Keto–Enol Tautomerism in the Thiophene Analogues of Naphthacen-5-one

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A study of the synthesis and keto–enol tautomerism in a naphtho and several anthrathiophene systems was undertaken with the objective of determining the structural features which influence the position of equilibrium in these fused systems. Thus 4,11-dihydroanthra[2,3-*b*]thiophen-4-one (**3**) and 4,11-dihydroanthra[2,3-*b*]thiophen-11-one (**4**) were synthesized and studied spectroscopically. Difficulties in the attempted synthesis of 4,11-dihydroanthra[2,3-*c*]thiophen-4-one (**5**) prompted the synthesis of 1,3-dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (**6**). This modification necessitated the synthesis of 1,3-dimethyl-4,9-dihydronaphtho[2,3-*c*]-thiophen-4-one (**7**) so that comparisons with the naphthothiophene system could be made. It was found that the *c*-fused ketones **6** and **7** gave no evidence of the presence of enolic material when their NMR spectra were studied in $CDCl_3$ or Me_2SO-d_6. A solution of **3** in $CDCl_3$ or $CDCl_3$–CF_3CO_2H gave no NMR spectroscopic evidence of enolic material on standing. In Me_2SO-d_6 only enolic material appeared to be present. In the case of **4** a freshly prepared solution in $CDCl_3$ showed only keto form, but when the solution was allowed to stand for 96 h, the NMR spectrum of the solution showed a 33% enol content. In $CDCl_3$–CF_3CO_2H at equilibrium a 39% enol content was observed. It is concluded that in these systems *c* fusion of a thiophene ring predisposes the compound to exist exclusively in the keto forms (**6k**,**7k**) since this avoids the intermediacy of the unstable anthra[*c*]- and naphtho[*c*]thiophenes. *b* fusion of a thiophene ring permits varying amounts of enol in the cases of **3** and **4**, depending on the solvent.

The synthesis and spectroscopic examination of keto–enol tautomerism in the thiophene analogues of anthrone were reported previously.[1,2] The naphthothiophene[1] and benzodithiophene[2] systems have been studied and the properties of the fushed thiophene systems were found to be dictated by the mode of fusion of the thiophene ring.

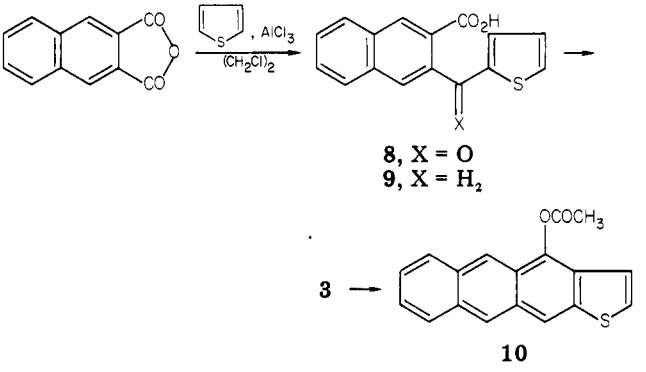
In this paper to report the results of a study of keto–enol tautomerism in the anthra[2,3]thiophene system, a heterocyclic analogue of the naphthacen-5-one system (**2**). While anthrone (**1k**) and anthrol (**1e**) have been isolated, the spectroscopically determined equilibrium constant in benzene ($K = 2.5 \times 10^{-3}$ at 20 °C) indicates the keto form **1k** greatly predominates in solution (Chart I).[3] Whereas naphthacen-5-one (**2**) has been shown to enolize in the presence of alkali[4] no evidence for enolization in the absence of strong base has been reported. In fact, Clar[5] was able to effect the addition of a Grignard reagent to the carbonyl group of **2**. Recent reviews dealing with keto–enol tautomerism in aromatic systems have been published.[6]

There are three possible isomeric anthrathiophenones, **3**–**5**, analogous to naphthacen-5-one. Difficulties in the attempted synthesis of **5** necessitated a slight alteration in that 1,3-dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (**6**) was substituted for **5**. This change made the synthesis and investigation of 1,3-dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**7**) necessary so that comparisons with the previously studied naphthothiophenones could be made.

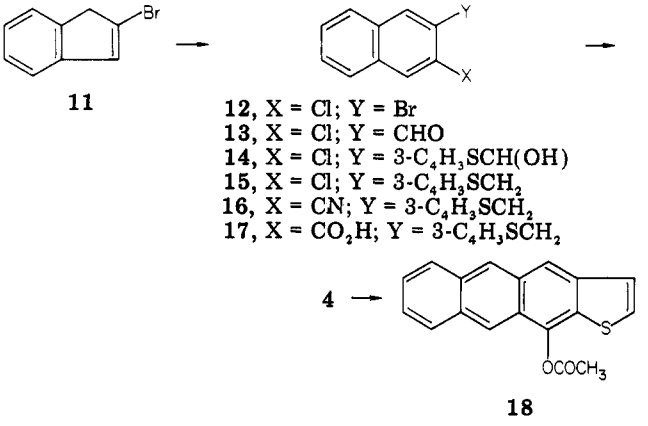
1. Synthesis of 4,11-Dihydroanthra[2,3-*b*]thiophen-4-one (3). The synthetic pathway leading to **3** is depicted in Scheme I.

