cm}^{-1} \); \( X_2 = 4795 \text{ G} \); \( Y_2 = 5425 \text{ G} \). Microwave frequency 9.7278 GHz, \( H_0 = 3471 \text{ G} \).
in accord with the extended conjugation, and the E/D ratios for 12Z,E follow the same trend as those for the parent vinylcarbenes.

In addition to the carbene signals described above, two triplet species are formed in the matrix photolyses of 8, particularly at 222 nm (Figure S4, Supporting Information). The strongest of these signals ($D = 0.636 \text{ cm}^{-1}$; $E = 0.0007 \text{ cm}^{-1}$) is indicative of a highly conjugated nitrene or an (almost) linear carbene. None of these unassigned signals match the cyanovinyl nitrene 23, which is formed from 2-pyrildinyl nitrene as described below. Some candidates for one or more of the unassigned triplet species are indicated in Scheme S1 in the Supporting Information. The same triplet signal is also obtained on photolysis or pyrolysis (FVT) of the isosteric tetrazolo[1,5-a]pyridazine 1T ($D = 0.637 \text{ cm}^{-1}$, $E = 0.0009 \text{ cm}^{-1}$). The signal looks very much like that of propynylidene, HCCCH,12 but it is too weak for a secure identification.

Photolysis of 8 at 254 or 222 nm in the IR cryostat gave, in addition to the peaks due to the diazo compounds 9 and 11 described above, new peaks at 3333 (m), 1955 (w), 889 (m), 852 (m), and 644 (m) cm$^{-1}$ and another set at 3338 (w), 2125 (v), 1661 (m), 986 (s), 945 (m), 613 (s), 605 (v), and 516 (m) cm$^{-1}$; as well as a single, weak peak at 1988 cm$^{-1}$ not belonging to any of the other sets of peaks (Figure 4 and in the Supporting Information Figures S5$^-$S7). The resulting IR spectrum is interpreted as a composite of two secondary photolysis products, derived from the carbene 12 (Scheme 3; Figure 4). The first set of absorptions is assigned to 1,2-pentadien-4-yne 13, and the second set to 3-ethylencyclopropene 14. The peaks due to 13 appeared first. Compounds 13 and 14 were identified by comparison with literature data13 and with the calculated spectra shown in the Supporting Information (see Figure S7). IR difference spectra show that 9 photolyses to 11, 13, and 14 at 222 and 254 nm (Figures S2 and S5). Both 9 and 11 photolyze to 13 and 14 at 281 nm (Figure S6, Supporting Information). Compounds 13 and 14 were also isolated from the preparative FVT described below.

Photolysis of the matrix containing a mixture of diazo compounds at $\lambda > 405$ nm caused the intensities of the triazole peaks to increase, thereby indicating that a portion of the diazo compounds 9Z,E reverted back to triazole 8, while another portion was converted to products 13 and 14.

Additional weak peaks appeared during the photolysis at 254 nm; the weak, single peak at 1988 cm$^{-1}$ (Figure 4 and in the Supporting Information Figure S5 and S7) does not belong to either 12 or 13. The most likely assignment is the 1,3-diazacycloheptatetraene 21 (see Scheme 4 and the discussion below), but the weakness prevented the observation of any other peaks belonging to 21; therefore, any assignment of the carrier must remain tentative.

A signal labeled K at 2042 cm$^{-1}$ in Figure 4 may be due to cyanovinylethenimine 26, one of the possible precursors of...
3-cyanopyrrole\textsuperscript{9} 29 (2260 cm\textsuperscript{-1}) (Scheme 4 and in the Supporting Information Figure S9). The presence of these compounds was confirmed by GC-MS and \textsuperscript{1}H NMR spectroscopy and comparison with samples prepared from tetrazolo[1,5-\textit{a}]pyridine 22\textit{T} (see below).\textsuperscript{9} Very weak peaks due to 27\textit{Z},\textit{E} were visible in the \textsuperscript{1}H NMR spectrum already at 500 °C, along with 13–15 as the main products, but the cyanopyrroles were not detectable at this temperature.

