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February 17, 1993

U. S. Department of Energy
Pittsburgh Energy Technology Center
Acquisition and Assistance Division
P. O. Box 10940
Pittsburgh, PA

Attention: John. N. Augustine

Dear Mr. Augustine:

The final Technical Report for Task I: Synthesis of 6-Methyl-9-propyldibenzothiophene-4-ol (DE-AC22-90PC 90035), as amended to 9-isopropyl-6-methyldibenzothiophene-4-ol, is enclosed.

According to Part III, Section J, Attachment B, of the contract, this is to be a draft copy. I have labeled this version of the report accordingly. I assume that you will contact us for changes which are to be included in the final draft.

Sincerely yours,

E. J. Eisenbraun
Regents Professor
Principal Investigator
(405) 744-6673

DISCLAIMER

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February 17, 1992

Final Technical Report (draft copy)

Report period: July 25, 1991-January 25, 1993

CONTRACT TITLE AND NUMBER:

Task I: Synthesis of 6-Methyl-9-propyldibenzothiophene-4-ol (DE-AC22-90PC90035)
amended to 9-isopropyl-6-methyldibenzothiophene-4-ol

CONTRACTOR NAME: Oklahoma State University, Stillwater, OK 74078

CONTRACT PERIOD: July 25, 1990- July 24, 1992, extended to January 25, 1993.

CONTRACT OBJECTIVE: Synthesis and purification of the amended title compound.

Technical Summary: This report is a compilation of data presented in earlier reports (Annual Reports 1991 and 1992, Quarterly Reports 1-7, and Monthly Status Reports 1-29). The first annual report (August 16, 1991) dealt with an attempted synthesis of 4-methoxy-6-methyl-9-propyldibenzothiophene (**6a**) (the original target compound, shown in **Scheme I**, p 25), the successful synthesis and delivery of 200 grams of the sulfide 1,4-diethyl-2-[(2'-methoxyphenyl)-thio]benzene (**11**) shown in Eq. 1 (p. 5), and initial work on a new synthesis route (**Scheme II**, p 26) for the preparation of the new target compound 9-isopropyl-6-methyldibenzothiophene-4-ol (**18**). The change to the new target compound (**18**) and the new synthesis route (**Scheme II**) became necessary when it was learned that the sulfide mixture **5a,5b** (**Scheme I**) could not be cyclized to the substituted dibenzothiophene mixture **6a, 6b**. This will be discussed later. The second Annual Technical Progress Report (August 17, 1993) described the successful preparation of 45 g of **18** using **Scheme II**. Subsequently funds were provided to synthesize an additional 5 g of **17** and 45 g of **18** using the reactions of **Scheme II**. This task has recently been completed.

Discussion of the Synthesis Route Shown in Scheme I: The selection of **Scheme I**, as a route to the original target compound 6-methyl-9-propyldibenzothiophene-4-ol (**7**), was based on literature precedents^{1,2} that 1-bromo-2-methyl-5-propylbenzene (**3a**) was formed exclusively during the bromination of 1-methyl-4-*n*-propylbenzene (**2**) and that a sulfide such as **5a** could be photocyclized⁷ to the 4-methoxy-6-methyl-9-propyldibenzothiophene (**6a**). Instead of the expected exclusive formation of **3a**, a mixture of **3a:3b** (2/1) was obtained and photocyclization⁷ failed to provide the cyclized products **6a,6b** as expected. This formation of a mixture (**3a,3b**) complicated the synthesis by introducing the need for separation of isomers at some later stage. However, the formation of the mixture of **3a** and **3b** did not block the synthesis. The synthesis failed because neither the sulfide mixture **5a,5b** nor the sulfones **8a,8b** could be cyclized to dibenzothiophenes.

Scheme I was carried to the diaryl sulfide mixture **5a,5b**. However, the reaction which produced **5a,5b** from the bromo compounds **3a,3b** was sluggish, with recovered starting material, despite 18 h of reflux. To determine whether the ortho-alkyl group of **3a** and its isomer could be exerting an adverse steric hindrance in the reaction and to learn whether the iodo analog of **3a** would be an improvement, a model reaction substituting 2-iodotoluene for **3a,3b** and benzenethiol for 2-methoxybenzenethiol was run.⁴ It is known that the reactivity of aryl halides in this coupling reaction is $\text{ArI} > \text{ArBr} > \text{ArCl}$. Gas chromatographic studies showed that all of the 2-iodotoluene was consumed and that the crude product showed two peaks in the ratio 97:3. The theoretical weight of crude product was observed. An additional change was the substitution of ethanol for 1-butanol. This provided an advantage because it was found that complete removal of 1-butanol from the product mixture, in the preparation of **5a,5b**, was difficult.

These findings suggested that the iodo-analog of **3a,3b** would be superior as a starting material. As expected, iodination of **2** gave a mixture of **4a,4b** and their subsequent use gave an improved yield of **5a,5b**. Reducing the consumption of the expensive tetrakis(tri-phenyl-phosphine)palladium (0) and 2-methoxybenzenethiol in step d also was a major factor in making this change. Accordingly, **2** was iodinated⁴ using iodine with periodic acid as an oxidant. As expected from our experience in the bromination of **2**, the iodination product was found by gas

chromatography to be a 2.8:1 mixture. This reaction was run with the hydrocarbon **2** in excess so recovery of **2** was expected. The gas chromatography ratio, including **2** (first peak) was 43:13:36 (**2/4b/4a**).

While we were able to prepare the mixture of sulfides **5a,5b** in good overall yield, the subsequent photocyclization (step e, **Scheme I**) to the corresponding dibenzothiophenes **6a,6b** failed to give an acceptable yield.⁷ A summary of yields, of the reactions used to prepare **5a,5b** in **Scheme I**, is presented as follows:

1 to **2** (step a) = (86 %)⁵

2 to **3a:3b** (step b) = (2.0/1, 69 %)⁶

2 to **4a:4b** (step c) = (2.8/1, 76 % based on recovered **2**)⁴

3a,3b to **5a,5b** (step d) = (1.7/1, 60 %)³

4a,4b to **5a,5b** (step d) = (2.7/1, 86 %)³

Attempts at converting **5a,5b** or **8a,8b** to **6a,6b** included unsuccessful use of the following reagents and conditions:

1. hv, I₂ in cyclohexane and in benzene under a variety of concentrations and light filters⁷
2. hv, I₂, propylene oxide⁷
3. H₂O₂ to form **8a,8b**⁸ followed by BuLi, CuCl₂ in THF^{9,10}
4. H₂SO₄, acetic acid¹¹

To avoid the formation of mixtures at the halogenation steps b and c of **Scheme I** which provided **3a,3b** and **4a,4b**, the use of the symmetrical 1,4-diethylbenzene (**9**, **Eq. 1**) as a substitute for 1-methyl-4-n-propylbenzene (**2**, **Scheme I**) was suggested. Use of 1,4-diethylbenzene offered the advantage of simplifying the reaction mixtures and thus facilitating the analysis of products during the exploratory work. In addition, **9** and its derivatives provided excellent models to study the various steps of **Scheme I**. Approval for the use of 1,4-diethylbenzene as starting material in the synthesis of 1,4-diethyl-2-[(2'-methoxyphenyl)thio]benzene (**11**, **Eq. 1**) was granted by DOE/PETC. Accordingly, the following reaction sequence, shown below as **Equation 1** which converts 1,4-diethylbenzene (**9**) to the sulfide **11** and the sulfone **12**, was carried out.