An aluminum chloride catalyzed Friedel–Crafts acylation of thiophene with naphthalene-2,3-dicarboxylic anhydride[7] in 1,2-dichloroethane afforded an 88% yield of 3-(2-thenoyl)-2-naphthoic acid (**8**). Reduction of **8** with zinc in ammonium hydroxide, utilizing the method of Schroeder and Weinmayr,[8] gave 3-(2-thenyl)-2-naphthoic acid (**9**) in quantitative yield. Conversion of **9** to its acid chloride with phosphorus pentachloride followed by cyclization with stannic chloride afforded an 86% yield of **3**. The ketone **3** could be converted to its enol acetate, 4-

Scheme I



Scheme II



(1) D. W. H. MacDowell and J. C. Wisowaty, *J. Org. Chem.*, **36**, 3999 (1971).
(2) (a) D. W. H. MacDowell and J. C. Wisowaty, *J. Org. Chem.*, **36**, 4004 (1971); (b) D. W. H. MacDowell and F. L. Ballas, *ibid.*, **39**, 2239 (1974).
(3) H. Baba and T. Takemura, *Bull. Chem. Soc. Jpn.*, **37**, 1241 (1964).
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(5) E. Clar and D. G. Stewart, *J. Chem. Soc.*, 4783 (1952).
(6) (a) S. Forsen and M. Nilsson in "The Chemistry of the Carbonyl Group", J. Zahicky, Ed., Interscience, New York, 1970, Vol. 2, Chapter 3; (b) H. Hart, *Chem. Rev.*, **79**, 515 (1979).
(7) M. P. Cava and J. P. VanMeter, *J. Org. Chem.*, **34**, 538 (1969).
(8) H. E. Schroeder and V. Weinmeyr, *J. Am. Chem. Soc.*, **74**, 4357 (1952).

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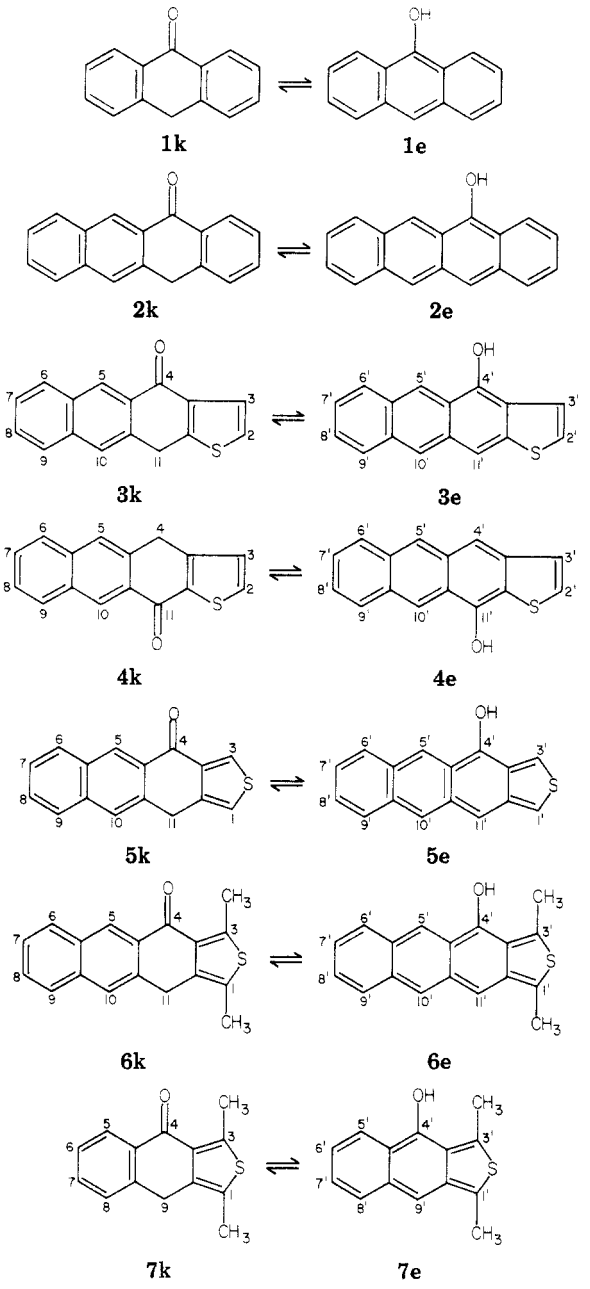
Chart I



acetoxyanthra[2,3-*b*]thiophene (**10**), by acetic anhydride and pyridine.

2. Synthesis of 4,11-Dihydroanthra[2,3-*b*]thiophen-11-one (4). Difficulties in the synthesis of **4** in a manner similar to that used to synthesize **3** necessitated a different route. Scheme II outlines the pathway followed in the synthesis of **4** and its acetate **18**.

2-Bromo-3-chloronaphthalene (**12**) was synthesized by a method which involved a phase-transfer catalysis of the reaction between 2-bromoindene (**11**) and dichlorocarbene.[9] Halogen–metal interchange between **12** and *n*-butyllithium in THF at −70 °C followed by addition of *N*,*N*-dimethylformamide gave an 80% yield of 3-chloro-2-naphthalenecarboxaldehyde (**13**). Reaction of **13** with 3-thienyllithium gave (2-chloro-3-naphthyl)-3-thienylcarbinol (**14**), which upon reduction with lithium aluminum hydride and aluminum chloride[10] gave 2-(3-thenyl)-3-chloronaphthalene (**15**). Reaction of **15** with cuprous cyanide in *N*-methylpyrrolidinone[11] gave following workup, 2-(3-thenyl)-2-naphthonitrile (**16**), which was hydrolyzed by base to give a 90% yield of 3-(3-thenyl)-2-naphthoic acid (**17**). Cyclization of **17** was effected as for **9** to provide an 86% yield of **4**.

The ketone **4** was also converted to its enol acetate, 11-acetoxyanthra[2,3-*b*]thiophene (**18**) by the action of pyridine and acetic anhydride.

