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Keto–Enol Tautomerism in the Thiophene Analogs of Anthrone. I. Derivatives of Naphtho[2,3-*b*]thiophene and Naphtho[2,3-*c*]thiophene

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The syntheses of 4,9-dihydronaphtho[2,3-*b*]thiophen-4-one (**2**), 4,9-dihydronaphtho[2,3-*b*]thiophen-9-one (**3**), and 4,9-dihydronaphtho[2,3-*c*]thiophen-4-one (**4**) are described. Keto–enol tautomerism in these compounds was studied by means of nmr spectroscopy and the results are compared with the calculated delocalization energy differences between the two tautomeric forms. Enol content in **2**–**4** was found to be dependent on the mode of fusion of the thiophene nucleus.

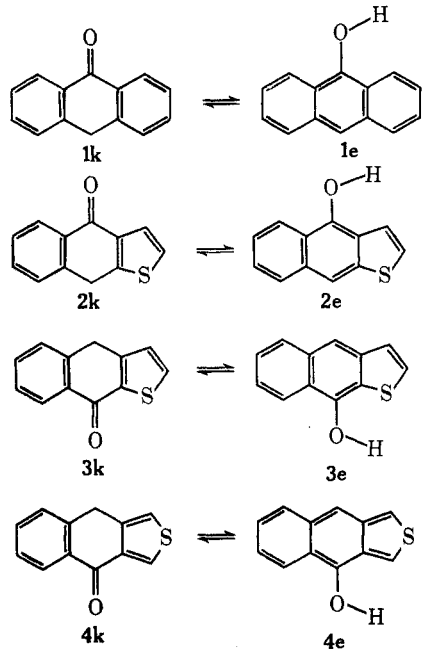
A comparison of the properties of polycyclic hydrocarbons with those of their thiophene analogs has provided some intriguing results. Anthracene and naphtho[2,3-*b*]thiophene proved to be very similar in physical and chemical properties;[2] however, the isomeric naphtho[2,3-*c*]thiophene has recently been shown to be a highly reactive species, whose transient existence could only be demonstrated in the form of two *N*-phenylmaleimide adducts.[3]

Keto–enol tautomerism has also been shown to be dependent on structure.[4] In the acene series, phenol and 1-naphthol have been isolated only in the enol form although the latter undergoes reactions which suggest the presence of both tautomers.[5] Even though both anthrone (**1k**) and anthrol (**1e**) have been isolated, the spectroscopically determined equilibrium constant ($K = 2.5 \times 10^{-3}$ at 20°) indicates that the keto form greatly predominates in benzene solution.[6] No evidence for enolization, in the absence of strong base, has been reported for the higher acene analogs.

There are three possible isomeric naphthothiophenones, **2**–**4**, analogous to anthrone.

In this paper we wish to report the preparation of these structurally related compounds and their corresponding keto–enol character.

Synthesis of 4,9-Dihydronaphtho[2,3-*b*]thiophen-4-one (2).—The synthesis of **2** was accomplished as outlined in Scheme I.



o-(2-Thenoyl)benzoic acid was prepared according to the procedure of Rajsner and coworkers[7] and converted to the known *o*-(2-thenyl)benzoic acid using zinc dust and aqueous ammonia as described by Schroeder and Weinmayr.[8] The overall yield was 80%. Cyclization of **6** *via* the acid chloride using stannic chloride afforded a mixture of the tautomers **2k** and **2e** in 75% yield after purification.

Synthesis of 4,9-Dihydronaphtho[2,3-*b*]thiophen-9-one (3).—The synthesis of **3** is outlined in Scheme II.

(1) NDEA Fellow, 1967–1970.

(2) (a) W. Carruthers, A. G. Douglas, and J. Hill, *J. Chem. Soc.*, 704 (1962); (b) W. Carruthers, *ibid.*, 4477 (1963).

(3) D. W. H. MacDowell, A. T. Jeffries, and M. B. Meyers, *J. Org. Chem.*, **36**, 1416 (1971).

(4) For a recent review on the subject of enolization, see S. Forsen and M. Nilsson in "The Chemistry of the Carbonyl Group," Vol. II, J. Zabicky, Ed., Intrscience, New York, N. Y., 1970, Chapter 3.

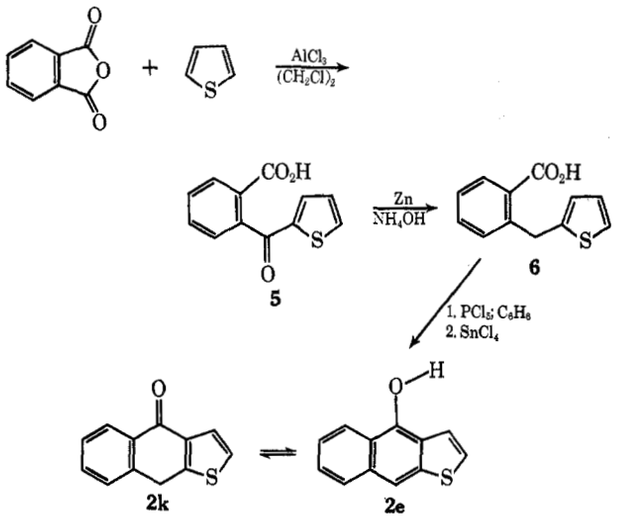
(5) Z. Majerski and N. Trinajstic, *Bull. Chem. Soc. Jap.*, **43**, 2648 (1970), and references contained therein.