2-Pyridylnitrene. The formation and photochemistry of 2-pyridylnitrene are now described. 2-Pyridylnitrene 19 is easily detected by its Ar matrix ESR spectrum when generated by FVT of tetrazolo[1,5-\textit{a}]pyridine/2-azidopyridine 22\textit{T}/22\textit{A} (see Scheme 4).\textsuperscript{9b} Photolysis of matrix-isolated 2-azidopyridine 22\textit{A} at 254 nm also affords a strong ESR signal due to triplet 2-pyridylnitrene 19 (Figure 5). However, a second signal at ca. 5000 G has the typical appearance of the $X_2Y_2$ transition of a strongly delocalized nitrene with a nonzero $E$ value ($D/hc = 0.425$ cm\textsuperscript{-1}; $E/hc = 0.006$ cm\textsuperscript{-1}) (Figure 5). The $D$ value of 0.425 cm\textsuperscript{-1} is too low to be due to an aliphatic or aromatic nitrene but would fit a conjugated vinylnitrene. This signal is ascribed to the ring-opened cyanodienynitrene 23.

This assignment is supported by the calculated natural spin density $\rho$ on the nitrene-N in 23 (1.2486), which makes this nitrene fit very well on our $D-i\rho$ correlation diagram\textsuperscript{6} (see Figure S10, Supporting Information). Nitrene 23 is the expected precursor of glutacononitriles 27\textit{Z},\textit{E} described below. The formation of open-chain ketenimines has been documented in the matrix photolyses of several substituted tetrazolo/azidopyridines,\textsuperscript{7,16} 2-Pyridylnitrene undergoes facile ring-expansion to the cyclic carboimidide 21 on both photolysis and FVT as observed by IR spectroscopy.\textsuperscript{9} Thus photolysis of 22\textit{T}/22\textit{A} in an Ar matrix at 254 nm affords a very clean IR spectrum of 21 in very good agreement with the calculated spectrum (Figure 6): 1989 (vs), 1318 (m), 975 (m), 747 (m), 551 (m) cm\textsuperscript{-1}. The UV spectrum of 21 has a maximum at 328 nm (Figures S11–S12, Supporting Information), and the compound therefore undergoes secondary photolysis in the 300–400 nm range.

\textbf{SCHEME 4.} Further Rearrangements of 3-Pyridazylcarbene 10 and 2-Pyridylnitrene 19

\textbf{FIGURE 5.} ESR spectrum obtained after mild FVT of tetrazolo-pyridine 22\textit{T} at 200 °C to generate 2-azidopyridine 22\textit{A}, isolation of the products in Ar matrix at 15 K, and photolysis at 254 nm. Signal at $X_2 = 7025$ G, $Y_2 = 7126$ G: $D/hc = 1.073$ cm\textsuperscript{-1}; $E/hc = 0.002$ cm\textsuperscript{-1} (assigned to 2-pyridylnitrene 19). Signal at $X_2 = 5055$ G, $Y_2 = 5281$ G: $D/hc = 0.425$ cm\textsuperscript{-1}; $E/hc = 0.006$ cm\textsuperscript{-1} (assigned to 23).

Most interestingly, further photolysis of 21 at 308 or 365 nm (using a 310—390 nm interference filter) leads to a new compound, the IR spectrum of which agrees very well with the calculated spectrum of the spiroazirene 25 (Scheme 4, Figure 7, and in the Supporting Information Figure S13).

In contrast, very poor agreement was found with the calculated IR spectra of a number of alternative structures, including cyanovinylazirenes 30 and isocyanovinylazirenes. The C=N stretching vibration of spiroazirene 25 appears at 1676 cm⁻¹. 1-Azaspiro[2.4]hepta-1,4,6-triene 31 (eq 2) has been prepared by photolysis of 6-azidofulvene

and is reported to absorb at 1676 cm⁻¹ in CCl₄ solution.¹⁷

The formation of spiroazirene 25 has precedent in the all-carbon series, where the analogous spirocyclopropene is postulated as a key intermediate in the thermal carbon scrambling in phenylcarbene (Scheme 5).¹⁸ Such a spirocyclopropene can actually be isolated in the indene series.¹⁹ The photochemical formation of 25 would be a logical consequence of an electrocyclic process yielding 24 (Scheme 4).

SCHEME 5. Phenylcarbene Rearrangements¹⁸

Either a concerted 1,5-shift or ring-opening to a vinylcarbene and reclosure leads to 25. This process is considered further in the Computational Method section below. The weak absorption at 2042 cm⁻¹ in Figure 7 and in the Supporting Information Figure S13 may be due to the ketenimine 26 (Schemes 4 and 6) or 39 (Scheme 7, described below). The weakness of this signal does not permit a distinction.

