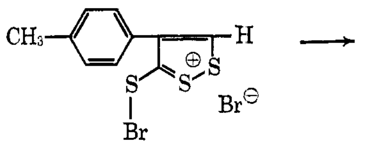
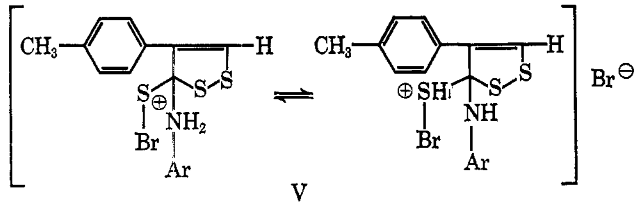
On the other hand, the 4-(*p*-tolyl)-1,2-dithiole-3-thione hydrobromide gave only trithione upon addition of aniline, and the trithione reacted very slowly with aniline in refluxing benzene solution. Direct refluxing with aniline opened the dithiole ring to provide materials that absorb in the 3.0-μ region.

The types of halogenated derivatives formed from trithiones depend on the solvent and the halogen. Chlorination in refluxing chloroform gives a 3,3,5-trichlorodithiole,[2b] whereas in acetic acid the 3,3-dichlorodithiole and a monochloro intermediate are formed.[3] Bromine and iodine trithione adducts have also been reported.[4]

In the work reported here, the room-temperature addition of 1 mole of bromine in carbon tetrachloride or benzene solution to 4-(*p*-tolyl)-1,2-dithiole-3-thione quantitatively precipitated a tan, high-melting solid. The solid did not absorb in the 8.9-μ region, evidence for reaction at the thiocarbonyl group. Isolation of trithione by aqueous acetic acid hydrolysis of the solid showed that the thione sulfur atom remained attached during the bromination. Reaction of the solid with primary aryl amines gave the 3-imines. Assuming that the solid is the bromotrithionium bromide IV, V was formed by addition of the amine. Loss of hydrogen bromide and sulfur yielded the imine hydrobromide. Aliphatic amines produced intractable tars.


IV


V

Experimental Section

Nuclear magnetic resonance spectra were measured at 52 Mc with a Varian Associates DP-60 spectrophotometer, with tetramethylsilane as internal standard.

4-(*p*-Tolyl)-1,2-dithiole-3-anil.—A solution of 2.24 g (0.010 mole) of 4-(*p*-tolyl)-1,2-dithiole-3-thione in 75 ml of carbon tetrachloride was treated with 1.70 g (0.0106 mole) of bromine dissolved in 25 ml of carbon tetrachloride. The tan solid that formed was collected, washed with carbon tetrachloride and pentane, and mixed with 10 ml of aniline; then ether was added. The ether-insoluble salt was collected and hydrolyzed with water, and the product was dissolved in benzene. The ether filtrate was diluted with pentane, and the small amount of solid that formed was collected and added to the benzene solution. The benzene was decolorized with Norit and concentrated. The addition of pentane produced 2.33 g (82%) of 4-(*p*-tolyl)-1,2-dithiole-3-anil: mp 139–141°, yellow-orange crystals; nmr ($CDCl_3$), 8.18 (singlet, 1 proton), 7.39 (complex 9 aromatic protons), and 2.34 ppm (singlet, 3 methyl protons); nmr for 4-(*p*-tolyl)-1,2-dithiole-3-thione (CCl_4), 8.26 (singlet, 1 proton), 7.28 (*para*-substituted aromatic, 4 protons), and 2.41 ppm (singlet, 3 methyl protons).

Anal. Calcd for $C_{16}H_{13}NS_2$: C, 67.80; H, 4.62; N, 4.94; S, 22.6. Found: C, 67.61; H, 4.57; N, 48.3; S, 22.9.