(6) H. Baba and T. Takemura, *ibid.*, **37**, 1241 (1964).

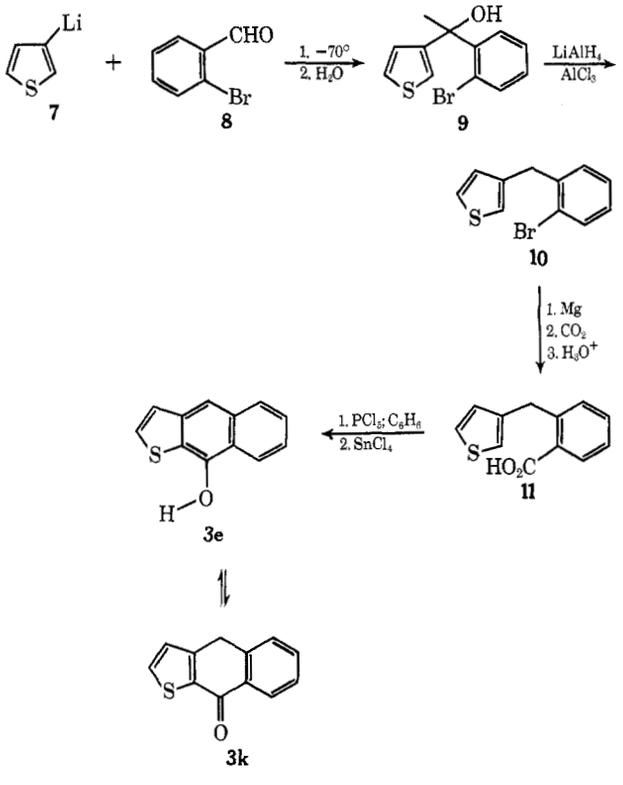
(7) M. Rajsner, J. Metysova, and M. Protiva, *Collect. Czech. Chem. Commun.*, **34**, 468 (1969).

(8) H. E. Schroeder and V. Weinmayr, *J. Amer. Chem. Soc.*, **74**, 4357 (1952).

Scheme I



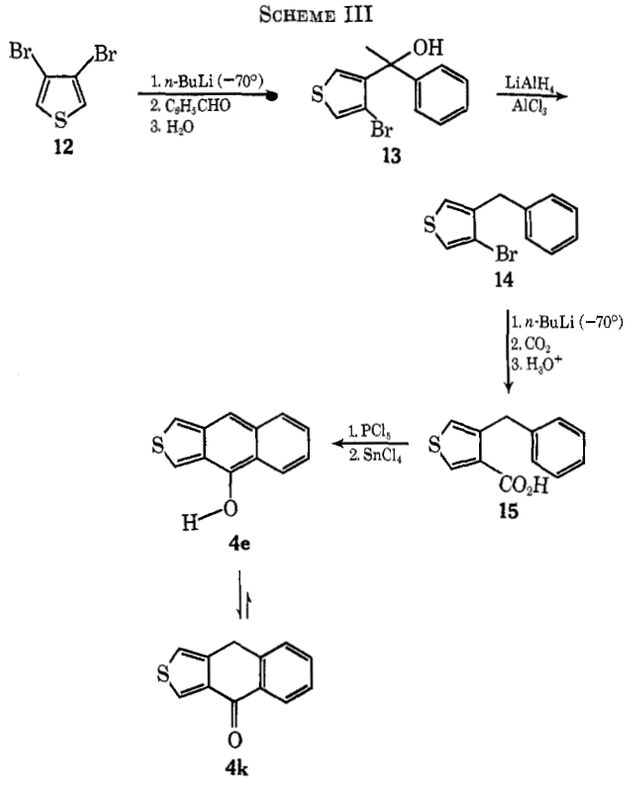
Scheme II



Treatment of 3-thienyllithium (**7**)[9] with *o*-bromobenzaldehyde (**8**) at −70° afforded *o*-bromophenyl-3-thienylcarbinol (**9**) in 61% yield. The reduction of **9** with equimolar amounts of lithium aluminum hydride and aluminum chloride in dry ether[10] provided *o*-bromophenyl-3-thienylmethane (**10**) in 82% yield. *o*-(3-Thenyl)benzoic acid (**11**) was obtained in 62% yield by carbonation of the Grignard reagent formed from **10**. Cyclization of **11** *via* the acid chloride using stannic chloride resulted in the formation of a mixture of the tautomers **3k** and **3e**. The ring closure proceeded in 78% yield.

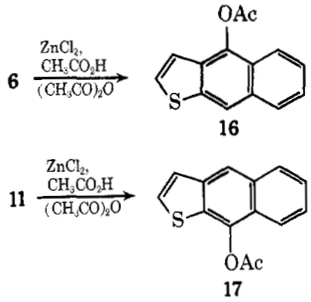
Synthesis of 4,9-Dihydronaphtho[2,3-*c*]thiophen-4-one (4).—The preparation of **4** is summarized in Scheme III.

Scheme III



4-Bromo-3-thienyllithium was allowed to react with benzaldehyde at −70° and the crude viscous product was promptly converted to 4-benzyl-3-bromothiophene (**14**) using an equimolar mixture of lithium aluminum hydride and aluminum chloride in dry ether. The overall yield was 73%. Halogen–metal exchange in **14** at −70°, followed by carbonation, afforded an 85% yield of 4-benzylthiophene-3-carboxylic acid (**15**), which was cyclized to **4k** *via* the acid chloride using stannic chloride in 82% yield.

