Synthesis and Tautomeric Properties of Some Potential 2-Hydroxythieno[3,2-*b*]thiophenes and 2-Hydroxythieno[2,3-*b*]thiophenes

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Several alkyl- and aryl-substituted potential 2-hydroxythieno[3,2-*b*]thiophenes and 2-hydroxythieno[2,3-*b*]thiophenes have been prepared by the hydrogen peroxide oxidation of the corresponding boronic acids; the structures of the compounds obtained have been determined by NMR spectroscopy. In no case could evidences be found for the presence of the hydroxy form of these compounds which instead exist as thiolactones; in the case of the thieno[2,3-*b*]thiophene system all of the compounds examined have the structure of thieno[2,3-*b*]thiophen-2(3*H*)-ones, while in the case of the thieno[3,2-*b*]thiophene the two isomeric thieno[3,2-*b*]thiophen-2(3*H*)-ones (B) and the thieno[3,2-*b*]thiophen-2(5*H*)-ones (D) could be identified. Compounds having the structure B were in every case those first obtained from the oxidation mixtures, but they sometimes isomerized to a mixture of B and D whose composition was influenced by the presence of substituents. The effects of the nature and of the position of substituents on the tautomeric equilibria have been explored; it was found that the isomers D were favored by the presence, in the 3 position, of substituents which could conjugate or hyperconjugate with the condensed thieno ring. The syntheses of a large number of thienothiophene derivatives, which were necessary as intermediates, are also described.

The properties of compounds having in principle the structure of hydroxythiophenes have been carefully investigated by Hörnfeldt and Gronowitz and by Lawesson, who have also developed easily available synthetic procedures which have made possible the study of the tautomeric properties of several differently substituted derivatives.[2] It has been observed that all the 2-hydroxythiophenes exist as thiolen-2-ones, with the exception of those holding substituents which can chelate with the OH function, which are instead true hydroxy heterocycles;[3] the enol form can also be observed in some aryl-substituted thiophenes.[4] 3-Hydroxythiophenes generally exist as a mixture of 4-thiolen-3-ones and 3-hydroxythiophenes[5] and also in this case chelation with electron-attracting groups causes these products to exist as intramolecularly hydrogen-bonded hydroxythiophenes.[6] Benzo[*b*]thiophenes exist exclusively as the benzo[*b*]thiophen-2(3*H*)-one and the benzo[*b*]thiophen-3(2*H*)-one, respectively.[7] Similar investigations have not been carried out with thienothiophenes; the few data available concern the cyclization of the 2- and 3-thienylthioacetic acids which both afforded the thieno[3,2-*b*]thiophen-3(2*H*)-one with no evidence of other tautomers.[8] In connection with ESR studies of nitroxides and radical anions of thienothiophene derivatives[9] and thieno[3,2-*b*]thiophene-2,5-diones[10] we have studied the tautomeric equilibria of some potential 2-hydroxy derivatives of thieno[3,2-*b*]thiophene and thieno[2,3-*b*]thiophene.[11]

All the products described in the present investigation were obtained through the hydrogen peroxide oxidation of the boronic acids of thienothiophenes, as described by Hörnfeldt and Gronowitz,[12] according to the following reactions.

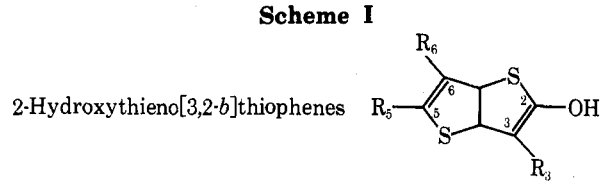
$$\text{Ar-Br} \xrightarrow{n\text{-BuLi}} \text{Ar-Li} \xrightarrow{B(OC_4H_9)_3} \text{Ar-B(OH)}_2 \xrightarrow{H_2O_2} \text{[Ar-OH]}$$

Ar = 2-thieno[3,2-*b*]thienyl and 2-thieno[2,3-*b*]thienyl

In one case the *p*-toluenesulfonic acid catalyzed dealkylation[13] of the *tert*-butoxythienothiophene was also employed. The products prepared and investigated are collected in Scheme I.

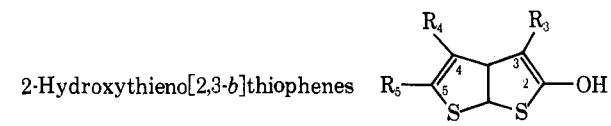
Compounds **7**, **8**, **14**, **15**, **17**, and **18** were not prepared with the general methods described above, but were obtained as by-products from the syntheses of the corresponding 2,5-dihydroxythienothiophenes which will be reported in a forthcoming paper;[10] their physical and spectral data and their tautomeric properties will, however, be described in this paper.

Scheme I



2-Hydroxythieno[3,2-*b*]thiophenes

1, $R_3 = R_5 = R_6 = H$
2, $R_3 = CH_3$; $R_5 = R_6 = H$
3, $R_3 = CH_2CH_3$; $R_5 = R_6 = H$
4, $R_3 = C_6H_5$; $R_5 = R_6 = H$
5, $R_5 = CH_3$; $R_3 = R_6 = H$
6, $R_3 = R_5 = CH_3$; $R_6 = H$
7, $R_6 = C(CH_3)_3$; $R_3 = R_5 = H$
8, $R_6 = C_6H_5$; $R_3 = R_5 = H$
9, $R_6 = CH_3$; $R_3 = R_5 = H$
10, $R_3 = R_6 = CH_3$; $R_5 = H$

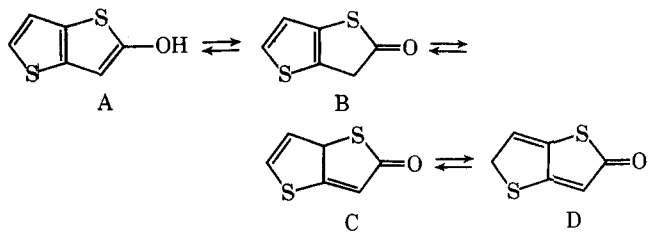


2-Hydroxythieno[2,3-*b*]thiophenes

11, $R_3 = R_4 = R_5 = H$
12, $R_3 = CH_3$; $R_4 = R_5 = H$
13, $R_3 = C_6H_5$; $R_4 = R_5 = H$
14, $R_4 = C(CH_3)_3$; $R_3 = R_5 = H$
15, $R_4 = C_6H_5$; $R_3 = R_5 = H$
16, $R_5 = CH_3$; $R_3 = R_4 = H$
17, $R_3 = R_4 = CH_3$; $R_5 = H$
18, $R_3 = R_4 = C_6H_5$; $R_5 = H$

2-Hydroxythieno[3,2-*b*]thiophenes. For this series of compounds the following four tautomeric forms can in principle be written (Scheme II).

Scheme II

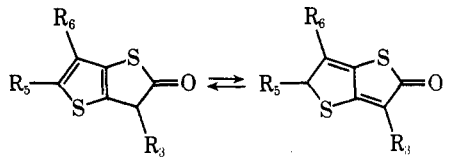


A B C D

The equilibrium compositions, in CS_2, for the tautomers of the variously substituted thieno[3,2-*b*]thiophen-2-ones, **1**–**10**, were established by NMR spectroscopy and are collected in Table I.