4-(*p*-Tolyl)-1,2-dithiole-3-benzylimine.—The trithione dibromide was prepared by addition of 4.89 g (0.0305 mole) of bromine in 30 ml of benzene to 6.72 g (0.030 mole) of the trithione in 120 ml of benzene. The crude dibromide was washed with benzene and treated with 11 ml of benzylamine. After the exothermic reaction had subsided, ether was added and the insoluble salt was collected and thoroughly washed with ether. The salt was hydrolyzed with water and the imine was dissolved in benzene and crystallized from benzene–hexane to yield 4.65 g (52%) of 4-(*p*-tolyl)-1,2-dithiole-3-benzylimine: mp 111–113°; nmr ($CDCl_3$), 7.91 (singlet, 1 proton), 7.31 (complex, 9 aromatic protons), 4.87 (singlet, 2 methylene protons), and 2.31 ppm (singlet, 3 methyl protons).

Anal. Calcd for $C_{17}H_{15}NS_2$: C, 68.64; H, 5.08; N, 4.71; S, 21.6. Found: C, 68.67; H, 5.44; N, 4.60; S, 21.8.

4-(*p*-Tolyl)-1,2-dithiole-3-(*p*-carboxyphenyl)imine.—The dibromide prepared from 8.96 g (0.040 mole) of trithione was treated with 16.5 g of *p*-aminobenzoic acid dissolved in 200 ml of methanol. The mixture was stirred for 15 min and the solid that formed was collected and washed with methyl ethyl ketone, benzene, and hexane. The crude imine was dissolved in 250 ml of pyridine, decolorized with Norit, and crystallized by the addition of 650 ml of ether. The yield of 4-(*p*-tolyl)-1,2-dithiole-3-(*p*-carboxyphenyl)imine was 9.85 g (75%): mp 252–258° dec; λ_{max}^{mull} 6.00 and 6.25 μ.

Anal. Calcd for $C_{17}H_{13}NO_2S_2$: C, 62.35; H, 4.01; N, 4.28; S, 19.6. Found: C, 62.40; H, 3.92; N, 4.30; S, 19.5.

---

[3] R. S. Spindt, D. R. Stevens, and W. E. Baldwin, *J. Am. Chem. Soc.*, **73**, 3693 (1951).

[4] A. S. Broun, M. D. Voronkov, and K. P. Katkova, *J. Gen. Chem. USSR*, **20**, 765 (1950).

4-Mercapto-5-(*p*-tolyl)-2H-thiapyrans

JULES L. ADELFANG[1]

Amoco Chemicals Corporation,
Research and Development Department, Whiting, Indiana

Received November 23, 1965

4-Aryl-1,2-dithiole-3-thiones,[2a] readily available from the reaction of sulfur with the appropriate cumene or α-methylstyrene, are a source of a large number of new sulfur chemicals. 4-(*p*-Tolyl)-1,2-dithiole-3-thione (I) reacted with several active methylene compounds to provide high yields of orange or red compounds containing two sulfur atoms. Condensations were carried out at room temperature using sodium ethoxide in benzene–ethanol solution. Other condensing agents were also used. *E.g.*, malonic ester condensed in a dimethoxyethane–benzene solvent pair with sodium amide as the condensing agent. Ethyl cyanoacetate and the trithione condensed very rapidly in benzene solution when piperidine was added. Acetoacetic ester or ethyl benzoylacetate did not react but malononitrile condensed very readily. In these condensations both the methylene and ester or cyano groups are involved and sulfur is lost.

