Further Studies on Heterocyclic Arene Imines. Preparation of 1a,9b-Dihydroazirino[*f*][1,7]phenanthroline, 3b,4a-Dihydroazirino-[2,3]phenaleno[1,9-*g*,*h*]quinoline and 1a,13b-Dihydro-dibenzo[1,2:6,7]phenazino[1,2-*b*]azirine

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The syntheses of the K-imine derivatives of 1,7-phenanthroline, phenaleno[1,9-*g*,*h*]quinoline, and dibenzo[*a*,*h*]phenazine are described. The parent heterocyclic compounds **4**, **9** and **14** were oxidized to the corresponding K-oxides, **5**, **10** and **15**, which in turn were reacted with sodium azide in aqueous acetone. The resulting *trans*-azido alcohols were then cyclized with tributylphosphine to the title compounds **6**, **11** and **16**.

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Although most K-region imines of polycyclic aromatic compounds were shown to be substantially more mutagenic than the corresponding K-region oxides [1-3], we found two exceptions. 1a,9b-Dihydrobenz[*h*]azirino[*f*]-quinoline (**1**) [4] and 1a,9b-dihydroazirino[*f*][1,10]phenanthroline (**2**) [4], that have nitrogen atoms at the bay region, proved less potent mutagens than the respective epoxides [5]. The mutagenicities of 1a,9b-dihydrobenz[*f*]azirino[*h*]quinoline (**3**) and its oxide analog [4] followed, however the general rule.

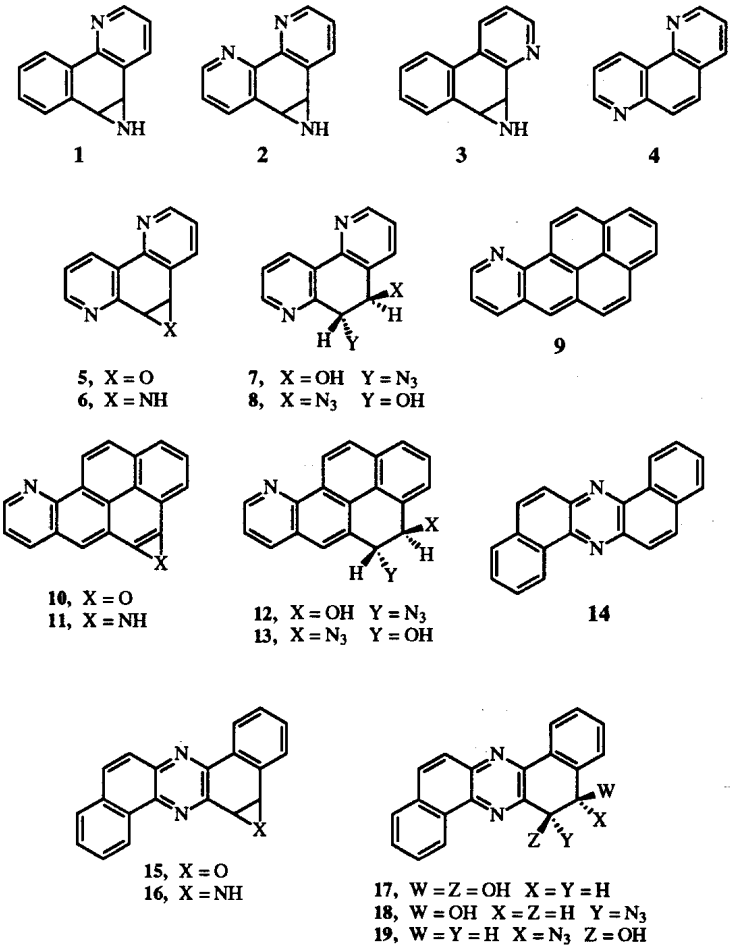
In order to understand the effect of the heteroatom at different locations on the mutagenic potency, we have now synthesized the K-region imine of 1,7-phenanthroline (**4**) which has one nitrogen atom at the bay-region and one at an M-region. In addition, we have prepared the imine derivative of phenaleno[1,9-*g*,*h*]quinoline (**9**) [6] (which is the bay-region aza analog of benzo[*a*]pyrene), and that of the potent carcinogen, dibenzo[*a*,*h*]phenazine (**14**) [7].

