Adducts of Phenanthrene 9,10-Imine and of Benz[*a*]anthracene 5,6-Imine to Some Nitrogen Heterocycles [1]

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Dedicated to the memory of Professor Nicholas Alexandrou

N-4-Pyridinyl-, *N*-2-quinolinyl-, and 2-pyrazinylphenanthrene 9,10-imines **4-6**, as well as *N*-4-pyridinyl- and *N*-2-pyrazinylbenz[*a*]anthracene 5,6-imines **12** and **13** were prepared by sodium hydride-mediated interaction of the parent arene imines, **1** and **10**, and the respective chloropyridine, chloroquinoline or chloropyrazine. *N*-Nicotynoyl-, *N*-2-pyridinoyl- and *N*-6-quinolinoylphenanthrene 9,10-imines **7-9** were obtained by interaction of *N*-trimethylsilylphenanthrene 9,10-imine (**2**) and the appropriate pyridine- or quinolinecarbonyl chlorides. Reaction of *N*-methylsulfonylphenanthrene 9,10-imine with thymine, cytosine, 5-fluorocytosine, purine, 6-chloropurine and adenine afforded, in the presence of either potassium carbonate or 1,5-diazabicyclo[3.4.0]non-5-ene, adducts **16-22**, respectively. The structures of the adducts were conformed by multinuclear nmr and by NOESY and C-H correlation 2D nmr spectrometry.

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Modern research on chemical carcinogenesis by polycyclic aromatic compounds is based on two concepts: (i) that the parent compounds undergo initially metabolic activation, and (ii) that the initiation step of tumor formation involves binding of the metabolites to nucleic acid [2]. The most explored metabolites of polycyclic aromatic compounds are the arene oxides and diol epoxides. These compounds react with DNA, as well as with other cellular nitrogen nucleophiles to give β-amino alcohols. Since some amino alcohols were shown to form in the presence of sulfotransferases, both *in vitro* and *in vivo*, cancer-producing aziridines [3] we have postulated that aziridine derivatives of polycyclic aromatic compounds (the so called arene imines) may also be involved in the mechanism of chemical carcinogenesis [4]. Support for this hypothesis was provided by comparative mutagenesis studies of numerous polycyclic arene oxides and imines, which revealed (a) that all arene imines have higher mutagenic potencies than the corresponding oxides [5-9], and (b) that a logarithmic correlation exists between the specific mutagenicities of the two classes of compounds [5]. In addition, it has been found that while many arene oxides are sensitive to microsomal and cytisolic epoxide hydrolases, the imines are resistant to these detoxifying enzymes [5]. Yet, in spite of these supporting results, the lack of appropriate reference compounds has prevented searching for DNA-arene imine adducts in polycyclic aromatic compound-induced tumor cells. Therefore, we find it imperative to develop suitable methods for the preparation of the required imine-nucleic acid standards.

In this paper we report the preparation of adducts of simple arene imines with several common nitrogen heterocycles, as well as with some representative purines and pyrimidines that may serve as models for adducts of carcinogenic polycyclic aromatic compounds and nucleic acid components.

Pyridine, quinoline and pyrazine proved not to react under mild conditions with 1a,9b-dihydro-1*H*-phenanthro[9,10-*b*]azirine (phenanthrene 9,10-imine) (**1**), however their halo-derivatives yielded, in the presence of a strong base, the corresponding **1**-substituted phenanthrene imines. Thus, 4-chloropyridine and **1** gave, in the presence of sodium hydride (2 hours at 35-40° in dimethyl sulfoxide) 93% of 4-[1a,9b-dihydrophenanthro[9,10-*b*]-azirin-1-yl]pyridine (**4**). In this reaction the aziridine ring retained its structure, as evidenced by the appearance of a two proton signal at 4.12 ppm in the ^{1}H nmr spectrum. Likewise, 1-chloroquinoline reacted with **1** to give 33% of the *N*-quinolinyl adduct **5**. Upon reacting **1** with chloropyrazine in dimethyl sulfoxide, a mixture of products was obtained. When, however the reaction was conducted in dimethylformamide, the expected 2-[1a,9b-dihydrophenanthro[9,10-*b*]azirin-1-yl]pyrazine (**6**) was obtained as the only isolable product.

In analogy to **1** also 1a,11b-dihydro-1*H*-benz[3,4]-anthra[1,2-*b*]azirine (benz[*a*]anthracene 5,6-imine (**10**) reacted with the above chloropyridine and chloropyrazine, to give adducts **12** and **13**, respectively.

In addition to compounds **4-6**, **12** and **13**, we prepared adducts in which **1** and **10** were attached to the heterocyclic moieties *via* carbonyl linkages. The starting materials in these cases were heterocyclic acid chlorides. In the presence of triethylamine nicotinoyl chloride in tetrahydrofuran reacted sluggishly with **1**. However, when the aziridine nitrogen proton was substituted by a trimethylsilyl group (by treatment with *N,O*-bis(trimethylsilyl)acetamide [10] the reaction proceeded smoothly even at 5°, and furnished within 10 minutes 65% of (1a,9b-dihydrophenanthro[9,10-*b*]azirin-1-yl)-3-pyridinylmethanone (**7**). The structure of **7** was confirmed by its characteristic ir spectrum in which the amide carbonyl appears at 1670 and 1580 cm^{-1}, and by the ^{1}H nmr spectrum which shows two aziridine ring protons at

4.32 ppm. By the same method 1a,9b-dihydro-1-(trimethylsilyl)-1*H*-phenanthro[9,10-*b*]azirine (**2**) was reacted with 2-pyridine- and 6-quinolinecarbonyl chloride to yield compound **8** and **9**, respectively. Likewise, the reaction of the pentacyclic imine **10** with 6-quinolinecarbonyl chloride afforded adduct **14** *via* **11**.

