# 1-Azabenz[a]anthracene and 9-Azabenz[a]anthracene



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The synthesis of 1-azabenz[a]anthracene and 9-azabenz[a]anthracene are presented.

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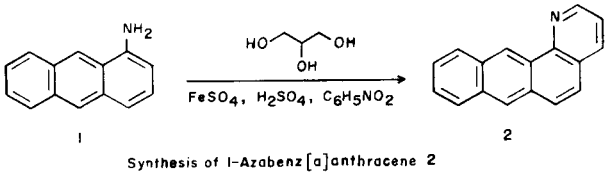
Azabenz[a]anthracenes have been detected in gc/ms spectra of recent lake sediments, street dust, and suspended urban particulate [1]. Azabenz[a]anthracenes are the nitrogen derivatives of benz[a]anthracene, the parent compound of a series that contain many carcinogenic members [2]. As aza-derivatives of the carcinogenic benz[a]anthracenes, these compounds may be responsible for the mutagenic activity that has been observed in the basic fraction of environmental pollutants. Thus it would be useful to have quantities of the pure materials available, both for confirmation of the structure of the materials isolated and to study the biological effects of the pure compounds.

Of the twelve possible isomeric mono-azabenz[a]anthracenes, the syntheses of all but 1-azabenz[a]anthracene (**2**) and 9-azabenz[a]anthracene (**5**) have been reported. We wish to describe the synthesis of both **2** and **5** and thus complete the series. As shown in Scheme 1, 1-azabenz[a]-anthracene (**2**) was synthesized in one step using a Skraup reaction. Glycerol, sulfuric acid, and iron(II) sulfate were reacted with 1-aminoanthracene (**1**) to give 1-azabenz[a]-anthracene (**2**).

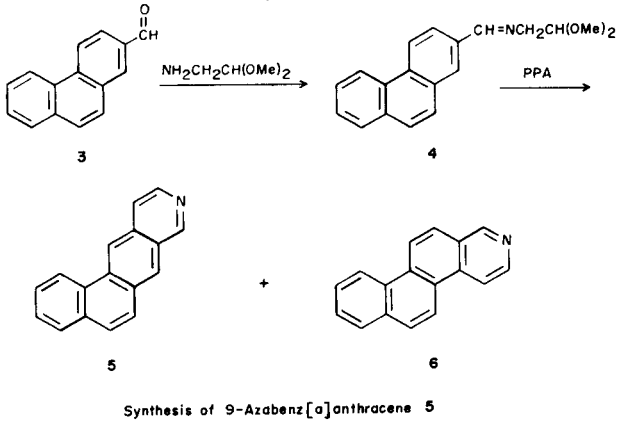
Scheme 1




1 2

Synthesis of 1-Azabenz[a]anthracene 2

Scheme 2




3 4 5 6

Synthesis of 9-Azabenz[a]anthracene 5

Scheme 2 shows the synthesis of 9-azabenz[a]anthracene (**5**) from phenanthrene-2-carboxaldehyde (**3**) [3,4]. Phenanthrene-2-carboxaldehyde (**3**) was converted to the Schiff base **4** with aminoacetaldehyde dimethyl acetal. The Schiff base **4** was cyclized in a Friedel-Crafts reaction using polyphosphoric acid to give 9-azabenz[a]anthracene **5** with a small amount of isomeric 2-azachrysene (**6**).

The structural assignments of the two isomers, 9-azabenz[a]anthracene (**5**) and 2-azachrysene (**6**) are based on nmr data. In 9-azabenz[a]anthracene (**5**) the proton spectra has a singlet at $\delta$ 8.51 and one at $\delta$ 9.12 which are characteristic for H-7 and H-12 respectively in azabenz[a]anthracenes. In 9-azabenz[a]anthracene (**5**) H-8 is a singlet at $\delta$ 9.50, while H-10 is a doublet, J = 5.9 Hz at $\delta$ 8.55 and H-11 is in a multiplet at $\delta$ 7.87-7.90. A 2-dimensional correlation spectra was done which confirms the assignments of the peaks. The spectrum of 2-azachrysene shows only one singlet at $\delta$ 9.38 for H-1 as is expected.

