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IDENTIFICATION OF SULFUR HETEROCYCLES IN COAL LIQUIDS AND
SHALE OILS

Technical Progress Report for the Period August 1, 1980—May 1, 1981

By
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MASTER

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U. S. DEPARTMENT OF ENERGY

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TECHNICAL PROGRESS REPORT

For Period

8/1/80 - 5/1/81

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Prepared for

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Office of Health and Environmental Research

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ABSTRACT

The sulfur heterocycle separation scheme which was described in the progress report for the last period was evaluated for quantitative recovery of individual components. The results indicate that recoveries can range from 10% to ~30% depending on the structure of the compound. For instance, dibenzothiophene is recovered to the extent of 30% while anthra[2,3-b]thiophene was found to oxidize at the 6 and 11 positions on the ring during the oxidation step, and subsequent reduction to the sulfide was low.

During this period, 23 unsubstituted sulfur-containing heterocyclic ring systems were synthesized in order to confirm GC/MS identifications and for biological testing. Since a number of the isomeric 4-ring sulfur heterocycles co-elute on SE-52 capillary columns, mixed phases containing SE-52 and a liquid crystal (BBBT) were used to resolve those compounds for positive identification. Of the thirteen possible 4-ring compounds, only benzo[b]naphtho[2,1-d]thiophene, benzo[b]naphtho[1,2-d]thiophene, and benzo[b]naphtho[2,3-d]thiophene are present in the studied coal liquids and shale oils.

The four possible 3-ring heterocycles and the thirteen possible 4-ring heterocycles were tested for mutagenic activity in the histidine reversion (Ames assay) system. One of the 3-ring isomers, naphtho[1,2-b]thiophene, and six of the 4-ring isomers induced mutations in Salmonella test strains. One of these compounds, phenanthro[3,4-b]thiophene, displayed approximately the same mutagenic activity as benzo[a]pyrene.

A two-step adsorption chromatographic procedure was developed in order to fractionate synthetic fuels into various chemical-type classes

for studying the relative concentrations and mutagenic activities of the various types. An SRC-II Heavy Distillate was fractionated into aliphatic hydrocarbons, polycyclic aromatic hydrocarbons, sulfur heterocycles, indoles and carbazoles, azaarenes, and amino polycyclic aromatic hydrocarbons. It was found that the amino-PAH fraction contained most of the mutagenic activity.

A survey was made for compounds containing both nitrogen and sulfur heteroatoms in their structures. A number of these compounds were detected by GC using nitrogen- and sulfur-selective detection.

I. ANALYTICAL CHEMISTRY

A. Quantitative Evaluation of the Sulfur Heterocycle Separation Scheme

The sulfur heterocycle separation scheme for coal liquids and shale oils developed in our laboratory (see previous progress report) consists of the following steps; (a) oxidation of sulfides to sulfones with 30% H_2O_2 , (b) extraction of PAH from the oxidized solution, (c) silica gel chromatography for the separation of sulfones and oxidized PAH from the unreacted PAH, (d) reduction of sulfones back to sulfides with LiAlH_4 , (e) extraction of PAH from the reduced solution, and (f) silica gel chromatography for the separation of sulfides from hydroquinones or quinones.

Ideally, the oxidation and reduction steps should selectively and completely convert the sulfides to sulfones and the sulfones back to sulfides, respectively. Furthermore, the extraction and adsorption chromatographic steps should exhibit 100% recovery at least for sulfides and sulfones. However, certain positions on the aromatic rings of some sulfur heterocycles are as reactive as the sulfur position to oxidation by H_2O_2 ,⁽¹⁾ and sulfur heterocyclic quinones may be produced. Under severe reduction conditions with LiAlH_4 , it is also possible that the thiophene ring would be reduced and sulfide would be finally recovered as hydrogenated thiophenes. Consequently, the analytical results would be unrepresentative of the original components in the real sample. Also, these side reactions could complicate the subsequent separation steps. In the adsorption chromatographic steps, irreversible adsorption of sulfides or sulfones on silica gel could also cause some non-recover-

able losses. The purpose of this study was to investigate the recovery for each step in the sulfur heterocycle separation scheme and to then estimate the total recovery of the heterocycle fraction.

Because of the complexity of the sulfur heterocycle fractions in the coal liquids and shale oils, only several representative standard sulfide heterocycles were selected for the evaluation of the sulfur heterocycle separation scheme.

Experimental:

To determine the sulfides and sulfones produced through the sulfur heterocycle separation scheme, a high performance liquid chromatographic (HPLC) system was used. The system consisted of a Model 6000 solvent delivery system (Waters Assoc., Milford, MA, USA), 3 cm x 2 mm i.d. Bondapak/Porasil precolumn (Waters), 25 cm x 4.6 mm i.d. Vydac 210 TP 4.6 Reversed-Phase C_{18} main column (SEP/A/RATIONS Group, P.O. Box 867, 16640 Spruce Street, Hesperia, CA 92345), a UV detector (Waters) operated at 254 nm, and a Model U6K Universal Liquid Chromatograph Injector (Waters), which allows the injection of samples up to 1 ml volume. The precolumn and main column were held at ambient temperature.

The mobile phase compositions were 80% CH_3CN/H_2O for the determination of sulfides, and 50% CH_3CN/H_2O for sulfones, with flow rates of 1 ml/min.

The standard compounds, dibenzothiophene, anthra[2,3-b]thiophene, 3-methylphenanthro[2,1-b]thiophene and phenanthro[2,1-b]thiophene, were used for evaluation of the oxidation and following separation steps; and dibenzothiophene sulfone, 6,11-diketoanthra[2,3-b]thiophene sulfone, and 3-methylphenanthro[2,1-b]thiophene sulfone were used for evaluation of the reduction and following separation steps.

A solution containing 15.4 mg of dibenzothiophene, 6.3 mg of anthra-[1,2-b]thiophene, and 14.8 mg of 3-methylphenanthro[2,1-b]thiophene in 50 ml benzene were prepared for the evaluation of the oxidation step and the extraction and adsorption chromatographic steps after reduction. For the evaluation of the reduction step and the extraction and adsorption chromatographic steps after oxidation, a solution containing 18.2 mg of dibenzothiophene sulfone, 8.0 mg of 6,11-diketoanthra[1,2-b]thiophene sulfone, and 16.8 mg of 3-methylphenanthro[2,1-b]thiophene sulfone were prepared. Two other solutions prepared were 200 mg dibenzothiophene in 100 ml benzene and 23.5 mg dibenzothiophene in 10 ml benzene for the evaluation of the oxidation step.

In the extraction step after the reduction, a gummy precipitate or emulsion was created when deionized water was added to decompose the unreacted LiAlH_4 . This complicated the extraction or separation of the PAH. To solve this problem, a 10% HCl solution was added to dissolve the precipitate $\text{Al}(\text{OH})_3$. Two easily separable organic and water layers were produced. The recoveries obtained using this new alternative extraction procedure was compared with those of the previous method using the standard sulfur heterocycles.

Results and Discussion

Table I shows the results of the oxidation and subsequent steps. For dibenzothiophene, the conversion is low when the starting material is only several mg, but high when the amount of starting material is high. For anthra[2,3-b]thiophene, 6,11-diketoanthra[1,2-b]thiophene sulfone was detected as the major product. This indicates that the 6 and 11 positions of anthra[2,3-b]thiophene are reactive. Other peaks in

the HPLC chromatograms remain to be identified. The conversion of 3-methylphenanthro[2,1-b]thiophene to its sulfone is about 30%.

Table II shows the results of the reduction and the following extraction steps. Over 90% of the dibenzothiophene sulfone was reduced by LiAlH_4 to dibenzothiophene, while about 60% of the 3-methylphenanthro[2,1-b]thiophene sulfone was converted to its sulfide. Longer reduction times only slightly increase the conversion.

Because the major product of the oxidized anthra[1,2-b]thiophene was 6,11-diketoanthra[1,2-b]thiophene sulfone, its conversion back to anthra[1,2-b]thiophene by LiAlH_4 was checked. No anthra[1,2-b]thiophene was found in the HPLC chromatograms. However, other peaks remain to be identified. Possible products are 6,11-dihydroxyanthra[1,2-b]thiophene and 2,2,3,3-tetrahydroanthra[1,2-b]thiophene. Tominaga (1) found that the carbonyl groups on the 6 and 11 positions are not easily reduced (10%) with LiAlH_4 . As a result, sulfur heterocycles with reactive positions such as these would not be recovered well when subjected to the whole sulfur heterocycle separation scheme.

Table III shows the results of the individual extraction and adsorption chromatographic steps. The recoveries of the two extraction steps were close to 90%. The values in parentheses represent the recoveries of the new alternative extraction procedure (step 5 with 10% HCl solution added to dissolve $\text{Al}(\text{OH})_3$). Better recoveries show that the addition of 10% HCl solution does not adversely affect the recovery. In the old procedure, the gummy precipitate could entrap some PAH and cause some loss of recovery; on the other hand, if an emulsion is produced, it would be difficult to separate the organic and water layers.

There is essentially no loss in the adsorption chromatographic step after the reduction, while some loss occurs in the adsorption chromatographic step after oxidation. Irreversible adsorption of more polar compounds, such as the ketones, could occur on the silica gel.⁽²⁾

According to the above results, the recoveries of various sulfur heterocycles subjected to the whole sulfur heterocycle separation scheme can be roughly estimated; about 30% recovery for dibenzothiophene, 12% for 3-methylphenanthro[2,1-b]thiophene, and 25% for anthra[2,3-b]thiophene (assuming that 10% of the 6,11-diketoanthra[1,2-b]thiophene sulfone can be reduced to anthra[2,3-b]thiophene, 90% of anthra[1,2-b]thiophene sulfone can be reduced to anthra[1,2-b]thiophene, and 90% recovery can be obtained for the extraction step after oxidation).

The extrapolation of these test results to the recoveries expected for the sulfur heterocycle fractions of synthetic fuels is not straightforward. However, these results do indicate several problems associated with this procedure. Recovery experiments are presently being conducted on the actual synfuel samples.

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Table I. Recoveries of the Sulfur Heterocycle Separation Scheme --
Oxidation and Extraction

Compound	No.	Amount(mg)	Product	Conversion (%)
Dibenzothiophene	1	3.1	Dibenzothiophene sulfone	35.3%
	2	7.7	Dibenzothiophene sulfone	39.5%
	3	100	Dibenzothiophene sulfone	96.8%
Anthra[1,2- <u>b</u>]- thiophene	1	1.3	Anthra[2,3- <u>b</u>]thiophene* sulfone	--
			6,11-diketoanthra- [1,2- <u>b</u>]thiophene sulfone	73.3%
	2	3.2	Anthra[1,2- <u>b</u>]thiophene sulfone	--
			6,11-diketoanthra[1,2- <u>b</u>]- thiophene sulfone	80.5%
3-methylphenan- thro[2,1- <u>b</u>]- thiophene	1	3.0	3-methylphenanthro- [2,1- <u>b</u>]thiophene sulfone	34.5%
	2	7.4	3-methylphenanthro- [2,1- <u>b</u>]thiophene sulfone	24.0%

*Because of the lack of standard compounds some peaks in the HPLC chromatogram were not identified yet.

Table II. Recoveries of the Sulfur Heterocycle Isolation Scheme --
Reduction and Extraction

Compound	Amount (mg)	Reaction Time (h)	Product	Conversion (%)
Dibenzothiophene sulfone	9.1	3	Dibenzothiophene	91.6%
		3	Dibenzothiophene	91.0%
		6	Dibenzothiophene	89.9%
		10	Dibenzothiophene	93.5%
6,11-Diketoanthra-[1,2-b]thiophene sulfone	4.0	3	Anthra[1,2-b]-thiophene	--
		3	Anthra[1,2-b]-thiophene	--
		6	Anthra[1,2-b]-thiophene	--
		10	Anthra[1,2-b]-thiophene	--
3-methylphenanthro-[2,1-b]thiophene sulfone	8.4	3	3-methylphenanthro-[2,1-b]thiophene	68.6%
		3	3-methylphenanthro-[2,1-b]thiophene	55.7%
		6	3-methylphenanthro-[2,1-b]thiophene	56.4%
		10	3-methylphenanthro-[2,1-b]thiophene	59.1%

*Other HPLC peaks were not yet identified.

Table III. Recoveries of the Sulfur Heterocycle Isolation Scheme --
Extraction and Adsorption Chromatography

Step	Compound	Amount (mg)	Recovery (%)
2. extraction after oxidation	Dibenzothiophene sulfone	2	89.5
3. adsorption chromatography after oxidation	Dibenzothiophene sulfone	0.36	83.4
		0.73	85.6
		2.0	99.8
	6,11-diketoanthra[1,2-b]thiophene sulfone	0.16	103.8
		0.32	105.9
	3-methylphenanthro[2,1-b]thiophene	0.34	84.7
		0.67	80.7
5. extraction after reduction	Dibenzothiophene	3.1	88.9 (95.4)*
	Anthra[1,2-b]thiophene	1.3	83.5 (91.0)*
	3-methylphenanthro[2,1-b]thiophene	3.0	89.1 (99.6)*
6. adsorption chromatography after reduction	Anthra[1,2-b]thiophene	4	95.4
	Anthra[1,2-b]thiophene	10	105.8
	3-methylphenanthro[2,1-b]thiophene	4	103.4
	3-methylphenanthro[2,1-b]thiophene	10	106.8

*Values in parentheses were obtained by an alternative procedure in which a 10% HCl was added to dissolve the $\text{Al}(\text{OH})_3$ precipitate of the decomposed LiAlH_4 solution.

B. Use of Liquid Crystal Capillary Columns for the Resolution of Isomeric Sulfur Heterocycles.

Although progress has been gained in the determination of polycyclic aromatic hydrocarbons (PAH) in coal liquids and shale oils by capillary column gas chromatography and gas chromatography/mass spectrometry, problems still exist in the identification of isomers which co-elute in GC and show identical mass spectra. As the ring number of the PAH increases, the identification of isomers become more difficult because of the geometrically increasing number of isomers. A useful approach in separating these isomers is the use of a highly selective liquid crystal column⁽¹⁾ which separates compounds according to their shape. However, the disadvantage in using a liquid crystal as the stationary phase is that the column usually exhibits poor efficiency. To increase the efficiency while at the same time maintaining its high selectivity is the approach that has been sought to solve this problem. Recently, Laub, et al.⁽²⁾ have demonstrated that blended stationary phases of liquid crystal and gum phases, such as N,N'-bis(p-butoxybenzylidene)- α,α' -bi-p-toluidine (BBBT) and SE-52, could improve the selectivity while maintaining the efficiency of columns for the separation of PAH.

A similar approach has been taken in this laboratory to improve the separation of isomeric sulfur heterocycles isolated from coal liquids and shale oils. Capillary columns coated with SE-52 and BBBT mixtures were used to separate the 4-ring sulfur heterocycle isomers.

EXPERIMENTAL

Column Preparation

Corning Pyrex glass was drawn with a Shimadzu GDM-1B glass-drawing machine into capillary tubes of 90m to 120 m lengths with different i.d. (0.2 mm, 0.26 mm, and 0.3mm). The capillary columns were first dynamically leached with 50 ml of 20% HCl at 105°C for approximately 48 hours, baked at 400°C for 12 hours, leached again with 20% HCl for another 48 hours, rinsed with deionized water, and then dried at 150°C for 12 hours.⁽³⁾ After leaching, the columns were cut into 20 m in length and dynamically silylated⁽⁴⁾ with a 5:1 mixture of hexamethyldisilazane (HMDS) and trimethylchlorosilane (TMCS) (Applied Science Labs., State College, PA, U.S.A.) at 400°C for 48 hours. The columns were coated statically⁽⁵⁾ with SE-52, 94% SE-52 and 6% BBT, 80% SE-52 and 20% BBT, or 50% SE-52 and 50% BBT, respectively. (BBT Liquid crystal; 180°C nematic → 303°C.) Appropriate amounts of stationary phases were dissolved in methylene chloride such that a 0.15- μ m thick film was deposited on 0.2 mm i.d. columns and 0.25- μ m film on 0.26 mm i.d. and 0.3 mm i.d. columns.

Gas Chromatography

A Perkin-Elmer Sigma 2 or Sigma 3B gas chromatograph equipped with FID and/or FPD was used. A Hewlett-Packard 5880A gas chromatograph equipped with only an FID was used to run chromatograms for the computation of the retention indices.⁽⁶⁾ A Hewlett-Packard 5982A GC/MS/DS equipped with SE-52 capillary column was also used occasionally to obtain mass spectral information for the confirmation of peak identifications. Helium carrier gas was used at a linear velocity of 50 cm/sec (measured at 40°C).

Samples

Solutions containing individual isomers of 4-ring sulfur heterocycles were prepared in methylene chloride. A solution containing all thirteen sulfur heterocycle isomers in hand was prepared. Another solution containing 6 difficult-to-separate isomers by SE-52 was also prepared.

RESULTS AND DISCUSSIONS

Although the liquid crystal column separates compounds in terms of their shapes at its nematic state, we found that a mild temperature programming on the column would not spoil the effect of the separation capability of the liquid crystal columns. Therefore one-ramp or two-ramp temperature programming from 40°C up to 220°C was used. The condensation of the injected sample at low temperature (40°C) at the beginning of the column reduced the band broadening caused by injection and improved the resolution.

Figure 1-a, 1-b, and 1-c show the chromatograms of the mixture of 13 isomers of 4-ring sulfur heterocycles on 0.2 mm x 20 m SE-52, 94% SE-52 + 6% BB BT, and 80% SE-52 + 20% BB BT columns. From SE-52 to 80% SE-52 + 20% BB BT columns, the column efficiency was reduced (band broadening), while the selectivity improved the resolution from 8 peaks for SE-52 to 10 peaks with two additional shoulder peaks for the 80 SE-52 + 20% BB BT. The third and fourth peaks consist of 6 sulfone heterocycles; phenanthro[9,10-b]thiophene, phenanthro[4,3-b]thiophene, anthra[1,2-b]thiophene and benzo[b]naphtho[2,3-d]thiophene in the third peak and phenanthro[2,3-b]thiophene and phenanthro[1,2-b]thiophene in the fourth peak. The chromatograms of this six-isomer mixture on the three different columns

are shown in Figures 2-a, 2-b, and 2-c respectively. The increasing separation power of columns by adding BBT to the SE-52 gum phase can be clearly seen. Figure 3 shows the complete separation of the six isomers with a 50% SE-52 + 50% BBT column (20 m x 0.26 mm i.d.). For the determination of PAC in complete coal liquids or shale oils, relatively large diameter columns (0.3 mm i.d.) coated with 0.25 μ m film of SE-52 to prevent overloading of the columns are used. Therefore, another 0.26 mm i.d. column coated with 0.25 μ m film of 50% SE-52 + 50% BBT was prepared. The column performance of the two above mentioned columns are shown in Figure 3-a and 3-b. Only 8 peaks appear in the chromatogram from the SE-52 column, while 11 peaks are obtained with the 50% SE-52 + 50% BBT column. The retention orders of the thirteen isomers are shown in the last two columns of Table I. Also shown in Table II are the retention indices of the isomers on the SE-52 column (column 4) and the retention time of isomers on the 50% SE-52 + 50% BBT column. Notice that compounds numbered 2,3,6 and 7 are not separated with the SE-52 column, but are separated with the 50% SE-52 + 50% BBT column (see Figure 4-a and 4-b); compounds 4 and 9 are not separated with the SE-52 column, but are separated with the 50% SE-52 + 50% BBT column; and compounds 8 and 11 not separated with the SE-52 column are separated with the 50% SE-52 + 50% BBT column. On the other hand, the two pairs of compounds (compounds 8 and 9, and compounds 10 and 11) not separated with the 50% SE-52 + 50% BBT column can be separated with an SE-52 column. Consequently, by using these two columns, the 13 isomers of the 4-ring sulfur heterocycles can be completely identified. With improved technology of column preparation and optimization of conditions, these mixed-phase columns should also improve the resolution or separation

power for other isomers and their complete identification could be possible, provided that standard compounds can be obtained.

These two columns have been used to identify the 4-ring isomers of the sulfur heterocycles in an SRC-II Heavy distillate coal liquid.

Figure 5 shows the SE-52 capillary column gas chromatogram of the sulfur fraction of an SRC-II heavy distillate. The marked peaks are identified and listed in TABLE IV in the following section I(C). The identification of peaks were confirmed with GC/MS equipped with an SE-52 column. However, the isomeric peaks still can not be identified with only an SE-52 column and/or GC/MS. For further identification, a chromatogram of the sulfur fraction was run with a 50% SE-52 + 50% BB BT column and is shown in Figure 6.

A selected-ion plot of the GC/MS run is shown in Figure 7. There are 3 peaks on the trace of $m/e = 234$ (4-ring isomers). This is consistent with the three relatively large peaks on the SE-52 chromatogram (see assigned peak 14 on Figure 5).

A different pattern of the three peaks can be seen on the 50% SE-52 + 50% BB BT chromatogram (see Fig. 5 and 6). Comparing the retention indices of these three peaks with the retention indices of standard 4-ring isomers on the SE-52 column and the retention times of these three peaks with the standard 4-ring isomers on the 50% SE-52 + 50% BB BT column, a positive identification was reached. The conclusion is that only the following three 4-ring isomers of sulfur heterocycles exist in the SRC-II heavy distillate: Benzo[b]naphtho[2,1-d]thiophene, Benzo[b]naphtho[2,3-d]thiophene and Benzo[b]naphtho[1,2-d]thiophene.

A positive identification of the 3-ring and 5-ring isomers of the sulfur heterocycles will be possible provided that all sets of standard compounds are obtained. This work is presently in progress.

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Table I. Identification of 4-ring Sulfur Heterocycle Isomers of an SRC-II Heavy Distillate Coal Liquid

No.	Compound	Retention ^a Time (min)	Retention ^b Index	Retention Order (SE-52)	(50% BBBT/ SE-52)
1	Benzo[b]naphtho[2,1-d]thiophene	22.2(22.2)	389.21	1	1
2	Phenanthro[4,3-b]thiophene	23.5	395.16(395.88)	3	2
3	Phenanthro[9,10-b]thiophene	24.1	394.64	3	3
4	Phenanthro[3,4-b]thiophene	25.0	396.46	4	4
5	Benzo[b]naphtho[1,2-d]thiophene ^c	25.2(25.2)	392.59(392.22)	2	5
6	Anthra[1,2-b]thiophene	26.0	394.82	3	6
7	Benzo[b]naphtho[2,3-d]thiophene ^c	27.4(27.2)	88.83(38.75)	3	7
8	Phenanthro[3,2-b]thiophene	28.0	401.52	7	8
9	Phenanthro[1,2-b]thiophene	28.0	395.79	4	8
10	Anthra[2,1-b]thiophene	30.1	397.45	5	9
11	Phenanthro[2,3-b]thiophene	30.1	402.13	7	9
12	Phenanthro[2,1-b]thiophene	32.2	399.58	6	10
13	Anthra[2,3-b]thiophene	43.2	---	8	11

- a. The three values in parentheses are the retention times of three peaks in the chromatograms of PASH SRC II Heavy Distillate Coal Liquid.
- b. Retention indices are from reference 7. The values in parentheses are those of the 3 peaks mentioned in a and do not necessarily belong to the compound indicated.
- c. Compounds as identified in PASH SRC-II Heavy Distillate Coal Liquid.

Table II. Compounds identified in the PASH fraction of an SRC-II Heavy Distillate Coal Liquid.

Peak No.	Mol wt. ^a	Compound	Retention Index ^b
1	166	Fluorene	269.51
2	180	C ₁ -Fluorene	286.93
3	188	Tetrahydrodibenzothiophene	293.38 (294.30)
4	184	Dibenzothiophene	295.62 (290.05)
5	18	Phenanthrene	300.00 (300.00)
6	178	Anthracene	301.70 (301.69)
7	198	C ₁ -Dibenzothiophene	312.57 316.41 316.60 320.24
8	212	C ₂ -Dibenzothiophene	332.85 332.85 333.5 336.15
9	226	Fluoranthene	342.15 (344.00)
10	226	C ₃ -Dibenzothiophene	343.78 349.69 351.46
11	208	Phenanthro[4,5- <u>bcd</u>]thiophene	348.51 (348.58)
12	202	Pyrene	350.52 (351.00)
13	222	C ₁ -Phenanthro[4,5- <u>bcd</u>]thiophene	362.67 363.78 365.63 367.22 369.20
14	234 ^c	Benzo[b]naphtho[2,1- <u>d</u>]thiophene Benzo[b]naphtho[1,2- <u>d</u>]thiophene Benzo[b]naphtho[2,3- <u>d</u>]thiophene	388.75 (398.21) 388.75 (388.83) 392.22 (392.59)

Table II. Continued.

Peak No.	Mol wt. ^a	Compound	Retention Index ^b
15	248	C ₁ -Benzonaphthothiophene	407.04
			414.25
16	262	C ₂ -Benzonaphthothiophene	439.98
			444.66
			447.38
			450.02

a. All compound molecular weights were obtained by GC/MS.

b. Values in parentheses are from reference 7.

c. The three isomers were separated on SE-52 and 50%/SE-52 + 50% BB BT columns.

