Polycyclic Arene Sulfides. Preparation of 1a,2,3,11b-Tetrahydrobenz-[5,6]anthra[1,2-*b*]thiirene, 6b,7a,8,9-Tetrahydrobenzo[10,11]-chryseno[1,2-*b*]thiirene, and 7,8,8a,9a-Tetrahydrobenzo-[10,11]chryseno[3,4-*b*]thiirene

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The title compounds **5**, **7** and **9** which are the first arene sulfides of 7,8-dihydrobenz[*a*]anthracene, 8,9- and 10,11-dihydrobenzo[*a*]pyrene, respectively, have been synthesized by treatment of the corresponding arene oxides **4, 6** and **8** with *N,N*-dimethylthioformamide in the presence of catalytic amounts of trifluoroacetic acid.

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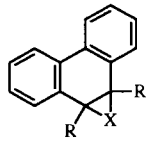
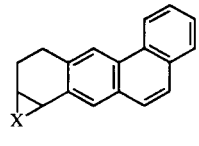
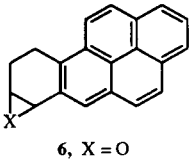
Arene oxides have been shown to be important metabolites of polycyclic aromatic hydrocarbons. Their interaction with nucleic acids, and their involvement in the induction of chemical mutagenesis and carcinogenesis have been well established and reviewed [1]. Arene imines, which are the nitrogen analogs of the arene oxides, seem to be of similar relevance to cancer research. It has been suggested that they are formed metabolically by interaction of the epoxides with cellular nitrogen-nucleophiles [2]. These compounds have been found to be extremely potent mutagens, resistant to detoxifying enzymes [3] and to react with DNA components [4]. In contrast, to the large volume of publications devoted to the oxides and imines only very little information is available on the corresponding polycyclic aromatic episulfides. The reason for this is probably associated with the instability of the *aromatic* thiiranes. Although the syntheses of 3,8-dithiatricyclo[5.1.0.$0^{2,4}$]-oct-5-ene [5] and 3,6,9-trithiatetracyclo[6.1.0.$0^{2,4}$.$0^{5,7}$]-nonane [6] (that may in a way be regarded as arene sulfides), have been announced in the early literature, attempts to prepare *polycyclic* arene sulfides has so far been unsuccessful and resulted in the formation of either sulfur-free aromatic compounds or in the generation of thiophenols. Polycyclic aromatic episulfides are cited in the literature mainly as reaction intermediates in the transformation of various sulfur-containing compounds to aromatic hydrocarbons [7]. Nevertheless, because it is assumed that arene sulfides might result from the interaction of arene oxides with cellular sulfur nucleophiles, substantial efforts have been made, in various laboratories, to prepare phenanthrene- and other polycyclic arene sulfides by the common methods established for non-aromatic thiiranes [8]. In our laboratories we attempted the preparation of phenanthrene 9,10-sulfide (9,10-dihydrophenanthrene-[9,10]thiirene (**1**)) by treatment of the parent hydrocarbon with (a) sulfuryl chloride and basic sodium sulfide, (b) various halothiocyanogens and bases, and (c) phthalimide *N*-sulfonyl chloride followed by lithiumaluminum hydride reduction. We tried in vain to obtain **1** from the corresponding epoxide **2** by treatment with (i) alkali thiocyanate and thiocyanic acid under a variety of conditions, (ii) thiourea, followed by reaction with an organic base, (iii) either 3-methylbenzothiazol-2-thione, *N,N*-dimethylthioformamide, or triphenylphosphine sulfide in the presence of trifluroacetic acid, (iv) aqueous sodium sulfide followed by dehydration with diethoxytriphenyl phosphine; and (v) phosphorus pentasulfide in the presence of either potassium carbonate or triethylamine. Attempts were also made to prepare **1** by photolysis of *cis*-stilbene sulfide, and by interaction of 2,2'-bis(diazomethyl)[1,1'-biphenyl] with elemental sulfur. In light of the observation that methoxyl groups increase the stability of certain episulfides [9] we repeated the above experiments using various mono- and polymethoxyphenanthrenes, phenanthrene oxides and derivatives of higher polycyclics as starting materials. Because of the exceptional stability of 9,10-diarylphenanthrene 9,10-oxides (see *e.g.*, [10]), the formation of thiiranes of type **3** was attempted. However, all efforts to substitute the oxygen of the oxirane ring in **2** by sulfur, as well



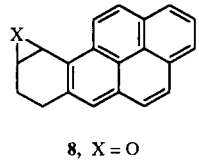
1, R = H, X = S
2, R = C_6H_5, X = O
3, R = C_6H_5, X = S