The carboxylic acid, **6** and **11**, were also cyclized to the enol acetates **16** and **17** according to the method of Fieser and Hershberg.[11]

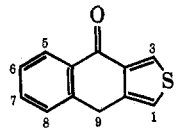


Spectral Data.—The nmr spectrum of **4k** was obobtained in both C_6D_6 and polysol-*d*[12] (see Table I).

The presence of the keto form (**4k**) in both solvents was confirmed by the appearance of a sharp singlet (2 H) in the methylene region. Neither spectrum contains a signal which can be assigned to an enol or meso proton in **4e**. The large chemical shift differences, which

(9) S. Gronowitz, *Ark. Kemi*, **7**, 361 (1954).
(10) J. Blackwell and W. J. Hickinbottom, *J. Chem. Soc.*, 1405 (1961).
(11) L. Fieser and E. B. Hershberg, *J. Amer. Chem. Soc.*, **59**, 1028 (1937).
(12) Available from Stohler Isotope Chemicals, Rutherford, N. J.; found to have solvent properties approximating those of dimethyl sulfoxide.

TABLE I



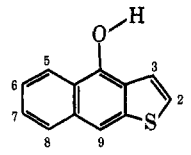
Solvent	Absorption, τ	Proton
Polysol-*d*	1.55 (d, 1 H), $J_{1,3}$ = 3 Hz	3
	1.62–1.85 (m, 1 H)	5
	2.17–2.73 (m, 4 H)	1, 6, 7, 8
	5.72 (s, 2 H)	9
Benzene-d_6	1.25–1.47 (m, 1 H)	5
	1.80 (d, 1 H), $J_{1,3}$ = 3 Hz,	3
	2.67–3.23 (m, 3 H)	6, 7, 8
	3.38–3.56 (m, 1 H), $J_{1,3}$ = 3 Hz, $J_{1,9}$ = 1 Hz	1
	6.48 (s, 2 H)	9

were induced by the utilization of an aromatic solvent, simplified the interpretation of these spectra. Since *only* the C_5 hydrogen exists on the deshielding side of a plane drawn through the C_4 carbon and perpendicular to the carbon–oxygen bond,[13] a downfield shift is observed for it while the remainder of the spectrum is shifted upfield.

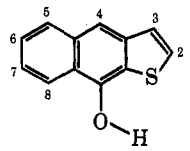
In polysol-*d* solution, both **2** and **3** give spectra which are consistent with the corresponding enol forms **2e** and **3e** (see Table II). Analogous results were obtained when acetone-d_6 was employed as the solvent. Since no absorption above τ 3.0 was observed, the existence of the keto forms **2k** and **3k** could not be verified.

TABLE II

NMR SPECTRA OF 2 AND 3 IN POLYSOL-*d*



2e



3e

Proton	τ	Proton	τ
–OH	−0.29 (s, 1 H)	OH	−0.29 (s, 1 H)
5	1.36–1.68 (m, 1 H)	8	1.40–1.71 (m, 1 H)
9	2.04 (s, 1 H)	4	2.08 (s, 1 H)
2, 8	1.94–2.26 (m, 2 H)	5	1.94–2.21 (m, 1 H)
3, 6, 7	2.32–2.68 (m, 3 H)	2, 3, 6, 7	2.27–2.69 (m, 4 H)

The nmr spectrum of **2** in C_6D_6 is composed of two complex multiplets in the aromatic region and a sharp singlet at τ 6.7 (see Table III). The singlet, due to the methylene protons in **2k**, furnishes a measure of the keto tautomer. The low field multiplet, which is assigned to the C_5 proton in both **2k** and **2e**, provides a measure of the sum of both tautomeric forms. The anisotropic effect of the ketone function results in a deshielding of the C_5 proton in **2k**. A similar deshielding by a phenolic oxygen has recently been reported[14] for the peri proton of hydroxynaphthalene systems. Analogously, the C_5 proton in **2e** appears downfield from the remainder of the aromatic absorptions.

TABLE III

NMR SPECTRA OF THE MIXTURE OF **2k** AND **2e**

Solvent	τ	Relative area[a] under absorption
C_6D_6	1.46–1.78 (m)	1.22
	2.26–3.55 (m)	6.77[b]
	6.73 (s)	1
C_6D_6	1.53–1.94 (m)	1
and	2.27–3.38 (m)	5.25[b]
CF_3CO_2H	6.75 (s)	1.71

[a] The values are an average of three experiments, none of which vary from the mean by more thn 3%. [b] Corrected for the residual signal from C_6D_6.

In order to ensure the establishment of an equilibrium condition, a drop of trifluoroacetic acid was added to the original solution and the spectrum was again recorded. The initial mixture was found to contain 40% ketone (**2k**) and 60% enol (**2e**). After equilibration, 85% of **2k** and 15% of **2e** were present in the solution. This proportion remained unchanged over the subsequent 48 hr. The appearance of two distinct doublets, τ 2.45 and 3.40 (J = 5 Hz), was an immediate indication that equilibration had taken place. These signals are assigned to the C_2 and C_3 protons of **2k**.