From the oxidation of the 2-thieno[3,2-*b*]thienylboronic

Table I
Equilibrium Compositions for the Tautomer of the Thieno[3,2-*b*]thiophen-2-ones 1-10 in CS_2



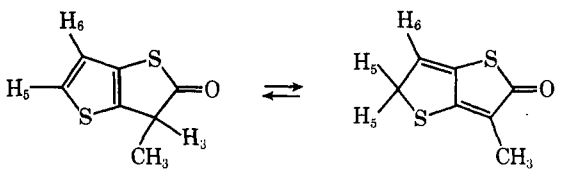
B D

	B	D
1, $R_3 = R_5 = R_6 = H$	100	
2, $R_3 = CH_3$; $R_5 = R_6 = H$	40	60
3, $R_3 = C_2H_5$; $R_5 = R_6 = H$	75	25
4, $R_3 = C_6H_5$; $R_5 = R_6 = H$	10	90
5, $R_5 = CH_3$; $R_3 = R_6 = H$	100	
6, $R_3 = R_5 = CH_3$; $R_6 = H$	100	
7, $R_6 = C(CH_3)_3$; $R_3 = R_5 = H$	100	
8, $R_6 = C_6H_5$; $R_3 = R_5 = H$	100	
9, $R_6 = CH_3$; $R_3 = R_5 = H$	85	15
10, $R_3 = R_6 = CH_3$; $R_5 = H$		100

acid a single crystalline product was obtained in good yield whose NMR spectrum, in CS_2, presented absorptions at δ 7.35 (1 H, doublet of triplets, J = 5.25 and 1.1 Hz), 6.9 (1 H, doublet of triplets, J = 5.25 and 0.5 Hz), and 3.78 (2 H, two doublets, J = 1.1 and 0.5 Hz). No other absorptions were detected and attempts to produce modifications by treatment with traces of acids or bases, which are known to catalyze the isomerization of hydroxythiophenes,[4] did not give any appreciable change. These results indicate that we are dealing with a single, relatively stable tautomer, to whom the structure of thieno[3,2-*b*]thiophen-2(3*H*)-one, (**1b**) can be confidently assigned; this attribution is also confirmed by the strong band at 1725 cm^{-1} in the ir spectrum and by the absence of the characteristic[14] uv spectrum of the thieno[3,2-*b*]thiophene ring.

The oxidation of the 3-methylthieno[3,2-*b*]thienylboronic acid afforded a reaction mixture in which only one isomer was present; the structure of the 3-methylthieno[3,2-*b*]thiophen-2(3*H*)-one (**2b**) was assigned to this compound on the basis of its NMR spectrum (Scheme III). After

Scheme III



40% 60%

2b **2d**

δ_{CH_3} = 1.41, J_{3-6} = 0.45 Hz
δ_3 = 3.78, J_{3-5} = 1.1 Hz
δ_6 = 6.9, J_{5-6} = 5.25 Hz
δ_5 = 7.35, J_{3-CH_3} = 7.5 H

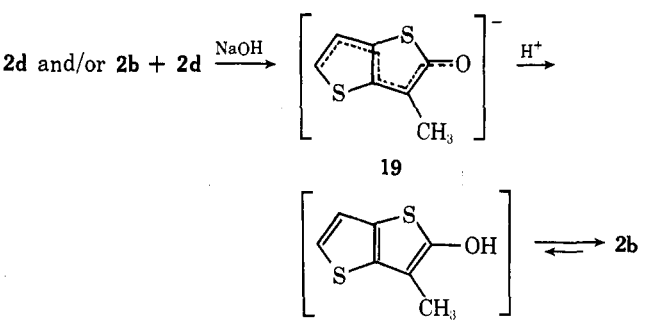
δ_{CH_3} = 1.87, J_{6-CH_3} = 0.45 Hz
δ_6 = 6.52 J_{5-CH_3} = 1.3 Hz
δ_5 = 4.25, J_{5-6} = 3.2 Hz

standing at room temperature or attempted purification by distillation or by column chromatography, this oily product invariably afforded a mixture with a second compound, which from the NMR spectrum is 3-methylthieno[3,2-*b*]thiophen-2(5*H*)-one (**2d**).

The ir spectra are in agreement with the proposed structures, the carbonyl stretching vibrations occurring at 1725 cm^{-1} for **2b** and at 1695 cm^{-1} for the isomer **2d** in which the carbonyl group is conjugated. Absorptions at 3450 and 3370 cm^{-1} observed for **2b** and **2d**, respectively, are attributed to the first overtone of the carbonyl stretching,[15] rather than to the presence of traces of hydroxy form **2a**. Integration of the NMR spectrum in CS_2 indicated an equilibrium composition of the two isomers **2b** and **2d** in the ratio of 40:60 ± 5. Equilibration could be greatly accelerated by the presence of catalytic amounts of gaseous HCl, triethylamine, or pyridine and the composition remained unchanged; the same equilibrium mixture was obtained starting from both pure **2b** or pure **2d** which could be prepared as described below.

The more stable form **2d** (or the tautomeric mixture) can be converted to the pure thieno[3,2-*b*]thiophen-2(3*H*)-one (**2b**) by the base-extraction method;[16] for this purpose, it was dissolved in cold dilute NaOH and the solution acidified in the presence of ether so that the lactones could be extracted in the organic phase as soon as they form (Scheme IV). The behavior of the 3-methyl-2-hydroxy-

Scheme IV



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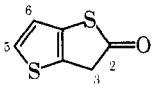
thieno[3,2-*b*]thiophene parallels that of 5-alkyl-substituted thiolen-2-ones,[4] studied by Hörnfeldt, and is in agreement with Ingold's rule[4] that in the protonation of a mesomeric anion of a weakly acidic tautomer, like **19**, the thermodynamically less stable tautomer is formed first.[17] The protonation of the mesomeric anion **19** should be an exothermic process in which the main factor governing the direction of attack by the proton will be the charge distribution in the anion; owing to its closer proximity to the electron-withdrawing oxygen atom, position 3 is thought to have the higher charge density and therefore the isomer **2b** will be formed more rapidly under conditions of kinetic control.[17]

Pure 3-methylthieno[3,2-*b*]thiophen-2(5*H*)-one (**2d**) can be obtained by taking advantage of its lower solubility. Treatment of the tautomeric mixture (or pure **2b**), dissolved in the minimum amount of ethanol, with a few drops of pyridine caused crystallization of **2d**. Thus the introduction of a methyl group in the 3 position of the thieno[3,2-*b*]thiophene nucleus increases the relative stability of conjugated form **2d** owing to hyperconjugation with the CH_3 group. This structure, which is not present at the equilibrium in the parent compound, becomes more stable than the thieno[3,2-*b*]thiophen-2(3*H*)-one (**2b**), in which one thiophene ring is still preserved. This modification is not unprecedented, since similar effect caused by the introduction of a methyl group in the 3 position was also observed in the simpler thiolen-2-ones.[4]

Table II[a]
Physical and Spectral (NMR in CS_2 and Ir in CCl_4) Data of the Thieno[3,2-*b*]thiophen-2(3*H*)-ones



Compd	Mp or bp, °C (mm)	>C=O, cm^{-1}	Chemical shifts, δ				Coupling constants, Hz			
			3	6	5	3'	J_{3-6}	J_{3-5}	J_{5-6}	$J_{3-3'}$
1b	94–95	1725	3.78	6.9	7.35		0.5	1.1	5.25	
2b	95–97 (1)	1725	3.78	6.9	7.35	1.41[b]	0.45	1.1	5.25	7.5
3b	98–100 (1)	1725	3.62	6.9	7.35	1.88, [c]0.95[b]	0.45	1.1	5.25	5.5,[d] 6.6,[d] 7.5[e]
4b	*h*	1730	4.75	6.9	7.35	7.2[f]	0.45	1.1	5.25	
5b	82–84	1725	3.73	6.6	2.52[b]		0.5	1.1	1.1	
6b	32–34	1720	3.65	6.55	2.48[b]	1.41[b]	0.4	1.1	1.1	7.5
7b[i]	53–55	1730	3.72	1.29[g]	6.92			1.05		
8b[i]	70–71	1730	3.82	7.32[f]	7.26			1.05		
9b	61–62	1725	3.78	2.22[b]	6.9		0.3	1.1	1.1	
10b	*h*	1725	3.75	2.21[b]	6.88	1.45[b]	0.3	1.1	1.1	7.5

[a] Satisfactory analytical data were reported for all the compounds listed in the table. [b] Methyl group. [c] CH_2 of the ethyl group. [d] Coupling constants between the H_3 and the two geminal hydrogens of the ethyl group. [e] $J_{CH_2-CH_3}$. [f] Phenyl group. [g] *tert*-Butyl group. [h] Not isolated (the NMR and ir data were determined from the mixture with the -2(5*H*)-one isomer). [i] Obtained as a by-product from the synthesis of the corresponding 2,5-dihydroxythieno[3,2-*b*]thiophene.

