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9-Azidoacridine and 9-acridinylnitrene

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Matrix photolysis as well as flash vacuum thermolysis (FVT) of 9-azidoacridine affords 9-acridinylnitrene, which is characterized by its IR and ESR spectra and is photochemically inert. FVT above 600 °C yields a mixture of the five isomeric cyanocarbazoles. Microwave-assisted reaction with diethyl- and dipropylamines in solution affords acridinylformamidine and acridinylpropionamidine, respectively. Microwave-assisted reaction with dimethylamine causes nucleophilic displacement of the azido group. Microwave-assisted 1,3-dipolar cycloaddition with phenylacetylene yields the two regioisomeric 9-(4- and 5-phenyl-1,2,3-triazol-1-yl)acridines, whose structures were established by X-ray crystallography. Copyright © 2010 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this paper.

Keywords: azides; FVT; nitrenes; matrix isolation; photolysis

INTRODUCTION

The ring expansion of 2-pyridylnitrenes **1** to 1,3-diazacycloheptatetraenes **2** is a very convenient way of preparing 1,3-diazepines **3** by photolysis of 2-azidopyridines/tetrazolo[1,5-*a*]pyridines in solution.[1–3] The intermediates **2** are stable in low temperature matrices and absorb strongly in the infrared at 1980–2000 cm^{-1}. 4-Quinolylnitrene **4** undergoes a similar ring expansion to a benzo-1,4-diazacycloheptatetraene **6** (1902 and 1904 cm^{-1} in Ar matrix), even though this has to take place via a strained transition state **5**.[4] 1-Isoquinolylnitrene undergoes analogous ring expansion to a benzo-1,3-diazocycloheptatetraene, which again must involve a strained transition state.[5] Flash vacuum thermolysis (FVT) of 9-Azidophenanthridine/tetrazolo[1,5-*d*]phenanthridine **7A/7T** produces the relatively stable and long-lived dibenzodiazacycloheptatetraene **9**, presumably via 9-phenanthridylnitrene **8**.[6] Compound **9** absorbs at 2010 cm^{-1} in the IR and dimerizes to the diiminodiazete **10**, a typical carbodiimide dimer, at −40 °C.[6] 9-Phenanthrylnitrene **11** as well as 6-phenanthridylcarbene undergo thermal ring expansion to the dibenzoazacycloheptatetraene **12** on FVT, but an isomeric zwitterionic cumulene **13** is formed on matrix photolysis (Scheme 1).[7] 1- and 2-Naphthylnitrenes undergo photochemical ring expansion to both conventional ketenimines and zwitterionic cumulenes on matrix photolysis.[8] In contrast, 9-anthracenylnitrene does not undergo such ring expansion.[9]

We have now investigated 9-azidoacridine **14** (Scheme 2) and find that the derived nitrene **15** is very stable and does not rearrange on matrix photolysis. However, it does undergo ring contraction to cyanocarbazoles on FVT.

EXPERIMENTAL

The apparatus and procedures for preparative FVT[10] and for Ar matrix isolation[11,12] were as previously described. KBr or CsI windows were used for IR spectroscopy, quartz for UV, and a Cu rod (7 cm long, 1.5 mm i.d.) for ESR spectroscopy. IR spectra are shown in Figs 1 and S1–S4, ESR spectra in Figs 2 and S5, and a UV spectrum in Fig. S7. FVT products were isolated in liquid nitrogen (77 K) in the preparative thermolyses, at 7–22 K with Ar for matrix isolation IR experiments, and at 15–20 K with Ar for ESR experiments. Photolysis experiments used a 1000 W high pressure Xe/Hg lamp equipped with a monochromator and appropriate filters, a 75 W low pressure Hg lamp (254 nm), and excimer lamps operating at 222 nm (25 mW cm^{-2}) and 308 nm (50 mW cm^{-2}). IR spectra were recorded with a resolution of 1 cm^{-1}. ESR spectra were recorded on a Bruker ER200D X-band spectrometer. GC for GCMS analysis was performed on a Shimadzu QP5050A GCMS instrument, injector 200 °C; temperature program: 100 °C (2 min), then 16 °C per min till 250 °C on a Zebron capillary column ZB-5 (0.25 μm thickness, 0.32 mm diameter, 30 m length). A CEM Labmate microwave reactor was used for the MW-assisted syntheses; temperatures were measured externally by infrared fibre optics. Melting points are uncorrected.

Syntheses

9-Chloroacridine

Caution: the procedures should be carried out in an efficient hood, and exposure to $POCl_3$ should be avoided.

N-Phenylanthranilic acid (213 mg, 1 mmol) was suspended in phosphorus oxychloride (0.5 ml, 5 mmol) and heated in the microwave reactor at 100 °C for 1.5 min. The mixture was poured onto ice and neutralized dropwise to pH 7 at 0 °C with cold 2M