The presence of strong absorptions at 3400 and 1635 cm^{-1} in the ir spectrum of **2** confirms the presence of both the enol and ketone forms. The preference for the enol tautomer in polar solvents was verified by the striking similarities in the uv spectra (95% ethanol) of **2** and its enol acetate **16**.

The nmr spectrum of **3** in C_6D_6 (Table IV) shows a mixture of the keto and enol tautomers **3k** and **3e**. In this case a determination of the relative quantities is simplified by the fact that the signals due to the C_8 protons of the keto and enol forms are not superimposed upon each other. By a comparison of the peak areas, the original mixture was found to contain 50% of each tautomeric form. Equilibration was accomplished as before and the spectrum was recorded; 73% ketone and 27% enol are present in the equilibrium mixture. The ir and uv spectra of **3** substantiate the nmr data in the same manner as for the preceeding isomers.

TABLE IV

NMR SPECTRA OF THE MIXTURE OF **3k** AND **3e**

Solvent	τ	Relative area[a] under absorption
C_6D_6	1.34–1.58 (m)	1.00
	1.67–2.00 (m)	1.00
	2.10–3.35 (m)	10.05[b]
	3.67 (d), J = 5 Hz	1.00
	6.74 (s)	1.96
C_6D_6	1.53–1.83 (m)	2.75
and	1.87–2.04 (m)	1.00
CF_3CO_2H	2.21–3.42 (m)	16.67[b]
	3.67 (d), J = 5 Hz	2.67
	6.77 (s)	5.50

[a] The values are an average of three experiments, none of which vary from the mean by more than 3%. [b] Corrected for the residual signal from C_6D_6.

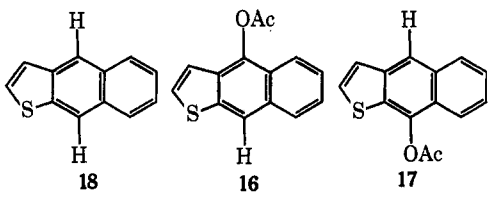
The enol acetates **16** and **17** were synthesized in order to compare their spectral properties with the

(13) E. D. Becker, "High Resolution NMR," Academic Press, New York, N. Y., 1969, p 230.

(14) G. Dudek, *Spectrochim. Acta*, **19**, 691 (1963).

corresponding enols **2e** and **3e**. Wynberg, *et al.*,[15] reported the nmr spectrum of naphtho[2,3-*b*]thiophene (**18**) and from a consideration of its 4-acetoxy derivative **16** concluded that the C_4 proton in **18** is more deshielded than the C_9 proton. As shown on Table V,

TABLE V



Solvent	18 τ	16 τ	17 τ
Acetone-d_6	1.50, 1.56	1.65	1.73
CCl_4	1.68, 1.75	1.87	1.96

this conclusion appears to be erroneous, since the C_9 proton of **16** occurs at lower field than the C_4 proton of **17**.

Discussion

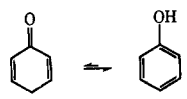
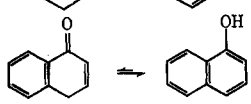
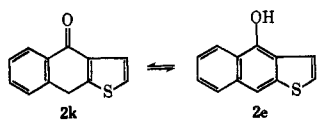
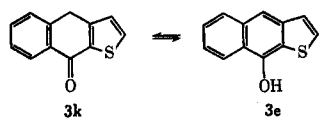
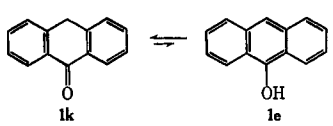
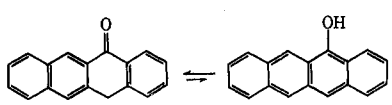
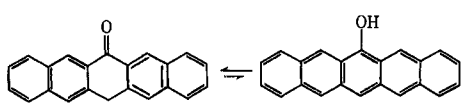
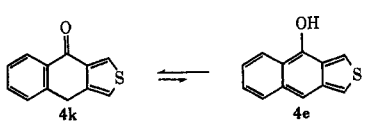
The keto–enol equilibrium position in hydroxyacene systems has been correlated with the free-energy loss which is experienced in the formation of the keto tautomer. For a series of structurally related compounds, this energy can be formulated as the π delocalization energy difference (ΔDE) between the two forms. The DE of the enol tautomer is taken as that of the parent system and the DE of the keto form as that of the corresponding *exo*-methylene derivative.[16] The values for ΔDE, which are given on Table VI, were computed using a general Hückel molecular orbital program.[17]

Compounds **2k,e** and **3k,e** possess calculated ΔDE values which are higher than the value for anthrone–anthrol (**1k,e**). This indicates an increased preference for the enol tautomer in the two systems which contain a *b*-fused thiophene ring. This prediction was supported experimentally by the observation that only **2e** and **3e** were present in hydrogen bonding solvents. Although both forms were detected in a benzene solution, the keto tautomer was found to predominate.

In contrast to the findings for the *b*-fused isomers **2** and **3**, compound **4**, which contains a *c*-fused thiophene ring, shows little tendency to enolize. Although **4k** was unaffected by 1 *M* sodium hydroxide, a deep red-orange solution was formed with ethanolic potassium hydroxide. The resulting solution soon exhibited the presence of a brown precipitate. The lack of enol character in **4** is reflected in a ΔDE value approximating that of 6-hydroxypentacene.