FVT of 22T/22A affords the cyclic carbodiimide 21 as the main product at temperatures below ca. 500 °C.² At higher temperatures, 21 gradually disappears, to be replaced by 2- and 3-cyanopyrroles 28 and 29 along with minor amounts of 2-aminopyridine (formed from triplet 2-pyridylnitrene by H-abstraction, in yields of 1—10% depending on conditions) and Z- and E-glutacononitriles 27Z,E (ca. 10%).²⁹ 2-Cyanopyrrole 28 appears first, but since 2- and 3-cyanopyrroles interconvert by means of a series of 1,5-H and 1,5-CN shifts, a mixture of 28 and 29 inevitably forms at elevated temperatures.²⁹ The cyclization of dienylazarene 23 and a concerted ring-contraction of 2-pyridylnitrene 19 are attractive mechanisms of formation of the cyanopyrroles (see several routes to cyanopyrroles in Schemes 4, 6, and 7). Although spiroazirene 25 is a photochemical product, and the cyanopyrroles are not obtained in any significant quantities on photolysis, the question has to be asked whether 25 could be a precursor of the cyanopyrroles in FVT reactions. The analogous spiroazirenes 31 (eq 2) rearranges to isocyanocyclopentadiene on both photolysis and thermolysis, and on FVT above 420 °C only cyanocyclopentadiene was obtained.¹⁷ A similar reaction could be the source of weak isocyanide absorptions seen at 2127—2133 cm⁻¹ in IR spectra of the photolyses of 22. The question of involvement of 25 in cyanopyrrole formation will be considered in the Computational Method section.

Relationship between 3-Pyridazylcarbene and 2-Pyridylnitrene. The high-temperature formation of compounds 27—29 from 8 could suggest the possible isomerization of 3-pyridazylcarbene to 2-pyridylnitrene as illustrated in Scheme 4. This reaction would have to pass through molecules or transition structures resembling the cyclopropene 16, the seven-membered ring ketenimine 17 (a ketene hydrazone; not observed experimentally; see Figure S14 in the Supporting Information), and the formally antiaromatic diazirene 18 (Scheme 4). The 2-pyridylnitrene energy surface

is usually accessed from tetrazopopyridine/2-azidopyridine 22T/22A. However, the ratio of yields of glutacononitriles 27E,Z and cyanopyrroles 28 and 29, [27E.Z]:[28 + 29] is much higher from 8 than from 22 (ratio \( \sim 6:1 \) from triazole 8 at 600 °C; ratio \( \sim 1:7 \) from tetrazole 22T). This suggests that the unobserved seven-membered-ring ketenimine 17 can undergo Type II ring-opening to cyanodienylnitrene 23, thus leading to an excess of glutacononitriles when proceeding from the pyridazine side (see Scheme 4). Moreover, no 2-aminopyridine was detectable by either GC-MS or NMR spectroscopy of the products of FVT of 8, whereas this compound is always formed as a minor product (1–10%, depending on conditions) from (triplet) 2-pyridylnitrene. Instead, 3-methylpyridazine was formed on FVT of 8, a characteristic (triplet) carbene H-abstraction product. Conversely, when 2-pyridylnitrene is generated from 22, there is no formation of either 3-methylpyridazine or the low molecular weight compounds derived from triazopyridazine, viz. 13–15. 2-Pyridylnitrene 19 is easily detected by its Ar matrix ESR spectrum when generated by FVT of 22T, but FVT of 8 with Ar matrix isolation in the ESR cryostat affords at best a trace of a triplet ESR signal, which may be due to 2-pyryldinitren 19, but it is too weak to assign it with any degree of certainty. As described above, 2-pyridylnitrene undergoes facile ring-expansion to the cyclic carbodiimide 21 on both photolysis and FVT; 21 is detectable by its strong absorption at 1988–1989 cm\(^{-1}\) in the IR spectrum (Figure 6). A weak band was observed at 1988 cm\(^{-1}\) in the photolyses of 8 (Figure 4 and in the Supporting Information Figures S5 and S14), but it was too weak for any secure assignment; none of the other absorptions belonging to 21 were detectable. Thus, if 3-pyrazylcarbene rearranges to 2-pyridylnitrene, this leads at best to trace amounts of nitrene 19 and carbodiimide 21 being observable.

