Synthesis of 2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran and Its Reaction with *o*-Chloranil[1]

THOMAS E. YOUNG,* LAURENCE J. HEITZ,[1,2] AND DAVID J. STEKLENSKI[1]

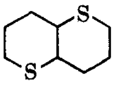
William H. Chandler Chemistry Laboratory, Lehigh University, Bethlehem, Pennsylvania 18015

Received July 13, 1972

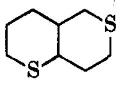
2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one (**9**), the first example of a new fused-ring heterocyclic system, has been synthesized *via* a stepwise condensation sequence from thiophenol and 2-carbomethoxythiacyclohexan-3-one (**5**). Reduction of this ketone (**9**) with aluminum hydride afforded 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran (**11**), which was inert to further catalytic (Pd/C) dehydrogenation up to 200°. Dehydrogenation of **11** with *o*-chloranil yielded a product characterized as a 1:1 adduct (**12**) of thiopyrano[3,2-*b*]-1-benzothiopyran (**3**) with *o*-chloranil.

In view of the many thousands of heterocyclic ring systems known in the literature, it is quite surprising that virtually no attention has been given to the thiopyranothiopyrans having various modes of ring fusion. Indeed, prior to our recently completed syntheses of *trans*-octahydrothiopyrano[3,2-*b*]thiopyran (**1**)[3] and of octahydrothiopyrano[4,3-*b*]thiopyran (**2**)[4] only one example of this general class, *viz.*, 1,2,3,4-tetrahydro-8-amino-5-methyl-2,10-dithiaxanthone, had been disclosed as an incidental item in a patent.[5]

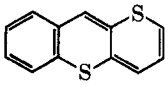
Interest in these kinds of structures stems from the potential aromaticity of fully conjugated, nonclassical dithia heterocycles such as thiopyrano[3,2-*b*]-1-benzothiopyran (**3**) and the dicationic species, 2,10-dithioniaanthracene (**4**), as well as analogs derived from **1** and **2**.



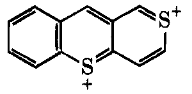
1



2



3

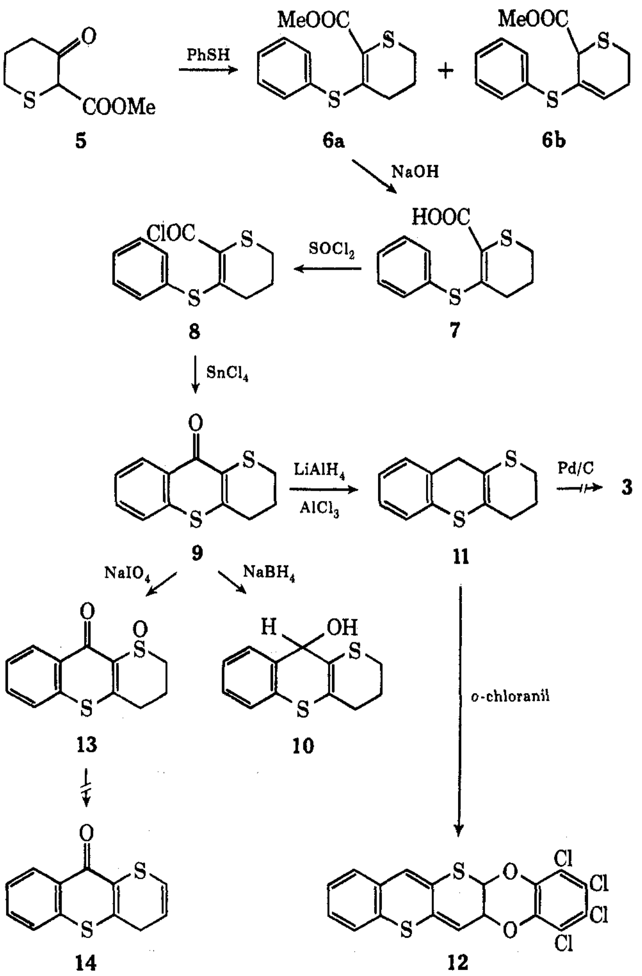


4

As a prelude to further studies of such theoretically interesting systems, we have explored syntheses of the prerequisite skeletal structures, and report here an explicit preparation of 2,3,4,10-tetrahydrothiopyrano-[3,2-*b*]-1-benzothiopyran (**11**), along with the response of this compound toward selected dehydrogenating reagents.