Equation 1

Interest in an additional supply of sulfide **11** was expressed by DOE/PETC and accordingly a large sample (10 X 20 g) of **11** was prepared, purified, and shipped to DOE/PETC. The identity and purity of this sample was established by gas chromatography and ^1H and ^{13}C NMR spectroscopy. Gas chromatographic analysis showed the purity of the distilled **11** to be about 97 % (triangulation of GC peaks). The closely-related impurities (*ca.* 3 %) arose during the coupling reaction step and were not removed by fractional distillation. They are believed to be 2,2'-dimethoxydiphenyl sulfide and $\text{C}_{10}\text{H}_{13}\text{-S-C}_{10}\text{H}_{13}$. As expected, the yields in the preparation **11** and **12** parallel those of the reactions in **Scheme I**. In the case of **11** and **12**, the materials did not contain isomeric impurities.

Samples of sulfide **11** and the corresponding sulfone **12** were subjected to cyclization reactions in an attempt to find conditions for conversion to a dibenzothiophene and then to apply these conditions to the cyclization of **5a,5b** to **6a,6b** in **Scheme I**. The reagents were:

1. $(\text{Ph}_2\text{Li})_2\text{Na}$ in diethyl ether-applied to **11**¹²
2. hn/Pyrex , CH_2Cl_2 , $(\text{CN})_2\text{C}=\text{C}(\text{CN})_2$ -applied to **11**¹³
3. Amberlyst-15, 1,2-dichlorobenzene, reflux-applied to **11**¹⁴
4. hv/Pyrex , I_2 , CH_2Cl_2 -applied to **12**⁷
5. VOCl_3 , $\text{CF}_3\text{CO}_2\text{H}$ in CH_2Cl_2 at $^\circ\text{C}$ -applied to **12**¹⁵

The above reactions failed to give a satisfactory cyclized product and consequently an alternate synthesis route, shown in **Scheme II** (p 28) was devised.

Discussion of the Synthesis Route in Scheme II: As stated above, the failure to convert the sulfide mixture **5a,5b** of **Scheme I** or sulfide **11** to a dibenzothiophene prompted development of the reaction sequence in **Scheme II**. Since the starting material, 2-n-propyl-5-

methylcyclohexanone, needed to synthesize **7a** of **Scheme I**, using **Scheme II**, is not commercially available nor is it easily synthesized, the target compound was modified to 4-hydroxy-9-isopropyl-6-methyldibenzothiophene (**18**, **Scheme II**). This substitute structure permits use of the commercially available (-)-2-isopropyl-5-methylcyclohexan-one [(-)-menthone]. Thus, the two phenols (**7a** of **Scheme I** and **18** of **Scheme II**) differ only in the structure of the three-carbon side chain.

The rationale for the synthesis of **18** via **17** (**Scheme II**) was menthone (**13**) being available, the synthesis was short, and precedents for the reaction steps were well documented. We carried out the synthesis of **17** on a small scale using equilibrated menthone that was on hand. We did not attempt to optimize the reaction conditions or yields, nor did we purify intermediates. Our aim was to carry the sequence to the end to learn if any of **17** ($M^+ = 270$) is formed. These efforts are described in the Experimental Section.¹⁶⁻¹⁸ GC and GC-MS analyses of the crude product, corresponding to **17**, showed it to be a mixture consisting of three isomeric **17**'s (35 %), demethylated **17** (4 %), two isomeric **17**'s lacking an isopropyl group (15 %), and several unidentified side-products (46 %). The three isomeric **17**'s were present in the relative ratios of 23:11:1.0.

This experience suggested that the yields and purity of the intermediates and final product could be improved by using pure l-(-)-menthone, running the PPA-cyclization (**Scheme II**, step d) reaction at a lower temperature, and substituting Pd/C for selenium in the dehydrogenating **16** to **17** (**Scheme II**, step e). We observed from the GC-MS results that the PPA cyclization conditions (based on literature precedent) resulted in partial cleavage of the isopropyl group and in partial cleavage of the methoxy methyl group. Cleavage of the methoxy methyl group at this step is acceptable, in principle, since this leads to the target **18**.

Once it became established that **17** (**Scheme II**) had been formed, the first two steps of this synthetic sequence, using purer menthone starting material, and on a larger scale were carried out. The objective in this larger-scale preparation was to characterize the intermediates, to decide on suitable points for purification, and to modify the literature conditions in order to reduce the number of side-products that were observed in the small-scale run. These large-scale experiments are described in the Experimental Section. GC analyses indicate that these reactions proceed as

anticipated with the expected isomers forming the major constituents of the crude product mixture. The conversion in the bromination reaction (formation of **14a**, **14b**) was substantial but not complete and they were accompanied by some equilibration of the unreacted menthone. The keto sulfide **15**, on the other hand, proceeded to completion but it was accompanied by some dimerization of 2-methoxybenzenethiol to 2,2'-dimethoxydiphenyl disulfide, a white crystalline solid. This, however, is not a major problem since this disulfide is separable from **15**, to a large extent, by selective precipitation. We have observed that the unreacted menthone (**13**, carried over from the bromination step) can also be separated readily from the keto sulfide **15** by steam distillation of the former.

Small-scale aromatization experiments on the tetrahydrodibenzothiophene intermediate **16** (**Scheme II**, step e) using Palladium-on-carbon (Pd/C) or selenium metal powder gave, regardless of reaction conditions, product mixtures of the desired methoxydibenzothiophene **17** and the side-product 4-methoxy-6-methyldibenzothiophene (**19**) as shown by GC-MS analysis. In order to extract the desired **17** from the crude reaction product, several purification techniques were tried (*vide infra*). Of these, the use of picric acid to form crystalline picrates of **17** and **19** was successful in separating **17** and **19** from the rest of the impurities. Decomposition of the picrates on basic alumina with hexanes afforded 17:19 (62/38) as determined by GC and ^1H NMR. In this mixture, the desired **17** co-crystallized with **19** but we were able to separate it from **19** by eluting twice through acidic and basic alumina with hexanes-toluene. Methoxydibenzothiophene **17**, obtained this way, was $\geq 98\%$ pure and is an odorless, crystalline solid showing good stability to neutral and basic alumina, silica gel, and thermal stability except under the aromatization conditions (Pd/C or Se present, $T > 245^\circ\text{C}$). Other purification techniques that were either unsuccessful or only partially successful include: Kugelrohr distillation under reduced pressure, sublimation, silica gel flash chromatography, elution through neutral and basic alumina contained in a Soxhlet extractor, and fractional crystallization from ethyl acetate or methanol-ether.