Unlike the above chloro heterocycles and carbonyl chlorides, the corresponding derivatives of purines and pyrimidines failed to give similar adducts of arene imines. Purines and pyrimidines were found however to react slowly with **1** in dimethyl sulfoxide in the presence of either potassium carbonate or an organic base. The rate could be increased substantially when the imine was activated by a methanesulfonyl group. Thus, when 1a,9b-dihydro-1-(methylsulfonyl)-1*H*-phenanthro[9,10-*b*]azirine (**3**) (prepared from **2** and methanesulfonyl chloride [10]) was treated with two equivalents of thymine and two equivalents of potassium carbonate in dimethyl sulfoxide for 24 hours, the aziridine ring cleaved and *trans*-1-[(9,10-dihydro-*N*-9-methanesulfonamidophenanthren)-10-yl]-5-methyl-2,4-pyrimidinedione (**16**) was obtained in 55% yield. The only side product was isomerized **3**, *N*-9-phenanthrenylmethanesulfonamide (**15**) [10]. Acid hydrolysis of **16** formed the mesyl-free amine (*cf.* reference [11]). The structure of **16** has been deduced from its elemental analysis, and from its multinuclear spectra which closely resemble those of the free thymine (Table 1). Binding of the nitrogen base to **3** caused H6' of thymine to be deshielded by 0.09 ppm. The C5' and C6' resonance peaks in the adduct were found to be shifted downfield by *ca.* 2 ppm, while that of the carbonyl carbon atom C4' was shifted upfield. The absence of peaks corresponding to etheral carbon atoms in the ^{13}C nmr spectrum indicates that the thymine is not linked to the phenanthrene residue through an oxygen atom, *i.e.* the bond must involve either N1' or N3'. The 2D NOESY measurements [12] (in hexadeuterioacetone) clearly showed nuclear Overhauser enhancement between H6' at 6.99 ppm and both H9 and H10 of the phenanthrene moiety at 5.19 and 5.86 ppm, respectively, and a resonance peak at 10.15 ppm indicated the presence of a hydrogen atom on N3'. These facts exclude the existence of a C10-N3' bond. Thus, the only possible binding of the thymine to the phenanthrene moiety must involve N1'.

The adducts of **3** and cytosine as well as 5-fluorocytosine were synthesized by the same method as **16** (see Experimental), and were characterized by virtue of their nmr spectra. In both adducts the H5' and H6' signals were deshielded by *ca.* 0.5 ppm as compared with the peaks of the free bases (Table 1). The C2', C5' and C6' signals in both **17** and **18** were strongly shifted downfield, and only the peaks of C4' moved upfield. The appearance of two NH_2 protons in the ^1H nmr spectra excludes the binding of cytosine and 5-fluorocytosine through their free amino groups. The absence of etheral ^{13}C signals proved that the oxygen atoms are not involved in the bonding. Unlike the 2D NOESY measurements of **16**, those of **17** and **18** (in hexadeuterioacetone) do not reveal nuclear Overhauser enhancement between H6' and the phenanthrene protons H9 and H10. However, this does not exclude the possibility of binding through N1'. If in **17** and **18** the linkages involved N1' atoms, the high field ^{13}C peaks at 157.3 and 141.2 ppm would correspond to the C6' atoms, and the low field peaks at 165.4 and 156.3 ppm, would correspond to the methine carbon atoms C4'. If however, the bond involved N3', the low field peaks would correspond to C6' (now the methine carbon atom) and those at 157.3 and 141.2 ppm, to C4'. Since 2D ^{13}C-^1H correlation measurements (in deuterioacetone) have indicated that in **17** the H6' doublet at 7.94 ppm is coupled with the signal of C6' at 157.3 ppm rather than with that of the methine carbon atom that shows up at 165.4 ppm, the binding atom is in fact N1'. A similar correlation for **18** indicates that in this adduct too the binding is through N1'.

The reaction of **3** with purine gave, in the presence of potassium carbonate, two adducts in the ratio 2.2:1 in 63% yield. The two isomeric products **19** and **20** have been separated by column chromatography on silica gel. As their ^1H

Table 1

Significant ^1H and ^{13}C Chemical Shifts of Some Free Pyrimidines, Methyladenines and Phenanthrene Imine Adducts [a]