The reactions investigated are summarized in Scheme I, in which 2-carbomethoxythiacyclohexan-3-one (**5**)[3] was first condensed with thiophenol in benzene in the presence of *p*-toluenesulfonic acid as catalyst and with azeotropic separation of water. The products, obtained in 46% yield, were comprised of a mixture of methyl 3-phenylmercaptothiacyclohex-2-ene-2-carboxylate (**6a**) and the isomeric 3-ene (**6b**) whose presence was evident from a vinyl triplet (H-4, δ 6.50 ppm, J = 4 Hz) in the nmr spectrum. The ratio of **6a**:**6b** was about 4:1 as estimated from the integrated intensities of the separate methyl (ester) resonance bands. Fractional distillation of the isomeric esters and recrystallization of the higher boiling fraction from hexane afforded pure crystalline samples of the conjugated isomer **6a** whose structure was verified by its nmr spectrum, which clearly lacked the vinyl proton absorption characteristic of the unconjugated isomer **6b**.

SCHEME I



Saponification of pure ester **6a** gave a 69% yield of the corresponding carboxylic acid **7**, which was used in subsequent cyclization experiments. Reaction of this acid with thionyl chloride gave the acid chloride **8**, which underwent ring closure on treatment with stannic chloride to yield (86% for two steps) 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one (**9**). This yellow crystalline ketone (**9**) exhibited an nmr spectrum consistent with the assigned structure and displayed an intense carbonyl stretching band at 1600 cm^{-1} in the infrared spectrum. This carbonyl frequency, which is comparable with that of 4*H*-thio-

---

[1] Based in part on the Ph.D. dissertation of L. J. Heitz, 1971, and the senior B.S. thesis of D. J. Steklenski, 1969, both at Lehigh University. Supported by National Science Foundation Grant GP-8597.

[2] National Defense Education Act Fellow, 1966–1969; Research Assistant, 1969–1971.

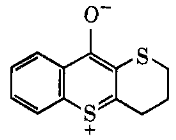
[3] T. E. Young and L. J. Heitz, *J. Org. Chem.*, **38**, 1562 (1973).

[4] T. E. Young and L. J. Heitz, unpublished work.

[5] Farbenfabriken Bayer, A.-G., British Patent 803,803 (Nov 5, 1958); *Chem. Abstr.*, **53**, 11412*h* (1959); *cf.* F. Bossert and R. Goennert, *Med. Chem. Abhandl. Med. Chem. Forschungstaetten Farbwerke Hoechst A.-G.*, **7**, 36 (1963); *Chem. Abstr.*, **60**, 9236*g* (1964).

pyran-4-one (1609 cm^{-1}),[6a] is indicative of an unusually low double-bond character of the carbonyl group, probably resulting from delocalization *via* a thiopyrylium-like structure as illustrated by the following canonical form.[6b]

9 ↔



The resulting redistribution of charge would account for the low carbonyl reactivity of ketone **9**, which could not be derivatized with hydroxylamine or phenylhydrazine in the usual manner. Furthermore, repeated attempts to reduce the ketone **9** by variations of the Huang-Minlon and Meerwein–Ponndorf reductions all yielded varying amounts of unreacted ketone but no reduction products. Reaction with lithium aluminum hydride was also ineffective, yielding about 30% of the expected weight of a solid, noncrystalline product which could neither be crystallized nor sublimed. However, sodium borohydride in aqueous ethanol gave a trace of the carbinol **10**, isolated as white crystals which showed a broad, hydrogen-bonded hydroxyl absorption at 3310 cm^{-1} in the infrared spectrum, but virtually no olefinic absorption in the expected region above 1600 cm^{-1}. Possible reduction of the ring-juncture double bond was excluded, however, since the mass spectrum of **10** showed the correct molecular ion parent peak at *m/e* 236 (calcd 236). In any case, the exceedingly poor yield of the carbinol **10** obviated further synthetic experiments with this material, and variations of the reduction procedure did not improve its availability.

