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Interconversion of Nitrenes, Azirenes, and Diradicals: Rearrangement of 3-Isoquinolylnitrene to *o*-Cyanophenylketenimine and 1-Cyanoisoindole

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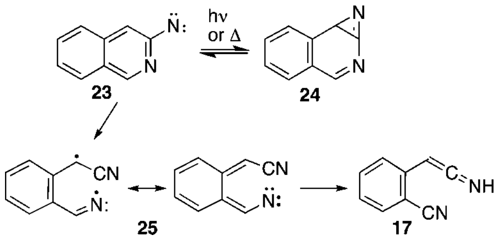

Photolysis of tetrazolo[1,5-*b*]isoquinoline/3-azidoisoquinoline **22T/22A** generates 3-isoquinolylnitrene **23**, which has been characterized together with a diradical species (**25**) by Ar matrix ESR spectroscopy. Photolysis at $\lambda > 300$ nm generates azirene **24**, characterized by IR spectroscopy, whereas further broadband UV photolysis destroys the azirene to produce *o*-cyanophenylketenimine **17**. The use of ^{15}N-labeled tetrazole/azide **22T′/22A′** demonstrates rapid equilibration of two regioisomeric ^{15}N-labeled azirenes **24′** and **24″** prior to formation of **17**. Flash vacuum thermolysis (FVT) of **22T/22A** affords 1-cyano-2*H*-isoindole **27** in quantitative yield. FVT of ^{15}N-labeled tetrazole/azide **22T′/22A′** causes scrambling of ^{15}N label in the 1-cyano-2*H*-isoindole product. It is concluded that the interconversion of azirenes **24** takes place via the unobserved diazacycloheptatetraene/diazacycloheptatrienylidene **32/33**, and that the rearrangement of azirene to ketenimine **17** and 1-cyanoisoindole **27** takes place via reversion to nitrene **23** followed by ring opening to diradical **25**.

Introduction

Thermal and photochemical rearrangements of pyridylnitrenes have been described in recent papers.[1,2] Thus, 2-pyridylnitrene **2**, generated from tetrazolo[1,5-*a*]pyridine **1T** and/or 2-azidopyridine **1A**, undergoes ring expansion to 1,3-diazacyclohepta-1,2,4,6-tetraene **4**. This reaction is assumed to take place via transient azirene **3**, which has not, however, been observed directly. The corresponding azirenes have been observed in the photochemical rearrangements of the naphthylnitrenes[3] in Ar matrixes and in the photolyses of fluorinated[4] phenyl azides. The formation of diazacycloheptatetraenes **4** is a preparatively useful process, which can be applied in the synthesis of a variety of 1,3-diazepines, usually in high yields, from substituted tetrazolopyridines.[5,6] Nevertheless, this ring expansion reaction is often accompanied by a minor ring opening reaction, leading to ketenimines **9**, presumably via the unobserved dienylnitrene/diradical **5**, termed a type II ring opening.[7] Small amounts of ketenimines **9** have been observed in matrix photolysis reactions,[5,6] whereas tautomeric glutacononitriles **10** are obtained in yields on the order of 10% in flash vacuum thermolysis (FVT) reactions.[2] FVT affords mixtures of 2- and 3-cyanopyrroles **7** and **8** as major products;[2] they are believed to be formed via the unobserved 2-cyano-2*H*-pyrrole **6**, and they interconvert by means of a series of thermal 1,5-H and 1,5-CN shifts (Scheme 1).

In 2-quinolyl- and 1-isoquinolylnitrenes **11** and **13**, which interconvert via observable diazacycloheptatetraene **12**, photo-

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(5) (a) Reisinger, A.; Bernhardt, P. V.; Wentrup, C. *Org. Biomol. Chem.* **2004**, *2*, 246. (b) Reisinger, A.; Koch, R.; Bernhardt, P. V.; Wentrup, C. *Org. Biomol. Chem.* **2004**, *2*, 1227.

(6) Addicott, C.; Wentrup, C. *Aust. J. Chem.* **2008**, *61*, 592.

(7) Kvaskoff, D.; Bednarek, P.; George, L.; Waich, K.; Wentrup, C. *J. Org. Chem.* **2006**, *71*, 4049.

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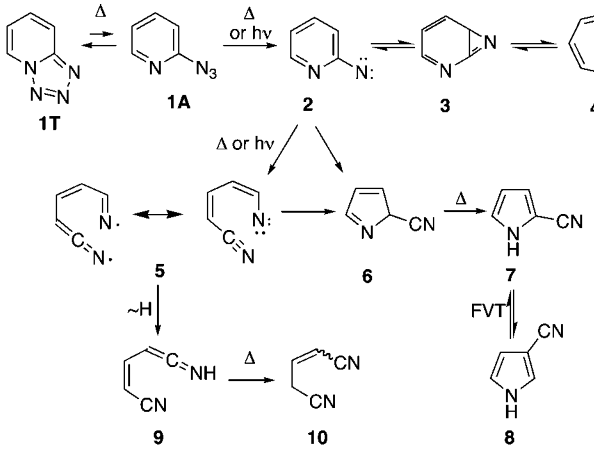
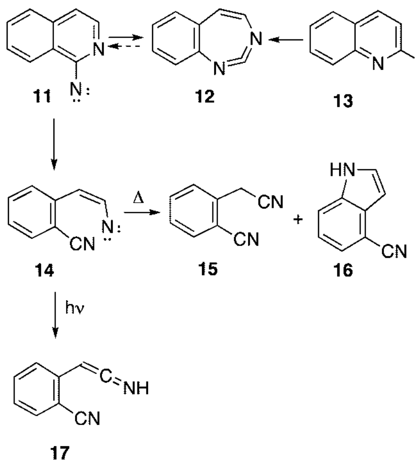
SCHEME 1. Pyridylnitrene Rearrangements



SCHEME 2. 2-Quinolylnitrene and 1-Isoquinolylnitrene Rearrangements



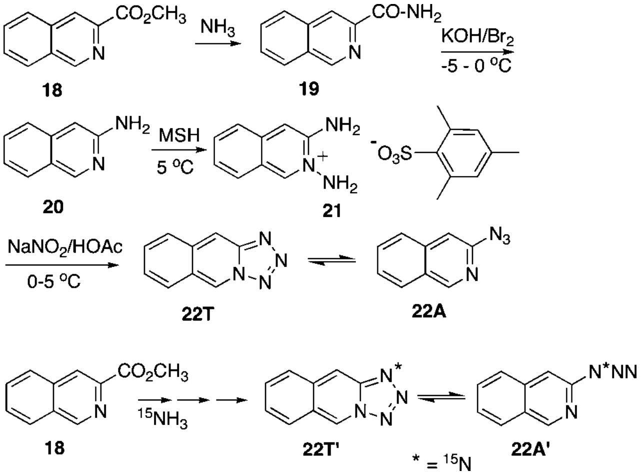
chemical ring opening to 2-*o*-cyanophenylketenimine **17** is a major process, whereas FVT leads to nitriles **15** and **16** (Scheme 2).[8] Again, ring opening to vinylnitrene **14** is assumed. The azirenes corresponding to **11** and **13** were not observed, and they are calculated to be transition states, not energy minima.