Since the keto forms **2k** and **4k** would be of equal energy according to this method of approximation, the difference in their ΔDE values is due to a difference in the calculated DE values for naphtho[2,3-*b*]thiophene and naphtho[2,3-*c*]thiophene.

TABLE VI

Compd	ΔDE (β units)	Preferred tautomer
	1.10	Enol
	0.83	Enol
 2k 2e	0.66[a]	Mixture
 3k 3e	0.62[a]	Mixture
 1k 1e	0.50	Keto
	0.43	Keto
	0.38	Keto
 4k 4e	0.37[a]	Keto

[a] The parameters for these calculations are $\alpha_s = \alpha + \beta$; $\beta_{cs} = 0.7\beta$.

Experimental Section[18]

Cyclization of *o*-(2-Thenyl)benzoic Acid (6).—A solution of *o*-(2-thenyl)benzoic acid (6.54 g, 30 mmol) in dry benzene (200 ml) was placed in a 500-ml, three-necked flask which was fitted with a reflux condenser and kept under a constant stream of nitrogen. After the solution was cooled to 4°, phosphorus pentachloride (6.24 g, 30 mmol) was added portionwise over 20 min with stirring. The mixture was then warmed until the evolution of hydrogen chloride ceased. The faintly yellow solution was then cooled to 4° and a solution of stannic chloride (4.0 ml, 8.9 g, 34 mmol) in dry benzene (50 ml) was added dropwise over a 1-hr period resulting in the formation of a yellow-green precipitate. Stirring was continued for an additional hour and the mixture was poured into ice and hydrochloric acid (200 ml, 2 *M*) and shaken vigorously. The layers were separated and the aqueous portion was extracted with benzene (100 ml). The combined benzene portions were washed successively with saturated sodium bicarbonate solution and water, then dried ($MgSO_4$), and concentrated to 50 ml. The resulting warm solution was chromatographed on a 15 × 2 cm column packed with neutral silica gel. Elution with benzene–chloroform (3:1) followed by concentration yielded 4.5 g (75%) of a yellow crystalline solid. Recrystallization from benzene–hexane afforded analytical sample (mp 130–132°): uv max (95% C_2H_5OH) 258 mμ (ε 49,800), 340 (6300), 352 (7400), and 367 (7310); ir (KBr) 3400 (OH) and 1635 cm^{-1} (ketone C=O); for nmr spectra (polysol-*d*) see Table II, (C_6D_6) see Table III.

(15) H. Wynberg, J. de Wit, and H. Sinnige, *J. Org. Chem.*, **35**, 711 (1970).

(16) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, p 250.

(17) HMO program written by Dr. J. Gruninger, West Virginia University.

(18) All temperatures are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nuclear magnetic resonance spectra were recorded on a Varian HA-60 spectrometer using tetramethylsilane as an internal standard (τ 10) and solvents as specified. The ultraviolet spectra were determined in 95% ethanol on a Bausch and Lomb spectronic 505 spectrophotometer. Infrared spectra were recorded on a Beckman IR-8 spectrophotometer.

Anal. Calcd for $C_{12}H_8OS$: C, 71.97; H, 4.02; S, 16.01. Found: C, 72.08; H, 4.11; S, 15.88.

o-Bromophenyl-3-thienylcarbinol (9).—Ethereal *n*-butyllithium (125 ml, 1.1 *M*, 0.138 mol) was transferred into a 500-ml, flame-dried, three-necked flask and kept under a constant stream of nitrogen. After cooling to −70°, a solution of 3-bromothiophene (25 g, 0.138 mol) in absolute ether (50 ml) was added over 15 min. The solution was stirred at −70° for an additional 30 min and a solution of *o*-bromobenzaldehyde (25.6 g, 0.138 mol) in absolute ether (50 ml) was added over a 1-hr period.

After the solution was stirred for an additional hour, it was allowed to slowly warm to 0°. Water (150 ml) was cautiously added to affect hydrolysis. The layers were separated and the aqueous layer was extracted with ether. The combined ether portions were washed neutral to litmus with copious quantities of water and dried ($MgSO_4$). Removal of the solvent left a viscous oil which crystallized on a short-path distillation. Recrystallization of the white solid from benzene–hexane gave an analytical sample of *o*-bromophenyl-3-thienylcarbinol (22.6 g, 61%): mp 58.5–60°; ir (melt) 3360 cm^{-1} (broad OH); nmr (CCl_4) τ 2.4–3.2 (m, 7 H, aromatic), 3.95 (d, J = 4 Hz, 1 H, methine), 6.90 (d, J = 4 Hz, 1 H, OH).

Anal. Calcd for $C_{11}H_9BrOS$: C, 49.08; H, 3.37; S, 11.91; Br, 29.69. Found: C, 48.91; H, 3.38; S, 11.73; Br, 29.83.