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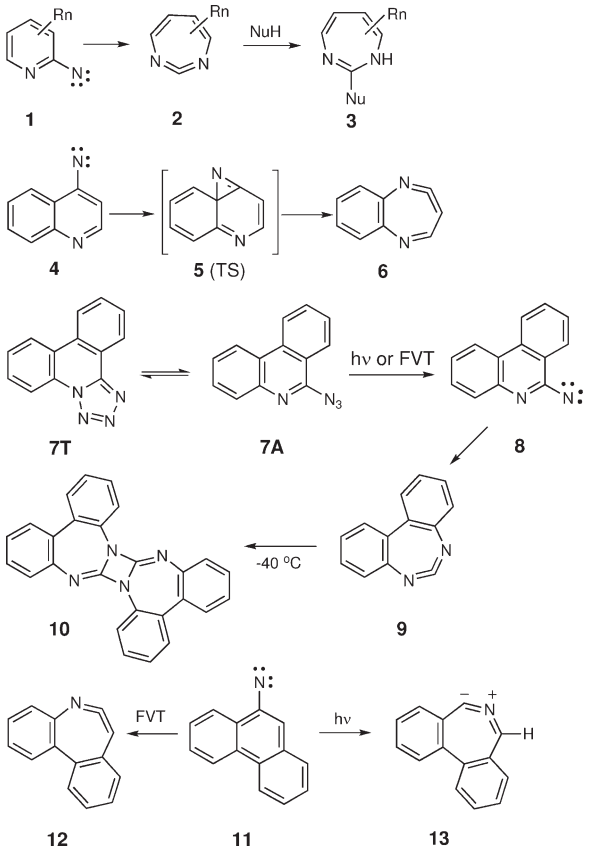
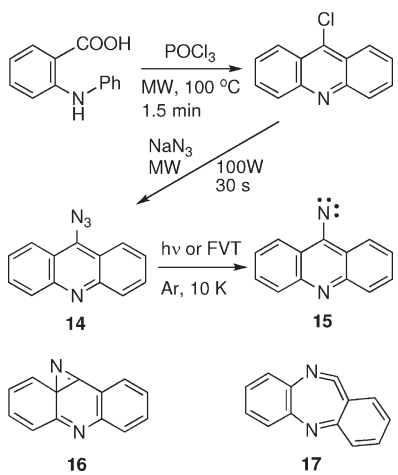


Scheme 1. Nitrene ring expansions

NaOH (6.5 ml). The white precipitate obtained was filtered, dried by suction, and sublimed at 60 °C (10^{-5} mbar). Yield 209 mg (98%), mp 117–119 °C (Lit.[13] 117–118 °C; lit.[14] 117–119 °C). IR (KBr cm^{-1}) 3043, 1628, 1590, 1447, 1404, 1261, 1080, 1019, 804, 757. ^{1}H-NMR δ (ppm) 8.43 (d, 1H, $J = 8.7$ Hz), 8.22 (d, 1H, $J = 8.7$ Hz), 7.81 (dd, 1H, $J = 7.3$ Hz), 7.63 (dd, 1H, $J = 7.3$ Hz). GCMS: t_R 11.1 min, *m/z* 215 (26.5), 213 (100), 178 (20.5%). Anal. Calcd for C_{13} H_8 N Cl: C, 73.08; H, 3.77; N, 6.56. Found: C, 73.26; H, 3.57; N, 6.58.



Scheme 2. 9-Azidoacridine and 9-acridinylnitrene

9-Azidoacridine

Caution: Azides are potentially explosive, and appropriate safety precautions should be taken. 9-Azidoacridine is extremely sensitive to visible light. The yellow compound turns brown in the course of several minutes in daylight at room temperature, with formation of 9,9′-azoacridine[15] and 9-aminoacridine as major products. The synthesis, chromatography, and other workup procedures should be carried out in the absence of light.

To a solution of 9-chloroacridine (25 mg; 0.117 mmol) in 7.5 ml of acetone in a Teflon vessel was added a solution of NaN_3 (25 mg; 0.385 mmol) in 2 ml of distilled water. The vessel was closed and irradiated in a microwave oven at 100 W for 30 s. After cooling to room temperature and concentrating the solution *in vacuo*, 9-azidoacridine was obtained as a yellow solid, which was filtered with suction and washed with 5 ml of water to afford 19.7 mg (76%) of crude product, which can be purified by vacuum sublimation at 55–60 °C (5×10^{-5} mbar) or by flash chromatography on silica gel, eluting with hexane-ethyl acetate 2:1 to yield 17.6 mg (68%), mp 83–85°C (lit.[15] 85–87 °C). IR (KBr) 2114 (asym. N_3), 1594, 1401, 1352 (sym. N_3), 1286, 1260, 1141, 747 cm^{-1}. UV (CCl_4) λ_{max}/nm (ε) 260 (17,500), 266 (25 000), 273 (11 000), 345 (5500), 362 (9000), 393 (5800). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.11 (d, $^3J = 8.8$ Hz, $J = 1.5$ Hz, 2H, H-4/5), 7.99 (d, $^3J = 8.8$ Hz, $J = 1.5$ Hz, 2H, H-1/8), 7.58 (dd, $^3J = 8.8$ Hz, $J = 1.5$ Hz, 2H, H-3/6), 7.36 (dd, $^3J = 8.8$ Hz, $J = 1.5$ Hz, 2H, H-2/7). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 148.1 (C-4a/10a), 140.8 (C-9), 130.4 (C-4), 128.9 (C-3), 125.7 (C-2), 121.7 (C-1), 119.5 (C-8a/9a). MS (ESI) *m/z* 221 (100%) $[M+H]^+$. Anal. Calcd for C_{13} H_8 N_4: C, 70.90; H, 3.66; N, 25.44. Found: C, 70.14; H, 3.68; N, 25.07.