We have now investigated 3-isoquinolylnitrene **23** and present direct ESR spectroscopic evidence for the nitrene, IR evidence for azirene **24**, ^{15}N-labeling evidence for rapid interconversion of regioisomeric azirenes via the unobserved diazacycloheptatetraene, and type II ring opening of the nitrene to form 2-*o*-cyanophenylketenimine **17**.

Results and Discussion

1. Tetrazolo[1,5-*b*]isoquinoline 22T/3-Azidoisoquinoline 22A. Three different syntheses of this material have been described.[9] In order to investigate the reaction mechanisms by ^{15}N labeling, we modified the third method[9c] to permit the late and reliable introduction of the ^{15}N label using only a small amount of ammonia (Scheme 3). 3-Aminoisoquinoline **20** is accessible by amidation of methyl isoquinoline-3-carboxylate **18** followed by a Hofmann degradation of amide **19**. Amination of **20** with *o*-mesitylsulfonylhydroxylamine (MSH)[10] followed by diazotization of salt **21** afforded tetrazole **22T**/azide **22A**. The use of ammonia-^{15}N (98 atom %) in the first step afforded N$_1$-labeled tetrazole/azide **22T′/22A′**. In the following, unlabeled compounds have numbers **19**−**22**, etc.; ^{15}N-labeled compounds have numbers **19′**−**22′**, etc.

SCHEME 3. Synthesis of 22T/22A



Compound **22** exists as a mixture of tetrazole **22T** and 3-azidoisoquinoline **22A** already in the solid state at rt;[9] the IR spectrum of the solid in KBr features a medium-intensity azide band at 2120 cm^{-1}. Varying proportions of azide **22A** have been described for solutions.[9] We measured the equilibrium concentrations in DMSO-d_6 at temperatures between 301 and 373 K by ^{1}H NMR spectroscopy and determined $\Delta S° = 52.4 \pm 1.5$ J K^{-1} mol^{-1}, $\Delta H° = 17.7 \pm 0.6$ kJ/mol, and $\Delta G° = 2.05 \pm 1$ kJ/mol for the isomerization **22T** → **22A** at 25 °C, i.e., the tetrazole and the azide are nearly isoergic. The values are in line with those determined for several tetrazolopyridines.[11] In general, DMSO favors the tetrazole, whereas chloroform favors the azide in the tetrazole/azide equilibrium.[12] The azide/tetrazole ratio for **22** was 0.36 in DMSO-d_6 and 4.1 in CDCl$_3$ at 19 °C. The compound exists exclusively as azide **22A** in the gas phase. Gentle evaporation of the compound at 45−55 °C (3.3×10^{-6} mbar) and condensation of the material with Ar to form a matrix at 7 K results in pure azide with strong absorptions at 2139 and 2122 cm^{-1} (Figure 1A). Comparison of the solid in KBr with the IR spectrum reveals that no tetrazole is present in the matrix. Moreover, on subsequent photolysis of this matrix, all IR bands decrease with the same rate. This is strong evidence that only one species is present, viz. azide **22A**, because we have observed in many cases that azides photolyze much faster than the valence isomeric tetrazoles.

2. Photolysis. Photolysis of an Ar matrix of azide **22A** in a cryostat for ESR spectroscopy at $\lambda = 254$ nm or $\lambda > 300$ nm afforded intense X_2Y_2 ESR transitions around 6600−6850 G characteristic of a heteroaromatic nitrene ($D = 0.943$; $E = 0.005$ cm^{-1}) (Figure 2A). The spectrum is ascribed to 3-isoquinolylnitrene **23** in its triplet ground state (T$_0$). The open shell (S$_1$) and closed shell (S$_2$) nitrenes are calculated to lie 60.7 and 146.9 kJ/mol above the triplet, respectively, at the B3LYP/6-31G*

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[8] Addicott, C.; Reisinger, A.; Wentrup, C. *J. Org. Chem.* **2003**, *68*, 1470.

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[10] Krause, J. G. *Synthesis* **1972**, 140.

[11] Evans, R. A.; Wong, M. W.; Wentrup, C. *J. Am. Chem. Soc.* **1996**, *118*, 4009.

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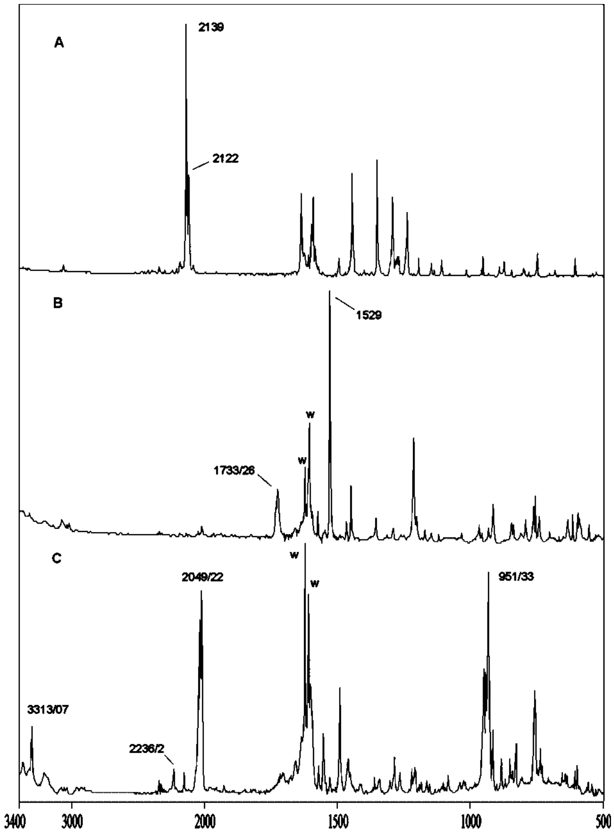

FIGURE 1. IR spectra of (A) 3-azidoisoquinoline **22A** deposited in Ar matrix at 7 K, (B) azirene **24** formed by photolysis at $\lambda > 300$ nm for 6.5 min, and (C) ketenimine **17** formed by further photolysis without a filter for 10 h (abscissa in cm^{-1}, w = water).

computational level, whereby the Cramer−Ziegler method[13] was used to estimate the S_1 energy (see Table S2, Supporting Information, for a summary of computational data).