The enolic form **2a** and the thiolactonic compound, **2c**, which is conceivably less stable than **2b** and **2d**, could never be evidenced in the experiments described above.

Oxidation of the 3-ethylthieno[3,2-*b*]thienylboronic acid also afforded as the first-formed compound the pure 3-ethylthieno[3,2-*b*]thiophen-2(3*H*)-one (**3b**); this, however, rapidly isomerized to a mixture of the **3b** and **3d** forms in the ratio of 75:25, respectively, in agreement with the lower hyperconjugative effect of the ethyl in respect to the methyl group. Compound **3b** showed the peculiarity, which also constituted a proof of its structure, of giving an NMR pattern due to two magnetically different geminal hydrogens in the ethyl group indicating that it is linked to a chiral center; the different staggered conformations of the rotating ethyl group are not equally populated, thus making the two methylene protons nonequivalent. This is clearly revealed in the multiplicity shown by the H_3 proton which allowed the coupling constants reported in Table II to be determined; a complete analysis of the ethyl group was not undertaken.

Also in this case the base-extraction method applied to the pure isomers or to a tautomeric mixture afforded the kinetically favored tautomer **3b** in pure state.

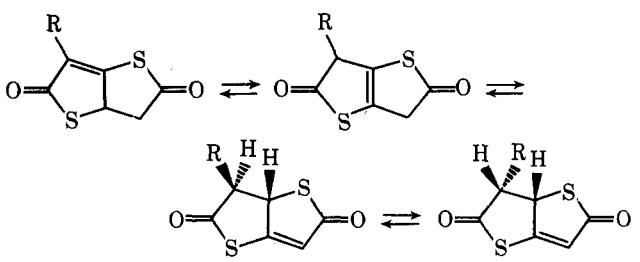
On passing to the 3-phenyl-substituted compound, **4**, the picture is modified in the expected way. The first-formed tautomer is still the kinetically favored 3-phenylthieno[3,2-*b*]thiophen-2(3*H*)-one (**4b**), but this is easily and rapidly isomerized to a mixture in which the 3-phenylthieno[3,2-*b*]thiophen-2(5*H*)-one (**4d**) largely predominates (**4b:4d** 10:90), a result which can be anticipated on the basis of the conjugation of the phenyl group with the carbon–carbon double bonds.

In this case the treatment of an alkaline solution of **4d** with acid did not give pure **4b** but a mixture in almost equimolecular amounts of the two, indicating that the base-extraction method is not so efficient to avoid a partial isomerization of **4b** to **4d** to occur; as a consequence a pure sample of the 3-phenylthieno[3,2-*b*]thiophen-2(3*H*)-one could not be obtained and analyzed.

Substituents in the 5 position cannot obviously contribute to the stabilization of the -2(5*H*)-one forms (D), whereas they can conjugate or hyperconjugate with the thiophene ring in the -2(3*H*)-one structures (B); accordingly only this latter tautomer is expected. Actually, the oxidation of the 5-methylthieno[3,2-*b*]thienylboronic acid afforded the 5-methylthieno[3,2-*b*]thiophen-2(3*H*)-one (**5b**); no indication of the formation of other tautomers could be found on attempted equilibration with acids or after treatment with alkali.

The strong stabilization of the thiophenic structure (B) by the methyl group in the 5 position is clearly demonstrated also in the case of 3,5-dimethylthieno[3,2-*b*]thiophen-2-one (**6**), where, notwithstanding the presence of a methyl group in 3, the fully conjugated tautomer (D) could not be detected and the only product obtained was 3,5-dimethylthieno[3,2-*b*]thiophen-2(3*H*)-one (**6b**).

The effect of substituents in the 6 position cannot easily be predicted and a rather complex situation should result from the fact that from this position they can exert their stabilizing properties on both the -2(3*H*)-one and the -2(5*H*)-one tautomers; the relative stability of the two isomers should reflect the balance of these effects for the various substituents. The first two compounds of this group investigated were the 6-*tert*-butyl (**7**) and the 6-phenyl (**8**), which were formed as by-products from the synthesis of the corresponding 2,5-dihydroxythieno[3,2-*b*]thiophenes (**20**), in connection with a parallel investigation of their tautomeric properties,[10] and their oxidation to the diones **21**.



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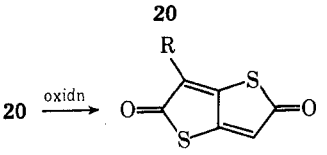

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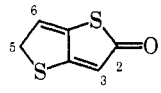
Both compounds **7** and **8** exist exclusively as thieno[3,2-*b*]thiophen-2(3*H*)-ones (B) and no indication of the pres-

Table III[a]
Physical and Spectral (NMR in CS_2, Ir in CCl_4) Data of the Thieno[3,2-*b*]thiophen-2(5*H*)-ones



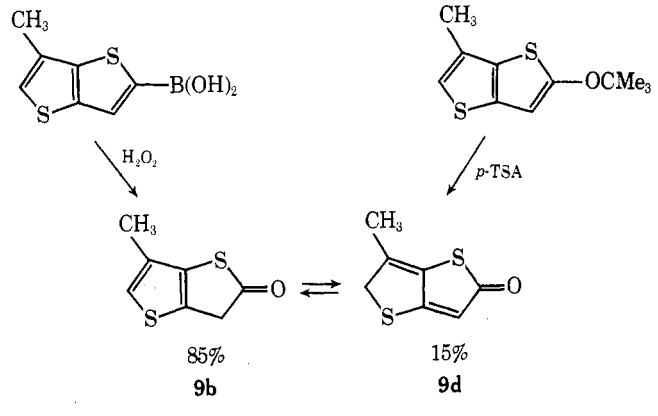
Compd	Mp, °C	>C=O, cm^{-1}	Chemical shifts, δ				Coupling constants, Hz			
			3	6	5		J_{3-6}	J_{3-5}	J_{5-6}	
2d	109–110	1695	1.87[b]	6.52	4.25		0.4	1.3	3.2	
3d	98–99	1695	2.3[c]	6.38	4.25	1.1[b]		1.0	3.2	7.5[d]
4d	101–102	1695	7.55–7.2[e]	6.47	4.30				3.3	
9d	*g*	1695	5.8	2.15[b]	4.15		0.4	1.35	1.35	
10d[f]	127–128	1690	1.82[b]	2.13[b]	4.1		0.4	1.2	1.4	

[a] Satisfactory analytical data were reported for all the compounds listed in the table. [b] Methyl group. [c] CH_2 of the ethyl group. [d] $J_{CH_2-CH_3}$. [e] Phenyl group. [f] The attribution has been made with reference to the chemical shifts of the methyl group in compounds **2b** and **9b**. [g] Not isolated (the NMR and ir data were determined from the mixture with the -2(3*H*)-one isomer).

ence of the -2(5*H*)-one form could be found on attempted isomerization with acids or bases.

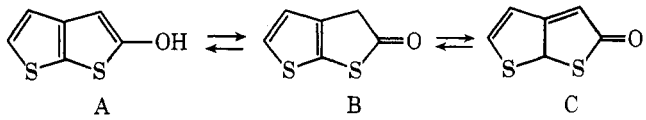
The oxidation of 6-methylthieno[3,2-*b*]thienylboronic acid afforded instead a mixture of the two isomers **9b** and **9d** in the ratio of 85:15; only the -2(3*H*)-one **9b** isomer could, however, be obtained after work-up of the reaction mixture. Essentially the same results were obtained when the *p*-toluenesulfonic acid catalyzed dealkylation of the 2-*tert*-butoxy-6-methylthieno[3,2-*b*]thiophene (**22**) was utilized for the synthesis of the potential hydroxy derivative (Scheme V).

