Experimental Section

Polarographic and cyclic voltammetric measurements were carried out with the aid of a Princeton Applied Research Model 170 electrochemical instrument. Polarograms were measured in the conventional manner before and after addition of known amounts of proton donor.

Cyclooctatetraene was purified by vacuum distillation under nitrogen. Purity of the other hydrocarbons was assessed by thin layer chromatography. If more than one spot was observed, the hydrocarbon was purified by column chromatography, sublimation, and/or recrystallization. Dimethyl sulfoxide (Matheson Coleman and Bell) was used as received. Tetrabutylammonium perchlorate (Southwestern Analytical Labs), the supporting electrolyte, was dried in an Abderhalden drying pistol.

Acknowledgment. Financial support was provided by the National Science Foundation. The Uniroyal Corp. provided a summer research assistantship for A. S. Miss Ling Ling Chung made the initial observations upon 9,10-diphenylanthracene and anthracene which led to this study.

Registry No.—**1a**, 120-12-7; **1b**, 779-02-2; **1c**, 602-55-1; **1d**, 781-43-1; **1e**, 1499-10-1; **2**, 85-01-8; **3**, 129-00-0; **4**, 206-44-0; **5**, 198-55-0; **6**, 191-07-1; **7**, 217-59-4; COT, 629-20-9.

References and Notes

(1) (a) M. E. Peover, *Electroanal. Chem.*, **2**, 1 (1967); (b) G. J. Hoijtink, *Advan. Electrochem. Electrochem. Eng.*, **7**, 221 (1970); (c) A. J. Fry, "Synthetic Organic Electrochemistry," Harper and Row, New York, N. Y., 1972, p 258 ff.

(2) K. S. V. Santhanam and A. J. Bard, *J. Amer. Chem. Soc.*, **88**, 2669 (1966).

(3) However, see J. R. Jezorek and H. B. Mark, Jr., *J. Phys. Chem.*, **74**, 1627 (1970).

(4) A. J. Fry, L. L. Chung, and V. Boekelheide, *Tetrahedron Lett.*, 445, 1354 (1974).

(5) A. J. Fry, C. S. Hutchins, and L. L. Chung, submitted for publication.

(6) TMP was used because it is less hydroscopic and more easily purified (sublimation) than phenol.

(7) Reference 1c, p 137.

(8) (a) 9-Phenylfluorene: C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **90**, 2821 (1968). (b) Phenol: L. M. Kolthoff, M. K. Chamtooni, Jr., and S. Bhowmik, *ibid*, **90**, 23 (1968).

(9) R. S. Nicholson, J. M. Wilson, and M. L. Olmstead, *Anal. Chem.*, **38**, 542 (1966).

(10) J. Janata and H. B. Mark, Jr., *J. Phys. Chem.*, **72**, 3616 (1968).

(11) S. W. Feldberg, *Electroanal. Chem.*, **3**, 199 (1969).

(12) (a) L. S. Marcoux, J. M. Fritsch, and R. N. Adams, *J. Amer. Chem. Soc.*, **89**, 5766 (1967); (b) R. N. Adams, *Accounts Chem. Res.*, **2**, 175 (1969).

(13) (a) R. D. Rataiczak and M. T. Jones, *J. Chem. Phys.*, **56**, 3898 (1972); (b) M. G. Townsend and S. I. Weissman, *ibid.*, **32**, 309 (1960); (c) H. M. McConnell and A. D. McLachlan, *ibid.*, **34**, 1 (1961); (d) R. E. Jesse, P. Biloen, R. Prins, J. D. W. v. Voorst, and G. J. Hoijtink, *Mol. Phys.*, **6**, 633 (1963).

(14) J. R. Jezorek, A. Lagu, T. M. Seigel, and H. B. Mark, Jr., *J. Org. Chem.*, **38**, 788 (1973).

(15) Phenol has the same pK_a as 9-phenylfluorene;[8] with three methyl groups, TMP must be less acidic than phenol.

(16) R. L. Benoit and C. Buisson, *Electrochim. Acta*, **18**, 105 (1973).