The strong ESR signals ascribed to triplet **23** were obtained in many experiments under a variety of UV photolysis conditions. However, depending on wavelength and time, further signals ascribed to diradical **25** appeared in the 1600 and 2500−4000 G range, and in the 5000−5500 G range ascribed to carbene **21**, as is seen in Figure 2B−D (see also Figure S1, Supporting Information, for larger-scale spectra). They will be discussed later in this section.

A similar photolysis of an Ar matrix of **22A** using $\lambda > 300$ nm and IR spectroscopic detection caused complete depletion of azide (Figure 1A) within about 6 min with simultaneous formation of a new compound absorbing at 1733 and 1726 cm^{-1} (Figure 1B). The IR spectrum is ascribed to azirene **24** because of an excellent correlation with the calculated spectrum at the B3LYP/6-31+G* level (Figure 3). It is normal for azirenes of this type to show split bands of medium intensity for the C=N stretching vibration in the 1700 cm^{-1} region.[3,14] A strong band at 1529 cm^{-1} is due to the C=N group of the isoquinoline ring. Azide **22A** was also deposited as a neat solid and photolyzed at 7 K to produce azirene **24** as a virtually pure substance, now absorbing at 1723 and 1523 cm^{-1} (Figure S2, Supporting Information). The azirene was remarkably stable, surviving to 110 K on warm-up, and then disappearing on further warming between 110 and 140 K.

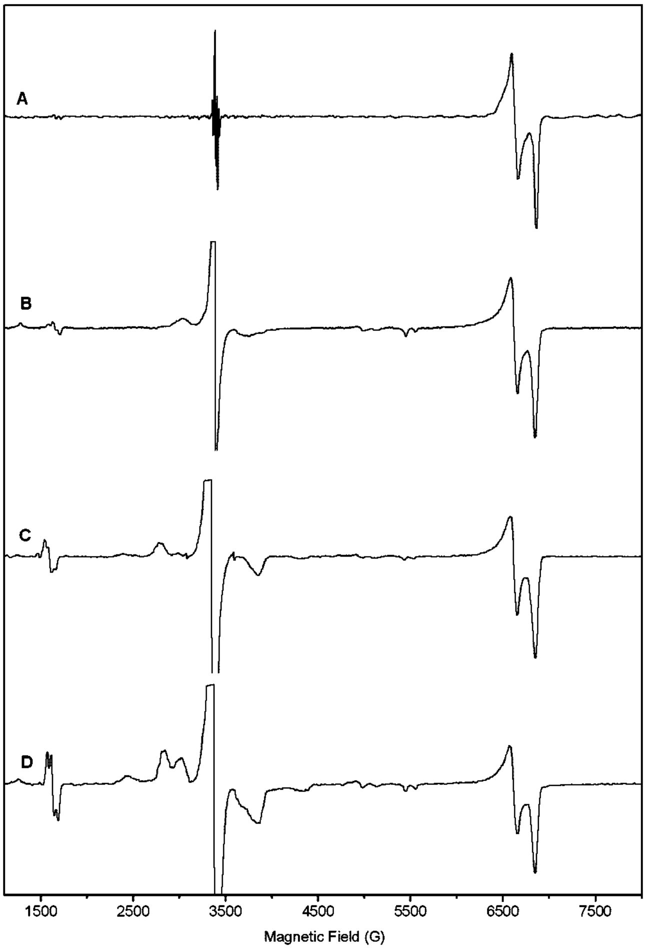

FIGURE 2. ESR spectra obtained by photolysis of **22A** in Ar matrixes. (A) Photolysis of **22A** at about 11 K using light of $\lambda = 332$ nm for 1 h. Nitrene **23** appears at $X_2 = 6625$ G, $Y_2 = 6860$ G; $D = 0.9444$ cm^{-1}, $E = 0.0049$ cm^{-1}; a monoradical appears at $g = 2$, and very weak $\Delta m_s = 2$ signals are ascribed to diradicals at 1625−1665 G, assigned to geometrical isomers of **25**; $H_0 = 3374.0$ G, $\nu = 9.4544$ GHz. (B) Photolysis of **22A** at 13 K, $\lambda = 332$ nm for 2 h. Besides nitrene **23**, signals for two diradicals and two carbenes [assigned as two conformers of **31**, most likely the *EZE* and *EEE* conformers (see below)] are seen. First carbene: $Z_1 = 1258$ G, $X_2 = 4950$ G, $Y_2 = 5443$ G; $D = 0.4336$ cm^{-1}, $E = 0.0123$ cm^{-1}. Second carbene: $X_2 = 5069$ G, $Y_2 = 5547$ G; $D = 0.4664$ cm^{-1}, $E = 0.0115$ cm^{-1}. First diradical (assigned to a geometrical isomer of **25**): $X_1 = 3126$, $X_2 = 3611$, $Y_1 = 3033$, $Y_2 = 3750$, $Z_1 = 2841$, $Z_2 = 3907$ ($\Delta m_s = 2$) 1645 G; $D = 0.0518$, $E = 0.0036$ cm^{-1}; $H_0 = 3372.5$ G, $\nu = 9.45141$ GHz. (C) Photolysis of **22A** at about 13 K, $\lambda = 254$ nm for 2 h. Stronger signals for diradicals are seen. $H_0 = 3372.5$ G, $\nu = 9.45131$ GHz. (D) Photolysis of **22A** at 12 K, $\lambda = 364$ nm for 1.5 h. Nitrene **23**, strong signals for two diradicals, assigned to geometrical isomers of **25**, and weak signals for the two carbenes **31** are seen. Second diradical (assigned to a geometrical isomer of **25**): $X_1 = 2935$ G, $X_2 = 3720$ G, $Y_1 = 2830$ G, $Y_2 = 3850$ G, $Z_1 = 2436$ G, $Z_2 = 4344$ G ($\Delta m_s = 2$) 1582 G; $D = 0.0874$ cm^{-1}, $E = 0.0037$ cm^{-1}; $H_0 = 3372.4$ G, $\nu = 945101$ GHz. Signs of D and E were not determined.

The azirene in the Ar matrix (Figures 1B and 3) changed very slowly on further irradiation at $\lambda > 300$ nm, but irradiation using either the unfiltered light of a high-pressure Hg/Xe lamp or the 254 nm line of a low-pressure Hg lamp caused the development of a new, strong, and complex band with maxima at 2049 and 2022 cm^{-1} (Figure 1C). The azirene was fully converted after 10 h of irradiation. The compound formed is unambiguously identified as the open-chain ketenimine **17** (Scheme 4), which has been obtained previously from iso-

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[14] Dunkin, I. R.; Thomson, P. C. P. *Chem. Commun.* **1980**, 499.

