Thirteen grams of the pure 127° acid was distilled in vacuum. The distillate upon hydrolysis and crystallization from water and from benzene yielded 10 g. of the original acid and about 3 g. of an oil-like substance from which the 115–117° body could be isolated.

The pure 127° acid was obtained in quantitative yield by the following procedure. One gram of α-carboxy-α-methyl-β-phenylglutaric acid was heated in a sealed tube in 30 cc. of water for one-half hour at 140–150°, the carbon dioxide removed, and the solution heated as above for two more hours at 175°. In the final product no trace of an oil was detected.

The authors are indebted to Mr. Hubert Liehe and especially to Mr. Herman Koch for assistance in the preparation and identification of certain of the compounds mentioned in this paper. To Dr. W. E. Craig is due the credit for checking and extending the work on the optically active compounds and the tricarboxylic acid.

Summary

1. The action of cold alcoholic potassium hydroxide on the stereomeric ethyl α-cyano-α-methyl-β-phenylglutarates is that of simple saponification leading to stereomeric acids. It does not in the case of the A (α or *trans*) series yield a salt of α-carboxy-α-methyl-β-phenylglutarimide as Carter and Lawrence believed. The derivatives formed by the action of acetyl chloride on the acids are true anhydrides. The A acid does not yield an acetylated imide.

2. The two racemic stereomeric α-cyano-α-methyl-β-phenylglutaric acids have been resolved into their optically active components.

3. The methyl group in the alpha position has been found to have an inhibiting effect on the hydrolysis in acid solution of substituted α-cyanoglutaric esters. Two stereomeric methyl and two ethyl esters of α-carboxy-α-methyl-β-phenlyglutarimide were formed by inhibited hydrolysis and from them the corresponding monoamides were obtained.

4. The compounds under consideration on complete saponification lead to α-methyl-β-phenylglutaric acid and an oil-like substance. From the latter a crystalline product believed to be a mixture of isomers has been obtained.

5. The mixture of esters originally synthesized by Carter and Lawrence and their derivatives were found more easily separable into stereomers than any of a number of similar esters containing other groups.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE]

Addition Reactions of Unsaturated Alpha-Ketonic Acids. IV

BY MARIE REIMER, ELISE TOBIN AND MARGARET SCHAFFNER

In former papers of this series it has been shown that the behavior of benzalpyruvic acid and its bromination products is influenced to a marked degree by the introduction of a methoxyl group in different positions in the benzene ring. A recent study[1] of *m*-methoxybenzalpyruvic acid shows, for example, that it differs in many ways from its para isomer. *p*-Methoxybenzalpyruvic acid[2] is unaffected by light; it readily combines with solvents of crystallization, forms a fairly stable dibromide from which a hydrated, unsaturated bromo compound can be prepared; the acid and all its derivatives give brilliant color reactions with concentrated sulfuric acid. *m*-Methoxybenzalpyruvic acid, on the other hand, is sensitive to light; its dibromo addition product is relatively unstable; the acid and its bromination products are not hydrated in solution and the latter form no brilliantly colored complexes with concentrated sulfuric acid. Because of these differences, the behavior of the ketonic acid with both a meta and a para methoxyl group in the same molecule becomes of interest. Since the 3,4-dimethoxyphenyl group is a common one in many natural products[3] a study of the influence of methoxyl groups in these positions may not be without wider significance. The present paper describes results obtained with 3,4-dimethoxybenzalpyruvic acid.

In earlier work, methoxycinnamic acids corresponding to the ketonic acids under observation have been prepared for purposes of identification

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(1) Reimer and Kamerling, THIS JOURNAL, **55**, 4643 (1933).

(2) Reimer, *ibid.*, **48**, 2454 (1926).