Matrix isolation

9-Azidoacridine **14** was sublimed at 55–60 °C (10^{-6} mbar) with protection from daylight and deposited with Ar on a KBr window at 20 K in the course of 40 min. IR (Ar, 20 K cm^{-1}) 2258 w, 2124 vs, 1623 m, 1556 s, 1522 s, 1484 s, 1439 w, 1410 vs, 1396 w, 1374 s, 1358 s, 1290 m, 1258 m, 1242 m, 1146 w, 1002 w, 938 w, 847 vw, 761 s, 751 s, 643 m, 613 w.

Irradiation of the sample at 308 nm caused an immediate decrease in the intensities of the azide bands and concomitant development of new bands ascribed to 9-acridinylnitrene **15** (Fig. 1). IR (Ar, 12 K cm^{-1}) 1526 w, 1321 s, 1250 m, 1198 m, 1135 m, 763 vs, 615 m, 609 m, 428 w. The nitrene spectrum remained unchanged upon further irradiation at 308 nm for 17 h.

The same nitrene IR spectrum was also obtained on irradiation of the azide at 222 nm. No rearrangement products (azirene or diazacycloheptatetraene) were detected on further irradiation at 222 nm for 8 h. The nitrene was also stable to irradiation at $\lambda > 410$, 470, 500–505 660, and 740 nm. Additional matrix IR spectra obtained under different conditions of photolysis are shown in Figs. S1 and S2.

The nitrene IR spectrum was also obtained by FVT of the azide at 400 °C with co-deposition of the product with Ar at 20 K (Fig. 1). The nitrene was still observable in the matrix IR spectra resulting from FVT up to 600 °C, but at higher temperatures 9,9′-azoacridine and a mixture of cyanocarbazoles (see below) was obtained (Figs S3 and S4). It is known that FVT of phenyl azide affords a high yield of azobenzene.[16]

The nitrene UV spectrum obtained by the photolysis of azide **14** (308 nm, 1 min, Ar, 20 K) is shown in Fig. S7 and features a broad maximum near 500 nm with pronounced vibrational fine structure.

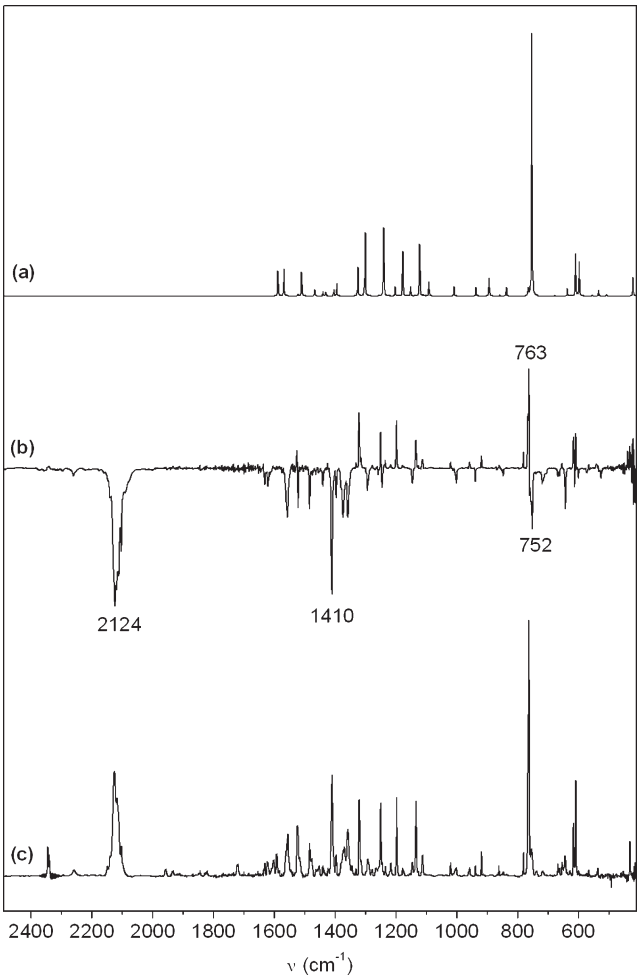


Figure 1. IR spectra of (a) triplet 9-acridinylnitrene **15**, calculated at the B3LYP/6-31+G** level; frequencies scaled by 0.9613. (b) Difference spectrum from the photolysis of an Ar matrix of 9-azidoacridine **14** at 308 nm (20 K; 6 min). Positive peaks assigned to triplet **15**, negative peaks to **14**. (c) FVT of **14** at 400 °C (7×10^{-6} mbar) with co-deposition of the product with Ar at 20 K, showing a mixture of **14** and **15**

The ESR spectrum of 9-acridinylnitrene **15** was obtained by depositing the azide with Ar at 15 K and photolysing at 308 nm for 30 s (Fig. 2). $H_o = 3471.4$ G, microwave frequency = 9.72857 GHz, $X_2 = 5550$, $Y_2 = 5647$ G. $|D| = 0.5196\ cm^{-1}$, $|E| = 0.0023\ cm^{-1}$. Calculated nitrene spin density $\rho = 1.28946$ (UB3LYP/EPR-III). The correlation between nitrene $|D|$ values and the calculated spin densities ρ on the nitrene N is shown for several nitrenes in Fig. S6. The same ESR spectrum of **15** was also obtained on the photolysis of the azide at 222 nm or by using a high-pressure Hg lamp equipped with a water filter and various visible light filters.