In addition to the above, the methoxy methyl cleavage reaction was carried out with boron tribromide on the mixture of **17** and **19**. The intent was to learn if this reaction takes place cleanly and if boron tribromide can be substituted for the more expensive boron tribromide-dimethyl sulfide complex that we originally planned to use. The reaction with boron tribromide was adapted from the

literature procedure for cleavage of catechol ethers¹⁹. The reaction proceeded smoothly in dry dichloromethane at 0 °C to give the expected mixture of **18** and **20** in about 88% yield. The ¹H NMR spectrum of the mixture of **18** and **20** clearly lacked the methoxy methyl signals and contained a broad singlet at $\delta = 5.4$ attributed to their phenolic OH resonances. This spectrum also showed that the conversion in this reaction was quantitative and that no side-products were observed. Moreover, there was no evidence of ring bromination. The mixture of phenols **18** and **20** consisted of a white fluffy solid.

Though we were initially hesitant to use 1,4-benzoquinones (DDQ and chloranil -owing to reported side-reactions, such as side-chain oxidation and/or Diels-Alder cycloaddition) for the dehydrogenation of **16**, we carried out trial aromatizations using DDQ in benzene at 25 °C and at 80 °C. The thought was that the lower reaction temperature (80 °C as compared with 245-300 °C) would minimize loss of isopropyl group. The reaction progress in each case was carefully monitored by removing aliquots at regular time intervals, diluting each with benzene and then filtering the resulting solutions through short plugs of basic alumina, magnesium sulfate, and Dicalite. GC analysis showed that the reaction was slow: 28 % (24 h at 25 °C), 55 % (24 h at 80 °C) and 67 % complete (168 h at 25 °C or 48 h at 80 °C). The desired methoxy dibenzothiophene **17** was the predominant product of the reaction and loss of the isopropyl group did not occur to any observable extent as determined by GC-MS. The reactions involving use of chloranil gave similar results but they were exceedingly slow: only 8 % conversion after 72 h at 80 °C. Moreover, increasing the ratio of chloranil from 1.4 to 4.1 equivalents did not improve the conversion. Thus, DDQ was the best of the reagents tried, however, the reaction at 80 °C was too slow and a higher boiling reaction solvent was indicated. The use of dioxane (bp 100-102 °C, described later) provided an increased yield.

An intermediate-scale synthesis of **18** also was carried out starting with 355 g of (-)-menthone (**13**). The resulting crude product contained about 75 % by weight of 2-bromomenthone (**14**) and reflected a conversion of *ca.* 76 % as determined by GC. We feel that these results are satisfactory for this step considering the scale and complexity of the run. An attempt on a 5-g scale to purify the crude 2-bromomenthone by Kugelrohr distillation gave a colorless distillate that exhibited new GC peaks. These peaks correspond to loss of hydrogen bromide. This finding confirmed our

suspicion that the 2-bromomenthone is thermally unstable which prompted direct use in the next step without purification. Keto sulfide **15** was thus prepared using 265 g of 2-methoxybenzenethiol and an equivalent amount of the crude monobromide. The weight recovery from the reaction was high (90 % w/w). The crude product was treated with low-boiling petroleum ether in order to precipitate most of the disulfide side-product.

An attempt to purify the keto sulfide **15** on a 5-g scale by Kugelrohr distillation led to the formation of five new impurities (by GC). Therefore, the bulk of the keto sulfide was treated with steam, before use, to remove volatile impurities. Since the earlier small-scale exploratory synthesis showed that the PPA cyclization was the lowest yield step in the overall scheme, we attempted to improve this step by running the reaction on a small-scale in refluxing toluene. GC analysis, however, showed a much slower reaction, no improved conversion and the formation of three new impurity peaks. The bulk of **15** was then converted to **16** by heating in PPA at 100-110 °C in the absence of solvent to give **16** in about 41 % yield.

At this point we had established that 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ) effected the aromatization of **16** to **17** in refluxing benzene (bp 80 °C) without loss of the isopropyl group. The reaction, however, did not proceed to completion at that temperature and with the DDQ ratio used. In order to achieve complete reaction of **16**, exploratory small-scale reactions with DDQ in refluxing anhydrous p-dioxane (bp 101 °C) were carried out using varying ratios of DDQ to **16**. A four-fold excess of DDQ was required to convert all of **16** to **17**. Thus, the larger-scale dehydrogenation run using an excess of DDQ was made as described in the experimental section.

Following reaction and extractive workup, crude **17** was passed twice through fresh plugs of acidic and basic alumina and the filtrate was then concentrated and pumped. The dark-brown viscous oil that resulted was treated with picric acid in boiling ethanol and the resulting orange picrate that precipitated was collected, partially dried and then recrystallized from boiling ethanol. The recrystallized picrate was collected, dried, and decomposed over basic alumina with n-hexanes and then toluene. This afforded a total of 35 g of the first crop of **17** as glistening white crystals, mp 108-110 °C. Gas chromatographic analysis of this material showed it to be better than 99 % pure (see GC trace). These 35 g of **17** represent a 9.5 % overall yield from menthone.

Reprocessing of the mother liquor from the picrate of crude **17** yielded an additional 10.5 g of **17**. This raised the total yield of purified **17** to 45.5 g representing an overall yield increase (from menthone) of pure material to 12.2 %. When the demethylation reaction (last step in Scheme II) was carried out initially at 0 °C on 10.5 g of pure **17**, the reaction proceeded smoothly with no side products observed, but despite the use of an excess of boron tribromide (4.6 equivalents of bromine atoms), there remained about 10 % unreacted **17** accompanying the phenol product **18**. Compounds **17** and **18** were separated by chromatography on basic alumina. However, when the bulk of **17** was converted to **18**, the reaction was carried out at room temperature. This resulted in essentially a quantitative conversion.

Phenol **18** is a white, crystalline solid melting without decomposition at 155-156 °C. It is soluble in ether, chloroform, dichloromethane, and acetone. It is slightly soluble in low-boiling petroleum, insoluble in water and forms a dispersion in dilute sodium hydroxide. It is stable to neutral alumina and to air during normal handling.

On February 19, 1992 the following samples of the pure (≥ 99 % by GC) phenol **18** (Scheme II) were shipped to DOE/PETC :

Sample ID	Grams	Purity	Melting Pt	Structure
SJF-IX-11-B	0.108 g	>99 %	155-156 °C	18
SJF-IX-11-B1	0.105	>99	155-156	18
SJF-IX-11-B5	0.113	>99	155-156	18
SJF-IX-11-B6	2.472	>99	155-15	18

2.798.g total

The relevant gas chromatography trace and proton and ^{13}C nuclear magnetic resonance spectra were enclosed with the samples. These data are consistent with the structure assigned to phenol **18**. This assignment has since been confirmed by a high-resolution mass spectrum and by C, H and S elemental analysis.

The following analytical data were collected on **17** and **18** (Galbraith Laboratories, Inc.):

The methoxy ether, 9-isopropyl-4-methoxy-6-methyl-dibenzothiophene (**17**, SJF-VIII-94-A) showed % carbon 75.41, % hydrogen 6.74, and % sulfur 11.93. The calculated values are 75.53, 6.71, and 11.84 % respectively.

The phenol, 6-methyl-9-(1'-methylethyl)dibenzothiophene-4-ol (**18**, SJF-IX-11B) showed % carbon 74.80, % hydrogen 6.35, and % sulfur 12.54. The calculated values are 74.98, 6.29, and 12.49 % respectively.