Scheme V

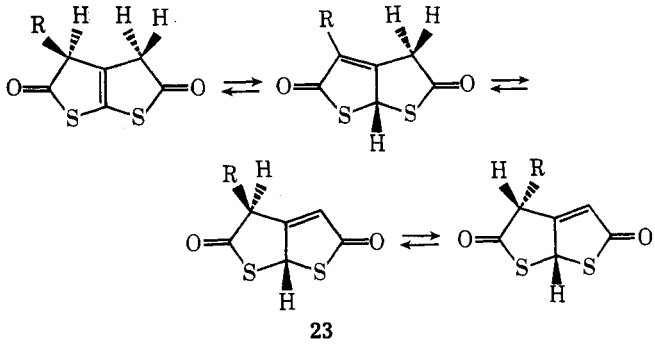


A similar mixture of the two tautomers was also obtained by the base-extraction method applied to **9b**. These results indicate that a methyl group stabilizes to a certain extent the -2(5*H*)-one tautomeric form (D) also when it is present in the 6 position and, as a final example of this group of compounds, the 3,6-dimethyl derivative, **10**, was synthetized with the expectation that in this case the carbonyl conjugated form (D) should have a much greater stability than the isomeric -2(3*H*)-one, **10b**. Actually the 3,6-dimethylthieno[3,2-*b*]thiophen-2(3*H*)-one (**10b**), which exclusively formed from the oxidation of the boronic acid, very easily isomerized completely to the more stable 3,6-dimethylthieno[3,2-*b*]thiophen-2(5*H*)-one (**10d**). When **10d** was dissolved in alkali and then acidified in the presence of ether a mixture of the two tautomers was obtained in which **10d** predominated (**10b:10d** 20:80); this mixture, on standing or on attempted manipulation, afforded pure **10d**.

2-Hydroxythieno[2,3-*b*]thiophenes. The following three tautomeric structures can in principle be expected for this class of compounds. The synthesis of these compounds has been carried out in the usual way by the oxidation of



the corresponding boronic acids; several of them were, however, formed as by-products[10] in the preparation of the 2,5-dihydroxythieno[2,3-*b*]thiophenes (**23**). All the potential 2-hydroxythieno[2,3-*b*]thiophenes investigated existed as a single product which remained unchanged on treatment with acids or bases; dissolution of these compounds in alkali followed by acidification in the presence of ether afforded the starting products without any evidence of the formation of other tautomers. NMR and ir data (see Table IV) indicated that these compounds have the structure of thieno[2,3-*b*]thiophen-2(3*H*)-ones (B).

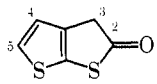


In this case, therefore, at variance with what is observed in the thieno[3,2-*b*]thiophenes, the condensed thieno ring is not involved in the tautomeric equilibrium, notwithstanding that in the thieno[2,3-*b*]thiophen-2(7*H*)-one structure (C) the carbonyl group could conjugate with the two carbon–carbon double bonds as in the case of the thieno[3,2-*b*]thiophen-2(5*H*)-ones; ring strain effects, which will prevent the two rings from reaching complete coplanarity, are probably responsible for the unstability of the tautomeric -2(7*H*)-one structure (C).

In order to test their chemical behavior, few reactions have been carried out with some of the potential 2-hydroxythienothiophenes here described with the expectation that derivatives could be obtained both from the enol and from the thiolactone forms; the reactions with acyl chlorides, aldehydes, ketones, and diazoalkanes indeed occurred at the oxygen and/or at the carbon atoms holding the active methylene groups. The results of these experiments are discussed in the accompanying paper.

Compounds **11–18** as well as **1–10** in both the tautomeric

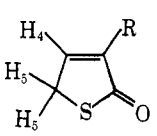
Table IV[a]
Physical and Spectral (NMR in CS_2 and Ir in CCl_4) Data of the Thieno[2,3-*b*]thiophen-2(3*H*)-ones



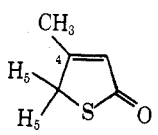
Compd	Mp or bp, °C (mm)	>C=O, cm^{-1}	Chemical shifts, δ				Coupling constants, Hz			
			3	4	5	3'	J_{3-4}	J_{3-5}	J_{4-5}	$J_{3-3'}$
11	84–86	1735	3.70	6.90	7.21		0.5	0.2	5.2	
12	94–96 (0.8)	1730	3.61	6.88	7.18	1.41[b]	0.5	0.2	5.2	7.5
13	102–104	1730	4.65	6.7	7.13	7.05[c]	0.5	0.2	5.2	
14[e]	143–145 (1.5)	1735	3.65	1.25[d]	6.70			*f*		
15[e]	106–107	1735	3.70	7.1[c]	6.95			*f*		
16	109–110	1730	3.59	6.55	2.49[b]		0.5	0.2	1.1	
17[e]	95–96 (0.5)	1730	3.55	2.24[b]	6.76	1.46[b]		*f*	1.1	7.5
18[e]	86–88	1735	4.55	6.88	7.0[c]	6.88[c]		*f*		

[a] Satisfactory analytical data were recorded for all the compounds listed in the table. [b] Methyl group. [c] Phenyl group. [d] *tert*-Butyl group. [e] Obtained as a by-product from the synthesis of the corresponding 2,5-dihydroxythieno[2,3-*b*]thiophene. [f] Not resolved.

forms B and D give rise to NMR spectra which can be easily interpreted by first-order treatment and which are extremely useful in the structural assignments. Thus the aromatic protons or the methyl groups in positions 4 and 5 in the series of the thieno[2,3-*b*]thiophen-2(3*H*)-ones or in the 5 and 6 positions of the thieno[3,2-*b*]thiophen-2(3*H*)-ones have chemical shifts and coupling constants in excellent agreement with the values expected for a 2,3-disubstituted thiophene or methylthiophene. The same groups in the thieno[3,2-*b*]thiophen-2(5*H*)-ones (D) have J_{5-6} coupling constants of 3.2–3.3 Hz which become 1.4 Hz when a methyl group is present in the 6 position; these values are quite similar to those reported by Hörnfeldt and Gronowitz[4] for the coupling between the protons in the 5 and 4 positions of the 3-thiolen-2-one **24** (J_{5-4} = 3–3.4 Hz) and of the 4-methyl-3-thiolen-2-one **25** ($J_{5\text{-}CH_3}$ = 1.5 Hz).



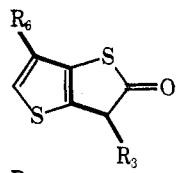
24



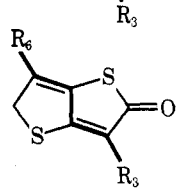
25

Interesting long-range couplings are observed in the thieno[3,2-*b*]thiophen-2-ones between protons in the 3 position and those in the 5 and 6 positions in both the systems of the -2(3*H*)-one (B) and of -2(5*H*)-one (D) (Scheme VI). J_{3-6} is 0.4–0.5 Hz in the thieno[3,2-*b*]thiophen-2(3*H*)-ones **1b–6b** and becomes 0.3 Hz when a methyl group is placed in 6 position (**9b** and **10b**); a 0.4-Hz coupling is also observed in the thieno[3,2-*b*]thiophen-2(5*H*)-ones holding a methyl group in the 3 position, **2d**, or in the 6 position, **9d**, and this coupling remains of the same magnitude even in compound **10d**, where two methyls are present at the two extreme carbon atoms. A 0.4-Hz coupling is also observed[10] in 3-methylthieno[3,2-*b*]thiophene-2,5-dione (**26**), which is structurally very similar to the corresponding -2(5*H*)-ones. The J_{3-6} observed in these compounds may be related to the J_{3-6} observed in the thieno[3,2-*b*]thiophene[18] or its 2-bromo[18] or 2-methyl[19] derivatives, which have couplings of 0.7, 0.69, and 0.5 Hz, respectively; a J_{3-6} = 0.6 Hz is also found in the 2-bromo-5-methylthieno[3,2-*b*]thiophene described in the present paper. A similar coupling has been reported for benzo[*b*]thiophene[20] between the protons in the 3 and 7 positions. The 0.4-Hz coupling between the two methyl groups of **10d** represents an example of coupling over as many as seven bonds which has previously been observed only in a few cases such as the polyacetylenic compounds[21] and 5-methyl-3-acetonylidene-4-thiolen-2-one (**27**).[4]