The synthesis of 1a,9b-dihydroazireno[*f*][1,7]phenanthroline (1,7-phenanthroline 5,6-imine (**6**)) was accomplished in four steps by initial hypochlorite oxidation [8] of **4** to **5**. The crude epoxide, which proved too labile to be purified, was treated with sodium azide in aqueous acetone to give *trans*-5-azido-5,6-dihydro-1,7-phenanthrolin-6-ol (**8**) as the sole isolable product. The fact that no azido-alcohol **7** has been formed is in accord with quantum-mechanical calculations which reveal that the intermediate leading to **8** is favored by -0.0706 β over the precursor of **7**. (*Cf.*, the values of 0.0138 and -0.0532 β for the oxirane ring opening of 1a,9b-dihydrobenz[*h*]oxireno[*f*]quinoline and 1a,9b-dihydrobenz[*f*]oxireno[*h*]quinoline, respectively [9]). Reaction of **8** with tributylphospine [10] gave the expected aziridine **6**.

3b,4a-Dihydroazirino[2,3]phenaleno[1,9-*g*,*h*]quinoline (10-azabenzo[*a*]pyrene 4,5-imine (**11**)) was obtained in two steps from the known oxide **10** [11]. Reaction of the latter with sodium azide yielded nearly a 1:1 mixture of azido alcohols **12** and **13**. (Quantum-mechanical calculations favor the formation of the precursor of **12** over that of **13** by an insignificant value of ΔE = 0.0024 β).

Treatment of this mixture with tributylphosphine in the cold, gave tributylphosphoazido adducts [12] which decomposed upon heating to imine **11**.

1a,13b-Dihydrodibenzo[1,2:6,7]phenazino[1,2-*b*]-azirine (dibenzo[*a*,*h*]phenazine 5,6-imine (**16**)) was prepared from **14** in a four step process. The parent compound was converted into epoxide **15** by two alternative



routes. (i) The dibenzophenazine was initially oxidized with osmium tetroxide in pyridine to *cis*-diol **17**, which in turn, was reacted with orthoacetic ester-trimethylchlorosilane [13]. (ii) The parent compound in chloroform was treated with an eight-fold molar excess of 3-chloroperbenzoic acid under reflux. Both methods gave the same yield (52%) of epoxide. Reaction of **15** with sodium azide afforded a 1:2 mixture of the *trans*-azido alcohols **13** and **19**. Cyclization of the azido alcohols to **16** was accomplished, as in the previous cases, with tributylphosphine.

EXPERIMENTAL

1a,9b-Dihydrooxireno[*f*][1,7]phenanthroline (**5**).

To 28.4 ml of commercial 10% aqueous sodium hypochlorite buffered to *p*H 8.5 with 0.8 *M* aqueous sodium hydrogen phosphate, was added 225 mg (0.67 mmole) of tetrabutylammonium hydrogen sulfate and 300 mg (1.6 mmoles) of **4** [8] in 33 ml of chloroform. The mixture was stirred vigorously at 25° for 4 hours. The organic phase was separated, washed (x3) with water and dried on sodium sulfate. Removal of the solvent under reduced pressure afforded 235 mg (75%) of **5**, mp 121-122°; ^{1}H nmr (deuteriochloroform): 200 MHz δ 4.55 (d, 1H, $J_{1a,9b}$ = 3.6 Hz, H1a or H9b), 4.73 (d, 1H, $J_{1a,9b}$ = 3.6 Hz, H1a or H9b). 7.28-7.46 (m, 2H, H4, H8), 7.92 (d, 1H, $J_{8,9}$ = 7.5 Hz, H9), 8.59-8.67 (m, 3H, H3, H5, H7). The epoxide could not be purified without decomposition.

trans-5-Azido-5,6-dihydro-1,7-phenanthrolin-6-ol (**8**).

A mixture of 200 mg (1.02 mmoles) of crude **5**, 5 g (77 mmoles) of sodium azide, 100 ml of acetone and 50 ml of water was stirred under exclusion of air at room temperature for 60 hours. The acetone was removed under reduced pressure and the resulting precipitate was extracted with dichloromethane. The dried organic solution was concentrated and chromatographed on alumina deactivated with 20% of water, using hexane-ether mixtures (ether content 5-50%) as eluent. There was obtained 152.5 mg (67%) of pure **8**, mp 123-125°; ir (nujol): 3310 (OH), 2150 cm^{-1} (N_3); ^{1}H nmr (deuteriochloroform): 200 MHz δ 4.74 (d, 1H, $J_{5,6}$ = 11 Hz, H5 or H6), 4.92 (d, 1H, $J_{5,6}$ =11 Hz, H5 or H6), 7.19-7.38 (m, 2H, H3, H9), 7.87 (d, 1H, $J_{3,4}$ = 8 Hz, H4), 8.44-8.55 (m, 3H, H2, H8, H10); lc-ms: (70 eV, particle beam 65°) m/z (relative intensity) 239 ($M^{+\cdot}$, 9), 211 ($C_{12}H_9N_3O^{+\cdot}$, 3), 210 ($C_{12}H_8N_3O^+$, 8), 197 ($C_{12}H_9N_2O^+$, 4), 182 ($C_{11}H_6N_2O^{+\cdot}$ or $C_{11}H_8N_3^+$, 100), 155 ($C_{10}H_7N_2^+$, 33).