Figure 1a. Chromatogram of 13 isomers: Anthra[1,2-b]-thiophene, Anthra[2,1-b]thiophene, Anthra[2,3-b]thiophene, Benzo[b]naphtho[1,2-d]thiophene, Benzo[b]naphtho[2,1-d]thiophene, Benzo[b]naphtho[2,3-b]thiophene, Phenanthro[1,2-b]thiophene, Phenanthro[2,1-b]thiophene, Phenanthro[2,3-b]thiophene, Phenanthro[3,2-b]thiophene, Phenanthro[4,3-b]thiophene, Phenanthro[9,10-b]thiophene, and Phenanthro[3,4-b]thiophene.

Conditions: 20 m x 0.2 mm glass capillary column coated with SE-52, temperature programmed 40°C-----20°C/min-----190°C

-----2°C/min-----220°C

Figure 1b. Chromatogram of 13 isomers (same as in Figure 1a).
Conditions: 20 m x 0.2 mm glass capillary column
coated with 6% BBBT + 94% SE-52, same temperature
program as in Figure 1a.

Figure 1c. Chromatogram of 13 isomers (as in Figure 1a).
Conditoins: 20 m x 0.2 mm glass capillary column
coated with 20% BBT + 80% SE-52, same temperature
program as in Figure 1a.

Figure 2a. Chromatogram of 6 isomers: Phenanthro[9,10-b]thiophene, Phenanthro[4,3-b]thiophene, Anthra[1,2-b]thiophene, Benzo[b]naphtho[2,3-d]thiophene, Phenanthro[2,3-b]thiophene, and Phenanthro[1,2-b]thiophene. Conditions: 20 m x 0.2 mm glass capillary column coated with SE-52, same temperature programming as in Figure 1a.

Figure 2b. Chromatogram of 6 isomers (same as in Figure 2a).
Conditions: same as in Figure 1b.

Figure 2c. Chromatogram of 6 isomers (same as in Figure 2a).
Conditions: same as in Figure 1c.

Figure 3. Chromatogram of 6 isomers (same as in Figure 2a).
Conditions: 20 m x 0.26 mm glass capillary column
coated with 50% BB8T + 50% SE-52.
Temperature programmed: same as in Figure 1a.

Figure 4a. Chromatogram of 13 isomers (same as in Figure 1a).
Conditions: 20 m x 0.3 mm column coated with SE-52.
Temperature programmed: 60°C---20°C/min---220°C

Figure 4b. Chromatogram of 13 isomers (same as in 1a).

Conditions: 20 m x 0.26 mm column coated
with 50% BBBT + 50% SE-52.

Temperature programmed:

60°C--20°C/min--220°C

Figure 5. Chromatogram of SRC-II Heavy Distillate.
 Conditions: 20 m x 0.3 mm capillary column coated with SE-52.
 Temperature programmed: 40°C --10°C/min-- 60°C --4°C/min-- 250°C

Figure 6. Chromatogram of SRC-II Heavy Distillate.
Conditions: same column as in Figure 3, temperature programmed
from 60°C to 220°C at 20°C/min.

Figure 7. Selected-ion plot of SE-52 GC/MS chromatogram -- SRC-II Heavy Distillate

C. Appication of the Developed Methodology to the Complete Chemical Characterization of an SRC II Heavy Distillate.

ABSTRACT

A separation method is described for the detailed identification of organic compounds in synthetic fuel products. Prefractionation of crude synfuel materials into discrete chemical classes was performed by adsorption column chromatography using small quantities of neutral aluminum oxide and silicic acid. Subsequent high resolution separation of individual components was achieved using capillary column gas chromatography and specific compound types were determined by gas chromatographic retention data and combined gas chromatography-mass spectrometry. The principal chemical classes investigated in a solvent refined coal liquid were: aliphatic hydrocarbons, polycyclic aromatic hydrocarbons, polycyclic aromatic sulfur heterocycles, nitrogen polycyclic aromatic compounds, and hydroxyl polycyclic aromatic hydrocarbons. The nitrogen-containing aromatic compounds were further separated into secondary nitrogen polycyclic aromatic heterocycles, amino polycyclic aromatic hydrocarbons, and tertiary nitrogen polycyclic aromatic heterocycles to facilitate their identification.

INTRODUCTION

Current emphasis on the development of alternate energy sources has stimulated production of synthetic fuels derived from oil shale, tar sands, and coal. Although technology for producing liquid and solid fuels from these feed stocks has been available since the early 1900's (1), the chemical characterization of these products has recently received increased attention. There are several reasons for determining specific compound types in synfuels. The identification and elimination of specific toxic and carcinogenic compounds would reduce the environmental and occupational health hazards associated with the production and combustion of these materials (2,3,4). Certain heteroatom species are known to decrease the efficiency of catalytic processes and contribute to the instability of liquid fuels during storage (5,6). Synthetic fuels are also a valuable source of chemical materials for the manufacture of pharmaceuticals, pesticides, herbicides, and dyes (3,7).

Because of the complex nature of synthetic fuel materials, fractionation according to chemical class is usually required before identification of individual components can be achieved. Traditionally, separation schemes have been developed using solvent partitioning methods and column chromatography. The organic analytical group at the National Bureau of Standards has isolated neutral oils, acids, and bases using a solvent extraction method with subsequent high performance liquid chromatographic (HPLC) and gas chromatographic analysis to separate and identify individual organic compounds in synfuels (8). The analytical group at Oak Ridge National Laboratory has developed a fractionation scheme using an acid-base extraction followed by solid-liquid chromatography on Sephadex LH-20, silicic acid, and basic alumina (1,9,10). They reported the separation of aliphatic and aromatic hydrocarbons as well as

nitrogen heterocyclic and polar aromatic compounds. Wilson et al. (11) used a similar solvent fractionation scheme to analyze coal liquefaction products before and after hydrotreatment. They reported the occurrence of neutral polycyclic aromatic hydrocarbons and sulfur, oxygen, and nitrogen heterocyclic aromatic compounds. In another separation scheme developed for solvent refined coal (12), nine fractions were isolated from silica gel on the basis of chemical functionality. Schiller and Mathiason (13) reported the development of a chromatographic procedure using neutral alumina to fractionate a wide variety of coal-derived solids and liquids for analysis by mass spectrometry and other spectral methods. The principal compound types investigated were: saturated hydrocarbons, aromatic hydrocarbons, benzofurans, ethers, nitrogen compounds, and hydroxyl compounds. A combination of ion-exchange, coordination, and adsorption chromatography was employed by Jewell et al. (14) for the separation of petroleum distillates. This method has also been used to separate coal-derived products into five fractions: acids, bases, neutral nitrogen compounds, saturated hydrocarbons, and aromatic hydrocarbons. This method is commonly known as the SARA technique and has been widely used.

Several problems exist with the previously described separation methods. First, most schemes are complicated, time consuming, tedious, and require highly trained personnel to execute each step with precision and accuracy. Long periods of time are required for pretreatment, cleaning, preparation, and activation of resins and adsorbent packings. Many methods use expensive materials, and large volumes of high purity solvents are necessary for each chromatographic or partitioning step. Solvent extraction and partitioning of polar types of compounds can cause formation of tars and stable emulsions (15) which contribute to the loss of components and inefficient separations.

Finally, many separation schemes are hindered by incomplete chemical class separation and overlap of compound types into adjacent fractions. Improvement of existing separation technology is necessary if faster analysis and better evaluation of the numerous types of synfuel products are to be achieved.

In this paper, the development of a two step separation method using neutral alumina and silicic acid adsorption chromatography is described. This procedure minimizes the problems previously discussed and is rapid, reproducible, economical, and efficient. Crude solid and liquid synfuel products can be fractionated into seven chemical classes by this method. This separation scheme can be completed in less than 6 hours and uses less than 500 mL of solvent and approximately 12 grams of adsorbent packing. The applicability of this fractionation method is demonstrated by the characterization of a solvent refined coal (SRC) liquid heavy distillate.

EXPERIMENTAL SECTION

An SRC II heavy distillate sample (boiling point range 260°C to 450°C) from the Fort Lewis, Washington, Pilot Plant (using West Virginia coal from the Pittsburgh seam) was provided by Pacific Northwest Laboratory for analysis. This material is of pilot plant origin and should not necessarily be considered representative of commercial scale production. A schematic diagram of the separation method is shown in Figure 1. First, neutral aluminum oxide (Brockman Activity I, 80-200 mesh, Fisher No. A950) was used as purchased to separate the raw material into four initial fractions: A-1, aliphatic hydrocarbons; A-2, neutral polycyclic aromatic compounds (PAC); A-3, nitrogen polycyclic aromatic compounds (N-PAC); and A-4, hydroxyl polycyclic aromatic hydrocarbons (HPAH). [The acronyms used in this paper are assigned according to the format defined by Bartle et al. (16)]. Approximately 0.1 to 0.3g of

crude sample was dissolved in a few mL of chloroform and adsorbed onto 3g of neutral alumina. The solvent was removed from the alumina by vigorously stirring the mixture under a gentle stream of dry nitrogen gas. The alumina with sample was then packed on top of an 11-mm i.d. column which already contained 6g of neutral alumina. The sample was then eluted with the following chromatographic grade solvents: fraction A-1, 20 mL of hexane; fraction A-2, 50 mL of benzene; fraction A-3, 70 mL of chloroform (containing 0.75% ethanol preservative); fraction A-4, 50 mL of 10% ethanol in tetrahydrofuran (containing no inhibitors).

Polycyclic aromatic oxygen heterocycles (PAOH) and polycyclic aromatic sulfur heterocycles (PASH) are eluted with the polycyclic aromatic hydrocarbons (PAH) in fraction A-2. Because the PASH are in such low concentration in coal-derived materials, the alumina column procedure was scaled-up and 10g of starting material was used to obtain a neutral PAC fraction. The PASH were then separated from the PAH and PAOH by a procedure previously reported by Willey et al. (17). Briefly, the PASH were oxidized with H_2O_2 to their corresponding sulfones, the sulfones were then separated from the other unoxidized neutral PAC on silica gel (fraction A-2a), reduced with $LiAlH_4$ to the original PASH and re-purified on silica gel (fraction A-2b).

Several distinct classes of nitrogen heterocyclic compounds were present in the initial N-PAC, fraction A-3. Consequently, a method was developed to subfractionate the N-PAC into three additional classes of compounds using silicic acid adsorption chromatography. The alumina N-PAC fraction was adsorbed onto 0.5 g of silicic acid (Mallinckrodt No. 2847, 100 mesh powder, used as received from supplier) and the solvent removed by stirring the mixture under dry nitrogen gas. A 22-mm i.d. column was packed with a hexane slurry of 2g of silicic acid. The silicic acid with the adsorbed sample was then packed

on top of the 2g column and eluted to give the following fractions and compound types: fraction S-1, 50 mL 1:1 (v:v) hexane:benzene, secondary nitrogen polycyclic aromatic heterocycles (2°-PANH); fraction S-2, 30 mL benzene, enriched amino polycyclic aromatic hydrocarbons (APAH); fraction S-3, 50 mL 1:1 (v:v) benzene: anhydrous ethyl ether, tertiary nitrogen polycyclic aromatic heterocycles (3°-PANH).

Each of the alumina and silicic acid fractions was concentrated to approximately 2 mL on a rotary evaporator, taken to dryness under nitrogen gas, weighed, and dissolved in an appropriate volume of benzene for capillary column gas chromatographic analysis. A Hewlett-Packard 5880 gas chromatograph equipped with a fused-silica capillary column (20 m x 0.30 mm i.d.) coated with SE-52 methylphenylsilicone stationary phase (film thickness 0.25 μ m) was used to obtain chromatograms of each fraction. The oven was held at 50°C for 2 minutes during injection and then temperature programmed at 3°C/min (alumina fractions) or 4°C/min (PASH and silicic acid fractions) to a final temperature of 250°C and held for 5 minutes. A flame ionization detector (FID) was generally used, but nitrogen and sulfur heterocycle fractions were also analyzed using a nitrogen-selective detector (NPD) and a sulfur selective detector (FPD). A Perkin-Elmer Sigma 2 gas chromatograph equipped with these detectors was used.

Identification of specific compounds was accomplished using gas chromatographic retention data and combined gas chromatography-mass spectrometry (GC-MS). Gas chromatographic conditions were similar to those already described. A Hewlett-Packard 5982A quadrupole mass spectrometer was operated in the electron impact mode (70 eV electron energy). Spectra were acquired and processed with a Hewlett-Packard 5934A data system.

Infrared spectroscopy of the HPAH fraction was performed by evaporating the solvent from the sample and placing an aliquot between two salt plates. The sample was then analyzed by scanning from 4000 cm^{-1} to 600 cm^{-1} on a Beckman ACCULAB 2 infrared spectrometer.

RESULTS AND DISCUSSION

The separation of oxygen and nitrogen heterocyclic compounds in petroleum products by adsorption chromatography on alumina has been extensively studied by Snyder and co-workers (18). Similarly, Schiller (13,19) used alumina chromatography to develop a rapid, simple separation method for heterocyclic compounds in synthetic fuels. The alumina step reported in this paper is a modified version of the method developed by Schiller. It was found in this study that column chromatography on neutral alumina minimized sample loss due to irreversible adsorption, eluted a wide range of solutes rapidly, and provided reproducible class separation according to the functionality of the heteroatom present in the polycyclic aromatic structure.

Compounds which contain nitrogen heteroatoms of different functionality can be separated on silicic acid by varying the eluent polarity. Silicic acid has previously been used to separate indoles and carbazoles from other N-PAC in tobacco smoke (20) and synfuels (9). The silicic acid procedure reported in this paper was developed to complement the alumina method by providing an equally simple and rapid method for subsequent chemical class separation of the nitrogen-containing polycyclic aromatic compounds. Using a small quantity of adsorbent (2.5g) reduces the contact time of the sample components with the silica structure and decreases degradation, artifact formation, and sample loss normally associated with chromatography on silica adsorbents.

Numerous compounds are present in each chemical class, even after extensive prefractionation, and further high resolution separation is required prior to the identification of specific components. The application of capillary column GC-MS to resolve and determine compounds in complex mixtures of PAC has been well established (21). This simple alumina-silica fractionation scheme combined with capillary column GC-MS provides a rapid, effective, and reproducible method for the detailed chemical characterization of synthetic fuels. Additionally, this two-step separation method can easily be scaled-up to produce larger quantities of sample which is sometimes required for the concentration of trace components and for bioassay to determine mutagenicity or carcinogenicity.

The quantitative data obtained using this procedure are presented in Tables I and II. A total recovery of greater than 90% was obtained by this method for the separation of an SRC II heavy distillate into chemical classes. A chromatogram of each of the fractions is shown in Figures 2-9. Tables III, IV and V list the compound types identified in each fraction.

Aliphatic Hydrocarbons. Due to the non-polar nature of the aliphatic hydrocarbons, this class of compounds elutes immediately from alumina with hexane. The gas chromatographic retention time of standard octadecane, $n\text{-C}_{18}$, was used to determine $n\text{-C}_{18}$ in the aliphatic fraction. Mass spectral data supplemented the identification of $n\text{-C}_{18}$ and was used to determine the other constituents in the homologous series of straight-chain hydrocarbons. The non-linearity of the baseline in the $n\text{-C}_{16}$ - $n\text{-C}_{20}$ region (see Figure 2) is caused by the numerous unresolved components (related olefins and branched isomers of the straight-chain parent hydrocarbons). The relatively low concentration of the aliphatic hydrocarbons in this coal liquid illustrates the highly aromatic nature of this product. The structural features of saturates

in coal liquids are similar to those of some petroleums and both can be correlated to the distribution of similar compounds found in plant material (22).

Neutral PAC. Naphthalene and triphenylene standards were used to ascertain the retention parameters of the neutral PAC fraction eluted from the alumina column. Benzene was chosen over toluene as the eluent because it is a slightly more polar solvent and reduced the overlap of the polycyclic furans (PAOH) into the chloroform fraction. The PAH (see Figure 3) are the chemical class of highest concentration in this SRC II heavy distillate and generally are major constituents in most coal-derived fuel products. The literature in this area is too extensive to cover here, but has recently been reviewed (23,24). The high degree of alkylation in this PAH fraction is of particular interest. A rough correlation between degree of alkylation of PAH structures in energy-related materials and mutagenicity has been reported by Griest and co-workers (25). Extensive alkylation is observed in all fractions of this SRC II liquid, and in some instances the alkylated species are more abundant than the parent PAC.

Although the PASH, Figure 4, comprise less than 1% of the total heavy distillate, the detailed characterization of the sulfur-containing compounds in synthetic fuel products is important in light of recent evidence that specific sulfur heterocycles have been shown to possess significant mutagenic activity (26,27). Furthermore, the removal of sulfur from fuels is desirable to prevent the formation of noxious sulfur gases during combustion and to prevent catalyst poisoning in coal conversion reactors. The identification of specific sulfur-containing species in synthetic fuels can provide insights into better methods of sulfur removal.

N-PAC. The elution of the N-PAC from neutral alumina with chloroform could be visually observed by the migration of a dark band down the column. Analysis by gas chromatography using a nitrogen-selective NPD verified that essentially all of the components in this fraction were nitrogen-containing compounds. Figure 5 is an FID chromatogram of the N-PAC fraction.

Primary (APAH), secondary (2° -PANH) and tertiary (3° -PANH) nitrogen heterocycles (see Figures 6-8) occur collectively in the alumina N-PAC fraction. Additional chemical class separation was essential for three reasons. First, the difficulty of identifying individual constituents in this fraction was increased by the fact that more than one compound eluted from the capillary column at the same time. For example, tetrahydrocarbazole co-eluted with two benzoquinoline isomers. This was also the case with many of the alkylated carbazoles, alkylated benzoquinolines, and three-ring APAH. Second, different concentration levels between chemical classes obscured groups of compounds which are important to the overall chemical behavior of the sample. Although the APAH were lower in concentration than either the secondary or tertiary PANH (see Table II), it has been suggested that the APAH are largely responsible for the biological activity of synfuel products (9,28). Third, detailed assignment of structure was complicated by the presence of isomeric compounds which had different molecular structures and functionalities but produced nearly identical mass spectra. For example, the methylbenzoquinolines and the aminoanthracenes have molecular weights of 193 amu and all fragment similarly by mass spectrometry making exact structural identification nearly impossible. Therefore, it was necessary to separate the nitrogen-containing compounds into subfractions.

The N-PAC constitute a major fraction of not only this coal liquid but also other coal liquefaction products, shale oils, and coal tars (3). Exten-

sive work has been reported on the separation and identification of several pyridines and anilines; a number of two and three ring N-PAC have also been identified in synthetic fuel products (7,13,19,29-33). Relatively fewer studies have been reported on the isolation and determination of compounds containing a larger number of rings. The one- and two-ring N-PAC systems are of general interest because they are present in higher concentration levels, are more volatile, some are commercially useful, and a few are biologically active. However, it is believed that isomers of increasing ring number generally display a higher degree of mutagenicity and carcinogenicity. For example, carbazole is non-carcinogenic, benzo[a]carbazole is moderately carcinogenic and dibenzo[c,g]carbazole is a potent carcinogen (34). Therefore, it is important to isolate and identify the larger compounds in synfuel products. Several 2-, 3-, and 4-ring N-PAC have been identified in the silicic acid subfractions of the alumina N-PAC fraction. The concentration envelope for this SRC II distillate cut is comprised mostly of 2-, 3-, and 4-ring N-PAC. However, work has been done with standard N-PAC of up to five rings (dibenzacridines and dibenzocarbazoles) and other synfuel products which shows the applicability of this separation method to the isolation of compounds containing more than four rings.

The enriched APAH fraction, Figure 7, is of particular interest. Wilson et al. (28) initially suggested the presence of 2-, 3-, and 4-ring primary aromatic amines in a similar SRC II heavy distillate. The results presented in this paper confirm the presence of these APAH and also report the occurrence of several alkylated species of the parent APAH. The APAH were not completely separated from the 3°-APAH. Preliminary data suggest that the tertiary nitrogen heterocycles overlapping into the APAH fraction are either alkylated or angular-structured species where the lone pair of electrons on the nitrogen

heteroatom is shielded. Therefore, some of the 3°-PANH and the APAH have similar retention characteristics. Many of the 3°-PANH that eluted in this fraction were more than twice as concentrated as the APAH and frequently obscured their presence. Thus, in addition to the retention and GC/MS data used, a derivatization method has been used (35) to ensure positive identification of the APAH listed in Table V. Although there was overlap between these two classes of N-PAC compounds in this fraction, the APAH were sufficiently enriched to verify their presence.

HPAH. The hydroxyl PAH (see Figure 9) were eluted last from neutral alumina with 10% ethanol in tetrahydrofuran. Many HPAH have been shown to be present in synthetic fuel products and several methods have been developed for their isolation and determination (8,29,30,36). The major acidic compounds found in synfuels are phenol and the alkylphenols. Also, HPAH such as hydroxybiphenyls, indanols, naphthols, acenaphthenols and hydroxyfluorenes have been reported to occur in these matrices (29).

Infrared spectroscopy of the HPAH fraction showed the strong presence of hydroxyl functional groups and indicated that there was little if any carbonyl oxygen. This observation agrees well with others who have reported the absence of carbonyl groups in coal liquefaction products (29). The major components identified by GC-MS in this fraction were indanols, hydroxybiphenyls, hydroxyfluorenes and naphthylphenols. Low levels of naphthols were also detected. As with the other fractions of this coal liquid, a high alkyl content was observed.

CONCLUSION

The projected increase in use of synthetic fuels produced from coal, shale, and tar sands to meet growing energy demands has created a need for

faster and more reliable methods of analysis of products and by-products from these processes. The methodology presented in this paper and applied to the analysis of a representative solvent refined coal liquid has been shown to be a rapid, effective, and reproducible means to a complete chemical analysis of these materials. Although not discussed, this separation method has been applied to the analysis of other SRC II products, coal tar, SRC recycle solvents, and SRC I process materials. In each case, the compounds in these materials were successfully separated according to chemical functionality as described for the SRC II heavy distillate.

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TABLE I. Weight percent of neutral alumina fractions from an SRC II heavy distillate coal liquid.

<u>FRACTION</u>	<u>COMPOUND TYPE</u>	<u>FRACTION [‡] WEIGHT PERCENT</u>
A-1	Aliphatic Hydrocarbons	5.5%
A-2	Neutral PAC	56.6%
A-3	N-PAC	20.0%
A-4	HPAH	<u>14.0%</u>
	TOTAL	96.1%

[‡] Average values for three different assays of SRC II heavy distillate.

TABLE II. Weight percent of silicic acid subfractions from an SRC II heavy distillate coal liquid.

<u>FRACTION</u>	<u>COMPOUND TYPE</u>	<u>WEIGHT PERCENT OF N-PAC</u>	<u>WEIGHT PERCENT OF HEAVY DISTILLATE</u>
S-1	2° PANH	59.6%	11.9%
S-2	Enriched APAH	8.5%	1.7%
S-3	3° PANH	<u>14.9%</u>	<u>3.0%</u>
	TOTAL	83.0%	16.6%

TABLE III. Compounds identified in the alumina chromatographic fractions of an SRC II heavy distillate coal liquid.

Peak No.	Molecular Weight	Compound	Peak No.	Molecular Weight	Compound
<u>Aliphatic Hydrocarbon Fraction A-1 (Figure 2)</u>					
1	226	$n\text{-C}_{16}$	8	324	$n\text{-C}_{23}$
2	240	$n\text{-C}_{17}$	9	338	$n\text{-C}_{24}$
3	254	$n\text{-C}_{18}$	10	352	$n\text{-C}_{25}$
4	268	$n\text{-C}_{19}$	11	366	$n\text{-C}_{26}$
5	282	$n\text{-C}_{20}$	12	380	$n\text{-C}_{27}$
6	296	$n\text{-C}_{21}$	13	394	$n\text{-C}_{28}$
7	310	$n\text{-C}_{22}$	14	408	$n\text{-C}_{29}$
<u>PAC Fraction A-2 (Figure 3)</u>					
1	142	C_1 -Naphthalene	14	196	C_3 -Biphenyl/ C_1 -Dibenzothiophene
	156	C_2 -Naphthalene	15	204	1-Phenylnaphthalene
	170	C_3 -Naphthalene	16	192	C_1 -Phenanthrene
	154	Biphenyl	17	204	2-Phenylnaphthalene
	154	Acenaphthene	18	206	C_2 -Phenanthrene
	168	Dibenzofuran	19	202	Fluoranthene
2	166	Fluorene	20	202	Pyrene
3	168	C_1 -Biphenyl/ C_1 -Acenaphthene	21	---	Not identified
4	168	C_1 -Biphenyl/ C_1 -Acenaphthene	22	216	Benzo[<u>a</u>]fluorene
5	184/180	C_4 -Naphthalene/ C_1 -Fluorene	23	216	Benzo[<u>b</u>]fluorene

TABLE III. Continued.