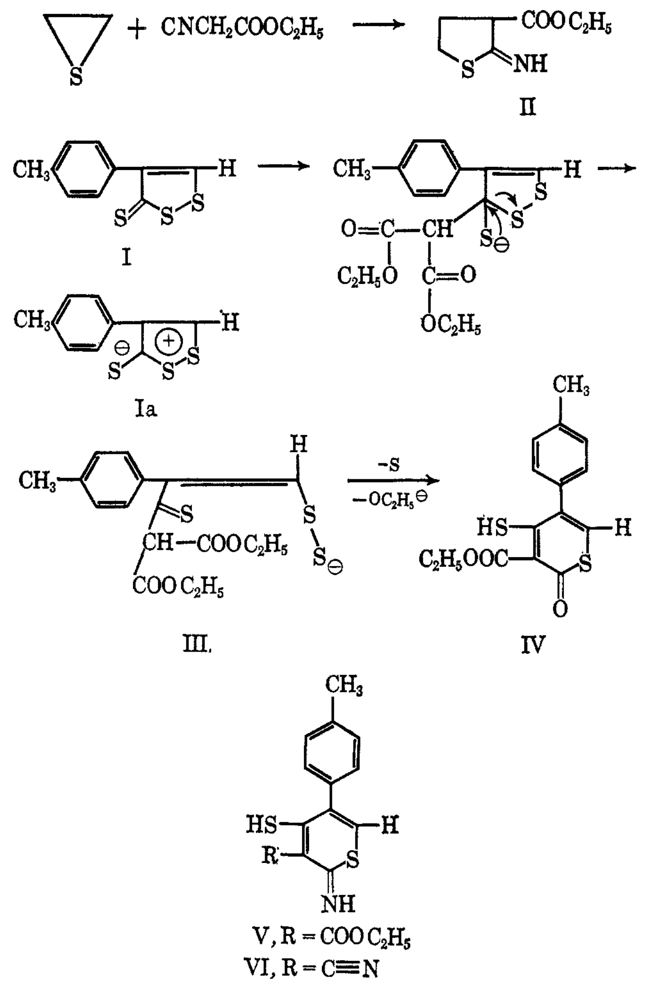
The addition of ethyl cyanoacetate to ethylene sulfide,[2b] gives an imino tetrahydrothiafuran existing as a mixture of tautomers. In a similar manner the addition of malonate ion to the trithione I caused cleavage of the dithioester to yield the intermediate III. Successive loss of sulfur, ring closure, and loss of ethoxide gave the 3-carbethoxy-4-mercapto-5-(*p*-tolyl)-2H-thiapyran-2-one (IV) in 86% yield. The 2-imino-2H-thiapyrans V and VI were obtained in 86 and 77% yield, respectively. (See Scheme I.)

---

[1] Arapahoe Chemicals Inc., Boulder, Colo.

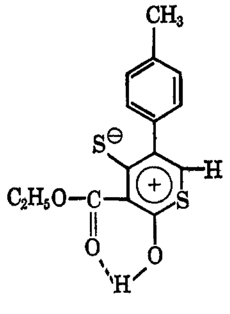
[2] (a) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. III, Chemical Publishing Co., Inc., New York, N. Y., 1960, pp 43–58; (b) H. R. Snyder and Wyvona Alexander, *J. Am. Chem. Soc.*, **70**, 217 (1948).

SCHEME I

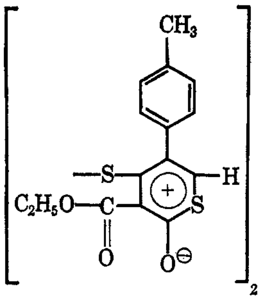


II, I, Ia, III, IV

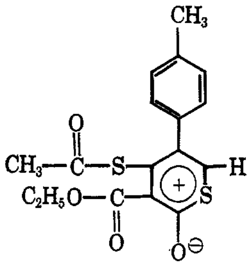
V, R = $COOC_2H_5$
VI, R = C≡N



VII



VIII

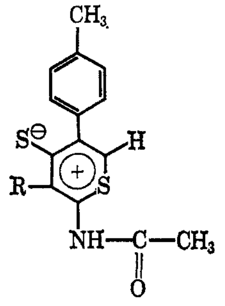


IX

The thiapyran-2-one IV is acidic and formed stable salts that yield the original thiapyran upon acidification. The favored tautomer of IV is the hydrogen-bonded enol where a polarized structure VII, similar to Ia, accounts for the observed spectral properties. The solid is a vivid red, and the thiocarbonyl absorption is strong in the 8.9-μ region, while the carbonyl region exhibits only a single, somewhat polar carbonyl band at 5.98 μ. The aromatic character of the hydrogen atom at the 6 position was confirmed by the nuclear magnetic resonance band at 7.6 ppm. The acidic hydrogen can be removed by oxidation with either hydrogen peroxide or iodine to yield the yellow disulfide VIII. This material could not be readily purified but gave the expected doublet carbonyl absorption at 5.75 and 6.05 μ.

