Reaction of Some Benzo[b]thiophene 1,1-Dioxides with Hydroperoxide Ion

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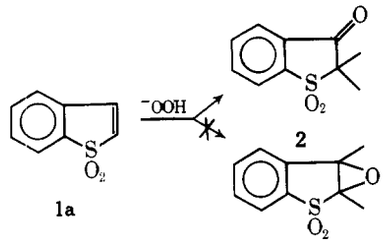
Received December 30, 1976

Unlike open-chain α,β-unsaturated sulfones, benzo[b]thiophene 1,1-dioxide (**1a**) and 3-R-benzo[b]thiophene 1,1-dioxides (**1b**, R = Me; **1c**, R = Et; **1d**, R = Ph) react anomalously with hydroperoxide ion. Rather than the epoxide, 3-oxo-2*H*-benzo[b]thiophene 1,1-dioxide (**2**) is obtained from **1a**, and **1b–d** react to form the corresponding 3-hydroxy-2*H* derivatives **5**. Hydration of **1b–d** is presumed to involve decomposition of the hydroperoxide intermediate and is not merely hydroxide ion catalyzed addition of water, since the rate of reaction with aqueous sodium hydroxide is far slower than with alkaline hydrogen peroxide. Compound **1c** was also isomerized to 3-ethylidene-2*H*-benzo[b]thiophene 1,1-dioxide (**6**) with alkaline hydrogen peroxide, but was converted to **5** (R = Et) only with sodium hydroxide. Possible mechanisms are considered.

The conversion of phenyl styryl sulfone and related compounds to the corresponding epoxides via the reaction with alkaline hydrogen peroxide[1] appears to parallel the behavior of α,β-unsaturated carbonyl compounds.[2] The reaction was shown to be stereoselective, resulting in the formation of the trans epoxide, and presumably follows the accepted mechanism for the epoxidation of enones.[3] However, application of the reaction to the cyclic unsaturated sulfone, benzo[b]thiophene 1,1-dioxide (**1a**), has been found to lead to an apparently anomalous result.

Treatment of **1a** with hydrogen peroxide and aqueous sodium hydroxide in pyridine[4] results in the formation of 3-oxo-2,3-dihydrobenzo[b]thiophene 1,1-dioxide (**2**), rather than the expected epoxide **3**. The identity of the ketone was verified by comparison of the infrared and NMR spectra with those of an authentic sample prepared by an alternate route.[5]



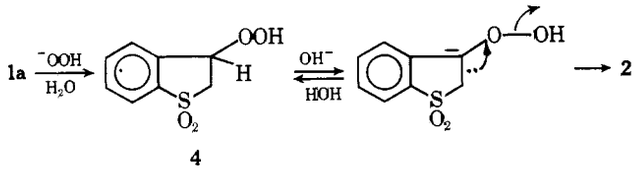
1a **2** **3**

The possibility of a rapid rearrangement of initially formed **3** to **2** is considered unlikely, since such rearrangements normally are effected by acid catalysis or occur at elevated temperatures,[6a–c] or via prolonged heating with a strong base such as lithium diethylamide.[6d] One possible route to the ketone, which requires removal of the proton from C-3, is shown in Scheme I.

Subjection of some 3-substituted benzo[b]thiophene 1,1-dioxides to the reaction also led to some unexpected results, as shown below (yield data in Table I). It was also observed that 2,3-dimethylbenzo[b]thiophene 1,1-dioxide did not react at all with OOH^-.

The formation of **6** from **1c** would appear to be a simple base-catalyzed isomerization. However, treatment of **1c** with NaOH with or without pyridine gave no **6**; this reaction is being further examined. It is noteworthy that dehydration of **5** (R = Et) by treatment with benzoyl chloride led to **6**, rather than **1c**, pointing to the higher degree of stability of the exocyclic double-bond structure. The 3-methylene isomer was not obtained either in the reaction of **1b** with hydroperoxide ion or of **5** (R = Me) with benzoyl chloride. However, **5** (R = Ph) was dehydrated with PhCOCl to **1d**, as expected.