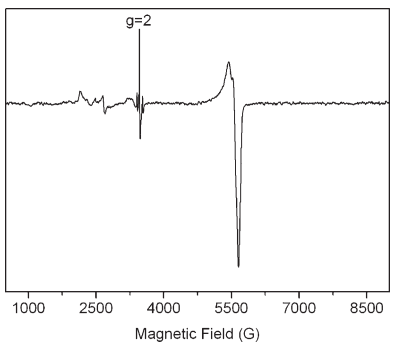


Figure 2. ESR spectrum obtained by the photolysis of an Ar matrix of 9-azidoacridine **14** at 308 nm (15 K; 30 s). $X_2 = 5550$, $Y_2 = 5647$ G. The $g = 2$ signal is due to adventitious monoradicals. Some signals in the 2000–3000 G region may be due to Z_1 and diradical transitions

Warm-up to room temperature and GCMS analysis of the material remaining on the cold window after 2.5 h photolysis at 308 nm revealed 9-aminoacridine as the major product ($t_R = 15.0$ min, $m/z = 194$).

The ESR spectrum of nitrene **15** was also obtained by FVT of the azide (Fig. S5).

Flash vacuum thermolysis

9-Azidoacridine **14** was subjected to FVT at 520 °C in a stream of Ar, and the product was isolated as an Ar matrix at 15 K. A strong ESR signal of the nitrene **15** was obtained (Fig. S5), identical with that generated by photolysis (*vide supra*, Fig. 2). The IR spectrum also demonstrated the presence of the nitrene, identical with that generated by photolysis (*vide supra*, Fig. 1), and, in addition, several nitrile group absorptions were present in the 2220–2240 cm^{-1} range.

9-Azidoacridine **14** was subjected to preparative FVT at 600 °C (10^{-3} mbar). The product was collected on a liq. N_2-cooled coldfinger and dissolved in $CHCl_3$ after the end of the thermolysis. GCMS analysis revealed five major products ($t_R = 10.2$–13.04 min), all with a mass of 192, corresponding to the mass of the nitrene and assigned to the five isomeric 9-, 1-, 2-, 4-, and 3-cyanocarbazoles, eluting in that order. Two additional, very minor peaks ($t_R = 11.2$ and 12.6 min) also had a mass of 192 and may be due to different cyanocarbazole tautomers or other isomeric compounds. A very weak peak indicated the presence of 9-aminoacridine ($t_R = 13.8$ min, $m/z = 194$).

The five cyanocarbazoles were identified by spiking with authentic samples. Reference samples of 4- and 9-cyanocarbazoles were obtained by FVT of tetrazolophenanthridine **7T** as described previously.[17] Reference samples of 1-cyanocarbazole,[18] 2-cyanocarbazole,[19,20] and 3-cyanocarbazole[21] were prepared according to literature procedures.

Reactions in solution

N′-Acridin-9-yl-N,N-diethylformamidine ***25a***

9-Azidoacridine **14** (2 mg; 0.009 mmol) was dissolved in 2 ml of diethylamine in a thick-walled Pyrex tube, which was closed and irradiated in the microwave reactor at 200 W (55 °C) for 10 min. After cooling and evaporating the excess amine, the material was taken up in $CHCl_3$ and purified by filtration through a short column of silica gel to yield 1.5 mg (60%) of product, mp 120–124 °C (decomp.), which was pure according to GCMS ($t_R = 18.2$ min, $m/z = 277$) and strongly fluorescent in solution. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.00 (d, 2H, $J = 8.7$ Hz), 7.89 (d, 2H, $J = 8.7$ Hz), 7.72 (s, 1 H), 7.65 (apparent t, 2H, $J = 6.6$ Hz), 7.36 (apparent t, 2H, $J = 6.6$ Hz), 3.70 (q, 4H, $J = 7.1$ Hz), 1.35 (t, 3H, $J = 7.1$ Hz), 1.23 (t, 3H, $J = 7.1$ Hz). ^{13}C NMR (DMSO-d_6) δ (ppm) 154.3, 130.4, 139.0, 128.4, 125.8, 125.1, 123.8, 120.0, 56.2, 45.3, 18.8, 15.2.

N′-Acridin-9-yl-N,N-dipropylpropionamidine **25b**

This compound was prepared by the method described above using dipropylamine (200 W, 84 °C, 10 min). A brightly fluorescent

yellow product was obtained (1.8 mg; 60%), which was pure according to GC-MS ($t_R = 22.0$ min, $m/z = 333$). ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.72 (d, 2H, $J = 8.6$ Hz), 7.86 (apparent t, 2H), 7.84 (d, 2H, $J = 8.0$ Hz), 7.45 (apparent t, 2H, $J = 8.7$ Hz), 3.60 (t, 2H, $J = 8.1$ Hz), 3.46 (t, 2H, $J = 8.2$ Hz), 2.31 (q, 2H, $J = 7.5$ Hz), 1.83 (sextuplet, 4H, $J \sim 7.5$ Hz), 1.07 (t, 3H, $J = 7.5$ Hz), 0.99 (t, 3H, $J \sim 7.5$ Hz), 0.92 (t, 3H, $J = 7.5$ Hz).