The cyclic ketone **9** was finally reduced by aluminum hydride generated *in situ* from lithium aluminum hydride and aluminum chloride in ether solution. This procedure, based on a similar one devised by Urberg and Kaiser[7] for reduction of thioxanthones, gave a 70% yield of 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran (**11**) as a viscous yellow oil whose infrared and nmr spectra clearly confirmed the assigned structure.

Attempts to dehydrogenate the tetrahydro compound **11** directly to the fully conjugated system **3** with palladium on charcoal at 200° yielded only recovered starting material, while reaction of **11** with *o*-chloranil in acetic acid solution afforded a colorless, crystalline compound which appeared to be a 1:1 adduct of thiopyrano[3,2-*b*]-1-benzothiopyran (**3**) with *o*-chloranil (*i.e.*, **12** or possibly an isomer thereof). Although this product was too insoluble in available solvents (*cf.* Experimental Section) to permit nmr characterization, it had an acceptable elemental analysis and showed a molecular ion parent peak at *m/e* 460 (calcd 460) in the mass spectrum, and an intensity ratio [(P + 2):P] of 1.35, about that expected for a tetrachloro compound.[8] In addition, this substance exhibited an intense infrared absorption band at 1450 cm^{-1}, which is comparable with the strong band (*ca.* 1428 cm^{-1}) characteristic of other 1,4-dioxin adducts of *o*-chloranil with olefins.[9] The high degree of unsaturation of this compound was further substantiated by an exceedingly weak aliphatic C–H stretching frequency at 2920 cm^{-1}, while the low frequency of the olefinic absorption (1600 cm^{-1}) strongly favored assignment of the conjugated structure **12** to this adduct. The ostensible intermediacy of **3** in the formation of this product **12** cannot, of course, be verified on the basis of the present experiments. Hence, unambiguous characterization of the theoretically interesting, but elusive, **3** must await its ultimate isolation by other means.

As a possible alternative route to introducing further unsaturation into the terminal thiopyran ring, the intermediate ketone **9** was converted by reaction with sodium metaperiodate[10] in dioxane to the 1-oxide **13** in 81% yield. The infrared spectrum of this product showed a typical sulfoxide stretching frequency at 1030 cm^{-1} and an intense absorption at 1610 cm^{-1} characteristic of the carbonyl group of the thiochromen-4-one system, thus confirming the assigned site of oxidation at S-1. Attempts to effect a Pummerer dehydration[11] of the sulfoxide with acetic anhydride, in the hope of obtaining **14**, yielded poorly defined products which could not be characterized, while a variation involving the use of benzoic anhydride afforded only recovered starting material.

Experimental Section[12]

Methyl 3-Phenylmercaptothiacyclohex-2-ene-2-carboxylate (6a) and Methyl 3-Phenylmercaptothiacyclohex-3-ene-2-carboxylate (6b).—A solution of 87.0 g (0.500 mol) of 2-carbomethoxythiacyclohexan-3-one (**5**),[3] 55.1 g (0.500 mol) of thiophenol, and 6.0 g (0.035 mol) of *p*-toluenesulfonic acid monohydrate in 500 ml of benzene was refluxed for 18 hr under a Dean–Stark trap. A total of 9.0 ml of water was collected. The solution was cooled and washed with four 150-ml portions of 10% sodium hydroxide, followed by two 150-ml portions of water. The benzene fraction was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The viscous, straw-yellow residual oil (108.7 g) was fractionally distilled to give 73.6 g of crude product, bp 150–175° (0.2–0.3 mm). Redistillation of this material gave two major fractions.

Fraction 1 (21.1 g), bp 138–145° (10.10 mm), whose nmr spectrum showed two distinct methyl ester peaks at δ 3.83 and 3.71 ppm for **6a** (*vide infra*) and **6b**, respectively, in about a 1:1 ratio, yielded a middle cut, bp 139.5–140° (0.10 mm), which was analyzed.