Scheme I



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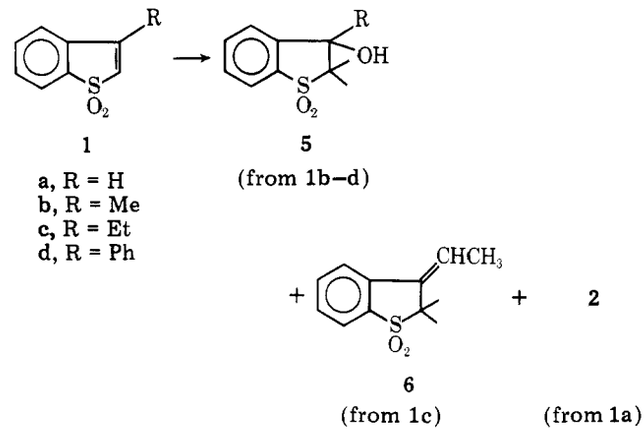

1 **5**

a, R = H
b, R = Me
c, R = Et
d, R = Ph

(from 1b–d)

6

(from 1c) (from 1a)

The formation of the 3-hydroxy products **5** appears on the surface to be a simple case of base-catalyzed hydration. However, the unusual character of the reaction is evident when comparisons are made of the attempts to prepare the alcohols via direct hydration of the parent compounds, using aqueous sodium hydroxide, with the reactions involving the alkaline hydrogen peroxide reagent. Using a modification of the method reported[7] for the preparation of 3-hydroxy-2,3-dihydrobenzo[b]thiophene 1,1-dioxide, **5** (R = Me) was obtained in 85% yield, and **5** (R = Et) in 47% yield (71% unreacted starting material recovered), only after mixtures of the parent compounds and aqueous sodium hydroxide in pyridine were refluxed for extended periods (7–30 h). On the other hand, with hydroperoxide ion the exothermic reaction was found to be essentially complete after 4 h at temperatures no higher than 35 °C. To account for the difference, an analogy may be drawn to the recently reported rapid hydrolysis of amides with hydroperoxide ion.[8] The postulated intermediate adduct was believed to decompose to ammonia and peroxycarboxylate ion, the latter in turn decomposing to carboxylate. It may, therefore, be presumed that the anion resulting from the initial attack of hydroperoxide ion on **1b–d** decomposes to the anion of **5**. Further studies involving other substituted benzo[b]thiophene 1,1-dioxides, as well as other five- and six-membered heterocyclic unsaturated sulfone systems are in progress.

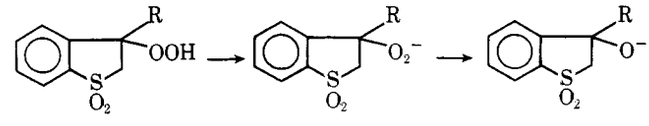

Table I. Reactions of 1 with OOH^- in Pyridine

Registry no.		R	Products (% yield)
825-44-3	**1a**	H	**2** (47%)
6406-91-3	**1b**	Me	**5**, R = Me (65%)[a]
16958-00-2	**1c**	Et	**6** (62%); **5**, R = Et (20%); **2** (1%)
27183-55-7	**1d**	Ph	**5**, R = Ph (47%)[a]

[a] Based on amount of starting material converted to product.

Experimental Section

Infrared spectra were obtained on a Beckman Acculab 2 or 4250 spectrophotometer; NMR spectra were recorded on a Varian Associates T-60 instrument. All melting points are uncorrected. Elemental analyses were done by Galbraith Laboratories, Knoxville, Tenn.

Materials. Benzo[*b*]thiophene 1,1-dioxide was prepared from benzo[*b*]thiophene (Aldrich Chemical Co.) by oxidation[9] with hydrogen peroxide in acetic acid. 3-Methylbenzo[*b*]thiophene was prepared by cyclization of 1-phenylthio-2-propanone (Parish Chemical Co.) with P_2O_5.[10] 3-Ethylbenzo[*b*]thiophene was obtained via the reaction of 1-bromo-2-butanone[11] with sodium thiophenoxide, followed by cyclization,[10] or by acetylation of benzo[*b*]thiophene, followed by Clemmensen reduction.[12] 2,3-Dimethylbenzo[*b*]thiophene was formed by cyclization[10] of 3-phenylthio-2-butanone (from 3-bromo-2-butanone[11] + PhSNa). The alkylbenzothiophenes were then converted to the 1,1-dioxides by oxidation with hydrogen peroxide in acetic acid. 3-Phenylbenzo[*b*]thiophene 1,1-dioxide was prepared through the sequence of reactions described by Bordwell et al.[13] from 1,1-diphenylethene.[14]

General Procedure for Reaction of Benzo[*b*]thiophene 1,1-Dioxides with Hydroperoxide Ion. To a solution of 1 mmol of **1** in pyridine (2–6 mL/mmol; sufficient to produce a homogeneous solution when the aqueous reagents are included) was added an excess of 30% hydrogen peroxide (2.5–3.0 mmol/mmol of **1**). A 10% excess of 1 or 2 M NaOH was then added[15] over a period of 10 min, while maintaining the temperature at 30–35 °C. Stirring was continued at 30–35 °C until titration of aliquots with 0.1 N Ce(IV)[16] indicated no further consumption of H_2O_2. The reaction mixture was poured into ice–water (10–15 mL/mmol of **1**) and processed as noted below.