9-Dimethylaminoacridine

9-Azidoacridine **14** (5 mg; 0.023 mmol) was dissolved in 3 ml of dioxane, and 4 ml of dimethylamine (40% aq. solution) was added. The mixture was irradiated in a closed, thick-walled Pyrex tube in the MW reactor at 200 W (100 °C) for 5 min. After cooling and evaporating the excess amine and solvent, the material was taken up in 5 ml of CH_2Cl_2, and 5 ml of water was added. The organic layer was separated, dried over $CaCl_2$, filtered and concentrated to yield 4 mg (79%) of product, mp 236–237 °C (lit.[22] 240 °C), which was pure according to GC-MS ($t_R = 14.9$ min, $m/z = 222$). ^{1}H NMR ($CDCl_3$) δ (ppm) 8.75 (d, 2H, $J = 8.6$ Hz), 8.23 (d, 2H, $J = 8.7$ Hz), 7.81 (apparent t, 2H, $J = 8.3$ Hz), 7.48 (apparent t, 2H, $J = 8.6$ Hz), 3.77 (s, 6H).

9-(4-Phenyl-1,2,3-triazole-1-yl)acridine **25** and 9-(5-Phenyl-1,2,3-triazole-1-yl)acridine **26**

In a dried 10 ml heavy-walled Pyrex tube, 89 mg (0.87 mmol) of phenylacethylene was added to 5 mg (0.022 mmol) of 9-azidoacridine **14**. The tube was sealed and irradiated in the microwave oven for 15 min at 60 W (100°C). After cooling, excess phenylacetylene was evaporated *in vacuo*. CH_2Cl_2 (2 ml) was added, and the resulting solution was evaporated to yield a yellow powder (5.3 mg; 71%). The regioisomeric triazoles **26** and **27** were separated by chromatography on alumina 90 (Merck, active, neutral (0.063–2.00 mm, 70–230 mesh) eluting with hexane-ethyl acetate 1:1. Crystals of the two triazoles were obtained by allowing diethyl ether to diffuse into solutions in $CHCl_3$.

4-Phenyl isomer **26**: yellow-brown crystals, mp 248–250 °C (lit.[23] 249–250 °C, but assigned to the 1,5-isomer; lit.[24] 281-282 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.44 (broad s at 298 K, resolving into d at 288 K, 2H, $J = 8$ Hz), 8.26 (s, 1H), 8.01 (d, 2H, $J = 8.4$ Hz), 7.90 (t, 2H, $J = 8$ Hz), 7.61 (m, 3H), 7.52 (t, 2H, $J = 7.2$ Hz), 7.43 (t, 1H, $J = 7.5$ Hz).

5-Phenyl isomer **27**: yellow crystals, mp 238–240 °C (lit.[23] 239 °C, but assigned to the 1,4-isomer; lit.[24] 239–241 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.43 (broad s at 298 K, resolving into d at 288 K, 2H, $J = 8$ Hz), 8.18 (s, 1H), 7.85 (t, 2H, $J = 8.1$Hz), 7.55 (t, 2H, $J = 8.1$ Hz), 7.42 (d, 2 H, $J = 8.8$ Hz), 7.15 (t, 1H, $J = 7.0$ Hz), 7.06 (t, 2H, $J = 7.7$ Hz), 6.98 (m, 2H).

The two triazoles are converted to the corresponding pyridoacridines on further heating.[23] This reaction, too, is conveniently carried out by microwave irradiation (100 °C, 60 W, 60–90 min) in toluene solution.

Crystallography

Crystallographic data were collected at 293 K on an Oxford Diffraction Gemini Ultra S CCD diffractometer employing Mo-K_α radiation and operating in the ω-scan mode. Data reduction and empirical absorption corrections were carried out with the CrysAlisPro program (Oxford Diffraction, version 171.33.34d). Structures were solved by direct methods with SHELXS-86 and refined by full matrix least squares analysis with SHELXL-97.[25] The thermal ellipsoid diagrams were produced with ORTEP3[26] and all programs were run within the WinGX package.[27] Packing diagrams were produced with the program Mercury (version 2.2).[28] Crystal data are presented in Table 1. Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre (CCDC 748456 and 748457). Copies of this information may be obtained from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Computational methods

The energies and IR spectra of the relevant molecules and transition structures were calculated at the (U)B3LYP/6-31+G** level using the Gaussian 03 suite of programs.[29] Energies were corrected for zero-point vibrational energies (ZPE), and all wavenumbers were scaled by a factor of 0.9613.[30] The energy of

Table 1. Crystal data for isomeric triazolylacridines **26** and **27**

Compound	4-Phenyl isomer **26**	5-Phenyl isomer **27**
Empirical formula	$C_{21}H_{14}N_4$	$C_{21}H_{14}N_4$
Formula weight	322.36	322.36
Temperature (K)	293(2)	293(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Triclinic	Triclinic
Space group	$P\,\bar{1}$	$P\,\bar{1}$
a (Å)	8.8707(8)	9.1244(8)
b (Å)	9.4278(9)	9.4017(8)
c (Å)	10.772(1)	9.8498(8)
a°	95.641(8)	96.959(7)
b°	90.124(8)	97.383(7)
g°	117.273(9)	104.635(7)
Volume (Å^3)	795.7(1)	800.3(1)
Z	2	2
r (calcd, g cm^{-3})	1.345	1.338
m (mm^{-1})	0.083	0.082
F(000)	336	336
Crystal size (mm)	0.4 × 0.1 × 0.05	0.5 × 0.5 × 0.1
q range °	3.13–25.00	3.34–25.00
Index ranges	$-10 \le h \le 10$	$-10 \le h \le 9$
	$-11 \le k \le 11$	$-11 \le k \le 11$
	$-8 \le l \le 12$	$-11 \le l \le 11$
Reflections collected	5202	5194
Independent reflections	2798	2805
	($R_{int} = 0.0383$)	($R_{int} = 0.0286$)
Completeness to $q = 25.00°$	99.6%	99.8%
Data/restraints/parameters	2798/0/226	2805/0/227
Goodness-of-fit on *F*2	0.676	0.804
R indices [*I*>2s(*I*)]	$R_1 = 0.0385$	$R_1 = 0.0378$
	$wR_2 = 0.0564$	$wR_2 = 0.0684$
R indices (all data)	$R_1 = 0.1297$	$R_1 = 0.0755$
	$wR_2 = 0.0664$	$wR_2 = 0.0751$
Max./min. res. (e A^{-3})	0.095/−0.131	0.145/−0.144