3. Attempts to synthesize 4,11-dihydroanthra[2,3-*c*]thiophen-4-one (5) involved an approach which sought to prepare naphthalene-2,3-dicarbonyl chloride and interact it with 2,5-dichlorothiophene under Friedel–Crafts conditions.[2b] Under a variety of conditions tried, the necessary naphthalene-2,3-dicarbonyl chloride could not be obtained.

4. Synthesis of 1,3-Dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (7) and 1,3-Dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (6). The difficulties in the synthesis of **5** prompted the substitution of 2,5-dimethylthiophene (**20**) for 2,5-dichlorothiophene. By adopting this modification, the synthesis utilizing a diacid chloride was circumvented; **20** is more reactive than 2,5-dichlorothiophene and was found to react readily with naphthalene-2,3-dicarboxylic anhydride.

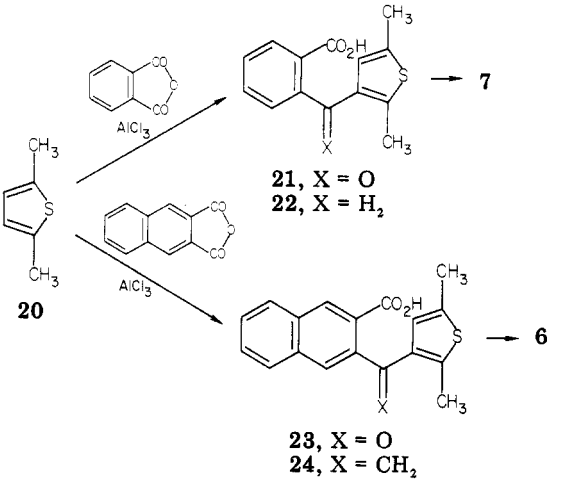
However, to make comparisons to the previously reported[1] 4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**19**), it was necessary to synthesize and examine the 1,3-dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**7**) system and verify that it was a satisfactory model for **19**.

Scheme III outlines the synthetic pathways leading to **6** and **7**.

An aluminum chloride catalyzed acylation of **20** with phthalic anhydride afforded the known[14] 2-(2,5-dimethyl-3-thenoyl)benzoic acid (**21**) in 69% yield. Reduction of **21** with zinc in ammonium hydroxide gave a quantitative yield of 2-(2,5-dimethyl-3-thenyl)benzoic acid (**22**). Cyclization of **22** by conversion to the corresponding acid chloride followed by ring closure with stannic chloride gave **7** in 74% yield.

An aluminum chloride catalyzed acylation of **20** with naphthalenedicarboxylic anhydride gave a 94% yield of 3-(2,5-dimethyl-3-thenoyl)-2-naphthoic acid (**23**). A zinc and ammonium hydroxide reduction of **23** gave 3-(2,5-

Scheme III



(9) W. E. Billups, private communication.
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(12) L. Friedman and H. Shechter, *J. Org. Chem.*, **26**, 2522 (1961).
(13) D. W. H. MacDowell and J. C. Wisowaty, *J. Org. Chem.*, **37**, 1712 (1972).
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Table I. NMR Spectral Data

compd	solvent	chemical shifts, δ
7	$CDCl_3$	8.17–8.26 (1, m, H_5), 7.22–7.49 (3, m, $H_{6,7,8}$), 3.95 (2, s, H_9), 2.85 (3, s, C_3-CH_3), 2.34 (3, s, C_1-CH_3)
	Me_2SO-d_6	8.1–8.25 (1, m, H_5), 7.4–7.8 (3, m, $H_{6,7,8}$), 4.15 (2, s, H_9), 2.85 (3, s, C_3-CH_3), 2.40 (3, s, C_1-CH_3)
6	$CDCl_3$	8.69 (1, s, H_5), 7.20–7.44 (5, m, $H_{6,7,8,9,10}$), 3.96 (2, s, H_{11}), 2.89 (3, s, C_3-CH_3), 2.29 (3, s, C_1-CH_3)
	$CDCl_3$ + Me_2SO-d_6	8.9 (1, s, H_5), 7.45–8.3 (5, m, $H_{6,7,8,9,10}$), 4.3 (2, s, H_{11}), 3.35 (3, s, C_3-CH_3, 2.85 (3, s, C_1-CH_3)
3	$CDCl_3$	8.85 (1, s, H_5), 7.25–7.85 (7, m, $H_{2,3,6,7,8,9,10}$), 4.52 (2, s, H_{11})
	$CDCl_3$ + CF_3CO_2H	8.84 (1, s, H_5), 7.30–7.93 (7, m, $H_{2,3,6,7,8,9,10}$), 4.52 (2, s, H_{11})
	Me_2SO-d_6	8.75–9.20 (2, m, 4′-OH), 7.40–8.55 (m, 9, $H_{2',3',5',6',7',8',9',10',11'}$)
4	$CDCl_3$ (t = 0)	8.82 (1, s, H_{10}), 7.07–8.01 (7, m, $H_{2,3,5,6,7,8,9}$), 4.48 (2, s, H_4)
	Me_2SO-d_6	10.7 (1, m, 11′-OH), 9.2 (1, s, $H_{10'}$), 8.8 (1, s, $H_{4'}$), 7.4–8.5 (7, m, $H_{2',3',5',6',7',8',9'}$)
	$CDCl_3$ (t = 96 h)	8.5–8.7 (m) and 8.85 (s), total 0.75, (H_{10}, $H_{10'}$, $H_{4'}$), 7.2–8.2 (5.3, m, aromatic), 4.35 (1, s, H_4)
	$CDCl_3$ + CF_3CO_2H	9.05 (s) and 8.6–8.9 (m), total 0.82 (H_{10}, $H_{10'}$, $H_{4'}$), 7.3–8.2 (m, 5.27, aromatic), 4.45 (s, 1, H_4)

dimethyl-3-thenoyl)-2-naphthoic acid (**24**) in 98% yield. Cyclization of **24** was effected by conversion to the corresponding acid chloride followed by ring closure with stannic chloride and gave a 77% yield of 1,3-dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (**6**).