There was no direct spectroscopic evidence for the cyclic 7-membered-ring ketenimine 17 in the photolyses or thermolyses of 8. The calculated frequency for this compound at the B3LYP/6-31G* level of theory is 1898 cm\(^{-1}\), no matching peak was observable in the experimental spectra (see Figure S14, Supporting Information). A rearrangement of 17 to 2-pyridylnitrene 19 would be possible via the diazirene 18 as an intermediate or transition state (see the Computational Method section below). Rearrangements via 1,3-diazirenes have been invoked in other, similar ring-expansions of hetarylnitrenes such as 2-pyrimidyl-\(^{5}\), 2-quinazolyl-\(^{6}\), and s-triazolo-\(^{27}\)nitrenes. When the reaction proceeds from 2-pyridylnitrene 19, type II ring-opening to 26 and 27 is a minor process under both thermal\(^{9,21}\) and photochemical\(^{16,22}\) conditions, whereas formation of the cyanopyrroles 28 and 29 is the major process under FVT conditions.\(^{9,21}\) FVT of 3-azidopyridine also leads to a mixture of 2- and 3-cyanopyrroles as end products, but no glutacononitrile is formed. Here, 3-cyanopyrrole is probably formed via the open-chain nitrile ylide in a Type I ring-opening–ring-closure.\(^{1}\) The reaction paths will now be discussed in more detail in light of theoretical calculations.

**Calculations.** For further insight, the thermal reaction paths were explored by calculating the relative energies of most of the species of interest at the B3LYP/6-31G* level of theory. The ground state of 2-pyridylnitrene 19 is the triplet (\(^3\)A\(^{2}\)), which is the reference point for all the energies in Scheme 6. It is now well-known that singlet nitrenes have an open shell electronic structure,\(^{23}\) therefore a detailed exploration of the reaction path 18 \(\rightarrow\) 19 requires CASSCF and CASPT2 calculations, the results of which are reported in Scheme 6. It is possible to make reasonable estimates for open-shell singlet species at the B3LYP/6-31G* level with use of the Cramer–Ziegler sum method.\(^{24}\) The latest Value

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**FIGURE 7.** (a) Calculated spectrum of spiroazirene 25 at the B3LYP/6-311G** level, wavenumbers scaled by 0.967, and (b) difference IR spectrum obtained after photolysis of tetrazolopyridine 22T at 222 nm for 30 min to generate 21 (negative spectrum), followed by 308 nm for 30 min to generate 25 (positive spectrum). The weak signal at 2042 cm\(^{-1}\) may be due to ketenimine 26 or 39.
for the energy gap between the triplet and the open-shell singlet (OSS) phenylnitrene is ca. 15 kcal/mol, whereas a value of ca. 18 kcal/mol has been assumed previously. We calculate the $T_0 - S_1$ gap in 19 as 18.6 (19.7) kcal/mol at the CASSCF (CASPT2) levels, and 16.2 kcal/mol at the B3LYP/6-31G* level using the Cramer-Ziegler correction. Thus, were it to occur, the overall carbene-nitrene rearrangement reaction, $10 \rightarrow 19$, would be exothermic by about 39-48 kcal/mol. The calculated activation energy for N$_2$ loss from diazo compound 9 is 41 kcal/mol (B3LYP/6-31G*). The cyclization of 10 to the cyclopropene 16 requires a very modest energy barrier (Scheme 6), and its rearrangement to the seven-membered-ring 17 is strongly exothermic. The activation energy for 16 → 17 at the CASPT2 level is seemingly below the energy of 16. The problem stems from the fact that the CASPT2 energy is calculated at the CASSCF geometry. The correctness of the CASSCF TS was confirmed by IRC calculations in both directions. A QCISD(T)/6-31G* single point calculation confirmed that the barrier is very low, with the transition state for 16 → 17 lying 1.3 kcal/mol above 16. The further isomerization of ketenimine 17 to diazirene 18 is approximately thermoneutral or modestly endothermic. Diazirine 18 was optimized as an energy minimum at the B3LYP level, but it is a transition state for the reaction 17 → 19 at the CASSCF level. The ring-opening of 18 to 19 (OSS) has a calculated barrier of ca. 2 kcal/mol at the B3LYP/6-31G* level. The cyclic carbodiimide 21 has been the subject of prior calculations, and its energy is close to that of the triplet nitrene 19. The bicyclic azirene 20 lies 10-13 kcal/mol above 21.

The ring-opened species 23 may be described as a resonance hybrid of a nitrene (23N) and a diradical (23R). The calculated bond lengths indicate that the dienylnitrene canonical structure 23N has higher weight than the diradical structure 23R in agreement with the experimental observation that the species is a nitrene. Note, however, that suitable benzannelation can cause the diradical character to predominate.

However, two different conformers of 23, namely 23EZ and 23ZZ (Scheme 6), are formed from cyclic ketenimine 17 and 23.

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pyridylnitrene 19, respectively. The two conformers can interconvert via a small barrier (5–10 kcal/mol at the B3LYP/6-31G* level) in both the singlet and triplet states. It is important to note that although the barrier is low, there is no reason to expect that thermally equilibrated intermediates are formed. Therefore, reaction dynamics can cause the formation of different products or product ratios from 17 and 19. The geometry of 23ZZ could not be optimized at the CASSCF level, because the species undergoes ring-closure to 2-cyano-2H-pyrrole 32 (Scheme 6).

