Degradation of 4(5)-Methyl-2-thiocyanoimidazole.—About 0.7 g. of 4(5)-methyl-2-thiocyanoimidazole was dissolved in 5 ml. of 4% hydrochloric acid and the solution treated with zinc. After standing overnight, a precipitate had formed which was slightly gray due to undissolved zinc. It was extracted with 95% ethanol, the extract being concentrated to a small volume and treated with water to yield a white product, the zinc chloride complex of 4(5)-methyl-2-mercaptoimidazole, m.p. 223° (dec.). This material gave an immediate orange color with methanolic gold chloride[4] and produced no depression of melting point when mixed with an authentic sample prepared as below.

When solid zinc chloride was added to a suspension of 4-methyl-2-mercaptoimidazole in 4% hydrochloric acid, solution occurred, followed almost immediately by precipitation. The white product, after washing with ethyl acetate and chloroform melted at 221° dec. This material also gave a deep orange color with methanolic gold chloride.

1-Methyl-2-thiocyanoimidazole.—Cyanogen bromide (1.2 g., 0.011 mole) and 1-methyl-2-mercaptoimidazole (0.4 g., 0.0035 mole) were thoroughly mixed, heated at 50–65° for 0.5–1 hr., and then allowed to stand for several hours. The resulting powder was dissolved in 4 ml. of water, the solution was neutralized with 10% sodium carbonate (no precipitation) and then continuously extracted with ether for 14 hr. Concentration of this ether extract yielded a slightly yellowish oil which solidified on cooling. This semi-solid material, 1-methyl-2-thiocyanoimidazole, contaminated with 1-methyl-2-mercaptoimidazole, was repeatedly extracted with warm petroleum ether (35–60°). Concentration of the petroleum ether extracts to dryness *in vacuo* resulted in white microscopic plates of pure 1-methyl-2-thiocyanoimidazole, yield 210 mg. (43%), m.p. 64–65°. The product yielded no gold chloride test for mercaptoimidazole. Paper chromatographs showed one spot only.

Anal. Calcd. for $C_5H_5N_3$: S, 23.0; C, 43.1; H, 3.59; N, 30.2. Found: S, 22.8; C, 42.9; H, 3.81; N, 29.6.

Imidazole Sulfate.—To a solution of 1 g. (0.015 mole) of imidazole in 8 ml. of dry pyridine was added 1.7 g. (0.015 mole) of thiocyanogen in 25 ml. of nitromethane. Thiocyanogen was prepared from lead thiocyanate and bromine.[5] The solution was mixed by stirring, and after 0.5 hr. the addition of thiocyanogen was repeated. After standing overnight the solution was brought to a boil and 1 volume of acetone was added. The suspension was then cooled and filtered and the somewhat gummy precipitate was washed with acetone. It was recrystallized from boiling ethanol, using charcoal to decolorize the solution, giving a white, crystalline product, imidazole sulfate, m.p. 84–85°, yield 0.97 g. (56%). In aqueous solution this compound gave an immediate white precipitate with barium chloride or benzidine hydrochloride.

Anal. Calcd. for $2C_3H_4N_2 \cdot H_2SO_4$: S, 13.67. Found: S, 13.64.

The same compound was prepared by addition of sulfuric acid to an ethanolic imidazole solution, m.p. 84–85°.

Histamine Sulfate.—To 100 ml. of dry pyridine was added 1 g. (0.0054 mole) of histamine dihydrochloride, most of which was dissolved. This suspension was treated with 1.8 g. (0.016 mole) of thiocyanogen in 30 ml. of nitromethane. The solution, which rapidly turned reddish, was stirred for complete mixing and allowed to stand overnight. A precipitate formed; the suspension was brought to a boil, a small amount of nitromethane added and the mixture was cooled. The precipitate was removed by filtration, washed with acetone and recrystallized three times from ethanol–water, using charcoal for decolorization. White needles of histamine sulfate were obtained, m.p. 254° (dec. 254–255°), yield 0.45 g. (39%). In aqueous solution this compound gave an immediate precipitate with barium chloride or benzidine hydrochloride.

Anal. Calcd. for $C_5H_9N_3 \cdot H_2SO_4$: S, 15.33. Found: S, 15.31.

