New Benzo[b]thiophene Derivatives of Anthracene and Benz[a]anthracene[1]

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Using several multistep synthetic paths, the title compounds and the required intermediates were prepared and properly characterized by both chemical and physical methods. In addition, 12-(2-benzo[b]thienyl)benz[a]anthracene was cyclodehydrogenated to give benzo[b]benzo[b]thieno[2,3-e]pyrene.

The preparation and study of polynuclear aromatic compounds containing sulfur has received considerable attention in recent years.[3] As a continuation of our research in sulfur-containing derivatives of anthracene[4] and benz[a]anthracene,[5] synthesis of the title compounds was undertaken.

Initial thinking dictated that the desired aromatic compounds, **18–23**, could be prepared by extensions of known reactions.[6] However, several experimental observations made during the course of our investigation proved to be far from routine.

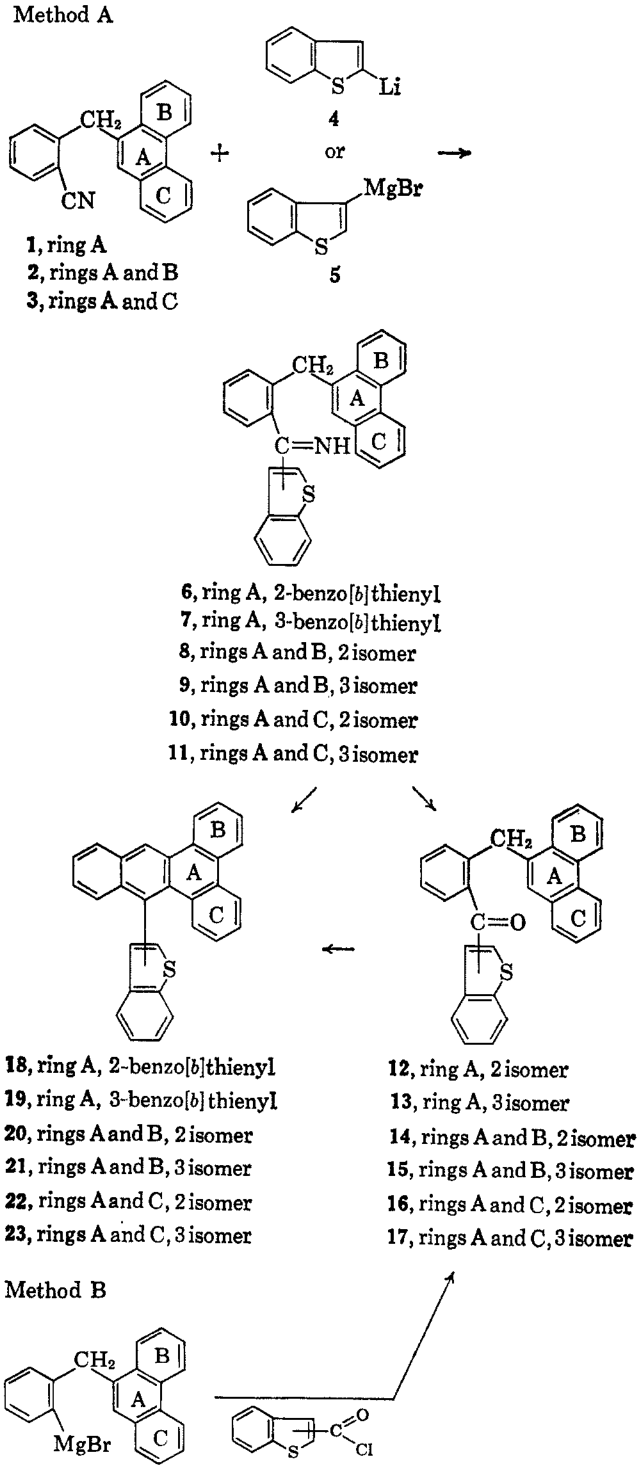
The two methods considered applicable for the preparation of ketones, **12–17**, which could be cyclized to the desired aromatic products, **18–23**, are illustrated in Chart I. Method A involves the reaction of an appropriate nitrile, **1–3**, with either 2-benzo[b]thienyllithium (**4**) or 3-benzo[b]thienylmagnesium bromide (**5**) followed by hydrolysis of the resulting ketimine,[7,8] **6–11**.