Anal. Calcd for $C_{13}H_{14}O_2S_2$: C, 58.61; H, 5.30; S, 24.08. Found: C, 58.81; H, 5.36; S, 24.15.

Fraction 2 (39.4 g), bp 146–156° (0.10 mm), showed an nmr spectrum with only a trace of vinyl absorption and consisted mainly of isomer **6a**. Redistillation gave pure **6a**, bp 159–160° (0.10 mm), which crystallized on cooling. Recrystallization from

---

[6] (a) D. S. Tarbell and P. Hoffman, *J. Amer. Chem. Soc.*, **76**, 2451 (1954). (b) On the basis of more detailed infrared studies, A. R. Katritzky and R. A. Jones, *Spectrochim. Acta*, **17**, 64 (1961), concluded that similarly polarized canonical forms are important contributors to the structure of 4*H*-thiopyran-4-one.

[7] M. M. Urberg and E. T. Kaiser, *J. Amer. Chem. Soc.*, **89**, 5931 (1967).

[8] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

[9] L. M. Jackman in R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., "Advances in Organic Chemistry. Methods and Results," Vol. 2, Interscience, New York, N. Y., 1962, pp 334–335.

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

[11] W. E. Parham and L. D. Edwards, *ibid.*, **33**, 4150 (1968).

[12] Melting points were determined using a Mel-Temp apparatus, precalibrated with a standard series of compounds having known corrected melting points. The microanalyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn., and by Dr. George I. Robertson, Florham Park, N. J. Infrared spectra were recorded on a Perkin-Elmer Model 257 instrument. Solids were run at 1% weight concentration in KBr disks, and liquids were run neat between NaCl plates. Nmr spectra were determined on a Varian A-60 or a Perkin-Elmer Hitachi R-20A spectrometer using tetramethylsilane as internal standard. Data are presented in the order δ (multiplicity, coupling constant, number of protons, assignment). Mass spectra were run by Dr. J. E. Sturm (Lehigh University) on a Hitachi RMU-6E high-resolution instrument equipped with double-focusing sector.

hexane yielded white needles: mp 48–48.5°; ir (neat) 2950–2920, 1730 and 1710 (C=O), 1585 (C=C), 1480, 1440, 1290–1210, 1190, 1055, 1030, 750, and 695 cm^{-1}; nmr ($CDCl_3$) δ 7.38 (m, 5, ArH), 3.83 (s, 3, CH_3), 2.90 (t, J = 4.5 Hz, 2, 6-CH_2), 2.05 ppm (m, 4, 4- and 5-CH_2).

Anal. Calcd for $C_{13}H_{14}O_2S_2$: C, 58.61; H, 5.30; S, 24.08. Found: C, 58.40; H, 5.21; S, 24.32.

3-Phenylmercaptothiacyclohex-2-ene-2-carboxylic Acid (7).—A mechanically stirred mixture of 165 g (0.619 mol) of methyl 3-phenylmercaptothiacyclohex-2-ene-2-carboxylate (**6a**) and 600 ml of 10% sodium hydroxide solution was refluxed for 5 hr. The resulting solution was cooled in an ice bath and acidified to pH 1–2 with 10% hydrochloric acid. The foul-smelling brown precipitate was collected by filtration, air dried, and then recrystallized from 600 ml of benzene to yield 108 g (69.1%) of pale yellow acid (**7**): mp 122–125°; nmr ($CDCl_3$) δ 11.02 (s, 1, COOH), 7.58 (m, 5, ArH), 2.87 (t, J = 6 Hz, 2, 6-CH_2), 2.03 ppm (m, 4, 4- and 5-CH_2).

Anal. Calcd for $C_{12}H_{12}O_2S_2$: C, 57.11; H, 4.79; S, 25.41. Found: C, 57.40; H, 4.83; S, 25.51.

