Nonclassical Condensed Thiophenes. I.
1,3-Disubstituted Thieno[3,4-*c*]thiophenes

M. P. Cava,*[1] N. M. Pollack, and G. A. Dieterle

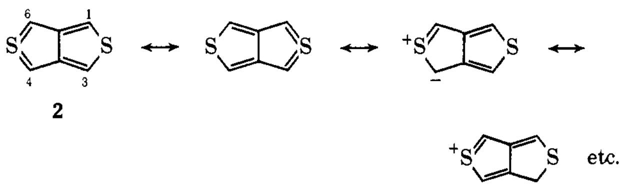
Contribution from the Department of Chemistry, Wayne State University, Detroit, Michigan 48202. *Received September 21, 1972*

Abstract: The sulfoxides 4,6-dimethyl-1*H*,3*H*-thieno[3,4-*c*]thiophene 2-oxide (**12**) and 4,6-dicarbomethoxy-1*H*,3*H*-thieno[3,4-*c*]thiophene 2-oxide (**20**) were dehydrated by hot acetic anhydride to generate 1,3-dimethylthieno[3,4-*c*]thiophene-5-S^{IV} (**8**) and 1,3-dicarbomethoxythieno[3,4-*c*]thiophene-5-S^{IV} (**21**), respectively. Neither **8** nor **21** could be isolated, but both could be trapped *in situ* by *N*-phenylmaleimide to give a pair of exo and endo adducts. The adducts of **8** (**13** and **14**), as well as those of **21** (**22** and **23**), arise by addition of *N*-phenylmaleimide to the thiophene ring of higher electron density.

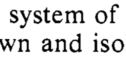
The greater chemical stability of thiophene as compared with either pyrrole or furan has long been known to organic chemists. In 1939, Schomaker and Pauling proposed that an expansion of the sulfur octet could be a factor in the stabilization of the thiophene molecule, as represented by the resonance contributor **1**.[2] This concept was later put into molecular orbital terms by Longuet-Higgins, who suggested pd^2 hybridization of the sulfur orbitals of thiophene.[3] In contrast, more recent theoretical studies of thiophene have led to the conclusion that d-orbital participation of sulfur is insignificant, and that only p-orbital sulfur conjugation is involved.[4,5]

1

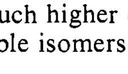
In connection with the problem of the possible tetracovalency of sulfur in thiophenes, we decided to undertake a study of the chemistry of the hitherto unknown heterocycle thieno[3,4-*c*]thiophene-5-S^{IV} (**2**). This system is a nonclassical one in the sense that, assuming a singlet ground state, its only uncharged resonance contributors are structures containing tetracovalent sulfur in one of the rings. Molecular orbital calculations for the parent heterocycle **2** have predicted that it should be a system of much higher energy than any of its three known and isolable isomers (**3**, **4**, or **5**); these calculations, in which sulfur d-orbital participation is rejected, predict also a triplet ground state (**2a**) for thieno[3,4-*c*]thiophene.[6]



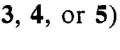
2



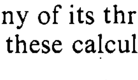
3



4



5



2a

Some time ago, in a preliminary communication, we reported evidence for the existence of a 1,3-dialkyl derivative of **2**.[7] In this paper, we report the details of this work, as well as a study of the generation of a derivative of **2** substituted in the 1,3 positions by electron-withdrawing groups.

1,3-Dimethylthieno[3,4-*c*]thiophene-5-S^{IV}. 1,3-Dihydrobenzo[*c*]thiophene 2-oxide (**6**) is easily dehydrated to benzo[*c*]thiophene (**7**) by heating with neutral alumina at 120–130°; adducts of **7** can be obtained directly by heating an acetic anhydride solution of sulfoxide **6** with a dienophile.[8] We therefore chose to attempt the synthesis of 1,3-dimethylthieno[3,4-*c*]thiophene-5-S^{IV} (**8**) by an analogous route. Thus, the reaction of 3,4-bis(chloromethyl)-2,5-dimethylthiophene (**9**)[9] with aqueous ethanolic sodium sulfide afforded, in 35% yield, 4,6-dimethyl-1*H*,3*H*-thieno[3,4-*c*]thiophene (**10**), mp 65–71°. A high-melting by-product of the same elemental composition as **10** was assigned the dimeric structure **11**. Periodate oxidation[10] of sulfide **10** in aqueous methanol gave the corresponding sulfoxide **12**, mp 115–119°, in 91% yield.