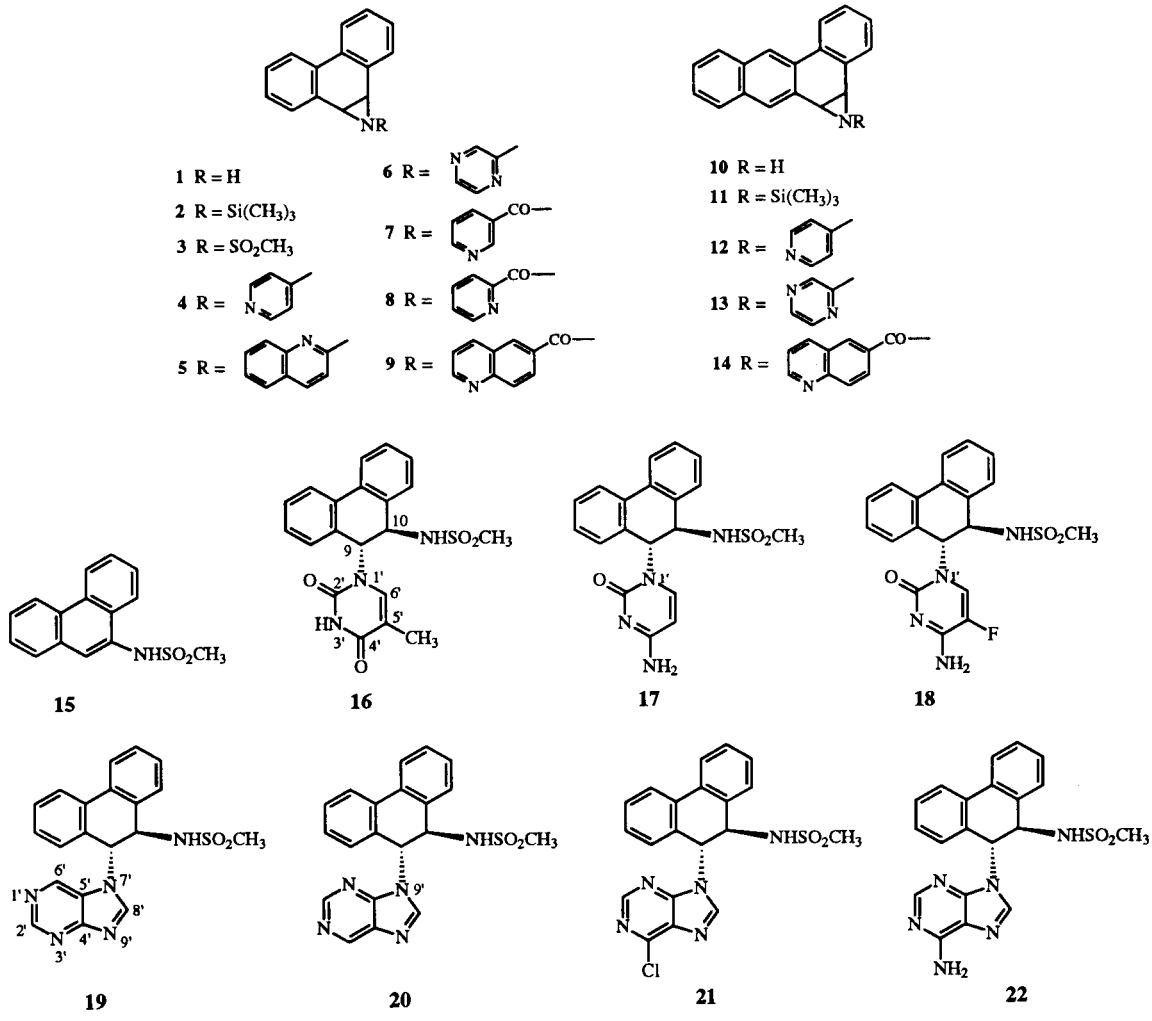
	Chemical Shifts (ppm)								
Compound	H2'	H5'	H6'	H8'	C2'	C4'	C5'	C6'	C8'
Thymine			7.24		151.4	164.9	107.6	137.7	
16			7.33		151.5	164.1	109.5	139.8	
Cytosine		5.58	7.33		156.9	166.6	92.5	142.7	
17		6.09	7.86		165.6	164.5	100.1	156.8	
5-Fluorocytosine			7.60		155.1	158.1	135.9	126.9	
18			7.96		159.8	155.3	142.4	140.4	
7-Methyladenine [13]	8.08			8.01	153.7	159.4	113.2	153.3	148.0
9-Methyladenine [13]	8.08			7.94	153.6	150.6	119.5	156.6	144.2
22	8.14			7.73	152.8	149.7	119.2	156.1	140.7

[a] In hexadeuteriodimethyl sulfoxide.

and ^{13}C nmr spectra are not very indicative, the binding of the phenanthrene backbone to the purine moiety could in principal involve any of the four nitrogen atoms. The 2D NOESY measurements revealed however, that both adducts show nuclear Overhauser enhancement between the purine H8' and the phenanthrene protons H9 and H10. This excludes the possibility of binding through N1' and N3' [13]. Since **19**, but not **20**, shows also nuclear Overhauser enhancement between the signal of H6' and H9 and H10, it can be concluded that the major and minor adducts are *trans*-7-, and *trans*-9-[(9,10-dihydro-*N*-9-methanesulfonamidophenanthren)-10-yl]purines **19** and **20**, respectively.

6-Chloropurine and **3** formed a single adduct **21** in 72% yield. The ^{1}H and ^{13}C nmr spectra of **21** resemble closely those of **20** rather than those of **19** (see Experimental) in which N9' is involved in the binding. The 2D NOESY measurements (in deuterioacetone) revealed nuclear Overhauser enhancement between H8' and H9 and H10. This indicates that neither N1' nor N3', is linked to H10. Since in 6-chloropurine N7' is sterically hindered by the halogen atom the exclusive binding through N9' is understandable.

The reaction between **3** and adenine took place only after replacement of the carbonate in the previous syntheses by 1,5-diazabicyclo[3.4.0]non-5-ene. The ^{1}H resonance peak of the isolated product, **22**, at 7.32 ppm suggests that the adenine amino group at position 6' is not involved in the binding of the base to the phenanthrene residue [14]. The 2D NOESY measurements indicated nuclear Overhauser enhancement between H8' and H9 and H10. This excludes the possibility that N1' and N3' are linked to C10. From the ^{13}C-^{1}H correlation measurements (in hexadeuteriodimethyl sulfoxide) we concluded that the ^{13}C peaks at 140.7 and 153.8 ppm correspond to C8' and C2', respectively. C5', which is linked to only one nitrogen atom appears upfield at 119.2 ppm [13]. The ^{1}H and ^{13}C nmr spectra of **22** resembles more closely those of 9- than of 7-methyladenine (see Table 1). This suggests that the isolated adduct **22** is *trans*-9-[(9,10-dihydro-*N*-9-methanesulfonamidophenanthren)-10-yl]-6(1*H*)-purinamine.



EXPERIMENTAL

4-[1a,9b-Dihydrophenanthro[9,10-*b*]azirin-1-yl]pyridine (**4**).