o-Bromophenyl-3-thienylmethane (10).—Lithium aluminum hydride (4.50 g, 0.118 mol) was suspended in absolute ether (50 ml) contained in a 500-ml, three-necked flask, which had previously been flame-dried under nitrogen and protected by a calcium chloride drying tube. The suspension was cooled in an ice bath while a solution of anhydrous aluminum chloride (15.6 g, 0.118 mol) in absolute ether (50 ml) was cautiously added. The ice bath was removed and a solution of *o*-bromophenyl-3-thienylcarbinol (21.0 g, 0.078 mol) in absolute ether (50 ml) was added at a rate such as to promote gentle reflux. The mixture was then refluxed for an additional 15 min and the ice bath replaced. Sulfuric acid (3 *M*) was added dropwise until vigorous refluxing subsided. The mixture was poured into ice and hydrochloric acid (200 ml, 2 *M*) and shaken. The layers were separated and the aqueous layer was extracted twice with ether (100 ml). The combined ethereal solution was successively washed with hydrochloric acid (2 *M*), saturated sodium bicarbonate solution, and water and then dried ($MgSO_4$). The liquid which remained after evaporation of the solvent was fractionally distilled giving 16.2 g (82%) of a clear colorless liquid, bp 95–97° (0.05 mm). On cooling the product crystallized as a white solid: mp 30–31°; nmr (CCl_4) τ 2.35–3.25 (m, 7 H, aromatic), 5.95 (s, 2 H, CH_2).

Anal. Calcd for $C_{11}H_9BrS$: C, 52.18; H, 3.58; Br, 31.51; S, 12.67. Found: C, 52.24; H, 3.50; Br, 31.75; S, 12.66.

o-(3-Thenyl)benzoic Acid (11).—The Grignard reagent, which was prepared from *o*-bromophenyl-3-thienylmethane (6.00 g, 24.7 mmol), magnesium metal (2.05 g, 84.5 g-atoms), 1,2-dibromoethane (8.92 g, 47.4 mmol), and ether (175 ml) according to the entrainment method,[19] was run onto excess Dry Ice and allowed to stand for 2 hr. Water (150 ml) was slowly added and the layers were separated. The organic layer was washed with 1 *M* sodium hydroxide solution (50 ml) and the aqueous portions were combined, cooled, and acidified with excess hydrochloric acid (1 *M*). The resulting precipitate was taken up in ether, washed with water, and dried ($MgSO_4$). The solvent was removed leaving a granular white solid, which was recrystallized from benzene-hexane to give white needles (3.2 g, 62%): mp 96–97°; ir (KBr) 1675 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 0.4 (hump, 1 H, CO_2H), 1.9–2.1 (m, 1 H, aromatic), 2.4–3.2 (m, 6 H, aromatic), 5.6 (s, 2 H, CH_2).

Anal. Calcd for $C_{12}H_{10}O_2S$: C, 66.03; H, 4.62; S, 14.69. Found: C, 65.99; H, 4.62; S, 14.48.

Cyclization of o-(3-Thenyl)benzoic Acid (11).—A solution of *o*-(3-thenyl)benzoic acid (2.00 g, 9.2 mmol) in dry benzene (75 ml) was run into a 300-ml, three-necked flask and kept at 4° under a constant stream of nitrogen. Phosphorus pentachloride (1.91 g, 9.2 mmol) was added portionwise with stirring over a 45-min period. The mixture was then warmed until the evolution of hydrogen chloride subsided. The resulting solution was cooled to 4° and a solution of stannic chloride (1.2 ml, 2.7 g, 10.3 mmol) in dry benzene (50 ml) was added over a 90-min period. The mixture was then stirred at room temperature for 2 hr, poured into ice and hydrochloric acid (1 *M*, 100 ml), and shaken vigorously. The layers were separated and the aqueous layer was extracted with benzene (100 ml). The benzene portions were combined, washed with saturated sodium bicarbonate solution and with water, dried ($MgSO_4$), and concentrated to 50 ml. The warm solution was chromatographed on a 15 × 2 cm column packed with neutral silica gel. Elution with benzene afforded 1.42 g (78%) of a yellow crystalline solid, mp 117–119°. An analytical sample was obtained by recrystallization from benzene–hexane: mp 120–121°; uv max (95% C_2H_5OH) 252 mμ (ϵ 52,100), 299 (5000), 338 (5070), 352 (6460), and 365 (6300); ir (KBr) 3400 (OH) and 1625 cm^{-1} (ketone C=O); for nmr spectra (polysol-*d*) see Table II, (C_6D_6) see Table III.

Anal. Calcd for $C_{12}H_8OS$: C, 71.97; H, 4.02; S, 16.01. Found: C, 72.13; H, 4.22; S, 16.22.

3-Bromo-4-thienylphenylcarbinol (13).—Ethereal *n*-BuLi (450 ml, 1.15 *M*, 0.52 mol) was run into a flame-dried, 1000-ml, three-necked flask under a constant stream of nitrogen. The solution was cooled to −70° and a solution of 3,4-dibromothiophene (125 g, 0.52 mol) in absolute ether (100 ml) was added dropwise. The resulting solution was stirred for an additional hour and then a solution of freshly distilled benzaldehyde (56 g, 0.53 mol) in absolute ether (75 ml) was added over a 1-hr period at −70°. The mixture was stirred for 30 min at −70°, allowed to warm to 0° slowly, poured into ice and water, and shaken vigorously. The layers were separated and the aqueous layer was extracted with ether (200 ml). The ether portions were combined, washed neutral to litmus with water, and dried ($MgSO_4$). The viscous oil (138 g, ~100%), which remained after evaporation of the solvent, was used withut further purification.