When a mixture of sulfoxide **12** and neutral alumina was heated under vacuum at 140–150° in a sublimer, a small amount of a bright yellow, fluorescent solid condensed onto the Dry Ice cold finger. On warming the cold finger to room temperature, the color and fluorescence vanished. In another experiment, the cold finger bearing the yellow solid was immersed in a solution of *N*-phenylmaleimide (NPM) in methylene chloride at −70°. If the yellow color was indeed due to the thienothiophene **8**, insufficient **8** was present to give a detectable amount of adducts (see Scheme I).

In contrast, a mixture of the exo and endo adducts (**13** and **14**) of **8** was obtained readily in 34% yield by refluxing a mixture of NPM and sulfoxide **12** in acetic anhydride; the adduct yield rose to 67% in a nitrogen atmosphere, attesting to the air sensitivity of interme-

---

[1] To whom inquiries should be addressed: Department of Chemistry, University of Pennsylvania, Philadelphia, Pa. 19174.

[2] V. Schomaker and L. Pauling, *J. Amer. Chem. Soc.*, **61**, 1769 (1939).

[3] H. C. Longuet-Higgins, *Trans. Faraday Soc.*, **45**, 173 (1949).

[4] D. T. Clark, *Tetrahedron*, **24**, 2663 (1968).

[5] M. J. S. Dewar and N. Trinajstic, *J. Amer. Chem. Soc.*, **92**, 1453 (1970).

[6] D. T. Clark, *Tetrahedron*, **24**, 2567 (1968).

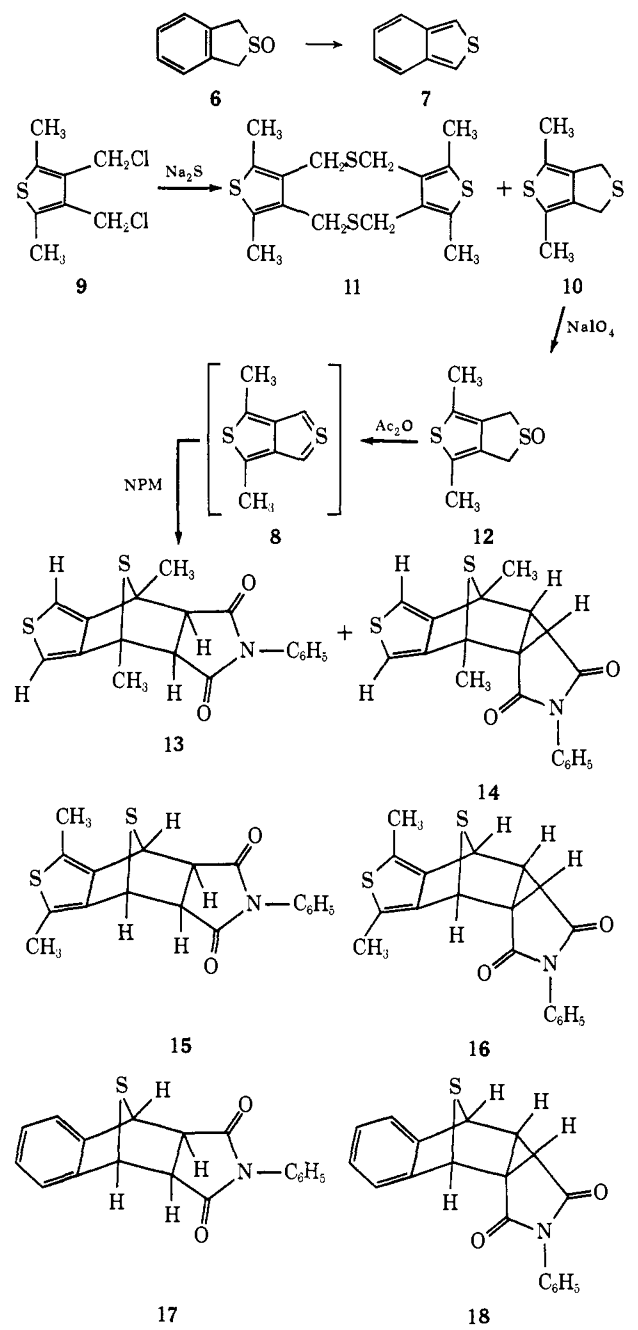
[7] M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **89**, 3639 (1967).