Acetylation of IV by acetyl chloride in pyridine yielded the thioacetate IX, a light yellow compound which hydrolyzes with cold alcohol and pyridine. The triplet carbonyl absorptions occur at 5.75, 5.85, and 6.02 μ and there is no absorption in the 8.9-μ region. The 3-μ region of the infrared spectra of V and VI, measured using Fluorolube mulling agent, exhibited a single band for the former, and the latter gave a well-defined doublet. The amino hydrogens of VI provide a single nuclear magnetic resonance signal and exchange with deuterium oxide. Study of VI in solution was hindered by low solubilities. It is possible that the second amino absorption is obscured by carbon-hydrogen absorptions. In this case, both V and VI would probably be best described by structures similar to VII.

The acetates, prepared with acetyl chloride in pyridine, are deep red and absorb strongly in the 8.9-μ region, indicating reaction at the nitrogen atom. The ester amide X does not absorb in the 3.0-μ region while XI exhibits a moderately strong singlet. The acetate XI is an imide analog and the remaining hydrogen atom is acidic. Aqueous ammonium hydroxide gives a salt that returns the imide upon acidification. The acetate X is not soluble in ammonium hydroxide.



X, R = $COOC_2H_5$
XI, R = C≡N

Experimental Section

Infrared spectra were measured with a Perkin-Elmer Model 21 spectrophotometer with sodium chloride optics. Ultraviolet spectra were determined with a Cary Model 11-MS recording spectrophotometer. Nuclear magnetic resonance measurements were carried out with the Varian Associates DP 60 spectrophotometer, with tetramethylsilane as internal standard.

3-Carbethoxy-4-mercapto-5-(*p*-tolyl)-2H-thiapyran-2-one (IV). —A solution of 6.10 g (0.265 mole) of sodium dissolved in 200 ml of absolute ethanol was treated with 43.5 g (0.27 mole) of diethyl malonate. After standing for 15 min the mixture was added to 35.8 g (0.16 mole) of 4-(*p*-tolyl)-1,2-dithiole-3-thione (I) dissolved in 200 ml of benzene. The reaction was allowed to stand at room temperature for 1 hr and the solid that formed upon addition to ice water was collected and washed with benzene and ether. The resulting yellow salt was decomposed with aqueous hydrochloric acid and the product was dissolved in benzene. Crystallization from benzene–hexane provided 42.0 g (86%) of 3-carbethoxy-4-mercapto-5-(*p*-tolyl)-2H-thiapyran-2-one (IV): mp 121–124°, as red needles; infrared (mull), 5.98 (C=O) and 8.86 μ (C=S); nmr (carbon tetrachloride) (parts per million from

TMS), 10 (broad OH), 7.60 (CH=), 7.16 (C_6H_4), 4.39 (CH_2 quadruplet), 2.38 (CH_3), 1.41 (CH_3 triplet); $\lambda_{max}^{CH_3OH}$ 270, 313, and 455 mμ (log ε 3.72, 3.60, and 3.99).

Anal. Calcd for $C_{15}H_{14}O_3S_2$: C, 58.81; H, 4.61; S, 20.9. Found: C, 58.15; H, 4.65; S, 20.8.

Treatment of IV with acetyl chloride and pyridine yielded an acetate that crystallized as yellow needles from benzene–hexane: mp 96–97.5°; infrared (mull), 5.75, 5.85, and 6.02 μ (C=O); nmr (carbon tetrachloride) (parts per million from TMS), 7.93 (CH=), 7.06 (C_6H_4), 4.20 (CH_2 quadruplet), 2.35 (CH_3C=O), 2.25 (CH_3), 1.35 (CH_3 triplet). The acetate was unstable in methanol solution when exposed to ultraviolet radiation, and rapidly hydrolyzed to IV in the presence of alcohol and pyridine.