To a solution of 100 mg (0.52 mmole) of **1** in 10 ml of dimethyl sulfoxide (freshly dried and distilled under nitrogen) was added 75 mg (1.5 mmoles) of sodium hydride (50% in parafin oil) and 78 mg (0.52 mmole) of 4-chloropyridine hydrochloride. The mixture was stirred at 35-40° for 2 hours. After cooling to 5°, cold water was added dropwise until the solution became yellow and **4** precipitated. The pale yellow solid was filtered, washed with water and recrystallized from a mixture of dichloromethane and hexane to give 130 mg (93%) of colorless crystals; mp 178-179°; ^{1}H nmr (deuteriochloroform): 200 MHz δ 4.12 (s, 2H, H1a, H9b), 6.66 (dd, 2H, $J_{2',3'} = J_{5',6'} = 4.6$ Hz, $J_{3',5'} = 1.5$ Hz, H3', H5'), 7.39-7.46 (m, 4H, H2, H3, H7, H8), 7.71 (dd, 2H, $J_{2,3} = J_{8,9} = 5.6$ Hz, $J_{2,4} = J_{7,9} = 3.3$ Hz, H2, H9), 7.96 (dd, 2H, $J_{3,5} = J_{6,8} = 3.4$ Hz, $J_{4,5} = J_{7,6} = 5.8$ Hz, H5, H6), 8.20 (dd, 2H, $J_{2',3'} = J_{5',6'} = 4.6$ Hz, $J_{2',6'} = 1.5$ Hz, H2', H6'); ms: lc (70 eV, particle beam 65°) m/z (relative intensity) 270 ($M^{+\cdot}$, 100), 269 ($C_{19}H_{13}N_2^+$, 72), 178 ($C_{14}H_{10}^{+\cdot}$, 48) 165 ($C_{13}H_9^+$, 23), 94 ($C_5H_6N_2^{+\cdot}$, 5).

Anal. Calcd. for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22; N, 10.36. Found: C, 84.14; H, 4.97; N, 10.04.

2-[1a,9b-Dihydrophenanthro[9,10-*b*]azirin-1-yl]quinoline (**5**).

By the manner described above **1** was reacted with 2-chloroquinoline at 40-45° for 30 minutes, yield 33% of yellow crystals, mp 121-122° (from a mixture of dichloromethane and hexane); ^{1}H nmr (hexadeuterioacetone): 200 MHz δ 4.45 (s, 2H, H1a, H9b), 7.26 (d, 1H, $J_{3',4'} = 8.7$ Hz, H3'), 7.40-7.52 (m, 5H, H3, H4, H7, H8, H8'), 7.69 (ddd, 1H, $J_a = 1.6$ Hz, $J_b = 6.8$ Hz, $J_c = 8.4$ Hz, H6'), 7.81-7.90 (m, 4H, H2, H4' or 5', H7', H9), 8.16-8.25 (m, 3H, H5' or H4', H5, H6); ms: lc (70 eV, particle beam 65°) m/z (relative intensity) 320 ($M^{+\cdot}$, 29), 319 ($C_{23}H_{15}N_2^+$, 40), 193 ($C_{14}H_{11}N^{+\cdot}$, 26), 178 ($C_{14}H_{10}^{+\cdot}$, 36), 177 ($C_{14}H_9^+$, 14), 165 ($C_{13}H_9^+$, 26), 129 ($C_9H_7N^{+\cdot}$, 100).

Anal. Calcd. for $C_{23}H_{16}N_2$: C, 86.22; H, 5.03; N, 8.75. Found: C, 86.01; H, 4.98; N, 8.46.

2-[1a,9b-Dihydrophenanthro[9,10-*b*]azirin-1-yl]pyrazine (**6**).

A mixture of 100 mg (0.52 mmole) of **1**, 38 mg (0.78 mmole) of 50% sodium hydride (in mineral oil) and 46.5 µl (0.53 mmole) of 2-chloropyrazine in 10 ml of dry dimethylformamide was stirred under argon at 35-40° for 24 hours. The cooled mixture was treated with cold water and the resulting precipitate was recrystallized from dichloromethane and hexane to give 81 mg (57%) of yellow **6**, mp 142-144°; ^{1}H nmr (deuteriochloroform): 400 MHz δ 4.32 (s, 2H, H1a, H9b), 7.38-7.47 (m, 4H, H3, H4, H7, H8), 7.71 (dd, 2H, $J_{2,3} = J_{8,9} = 7.3$ Hz, $J_{2,4} = J_{7,9} = 1.7$ Hz, H2, H9), 8.06 (dd, 2H, $J_{3,5} = J_{6,8} = 0.9$ Hz, $J_{4,5} = J_{6,7} = 7.6$ Hz, H5, H6), 8.17-8.20 (m, 2H, H5', H6'), 8.34 (s, 1H, H3'); ms: lc (70 eV, particle beam 65°), m/z (relative intensity) 271 ($M^{+\cdot}$, 46) 270 ($C_{18}H_{12}N_3^+$, 100), 178 ($C_{14}H_{10}^{+\cdot}$, 26), 177 ($C_{14}H_9^+$, 12), 165 ($C_{13}H_9^+$, 12).

Anal. Calcd. for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.29; H, 4.70; N, 15.01.

4-[1a,11b-Dihydrobenz[3,4]anthra[1,2-*b*]azirin-1-yl]pyridine (**12**).

This compound was prepared from **10** and 4-chloropyridine by the method described for **4**, yield 91%, colorless crystals, mp 192-193° (from a mixture of dichloromethane and hexane); ^{1}H nmr (deuteriochloroform): 400 MHz δ 4.10 (d, 1H, $J_{1a,11b} = 5.7$ Hz H1a or H11b), 4.25 (d, 1H, $J_{1a,11b} = 5.7$ Hz, H1a or H11b), 6.76 (dd, 2H, $J_{2',3'} = J_{5',6'} = 4.8$ Hz, $J_{3',5} = 1.4$ Hz, H3', H5'), 7.42-7.55 (m, 4H, H3, H4, H8, H9), 7.73 (dd, 1H, $J_{2,3} = 7.5$ Hz, $J_{2,4} = 1.4$ Hz H2), 7.89-7.92 (m, 2H, H7, H10), 8.17-8.19 (m, 2H, H5, H11), 8.24 (dd, 2H, $J_{2',3'} = J_{5',6'} = 4.8$ Hz, $J_{2',6'} = 1.4$ Hz, H2', H6'), 8.44 (s, 1H, H6); ms: lc (70 eV, particle beam 65°) m/z (relative intensity) 320 ($M^{+\cdot}$, 58), 319 ($C_{23}H_{15}N_2^+$, 15), 228 ($C_{18}H_{12}^{+\cdot}$, 100), 215 ($C_{17}H_{11}^+$, 21), 94 ($C_5H_6N_2^{+\cdot}$, 18).