The Type II ring-opening of cyclic ketenimine 17 to the open shell singlet state (OSS) of 23EZ is analogous to the ring-opening of 2-quinazolylnitrene, which has been examined by CASSCF and CASPT2 calculations previously, when it was found to have a barrier of ca. 20 kcal/mol. An activation barrier of 30–40 kcal/mol was calculated for 17 → 23EZ (OSS) (Scheme 6), and the reaction is exothermic. Therefore, on thermodynamic grounds, the ring-opening 17 → 23EZ appears to be a very favorable pathway. There will be enough energy in high-temperature FVT reactions to overcome the activation barriers. The reaction 17 → 23EZ, then, is the likely source of the glutacononitriles 27 found in the FVT reactions of diazomethylpyridazine 9.

The calculated barrier for the Type II ring-opening of triplet 2-pyridylnitrene 19 to triplet 23ZZ is ca. 30 kcal/mol (Scheme 6); the corresponding S1–S2 reaction has a slightly lower barrier. Both reactions are endothermic (Scheme 6). A transition state for the concerted ring-contraction of 2-pyridylnitrene 19 (OSS, S1) to 2-cyano-2H-pyrrole 32 (ca. 49 kcal/mol) could only be located at the B3LYP level. Corresponding TS values have been located for the ring-contractions of phenylnitrene10 and 1-naphthylnitrene29 to 5-cyanocyclopentadiene and 1-cyanoindene, respectively.

A transition state was located for the direct ring-contraction 19 (S1) → 1-cyanopyrrole 33, but this barrier is high (47–68 kcal/mol; Scheme 6). Previous substituent and 15N-labeling work has established that 2-pyrindynes do not undergo ring-contraction via 1-cyanopyrroles such as 33. Similarly, 2-quinolyl- and 1-isoquinolynitrenes do not undergo ring-contraction to 1-cyanoindole; the products are formed via ring-opening to o-cyano-β-styrylnitrene. Remarkably, 4- and 2-pyrimidynitrenes do undergo ring-contraction to 1-cyanomidaoloses and 1-cyanopyrazoles, respectively, but these reactions, too, may proceed via ring-opening.2,5,6,8a

Thus, the computational data for the ring-contraction of 2-pyridylnitrene 19 (Scheme 6) clearly indicate that the ring-opening/recyclization route 19 → 23ZZ → 32 → 28 is energetically preferred over the concerted ring-contractions to 2-cyano-2H-pyrrole 32 and the nonobserved 1-cyanopyrrole 33. The barrier for the 1,5-H shift in 2-cyano-2H-pyrrole 32 to 2-cyano-2H-pyrrole 28 is ca. 30 kcal/mol, and for the 1,5-CN shift to 3-cyano-3H-pyrrole 34 it is ca. 35 kcal/mol, in agreement with the observation that 2-cyano-2H-pyrrole is usually observed prior to 3-cyano-2H-pyrrole on FVT.9b

**Scheme 7. Spiroazirene Route to Cyanopyrroles**

The reaction 19 → 23 → 27 (Scheme 6) explains the formation of glutacononitriles in the thermolyses of the precursors of 2-pyridylnitrene 19. There are three possible routes to glutacononitriles 27: (i) a 1,4-H shift in 23EZ, (ii) a 1,2-H shift in 23ZZ, and (iii) a 1,2-H shift in 23EZ to afford the ketenimine 26E, which can isomerize to 27 in a 1,5-H shift through a small barrier (Scheme 6). As mentioned above, a weak band at 2042 cm⁻¹ in many photolysis IR spectra indicates the presence of an open-chain ketenimine. An alternative carrier of this signal is the azafulvenimine 39 described in Scheme 7.

**Spiroazirene Route to Cyanopyrroles.** Formation of cyanopyrroles from 2-pyridylnitrene via spiroazirene 25 (Schemes 4 and 7) will now be considered. The electrocyclic process forming 24 from 21 is calculated to be endothermic by 12–18 kcal/mol, but the spiroazirene 25 is ≤4 kcal/mol above 21 (Scheme 7). The reactions summarized in Scheme 7 indicate that rearrangement of diazacycloheptate 21 to diazabicyclo[3.2.0]heptadiene 24 and spiroazirene 25 constitutes a feasible route to cyanopyrroles, which is competitive with the concerted ring-contraction of...
2-pyridylnitrene 19, but not with ring-contraction via cyano
dienynitrenes 23 (Scheme 6). The activation energy for the
first step, 21 \rightarrow 24, is high (ca. 47 kcal/mol), but the reaction
would be achievable under high-temperature FVT condi-
tions.

