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.

Acknowledgment.—The authors wish to thank Mr. Robert Smith for his services in recording some of the nmr spectra and Dr. C. G. McCarty for his aid in the preparation of this manuscript.

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

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Received June 1, 1971

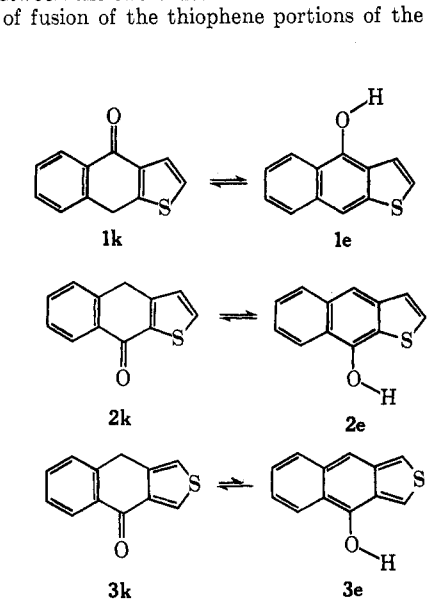
The syntheses of five benzodithiophene analogs of anthrone and anthrol are described. The keto–enol equilibrium position for each of these compounds was spectroscopically determined and a comparison of the experimental results with the calculated delocalization energy difference between the two tautomeric 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**.

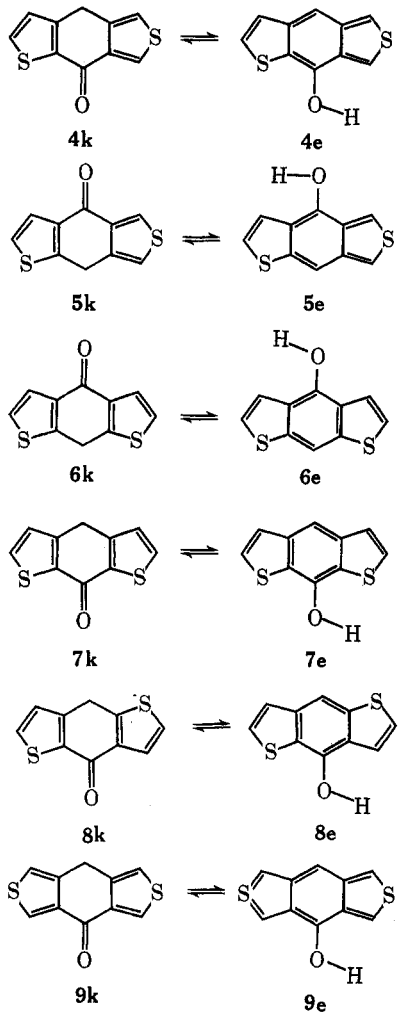
In this paper we wish to report the preparation of five of these compounds, **4–8**. The synthesis of the final isomer, 4,8-dihydrobenzo[1,2-*c*:4,5-*c*′]dithiophen-4-one (**9**), is underway and will be the subject of a future publication dealing with the chemistry of benzo-[1,2-*c*:4,5-*c*′]dithiophene.

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).



(1) NDEA Fellow, 1967–1970.

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

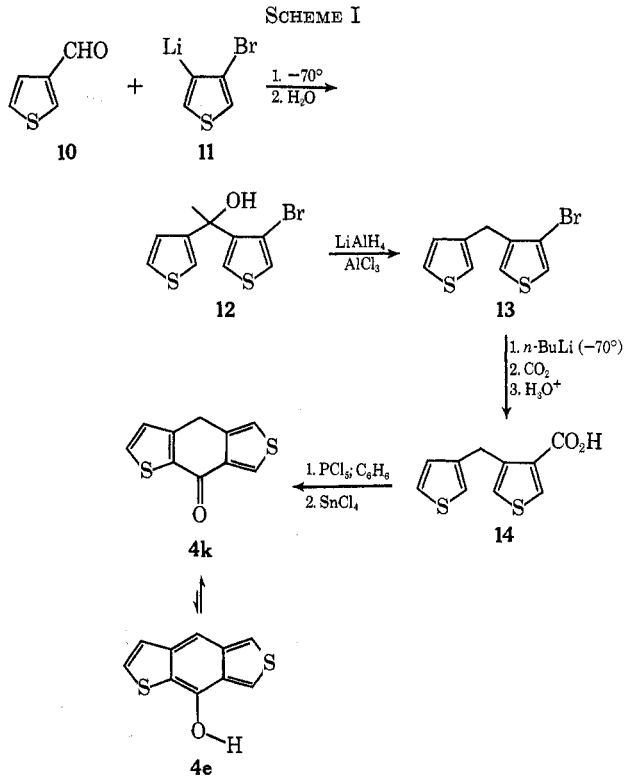


Treatment of 4-bromo-3-thienyllithium (**11**) with 3-thiophenecarboxaldehyde (**10**)[3] at −70° afforded 3-bromo-3′,4-dithienylcarbinol (**12**) in 95% yield. The reduction of **12** with lithium aluminum hydride and aluminum chloride in dry ether[4] provided 3-bromo-3′,4-dithienylmethane (**13**) in 91% yield. Halogen–metal exchange in **13** at −70°, followed by carbonation, resulted in an 84% yield of 3′,4-dithienylmethane-3-carboxylic acid (**14**) which was cyclized *via* the acid chloride using stannic chloride to **4k** in 63% yield. The presence of a sharp singlet (τ 6.67) in the methylene region of the nmr spectrum (C_6D_6) of **4k** (Table I) supports the keto structure for the cyclization product. The ir and uv spectra also uphold this assignment for the keto–enol character of **4**.

In cases where the free-energy difference between the two tautomeric forms is small, the enol content has been shown to be very solvent dependent, *i.e.*, **1k**,**e** and **2k**,**e**.[2] Both **1e** and **2e** were found to be present, exclusive of the corresponding keto forms, in a polysol-*d*[5] solution. However, no indication of the presence of **4e** was found in the nmr spectrum (polysol-*d*) of **4k** (Table I). The aromatic region of the spectrum, representing four hydrogens, shows the expected multiplicity and coupling constants. The methylene singlet appears at τ 5.82 and represents two hydrogens.

(3) S. Gronowitz, *Ark. Kemi*, **8**, 441 (1955).
(4) J. Blackwell and W. J. Hickinbottom, *J. Chem. Soc.*, 1405 (1961).
(5) Available from Stohler Isotope Chemicals, Rutherford, N. J.; it was found to have solvent properties, approximating those of dimethyl sulfoxide.

SCHEME I



In all its spectral properties, **4k** strongly resembles **3k**. However, unlike **3k** it is readily soluble in 1 *M* sodium hydroxide, giving rise to a bright yellow solution which rapidly darkens on standing.

Synthesis of 4,8-Dihydrobenzo[1,2-*b*:4,5-*c*′]dithiophen-4-one (5k).—The synthesis of **5k** is outlined in Scheme II.

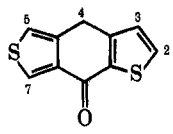
By simply substituting 2-thiophenecarboxaldehyde (**15**)[6] for 3-thiophenecarboxaldehyde (**10**) in Scheme I, the reaction sequence provided the same basic ring system as before with the ketone function now appearing in the 4 position. The individual reactions furnished compounds of unambiguous structure in yields of 56–86%.

The nmr spectrum (polysol-*d*) of **5k**, which is indicative of the keto tautomer, consists of a low field doublet for one hydrogen together with a complex multiplet for three hydrogens in the aromatic region and also a methylene singlet for two hydrogens at τ 5.58. The aromatic region was better resolved when C_6D_6 was employed as the solvent. The signal multiplicities and coupling constants support the presence of only the keto form (see Table I). The ir and uv spectra of **5k** also substantiate this conclusion. As was the case for **4k**, **5k** readily dissolves in 1 *M* sodium hydroxide solution.