On April 20, 1992, the following samples were shipped to DOE/PETC (the relevant GC traces were also included):

Sample ID	Grams	Purity	Melting Pt	Structure	Total Wt.
SJF-VIII-94-A	2.9 g	>99 %	108-110 °C	17	
SJF-VIII-94-A	1.6	>99	108-110	17	4.50 g
SJF-IX-35-A-1	1.98	>99	155-157	17	
SJF-IX-35-A-2	3.74	>99	155-157	17	
SJF-IX-35-A-3	3.53	>99	155-157	17	
SJF-IX-35-A-4	3.77	>99	155-157	17	
SJF-IX-35-A-5	3.59	>99	155-157	17	16.61 g

An additional sample (SJF-IX-38-A, 9.95 g, mp 154-156 °C) of the phenol, 6-methyl-9-(1'-methylethyl)dibenzothiophene-4-ol (**18**) was also shipped to DOE/PETC on May 6, 1992. The GC trace showed the sample to be 95.6 % pure. This trace was shown at two different attenuation but both were from a single injection.

Molecular Mechanics (MM2) calculations on dibenzothiophenes **17** and **18** were carried out on a modified Macintosh IIfx computer using the Tektronix CAChe™ Molecular Modeling System.²² The purpose of these calculations was to estimate the total strain energy for dibenzothiophenes **17** and **18** and some of the bond lengths and angles. These calculation results are preliminary in nature and should be used only as a rough guide. The data are found on p. 27 of this report

Funds to prepare an additional 5 g of **17** and 45 g of **18** were approved. To carry out this work, a six month extension to the contract was granted. The procedures used for the preparation of these samples were essentially those described elsewhere in this report. This resulted in 5.0 g of **17**

(p 108-110 °C, 99.5 % purity) and 38.5 g of **18** (p 156-157 °C, 97 % purity, distributed in 7 vials). These samples were shipped on December 26, 1992. A final 6.5 g sample (total 45 g) of **18** (92 % purity) was isolated from the remaining mother liquors and shipped on January 19, 1993.

EXPERIMENTAL

Wolff-Kishner Reduction of 4'-Methylpropiophenone (1) to 1-Methyl-4-n-propylbenzene (2, Scheme I, step a)⁵. 4'-Methylpropiophenone (101.4 g, 0.63 mol), hydrazine hydrate (150 mL), sodium hydroxide (27 g, 0.67 mol), potassium hydroxide (43 g, 0.66 mol) and diethylene glycol (500 mL) were added to a stainless-steel apparatus containing a magnetic stirring bar. The apparatus was fitted with a thermocouple probe, Dean-Stark trap, stainless-steel water condenser and a nitrogen inlet tube. This apparatus, constructed mainly of stainless steel, was specifically designed for this type of reaction in order to avoid the attack of alkali on glass.

The apparatus was flushed with nitrogen and heating with stirring was carried out at such a rate that nitrogen from the decomposing hydrazone was vigorous. As the reaction proceeded, the hydrocarbon product distilled and was collected in the Dean-Stark trap as an upper layer [107.4 mL (103.7 mL theoretical)].

The product was transferred to a separatory funnel, dissolved in ether (500 mL), washed with dilute hydrochloric acid (2x50 mL) and with water (3x50 mL), dried (MgSO₄), filtered, concentrated (rotary evaporation) to 87.0 g (98 %) of a pale yellow oil. Gas chromatography studies using OV-101 substrate at 130 °C showed approximately 95% purity. Vacuum distillation, using a Kugelrohr apparatus, gave a colorless liquid (76.2 g, 86 %). The ¹H and ¹³C NMR spectra, copies of which are enclosed, verified the structure of the product as 1-methyl-4-n-propylbenzene (**2**).

Bromination of 1-Methyl-4-n-propylbenzene (2, Scheme I, step b)⁶. A 500 mL, 3-neck flask was fitted with condenser, magnetic stir-bar, thermocouple probe and pressure-equalized dropping funnel. The top joint of the condenser was connected to an empty trap which, in turn, led to a second trap containing magnetically stirred 10 % sodium hydroxide. This alkali trap absorbs hydrogen bromide produced by the reaction. 1-Methyl-4-n-propylbenzene (134 g, 1.0

mol), iodine (2 crystals) and iron powder (2.5 g, 325 mesh) were added to the reaction flask. The flask was then immersed in an ice-salt bath and cooled to $-6\text{ }^{\circ}\text{C}$. Bromine (45 mL, 139.8 g, 0.88 mol, 0.9 equiv.) was added to the stirred reaction mixture during 2.5 h. The inside temperature was maintained around $-3\text{ }^{\circ}\text{C}$ during addition. The reaction mixture was allowed to warm to room temperature overnight.

The brown reaction mixture was poured into water (500 mL) and the mixture was then transferred to a separatory funnel. This operation was carried out in a hood. The layers were separated and the aqueous layer was extracted with hexane (3 x 300 mL). The organic layers were combined, washed with 10 % NaOH (200 mL) and water (3 x 200 mL), dried (MgSO_4), filtered, concentrated (rotary evaporation) and then pumped to constant weight (189 g, 102 % yield) of light brown oil. Kugelrohr distillation gave a clear colorless oil (128 g, 69 % yield) and a dark brown pot residue (12.6 g). The ^1H and ^{13}C NMR spectra of the distillate showed it to be a mixture of the expected product and an impurity. There is a characteristic ^1H NMR singlet at $\delta = 7.34$ (s, 1H, ArH). The **3a/3b** ratio was 2.0:1.0.

Coupling of 1-Bromo-2-methyl-5-n-propylbenzene (3a) and 1-Bromo-5-methyl-2-n-propylbenzene (3b) with 2-Methoxybenzenethiol (Scheme I, step d)³. A 500-mL, 3-neck, round-bottomed flask was fitted with two reflux condensers, stopper and Teflon-coated stir-bar. Nitrogen was introduced and vented through the two condensers. The system was purged with nitrogen while 1-butanol (200 mL) and freshly-cut pieces of sodium (3.05 g, 0.133 g. atom, 2.7 equiv.) were introduced. This heterogeneous mixture was stirred at room temperature until all of the sodium had reacted (0.5 h). A solution of the mixture of title bromo compounds (10.66 g, 0.050 mol) and 2-methoxybenzenethiol (5.75 g, 0.040 mol) in 50 mL of 1-butanol was then added followed by 0.62 g (5.37×10^{-4} mol, 1.1 mol %) of $\text{Pd}[\text{P}(\text{C}_6\text{H}_5)_3]_4$ catalyst. This reaction mixture was heated, under nitrogen, at reflux for 18 h during which a dark color developed.

The cooled reaction mixture was concentrated under vacuum (rotary evaporator) to a dark grey slush. Since washing the slush with hexane was ineffective, the product was transferred to a separatory funnel containing 300 mL of water and the mixture was extracted with hexane (3 x 300 mL). The combined extracts were washed with water (3 x 100 mL), dried (MgSO_4), and filtered through a pad of basic alumina. The filtrate was concentrated under vacuum (rotary evaporator) and

further stripped using a vacuum pump to 14.86 g (138 %) of colorless oil. At this point, some 1-butanol remained. GC analysis (programming from 120 to 290 °C at 20 °/min) of this liquid showed unreacted starting material (36 %) and two product peaks in the ratio of 57:33. The estimated yield of coupled product, based on GC studies, is 60%. Steam distillation of the distilled reaction mixture was effective in separating the starting bromo material from the product but some of the product slowly distilled with steam.