Thus, in summary, we have identified three potential
routes to cyanopyrroles: (i) ring-opening\textendash ring-closure via
dienynitrene 23 (Scheme 6); (ii) concerted ring-contraction of 2-pyridylnitrene 19 to 2-cyano-2H-pyrrole 32 (Scheme 6;
not likely here, but possible in other arylnitrenes); and
(iii) electrocyclic rearrangement of diazacycloheptatetraene
21 via spiroazirene 25 (Scheme 7). The latter pathway is
actually followed in the phenylcarbene rearrangement.18

While we have no experimental evidence for the spiroazirene
route to cyanopyrroles (Scheme 7), it will be necessary
to consider it in future work. It may well be that different
routes of ring-contraction will be followed in different
systems. Strong evidence for the ring-opening\textendash ring-closure
pathway has been adduced for other systems.2,6,27,29 The
existence of several potential pathways can also provide an
explanation for the different product ratios obtained from
pyridazine 8 and pyridine 22. The ring-opening\textendash ring-closure
mechanism (i) is fully consistent with the results of 15N-
and substituent labeling of 2-pyridylnitrenes.30 The spiroazir-
enne mechanism (iii) can explain the products obtained from
6-substituted tetrazolo[1,5-a]pyridine, but does not explain
the major product obtained from 8-substituted tetrazolo-
[1,5-a]pyridine.30

The potential formation of the azafulvenylnitrene 38
(Scheme 7) as a rearrangement product of diazacyclohepta-
tetraene 21 makes it necessary to consider this nitrene as an
alternative to the cyanodienynitrene 23 as carrier of the low-
field nitrene signal (5000\textendash 5300 G) in the ESR spectrum
(Figure 5). This ESR spectrum was obtained by photolysis
of tetrazole/azide 22T/22A at 254 nm. Under the same
photolysis conditions, diazacycloheptatetraene 21 is formed
cleanly as observed by IR spectroscopy (Figure 6). Compound
21 is stable at this wavelength and rearranges to 25
on irradiation at 308 or 365 nm. Thus, nitrene 38 should
not be formed at 254 nm. Hence, the evidence supports cyano-
dienynitrene 23 as the carrier of the low-field triplet ESR
signal.

Further Reactions of the Pyridazylcarbenes. We will now
consider the remaining reactions of the pyridazylcarbenes 10
(Schemes 8 and 9). The barriers for isomerization of carbene
12E to allene 13 and cyclopropene 14 are only ca. 4 and
2 kcal/mol, respectively. These are the first reactions to take
place on FVT. The isomerization of ethynylcyclopropene 14
to pentadiyne 15 is exothermic by ca. 14 kcal/mol, but that
of pentadienyne 13 to pentadiyne 15 would be endothermic
by ca. 11 kcal/mol (Scheme 8).

The alternative cyclization of carbene 10Z to azirene 42
has a calculated barrier of 14 kcal/mol, and 10E can form the
same product with a barrier of ca. 11 kcal/mol. The seven-
membered ring allene 43 is ca. 12 kcal/mol higher in energy
that the cyclic ketenimine 17, and ca. 37 kcal/mol above
cyclic carbodiimide 21. There was no experimental evidence
for the formation of 43 (Scheme 9 and in the Supporting
Information Figure S14).

Two isomers of 17, viz. the cyclic nitrile ylide 17 and
diazacycloheptatrienylidene 17′, were also considered
(Scheme 9). There was no experimental evidence for these

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**Scheme 8. Calculated Energies for Ring-Opening and Fragmentation of 3-Pyridazylcarbene**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10Z</td>
<td>55.0</td>
</tr>
<tr>
<td>12E + N₂</td>
<td>64.0</td>
</tr>
<tr>
<td>12Z + N₂</td>
<td>62.8</td>
</tr>
<tr>
<td>13 + N₂</td>
<td>4.4</td>
</tr>
</tbody>
</table>

*B3LYP/6-31G* in kcal/mol relative to 19 T₀ = 0.

**Scheme 9. Unobserved Ring-Expansions of 3-Pyridazylcarbene 10*  

*Calculations at the CASSCF (CASPT2) and B3LYP/6-31G* levels in kcal/mol relative to 19 T₀ = 0.