In our case, both methods were attempted but method A proved to be the only practical route since none of the desired ketones could be isolated *via* method B. This failure was not due to the reactions, *per se*, but resulted from the difficulty involved in isolation of the desired products.

Ketones **12**, **14**, and **16** were prepared as outlined in Chart I by direct hydrolyses of the 2-benzo[b]thienyllithium–nitrile reaction mixtures using 40% sulfuric acid and isolated as crystalline products. On the other hand, ketones **13**, **15**, and **17** required that the ketimines **7**, **9**, and **11** be precipitated and collected in crude form as their respective hydrochloride salts prior to hydrolysis.

Acid-catalyzed aromatic cyclodehydration[9] of the corresponding ketones was employed for the preparation of aromatic compounds **18–22**. Compound **23** could not be synthesized from its precursor ketone. Ketones **12**, **13**, and **15** favored conditions of heat and pressure (sealed tube at 180°) for cyclization, whereas ketones **14** and **16** were readily cyclized by heating in the acid mixture at atmospheric pressure. In addition, aromatic compounds **20** and **21** were prepared by cyclization of their corresponding ketimine hydrochlorides. The structures assigned to all the aromatic products are consistent with the elemental analyses, ultraviolet, and infrared data.

Chart I



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[2] Abstracted in part from the Ph.D. Thesis of P. D. H. presented to the Virginia Polytechnic Institute, 1964. National Defense Education Act Fellow, 1960–1963; Eastman Kodak Fellow, 1963–1964.

[3] (a) B. D. Tilak, *Tetrahedron*, **9**, 76 (1960); (b) G. N. Pillai, T. S. Murty, and B. D. Tilak, *Indian J. Chem.*, **1**, 112 (1963); (c) P. Faller, *Compt. Rend.*, **260**, 3686 (1965).

[4] F. A. Vingiello, S-G. Quo, P. Polss, and P. Henson, *J. Med. Chem.*, **7**, 832 (1964).

[5] F. A. Vingiello, S-G. Quo, and P. Polss, *J. Org. Chem.*, **30**, 266 (1965).

[6] For a recent example of syntheses in this area, see F. A. Vingiello and P. D. Henson, *ibid.*, **30**, 2842 (1965).

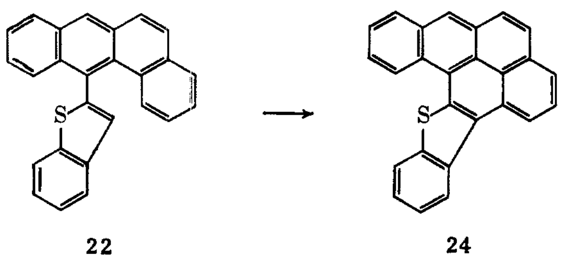
[7] F. A. Vingiello and M. M. Schlechter, *ibid.*, **28**, 2448 (1963).

[8] F. A. Vingiello and A. Borkovec, *J. Am. Chem. Soc.*, **78**, 1240 (1956).

[9] C. K. Bradsher, *ibid.*, **62**, 486 (1940).

The failure of ketone **17** to undergo acid-catalyzed aromatic cyclodehydration might be attributed to steric hindrance, a factor not uncommon with ketones of this type.[10] This idea is supported by consideration of the carbonyl absorption frequencies in the infrared of the isomeric ketones **16** and **17**. From the standpoint of resonance interaction,[11] one would expect the carbonyl adsorption band of **16** to occur at a higher frequency than that of **17**.[12] However, the reverse is actually observed (1647 cm^{-1} for **16** and 1664 cm^{-1} for **17**) which implies a steric inhibition of normal conjugation effects. Further cyclization attempts using alumina[10] and liquid hydrogen fluoride[13] also proved to be unsuccessful.