Anal. Calcd. for $C_{23}H_{16}N_2$: C, 86.23; H, 5.03; N, 8.74. Found: C, 86.01; H, 5.12; N, 8.59.

2-[1a,11b-Dihydrobenz[3,4]anthra[1,2-*b*]azirin-1-yl]pyrazine (**13**).

The yield was 42%, yellow crystals; mp 167-168° (from dichloromethane-hexane); ^{1}H nmr (deuteriochloroform): 400 MHz δ 4.32 (d, 1H, $J_{1a,11b} = 6.2$ Hz, H1a or H11b), 4.45 (d, 1H, $J_{1a,11b} = 6.2$ Hz, H1a or H11b), 7.42 (t, 1H, $J_{2,3,4} = 7.2$ Hz, H3), 7.47-7.52 (m, 3H, H4, H7, H8), 7.72 (d, 1H, $J_{2,3} = 7.2$ Hz, H2), 7.87-7.92 (m, 2H, H7, H10), 8.18-8.22 (m, 3H, H5', H6', H11), 8.26 (d, 1H, $J_{4,5} = 8$ Hz, H5), 8.33 (s, 1H, H3'), 8.52 (s, 1H, H6); ms: lc (70 eV particle beam 65°) m/z (relative intensity) 321 ($M^{+\cdot}$, 95), 320 ($C_{22}H_{14}N_3^+$, 100), 228 ($C_{18}H_{12}^{+\cdot}$, 60), 227 ($C_{18}H_{11}^+$, 31), 215 ($C_{17}H_{11}^+$, 20), 95, ($C_4H_5N_3^{+\cdot}$, 7).

Anal. Calcd. for $C_{22}H_{15}N_3$: C, 82.22; H, 4.71; N, 13.07. Found: C, 81.83; H, 4.91; N, 12.55.

(1a,9b-Dihydrophenanthro[9,10-*b*]azirin-1-yl)-3-pyridinylmethanone (**7**).

A solution of 190 mg (0.98 mmole) of **1** in 25 ml of freshly dried tetrahydrofuran was treated with 120 µl (0.49 mmole) of *N,O*-bis(trimethylsilyl)acetamide. The mixture was stirred under argon at room temperature for 30 minutes. To the mixture was injected 182 µl (1.3 mmoles) of triethylamine, followed by addition of 230 mg (1.3 mmoles) of nicotinoyl chloride hydrochloride. After an additional 30 minutes of stirring, the mixture was cooled to 5° and exessive 5% aqueous sodium bicarbonate was added. The reaction mixture was stirred for an additional 10 minutes and the precipitate was filtered, washed with water, dried and recrystallized from a mixture of ether and hexane to give 190 mg (65%) of yellow **7**, mp 126-128°; ir (nujol): 1670, 1580 cm^{-1} (amide I and II); ^{1}H nmr (deuteriochloroform): 400 MHz δ 4.32 (s, 2H, H1a, H9b), 7.34-7.42 (m, 3H, H3, H5', H8), 7.49 (td, 2H, $J_{2,4} = J_{7,9} = 1.4$ Hz, $J_{3,4,5} = J_{6,7,8} = 7.8$ Hz, H4, H7), 7.62 (dd, 2H, $J_{2,3} = J_{8,9} = 7.5$ Hz, $J_{2,4} = J_{7,9} = 1.4$ Hz, H2, H9), 8.13 (d, 2H, $J_{4,5} = J_{6,7} = 7.8$ Hz, H5, H6), 8.16 (dt, 1H, $J_{2',4',6'} = 2$ Hz, $J_{4',5'} = 7.8$ Hz, H4'), 8.75 (dd, 1H, $J_{4',6'} = 1.8$ Hz, $J_{5',6'} = 4.8$ Hz, H6'), 9.11 (dd, 1H, $J_{2',4'} = 2$ Hz, $J_{2',5'} = 0.7$ Hz, H2'); ms: lc (70 eV particle beam 65°) m/z (relative intensity) 298 ($M^{+\cdot}$, 65), 192 ($C_{14}H_{10}N^+$, 77), 178 ($C_{14}H_{10}^{+\cdot}$, 20), 165 ($C_{13}H_9^+$, 58), 106 ($C_6H_{14}NO^+$, 100), 78 ($C_5H_4N^+$, 55).

Anal. Calcd. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.02; H, 4.57; N, 9.45.

(1a,9b-Dihydrophenanthro[9,10-*b*]azirin-1-yl)-2-pyridinylmethanone (**8**).

The 2-pyridinoyl derivative **8** was obtained from **1** and 2-pyridinecarbonyl chloride hydrochloride by a similar procedure, yield 65%, colorless needles, mp 124-126° (from a mixture of ether and hexane); ir (nujol): 1685, 1595 cm^{-1} (amide I and II); ^{1}H nmr (deuteriochloroform): 200 MHz δ 4.41 (s, 2H, H1a, H9b), 7.33-7.48 (m, 5H, H3, H4, H5', H7, H8), 7.68-7.77 (m, 3H, H2, H4', H9), 7.90 (dd, 1H, $J_{3',4'} = 7.8$ Hz, $J_{3',5'} = 1.1$

Hz, H3'), 8.07 (dd, 2H, $J_{3,5} = J_{6,8} = 1.6$ Hz, $J_{4,5} = J_{6,7} = 7.5$ Hz, H5, H6), 8.71 (ddd, 1H, $J_{3',6'} = 0.9$ Hz, $J_{4',6'} = 1.7$ Hz, $J_{5',6'} = 4.7$ Hz, H6'); ms: lc (70 eV particle beam 65°), m/z (relative intensity) 298 ($M^{+\cdot}$, 100), 297, ($C_{20}H_{14}N_2O^{+\cdot}$, 9), 192 ($C_{14}H_{10}N^+$, 18), 178 ($C_{14}H_{10}^{+\cdot}$, 14), 165 ($C_{13}H_9^+$, 46), 106 ($C_6H_4NO^+$, 14), 79 ($C_5H_5N^{+\cdot}$, 86), 78 ($C_5H_4N^+$, 67).