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Conclusion

The isomeric 3-pyridazylcarbene 10 and 2-pyridylnitrene 19 were investigated. There is little evidence for interconversion of these two isomers, but each has a rich chemistry. Mild FVT of triazolopyridazine 8 generates the diazomethyl valence tautomer 9, which on either matrix photolysis or flash vacuum thermolysis (FVT) gives rise to 3-pyridazylcarbene 10. The carbene was detected by ESR spectroscopy in the photolysis reaction. Matrix photolysis with IR observation reveals ring-opening of the carbene to diazoalkyne 11, which again loses N2 to generate a new carbene, pent-2-en-4-yn-1-ylidene 12; this too was detected by ESR spectroscopy, and it rearranges to pentadienylene 13, ethynyl-cyclopentene 14, and, at elevated temperatures, 1,4-pentadiyne 15.

Photolysis of matrix-isolated tetratrazo[1,5-a]pyridine/2-azidopyridine 22T/22A yields both triplet 2-pyridylnitrene 19 and its ring-opened isomer, the cyanodienylinenitrile 23, which are detected by ESR spectroscopy. 1,3-Diazacycloheptatetraene 21 is formed cleanly on matrix photolysis as observed by IR spectroscopy. It is also a major product of FVT of 22T/22A under mild conditions. Photolysis of 21 above 300 nm causes its rearrangement to the spiroazirene 25, identified by its Ar-matrix IR spectrum.

FVT of 8,9 causes formation of Z- and E-gluconoconitriiles 27ZE and minor amounts of 2- and 3-cyanopyrroles 28 and 29 in addition to 13–15. FVT of tetratrazopyridine/2-azido-pyridine 22T/22A also affords compounds 27–29, but the ratios of yields of these products are very different in the two systems.

Calculations support the postulate that both 3-pyridazylcarbene (via 1,7-diazacycloheptatetraene 17) and 2-pyridyl nitrene 19 can undergo ring-opening to vinylidenetrane 23, but they can lead to different conformers of 23; one, 23EZ, is predominantly a precursor of gluconoconitriiles 27; the other, 23ZZ, is a precursor of 2- and 3-cyanopyrroles via 2-cyano-2H-pyrrole 32. Another potential route to cyanopyrroles proceeds via electrocyclization of 1,3-diazacycloheptatetraene 21 to diazabicyclo[3.2.0]heptatriene 24 and spiroazirene 25. The ring-opening–reclusion reaction via dienynitrene 23 emerges as the energetically most favorable mechanism of ring-contraction in 2-pyridylnitrenes.

Computational Method

Calculations of all species were performed with the B3LYP method, as implemented in the Gaussian 03 suite of programs, with the 6-31G* basis set for geometry and transition state optimizations. Energies of open-shell S1 nitrenes at the CASSCF wave function remained stable in the range 77–80%. Cartesian coordinates, energies, vibrational frequencies, and details of the correlated orbitals in the CASSCF active space are listed in the Supporting Information.

Experimental Section

General procedures have been published in matrix isolation for IR spectroscopy, Ar gas and sample vapor were codeposited on a CsI target maintained at 25 K. The Ar flow rate was maintained at ca. 4 mbar per min to obtain a thin, transparent matrix. After depositing the matrix for ca. 30 min, the CsI target was cooled to 10 K, and IR spectra were recorded with 1 cm⁻¹ resolution. For ESR spectroscopy a similar cryostat was used, where the sample and Ar were condensed on a Cu rod at ca. 15 K. Photolyses were carried out with use of a 1000 W high-pressure Xe/Hg lamp equipped with a monochromator and appropriate cut-off and interference filters, a 75 W low pressure Hg lamp (254 nm), or excimer lamps operating at 222 (25 mW/cm²) and 308 nm (50 mW/cm²).

The temperatures used for FVT experiments ranged from 500 to 700 °C.

In preparative FVT experiments, the sample was placed in a sublimation tube and sublimed into a 20 × 2 cm quartz pyrolysis tube. The FVT unit was evacuated with an oil diffusion pump capable of a vacuum of 10⁻⁶–10⁻⁴ mbar. The pyrolysis products were collected on a coldfinger cooled with liquid nitrogen (ca. 77 K). After the end of the experiment, the collected product was dissolved in CDCl³, and NMR and GC-MS analyses were carried out.

GC-MS analysis used a ZB-5 Zebron GC column (30 m, 0.22 mm i.d., 0.25 μm film thickness), He carrier gas at a flow rate of 3.7 mL/min, column head pressure 100 kPa, inlet temperature 200 °C, and GC-MS interface 250 °C. The temperature program started at 85 °C for 2 min, followed by a ramp of 12 deg/min up to 250 °C.