(17) The pK_a of phenol in DMF has not been measured, but *p*-chloro- and *m*-chlorophenol have pK_a = 16.8 and 16.3, respectively, in DMF.[18] The parent compound should therefore have $pK_a \gg 17$ in DMF; it is 16.4 in DMSO.[8b]

(18) C. D. Ritchie and G. H. Megerle, *J. Amer. Chem. Soc.*, **89**, 1447 (1967).

(19) S. Wawzonek and D. Wearring, *J. Amer. Chem. Soc.*, **81**, 2067 (1959).

Preparation of Some Thiovulpinic Acids

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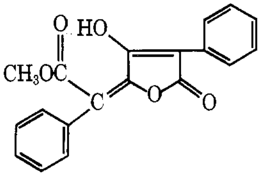
Recent findings of anti-inflammatory activity in the vulpinic acid series[1] prompted us to undertake the investigation of some thio analogs of this interesting series of lichen metabolites.[2] One thio analog of vulpinic acid (**1**) is the thiol ester **2**. Since the dilactone **3** is converted to **1** by reaction with sodium methoxide,[2] the reaction of **3** with the sodium salt of methyl mercaptan was studied. Two products were isolated from this reaction in about 50% yield each, both of which analyzed for the expected product.



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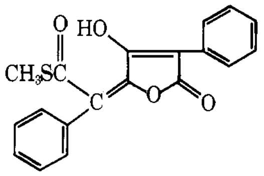

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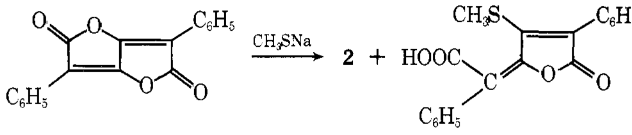
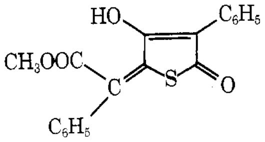


3 **4**

The structure of **2** was established by comparison of its nmr and mass spectra with that of **1**. Both **1** and **2** have very similar characteristic aromatic proton peaks at δ 7.4 (8 protons) and 8.2 (2 protons) and enolic protons at δ 13.8 and 13.65, respectively. The latter indicate chelate-type hydrogen bonding between the enol and the ester carbonyl, and provide strong evidence for the stereochemistry about the exocyclic double bond. The mass spectra of both **1** and **2** show molecular ion peaks, and also strong peaks at m/e 290 corresponding to the m/e for **3** formed by the primary elimination of the elements of methanol and methyl mercaptan, respectively.[3] The nmr of **4** showed a one-proton peak at δ 10.90 characteristic of a carboxylic acid, and the mass spectrum, in addition to the molecular ion peak, showed a strong peak at m/e 294 which is consistent with the loss of CO_2 from the molecular ion. Only a weak peak at m/e 290 was present.

Another thiovulpinic acid is **5**, in which the lactone is replaced by a thiolactone. Since, as shown above, sulfur anions can displace the ring oxygen of **3**, we attempted to prepare **6**, which could conceivably be converted to **5** *via* the monothiodilactone **7** by processes analogous to those used for the preparation of **1**. However, although reaction of **3** with hydrogen sulfide in the presence of sodium methoxide gave a base-soluble product, on attempted recrystallization from methanol of the crude product obtained by acidification of the basic solution, only **3** was isolated. This suggested that **3** was opened to give the



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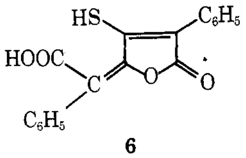

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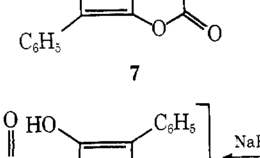

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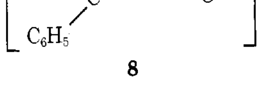

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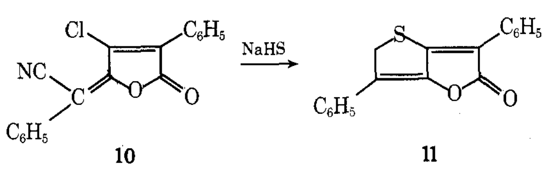
thiol acid **8**, which behaves like a mixed anhydride to thermally re-form **3**.