The same compound was prepared by addition of pyridine and sulfuric acid to an ethanol–water solution of histamine dihydrochloride, m.p. 252° dec.

MEMPHIS, TENN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

A New Method of Preparing Substituted Thiophenols

BY A. H. HERZ[1] AND D. S. TARBELL

RECEIVED MAY 12, 1953

Attempts to carry out Friedel–Crafts acylations of diphenyl disulfide or formaldehyde diphenyl mercaptal were unsuccessful; however, it was shown that the readily formed addition product of a thiophenol and 3-nitrobenzalacetophenone is amenable to electrophilic substitution, and that this substituted addition product may be nearly quantitatively converted to the correspondingly substituted thiophenol. It was demonstrated by the preparation of acetylated, brominated and nitrated thiophenols that this scheme constitutes a general method for the preparation of electrophilically substituted thiophenols.

Thiophenols and their esters, in marked contrast to phenols, have been found to give ordinary electrophilic substitution reactions only in exceptional cases. Attempts to nitrate or to brominate thiophenols give first the disulfides,[2] which may undergo some nuclear substitution; the nuclear acylation of thiophenol, either directly,[3] or *via* the Fries reaction on the ester,[4] has been unsuccessful. There seem to be almost no examples of electrophilic substitution in thiophenol esters.[5]

This resistance of thiophenols and their esters to electrophilic substitution makes it usually necessary to prepare substituted thiophenols by introducing the substituents before the thiol group.[6]

This problem of nuclear substitution in thiophenols arose in connection with our previous work.[4] It might be expected that diphenyl disulfide would undergo general electrophilic substitution satisfactorily, since it brominates well[2a,7]; Friedel–Crafts acetylation, however, does not occur with aluminum chloride and acetyl chloride[3]; with aluminum bromide and acetyl chloride, we have

(1) Eastman Kodak Fellow, 1952–1953.

(2) (a) E. Bourgeois and A. Abraham, *Rec. trav. chim.*, **30**, 422 (1911); (b) T. Van Hove, *Bull. soc. chim. Belg.*, **36**, 548 (1927); **37**, 88 (1928).

(3) G. B. Bachman and C. L. Carlson, THIS JOURNAL, **73**, 2857 (1951); the only case we have noted in which direct nuclear acylation is successful is 3-methoxythiophenol (German Patent 202,632; *Chem. Zentr.*, **79**, II, 1659 (1908), and ref. 4 below).

(4) D. S. Tarbell and A. H. Herz, THIS JOURNAL, **75**, 1668 (1953).

(5) *Cf.* E. Gehauer-Fülnegg and F. Meissner, *Monatsh.*, **50**, 59 (1928), for the chlorsulfonation of phenyl thiolacetate: chlorination of phenyl thiolbenzoate does not give simple nuclear substitution (R. Schiller and R. Otto, *Ber.*, **9**, 1634 (1876)).

(6) R. Connor, in Gilman's "Organic Chemistry," Second Edition, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 844 ff.

(7) T. Zincke and W. Frohneberg, *Ber.*, **43**, 837 (1910); the dibromodiphenyl disulfide is readily reduced to the *p*-bromothiophenol.

obtained 72% of phenyl thiolacetate, along with a small amount of *p*-bromophenyl thiolacetate.[7a]