The synthesis of aza-aromatic hydrocarbon pollutants is necessary in order to assess the health hazard posed by them. This knowledge is important because production of liquid fuels by gasification of nitrogen-rich oil shale and coal could release increasing amounts of aza-aromatic hydrocarbons into the environment. 1-Azabenz[a]anthracene (**2**), 9-azabenz[a]anthracene (**5**) and 2-azachrysene (**6**) are currently undergoing evaluation for mutagenic and carcinogenic activity [5] and will be compared to alkylbenz[a]-anthracenes some of which are very mutagenic and carcinogenic.

## EXPERIMENTAL

Melting points (uncorrected) were obtained using a Mel-Temp apparatus. The nmr spectra were recorded on a Jeol FX90Q or a Varian XL400 spectrometer. All chemical shifts are reported in parts per million ($\delta$) downfield from tetramethylsilane. The ir spectra were recorded on a Perkin Elmer 1310 spectrometer. The uv spectra were determined on a Varian DMS90 spectrometer.

1-Azabenz[a]anthracene (**2**).

Concentrated sulfuric acid (4.96 ml) was added dropwise to 5.0 g (0.03 mole) of 1-aminoanthracene (**1**), 10.0 g (0.11 mole) of glycerol and 1.0 g (3.6 mmoles) of iron(II) sulfate in 12 ml of nitrobenzene. The mixture was then heated at 145° for 1 hour and refluxed for 3 hours. After dilution

with water (100 ml) and evaporation to dryness, the residue was stirred with hot water (200 ml) and filtered. Upon addition of saturated sodium chloride (200 ml) solution, a precipitate formed. The filtrate was stirred with concentrated ammonium hydroxide solution (200 ml) and filtered. The solid was dissolved in hot toluene (150 ml), filtered and the solvent evaporated, to give a residue which was chromatographed on silica gel using chloroform/ethyl acetate (3/1) as the eluant. The desired component was rechromatographed on silica gel eluting with dichloromethane/hexane (3/1), yield 2.10 g (30%) of yellow crystals, mp 132-133°; $^1$H nmr (deuteriochloroform): δ 7.45 (m, H-8, H-9, H-10, H-11), 8.10 (m, H-3, H-4, H-5, H-6), 8.36 (s, H-7), 9.00 (dd, J = 6 and 1.5 Hz, H-2), 9.81 (s, H-12); $^{13}$C nmr (deuteriochloroform): δ 122.0 (C-3), 123.9 (C-9), 125.1 (C-10), 125.8 (C-8), 126.3 (C-5 and C-6), 126.4 (C-4a), 127.8 (C-11), 128.2 (C-7), 129.1 (C-12), 129.4 (C-7a), 131.6 (C-11a), 132.2 (C-6a), 132.9 (C-12a), 135.5 (C-4), 147.4 (C-12b), 148.2 (C-2); ir (nujol): 2950, 1450, 910, 790 cm$^{-1}$; uv (methanol): λ max 219 nm (ε 24,500), 253 (51,500), 276 (30,600), 293 (18,800), 304 (23,500), 388 (5800), 354 (5100), 385 (2000).

*Anal.* Calcd. for $C_{17}H_{11}N$-0.1$H_2O$: C, 88.36; H, 4.89; N, 6.06. Found: C, 88.38; H, 4.81; N, 6.01.

2-Aza-4,4-dimethoxy-1-(2-phenanthryl)-1-butene (**4**).

A mixture of 18.0 g (87.0 mmoles) of phenanthrene-2-carboxaldehyde (**3**) and 10.5 g (100.0 mmoles) of aminoacetaldehyde dimethyl acetal was heated at 100° for 1.5 hours. More acetal (1.4 g, 13.0 mmoles) was added and heating was continued for an additional hour. The water and excess acetal was removed *in vacuo* at room temperature. The Schiff base **4** was recrystallized from benzene/petroleum ether (30-60°), yield 22.0 g (86%); ir (nujol): 1636, 1130 cm$^{-1}$; ms: m/e 293 (20%) (MI), 262 (30%), M-OMe.