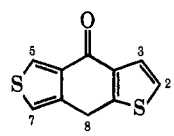
Synthesis of 4-Hydroxybenzo[1,2-*b*:5,4-*b*′]dithiophene (6e).—The synthesis of **6e** was accomplished in two steps from 3-bromo-2,2′-dithienylmethane (**21**) (see Scheme III). The alkylation of 3-bromothiophene (**19**) with 2-chloromethylthiophene (**20**)[7] under the influence of stannic chloride produced **21** in 29% yield. This compound was recently reported as a precursor in the preparation of benzo[1,2-*b*:5,4-*b*′]dithiophene,

(6) "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 915.
(7) "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 1955.

Table I



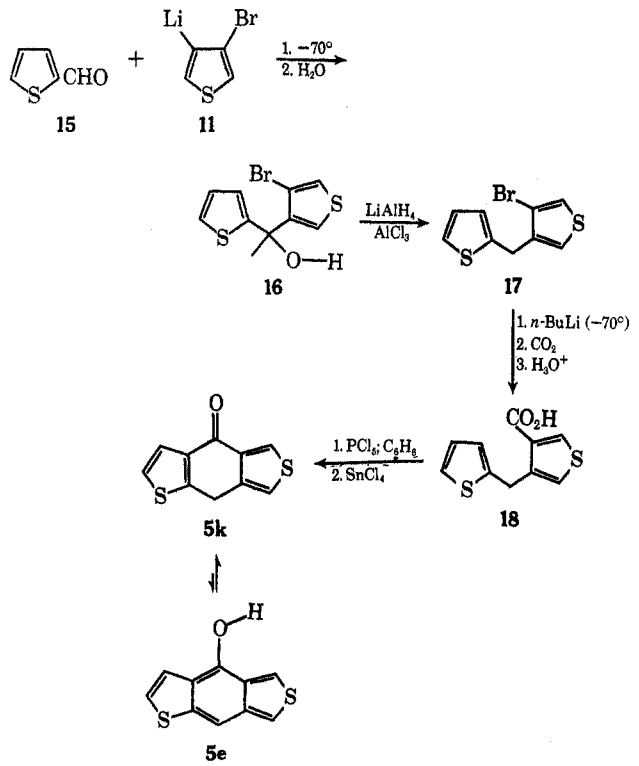
4k



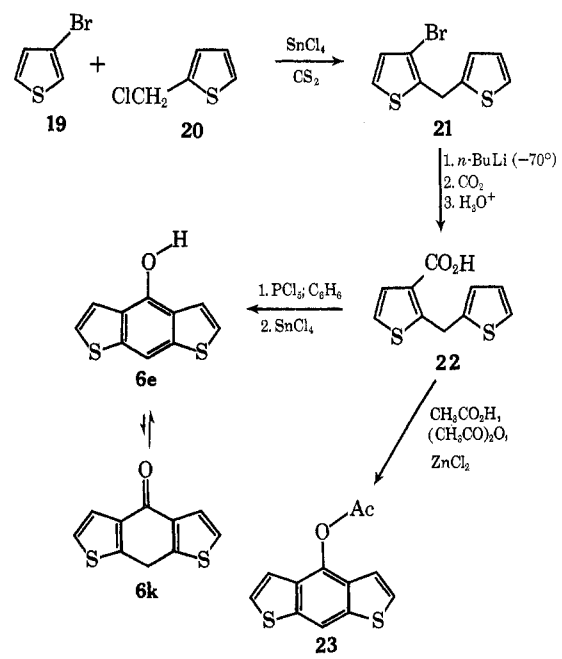
5k

Solvent	Proton	τ	Proton	τ
C_6D_6	7	1.87 (d, 1 H), $J_{5,7}$ = 3.5 Hz	5	1.88 (d, 1 H), $J_{5,7}$ = 3.5 Hz
	2	2.97 (d, 1 H), $J_{2,3}$ = 5 Hz	2	2.34 (d, 1 H), $J_{2,3}$ = 5 Hz
	3,5	3.31–3.58 (m, 2 H)	3	3.32 (d, 1 H), $J_{2,3}$ = 5 Hz
	4	6.67 (s, 2 H)	7	3.60 (m, 1 H), $J_{5,7}$ = 3.5, $J_{7,8}$ = 1 Hz
			8	6.62 (s, 2 H)
Polysol-*d*	7	1.69 (d, 1 H), $J_{5,7}$ = 3.5 Hz	5	1.64 (d, 1 H), $J_{5,7}$ = 3.5 Hz
	2	2.04 (d, 1 H), $J_{2,3}$ = 5 Hz	2, 3, 7	2.36–2.64 (m, 3 H)
	5	2.50 (m, 1 H), $J_{5,7}$ = 3.5, $J_{4,5}$ = 1 Hz	8	5.58 (s, 2 H)
	3	2.78 (d, 1 H), $J_{2,3}$ = 5 Hz		
	4	5.82 (s, 2 H)		

Scheme II



Scheme III



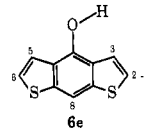
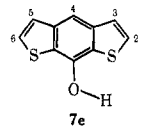
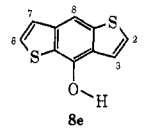
but its physical and spectral properties were not described.[8] Carbonation of **21** afforded 2,2′-dithienylmethane-3-carboxylic acid (**22**) in 64% yield. Cyclization of **22** *via* the acid chloride using stannic chloride provided a 40% yield of **6e**. The acid **22** was also converted to 4-acetoxybenzo[1,2-*b*:5,4-*b*′]dithiophene (**23**) according to the method of Fieser and Hershberg.[9]

The nmr spectrum (polysol-*d*) of **6e** consists of a broad singlet for the enol hydrogen, two doublets, $J_{2,3}$ = 5 Hz, which represent the four thiophene hydrogens, and a sharp singlet for the meso (C_8) hydrogen. No absorption above τ 2.7 was observed, thus indicating the absence of a significant quantity of the keto tautomer (see Table II). The spectrum of **6e** in C_6D_6 was also recorded. The signal multiplicities and coupling constants were identical with those in the spectrum which was obtained in polysol-*d*. The presence of the aromatic solvent caused a strong upfield shift of the entire spectrum. Trifluoroacetic acid had been used to ensure the formation of an equilibrium condition

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

(9) L. Fieser and E. B. Hershberg, *J. Amer. Chem. Soc.*, **59**, 1028 (1937).

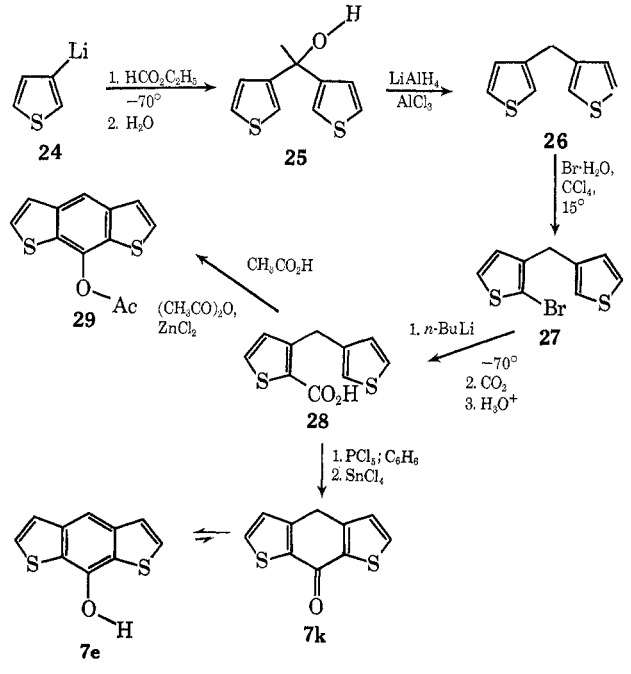
TABLE II

Compd	Polysol-*d* Proton	Polysol-*d* τ	C_6D_6 Proton	C_6D_6 τ
 6e	OH	−0.21 (s, 1 H)	OH	1.96 (s, 1 H)
	8	2.03 (s, 1 H)	2, 6	2.36 (d, 2 H), $J_{2,3}$ = 5 Hz
	2, 6	2.28 (d, 2 H), $J_{2,3}$ = 5 Hz	8	2.39 (s, 1 H)
	3, 5	2.62 (d, 2 H), $J_{2,3}$ = 5 Hz	3, 5	3.13 (d, 2 H), $J_{2,3}$ = 5 Hz
 7e	OH	−0.41 (s, 1 H)	4	2.32 (s, 1 H)
	4	2.10 (s, 1 H)	2, 6	2.92 (d, 2 H), $J_{2,3}$ = 5 Hz
	2, 6	2.43 (d, 2 H), $J_{2,3}$ = 5 Hz	3, 5	3.08 (d, 2 H), $J_{2,3}$ = 5 Hz
	3, 5	2.57 (d, 2 H), $J_{2,3}$ = 5 Hz	OH	4.87 (s, 1 H)
 8e	OH	0.33 (s, 1 H)		
	8	2.08 (s, 1 H)		
	2, 3, 6, 7	2.12–2.72 (m, 4 H)		