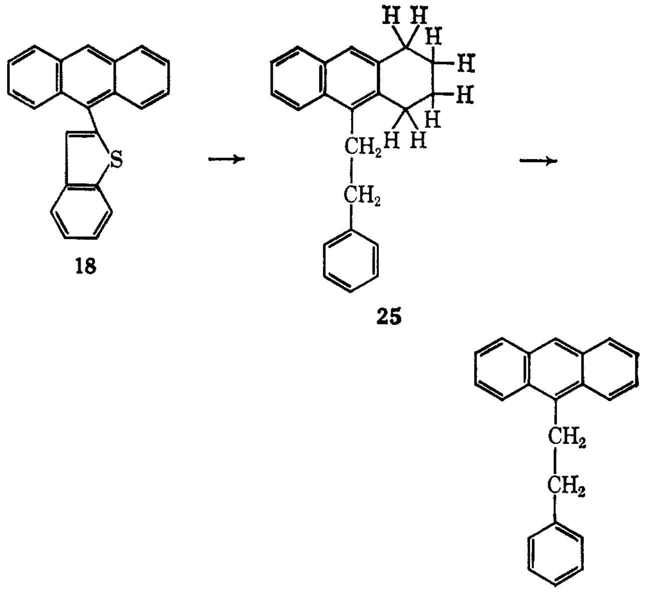
Compound **22** was considered of additional importance since it presents an opportunity to prepare a sulfur-containing aromatic system consisting of seven fused aromatic rings, **24**. Such compounds should be of physiological interest,[3,14] and of further interest for spectral comparisons with carbocyclic analogs.[15] Compound **24** was prepared by treatment of **22** with aluminum chloride in dry benzene in 30% yield.



22 **24**

Desulfurization studies[16] of compounds **18**, **20**, and **22** using Raney nickel were found to be interesting but not as straightforward as one might have expected. Initial desulfurization attempts using commercially available Raney nickel No. 28[17] resulted in multicomponent oils. Only in the case of compound **18** could an analytically pure product be isolated. This product was assigned the structure of 9-(2-phenylethyl)-1,2,3,4-tetrahydroanthracene (**25**) on the basis of its elemental analysis and infrared and ultraviolet spectra. Treatment of **25** with 10% palladium on charcoal gave **26**.

In order to investigate the problem of the Raney nickel desulfurizations, the expected products, **26** and the two corresponding benz[*a*]anthracene derivatives, were prepared and characterized.[18] The nickel catalyst was prepared according to the procedure of Mozingo,[19] except that various heating times and temperatures for digestion were used to produce catalysts of varying degrees of activity. In addition, deactivating procedures such as drying the catalyst or heating in boiling acetone or ethanol were employed.



18 **25** **26**

Using the previously prepared compounds[18] as standards and analyzing the products by gas chromatography, 27 desulfurization reactions were performed. Only for compound **20** was the desired product isolated from the reaction mixture. However, the yield was low and the reaction required that the catalyst be deactivated by boiling it in a 2:1 mixture of benzene and ethanol prior to desulfurization in mesitylene.

Experimental Section[20]

2-Benzylphenyl 2-Benzo[*b*]thienyl Ketone (12).—The 2-lithium reagent of benzo[*b*]thiophene was prepared by adding 26.8 g (0.20 mole) of benzo[*b*]thiophene in 150 ml of anhydrous ether to a solution of 14.0 g (0.21 mole) of *n*-butyllithium[21] in 150 ml of *n*-hexane. When the reaction was complete, a solution of 38.6 g (0.20 mole) of 2-benzylbenzonitrile in 150 ml of dry benzene was added and the resulting mixture was stirred and boiled overnight. An excess of 40% sulfuric acid was added and the heating was continued for 26 hr. The organic layer was separated, washed with water, and concentrated. The product was obtained from 95% ethanol, after treatment with charcoal, as white needles, 43.5 g (66%), mp 110–111°.

Anal. Calcd for $C_{22}H_{16}OS$: C, 80.45; H, 4.91; S, 9.76. Found: C, 80.25; H, 4.78; S, 9.81.