[8] (a) M. P. Cava and N. M. Pollack, *ibid.*, **88**, 4112 (1966); (b) M. P. Cava, N. M. Pollack, O. A. Mamer, and M. J. Mitchell, *J. Org. Chem.*, **36**, 3932 (1971).

[9] K. Dimroth, G. Pohl, and H. Follmann, *Chem. Ber.*, **99**, 634 (1966).

[10] N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

Scheme I



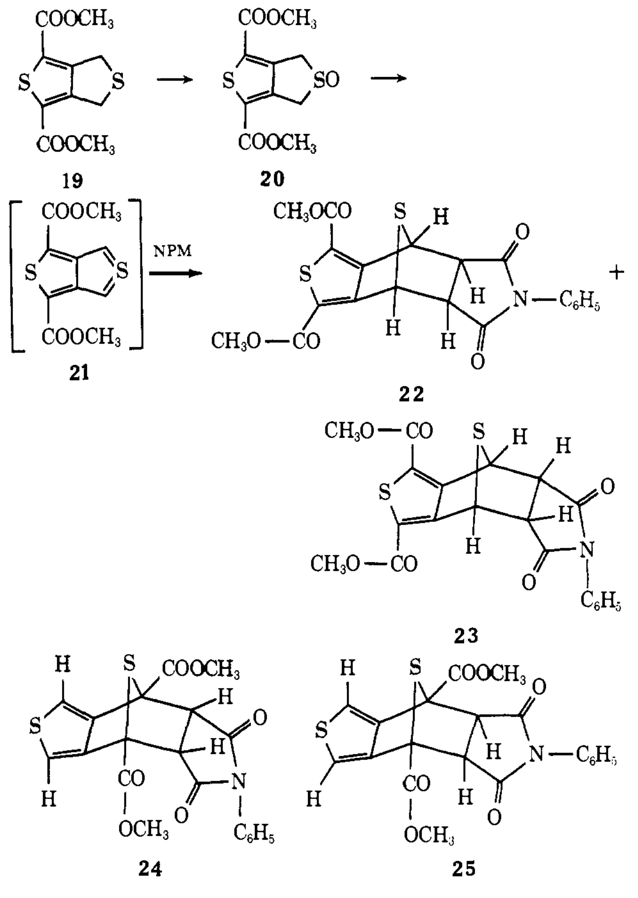
diate 8. The isomeric adducts were assigned the exo and endo structures 13 and 14, respectively, on the basis of their nmr spectra, which also eliminated from consideration the alternate possible structures 15 and 16. Thus, the two protons α to the imide carbonyls in the exo adduct 13 appear at δ 3.28, a position very close to that (δ 3.30) of the corresponding protons of the *exo*-isothianaphthene adduct 17.[8] In the endo adduct 14, the protons α to the carbonyls (δ 3.91) show the same deshielding effect of the sulfur bridge as the corresponding protons (δ 4.10) in the *endo*-isothianaphthene adduct 18. The isomeric structures 15 and 16 are easily eliminated for the adducts of 8 since neither adduct shows a proton in the δ 4.9 region, characteristic of the bridgehead protons of 17 and 18.[8]

1,3-Dicarbomethoxythieno[3,4-*c*]thiophene-5-S^{IV}. The synthesis of 4,6-dicarbomethoxy-1*H*,3*H*-thieno[3,4-*c*]thiophene (19) has been described by Wynberg and Zwanenburg.[11] Periodate oxidation of sulfide 19 in aqueous methanol gave the corresponding sulfoxide 20, mp 157–159°, in 92% yield.