in C_6D_6 solutions of **1k,e** and **2k,e**.[2] The addition of a drop of this acid to the C_6D_6 solution of **6e** had no observable effect on the aromatic portion of the spectrum but only served to eliminate the enol (OH) absorption. Since no absorption above τ 3.2 was observed, the equilibrium position in **6k,e** must strongly favor the enol tautomer. The ir and uv spectra were also consistent with the assignment of **6e** for the structure of the cyclized product. The uv spectrum of **6e** was found to be very similar to that of its enol acetate (**23**).

Synthesis of 8-Hydroxybenzo[1,2-*b*:5,4-*b*′]dithiophene (7e).—The synthesis of **7e** is outlined in Scheme IV. The known 3,3′-dithienylmethane (**26**)[10] was

SCHEME IV



obtainable in fair quantity by way of high-yield reactions; therefore it presented itself as a logical starting material in the preparation of **7e**.

Gronowitz and Eriksson[11] have reported a two-step conversion of 3-bromothiophene to 3,3′-dithienylcarbinol (**25**) *via* 3-thiophenecarboxaldehyde. The same transformation was accomplished in one-step by treating ethyl formate with 2 equiv of 3-thienyllithium (**24**) at −70°. The yield of the alcohol was 77%. The reduction of **25** to 3,3′-dithienylmethane (**26**) was achieved in high yield according to the procedure of Wynberg, *et al.*[10] Since the dibromination of **26** had been shown[10] to produce 2,2′-dibromo-3,3-dithienylmethane, similar conditions were used to affect a monobromination. The conversion proceeded in 68% yield and provided the expected 2-bromo compound. Halogen–metal exchange at −70° in **27**, followed by carbonation, provided a good yield of 3,3′-dithienylmethane-2-carboxylic acid (**28**) which was cyclized *via* the acid chloride using stannic chloride to **7e**. The enol acetate of **7e** was also formed from **28** in order to compare its spectral properties with those of the enol.

The nmr spectrum of **7e** was obtained in polysol-*d* and in C_6D_6 and as expected both were very similar to those earlier described for **6e** (see Table II). No indication for the presence of the keto tautomer (**7k**) in either solvent was found. The uv spectrum of **7e** was compatible with that of its enol acetate (**29**). The lack of a carbonyl absorption in the ir spectrum of **7e** confirmed the presence of only the enol tautomer.

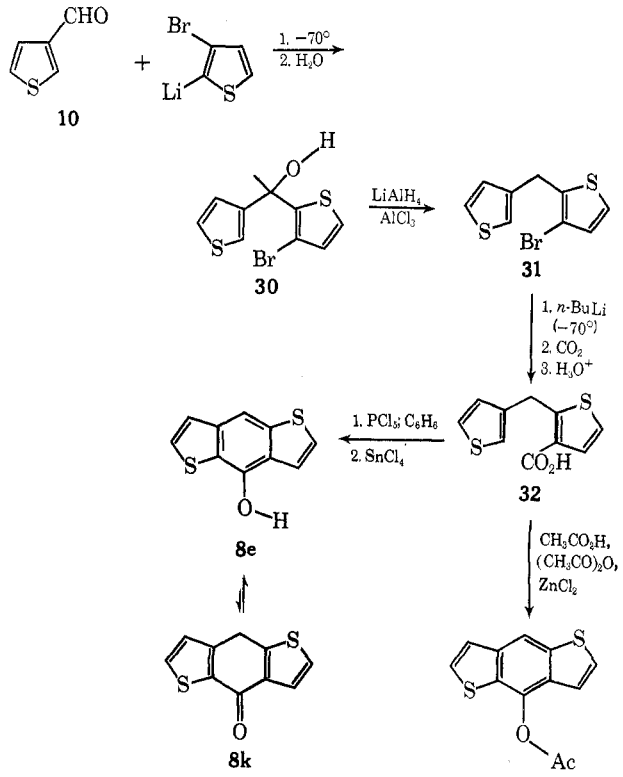
Synthesis of 4-Hydroxybenzo[1,2-*b*:4,5-*b*′]dithiophene (8e).—The preparation of the fifth isomer in this series was achieved by following a reaction sequence similar to that which proved successful in the synthesis of both **4k** and **5k** (see Scheme V).

Treatment of 3-bromo-2-thienyllithium with 3-thiophenecarboxaldehyde provided a 63% yield of 3-bromo-2,3-dithienylcarbinol (**30**) as a viscous oil. This alcohol had earlier been prepared by other workers,[10] who were unable to affect purification. Although we were successful in obtaining **30** as an analytically pure, low melting solid, the method was tedious. For this reason, the crude, viscous alcohol was allowed to react with equimolar quantities of lithium aluminum hydride and aluminum chloride, thus furnishing a 66% yield of 3-bromo-2,3′-dithienylmethane (**31**). The physical properties of **31** are comparable with those reported for it by Wynberg,[10] who obtained the bromide *via* an alternate route. Carbonation of **31** was affected in 83% yield and the resulting acid was cyclized to **8e** in 73% yield. The acid **32** was also converted to the enol acetate **33** of **8e**.

(10) A. Kraak, A. K. Wiersema, P. Jordens, and H. Wynberg, *Tetrahedron*, **24**, 3381 (1968).

(11) S. Gronowitz and B. Eriksson, *Ark. Kemi*, **21**, 335 (1964).

Scheme V



The nmr spectrum (polysol-*d*) of **8e** revealed the presence of only the enol tautomer. A broad singlet due to the enol (OH) hydrogen was found at τ 0.33. The lack of a signal in the methylene region of the spectrum, τ 5–7, indicates the absence of a significant amount of the keto form **8k** (see Table II). Unlike **6e** and **7e**, **8e** possesses four nonequivalent thiophene protons. For this reason the aromatic portion of the spectrum is highly complex. The meso (C_8) proton appears slightly downfield from the remainder of the aromatic protons. Since **8e** was not readily soluble in benzene, its nmr spectrum in C_6D_6 could not be obtained. However, the information which was provided by the ir and uv spectra of **8e** justifies the assignment of the enol form for the cyclization product. The uv spectrum of **33** very closely resembles that of **8e**.