Iodination of 1-Methyl-4-n-propylbenzene (Scheme I, step c)⁴. To a 1-L, round-bottomed flask containing a magnetic stir-bar and fitted with a thermometer, was added 1-methyl-4-n-propylbenzene (60.4 g, 0.45 mol), glacial acetic acid (170 mL), periodic acid (H₅IO₆, 15.40 g, 0.068 mol), iodine (33.90 g, 0.134 mol), and sulfuric acid (6.0 mL diluted with 32 mL of water). The resulting dark-brown reaction mixture was heated with stirring to 56 °C during 1 h and then maintained at 52-56 °C for four additional hours. The cooled reaction mixture was then transferred to a separatory funnel using water and dichloromethane. The layers were separated and the top (aqueous) layer was extracted with dichloromethane (4 x 200 mL). The dichloromethane layers were combined, washed with saturated sodium bicarbonate (2 x 200 mL), dilute sodium bisulfite (2 x 200 mL), and water (2 x 200 mL). The residual organic layer was dried (MgSO₄), filtered, concentrated (rotary evaporation) and pumped (oil pump) affording 92.5 g of crude product as a dark-pink liquid which was shown by gas chromatography (DB-1, 130 °C to 290 °C at 20 °C/min) to consist of unreacted hydrocarbon **2** (43 %), **4b** (13 %), **4a** (36 %) and diiodo impurity (9 %). The presence of unreacted hydrocarbon was expected since less than one equivalent of iodine was used in this trial run in order to minimize the formation of polyiodo side products. The unreacted hydrocarbon appears to be separable from the iodo products by fractional distillation.

Coupling of 2-Iodotoluene and Benzenethiol³. The apparatus described above (Scheme I, step d) was charged with absolute ethanol (200 mL) and freshly-cut sodium (5.52 g, 0.24 g-atom, 4.8 equiv.) was added in small pieces. After all of the sodium had reacted, a solution of 2-iodotoluene (11.12 g, 0.05 mol) and benzenethiol (5.52 g, 0.05 mol) in 50 mL of absolute ethanol was added followed by addition of Pd[P(C₆H₅)₃]₄ (0.51 g, 4.4 x 10⁻⁴ mol, 0.88 mol %).

A dark-brown color developed during 16 h of heating at reflux. The cooled reaction mixture was transferred to a separatory funnel, diluted with water (300 mL), extracted with hexane (4 x 75 mL) and the combined extracts were washed with 10% sodium hydroxide (2 x 30 mL), water (3 x 50 mL), dried (MgSO₄), filtered, concentrated under vacuum, and pumped (oil pump) for 4 h affording a crude brown-colored but clear oil (10.05 g, 100 %). GC analysis at 220 °C showed 2-iodotoluene (4.4 min) to be absent and the presence of a major product (97 %) and two minor impurities (3 %).

1,4-Diethyl-2-[(2'-methoxyphenyl)thio]benzene (11, Eq. 1)³ was prepared from **9** similarly to the preparation of sulfides **5a+5b** (Scheme I) starting with 79.1 g of **9**, 48.3 g of 2-methoxybenzenethiol, 28.8 g of sodium metal, 1.7 g of tetrakis(triphenylphosphine)-palladium(0) and 720 mL of anhydrous ethyl alcohol. After 10 h of reflux under nitrogen, subsequent workup and two fractional distillations using a 12-cm Vigreux column, gave 72 g of purified **11** as a clear and colorless liquid. Two additional runs afforded purified **11** (223 g total), bp 181-182 °C/3 mm.

2-[(2'-Methoxyphenyl)thionyl]-1-methyl-4-*n*-propylbenzene (8a) and 3-[(2'-methoxyphenyl)thionyl]-1-methyl-4-*n*-propylbenzene (8b, Scheme I, step f).⁸ A mixture of sulfides **5a,5b** (13.6 g, 0.050 mol) was dissolved in 100 mL of glacial acetic acid and 27 mL (0.26 mol) of 31% aqueous hydrogen peroxide was added over 5 min. The reaction mixture was stirred at room temperature for 23 h and then heated to reflux (35 min) and at reflux (0.5 h). It was then poured onto 500 mL of ice and most of the acetic acid was neutralized by the portion wise addition of 76 g of anhydrous solid sodium carbonate. The resulting solution was extracted with 6 x 50 mL of methylene chloride and the combined organic extracts were washed with 2 x 50 mL of sat'd sodium carbonate solution, 2 x 50 mL of water, dried (MgSO₄), filtered, concentrated (rotary evaporator) and pumped (24 h, 2 mm) affording the crude sulfones **8a+8b** (14.4 g, 95 %) as a white, somewhat sticky, crystalline solid. This solid was washed with low boiling petroleum ether (5 x 30 mL) and dried *in vacuo* (48 h) affording a white, crystalline, free-flowing solid, (12.7 g, 83 %), mp 97-100 °C.

1,4-Diethyl-2-[(2'-methoxyphenyl)thi-nyl]benzene (12, Eq. 1), mp 77-78 °C, was prepared similarly to **8a+8b** (Scheme I, step f) in 86% yield starting with 5.5 g of sulfide **11** (5.5 g), 31% aqueous hydrogen peroxide (13 mL) and glacial acetic acid (50 mL)⁸.

Attempted Cyclization of a Mixture of 2-methoxy-2'-methyl-5'-*n*-propyl-(5a) and 2-methoxy-5'-methyl-2'-*n*-propyldiphenylsulfide (5b) Using Sulfuric Acid/Acetic Acid.¹¹ Conc. sulfuric acid (20 mL) was charged into a 100-mL, 2-neck, round-bottomed flask equipped with thermometer, stopper and stir-bar. The apparatus was lowered into an ice-salt bath and when the inside temperature reached -12 °C, a solution of sulfides (2.74, 0.0098 mol) **5a+5b** in acetic acid (5 mL) was added dropwise over 1h such that the inner temperature remained between -10 °C and -5 °C. After addition was complete, the reaction solution was stirred at -10 °C for another 0.8 h and then poured into ice-water (500 mL). This was extracted with dichloro-methane (4 x 100 mL) and the combined dichloromethane extracts were washed with sodium carbonate solution (50m mL, 2 N), water (2 x 100 mL), saturated brine (100 mL), dried (MgSO₄), filtered, concentrated (rotary evaporator), and pumped (4h, 2 mm) affording 2.17 g of an almost colorless liquid that was 100% unreacted starting material **5a+5b** by GC analysis.