Anal. Calcd. for $C_{12}H_9N_5O$: C, 60.25; H, 3.79; N, 29.27. Found: C, 60.39; H, 3.88; N, 29.05.

1a,9b-Dihydroazirino[*f*][1,7]phenanthroline (**6**).

To a solution of 85 mg (0.38 mmole) of **8** in 60 ml of chloroform was added at 0° under exclusion of air, 88.5 µl (0.38 mmole) of tributylphosphine. The mixture was first stirred for 20 minutes at 0° and then for 20 minutes at 25°. Finally, the mixture was refluxed for 2 hours. The solvent was evaporated and the residue quickly chromatographed on silica gel deactivated with 36% of water, using hexane-ethyl acetate mixtures (ethyl acetate content 5-20%) as eluent, yield 27.5 mg (37%), mp 118-120°; ir (nujol): 3340 cm^{-1} (NH); ^{1}H nmr (deuteriochloroform): 200 MHz δ 3.63 (d, 1H, $J_{1a,9b}$ = 5 Hz, H1a or H9b), 3.84 (d, 1H, $J_{1a,9b}$ = 5 Hz, Hla or H9b), 7.19-7.36 (m, 2H, H4, H8), 7.84 (d, 1H, $J_{8,9}$ = 7.7 Hz, H9), 8.53-8.58 (m, 2H, H3, H7), 8.23 (dd, 1H, J3,5 = 1.6 Hz, $J_{4,5}$ = 8.1 Hz, H5); lc-ms: (70 eV, particle beam 65°) m/z (relative intensity) 195 ($M^{+\cdot}$, 100), 168 ($C_{11}H_8N_2^{+\cdot}$, 42), 167 ($C_{11}H_7N_2^+$, 23).

Anal. Calcd. for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.92; H, 4.75; N, 21.24.

trans-5-Azido-4,5-dihydro-4-phenaleno[1,9-*g*,*h*]quinolinol (**12**) and *trans*-4-Azido-4,5-dihydro-5-phenaleno[1,9-*g*,*h*]quinolinol (**13**).

As for the preparation of **5**, 100 mg, (0.37 mmole) of 4a,3b-dihydrooxireno[2,3]phenaleno[1,9-*g*,*h*]quioline (**10**) (prepared by the method of Kitahara *et al.* [11]) was reacted for 3 days at room temperature, under exclusion of air, with excess of sodium azide in aqueous acetone. Chromatography on alumina deactivated with 16% of water, using mixtures of hexane and ethyl acetate (containing 2-25% of the ester) as eluent afforded 71.5 mg (62%) of a nearly 1:1 mixture of **12** and **13** as pale yellow crystals, mp 205-207°; ir (nujol): 3406 (OH), 2113 cm^{-1} (N_3); ^{1}H nmr (deuteriochloroform): 200 MHz δ 5.07-5.21 (m, 2H, H4, H5), 7.44-7.71 (m, 3H, H1, H2, H7), 7.92-8.03 (m, 3H, H3, H8, H12), 8.19-8.97 (m, 2H, H9, H11), 9.16 (s, 0.5H, H6 of **13**), 9.20 (s, 0.5H, H6 of **12**); lc-ms: (70 eV, particle bean 65°) m/z (relative intensity) 312 ($M^{+\cdot}$, 48), 284 ($C_{19}H_{12}N_2O^{+\cdot}$, 21), 270 ($C_{19}H_{12}NO^+$, 65), 256 ($C_{18}H_{10}NO^+$, 25), 255 ($C_{18}H_9NO^{+\cdot}$ or $C_{18}H_{11}N_2^{+\cdot}$, 100), 254 ($C_{18}H_{10}N_2^{+\cdot}$, 26), 253 ($C_{19}H_{11}N^{+\cdot}$, 35), 240 ($C_{18}H_{10}N^+$, 12), 227 ($C_{17}H_9N^{+\cdot}$, 14).

Anal. Calcd. for $C_{19}H_{12}N_4O$: C, 73.07; H, 3.87; N, 17.94. Found: C, 72.90; H, 3.89; N, 17.61.

3b,4a-Dihydroazirino[2,3]phenaleno[1,9-*g*,*h*]quinoline (**11**).