the open shell singlet nitrene was estimated using the Ziegler-Cramer sum method.[31] The UV spectrum was calculated at the TD-B3LYP/6-31+G** level (Fig. S7). Natural spin densities of nitrene N-atoms were calculated using UB3LYP/EPR-III implemented in Gaussian 03.[32] Zero-field splitting parameters *D* and *E* (cm^{-1}) were calculated from experimental ESR spectra using Wasserman's equations.[33]

RESULTS AND DISCUSSION

9-Azidoacridine **14** has been prepared by diazotization of 9-hydrazinoacridine and by the treatment of 9-chloroacridine with sodium azide in refluxing aqueous acetone.[15] We found that 9-azidoacridine was prepared conveniently and rapidly by microwave-assisted reaction of 9-chloroacridine with sodium azide. 9-Chloroacridine was itself obtained rapidly in a fast, microwave-assisted reaction of *N*-phenylanthranilic acid, phosphorus oxychloride, and sulfuric acid.

Photolysis of 9-azidoacridine in low temperature Ar matrices caused rapid decrease of the IR bands due to the azide **14** with concomitant development of new bands assigned to the triplet nitrene **15**, whose observed and calculated IR spectra are in excellent agreement (Fig. 1). This took place by using a variety of wavelengths from 222 nm into the visible region, and the nitrene was inert to further photochemical reaction under these conditions. Additional IR spectra obtained under different photolysis conditions are shown in Figs S1 and S2.

It is most likely that it is the triplet state of the nitrene **15** that is being observed in the IR spectrum, because similar photolysis in a cryostat for ESR spectroscopy caused rapid appearance of signals assigned to the triplet nitrene (Fig. 2). The zero-field splitting parameter $|D|$ for the nitrene, 0.5196 cm^{-1}, is close to the value for 9-anthracenylnitrene (0.47 cm^{-1}).[34] The nitrene $|D|$ values show an excellent correlation[35] with the calculated spin densities on the nitrene–nitrogen (see Supporting Information, Fig. S6).

Calculations at the UB3LYP/6-31+G** level indicate the triplet nitrene ($^3A_2$ lies 7.8 kcal/mol below the open-shell singlet ($^1A_2$) (Fig. 3). Here, the Ziegler–Cramer method[25] was used to estimate the energy of the $^1A_2$ state. It is known that this method overestimates the singlet-triplet gap by about 1.9 kcal/mol.[9] The calculated energy data in Fig. 3 indicate that ring closure to an azirene **16** and ring expansion to a diazacycloheptatetraene **17** are feasible processes with an activation barrier of *ca*. 23 kcal/mol. The azirene exists in a very shallow minimum and would be difficult to detect, but the diazacycloheptatetraene should be a potentially observable compound. A very weak peak is observed in some IR spectra at 1720 cm^{-1} (e.g. Fig. 1c), but this is under FVT conditions. We do not expect azirene **16** to survive the FVT experiment. The 1720 cm^{-1} peak is never observed as a photolysis product. A strong absorption (475 km/mol) is calculated for **17** at 1863 cm^{-1} at the B3LYP/6-31+G** level (see Supporting Information). The failure of the nitrene to undergo rearrangement may be due to the fact that acridines are generally strongly fluorescent compounds;[22] hence, it may be that the aromatic π system absorbs and emits all the light. A similar lack of reactivity was observed for 9-anthracenylnitrene.[9]

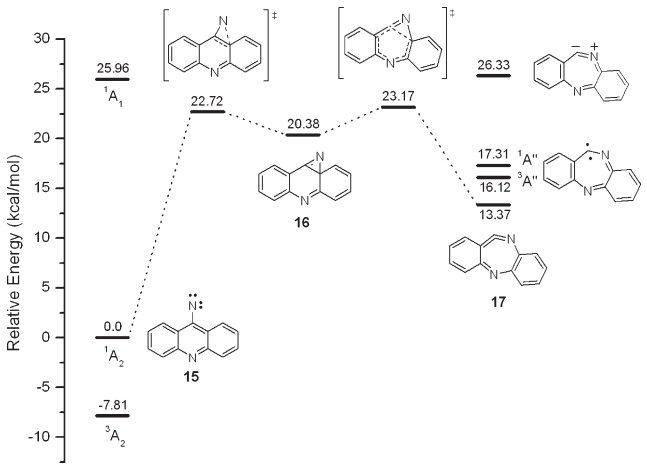
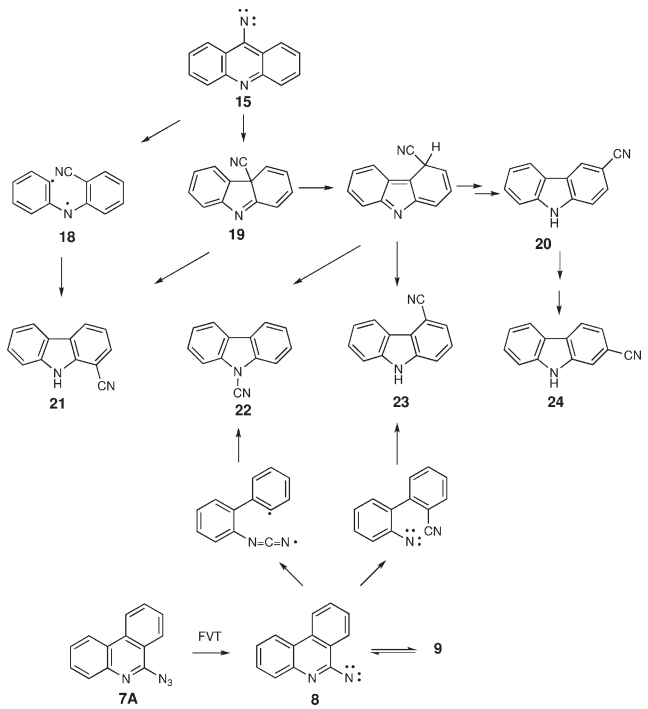