CASSCF optimizations and single-point CASPT2 calculations were performed for open-shell and related systems, and were carried out with the MOLCAS suite of programs, using the 6-31G* basis set. The CASSCF calculations used an 8-electron, 8-orbital active space, e.g. for 19: 3½, 3½*, and the 2 p-AOs on the nitrene-N atom. The reference weights of the CASSCF wave function remained stable in the range 77–80%. Cartesian coordinates, energies, vibrational frequencies, and details of the correlated orbitals in the CASSCF active space are listed in the Supporting Information.

References

(32) Frisch, M. J., et al. Gaussian 03, Revision E.01; Gaussian Inc., Wallingford, CT, 2004. (For the complete reference, see the Supporting Information.)
Matrix Isolation and Photolysis of Triazolo[1,5-b]pyridazine. Triazolo[1,5-b]pyridazine 8 was sublimed at 65–70 °C under vacuum (2.0 × 10⁻⁸ mbar) and codeposited with Ar on a CsI target at 25 K. The IR spectrum recorded at ca. 10 K showed the main triazole peaks at 1544 (m), 1494 (m), 1403 (m), 1321 (s), 1307 (m), 1256 (m), 957 (m), 815 (s), and 734 (m) cm⁻¹ (see Figure S1 in the Supporting Information for the IR and UV spectra).

Preparative FVT of Triazolopyridazine. Preparative FVT of 8 (150 mg) was carried out at 500–700 °C. The collected products were examined by ¹H NMR (CDCl₃; 500 MHz) and GC-MS. Data are presented below.

2-Ethynylcyclopropene 14:¹³a,¹⁴ IR (Ar, 10 K) 3338 (w), 2125 (vw), 1661 (m), 986 (s), 945 (m), 613 (s), 605 (vw), and 516 (m) cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) 7.10 (dd, 2H, J = 2.75, 2.07 Hz), 5.65 (dt, 1H, J = 7.0 and 2.6 Hz), 5.02 (dd, 2H, J = 6.8 and 1.7 Hz); ¹³C NMR (CDCl₃) 123.9, 120.1, 114.8, 109.8, 101.0.

Preparative FVT of Penta-1,2-dien-4-yne 13:IR (Ar, 10 K) 3333 (m), 1955 (w), 1417 (m), 1310 (m), 1238 (m), 1154 (m), 1142 (m), 1054, 1049, 21.2, 19.6; ¹H NMR (CDCl₃, 500 MHz) 5.35 (td, 1H, J = 7.0 and 1.6 Hz), 5.07 (dd, 2H, J = 6.8 and 1.7 Hz), 2.87 (dt, 1H, J = 7.0 and 2.6 Hz), 5.02 (dd, 2H, J = 6.8 and 1.7 Hz), 2.87 (dt, 1H, J = 2.6 and 1.6 Hz).

1,4-Pentadiyne 15:¹⁴,¹⁰ IR (Ar, 10 K) 3319 (s), 2140 (w), 1417 (m), 1300 (w), and 605 (w); ¹H NMR (CDCl₃, 500 MHz) 5.15 (t, 1H, J = 2.75, 2.07 Hz).

Z-Gluacononitrile 26Z:¹⁰,¹⁵ ¹H NMR (CDCl₃, 500 MHz) 6.47 (dt, 1H, J = 7.0 and 10.8 Hz), 5.65 (dt, 1H, J = 10.3 and 1.7 Hz), 3.35 (dd, 1H, J = 6.8 and 1.7 Hz); ¹³C NMR (CDCl₃) (mixture of Z and E isomers) 141.1, 140.7, 115.4, 114.2, 105.4, 104.9, 21.2, 19.6; ¹H NMR (Ar, 10 K) 2275 and 2235 cm⁻¹ (mixture of Z and E isomers).

E-Gluacononitrile 26E:¹⁰,¹⁵ ¹H NMR (CDCl₃, 500 MHz) 6.59 (dt, 1H, J = 5.0 and 16.25 Hz), 5.80 (dt, 1H, J = 16.25 and 2.1 Hz), 3.50 (dd, 2H, J = 6.7 and 1.65 Hz); ¹³C NMR (CDCl₃) see data for mixture under Z-gluacononitrile.

2-Cyanopyrrole 27:²⁰,⁴¹ IR (Ar, 10 K) 2235 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) 9.37 (br, 1H, J = 3.5, 2.7, and 1.4 Hz), 6.84 (m, 1H, apparent J = 3.8, 2.5, and 1.4 Hz), 6.25 (dt, 1H, J = 3.8 and 2.7 Hz); ¹³C NMR (CDCl₃) 123.9, 120.1, 114.8, 109.8, 101.0.

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