Peak No.	Molecular Weight	Compound	Peak No.	Molecular Weight	Compound
6	182	C ₁ -Dibenzofuran	24	216	C ₁ -Pyrene/C ₁ -Fluoranthene
7	182	C ₂ -Biphenyl	25	230	C ₂ -Pyrene/C ₂ -Fluoranthene
8	180/182	C ₁ -Fluorene/ C ₂ -Biphenyl	26	228	Benz[a]anthracene
9	198/194	C ₅ -Naphthalene/ C ₂ -Fluorene	27	228	Chrysene
10	184	Dibenzothiophene	28	242	C ₁ -Benz[a]anthracene/ C ₁ -Chrysene
11	182	Tetrahydrophenanthrene	29	252	Benzo[a]fluoranthene
12	196	C ₃ -Biphenyl	30	252	Benzo[a]pyrene
13	178	Phenanthrene			
N-PAC Fraction A-3 (Figure 5)					
1	131	C ₁ -Indole	19	193/207	C ₁ -Benzoquinoline/ C ₂ -Benzoquinoline
2	157	C ₂ -Quinoline	20	183	C ₁ -Carbazole
3	145	C ₂ -Indole	21	193	C ₁ -Benzoquinoline
4	159	C ₃ -Indole	22	207	C ₂ -Benzoquinoline
5	198	C ₂ -Diphenyl ether	23	197	C ₂ -Carbazole
6	185	C ₄ -Quinoline	24	207	C ₂ -Benzoquinoline

TABLE III. Continued.

<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>	<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>
7	183	Tetrahydro- benzoquinoline	25	197	C ₂ -Carbazole
8	178	Phenanthrene	26	197	C ₂ -Carbazole
9	179	Benzoquinoline	27	211	C ₃ -Carbazole
10	179	Benzoquinoline	28	203	Azafluoranthene
11	197	C ₁ -Tetrahydro- benzoquinoline	29	203	Azapyrene
12	171/179	Tetrahydro- carbazole/Benzo- quinoline	30	225	C ₄ -Carbazole
13	197	C ₁ -Tetrahydro- benzoquinoline	31	217/239	C ₁ -Azapyrene/ C ₁ -Azafluoranthene
14	167	Carbazole	32	231	C ₂ -Azapyrene/ C ₂ -Azafluoranthene
15	193	C ₁ -Benzoquino- line	33	221	Tetrahydrobenzo- carbazole
16	185	C ₁ -Tetrahydro- carbazole	34	229	Naphthoquinoline
17	193	C ₁ -Benzoquino- line	35	217	Benzocarbazole
18	181/193	C ₁ -Carbazole/ C ₁ -Benzoquino- line	36	231	C ₁ -Benzocarbazole

TABLE III. Continued.

Peak No.	Molecular Weight	Compound	Peak No.	Molecular Weight	Compound
<u>HPAH Fraction A-4 (Figure 9)</u>					
1	148	C ₁ -Indanol	17	198	C ₂ -Hydroxybiphenyl
2	170	Hydroxybiphenyl	18	182	Hydroxyfluorene
3	162	C ₂ -Indanol	19	182	Hydroxyfluorene
4	184	C ₁ -Hydroxybi-phenyl	20	198	C ₂ -Hydroxybiphenyl
5	184	C ₁ -Hydroxybi-phenyl	21	182	Hydroxyfluorene
6	176	C ₃ -Indanol	22	198	C ₂ -Hydroxybiphenyl
7	198	C ₂ -Hydroxybi-phenyl	23	226/196	C ₄ -Hydroxybiphenyl/ C ₁ -Hydroxyfluorene
8	170	Hydroxybiphenyl	24	212	C ₃ -Hydroxybiphenyl
9	170	Hydroxybiphenyl	25	212/196	C ₃ -Hydroxybiphenyl/ C ₁ -Hydroxyfluorene
10	190	C ₄ -Indanol	26	220	Naphthylphenol
11	212	C ₃ -Hydroxybi-phenyl	27	226/210	C ₄ -Hydroxybiphenyl/ C ₂ -Hydroxyfluorene
12	184/204	C ₁ -Hydroxybi-phenyl/C ₅ -Indanol	28	234	C ₁ -Naphthylphenol
13	184	C ₁ -Hydroxybi-phenyl	29	240/224	C ₅ -Hydroxybiphenyl/ C ₃ -Hydroxyfluorene

TABLE III. Continued.

<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>	<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>
14	184	C ₁ -Hydroxybi-phenyl	30	220	Naphthylphenol
15	212	C ₃ -Hydroxybi-phenyl	31	220	Naphthylphenol
16	182	Hydroxyfluorene	32	234	C ₁ -Naphthylphenol

TABLE IV. Compounds identified in the PASH subfraction A-2b (Figure 4) of an SRC II heavy distillate coal liquid.

<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>	<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>
1	166	Fluorene	9	202	Fluoranthene
2	180	C ₁ -Fluorene	10	226	C ₃ -Dibenzothiophene
3	188	Tetrahydrodi- benzothiophene	11	208	Phenanthro[4,5- <u>bcd</u>]- thiophene
4	184	Dibenzothiophene	12	202	Pyrene
5	178	Phenanthrene	13	222	C ₁ -Phenanthro[4,5- <u>bcd</u>]- thiophene
6	178	Anthracene	14	234	Benzonaphthothiophene
7	198	C ₁ -Dibenzothio- phene	15	248	C ₁ -Benzonaphthothio- phene
8	212	C ₂ -Dibenzothio- phene	16	262	C ₂ -Benzonaphthothio- phene

TABLE V. N-PAC compounds identified in the silicic acid subfraction of an SRC
II heavy distillate coal liquid.

<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>	<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>
<u>2°-PANH Fraction S-1 (Figure 6)</u>					
1	145	C ₂ -Indole	11	167	Carbazole isomer
2	159	C ₃ -Indole	12	181	C ₁ -Carbazole
3	184	C ₁ -Diphenyl ether	13	195	C ₂ -Carbazole
4	173	C ₄ -Indole	14	209	C ₃ -Carbazole
5	198	C ₂ -Diphenyl ether	15	223	C ₄ -Carbazole
6	178	Phenanthrene	16	237	C ₅ -Carbazole
7	171	Tetrahydro-carbazole	17	217	Benzocarbazole
8	212	C ₃ -Diphenyl ether	18	217	Benzocarbazole
9	167	Carbazole	19	231	C ₁ -Benzocarbazole
10	167	Carbazole isomer	20	245	C ₂ -Benzocarbazole

Enriched APAH Fraction S-2 (Figure 7)

1	143	Naphthylamine	11	221/207	C ₃ -Benzoquinoline/ C ₁ -Aminophenanthrene
2	169	Aminobiphenyl	12	235	C ₄ -Benzoquinoline
3	183	C ₁ -Aminobiphenyl	13	233	Tetrahydronaphtho-quinoline

TABLE V. Continued.

Peak No.	Molecular Weight	Compound	Peak No.	Molecular Weight	Compound
4	197	C ₂ -Aminobiphenyl	14	217	Aminopyrene/Amino-fluoranthene
5	181	Aminofluorene	15	233	Tetrahydronaphthoquinoline
6	179	Benzo[h]quinoline ^a	16	229	Naphthoquinoline (possibly Benz[c]-acridine ^a)
7	167	Carbazole	17	231	C ₁ -Aminopyrene/ C ₁ -Aminofluoranthene
8	193	C ₁ -Benzoquinoline	18	229	Naphthoquinoline (possibly Benz[a]-acridine ^a)
9	193	Aminophenanthrene/Aminoanthracene	19	230	Benzanthrone
10	207	C ₂ -Benzoquinoline	20	244	C ₁ -Benzanthrone
		line	21	—	Phthalate ester

TABLE V. Continued.

<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>	<u>Peak No.</u>	<u>Molecular Weight</u>	<u>Compound</u>
<u>3°-PANH Fraction S-2 (Figure 8)</u>					
1	157	C ₂ -Quinoline	8	197	C ₁ -Tetrahydroquinoline
2	171	C ₃ -Quinoline	9	193	C ₁ -Benzoquinoline
3	185/158/183	C ₄ -Quinoline/ Unidentified peaks	10	207/203	C ₂ -Benzquinoline/ Azafluoranthene
4	199	C ₅ -Quinoline	11	221	C ₃ -Benzoquinoline
5	183	Tetrahydroquino- line	12	203	Azapyrene
6	179	Acridine ^a	13	217	C ₁ -Azapyrene/ C ₁ -Azafluoranthene
7	179	Phenanthridine ^a / Benzo[f]quinoline ^a	14	229	Naphthoquinoline

^aPossible structures assigned by retention data comparisons with standard compounds.

FIGURE CAPTIONS

Figure 1. Chemical class separation scheme for synthetic fuel products.

Key: Neutral polycyclic aromatic compounds (PAC), nitrogen polycyclic aromatic compounds (N-PAC), hydroxy polycyclic aromatic hydrocarbons (HPAH), polycyclic aromatic oxygen heterocycles (PAOH), polycyclic aromatic sulfur heterocycles (PASH), secondary nitrogen polycyclic aromatic heterocycles (2°-PANH), amino polycyclic aromatic hydrocarbons (APAH), and tertiary nitrogen polycyclic aromatic heterocycles (3°-PANH).

Figure 2. Capillary column gas chromatogram of aliphatic hydrocarbon fraction A-1. Peak numbers refer to compounds listed in Table III. Conditions: 20 m x 0.30 mm fused-silica capillary column coated with SE-52, temperature programmed from 40°C to 250°C at 3°C/min.

Figure 3. Capillary column gas chromatogram of PAH fraction A-2. Peak numbers refer to compounds listed in Table III. Conditions as in Figure 2.

Figure 4. Capillary column gas chromatogram of PASH fraction A-2b. Peak numbers refer to compounds listed in Table IV. Conditions: 20 m x 0.30 mm fused-silica capillary column coated with SE-52, temperature programmed from 40°C to 250°C at 4°C/min.

Figure 5. Capillary column gas chromatogram of N-PAC fraction A-3. Peak numbers refer to compounds listed in Table III. Conditions as in Figure 2.

Figure 6. Capillary column gas chromatogram of 2°-PANH fraction S-1. Peak numbers refer to compounds listed in Table V. Conditions as in Figure 4.

Figure 7. Capillary column gas chromatogram of enriched APAH fraction S-2. Peak numbers refer to compounds listed in Table V. Conditions as in Figure 4.

Figure 8. Capillary column gas chromatogram of 3°-PANH fraction S-3. Peak numbers refer to compounds listed in Table V. Conditions as in Figure 4.

Figure 9. Capillary column gas chromatogram of HPAH fraction A-4. Peak numbers refer to compounds listed in Table III. Conditions as in Figure 2.

FIGURE 1

FIGURE 2

FIGURE 3

FIGURE 4

FIGURE 5

FIGURE 6

FIGURE 7

FIGURE 8

FIGURE 9

D. Survey of Compounds Containing both Nitrogen and Sulfur Heteroatoms

Polycyclic aromatic compounds that contain both nitrogen and sulfur atoms in the aromatic ring structure have been reported to occur in high-boiling petroleum distillates (1,2). In addition, polycyclic aromatic nitrogen-sulfur heterocycles (PANSN) have been found in high temperature coal tars (3). The PANSN in such complex mixtures are conventionally identified by either spectrophotometric (e.g. UV absorption) or high resolution mass spectrometric methods. However, recent research where the feasibility of chromatographic separation and analysis was investigated have shown it to be a promising alternative.

Several problems must be considered if the PANSN are to be successfully analyzed in complex mixtures by chromatographic methods. First, as with the polycyclic aromatic sulfur heterocycles (PASH), the PANSN occur in very low concentration levels in environmental samples making direct gas chromatographic analysis impossible. Next, if both PASH and PANSN are present in a sample matrix, then a method that distinguishes between these classes of compounds is required if a sulfur-selective gas chromatographic detector is used. Finally, the problem of greatest magnitude is exact molecular structure determination. For the three ring PANSN more than one combination of nitrogen-sulfur functionality is possible as shown in Figure 1. More than 40 isomeric structures are

FIGURE 1

possible for compound type II alone. The number of isomers for all the three ring compounds is phenomenally large. Conventional mass spectral methods alone are not applicable for structural determination because identical mass spectra are obtained for different isomers of the same compound. The solutions to these problems can be approached by isolating enriched, class specific fractions by liquid-solid column chromatographic methods prior to high resolution analysis by capillary column gas chromatography (GC) using a sulfur-specific flame photometric detector (FPD) or a mass spectrometer for detection and identification.

A chemical class separation scheme has recently been developed and was discussed in section C of this report. It was found that for those functionalities investigated the PANSH are quantitatively eluted in Fraction A-3 of the alumina column chromatographic step. Adsorption chromatography on silicic acid of those PANSH studied on alumina was also investigated. The results of both steps are presented in Table I. Some separation between PANSH of different functionality occurs on silicic acid.

TABLE I

<u>Compound</u>	<u>Structure</u>	<u>Alumina</u>				<u>Silicic Acid</u>		
		<u>A-1</u>	<u>A-2</u>	<u>A-3</u>	<u>A-4</u>	<u>S-1</u>	<u>S-2</u>	<u>S-3</u>
Thiazole				X				X
4-Methylthiazole				X				X
Benzothiazole				X			X	
Phenothiazine				X		X	X ^a	
a About 20% of the phenothiazine elutes in fraction S-2.								

It has been shown by nitrogen-selective gas chromatographic detection that virtually all compounds eluting in fraction A-3 of a solvent

refined coal (SRC-II) liquid contained a nitrogen heteroatom. Additionally, the PASH were eluted with the PAH in fraction A-2. Therefore, any compounds that are detected with the FPD in Fraction A-3 of this coal liquid sample should be PANS_H. PANS_H were not detected in fraction A-3 of the SRC-II product. However, further enrichment of the PANS_H by silicic acid column chromatography and subsequent capillary FPD-GC analysis provided positive evidence for the presence of PANS_H in this SRC-II coal liquid. Figures 2, 3 and 4 show capillary FPD-GC chromatograms of fractions S-1, S-2 and a 1:1 (v:v) composite of S-1 and S-2, correspondingly. From high resolution mass spectral data for this same SRC II material, it was determined that two and three ring PANS_H and alkyl homologues up to C₂ were present (4). As of yet, little is known about the exact molecular structure of the PANS_H found in this sample. Figure 5 is an FPD/FID dual trace chromatogram of fraction S-2 and illustrates that structural identification of the PANS_H in this fraction by coupled capillary column gas chromatography-mass spectrometry (GC-MS) is impossible due to the comparatively low concentration levels of PANS_H as compared to the nitrogen polycyclic aromatic compounds.

The chromatographic separation and detection described, supplemented by high resolution mass spectral data, provide strong evidence for the occurrence of PANS_H in coal-derived materials. The major obstacle that must still be considered prior to structural determination is the isolation of a PANS_H fraction that is significantly enriched to allow analysis by GC-MS without obscuring interferences from other classes of compounds. Finally, biological testing of standard compounds to determine the extent that PANS_H might contribute to the overall mutagenicity and carcinogenicity of coal liquids will be important to the emphasis placed on separating and identifying this class of compounds.

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FIGURE 2. Capillary FPD-GC chromatogram of fraction S-1 of an SRC. II coal liquid. Conditions: 15 m X 0.31 mm i.d. SE-52 fused silica capillary column; temperature programmed from 40°C (initial time: 2.0 min) to 250°C at 6°C/min.

FIGURE 3. Capillary FPD-GC chromatogram of fraction S-2 of an SRC II coal liquid. Conditions as in FIGURE 1.

FIGURE 4. Capillary FPD-GC chromatogram of a 1:1 (vol:vol) mixture of fraction S-1 and S-2 of an SRC II coal liquid. Conditions as in FIGURE 1.

FIGURE 5. Capillary FPD/FID-GC dual trace chromatogram of fraction S-2 of an SRC II coal liquid. Conditions: 25 m X 0.31 mm i.d. SE-52 fused silica capillary column equipped with a fused silica effluent splitter; temperature programmed from 40°C (initial time: 2.0 min) to 250°C at 4°C/min.

E. Work in Progress

A number of distillate cuts from an SRC II coal liquid and several SRC I samples (specific samples are listed in the renewal proposal) are being analyzed for sulfur heterocycles. The enrichment of larger compounds in the higher boiling point cuts should help considerably in the identification of the larger compounds.

Most of the 5-ring sulfur heterocycles (mol. wt. = 258) have been synthesized, and the remaining ones are in progress. The biological testing of these compounds is also in progress.

With the accumulation of many standard compounds for comparison, many exact identifications of mixture constituents will be possible in the near future.

II. SYNTHESIS OF STANDARD COMPOUNDS.

A. Synthesis of Anthra[b]thiophenes and Benzo[b]naphtho[d]thiophenes.

All isomers of the parent anthra[b]thiophenes and benzo[b]naphtho[d]thiophenes, namely anthra[2,3-b]thiophene, anthra[2,1-b]thiophene, anthra[1,2-b]thiophene, benzo[b]naphtho[2,3-d]thiophene, benzo[b]naphtho[2,1-d]thiophene and benzo[b]naphtho[1,2-d]thiophene were synthesized using a new procedure.

Recently, using glass capillary gas chromatography/mass spectrometry, a great many heterocyclic sulfur compounds have been separated and identified from coal gasification tar, coal liquid and shale oils (1). It is well known that several unsubstituted tetracyclic thiophene derivatives are contained within these polycyclic thiophene fractions. Iwao, *et al.*, have reported the synthesis of all isomers of the parent phenanthro[b]thiophene in order to provide samples for the measurement of retention data for programmed temperature capillary column gas chromatography, and have examined the carcinogenic and mutagenic activities of these compounds (2). As a continuation of this research plan to synthesize all of the remaining tetracyclic polycondensed thiophene derivatives, the present paper describes a new route for the preparation of all isomers of the anthra[b]thiophene and benzo[b]naphtho[d]thiophene ring systems.

The synthesis of anthra[2,3-b]thiophene was first reported by Faller, et al., in 1968 (3), using the Elbs reaction. The Elbs reaction is a useful method for the preparation of polycyclic aromatic compounds. Although the yields of products obtained via this procedure are usually quite low, the Elbs procedure is still quite valuable since it can be used to synthesize compounds which are difficult to prepare via other methods.

The cyclization of compounds which have an aldehyde group at the ortho-position with polyphosphoric acid to give polycyclic aromatic compounds is well known (4,5). Anthra[2,3-b]thiophene was prepared according to this method. The key intermediate compound for the synthesis of 7, 3-(2-thenyl)-2-naphthalenecarboxaldehyde (6), was prepared by the oxidation of 3-(2-thenyl)-2-naphthalenemethanol with chromium trioxide-pyridine complex in pyridine at room temperature. Compound 5 was obtained by the reduction of 3-(2-thenyl)naphthalenecarboxylic acid (4) with lithium aluminum hydride. Compound 4 was synthesized by the reduction of 3-(2-thenoyl)naphthalenecarboxylic acid (3) which was prepared from 2,3-naphthalenedicarboxylic acid and thiophene using the Friedel-Crafts condensation reaction. Cyclization of the crude aldehyde 6 by heating with polyphosphoric acid gave anthra[2,3-b]thiophene (7) as yellow crystals in 50.6% overall yield from 4.

Next, the synthesis of anthra[2,1-b]thiophene (13) and anthra[1,2-b]thiophene (20) is described using the Diels-Alder cycloaddition reaction of 1,4-naphthoquinone (9) with 2- or 3-vinylthiophene (8,17). In general, cycloaddition reactions of 1,4-naphthoquinone with various dienophiles is very useful; consequently, variations of this procedure have been frequently reported (6,7). It is well known that 2-vinylthiophene (8) reacts with

dienophiles such as benzoquinone and anhydrous maleic acid to yield naphthothiophene and benzo[b]thiophene derivatives (8,9). However, the reaction of vinylthiophenes (8,17) with 1,4-benzoquinone (9) has not been reported.

Scheme I outlines a new procedure for the preparation of anthra[2,1-b]- and anthra[1,2-b]thiophene (13,20) by an application of the Diels-Alder reaction, significantly enhancing the overall synthetic utility of the Diels-Alder approach to anthra[b]thiophenes. 2-Vinylthiophene (8) and 1,4-naphthoquinone (9) were refluxed in dry toluene for 24 hours giving the adduct 10 as red needles in 22% yield. The structure of this compound (10) was implied from the nmr data; namely, 10 has lost two protons relative to the first theoretical adduct, and four protons due to an ethylene group at 2.98 ppm are apparent. The mass spectrum and the elemental analysis also agree with this structure. Compound 10 was readily dehydrogenated by chloranil to the quinone 12 in 81% yield (yellow needles). Compound 12 has been previously prepared by other less convenient routes.

Reduction of 12 with lithium aluminum hydride in tetrahydrofuran gave two products, anthra[2,1-b]thiophene (13) and 6,11-dihydro-6-oxoanthra[2,1-b]thiophene (14) in 19.2% and 11% yield, respectively. The ir of 14 showed a peak at 1660 cm^{-1} due to the carbonyl group. The nmr spectrum of compound 14 indicated a methylene proton at 5.51 ppm, showing no low field shift for the deshielding effect of the carbonyl group. The nmr spectrum of compound 10 showed one hydrogen at the 1-position, which was deshielded by the carbonyl group at the 11-position, appearing as a doublet at 8.77 ppm ($J = 6\text{ Hz}$). When the reduction with lithium aluminum hydride was carried out in the presence of aluminum chloride, a mixture of 13 and 6,11-dihydroanthra[2,1-b]thiophene (15) was obtained. This mixture could

not be separated by fractional crystallization or column chromatography. This mixture, on treatment with 10% palladium on charcoal, gave a single product, 13, in 40.6% yield from 12.

Anthra[1,2-b]thiophene (20) was synthesized from 9 and 3-vinylthiophene (17), which was prepared by thermolysis of 3-methylcarbinolthiophene, in a manner similar to the preparation of 13. Reaction of 17 with 9 gave the dihydro product (18) in 43.9% yield, which was converted to 6,11-dihydro-6,11-dioxoanthra[1,2-b]thiophene (19) by treatment with chloranil. Compound 19 reacted with lithium aluminum hydride in tetrahydrofuran and zinc dust in ammonium hydroxide to give 20 in 5.6% and 6.8% yield, respectively. When 19 was treated with lithium aluminum hydride in the presence of aluminum chloride, a mixture of 20 and 6,11-dihydroanthra[1,2-b]thiophene (21) was obtained. This mixture was also reacted with 10% palladium on charcoal to give only one product, the desired compound 20 in 37% yield.

Finally, the synthesis of benzo[b]naphtho[2,3-d]thiophene (25), benzo[b]naphtho[2,1-d]thiophene (29) and benzo[b]naphtho[1,2-d]thiophene (34) are described. Compound 25 was synthesized from 22 in a manner similar to the preparation of 7. Reduction of 2-(2-benzo[b]thenyl)phenyl-carboxylic acid (22) to the corresponding primary alcohol (not purified) followed by oxidation with chromic oxide-pyridine reagent afforded the aldehyde 24, which was readily cyclized with polyphosphoric acid to the desired compound 25 in an overall yield of 58% from the acid 22. Recently, the required acid 22 was efficiently prepared in two steps from benzo[b]thiophene-2-carboxaldehyde (32) by condensation with phenyloxazoline using *n*-butyllithium, followed by reduction with hydrogen in the presence of palladium on charcoal (10). Various syntheses of compound 25 have been

reported (11-17). Of these procedures, Mayer's method was the most convenient and useful preparation due to its simplicity and wide range of applicability. Carruthers, et al. (18), reported the simple and convenient synthesis of 29 by irradiation of 3-styrylbenzo[b]thiophene (28), which was readily prepared using the Wittig reaction of 3-benzo[b]thenyltriposponium chloride with benzaldehyde (31). The styryl derivative 28 is the key intermediate in this reaction. We attempted the synthesis of 28 using the Wadsworth-Emmons reaction (19-21).

Thus, the reaction of benzo[b]thiophene-3-carboxaldehyde (26) with diethyl benzylphosphonate (27) gave 28 in good yield. Alternatively, compound 28 was obtained by the reaction of diethyl benzo[b]thenylphosphonate (29) with benzaldehyde (31) in 76% yield. Similarly, benzo[b]thiophene-2-carboxaldehyde (32) reacted with 27 to give 2-styrylbenzo[b]thiophene (33) in 72% yield. The photocyclization of these styryl derivatives was carried out in cyclohexane in the presence of iodine and air. As expected, the photocyclization of 2- or 3-styrylbenzo[b]thiophene (28, 33) proceeded smoothly and gave the desired benzo[b]naphtho[2,3-d]thiophene (29) and benzo[b]naphtho[1,2-d]thiophene (34) in 68% and 51% yield, respectively.

Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman Acculab-2 spectrometer. Nmr spectra were recorded on a Varian EM 390 spectrometer or a JEOL FX 90 Q spectrometer. The chemical shift values are expressed as δ values relative to tetramethylsilane as an internal standard. Mass spectra were obtained on a Hewlett-Packard model 5980 A mass spectrometer. Uv spectra were recorded for solutions in cyclohexane with a Perkin Elmer 320 spectrometer.

3-(2-Thenoyl)-2-naphthalenecarboxylic Acid (3).