Spectral Results. In the case of the *c*-fused naphthothiophene compound **7** and the analogous anthrathiophene **6**, only keto forms were evident in the NMR spectra whether in $CDCl_3$ or Me_2SO-d_6. No indication of any enolic material was found in the infrared spectrum.

For the *b*-fused derivatives **3** and **4**, the NMR spectrum of **3** indicated only keto form **3k** in $CDCl_3$ or $CDCl_3$–CF_3CO_2H. The NMR spectrum in Me_2SO-d_6, however, reduced the keto content below detectable limits. Compound **4** exhibited different behavior. A freshly prepared solution of **4** in $CDCl_3$ showed only the presence of the keto form **4k**. However, after the solution was allowed to stand at room temperature, the amount of keto compound dropped to 67%. In $CDCl_3$–CF_3CO_2H the equilibrated solution contained 61% keto form. In Me_2SO-d_6 solution no evidence of **4k** was obtained.

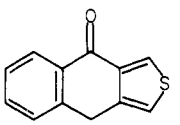
The NMR spectral data is given in Table I.

Discussion

Some significant observations result from these studies. The *c*-fused anthrathiophene system, 1,3-dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (**6**), was identical with 4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**19**) and 1,3-dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**7**) in that the keto form was the only form detected by NMR and IR spectroscopy.

On the other hand, 4,11-dihydroanthra[2,3-*b*]thiophen-4-one (**3**) differed from the smaller system 4,9-dihydronaphtho[2,3-*b*]thiophen-4-one (**27**).[1] Whereas **27** existed as a mixture of keto and enol forms, **3** was present solely as the keto form.

Since **3** was stable in the keto form and did not parallel the smaller system **27**, it is unclear why 4,11-dihydroanthra[2,3-*b*]thiophen-11-one (**4**) did parallel the smaller system 4,9-dihydronaphtho[2,3-*b*]thiophen-9-one (**26**)[1] in that both tautomers are present as keto–enol mixtures.



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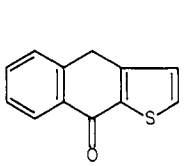

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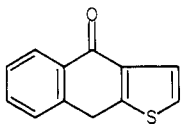

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The mode of fusion of the thiophene ring, *b* or *c* fusion, has an important influence on the extent of keto–enol tautomerism observed in these compounds. Whereas *b* fusion of the thiophene ring provides opportunity for enolization which would incorporate a naphtho[*b*]thiophene system or an anthra[*b*]thiophene system, enolization in the *c*-fused systems is unfavorable due to the necessary formation of the known unstable naphtho[*c*]thiophene[15] and the as yet unreported anthra[*c*]thiophene systems.

Experimental Section[16]

1. Synthesis of 4,11-Dihydroanthra[2,3-*b*]thiophen-4-one (3). 3-(2-Thenoyl)-2-naphthoic Acid (8). To a solution of 4.05 g (30.4 mmol) aluminum chloride in 1,2-dichloroethane (15 mL) was added a suspension of 2.70 g (13.6 mmol) of naphthalene-2,3-dicarboxylic anhydride[7] in 30 mL of 1,2-dichloroethane. The resulting yellow suspension was stirred for 30 min and then a solution of 1.15 g (13.7 mmol) of thiophene in 1,2-dichloroethane was added dropwise with stirring over a 1-h period such that the temperature of the reaction remained below 30 °C. The reaction mixture was then allowed to stir for 2 h at ambient temperature and then poured into a solution of 100 mL of water and 50 mL of 12 M HCl. The layers were separated, and the combined organic layer was extracted with 2 M NaOH solution. The basic extracts were treated with decolorizing carbon, filtered, and acidified to afford 3.38 g (88%) of a white solid, mp 215–216 °C. Four recrystallizations from aqueous ethanol provided an analytical sample: mp 215–216 °C; IR (Nujol) 1645 (ketone C=O), 1690 cm^{-1} (acid C=O); NMR (acetone-d_6) δ 8.6 (s, 1 H, naphthalene C_4-H), 6.9–8.1 (m, 8 H, remaining aromatic CH). Anal. Calcd for $C_{16}H_{10}O_3S$: C, 68.07; H, 3.57; S, 11.35. Found: C, 68.33; H, 3.66; S, 11.42.

3-(2-Thenyl)-2-naphthoic Acid (9). To a solution of 6.45 g (23.0 mmol) of 3-(2-thenoyl)-2-naphthoic acid in 500 mL of concentrated NH_4OH were added 14.58 g (0.223 mol) of zinc dust and 0.2 g of cupric sulfate. The reaction mixture was heated at reflux for 24.5 h with addition of 100-mL portions of concentrated NH_4OH every 4 h. At the end of the reflux period the reaction mixture was filtered while hot and the warm filtrate was acidified with HCl. The resulting solid was recrystallized from aqueous

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(16) All temperatures are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Nuclear magnetic resonance spectra were recorded on a Varian EM 360 (60 MHz) with tetramethylsilane as an internal standard. Infrared spectra were recorded on a Beckman IR-8 or a Perkin-Elmer 567 spectrophotometer. The ultraviolet spectra were recorded on a Bausch and Lomb 2000 spectrophotometer. Mass spectra were measured on a Nuclide 12-90-G single-focusing mass spectrometer or a Finnegan 4021 quadrupole mass spectrometer.

ethanol and afforded 6.1 g (99%) of 3-(2-thenyl)-2-naphthoic acid as white needles, mp 192–193 °C. An analytical sample was prepared by recrystallization from benzene/hexane: mp 193 °C; IR (Nujol) 1690 cm^{-1} (acid C=O); NMR (80 MHz, acetone-d_6) δ 8.56 (s, 1 H, naphthalene C_1-H), 6.81–8.04 (m, 8 H), remaining aromatic CH), 4.75 (s, 2 H, CH_2). Anal. Calcd for $C_{16}H_{20}O_2S$: C, 71.62; H, 4.51; S, 11.95. Found: C, 71.82; H, 4.77; S, 11.65.