Benzo[*b*]thiophene 1,1-Dioxide (1a). Following the oxidation of 1.0 g (6.0 mmol) of **1a**, which was carried out at 0–5 °C for 1 h, the resulting bright-yellow solution was acidified with concentrated HCl, which caused the separation of a small amount of solid (not removed by filtration). The mixture was extracted three times with 20-mL portions of methylene chloride, and the combined extracts were dried over $MgSO_4$. The solvent was removed by evaporation under reduced pressure, leaving 0.74 g of residue, mp 127–132 °C. After recrystallization from methanol, 0.51 g (47%) of **2**, mp 131–132 °C (lit. mp 133 °C,[5,17a] 136–137 °C[17b]), was obtained. Comparison of the infrared and NMR spectra with those of an authentic sample[5] verified the identity of **2**.

3-Methylbenzo[*b*]thiophene 1,1-Dioxide (1b). The diluted reaction mixture (from 3.0 g, 17 mmol of **1b**) was reduced to a volume of about 40 mL by rotary evaporation and the residue was extracted three times with 20-mL portions of methylene chloride. Evaporation of the dried ($MgSO_4$) combined extracts left 2.4 g of solid residue, mp 80–97 °C.

Five recrystallizations of the solid product from chloroform–hexane (1:1) raised the mp to 97.5–99.5 °C, but TLC on silica gel with chloroform revealed the presence of small amounts of two other substances which could not be removed by recrystallization. A portion of the solid product (1.81 g) was chromatographed on a silica gel column with chloroform, and 1.63 g of colorless solid (**5**, R = Me), mp 105–106 °C (recrystallized from chloroform–hexane, 1:1), was obtained. (The first fractions of eluate contained unreacted **1b** and a miniscule amount of another unidentified substance.)

NMR (in $CDCl_3$) δ 1.73 (s, 3, $-CH_3$), 3.53 (s, 2, CH_2), 3.67 (s, 1, OH), 7.63 (m, 4, Ar–H); infrared 3460 (s), 2930, 2990 (1600 cm^{-1} band in precursor absent in product). Anal. Calcd for $C_9H_{10}O_3S$: C, 54.53; H, 5.08; S, 16.17. Found: C, 54.42; H, 5.20; S, 16.17.

3-Ethylbenzo[*b*]thiophene 1,1-Dioxide (1c). The reaction was carried out with 4.0 g (21 mmol) of **1c**. After dilution, the initially homogeneous mixture was chilled, causing the separation of a white solid within a few minutes. The solid was filtered, washed, and air-dried; 1.4 g, mp 134–135.5 °C, was obtained. Evaporation of the filtrate to 50 mL resulted in the separation of an additional 1.1 g of solid, mp 133–134.5 °C. The combined solids were recrystallized twice from methanol, yielding pure **6**, mp 133.5–134.5 °C: NMR (in $CDCl_3$) δ 1.83 (d of t, 3, CH_3), 4.05 (s, 2, CH_2), 6.45 (m, 1, =CH), 7.59 (m, 4, Ar–H). Anal. Calcd for $C_{10}H_{10}O_2S$: C, 61.83; H, 5.19; S, 16.51. Found: C, 62.32; H, 5.40; S, 16.39.

The aqueous filtrate was acidified with concentrated HCl and the resulting solution was extracted with methylene chloride (3 × 20 mL). Evaporation of the organic solvent left a syrupy residue (1.1 g), which was chromatographed on silica gel with chloroform to yield three components: 0.04 g of **2**,[18] 0.91 g of a very viscous syrup (**5**, R = Et), and 0.01 g of a yellow solid which was not further identified. All attempts to crystallize the hydroxy compound failed. However, the NMR and infrared spectra were in conformity with the proposed structure: NMR (in $CDCl_3$) δ 0.82 (t, 3, CH_2CH_3), 2.22 (q, 2, CH_2CH_3), 3.5 (s, 2, CH_2), 4.48 (br s, 1, OH), 7.56 (m, 4, Ar-H); infrared 3468 (s).

An attempt to prepare the benzoate via the reaction with benzoyl chloride[7] resulted in the formation of **6**, mp 133–134 °C, as verified by mixture melting point and comparison of the infrared and NMR spectra with those obtained for **6** earlier (see above).