A solution of 2.7 g of anhydrous aluminum chloride and 1 g (5 mmoles) of 2,3-naphthalenedicarboxylic acid anhydride in 10 ml of dry nitrobenzene was prepared at 50°. To this solution, 0.5 g (5.9 mmoles) of thiophene was added uniformly over a period of 20 minutes while maintaining the reaction temperature at 40-50°. One hour later, the reaction temperature was raised to 50-55° and this temperature was maintained for one hour, after which time the hydrochloric acid evolution had practically ceased. The dark red colored reaction mass was poured into ice-water and the nitrobenzene layer was washed nearly acid free. The crude 2-(2-thenoyl)-3-naphthalenecarboxylic acid, obtained after steam distillation of the nitrobenzene, was washed acid free and dissolved at 90° in water containing an excess of sodium carbonate. The filtered solution was carefully acidified with hydrochloric acid. The product was recrystallized from ethanol-benzene giving 0.45 g (31.9%) of pale brown prisms, mp 212°; ir (potassium bromide): 3050-2400 (OH), 1670, 1635 (C=O); ms: m/e 282 (M⁺, 55), 238 (M - 44), 237 (M - 45, 48), 111 (100).

Anal. Calcd. for C₁₆H₁₀OS: C, 68.07; H, 3.57; S, 11.36. Found: C, 68.02; H, 3.68; S, 10.89.

3-(2-Thenyl)-2-naphthalenecarboxylic Acid (4).

3-(2-Thenoyl)-2-naphthalenecarboxylic acid (1.4 g, 5 mmoles) was dissolved in 20 ml of concentrated ammonium hydroxide and 12 ml of water; the resulting solution was heated at 90-95° in an oil bath for 4 hours with 3 g of zinc dust (activated with copper sulfate). During the reduction, the solution changed in color from reddish-orange to pale yellow. The cooled reaction mixture was filtered to remove excess zinc and the filtrate was extracted once with ether. The aqueous layer was acidified with hydrochloric acid and a tan oil separated which solidified on standing. The solid was filtered, washed with water, dried and recrystallized from benzene giving 1.1 g (81.5%) of colorless needles, mp 188°; ir (potassium bromide): 3100-2700 (OH, broad), 1690 (C=O); nmr (deuteriochloroform + trifluoroacetic acid): 4.69 (s, CH₂, 2H), 6.75 (dd, J = 1, 5 Hz, H-3', 1H), 6.83 (dd, J = 5, 6 Hz, H-4, 1H), 7.13 (dd, J = 1, 6 Hz, H-5', 1H), 7.48-7.98 (m, H-5, H-6, H-7, H-8, 4H), 7.77 (s, H-4, 1H), 8.68 (s, H-1, 1H); ms: m/e 268 (M⁺, 50), 250 (M - 18, 100), 221 (M - 47, 56).

Anal. Calcd. for C₁₆H₁₂O₂S: C, 71.06; H, 4.47; S, 11.86. Found: C, 71.33; H, 4.46; S, 11.59.

Anthra[2,3-b]thiophene (7).

A solution of 0.73 g (3.17 mmol) of 3-(2-Thenyl)-2-naphthalenecarboxylic acid in 20 ml of dry ether was added dropwise to a suspension of 0.14 g of lithium aluminum hydride in 30 ml of dry ether. After refluxing for 3 hours, 10% sodium hydroxide was added dropwise and the precipitated aluminum hydroxide was filtered. The dried filtrate (sodium sulfate) was evaporated to give the crude alcohol as a colorless oil; ir (neat): 3370 (OH, broad).

The solution of the above alcohol in 8 ml of dry pyridine was added slowly to a suspension of chromium trioxide-pyridine. After stirring for

2 hours at room temperature, the reaction mixture was filtered and washed with chloroform. The filtrate was washed with 10% hydrochloric acid and then 10% sodium carbonate. After drying over sodium sulfate, chloroform was evaporated to leave the crude aldehyde as a dark oil; ir (neat): 1690 (C=O).

A mixture of the crude aldehyde and 7 ml of polyphosphoric acid was heated at 100° for 15 minutes. After cooling, ice water was added to the mixture and the resulting precipitated yellow solid was collected by filtration. After drying, the product was recrystallized from benzene giving 0.32 g (50.6%) of yellow cotton needles, mp 320° dec. [lit. (3) mp 330° dec.); ms: 234 (M⁺, 100).

4,5,6,11-Tetrahydro-6,11-dioxoanthra[2,1-b]thiophene (10).

A solution of 6.2 g (40 mmol) of 1,4-naphthoquinone and 4.4 g (40 mmol) of 2-vinylthiophene (22,23) in 200 ml of toluene was refluxed for 2 days. After cooling, the precipitate which formed was removed by filtration. The product gave colorless needles, mp 187° and was identified as 1,4-dihydroxynaphthalene (24). The toluene layer was washed with 200 ml of 10% sodium hydroxide solution and dried with sodium sulfate. The toluene was removed at reduced pressure. The residue was chromatographed on silica gel using hexane followed by benzene-hexane (1:1) as the eluents giving 2.30 g (22%) of a red oil which slowly crystallized. This crude product was used without purification in the subsequent reaction step. The analytical sample was recrystallized from benzene to give red needles, mp 188°; ir (potassium bromide): 1660, 1645 (C=O); nmr (deuteriochloroform): 2.98 (s, -CH₂-CH₂-, 4H), 7.09 (d, J = 5.5 Hz, H-2, 1H), 7.63-7.75 (m, H-8, H-9, 2H), 7.96 (d, J = 5.5 Hz, H-1, 1H), 8.00-8.30 (m, H-7, H-10, 2H); ms: m/e 266 (M⁺, 30), 264 (M - 2, 100).

Anal. Calcd. for $C_{16}H_{10}OS$: C, 72.16; H, 3.78; S, 12.04. Found: C, 72.39; H, 3.58; S, 12.09.

6,11-Dihydro-6,11-dioxoanthra[2,1-b]thiophene (12).

A solution of 2.67 g (10 mmoles) of 4,5,6,11-tetrahydro-6,11-dioxoanthra[2,1-b]thiophene and 2.46 g (10 mmoles) of chloranil in 100 ml of toluene was refluxed for 15 hours. After cooling, the precipitate was removed by filtration and the toluene solution was poured into 300 ml of ice water and added to 50 ml of 10% sodium hydroxide solution. This mixture was then extracted with 200 ml of benzene and the organic layer was dried over sodium sulfate. The benzene and toluene were removed by evaporation to yield a dark yellow oil which was chromatographed on silica gel using benzene-hexane as the eluent giving 2.1 g (81%) of yellow needles, mp 196° [lit. (3) mp 196°]; ir (potassium bromide): 1660 ($C=O$); nmr (deuteriochloroform): 7.71-7.82 (m, aromatic H, 3H), 8.12-8.38 (m, aromatic H, 4H), 8.77 (d, $J = 6$ Hz, H-1, 1H); ms: m/e 264 (M^{+} , 100).
3-Thienylmethylcarbinol (16).

Into a stirred solution of 5.2 g of lithium aluminum hydride in 50 ml of dry ether was slowly dropped 12.6 g (100 mmoles) of 3-acetylthiophene. When the addition was complete (5 hours), the reaction mixture was quenched with the cautious addition of 50 ml of water and enough 10% hydrochloric acid to dissolve the inorganic salts. The ether phase was evaporated and the aqueous phase was extracted with 3 X 100 ml of ether. The dried (sodium sulfate) ether extracts were evaporated yielding a pale yellow oil which was distilled at $105-110^{\circ}/20$ mm to give 11.0 g (85.9%) of a colorless oil (25).

3-Vinylthiophene (17) (26).

3-Thienylmethylcarbinol (10 g) was heated at reflux temperature. In order to prevent possible loss of the monomeric 3-vinylthiophene through polymerization in the dehydrating flask, 0.1% hydroquinone was added to the

alcohol before dehydration. The temperature of the vapor rose rapidly to 100° and then gradually rose to 130-150°, remaining at this latter temperature until the dehydration was complete. The mixture of the product and water was extracted with ether. After drying the ether solution with anhydrous sodium sulfate, the ether was removed on a steam bath and the residue was distilled under reduced pressure at 55-59°/20 mm to give 4.6 g (53.5%) of a colorless liquid; ir (neat): 1790, 1630.

4,5,6,11-Tetrahydro-6,11-dioxoanthra[1,2-b]thiophene (18).

This compound was synthesized from 1,4-naphthoquinone and 3-vinylthiophene in 43.9% yield in a manner similar to the preparation of 4,5,6,11-tetrahydro-6,11-dioxoanthra[2,1-b]thiophene, and was obtained as red needles after recrystallization from benzene/hexane (1:1), mp 176-177°; ir (potassium bromide): 1655, 1635 (C=O); nmr (deuteriochloroform): 2.92 (s, -CH₂-CH₂-, 4H), 6.90 (d, J = 5 Hz, H-3, 1H), 7.56 (d, J = 5 Hz, H-2, 1H), 7.59-7.81 (m, H-8, H-9, 2H), 7.99-8.73 (m, H-7, H-10, 2H); ms: m/e 266 (M⁺, 100).

Anal. Calcd. for C₁₆H₁₄O₂S: C, 72.16; H, 3.78; S, 12.04. Found: C, 72.43; H, 3.70; S, 11.73.

6,11-Dihydro-6,11-dioxoanthra[1,2-b]thiophene (19).

This compound was synthesized from 4,5,6,11-tetrahydro-6,11-dioxoanthra[1,2-b]thiophene in 84.6% yield in a manner similar to the preparation of 6,11-dihydro-6,11-dioxoanthra[2,1-b]thiophene and was obtained as red needles after recrystallization from benzene, mp 219-220° [lit. (27) mp 221°]; ir (potassium bromide): 1665 (C=O); ms: m/e 264 (M⁺, 100).

Anthra[2,1-b]thiophene (13).

a)

Into a stirred solution of 0.86 g of lithium aluminum hydride in 50 ml of tetrahydrofuran, 1 g (3.79 mmol) of 6,11-dihydro-6,11-dioxoanthra[2,1-b]thiophene was slowly added dropwise. When the addition was complete,

the tetrahydrofuran was brought to reflux for 48 hours after which time it was quenched by cautiously adding 10 ml of water, and enough 10% hydrochloric acid to dissolve the inorganic salts. The mixture was poured into ice water and extracted with 100 ml of benzene. The extract was washed successively with water and saturated sodium bicarbonate solution, and was then dried (sodium sulfate) and evaporated. The residue was chromatographed on a column of silica gel using hexane as an eluent giving pale yellow crystals which were recrystallized from ethanol giving 0.17 g (19.2%) of white leaflets, mp 196° [lit. (3) mp 196°]; ms: m/e 234 (M^{+} , 100).

Subsequent elution using hexane-benzene (1:1) as the eluent gave 0.3 g of the starting material as yellow crystals.

Further elution using benzene afforded a brown crystalline substance which was recrystallized from benzene to give 0.1 g of 6,11-dihydro-6-oxoanthra[2,1-b]thiophene (14) as colorless needles, mp 260° ; ir (potassium bromide): 1660 (C=O); nmr (deuteriochloroform): 5.51 (s, CH_2 , 2H), 7.25-8.00 (m, aromatic proton, 8H); ms: m/e 250 (M^{+} , 27), 249 ($M - 1$, 100); gc-ms retention time: 1.7, this mass showed as a benzene peak at m/e 78.

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{OS} + 0.5\text{C}_6\text{H}_6$: C, 78.86; H, 4.53; S, 11.08. Found: C, 78.90; H, 4.42; S, 10.94.

b)

A solution of 1.2 g of aluminum chloride in 50 ml of absolute ether was added to a stirred suspension of 0.4 g of lithium aluminum hydride in 15 ml of absolute ether. The mixture was stirred for 15 minutes and then 0.5 g of 6,11-dihydro-6,11-dioxoanthra[2,1-b]thiophene was added portionwise. The gray ethereal suspension was maintained at reflux for 2 hours. Ethyl

acetate (15 ml) was added dropwise in order to decompose the excess hydride reagent. The reaction mixture was poured into ice and 5% hydrochloric acid. The ether layers were separated and the aqueous phase was extracted with 3 X 50 ml portions of ether. The combined ethereal solution was washed successively with saturated sodium bicarbonate solution and water, and was then dried with sodium sulfate and concentrated in vacuo. The pale yellow gummy solid was chromatographed on a silica gel column using hexane as an eluent to yield a white solid material. The nmr of the product showed two methylene protons at 4.12 and 4.28 ppm, and two singlet peaks at 8.48 and 8.84 ppm, due to the aromatic proton at the 6- and 11-positions. These peaks indicate a mixture of 6,11-dihydroanthra[2,1-b]thiophene (15) and anthra[2,1-b]thiophene (13). A mixture of 13 and 15, 0.05 g of palladium on charcoal and 20 ml of m-xylene was refluxed for 30 hours. After removing the palladium on charcoal, m-xylene was evaporated at reduced pressure. The residue was recrystallized from ethanol to give 0.18 g (40.6%) of the product as pale yellow leaflets, mp 196°; ms: m/e 234 (M⁺, 100). The picrate gave dark red needles, mp 157°.

Anthra[1,2-b]thiophene (20).

This compound was synthesized from 6,11-dihydro-6,11-dioxoanthra[1,2-b]thiophene by the following three methods: method a) and method b), in a manner similar to the preparation of anthra[2,1-b]thiophene and the method of reduction with zinc dust (method c). These yields were 5.6%, 37% and 6.8%, respectively. This compound gave colorless leaflets, mp 120° [lit. (3) mp 121°] and the picrate gave brown red needles, mp 145°.

c)

A mixture of 0.5 g of 6,11-dihydro-6,11-dioxoanthra[1,2-b]thiophene,

2 g of zinc dust (treated with 0.1% copper sulfate solution for 5 minutes), 50 ml of 2N sodium hydroxide solution and 30 ml of toluene was refluxed for 10 hours. The toluene layer was separated and the aqueous layer was extracted once with 50 ml of benzene. The combined toluene and benzene extracts were washed successively with saturated sodium bicarbonate solution and water, and were evaporated in vacuo following drying (sodium sulfate). The residue was chromatographed on a column of silica gel using hexane as the eluent to give pale yellow needles, which were recrystallized from ethanol giving 0.03 g (6.8%) of colorless crystals, mp 120°; ms: m/e 234 (M⁺, 100). Benzo[b]naphtho[2,3-d]thiophene (7).

A solution of 1.35 g (5 mmoles) of 2-(2-benzo[b]thenyl)benzenecarboxylic acid in 50 ml of dry ether was added dropwise to a suspension of 0.2 g of lithium aluminum hydride in 40 ml of dry ether. After refluxing for 3 hours, the reaction mixture was carefully quenched by cautiously adding 6 ml of water and enough 10% hydrochloric acid to dissolve the inorganic salts. The ether phase was separated and the aqueous phase was extracted with 3 X 50 ml portions of ether dried over sodium sulfate. Evaporation of the ether yielded colorless crystals, mp 92°; ir: 3370 (OH, broad).

The solution of the above crude alcohol in 15 ml of dry pyridine was added slowly to a suspension of chromium trioxide-pyridine complex made from 1.2 g of chromium trioxide and 12 ml of dry pyridine. After stirring for 2 hours at room temperature, the reaction mixture was filtered and washed with chloroform. The filtrate was washed with 10% hydrochloric acid and 10% sodium carbonate successively. After drying over sodium sulfate, the chloroform was evaporated to leave the crude aldehyde as a dark oil; ir (neat): 1690 (C=O).

A mixture of the crude aldehyde and 10 g of polyphosphoric acid was

heated at 100° for 30 minutes. After cooling, ice water was added to the reaction mixture and the precipitated brown solid was collected by filtration. After drying, the product was recrystallized from benzene-hexane (1:1) giving 0.68 g (58%) of colorless crystals, mp 158-159 [lit. mp (11) 158°, (14) 163°, (12) 160°]; ms: m/e 234 (M⁺, 100). The picrate gave red needles, mp 130°.

Diethyl Benzo[b]thenylphosphonate (29).

A mixture of 30 g (165 mmoles) of 3-chloromethylbenzo[b]thiophene (28) and 30 g (180 mmoles) of triethylphosphite was heated at 160° for 8 hours. The reaction product was distilled to give 42 g (89.7%) of a colorless oil, bp 176-182°/1.5 mm; nmr (deuteriochloroform): 1.13 (t, J = 7 Hz, -CH₂-CH₃, 6H), 3.21 (s, -CH₂- 1H), 3.46 (s, -CH_b, 1H), 3.94 (q, O-CH₂-, 4H), 7.89 (s, H-2, 1H), 7.19-7.36 (m, H-5, H-6, 2H), 7.66-7.79 (m, H-4, H-7, 2H).

Anal. Calcd. for C₁₃H₁₇O₃PS: C, 55.03; H, 6.03; P, 10.89; S, 11.28.

Found: C, ; H, ; P, ; S, .

3-Styrylbenzo[b]thiophene (28).

a)

Under a nitrogen atmosphere, 1.34 g (28 mmoles) of sodium hydride (the mineral oil was removed by washing with dry petroleum ether) was added to an ice cooled stirred solution of 4.06 g (25 mmoles) of 3-benzo[b]-thiophenecarboxaldehyde and 5.71 g (25 mmoles) of diethyl benzylphosphonate (29) in 50 ml of 1,2-dimethoxyethane. After stirring for 15 minutes, the ice bath was removed. The mixture was stirred at room temperature for 3 hours and poured into ice water. The precipitate was collected by filtration and recrystallized from ethanol giving 5.11 g (86%) of pale yellow crystals, mp 95-96°.

b)

Sodium hydride (50%, 0.98 g, 10 mmoles) was placed in 50 ml of dry 1,2-dimethoxyethane. The slurry was cooled to 20° and 2.84 g (10 mmoles) of diethyl benzo[b]thenylphosphonate was added dropwise with stirring. After the addition, the solution was stirred at room temperature for 30 minutes. To the pale yellow solution, maintained below 25°, was added dropwise 1.06 g (10 mmoles) of benzaldehyde. During the addition, a gummy precipitate appeared. The solution was stirred at room temperature for 1 hour and heated at 50° for 30 minutes. After cooling, a large excess of water was added and the product was collected by filtration. The product was recrystallized from ethanol giving 1.8 g (76%) of pale yellow crystals, mp 96° [lit. (18) mp 97°]; ms: m/e 234 (M^+ , 100).

Benzo[b]naphtho[2,1-d]thiophene (29).

A solution of 1.77 g (75 mmoles) of 3-styrylbenzo[b]thiophene and 0.10 g of iodine in 750 ml of cyclohexane was irradiated for 4 hours with a 450 Watt Hanovia medium pressure mercury lamp, through a corex filter. During the course of the reaction, a slow stream of air was passed through the solution. The solvent was evaporated in vacuo and the residue was effectively purified by silica gel chromatography using benzene as an eluent giving 2.38 g (68%) of colorless fine plates, mp 185-186° [lit. (30) mp 185-186°]; ms: m/e 234 (M^+ , 100). The picrate gave orange-red needles, mp 145°.

2-Styrylbenzo[b]thiophene (33).

This compound was synthesized from 2-benzo[b]thiophenecarboxaldehyde and diethyl benzylphosphonate in a manner similar to the preparation of 3-styrylbenzo[b]thiophene and was obtained as pale yellow leaflets (ethanol) in 72% yield, mp 196-197°; ms: m/e 236 (M^+ , 100), 234 ($M - 2$, 61).

Anal. Calcd. for $C_{16}H_{12}S$: C, 81.31; H, 5.12; S, 13.57. Found: C, 81.31; H, 5.18; S, 13.41.

Benzo[b]naphtho[1,2-b]thiophene (34).

This compound was synthesized by photocyclization from 2-styryl-benzo[b]thiophene in a manner similar to the preparation of benzo[b]naphtho[2,1-d]thiophene, and was obtained as colorless crystals, mp $103-104^{\circ}$ [lit. (31) mp $102-105^{\circ}$], in 51% yield; ms: m/e 234 (M^{+} , 100). The picrate was obtained as orange-red needles, mp 149° .

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+

+

+

LAH

LAH
AlCl₃

+

Pd/C

13

Scheme I

Scheme II

B. Synthesis of Phenaleno[1,9-bc]thiophene.

The cyclization of 2-acetylthionaphthalene, prepared from 2-mercaptanaphthalene (1) and chloroacetone in the presence of sodium hydroxide, with polyphosphoric acid gave 1-methylnaphtho[2,1-b]thiophene (4) in 64% overall yield from 1. By bromination with N-bromosuccinimide, 4 was converted in 40% yield into 1-bromomethylnaphtho[2,1-b]thiophene (8). Treatment of 8 with potassium cyanide in a phase-transfer medium gave 1-cyanomethylnaphtho[2,1-b]thiophene (10) in good yield. Compound 10 was reduced to the corresponding aldehyde (11) and then cyclized with polyphosphoric acid to phenaleno[1,9-bc]thiophene in 24% overall yield from 10.

Recently, we prepared all of the isomeric phenanthro[b]thiophenes, anthra[b]thiophenes and benzo[b]naphtho[b]thiophenes in order to assign the absolute structure of each tetracyclic thiophene in coal derived products (1). These compounds have a molecular formula and weight of either $C_{16}H_{10}S = 234$, or, in the case of two isomers, of $C_{14}H_8S = 208$. One of these last mentioned isomers is phenanthro[1,9-bcd]thiophene, which has already been isolated, identified (2) and synthesized by Klemm (3). However, the other isomer, phenaleno[1,9-bc]thiophene, is a ring system which is unreported in the literature. As a continuation of the work currently in progress in this laboratory, we now report the facile synthesis of phenaleno[1,9-bc]thiophene (12) according to a modification of Newman's method for the synthesis of benzo[a]pyrene (4). The Newman procedure has also been found to be

applicable to the preparation of other polycyclic aromatic hydrocarbons (5).

It has been reported that refluxing a mixture of potassium cyanide and a bromomethyl compound in benzene/water in the presence of methyltri-caprylammonium chloride (Aliquat 336) (6) gives the corresponding key intermediate cyanomethyl derivatives, which can be used for the synthesis of polycyclic compounds. 1-Cyanomethylnaphtho[2,1-b]thiophene (10), which was expected to be prepared by bromination of 1-methylnaphtho[2,1-b]thiophene (4) with N-bromosuccinimide followed by treatment with potassium cyanide, is a key intermediate for the synthesis of the desired phenaleno[1,9-bc]thiophene (12).

Dann reported the synthesis of 3-methylnaphtho[2,1-b]thiophene (4) from 2-mercaptanaphthalene (1) and chloroacetone (2) in the presence of sodium hydroxide in methanol followed by cyclization with hydrogen fluoride or concentrated sulfuric acid (7). In this procedure the total yield from 1 is only 40%, and therefore we attempted to improve the yield. Thus, a solution of sodium hydroxide was added portionwise to a solution of compounds 1 and 2 in methanol under stirring at room temperature to give compound 3, which was treated with polyphosphoric acid on a steam bath for 30 minutes without purification of 3 to afford 4 in 64% overall yield from 1.

We also attempted an alternative synthesis of 4 by photocyclization of styrylthiophene. Recently, Iwao, et al., have reported that phenanthro-[b]thiophene derivatives are conveniently prepared by the oxidative photocyclization of naphthylethenylthiophene (1). The synthesis of the parent naphtho[2,1-b]thiophene from 2-styrylthiophene in a similar photocyclization has also been reported (8). We applied this procedure for

the synthesis of 4. Compound 5 was readily prepared by the Wadsworth-Emmons reduction (9-11) between diethyl benzylphosphonate (6) and 4-methylthiophene-2-carboxaldehyde (7) in 87% yield. The photocyclization of 5 was carried out in cyclohexane in the presence of iodine and air. However, the yield using this procedure proved to be poor (40% yield). In general, the photocyclization of the methyl compounds does not proceed as well as that of the corresponding unsubstituted derivatives (12-13).

Bromination of aromatic methyl compounds with N-bromosuccinimide is most often reported to occur in nonpolar solvents, such as carbon tetrachloride. However, bromination of 4 with N-bromosuccinimide in carbon tetrachloride gave only 2-bromo-1-methylnaphtho[2,1-b]thiophene (9) in 79% yield. However, Campaigne reported the bromination of 3-methylbenzo[b]thiophene with N-bromosuccinimide in dry benzene to give only the corresponding bromomethyl compound in good yield (14). Thus, we attempted the bromination of 4 with N-bromosuccinimide in dry benzene. Compound 4 was allowed to react with N-bromosuccinimide in dry benzene in the presence of benzoylperoxide under reflux for 2 hours giving two products, 9 and 1-bromomethylnaphtho[2,1-b]thiophene (8) in 24.7% and 39.7% yield, respectively.