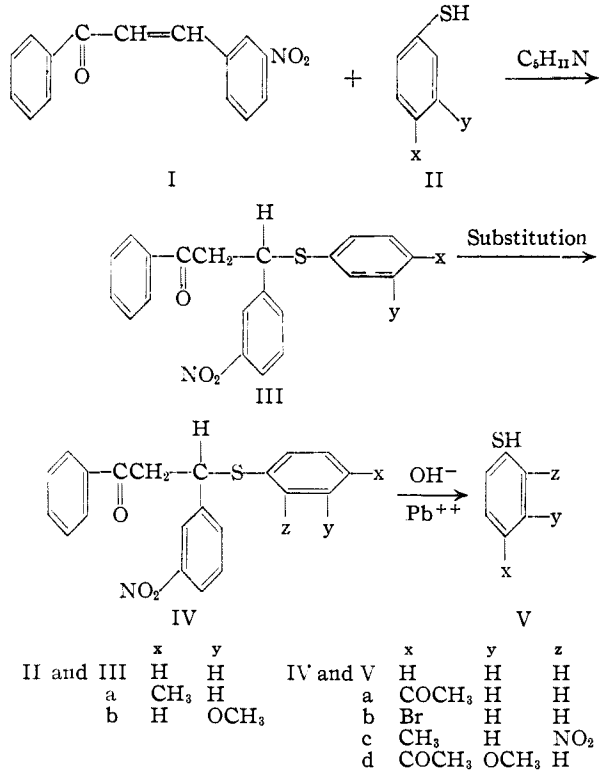
The alkyl aryl sulfides, RSAr, undergo most electrophilic substitution reactions smoothly,[8] but the removal of the alkyl group to liberate the thiol group is not usually practical.[9] The mercaptals and mercaptoles derived from thiophenols can be converted to the thiophenols more readily (ref. 9, p. 67), and we therefore investigated the Friedel–Crafts acetylation of formaldehyde diphenyl mercaptal $(C_6H_5S)_2CH_2$. This yielded up to 60% of phenyl thiolacetate, and a small amount of amorphous solid devoid of ketonic properties.

Since electrophilic substitution is usually carried out under acidic conditions, a blocking group for the thiol group which is stable in acid but is removed under weakly basic conditions is plainly required. It is known[10] that the products of addition of thiophenols and α,β-unsaturated ketones, such as III, are readily converted to the thiophenol lead mercaptide and the starting ketone by basic lead acetate.

This system has proved practical; we have found that sulfides such as III are amenable to substitution in the thiophenyl ring, and that they can then be readily converted to the substituted thiophenol. This appears to be a general method of preparing substituted thiophenols, some of which were only inconveniently accessible.

Thus, the nearly instantaneous piperidine-catalyzed reaction of thiophenol and 3-nitrobenzalacetophenone (I)[11] afforded a 96% yield of β-(3-nitrophenyl)-β-(phenylthio)-propiophenone (III) which with 3 moles of aluminum bromide and acetyl chloride, both as solvent and acetylating agent, gave β-(3-nitrophenyl)-β-(4-acetylphenylthio)-propiophenone (IVa) in 86% yield. Lead acetate and base converted IVa to 4-acetylphenyl lead mercaptide which, after treatment with dilute acid, gave 4-acetylthiophenol (Va) in 77% over-all yield. Alternatively, the intermediate lead mercaptide could be oxidized directly to the bis-(4-acetylphenyl) disulfide.

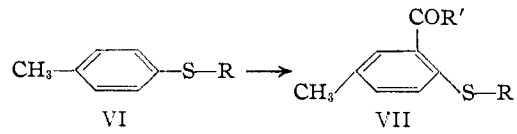
Similarly, III was brominated in the presence of three equivalents of aluminum bromide, to give IVb which, through the lead mercaptide intermediate, gave 4-bromothiophenol (Vb) in 58% yield based on thiophenol. In the absence of, or with merely catalytic amounts of aluminum bromide, or with pyridine hydrobromide perbromide[12] as the brominating agent, no IVb or other bromination product could be isolated; instead, large amounts of 3-nitrobenzalacetophenone (I)



	x	y		x	y	z
II and III	H	H	IV and V	H	H	H
a	CH_3	H	a	$COCH_3$	H	H
b	H	OCH_3	b	Br	H	H
			c	CH_3	H	NO_2
			d	$COCH_3$	OCH_3	H

were obtained. This indicates that unless nuclear bromination is rapid, bromine may oxidize and thus irreversibly remove any thiophenol in equilibrium with the sulfide III.

In view of the easy acetylation of III it was reasonable to expect that IIIa should be acetylated ortho to the sulfur atom. However, treatment of IIIa with acetyl chloride and aluminum bromide at low temperatures left the starting material unchanged, whereas at elevated temperature, only tars were obtained.[13]



On the other hand, the nitration product of IIIa gave rise, although in poor yield, to 2-nitro-4-methylthiophenol (Vc), which was quantitatively oxidized to the known bis-(2-nitro-4-methylphenyl) disulfide. In addition, a large amount of 3-nitrobenzalacetophenone was obtained, apparently for the same reason as in the bromination of (III). Even with simple aryl alkyl sulfides, nuclear nitration has been rarely successful (J. Pollak, ref. 8), since ordinarily the action of nitric acid on sulfides causes sulfoxide or sulfone formation.[2b]