Discussion

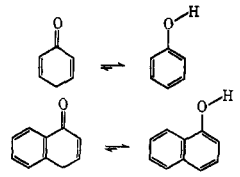
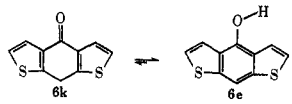
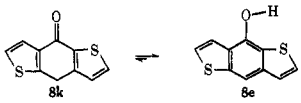
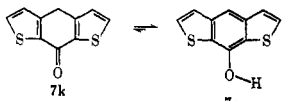
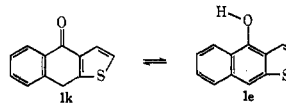
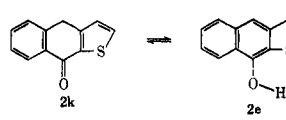
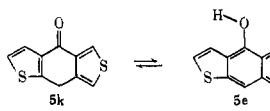
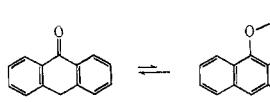
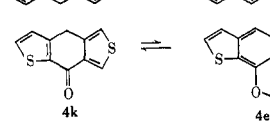
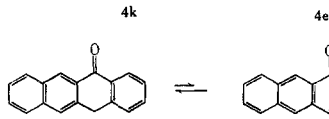
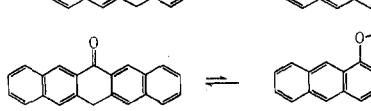
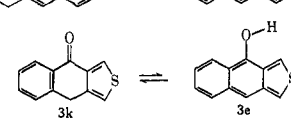
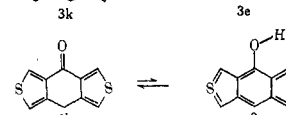
The keto–enol character of polycylic phenols is dictated by the free-energy difference between the two tautomeric forms. Since the individual compounds to be considered are very similar in structure, the change in σ bond energy for the transformation enol → ketone remains constant throughout the series. Thus the free-energy change can be represented by the π delocalization energy difference, ΔDE.

$$\Delta DE = DE_{enol} - DE_{keto}$$

In this approximation DE_{enol} is taken as the π delocalization energy of the parent system and DE_{keto} as that of the *exo*-methylene derivative.[12] A comprehensive list of ΔDE values was compiled and appears in Table III along with the experimentally determined equilibrium position for each substance.

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

Table III

Compd	ΔDE (β units)[a,b]	Preferred tautomer
	1.10	Enol
	0.83	Enol
 (6k, 6e)	0.80	Enol
 (8k, 8e)	0.76	Enol
 (7k, 7e)	0.72	Enol
 (1k, 1e)	0.66	Enol (polysol-*d*), mixture (C_6D_6)
 (2k, 2e)	0.62	Enol (polysol-*d*), mixture (C_6D_6)
 (5k, 5e)	0.53	Keto[c]
	0.50	Keto[c]
 (4k, 4e)	0.49	Keto[c]
	0.43	Keto[d]
	0.38	Keto
 (3k, 3e)	0.37	Keto[d]
 (9k, 9e)	0.21	?[e]

[a] HMO program written by Dr. J. Gruninger, West Virginia University. [b] The parameters for these calculations are $\alpha_s = \alpha + \beta$; $\beta_{cs} = 0.7\beta$. [c] Soluble in hot 1 *M* sodium hydroxide solution. [d] Soluble in ethanolic potassium hydroxide solution. [e] Has not been prepared but keto form is predicted from the ΔDE value.

For the vast majority of the compounds which appear in Table III only one tautomeric form could be

spectroscopically detected. Only in the C_6D_6 solutions of the two *b*-fused naphthothiophene derivatives, **1k,e** and **2k,e**, was a coexisting keto–enol pair observed. The extent of the ΔDE region where this phenomenon occurs is still somewhat ill-defined and is currently under investigation.

Earlier,[2] we domonstrated that a compound of greatly enhanced enol content was produced by replacing one of the benzene rings of anthrone by a *b*-fused thiophene moiety. It logically follows that a still higher degree of enolization would be expected for the benzodithiophene derivatives related to anthrone if both heterocyclic rings were *b* fused. Hence, the fact that only the enol tautomers were detected in the equilibrium mixtures, **6k,e**, **7k,e**, and **8k,e**, is not unreasonable.

The benzodithiophene derivatives **4k** and **5k**, in which one of the thiophene rings is fused across its 3,4 bond, highly favor the keto tautomer since enolization would necessitate the formation of an energetically unfavorable benzo[*c*]thiophene system.

The correlation of the experimentally observed equilibrium position with computed ΔDE values provided excellent results in both the acene and "heteroacene" series.

Experimental Section[13]

3-Bromo-3′,4-dithienylcarbinol (**12**).—A solution of 3-thiophenecarboxaldehyde (46 g, 0.41 mol) in absolute ether (100 ml) was added dropwise to a solution of 4-bromo-3-thienyllithium, which had been prepared at −70° from ethereal *n*-butyllithium (300 ml, 1.5 *M*, 0.45 mol) and a solution of 3,4-dibromothiophene (110 g, 0.45 mol) in absolute ether (100 ml). The reaction mixture was stirred at −70° for 45 min and then allowed to warm to room temperature. Water (200 ml) was cautiously added with stirring. The layers were separated and the aqueous phase was extracted with ether (100 ml). The combined ether portions were washed neutral with copious quantities of water and dried ($MgSO_4$). The solvent was removed and the resulting viscous oil was warmed (70°) *in vacuo* for 2 hr. On cooling, the oil solidified giving an off-white solid which was recrystallized from hexane as white clusters (106.6 g, 95%), mp 64–68°. Two additional recrystallizations from hexane provided the analytical sample: mp 72.5–73.5°; ir (melt) 3390 cm^{-1} (OH); nmr ($CDCl_3$) τ 2.58–3.00 (m, 5 H, thiophene), 4.03 (d, 1 H, *J* = 3.5 Hz, methine), 7.47 (d, 1 H, *J* = 3.5 Hz, OH).

Anal. Calcd for $C_9H_7BrOS_2$: C, 39.28; H, 2.57; Br, 29.04; S, 23.30. Found: C, 39.10; H, 2.49; Br, 29.34; S, 23.03.

3-Bromo-3′,4-dithienylmethane (**13**).—A solution of aluminum chloride (64 g, 0.48 mol) in absolute ether (250 ml) was slowly added to a cooled suspension of lithium aluminum hydride (9.1 g, 0.24 mol) in absolute ether (100 ml). The mixture was allowed to come to room temperature and a solution of 3-bromo-3′,4-dithienylcarbinol (33 g, 0.12 mol) in absolute ether (100 ml) was added at such a rate as to promote a gentle reflux. The suspension was maintained at reflux for an additional 30 min and then cooled by means of an ice bath. The excess hydride was decomposed by dropwise addition of ethyl acetate (200 ml). The mixture was poured into ice and 1 *M* hydrochloric acid and shaken vigorously. The layers were separated and the aqueous phase was extracted with ether (two 100-ml portions). The combined organic portions were washed successively with 1 *M* hydrochloric acid, saturated sodium bicarbonate solution, and water and dried ($MgSO_4$). The solution was concentrated and the resulting liquid was fractionated giving 28.2 g (91%) of a colorless liquid, bp 98–103° (0.1 mm). An additional distillation provided the analytical sample: bp 94–95° (0.05 mm); nmr (CS_2) τ 2.74–3.32 (m, 5 H, thiophene), 6.15 (s, 2 H, CH_2).

Anal. Calcd for $C_9H_7BrS_2$: C, 41.70; H, 2.72; Br, 30.83; S, 24.74. Found: C, 41.89; H, 2.79; Br, 31.07; S, 24.89.

3′,4-Dithienylmethane-3-carboxylic Acid (**14**).—A solution of 3-bromo-3′,4-dithienylmethane (43 g, 0.17 mol) in absolute ether (100 ml) was added under a constant stream of nitrogen to an ethereal n-butyllithium solution (143 ml, 1.28 M, 0.18 mol) which was maintained at −70°. After stirring at −70° for 30 min, the solution was run onto excess Dry Ice. The mixture was allowed to come to room temperature and water (250 ml) was cautiously added with stirring. The layers were separated and the organic phase was washed with water (150 ml). The combined aqueous portions were acidified with excess 2 *M* hydrochloric acid. The resulting white precipitate was taken up in ether (two 250-ml portions) and the ethereal solution was washed with water, dried ($MgSO_4$), and concentrated. The white product was recrystallized from acetonitrile as white needles (31.1 g, 84%). An additional recrystallization from acetonitrile afforded the analytical sample: mp 138–139°; ir (KBr) 1675 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 1.79 (d, 1 H, $J_{2,5}$ = 3.5 Hz, thiophene), 2.62–3.12 (m, 4 H, thiophene), 3.51 (broad s, 1 H, COOH), 5.75 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_{10}H_8O_2S_2$: C, 53.55; H, 3.59; S, 28.59. Found: C, 53.78; H, 3.68; S, 28.75.