(3) R Robinson, *J. Chem. Soc.*, **111**, 894 (1917); Schoepf and Bayerle, *Ann.*, **513**, 190 (1934).

of the latter. The comparison of the cinnamic acid and the corresponding ketonic acid was of especial interest in the case of the *m*-methoxy compounds since the influence of this group in the cinnamic acid is to direct bromine into the ring instead of to the unsaturated side-chain. The unusual behavior of this cinnamic acid makes important the study of 3,4-dimethoxycinnamic acid which is also found to be of interest when contrasted with 2,4-dimethoxycinnamic acid previously described.[4] The experiments with 3,4-dimethoxycinnamic acid are included in this paper.

The results with both series of acids show that the influence of the *p*-methoxyl group is more in evidence than is that of the meta group. Lack of ready decolorization in the sunlight, the formation of hydrated bromine compounds and brilliant solutions in concentrated sulfuric acid are characteristics of the ketonic compounds; ready addition of bromine to the ethylenic linkage of the side-chain and no bromination in the ring, except slowly in the presence of excess of bromine, differentiate the 3,4-dimethoxy- from the 3-methoxycinnamic acid. It is noteworthy that 2,4-dimethoxycinnamic acid[3] is much more readily brominated in the ring than the 3,4-isomer although the 2- and the 4-methoxycinnamic acids behave normally.

Experimental Part

3,4-Dimethoxybenzalpyruvic acid was prepared by alkaline condensation of veratric aldehyde with pyruvic acid. The aldehyde was made by a variety of methods, the best yields (over 90%) being secured by following the procedure described in "Organic Syntheses."[5] Nineteen grams (0.114 mole) of veratric aldehyde was stirred into 10 g. (0.114 mole) of pyruvic acid, the mixture cooled with ice and 64.4 cc. of 10% potassium hydroxide (0.114 mole) added slowly. To the thoroughly cooled mixture 8 cc. of 25% potassium hydroxide in methyl alcohol was then added and the whole shaken vigorously for about an hour until a clear orange colored solution resulted. This was diluted to 800 cc. and acidified with chilled, concentrated hydrochloric acid. As the yellow acid precipitating was always accompanied by potassium salt, the acid mixture was allowed to stand for twenty-four hours in the cold and the solid then filtered. The bright yellow veratral pyruvic acid can be crystallized from boiling water from which it separates in shining plates melting at 155°. It is readily soluble in boiling benzene, in alcohols and the other usual organic solvents.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.01; H, 5.08. Found: C, 60.89; H, 5.29.

The yields of pure acid were rarely more than 50%. When oxidized in alkaline solution with hydrogen peroxide a quantitative yield of 3,4-dimethoxycinnamic acid, melting at 179°, was obtained.

The acid is only very slightly sensitive to light. After several months' exposure the color had deepened slightly due evidently to a slight decomposition rather than to the polymerization reaction which is characteristic of these acids.

The methyl ester was prepared by dissolving the acid in a small volume of cold methyl alcohol saturated with hydrogen chloride. In a few minutes the ester separated in shining lemon-yellow crystals. Recrystallized from boiling methyl alcohol, it separates in stiff yellow needles melting at 118°.

Anal. Calcd. for $C_{13}H_{13}O_5Br$: C, 62.40; H, 5.60. Found: C, 62.39; H, 5.44.

The ethyl ester prepared in the same manner did not crystallize from the reaction mixture. The thick reddish liquid was poured onto crushed ice and excess of sodium carbonate solution. The yellow oil that separated slowly solidified. This was taken up with ether, the solution washed and dried. On evaporation of the ether, the yellow oily product slowly crystallized. The substance was recrystallized from boiling methyl alcohol to which a few drops of water were added. The ester separates in very small, deep yellow prisms melting at 71–72°.

Anal. Calcd. for $C_{14}H_{15}O_5Br$: C, 63.63; H, 6.06. Found: C, 63.72; H, 6.06.

Reactions with Bromine

3,4-Dimethoxybenzalpyruvic Acid Dibromide, $(CH_3O)_2$-$C_6H_3CHBrCHBrCOCOOH$.—The bromination was carried out with one mole of bromine in cooled chloroform solution in the usual manner. The yellowish white solid which separated was filtered and washed with cold chloroform. The crude product melted at 134–136°.