Attempted Cyclization of a Mixture of 2-Methoxy-2'-methyl-5'-*n*-propyl-diphenyl sulfone (8a) and 2-Methoxy-5'-methyl-2'-*n*-propyldiphenyl sulfone (8b) Using *n*-Butyllithium.^{9,10} A dry, 250-mL, 3-neck, round-bottomed flask was fitted with a stir-bar, a thermometer and two stoppers. Two syringe needles served as inlet and outlet for argon gas. The apparatus was flushed with argon, charged with a solution of sulfones **8a,8b** (3.04 g, 0.01 mol) in 150 mL of dry tetrahydrofuran (150 mL) and then lowered into a Dry Ice-acetone bath. When the inside temperature reached -78 °C, a solution of *n*-butyllithium in hexanes (Aldrich, 2.5 M, 14.0 mL, 0.035 mol, 3.5 equiv) was introduced followed by stirring at -78 °C for 0.5 h. Anhydrous cupric chloride (2.83 g, 0.021 mol, 2.1 equiv) was then added followed by stirring at -78 °C for 1h. The heterogeneous reaction mixture was allowed to reach 18 °C during 1h and was stirred at 18 °C for another hour. Water (10 mL) was then added followed by 5% hydrochloric acid (10 mL) and ether (150 mL). The two layers were separated and the ether layer was washed with

water (2 x 100 mL), dried (MgSO₄), filtered, concentrated (rotary evaporator) and pumped affording the crude product (3.5 g) as a viscous, light-brown oil consisting (by GC) of unreacted sulfones (**8a+8b**, 64 %), sulfones bearing one added butyl group (25 %) and three unidentified impurities (11 %).

Reaction of 1,4-Diethyl-2-[(2'-methoxyphenyl)thio]-benzene (11) With Diphenyl Lithium-Sodium¹². Phenyl lithium (3.9 mL, 7.02 mmol) and sodium (0.62 g) were added to a solution of diphenyl mercury (1.13 g) in anhydrous ether. After stirring for 2 h at 25 °C under argon, sulfide **11** (1.38 g) in anhydrous ether (7 mL) was added. The resulting dark-brown reaction mixture was stirred at 25 °C for 69 h and then heated at reflux for three days. Methanol (20 mL) and water (20 mL) were cautiously added to the cooled reaction suspension under argon. The mixture was made slightly acidic (pH 4) with dilute hydrochloric acid, the layers were separated and the aqueous layer was extracted with ether (3 x 100 mL). The combined ether extracts were washed with sat'd sodium bicarbonate (2 x 100 mL) and with water (30 mL), dried (MgSO₄), filtered, concentrated (rotorvap) and pumped (oil pump, 1 h) affording the crude product as a pale-yellow wax (1.43 g, 106 %). GC analysis of this material showed it to consist of more than 24 components.

Attempted Photocyclization of 1,4-Diethyl-2-[(2'-methoxy-phenyl)-thio]benzene (11)¹³. Sulfide **11** (1.37 g), tetracyanoethylene (0.65 g) and methylene chloride (500 mL) were charged into a photochemical reactor and the resulting solution was deaerated with a steady stream of argon bubbles for 1h. It was then irradiated thru a Pyrex filter with an UV lamp under argon at 25 °C for 36 h during which aliquots were removed at regular intervals. GC analysis of these aliquots showed that at short irradiation times (6h or 18 h) about 3 % conversion had taken place, but at long irradiation times (36 h), the reaction mixture consisted of: unreacted sulfide (88 %, *t_R* = 10.50 min), fragmentation product (4 %, *t_R* = 7.81min) and two unidentified products (6 %, *t_R* = 12.22 min and 2 %, *t_R* = 13.18 min).

Reaction of 1,4-Diethyl-2-[(2'-methoxyphenyl)-thio]benzene (11) With Amberlyst-15¹⁴. Sulfide **11** (1.40 g), Amberlyst-15 (5.0 g) and chlorobenzene (70 mL) were charged into a 100-mL, 2-neck, round-bottomed flask fitted with a thermocouple probe, a stir-bar, a

reflux condenser and a Dean-Stark trap. The reaction mixture was heated at reflux under nitrogen for 4 h and aliquots were removed after 1h, 2h, 3h and 4h for GC analysis. Most of the chlorobenzene (55 mL) was then removed by distillation and *o*-dichlorobenzene (30 mL) were added. Heating at reflux (164-166 °C) was then resumed for 29 h during which time more aliquots were taken at regular time intervals. During this second reflux period, two major new peaks (with *t_R*'s very close to that of the starting sulfide) grew with time. The heating was stopped after 29 h of reflux at which point the product mixture was shown by GC and GC-MS analysis to consist of unreacted **11** (36 %), demethylated **11** (30 %), C₁₀H₁₃SC₁₀H₁₃ (18 %) and three impurities (7 %).

Attempted Reaction of 1,4-Diethyl-2-[(2'-methoxyphenyl)thionyl]-benzene (12) With Vanadium Oxychloride.¹⁵ Sulfone **12** (1.52 g) in dichloromethane (5 mL) was added under argon at 0 °C to a solution of vanadium oxychloride (2.0 mL) in trifluoroacetic acid (15 mL). The resulting dark-brown reaction solution was stirred at 0 °C for 4 h. Water (50 mL) was cautiously added and the aqueous layer was extracted with dichloromethane (5 x 50 mL). The combined dichloromethane extracts were washed with sat'd sodium bicarbonate (30 mL), water (50 mL), dried (MgSO₄), filtered, concentrated, and pumped (oil pump, 2 h) affording the crude product (1.44 g, 99 %) as a dirty-white solid, mp 73-76 °C. GC analysis showed this solid to be the unreacted sulfone **12**.

Attempted Photocyclization of 1,4-Diethyl-2-[(2'-methoxy-phenyl)-thionyl]benzene (12).⁷ This reaction was carried out for 21 h as described for the corresponding sulfide **11** except that a stoichiometric amount of iodine was substituted for tetracyanoethylene. Again aliquots were removed at regular time intervals and analyzed by GC. Workup after 21 h resulted in a product mixture consisting of unreacted sulfone (95 %, *t_R* = 12.54 min) and two fragmentation products (2.5 %, *t_R* = 4.54 min and 2.0 %, *t_R* = 6.22 min).

Bromomenthone (14a, 14b, Scheme II, steps a,b).^{17,18} Lithium diisopropyl amide (LDA) was generated in anhydrous tetrahydrofuran (THF) at -78 °C and under an argon atmosphere by addition during 1.5 h of *n*-butyllithium in hexanes (0.690 mol) to diisopropyl amine

(0.660 mol). Cold THF solutions of chlorotrimethyl-silane (3.93 mol, 6.6 equiv) and (-)-menthone (0.600 mol; Aldrich; contaminated with 5% isomenthone) were then added at -78 °C over 1.6 h and 1.8 h, respectively. This was followed by the rapid addition (15 min) of a cold (-15 °C) solution of bromine (0.626 mol, 1.0 equiv) in dichloro-methane. After stirring for a short time at -78 °C, cold saturated sodium bicarbonate (200 mL) was added over 0.5 h. The Dry Ice-acetone bath was then replaced by an ice bath and the reaction mixture was diluted further with sat'd sodium bicarbonate (3.8 L) and then solid sodium bicarbonate was added until gas evolution ceased and the pH rose to 7-8. The resulting homogeneous solution was extracted with low-boiling petroleum ether (4 x 300 mL). The organic extracts were combined, washed with water, dried (MgSO₄), filtered, concentrated at room temperature, and pumped (oil pump, r.t., 2 mm, 16 h) affording 143 g of crude **14a,14b** as a brown liquid.