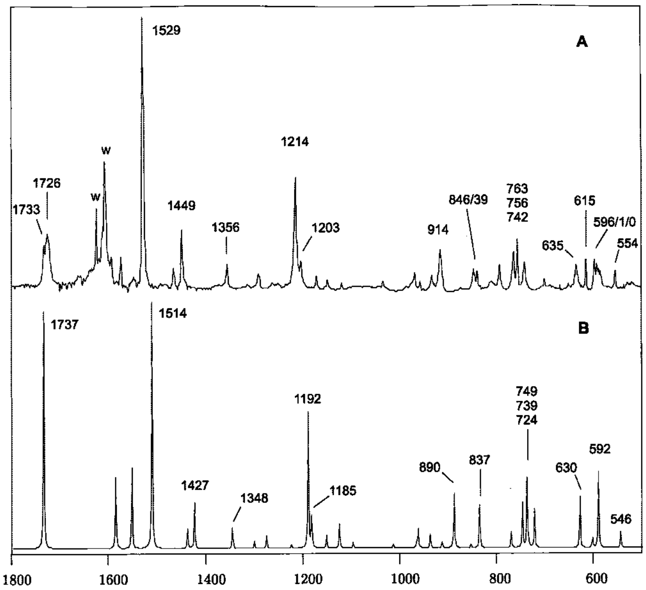
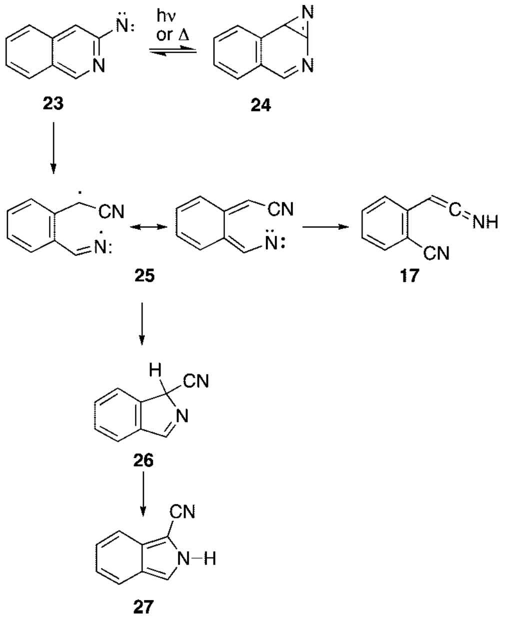


FIGURE 3. Experimental (A) and calculated (B) IR spectra of azirene **24** (B3LYP/6-31+G*, wavenumbers scaled by 0.9613). Abscissa in cm^{-1}, w = water.

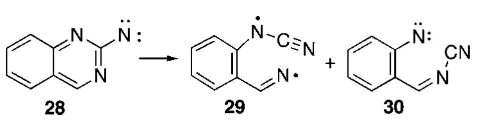
SCHEME 4. 3-Isoquinolylnitrene Rearrangements



quinolylnitrene **11** (Scheme 2)[8] (see Table S1 and Figure S3, Supporting Information). It is common for ketenes and ketenimines to feature multiple absorption maxima in the cumulene stretching region around 2000 cm^{-1}. This can be due to the existence of two conformers, s-*Z* and s-*E*, as well as several nonplanar conformers that may be populated in the Ar matrix. The integrated intensities of the IR bands due to azide **22A**, azirene **24**, and ketenimine **17** were monitored as a function of photolysis time (Figure S4, Supporting Information). This allowed a clear-cut attribution of IR bands to the individual compounds and also revealed a subset of bands in the IR spectrum in Figure 1C, which does not belong to **17**. These bands are at 2264, 1590, 1554, 1286, 1265, 1209, 884, 736, 720, and 600 cm^{-1}. The weak CN absorption at 2264 cm^{-1} is indicative of an unconjugated nitrile. This set of bands match the calculated IR spectrum of 1-cyano-1*H*-isoindole **26** (Figure S3, Supporting Information). The formation of compounds **17** and **26** is a logical consequence of a ring opening of 3-isoquinolylnitrene **23** to the diradical **25**, i.e., a type II ring opening of nitrene **23**. As described below, the more stable 2*H*-isomer **27** is formed by FVT, but not in the matrix photolysis. It is assumed that intersystem crossing between the singlet and triplet states of nitrene **23** can take place easily during photolysis. The reaction mechanism is summarized in Scheme 4.

We can now assign the diradical-type ESR signals in Figure 2B−D to diradical **25** (Scheme 4), which is analogous to the dienylnitrene/diradical **5** postulated to be formed from 2-pyridylnitrene (Scheme 1) and styrylnitrene **14** postulated in Scheme 2. In the pyridine case, this species will have a high degree of nitrene character. In the isoquinoline case, species **25** will have a high degree of diradical character because the nitrene canonical structure is *o*-quinoid. The strong and sharp half-field signals ($\Delta m_s = 2$) at 1588−1645 G in Figure 2B−D are characteristic of diradicals and are never seen with such intensity for hetaryl-nitrenes or -carbenes. The relative intensities of the two sets of signals change depending on the photolysis wavelength and time, thereby making it clear that there are two closely related diradical species. Only tiny amounts of the diradicals are seen in Figure 2A. Increasing amounts are seen in Figures 2B−D. The signals are assigned to s-*Z* and s-*E* conformational isomers of **25**. The lines in the range 2200−4200 G are typical Z_1, Y_1, and X_1 and X_2, Y_2, and Z_2 transitions of a triplet diradical.[15] The *D* values (0.0518 and 0.0874 cm^{-1}) are smaller than that determined for **29** (0.119 cm^{-1}, see eq 3), as would be expected for a diradical with one less nitrogen center. The *D* values of **25** and **29** are higher than those determined for several other organic 1,5-diradicals (~0.02 cm^{-1}).[15] This can be ascribed to the partial nitrene-type canonical structure (see formula **25**, Scheme 4), which puts a high electron spin density on N (see calculated spin densities in the Supporting Information).

The chemistry described here is analogous to that of 2-quinazolylnitrene **28**, where ring opening affords a diradical **29** as well as a secondary minor nitrene to which structure **30** was assigned (eq 3).[7]



(1)

Analogous ring opening in 3-isoquinolylnitrene **23** will generate diradical **25** (eq 2) and arylcarbene **31** (eq 3). Thus, a likely candidate for the weak carbene signals seen in Figure 2B−D around 5000−5500 G is the arylcarbene **31**, which can exist in several geometrically isomeric forms (eq 3) (further possible conformers are shown in the Supporting Information). An excellent linear correlation exists between experimental *D* values and calculated natural spin densities ρ on the carbene center of monosubstituted carbenes of the type RCH.[16] The $D-\rho$ correlation fits the equation $D = 0.78446\rho - 0.78316$ cm^{-1} with a standard deviation of $D \pm 0.015$ cm^{-1}; $R^2 = 0.990$ at the UB3LYP/EPR-III level of theory.