In another approach to **6**, we repeated (and confirmed) the 1894 preparation[4] of **10** from **9**. We hoped to react **10** with sodium hydrosulfide in order to displace the chlorine with a mercaptan. Reaction of **10** with H_2S and sodium methoxide gave a single product in 85% yield which has been assigned the structure **11**. Thus the mass spectrum had a molecular ion at *m/e* 292 containing (by isotope ratios) only one sulfur, the nmr showed as the only nonaromatic protons a single two-proton peak at δ 4.6, and the elemental analysis (C, H, S) was correct for $C_{18}H_{12}SO_2$. Apparently sulfur did displace the chlorine either before or after reaction with the nitrile. The resultant bicyclic product presumably was reduced by the excess hydrogen sulfide to the observed product. The reducing properties of H_2S and its conjugate anions are well known.[5]

$C_6H_5CH(CN)COCOCH(CN)C_6H_5 \xrightarrow{POCl_3}$

9



10 **11**

The successful preparation of **7** was suggested by the report[6] that thiolacetic acid and pyridine convert certain simple butenolides to the corresponding thiolactones. Treatment of **3** with 1 mol of thiolacetic acid and pyridine in chloroform gave the desired monothiolactone **7**; excess thiolacetic acid gave the dithiolactone **12**. A rationalization of this reaction may be that thiolacetate attacks **3** to give both **13** and **14** in a manner similar to the reaction of **3** with methylmercaptide ion. Since **13** is able to revert readily to **3** by loss of thioacetate, no net reaction results. However, **14** is unable to re-form **3** readily, and the carboxylate anion can be acylated either by the adjacent thioacyl group or by thiolacetic acid. The mixed anhydride **15** now can form **7** by a sterically favored cyclization.

Reaction of **7** with methanolic sodium methoxide gave the desired thiovulpinic acid **5**. The thiolactone structure for **5** was suggested by the presence of carbonyl peaks in the ir at 5.94 and 6.03 μ and the absence of a strong peak near 5.65 μ characteristic of vulpinic acids due to the lactone carbonyl. The cis relationship of the ester and enol is most clearly indicated by the chelated OH peak in the nmr at δ 13.97. Prolonged refluxing of **5** during attempted recrystallization from methanol or melting at 110° converted **5** back to **7**. Lactonization of **1** to give **3** is not observed under such mild conditions; so the presence of sulfur in the thiolactone ring greatly increases the rate of ring formation of the adjacent five-membered ring, possibly because the larger size of sulfur in comparison to oxygen decreases strain energy. Treatment of **12** with sodium methoxide formed a soluble salt, presumably **16**, but acidification even at 0° caused recyclization to **12**. Presumably ring formation is aided by the low strain energy of two thiolactone rings and the nucleophilicity of the mercapto group.

Experimental Section

Melting points (uncorrected) were determined using a Thomas-Hoover capillary melting point apparatus. Mass spectra were determined using a Hitachi Perkin-Elmer RMN-6E spectrometer. Nmr spectra were obtained on a Varian T-60 instrument, and ir on a Perkin-Elmer 137 Infracord.

Thiolpulvinic Acid Methyl Ester (2) and 2,5-Diphenyl-4-hydroxy-3-methylthio-2,4-hexadienedioic Acid γ-Lactone (4). Pulvinic acid lactone (16.0 g, 0.055 mol) was added to a suspension of 2.88 g (0.06 mol) of 50% sodium hydride in oil in 100 ml of glyme. Methyl mercaptan was bubbled through the solution until a clear brown solution was obtained and tlc indicated that no dilactone remained. The reaction mixture was diluted with about 400 ml of water and extracted with ether, and the aqueous layer was acidified with hydrochloric acid to give an oily solid. Recrystallization from acetone–water gave 7.0 g (37%) of **2** as orange needles, mp 156–158°. A second recrystallization from the same solvent mixture gave 3.87 g of orange needles: mp 165–168°; ir (Nujol) 4.3 (broad, chelate OH), 5.65, 6.20, 6.30 μ; nmr ($CDCl_3$) δ 2.36 (s, 3, SCH_3), 7.40 (m, 8 H, 3′-, 4′-, 5′-, 2-, 3-, 4-, 5-, 6-phenyl H), 8.14 (m, 2 H, 2′-, 6′-phenyl H), 13.65 (s, 1, OH); mass spectrum *m/e* 338 (M^+), 290 ($M^+ - CH_3SH$), 263 ($M^+ - COSCH_3$), 235, 207, 178, 145.