In a similar manner as for the preparation of **6**, 70 mg (0.22 mole) of the mixture of **12** and **13** in chloroform was treated at 0° with 60.5 µl (0.24 mmole) of tributylphosphine followed by decomposition of the adduct, so formed, by heating at reflux for 5 hours. The resulting yellow oil was purified by chromatography on silica gel deactivated with 25% of water using hexane containing 2-20% of ethyl acetate as eluent, yield 28.8 mg (48%) of yellow crystals, mp 188-189°; ir (nujol): 3310 cm^{-1} (NH); ^{1}H nmr (deuteriochloroform): 200 MHz δ 3.89 (d, 1H, $J_{3b,4a}$ = 4.7 Hz, H3b or H4a), 3.96 (d, 1H, $J_{3b,4a}$ = 4.7 Hz, H3b or H4a), 7.55 (m, 1H, H2), 7.68 (d, 1H, $J_{1,2}$ = 8 Hz, H1), 7.88 (1H, $J_{10,11}$ = 9 Hz, H11), 7.97 (d, 1H, $J_{10,11}$ = 9 Hz, H10), 8.08-8.13 (m, 2H, H3, H7), 8.27 (dd, 1H, $J_{6,8}$ = 2 Hz, $J_{7,8}$ = 8.5 Hz, H8), 9.05 (dd, 1H, $J_{6,7}$ = 5 Hz, $J_{6,8}$ = 2 Hz, H6), 9.32 (s, 1H, H5); gc-ms: (70 eV, 100-280°) m/z (relative intensity) 268 ($M^{+\cdot}$, 100), 241 ($C_{18}H_{11}N^+$, 15), 240 ($C_{18}H_{10}N^{+\cdot}$, 23)

Anal. Calcd. for $C_{19}H_{12}N_2$: C, 85.05; H, 4.51; N, 10.44. Found: C, 85.32; H, 4.42; N, 10.21.

1a,13b-Dihydrodibenzo[1,2:6,7]phenazino[1,2-*b*]oxirene (**15**).

Method A.

A solution of 980 mg (3.5 mmoles) of **14**, 1 g (3.94 mmoles) of osmium tetroxide in 30 ml of anhydrous pyridine was stirred in the dark under exclusion of air for 14 days at room temperature. The mixture was then stirred for 3.5 hours with 50 ml of 6% aqueous sodium bisulfite, diluted with 100 ml of water and allowed to stand overnight. There was obtained 879 mg (80%) of

cis-diol **17** as pale yellow crystals, mp 187-189; ir (nujol): 3350 cm^{-1} (OH); ^1H nmr (deuteriochloroform): 200 MHz δ 5.26 (d, 1H, $J_{5,6}$ = 4.9 Hz, H5 or H6), 5.33 (d, 1H, $J_{5,6}$ = 4.9 Hz, H5 or H6), 7.57-8.18 (m, 8H, H2, H3, H4, H9, H10, H11, H12, H13), 8.52 (dd, 1H, $J_{1,2}$ = 10 Hz, $J_{1,3}$ = 2 Hz, H1), 9.24 (dd, 1H, $J_{8,9}$ = 10 Hz, $J_{8,10}$ = 2Hz, H8). A mixture of 300 mg (0.955 mmole) of crude **17** in 9 ml of dry benzene, 0.38 ml (3.17 x 10^{-3} mmole) of trimethyl orthoacetate and 12 mg (0.098 mmole) of benzoic acid was stirred under reflux for 90 minutes. After cooling to 25°, 75 mg (0.71 mmole) of solid sodium carbonate was added. The solids were filtered off and the resulting solution evaporated to dryness. The yellow crystals were dissolved in 9 ml of dichloromethane. This solution was added at 0° to a solution of 0.3 ml (1.84 x 10^{-3} mmole) of trimethylchlorosilane and 30 µl (2.97 x 10-4 mmole) of triethylamine in 3 ml of dichloromethane. The mixture was stirred for 3 hours at 4°. After removal of the solvent under reduced pressure, the residue was dissolved in 25 ml of dry tetrahydrofuran and cooled to -78°. A solution of 750 mg of sodium methoxide in 15 ml of the same solvent was added, and the mixture was stirred at 4° for 18 hours. Addition of 150 ml of dry ether afforded a voluminous precipitation. The salts were filtered off and the resulting tetrahydrofuran solution was concentrated and washed (x3) with cold water. Evaporation of the residual solvent gave 147.8 mg (52%) of **15** as a viscous dark yellow oil that was used in the next step without further purification; ^1H nmr (deuteriochloroform): 200 MHz δ 4.63 (d, 1, $J_{1a,13b}$ = 4 Hz, H1a or H13b), 4.92 (d, 1H, $J_{1a,13b}$ = 4Hz, H1a or H13b), 7.50-8.19 (m, 8H, H2, H3, H4, H7, H8, H9, H10, H11), 8.29 (dd, 1H, $J_{3,5}$ = 2Hz, $J_{4,5}$ = 11 Hz, H5), 9.25 (dd, 1H, $J_{10,12}$ = 1.8 Hz, $J_{11,12}$ = 10 Hz, H12).