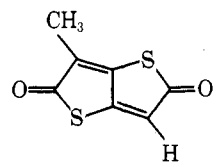
Scheme VI



$R_3 = R_6 = H$; J_{3-6} = 0.4–0.5 Hz
$R_3 = R_6 = CH_3$; J_{3-6} = 0.3 Hz

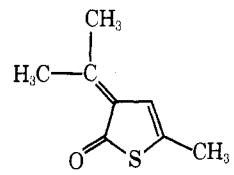


$R_3 = CH_3$, $R_6 = H$; J_{3-6} = 0.4 Hz
$R_3 = H$, $R_6 = CH_3$; J_{3-6} = 0.4 Hz
$R_3 = R_6 = CH_3$; J_{3-6} = 0.4 Hz



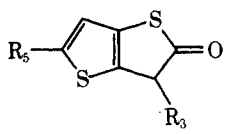
J_{3-6} = 0.4 Hz

26

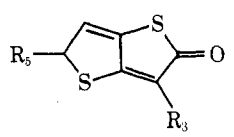


J = 0.7–0.8 Hz

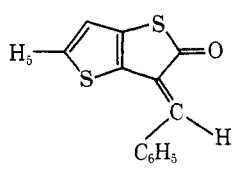
27



$R_3 = R_5 = H$; J_{3-5} = 1.1 Hz
$R_3 = H$, $R_5 = CH_3$; J_{3-5} = 1.1 Hz



$R_3 = R_5 = H$; J_{3-5} = 1.35 Hz
$R_3 = CH_3$, $R_5 = H$; J_{3-5} = 1.2–1.35 Hz



J_{CH-5} = 0.7 Hz

28

A long-range coupling is also observed in the lactones of the thieno[3,2-*b*] series between protons in positions 3 and 5. In the thieno[3,2-*b*]thiophene this coupling is small and negative;[18] in the products here described J_{3-5} has the value of 1.0–1.1 Hz in the -2(3*H*)-ones (B) and of 1.2–1.3 Hz in the -2(5*H*)-ones (D); in both cases the coupling remains practically unaffected when a hydrogen linked to the unsaturated carbon [R_5 in the -2(3*H*)-ones and R_3 in the -2(5*H*)-ones] is replaced by a methyl group. A similar long-range coupling (0.7 Hz) was also detected[22] in compound **28** between the benzylidene proton and the ring proton in position 5. The fact that the magnitude of the proton–proton coupling constants, J_{3-5} and J_{3-6}, remains practically unchanged when an olefinic or ring proton is substituted by a methyl group can be taken as an indication of a π-electron transmitted interaction.[21,23]

Finally, in the case of 3-ethylthieno[3,2-*b*]thiophen-2(5*H*)-one (**3d**), the J_{3-6} becomes so small that it could not be resolved and the J_{3-5} was reduced to 1 Hz; this can probably be associated with the conformational requirements of the ethyl group which causes the C–CH_3 bond to lie preferentially perpendicular to the molecular plane. A similarly interpretable decrease of the hyperfine splitting constant of the alkyl protons was observed in the radical anions of the thieno[3,2-*b*]thiophene-2,5-diones on passing from the 3-methyl to the 3-ethyl derivatives.[10]

Experimental Section[24]

2-Bromothieno[3,2-*b*]thiophene (**29**) and 2-bromothieno[2,3-*b*]thiophene (**30**) were prepared as described in the literature.[25]

2-Bromo-3-methylthieno[3,2-*b*]thiophene (31). To a solution of 3-methylthieno[3,2-*b*]thiophene[26] (4.2 g) in acetic acid (100 ml), *N*-bromosuccinimide (NBS, 4.9 g) was added in small portions and the mixture was stirred at room temperature for 2 hr. The solution was poured on water and extracted with chloroform several times; the organic layer was separated, washed with water and $NaHCO_3$ solution, and dried. The solvent was evaporated and the residue distilled: bp 106–108° (1 mm) (5.5 g); NMR (CS_2) δ_{CH_3} 2.25, δ_5 7.25, δ_6 7.01, J_{5-6} = 5.2 Hz.

Anal. Calcd for $C_7H_5BrS_2$: C, 36.06; H, 2.16; Br, 34.28; S, 27.50. Found: C, 36.02; H, 2.23; Br, 35.0; S, 27.35.

3-Acetylthieno[3,2-*b*]thiophene (32). To a solution of *n*-butyllithium (prepared from 0.85 g of lithium) in ether cooled at −70°, 3-bromothieno[3,2-*b*]thiophene[25] (12 g) was added and the mixture was stirred for 1 hr. Then *N*,*N*-dimethylacetamide (12 ml) dissolved in ether was added dropwise and the reaction mixture was stirred at −70° for 3 hr and then overnight at room temperature. Water was added and the ether layer was treated with dilute HCl, washed with water, dried, and evaporated. The solid residue (11 g) was chromatographed through silica gel with light petroleum–ether (9:1) as eluent. A solid product was collected which melted at 81–82° after crystallization from ethanol, NMR (CS_2) δ_2 7.95, δ_5 7.4, δ_6 7.1, δ_{COCH_3} 2.45, J_{5-6} = 5.1, J_{2-5} = 1.6 Hz.

Anal. Calcd for $C_8H_6OS_2$: C, 52.72; H, 3.32; S, 35.18. Found: C, 52.75; H, 3.29; S, 35.10.

3-Ethylthieno[3,2-*b*]thiophene (33). A mixture of **32** (7 g), 85% hydrazine (3.5 ml), KOH (4.4 g), and diethylene glycol (35 ml) was refluxed for 2 hr and the water formed slowly distilled off. The resulting mixture was boiled for 3 hr more and then poured on water and extracted with ether. The organic solution was washed with water, dried, and evaporated. The residue was distilled to give 4.5 g of **33**: bp 85–86° (0.3 mm); NMR (CS_2) δ_2 6.82, δ_5 7.16, δ_6 7.05, δ_{CH_2} 2.62, δ_{CH_3} 1.29, $J_{CH_2-CH_3}$ = 7.5, J_{2-CH_2} = 1.1, J_{2-5} = 1.5, J_{5-6} = 5.2 Hz.

Anal. Calcd for $C_8H_8S_2$: C, 57.10; H, 4.79; S, 38.11. Found: C, 57.04; H, 4.80; S, 38.21.

2-Bromo-3-ethylthieno[3,2-*b*]thiophene (34) and 2,5-Dibromo-3-ethylthieno[3,2-*b*]thiophene (35). Treatment of **33** (4.5 g) with NBS (2.67 g) as described above for **31** afforded a mixture (3.5 g) of mono- and dibromo derivatives together with some unreacted **33** which was separated by column chromatography through silica gel with light petroleum as eluent. The dibromo compound was eluted first: NMR (CS_2) δ_6 7.02, δ_{CH_2} 2.68, δ_{CH_3} 1.24, $J_{CH_2-CH_3}$ = 7.5 Hz. This was not further analyzed. Then the desired product **34** was obtained as an oil: bp 115° (1 mm); NMR (CS_2) δ_5 7.25, δ_6 7.02, δ_{CH_2} 2.69, δ_{CH_3} 1.25, $J_{CH_2-CH_3}$ = 7.5, J_{5-6} = 5.1 Hz.

Anal. Calcd for $C_8H_7BrS_2$: C, 38.87; H, 2.85; S, 25.94; Br, 32.33. Found: C, 39.0, H, 2.85; S, 26.05; Br, 32.80.

