JOC Article

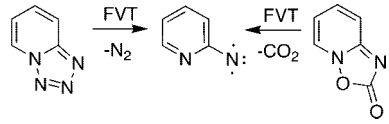
2-Pyridylnitrene from Tetrazolo[1,5-*a*]pyridine and Pyrido[2,3-*a*][1,2,4]oxadiazol-2-one

Adam McCluskey[†] and Curt Wentrup*

Chemistry Building, School of Molecular and Microbial Sciences, The University of Queensland, Brisbane QLD 4072, Australia

wentrup@uq.edu.au

Received April 25, 2008



Flash vacuum thermolyses of tetrazolo[1,5-*a*]pyridine and pyrido[2,3-*a*][1,2,4]oxadiazol-2-one generate 2-pyridylnitrene, which was detected by Ar matrix ESR spectroscopy. The thermolysis products are 2-aminopyridine, *Z*- and *E*-glutacononitriles, and 2- and 3-cyanopyrroles. The products are formed in the same ratios from the two precursors.

Introduction

In recent papers we have demonstrated the occurrence of two types of ring-opening reactions of (hetero)aromatic nitrenes and carbenes: Type I causes ring opening to ylides (nitrile ylides or diazo compounds), exemplified by 3-pyridylcarbene, 3-pyridylnitrene, and 2-pyrazinylnitrene/4-pyrimidylnitrene, as has been elucidated particularly in matrix photolysis studies.[1,2] Type II causes ring opening to diradicals or nitrenes **4**, exemplified by (substituted) 2-pyridylnitrenes, 1-isoquinolylnitrene, and 2-quinoxalylnitrene (Scheme 1), and it may take place under both thermal (flash vacuum thermolysis, FVT) and photochemical conditions.[3,4] The open-chain diradicals/nitrenes **4** are postulated to be the source of cyanovinylketenimines **5**, which tautomerize to glutacononitriles **6** under thermal reaction conditions (Scheme 1).

2-Pyridylnitrene **2** also undergoes H-abstraction to form small amounts of 2-aminopyridine **9**, even under conditions of high vacuum FVT, but the major products are the cyanopyrroles **7** and **8**. Type II ring opening to **5** or **6** is a minor process under both thermal[5,6] and photochemical[7] conditions; thus the yields of glutacononitriles are typically of the order of 10%. The formation of the cyanopyrroles **7** and **8** is the major process under FVT conditions. There may be more than one mechanism of formation of **7** and **8**. One is via vinylnitrene **4**; another is a concerted ring contraction of 2-pyridylnitrene **2** (Scheme 1).[8,9]

Here we report an investigation of two different precursors of 2-pyridylnitrene, viz., the title compounds tetrazolo[1,5-*a*]-pyridine[5,6] (**1T**) and pyrido[2,3-*a*][1,2,4]oxadiazol-2-one[10] (**10**), which have been reported to afford the same products, but in very different ratios, on FVT. In the FVT of **1**, only minor amounts of glutacononitriles **6** and 2-aminopyridine **9** are formed (of the order of 10%), and the cyanopyrroles are the major products. 2-Cyanopyrrole **7** is formed first, but it interconverts with 3-cyanopyrrole **8** via a series of sigmatropic 1,5-shifts of H and CN under FVT conditions. Furthermore, chemical activation can cause significant isomerization of **7** to **8** at low pressure.[9] Therefore, a mixture of 2- and 3-cyanopyrroles is always formed.[9a,11] In the FVT of pyrido[2,3-*a*][1,2,4]oxadiazol-2-one (**10**), yield ratios of **6**:**7**:**8** = 1:3:3 at 600 °C and 3:1:3 at 700 °C were reported, and no presence of 2-aminopyridine was mentioned (Scheme 2).[10] The high proportion of glutacononitrile **6** has been an enigma for many years. Such large differences in product ratios from different precursors would normally imply different reaction mechanisms. Herein we report conclusive evidence that FVT of both precursors generates 2-pyridylnitrene **2**, and the products ratios from the two precursors are in fact identical.

[†] Current address: Discipline of Chemistry, School of Environmental and Life Sciences, University of Newcastle, Callaghan NSW 2308, Australia.