4, X = O
5, X = S



6, X = O
7, X = S



8, X = O
9, X = S

as to cyclize 2,2'-bis(thiobenzoyl)[1,1'-biphenyl] (formed from 2,2'-bis(benzoyl)[1,1'-biphenyl] and the Lawesson Reagent [11], led only to the formation of mixtures of 9,10-diphenylphenanthrene, 10,10-diphenyl-9-phenanthrenone and 10,10-diphenyl-9-phenanthrenethione. To the best of our knowledge, other researchers met similar difficulties in their attempts to prepare polycyclic arene sulfides. The few examples of polycyclic thiiranes reported in the literature (*e.g.*, 1a,7a-dihydronaphtho[2,3-*b*]thiirene-1a,7a-dicarboxylic acid [12] and 1a,7a-dihydrothiireno[*b*]-quinoxaline [13]) were subsequently proven to have different structures [14], and one of the lithiation products of 5,7-dihydrodibenzo[*c,e*]thiepin that was tentatively assigned as **1** [15] has now been shown to be an error.

It seems therefore, that if the sulfur analogs of arene oxides are formed during the metabolism of carcinogenic polycyclic aromatic compounds, they might be too unstable to be of biological significance. However, thiiranes derived from carcinogenic hydroaromatics [16] that resemble alicyclic thiiranes, may be more likely to withstand ambient conditions and to play a role in carcinogenicity.

In this paper we report the syntheses of the title compounds **5, 7** and **9** which are the sulfide derivatives of 10,11-dihydrobenz[*a*]anthracene, and 7,8- and 9,10-dihydrobenzo[*a*]pyrene. When 1a,2,3,11b-tetrahydrobenz-[5,6]anthra[1,2-*b*]oxirene (**4**) (which was prepared according to the known procedure [17]) was treated at *room temperature* with two equivalents of *N,N*-dimethylthioformamide followed by addition of 0.1 equivalent of trifluoroacetic acid, episulfide **5** was obtained in 32% yield provided that the addition of the acid was in the form of a fine continuous stream obtained with the aid of a micro-syringe during 10 minutes. Under the conditions of Takido *et al* [18] where the reaction mixture has been heated at 60° no **5** could be isolated. Although the yield of **5** was rather low, the application of *N,N*-dimethylthioformamide proved superior to the other methods of conversion of epoxides to episulfides described above.

In the same manner 6b,7a,8,9-tetrahydrobenzo-[10,11]chryseno[1,2-*b*]oxirene (**6**) [19] and the bay-region oxide, 7,8,8a,9a-tetrahydro[10,11]chryseno[3,4-*b*]oxirene (**8**) were converted into the corresponding arene sulfides **7** and **9**. The structures of the thiiranes were established by virtue of their elemental analyses and their characteristics ^{1}H nmr. The episulfide ring protons appear between 3.80 and 4.98 ppm. These chemical shifts are in the same region of those recorded for the corresponding epoxides. While thiiranes **5** and **7** were found to be perfectly stable at room temperature, compound **9** slowly lost elemental sulfur when left to stand for several days. It did not deteriorate even after four months however, when stored in the freezer at -18°. Attempts to dehydrogenate the three episulfides by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in benzene, resulted in their quantitative transformation to the corresponding sulfur-free aromatic hydrocarbons.

EXPERIMENTAL

1a,2,3,11b-Tetrahydrobenz[5,6]anthra[1,2-*b*]thiirene (**5**).

Into a solution of 200 mg (0.82 mmole) of 1a,2,3,11b-tetrahydrobenz[5,6]anthra[1,2-*b*]oxirene (**4**) [17] and 138 µl (1.65 mmoles) of *N,N*-dimethylthioformamide in 10 ml of dry dichloromethane, was syringed during 10 minutes, 6.2 µl (8.2 x 10^{-2} mmole) of trifluoroacetic acid. The mixture was stirred under nitrogen atmosphere until the entire oxide was consumed (1 hour, as indicated by tlc on silica gel with a mixture of 10% ether and 90% hexane as eluent). The solvent was evaporated under reduced pressure and the residue was dissolved in 5 ml of tetrahydrofuran. Addition of ice cold deionized water precipitated 75 mg (32%) of colorless **5**, mp 126-128°; ^{1}H nmr (deuteriochloroform): 200 MHz δ 2.21 (m, 1H, H2), 2.54 (m, 1H, H2'), 2.81 (dd, 1H, $J_{1a,3}$ = 4.4 Hz, $J_{2,3}$ = 15.5 Hz, H3), 3.09 (m, 1H, H3'), 3.80 (m, 1H, H1a), 4.22 (d, 1H, $J_{1a,11b}$ = 6.4 Hz, H11b), 7.57-7.69 (m, 4H, H6, H7, H9, H10), 7.87 (dd, 1H, $J_{6,8}$ = 1.8 Hz, $J_{7,8}$ = 7.5 Hz, H8), 7.92 (s, 1H, H11), 8.34 (s, 1H, H4), 8.62 (dd, 1H, $J_{5,7}$ = 1.7 Hz, $J_{5,6}$ = 8.0 Hz, H5); ms: lc (70 eV, particle beam 65°) m/z (relative intensity) 230 [(M-S)$^{+\cdot}$, 100], 229 ($C_{18}H_{13}^+$, 81), 228 ($C_{18}H_{12}^{+\cdot}$, 51), 215 ($C_{17}H_{11}^+$, 34).