2-Bromo-3-phenylthieno[3,2-*b*]thiophene (36). Treatment of 3-phenylthieno[3,2-*b*]thiophene[7] (2.16 g) with NBS (1.78 g) as described above for **31** afforded a product which was purified by column chromatography on silica gel, using light petroleum as eluent. Pure **36** (3.15 g) melted at 77–78°; NMR (CS_2) δ_5 7.3, δ_6 7.05, $\delta_{C_6H_5}$ 7.4, J_{5-6} = 5.1 Hz.

Anal. Calcd for $C_{12}H_7BrS_2$: C, 48.82; H, 2.39; Br, 27.07, S, 21.72. Found: C, 48.9; H, 2.45; Br, 27.25; S, 22.00.

2-Bromo-5-methylthieno[3,2-*b*]thiophene (37). Treatment of 2-methylthieno[3,2-*b*]thiophene[19] (4.3 g) with NBS (4.9 g) in CH_3COOH (90 ml) as described above for **31** afforded the desired product (6 g) with mp 128–129° after crystallization from ethanol; NMR (CS_2) δ_{CH_3} 2.52, J_{3-6} = 0.6 and J_{CH_3-6} = 1.1 Hz.

Anal. Calcd for $C_7H_5BrS_2$: C, 36.06; H, 2.16; Br, 34.28; S, 27.50. Found: C, 36.17; H, 2.16; Br, 34.24; S, 27.60.

3,5-Dimethylthieno[3,2-*b*]thiophene (38). To a solution of *n*-butyllithium (prepared from 0.35 g of lithium) cooled at −70°, 3-bromo-5-methylthiophene[27] (4 g) was added dropwise and the mixture was kept at this temperature for 30 min. Sulfur (1 g) was then added and the temperature was allowed to gradually rise to −10°; to this solution containing the lithium salt of the 5-methyl-3-mercaptothiophene chloroacetone (3 g) was added and the mixture was stirred at room temperature overnight. The mixture was poured on water and the ether layer was washed, dried, and evaporated. The residue was distilled to afford (5-methyl-3-thienylthio)acetone (**39**) (3.5 g): bp 125–126° (1 mm); NMR (CS_2) δ 2.15 (t, 3 H, CH_3CO, J = 0.3 Hz), 2.41 (d, 3 H, CH_3 in 5, J = 1.1 Hz), 3.38 (g, 2 H, CH_2CO, J = 0.3 Hz), 6.53 (d, q, 1 H, J = 1.5, J' = 1.1 Hz), 6.78 (d, 1 H, J = 1.5 Hz).

Anal. Calcd for $C_8H_{10}OS_2$: C, 51.58; H, 5.41; S, 34.42. Found: C, 51.49, H, 5.47; S, 34.86.

To a stirred mixture of $AlCl_3$ (3 g) and CS_2 (60 ml) a solution of **39** (3.2 g) in CS_2 was added and the mixture was stirred at room temperature for 24 hr. Water was added and the organic layer was separated, washed, and dried. Evaporation of the solvent afforded an oil which was distilled under vacuum to afford 2 g of **38**: bp 98–100° (2 mm); NMR (CS_2) δ_3 2.21, δ_5 2.46, δ_6 6.65, δ_2 6.67, J_{2-3} = 1.2, J_{6-5} = 1.2, and J_{2-5} = 0.3 Hz.

Anal. Calcd for $C_8H_8S_2$: C, 57.10; H, 4.79; S, 38.11. Found: C, 57.19; H, 4.74; S, 38.20.

2-Bromo-3,5-dimethylthieno[3,2-*b*]thiophene (40) and 2,6-Dibromo-3,5-dimethylthieno[3,2-*b*]thiophene (41). Treatment of **38** (1.7 g) with NBS (1.8 g) in CH_3COOH (30 ml) afforded a mixture of products which was separated by column chromatography on Florisil using hexane as eluent. Compound **41** was eluted first (0.4 g), mp 127–129° from ethanol, NMR (CS_2) δ_3 2.22, δ_5 2.45.

Anal. Calcd for $C_8H_6Br_2S_2$: C, 29.47; H, 1.85; S, 19.66. Found: C, 30.21; H, 1.90; S, 20.01.

A second fraction contained the monobromo derivative **40** (1.7 g), bp 148–150° (2 mm), NMR (CS_2) δ_3 2.18, δ_5 2.48, δ_6 6.65, J_{5-6} = 1.1 Hz.

Anal. Calcd for $C_8H_7BrS_2$: C, 38.87; H, 2.85; Br, 32.33; S, 25.94. Found: C, 38.76; H, 2.90; Br, 32.71; S, 26.02.

2-Bromo-6-formylthieno[3,2-*b*]thiophene (42). Treatment of 3-formylthieno[3,2-*b*]thiophene[28] (2 g) with NBS (1.9 g) as described above for **31** afforded a solid product (2.9 g) which was purified by chromatography on silica gel using a 1:1 mixture of light petroleum–ether as eluent, mp 104–105°, NMR (CS_2) δ_{CHO} 9.89 (s), δ_5 8.2 (s), δ_3 7.25 (s).

Anal. Calcd for $C_7H_3BrS_2O$; C, 34.02; H, 1.22; Br, 32.34; S, 25.95. Found: C, 34.10; H, 1.22; Br, 32.28; S, 25.70.

2-Bromo-6-methylthieno[3,2-*b*]thiophene (43). A mixture of **42** (3.5 g), diethylene glycol (12 ml), KOH (1.9 g), and 85% hydrazine (1.2 ml) was refluxed for 1 hr and the water formed distilled off. The temperature was raised to 170–180° and the mixture was stirred at this temperature for 3 hr and then poured on water. Extraction with ether afforded, after evaporation of the solvent, an oil which was purified by distillation: bp 120° (2 mm) (1.3 g); NMR (CS_2) δ_3 7.06, δ_5 6.85, δ_{CH_3} 2.26, J_{CH_3-5} = 1.1 Hz.

2,3,5-Tribromo-6-methylthieno[3,2-*b*]thiophene (44). To a solution of 3-methylthieno[3,2-*b*]thiophene[26] (1.54 g) in CS_2 (15 ml), bromine (5.3 g) in CS_2 (5 ml) was added dropwise and the resulting mixture was stirred at room temperature for 14 hr and then poured on 2 *N* NaOH solution. More CS_2 was added and the organic layer was separated, washed, and dried. A solid compound

was obtained (3.25 g), mp 179–180° from chloroform, NMR (CS_2) δ_{CH_3} 2.25.

Anal. Calcd for $C_7H_3Br_3S_2$: C, 21.50; H, 0.77; Br, 61.32; S, 16.40. Found: C, 21.48; H, 0.75; Br, 60.95; S, 16.42.

3,5-Dibromo-2-*tert*-butoxy-6-methylthieno[3,2-*b*]thiophene (45) and 3,5-Dibromo-6-methylthieno[3,2-*b*]thiophene (46). A solution of *n*-butyllithium (from 0.6 g of lithium) in ether was added dropwise to a suspension of **44** (11.7 g) in ether cooled at −70° and the mixture was kept at this temperature for 30 min and then at −30° for 1 hr. A 0.5 *M* solution of $MgBr_2$ in ether (100 ml) was added and the mixture was left to reach room temperature during 1 hr. After cooling at 0° a solution of *tert*-butyl perbenzoate (5 g) in ether was added and the solution was stirred for 3 hr. The mixture was poured on dilute HCl and the organic layer was washed with water and 10% NaOH solution and finally washed neutral with water and dried. The ether was removed and the residue was purified by column chromatography on Florisil using light petroleum as eluent. The first fractions contained **46** (1 g), mp 86–87°, NMR (CS_2) δ_2 7.17, δ_{CH_3} 2.27.

Anal. Calcd for $C_7H_4Br_2S_2$: C, 26.94; H, 1.29; Br, 51.22; S, 20.55. Found: C, 27.04; H, 1.39; Br, 51.07; S, 20.42.

The desired product **45** was then eluted (4.9 g), mp 65–66°, NMR (CS_2) δ_{CH_3} 2.18, $\delta_{C(CH_3)_3}$ 1.42.