A small portion of the product obtained in a similar experiment was chromatographed on neutral alumina using benzene as the eluent. Repeated short-path distillation of the alcohol-containing fraction provided an analytical sample of 3-bromo-4-thienylphenylcarbinol as a slightly yellow, clear oil [100° bath (0.1 mm)]: ir (neat) 3350 cm^{-1} (broad OH); nmr (CS_2) τ 2.7–3.1 (m, 7 H, aromatic), 4.35 (d, J = 4 Hz, 1 H, methine), 7.52 (d, J = 4 Hz, 1 H, OH).

Anal. Calcd for $C_{11}H_9BrOS$: C, 49.08; H 3.37; Br, 29.69; S, 11.91. Found: C, 49.23; H, 3.46; Br, 29.50; S, 12.03.

4-Benzyl-3-bromothiophene (14).—Lithium aluminum hydride (29.5 g, 0.778 mol) was suspended in absolute ether (150 ml) contained in a 1000-ml, flame-dried, three-necked flask. The mixture was cooled in an ice–water bath while a solution of anhydrous aluminum chloride (104 g, 0.78 mol) in absolute ether (200 ml) was added over a 5-min period. External cooling was halted and a solution of crude 3-bromo-4-thienylphenylcarbinol (138.4 g, ~0.5 mol) in absolute ether (200 ml) was added at a rate such as to promote gentle reflux. The mixture was maintained at reflux for an additional 15 min and the ice bath was then replaced. Excess hydride was destroyed by cautious, dropwise addition of sulfuric acid (3 *M*). The mixture was poured into ice and hydrochloric acid (400 ml, 2 *M*) and shaken vigorously. The layers were separated and the aqueous layer was extracted twice with ether (150 ml). The combined ether portions were successively washed with hydrochloric acid (2 *M*), saturated sodium bicarbonate solution, and water, and dried ($MgSO_4$). After concentration, the liquid was fractionally distilled to give 94.7 g (73%) of a clear, colorless liquid: bp 105–110° (0.1 mm); nmr (CCl_4) τ 2.8 (broad s, 6 H, aromatic), 3.25–3.35 (m, 1 H, 5 position of thiophene), 6.11 (s, 2 H, CH_2).

Anal. Calcd for $C_{11}H_9BrS$: C, 52.18; H, 3.58; Br, 31.51; S, 12.67. Found: C, 52.37; H, 3.59; Br, 31.66; S, 12.70.

4-Benzylthiophene-3-carboxylic Acid (15).—Ethereal *n*-BuLi (84 ml, 1.32 *M*, 0.11 mol) was run into a 500-ml, three-necked, flame-dried flask under a constant stream of nitrogen. The solution was cooled to −70° and a solution of 4-benzyl-3-bromothiophene (25.3, g, 0.10 mol) in absolute ether (50 ml) was added dropwise over a 15-min period. The resulting mixture was maintained at −70° for 30 min and run onto excess Dry Ice under a stream of nitrogen. The mixture was allowed to warm to 0°, water (150 ml) was added, and the layers were separated. The ether layer was extracted with sodium hydroxide solution (100 ml, 1 *M*). The aqueous portions were combined, cooled, and acidified with excess hydrochloric acid (1 *M*). The white precipitate was taken up in ether and dried ($MgSO_4$). Removal of the solvent left 21.5 g of a white solid which was recrystallized as white needles (18.3 g, 85%) from acetonitrile: mp 143.5–

(19) E. C. Horning, Ed., "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 553.

144°; ir (KBr) 1675 cm^{-1} (acid C=O); nmr (polysol-*d*) τ 1.8 (d, J = 3.5 Hz, 1 H, thiophene 2 position), 2.78 (s, 5 H, C_6H_5), 3.02 (d, J = 3.5 Hz, 1 H, thiophene 5 position), 5.75 (s, 2 H, CH_2).

Anal. Calcd for $C_{12}H_{10}O_2S$: C, 66.03; H, 4.62; S, 14.69. Found: C, 66.25; H, 4.64; S, 14.82.

Cyclization of 4-Benzylthiophene-3-carboxylic Acid (15).—Phosphorus pentachloride (2.72 g, 13 mmol) was added portionwise to a stirred solution of 4-benzylthiophene-3-carboxylic acid (2.85 g, 13 mmol) in dry benzene (15 ml) at 5°. The mixture was allowed to warm to room temperature and then heated on a steam bath until the evolution of hydrogen chloride had ceased.

The acid chloride solution was added dropwise to a solution of stannic chloride (1.6 ml, 3.5 g, 14 mmol) in dry benzene (75 ml) at 5° over a 30-min period. The mixture was allowed to stir at room temperature for 2 hr, refluxed for 15 min, allowed to cool, and poured into ice and hydrochloric acid (2 *M*). The layers were separated and the aqueous phase was extracted with benzene (100 ml). The combined organic portions were washed with saturated sodium bicarbonate solution and with water and dried ($MgSO_4$). The yellow solid which remained after removal of the solvent was chromatographed on neutral silica gel using benzene as the eluent. The benzene solution was concentrated and diluted with hexane. 4,9-Dihydronaphtho-[2,3-*c*]thiophen-4-one (2.15 g, 82%) was obtained as yellow plates: mp 103.5–105°; uv max (95% C_2H_5OH) 281 mμ (ϵ 13,700); ir (KBr) 1650 cm^{-1} (ketone C=O); for nmr spectra (polysol-*d*) and (C_6D_6) see Table I.

Anal. Calcd for $C_{12}H_8OS$: C, 71.97; H, 4.02; S, 16.01. Found: C, 71.99; H, 4.11; S, 15.85.