Treatment of 8 with potassium cyanide in benzene/water in the presence of methyltricaprylammonium chloride (Alliquat 336) gave 1-cyanomethylnaphtho[2,1-b]thiophene (10) in 68.3% yield. This compound was reduced to the corresponding aldehyde (not isolated) and then cyclized with polyphosphoric acid to give the desired phenaleno[1,9-bc]thiophene (12) in 23.6% overall yield from 10. However, cyclization of 14 under similar conditions did not give the desired product. Compound 14 was successfully prepared by the bromination of 9 with N-bromosuccinimide in dry benzene followed by cyanation with potassium cyanide in good yield.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Ir spectra were obtained on a Perkin Elmer model 457 spectrophotometer and a Beckman Acculab 2 spectrophotometer. ^1H Nmr spectra were obtained on a Varian EM 390 spectrometer and a JEOL FX 90 Q spectrometer in the solvents as indicated. Chemical shifts are reported in ppm from TMS as an internal standard and are given in δ units. Mass spectra were obtained on a Hewlett-Packard model 5980A mass spectrometer. Uv spectra were recorded for solutions in cyclohexane with a Perkin Elmer 320 spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona.

1-Methylnaphtho[2,1-b]thiophene (1).

a)

A solution of sodium hydroxide (2 g of sodium hydroxide + 4 ml of water) was added dropwise to a stirred solution of 4.8 g (30 mmols) of 2-naphthalenethiol and 2.8 g (30 mmols) of chloroacetone in 30 ml of methanol. The mixture was stirred for 1 hour at room temperature and then heated to reflux for 30 minutes. The reaction mixture was chilled, poured into 300 ml of water and acidified with 10% hydrochloric acid. The resulting precipitates were collected by filtration.

Polyphosphoric acid (15 g) was prewarmed on a steam bath and the above product was thoroughly mixed in. The mixture was heated for 30 minutes on a steam bath and was then poured into 300 ml of ice water. An oily product appeared, from which the aqueous layer was decanted, and the crude product was dissolved in 200 ml of benzene. The solution was dried with sodium sulfate and evaporated to give a dark oil. The residue was

mixed with 5 g of silica gel (60-200 mesh) and this mixture was loaded onto a silica gel column. Using hexane as an eluent gave colorless crystals, which were recrystallized from methanol yielding 3.3 g (64%) of colorless prisms, mp 60° [lit. (7) mp 58-60].

b)

A solution of 1 g (5 mmoles) of 4-methyl-2-styrylthiophene and 0.05 g of iodine in 500 ml of cyclohexane was irradiated for 6 hours with a 450 Watt Hanovia medium pressure mercury lamp, through a corex filter. During the course of the reaction, a slow stream of air was passed through the solution. The solvent was evaporated in vacuo and the residue was effectively purified by silica gel chromatography using hexane as the eluent giving 0.41 g (41%) of 1-methylnaphtho[2,1-b]thiophene; nmr (deuteriochloroform): 2.89 (s, CH₃, 3H), 7.49-7.99 (m, H-2, H-5, H-6, H-7, H-8, 6H), 8.69 (dd, J = 1, 7 Hz, H-9, 1H); ms: m/e 198 (M⁺, 100).

4-Methyl-2-styrylthiophene (5).

Sodium hydride (50%, 1 g, 22 mmoles) was placed in 50 ml of dry 1,2-dimethoxyethane. The slurry was cooled to 20° and 2.28 g (10 mmoles) of dimethylbenzylphosphonate was added dropwise with stirring. After the addition, the solution was stirred at room temperature for 30 minutes. To the pale yellow solution, maintained below 25°, was added dropwise 1.26 g (10 mmoles) of 4-methyl-2-thiophenecarboxaldehyde (15). During the addition, a gummy precipitate appeared. The solution was stirred at room temperature for 1 hour and then heated at 50° for 30 minutes. After cooling, a large excess of water was added and the resulting precipitate was collected by filtration. The product was recrystallized from hexane giving 0.87 g (87%) of pale yellow leaflets, mp 67°; nmr (deuteriochloroform): 2.23 (s, CH₃, 3H), 6.78 (s, H-5, 1H), 6.89 (s, H-3, 1H), 6.96 (d, J = 16 Hz, ethylene proton, 1H),

7.19 (d, $J = 16$ Hz, ethylene proton, 1H), 7.28-7.46 (m, phenyl protons, 5H).

Anal. Calcd. for $C_{13}H_{12}S$: C, 77.95; H, 6.04; S, 16.01. Found: C, 78.02; H, 6.15; S, 16.19.

2-Bromo-1-methylnaphtho[2,1-b]thiophene (9).

A mixture of 0.95 g (5.3 mmol) of N-bromosuccinimide, 1 g (5 mmol) of 1-methylnaphtho[2,1-b]thiophene, 0.005 g of benzoylperoxide and 50 ml of dry carbon tetrachloride was refluxed. Boiling was continued for 2 hours, the mixture was cooled in an ice bath, and the crystals of succinimide were removed by filtration. The filtrate was washed with 10% sodium hydroxide solution and then with water. The benzene layer was dried with sodium sulfate and evaporated to give brown crystals. The crude product was purified by chromatography on a silica gel column using hexane as the eluent giving 1.1 g (79%) of the product as colorless needles, mp 89° . An analytical sample was recrystallized from methanol; nmr (deuteriochloroform): 2.83 (s, CH_3 , 3H), 7.50-7.68 (m, H-7, H-8, 2H), 7.69 (s, H-4, H-5, 2H), 7.89-7.92 (m, H-6, 1H), 8.60 (dd, $J = 2, 6$ Hz, H-9, 1H); ms: m/e 278 ($M + 2$, 100), 276 (M^+ , 99), 197 ($M - HBr$).

Anal. Calcd. for $C_{13}H_9BrS$: C, 56.33; H, 3.27; S, 11.57. Found: C, 56.56; H, 3.52; S, 11.38.

1-Bromomethylnaphtho[2,1-b]thiophene (8).

A mixture of 3.8 g (21.5 mmol) of N-bromosuccinimide, 3.96 g (20 mmol) of 1-methylnaphtho[2,1-b]thiophene, 0.01 g of benzoyl peroxide and 100 ml of dry benzene was gently refluxed. Boiling was continued for 2.5 hours, the mixture was cooled in an ice water bath and the crystals of succinimide were removed by filtration. The filtrate was washed with 10% sodium hydroxide solution and water. The benzene layer was dried with sodium sulfate and evaporated to give crystals. After washing with

hexane, the colorless crystals were recrystallized from hexane giving 2.20 g (39.7%) of **8** as colorless needles, mp 142° ; nmr (deuteriochloroform): 5.04 (s, CH_2 , 2H), 7.45-7.94 (m, H-2, H-4, H-5, H-7, H-8, 6H), 8.54 (dd, $J = 2, 7$ Hz, 1H); ms: m/e 278 ($M + 2$, 38), 276 (M^+ , 37), 197 ($M - \text{Br}$, 100).

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{BrS}$: C, 56.33; H, 3.27; S, 11.57. Found: C, 56.38; H, 3.40; S, 11.60.

The hexane layer wash was evaporated and the residual brown oil was chromatographed over a silica gel column using hexane as the eluent to give 1.37 g (24.7%) of 2-bromo-1-methylnaphtho[2,1-b]thiophene (**9**). 1-Cyanomethylnaphtho[2,1-b]thiophene (**10**).

A mixture of 2 g (7.2 mmol) of 1-bromomethylnaphtho[2,1-b]thiophene, 2.5 g of potassium cyanide, 100 ml of benzene, 15 ml of water and 10 drops of Aliquat 336 was refluxed for 2.5 hours. After the addition of 100 ml of benzene, the benzene layer was washed successively with water, 10% hydrochloric acid and water. After drying with sodium sulfate, the benzene was evaporated. The residue was recrystallized from benzene/hexane (1:1) giving 1.1 g (68.3%) of pale brown needles, mp 102° ; ir (potassium bromide): 2245 (CN); nmr (deuteriochloroform): 4.17 (s, CH_2 , 2H), (7.47-8.16 (m, H-2, H-4, H-5, H-6, H-7, H-8, H-9, 7H); ms: m/e 223 (M^+ , 100), 195 ($M-28$, 14).

Anal. Calcd. for $\text{C}_{14}\text{H}_9\text{NS}$: C, 75.31; H, 4.06; N, 6.27; S, 14.36. Found: C, 75.20; H, 4.33; N, 6.23; S, 14.08.

Phenaleno[1,9-bc]thiophene (**12**).

Diisobutylaluminum hydride (25% solution in toluene, 2 ml, 3 mmol) was added with a syringe to a solution of 0.5 g (2.24 mmol) of

1-cyanomethylnaphtho[2,1-b]thiophene in 15 ml of dry benzene. The reaction mixture was stirred at room temperature for 2 hours. Dilute hydrochloric acid was added and the product was extracted with chloroform. Evaporation of the dried extract gave the aldehyde as an oil which slowly crystallized; ir (neat): 1710 (C=O).

A mixture of the above crude aldehyde and 10 g of polyphosphoric acid was heated on a steam bath for 1 hour. The reaction mixture was poured into ice water and extracted with benzene. The extract was washed with water, dried and evaporated. The residue was chromatographed on a column of silica gel using cyclohexane as the eluent giving 0.13 g of red crystals. This product was purified by sublimation at 130-140°/1.5 mm giving colorless crystals which were recrystallized from methanol yielding 0.11 g (23.6%) of colorless prisms, mp 156°. The picrate of this compound gave red violet needles, mp 195° dec, recrystallized from ethanol; ir (potassium bromide): 3100, 3050 (w), 2930 (w), 1730 (w), 1485 (w), 830, 800, 675; uv: λ max nm (log ϵ) 230 (4.24), 252 (4.13), 263 (4.30), 269 (4.25), 337 (4.08), 344 (4.22), 350 (4.21), 364 (4.21); nmr (deuteriochloroform): 7.66 (s, H-2, 1H), 7.61-8.17 (m, aromatic protons, 7H); ms: m/e 208 (M^+ , 100), 163 ($M - 45$, 29).

Anal. Calcd. for $C_{14}H_8S$: C, 80.73; H, 3.87; S, 15.39. Found: C, 80.49; H, 4.09; S, 15.13.

2-Bromo-1-bromomethylnaphtho[2,1-b]thiophene (13).

A mixture of 1.13 g (4.08 mmoles) of 2-bromo-1-methylnaphtho[2,1-b]thiophene, 0.6 g (2.1 mmoles) of 1,3-dibromo-5,5-dimethylhydantoin, 0.005 g of benzoyl peroxide and 50 ml of dry benzene was refluxed for 2 hours. The reaction mixture was cooled in an ice bath and the precipitate was removed by filtration. The filtrate was washed with 10% sodium hydroxide

solution and water. The benzene layer was dried with sodium sulfate and evaporated giving 1.3 g (90%) of colorless crystals. An analytical sample was recrystallized from hexane/benzene (1:1). In a similar manner, the reaction of 2-bromo-1-methylnaphtho[2,1-b]thiophene with N-bromosuccinimide gave the dibromo compound in 79% yield; nmr (deuteriochloroform): 5.09 (s, CH₃, 3H), 7.51-7.84 (m, H-4, H-5, H-7, H-8, 4H), 7.99 (dd, J = 1, 7 Hz, H-6, 1H), 8.68 (dd, J = 2, 6 Hz, H-9, 1H); ms: m/e (M + 2, 46), 275 (M⁺, 42), 196 (M - Br, 100).

Anal. Calcd. for C₁₃H₈BrS: C, 43.85; H, 2.26; Br, 4.49; S, 9.00. Found: C, 43.69; H, 2.46; Br, 4.26; S, 8.79.

2-Bromo-1-cyanomethylnaphtho[2,1-b]thiophene (14).

A mixture of 1.15 g (3.23 mmoles) of 2-bromo-1-bromomethylnaphtho[2,1-b]thiophene, 2 g of potassium cyanide, 4 drops of Aliquat 336, 50 ml of benzene and 10 ml of water was refluxed for 2 hours. After the addition of 50 ml of benzene, the benzene layer was washed successively with water, 10% hydrochloric acid, and water. After drying, the benzene was evaporated. The residue was recrystallized from benzene/hexane giving 0.53 g (53%) of colorless needles, mp 172-173°; ir (potassium bromide): 2260 (CN); nmr (deuteriochloroform): 4.28 (s, CH₂, 2H), 7.57-7.80 (m, H-4, H-5, H-7, H-8, 4H), 7.98 (dd, J = 2, 7 Hz, H-6, 1H), 8.45 (dd, J = 1, 6 Hz, H-9, 1H); ms: m/e 303 (M + 2, 100), 301 (M⁺, 100).

Anal. Calcd. for C₁₄H₈BrNS: C, 55.64; H, 2.67; N, 4.64; S, 10.61. Found: C, 55.46; H, 2.81; N, 4.57; S, 10.55.

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C. Synthesis of Benzo[b]phenanthro[d]thiophenes.

Abstract: The synthesis of benzo[b]phenanthro[1,2-d]thiophene (1), benzo[b]phenanthro[4,3-d]thiophene (2), benzo[b]phenanthro[2,1-d]thiophene (3) and benzo[b]phenanthro[3,4-d]thiophene (4) from appropriately substituted stilbenes by photochemical cyclodehydrogenation is described. The photolysis of stilbene 2 gave a mixture of 4 and anthra[1,2-b]benzo[d]thiophene (5).

The majority of polycyclic hydrocarbons, that have proved to be carcinogenic, are phenanthrene derivatives suitably, substituted by alkyl or aryl ring attached to the phenanthrene ring (1). Robinson, after studying a large number of carcinogenic hydrocarbons, proposed an hypothesis that for carcinogenicity, the 9,10-position of the activated phenanthrene system should be unsubstituted (2). Recently we have become interested in ascertaining which of the polycyclic sulfur-containing heterocycles are carcinogenic in coal and coal derived products (3). In that connection it has already been confirmed that benzo[b]naphtho[2,1-d]thiophene is present in coal products, but found to be void of the mutagenic activity (4). This may be due to the absence of a 9,10-unsubstituted phenanthrene system. Therefore based on Robinson's hypothesis, it appeared of interest to synthesize some homologs of benzo[b]naphtho[d]thiophene such as benzo[b]phenanthro[1,2-d]thiophene (1), benzo[b]phenanthro[4,3-d]thiophene (2) benzo[b]phenanthro[2,1-d]thiophene (3) and benzo[b]phenanthro[3,4-d]thiophene (4).

These compounds were basically prepared by photochemical cyclodehydrogenation of appropriately substituted stilbenes (6, 7, 8 and 9) and is depicted in the scheme below. The Wadsworth-Emmons reaction between 2-benzo[b]thiophene-carboxaldehyde and diethyl 1-naphthylmethylphosphonate and diethyl 2-naphthylmethylphosphonate gave stilbenes 6 and 7, respectively. The photocyclization of stilbenes 6 and 7 with a 450 Watt Hanovia medium pressure mercury lamp gave benzo[b]phenanthro[1,2-d]thiophene (1) and benzo[b]phenanthro[4,3-d]thiophene (2). Davies, *et al.*, prepared 1 involving a multistep synthesis starting from 3-vinylthiophene and naphthoquinone (5). The compounds 3 and 4 were also prepared by photochemical cyclodehydrogenation of stilbenes 8 and 9, respectively. This reaction was earlier studied by Croisy, *et al* (6). In the photolysis of 9, we isolated both benzo[b]phenanthro[3,4-d]thiophene (4) and anthra[1,2-b]benzo[d]thiophene (5) in the ratio of 1:3, whereas Croisy, *et al.*, obtained only 5 as the sole product. We prepared stilbenes 8 and 9 by the Wadsworth-Emmons reaction in higher yields than those reported (6).

EXPERIMENTAL

¹H-Nmr were obtained on a Varian M390 spectrometer and a JEOL FX 9Q spectrometer in the solvents indicated. Chemical shifts are reported in ppm from TMS as an internal reference and are given in δ units. Mass spectra were recorded on a Hewlett-Packard model 5980A mass spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Melting points were determined on a Thomas-Hoover melting points apparatus and are uncorrected.

1-(Benzo[b]thiophen-2-yl)-2-(1'-naphthyl)ethene (6).

Sodium hydride (50% oil suspension, 0.6 g, 12 mmoles) was placed in 1,2-dimethoxyethane. Diethyl 1-naphthylmethylphosphonate (2.62 g, 10 mmoles) was added dropwise to the above suspension. After addition, the solution was stirred at room temperature for about 1 hour. To the yellow solution, was

added dropwise 2-benzo[b]thiophenecarboxaldehyde and the reaction mixture was stirred at room temperature for 1 additional hour. The reaction mixture was decomposed with water and the solid was collected by suction filtration, yield 2.5 g (87%), mp 155°; nmr (deuteriochloroform): 7.0-8.3 (m, all aromatic and olefinic protons, 14H); ms: 286 (M^+ , 100).

1-(Benzo[b]thiophen-2-yl)-2-(2'-naphthyl)ethene (**7**).

This compound was prepared according to the above procedure, yield, 79.5%, mp 255°; nmr (deuteriochloroform): 7.3-8.2 (m, all aromatic and olefinic protons, 14H); ms: 286 (M^+ , 100).

Benzo[b]phenanthro[1,2-d]thiophene (**1**).

A solution of 1-(benzo[b]thiophen-2-yl)-2-(1'-naphthyl)ethene (0.5 g, 17 mmoles) and iodine (0.5 g) in cyclohexane (500 ml) was irradiated for 4 hours with a 450 Watt Hanovia medium pressure mercury lamp through a Corex filter. During the course of reaction a slow stream of air was also passed through the solution. The solvent was evaporated in vacuo and the residue was chromatographed on a silica gel column using hexane as a eluant to give after crystallization from hexane 0.2 g (41%) of **1** as white crystals, mp 162-164° (lit 168°); ms: 284 (M^+ , 100); nmr (deuteriochloroform): 7.36-8.20 (m, H-2, H-3, H-6, H-8, H-9, H-10, H-11, H-12, 8H), 8.76 (d, $J = 10$ Hz, H-1, H-13, 2H), 8.98 (d, $J = 10$ Hz, H-4, H-5, 2H).

Anal. Calcd. for $C_{20}H_{12}S$: C, 84.47; H, 4.25; S, 11.27. Found: C, 84.32; H, 4.41; S, 11.05.

Benzo[b]phenanthro[4,3-d]thiophene (**2**).

This compound was prepared following the above procedure described for **1**, yield, 25%, mp 132-133°; ms: 284 (M^+ , 100); nmr (deuteriochloroform): 7.25-8.0 (m, H-1, H-2, H-3, H-4, H-7, H-8, H-10, H-11, H-12, H-13, 10H), 8.70 (near dd, $J = 10$ Hz, H-6, 1H), 9.04 (near dd, $J = 10$ Hz, H-5, 1H).

Anal. Calcd. for $C_{20}H_{12}S$: C, 84.47; H, 4.25; S, 11.27. Found: C, 84.46; H, 4.32; S, 11.00.

Diethylbenzo[b]thiophen-3-ylphosphonate (10).

Compound 10 was prepared by the reaction of 3-chloromethylbenzo[b]thiophene and triethylphosphite following the procedure of Yoshinori, et al. (7).

1-(Benzo[b]thiophen-3-yl)-2-(1'-naphthyl)ethene (8).

This compound was prepared by Wadsworth-Emmons reaction between 10 and 1-naphthalenecarboxaldehyde following the method used for 6, yield 56%, mp 130° (lit. 134°).

1-(Benzo[b]thiophen-3-yl)-2-(2'-naphthyl)ethene (9).

This compound was also prepared in same way as 8 by the reaction of 10 and 2-naphthaldehyde, yield 56%, mp 150° (lit. 152°).

Benzo[b]phenanthro[2,1-d]thiophene (3).

This compound was prepared by photocyclization of 8 following the method used for 1, yield 10%, mp 230° (lit. 331°); ms: 284 (M^+ , 100).

Benzo[b]phenanthro[4,3-d]thiophene (4) and Anthra[1,2-b]benzo[d]thiophene (5).

The stilbene 9 was irradiated following the procedure used for 1. The solid obtained (yield 5%) after chromatography on a silica gel column was crystallized from hexane to give 5, mp 227° (lit. 228°), ms: 284 (M^+ , 100), and concentration of the mother liquor gave 4 in the ratio of 3:1, mp 120° (lit. 127°), ms: 284 (M^+ , 100).

Anal. Calcd. for $C_{20}H_{12}S$: C, 84.47; H, 4.25; S, 11.27. Found: C, 84.26; H, 4.24; S, 11.26.

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SCHEME

D. Synthesis of Benzo[3,2]phenanthro[4,5-bcd]thiophene and Chryseno- [4,5-bcd]thiophene

Previously, we have reported the synthesis of the phenanthro[b]thiophenes (1). To further our investigation of polycyclic thiophenes, the study of benz[2,3]phenanthro[4,5-bcd]thiophene (1) and chryseno[4,5-bcd]thiophene (2) was desired. Karcher, et al., have shown that compounds 1 and 2 are present in polynuclear aromatic hydrocarbons derived from coal tar and that compound 1 possessed high mutagenic activity (2). Therefore, in order to assign the

absolute structure via synthetic routes and to obtain a sufficient sample for carcinogenic and mutagenic testing, it was desired to synthesize compounds 1 and 2.

Newman and Kannan (3) have reported the synthesis of benzo[a]pyrenes from methyl benz[a]anthracenes in four steps. Thus, it appeared that compounds 1 and 2 could be obtained from 6-methylbenzo[b]naphtho[2,1-d]thiophene (7) (Scheme I) and 11-methylbenzo[b]naphtho[2,3-d]thiophene (19) (Scheme III). The 6-methylbenzo[b]naphtho[2,1-d]thiophene (19) was readily obtained from the Wittig reaction of benzyltriphenylphosphonium chloride (3)(4) and 3-acetylbenzo[b]thiophene (14) followed by photocyclization of the alkene 5. This method has been shown to be an effective route to polycyclic thiophenes (1).

The methyl compound (6) was brominated with N-bromosuccinimide to yield 6-bromomethylbenzo[b]naphtho[2,1-d]thiophene (7). This bromomethyl compound 7 was converted to 6-cyanomethylbenzo[b]naphtho[2,1-d]thiophene (8) with potassium cyanide and Aliquat-336 in good yield. Reduction of the cyano com-

pound 8 with diisobutylaluminum hydride afforded the aldehyde 9, which was not purified, but reacted directly with polyphosphoric acid to give the desired polycyclic thiophene 1.

Synthesis of 11-methylbenzo[b]naphtho[2,3-d]thiophene (18) was first attempted by the cyclization of the methyl ketone 10 (5) (Scheme II). However, instead of producing the desired methyl compound 18, deacetylation occurred to afford 2-benzylbenzo[b]thiophene (11) in low yield. Since cyclization onto the benzene ring proved to be unsuccessful, it was presumed that the 3-position of the thiophene ring should be more suitable for cyclization.

Newman and Kannan (3) have shown the synthesis of 9-fluoro-12-methylbenzo[a]anthracene, where the methyl ketone was cyclized onto the naphthalene ring. This method also proved to be successful in our case. Therefore, reaction of the oxazoline 12 (6) with *sec*-butyllithium followed by condensation with benzo[b]thiophene-2-carbaldehyde (13) (7) afforded compound 14. Hydrolysis of compound 14 with hydrochloric acid in dioxane yielded the lactone 15. Reduction of compound 16 with hydrogen and palladium on carbon in acetic acid gave the acid 16. When the acid 16 was allowed to react with methyllithium at room temperature the methyl ketone 17 and a small amount of the cyclized methyl compound 18 was obtained. Separation of this mixture was easily achieved by chromatography. The methyl ketone 17 was reacted with polyphosphoric acid to yield 11-methylbenzo[b]naphtho[2,3-d]thiophene (18). The same sequence of reaction which converted the methylbenzo[b]naphtho[2,1-d]thiophene (6) to benz[2,3]phenanthro[4,5-bcd]thiophene (1), also proved to be successful in the conversion of 11-methylbenzo[b]naphtho[2,3-d]thiophene (18) to the desired chryseno[4,5-bcd]thiophene (2).

It should be noted that tlc (cyclohexane as eluent) of compound 2 showed a small impurity of lower R_f value. This small impurity was removed by recrystallization to give pure compound 2.

EXPERIMENTAL

All melting points are uncorrected. Ir spectra were obtained on a Beckman Acculab-2 spectrometer. Nmr spectra were obtained on a Varian EM 390 spectrometer or a JEOL FX 90 Q spectrometer. Mass spectra were obtained on a Hewlett-Packard model 5890A mass spectrometer. Uv spectra were recorded for solutions in 95% ethanol with a Perkin Elmer 320 spectrometer.

3-Acetylbenzo[b]thiophene (4).

The synthesis of compound 4 from 3-lithiobenzo[b]thiophene and acetonitrile has been reported by Dickinson and Iddon (8). However, reaction of the lithio compound with *N,N*-dimethylacetamide gave a much better yield. Thus, a solution of 3-bromobenzo[b]thiophene (21.3 g, 0.10 mole) in 150 ml of absolute ether was added to a mixture of 63 ml (0.10 mole) of 1.6 M *n*-butyllithium solution in hexane and 250 ml of absolute ether keeping the temperature below -70°. A white suspension of 3-lithiobenzo[b]thiophene was obtained after 30 minutes. A solution of *N,N*-dimethylacetamide (10.5 g, 0.12 mole) in 10 ml of absolute ether was added. The mixture was stirred at -78° for 4 hours and allowed to warm up to room temperature. Hydrochloric acid (2*N*) was added and the ether layer was separated, followed by extraction of the aqueous layer with ether. The combined extracts were washed with water, dried and evaporated. The residue was distilled in vacuo to give 10.4 g (59%) of 4 as a pale yellow liquid, b.p. 104-107°/0.2 mm.