Anal. Calcd. for $C_{12}H_{12}O_5Br_2$: C, 36.36; H, 3.03. Found: C, 36.29; H, 3.02.

A 72% yield of the dibromide was obtained. The chloroform filtrates, on evaporation of the solvent in a current of dry air, deposited an oil from which crystals slowly separated. These were found to be the unsaturated bromine compound formed by loss of hydrogen bromide from the dibromide. This loss of hydrogen bromide takes place so readily that it was not found possible to crystallize the dibromide from any solvent.

β-Bromo-3,4-dimethoxybenzalpyruvic Acid, $(CH_3O)_2$-$C_6H_3CH{=}CBrCOCOOH$.—The dibromo acid just described reacts readily with cold water; hydrogen bromide is eliminated and the unsaturated acid thus formed separates as a pure white flocculent solid. The behavior of the substance on melting varies, as the acid separates with different amounts of water. A sample which had stood in contact with water several hours became yellow and softened at 150°, melted with vigorous effervescence at 157°.

Anal. Calcd. for $C_{12}H_{11}O_5Br \cdot 2H_2O$: C, 41.02; H, 4.27. Found: C, 41.37; H, 4.54.

After standing overnight over sulfuric acid the behavior was the same but analysis showed that part of the water had been lost.

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(4) Reimer and Tobin, THIS JOURNAL, **52**, 341 (1930).

(5) "Organic Syntheses," John Wiley and Sons, Inc., New York, 1933, Vol. XIII, p. 102.

Anal. Calcd. for $C_{12}H_{11}O_5Br\ H_2O$: C, 43.24; H, 3.90. Found: C, 43.27; H, 4.04.

After longer standing over sulfuric acid or after several months' exposure to the air, the acid melted at 158° with reddening and slow decomposition.

Anal. Calcd. for $C_{12}H_{11}O_5Br$: C, 45.71; H, 3.46. Found: C, 45.72; H, 3.52.

The best method for preparation of the unsaturated acid is to boil the dibromo acid in methyl alcoholic solution. The unsaturated acid separates from this solution on addition of a small volume of water, in rosets of firm needles. It is soluble in the usual organic solvents. Oxidation of an alkaline solution with hydrogen peroxide gave α-bromo-2,4-dimethoxycinnamic acid to be described later.

The methyl ester of β-bromo-3,4-dimethoxybenzalpyruvic acid was prepared by action of diazomethane in ethereal solution. On evaporation of the ether, a white solid separated which crystallized from boiling methyl alcohol in shining white plates melting at 141–142°. It is soluble in chloroform, benzene, acetone and boiling alcohols.

Anal. Calcd. for $C_{13}H_{13}O_5Br$: C, 47.41; H, 3.95. Found: C, 47.02; H, 3.53.

Reactions with Excess of Bromine

When two molecular proportions of bromine were used with a chloroform solution of 3,4-dimethoxybenzalpyruvic acid, the second mole of bromine reacted with extreme slowness, the color of the bromine disappearing completely only after several weeks. The heavy oil left after spontaneous evaporation of the solvent gradually solidified to a deep corn colored solid melting 100 to 110°. Analysis indicated the substance to be a mixture of a tribromo acid and an unsaturated acid formed from it by loss of hydrogen bromide. This unsaturated acid can be obtained by washing out the crude tribromide with glacial acetic acid but no pure tribromo acid could be prepared. When the crude tribromide was oxidized in alkaline solution with hydrogen peroxide the reaction proceeded slowly. After twenty-four hours the solution was warmed slightly to complete the reaction and hydrochloric acid was added. The characteristic, white gelatinous precipitate of α-bromo-3,4-dimethoxy-6-bromocinnamic acid, melting at 233°, described later in this paper, was obtained. The formation of this compound determines the position of the nuclear bromine atom in these ketonic acids.