4,11-Dihydroanthra[2,3-*b*]thiophen-4-one (3). To a suspension of 0.5 g (1.86 mmol) of 3-(2-thenyl)-2-naphthoic acid in 25 mL of benzene under nitrogen at 5 °C was added 0.39 g (1.86 mmol) phosphorus pentachloride over a 5-min period. The suspension was allowed to warm to room temperature slowly and was then warmed slowly to reflux, heated at reflux for 10 min, and then cooled to 5 °C. A solution of 1.04 g (3.99 mmol) of stannic chloride in 10 mL of dry benzene was added dropwise over a 30-min period and the reaction mixture was allowed to warm to room temperature and to stir for 3 h. It was then poured into ice and HCl and extracted with benzene. The combined organic layer was treated with $NaHCO_3$ and dried (Na_2SO_4). Evaporation left a dark solid which was dissolved in a small amount of chloroform and chromatographed on neutral silica gel. Elution with 1:1 chloroform–benzene gave 0.4 g (86%) of 4,11-dihydroanthra[2,3-*b*]thiophen-4-one as a yellow solid (mp 165 °C). Two crystallizations from benzene/hexane afforded an analytical sample: mp 166–168 °C dec; IR (KBr) 1650 cm^{-1} (ketone), no OH band; NMR (80 MHz, $CDCl_3$) δ 8.85 (s, 1 H, C_5-H), 7.18–8.07 (m, 7 H, remaining aromatic CH), 4.52 (s, 2 H, CH_2); mass spectrum (70 eV), *m/e* calcd 250, found 250; UV max (95% C_2H_5OH) 254 nm (log ϵ 5.88). Anal. Calcd for $C_{16}H_{10}OS$: C, 76.77; H, 4.03; S, 12.81. Found: C, 76.72; H, 4.10; S, 12.95.

4-Acetoxyanthra[2,3-*b*]thiophene (10). A mixture of 0.1 g (0.4 mmol) of 4,11-dihydroanthra[2,3-*b*]thiophen-4-one (3) in 20 mL of acetic anhydride and 4 mL of pyridine was warmed on a steam bath to effect solution. The bright yellow solution was allowed to stand at ambient temperature for 30 min and then heated on a steam bath for 10 min. The warm solution was poured onto 50 g of ice and the yellow solid which separated was filtered and recrystallized from cyclohexane to give 0.09 g (77%) of a bright yellow solid, mp 192–198 °C. A second recrystallization from cyclohexane afforded an analytical sample, mp 193–194 °C dec; IR (Nujol) 1760 cm^{-1} (acetate C=O); NMR (acetone-d_6) δ 7.2–8.6 (m, 9 H, aromatic), 2.6 (s, 3 H, acetate CH_3); UV max (95% C_2H_5OH) 270 nm (log ϵ 4.98), 272 (4.98). Anal. Calcd for $C_{18}H_{12}O_2S$: C, 73.95; H, 4.14; S, 10.97. Found: C, 73.81; H, 4.38; S, 10.77.

2-Bromoindene (11). A solution of 30.0 g (0.258 mol) of freshly distilled indene in 300 mL of Me_2SO and 10 mL of H_2O was cooled in an ice bath and then 91.7 g (0.258 mmol) of *N*-bromosuccinimide was added in one portion. After a short induction period the solution became light orange and the cooling bath was removed. The solution was stirred for 15 min and then poured into 600 mL of saturated $NaHCO_3$ solution. The resulting solid was filtered and recrystallized from chloroform/hexane to give 43.0 g (78%) of indene bromohydrin, mp 126–128 °C (lit.[17] mp 128–129 °C).

A solution of 20.0 g (0.094 mol) of indene bromohydrin in 250 mL of toluene was heated at reflux (Dean–Stark trap) to remove any H_2O. To the solution was added 1 mL of H_2SO_4 (18 M) and heating was continued for 1 h. Most of the toluene was then removed in vacuo and 100 mL of ether added. The organic layer was washed with H_2O and $NaHCO_3$ and dried ($MgSO_4$). Evaporation of the solvent left an oil which upon distillation afforded 11.9 g (65%) of 2-bromoindene, bp 135 °C (18 mm) [lit.[18] bp 123–124 °C (23 mm)].

Dehydration with *p*-toluenesulfonic acid in benzene gave a 66% yield of 2-bromoindene.

2-Bromo-3-chloronaphthalene (12). In a procedure modeled after that of Billups,[9] to a solution of 20.87 g (0.107 mol) of 2-bromoindene in 115 mL of dry (distilled from P_4O_{10}) chloroform was added 0.4 g (1.1 mmol) of hexadecyltrimethylammonium bromide. To this solution was added with stirring a solution of 69.6 g (1.74 mol) of sodium hydroxide in 125 mL of H_2O over a 30-min period. The resulting dark reaction mixture was stirred for 2 h at room temperature. After the solution was heated at reflux for 2 h, 50 mL of chloroform was added and reflux was continued for an additional 6 h. At the end of the reflux period the solution was filtered to remove a black solid. The filter cake was washed with benzene and then with ether. The filtrate was separated and the organic portion washed several times with H_2O and then with saturated NaCl solution and dried ($MgSO_4$). Evaporation gave a brown solid which was sublimed at 80 °C (0.005 mm) to give 9.79 g (38%) of a white solid. Recrystallization of the solid from ethanol afforded 2-bromo-3-chloronaphthalene as a white solid, mp 128–129.5 °C (lit.[19] mp 115 °C). Anal. Calcd for $C_{10}H_6BrCl$: C, 49.73; H, 2.50. Found: C, 50.04; H, 2.60.