Figure 3. Calculated energy surface at the B3LYP/6-31+G** level including zero-point vibrational energy corrections

Flash vacuum thermolysis

The nitrene **15** was also obtained by FVT of 9-azidoacridine at 400–600 °C and identified by its ESR and IR spectra of the Ar matrix-isolated products, which were identical with the spectra obtained by photolysis. Only minute bands were present in the 1800–2000 cm^{-1} range, where cyclic ketenimines such as **17** are expected to absorb (Figs 1 and S3 and S4).[4,7] However, at FVT temperatures above 600 °C, a series of bands in the range of 2220–2240 cm^{-1} in the IR spectra indicated the additional presence of nitriles. It is well known that phenylnitrene ring contracts to cyanocyclopentadiene on FVT.[36,37] 2-Pyridylnitrenes afford cyanopyrroles.[38] 9-Phenanthrylnitrene **8** affords 9- and 4-cyanofluorenes **22** and **23** (Scheme 3).[7] 9-Phenanthridylnitrene affords 4- and 9-cyanocarbazoles.[6,16–17] 9,9′-Azoacridine was also formed above 600 °C (Figs S3 and S4) by gas phase dimerization of the (triplet) nitrene. This is analogous to the



Scheme 3. Ring contraction in 9-acridinylnitrene **15**. Not all possible *XH*-cyanocarbazole intermediates are shown

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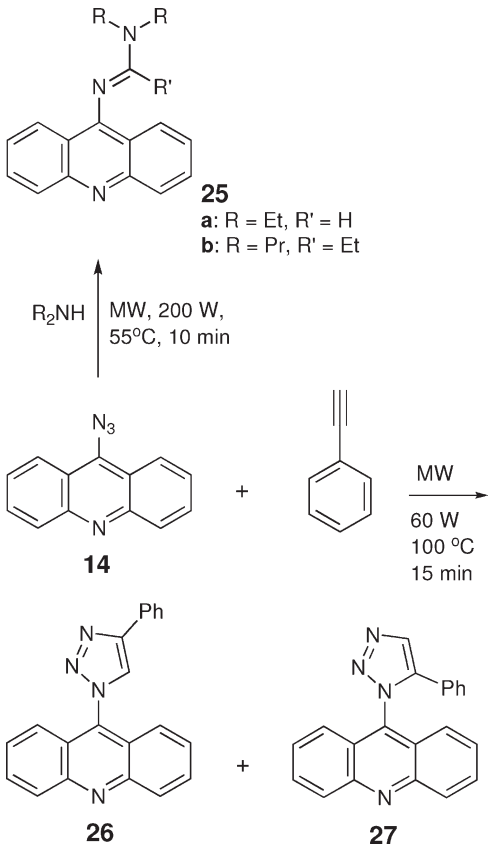
known dimerization of phenylnitrene to azobenzene on FVT.[16,36,37]

Ring contraction of 9-acridinylnitrene **15** to cyanocarbazoles was verified by preparative FVT at 600 °C. All five isomeric carbazoles **20**–**24** (Scheme 3) were formed. The initial ring contraction would generate the ring-opened diradical or carbene **18**, or 4a*H*-carbazole **19**, which by ring closure and sequential sigmatropic shifts of CN and H can isomerize to all the isomeric cyanocarbazoles (Scheme 3). It is known that 2- and 3-cyanoindenes not only interconvert but also isomerize to all the isomeric cyanoindenes on high temperature FVT.[39] It is possible that two minor peaks with *m/z* 192 observed in the GCMS of the FVT product are due to trace amounts of **19** and/or isomeric X*H*-cyanocarbazoles ($X = 1$, 2, 3, or 4) or other isomeric compounds.