4-Acetoxynaphtho[2,3-*b*]thiophene (16).—A stirred mixture of *o*-(2-thenyl)benzoic acid (0.95 g, 4.3 mmol), glacial acetic acid (10 ml), acetic anhydride (7 ml), and anhydrous zinc chloride (0.10 g, 0.74 mmol) was heated at reflux for 15 min and while still hot was cautiously diluted with water (17 ml). The yellow crystalline solid was filtered and recrystallized from cyclohexane as yellow needles (0.82 g, 78%): mp 120–121° (lit.[2a] 119–120°); uv max (95% C_2H_5OH) 250 mμ (ϵ 63,100) 256 (63,200), 317 (sh, 4020), 331 (sh, 5930), 340 (7050), and 356 (8930); ir (KBr) 1755 cm^{-1} (acetate C=O); nmr (CCl_4) τ 1.87 (s, 1 H, aromatic 9 position), 2.05–2.4 (m, 2 H, aromatic 5 and 8 positions), 2.5–2.9 (m, 4 H, aromatic, 2, 3, 6, and 7 positions), 7.60 [s, 3 H, $CH_3C(=O)O$].

9-Acetoxynaphtho[2,3-*b*]thiophene (17).—A stirred mixture of *o*-(3-thenyl)benzoic acid (0.47 g, 2.2 mmol), glacial acetic acid (5 ml), acetic anhydride (3.5 ml), and anhydrous zinc chloride (50 mg, 0.37 mmol) was heated at reflux for 15 min and while still hot was slowly diluted with water (8.5 ml). The yellow crystalline solid was filtered and recrystallized from cyclohexane as yellow needles (0.41 g, 78%): mp 106–107°; uv max (95% C_2H_5OH) 249 mμ (ϵ 72,800), 255 (72,300), 316 (sh, 4640), 329 (6060), 338 (7270), and 354 (8890); ir (KBr) 1760 cm^{-1} (acetate C=O); nmr (CCl_4) τ 1.96 (s, 1 H, aromatic 4 position), 2.05–2.20 (m, 2 H, aromatic 5 and 8 positions), 2.35–2.90 (m, 4 H, aromatic 2, 3, 6, and 7 positions), 7.60 [s, 3 H, $CH_3C(=O)O$].

Anal. Calcd for $C_{14}H_{10}O_2S$: C, 69.39; H, 4.16; S, 13.24. Found: C, 69.56; H, 4.02; S, 13.09.

Registry No.—**2e**, 31926-61-1; **2k**, 31926-62-2; **3e**, 31926-63-3; **3k**, 31926-64-4; **4k**, 31926-65-5; **9**, 31926-66-6; **10**, 31926-67-7; **11**, 31926-68-8; **13**, 31981-25-6; **14**, 31926-69-9; **15**, 31926-70-2; **16**, 22566-41-2; **17**, 31926-72-4.

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Keto–Enol Tautomerism in the Thiophene Analogs of Anthrone. II. Benzodithiophenes

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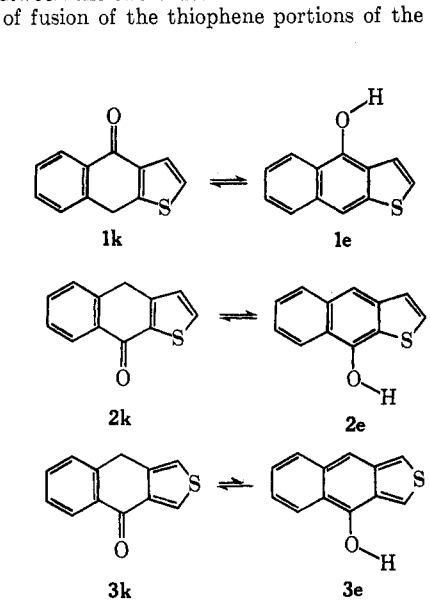
The syntheses of five benzodithiophene analogs of anthrone and anthrol are described. The keto–enol equilibrium position for each of these compounds was spectroscopically determined and a comparison of the experimental results with the calculated delocalization energy difference between the two tautomeric forms was made for each isomer. The results are explained in terms of the modes of fusion of the thiophene portions of the molecule.

As was demonstrated in the initial paper[2] in this series, substituting a thiophene nucleus for one of the benzene moieties of anthrone gives rise to a significant change in the conditions necessary to promote enolization. The direction of this change was found to be dictated by the mode of fusion of the thiophene ring.[2]

In order to further define the structural conditions which govern keto–enol tautomerism, the earlier study was extended to the benzodithiophene systems **4–9**.

In this paper we wish to report the preparation of five of these compounds, **4–8**. The synthesis of the final isomer, 4,8-dihydrobenzo[1,2-*c*:4,5-*c*′]dithiophen-4-one (**9**), is underway and will be the subject of a future publication dealing with the chemistry of benzo-[1,2-*c*:4,5-*c*′]dithiophene.

Synthesis of 4,8-Dihydrobenzo[1,2-*b*:4,5-*c*′]thiophen-8-one (4k).—The reaction sequence which had been successfully employed in the preparation of the naphthothiophenones **2k** and **3k** was easily adapted to the synthesis of the first benzodithiophenone **4k** (see Scheme I).



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(2) D. W. H. MacDowell and J. C. Wisowaty, *J. Org. Chem.*, **36**, 3999 (1971).