2,3-Dimethylbenzo[*b*]thiophene 1,1-Dioxide. The reaction with hydrogen peroxide and aqueous NaOH was carried out as described above, and at temperatures ranging from 0 to 50 °C. In every case, the starting material was recovered almost quantitatively.

3-Phenylbenzo[*b*]thiophene 1,1-Dioxide (1d). After a 7-h reaction period, during which 1.6 g (6.6 mmol) of **1d** was oxidized, the mixture was diluted with water. After chilling in an ice bath, a solid precipitated and 0.52 g of unreacted **1d**, mp 158–160.5 °C, was collected. The volume of the filtrate was reduced by evaporation under reduced pressure to about 40 mL. The residue, a clear aqueous solution plus some insoluble tacky material, was extracted with three 15-mL portions of methylene chloride. After washing once with 20 mL of 3 M HCl and drying over $MgSO_4$, the solvent was removed, leaving 0.55 g of a colorless semisolid residue. All attempts to crystallize the product were futile. No chromatographic evidence that the product was a mixture was obtained. The NMR and infrared spectra indicate the product is **5** (R = Ph): NMR (in $CDCl_3$) δ 3.81 (s, 2, CH_2), 4.0 (br s, 1, OH), 7.46 (m, 4, Ar–H), 7.63 (m, 5, Ar–H); infrared 3461 (s) (1600 cm^{-1} band present in spectrum of parent compound absent in product).

Reaction of 0.10 g of the hydroxy compound with benzoyl chloride resulted in the formation of 0.075 g of **1d**, mp 159–160 °C, whose infrared spectrum was identical with that of an authentic sample.

Base-Catalyzed Hydration of 3-Alkylbenzo[*b*]thiophene 1,1-Dioxides. A solution of 1 mmol of **1b** or **1c** in pyridine (2.5–4 mL/mmol; sufficient to produce a homogeneous solution after addition of aqueous reagent) was combined with 0.5 M NaOH (4–6 mL/mmol). The solution was stirred and heated to reflux (**1b**, 7 h, followed by 18 h at 25 °C; **1c**, 30 h). The mixture was then evaporated under reduced pressure to remove all solvent. Water (3 mL/mmol) was added to the residue and insoluble solid (unreacted starting material) was removed by filtration. The basic filtrate was acidified with concentrated HCl and extracted three times with methylene chloride. Removal of the solvent under reduced pressure left a syrupy residue. Specific results for the individual compounds are given below.

3-Hydroxy-3-methyl-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (5, R = Me). From 0.634 g (3.52 mmol) of **1b** there was obtained 0.052 g of unreacted starting material and 0.60 g of syrup, which solidified on vigorous stirring. Recrystallization from chloroform–hexane (1:1) afforded 0.50 g of product, mp 99.5–101 °C; a second recrystallization raised the melting point to 100–101 °C. Chromatography of 110 mg of the product on a silica gel column (chloroform) resulted in the separation of 10 mg of unreacted **1b** (identity from infrared spectrum), and the remaining material which was eluted was essentially pure **5** (R = Me). Recrystallization from chloroform–hexane (1:1) gave white crystals, mp 107–107.5 °C. The infrared and NMR spectra were identical with those obtained for the product isolated from the reaction of **1b** with OOH^-.

3-Hydroxy-3-ethyl-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (5, R = Et). A total of 1.42 g of unreacted starting material was recovered from the reaction of 2.0 g (10 mmol) of **1c**. The viscous syrup residue (0.30 g) left after the removal of the methylene chloride could not be induced to crystallize. The infrared and NMR spectra of this material were identical to those of the product **5** (R = Et), obtained in the reaction of **1c** with OOH^-. Treatment of the product with benzoyl chloride (reflux for 1 h) also resulted in the formation of **6**, as verified by infrared and NMR spectra comparisons.

Acknowledgments. I am indebted to Dr. James Lyle for helpful discussions. Technical assistance provided by Laura Wright and Clayton Harris is gratefully noted.

Registry No.—5 (R = Me), 62521-48-6; 5 (R = Et), 62521-49-7; 5 (R = Ph), 62521-50-0; 6, 62521-51-1; hydroperoxide ion, 14691-59-9; 2,3-dimethylbenzo[*b*]thiophene 1,1-dioxide, 16958-01-3.