Recrystallization from ether/hexane gave colorless prisms, mp 64° (lit. mp 64-65°); ¹H-nmr (deuteriochloroform): δ 2.52 (s, 3H, CH₃), 7.35 (m, 2H, H₅ and H₆), 7.75 (m, 1H, H₇), 8.10 (s, 1H, H₂) and 8.75 (m, 1H, H₄).

3-(1-Phenyl-1-propen-2-yl)benzo[b]thiophene (5).

Carruthers and Stewart (9) have reported the formation of compound 5 via the Grignard reaction followed by dehydration. However, the Wittig reaction gave a much better yield.

Therefore, a solution of 38.9 g (0.10 mole) of **3** in 100 ml of absolute ethanol was added to a solution of sodium (2.4 g, 0.105 mole) in 400 ml of absolute ethanol. After 10 minutes of stirring, a solution of 17.6 g (0.10 mole) of **4** in 50 ml of absolute ethanol was added. The mixture was refluxed for 5 hours. The ethanol was removed in vacuo and water was added to the residue. The product was extracted with ethyl ether and dried with anhydrous sodium sulfate. The ether was removed and the residue was dissolved in cyclohexane after which the insoluble triphenylphosphine oxide was filtered off. After removal of the cyclohexane, the product was chromatographed on a column of silica gel using cyclohexane as eluent to yield 20.1 g (80%) of a trans-cis mixture of **5** as colorless crystals. Recrystallization from hexane gave colorless plates, mp 67-68°; ir: (potassium bromide) 1600 and 3090 cm^{-1} (C=C), 680, 780, 900 and 3000 cm^{-1} (aromatic); ^1H -nmr (deuteriochloroform): δ 2.24 (3H, cis CH_3), 2.31 (s, 3H trans CH_3), 6.68 (d, $J = 1.5$ Hz, 1H cis C=C-H), 6.78 (d, $J = 1.5$ Hz, 1H, trans C=C-H), 6.90-8.07 (m, 10H, aromatic); ms: 250 (M^+ , 48.5), 235 ($\text{M}-\text{CH}_3$, 100).

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{S}$ (250.37): C, 81.32; H, 5.12; S, 13.57. Found: C, 81.51; H, 5.24; S, 13.34.

6-Methylbenzo[b]naphtho[2,1-d]thiophene (**6**).

A solution of **5** (2.0 g, 0.008 mole) and 0.10 g of iodine in 750 ml of cyclohexane was irradiated for four hours with a 450 Watt Hanovia medium pressure mercury lamp through a corex filter. During the course of the reaction a slow stream of air was passed through the solution. The cyclohexane was removed in vacuo and the residue was passed through a column of silica gel (60-20 mesh) using cyclohexane as eluent to yield 1.97 g of **6** as a colorless needles, mp 95.5-96° (lit mp 96° (10)); ir: 1385 cm^{-1} (CH_3), 740, 795 and 3060 cm^{-1} (aromatic); ^1H -nmr (deuteriochloroform): δ 3.00 (s, 3H, CH_3), 7.32-8.52 (m, 9H, aromatic); ms: 248 (M^+ , 100).

6-Bromomethylbenzo[b]naphtho[2,1-d]thiophene (7).

A mixture of 7 (0.5 g, 2.0 mmoles), N-bromosuccinimide (0.38 g, 2.1 moles), 15 ml of carbon tetrachloride and 10 mg of benzoyl peroxide was refluxed for two hours (tlc showed a small amount of starting material). The succinimide was filtered off and washed with carbon tetrachloride. The filtrate was concentrated and cooled to give 0.3 g of light yellow needles. Further concentration of the mother liquor gave an additional 0.2 g, to give a total yield of 0.5 g (77.5%), mp 169-170°. Recrystallization of a small amount gave colorless needles, mp 176°; ir (potassium bromide): 690 cm^{-1} (Br), 720, 750 and 3020 cm^{-1} (aromatic); ^1H -nmr (deuteriochloroform): δ 5.08 (s, 2H, CH_2), 7.35-8.52 (aromatic); ms: 328 (M^+ , ^{81}Br , 14.0), 326 (M^+ , ^{79}Br , 13.2), 247 ($\text{M}-\text{Br}$, 100).

Anal. Calcd. for $\text{C}_{17}\text{H}_{11}\text{BrS}$ (327.25): C, 62.40; H, 3.39; Br, 24.42; S, 9.80. Found: C, 62.56; H, 3.48; Br, 24.50; S, 9.65.

6-Cyanomethylbenzo[b]naphtho[2,1-d]thiophene (8).

A stirred mixture of 8 (5.0 g, 15.3 mmoles), potassium cyanide (2.0 g, 30.8 mmoles), 10 drops of Aliquat-336, 200 ml of benzene and 100 ml of water was refluxed for 3 hours. The benzene layer was separated and the aqueous layer was extracted with benzene. The combined benzene extracts were washed with water, dilute hydrochloric acid and then with water again. The benzene extracts were dried with anhydrous sodium sulfate and removed in vacuo to give a light brown solid. Recrystallization from benzene/cyclohexane (charcoal) gave 3.55 g (85%) of colorless needles, mp 162-164°. An analytical sample was obtained by two recrystallizations from benzene/cyclohexane, mp 165.5-166°; ir (potassium bromide): 2125 cm^{-1} (CN), 730, 760 and 3030 cm^{-1} (aromatic); ^1H -nmr (deuteriochloroform): δ 4.32 (s, 2H, CH_2), 7.45-8.17 (m, 9H, aromatic); ms: 273 (M^+ , 100).

Anal. Calcd. for $C_{18}H_{11}NS$ (273.36): C, 79.09; H, 4.06; N, 5.12; S, 11.73.

Found: C, 78.88; H, 4.03; N, 4.92; S, 11.36.

Benz[2,3]phenanthro[4,5-bcd]thiophene (1).

A solution of diisobutylaluminum hydride (2.0 ml, Ventron, 25%) in toluene was syringed into a dry stirred solution of 8 (0.5 g, 1.83 mmoles) in 30 ml of benzene under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 2 hours. Dilute hydrochloric acid was added to the mixture, followed by extraction with chloroform. The chloroform extractions were dried with anhydrous sodium sulfate followed by removal of the chloroform in vacuo to give the aldehyde as a solid (ir, 1720 cm^{-1} aldehyde). Polyphosphoric acid (6 g) was added to the crude aldehyde dissolved in 10 ml of m-xylene. The mixture was heated at 100° for 2 hours with vigorous stirring. Ice was added to decompose the acid, after which the aqueous mixture was extracted with chloroform, dried with anhydrous sodium sulfate and evaporated in vacuo to dryness. The residue was chromatographed on a column of alumina using cyclohexane: benzene (3:1) as eluent to give 0.2 g (42%) of 1 as a pale yellow solid, mp $151\text{--}152^\circ$. An analytical sample was recrystallized from cyclohexane to give pale yellow needles, mp $152\text{--}153^\circ$; ir (potassium bromide): 730, 750, 800, 840, 860 and 3020 cm^{-1} (aromatic); ^1H -nmr (deuteriochloroform): δ 7.53-8.33 (m, 9H, aromatic), 8.28 (s, 1H, H_6); uv: λ max (log ϵ) 208 (3.94), 221 (2.93), 262 (4.02), 277 (3.93), 288 (4.00), 298 (3.98), 331 (3.09), 347 (3.38), 364 (3.62) 385 nm (3.56); ms: 258 (M^+ , 100).

Anal. Calcd. for $C_{18}H_{10}S$ (258.34): C, 83.69; H, 3.90; S, 12.41. Found:

C, 83.80; H, 3.80; S, 12.14.

2-Benzylbenzo[b]thiophene (11).

Compound 10 (1.0 g, 3.75 mmoles) was heated with 10 g of polyphosphoric acid at 150° for 20 minutes. Ice was added to decompose the acid. The aqueous

mixture was extracted with ether, washed with aqueous sodium bicarbonate, water and then dried with anhydrous sodium sulfate. The ether was removed in vacuo to give an oily solid (tlc in cyclohexane showed one spot, however in benzene many spots were present). Chromatography on silica gel with cyclohexane as eluent gave 0.08 g (9.5%) of a white solid (mixed melting point and nmr showed this compound to be identical with 11), mp 84-85° (lit mp 86-87° (10); ¹H-nmr (deuteriochloroform): δ 4.20 (s, 2H, CH₂), 6.96 (s, 1H, H₃), 7.20-7.45 (m, 7H, H₅, H₆, and phenyl), 7.56-7.83 (q, 2H, H₄ and H₇). 2-[2-(1-Benzo[b]thiophen-2-yl-1-hydroxymethyl)phenyl]-4,4-dimethyl-2-oxazoline (14).

sec.-Butyllithium (48.3 ml of 1.3 M solution in hexane, 0.063 moles) was syringed over a period of 30 minutes into a dry solution of 12 (10 g, 0.057 mole) and 600 ml of ethyl ether under nitrogen at -78°. The solution turned yellow followed by a yellow precipitate. The mixture was allowed to warm slowly to -15° and then cooled back to -78°, after which 13 (9.3 g, 0.057 mole) dissolved in 200 ml of dry ethyl ether was added dropwise. The mixture was allowed to slowly warm to room temperature and then stirred overnight at room temperature. The mixture was then poured into 400 ml of ice water and the layers separated. The aqueous layer was extracted with ethyl ether and the combined extracts were dried with anhydrous sodium sulfate. The ether was removed in vacuo to give a yellow solid. The solid was filtered and washed with ether to give a white solid. The mother liquor was concentrated to give more product, total yield, 6 g (62%), mp 134-135°. An analytical sample was recrystallized from benzene/hexane to give colorless prisms, mp 135-136°; ir (potassium bromide): 700, 760 and 2990 cm⁻¹ (aromatic), 3090 cm⁻¹ (OH), 1640 cm⁻¹ (C=N); ¹H-nmr (deuteriochloroform): δ 0.87 (s, 3H, CH₃), 1.29 (s, 3H, CH₃), 3.88 (q, 2H, CH₂), 6.08 (d, J = 9 Hz, 1H, C-H), 6.74 (s, 1H, H₃), 7.15-7.98 (m, 8H, aromatic), 8.65 (d, J = 9 Hz, 1H, OH); ms: 337 (M⁺, 100).

Anal. Calcd. for $C_{20}H_{19}NO_2S$ (337.44): C, 71.12; H, 5.68; N, 4.15; S, 9.50. Found: C, 71.33; H, 5.74; N, 4.13; S, 9.61.

5-Benzo[b]thiophen-2-yl-2,5-dihydrobenzo[c]furan-2-one (15).

A solution of 14 (1.7 g, 5.04 mmoles), 40 ml of 10% hydrochloric acid and 50 ml of 1,4-dioxane was refluxed for 18 hours. The solution was allowed to cool slowly to give light brown needles. Filtration and recrystallization from benzene/ methanol (charcoal) gave 1.2 g (89%), mp 171-172°; ir (potassium bromide): 1750 cm^{-1} (C=O), 1050 and 1280 cm^{-1} (C-O), 690, 745 and 3030 cm^{-1} (aromatic); $^1\text{H-nmr}$ (deuteriochloroform): δ 6.72 (s, 1H, CH), 7.26-8.13 (m, 9H, aromatic); ms: 266 (M^+ , 100).

Anal. Calcd. for $C_{16}H_{10}SO_2$ (266.32): C, 72.16; H, 3.78; S, 12.04. Found: C, 72.13; H, 3.87; S, 11.88.

2-(2-Carboxyphenylmethylbenzo[b]thiophene (16).

A mixture of 16 (1.6 g, 6.0 mmoles), 0.5 g of 5% palladium on carbon and 200 ml of acetic acid was hydrogenated at 80-90° and atmospheric pressure. The solution was then boiled and filtered to remove the catalyst. The acetic acid was removed in vacuo to give a white solid, which was recrystallized from benzene/hexane (charcoal) to give 1.4 g (87%), mp 142-144°; ir (potassium bromide): $2580\text{-}3030\text{ cm}^{-1}$ (OH), 1670 cm^{-1} (C=O), 1240 cm^{-1} (C-O); $^1\text{H-nmr}$ (DMSO- d_6): δ 4.64 (s, 2H, CH_2), 7.04 (s, 1H, H_3), 7.15-7.96 (m, 8H, aromatic), 11.0-13.6 (broad s, 1H, COOH); ms: 268 (M^+ , 67), 250 ($M\text{-H}_2\text{O}$, 100).

Anal. Calcd. for $C_{16}H_{12}SO_2$ (268.34): C, 71.62; H, 4.51; S, 11.95. Found: C, 71.37; H, 4.56; S, 11.81.

2-(2-Acetylphenylmethyl)benzo[b]thiophene (17) and 11-Methylbenzo[b]naphtho-[2,3-d]thiophene (18).

Methylolithium (6.9 ml of a 1.4 M solution in ethyl ether, 9.7 mmoles) was added rapidly to a stirred solution of 16 (1.0 g, 3.7 mmoles) dissolved in 40 ml of dry ethyl ether. The solution was stirred for an additional hour,

followed by decomposition with saturated ammonium chloride. The ether was separated and the aqueous layer was extracted with ether. The combined ether extracts were dried with anhydrous sodium sulfate. The ether was removed in vacuo to give an oily solid. Chromatography on silica gel using toluene:hexane (1:1) as eluent gave 0.15 g (14%) of **18** and 0.5 g (50%) of **17** (ir, 1670 cm^{-1} , C=O). The crude methyl ketone **17** (0.5 g, 1.9 mmoles) was heated with 6 ml of polyphosphoric acid at $80-90^\circ$ for 15 minutes. Ice was added to decompose the acid. The aqueous mixture was extracted with benzene, dried with anhydrous sodium sulfate and the benzene removed in vacuo to give a dark yellow solid. Chromatography on silica gel using hexane:toluene (5:1) as eluent gave 0.25 g. Total yield of **18** was 0.4 g (43% overall yield from **16**), mp $160-161^\circ$. An analytical sample was recrystallized from benzene/cyclohexane to give colorless needles, mp $161-162^\circ$; ir (potassium bromide): 1390 cm^{-1} (CH_3), 730, 755 and 3030 cm^{-1} (aromatic); $^1\text{H-nmr}$ (deuteriochloroform): δ 3.15 (s, 3H, CH_3), 7.49-8.41 (m, 9H, aromatic); ms: 248 (M^+ , 100).

Anal. Calcd. for $\text{C}_{17}\text{H}_{12}\text{S}$ (248.35): C, 82.22; H, 4.87; S, 12.91. Found: C, 82.10; H, 4.91; S, 12.76.

11-Bromomethylbenzo[b]naphtho[2,3-d]thiophene (**19**).

Bromination was achieved in the same manner as described for compound **6**, thus, 1.33 g (5.36 mmoles) of **18**, 1.24 g (6.97 mmoles) of N-bromosuccinimide, 30 mg of benzoyl peroxide and 50 ml of carbon tetrachloride gave 1.33 g (76%) of yellow needles, mp $201-203^\circ$; ir (potassium bromide): 695 cm^{-1} (Br), 720, 750 and 2910 cm^{-1} (aromatic); $^1\text{H-nmr}$ (deuteriochloroform): δ 5.52 (s, 2H, CH_2), 7.43-8.62 (m, 9H, aromatic); ms: 328 (M^+ , ^{81}Br , 12.3), 326 (M^+ , ^{79}Br , 11.7), 247 (M-Br, 100). A satisfactory analysis was not obtainable after repeated recrystallization from benzene/cyclohexane.

Anal. Calcd. for $C_{17}H_{11}BrS$ (327.25): C, 62.40; H, 3.39; Br, 24.42; S, 9.80. Found: C, 60.61; H, 3.57; Br, 26.00; S, 9.66.

11-Cyanomethylbenzo[b]naphtho[2,3-d]thiophene (20).

Conversion of compound 19 to the cyano compound 20 was achieved in the same manner as described for compound 7. Thus, 1.25 g (3.82 mmoles) of 19, 0.5 g (77 mmoles) of potassium cyanide, 50 ml of benzene, 25 ml of water and 3 drops of Aliquat-336 gave 0.75 g (72%) of light brown needles, mp 230-230.5°; ir (potassium bromide): 2120 cm^{-1} ($C\equiv N$), 700, 730, 760 and 2910 cm^{-1} (aromatic); 1H -nmr (deuteriochloroform): δ 4.70 (s, 2H, CH_2), 7.47-8.43 (m, 9H, aromatic); ms: 273 (M^+ , 100).

Anal. Calcd. for $C_{18}H_{11}NS$ (273.36): C, 79.09; H, 4.06; N, 5.12; S, 11.73. Found: C, 79.23; H, 4.29; N, 5.13; S, 11.78.

Chryseno[4,5-bcd]thiophene (2).

Conversion of compound 20 to compound 2 was achieved in the same manner as described for compound 8. Thus, 1 g (3.66 mmoles) of 20, 60 ml of dry benzene and 4 ml of diisobutylaluminum hydride (25% solution in toluene) gave the aldehyde (ir, 1715 cm^{-1} , $C=O$) as a light brown solid. The crude aldehyde, 12 g of polyphosphoric acid and 20 ml of dry xylene gave after chromatography 0.35 g (tlc in cyclohexane showed the presence of an impurity). Recrystallization from cyclohexane gave 0.3 g (32%) of colorless needles, mp 172-173°; ir (potassium bromide): 690, 740 and 2960 cm^{-1} (aromatic); 1H -nmr (deuteriochloroform): δ 7.60-8.31 (m, 8H, aromatic), 8.70 (d, $J_{10,11} = 9$ Hz, 1H, H_{10}), 8.77 (near dd, 1H, H_9). uv: λ max (log ϵ) 202 (3.61), 213 (3.48), 246 (3.87), 253 (3.07), 268 (3.75), 278 (3.74), 340 (3.32), 357 (3.40) and 380 nm (2.44); ms: 258 (M^+ , 100).

Anal. Calcd. for $C_{19}H_{10}S$ (258.34): C, 83.69; H, 3.90; S, 12.41. Found: C, 83.46; H, 3.66; S, 12.19.

Scheme 1

Scheme II

Scheme III

Scheme III

NBS

KCN

DIBAL

PPA

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E. Synthesis of Benzo[4,5]phenaleno[1,9-bc]thiophene.

The pentacyclic thiophene benzo[4,5]phenaleno[1,9-bc]thiophene was synthesized via the corresponding 3-methylphenanthro[2,1-b]thiophene.

It is known that benzo[a]pyrene has been the most extensively investigated among the large number of polycyclic hydrocarbons (1). Many heterocyclic analogs of these carcinogenic hydrocarbons, such as acridine, carbazole and thiophene derivatives, have been prepared and the relationship between their chemical structure and biological activity have been studied (2). However, the report of heterocyclic analogs of benzo[a]pyrene occurs much less frequently. Further, little research concerning the carcinogenicity of these compounds appears in the literature. The synthesis and carcinogenic evaluation of pyreno[1,2-b]thiophene, a benzo[a]pyrene analog, was reported by Tilak, who published a review concerning the synthesis and carcinogenesis of thiophene isosteres of several polycyclic hydrocarbons (3). Recently, we have synthesized tricyclic and tetracyclic thiophene derivatives and have tested these compounds for mutagenic and carcinogenic activity (4). Karcher, et al., reported the separation and determination of structure for two isomers of pentacyclic thiophenes, benzo[2,3]phenanthro[4,5-bcd]-thiophene and chryseno[4,5-bcd]thiophene, which were found in coal tar (5). At this time, the preparation of these two compounds had

already been accomplished by our group (6). We now wish to report the synthesis of one of the remaining two thia analogs of benzo[a]pyrene, benzo[4,5]phenaleno[1,9-bc]thiophene (1).

The key intermediate in this study is the corresponding methyl compound 3-methylphenanthro[2,1-b]thiophene (7). Recently, Iwao, et al., reported a convenient synthesis of phenanthro[b]thiophenes by a combination of the Wadsworth-Emmons procedure and photocyclization (4). We applied the above reaction sequence to the preparation of the corresponding methyl compound 7.

The reaction of 4-methyl-2-thiophenecarboxaldehyde (4), which was prepared by the oxidation of 4-methyl-2-thiophenemethanol (3) with chromium trioxide, with diethyl naphthylmethylphosphonate (5) in the presence of sodium hydride in dimethoxyethane gave 4-methyl-2-(1-naphthyl)ethenylthiophene (6) in 68% yield. Compound 6 was irradiated with a 450 watt Hanovia medium pressure mercury lamp in the presence of iodine to give 3-methylphenanthro[2,1-b]thiophene (7) in 84.2% yield. The attempted bromination of 7 with N-bromosuccinimide in carbon tetrachloride proved unsuccessful. This reaction gave only the 2-bromo compound (8) in 50% yield. However, by using dry benzene as the solvent instead of carbon tetrachloride, the desired 3-bromomethylphenanthro[2,3-b]thiophene (9) was obtained in 62% yield. This phenomenon was observed in the bromination of 1-methylnaphtho[2,1-b]thiophene with N-bromosuccinimide (7). Campaigne has also reported a similar reaction in the case of the bromination of 3-methylbenzo[b]thiophene (8).

Recently, Newman (9) reported the convenient cyanation of bromomethyl compounds with potassium cyanide in the presence of methyl tricaprylammonium chloride (Aliquat 336) (10). It was anticipated that this method could be

applied to the preparation of 1-cyanomethylphenanthro[2,1-b]thiophene (10). Thus, treatment of 9 with potassium cyanide in the presence of Aliquat 336 in benzene-water gave 10 in 70.8% yield. Compound 10 was then reacted with diisobutylaluminum hydride to give the corresponding aldehyde, which was cyclized with polyphosphoric acid to the final product, benzo[4,5]phenaleno-[1,9-bc]thiophene (1) in 23.4% overall yield from 10. Conversely, cyclization of 2-bromo-3-cyanomethylnaphtho[2,1-b]thiophene (13) under conditions similar to those employed in the preparation of 1, did not afford the desired product. Compound 13 was prepared in good yield by the bromination of 7 with N-bromosuccinimide in dry benzene followed by cyanation with potassium cyanide. However, treatment of 13 with zinc dust in acetic acid under reflux for 1.5 hours gave the debrominated product 10 in 34% yield.

EXPERIMENTAL

Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman Acculab-2 spectrometer. Nmr spectra were recorded on a Varian EM 390 spectrometer or a JEOL FX 90 Q spectrometer. The chemical shift values are expressed as δ values relative to internal tetramethylsilane. Mass spectra were obtained on a Hewlett-Packard model 5980A mass spectrometer. Uv spectra were recorded for solutions in cyclohexane with a Perkin Elmer 320 spectrometer.

4-Methylthiophene-2-methanol (3).

Into a stirred solution of 5.2 g of lithium aluminum hydride in 400 ml of absolute ether, 14.22 g of 4-methyl-2-thiophenecarboxylic acid (2) was slowly added dropwise. When the addition was complete, the ether was

brought to reflux for 5 hours, after which time it was carefully quenched by cautiously adding 80 ml of water and enough 10% hydrochloric acid to dissolve the inorganic salts. The ether phase was separated and the aqueous phase was extracted with 300 ml of ether. The combined ether layers were washed successively with 100 ml of 5% sodium hydroxide and water, and were dried over sodium sulfate. Evaporation of the ether yielded a colorless oil which was distilled at $78-80^{\circ}/1.5$ mm to give 11.0 g (85.9%) of a colorless oil; ir (neat): 3400 (OH, broad); nmr (deuteriochloroform): 2.18 (s, CH_3 , 3H), 2.52 (t, $J = 6$ Hz, OH, 1H), 4.64 (d, $J = 6$ Hz, $-\text{CH}_2-\text{O}$, 2H), 6.76 (s, H-3, H-5, 2H).

Anal. Calcd. for $\text{C}_6\text{H}_8\text{OS}$: C, 56.22; H, 6.30; S, 25.01. Found: C, 56.41; H, 6.09; S, 24.82.

4-Methyl-2-thiophenecarboxaldehyde (4).

A solution of 12.8 g (100 mmoles) of 4-methylthiophene-2-methanol (3) in 180 ml of dry pyridine was added slowly to a suspension of chromium trioxide and 220 ml of dry pyridine. After stirring for 2 hours at room temperature, the reaction mixture was filtered and washed with chloroform. The filtrate was washed successively with 10% hydrochloric acid and saturated sodium carbonate and was then dried over sodium sulfate. Evaporation of the chloroform yielded a brown oil which was distilled at $65-68^{\circ}/0.75$ mm to give 9.05 g (71.7%) of colorless oil. This aldehyde had the odor of an aromatic aldehyde, such as benzaldehyde, and changed to a yellow oil on standing at room temperature for about 2 days; ir (neat): 1660 ($\text{C}=\text{O}$); nmr (deuteriochloroform): 2.28 (s, CH_3 , 3H), 7.35 (s, H-5, 1H), 7.53 (s, H-3, 1H), 9.85 (s, $-\text{CH}=\text{O}$, 1H).