(1) Bednarek, P.; Wentrup, C. *J. Am. Chem. Soc.* **2003**, *125*, 9083–9089.
(2) Addicott, C.; Wong, M. W.; Wentrup, C. *J. Org. Chem.* **2002**, *67*, 8538–8546.
(3) Addicott, C.; Reisinger, A.; Wentrup, C. *J. Org. Chem.* **2003**, *68*, 1470–1474.
(4) Kvaskoff, D.; Bednarek, P.; George, L.; Waich, K.; Wentrup, C. *J. Org. Chem.* **2006**, *71*, 4049–4058.
(5) Crow, W. D.; Wentrup, C. *Chem. Commun.* **1969**, 1387–1388.
(6) Wentrup, C.; Winter, H.-W. *J. Am. Chem. Soc.* **1980**, *102*, 6159–6161.
(7) Reisinger, A.; Bernhardt, P. V.; Wentrup, C. *Org. Biomol. Chem.* **2004**, *2*, 245–256.
(8) Harder, R.; Wentrup, C. *J. Am. Chem. Soc.* **1976**, *98*, 1259.
(9) (a) Wentrup, C. *Top. Curr. Chem.* **1976**, *62*, 173–251. (b) Wentrup. C. *In Reactive Intermediates*; Abramovitch, R. Ed., Plenum: New York, 1980, Vol. 1, p 263−319.
(10) Brown, R. F. C.; Smith, R. J. *Aust. J. Chem.* **1972**, *25*, 607–624.
(11) Wentrup, C.; Crow, W. D. *Tetrahedron* **1970**, *26*, 3965–3970.

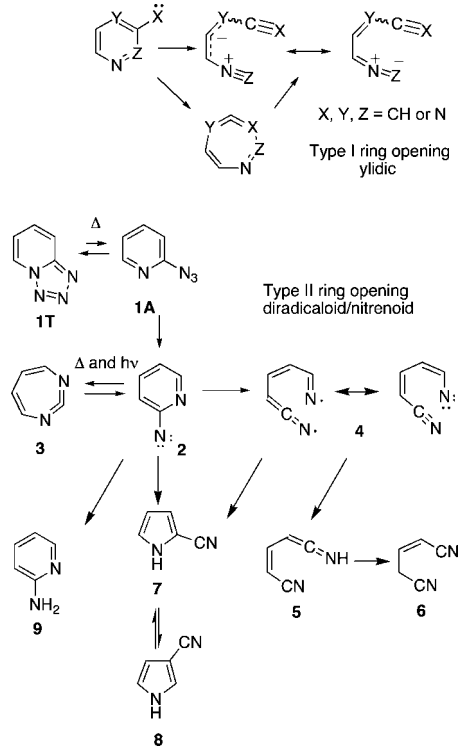
10.1021/jo800899t CCC: $40.75
Published on Web 07/23/2008

TABLE 1. Products of FVT of 1T and 10[a]

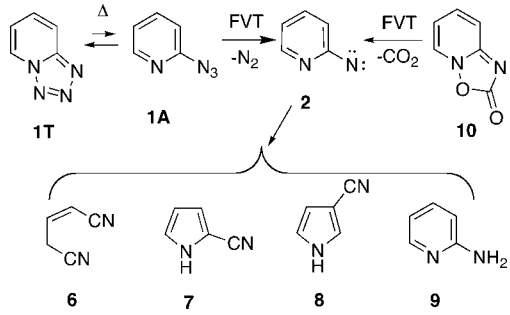
	starting materials **1T** and **10**							
	500 °C		600 °C		700 °C		800 °C	
	1T	**10**	**1T**	**10**	**1T**	**10**	**1T**	**10**
	500 °C	500°C	600°C	600°C	700°C	700°C	800°C	800°C
6	12.3	0	11.5	8.1	17.2	16.6	17.1	19.2
7	37.8	0	44.7	24.2	39.2	38.1	41.2	40.5
8	35.4	0	40.9	18.3	37.2	37.0	37.3	36.7
9	2.8	0	0.7	18	1.1	2.8	<0.5	1.7
recovered **1T**	3.9		0		0		0	
recovered **10**		91.6		14.2		0		0

[a] Absolute yields by GC.

SCHEME 1. Type I and Type II Ring Openings



SCHEME 2. 2-Pyridylnitrene from 1 and 10



Results and Discussion

Tetrazole **1T** and oxadiazolone **10** were subjected to FVT under identical conditions, and the products and yields were analyzed by GC-IR, GC-MS, and ^{1}H NMR spectroscopy. The results are presented in Table 1. The activation energy for decomposition of **10** is significantly higher than that for **1**. Thus, **1** starts to thermolyze already at 380 °C, while **10** is unreactive below 600 °C in our apparatus. Both compounds react completely in the 700−800 °C range. It is evident from Table 1 that the two precursors give the same products with very nearly the same yields. The only apparently abnormal result is the 18% yield of 2-aminopyridine **9** obtained from **10** at 600 °C, i.e., at the onset of thermolysis. However, also **1T** gives a relatively high yield of 15% of **9** at the onset of thermolysis, at 380 °C.[9a] The reason for this is uncertain, but it may be observed that it is at the onset of pyrolysis that the nascent nitrene has least excess energy available for rearrangement. Therefore, a higher proportion may undergo intersystem crossing to the triplet ground state, which undergoes H-abstraction. This is necessarily an intermolecular reaction, and it is therefore far more sensitive to pressure and concentrations than the other (unimolecular) reactions.