References and Notes

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(4) Dioxane may be used, but yields are generally lower. In methanol, 3-methoxy-2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide is also formed and complicates the separation procedure. Acetone (see ref 1) is satisfactory if the temperature is maintained at 40–50 °C.
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(17) (a) H. Kloosterziel and H. J. Backer, *Recl. Trav. Chim. Pays-Bas*, **71**, 361 (1952); (b) F. G. Bordwell and C. J. Albisetti, *J. Am. Chem. Soc.*, **70**, 1558 (1948); (c) F. Arndt, A. Kirsch, and P. Nachtwey, *Ber.*, **B59**, 1074 (1926).
(18) In another run, in which the temperature was maintained at 20–25 °C, compound **2** comprised 15% of the product mixture.

Notes

3,3,5,5- and 3,3,7,7-Tetraphenylpyromellitide and Their Tetrathio Analogues

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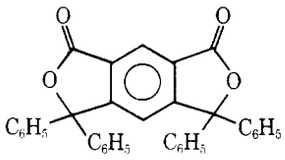
Received January 11, 1977

A synthesis of 3,3,7,7-tetraphenylpyromellitide (**2**) from pyromellityl chloride via a Friedel–Crafts reaction has been reported;[2] however, on the basis of the present work it appears that the reported compound was actually the 3,3,5,5-tetraphenylpyromellitide (**1**). Apparently the trans isomer was lost



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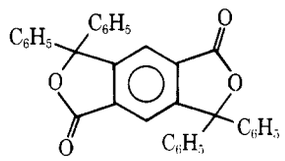

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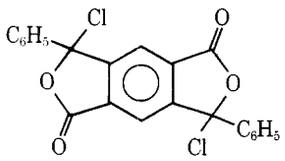
in the purification procedure owing to its greater reactivity. The pseudo acid chloride (**3**) of 2,5-dibenzoylterephthalic acid has also been isolated and identified[3,4] as has the pseudo-4,6-dibenzoylisophthaloyl chloride (**4**).[4] These materials were used to produce polyamides or polyanthrazolines and were not reacted further to the tetraphenylpyromellitides.



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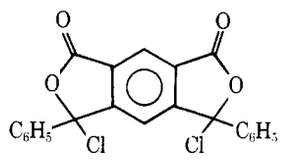

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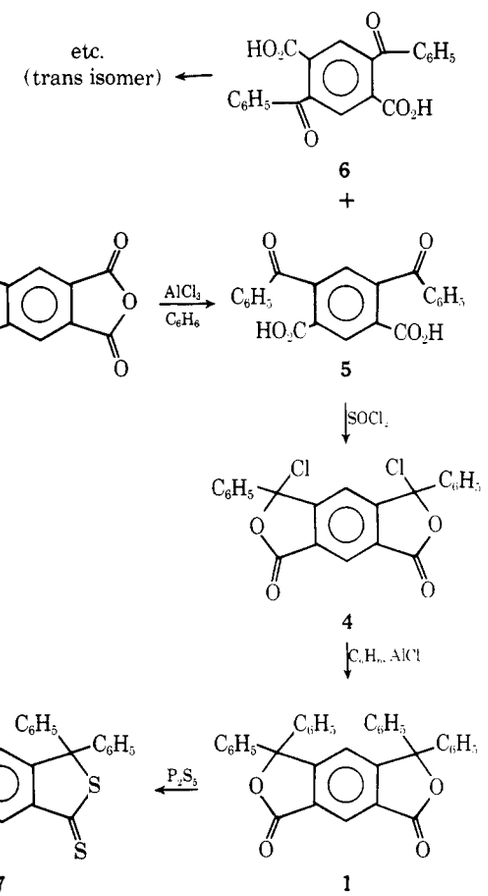
It is the purpose of this paper to report the novel, high-yield, unequivocal syntheses of the cis and trans isomers, **1** and **2**, of tetraphenylpyromellitide. Further the tetrathio analogue of each was prepared.

The cis oxo- and thiotetraphenylpyromellitides have been used as monomers for a new type of heterocyclic polymer, polyimidines.[7,8]

The salient features of this reaction scheme are twofold. First, the isomeric dibenzoylphthalic acids, **5** and **6**, can be



separated as their potassium salts. The potassium salt of the terephthalic acid isomer crystallizes from aqueous KOH whereas the sodium salts of both isomers are soluble in NaOH solutions. Previous investigators also have used KOH solutions but apparently neutralized them soon after dissolution without waiting for a crystalline precipitate to form. In earlier work[4,5] the isomer separation was performed with more difficulty and lower yields by crystallizing the acids from acetic acid or aqueous ethanol or methanol.

The second important finding is the fact that the pseudo