Anal. Calcd for $C_{19}H_{14}O_4S$: C, 67.44; H, 4.17; S, 9.48. Found: C, 67.53; H, 4.30; S, 9.28.

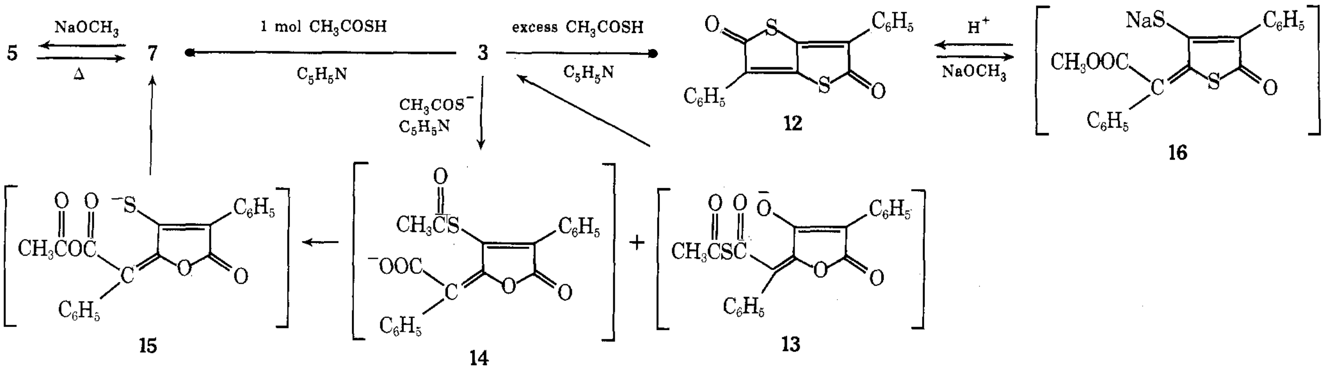
Evaporation of the mother liquor of the first crystallization above gave a red oil which on drying under vacuum and trituration with cyclohexane gave 5.0 g of a yellow solid. Recrystallization from benzene gave 1.4 g of **4** as yellow needles: mp 166.5–167°; ir (Nujol) 5.7 and 6.0 μ; nmr ($CDCl_3$) δ 2.08 (s, 3, SCH_3), 7.55 (m, 10, phenyl H), 10.90 (s, 1, OH); mass spectrum *m/e* 338 (M^+), 294 ($M^+ - CO_2$), 290, 279, 148 ($C_6H_5C{\equiv}CSCH_3^+$).

Anal. Calcd for $C_{19}H_{14}O_4S$: C, 67.44; H, 4.17; S, 9.48. Found: C, 67.53; H, 4.25; S, 9.38.

3,6-Diphenyl-2*H*,5*H*-thieno[3.2-*b*]furan-2-one (11). A suspension of 0.174 g (0.00325 mol) of sodium methoxide in 20 ml of dry glyme was saturated with hydrogen sulfide gas and a slurry of 1.0 g (0.00325 mol) of 4-chloropulvinonitrile in glyme was added in portions. After 1 hr a yellow solid had formed. The reaction mixture was diluted with water and the solid was collected by filtration and washed with water to give 0.85 g (90%) of brown-yellow needles. Recrystallization from methanol-chloroform and then chlorobutane gave golden needles: mp 208.5–210° dec; ir (Nujol) 5.8 μ; nmr ($CDCl_3$) δ 4.56 (s, 2, CH_2S), 7.37 (m, 6, phenyl H), 7.76 (m, 4, phenyl H); mass spectrum *m/e* 292 (M^+, isotope peak indicates 1 S), 291, 263, 247, 235.

Anal. Calcd for $C_{18}H_{12}O_2S$: C, 73.95; H, 4.14; S, 10.97. Found: C, 73.89; H, 3.96; S, 10.78.