4,8-Dihydrobenzo[1,2-*b*:4,5-*c*′]dithiophen-8-one (**4k**).—Phosphorus pentachloride (4.16 g, 20 mmol) was added portionwise to a stirred solution of 3′,4-dithienylmethane-3-carboxylic acid (4.48 g, 20 mmol) in dry benzene (150 ml) which was maintained at 4°. The mixture was then warmed until the evolution of hydrogen chloride ceased. The resulting solution was cooled to 4° and a solution of stannic chloride (3 ml, 6.7 g, 26 mmol) in dry benzene (50 ml) was dropwise added. The mixture was stirred at 4° for 1 hr and at room temperature for an additional hr, then poured into ice and 2 *M* hydrochloric acid. After vigorous shaking, 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, dried ($MgSO_4$), and concentrated to 75 ml. The resulting solution was chromatographed on a 20 cm × 2 cm column packed with neutral silica gel. Elution with benzene–chloroform (3:1), followed by concentration of the effluent, yielded a tan solid which was sublimed (100°, 0.05 mm) to give 2.6 g (63%) of a light-colored solid, mp 129–131°. Recrystallization from benzene–hexane provided an analytical sample: mp 132°; uv max (95% C_2H_5OH) 303 mμ (ε 15,900); ir (KBr) 1630 cm^{-1} (ketone C=O), no enol (OH) absorption was observed. Nmr spectra appear in Table I.

Anal. Calcd for $C_{10}H_6OS_2$: C, 58.22; H, 2.93; S, 31.09. Found: C, 58.16; H, 3.02; S, 30.92.

3-Bromo-2′,4-dithienylcarbinol (**16**).—A solution of 2-thiophenecarboxaldehyde (11.2 g, 0.10 mol) in absolute ether (50 ml) was dropwise added to a solution of 4-bromo-3-thienyllithium, which had been prepared at −70° from ethereal *n*-butyllithium (110 ml, 1.1 *M*, 0.12 mol) and a solution of 3,4-dibromothiophene (30 g, 0.12 mol) in absolute ether (50 ml). The mixture was stirred at −70° for 1 hr and then allowed to come to room temperature. Following normal work-up, the solvent was removed and the resulting liquid was dissolved in 50 ml of a 1:1 benzene–hexane solution. The solution was placed on a column of neutral alumina followed by 200 ml of the benzene–hexane solution. The eluent was then changed to chloroform and the alcohol containing fractions were combined and recrystallized from benzene–hexane giving 15.3 g (56%) of 3-bromo-4,2′-dithienylcarbinol as large white crystals. An additional recrystallization from benzene–hexane provided the analytical sample: mp 61.5–63°; ir (melt) 3380 cm^{-1} (OH); nmr (CS_2) τ 2.77–3.33 (m, 5 H, thiophene), 4.18 (d, 1 H, *J* = 4 Hz, methine), 7.22 (d, 1 H, *J* = 4 Hz, –OH).

Anal. Calcd for $C_9H_7BrOS_2$: C, 39.28; H, 2.57; Br, 29.04; S, 23.30. Found: C, 39.46; H, 2.36; Br, 29.20; S, 23.04.

3-Bromo-2′,4-dithienylmethane (**17**).—A solution of aluminum chloride (6.1 g, 46 mmol) in absolute ether (100 ml) was slowly added to a cooled suspension of lithium aluminum hydride (1.75 g, 46 mmol) in absolute ether (50 ml). The mixture was allowed to come to room temperature and a solution of 3-bromo-2′,4-dithienylcarbinol (11 g, 40 mmol) in absolute ether (50 ml) was added at such a rate as to promote a gentle reflux. The suspension was maintained at reflux for an additional 30 min and then cooled by means of an ice bath. The excess hydride was decom-

(13) 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.

posed by dropwise addition of 3 *M* sulfuric acid. The mixture was poured into ice and 1 *M* hydrochloric acid. Work-up followed the procedure which was previously outlined in the preparation of **13**. The resulting liquid was fractionated giving 8.9 g (86%) of a colorless liquid: bp 94–98° (0.1 mm); nmr (CS_2) τ 2.79–3.33 (m, 5 H, thiophene), 5.95 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_9H_7BrS_2$: C, 41.70; H, 2.72; Br, 30.83; S, 24.74. Found: C, 41.75; H, 2.87; Br, 30.58; S, 24.92.

2′,4-Dithienylmethane-3-carboxylic Acid (18).—A solution of 3-bromo-2′,4-dithienylmethane (23 g, 89 mmol) in absolute ether (50 ml) was added under a constant stream of nitrogen to an ethereal *n*-butyllithium solution (85 ml, 1.18 *M*, 100 mmol) which was maintained at −70°. After stirring at −70° for 30 min, the solution was run onto excess Dry Ice. The mixture was allowed to come to room temperature and water (200 ml) was cautiously added. After normal work-up as previously described, the solvent was removed and the white solid was recrystallized from benzene–hexane as white needles (13.8 g, 69%). An additional recrystallization from benzene–hexane afforded the analytical sample: mp 136–137°; ir (KBr) 1675 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 1.71 (d, 1 H, $J_{2,5}$ = 3.5 Hz, thiophene), 2.66–3.17 (m, 4 H, thiophene), 3.63 (broad s, 1 H, COOH), 5.52 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_{10}H_8O_2S_2$: C, 53.55; H, 3.59; S, 28.59. Found: C, 53.51; H, 3.61; S, 28.56.

4,8-Dihydrobenzo[1,2-*b*:4,5-*c*′]dithiophen-4-one (5k).—Phosphorus pentachloride (2.88 g, 14 mmol) was added portionwise to a stirred solution of 2′,4-dithienylmethane-3-carboxylic acid (3.1 g, 14 mmol) in dry benzene (25 ml) which was maintained at 4°. The mixture was then warmed on a steam bath until the evolution of hydrogen chloride had ceased. The resulting acid chloride solution was added dropwise to a stirred solution of stannic chloride (2.1 ml, 4.7 g, 18 mmol) in dry benzene (100 ml) at 4°. The mixture was allowed to come to room temperature and was stirred for 1 hr. The yellow suspension was poured into ice and 2 *M* hydrochloric acid (100 ml). 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, then dried ($MgSO_4$), and concentrated to 100 ml. The warm solution was chromatographed on neutral silica gel, using benzene (500 ml) as the eluent followed by benzene–chloroform (3:1) solution (1000 ml), which, after evaporation of the solvent, gave a slightly pink solid. Sublimation (90°, 0.1 mm) provided 1.65 g (58%) of a yellow solid. Recrystallization from ethanol–water afforded an analytical sample: mp 151–153°; uv max (95% C_2H_5OH) 279 mμ (ε 13,700); ir (KBr) 1635 cm^{-1} (ketone C=O), no enol (OH) absorption was observed. The nmr spectra of **5k** appear in Table I.

Anal. Calcd for $C_{10}H_6OS_2$: C, 58.22; H, 2.93; S, 31.09. Found: C, 57.99; H, 2.84; S, 30.80.

3-Bromo-2,2′-dithienylmethane (21).—A solution of 2-chloromethylthiophene (26.5 g, 0.20 mol) in carbon disulfide (120 ml) was dropwise added to a vigorously stirred solution of 3-bromothiophene (97.8 g, 0.60 mol) and stannic chloride (2 g, 7.7 mmol) in carbon disulfide (300 ml). The mixture was stirred for 4 hr, then poured into ice and 2 *M* hydrochloric acid, and shaken vigorously. Ether (500 ml) was added and the layers were separated. The aqueous phase was extracted with either (200 ml) and the ethereal portions were combined and filtered. The solution was washed with saturated sodium bicarbonate solution and with water, then dried ($MgSO_4$), and concentrated. The resulting yellow liquid was fractionated giving a 3-bromothiophene (60 g), bp 60–62° (15 mm), and 3-bromo-2,2′-dithienylmethane (15.2 g, 29%), bp 91–98 (0.05 mm). The product was redistilled, bp 95–97° (0.1 mm), to given an analytical sample of the clear, colorless liquid: nmr (CS_2) τ 2.83–3.23 (m, 5 H, thiophene), 5.78 (d, 2 H, $-CH_2-$).