When a solution of sulfoxide 20 in acetic anhydride was heated to reflux under nitrogen, an intense red-orange color accompanied by a bright orange fluorescence developed rapidly. This color, which we attribute to thienothiophene 21, remained unchanged after an additional 2 hr of refluxing. We could not isolate the orange product due to its sensitivity to light and air, but the fact that it moved rapidly on a silica plate with benzene as the developer attests to its nonpolar nature.

In a similar dehydration of 20 run under nitrogen in the presence of NPM, the orange color vanished in somewhat over 2 hr, and a mixture of exo and endo adducts (22 and 23) of 21 was obtained in 67% yield. The nmr spectra of these adducts clearly supported structures 22 and 23 and eliminated the alternate possibilities 24 and 25 (Scheme II). Thus, the protons α to the imide carbonyls in endo adduct 23 (δ 4.27) were deshielded by the sulfur bridge, while the corresponding protons of the exo adduct 22 (δ 3.52) were not. The bridgehead protons of both 22 and 23 were clearly detectable in the δ 5.4 region. In exo adduct 22, the bridgehead protons and those of the adjacent carbons appear as sharp singlets; in endo adduct 23, the corresponding sets of protons interact and are observed as two sets of apparent quartets as a result of the phenomenon of virtual coupling.[12]

Scheme II



---

[11] H. Wynberg and D. J. Zwanenburg, *J. Org. Chem.*, 29, 1919 (1964).

[12] F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969.

Discussion

The evidence presented above indicates both the existence of the thieno[3,4-*c*]thiophene system and the suitability of a Pummerer-type sulfoxide dehydration for the generation of this nonclassical heterocyclic system.

It is of some interest to compare the addition of the dienophile NPM to the two 1,3-disubstituted thieno[3,4-*c*]thiophenes **8** and **21**. The examples **8** and **21** represent thienothiophenes which are electronically unsymmetrical due to substitution at one ring only by electron-releasing and electron-withdrawing substituents, respectively. The enhanced reactivity of the methylated 1,3 positions of **8** toward NPM results in exclusive addition to these positions; this effect parallels the activating effect toward dienophiles of methyl groups in the 9,10 positions of anthracene.[13] Exactly the opposite effect is observed in the case of **21**, where the deactivating ester groups at the 1,3 positions lead to exclusive addition of NPM to the unsubstituted ring.

Experimental Section

General. Melting points are uncorrected. Elemental analyses were reported in the original manuscript and were consistent with the assigned formulas within the limits ±0.3% for compounds **10**, **11–14**, **20**, and **23**. Spectra were recorded on a Perkin-Elmer Model 137 ir spectrophotometer and a Varian A-60A nmr spectrometer. Separations by preparative thin layer chromatography (ptlc) were carried out on silica plates using 1:6 ethyl acetate-benzene as the developer.

4,6-Dimethyl-1*H*,3*H*-thieno[3,4-*c*]thiophene (10). Finely powdered 3,4-bis(chloromethyl)-2,5-dimethylthiophene[9] (**9**, 20.9 g) was added in small portions, over a period of 3.5 hr, to a stirred slurry of pulverized sodium sulfide nonahydrate (26.5 g) in 95% ethanol (250 ml). After stirring for a further 15 hr, the mixture was concentrated to half of its volume, diluted with water (100 ml), and extracted with several 100-ml portions of chloroform. Evaporation of the solvent, followed by steam distillation, gave the steam-volatile sulfide **10** (5.87 g, 35%), mp 65–71°. The analytical sample, mp 67–70°, was crystallized from methanol.

In a separate run, a nonvolatile by-product was isolated in 11% yield. This compound, assigned structure **11**, had mp 234–238° after crystallization from benzene; nmr ($CDCl_3$) δ 2.38 (12 H, s, 4 × CH_3) and 3.50 (8 H, s, 4 × CH_2).