3,6-Diphenyl-2*H*,5*H*-thieno[3,2-*b*]furan-2,5-dione (7). A mixture of 2.90 g (0.01 mol) of pulvinic acid lactone, 0.76 g (0.01 mol) of thiolacetic acid, and 1.01 g (0.01 mol) of triethylamine in 15 ml of dry pyridine was stirred at room temperature for 30 min. The reaction mixture was chilled, diluted with water, and acidified to give red crystals which were recrystallized from chlorobutane. Since previous experience indicated that this product, although mostly the desired **7**, was contaminated with both pulvinic acid



lactone 3 and the dithiolactone 12, it was dissolved in methanolic sodium methoxide, cooled, diluted with water, and acidified. The crude 5 thus obtained was dissolved in 5% sodium carbonate, the insoluble fraction was removed by filtration, and the solution was extracted with ether. Acidification gave pure 5, which was dissolved in 50 ml of methanol and refluxed for 35 min to give 1.5 g of 7 as long yellow needles: mp 175–176.5°; ir (Nujol) 5.6, 5.9, 6.2 μ; nmr ($CDCl_3$) δ 7.30 (m, 6, phenyl H), 7.80 (m, 4, phenyl H); mass spectrum *m/e* 306 (M^+), 278, 250.

Anal. Calcd for $C_{18}H_{10}O_3S$: C, 70.57; H, 3.29; S, 10.47. Found: C, 70.89; H, 3.41; S, 10.23.

5-Carbomethoxy-2,5-diphenyl-3-hydroxy-4-mercapto-2,4-pentadienoic Acid γ-Thiolactone (*E*) (5). A solution of 1.6 g (0.00523 mol) of 7 and 1.6 g (0.03 mol) of sodium methoxide in 35 ml of methanol was kept at 0–5° for 30 min. The solution was treated with charcoal and diluted with water, and the chilled solution was acidified with HCl to give a yellow solid. This was dissolved in about 200 ml of 5% Na_2CO_3 and extracted twice with ether, and the aqueous layer was acidified in the cold with acetic acid to give 1.50 g (84%) of a yellow-orange, flocculent solid: mp 115–116° (resolidified and remelted at 173–175°); ir (Nujol) broad peak at 3.9–4.4 (chelated OH), 5.94 and 6.03 μ; nmr ($CDCl_3$) δ 3.76 (s, 3, OCH_3), 7.31 (m, 8, phenyl H), 7.72 (m, 2, phenyl H), 13.97 (br s, 1, OH); mass spectrum *m/e* 338 (M^+), 306 ($M^+ - CH_3OH$), 278.

Anal. Calcd for $C_{19}H_{14}O_4S$: C, 67.44; H, 4.17; S, 9.48. Found: C, 67.74; H, 4.29; S, 9.19.

3,6-Diphenyl-2*H*,5*H*-thieno[3,2-*b*]thiophene-2,5-dione (12). A mixture of 5.0 g (0.0172 mol) of pulvinic acid lactone, 4 ml of thiolacetic acid, 8 ml of chloroform, and 22 ml of dry pyridine was refluxed for 3 hr. Then another 4 ml of thiolacetic acid was added, the refluxing was continued for an additional 1 hr, and the reaction mixture was allowed to stand at room temperature for 18 hr. This gave 0.90 g (16%) of an orange solid, mp 219–221.5°. For purification this was dissolved in warm methanolic sodium methoxide to give a red solution. The chilled solution was diluted with water and acidified to give a yellow solid, which was slurried with sodium carbonate and washed with water to give 0.65 of a yellow solid: mp 221–222.5° dec; ir 5.9 μ; mass spectrum *m/e* 322 (M^+).

Anal. Calcd for $C_{18}H_{10}O_2S_2$: C, 67.06; H, 3.13; S, 19.89. Found: C, 67.08; H, 3.32; S, 19.55.

Acknowledgments. We are indebted to our Analytical and Physical Chemistry Section personnel for analytical and physical data: Miss Edith Reich for elemental analysis and Dr. Edward White and Mr. Gerald Roberts for mass spectra.

Registry No.—**2**, 51751-95-2; **3**, 6273-79-6; **4**, 51751-96-3; **5**, 51751-97-4; **7**, 51751-98-5; **10**, 51751-99-6; **11**, 51751-00-2; **12**, 51751-01-3.