3-Chloro-2-naphthalenecarboxaldehyde (13). A solution of 10.0 g (41.4 mmol) of 2-bromo-3-chloronaphthalene in 100 mL of THF (N_2) was cooled to −70 °C and 27.2 mL of 1.52 M (41.4 mmol) of *n*-butyllithium was added with stirring over a 15-min period. The resulting solution was stirred at −70 °C for 45 min and then a solution of 4.4 g (60.0 mmol) of distilled DMF in 50 mL of THF was added over a 15-min period. The solution was then stirred for 45 min at −70 °C and allowed to slowly warm to room temperature and finally to stir at the temperature for 12 h. The reaction mixture was poured on to ice and the mixture was extracted with ether, washed with HCl, H_2O, and $NaHCO_3$, and dried ($MgSO_4$). Evaporation afforded a yellow solid which was recrystallized from hexane to give 6.3 g (80%) of 3-chloro-2-naphthalenecarboxaldehyde as white needles, mp 115–118 °C. An analytical sample was prepared by two additional recrystallizations from hexane: mp 121–122 °C (lit.[20] mp 121 °C); IR (Nujol) 1690 cm^{-1} (aldehyde C=O); NMR ($CDCl_3$) δ 10.6 (s, 1 H, aldehyde CH), 8.5 (s, 1 H, C_1-H), 7.3–8.2 (m, 5 H, $C_{4,5,6,7,8}$-H). Anal. Calcd for $C_{11}H_7ClO$: C, 69.31; H, 3.70. Found: C, 69.30; H, 4.00.

(3-Chloro-2-naphthyl)-3-thienylcarbinol (14). To a stirred ethereal solution of 3-lithiothiophene[21] prepared from 3-bromothiophene (4.4 g, 27.0 mmol) at −70 °C was added dropwise a solution of 5.00 g (26.2 mmol) of 3-chloro-2-naphthalenecarboxaldehyde in 80 mL of a 1:1 mixture of THF and benzene with stirring at −70 °C. After being stirred at −70 °C for 1 h, the mixture was allowed to warm to room temperature and was then hydrolyzed with water and extracted with ether. Workup left a light yellow oil which was chromatographed on neutral silica gel (elution with benzene) to give 6.6 g (97%) of (2-chloro-3-naphthyl)-3-thienylcarbinol as an oil: IR (neat) 3400 cm^{-1} (OH); NMR ($CDCl_3$) δ 6.8–8.1 (m, 9 H, aromatic CH), 6.2 (s, 1 H >CH), 3.15 (s, 1 H, COH). The oil could not be purified via short path or other distillation means due to decomposition, so no analytical sample was prepared.

2-(3-Thenyl)-3-chloronaphthalene (15). To a suspension of 1.74 g (45.7 mmol) of lithium aluminum hydride in 50 mL of ether at 5 °C was added a suspension of 6.1 g (45.7 mmol) of aluminum chloride in 50 mL of ether and a solution of 6.6 g (24.02 mmol) of (3-chloro-2-naphthyl)-3-thienylcarbinol in 100 mL of ether was added at such a rate so as to promote a gentle reflux. The solution was then heated at reflux for 20 min, allowed to cool, hydrolyzed with dilute H_2SO_4, and worked up to provide a yellow oil which was chromatographed on silica gel (elution with hexane) to give 4.6 g of 2-(3-thenyl)-3-chloronaphthalene as a light yellow oil: IR (neat) 3090 (aromatic CH), 2950 cm^{-1} (alkyl CH); NMR ($CDCl_3$) δ 6.8–8.05 (m, 9 H, aromatic CH), 4.15 (s, 2 H, CH_2). Attempts to vacuum distill the oil resulted in decomposition; therefore, no analytical sample was prepared.

3-(3-Thenyl)-2-naphthonitrile (16). To a solution of 4.6 g (17.8 mmol) of 2-thenyl-3-chloronaphthalene in 50 mL of *N*-methylpyrrolidinone was added 2.86 g (32.0 mmol) of dry cuprous cyanide). The solution was heated at reflux for 24 h, cooled, and poured into a solution of 7.31 g of ferric chloride hexahydrate, 2.4 mL of HCl (12 M), and 50 mL of H_2O, and the mixture was stirred at 60–70 °C for 30 min. Extraction with benzene followed by washing with HCl and NaOH and drying ($MgSO_4$) gave upon evaporation of the solvent a dark red oil, which was chromatographed on alumina (benzene) to give a yellow oil, which was

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hydrolyzed to the acid without further purification: IR (neat) 2220 cm^{-1} (CN); NMR (80 MHz, $CDCl_3$) δ 8.17 (s, 1 H, naphthalene C_4-H), 6.93–7.79 (m, 8 H, remaining aromatic CH), 4.30 (s, 2 H, $>CH_2$).