2-Benzylphenyl 3-Benzo[*b*]thienyl Ketone (13).—A Grignard reagent was prepared from 3.0 g (0.12 g-atom) of magnesium turnings and 26.5 g (0.12 mole) of 3-bromobenzo[*b*]thiophene in 150 ml of anhydrous ethyl ether. After the reaction was complete, the ether was replaced with dry benzene, and a solution of 20.0 g (0.11 mole) of 2-benzylbenzonitrile in 100 ml of dry benzene was added. The mixture was stirred and heated under reflux overnight, cooled, and decomposed with a 20% ammonium chloride solution. The organic layer was separated, washed with water, and dried over anhydrous calcium chloride. The solution was filtered and concentrated, and the residual oil was dissolved in 500 ml of dry ether. Hydrogen chloride gas was bubbled into the ether solution and 20 g of crude ketimine hydrochloride was collected. This crude product along with 200 ml of benzene and 150 ml of 40% sulfuric acid was heated under reflux for 19 hr.

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(10) F. A Vingiello, A. Borkovec, and W. W. Zajac, *J. Am. Chem. Soc.*, **80**, 1714 (1958).

(11) R. S. Rasmussen, D. D. Tunnicliff, and R. R. Brittain, *ibid.*, **71**, 1068 (1949).

(12) R. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," Interscience Publishers, Inc., New York, N. Y., 1960, p 154.

(13) C. K. Bradsher, T. W. G. Solomons, and F. R. Vaughan, *J. Org. Chem.*, **25**, 757 (1960).

(14) F. A. Vingiello, W. W. Zajac, and L. G. Mahone, *ibid.*, **28**, 3253 (1963).

((15) L. Ojakaar, Ph.D. Thesis, Virginia Polytechnic Institute, 1964.

(16) H. Huptmann and W. F. Walter, *Chem. Rev.*, **62**, 347 (1962).

(17) Purchased from W. R. Grace and Co., Raney Catalyst Division, Chattanooga, Tenn.

(18) Prepared according to method A by substituting the Grignard reagent of 2-phenylethyl bromide for the benzo[*b*]thiophene moiety in the scheme.

(19) R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 176.

(20) All boiling points are uncorrected and all melting points were taken on a Fisher-Johns melting apparatus and are corrected. The infrared spectra were determined with a Beckman Model IR-5 recording spectrophotometer and the ultraviolet spectra with a Beckman Model DK-2A recording spectrophotometer using a 1-cm quartz cell and 95% ethanol as the solvent. The microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(21) Commercially available from Foote Mineral Co., Exton, Pa.

TABLE I

NEW KETONES

Compound	% yield	Mp, °C	Carbon, %		Hydrogen, %		Sulfur, %	
			Calcd	Found	Calcd	Found	Calcd	Found
2-Benzylphenyl 2-benzo[*b*]thienyl ketone (**12**)	66	110–111	80.45	80.25	4.91	4.78	9.76	9.81
2-Benzylphenyl 3-benzo[*b*]thienyl ketone (**13**)	17	78–79	80.45	80.32	4.91	4.83	9.76	9.91
2-(1-Naphthylmethyl)phenyl 2-benzo[*b*]thienyl ketone (**14**)	44[a]	100–101	82.51	82.14	4.79	4.92	8.47	8.40
2-(1-Naphthylmethyl)phenyl 3-benzo[*b*]thienyl ketone (**15**)	30[b]	120–121	82.51	82.47	4.79	4.74	8.47	8.55
2-(2-Naphthylmethyl)phenyl 2-benzo[*b*]thienyl ketone (**16**)	65[a]	107–108	82.51	82.10	4.79	4.82	8.47	8.79
2-(2-Naphthylmethyl)phenyl 3-benzo[*b*]thienyl ketone (**17**)	15[b]	231–232[c]	82.51	82.04	4.79	4.31	8.47	8.11
2-Benzylphenyl 2-phenylethyl ketone	76[b]	*d*	87.96	87.68	6.71	6.44	..	..
2-(1-Naphthylmethyl)phenyl 2-phenylethyl ketone	64[b]	*e*	89.11	89.25	6.33	6.16	..	..
2-(2-Naphthylmethyl)phenyl 2-phenylethyl ketone	86[b]	69–70	89.11	89.69	6.33	6.33	..	..