Anal. Calcd. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.36; H, 4.65; N, 9.53.

(1a,9b-Dihydrophenanthro[9,10-*b*]aziridin-1-yl)-6-quinolinylmethanone (**9**).

Under the same conditions **1** and 6-quinolinecarbonyl chloride hydrochloride reacted to give colorless **9** in 85% yield, mp 151-152° (from a mixture of ether and hexane); ir (nujol): 1669 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): 400 MHz δ 4.33 (s, 2H, H1a, H9b), 7.41-7.47 (m, 3H, H3, H3', H8), 7.51 (ddd, 2H, $J_{2,4} = J_{7,9} = 1.4$ Hz, $J_{3,4} = J_{7,8} = 7.4$ Hz, $J_{4,5} = J_{6,7} = 8$ Hz, H4, H7), 7.63 (dd, 2H, $J_{2,3} = J_{8,9} = 7.5$ Hz, $J_{2,4} = J_{7,9} = 1.4$ Hz, H2, H9), 8.11-8.18 (m, 4H, H5, H6, H7', H8'), 8.22 (dd, 1H, $J_{2',4'} = 1.8$ Hz, $J_{3',4'} = 8.9$ Hz, H4'), 8.46 (d, 1H, $J_{5',7'} = 1.8$ Hz, H5'), 9.00 (dd, 1H, $J_{2',3'} = 4.2$ Hz, $J_{2',4'} = 1.8$ Hz, H2'); ms: lc (70 eV particle beam 65°) m/z (relative intensity) 348 ($M^{+\cdot}$, 28), 178 ($C_{14}H_{10}^{+\cdot}$, 100), 177 ($C_{14}H_9^+$, 26), 165 ($C_{13}H_9^+$, 70), 156 ($C_{10}H_6NO^+$, 60), 128 ($C_9H_6N^+$, 32).

Anal. Calcd. for $C_{24}H_{16}N_2O$: C, 82.74; H, 4.62; N, 8.04. Found: C, 82.72; H, 4.89; N, 7.85.

(1a,11b-Dihydrobenz[3,4]anthra[1,2-*b*]azirin-1-yl)-6-quinolinylmethanone (**14**).

The reaction of **11** (prepared from **10**) and 6-quinolinecarbonyl chloride hydrochloride gave colorless **14** in 60% yield, mp 166-168° (from ether-hexane); ir (nujol): 1655 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): 400 MHz δ 4.34 (d, 1H, $J_{1a,11b} = 6.1$ Hz, H1a or H11b), 4.43 (d, 1H, $J_{1a,11b} = 6.1$ Hz, H1a or H1b), 7.42-7.57 (m, 5H, H3, H3', H4, H8, H9), 7.65 (dd, 1H, $J_{2,3} = 7.4$ Hz, $J_{2,4} = 1.2$ Hz, H2), 7.87 (m, 1H, H7 or H10), 7.96 (m, 1H, H7 or H10), 8.09 (s, 1H, H11), 8.10-8.14 (m, 2H, H7', H8'), 8.23 (dd, 1H, $J_{2',4'} = 1.8$ Hz, $J_{3',4'} = 8.9$ Hz, H4'), 8.35 (d, 1H, $J_{4,5} = 7.8$ Hz, H5), 8.47 (d, 1H, $J_{5',7'} = 1.7$ Hz, H5'), 8.61 (s, 1H, H6), 8.99 (dd, 1H, $J_{2',3'} = 4.2$ Hz, $J_{2',4'} = 1.8$ Hz, H2'); ms: lc (70 eV particle beam 65°) m/z (relative intensity) 398 ($M^{+\cdot}$, 38) 228 ($C_{18}H_{12}^{+\cdot}$, 18), 215 ($C_{17}H_{11}^+$, 34), 202 ($C_{16}H_{10}^{+\cdot}$, 33), 156 ($C_{10}H_6NO^+$, 100), 128 ($C_9H_6N^+$, 48).

Anal. Calcd. for $C_{28}H_{18}N_2O$: C, 84.40; H, 4.55; N, 7.03. Found: C, 84.15; H, 4.97; N, 6.84.

trans-1-[9,10-Dihydro-10-(methanesulfonamido)-9-phenanthrenyl]-5-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**16**).

To a solution of 100 mg (0.8 mmole) of thymine in 10 ml of freshly dried and distilled dimethyl sulfoxide, was added under argon atmosphere 110 mg (0.8 mmole) of potassium carbonate and 100 mg (0.37 mmole) of **3** [10]. The mixture was stirred at room temperature for 24 hours. Cold water (50 ml) was added and the organic material was extracted twice with 25 ml of ethyl acetate. The solution was concentrated and chromatographed on silica gel, using a 9:1 mixture of ethyl acetate-hexane as eluent to give 81 mg (55%) of **16** as colorless crystals, mp 284-285°; ^1H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 1.71 (s, 3H, CCH_3), 2.90 (s, 3H, SCH_3), 5.19 (m, 1H, H10; upon addition of deuterium oxide, m is transferred to d, $J_{9,10} = 10.8$ Hz), 5.63 (d, 1H, $J_{9,10} = 10.8$ Hz, H9), 7.04 (d, 1H, $J_{7,8} = 7.6$ Hz, H8), 7.33-7.47 (m, 5H, H2, H3, H6, H6', H7; upon addition of deuterium oxide, proton 6' appears as d at 7.29, $J_{6',CH_3} = 0.9$ Hz), 7.57 (d, 1, $J_{1,2} = 7.1$ Hz, H1), 7.91 (d, 1H, J = 7.3 Hz, H4 or H5), 7.98 (d, 1H, J = 8 Hz, H4 or H5), 8.01 (br s, 1H, SN*H*), 11.45 (br s, 1H, CON*H*); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 12.3 (CH_3 of thymine), 42.1 (SCH_3), 54.3 (overlapping C9 and C10), 109.5 (C5'), 124.4, 124.5, 126.6, 127.4, 128.7, 128.9, 129.0, 129.3, 132.3, 132.6, 133.4, 135.0, 139.8, (C6'), 151.5 (C2'), 164.1 (C4').