Polysubstituted thiophenols may also be prepared by this method. Thus 4-acetyl-3-methoxythiophenol (Vd) was obtained through the lead mercaptide intermediate of the acetylated addition product of 3-nitrobenzalacetophenone and 3-methoxythiophenol (IIb). The acetyl group was as-

(7a) ADDED IN PROOF.—Dr. A. H. Weinstein, of the Goodyear Tire and Rubber Company, has obtained phenyl chlorothiolacetate by the action of chloroacetyl chloride on diphenyl disulfide in carbon disulfide solution (private communication).

(8) Bromination,[2] sulfonation,[2b] nitration (J. Pollack, L. Fiedler and H. Roth, *Monatsh.*, **39**, 189 (1918), Friedel–Crafts acylation (R. A. Cutler, R. J. Stenger and C. M. Suter, THIS JOURNAL, **74**, 5475 (1952)) and even the Gattermann aldehyde reaction (F. Krollpfeiffer, H. Hartmann and F. Schmidt, *Ann.*, **563**, 22 (1949)).

(9) *Cf.* D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 39 (1951).

(10) (a) B. H. Nicolet, THIS JOURNAL, **53**, 3066 (1931); (b) for recent references *cf.* R. Adams, E. F. Elslager and T. E. Young, *ibid.*, **75**, 663 (1953).

(11) R. Sorge, *Ber.*, **35**, 1068 (1902). This reagent was chosen because it is inactive toward electrophilic substitution.

(12) C. Djerassi and C. Scholz, THIS JOURNAL, **70**, 417 (1948).

(13) Although F. Krollpfeiffer and A. Wissner, *Ann.*, **572**, 195 (1951), were able to obtain VII by low temperature acetylation of VI, K. Auwers and F. Arndt, *Ber.*, **42**, 2707 (1909), noted that steric requirements of R and R' may be of critical importance for the success of the acetylation reaction.

signed the 4-position, since our product, upon alkaline oxidation, was quantitatively converted to a colorless bis-(acetyl-3-methoxyphenyl) disulfide. If the acetyl group was ortho to the sulfur atom, oxidation in the presence of alkali would have yielded a thioindigo dye[14]; moreover, neither Vd nor the analytically pure disulfide derived from it, was identical with 2-acetyl-5-methoxythiophenol or its disulfide (*cf.* German Patent, ref. 3; also ref. 4).

Experimental[15]

Attempted Acetylation of Diphenyl Disulfide.—A mixture of aluminum bromide (19.6 g.), diphenyl disulfide (8 g.), acetyl chloride (6 g.) and 30 cc. of carbon disulfide was refluxed until no more hydrogen halide was given off (about 5 hr.). After the reaction was completed, the mixture was worked up with ice, extracted with ether, washed, dried and vacuum distilled, yielding 8 g. of colorless oil, b.p. 66° (1.5 mm.), $n^{20}D$ 1.5700. The properties of this oil, which solidified upon chilling, m.p. (uncorrected) 18–19.5°, are identical with the previously described properties of phenyl thiolacetate.[4] Upon basic hydrolysis and oxidation with hypoiodite solution, the oil was quantitatively converted to diphenyl disulfide, which was identical with starting material.

Treatment of the distillation residue with methyl alcohol yielded 1 g. of colorless solid which after recrystallization from methyl alcohol melted at 51–52°, and was shown to be *p*-bromophenyl thiolacetate by mixed m.p. with an authentic sample.[16]

Practically identical yields of phenyl thiolacetate and *p*-bromophenyl thiolacetate were obtained by running the reaction at 0°; however, substituting boron fluoride and acetic acid for the aluminum bromide, and running the reaction at 80° in a sealed tube, gave back 80% of unchanged starting material.

Attempted Acetylation of Formaldehyde Diphenyl Mercaptal.—To formaldehyde diphenylmercaptal (10 g.) dissolved in 40 cc. of carbon disulfide, there was added slowly at −10° a mixture of aluminum bromide (23 g.) and acetyl chloride (10 g.) in 30 cc. of carbon disulfide. After the addition was completed, the mixture was worked up as in the preceding experiment and yielded 7.4 g. of phenyl thiolacetate. From the distillation residue there was also obtained 2.5 g. of a tan, amorphous solid of unknown constitution, which did not exhibit ketonic properties.