Method B.

A solution of 140 mg (0.5 mmole) of **14** and 800 mg (3.9 mmoles) of 85% 3-chloroperbenzoic acid in 100 ml of chloroform was refluxed for 6 hours. After removal of the solvent the mixture was digested with a mixture of 150 ml of cold ether and 150 ml of 7.5% aqueous sodium hydroxide. The organic layer was separated and washed (x 3) with cold water, dried and the solvent evaporated. There was obtained 77 mg (52%) of **15** as a dark yellow oil which had the same ^1H nmr spectrum as the compound obtained by method A.

trans-6-Azido-5,6-dihydro-5-dibenzo[*a,h*]phenazinol (**18**) and *trans*-Azido-5,6-dihydro-6-dibenzo[*a,h*]phenazinol (**19**).

Treatment of 200 mg (0.64 mmole) of **15** with 5 g (77 mmoles) of sodium azide yielded, after chromatography on deactivated alumina with hexane-ethyl acetate mixtures as eluent, 103.6 mg (48%) of a 1:2 mixture of **18** and **19**, mp 183° dec; ir (nujol): 3305 (OH), 2150 cm^{-1} (N_3); ^1H nmr (deuteriochloroform): 200 MHz δ 4.82-5.14 (m, 2H, H5, H6), 7.42-7.94 (m, 8H, H2, H3, H4, H9, H10, H11, H12, H13), 8.40 (dd, 0.67H, $J_{1,2}$ = 8.6 Hz, $J_{1,3}$ = 2 Hz, H1 of **19**), 8.52 (dd, 0.33H, $J_{1,2}$ = 6.2 Hz, $J_{1,3}$ = 1.5 Hz, H1 of **18**), 9.14 (two overlapping dd, 1H, $J_{8,9}$ = 9 Hz, $J_{8,10}$ = 2 Hz, H8 of **18** and **19**), lc-ms: (70 eV, particle beam 65°) m/z (relative intensity) 339 ($M^{+\cdot}$, 42), 311 ($C_{20}H_{13}N_3O^{+\cdot}$, 33), 297 ($C_{20}H_{13}N_2O^+$, 25), 283 ($C_{19}H_{11}N_2O^+$, 48), 282 ($C_{19}H_{12}N_3^+$, 100), 267 ($C_{19}H_{11}N_2^+$, 22), 254 ($C_{18}H_{10}N_2^{+\cdot}$, 15).

Anal. Calcd. for $C_{20}H_{13}N_5O$: C, 70.79; H, 3.86; N, 20.64. Found: C, 70.95; H, 3.89; N, 20.23.

1a,13b-Dihydrodibenzo[1,2:6,7]phenazino[1,2-*b*]azirine (**16**).

In the manner described for the preparation of **6**, 100 mg (0.29 mmole) of the above mixture of **18** and **19** was reacted with 369 µl (0.3 mmole) of tributylphosphine, yield 30 mg (35%) of pale yellow crystals, mp 171-173°; ir (nujol): 3330 cm^{-1} (NH); ^1H nmr (deuteriochloroform): 200 MHz δ 3.77 (d, 1H, $J_{1a,13b}$ = 8.5 Hz, H1a or H13b), 4.15 (d, 1H, $J_{1a,13b}$ = 8.5 Hz, H1a or H13b), 7.40-8.17 (8H, H2, H3, H4, H7, H8, H9, H10, H11), 8.75 (dd, 1H, J_1 = 2 Hz, J_2 = 11Hz, H5 or H12), 9.23 (dd, 1H, J_1 = 1.8 Hz, J_2 = 10 Hz, H5 or H12); lc-ms: (70 eV, particle beam 65°) m/z (relative intensity) 295 ($M^{+\cdot}$, 100), 280 ($C_{20}H_{12}N_2^{+\cdot}$, 64), 268 ($C_{19}H_{12}N_2^{+\cdot}$, 30), 267 ($C_{19}N_{11}N_2^+$, 21).

Anal. Calcd. for $C_{20}H_{13}N3$: C, 81.34; H, 4.44; N, 14.23. Found: C, 81.09; H, 4.48; N, 14.42.

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