4-Methyl-2-(1-naphthyl)ethenylthiophene (6).

Sodium hydride (50%, 1.92 g, 40 mmoles) was placed in 200 ml of 1,2-dimethoxyethane. Sodium hydride was used after washing two times with 20 ml of petroleum ether. The slurry was cooled to 20° and 5.56 g (20 mmoles) of diethyl 1-naphthylmethylphosphonate (11) was added dropwise with stirring. After the addition, the solution was stirred at room temperature for 30 minutes until the gas evolution had ceased. To the pale yellow solution, maintained below 25°, was added dropwise 2.52 g (20 mmoles) of 4-methylthiophene-2-carboxaldehyde (4). During the addition, a gummy precipitate appeared. The solution was stirred at room temperature for 2 hours and was heated at 50° for 20 minutes. After cooling, a large excess of water was added and the resulting precipitate was collected by filtration. The crude product was purified by chromatography on a silica gel column using hexane as the eluent giving 3.41 g (68%) of product as pale yellow crystals, mp 74-75°. An analytical sample was recrystallized from hexane; nmr (deuteriochloroform): 2.25 (s, CH₃, 3H), 6.82 (s, H'-5 or H'-3, 1H), 6.93 (s, H'-5 or H'-3, 1H), 7.20 (d, J = 15 Hz, ethenyl proton, 1H), 7.42-7.92 (m, naphthyl and ethenyl protons, 7H), 8.17 (m, H-8, 1H); ms: m/e 250 (M⁺, 100), 249 (M - 1, 35), 235 (M - 15, 20).

Anal. Calcd. for C₁₇H₁₄S: C, 81.56; H, 5.64; S, 12.81. Found: C, 81.80; H, 5.66; S, 12.68.

3-Methylphenanthro[2,1-b]thiophene (7).

A solution of 2 g (8 mmoles) of 4-methyl-2-(1-naphthyl)ethenylthiophene and 0.1 g of iodine in 750 ml of cyclohexane was irradiated for 4 hours with a 450 watt Hanovia medium pressure mercury lamp through a corex filter. During the course of the reaction, a slow stream of air was passed through the solution. The solvent was evaporated in vacuo and the

residue was added to 10 ml of ethanol, filtered and washed with a small amount of ethanol to give pale brown crystals. This product was recrystallized from ethanol giving 1.67 g (84.2%) of colorless crystals, mp 153-154°; ir (potassium bromide): 3040 (small peak), 860, 810, 745; nmr (deuteriochloroform): 2.96 (s, CH₃, 1H), 7.23 (s, H-1, 1H), 7.59-7.75 (m, H-7, H-8, 2H), 7.86 (d, J = 9 Hz, H-5 or H-11, 1H), 7.93 (d, J = 9 Hz, H-5 or H-11, 1H), 8.03 (d, J = 9 Hz, H-4, 1H), 8.66 (d, J = 9 Hz, H-10, 1H), 8.66-8.83 (m, H-7, H-8, 2H); ms: m/e 248 (M⁺, 100).

Anal. Calcd. for C₁₇H₁₂S₄: C, 82.22; H, 4.87; S, 12.91. Found: C, 81.99; H, 4.89; S, 13.17.

Reactions of 3-Methylphenanthro[2,1-b]thiophene with NBS in Carbon Tetrachloride.

A mixture of 1.24 g (5 mmoles) of 3-methylphenanthro[2,1-b]thiophene (7), 0.88 g (5 mmoles) of N-bromosuccinimide, 5 mg of benzoyl peroxide and 30 ml of carbon tetrachloride was shaken vigorously and then heated. During the first ten minutes of the reaction, an additional 5 mg of benzoyl peroxide was added. The flask and contents were shaken frequently during the first hour and the mixture was refluxed for an additional 2 hours. The mixture was then cooled in an ice bath. The succinimide was removed by filtration and washed with an additional 10 ml of carbon tetrachloride. The carbon tetrachloride was removed under reduced pressure and the residue was chromatographed on a silica gel column using hexane as an eluent to give pale brown crystals, mp 138-139°. An analytical sample was recrystallized from hexane giving 0.82 g (50%) of colorless prisms, mp 139°; nmr (deuteriochloroform): 2.88 (s, CH₃, 3H), 7.57-7.72 (m, H-7, H-8, 2H), 7.79-7.98 (m, H-5, H-6, H-11, 3H), 8.58-8.75 (m, H-4, H-9, H-10, 3H);

ms: m/e 328 (M + 2, 97.7), 326 (M⁺, 100), 247 (M - 79, 40).

Anal. Calcd. for C₁₇H₁₁BrS: C, 62.40; H, 3.39; S, 9.80. Found: C, 62.80; H, 3.36; S, 9.90.

2-Bromomethylphenanthro[2,1-b]thiophene (9).

A mixture of 0.89 g (5 mmoles) of N-bromosuccinimide, 1.24 g (5 mmoles) of 3-methylphenanthro[2,1-b]thiophene, 0.005 g of benzoyl peroxide and 50 ml of dry benzene was gently refluxed. After refluxing 2.5 hours, the mixture was cooled in an ice water bath and the crystals of succinimide which formed were removed by filtration. The filtrate was washed with 10% sodium hydroxide solution and water. The benzene layer was dried with sodium sulfate and evaporated to give crystals. After washing with hexane, the white crystals were recrystallized from hexane giving 1.0 g (62%) of colorless needles, mp 146°. The hexane solvent was evaporated in vacuo and the residue was chromatographed on a silica gel column using hexane as an eluent to give 0.11 g (6.7%) of 2-bromo-3-methylphenanthro[2,1-b]thiophene (8), mp 137°; nmr (deuteriochloroform): 5.15 (s, -CH₂-, 2H), 7.22 (s, H-2, 1H), 7.56-7.77 (m, H-7, H-8, 2H), 7.87-8.09 (m, H-5, H-6, H-11, 3H), 8.58-8.81 (m, H-4, H-9, H-10, 3H).

Anal. Calcd. for C₁₇H₁₁BrS: C, 62.40; H, 3.39; S, 9.80. Found: C, 62.35; H, 3.51; S, 9.28.

3-Cyanomethylphenanthro[2,1-b]thiophene (10).

A mixture of 1.13 g (5 mmoles) of 3-bromomethylphenanthro[2,1-b]thiophene (9), 2.5 g of potassium cyanide, 100 ml of benzene, 15 ml of water and 10 drops of Aliquat 336 was refluxed for 2.5 hours. After the addition of 100 ml of benzene, the benzene layer was washed successively with water, 10% hydrochloric acid and water. After drying (sodium sulfate) the benzene was evaporated. The residue was recrystallized from benzene-hexane (1:1)

giving 0.97 g (70.8%) of pale brown needles, mp 148-150°; ir (potassium bromide): 2460 (C≡N); nmr (deuteriochloroform): 4.34 (s, CH₂, 2H), 7.60-8.17 (m, H-2, H-4, H-5, H-7, H-8, H-11, 6H), 8.59-8.79 (m, H-9, 1H), 8.66 (d, J = 9 Hz, H-10, 1H); ms: m/e 258 (M⁺, 100), 234 (M - 24, 7).

Anal. Calcd. for C₁₈H₁₁NS: C, 79.09; H, 4.06; N, 5.13; S, 11.73. Found: C, 78.69; H, 4.28; N, 5.02; S, 11.39.

Benzo[4,5]phenaleno[1,9-bc]thiophene (1).

Diisobutylaluminum hydride (25% solution in toluene, 2 ml, 3 mmoles) was added with a syringe to a solution of 0.5 g (1.83 mmoles) of 3-cyanometthyl-phenanthro[2,1-b]thiophene (10) in 15 ml of dry benzene. The mixture was stirred at room temperature for 2 hours. Dilute hydrochloric acid was added and the product was extracted with chloroform. Evaporation of the dried extract gave the aldehyde (11) as an oil, which slowly crystallized; ir (neat): 1700 (C=O).

A mixture of the above crude aldehyde (11) and 10 g of polyphosphoric acid was heated on a steam bath for 1 hour. The reaction mixture was poured into ice water and extracted with chloroform. The chloroform was washed successively with water and sodium carbonate, and then was dried (sodium sulfate) and evaporated. The residue was chromatographed on a column of silica gel using hexane as the eluent giving 0.11 g (23.4% of pale yellow crystals. An analytical sample was recrystallized from hexane giving pale yellow leaflets, mp 154°; ir (potassium bromide): 3040 (s), 2930 (s), 1720 (s), 875, 825, 790, 750; uv (cyclohexane): λ_{max} nm (log ε) 264 (4.82), 285 (4.42), 297 (4.37), 311 (4.38), 338 (4.35), 354 (4.59), 373 (4.78), 395 (3.96); nmr (deuteriochloroform): 7.51 (s, H-2 or H-5, 1H), 7.54 (s, H-2 or H-5, 1H), 7.61-7.70 (m, H-4, H-7, H-8, 3H), 8.06-8.17 (m, H-3, H-6, 2H), 8.26 (d, J = 9 Hz, H-11, 1H), 8.79 (d, J = 9 Hz, H-10, 1H), 8.70-8.82 (m, H-9, 1H). The picrate was obtained as brown needles, mp

184-185° (from ethanol).

Anal. Calcd. for $C_{18}H_{10}S$: C, 83.69; H, 3.90; S, 12.41. Found: C, 83.74; H, 4.04; S, 12.50.

2-Bromo-3-bromomethylphenanthro[2,1-b]thiophene (12).

A mixture of 0.65 g (2 mmoles) of 2-bromo-3-methylphenanthro[2,1-b]thiophene (8), 0.35 g (2 mmoles) of N-bromosuccinimide, 0.005 g of benzoyl peroxide and 50 ml of dry benzene was refluxed for 2 hours.. The reaction mixture was cooled in an ice bath and the precipitate was removed by filtration. The filtrate was washed with 10% sodium hydroxide solution and water. The benzene layer was dried with sodium sulfate and evaporated to yield white crystals which were recrystallized from benzene giving 0.71 g (87.7%) of colorless needles, mp 188-189°; nmr (deuteriochloroform): 5.11 (s, -CH₂-, 2H), 7.57-7.75 (m, H-7, H-8, 2H), 7.82-8.03 (m, H-5, H-6, H-11, 3H), 8.56-8.77 (m, H-4, H-9, H-10); ms: m/e 408 (M + 2, 12), 406 (M⁺, 23), 327 (53), 325 (52), 246 (100).

Anal. Calcd. for $C_{13}H_8Br_2S$: C, 43.85; H, 2.26; Br, 4.49; S, 9.00. Found: C, 43.69; H, 2.46; Br, 4.26; S, 8.79.

2-Bromo-3-cyanomethylphenanthro[2,1-b]thiophene (13).

A mixture of 0.81 g (2 mmoles) of 2-bromo-3-bromomethylphenanthro[2,1-b]thiophene (12), 1.5 g of potassium cyanide, 5 drops of Aliquat 336, 50 ml of benzene and 10 ml of water was refluxed for 2 hours. After the addition of 50 ml of benzene, the benzene layer was washed successively with water. After drying, the benzene was evaporated and the residue was recrystallized from benzene to give 0.33 g (47.3%) of pale brown needles, mp 233°; ir (potassium bromide): 2250 (CN); ms: m/e 353 (M⁺, 100), 351 (M - 2, 96).

Anal. Calcd. for $C_{18}H_{10}BrNS$: C, 61.25; H, 2.86; N, 3.97; S, 9.05.

Found: C, 61.70; H, 3.30; N, 3.91; S, 9.22.

Diethyl 1-Naphthylmethylphosphonate (5).

A mixture of 15.2 g (100 mmoles) of 1-chloromethylnaphthalene and 16.6 g (100 mmoles) of triethyl phosphite was heated at 160° for 8 hours. After distillation of the unreacted triethyl phosphite, the product was distilled ($165-175^{\circ}/0.75$ mm) to give 20 g (71.9%) of colorless oil.

Debromination of 2-Bromo-3-cyanomethylphenanthro[2,1-b]thiophene (13).

A mixture of 0.5 g (1.66 mmoles) of 2-bromo-3-cyanomethylphenanthro[2,1-b]thiophene, 1 g of zinc dust and 30 ml of acetic acid was refluxed for 1.5 hours. After cooling, the reaction mixture was poured into 200 ml of ice water and extracted with benzene. The benzene layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was recrystallized from ethanol to give 0.21 g of 3-cyanomethylphenanthro[2,1-b]thiophene (10), mp 150° .

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F. Synthesis of Pyreno[b]thiophenes.

Abstract: The synthesis of all the isomers of pyreno[b]thiophene namely, pyreno[1,2-b]thiophene, pyreno[2,1-b]thiophene and pyreno[4,5-b]thiophene is described. Their spectral characteristics are also discussed.

The presence of polycyclic aromatic hydrocarbons (PAH) in coal derived products and their mutagenic activity have been extensively studied (1a,b). Recently from this as well as other laboratories (2-4) it has been shown that many commercial PAH materials derived from coal, contain sulfur heterocycles as major impurities in which one aromatic ring has been replaced by a thiophene ring. However, the mutagenic and carcinogenic potential of these sulfur compounds are rarely reported because of the difficulties encountered in obtaining pure samples from coal in sufficient amount. Therefore, we have initiated a systematic synthetic effort to obtain authentic specimens of polycyclic thiophenes in high purity in order to compare their mass spectra with those obtained from coal derived products and to test their mutagenic activity. Thus we can identify polycyclic thiophenes occurring in coal with certainty.

There are three different thiophene isomers which can result when a thiophene ring is fused to a pyrene ring. Of these, pyreno[1,2-b]thiophene (1) has been reported by Tilak, et al (5). The other two isomers, namely,

pyreno[2,1-b]thiophene (2) and pyreno[4,5-b]thiophene (3) have been prepared as described below.

The synthesis of pyreno[2,1-b]thiophene is depicted in Scheme I. 10-Methylphenanthro[2,1-b]thiophene (7), a key intermediate, was prepared by photocyclization of 2-[2-methyl-2-(1-naphthylethenyl)]thiophene (6), from which the required compound can be made by homologation of an easily functionalizable methyl group. The olefin 6 was prepared by a Wadsworth-Emmons reaction between diethyl 2-thenylphosphonate (5) and 1-acetylnaphthalene. The compound 6 appeared to be a mixture of cis and trans isomers as evidenced by the presence of two methyl signals at δ 2.19 and δ 2.48 in the nmr spectrum. The bromination of 7 with N-bromosuccinimide in the presence of benzoyl peroxide as a radical initiator, gave exclusively bromomethylphenanthrothiophene (8). The bromine in 8 was replaced by one carbon nucleophile required for ring closure at C-1 of the phenanthrene ring. Thus the reaction of 8 with potassium cyanide in a phase transfer medium, gave 10-cyanomethylphenanthrothiophene (9). The cyano compound 9 was reduced to the aldehyde with diisobutylaluminium hydride and the resulting aldehyde was cyclized with polyphosphoric acid to the desired compound 2.

The steps involved in synthesis of pyreno[4,5-b]thiophene are depicted in Scheme II. The pyrene was converted to 4-bromo-1,2,3,6,7,8-hexahydropyrene (13) by reduction with sodium in amyl alcohol followed by bromination using literature methods (6,7). The reaction of 4-bromopyrene 14 with

phenyllithium gave 4-prenyllithium and the latter on reaction with 2,2,2',2',-tetraethoxydiethyl disulfide yielded w-diethoxyethyl-4-prenyl sulfide (15). We were, however, unsuccessful in our attempt to make the lithio derivative of 13. The diethyl acetal 15 was cyclized with polyphosphoric acid to pyreno-[4,5-b]thiophene [3], though in poor yield.

The fusion of the thiophene ring at different positions of the pyrene ring caused deshielding of the peri protons around the thiophene ring. This deshielding caused diagnostic differences among all three isomers. In pyreno-[1,2-b]thiophene, proton H-6 was more deshielded and gave a singlet at δ 8.70. The most deshielded protons H-6 and H-10 of pyreno[2,1-b]thiophene gave a singlet at δ 8.56 and a doublet ($J = 8$ Hz) at δ 8.60, respectively. The most deshielded proton, H-1 of pyreno[4,5-b]thiophene appeared at δ 8.70 as a double doublet ($J = 10$ and 2.5 Hz) due to coupling with its ortho and meta protons. There is no characteristic difference in the uv absorption pattern in all three isomers and these spectra are similar to that of benzo[a]-pyrene.

EXPERIMENTAL

Ir spectra were recorded on a Beckman Acculab-2 Spectrometer. ^1H Nmr spectra were obtained on a Varian EM 390 Spectrometer and a JEOL FX 90Q spectrometer in the solvents indicated. Chemical shifts are reported in ppm from TMS as an internal reference and are given in δ units. Mass spectra were recorded on a Hewlett Packard model 5980 A mass spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

Pyreno[1,2-b]thiophene (1).

This was prepared starting from 3-bromopyrene according to Tilak's procedure (5), m.p. 145° (lit 145-146°); ir (potassium bromide): 3040 (s), 1590 (s), 1420 (s), 1320 (s), 840 (s), 820 (s), 700 (s); nmr (deuteriochloroform): 8.70 (s, H-6, 1H), 8.48-7.59 (m, H-1, H-2, H-3, H-4, H-5, H-7, H-8, H-10, H-11, 9H); ms: 258 (M^+ , 100), 226 (M^+-32 , 8), 200 (M^+-58 , 2); uv (cyclohexane): λ max nm (log ϵ), 220 (4.56), 258 (4.67), 264 (4.73), 272 (4.69), 284 (4.69), 296 (4.60), 310 (3.79), 325 (4.04), 340 (4.42), 360 (4.63), 370 (4.05), 390 (3.93).

2-[2-Methyl-2-(1-naphthyl)ethenyl]thiophene (6).

Sodium hydride (50% oil suspension, 3 g, 62.5 mmoles) was placed in 1,2-dimethoxyethane (200 ml). The slurry was cooled to 20° and diethyl 2-thenylphosphonate (9.36 g, 40 mmoles) was added dropwise with stirring. After addition, the solution was stirred at room temperature for about one hour until the gas evolution had ceased. To the yellow solution, maintained below 25°, was added dropwise 1-acetylnaphthalene (Aldrich, contains 30% 2-acetylnaphthalene). The reaction mixture was stirred at room temperature for an additional hour and then refluxed for 0.5 hour. After cooling, the reaction mixture was decomposed with a large excess of water and the product was extracted with benzene. The benzene, after drying over sodium sulfate, was removed and the residue was chromatographed over a silica gel column using hexane as an eluant to give 5.5 g (82%) as a pale greenish yellow oil; nmr (deuteriochloroform): 2.19 and 2.48 (s, CH_3 , 3H), 6.5-8.3 (m, 1 olefinic proton, 10 aromatic protons, 11H).

10-Methylphenanthro[2,1-b]thiophene (7).

A solution of 2-[2-methyl-2-(1-naphthyl)ethenyl]thiophene (1.24 g, 5 mmoles) and iodine (0.05 g) in cyclohexane (500 ml) was irradiated for four

hours with a 450 Watt Hanovia medium pressure mercury lamp through a Corex filter. During the course of reaction a slow stream of air was also passed through the solution. The solvent was evaporated in vacuo and the residue was chromatographed over a silica gel column using hexane as the eluant to give white crystals which were recrystallized from hexane, yield 0.23 g (18.5%), m.p. 121-122°; nmr (deuteriochloroform): 3.3 (s, CH₃, 3H), 7.5-8.2 (m, H-2, H-4, H-5, H-6, H-7, H-8, 6H), 8.35 (d, H-3, J = 9 Hz, 1H), 9.0 (near dd, H-9, J = 9 Hz, 1H).

Anal. Calcd. for C₁₇H₁₂S: C, 82.22; H, 4.87; S, 12.91. Found: C, 82.48; H, 4.78; S, 12.63.

10-Bromomethylphenanthro[2,1-b]thiophene (8).

A mixture of N-bromosuccinimide (0.89 g), 10-methylphenanthro[2,1-b]-thiophene (1.24 g, 5 mmoles), benzoyl peroxide (0.01 g) in dry benzene (50 ml) was gently refluxed for two hours. The reaction mixture was cooled in an ice bath and succinimide was separated by suction filtration. The last traces of imide were removed by shaking the filtrate with an ice-cooled sodium hydroxide (5%) solution followed with water. The organic layer was dried over sodium sulfate, evaporated and the residue was washed with hexane (10 ml) and was then recrystallized from hexane-benzene (2:1) to give (1.22 g, 75%) of colorless needles, m.p. 147°; nmr (deuteriochloroform): 5.30 (s, CH₃, 3H), 7.67 (d, J = 5 Hz, H-2, 1H), 7.62-7.79 (m, H-7, H-8, 2H), 7.91 (d, J = 10 Hz, H-5, 1H), 7.92-8.05 (m, H-6, 1H), 8.00 (d, J = 6 Hz, H-3, 1H), 8.23 (s, H-11, 1H), 8.30 (d, J = 10 Hz, H-4, 1H), 9.05 (near dd, J = 1 and 7 Hz, H-9, 1H).

Anal. Calcd. for C₁₇H₁₁BrS: C, 62.40; H, 3.39; S, 9.80. Found: C, 62.62; H, 3.54; S, 9.67.

10-Cyanomethylphenanthro[2,1-b]thiophene (9).

A mixture of (1.13 g, 5 mmoles) of 8, potassium cyanide (2.5 g) in a mixture of benzene (100 ml) and water (15 ml) with 10 drops of Aliquat-336 (tricaprylmethyl ammonium chloride) was refluxed for 2.5 hours. After the addition of 100 ml of benzene, the benzene layer was separated, washed successively with water, 10% hydrochloric acid and water. After drying over sodium sulfate, the benzene was removed under reduced pressure. The residue was crystallized from benzene-ethanol (1:1) giving (0.86 g, 63%) a pale yellow needles, m.p. 155-157°; ir (potassium bromide): 2260 (C≡N); nmr (deuteriochloroform): 4.56 (s, CH₂-CN, 2H), 7.65 (d, J = 6 Hz, H-2, 1H), 7.59-7.76 (m, H-7, H-8, 2H), 7.88 (d, J = 10 Hz, H-5, 1H), 7.98 (d, J = 6 Hz, H-3, 1H), 8.03 (near dd, J = 4 Hz, H-6, 1H), 8.24 (s, H-11, 1H), 8.30 (d, J = 1 Hz, H-4, 1H), 8.44 (near dd, J = 6 Hz, H-9, 1H).

Anal. Calcd. for C₁₈H₁₁NS: C, 79.09; H, 4.06; N, 5.13; S, 11.73. Found: C, 78.96; H, 4.20; N, 5.13; S, 11.83.

Pyreno[2,1-b]thiophene (2).

Diisobutylaluminium hydride (25% solution in toluene, 2 ml, 3 mmoles) was added to a solution of (0.5 g, 1.83 mmoles) of 9 in dry benzene (15 ml). The mixture was stirred at room temperature for two hours. Dilute hydrochloric acid was added and the product was extracted with chloroform. The evaporation of the dried extracts over sodium sulfate, gave an aldehyde as an oil which slowly crystallized; ir (neat): 1720 (C=O). A mixture of the above aldehyde and polyphosphoric acid (10 g) was heated on a steam bath for one hour. The reaction mixture was poured into ice water and extracted with chloroform. The chloroform was washed successively with water and sodium carbonate solution, dried over sodium sulfate and evaporated. The residue was chromatographed on a silica gel column using hexane as the eluant giving

pale yellow leaflets (0.1 g, 21%), m.p. 156-157°. The picrate was obtained as brown needles, m.p. 198°; ir (potassium bromide): 3040 (s), 1580 (s), 1245 (m), 862, 835, 820, 740; uv (cyclohexane): λ max nm (log ϵ) 247 (4.64), 256 (4.67), 268 (4.19), 280 (4.45), 291 (4.59), 323 (3.67), 336 (4.13), 352 (4.51), 372 (4.69), 386 (3.62); nmr (deuteriochloroform): 7.75 (d, J = 5.5 Hz, H-8, 1H), 8.0-8.27 (m, H-1, H-2, H-3, H-4, H-5, H-9, 6H), 8.56 (s, H-6, 1H), 8.60 (d, J = 8 Hz, H-10, 1H); ms: 258 (M^+ , 100), 226 (M^+ -32, 10), 200 (M^+ -58, 2).

Anal. Calcd. for $C_{18}H_{10}S$: C, 83.37; H, 3.90; S, 12.41. Found: C, 83.59; H, 3.89; S, 12.27.

S-1,2,3,6,7,8-Hexahdropyrene (12).

This was prepared by the reduction of pyrene following Cook and Hewlett's procedure (6) with sodium in amyl alcohol, m.p. 132° (lit 132-133°).

4-Bromo-1,2,3,6,7,8-hexahdropyrene (13).

Hexahdropyrene was brominated with bromine in glacial acetic acid according to the procedure of Streitweiser (7) m.p. 120° (lit 127°).

4-Bromopyrene (14).