Anal. Calcd. for $C_{20}H_{19}N_3O_4S$: C, 60.44; H, 4.82; N, 10.57; S, 8.07. Found: C, 60.15; H, 4.60; N, 10.43; S, 7.80.

trans-4-Amino-1-[9,10-dihydro-10-(methanesulfonamido)-9-phenanthrenyl]-2(3*H*)-pyrimidinone (**17**).

In the same manner described for **16** 160 mg (1.44 mmoles) of cytosine was reacted with 190 mg (0.7 mmole) of **3**. Chromatography on silica gel with ethyl acetate eluted some **15** [10] as the first fraction. The second fraction consisted of 11 mg (4%) of **13** as colorless crystals, mp 168-169°; ^1H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 3.07 (s, 3H, CH_3), 4.75 (t, 1H, $J_{9,10,NH} = 7$ Hz, H10; upon addition of deuterium oxide, the t changed to d), 6.09 (d, 1H, $J_{5',6'} = 5.7$ Hz, H5'), 6.20 (d, 1H, $J_{9,10} = 7$ Hz, H9), 6.89 (br s, 2H, NH_2), 7.29-7.47 (m, 5H, H2, H3, H6, H7, H8), 7.57 (d, 1H, $J_{1,2} = 7.3$ Hz, H1), 7.66 (d, 1H, $J_{10,NH} = 7$ Hz, N*H*), 7.86 (d, 1H, $J_{5',6'} = 5.7$ Hz, H6'), 7.92 (m, 2H, H4, H5); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.7, 55.1, 73.9, 100.1 (C5'), 124.3, 124.4, 128.3, 128.8, 129.1, 129.4, 129.6, 129.8, 133.0, 133.1, 133.2, 133.4, 134.1, 156.8 (C6'), 164.5 (C4'), 165.6 (C2').

Anal. Calcd. for $C_{19}H_{18}N_4O_3S$: C, 59.67; H, 4.74; N, 14.65; S, 8.38. Found: C, 59.42; H, 4.52; N, 14.23; S, 8.05.

trans-4-Amino-5-fluoro-1-[9,10-dihydro-10-(methenesulonamido)-9-phenanthrenyl]-2(3*H*)-pyrimidinione (**18**).

The reaction of **3** and 5-fluorocytosine afforded, after chromatography on silica gel (with ethyl acetate containing 40-60% hexane as eluent), 32% of **18** as colorless crystals; mp 198-199°: ^1H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 3.07 (s, 3, CH_3), 4.75 (t, 1H, $J_{9,10,NH} = 7$ Hz, H10; upon addition of deuterium oxide, t changes to d), 6.12 (d, 1H, $J_{9,10} = 7$ Hz, H9), 7.31-7.48 (m, 7H, H2, H3, H6, H7, H8, NH_2), 7.58 (d, 1H, $J_{1,2} = 7.3$ Hz, H1), 7.64 (d, 1H, $J_{10,NH} = 7$ Hz, N*H*), 7.92 (m, 2H, H4, H5), 7.96 (d, 1H, $J_{6',F} = 3.3$ Hz, H6'); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.6, 55.0, 74.8, 124.4, 124.5, 128.4, 128.8, 129.2, 129.5, 129.6, 129.6, 132.7, 133.1, 133.4, 133.9, 140.4 (d, $J_{6'F} = 20$ Hz, C6'), 142.4 (d, $J_{5',F} = 245$ Hz, C5'), 155.3 (d, $J_{4',F} = 14$ Hz, C4'), 159.8 (d, $J_{2',F} = 1$ Hz, C2').

Anal. Calcd. for $C_{19}H_{17}FN_4O_3S$: C, 56.99; H, 4.28; N, 13.99. Found: C, 57.14; H, 4.44; N, 13.59.

trans-7- and *trans*-9-[9,10-Dihydro-10-(methanesulfonamido)-9-phenanthrenyl]-1*H*-purines **19** and **20**, Respectively.

Reaction of 177 mg (1.47 mmoles) of purine and 200 mg (0.74 mmole) of **3** afforded, after chromatography on silica gel (with ethyl acetate as eluent) a 2.2:1 mixture of the isomeric adducts **19** and **20**. The isomers were separated by a second chromatography on silica gel using ethyl acetate with a gradient of 0-60% hexane as eluent.

Compound **19** was obtained as colorless crystals, mp 272-274°; ^1H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 2.73 (s, 3H, CH_3), 5.25 (d, 1H, $J_{9,10} = 7.5$ Hz, H10), 6.10 (d, 1H, $J_{9,10} = 7.5$ Hz, H9), 7.13 (d, 1H, $J_{7,8} = 7.7$ Hz, H8), 7.34-7.40 (m, 2H, H2, H7), 7.49 (d, 1H, $J_{1,2} = 7.6$ Hz, H1), 7.53-7.58

(m, 2H, H3, H6), 7.91 (br s, 1H, N*H*), 8.03 (d, 1H, J = 7.9 Hz, H4 or H5), 8.11 (d, 1H, J = 7.7 Hz, H4 or H5), 8.19 (s, 1H, H8'), 8.98 (s, 1H, H2'), 9.05 (s, 1H, H6'); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.1, 55.3, 60.0, 124.8, 125.0, 128.7, 128.9, 129.1, 129.2, 129.7, 130.2, 130.4, 132.7, 132.8, 133.6, 142.2, 148.6, 152.6, 160.2 (one aromatic carbon signal is overlapping).