References and Notes

(1) B. M. Sutton, D. T. Walz, and J. W. Wilson, Belgian Patent 775,871 (1972); F. R. Foden and D. M. O'Mant, U. S. Patent 3,676,464 (1972).
(2) Y. Asohina, "Chemistry of Lichen Substances," Japan Society for the Promotion of Science, Tokyo, 1954.
(3) See R. M. Letcher and S. H. Eggers, *Tetrahedron Lett.*, 3541 (1967), for a discussion of the mass spectra of pulvinic acid derivatives.
(4) J. Volhard and F. Hencke, *Justus Liebigs Ann. Chem.*, **282**, 59 (1894).
(5) J. P. Idoux, *J. Chem. Soc. C*, 435 (1970); H. K. Porter, *Org. React.*, **20**, 455 (1973).
(6) Y. S. Rao and R. Filler, *J. Heterocycl. Chem.*, **1**, 210 (1964).

An Improved Synthesis of Tetrathiafulvalene

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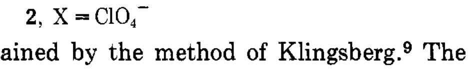
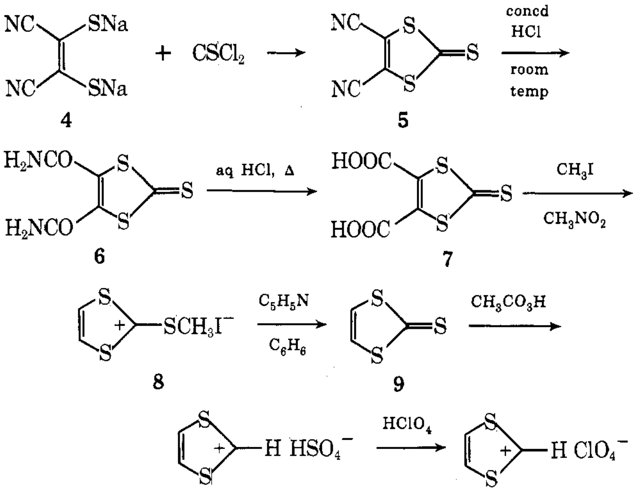
The phenomenon of metallic electrical conductivity in the complex of tetrathiafulvalene (TTF, 3) with tetracyanoquinodimethane has recently been a subject of intense interest.[2-4] Extensive physical study of this complex depends, among other things, upon a reliable source of TTF, which must be unusually pure.[5] In our hands existing routes to TTF proved to be tedious and difficult to reproduce, and often gave product of dubious or unsatisfactory purity. We now report an improved synthesis of TTF.

Typical preparative procedures for TTF ultimately rely on coupling the 1,3-dithiolium hydrogen sulfate (1) or perchlorate (2)[2,6-8] with a tertiary amine, the thiolium salts



1, $X = HSO_4^-$
2, $X = ClO_4^-$
3

being obtained by the method of Klingsberg.[9] The latter entails the multistep sequence depicted in transformations 4 through 9.



In this sequence we encountered particular difficulty in obtaining reasonable yields of thione 9 by demethylation of the methiodide 8. This in turn complicated preparing pure hydrogen sulfate 1. Furthermore, although the hydrogen sulfate can be directly coupled to TTF without conversion to an intervening salt form, the fact that it is hygroscopic and difficult to purify seriously compromises its use as a coupling substrate. The hydrogen sulfate can be readily converted to very pure perchlorate 2, which is chemically satisfactory for coupling, but which entails a serious explosion hazard particularly if large quantities are to be used.

Our improved procedure begins with the diester 10 prepared according to the directions of O'Connor and Jones.[10]

By this means we have reproducibly obtained recrystallized TTF of very high purity in 65% yields based on diester 10, or 55% overall yields based on commercially available dimethyl acetylenedicarboxylate and ethylene trithiocarbonate; the yields cited are reproducible to within ±2%.

In addition to high yields, the main points of advantage and novelty in this sequence are (1) a simplified route to diacid 7, (2) direct decarboxylation of the diacid to thione 9 in high yield and purity and consequent improved accessibility of the hydrogen sulfate 1, (3) formation of analytically pure PF_6^- salt 11, which is an ideal coupling substrate both with respect to the chemistry of coupling and safety of handling even on a large scale.[11]

For spectral studies we also required highly deuterated TTF. By hydrolyzing the ester 10 with a mixture of DCl and DOAc in D_2O (from acetyl chloride and D_2O), and