9-Azabenz[*a*]anthracene (**5**) and 2-Azachrysene (**6**).

To 100 ml of polyphosphoric acid under nitrogen was added 10.4 g (35.5 mmoles) of finely powdered Schiff base **4**. The mixture was heated at 100° for 1.5 hours. The red syrup was poured into ice-water (200 ml) and stirred until all the gummy material was dissolved. The solution was washed with ether. The aqueous solution was basified with ammonium hydroxide solution and extracted with benzene (4 × 500 ml). The combined extracts were dried (magnesium sulfate) and evaporated to give 1.6 g (18%) of a mixture of two isomers (3/1, 9-azabenz[*a*]anthracene (**5**) and 2-azachrysene (**6**)). The isomers were separated by silica gel chromatography eluting with 1% acetic acid, 1.5% methanol and 97.5% dichloromethane to give 1.1 g of 9-azabenz[*a*]anthracene (**5**) and 0.4 g of 2-azachrysene (**6**).

The physical properties of 9-azabenz[*a*]anthracene (**5**) are: mp 138-140°; $^1$H nmr (deuteriochloroform, 400 MHz): δ 7.70 (d, J = 9.1 Hz, H-5 (or 6)), 7.66-7.74 (m, H-2, H-3), 7.84 (d, J = 9.1 Hz, H-6 (or 5)), 7.87-7.90 (m, H-4, H-11), 8.51 (s, H-7), 8.55 (d, J = 5.9 Hz, H-10), 8.83 (dd, J = 7.8 and 1.0 Hz, H-1), 9.12 (s, H-12), 9.50 (s, H-8); $^{13}$C nmr (deuteriochloroform): δ 119.996 (C-11), 129.429 (C-1), 123.355 (C-12), 126.985 (C-7a), 127.147 (C-5, C-6), 127.905 (C-7), 128.122 (C-2, C-3), 128.772 (C-4), 129.802 (C-4a), 131.481 (C-12b), 132.294 (C-6a), 132.456 (C-12a), 132.944 (C-11a), 141.557 (C-10), 153.313 (C-8); ir (potassium bromide): 3100, 1600, 1200, 845, 810 cm$^{-1}$; uv (95% ethanol): λ max 215 nm (ε 25,500), 224 (32,700), 252 (22,200), 264 (30,100), 274 (56,200), 282 (79,200), 302 (10,400), 320 (5500, 334 (5600), 350 (3400), 372 (2700), 393 (2800); ms: m/e 229 (100%) (MI).

*Anal.* Calcd. for $C_{17}H_{11}N$: C, 89.05; H, 4.84; N, 6.11. Found: C, 88.74; H, 4.65; N, 6.04.

The physical properties of 2-azachrysene (**6**) are: mp 236-237°, lit [6] 224-226°; $^1$H nmr (deuteriochloroform): δ 7.62-7.89 (m, H-8, H-9), 7.95-8.19 (m, H-6, H-7, H-12), 8.49 (d, J = 7 Hz, H-4), 8.63 (d, J = 9 Hz, H-5), 8.72-8.96 (m, H-10, H-11, H-3), 9.38 (s, H-1); ir (nujol): 2950, 1460, 885, 810 cm$^{-1}$; uv (95% ethanol): λ max 216 nm (ε 35,700), 237 (15,400), 268 (88,100), 318 (9200), 349 (2500), 366 (2980).

*Anal.* Calcd. for $C_{17}H_{11}N$: C, 89.06; H, 4.84; N, 6.11. Found: C, 88.90; H, 5.09; N, 6.12.

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[5] 1-Azabenz[*a*]anthracene and 2-azachrysene are presently available as reference materials from Dr. David G. Longfellow, Division of Cancer Etiology, National Cancer Institute, Landow Building, Room 8C-33, Bethesda, MD 20205.

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