Anal. Calcd for $C_{17}H_{16}O_4S_2$: C, 58.60; H, 4.63; S, 18.4. Found: C, 58.22; H, 4.70; S, 18.2.

2-Imino-3-carbethoxy-4-mercapto-5-(*p*-tolyl)-2H-thiapyran (V). —Ethyl cyanoacetate, 1.80 g (0.015 mole), was added to a solution of 0.015 mole of sodium ethoxide in 10 ml of ethanol and the resulting mixture was treated with 1.70 g (0.0076 mole) of 4-(*p*-tolyl)-1,2-dithiole-3-thione dissolved in 15 ml of benzene. Reaction was immediate and the orange-yellow solid that formed was collected and washed with water, benzene, and ether. The yield of crude 2-imino-3-carbethoxy-4-mercapto-5-(*p*-tolyl)-2H-thiapyran, mp 240–245° dec, was 2.0 g (86%). A purified sample, mp 246–248° dec, was obtained by crystallization from methyl ethyl ketone: infrared (mull), 3.02 (NH), 5.91 (C=O), and 8.90 μ (C=S); $\lambda_{max}^{CH_3OH}$ 334 and 390 mμ (log ε 3.95 and 3.34).

Anal. Calcd for $C_{15}H_{15}NO_2S_2$: C, 58.99; H, 4.95; N, 4.59; S, 21.0. Found: C, 59.59; H, 4.91; N, 4.29; S, 21.5.

The acetate, prepared with acetyl chloride in pyridine solution, was isolated as dark red crystals from ethyl acetate: mp 193–196°; infrared (mull), 5.85 (C=O), 6.00 (C=O), and 8.88 μ (C=S).

Anal. Calcd for $C_{17}H_{17}NO_3S_2$: N, 4.03. Found: N, 3.98.

2-Imino-3-cyano-4-mercapto-5-(*p*-tolyl)-2H-thiapyran (VI).—A solution of 24.6 g (0.110 mole) of 4-(*p*-tolyl)-1,2-dithiole-3-thione and 9.1 g (0.14 mole) of malononitrile in 330 ml of benzene was added to 8.9 g (0.165 mole) of sodium methoxide in 500 ml of methanol. After standing for 1 hr the reaction mixture was added to an excess of dilute hydrochloric acid and the red solid was collected and washed with water and benzene. The yield of crude product, mp 245–250° dec, was quantitative. Samples of VI were purified in 77% yield, by crystallization from acetone–benzene, without any change in the melting point: infrared (fluorolube), 3.06 and 3.23 μ (NH_2); (mull), 4.50 (C≡N), 6.03 (C=N), and 8.92 (C=S); nmr (deuterated DMSO) (ppm from TMS), 9.09 (NH_2), 7.34 (CH=), 6.85 (C_6H_4), 2.30 (CH_3) (all singlets); $\lambda_{max}^{CH_3OH}$ 248, 331, and 472 mμ (log ε 4.08, 4.36, and 4.30).

Anal. Calcd for $C_{13}H_{10}N_2S_2$: C, 60.43; H, 3.90; N, 10.85; S, 24.8. Found: C, 60.55; H, 3.90; N, 10.73; S, 24.9.

With ammonium hydroxide the thiapyran gives a yellow solution from which the starting material can be recovered upon acidification. The amino hydrogens, observed *via* nmr spectroscopy, readily exchange with deuterium oxide in deuterated dimethyl sulfoxide. Acetylation with acetyl chloride–pyridine gives a purple-red monoamide that was crystallized from acetone–benzene: mp 245–248°; infrared (mull), 3.08 (NH), 4.50 (C≡N), 5.82 (C=O), and 8.95 μ (C=S). The amide is soluble in aqueous ammonium hydroxide giving an orange-red solution. Acidification with hydrochloric acid precipitates the amide.

Anal. Calcd for $C_{15}H_{12}N_2OS_2$: C, 59.98; H, 4.03; N, 9.33; S, 21.4. Found: C, 60.47; H, 4.35; N, 9.33; S, 21.6.