Anal. Calcd. for $C_9H_7BrS_2$: C, 41.70; H, 2.72; Br, 30.83; S, 24.74. Found: C, 41.78; H, 2.78; Br, 31.04; S 24.81.

2,2′-Dithienylmethane-3-carboxylic Acid (22).—A solution of 3-bromo-2,2′-dithienylmethane (23 g, 89 mmol) in absolute ether (50 ml) was added under a constant stream of nitrogen to an ethereal *n*-butyllithium solution (80 ml, 1.28 *M*, 102 mmol) which was maintained at −70°. After stirring at −70° for 30 min, the solution was run onto excess Dry Ice. The mixture was allowed to come to room temperature and stand for 10 hr. Water (200 ml) was cautiously added and the layers were separated. Following acidification and normal work-up, the solvent was removed and the resulting white solid was recrystallized from benzene–hexane. The yield was 16.2 g (81%). An additional recrystallization from benzene–hexane provided the analytical sample: mp 122.5–123.5°; ir (KBr) 1675 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 2.46–3.15 (m, 5 H, thiophene), 4.08 (broad s, 1 H, COOH), 5.20 (s, 2 H, $-CH_2-$).

Anal. Calcd. for $C_{10}H_8O_2S_2$: C, 53.55; H, 3.59; S, 28.59. Found: C, 53.50; H, 3.54; S, 28.48.

Benzo[1,2-*b*:5,4-*b*′]dithiophen-4-ol (6e).—Phosphorus pentachloride (4.16 g, 20 mmol) was added portionwise to a stirred solution of 2,2′-dithienylmethane-3-carboxylic acid (4.48 g, 20 mmol) in dry benzene (50 ml) which was maintained at 4°. The mixture was then gently warmed until the evolution of hydrogen chloride had ceased. The resulting solution was cooled to 4° and a solution of stannic chloride (3 ml, 6.7 g, 26 mmol) in dry benzene (50 ml) was dropwise added during 30 min. The mixture was stirred at room temperature for 2 hr and then heated to reflux, cooled, and poured into ice and 2 *M* hydrochloric acid. Following a vigorous shaking, the layers were separated and the aqueous phase was extracted with ether (150 ml). The combined organic portions were washed with saturated sodium bicarbonate solution and with water, dried ($MgSO_4$), and concentrated to 50 ml. The resulting solution was chromatographed on a 20 cm × 2 cm column packed with neutral silica gel. Elution with benzene provided a white granular solid which was recrystallized from benzene–hexane as off-white clusters, 1.65 g (40%). An additional recrystallization from benzene–hexane provided the analytical sample: mp 179–180°; uv max (95% C_2H_5OH) 245 mμ (ε 58,600), 252 (66,500), 300 (8430), 325 (8000), 340 (9400); ir (KBr) 3330 cm^{-1} (OH), no carbonyl absorption was observed. The nmr spectra of **6e** appear in Table II.

Anal. Calcd for $C_{10}H_6OS_2$: C, 58.22; H, 2.93; S, 31.09. Found: C, 57.96; H, 3.00; S, 31.35.

4-Acetoxybenzo[1,2-*b*:5,4-*b*′]dithiophene (23).—A stirred mixture of 2,2′-dithienylmethane-3-carboxylic acid (10 g, 45 mmol), glacial acetic acid (100 ml), acetic anhydride (70 ml), and freshly fused zinc chloride (0.87, 6.4 mmol) was heated at reflux for 15 min and while still hot was cautiously diluted with water (170 ml). The resulting yellow-green crystalline solid was filtered, dried *in vacuo*, and sublimed (110°, 0.1 mm) to give 7.1 g (64%) of the yellow solid. An analytical sample was obtained by recrystallization from benzene–hexane: mp 131.5–133°; uv max (95% C_2H_5OH) 246 mμ (ε 66,000), 253 (76,200), 307 (9000), 328 (2650); ir (KBr) 1750 cm^{-1} (acetate C=O); nmr (CCl_4) τ 1.84 (s, 1 H, C_8 hydrogen), 2.68 (d, 2 H, $J_{2,3}$ = 5 Hz, thiophene), 2.82 (d, 2 H, $J_{2,3}$ = 5 Hz, thiophene), 7.60 [s, 3 H, $-OC(=O)CH_3$].

Anal. Calcd for $C_{12}H_8O_2S_2$: C, 58.04; H, 3.25; S, 25.83. Found: C, 57.81; H, 3.25; S, 25.80.

3,3′-Dithienylcarbinol (25).—A solution of freshly distilled ethyl formate (36 g, 0.49 mol) in absolute ether (100 ml) was dropwise added to a solution of 3-thienyllithium, which had been prepared at −70° from ethereal *n*-butyllithium (640 ml, 1.52 *M*, 0.97 mol) and a solution of 3-bromothiophene (170 g, 1.04 mol) in absolute ether (300 ml). The reaction mixture was stirred at −70° for 1 hr and then allowed to warm to 0°. Water (600 ml) was cautiously added with stirring. The layers were separated and the ethereal solution was washed neutral with copious quantities of water and dried ($MgSO_4$). The solvent was removed and the viscous oil which remained was warmed *in vacuo* for 3 hr. On cooling the oil solidified. The solid was recrystallized from hexane, to give 73.2 g (77%) of the alcohol: mp 65–68° (lit.[11] 68–69°); ir (melt) 3230 cm^{-1} (OH); nmr (CS_2) τ 2.79–3.27 (m, 6 H, thiophene), 4.40 (d, 1 H, *J* = 4 Hz, methine), 6.85 (d, 1 H, *J* = 4 Hz, OH).

2-Bromo-3,3′-dithienylmethane (27).—A solution of 3,3′-dithienylmethane (16.7 g, 93 mmol) in carbon tetrachloride (65 ml) was briskly added to a vigorously stirred mixture of bromine (14.85 g, 0.186 g-atom) and water (500 ml) at 15°. After 15 min the solution had turned colorless. Stirring was continued for an additional 10 min and ether (300 ml) was added. The layers were separated and the organic layer was extracted with ether (100 ml). The combined organic portions were washed with saturated sodium bicarbonate solution, then with water, and dried ($MgSO_4$). The ethereal solution was concentrated and the resulting oil was fractionated giving 3,3′-dithienylmethane (3.2 g), bp 65–75° (0.05 mm), and 2-bromo-3,3′-dithienylmethane (13.2, g, 68% based on unrecovered starting material), bp 85–95° (0.05 mm). An analytical sample was obtained by repeated distillation: bp 95–99° (0.1 mm); nmr (CS_2) τ 2.77–3.45 (m, 5 H, thiophene), 6.18 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_9H_7BrS_2$: C, 41.70; H, 2.72; Br, 30.83; S, 24.74. Found: C, 41.59; H, 2.50; Br, 30.62; S, 24.49.

Fair quantities of both 2,2-dibromo-3,3-dithienylmethane (mp 41–43°, lit.[10] 43°) and 2,2′,5,5′-tetrabromo-3,3′-dithienylmethane were isolated when the addition rate for 3,3′-dithienylmethane was slow. The tetrabromide was recrystallized from hexane as white needles: mp 102–103°; nmr (CS_2) τ 3.32 (s, 2 H, thiophene), 6.25 (s, 2 H, $-CH_2-$).

Anal. Calcd. for $C_9H_4Br_4S_2$: C, 21.80; H, 0.81; Br, 64.46; S, 12.93. Found: C, 21.76; H, 0.76; Br, 64.31; S, 13.05.