2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one (9).—To a mechanically stirred solution of 23.2 g (0.092 mol) of 3-phenylmercaptothiacyclohex-2-ene-2-carboxylic acid (**7**) in 250 ml of anhydrous ether was added 34.5 ml (0.52 mol) of thionyl chloride and 5 drops of pyridine. A condenser and drying tube were attached and the mixture was then refluxed for 2 hr. The ether and excess thionyl chloride were then removed on a rotary evaporator, leaving the crude acid chloride **8** as a dark brown oil. The acid chloride was dissolved in 250 ml of anhydrous benzene, the solution was cooled in an ice bath, and 23.4 ml (0.200 mol) of stannic chloride was added. The mixture was allowed to come to room temperature during 2 hr, after which it was poured into a mixture of 250 ml of concentrated hydrochloric acid and 700 g of ice. The resulting mixture was stirred thoroughly and the solid was collected by filtration. Benzene extraction of the mother liquor yielded more brown solid upon evaporation of the solvent. The combined solids were recrystallized from absolute ethanol to give 8.60 g (40%) of 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one (**9**) as yellow crystals, mp 174–176°. Further recrystallization produced an analytical sample: mp 178–180°; ir (KBr) 1600 (C=O), 1580, 1560, 1530, 1430, 1320, 1145, 830, 810, and 750 cm^{-1}; nmr ($CDCl_3$) δ 8.50 (m, 1, H-9), 7.55 (m, 3, H-6, 7, and 8), 3.07 (t, J = 6 Hz, 2, 2-CH_2), 2.78 (t, J = 6 Hz, 2, 4-CH_2), 2.20 ppm (m, 2, 3-CH_2).

Anal. Calcd for $C_{12}H_{10}OS_2$: C, 61.50; H, 4.30; S, 27.27. Found: C, 61.30; H, 4.48; S, 27.28.

2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-ol (10).—To a suspension of 1.00 g (0.00428 mol) of ketone **9** in 130 ml of 95% ethanol was added a solution of 3.00 g (0.079 mol) of sodium borohydride in 20 ml of 3% sodium hydroxide solution. The mixture was then stirred under reflux for 5.5 hr, cooled, and diluted with 500 ml of water. The resulting emulsion was acidified with acetic acid to pH *ca.* 6, and the yellow precipitate was collected and dried. This material weighed 0.52 g and gelled around 115–120°, but could neither be crystallized nor sublimed. Concentration of the filtrates yielded 50 mg of cream-colored solid which on sublimation at 110° (0.15 mm) afforded white crystals of the carbinol **10**: mp 133–135°; ir (KBr) 3310 broad (OH), 3050 (ArH), 2935, 2910, 2850 (CH aliphatic), 1590, 1565, 1470, 1430, 1270, 1040, and 750 cm^{-1}; mass spectrum m/e 236 (calcd 236 for M^+).

Anal. Calcd for $C_{12}H_{12}OS_2$: C, 60.98; H, 5.12; S, 27.13. Found: C, 60.81; H, 5.06; S, 26.92.

2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran (11).—To a mechanically stirred slurry of 1.29 g (0.034 mol) of lithium aluminum hydride in 50 ml of anhydrous ether (distilled from NaH) was added slowly a solution of 9.10 g (0.0685 mol) of anhydrous aluminum chloride in 75 ml of dry ether. After the mixture was cooled in an ice bath, 4.00 g (0.0171 mol) of 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one (**9**) was added portionwise during 10 min. The resultant solution was refluxed for 0.5 hr and cooled, and the excess lithium aluminum hydride was carefully destroyed by addition of ethyl acetate. Water was then added dropwise to coagulate the solids. The mixture was filtered, and the solids were washed with three 50-ml portions of ether. The combined ether extracts were dried ($MgSO_4$), filtered, and evaporated. The residual oil was distilled through a short-path column to give 2.85 g (76%) of 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran (**11**) as a pale yellow oil: bp 133–136° (0.15 mm); ir (neat) 3060 (ArH), 2920, 2860, 2840, 2820 (CH aliphatic), 1620 (C=C), 1590, 1575, 1470, 1450, 1440, and 750 cm^{-1}; nmr (CCl_4) δ 7.08 (m, 4, ArH), 3.20 (s, 2, 10-CH_2), 2.75 (t, J = 5.5 Hz, 2, 2-CH_2), 2.08 ppm (m, 4, 3- and 4-CH_2).