Variations of experimental conditions, such as changing the catalyst and catalyst concentrations as well as the addition sequence, did not bring about any detectable nuclear acetylation.

β-(3-Nitrophenyl)-β-(phenylthio)-propiophenone (III).—To 3-nitrobenzalacetophenone (I) (18 g.), dissolved in minimum amount of boiling benzene, thiophenol (8 g.) was added, the heat source was removed and piperidine (1.5 cc.) was dropped into the solution, which immediately boiled up. The solution was permitted to return to room temperature, acetic acid (approx. 10 cc.) followed by methyl alcohol (approx. 200 cc.) was added, and after chilling, was filtered. Thus 25 g. (96%) crude III was obtained which was used without further purification in the subsequent experiments. After recrystallization from ethyl alcohol, III melts at 105–106°.

Anal. Calcd. for $C_{21}H_{17}O_3SN$: C, 69.41; H, 4.72. Found: C, 69.69; H, 5.05.

Acetylation of III.—A solution of III (10 g.) in acetyl chloride (60 cc.) and carbon disulfide (50 cc.) was added dropwise with stirring at −10° to aluminum bromide (25 g.) in carbon disulfide (50 cc.). After the addition was completed, the reaction mixture was worked up with ice, extracted with chloroform, washed and dried. The solution was then evaporated to about 15 cc., 100 cc. of methyl alcohol was added, and upon chilling and filtering, β-(3-nitrophenyl)-β-(4-acetylphenylthio)-propiophenone (IVa) (9.5 g.) was collected. After recrystallization from ethyl alcohol, IVa melted at 96–97°.

Anal. Calcd. for $C_{23}H_{19}O_4SN$: C, 68.14; H, 4.72. Found: C, 68.27; H, 5.01.

Transformation of IVa to 4-Acetylthiophenol (Va).—To a well stirred solution of IVa (12 g.) dissolved in a mixture of chloroform (200 cc.) and ethyl alcohol (200 cc.) was added 175 cc. of 20% lead acetate trihydrate in 50% ethyl alcohol, followed by enough 10% aqueous sodium hydroxide to keep the solution at *p*H 8–10. (With concentrated alkali and high *p*H, the insoluble lead mercaptide will dissolve forming sodium mercaptide.) The yellow lead mercaptide precipitated, it was collected and washed first with alcohol and then with chloroform. From this wash solution and the filtrate, a nearly quantitative amount of I could be recovered. The mercaptide was carefully triturated with dilute hydrochloric acid at 0° (with concd. acid or at elevated temperature, mercaptole formation may interfere) and the resulting solution which contained precipitated lead chloride was repeatedly extracted with chloroform which in turn was treated with 10% aqueous sodium hydroxide to remove the alkali-soluble thiophenolic fraction. This water solution was acidified and the chloroform extract obtained from it was washed, dried and distilled, yielding 4.2 g. of colorless oil. The properties of this oil which solidified upon chilling, m.p. (uncorrected) 27–28.5°, are identical with the previously described[4] 4-acetylthiophenol.

The identity of this low melting colorless solid which turns quickly yellow in contact with air and which gives yellow solutions with alkali, was definitely established by oxidizing it with ferric chloride in acetic acid to give a quantitative yield of bis-(4-acetylphenyl) disulfide, m.p. 99–100°, which did not depress the melting point of an authentic sample.[4]

This disulfide could also be obtained directly by triturating the lead mercaptide with a hot solution of ferric chloride in acetic acid.

The piperidine-catalyzed addition of Va to I gave a product in excellent yield, m.p. 96–97°, which by mixed melting point determination was shown to be identical with previously obtained IVa.

Bromination of III.—Bromine (0.88 g.) in chloroform (20 cc.) was added at 0° to III (2 g.) dissolved in chloroform (80 cc.). Into this well-stirred solution, and while maintaining the temperature at −5 to 0°, was slowly dropped a solution of aluminum bromide (4.4 g.) in carbon disulfide (100 cc.). The mixture was vigorously stirred until no more hydrogen bromide was given off (about 0.5 hr.); it was then worked up with ice, aqueous bisulfite and chloroform in the usual manner. Upon addition of methyl alcohol, chilling and filtering, there was obtained β-(3-nitrophenyl)-β-(4-bromophenylthio)-propiophenone (IVb) (1.6 g.). Recrystallizing from a methyl–ethyl alcohol mixture gave faintly yellow crystals, m.p. 130–131°.