3,3′-Dithienylmethane-2-carboxylic Acid (28).—A solution of 2-bromo-3,3′-dithienylmethane (33 g, 0.13 mol) in absolute ether (75 ml) was added dropwise to an ethereal *n*-butyllithium solution (92 ml, 1.55 *M*, 0.14 mol) which was maintained at −70°. The mixture was stirred for 30 min and run to excess Dry Ice. After warming to room temperature, the reaction mixture was poured into ice and water (400 ml) and shaken vigorously. The layers were separated and the organic phase was washed with water (150 ml). The combined aqueous portions were acidified with excess 2 *M* hydrochloric acid. The resulting precipitate was taken up in ether and dried ($MgSO_4$). The solvent was evaporated leaving 25.8 g of white solid, which was recrystallized from acetonitrile as white clusters (24.2 g, 85%): mp 135–136°; ir (KBr) 1655 cm^{-1} (acid C=O); nmr (CS_2) τ −2.8 (s, 1 H, COOH), 2.67 (d, 1 H, $J_{2,3}$ = 5 Hz, thiophene), 2.82–3.02 (m, 1 H, thiophene), 3.07–3.29 (m, 3 H, thiophene), 5.72 (s, 2 H, $-CH_2-$).

Anal. Calcd. for $C_{10}H_8O_2S_2$: C, 53.55; H, 3.59; S, 28.59. Found: C, 53.33; H, 3.77; S, 28.77.

Benzo[1,2-*b*:5,4-*b*′]dithiophen-8-ol (7e).—Phosphorus pentachloride (6.24 g, 30 mmol) was added portionwise to a stirred solution of 3,3′-dithienylmethane-2-carboxylic acid (6.72 g, 30 mmol) in dry benzene (25 ml) which was maintained at 4°. The mixture was then warmed on a steam bath until the evolution of hydrogen chloride had ceased. The resulting acid chloride solution was dropwise added to a stirred solution of stannic chloride (4.8 ml, 10.6, g 40 mmol) in dry benzene (100 ml) at 4°. The mixture was allowed to come to room temperature and was stirred for 2 hr. The green suspension was heated to reflux, then was cooled, and poured into ice and 2 *M* hydrochloric acid (100 ml). The layers were separated and the aqueous phase was extracted with a benzene–ether solution (1:1, 150 ml). The combined organic portions were washed with saturated sodium bicarbonate solution and with water, then dried ($MgSO_4$), and concentrated to 100 ml. The warm solution was chromatographed on neutral silica gel, using benzene as the eluent. Evaporation of the solvent left a green-brown solid which was recrystallized from benzene–hexane giving large green-black clusters (1.6 g, 26%). An addition recrystallization from benzene–hexane provided an analytical sample: mp 140.5–142°; uv max (95% C_2H_5OH) 246 mμ (ε 54,500), 253 (61,600), 298 (7770), 309 (9500), 321 (8120), 335 (7550); ir (KBr) 3330 cm^{-1} (OH), no carbonyl absorption was observed. The nmr spectra of **7e** appear in Table II.

Anal. Calcd for $C_{10}H_6OS_2$: C, 58.22; H, 2.93; S, 31.09. Found: C, 58.07; H, 3.05; S, 30.97.

8-Acetoxybenzo[1,2-*b*:5,4-*b*′]dithiophene (29).— A stirred mixture of 3,3′-dithienylmethane-2-carboxylic acid (2.24 g, 10 mmol), glacial acetic acid (28 ml), acetic anhydride (20 ml), and dry zinc chloride (0.23 g, 1.7 mmol) was heated at reflux for 15 min and while still hot was cautiously diluted with water (48 ml). The resulting white crystalline solid was filtered, dried *in vacuo*, and sublimed (100°, 0.1 mm). The yield was 1.9 g, 77%. An analytical sample was obtained by recrystallization from acetic acid–water as long white needles: mp 127.5–128.5°; ir (KBr) 1765 cm^{-1} (acetate C=O); uv max (95% C_2H_5OH) 244 mμ (ε 53,600), 252 (57,600), 294 (7250), 303 (8160), 314 (sh, 4400), 328 (2210); nmr (acetone-d_6) τ 1.75 (s, 1 H, C_4 hydrogen), 2.36 (d, 2 H, $J_{2,3}$ = 5 Hz, thiophene), 2.50 (d, 2 H, $J_{2,3}$ = 5 Hz, thiophene), 7.52 [s, 3 H, $-OC(=O)CH_3$].

Anal. Calcd. for $C_{12}H_8O_2S_2$: C, 58.04; H, 3.25; S, 25.83. Found: C, 57.78; H, 3.31; S, 25.95.

3-Bromo-2,3′-dithienylcarbinol (30).—A solution of 2,3-dibromothiophene (95.3 g, 0.39 mol) in dry ether (100 ml) was added dropwise to a freshly prepared ethereal solution of *n*-butyllithium (250 ml, 1.65 *M*, 0.41 mol) at −70° under nitrogen. The mixture was stirred at −70° for 30 min and then a solution of 3-thiophenecarboxaldehyde (44 g, 0.39 mol) in dry ether (100 ml) was added. After the addition was complete, the mixture was allowed to warm slowly to room temperature. Stirring was continued for an additional 12 hr. The mixture was poured into ice and water and shaken vigorously. The layers were separated and the aqueous phase was extracted with ether (100 ml). The combined organic portions were washed neutral with water and dried ($MgSO_4$). The solvent was removed leaving 68 g (63%) of a reddish brown oil, which was used without further purification.

A small portion of the product obtained from a similar experiment was chromatographed on neutral alumina using benzene–hexane (1:1) as the eluent. Repeated short-path distillation of the alcohol containing fraction provided an analytical sample of 3-bromo-2,3′-dithienylcarbinol as a clear, slightly yellow-green oil (80° bath, 0.05 mm) which solidified during prolonged refrigeration: mp 39–40°; ir (neat) 3400 cm^{-1} (OH); nmr (CS_2) τ 2.75–3.25 (m, 5 H, thiophene), 4.15 (s, 1 H, methine), 7.40 (s, 1 H, OH).

Anal. Calcd for $C_9H_7BrOS_2$: C, 39.28; H, 2.57; Br, 29.04; S, 23.30. Found: C, 39.42; H, 2.70; Br, 28.84; S, 23.09.

3-Bromo-2,3′-dithienylmethane (31).—A solution of aluminum chloride (42 g, 0.31 mol) in absolute ether (150 ml) was cautiously added to a cooled suspension of lithium aluminum hydride (12 g, 0.31 mol) in absolute ether (100 ml). The mixture was allowed to come to room temperature and a solution of unpurified 3-bromo-2,3′-dithienylcarbinol (68 g, ~0.25 mol) in absolute ether (200 ml) was added at such a rate as to promote a gentle reflux. The suspension was maintained at reflux for an additional 30 min and then cooled by means of an ice bath. The excess hydride was decomposed by dropwise addition of 3 *M* sulfuric acid. The mixture was poured into ice and 1 *M* hydrochloric acid and worked up in the manner described for **13**. After the solvent was removed, the residue was fractionated yielding 3-bromo-2,3′ dithienylmethane (42 g, 66%) as a colorless liquid: bp 95–100° (0.1 mm) [lit.[10] bp 102–106° (0.2 mm)]; nmr (CS_2) τ 2.77 3.21 (m, 5 H, thiophene), 5.95 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_9H_7BrS_2$: C, 41.70; H, 2.72; Br, 30.83; S, 24.74. Found: C, 41.75; H, 2.56; Br, 30.59; S, 25.02.

2,3′-Dithienylmethane-3-carboxylic Acid (32).—A solution of 3-bromo-2,3′-dithienylmethane (32 g, 0.12 mol) in absolute ether (100 ml) was added under a nitrogen atmosphere to an ethereal *n*-butyllithium solution (135 ml, 1.05 *M*, 0.14 mol) which was maintained at −70°. After stirring at −70° for 30 min, the solution was run onto excess Dry Ice. The mixture was allowed to come to room temperature and water (300 ml) was cautiously added. The layers were separated and the organic phase was washed with water (100 ml). The combined aqueous portions were acidified and worked up as described in the preparation of **14**. The resulting ethereal solution was concentrated leaving 26.8 g of a white solid. Recrystallization from acetonitrile gave 23 g (83%) of a white crystalline solid. An additional recrystallization from benzene–hexane provided the analytical sample: mp 132–133.5; ir (KBr) 1665 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 2.48–3.00 (m, 5 H, thiophene), 5.38 (s, 2 H, $-CH_2-$).