Anal. Calcd for $C_{12}H_{12}S_2$: C, 65.41; H, 5.49; S, 29.10. Found: C, 65.50; H, 5.58, S, 28.90.

Reaction of 2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran (11) with *o*-Chloranil.—To a magnetically stirred refluxing solution of 2.20 g (0.01 mol) of 2,3,4,10-tetrahydrothiopyrano-[3,2-*b*]-1-benzothiopyran (**11**) in 30 ml of glacial acetic acid was added dropwise 4.90 g (0.02 mol) of *o*-chloranil in 20 ml of acetic acid over a period of 15 min. After the addition was complete, the resulting mixture was refluxed for 2 hr. The mixture was then cooled to room temperature and the precipitate was collected by filtration go give 4.00 g of white solid, mp 260° dec. The very low solubility of this material in all of the usual solvents, including such powerful media as DMSO, DMF, pyridine, trifluoroacetic acid, and hexamethylphosphoramide, dictated purification[13] by extraction of impurities with refluxing xylene to give an analytical sample of white powder: mp 265° dec; ir (KBr) 3060 w (ArH), 2920 w (CH aliphatic), 1600 (C=C), 1450 s, 1385, 1310, 1285, 1230, 1165, 1110, 1090, 1010, 1000, 865, 835, and 755 cm^{-1}; mass spectrum m/e (rel intensity) 460 (29), 203 (100), 171 (51), 91 (49), and 69 (70) (calcd for M^+, 460). Additionally, the molecular ion cluster, m/e (rel intensity normalized to total unity) 460 (0.125), 461 (0.060), 462 (0.290), 463 (0.070), 464 (0.207), 465 (0.045), 466 (0.079), 467 (0.017), 468 (0.017), yielded a molecular weight value of 462.6 (calcd 462.2).

Anal. Calcd for $C_{18}H_8Cl_4O_2S_2$: C, 46.78; H, 1.74; Cl, 30.68; S, 13.87. Found: C, 47.03; H, 2.06; Cl, 30.45; S, 14.17.

2,3,4,10-Tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one 1-Oxide (13).—To a magnetically stirred solution of 2.72 g (0.0128 mol) of sodium metaperiodate in 50 ml of water was added in one portion a solution of 3.00 g (0.0128 mol) of **9** in 50 ml of dioxane. The solution immediately became cloudy with precipitation of a white solid occurring after a few minutes. Stirring was continued overnight at room temperature. The mixture was then diluted with 100 ml of water and extracted with three 75-ml portions of chloroform. The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The resulting crude solid was recrystallized from absolute ethanol to give 2.60 g (81%) of 2,3,4,10-tetrahydrothiopyrano[3,2-*b*]-1-benzothiopyran-10-one 1-oxide (**13**), mp 166° dec. Two more recrystallizations afforded an analytical sample of **13**: mp 166° dec; ir (KBr) 3050 (ArH), 2900 (CH aliphatic), 1610 (C=O), 1590, 1565, 1530, 1440, 1315, 1050, 1030 ($^+SO^-$), 990, and 750 cm^{-1}; nmr (CF_3COOD) δ 8.55 (m, 1, H-9), 7.83 (m, 3, H-6, 7, 8), 4.2–2.2 ppm (m, 6, 2-, 3-, and 4-CH_2).

Anal. Calcd for $C_{12}H_{10}O_2S_2$: C, 57.57; H, 4.03; S, 25.62. Found: C, 57.36; H, 4.19; S, 25.41.

Registry No.—**5**, 38555-41-8; **6a**, 38555-58-7; **6b**, 38555-59-8; **7**, 38555-60-1; **8**, 38555-61-2; **9**, 38555-62-3; **10**, 38555-63-4; **11**, 38555-64-5; **12**, 38555-65-6; **13**, 38555-66-7; thiophenol, 108-98-5; *o*-chloranil, 2435-53-2.

---

[13] Confidence in the purity of this product rests on the concordance of four different elemental analyses, the m/e value for the molecular ion, and the molecular weight based on the molecular ion cluster.