Anal. Calcd. for $C_{17}H_{14}S$: C, 82.40; H, 5.38; S, 12.22. Found: C, 82.14; H, 5.41; S, 11.91.

6b,7a,8,9-Tetrahydrobenzo[10,11]chryseno[1,2-*b*]thiirene (**7**).

In a similar manner, 1.0 g (3.7 mmoles) of 6b,7a,8,9-Tetrahydrobenzo[10,11]chryseno[1,2-*b*]oxirene (**6**) [19] and 0.63 ml of *N,N*-dimethylthioformamide was treated with 29 µl (0.37 mmole) of trifluoroacetic acid. The reaction was completed after 75 minutes and was worked up as above to give 560 mg (52%) of colorless **7**, mp 118-120°; ^{1}H nmr (deuteriochloroform): 200 MHz δ 2.32 (m, 1H, H8), 2.77 (m, 1, H8'), 3.10 (m, 1H, H9), 3.61 (dd, 1H, $J_{7a,9'}$ = 4.3 Hz, $J_{8,9'}$ = 15.8 Hz, H9'), 3.92 (m, 1H, H7a), 4.44 (d, 1H, $J_{6b,7a}$ = 6.5 Hz, H6b), 7.93-8.28 (m, 8H, H1, H2, H3, H4, H5, H6, H10, H11); ms: lc (70 eV, particle beam 65°) m/z (relative intensity) 286 [($M^{+\cdot}$, 5), 254 ($C_{20}H_{14}^{+\cdot}$, 84), 253 ($C_{20}H_{13}^+$, 100), 252 ($C_{20}H_{12}^{+\cdot}$, 82), 239 ($C_{19}H_{11}^+$, 27).

Anal. Calcd. for $C_{20}H_{14}S$: C, 83.87; H, 4.93; S, 11.20. Found: C, 83.57; H, 4.91; S, 10.90.

7,8,8a,9a-Tetrahydrobenzo[10,11]chryseno[3,4-*b*]thiirene (**9**).

The reaction of 560 mg (2.1 mmoles of 7,8,8a,9a-tetrahydro[10,11]chryseno[3,4-*b*]oxirene (**8**) [19] with 0.353 ml (4.1 mmoles) of *N,N*-dimethylthioformamide in the presence of 16 µl (0.21 mmole) of trifluoroacetic acid gave after 1 hour 220 mg (37%) of **9** as pale yellow crystals, mp 115-116° (from hexane); ^{1}H nmr (deuteriochloroform): 400 MHz δ 2.35 (m, 1H, H8), 2.65 (m, 1H, H8'), 2.99 (dd, 1H, $J_{7,8}$ = 15.6 Hz, $J_{7,8a}$ = 4.1 Hz, H7), 3.23 (m, 1H, H7'), 3.92 (m, 1H, H8a), 4.98 (d, 1H, $J_{8a,9a}$ = 6.5 Hz, H9a), 7.86 (s, 1H, H6), 7.92-8.05 (m, 3H, Ar*H*), 8.15-8.19 (m, 3H, Ar*H*), 8.51 (d, 1H, $J_{10,11}$ = 9.3 Hz, H10); ms: lc (70 eV, particle beam 65°), m/z (relative intensity) 254 [(M-S)$^{+\cdot}$, 100],

253 ($C_{20}H_{13}^+$, 54), 252 ($C_{20}H_{12}^{+\cdot}$, 61), 239 ($C_{19}H_{11}^+$, 49).

Anal. Calcd. for $C_{20}H_{14}S$: C, 83.87; H, 4.93; S, 11.20. Found: C, 83.61; H, 5.02; S, 10.88.

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