The formation of CO_2 as the byproduct of thermolysis of **10** was confirmed by IR spectroscopy when the products of FVT were isolated on a KBr target in a liquid nitrogen-cooled (ca. 77 K) cryostat. Under these conditions, tetrazole **1T** is seen to be completely converted to the azide **1A** already on sublimation at 40 °C and deposition of the material on the KBr target (see Figure S1 in the Supporting Information). The formation of 1,3-diazacyclohepta-1,2,4,6-tetraene **3** (1988−1989 (vs) cm^{-1}) is observed on FVT between 370 and 600 °C as previously reported.[6,12] The formation of cyanopyrroles **7** and **8** is observed above 400 °C, and these compounds begin to dominate above 550 °C. Relevant spectra are shown in the Supporting Information. This gives only a narrow window around ca. 550 °C where strong signals for **3** are observable in the IR spectra following FVT of **1**. Compound **10** barely reacts at this temperature; therefore, it is not surprising that only a weak band for **3** is observable at 1988 cm^{-1} in the product of FVT of **10** at 600 °C (Figure S8, Supporting Information). At higher FVT temperatures, nitrene **2** does not survive, as it is converted to products **6**−**9**.

Direct evidence for the formation of 2-pyridylnitrene **2** from both precursors was obtained by ESR spectroscopy of the products of FVT isolated in Ar matrices. Thus, FVT of **1T** at 500 °C produced an ESR spectrum of **2** in agreement with previously reported data[13] (D/hc = 1.049 cm^{-1}; $E/hc \leq$ 0.0016 cm^{-1}) (Figure 1b). The same signal was obtained on FVT of **10** at 570 °C (Figure 1a). The signal is much weaker in this case because **10** only just starts to react at this temperature (cf. Table 1), and at higher temperatures the nitrene is converted to products.

(12) The main absorption of **2** was previously reported as 1975 cm^{-1};[6] this was due to the use of an inferior dispersive IR spectrometer.

(13) Kuzaj, M.; Lüerssen, H.; Wentrup, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 480–482.

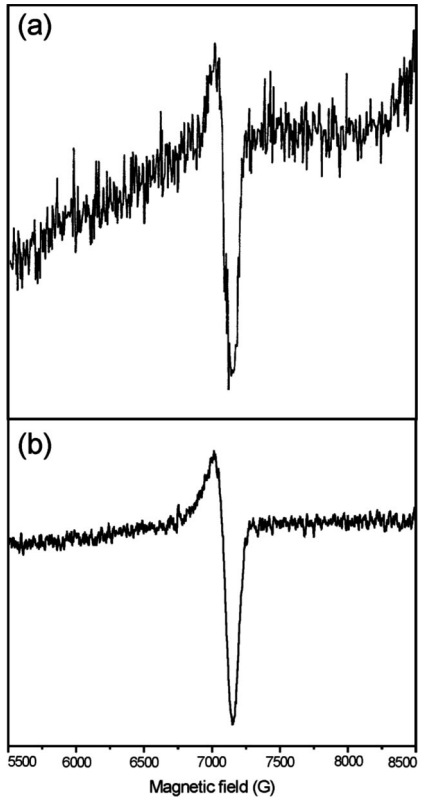


FIGURE 1. ESR spectra (Ar matrix, 20 K) of 2-pyridylnitrene **2** obtained by FVT of (a) [1,2,4]oxadiazolo[2,3-*a*]pyridin-2-one (**10**) at 570 °C, $D/hc = 1.049$ cm^{-1}, $E/hc = 0.0$ cm^{-1}, and (b) tetrazolo[1,5-*a*]pyridine (**1T**) at 500 °C, $D/hc = 1.049$ cm^{-1}, $E/hc \leq 0.0016$ cm^{-1}.

Conclusion

Tetrazolopyridine **1T** undergoes FVT via 2-azidopyridine **1A**. Pyridooxadiazolone **10** undergoes FVT by elimination of CO_2. In both cases, the formation of 2-pyridylnitrene **2** in its triplet ground state was detected by ESR spectroscopy. The isolable products of FVT are the *Z*- and *E*-glutacononitriles **6**, formed by type II ring opening, 2- and 3-cyanopyrroles **7** and **8**, and 2-aminopyridine **9**. The relative and absolute yields of the products are nearly identical from the two precursors, and it is concluded that both reactions proceed by the same mechanism, initiated by the formation of 2-pyridylnitrene **2**. There may be several reasons why different results were obtained by the two original groups,[5,9a,10] but the most likely explanation is different apparatus design and different experimental conditions, in particular the higher pressure used in ref 10.