4,6-Dimethyl-1*H*,3*H*-thieno[3,4-*c*]thiophene 2-Oxide (12). A solution of sodium periodate (6.86 g) in water (100 ml) was added to a stirred solution of sulfide **10** (5.10 g) in methanol (375 ml). After stirring for a further 15 hr, the mixture was concentrated to half of its volume and extracted with several 100-ml portions of chloroform. Evaporation of the extracts, followed by crystallization from cyclohexane, gave sulfoxide **12** (5.08 g, 91%), mp 115–119°. The analytical sample, mp 116–120°, was recrystallized from the same solvent.

Adducts (13 and 14) of 1,3-Dimethylthieno[3,4-*c*]thiophene-5-S^{IV} (8) with *N*-Phenylmaleimide. A mixture of sulfoxide **12** (0.930 g) and *N*-phenylmaleimide (0.908 g) in acetic anhydride (50 ml) was heated under reflux for 4 hr. Evaporation of the solvent, followed by crystallization from benzene (10 ml), gave exo adduct **13** (0.245 g, 14%), mp 220–228°. Chromatography of the residue on NI alumina (1:1 benzene–ether eluent), followed by crystallization from benzene–cyclohexane, afforded additional **13** (total yield 24%). The analytical sample of **13**, mp 227–229°, was crystallized from ethanol: nmr ($CDCl_3$) δ 2.05 (6 H, s, 2 × CH_3), 3.28 (s, 2 H, 2 × HCCO), 6.76 (s, 2 H, 2 × thiophene CH), 7.2–7.6 (5 H, m, C_6H_5).

The residues from **13** were subjected to ptlc to give endo adduct **14** (0.165 g, 10%), mp 160–188°. Recrystallization from ethanol afforded pure **14**: mp 181–183°; nmr ($CDCl_3$) δ 2.03 (s, 6 H, 2 × CH_3), 3.90 (2 H, s, 2 × HCCO), 6.76 (2 H, s, 2 × thiophene CH), 6.55–6.85 (2 H, m, shielded ortho protons of C_6H_5), 7.2–7.4 (3 H, m, remaining protons of C_6H_5).

When the original reaction was repeated under nitrogen, ptlc separation gave adducts **13** and **14** in yields of 49 and 18%, respectively.

4,6-Dicarbomethoxy-1*H*,3*H*-thieno[3,4-*c*]thiophene 2-Oxide (20). A solution of sodium periodate (0.414 g) in the minimum amount of hot water was added dropwise to a solution of 1,3-dihydro-4,6-dicarbomethoxythieno[3,4-*c*]thiophene[11] (**19**, 0.500 g) in refluxing methanol (110 ml). After refluxing for an additional 45 min, the solution was concentrated, diluted with water, and extracted with chloroform. Evaporation of the dried extract, followed by crystallization from benzene–cyclohexane, gave sulfoxide **20** (0.486 g, 92%), mp 157–159°.

Adducts (22 and 23) of 1,3-Dicarbomethoxythieno[3,4-*c*]thiophene-5-S^{IV} (21) with *N*-Phenylmaleimide. A mixture of sulfoxide **20** (0.400 g), *N*-phenylmaleimide (0.318 g), and acetic anhydride (60 ml) was refluxed with stirring under nitrogen for 3 hr, during which time the initially developed bronze color faded to a pale yellow. Evaporation of the solvent gave a residue which, on crystallization from benzene–cyclohexane, afforded white needles of exo adduct **22** (0.252 g), mp 204.5–205°. Separation of the residues by ptlc gave a further 0.073 g of **22** (mp 205°, total yield 54%) and 0.078 g of endo adduct **23** (13%), mp 175–176°.

The exo adduct **22** gave somewhat erratic analytical results. Its mass spectrum confirmed its molecular weight as 429 (29%). It is noteworthy that the base peak at *m/e* 256 corresponds to thienothiophene **21**, formed by a retro-Diels–Alder reaction of **22**.

Acknowledgment. We thank the U. S. Army Research Office (Durham) for a grant in partial support of this work.

---

[13] J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967).