Compound **20** was obtained as colorless crystals, mp 285-287°; ^{1}H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 2.50 (s, 3H, CH_3), 5.48 (d, 1H, $J_{9,10}$ = 9.5 Hz, H10), 6.06 (d, 1H, $J_{9,10}$ = 9.5 Hz, H9), 6.79 (d, 1H, $J_{7,8}$ = 7.6 Hz, H8), 7.27 (t, 1H, $J_{6,7,8}$ = 7.6 Hz, H7), 7.42 (t, 1H, $J_{1,2,3}$ = 7.5 Hz, H2), 7.48-7.52 (m, 2H, H3, H6), 7.56 (d, 1H, $J_{1,2}$ = 7.5 Hz, H1), 8.00 (br s, 1H, N*H*), 8.01 (d, 1H, J = 8 Hz, H4 or H5), 8.06 (d, 1H, J = 7.9 Hz, H4 or H5), 8.23 (s, 1H, H8'), 8.94 (s, 1H, H2' or H6'), 9.20 (s, 1H, H2' or H6'); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.3, 54.7, 58.2, 124.6, 124.6, 127.4, 127.9, 128.9, 128.9, 129.4, 129.8, 131.5, 132.6, 133.0, 133.9, 134.1, 146.5, 148.4, 151.3, 152.2.

Anal. of **19** and **20** Calcd. for $C_{20}H_{17}N_5O_2S$: C, 61.37; H, 4.38; N, 17.89; S, 8.19. Found: C, 61.09; H, 4.46; N, 17.53; S, 7.94.

trans-6-Chloro-9-[9,10-dihydro-10-(methanesulfonamido)-9-phenanthrenyl]-1*H*-purine (**21**).

6-Chloropurine and **3** were reacted as described above to give **21** in 72% yield, colorless crystals, mp 258-260°; ^{1}H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 2.62 (s, 3H, CH_3), 5.45 (m, 1H, H10; upon addition of deuterium oxide, d, $J_{9,10}$ = 9.6 Hz), 6.05 (d, 1H, $J_{9,10}$ = 9.6 Hz, H9), 6.83 (d, 1H, $J_{7,8}$ = 7.7 Hz, H8), 7.26 (t, 1H, $J_{6,7,8}$ = 7.7 Hz, H7), 7.42 (t, 1H, $J_{1,2,3}$ = 7.4 Hz, H2), 7.48-7.52 (m, 2H, H3, H6), 7.55 (d, 1H, $J_{1,2}$ = 7.4 Hz, H1), 8.00 (d, 1H, $J_{3,4}$ = 7.4 Hz, H4), 8.01 (br s, 1H, N*H*), 8.05 (d, 1H, $J_{5,6}$ = 7.7 Hz, H5), 8.34 (s, 1H, H8'), 8.78 (s, 1H, H2'); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.4, 54.7, 59.1, 124.6, 124.7, 127.5, 127.8, 128.9, 129.0, 129.5, 129.9, 131.2, 131.5, 132.6, 133.0, 133.6, 147.1, 149.6, 151.7, 152.2.

Anal. Calcd. for $C_{20}H_{16}ClN_5O_2S$: C, 56.40; H, 3.79; Cl, 8.32; N, 16.44; S, 7.53. Found: C, 56.11; H, 3.86; Cl, 8.31; N, 16.14; S, 7.62.

trans-9-[9,10-Dihydro-10-(methanesulfonamido)-9-phenanthryl]-6(1*H*)-purinamine (**22**).

To a solution of 250 mg (1.85 mmoles) of adenine in 16 ml of dry dimethyl sulfoxide was added under argon atmosphere 377 µl of 1,5-diazabicyclo[3.4.0]non-5-ene and 250 mg (0.92 mmole) of **3**. The mixture was stirred at room temperature for 24 hours. Cold water (50 ml) was added and the organic material was extracted twice with 30 ml of ethyl acetate. The organic solution was dried, concentrated and the residue was chromatographed on silica gel using ethyl acetate and 0-20% hexane as eluent, yield 51 mg (13%) of colorless **22**, mp 181-182°; ^{1}H nmr (hexadeuteriodimethyl sulfoxide): 400 MHz δ 2.46 (s, 3H, CH_3), 5.46 (m, 1H, H10; upon addition of deuterium oxide, d, $J_{9,10}$ = 9.2 Hz), 5.88 (d, 1H, $J_{9,10}$ = 9.2 Hz, H9), 6.77 (d, 1H, $J_{7,8}$ = 7.6 Hz, H8), 7.28 (t, 1H, $J_{6,7,8}$ = 7.6 Hz, H7), 7.32 (br s, 2H, NH_2), 7.43 (t, 1H, $J_{1,2,3}$ = 7.4 Hz, H2), 7.47-7.52 (m, 2H, H3, H6), 7.56 (d, 1H, $J_{1,2}$ = 7.4 Hz, H1), 7.73 (s, 1H, H8'), 7.96 (d, 1H, $J_{10,NH}$ = 6.6 Hz, N*H*), 8.00 (d, 1H, J = 7.7 Hz, H4 or H5), 8.04 (d, 1H, J = 7.8 Hz, H4 or H5), 8.14 (s, 1H, H2'); ^{13}C nmr (hexadeuteriodimethyl sulfoxide): 100 MHz δ 41.3, 54.8, 58.0, 119.2, (C5'), 124.6, 124.6, 127.5, 128.1, 128.9, 129.0, 129.4, 129.7, 132.1, 132.7, 133.0, 134.3, 140.7, (C8'), 149.7, (C4'), 152.8, (C2'), 156.1, (C6').

Anal. Calcd. for $C_{20}H_{18}N_6O_2S$: C, 59.10; H, 4.46; S, 7.89. Found: C, 58.83; H, 4.66; S, 7.64.

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