3-(3-Thenyl)-2-naphthoic Acid (17). A solution of 2.0 g (8.02 mmol) of 3-(3-thenyl)-2-naphthonitrile and 1.8 g (32.18 mmol) of KOH in 20 mL of diethylene glycol was heated at reflux for 22 h, cooled, diluted with H_2O, filtered through a bed of charcoal, and then acidified with HCl to provide 2.05 g (90%) of 3-(3-thenyl)-2-naphthoic acid as white needles, mp 183.5–186 °C. An analytical sample was prepared by recrystallization from aqueous ethanol, mp 189.5–190.5 °C. Subsequently benzene/hexane was found to be a better recrystallization solvent: IR (Nujol) 1680 cm^{-1} (acid C=O); NMR (acetone-d_6, 80 MHz) δ 8.52 (s, 1 H, naphthalene C_1-H), 6.93–8.01 (m, 8 H), remaining aromatic CH), 4.54 (s, 2 H, $>CH_2$). Neutralization equivalent calcd 268, found 261. Anal. Calcd for $C_{16}H_{12}O_2S$: C, 71.62; H, 4.51; S, 11.95. Found: C, 71.87; H, 4.61; S, 12.14.

4,11-Dihydroanthra[2,3-*b*]thiophen-11-one (4). A suspension of 0.500 g (1.86 mmol) of 3-(3-thenyl)-2-naphthoic acid in 35 mL of dry benzene under N_2 was cooled to 5 °C and 0.39 g (1.86 mmol) of phosphorus pentachloride was added in one portion. The reaction mixture was allowed to slowly warm to room temperature with stirring and was then heated at reflux for 3 h. The yellow solution was then cooled to 5 °C and to this was added 1.04 g (4.0 mmol) of stannic chloride in 10 mL of dry benzene over a 30-min period. Following the addition the reaction mixture was allowed to warm to room temperature with stirring for 2 h and was then poured into HCl and ice and extracted with ether and benzene. The organic layer was washed with H_2O and $NaHCO_3$ and dried (Na_2SO_4). Evaporation of the solvent left a reddish yellow solid. All manipulations with this product were carried out as rapidly as possible due to its air sensitivity (oxidation to dione). Also it was not left dissolved in any solvent for no more than bried periods of time. The product was stored as a solid under N_2 at 0 °C. Chromatography over silica gel (elution with 1:1 chloroform/benzene) gave a yellow solid which was rechromatographed to give 0.4 g (86%) of 4,11-dihydroanthra[2,3-*b*]thiophen-11-one as a light yellow solid, mp 168–170 °C. An analytical sample was prepared by rapid recrystallization from benzene/hexane: mp 166–168 °C; IR (Nujol) 1670 cm^{-1} (ketone C=O), no enol; NMR ($CDCl_3$, 80 MHz; upon mixing, keto form) δ 8.82 (s, 1 H, C_{10}-H), 7.07–8.01 (m, 7 H, $C_{2,3,5,6,7,8,9}$-H), 4.48 (s, 2 H, CH_2); UV max (95% C_2H_5OH) 263 nm (log ϵ 4.37), 317 (log ϵ 4.32). Anal. Calcd for $C_{16}H_{10}OS$: C, 76.77; H, 4.03; S, 12.81. Found: C, 76.59; H, 3.99; S, 12.83.

11-Acetoxyanthra[2,3-*b*]thiophene (18). To a suspension of 100 mg (0.40 mmol) of 4,11-dihydroanthra[2,3-*b*]thiophen-11-one in 20 mL of acetic anhydride under N_2 was added 4 mL of pyridine followed by gentle warming to dissolve the solid. After standing for 0.5 h at room temperature, the mixture was poured onto ice and the resultant yellow solid was filtered and recrystallized benzene/hexane to afford 0.1 g (85%) of 11-acetoxyanthra[2,3-*b*]thiophene. An analytical sample was prepared by two additional recrystallizations from benzene/hexane: mp 227–228 °C; IR (Nujol) 1750 cm^{-1} (acetate C=O); NMR ($CDCl_3$) δ 7.2–8.6 (m, 9 H, aromatic CH), 2.6 (s, 3 H, acetate CH_3); UV max (95% C_2H_5OH) 273 nm (log ϵ 5.41). Anal. Calcd for $C_{18}H_{12}O_2S$: C, 73.95; H, 4.14; S, 10.97. Found: C, 73.85; H, 4.17; S, 10.79.

4. Synthesis of 1,3-Dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (7). 2-(2,5-Dimethyl-3-thenyl)benzoic Acid (22). From 5.00 g (19.2 mmol) of 2-(2,5-dimethyl-3-thenoyl)benzoic acid (21) in 400 mL of 28% ammonium hydroxide, 12.2 g (0.186 mol) of zinc dust, and 0.4 g of cupric sulfate, following the procedure for 9, there was obtained after recrystallization from heptane 4.75 g (100%) of 2-(2,5-dimethyl-3-thenyl)benzoic acid as white stars, mp 139–140 °C. A second recrystallization from heptane afforded an analytical sample: mp 139–140 °C; IR (Nujol) 1740 cm^{-1} (acid C=O); NMR ($CDCl_3$, 80 MHz) δ 7.96–8.08 (m, 1 H, benzene C_6-H), 7.04–7.51 (m, 3 H, benzene $C_{3,4,5}$-H), 4.23 (s, 2 H, CH_2), 2.30 (s, 6 H, thiophene C_2- and C_5-CH_3). Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.26; H, 5.73; S, 13.02. Found: C, 68.42; H, 5.73; S, 13.26.