Anal. Calcd for $C_{11}H_{12}Br_2OS_2$: C, 34.39; H, 3.15; Br, 41.61; S, 16.69. Found: C, 34.37; H, 3.18; Br, 41.82; S, 16.59.

2-*tert*-Butoxy-6-methylthieno[3,2-*b*]thiophene (22). To a solution of *n*-butyllithium (from 0.5 g of lithium), cooled at −70°, a solution of **45** (2.95 g) in ether was added and the mixture was kept at −50° for 30 min. Water was added and the ether layer was separated, washed, dried, and evaporated. The residue was purified on silica gel using light petroleum as eluent to afford **22** (1 g), mp 39–40°, NMR (CS_2) δ_5 6.7, δ_3 6.4, δ_{CH_3} 2.25, $\delta_{C(CH_3)_3}$ 1.37, $J_{CH_3\text{-}5}$ = 1.1 Hz.

Anal. Calcd for $C_{11}H_{14}OS_2$: C, 58.37; H, 6.24; S, 28.33. Found: C, 58.92; H, 6.33; S, 29.02.

3,6-Dimethylthieno[3,2-*b*]thiophene (48). Reaction of 3-bromo-4-methylthiophene[29] (4 g) with *n*-butyllithium (from 0.35 g of Li), sulfur (1 g), and chloroacetone (3 g), carried out as described above for **39**, afforded the (4-methyl-3-thienylthio)acetone, **47** (3.5 g), bp 95° (0.2 mm).

Anal. Calcd for $C_8H_{10}OS_2$: C, 51.58; H, 5.41; S, 34.42. Found: C, 51.69, H, 5.36; S, 34.05.

To a stirred mixture of $AlCl_3$ (3 g) and CS_2 (60 ml) a solution of **47** (3.2 g) in CS_2 was added and the mixture was worked up as described above for **38**. The solid product **48** was purified by crystallization from pentane, mp 88–89°, NMR (CS_2) δ_{CH_3} 2.3, δ_2 6.87, $J_{2\text{-}CH_3}$ = 1.1 Hz.

2-Bromo-3,6-dimethylthieno[3,2-*b*]thiophene (49) and 2,5-Dibromo-3,6-dimethylthieno[3,2-*b*]thiophene (50). Treatment of **48** (1.7 g) with NBS (1.8 g) in CH_3COOH (50 ml) as described above for **31** afforded a mixture of **50, 49,** and **48,** which were eluted in order from a silica gel column using light petroleum as eluent. The dibromo derivative **50** (0.3 g) melted at 140–142°, NMR (CS_2) δ_{CH_3} 2.22.

Anal. Calcd for $C_8H_6Br_2S_2$: C, 29.47; H, 1.85; Br, 49.02; S, 19.66. Found: C, 29.72; H, 1.97; Br, 48.86; S, 20.02.

The desired product **49** (2.1 g) had mp 47–48°, NMR (CS_2) δ_5 6.83, δ_3 2.27, δ_6 2.2, $J_{5\text{-}6}$ = 1.1 Hz.

Anal. Calcd for $C_8H_7BrS_2$: C, 38.87; H, 2.85; Br, 32.33; S, 25.94. Found: C, 39.02; H, 2.84; Br, 32.50; S, 26.05.

2-Bromo-3-methylthieno[2,3-*b*]thiophene (51). Treatment of 3-methylthieno[2,3-*b*]thiophene[28] (2.1 g) with NBS (2.4 g) in CH_3COOH (40 ml) as described above for **31** afforded **51** as an oil (3 g), bp 112–113° (0.8 mm), NMR (CS_2) δ_5 7.32, δ_4 7.05, δ_{CH_3} 2.25, $J_{4\text{-}5}$ = 5.25 Hz.

Anal. Calcd for $C_7H_5BrS_2$: C, 36.06; H, 2.16; Br, 34.28; S, 27.50. Found: C, 36.50; H, 2.22; Br, 34.31; S, 27.46.

2-Bromo-3-phenylthieno[2,3-*b*]thiophene (52). Treatment of 3-phenylthieno[2,3-*b*]thiophene[7] (2.24 g) with NBS (1.85 g) in acetic acid (60 ml) as described for **31** afforded an oil, bp 176–178° (0.8 mm) (3 g).

Anal. Calcd for $C_{12}H_7BrS_2$: C, 48.82; H, 2.37; Br, 27.07; S, 21.72. Found: C, 48.86; H, 2.31; Br, 27.40; S, 21.82.

2-Bromo-5-methylthieno[2,3-*b*]thiophene (53). Treatment of 2-methylthieno[2,3-*b*]thiophene[19] (4.3 g) with NBS (4.9 g) in CH_3COOH (90 ml) afforded a solid product (5.6 g) which was purified by column chromatography on silica gel using light petroleum as eluent, mp 79–80°, NMR (CS_2) δ_3 6.72, δ_4 6.98, δ_{CH_3} 2.53, $J_{3\text{-}CH_3}$ = 1.2 Hz.

Syntheses of the Thieno[3,2-*b*]thiophen-2-ones. The syntheses of these compounds have been carried out according to the general procedure described below for the parent compound **1b.** Details of preparations are also reported for the single products, whose physical and spectral data are collected in Tables II and III. In these tables data are also reported for compounds **7b** and **8b,** which were not prepared as described for **1b,** but were isolated as by-products from the syntheses of the corresponding 2,5-diones which will be described in a forthcoming paper.

Thieno[3,2-*b*]thiophen-2(3H)-one (1b). To a stirred solution of *n*-butyllithium (prepared from 0.45 g of Li) in ether, cooled at −70°, an ethereal solution of the 2-bromothieno[3,2-*b*]thiophene **29** (6.5 g) was added dropwise; the resulting solution of the 2-thieno[3,2-*b*]thienyllithium compound was stirred for 1 hr at −70° and then treated with *n*-butyl borate (9.2 g). The mixture was left to gradually reach room temperature during 5 hr and then shaken with 2 *N* HCl (25 ml). The layers were separated and the aqueous phase extracted with ether. The ethereal solution was extracted with three portions of 100 ml of cold 2 *N* NaOH and the alkaline solution was acidified with cold 2 *N* H_2SO_4; the separating boronic acid was dissolved in ether and 35% hydrogen peroxide (25 ml) was added. The mixture was vigorously stirred, under nitrogen, for 12 hr. The ethereal solution was washed several times with water and dried over Na_2SO_4, and the solvent was evaporated under nitrogen. A solid residue was obtained (2.1 g), which was purified by column chromatography. The physical and spectral data of **1b** are collected in Table II.

3-Methylthieno[3,2-*b*]thiophen-2(3*H*)-one (2b) and 3-Methylthieno[3,2-*b*]thiophen-2(5*H*)-one (2d). Treatment of **31** (7.8 g) as described above for **1b** afforded an oil (4 g), which was shown by NMR to be pure **2b.** Distillation of this product, bp 95–97° (1 mm), or elution through a silica gel column afforded a mixture of **2b** and **2d;** a mixture of the two isomers was also obtained when the oil was left to stand at room temperature for few hours. The isomerization was rapidly obtained if gaseous HCl was bubbled into the solutions of pure **2b** or **2d,** prepared as described below, or if a few drops of triethyllamine were added; the equilibrium composition, in CS_2, determined by NMR was **2b:2d** 40:60 ± 5.

Pure **2b** could be obtained with the base-extraction method. Pure **2d,** or a mixture of the two isomers, was dissolved in an excess of cold 2 *N* NaOH solution and ether was added; the mixture was vigorously stirred in an ice bath and acidified by the dropwise addition of a cold 2 *N* H_2SO_4 solution. The ether layer was separated, washed, dried, and evaporated under nitrogen; the oily residue consisted of pure **2b.**

Pure **2d** was obtained when to a saturated methanolic solution of **2b,** or a mixture of the two isomers, a few drops of pyridine were added; the **2d** which crystallized down from the solution was filtered and washed with cold methanol (mp 109–110°).