6-Isopropyl-2-[(2'-methoxyphenyl)thio]-3-methyl-cyclohexanone (15, Scheme II, step c).¹⁸ Sodium hydroxide (0.654 mol), ethyl alcohol (350 mL), water (150 mL), and 2-methoxybenzenethiol (0.656 mol) were stirred under nitrogen at room temperature for one hour. Crude bromomenthone (0.595 mol) in ethyl alcohol (250 mL) was then added dropwise during 0.7 h. The resulting heterogeneous mixture was heated under nitrogen to reflux during 0.7 h and at reflux for 4 h. After cooling to room temperature under nitrogen, the mixture was treated with water (700 mL) and extracted with ether (6 x 200 mL). The combined ether extracts were washed with brine (4 x 100 mL), dried (MgSO₄), filtered, rotorvaped and pumped affording presumed crude **15** as a brown liquid (141 g). After steam-distillation and similar workup, there was obtained a steam-volatile fraction (14 g) as a clear minty-smelling liquid, which is presumably unreacted menthone (**13**), and a non-steam-volatile fraction (124 g) as a brown, viscous liquid.

9-Isopropyl-4-methoxy-6-methyl-6,7,8,9-tetrahydrodibenzothiophene (16, Scheme II, step d). Crude **15** (1.6 mol) and polyphosphoric acid (1.9 kg PPA) were heated with mechanical stirring under nitrogen to 100 °C during 0.5 h and at 100-110 °C for 1.5 h. The chocolate-brown, syrupy reaction mixture was poured onto 5 L of ice, stirred for 1h to decompose all the unreacted PPA, saturated with sodium chloride and extracted with ether. The combined

organic extracts were washed with water and brine and subjected to steam-distillation. Extractive workup of the residue from the steam distillation afforded the tetrahydro product in an estimated 41% yield as the major constituent of a dark-brown viscous oil possessing a moderate mercaptan odor.

Dehydrogenation of 16 to 9-Isopropyl-4-methoxy-6-methyldibenzothiophene (17, Scheme II, step e) Using Selenium.¹⁸ Crude 16 (15.3 g) and powdered selenium metal (16.0 g) were heated with stirring under an argon atmosphere in a well-ventilated hood to 300 °C over 0.5 h and at 300 °C for 2.3 h. The effluent gas from this reaction was passed first through an empty trap and then through a trap containing copper sulfate solution in order to scrub the hydrogen selenide produced. Ethyl alcohol (80 mL) was then added to the reaction flask and the heterogeneous mixture was heated at reflux under argon for 1h. This was filtered while hot and the filter cake was washed repeatedly with hot dichloromethane. The resulting black filtrate was boiled with activated charcoal, filtered again and the new filtrate was rotorvaped and pumped (oil pump) affording 17 (10.3 g) as a black amorphous paste. This material was eluted with hexanes (3 h) through neutral alumina in a Soxhlet apparatus. Concentration of the hexane extract afforded a first fraction (2.6 g) that was shown by GC and GC-MS analysis to be made up of three isomeric 17's (35%), de-methylated 17 (4%), two isomeric 17's lacking an isopropyl group (15%), and several unidentified side-products (46%). The three isomeric 17's were present in the relative ratios of 23:11:1.0.

Dehydrogenation of 16 to 17 with palladium on carbon.^{20,21} Crude 16 (4.6 g), Pd/C (1.0 g) and 10.0 g of 1-naphthoic acid solvent were heated at 300 °C for 4 h. After cooling to room temperature, the black, solid residue was dissolved in ether and filtered through dicalite. The ether filtrate was washed with saturated sodium bicarbonate, brine, dried, filtered, rotorvaped and pumped affording 6.0 g of a black, syrupy liquid, which was passed through neutral alumina with ether and then steam-distilled. Workup of the residue from the steam distillation afforded 2.6 g of a dark-brown, viscous liquid consisting of 17 (35 %), 19 (13 %) and several impurities (52 %). Other Pd/C reactions gave similar results.

Dehydrogenation of 16 to 17 with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) at 80 °C and at 25 °C. 9-Isopropyl-4-methoxy-6-methyl-6,7,8,9-tetrahydrodibenzothiophene (**16**; 0.25 g, 0.364 mmol), DDQ²³ (0.22 g, 0.950 mmol) and dry benzene were charged into a dry, 15-mL, round-bottom flask fitted with stirring bar, reflux condenser, and drying tube. The resulting black solution was stirred and heated at reflux. Aliquots were removed at regular time intervals and then diluted with benzene. Each such solution was filtered through short plugs of basic alumina, magnesium sulfate, and Dicalite and then concentrated and analyzed by gas chromatography.

A similar experiment was carried out at 25 °C for a total of 24 h. During this period aliquots were taken, treated as described in the preceding paragraph, and analyzed by gas chromatography. The GC analysis showed that the reaction was slow under these conditions: 28 % (24 h at 25 °C), 55 % (24 h at 80 °C), and 67 % complete (168 h at 25 °C or 48 h at 80 °C).

Dehydrogenation of 16 to 17 With DDQ in Refluxing Dioxane. Tetrahydrodibenzothiophene **16** (0.38 mol), was heated at reflux in dry p-dioxane (bp 94 °C) in the presence of 720 g of DDQ under a nitrogen atmosphere for 1.8 h. The resulting black reaction suspension was allowed to cool to room temperature under nitrogen and was then diluted with 4 L of water and 2 L of petroleum ether. The aqueous layer was made basic (pH $\geq$ 10) with sodium hydroxide and was then extracted with 6 x 500 mL of petroleum ether. The combined dark-brown organic extracts were washed with water, brine, dried (MgSO₄) and filtered twice through fresh 200 g-pads each of acidic and basic alumina. The resulting brown filtrate was concentrated and pumped and the residual viscous oil was dissolved in hot ethanol and treated with a saturated solution of picric acid in boiling ethanol. The precipitated orange picrate was collected, dried partially and recrystallized from fresh ethanol. The recrystallized picrate, mp 158-159 °C, was then collected, dried and decomposed over basic alumina using petroleum ether and then toluene. This afforded the first crop of 35 grams of **17** as glistening white crystals, mp 108-110 °C, of >99% purity (by GC). Further processing of the picrate mother liquors yielded another 10.5 grams of **17** ($\geq$ 95% purity) as the second crop. The overall yield of purified **17** from (-)-menthone is 12.2%.

Dehydrogenation of 16 to 17 with 2,3,5,6-tetrachloro-1,4-benzoquinone (Chloranil) in Refluxing Benzene. 9-Isopropyl-4-methoxy-6-methyl-6,7,8,9-tetrahydrodibenzothiophene (**16**, 0.25 g, 0.364 mmol), Chloranil²⁴ (1.4 equiv) and dry benzene were charged into a dry, 15-mL, round-bottom flask fitted with a magnetic stirring bar, a reflux condenser and a drying tube. The resulting black solution was stirred and heated at reflux. Aliquots were removed at regular intervals and then diluted with benzene. Each aliquot was then filtered through basic alumina, magnesium sulfate, Dicalite, concentrated, and analyzed by gas chromatography. The final aliquot, taken after 72 h of reflux, showed (by GC) that only 8 % of **16** was converted to **17** and that none of **19** was present. A second run was carried out in the same way at 80 °C using 4.1 equivalents of Chloranil. GC analysis showed that again only 8 % of **16** was converted to **17** and that **19** was absent.