The data for the *EZE* and *EEE* isomers of carbene **31** (eq 3) fit extremely well with this correlation (**31**-*EZE*: $D = 0.4336$,

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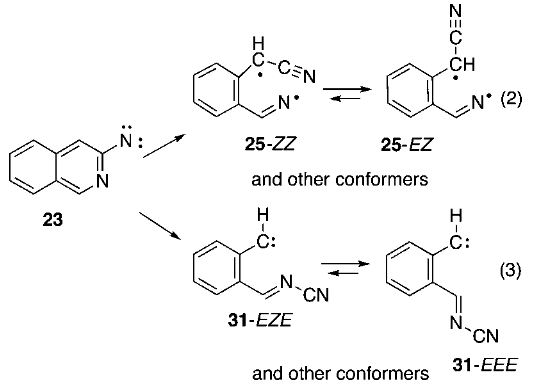
$E = 0.0123$ cm^{-1}, $\rho = 1.5245$; **31**-*EEE*: $D = 0.4664$, $E = 0.0118$ cm^{-1}, $\rho = 1.5939$), but other conformations are not excluded. The correlation is illustrated in Figure S5 of the Supporting Information.



The intensities as well as the ratios of geometrical isomers of the carbene varied as a function of photolysis wavelength and time (Figure 2 and Figure S1, Supporting Information).

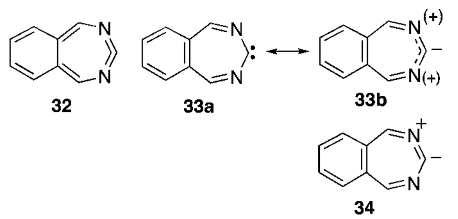
The activation barriers for conversion of triplet nitrene **23** to triplet diradical **25** and triplet carbene **31** were calculated at the UB3LYP/6-31 G* level of theory as 110.9 and 199.6 kJ/mol, respectively, i.e., the formation of the diradical is less costly energetically, in accord with the observed relative intensities in the ESR spectra (Figure 2). Moreover, the barrier for conversion of the open-shell singlet nitrene $^1A''$ to the open-shell singlet diradical $^1A''$ (139.7 kJ/mol) was higher than for the triplet−triplet reaction.

It must be noted that ESR spectroscopy is far more sensitive than IR spectroscopy. Comparison with the calculated vibrational frequencies of nitrene **23** and diradicals **25** (Supporting Information) clearly shows that these are not the species being observed in the IR spectra, where azirene formation is observed very rapidly and quantitatively (Figures 1B and 3). We have observed several other related nitrenes, e.g., **28**, by IR and UV−vis spectroscopy,[7] but this would not be possible under these reaction conditions ($\lambda > 300$ nm) because the nitrenes themselves undergo rapid photolysis at visible wavelengths.

3. FVT. Preparative FVT of **22A** at 550 °C afforded 1-cyano-2*H*-isoindole **27** in quantitative yield. FVT with Ar matrix isolation and IR spectroscopy of the product at 7 K demonstrated that **27** starts forming at about 350 °C, and its formation is complete at 500−550 °C. No other product or intermediate was discernible. It is logical to assume that **27** is formed by tautomerization of **26** (Scheme 4). This tautomerization reaction is calculated to have a barrier of about 160 kJ/mol at the B3LYP/6-31G* level. **27** is calculated to lie 37 kJ/mol below **26** (see computational data in the Supporting Information). Therefore, the tautomerization **26** → **27** will take place easily under FVT conditions but not in low-temperature matrixes.

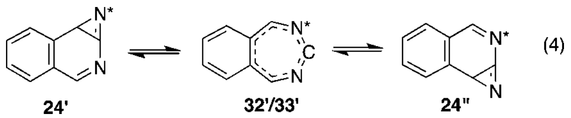
It is postulated that ring opening to diradical **25** is a key step in both photolysis and thermolysis reactions. The mechanism is summarized in Scheme 4.

4. ^{15}N Labeling. In none of the experiments described so far was there any evidence for the existence of diazacycloheptatetraene **32**. This molecule is calculated to absorb strongly at about 1930 cm^{-1} in the IR.[17] Calculations also indicate that molecule **33** is virtually isoergic with **32**, both of them lying 76−80 kJ/mol above ground state nitrene **23** (T_0), i.e., about 20 kJ/mol above the open-shell singlet nitrene (S_1) (vide supra).[17] Azirene **24** was found to be about 40 kJ/mol more stable than **32** or **33**.[17]



While compound **32** is a twisted *o*-quinoid carbodiimide benefiting from some Möbius-aromatic stabilization, **33** is best described as a resonance hybrid of a carbene **33a** and an ylidic zwitterion **33b**.[17] Bond-localized cyclic nitrile ylide **34** was not located as an energy minimum.[17] Comparison of the experimental IR spectra with the calculated data[17] for **32** and **33** makes it clear that these compounds were not present in any of our experiments. This is in stark contrast to the situation with 2-pyridylnitrene **2** (Scheme 1), where the diazacycloheptatetraene **4** is the major and easily detected reaction product under both thermal and photochemical conditions, azirene **3** is not observable, and ring opening to **9/10** is a minor process.

The use of ^{15}N-labeled tetrazole/azide **22T′/22A′** (98 atom % ^{15}N, see Scheme 3) proved that azirenes **24′** and **24″** interconvert rapidly as they are being formed by photolysis. This interconversion is complete before the ring-opened ketenimines **17′/17″** are formed. 1-Cyanoisoindole **27** formed by FVT also has complete scrambling of the ^{15}N label. We postulate that the ^{15}N scrambling takes place, both photochemically and thermally, via facile interconversion of azirene with the 7-membered ring species **32** or **33** (eq 4). The activation barrier for this process is calculated to be only 55 kJ/mol at the B3LYP/6-31G* level.



It is also conceivable that the two azirenes **24′** and **24″** could interconvert directly in a concerted pericyclic reaction, but we were unable to locate a TS for such a process at either the HF or B3LYP computational level.