Experimental Section

Preparative FVT experiments were carried out using a 20 × 2 cm^2 unfilled quartz tube, pumped continuously with the aid of an oil diffusion pump capable of an end vacuum of ca. 10^{-4} mbar. The operating vacuum was ca. 10^{-2} mbar. A sample of 100 mg of the starting material was used in each experiment. Products were trapped in a liquid N_2 trap. All experiments were carried out in duplicate. The data in Table 1 are averages of two runs. The deviation between runs was better than ±5%.

For 77 K IR spectroscopy, a 10 cm long, 1.2 cm i.d. electrically heated quartz tube suspended in a vacuum chamber (2.0×10^{-6} mbar) was directly flanged to a cryostat cold head, with a wall-free flight path of ca. 3 cm between the exit of the quartz tube and the KBr target.

For matrix isolation ESR spectroscopy of 2-pyridylnitrene **2**, the above-mentioned pyrolysis oven was flanged to the cold head of a closed-cycle liquid He cryostat. The FVT products were codeposited with Ar at 20−25 K on a Cu rod. **1T** was subjected to FVT at 490−510 °C and **10** at 570 °C.

ESR data for **2** generated from **1T**: $D = 1.049$ cm^{-1}, $E \leq 0.0016$ cm^{-1}, $H_0 = 3470.9$, $X_2 = 7090$ G, $Y_2 = 7164$ G, microwave frequency = 9.72717 GHz. Data for **2** generated from **10**: $D = 1.049$ cm^{-1}, $E = 0.0$ cm^{-1}, $H_0 = 3476.2$, $XY_2 = 7150$ G, microwave frequency = 9.7420 GHz.

Products of the preparative pyrolyses were identified by GC-IR, GC-MS, and NMR spectroscopy. Yields were determined by GC on a capillary column (50 m × 0.5 mm i.d., BP 10 stationary phase), He carrier gas, column head pressure 250 kPa, inlet temperature 200 °C. The temperature program started at 40 °C for 1 min, followed by a ramp of 15 deg/min up to 200 °C.

Retention times (min): 2-aminopyridine 7.4; glutacononitrile 7.9; 2-cyanopyrrole 9.6; 3-cyanopyrrole 12.3. The accuracy of the GC yields was checked by ^{1}H NMR spectroscopy of crude product mixtures. All experiments were performed in duplicate.

IR data: In the GC-IR, 2-cyanopyrrole appears at 2232 cm^{-1}; 3-cyanopyrrole appears at 2242. In the neat solid at 77 K 2- and 3-cyanopyrroles both appear at 2230 cm^{-1}. In Ar matrices at 10 K, glutacononitrile appears at 2275 and 2235 cm^{-1}, 2-cyanopyrrole at 2235 cm^{-1}, and 3-cyanopyrrole at 2260 cm^{-1}.

NMR data: *Z*-Glutacononitrile.[14] The *Z*:*E* ratio of glutacononitriles was close to 1:1 as determined by ^{1}H NMR spectroscopy. ^{1}H NMR ($CDCl_3$, 500 MHz) of *Z*-glutacononitrile: δ 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). ^{13}C NMR ($CDCl_3$) (mixture of *Z* and *E* isomers): δ 141.1, 140.7, 115.4, 114.2, 105.4, 104.9, 21.2, 19.6.

***E*-Glutacononitrile.**[14] The *Z*:*E* ratio of glutacononitriles was close to 1:1 as determined by ^{1}H NMR spectroscopy. ^{1}H NMR ($CDCl_3$, 500 MHz) of *E*-glutacononitrile: δ 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). ^{13}C NMR ($CDCl_3$): see data forthe mixture under *Z*-glutacononitrile.

2-Cyanopyrrole.[15] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.37 (br, 1H), 6.94 (m, 1H, apparent 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). ^{13}C NMR ($CDCl_3$) δ 123.9, 120.1, 114.8, 109.8, 100.1.

3-Cyanopyrrole.[16] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.96 (br, 1H), 7.30 (m, 1H, apparent J = 3.3 and 1.9 Hz), 6.78 (m, 1H, apparent J = 2.7, 2.1, and 0.7 Hz), 6.47 (m, 1H, apparent J = 2.6 and 1.3 Hz).

Acknowledgment. This research was supported by the Australian Research Council.

Supporting Information Available: IR spectra of the thermolyzates from **1**, collected at 77 K, resulting from FVT at 340−650 °C and IR spectrum of the thermolyzate from **10** at 600 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800899T

(14) Boate, D. R.; Hunter, D. H. *Org. Magn. Reson.* **1984**, *22*, 167–170.
(15) Anderson, H. J. *Can. J. Chem.* **1959**, *37*, 1959.
(16) den Hertog, H. J.; Martan, R. J.; van der Plas, H. C.; Bon, J. *Tetrahedron Lett.* **1966**, 4325–4328.