3-Ethylthieno[3,2-*b*]thiophen-2(3*H*)-one (3b) and 3-Ethylthieno[3,2-*b*]thiophen-2(5*H*)-one (3d). Treatment of **33** (5.2 g) as described above for **1b** afforded an oil (2.8 g) which consisted of pure **3b,** as shown by NMR. A mixture of **3b** and **3d** was obtained after chromatography on silica gel using light petroleum–ether (8:2) as eluent; fractions could be obtained in which pure **3d** was present (mp 98–99°). Pure **3b** could be regenerated by dissolving the mixture in alkali and acidifying in the presence of ether. The acid- or base-catalyzed equilibrium mixture in CS_2 contained **3b** and **3d** in the ratio of 75:25.

3-Phenylthieno[3,2-*b*]thiophen-2(3*H*)-one (4b) and 3-Phenylthieno[3,2-*b*]thiophen-2(5*H*)-one (4d). The oxidation of the boronic acid obtained from **36** (3 g) as described for **1b** afforded **4b** (1.6 g) as an oil which on attempted distillation gave rise to a mixture with the isomeric **4d;** the isomerization occurred also on standing or when passing the product through a silica gel column. At the equilibrium the mixture contained **4b** and **4d** in the ratio of 10:90. The base extraction method in this case did not give pure **4b** but a mixture in approximately equimolecular amounts.

5-Methylthieno[3,2-*b*]thiophen-2(3*H*)-one (5b). This compound was obtained in 70% yield starting from **37** (5.8 g) according to the usual procedure. The solid compound, mp 82–84°, did not suffer isomerization on crystallization or on treatment with acids or bases.

3,5-Dimethylthieno[3,2-*b*]thiophen-2(3*H*)-one (6b). This product was prepared in 65% yield from **40** (1.3 g) and could be distilled without suffering isomerization, bp 118° (1 mm). No changes were observed after treatment with acids or bases.

6-Methylthieno[3,2-*b*]thiophen-2(3*H*)-one (9b) and 6-Methylthieno[3,2-*b*]thiophen-2(5*H*)-one (9d). A. Treatment of **43** (3.5 g) as described above for **1b** afforded a residue (2 g) which was shown by NMR to contain 85% of **9b** and 15% of **9d.** Column chro-

matography of the reaction mixture on silica gel afforded pure **9b**, mp 61–62°. When this product was dissolved in alkali and the solution acidified in the presence of ether a mixture of the two isomers, **9b** and **9d**, in the ratio of 85:15 was obtained.

B. 2-*tert*-Butoxy-6-methylthieno[3,2-*b*]thiophene (**22**, 0.9 g) was warmed at 65°, under nitrogen, for 5 hr in the presence of traces of *p*-toluenesulfonic acid. The cooled mixture was dissolved in CS_2 and the NMR spectrum recorded; a mixture of **9b** and **9d** in the ratio of 80:20 was obtained. Column chromatography on silica gel of this mixture afforded pure **9b**, mp 61–62°.

3,6-Dimethylthieno[3,2-*b*]thiophen-2(3*H*)-one (10b) and 3,6-Dimethylthieno[3,2-*b*]thiophen-2(5*H*)-one (10d). From the oxidation of the boronic acid obtained from **49** (2.8 g), according to the procedure reported above for **1b**, an oily residue was obtained which was identified from its NMR spectrum as the pure tautomer **10b**. This compound spontaneously isomerized very rapidly to the isomeric **10d**; the transformation occurred almost instantaneously when HCl was bubbled into the CS_2 solution of **10b**. Column chromatography on silica gel of the reaction mixture gave rise to the pure 3,6-dimethylthieno[3,2-*b*]thiophen-2(5*H*)-one (**10d**), mp 127–128°. An alkaline solution of **10d**, treated with sulfuric acid in the presence of ether in the usual way, afforded a mixture of **10b** and **10d** in the ratio 30:70.

Syntheses of Thieno[2,3-*b*]thiophen-2-ones. The preparation of compounds **11**, **12**, **13**, and **16** from the bromo derivatives **38**, **51**, **52**, and **53**, respectively, was carried out according to the procedure described above for **1b** and their physical and spectral data are collected in Table IV. This table also contains the data concerning the products **14**, **15**, **17**, and **18**, which were obtained as by-products from the syntheses of the corresponding 2,5-diones.[10]

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Registry No.—**1b**, 56411-71-3; **2b**, 56411-72-4; **2d**, 56411-73-5; **3b**, 56411-74-6; **3d**, 56411-75-7; **4b**, 56411-76-8; **4d**, 56411-77-9; **5b**, 56411-78-0; **6b**, 56411-79-1; **7b**, 56411-80-4; **8b**, 56411-81-5; **9b**, 56411-82-6; **9d**, 56411-83-7; **10b**, 56411-84-8; **10d**, 56411-85-9; **11**, 56411-86-0; **12**, 56411-87-1; **13**, 56411-88-2; **14**, 56411-89-3; **15**, 56411-90-6; **16**, 56411-91-7; **17**, 56411-92-8; **18**, 56411-93-9; **22**, 56411-94-0; **29**, 25121-82-8; **31**, 56411-95-1; **32**, 56411-96-2; **33**, 56411-97-3; **34**, 56411-98-4; **35**, 56411-99-5; **36**, 56412-00-1; **37**, 56412-01-2; **38**, 31486-84-7; **39**, 56412-02-3; **40**, 56412-03-4; **41**, 56412-04-5; **42**, 56412-05-6; **43**, 56412-06-7; **44**, 56412-07-8; **45**, 56412-08-9; **46**, 56412-09-0; **47**, 56412-10-3; **48**, 56412-11-4; **49**, 56412-12-5; **50**, 56412-13-6; **51**, 56412-14-7; **52**, 56412-15-8; **53**, 56412-16-9; 3-methylthieno[3,2-*b*]thiophene, 1723-34-8; 3-bromothieno[3,2-*b*]thiophene, 25121-83-9; *N*,*N*-dimethylacetamide, 127-19-5; 3-phenylthieno[3,2-*b*]thiophene, 35022-15-2; 2-methylthieno[3,2-*b*]thiophene, 13393-75-4; 3-formylthieno[3,2-*b*]thiophene, 31486-88-1; 3-bromo-4-methylthiophene, 30318-99-1; chloroacetone, 78-95-5; 3-methylthieno[2,3-*b*]thiophene, 5911-97-7; 3-phenylthieno[2,3-*b*]thiophene, 35022-13-0; 2-methylthieno[2,3-*b*]thiophene, 26238-22-2.

References and Notes

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(17) Charge distributions have been calculated for the anions derived from compounds **1**, **2**, **9**, and **10** by using the CNDO/2 method and in every case it was found that the 3 position has a charge density considerably higher than the 5 position; position 7 also resulted to be slightly negative. The difference between charge densities in the 3 and 5 positions becomes less pronounced in compound **10**. The most relevant data were as follows: **1**, C_3 −0.1826, C_5 −0.1121, C_7 −0.0652; **2**, C_3 −0.1401, C_5 −0.1087, C_7 −0.0624; **9**, C_3 −0.1826, C_5 −0.1256, C_7 −0.0758; **10**, C_3 −0.1391, C_5 −0.1234, C_7 −0.0717. A CNDO/2 study was also carried out in order to investigate the influence of substituents on the relative stability of the two tautomers B and D; in qualitative agreement with the experimental results, it was found that, while in the unsubstituted product **1** form B is 4.33 kcal/mol more stable than **1d**, the introduction of a methyl group in the 3 position renders the form **2d** 4.71 kcal/mol more stable than **2b**, the effect becoming even more pronounced (5.19 kcal/mol) in the case of compound **10**, in which two methyl groups are present in the 3 and 6 position. In compound **9** the -2(3*H*)-one structure (B) is 1.56 kcal/mol more stable than the -2(5*H*)-one isomer (D). Details on calculations will be supplied on request.
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