Anal. Calcd. for $C_{21}H_{16}O_3SNBr$: C, 57.02; H, 3.65. Found: C, 57.14; H, 3.65.

IVb (0.7 g.) gave a yellow lead mercaptide which was formed and treated as was the lead mercaptide from IVa, except that the resulting 4-bromothiophenol (Vb) was not distilled but crystallized from an aqueous methanol solution. Vb (0.28 g.) thus obtained, melted at 74–75°; the melting point was not depressed by admixture with an authentic sample.[16]

The piperidine-catalyzed addition of Vb to I gave an 86% yield of a product, m.p. 130–131, which, by a mixed melting point procedure, was shown to be identical with IVb obtained above.

β-(3-Nitrophenyl)-β-(4-methylphenylthio)-propiophenone (IIIa) was obtained in 93% yield from *p*-thiocresol and I in a manner analogous to III; colorless crystals, m.p. 103–104°.

Anal. Calcd. for $C_{22}H_{19}O_3SN$: C, 70.02; H, 5.07. Found: C, 70.15; H, 5.27.

Nitration of IIIa.—To IIIa (4 g.) dissolved in acetic anhydride (35 cc.) was added at 0°, 0.7 g. of concentrated nitric acid (d. 1.42) in acetic acid (10 cc.). The solution, which turned green, was kept for approx. 10 minutes at 0°, it was then poured onto crushed ice to which 10 cc. of 10% aqueous alkali had been added previously. With completed hydrolysis of the acetic anhydride, the precipitated yellow solid was filtered and taken up in the minimum amount of a benzene–ethanol mixture. Upon chilling, 1 g. of I was collected.

Without isolating the primary nitration product IVc, the

(14) German Patent 198,509 (*Chem. Zentr.*, **79**, I, 2118 (1908)); *cf.* ref. 4.

(15) Analyses by Miss Viola Williams; m.p.'s are corrected.

(16) H. F. Wilson and D. S. Tarbell, THIS JOURNAL, **72**, 2500 (1950).

filtrate was treated in the same manner as was IVb. There was thus obtained, through the lead mercaptide intermediate, Vc (0.2 g.) as yellow needles, m.p. 55–58°, which, because of their rapid oxidation, were not obtained analytically pure but were quantitatively converted by hypoiodite to bis-(4-methyl-2-nitrophenyl) disulfide, m.p. 174–175°; the melting point was not depressed by admixture with an authentic sample.[17]

Acetylation of IIIb.—IIIb was formed, in a manner analogous to III, by the piperidine-catalyzed addition of 3-methoxythiophenol (IIb)[3] to I; there was thus obtained a 35% crude yield of IIIb, m.p. 72–75°. Without further purification, IIIb (3.3 g.) was acetylated under the same conditions as III, except that the reaction mixture was stirred for at least 0.5 hr. at −10° before it was worked up. There was thus obtained β-(3-nitrophenyl)-β-(4-acetyl-3-methoxyphenylthio)-propiophenone (IVd) (2.6 g.); colorless crystals, m.p. 120–121°.

Anal. Calcd. for $C_{24}H_{21}O_5SN$: C, 66.20; H, 4.86. Found: C, 66.30; H, 4.83.

IVd (0.8 g.) was converted through the lead mercaptide intermediate to Vd (0.3 g.) in the same manner as was given for IVb. Because of its ready oxidation Vd, m.p. 75–80°, was not obtained in a pure form but was converted by a hot solution of ferric chloride in acetic acid to bis-(4-acetyl-3-methoxyphenyl) disulfide; colorless crystals, m.p. 179–180°.

Anal. Calcd. for $C_{18}H_{18}O_4S_2$: C, 59.66; H, 5.01. Found: C, 59.75; H, 5.29.

ROCHESTER, N. Y.