[a] Prepared essentially as has been described for compound **12**. [b] Prepared essentially as has been described for compound **13**. [c] The crystals first obtained melted at 211–212°. These were converted to the higher melting dimorph by boiling them in acetic acid. [d] Bp 180–186° (0.3 mm). [e] Bp 225–232° (0.2 mm).

TABLE II

NEW ANTHRACENES AND BENZ[*a*]ANTHRACENES[a]

Compound	% yield	Mp, °C	Carbon, %		Hydrogen, %		Sulfur, %	
			Calcd	Found	Calcd	Found	Calcd	Found
9-(2-Benzo[*b*]thienyl)anthracene (**18**)	95	260–261	85.12	85.24	4.55	4.58	10.33	10.33
9-(3-Benzo[*b*]thienyl)anthracene (**19**)	74	165–166	85.12	85.31	4.55	4.55	10.33	10.27
7-(2-Benzo[*b*]thienyl)benz[*a*]anthracene[b] (**20**)	Quant	244–245	86.61	86.37	4.48	4.79	8.91	8.90
7-(3-Benzo[*b*]thienyl)benz[*a*]anthracene (**21**)	66	186–187	86.61	86.73	4.48	4.63	8.91	8.95
12-(2-Benzo[*b*]thienyl)benz[*a*]anthracene (**22**)	97	200–201	86.61	86.69	4.48	4.45	8.91	8.46
7-(2-Phenylethyl)benz[*a*]anthracene (**27**)	76	125–126	93.94	93.63	6.06	6.27	...	...
12-(2-Phenylethyl)benz[*a*]anthracene (**28**)	86	140–141	93.94	93.92	6.06	6.08	...	...

[a] The wavelength maxima for **18** are 338, 368, 349, and 254 mμ; for **19**, 386, 366, 348, and 254 mμ; for **20**, 372, 354, 336, 291, 281, and 271 mμ; for **21**, 370, 353, 335, 291, 281, and 271 mμ; for **22**, 370, 350, 345, 289, 279, and 269 mμ; for **27**, 338, 322, 303, 292, 281, 271, and 260 mμ; and for **28**, 338, 290, 279, 269, and 260 mμ. [b] Formed a 1:1 adduct with TNF. *Anal.* Calcd for $C_{39}H_{21}N_3O_7S$: C, 69.33; H, 3.13; N, 6.22; S, 4.75. Found: C, 69.53; H, 3.33; N, 6.46; S, 4.37.

After the usual work-up, the product crystallized from 95% ethanol as white platelets, 6.0 g (17%), mp 78–79°.

Anal. Calcd for $C_{22}H_{16}OS$: C, 80.45; H, 4.91; S, 9.76. Found: C, 80.32; H, 4.83; S, 9.91.

The remaining new ketones were prepared essentially as was compound **12** or **13** as illustrated in Chart I. The data are shown in Table I.

9-(2-Benzo[*b*]thienyl)anthracene (18).—A mixture of 1.0 g (0.003 mole) of 2-benzylphenyl 2-benzo[*b*]thienyl ketone, 70 ml of glacial acetic acid, and 30 ml of 48% hydrobromic acid was sealed in a Carius tube and heated in a Carius furnace at 188° for 4 hr. After cooling to room temperature, the tube was opened, and the crude crystalline product was collected by filtration. The filtrate was neutralized with a saturated carbonate solution and extracted with benzene. The initially collected solid was dissolved in the benzene extract, ethanol was added, and the resulting solution was treated with charcoal. The product crystallized as yellow platelets, 0.9 g (95%), mp 258–259°.

An analytical sample was prepared by repeated recrystallizations from a 1:1 benzene–ethanol solution: mp 260–261°.

Anal. Calcd for $C_{22}H_{14}S$: C, 85.12; H, 4.55; S, 10.33. Found: C, 85.24; H, 4.58; S, 10.33.

The wavelength maxima for **18** are 388, 368, 349, and 254 mμ.

The remaining cyclodehydration reactions were effected in essentially the same way. The data are shown in Table II.