β-Bromo-3,4-dimethoxy-6-bromobenzalpyruvic Acid, $(CH_3O)_2C_6H_2BrCH{=\!=}CBrCOCOOH$.—The acid can be prepared most readily by boiling the crude tribromide in glacial acetic acid and adding an equal volume of water to the cooled solution when the evolution of hydrogen bromide has ceased. The crystalline product is fairly soluble in boiling benzene, readily soluble in alcohol, ether, acetone and chloroform, insoluble in ligroin. It crystallizes from benzene in colorless needles. On heating it becomes yellow at about 150°, softens at 158° and melts 162–164° with slow effervescence.

Anal. Calcd. for $C_{12}H_{10}O_5Br_2$: C, 36.54; H, 2.33. Found: C, 36.89; H, 2.48.

When this unsaturated acid is heated above its melting point the clear, yellow melt solidifies. This new compound crystallizes from benzene in fine, deep yellow needles, melting with decomposition at 180°. It is readily soluble in the usual organic solvents except benzene, in which it is sparingly soluble, and ligroin. It is an unsaturated bromine compound not soluble in alkaline solution. When it was suspended in sodium carbonate solution and hydrogen peroxide added there was vigorous reaction; the yellow compound dissolved rapidly to give a colorless solution from which hydrochloric acid precipitated the characteristic colorless jelly of α-bromo-3,4-dimethoxy-6-bromocinnamic acid, melting at 233°. The yellow compound is α-bromo-3,4-dimethoxy-6-bromo-cinnamic aldehyde formed by loss of carbon dioxide from the ketonic acid.

Anal. Calcd. for $C_{11}H_{10}O_3Br_2$: C, 37.71; H, 2.85. Found: C, 37.79; H, 2.75.

The aldehyde forms a semicarbazone melting with decomposition at about 215°.

This ready loss of carbon dioxide above the melting point has not been observed with any of the other ketonic acids studied.

The methyl ester of the unsaturated bromo ketonic acid (162–164°) was prepared with diazomethane in ethereal solution. Fine, colorless compact crystals of the ester separated rapidly. It crystallized in shining granules from methyl alcohol, in fine shining needles from acetone. It melts at 171–172°.

Anal. Calcd. for $C_{13}H_{12}O_5Br_2$: C, 38.23; H, 2.94. Found: C, 38.55; H, 3.12.

The effect of concentrated sulfuric acid on these bromo ketonic acids is of interest since the bromination products of 4-methoxybenzalpyruvic acid give a series of brilliantly colored compounds with this reagent,[6] while those of 3-methoxybenzalpyruvic acid do not. Colored products were obtained with 3,4-dimethoxybenzalpyruvic acid. The acid and its esters form bright cherry-red solutions changing to green and then to blue. With bromine in the side chain, the final color is green; with bromine also in the ring the color change is from red to brown. These colors are not so deep nor are they the same as with the *p*- and *o*-methoxy acids formerly studied.[6]

Reactions with 3,4-Dimethoxycinnamic Acid

The acid was obtained by hydrolysis of its ethyl ester prepared from veratric aldehyde and ethyl acetate according to the directions of Perkin and Schiess.[7]

The crude ester, formed in 95% yield, was purified by crystallization from diluted methyl alcohol instead of from petroleum ether as recommended by Perkin and Schiess. The acid, obtained in 85% yield, calculated from the aldehyde used, crystallized from hot glacial acetic acid. It melted at 179–181°.

3,4-Dimethoxycinnamic Acid Dibromide.—Ten and four-tenths grams (0.05 mole) of the cinnamic acid was suspended in 150 cc. of chloroform, the mixture cooled with ice and 8 g. (1 molecular proportion) of bromine added slowly. The bromine was decolorized instantly. There was no evidence of hydrogen bromide during the reaction. On evaporation of the solvent the clear solution deposited a practically quantitative yield of a pale yellow dibromide,

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[6] Reimer and Howard, THIS JOURNAL, **50**, 2506 (1928).