(17) M. T. Bogert and R. W. Allen, *Ind. Eng. Chem.*, **18**, 532 (1926).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF SWARTHMORE COLLEGE]

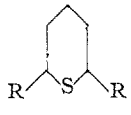
Thiapyran Derivatives. IV. Some Symmetrical 2,6-Disubstituted Tetrahydrothiapyrans and 1,1-Dioxides

BY EDWARD A. FEHNEL AND GEORGE C. OPPENLANDER

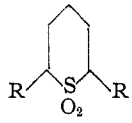
RECEIVED MAY 2, 1953

Some new symmetrical 2,6-disubstituted tetrahydrothiapyrans and related 1,1-dioxides have been prepared and characterized. The preparation of α,ε-dibromopimelic acid has been reinvestigated and a stereochemically pure form of this compound has been isolated and identified as the *meso* isomer.

While searching for intermediates which might prove useful in the synthesis of certain thiapyran derivatives, we have had occasion to prepare a number of new tetrahydrothiapyrans and tetrahydrothiapyran 1,1-dioxides, some of which have been described in the preceding papers in this series.[1] The present communication describes the preparation of some symmetrical 2,6-disubstituted tetrahydrothiapyrans (I–III) and 1,1-dioxides (IV–VI) which were obtained in the course of this work but which have not previously been reported.



I, R = COOH
II, R = $COOCH_3$
III, cyclic anhydride of I



IV, R = COOH
V, R = $COOCH_3$
VI, R = Br

The dicarboxylic acid I and its dimethyl ester II were prepared by the action of sodium sulfide on α,ε-dibromopimelic acid (VII) and methyl α,ε-dibromopimelate (VIII), respectively, under conditions similar to those previously employed[2,3] in the synthesis of the analogous 2,5-disubstituted thiophanes. A consideration of the stereochemical factors involved in cyclizations of this type shows that the *meso*-dihalides should lead to *cis* products, while the racemic dihalides should furnish the *trans* isomers. These results have been verified in the thiophane series,[2,3] where both the *meso* and the racemic forms of α,δ-dibromoadipic acid were available for cyclization. In the present investigation, however, an examination of the literature failed to provide any information on the stereoisomeric forms of α,ε-dibromopimelic acid. In 1895, Willstätter[4] reported, in what appears to be the only published reference to this compound, the isolation of almost quantitative yields of crude α,ε-dibromopimelic acid from the reaction between pimelic acid and excess bromine in the presence of red phosphorus. Willstätter's purified product is described as a colorless crystalline compound with m.p. 140–142°, but no indication is given as to whether this product was a *meso* form, a racemic form or a mixture of diastereomers.

Since it seemed desirable to employ a definite stereoisomeric form[5] of the dibromoacid in the cyclization reaction, we have reinvestigated the preparation of this compound and, by slightly altering Willstätter's original procedure, have succeeded in isolating and characterizing a stereochemically pure product. In our method the diacid chloride of pimelic acid, prepared by the action of thionyl chloride on the acid, was treated with slightly more than the theoretical amount of bromine, and the resultant dibromodiacid chloride was converted to the dibromoacid by reaction with hot formic acid.[6] The crude product (m.p. *ca.* 135–145°) which crystallized out of the reaction mixture on cooling was recrystallized repeatedly from formic acid until it gave a constant m.p. of 154.5–155°; no material comparable to Willstätter's 140–142° product was isolated at any stage of the purification, although the experiment was repeated many times. Attempts to isolate the other (presumably lower melting and more soluble) isomer from the combined mother liquors from the above operations were unsuccessful. Rapid concentration or removal of the solvent furnished

(1) E. A. Fehnel and M. Carmack, THIS JOURNAL, **70**, 1813 (1948); E. A. Fehnel and P. A. Lackey, *ibid.*, **73**, 2473 (1951); E. A. Fehnel, *ibid.*, **74**, 1569 (1952).

(2) A. Fredga, *J. prakt. Chem.*, **150**, 124 (1938).

(3) R. J. Turner and A. J. Hill, *J. Org. Chem.*, **14**, 476 (1949).

(4) R. Willstätter, *Ber.*, **28**, 655 (1895).

(5) *I.e.*, either *meso* or racemic.

(6) *Cf.* the preparation of α,δ-dibromoadipic acid, H. R. Le Sueur *J. Chem. Soc.*, **93**, 716 (1908).