Picrate of 17 and 19. A hot solution of 10.1 g of picric acid in ethanol was added to a hot ethanol solution of a crude mixture (7.84 g) containing **17** & **19** and several impurities. The resulting dark-brown solution was allowed to cool and stand at room temperature for several hours. The precipitated muddy-orange crystals were filtered, washed once with ethanol and dried partially by pumping. This material was then placed on top of a column of basic alumina, in a modified Soxhlet apparatus, and eluted with refluxing n-hexanes for 0.5 h. Evaporation and pumping of the yellow hexane solution afforded 1.34 g of a colorless, odorless, viscous oil that crystallized completely upon standing at room temperature. Gas chromatography and proton nuclear magnetic spectroscopy showed this material to consist of a 62:38 mixture of **17/19**.

6-Methyl-9-(1-methylethyl)dibenzothiophene-4-ol (18**).**¹⁹ Methoxydibenzothiophene **17** (10.45 g) and boron tribromide (5.6 mL) were combined in dichloromethane at -78 °C under a nitrogen atmosphere. The Dry Ice-acetone bath was then replaced with an ice bath and the reaction mixture allowed to warm to 0 °C. Stirring at 0 °C under nitrogen was continued for 1 h. The reaction mixture was then poured onto 500 mL of ice and the aqueous layer was extracted with 5 x 100 mL of dichloromethane. The combined dichloromethane extracts were washed with water, brine, dried (MgSO₄), filtered, rotorvaped and pumped to give 8.92 g of a white crystalline solid,

mp 155-156 °C, consisting (by GC analysis) of phenol **17** (90 %) and methoxy precursor **17** (10 %). Compounds **17** and **18** were separated by chromatography on basic alumina.

References and Notes

- (1) Pines, H.; Strehlau, D.R.; Ipatieff, V. N. *J. Am. Chem. Soc.* **1949**, *71*, 3534.
- (2) Taylor, E. P.; Watts, G. E. *J. Chem. Soc.* **1952**, 1123.
- (3) Migita, T.; Shimizu, T.; Asami, Y.; Shiobara, J.-i.; Kato, Y.; Kosugi, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1385.
- (4) Suzuki, H.; Nakamura, K.; Goto, R. *Bull. Chem. Soc. Jpn.* **1966**, *35*, 128.
- (5) Eisenbraun, E. J.; Hall, H. *Chem. Ind.* **1970**, 1535.
- (6) Wisansky, W. A.; Ansbacher, S. *Org. Synth. Coll. Vol. III*, **1955**, 138.
- (7) Zeller, K.P.; Petersen, H. *Synthesis* **1975**, 532.
- (8) (a) The general procedure for the oxidation of sulfides to sulfones is described on p 453 of Pasto, D. J.; Johnson, C. R. *Organic Structure Determination*, Prentice-Hall, Inc.: Englewood Cliffs, NJ (1969) was adapted to the compounds at hand. (b) A sulfone can be converted back to the corresponding sulfide with lithium aluminum hydride, and a sulfoxide can be reduced to the sulfide with stannous chloride-hydrochloric acid (Ho, T.-L.; Wong, C.M. *Synthesis* **1973**, 206).
- (9) (a) Gilman, H.; Esmay, D.L. *J. Am. Chem. Soc.* **1953**, *75*, 278. (b) Oita, K.; Gilman, H. *J. Org. Chem.* **1957**, *22*, 336.
- (10) (a) Gogte, V.N.; Palkar, V.S.; Tilak, B.D. *Tetrahedron Lett.* **1960**, (6), 30. (b) Pandya, L.J.; Rao, D.S.; Tilak, B.D. *J. Sci. Industr. Res. India* **1959**, *18B*, 516.
- (11) Wieland, H.; Mueller, C. *Chem. Ber.* **1913**, *46*, 3304.
- (12) Wittig, G.; Benz, E. *Chem. Ber.* **1958**, *91*, 873.
- (13) Bendig, J.; Beyermann, M.; Kreysig, D. *Tet. Lett.* **1977**, 3659.
- (14) (a) Amberlyst-15 is a strongly acidic ion-exchange resin commonly used for effecting electrophilic aromatic substitution/cyclization reactions. (b) Since the boiling point of chlorobenzene is 132 °C, sulfide **17** has some thermal stability. This treatment also demonstrated the stability of **17** under these acidic conditions.

- (15) Liepa, A.J.; Summons, R.E. *J. Chem. Soc., Chem. Commun.* **1977**, 826.
- (16) Corey, E.J.; Gross, A.W. *Tetrahedron Lett.* **1984**, 25, 495.
- (17) Stotter, P.L.; Hill, K.A. *J. Org. Chem.* **1973**, 38, 2576.
- (18) Tedjamulia, M.L.; Tominaga, Y.; Castle, R.N.; Lee, M.L. *J. Heterocycl. Chem.* **1983**, 20, 1485.
- (19) Vickery, E.H.; Pahler, L.F.; Eisenbraun, E.J. *J. Org. Chem.* **1979**, 44, 4444.
- (20) Findlay, J.W.A.; Turner, A.B. *Org. Synth.* **1973**, Coll. Vol. V, 428.
- (21) Walker, D.; Hiebert, J.D. *Chem. Rev.* **1967**, 67, 153.
- (22) CAChe™ = Computer-Aided Chemistry.
- (23) Fieser, M. *Reagents for Organic Synthesis*; Wiley and Sons: New York, 1989; Vol. 12, p174.
- (24) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley and Sons: New York, 1967; Vol 1, p 125.

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Scheme 1

a NH_2NH_2 , NaOH, DEG, heat. **b** Br_2 , Fe, I_2 catalyst. **c** I_2 , HgIO_6 , HOAc, heat. **d** Na, EtOH, 2-Methoxybenzenethiol, $\text{Pd}(\text{PPh}_3)_4$, heat. **e** hn, I_2 , cyclohexane. **f** H_2O_2 (30%), HOAc. **g** BBT_3 , CH_2Cl_2 .

Scheme II

• LDA, TMSCl, THF, -78 °C. **b** Br₂, CH₂Cl₂, -78 °C. **c** 2-Methoxybenzenethiol, NaOH, EtOH-H₂O, Reflux. **d** PPA, heat. **e** DDQ, p-Dioxane, 101 °C. **f** BBr₃, CH₂Cl₂, 0 °C.

Augmented MM2 Calculation Results
(On The Tektronix CAChe™ Molecular Modeling System)

Total Strain Energy = -7.18 Kcal/mol

$d_1 = 2.418 \text{ \AA}$, $d_2 = 2.962 \text{ \AA}$, $d_3 = 3.040 \text{ \AA}$

$\alpha = 122.98^\circ$, $\beta = 123.89^\circ$

$\gamma = 124.23^\circ$, $\delta = 122.71^\circ$

Total Strain Energy = -3.23 Kcal/mol

Total Strain Energy = +0.27 Kcal/mol

**DATE
FILMED**

6/15/94

END