Photolysis of ^{15}N-labeled azide **22A′** at $\lambda > 300$ nm led initially (within 30 s) to labeled azirene **24′**, as seen in a red shift of the complex azirene C=N band from 1733 to 1711 cm^{-1} (Figure 4). However, within a few minutes of photolysis, the unshifted band at 1733 cm^{-1} started growing, and the red-shifted band at 1711 cm^{-1} decreased, eventually reaching about a 1:1 ratio of the two azirenes **24′** and **24″** (Figure S6 of the Supporting Information). At the same time, the C=N band of the isoquinoline moiety, which appeared at first in the unshifted position of 1529 cm^{-1}, decreased, and a red-shifted band at 1521 cm^{-1} grew in intensity, indicating that isoquinoline-N was becoming labeled (Figure S6 of the Supporting Information). The isotopic shifts of about 20 and 8 cm^{-1} for azirene and isoquinoline C=N moieties are in excellent agreement with calculations (19 and 8 cm^{-1}, respectively).[17] There were no other significant differences between labeled and unlabeled spectra.

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[17] Kuhn, A.; Vosswinkel, M.; Wentrup, C. *J. Org. Chem.* **2002**, *67*, 9023.

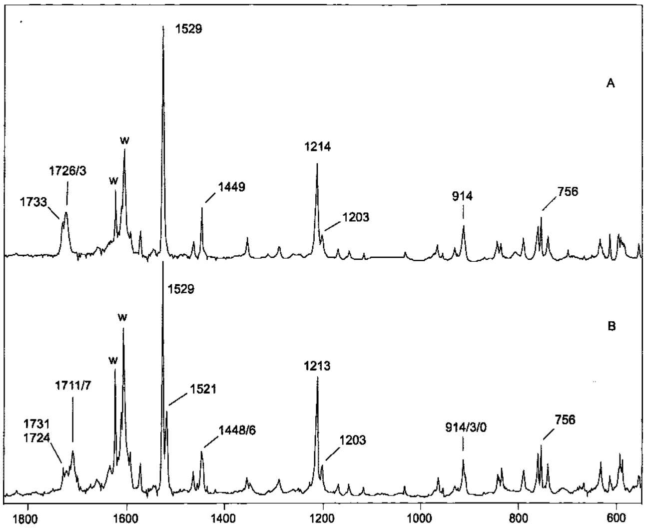

FIGURE 4. IR spectra of unlabeled and ^{15}N-labeled azirenes **24** (A) and **24′/24″** (B) (Ar matrix, 7 K).

Further broad-band photolysis of labeled azirene afforded labeled ketenimine **17′/17″**, showing red shifts of the complex C=C=N absorption band at 2049−2016 cm^{-1} (unlabeled) to 2050−2006 cm^{-1} (labeled); the band maxima at 2040/2022 cm^{-1} shifted to 2032/2013 cm^{-1} in agreement with a calculated isotopic shift of 13 cm^{-1} (Figure S7 of the Supporting Information). The absorption of the CN group was split into two with a shift of 26 cm^{-1}. Unlike the situation for the azirenes, there was no dynamic evolution pattern for the labeling of the ketenimines; the ratio of labeled and unlabeled substances remained constant throughout the photolysis and is assumed to be 1:1.

Labeled azide **22A′** was also subjected to FVT at 550 °C. Examination of the isolated 1-cyano-2*H*-indole **27′** by ^{13}C and ^{15}N NMR spectroscopy demonstrated complete scrambling of the ^{15}N label. In particular, the IR spectrum featured two peaks of equal intensity for the CN group, viz. 2200 (C^{14}N) and 2180 cm^{-1} (C^{15}N).

Conclusion

Photolysis of 3-azidoisoquinoline **22A** causes rapid formation of 3-isoquinolylnitrene **23** (observed by ESR) and ring closure to azirene **24** (observed by IR spectroscopy). ^{15}N labeling reveals that the azirene undergoes photochemical automerization (**24′** $\rightleftharpoons$ **24″**), and it is concluded that this takes place via a symmetrical intermediate, viz. the 7-membered ring carbodiimide or carbene/ylide **32/33** (eq 4). The azirene is obtained virtually pure and is stable to temperatures above 110 K. UV photolysis of the azirene causes rearrangement to *o*-cyanophenylketenimine **17**.

In addition to the ESR signal for the triplet nitrene, signals due to triplet diradicals also develop rapidly upon UV photolysis. These diradicals are assigned structure **25**, which can form by ring opening of the nitrene (eq 2). Thus, azirene **24** can rearrange to ketenimine **17** via reversion to nitrene **23**, followed by ring opening to diradical **25** (Scheme 4). Diradical **25** can undergo a 1,6-H shift to give ketenimine **17** or cyclize to 1*H*-1-cyanoisoindole **26**. Finally, a 1,5-H shift in **26** affords 2*H*-1-cyanoisoindole **27**, which is obtained in quantitative yield on FVT, with complete nitrogen scrambling when labeled azide **22A′** is used.

This is the first direct observation of a fused azirene in the hetarylnitrene series. Azirenes have been postulated but never observed as intermediates in the ring expansion of 2-pyridylnitrenes, 2-quinolylnitrene, 2-pyrazinylnitrene, and 4-pyrimidylnitrene to cyclic carbodiimides. Ring opening of 2-pyridylnitrenes to dienylnitrenes/diradicals analogous to **25** has long been postulated as a mechanism of formation of open-chain ketenimines and glutacononitriles but not previously observed.

Computational Method. Standard DFT calculations were performed using the Gaussian 98 suite of programs.[18] Geometry optimizations and frequency calculations were computed at the B3LYP/6-31G* and in some cases the B3LYP/6-31+G* level of theory. A scaling factor of 0.9613 was used for wavenumbers.[19] The nature of transition states was established by intrinsic reaction coordinate (IRC) calculations. The energy of open-shell singlet nitrene **23** (S_1, $^1A''$) was estimated using the Cramer−Ziegler method.[13] An overview of calculated relative energies is given in Table S2 of the Supporting Information.

Experimental Section

General. Apparatus for matrix isolation, photolysis, ESR and IR spectroscopy, and FVT have been described.[7,20]

Isoquinoline-3-carboxamide-^{15}N 19′. The efficient synthesis of amide **19**, using only small amounts of ammonia, was achieved by means of a vacuum line. Ammonia-^{15}N (98 atom % ^{15}N, 400 mg, 22.22 mmol) was condensed into a degassed and frozen solution of 700 mg (3.74 mmol) of isoquinoline-3-methylcarboxylate in 10 mL of dry methanol in a 50 mL flask cooled in liquid N_2 and containing a magnetic stirring bar. The flask was closed, and the stopcock and the attachment of the flask were secured with springs. The content was allowed to warm to rt and then stirred magnetically for 12 h at rt, after which time a white precipitate had formed. Excess ammonia was condensed from the reaction flask into another container for reuse. The white product was isolated by filtration, yielding 503 mg (2.91 mmol, 77.7%) of **19′**: mp 206−208 °C; mp of unlabeled material 206−208 °C; lit.[21] mp 206−207 °C.