Anal. Calcd for $C_{10}H_8O_2S_2$: C, 53.55; H, 3.59; S, 28.59. Found: C, 53.71; H, 3.62; S, 28.30.

Benzo[1,2-*b*:4,5-*b*′]dithiophen-4-ol (8e).—A solution of 2,3′-dithienylmethane-3-carboxylic acid (4.48 g, 20 mmol) in dry benzene (50 ml) was transferred to a flame-dried, 300-ml, three-necked flask and maintained at 4° under a constant flow of nitrogen. Phosphorus pentachloride (4.16 g, 20 mmol) was added portionwise with stirring over a 45-min period. The mixture was then warmed until the evolution of hydrogen chloride ceased. The resulting solution was cooled to 4° and a solution of stannic chloride (3 ml, 6.7 g, 26 mmol) in dry benzene (50 ml) was added during 30 min. The mixture was stirred at room temperature for 2 hr and then heated to reflux, cooled, and poured into ice and 2 *M* hydrochloric acid. After vigorous shaking, 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, dried ($MgSO_4$), and concentrated to 50 ml. The resulting solution was chromatographed on a 20 cm × 2 cm column packed with neutral silica gel. Elution with benzene yielded a yellow-green solid, which was recrystallized from benzene–hexane to give 3.0 g (73%) of a lustrous black crystalline solid. Repeated recrystallization from benzene–hexane provided an analytical sample: mp 180–181°; uv max (95% C_2H_5OH) 227 mμ (ε 30,000), 246 (38,400), 253 (51,100), 276 (4600), 285 (6740), 296 (6370), 335 (10,450), 349 (12,450); ir (KBr) 3300 cm^{-1} (–OH), no carbonyl absorption was observed; nmr (polysol-*d*) τ 0.33

(broad s, 1 H, -OH), 2.08 (s, 1 H, C_8 hydrogen), 2.12–2.72 (m, 4 H, thiophene).

Anal. Calcd for $C_{10}H_6OS_2$: C, 58.22; H, 2.93; S, 31.09. Found: C, 58.37; H, 2.83; S, 30.90.

4-Acetoxybenzo[1,2-*b*:4,5-*b'*]dithiophene (33).—A stirred mixture of 2,3′-dithienylmethane-3-carboxylic acid (15 g, 67 mmol), glacial acetic acid (150 ml), acetic anhydride (105 ml), and freshly fused zinc chloride (1.3 g, 9.6 mmol) was heated at reflux for 15 min and while still hot was cautiously diluted with water (255 ml). The resulting yellow crystalline solid was filtered, dried *in vacuo* and purified by sublimation (90°, 0.1 mm). The yield was 12.5 g (75%). An analytical sample was obtained by recrystallization from benzene–hexane: mp 113–115°; uv max (95% C_2H_5OH) 231 mμ (ε 22,900), 246 (44,200), 254 (61,900), 289 (7680), 299 (8500), 323 (9620), 337 (14,900); ir (KBr) 1755 cm^{-1} (acetate C=O); nmr (CCl_4) τ 1.96 (s, 1 H, C_8 proton), 2.60–3.00 (m, 4 H, thiophene), 7.62 [s, 3 H, $-OC(=O)CH_3-$].

Anal. Calcd. for $C_{12}H_8O_2S_2$: C, 58.04; H, 3.25; S, 25.83. Found: C, 57.97; H, 3.39; S, 25.83.

Registry No.—**4k**, 31936-79-5; **5k**, 31981-26-7; **6e**, 31936-80-8; **7e**, 31936-81-9; **8e**, 31936-82-0; **12**, 31936-83-1; **13**, 17965-66-1; **14**, 31936-85-3; **16**, 31936-86-4; **17**, 31936-87-5; **18**, 31936-88-6; **21**, 31936-89-7; **22**, 31936-90-0; **23**, 31936-91-1; **25**, 31936-92-2; **27**, 31936-93-3; **27** tetrabromide, 31936-94-4; **28**, 31936-95-5; **29**, 31936-96-6; **30**, 17964-88-4; **31**, 17965-56-9; **32**, 31936-99-9; **33**, 31937-00-5.

Acknowledgment.—The authors wish to thank Dr. C. G. McCarty and Dr. J. Gruninger for their aid in the preparation of this manuscript and Mr. Robert Smith for recording some of the nmr spectra.

Pteridines. XXVI. Preparation and Properties of Some 3,4- and 5,6-Dihydropteridines[1,2]

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Received December 9, 1970

Treatment of 8-alkyl-7(8*H*)-pteridinone-6-carboxylic acid derivatives (substituted at position 4 with hydrogen or methyl) with sodium borohydride leads to the formation in high yield of bright yellow dihydro compounds which are 10,000 times weaker acids, and exhibit uv absorption maxima some 50–60 nm higher, than the starting pteridinones. The influence of 2 and 4 substituents on this reduction has been carefully examined, and evaluation of both spectroscopic (uv, ir, and nmr) and chemical data has shown conclusively that these reduction products are 3,4-dihydro derivatives, and not 4,8- (or 5,8-) dihydro derivatives as previously suggested. By contrast, catalytic reduction of the same series of 8-alkyl-7(8*H*)-pteridinone-6-carboxylic acids and esters has been shown to give 5,6-dihydro compounds with very different chemical and physical properties. It has been demonstrated that the 3,4-dihydro compounds rearrange quantitatively and irreversibly to the 5,6-dihydro isomers in trifluoroacetic acid solution. The preparation of 22 new 8-alkyl-7(8*H*)-pteridinone-6-carboxylic acids and esters, as well as the requisite pyrimidine precursors, is described.

Dihydropteridines are attracting considerable current attention because of their role as naturally occurring cofactors in one-carbon transfer reactions involving the folic acid coenzymes,[3] the enzymatic hydroxylation of phenylalanine to tyrosine,[4] and a variety of other oxygenase reactions,[5] and as intermediates in photosynthetic electron transport processes in higher plants and photosynthetic bacteria.[6] Previous uncertainties as to the location of the hydrogen atoms in certain dihydropteridines (such as drosopterin, isodrosopterin, neodrosopterin, dihydrofolic acid, etc.)[7] have led to numerous efforts to prepare model dihydropteridines of known structure. For these reasons we have reinvestigated and extended our finding of several years ago[8,9] that a number of 7(8*H*)-pteridinone-6-carboxylic acid derivatives were reduced with sodium borohydride to dihydro compounds with unusual chemical and physical properties. The present work was undertaken in an effort to delineate the structural features (primarily the substitution pattern in the pyrimidine ring) necessary for sodium borohydride reduction of 7(8*H*)-pteridinone-6-carboxylic acids to these novel dihydro derivatives and to settle the controversy which has developed concerning their structure.[10] We describe herein the preparation of the requisite pteridine precursors, and the pyrimidine intermediates required for their preparation, the reduction experiments carried out on these pteridines, both with sodium borohydride and with hydrogen in the presence of various catalysts, and, finally, both spectroscopic and chemical evidence which firmly establishes the sodium borohydride reduction products as 3,4-dihydro derivatives, and the catalytic reduction products as their 5,6-dihydro isomers.

Synthesis of Intermediates. Pyrimidines.—Most of the requisite 4-alkylamino-5-aminopyrimidines required in this work were prepared by standard procedures and used directly in the pteridine preparations. Some special cases are described below.

(1) For the previous paper in this series, see E. C. Taylor and K. Lenard, *Justus Liebigs Ann. Chem.*, **726**, 100 (1969).

(2) A part of this work was supported by a grant (CA-02551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service.

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