Benzo[*b*]benzo[*b*]thieno[2,3-*e*]pyrene (24).—To a solution of 0.5 g (0.0014 mole) of 12-(2-benzo[*b*]thienyl)benz[*a*]anthracene (**22**) in 50 ml of dry benzene was added 0.8 g of aluminum chloride. The reaction mixture was heated to reflux for 10 min, cooled, and poured into 200 ml of a 10% hydrochloric acid solution. The benzene layer was separated and the aqueous layer was extracted with benzene. The combined benzene solutions were washed with water, concentrated to *ca* 15 ml, and 100 ml of 95% ethanol was added. The resulting yellow-brown precipitate was collected and chromatographed on an alumina column using petroleum (bp 30–60°) ether as the eluent. The greenish yellow, blue-fluorescing band was collected and, following solvent removal, the product was crystallized from a benzene–ethanol solution as fluffy orange needles, mp 232–233°, yield 0.15 g (30%).

An analytical sample was prepared by vacuum sublimation followed by recrystallization from a benzene–ethanol solution.

Anal. Calcd for $C_{28}H_{14}S$: C, 87.12; H, 3.94; S, 8.94. Found:[22] C, 86.90; H, 4.01; S, 8.98.

A 2,4,7-trinitrofluorenone (TNF) adduct was prepared as has been described for 20 and was obtained as a green granular solid, mp 258–260°.

Anal. Calcd for $C_{39}H_{19}N_3O_7S$: C, 69.53; H, 2.86; N, 6.24; S, 4.75. Found: C, 69.37; H, 3.24; N, 6.13; S, 4.59.

The wavelength maxima for **24** are 445, 422, 410, 402, 390, 370, 355, and 303 mμ.

Desulfurization of 9-(2-Benzo[*b*]thienyl)anthracene (18).—Raney nickel[17] (5.0 g) was added to a solution of 2.0 g (0.006 mole) of 9-(2-benzo[*b*]thienyl)anthracene in 300 ml of a 2:1 benzene–ethanol solution. The reaction mixture was heated to reflux for 2 hr and cooled, and the nickel catalyst was removed by filtration. The filtrate was concentrated and the residual oil was dissolved in 95% ethanol. After treatment with charcoal 9-(2-phenylethyl)-1,2,3,4-tetrahydroanthracene (**25**) crystallized as white platelets, mp 99–100°, yield 0.65 g (36%).

Anal. Calcd for $C_{22}H_{22}$: C, 92.26; H, 7.74. Found: C, 92.30; H, 7.74.

The wavelength maxima for **25** are 325, 321, 305, 292, 281, and 271 mμ.

A mixture of 0.25 g of the tetrahydroanthracene and 1.0 g of 10% palladium on charcoal in 40 ml of *p*-cymene was heated to reflux for 3.5 hr. After cooling, the mixture was poured onto an alumina column and eluted with benzene. Following solvent removal under reduced pressure, the residual oil was crystallized from ethanol as yellow needles, mp 102°. The product was identified as 9-(2-phenylethyl)anthracene, yield 0.22 g (95%).

Desulfurization of 7-(2-Benzo[*b*]thienyl)benz[*a*]anthracene (20).—Raney nickel W7 was prepared from 12.5 g of a nickel–aluminum alloy and 16.0 g of sodium hydroxide in 200 ml of water according to Mozingo[19] except that digestion was conducted at 60–65° for 1 hr. The nickel catalyst was added to 1.0 g of 7-(2-benzo[*b*]thienyl)benz[*a*]anthracene in 300 ml of a 2:1 benzene–ethanol solution. After boiling for 1.5 hr, the solvent was removed and substituted with 150 ml of mesitylene. Boiling was continued for 2 hr. After cooling, the catalyst was removed by filtration and washed with 100 ml of benzene. Following solvent removal under reduced pressure, fractional crystallization of the residual oil from 95% ethanol afforded 0.6 g of the unreacted starting material and 0.2 g of the desulfurized product, 7-(2-phenylethyl)benz[*a*]anthracene, mp 122–124°.

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(22) Average of two analyses on duplicate samples.