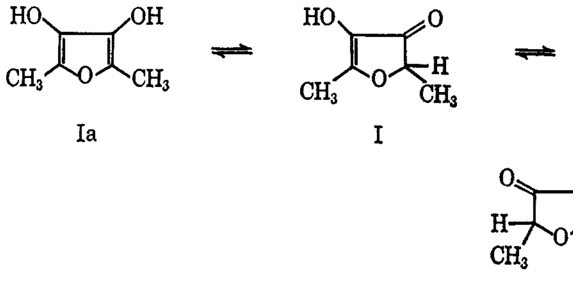
A Rational Synthesis of 4-Hydroxy-2,5-dimethyl-3(2H)-furanone, a Flavor Component of Pineapple

David W. Henry and Robert M. Silverstein

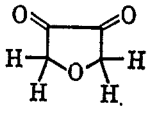
Department of Pharmaceutical Chemistry, Stanford Research Institute, Menlo Park, California 94025

The title compound (I), recently isolated from pineapple flavor concentrate by Rodin, *et al.*,[1] was identified on the basis of its spectral characteristics. It was known also from the work of Hodge, *et al.*, to be produced by a complex reaction between piperidine acetate and the deoxy sugar, rhamnose.[2,3] The product of this reaction was identified on the basis of its spectral properties and on a degradative sequence.[3,4] This Note presents a rational synthesis of furanone I, which confirms the previous structural assignments.

4-Hydroxy-2,5-dimethyl-3(2H)-furanone may be considered as one of three possible tautomers (I, Ia, and Ib). Dienolic tautomer Ia is formally a furan, and a synthetic approach utilizing intermediates containing this relatively stable heteroaromatic ring could be expected to avoid some of the well-documented instability problems associated with the monoenolic final product.[1,5,6] Almost all α- or β-hydroxyfurans tend to assume the carbonyl tautomeric form[7]; thus, the lower homolog of I, tetrahydrofuran-3,4-dione (II), is reported to exist solely in the diketo form.[8] In the special case where carbalkoxy groups are present in the 2 and 5 positions, however, 3,4-dihydroxyfurans exist as such, and several examples of this class of compound are known.[9] The behavior of these hydroxyl groups parallels that of phenols and they may be alkylated or acylated in the normal manner.[9]



Ia I Ib



II

In the present work, dimethyl 3,4-dihydroxyfuran-2,5-dicarboxylate (III), prepared by base-catalyzed condensation of dimethyl oxalate and dimethyl diglycolate,[10] was readily converted to dibenzyl derivative IV by treatment with excess benzyl chloride in the presence of base. Reduction of IV with lithium aluminum hydride gave a viscous diol (V), which was transformed directly to dibenzoate ester VI with benzoyl chloride and pyridine (see Scheme I). Catalytic hydrogenolysis of a tetrahydrofuran solution of the dibenzoate,

---

(1) J. O. Rodin, C. M. Himel, R. M. Silverstein, R. W. Leeper, and W. A. Gortner, *J. Food Sci.*, **30**, 280 (1965).

(2) J. E. Hodge, B. E. Fisher, and E. C. Nelson, *Proc. Am. Soc. Brewing Chemists*, **84** (1963).

(3) J. E. Hodge and B. E. Fisher, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept 1963, p 3D.

(4) B. E. Fisher and J. E. Hodge, Abstracts, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1965, p 4D.

(5) J. E. Hodge, personal communication.

(6) B. Willhalm, M. Stoll, and A. F. Thomas, *Chem. Ind.* (London), **38**, 1629 1965.

(7) R. Rosenkranz, K. Allner, R. Good, W. V. Philipsborn, and C. Eugster, *Helv. Chim. Acta*, **46**, 1259 (1963), and references therein.

(8) E. C. Kendall and Z. G. Hajos, *J. Am. Chem. Soc.*, **82**, 3219 (1960).

(9) A. P. Dunlop and F. N. Peters, "The Furans," Reinhold Publishing Corp., New York, N. Y., 1953, pp 180–183.

(10) O. Hinsberg, *Chem. Ber.*, **45**, 2413 (1912).