Streitweiser procedure (7) was followed for dehydrogenation of hexahdropyrene m.p. 130° (lit 138°).

Pyreno[4,5-b]thiophene (3).

4-Bromopyrene (2.5 g, 9 mmoles) dissolved in dry benzene (15 ml) and diluted with dry ether (30 ml) was treated with phenyllithium (6 ml, 1.85 M solution) and the reaction mixture was left overnight. The prenyllithium was separated as a yellow solid. The solvent was decanted and the solid was washed with ether 2-3 times. The solid was then suspended in ether and treated with the solution of 2,2,2',2'-tetraethoxydiethyl disulfide (8) (2.5 g, 9 mmoles) and the reaction mixture was stirred overnight. The reaction was

decomposed with water and the ether layer was separated. The aqueous layer was again extracted with ether. The combined ether layers were dried over sodium sulfate and concentrated to give an oil which was used for next step as such.

The above oil was dissolved in chlorobenzene (100 ml) and refluxed with polyphosphoric acid (10 g) for 0.5 hour. The chlorobenzene was decanted off and the residue was washed three times with chlorobenzene. The chlorobenzene was removed in vacuo and the residue was chromatographed on a silica gel column using hexane as the eluant. The solid obtained was crystallized from hexane to give yellow crystals (0.1 g, 5%), m.p. 185°; ir (potassium bromide): 3040 (s), 1580 (s), 820 (s), 710 (s); nmr (deuterioacetone): 8.70 (dd, $J = 10$ and 2.5 Hz, H-1, 1H), 8.53-7.36 (m, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-10, H-11, 9H); ms: 258 (M^+ , 100), 226 ($M^+ - 32$, 12), 200 ($M^+ - 58$, 2); uv (hexane): λ max nm (log ϵ): 223 (4.59), 250 (4.50), 260 (4.45), 284 (4.51), 288 (4.49), 316 (4.14), 330 (4.36), 348 (4.49), 367 (3.62).

Anal. Calcd. for $C_{18}H_{10}S$: C, 83.37; H, 3.90; S, 12.41. Found: C, 83.35; H, 3.91; S, 12.12.

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SCHEME-I

SCHEME-II

III. BIOLOGICAL TESTING

A. Microbial Mutagenicity of Three- and Four-Ring Polycyclic Aromatic Sulfur Heterocycles.

ABSTRACT

The stable isomers of three- and four-ring polycyclic aromatic sulfur heterocycles were tested for mutagenicity in the Ames standard plate incorporation test and a liquid pre-incubation modification of the Ames test. Of the four three-ring compounds tested only naphtho[1,2-b]thiophene was mutagenic. Of the four-ring compounds, 6 of 13 were mutagenic in the standard Ames or pre-incubation Ames test. The highest activity for the four-ring compounds was observed for phenanthro[3,4-b]thiophene, a compound of approximately the same mutagenic potency in the Ames test as benzo[a]pyrene. The other active four-ring compounds were of considerably less mutagenic potency than phenanthro[3,4-b]thiophene. Mutagenicity for two of the four-ring aromatic thiophenes could only be detected in the liquid pre-incubation Ames test.

S. typhimurium TA100 was the most sensitive strain to mutagenesis by these compounds followed by TA98. All mutagenesis was indirect, requiring metabolic activation.

INTRODUCTION

The biological activity of the polycyclic aromatic sulfur heterocycles (PASH) is not well characterized. Limited data suggest that larger PASH are mutagenic (Karcher et. al., 1981) and carcinogenic in laboratory animals (Tilak, 1960). In practical terms, the genetic activity of PASH is of interest because these compounds are significant constituents of synthetic fuels. For example, coal-derived materials and shale oils both contain a variety of 2-,3-,4- and 5-ring PASH (Willey et al., 1981; Lee et. al., 1980).

A major difficulty in studying the genetic activity of PASH has been the lack of standards, particularly, of higher-molecular-weight compounds. As part of a systematic program of organic synthesis in one of our laboratories, most of the stable 3-,4- and 5-ring PASH have been synthesized (??). The present communication deals with the mutagenicity of the stable 3- and 4-ring PASH in the Ames test system.

Mutagenesis Assays

Agar plate mutagenicity assays were performed as described by Ames et. al. (1975) using four of the Ames-Salmonella test strains; Salmonella typhimurium TA98, TA100, TA1535 and TA1537. The mutagen phenotype defining these strains was determined in each experiment as shown in Table 1.

Dimethylsulfoxide (DMSO) was the solvent used in the bioassay work reported. In addition to the use of the mutagens in Table 1 to check the phenotypes of the Ames Salmonella strains, fixed concentrations of 2-aminoanthracene, benzo[a]pyrene and a complex basic fraction from SRC II heavy distillate were tested against the rat liver (S9) homogenates used for metabolic activation. Optimum levels for S9 were thus established and monitored on a daily basis during the course of the Ames experiments reported herein. Negative controls included the Ames/Salmonella typhimurium test

strains, plus and minus microsomal enzymes (S9), and appropriate solvent controls. Mutagenic response, measured as revertant colonies were counted electronically using a Biotran II automated colony counter (New Brunswick Scientific Co., Inc., Edison, NJ).

The chemicals in this study were assayed for mutagenicity at concentrations of 2, 4, 8, 10, 20 and 50 μg or 20, 40, 80, 100, 200 and 500 μg per petri plate. Each concentration was assayed in duplicate. Stock solutions 10,000 $\mu\text{g}/\text{ml}$ in DMSO of the various PASH were stored at -80°C when not in use.

RESULTS

Three- and 4-ring PASH compounds were tested for mutagenicity in the Ames standard plate incorporation test (Ames et. al., 1975) and a variant of the Ames test based on a liquid pre-incubation step (Yahagi et. al., 1975).

All possible 3 and 4 ring isomers were synthesized and tested for biological activity except for those compounds in which ring fusion is on side c of the thiophene ring. Fusion at this position reduces resonance stabilization of the thiophene ring portion of the molecule rendering it less stable and most likely unable to survive coal liquefaction or shale oil retorting processes.

The mutagenicity for the 3-ring PASH compounds is shown in Table 2. Both linear and nonlinear condensed structures were treated. Of these compounds only naphtho[1,2-b]thiophene was active, inducing an estimated 22 (revertants/g against TA100 (rev TA100/ μg) tested by the standard plate incorporation method. Much less mutagenicity was demonstrated against TA98 (ca. 2 rev/ μg), and no mutagenesis was induced against TA1535 or TA1537 (data not shown). All mutagenesis was indirect, requiring metabolic activation. Dose response data from Table 2 comparing TA98 with TA100 is shown in Figure 1.

Naphtho[2,1-b]thiophene, which differs from the genetically active [1,2-b]isomer only in the position of the sulfur atom, showed no activity in either the standard or pre-incubation Ames tests. The two linear structures, naphtho[2,3-b]thiophene and dibenzothiophene were inactive against the four Ames tester strains used in this study, and TA98 and TA100 in the Ames pre-incubation test (Table 2).

Twelve 4-ring PASH were also tested for mutagenicity, as shown by the data in Table 3. Of the 13, 5 were mutagenically active. Four of these compounds induced mutation in both TA98 and TA100. As for the 3-ring PASH, TA100 was more sensitive to induced mutation than TA98. No mutagenesis was detected with either TA1535 or TA1537. All mutagenesis with the 4-ring PASH required metabolic activation.

In quantitative terms, phenanthro[3,4-b]thiophene was the most mutagenic of the 4-ring PASH. This compound, induced an estimated 195 rev TA100/ μ g and 29 rev TA98/ μ g in the Ames standard plate incorporation test. In comparative terms, phenanthro[3,4-b]thiophene is about as active in the Ames test as benzo[a]pyrene. The results of the pre-incubation tests with TA98 and TA100 were inconclusive because of extensive killing.

The two anthrathiophenes were next in potency. For example, anthra-[2,1-b]thiophene induced approximately 7 rev TA100/ μ g and less than 1 rev TA98/ μ g in the standard Ames test. Anthra[1,2-b]thiophene, which differs from the [2,1-b] isomer only in the position of the sulfur atom induced about 3 rev TA100/ μ g and less than 0.5 rev TA98/ μ g. TA98 responded better in the pre-incubation test of both anthrathiophenes, but remained less active than TA100 in the standard or pre-incubation tests.

The least mutagenically active of the 4-ring PASH induced mutation only in the Ames pre-incubation assay. Phenanthro[3,2-b]thiophene induced approximately 1 rev/ μ g tested in both TA100 and TA98. Benzo[b]naphtho[2,1-d]thiophene was active only against TA100 and induced mutations at the rate of approximately 1 rev/ μ g.

Although the data are limited, they suggest that both the aromatic ring system and the position of the sulfur heteroatom in the thiophene ring influence the mutagenicity of the 3- and 4-ring PASH in the Ames assay. For example, both anthrathiophenes were of roughly the same mutagenicity although the positions of their sulfur atoms were different relative to the anthracene portion of the molecule. Thus the aromatic portion of these compounds may play a more important role than the thiophene ring in determining genotoxicity.

The mutagenicity of the two most active of the PASH compounds studied was apparently determined largely by the position of the sulfur atom. For example, the highly active phenanthro[3,4-b]thiophene (ca. 195 rev TA100/ μ g) differed from the genetically inactive phenanthro[4,3-b]thiophene only in the location of its sulfur atom. Otherwise both compounds had identical geometry, e.g. an aromatic phenanthrene fused to a thiophene ring. In exactly this same way, the 3-ring naphtho[1,2-b]thiophene (ca. 22 rev TA100/ μ g) differed from the inactive naphtho[1,2-b]thiophene only in the position of the sulfur atom.

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TABLE 1. Mutagen Phenotypes of Ames Tester Strains Used to Bioassay Pure PASH
Response for Ames Test Strain:

Compound	µg/Plate	S9	TA98	TA100	TA1537	TA1535
2-Aminoanthracene	1	+	(+)	(+)	(+)	(+)
9-Aminoacridine	50	+	(-)	(-)	(+)	(-)
Nitrosoguanidine	1	-	(-)	(+)	(-)	(+)
7,9-Dimethylbenz[<u>c</u>]- acridine	10	+	(-)	(+)	(-)	(-)

+ indicates a response in revertant colonies at least 2 times above background.

- indicates less than a two-fold response above background.

TABLE 2. Mutagenicity of polycyclic aromatic sulfur heterocycles (PASH): Three-ring compounds.

Name	Structure	Strain: TA98 ^a		+ S9	TA100 -S 9	TA98(pi) ^b		TA100(i)
		+ S9	- S9			+ S9	+ S9	
Dibenzothiophene		101±17(0) ^c	85±8(0)	221±20(0)	221±20(0)	26±2		180±13(0)
		145±1(33)	ND		ND	ND		
		102±0(82)	ND		ND	ND		
		126±14(164)	80±10(164)	284±21(250)	304±21(250)	88±8(100)		206±13(100)
		88±4(328)	83±3(328)	294±34(500)	294±34(500)	75±2(500)		216±4(250)
naphtho[2,3-b]thiophene		62±6(0)	85±8(0)	223±16(0)	221±29(0)			160±13(0)
		63±7(20)	ND	216±6(20)	ND			---
		70±17(40)	ND	215±16(40)	ND			---
		84±29(80)	ND	194±16(80)	ND			---
		18±2(100)	76±2(120)	165±21(100)	ND			
		66±8(200)	76±10(250)	222±32(200)	228±18(250)			207±5(250)
		ND	ND	294±18(500)	245±17(500)			218±5(250)
naphtho[2,1-b]thiophene		62±6(0)		223±16(0)	221±20(0)	26±2(0)		180±13(0)
		69±3(20)		196±7(20)	ND	---		---
		61±18(40)		211±28(40)	ND	---		---
		62±4(80)		162±5(80)	ND	---		---
		49±1(100)		157±3(100)	ND	---		---
		41±4(200)		173±23(200)	167±11(250)	45±1(250)		186±14(100)
		45±6(500)		130±8(500)	152±12(500)	38±3(500)		130±5(250)
naphtho[1,2-b]thiophene		34±4(0)		217±19(0)	221±20(0)	26±2		180±13(0)
		56±3(20)		657±38(20)	ND	ND		---
		85±26(40)		746±65(40)	ND	ND		---
		100±2(80)		1026±99(80)	ND	ND		---
		186±50(100)		1185±11(100)	ND	ND		34±13(100)K
		142±2(200)		1247±3(200)	174±10(250)	9±4(250)		16±10(250)K
		19±2(500)		48±59(500)	93±1(500)	25±1(500)		---

- a. *S. typhimurium* TA98 or TA100 in the standard Ames plates incorporation test. b. *S. typhimurium* TA98 or TA100 in the Ames pre-incubation test. c. Number outside parenthesis indicate average number of revertant colonies per petri plates ± SE for duplicate samples. Number inside parenthesis indicates the concentration of chemical in µg per plate.

TABLE 3. Mutagenicity of polycyclic aromatic sulfur heterocycles (PASH): Four-ring compounds.

Name	Structure	Strain: TA98 ^a		TA100		TA98(pi) ^b		TA100(Pi)	
		+ S9	- S9	+ S9	-S 9	+ S9	-S 9	+ S9	-S 9
benzo[b]naphto- [2,3-d]thiophene		31±2(0) ^c	38±2(0)	193±13(0)	221±20(0)	26±2(0)		180±13(0)	
		41±5(20)		244±17(20)	ND	---		---	
		41±2(40)		186±14(40)	ND	---		---	
		36±6(80)		194±9(80)	ND	---		---	
		34±2(100)		220±3(100)	ND	42±1(100)		238±23(100)	
		36±9(200)	42±1(250)	170±1(200)	231±15(200)	44±1(200)		232±9(250)	
		29±1(500)	27±4(500)	167±2(500)	218±12(500)	---		---	
Anthra[1,2-b]thiophene		34±2(0)	38±2(0)	193±13(0)	221±20(0)	26±2(0)		180±13(0)	
		37±5(20)		260±52(20)	ND	ND			
		57±8(40)		368±31(40)	ND	ND			
		49±15(80)		431±12(80)	ND	ND			
		77±19(100)		415±23(100)	ND	234±(100)			
		104±4(200)	31±5(250)	416±10(200)	231±15(200)	218±1(250)		715±33(100)*?	
		114±3(500)	36±4(500)	374±38(500)	218±11(500)	---		218±0(250)	
Anthra[2,1-b]thiophene		34±2(0)	38±2(0)	193±13(0)	221±20(0)	26±2(0)		180±13(0)	
		32±4(20)	---	295±10(20)	ND	ND		---	
				466±32(40)	ND	ND		---	
		50±1(40)	---	702±25(80)	ND	ND		---	
		61±9(80)	---	639±6(100)	ND	197±3(100)		695±104(100)	
		54±5(100)	---	584±28(200)	276±6	251±6(250)		838±0(250)	
		110±3(200)	23±4(250)	521±17(500)	235±36	ND		---	
		72±1(500)	34±5(500)						
benzo[b]naphto- [1,2-d]thiophene		36±1(0)		217±19(0)	221±20(0)	26±2(0)		180±13(0)	
		33±2(20)		212±6(20)	ND	ND			
		27±2(40)		194±19(40)	ND	ND			
		30±1(80)		166±11(80)	ND	ND			
		26±2(100)		186±4(100)	ND	38±2(100)		198±5(100)	
		24±7(200)		164±21(200)	259±11(250)	44±15(250)		204±12(250)	
		39±2(500)		139±11(500)	247±10(500)	ND			

TABLE 3. Continued.

Name	Structure	Strain:		TA98		TA100		TA98(pi) ^a		TA100(Pi)	
				+ S9	- S9	+ S9	- S9	+ S9	- S9	+ S9	- S9
benzo[b]naphto- [2,1]thiophene				36±1(0)		217±19(0)	221±20(0)	26±2(0)		180±13(0)	
				32±4(20)		243±26(20)	ND	ND		---	
				31±2(7)		228±2(40)	ND	ND		---	
				45±3(80)				ND		---	
				31±6(100)		321±19(80)	ND			---	
				49±2(200)		305±6(100)	ND	62±1(100)		363±39(100)	
				42±3(500)		312±4(200)	260±7(250)	63±2(250)		350±1(250)	
						277±34(500)	215±18(500)	ND		---	
phenanthro[2,3-b]thiophene				62±6(0)							
				62±8(20)		217±19(0)	221±20(0)	26±2(0)		180±13(0)	
				69±0(40)		242±24(10)	ND	ND		---	
				60±3(80)		258±6(40)	ND	ND		---	
				59±5(100)		251±13(80)	ND	ND		---	
				50±5(200)		244±4(100)	ND	50±6(100)		239±22(100)	
				58±3(500)		244±3(200)	207±7(250)	50±1(250)		298±2(250)	
						239±3(500)	166±8(500)	ND		---	
phenanthro[3,2-b]thiophene				62±6(0)		223±16(0)	221±20(0)	261±2(0)		180±3(0)	
				59±1(20)		241±49(30)	ND	ND		---	
				60±2(40)		297±17(40)	ND	ND		---	
				67±11(0)		234±68(80)	ND	ND		---	
				76±12(100)		271±11(100)	ND	117±1(100)		382±22(100)	
				67±9(200)		269±4(200)	232±26(250)	79±7(250)		317±38(250)	
				73±4(500)		287±15(500)	221±2(500)	ND		---	
phenanthro[1,2-b]thiophene				62±6(0)		223±16(0)	221±20(0)	26±2(0)		180±3(0)	
				65±3(20)		239±10(20)	ND	ND			
				56±2(40)		224±6(40)	ND	ND			
				49±4(80)		196±7(80)	ND	ND			
				49±1(100)		197±5(100)	ND	ND		270±2(100)	
				60±1(200)		224±6(200)	238±4(250)	69±8(250)		189±4(250)	
				74±9(500)		203±3(500)	227±12(500)	58±3(500)			

TABLE 3. Continued.

Name	Structure	Strain: TA98 ^a		TA100		TA98(Pi) ^b		TA100(Pi)	
		+ S9	- S9	+ S9	- S9	+ S9	- S9	+ S9	- S9
phenanthro[2,1-b]thiophene		62±6(0) ^c		223±16(0)	22±20(0)	261±2(0)		180±13(0)	
		68±1(20)		318±31(20)	---				
		66±6(40)		294±3(40)	---				
		62±1(80)		308±19(80)	---				
		61±5(100)		278±26(100)	---			276±40(100)	
		53±10(200)		285±9(200)	280±12(250)	68±4(250)		263±13(250)	
		65±12(500)		260±0(500)	26±1(500)	60±2(500)			
phenanthro[3,4-b]thiophene		93±10(0)	85±8(0)	223±16(0)	221±20(0)	26±2(0)		180±13(0)	
		124±9(22)	---	386±92(2)	---			---	
		191±3(5.5)	---	907±397(4)	---			---	
				1585±25(8)	---			---	
		412±15(11.0)	70±5(11.0)	1277±243(10)				240±6(100)	
		741±22(22.0)	75±2(22.0)	1158±19(20)	215±10(25)	76±3(250)		163±16(250)	
				681±50(50)	201±5(50)	88±19(500)		---	
phenanthro[4,3-b]thiophene		62±6(0)	85±8(0)	223±16(0)	221±20(0)	261±2(0)		180±3(0)	
		19±2(20)		280±24(20)					
		19±6(40)		360±1(40)					
		21±1(0)		273±13(80)					
		14±1(100)		256±8(100)				252±38(100)	
		30±3(200)	81±10(250)	219±44(200)	127±12(250)	106±6(250)		250±2(250)	
		19±4(500)	95±5(500)	207±7(500)	112±(500)	100±19(500)			
phenanthro[9,10-b]thiophene		62±6(0)	85±8	223±16(0)	221±20(0)	26±2(0)		180±3(0)	
		37±10(20)	---	254±23(20)	---			---	
		71±4(40)	---	222±12(40)	---			---	
		49±16(80)	---	229±10(80)	---			---	
		62±3(100)	---	224±3(100)	---			284±17(100)	
		55±3(200)	71±9(250)	216±34(100)	232±45(250)	47±3(250)		204±11(250)	
		52±1(500)	77±7(250)	245±4(500)	228±7(500)	35±1(500)			

a. *S. typhimurium* TA98 or TA100 in the standard Ames plates incorporation test. b. *S. typhimurium* TA98 or TA100 in the Ames pre-incubation test. c. Number outside parenthesis indicate average number of revertant colonies per petri plates ± SE for duplicate samples. Number inside parenthesis indicates the concentration of chemical in µg per plate.

FIGURE 1

FIGURE 2

APPENDIX 1: COMPOUNDS SYNTHESIZED TO DATE.

Name	Quantity	MW	Structural Formula
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Three Ring Systems:

Naphtho[2,3- <u>b</u>]thiophene	170 mg	184	
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Four Ring Systems

Phenaleno[6,7- <u>bc</u>]thiophene	110 mg	208	
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Anthra[1,2- <u>b</u>]thiophene	200 mg	234	
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Anthra[2,1- <u>b</u>]thiophene	200 mg	234	
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Anthra[2,3- <u>b</u>]thiophene	300 mg	234	
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Benzo[<u>b</u>]naphtho[1,2- <u>d</u>]-thiophene	3 g	234	
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Name	Quantity	MW	Structural Formula
Phenanthro[3,2- <u>b</u>]thiophene	700 mg	234
Phenanthro[9,10- <u>b</u>]thiophene	2 g	234
Five Ring Systems			
Benzo[4,5]phenaleno[1,9- <u>bc</u>]-thiophene	200 mg	258
Benzo[4,5]phenaleno[9,1- <u>bc</u>]-thiophene	5 mg unstable	258
Benzo[1,2]phenaleno[4,3- <u>bc</u>]-thiophene	200 mg	258
Benzo[2,3]phenanthro[4,5- <u>bcd</u>]-thiophene	700 mg	258
Chryseno[4,5- <u>bcd</u>]thiophene	350 mg	258

Name	Quantity	MW	Structural Formula
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Benzo [<u>b</u>] naphtho [2,1- <u>d</u>]- thiophene	2 g	234	
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Benzo [<u>b</u>] naphtho [2,3- <u>d</u>]- thiophene	100 mg	234	
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Phenanthro [1,2- <u>b</u>] thiophene	2 g	234	
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Phenanthro [2,1- <u>b</u>] thiophene	2 g	234	
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Phenanthro [3,4- <u>b</u>] thiophene	1.5 g	234	
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Phenanthro [4,3- <u>b</u>] thiophene	1 g	234	
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Phenanthro [2,3- <u>b</u>] thiophene	700 mg	234	
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Name	Quantity	MN	Structural Formula
Pyreno[1,2- <u>b</u>]thiophene	300 mg	258
Pyrene[2,1- <u>b</u>]thiophene	200 mg	258
Pyreno[4,5- <u>b</u>]thiophene	100 mg	258
Anthra[1,2- <u>b</u>]benzo[<u>d</u>]-thiophene	30 mg	284
Benzo[<u>b</u>]phenanthro[1,2- <u>d</u>]-thiophene	200 mg	284
Benzo[<u>b</u>]phenanthro[2,1- <u>d</u>]-thiophene	30 mg	284
Benzo[<u>b</u>]phenanthro[3,4- <u>d</u>]-thiophene	50 mg	284

Name	Quantity	MW	Structural Formula
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Benzo [<u>b</u>]phenanthro[4,3- <u>d</u>]- thiophene	200 mg	284	
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Triphenyleno[1,2- <u>b</u>]thiophene	400 mg	284	
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Triphenylene[2,1- <u>b</u>]thiophene	400 mg	284	
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APPENDIX 2

PAPERS PUBLISHED OR SUBMITTED FOR PUBLICATION

DURING THIS PERIOD

1. M. Iwao, M.L. Lee, and R.N. Castle, "Synthesis of Phenanthro[b]thiophenes," J. Heterocyclic Chem., 17, 1259 (1980).
2. K.D. Bartle, M.L. Lee, and S.A. Wise, "Factors Affecting the Retention of Polycyclic Aromatic Hydrocarbons in Gas Chromatography," Chromatographia, 14 69 (1981).
3. C. Willey, M. Iwao, R.N. Castle, and M.L. Lee, "Determination of Sulfur Heterocycles in Coal Liquids and Shale Oils," Anal. Chem., 53 400 (1981).
4. D.W. Later, M.L. Lee, K.D. Bartle, R.C. Kong, and D.L. Vassilaros, "Rapid Chemical Class Separation and Detailed Characterization of Organic Compounds in Synthetic Fuels," Anal. Chem., submitted.
5. R.A. Pelroy, Y. Tominaga, M. Iwao, R.N. Castle, and M.L. Lee, "Microbial Mutagenicity of Three- and Four-Ring Polycyclic Aromatic Sulfur Heterocycles," Mut. Res., submitted.
6. Y. Tominaga, M.L. Lee, and R.N. Castle, "Synthesis of Anthra[b]thiophenes and Benzo[b]naphtho[d]thiophenes," J. Heterocyclic Chem., submitted.
7. R. Pratap, Y. Tominaga, M.L. Lee, and R.N. Castle, "Synthesis of Pyreno[b]thiophenes," J. Heterocyclic Chem., submitted.