Reactions in solution

Photolysis of 9-azidoacridine **14** in dialkylamine solutions in dioxane did not lead to the desired dialkylamino-dibenzo-1,4-diazepine derivatives under conditions that are successful in the pyridine series.[1,2] Instead, 9-diethylaminoacridine was a major product of the photolysis in the presence of diethylamine. In contrast, the azide underwent an efficient thermal reaction with diethyl- and dipropylamines to form amidines **25** (Scheme 4). This reaction was accomplished in minutes by microwave irradiation. The mechanism is complex and believed to involve dehydrogenation of dialkylamines to vinylamines, followed by 1,3-dipolar cycloaddition of the azide and cleavage of the resulting triazoline.[40] Other examples have been published, and the reaction only takes places with electronegatively substituted aryl and heteroaryl azides.[41–43] Electron transfer to form azide radical anion/amine radical cation pairs may be involved.[44]

It is also known that electronegatively substituted aromatic compounds undergo S_NAr reactions readily, via radical anion/radical cation pairs and/or Meisenheimer complexes. Nucleophilic substitutions of the azido group in 9-azidoacridine hydrochloride have been reported.[15] We found that the azido group in **14** is readily displaced by dimethylamine and methanol under microwave irradiation, to form 9-dimethylamino- and 9-methoxyacridines, respectively.



Scheme 4. Reactions in solution

Another consequence of electronegative substitution of aryl azides is that the usual Cu(I) catalysed 'click reaction'[45–47] with acetylenes is inefficient or does not take place at all. Reduction to amines may occur instead.[48] We did not obtain any triazoles in the click reaction between 9-azidoacridine and phenylacetylene with the habitual $CuSO_4$/sodium ascorbate catalyst or with Cu on charcoal.[49] Small amounts of the 1,4-isomer **26** were obtained using Cu wire or Cu powder. It is likely that the yield can be

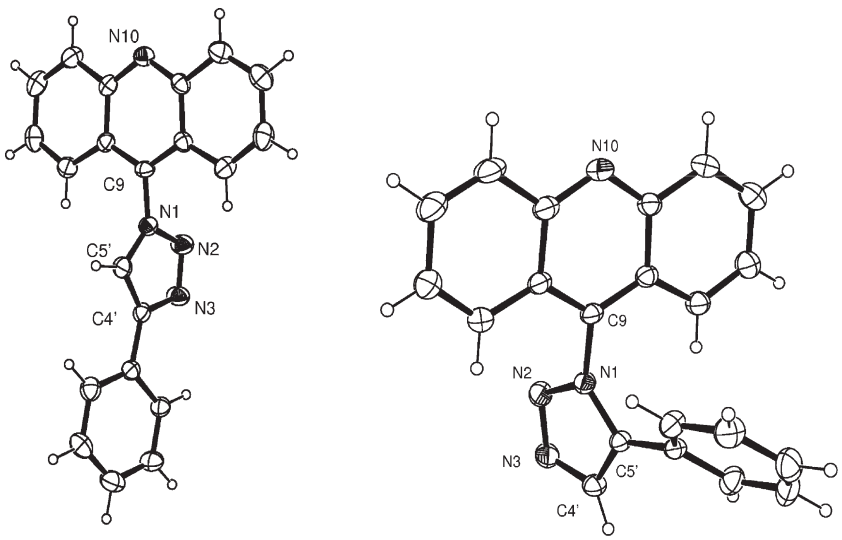


Figure 4. ORTEP plots (30% probability ellipsoids) of (left) 9-(4-phenyl-1,2,3-triazol-1-yl)acridine **26** and (right) 9-(5-phenyl-1,2,3-triazol-1-yl)acridine **27**

improved by using a new variant of the click reaction using Cu nanoparticles in the presence of amine hydrochlorides.[50] However, the cycloaddition takes place under the conventional, thermal Huisgen conditions, i.e in boiling toluene for 24–48 h and affords a mixture of the two regioisomeric addition products **26** and **27**,[23] but there is a controversy in the literature concerning the assignment of NMR spectra to the two isomers.[23,24] We have examined this cycloaddition under microwave conditions and find that neither of the previous assignments of ^{1}H NMR spectra was correct. In other words, it was still not known which isomer is which. In order to resolve the issue, we have obtained X-ray crystal structures of the two isomers (Fig. 4, Scheme 4) as well as 400 MHz ^{1}H NMR spectra. This has permitted a definitive assignment of spectra and melting points to the structures.

The bond lengths and angles of the two isomers are not significantly different. The main structural differences are found in their inter-ring torsional angles. In the 1,4-isomer **26**, the acridine and triazole rings are twisted by ~72° relative to each other while the phenyl and triazole rings are close to coplanar (~6° twist angle). In the 1,5-isomer, the acridine/triazole interplanar twist angle is again marked (~63°), but in this isomer the phenyl/triazole rings must also twist significantly (~45°) to avoid clashing between the phenyl and acridine rings. In both structures, the space group symmetry dictates that all acridine rings are parallel and intermolecular stacking is a feature of their structures (see Supporting Information).

Thermal elimination of N_2 from acridinyltriazoles causes cyclization to pyridoacridines with anti-tumour properties, as reported by Stevens and colleagues.[23] This reaction, too, can be carried out conveniently by using MW irradiation.

CONCLUSION

Photolysis of matrix-isolated 9-azidoacridine **14** affords 9-acridinylnitrene **15**, which is characterized by its IR and ESR spectra. The nitrene can also be generated and matrix-isolated by FVT of **14**. The nitrene is long-lived and photochemically stable in low temperature Ar matrices. FVT of **14** causes ring contraction to a mixture of isomeric cyanocarbazoles. Thermal reaction of **14** with diethylamine and dipropylamine in solution affords acridinylamidines **25**. Thermal cycloaddition with phenylacetylene affords the triazolylacridines **26** and **27**. The syntheses of 9-chloroacridine, 9-azidoacridine **14**, amidines **25** and triazoles **26** and **27** were carried out conveniently and rapidly under microwave irradiation.

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