3-Aminoisoquinoline-^{15}N 20′. Bromine (0.13 mL, 2.7 mmol) was added to a stirred solution of 2.13 g (41.4 mmol) of KOH in 5 mL of H_2O at −5 to −3 °C. Another 5 mL of water was then added, and stirring was continued for 10 min. Labeled 3-aminoisoquinoline (500 mg, 2.89 mmol) was now added in portions with 5 mL of H_2O with vigorous stirring at −5 to 0 °C over 1 h. The thick, white suspension was warmed to rt, heated at 80 °C for 1 h, and then heated at 100−110 °C for 10 min. A clear yellow solution formed for a short time, followed by a yellow precipitate. The mixture was cooled to rt. Another 2.70 g of KOH was added, and the mixture was allowed to stand for 12 h. A yellow solid was filtered off, and the solution was concentrated and filtered. The combined precipitates were extracted with boiling toluene and filtered hot. Evaporation of the filtrate afforded 0.236 g (56.4%) of yellow plates of **20′**: mp 176−178 °C; mp of unlabeled material 174−180 °C; lit.[21] mp 178 °C.

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Tetrazolo[1,5-*b*]isoquinoline-^{15}N/3-Azidoisoquinoline-^{15}N 22T′/22A′. Labeled 3-aminoisoquinoline (0.171 g, 1.18 mmol) was dissolved in 7 mL of DCM and cooled to 5−7 °C, affording a yellow suspension. A suspension of MSH (0.280 g, 1.30 mmol) in 7 mL of DCM was cooled to 5 °C and added to the above suspension at 5 °C with stirring. The DCM was previously freed of acid by passing it through a column of basic alumina. When a clear lemon solution had formed, stirring was stopped, and the solution was allowed to stand for 1 h, after which time a precipitate had formed. After addition of 2 mL of diethyl ether, the mixture was allowed to stand at 5 °C for 12 h. The product was filtered, washed thoroughly with diethyl ether, and dried in vacuo to afford 319 mg (0.88 mmol, 75.0%) of a yellow solid: mp 170−172 °C. This material was dissolved in 6 mL of acetic acid (50%), and a cold solution of 97 mg (1.41 mmol) of sodium nitrite in 2 mL of water was added dropwise at 0−5 °C. After the mixture had been stirred in ice in the dark for 2 h, the crude product (48 mg, 32%) was filtered and purified by vacuum sublimation to yield 13 mg (9%) of **22T′/22A′**: mp 126−128 °C. Unlabeled tetrazole **22T/22A** was obtained in the same manner: mp 126−128 °C; lit.[9b] mp 122 °C.

Argon Matrix Photolysis of 3-Azidoisoquinoline 22A. The tetrazole/azide mixture **22T/22A** was sublimed at 45−55 °C (3.3 × 10^{-6} mbar) and codeposited in argon (flow rate about 3 mbar/min). The condensate consisted only of 3-azidoisoquinoline **22A**, as evidenced by comparison with the IR spectrum of the solid tetrazole/azide mixture: IR (Ar matrix, 7 K) ν 3069, 3048, 2345, 2301, 2244, 2215 (all vw), 2191 w, 2185 w, 2147 w (N$_3$), 2139 vs (N$_3$), 2122 s (N$_3$), 2091 w, 1636 s, 1627 m, 1598 m, 1593 s, 1584 m, 1578 w, 1573 vw, 1495 w, 1457 vw, 1450 m, 1444 s, 1440 m, 1400 vw, 1351 s, 1345 sh, 1340 vw, 1302 w, 1299 m, 1293 s, 1291 m, 1282 w, 1280 w, 1275 m, 1270 m, 1245 w, 1243, 1241, 1239, 1237 (all m), 1197 sh, 1194 w, 1150 sh, 1147 w, 1142 sh, 1138 sh, 1136 vw, 1109 w, 1107 w, 1080 vw, 1016 vw, 961 br w, 958 w, 953 w, 931 vw, 892 w, 889, 886, 883, 880, 877 (all vw), 875 w, 873 w, 848, 845, 801, 796, 780, 753 (all vw), 749 m, 682 vw, 606 w, 526 vw, 472 vw, and 468 w cm^{-1}.

For quantitative, time-dependent IR measurements, **22A** was irradiated in discrete intervals. Initially, the condensate was photolyzed with light of λ > 300 nm. After 6.5 min photolysis, the starting material was fully converted, leading to a spectrum that presented only negligible amounts of secondary photolysis product **17**. The dominating bands originate from 7b*H*-azireno[3,2-*c*]isoquinoline **24**: IR (Ar matrix, about 7 K) ν 1733 w, 1726 m, 1723 m (all C=N), 1574 w, 1529 s (C=N), 1466 w, 1449 m, 1356 w, 1292 w, 1290 w, 1214 m, 1203 br w, 1172 vw, 969 vw, 967 vw, 914 w, 846 vw, 839 br vw, 792 w, 791 sh, 766 vw, 763 w, 756 w, 742 br w, 637 vw, 635 w, 632 sh, 615 w, 596 w, 593 vw, 591 vw, 588 vw, 586 vw, 584 vw, 556 sh, and 554 vw cm^{-1} (Figure 1B).

After removal of the filter, the sample was subjected to broad-band photolysis for 605 min (high-pressure Hg/Xe lamp). This resulted in a slow decay of the bands of azirene and a gradual increase of the bands of *o*-cyanophenylketenimine **17**, to which the major bands in the final spectrum are ascribed: IR (Ar matrix, 7 K) ν 3316 sh, 3313 w, 3307 w, 3297 vw (all NH), 2236 w, 2232 w (all C≡N), 2055 w, 2049 m, 2040 s, 2031 m, 2022 s, 2016 m (all C=C=N), 1573 vw, 1492 m, 1465 w, 1464 w, 1460 m, 1418 w, 1411 w, 1346 w, 1341 br w, 1303 vw, 1085 br vw, 1083 vw, 955 w, 951 m, 949 m, 942 m, 937 m, 935 m, 933 s, 928 m, 916 w, 851 vw, 828 w, 765 w, 761 m, 758 m, 755 m, 607 vw, 464 vw, 420 w cm^{-1} (Figure 1C). A set of weak bands at 2264, 1590, 1554, 1286, 1265, 1209, 884, 736, 720, and 600 cm^{-1} is ascribed to 1-cyano-1*H*-isoindole **26** (Figure S3 in the Supporting Information).