1,3-Dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (7). A solution of 0.50 g (2.03 mmol) 2-(2,5-dimethyl-3-thenyl)benzoic acid in 30 mL of dry benzene at 4 °C was treated with 0.423 g (2.03 mmol) of phosphorus pentachloride. The yellow mixture was then slowly heated until HCl was no longer evolved and was then cooled to 4 °C and 1.07 g (4.1 mmol) of stannic chloride in 20 mL of dry benzene was added dropwise. The mixture was stirred for 1 h at 4 °C and then allowed to warm slowly to room temperature over 3 h and was then poured into ice and HCl and extracted with ether. Evaporation of the washed and dried organic extract gave a yellow solid which was chromatographed on neutral silica gel and recrystallized from hexane to give 0.34 g (74%) of 1,3-dimethyl-4,9-dihydronaphtho[2,3-*c*]thiophen-4-one, mp 123–124 °C. Two recrystallizations from hexane afforded an analytical sample: mp 124–125 °C; IR (Nujol) 1650 cm^{-1} (ketone C=O), no enol present; NMR ($CDCl_3$, 80 MHz) δ 8.17–8.26 (m, 1 H, C_5-H), 6.22–7.49 (m, 3 H, $C_{6,7,8}$-H), 4.02 (s, 2 H, CH_2), 2.85 (s, 3 H, C_3-CH_3), 2.34 (s, 3 H, C_1-CH_3): UV max (95% C_2H_5OH) 248 nm (log ϵ 5.52). Anal. Calcd for $C_{14}H_{12}OS$: C, 73.65; H, 5.30; S, 14.04. Found: C, 73.54; H, 5.44; S, 14.19.

5. Synthesis of 1,3-Dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (6k). 3-(2,5-Dimethyl-3-thenoyl)-2-naphthoic Acid (23). From naphthalene-2,3-dicarboxylic anhydride (5.00 g, 25.2 mmol) and 2,5-dimethylthiophene (20) there was obtained by the same procedure as for 8 a 94% yield of 3-(2,5-dimethyl-3-thenoyl)-2-naphthoic acid as white needles (2-propanol–water), mp 205–208 °C. Analytical sample, same solvent pair: mp 208–209 °C; IR (Nujol) 1670 cm^{-1} (acid C=O); NMR (Me_2SO-d_6) δ 8.65 (s, 1 H, naphthalene C_4-H), 7.5–8.3 (m, 5 H, naphthalene $C_{1,5,6,7,8}$-H), 6.65 (s, 1 H, thiophene C_4-H), 2.5 (s, 3 H, thiophene C_2-CH_3), 2.3 (s, 3 H, thiophene C_5-CH_3). Anal. Calcd for $C_{18}H_{14}O_3S$: C, 69.66; H, 4.55; S, 10.33. Found: C, 69.62; H, 4.67; S, 10.10.

3-(2,5-Dimethyl-3-thenyl)-2-naphthoic Acid (24). From 5.00 g (16.1 mmol) of 3-(2,5-dimethyl-3-thenoyl)-2-naphthoic acid, using zinc and ammonium hydroxide as for 22, there was obtained a white solid which was recrystallized from aqueous ethanol to give 4.64 g (98%) of 3-(2,5-dimethyl-3-thenyl)-2-naphthoic acid as white needles, mp 192–195 °C. Analytical sample (same solvent): mp 193–195 °C; IR (Nujol) 1690 cm^{-1} (acid C=O); NMR (acetone-d_6, 80 MHz) δ 8.5 (s, 1 H, naphthalene C_1-H), 7.45–8.02 (m, 5 H, naphthalene $C_{1,5,6,7,8}$-H), 6.29 (s, 1 H, thiophene C_4-H), 2.31 (s, 3 H, thiophene C_2-CH_3), 2.27 (s, 3 H, thiophene C_5-CH_3). Anal. Calcd for $C_{18}H_{16}O_2S$: C, 72.94; H, 5.44; S, 10.82. Found: C, 73.03; H, 5.48; S, 10.93.

1,3-Dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one (6). From 0.500 g (1.69 mmol) of 3-(2,5-dimethyl-3-thenyl)-2-naphthoic acid there was obtained, using the procedure for the cyclization of 22 to give 7, a yellow solid which was recrystallized from benzene/hexane to give 0.36 g (77%) of 1,3-dimethyl-4,11-dihydroanthra[2,3-*c*]thiophen-4-one as nearly colorless cubes, mp 173–176 °C. An analytical sample was prepared by several recrystallizations from benzene/hexane: mp 175.5–177 °C; IR (Nujol) 1655 cm^{-1} (ketone C=O), no enol present; NMR ($CDCl_3$, 80 MHz) δ 8.60 (s, 1 H, C_5-H), 7.20–7.94 (m, 5 H, $C_{6,7,8,9,10}$-H), 3.96 (s, 2 H, CH_2), 2.84 (s, 3 H, C_3-CH_3), 2.29 (s, 3 H, C_1-CH_3); UV max (95% C_2H_5OH) 255 nm (log ϵ 4.99). Anal. Calcd for $C_{18}H_{14}OS$: C, 77.67; H, 5.07; S, 11.52. Found: C, 77.59; H, 5.10; S, 11.71.

Registry No. 3e, 80228-29-1; **3k**, 80228-30-4; **4e**, 80228-31-5; **4k**, 80228-32-6; **6**, 80228-33-7; **7**, 80228-34-8; **8**, 80090-33-1; **9**, 80090-34-2; **10**, 80228-35-9; **11**, 10485-09-3; **12**, 71436-67-4; **13**, 80228-36-0; **14**, 80228-37-1; **15**, 80228-38-2; **16**, 80228-39-3; **17**, 80228-40-6; **18**, 80228-41-7; **20**, 638-02-8; **21**, 80228-42-8; **22**, 80228-43-9; **23**, 80228-44-0; **24**, 80228-45-1; naphthalene-2,3-dicarboxylic anhydride, 716-39-2; thiophene, 110-02-1; 3-bromothiophene, 872-31-1; indene bromohydrin, 5400-80-6.