Photolysis of Neat 3-Azidoisoquinoline 22A. Azide was sublimed at 46−48 °C (2 × 10^{-6} mbar) over a 2.5 h period and deposited neat, without Ar. Azide was then photolyzed (λ > 300 nm) for 8 min, which yielded the IR spectrum of neat azirene **24** (Figure S2 in the Supporting Information): IR (neat, 7 K) ν 1723 w, 1603 w, 1523 s, 1448 w, 1359 vw, 1219 m, 917 w, 848 vw, 793 vw, 768 w, 757 w, 744 w, 630 w, 615 w, and 586 w cm^{-1}. On subsequent warming, the bands of azirene disappeared between 110 and 140 K.

Argon Matrix Photolysis of 3-Azidoisoquinoline-^{15}N 22A′. The tetrazole/azide mixture was sublimed at 46−49 °C (2 × 10^{-6} mbar) over 2 h and 15 min and codeposited in argon (flow rate about 4 mbar/min): IR (Ar matrix, 7 K) ν 3069, 2330, 2293, 2207, 2182, 2175, 2154 (all vw), 2143 w, 2133 vs, 2116 w, 2111 w, 2105 vw, 1636 m, 1595 m, 1588 vw, 1585 w, 1498 vw, 1496 vw, 1450 vw, 1444 sh, 1443 m, 1438 vw, 1349 m, 1345 sh, 1344 sh, 1340 vw, 1294 vw, 1288 w, 1286 m, 1279 vw, 1274 w, 1270 w, 1236 vw, 1232 w, 1228 m, 1225 vw, 1222 vw, 1193 vw, 1191 w, 1145, 1136, 1107, 1103, 1016, 958, 952, 890, 875, 873, 845, 791, 777, 748, 681, 606, 526, and 468 (all vw) cm^{-1}.

The azide was then photolyzed with light of λ > 300 nm. The progress of the photolysis was followed in discrete intervals. After 10.5 min, the azide had almost disappeared, and only a negligible amount of final photolysis product **17** was present. The bands of ^{15}N-labeled azirines **24′** and **24″** were observed: IR (Ar matrix, 7 K) ν 1731 vw, 1724 vw, 1717 vw, 1711 w, 1574 vw, 1529 s, 1521 w, 1465 vw, 1448 w, 1446 w, 1356 vw, 1349 vw, 1291 vw, 1216 sh, 1213 m, 1203 br w, 1170 vw, 966 vw, 964 vw, 914 w, 913 w, 910 vw, 908 sh, 844 vw, 842 vw, 836 vw, 834 sh, 792 vw, 790 vw, 766 vw, 762 w, 756 w, 741 vw, 636 vw, 633 vw, 614 vw, 596 vw, 593 w, 591, 589, 587, 555, and 553 (all vw) cm^{-1} (Figure 4).

After 42 min, the filter was removed, and the sample was exposed to broad-band UV light. After 5 h and 15 min, only minor amounts of azirines were visible. The dominant bands in the spectrum are assigned to two ^{15}N-labeled *o*-cyanophenylketenimines **17′** and **17″**: IR (Ar matrix, 7 K) ν 3316 vw, 3313 w, 3300 w, 3290 vw, 2235 vw, 2231 vw, 2208 vw, 2201 vw, 2068 vw, 2050 m, 2040 s, 2032 s, 2025 s, 2013 s, 2006 s, 1573 vw, 1495 w, 1491 m, 1465 vw, 1462 vw, 1460 vw, 1344 br w, 1303 vw, 1080 vw, 956 w, 948 s, 939 s, 937 s, 934 s, 933 s, 930 s, 928 s, 926 s, 916 m, 914 m, 884 w, 850 vw, 841 vw, 832 vw, 827 w, 765 w, 760 m, 757 m, 755 m, 598 vw, 464 vw, 457 vw, and 420 w cm^{-1}.

Preparative FVT of 3-Azidoisoquinoline 22A: FVT/Argon Matrix Isolation of 3-Azidoisoquinoline 22A. The tetrazole/azide mixture was sublimed at 70−75 °C (5 × 10^{-5} mbar) over a period of 2 h and 20 min, and the vapor was passed through a FVT tube at 500−550 °C. The thermolysate was codeposited in Ar (flow rate about 3 mbar/min) and consisted entirely of 2*H*-1-cyanoisoindole **27** as evidenced by comparison with a pure, isolated sample: IR (Ar matrix, 15 K) ν 3480 vs, 2224 vw, 2219 s, 2209 vw, 1660 br vw, 1590 w, 1453 m, 1410 m, 1386 m, 1311 m, 1304 w, 1240 m, 1137 m, 1110 m, 1105 m, 1045 w, 995 w, 769 m, 750 m, 632 w, 595 w, 589 m, 553 m, 529 w, 476 w, and 427 w cm^{-1}.

Preparative FVT of 3-Azidoisoquinoline-^{15}N 22A′. Over 2 h, a sample of 200 mg of **22T′/22A′** was sublimed at 40−50 °C (10^{-2} mbar) into the quartz tube of the FVT apparatus held at 550 °C. The product of FVT was isolated on a coldfinger cooled in liquid N$_2$. At the end of the thermolysis, the isolated substance was dissolved in acetone and purified by thick layer chromatography on silica gel, eluting with diethyl ether. Only one band eluted with isolable quantities of a substance. This material dissolved in acetone to give a green solution. Evaporation of the solvent and sublimation at 80 °C (10^{-2} mbar) afforded 160 mg (96%) of white crystals: mp 130−132 °C dec; mp for unlabeled material 130−132 °C; lit.[22] mp 132−134 °C; MS *m*/*z* 143 (100%), 144 (10%); IR (KBr) ν 3260 s, 2930 w, 2200 s (C^{14}N), 2180 s (C^{15}N, same intensity as 2200 cm^{-1} band), 1450 m, 1410 m, 1400, s, 1285 m, 1315 m, 1240 s, 1135 s, 1110 s, 765 s, 755 s, 730 s cm^{-1}; ^{13}C NMR (acetone-*d*$_6$) δ 90.3 (m), 115.5 (m), 117.5 (d, J_{NC} = 14 Hz), 117.5 (s), 125.2 (s), 118.4, 122.3, 122.9, 125.9, 131.5 (d, J_{NC} = 4 Hz); ^{15}N NMR

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(acetone-d_6 referenced to saturated $^{15}NH_4Cl$ in H_2O, $\delta_N = 27.34$ ppm) δ 272.2 (tertiary N), 174.5 (secondary N, d, $J_{NH} = 97$ Hz).

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Supporting Information Available: ESR and IR spectral Figures S1−S6, tables of IR spectral data for ketenimine **17**, and tables of computational data (Cartesian coordinates, absolute and relative energies, and vibrational frequencies for all calculated structures). This material is available free of charge via the Internet at http://pubs.acs.org.

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