[7] Perkin and Schiess, *J. Chem. Soc.*, **85**, 163 (1904).

melting when pure at 149° as described by Van Duin.[8] Oxidation of a sample of this acid with potassium permanganate in alkaline solution gave a quantitative yield of veratric acid showing that there had been no trace of substitution in the ring, a behavior very different from that of 2,4-dimethoxycinnamic acid in which bromine enters the ring simultaneously with addition to the side chain, and from that of 3-methoxycinnamic acid in which the first mole of bromine enters the ring exclusively with no addition to the unsaturated side chain.

α-Bromo-3,4-dimethoxystyrene, $(CH_3O)_2C_6H_3CH{=\!=}CH\text{-}Br$.—When α-bromo-3,4-dimethoxycinnamic acid was shaken with cold water there was copious evolution of carbon dioxide and a flocculent white solid separated at once. This is an unsaturated, neutral, bromine compound which crystallizes from a small volume of methyl alcohol in shining, stiff, colorless needles melting at 67°. Analysis and behavior of the compound prove it to be a styrene derivative. It is the chief product of the reaction.

Anal. Calcd. for $C_{10}H_{11}O_2Br$: C, 49.38; H, 4.52. Found: C, 49.38; H, 4.77.

α-Bromo-β-hydroxy-3,4-dimethoxycinnamic Acid, $(CH_3O)_2C_6H_3CHOHCHBrCOOH$.—The aqueous filtrate from the styrene derivative was extracted repeatedly with ether, the ether extracts washed and dried and the solvent allowed to evaporate. The residue was a colorless, crystalline acid, soluble in water and alcohols, very slightly soluble in other organic solvents. It was crystallized from a large volume of boiling ether, from which it separated in hard compact crystals, melting with vigorous effervescence at 166°.

Anal. Calcd. for $C_{11}H_{12}O_5Br$: C, 43.27; H, 4.26. Found: C, 43.52; H, 4.15.

The methyl ester was prepared by reaction of an excess of an ethereal solution of diazomethane on a suspension of the acid in the same solvent. It separated at once from the ether in fine hard crystals. It crystallizes from boiling methyl alcohol in large, colorless, rhombic crystals melting at 145–147°.

Anal. Calcd. for $C_{12}H_{15}O_5Br$: C, 45.14; H, 4.70. Found: C, 45.31; H, 5.09.

α-Bromo-3,4-dimethoxycinnamic Acid, $(CH_3O)_2C_6H_2\text{-}CH{=\!=}CBrCOOH$.—Attempts to prepare this acid from the cinnamic acid dibromide by the usual methods were unsuccessful. The styrene derivative (67°) was obtained in all cases with admixture of reddish oils from which no pure compound could be separated. The acid was readily formed, however, by hydrogen peroxide oxidation of β-bromo-3,4-dimethoxybenzalpyruvic acid as previously described. It separates from benzene in yellowish, flattened needles containing benzene of crystallization; from boiling water in deep cream-colored needles, melting, without effervescence, at 167–168°. It is readily soluble in the usual organic solvents with the exception of petroleum ether.

Anal. Calcd. for $C_{11}H_{11}O_4Br$: C, 45.99; H, 3.83. Found: C, 46.02; H, 4.38.

The methyl ester was obtained by adding an ethereal solution of diazomethane to the acid. On evaporation of the ether, the ester separated in soft, fine colorless needles melting at 83°. It is soluble in the usual organic solvents.

Anal. Calcd. for $C_{12}H_{13}O_4Br$: C, 47.84; H, 4.31. Found: C, 48.02; H, 4.64.

Reaction with Excess of Bromine.—Because of the fact that the β-bromine atom in 2,4-dimethoxy-5-bromocinnamic acid dibromide is so extraordinarily reactive, the corresponding 3,4-dimethoxy compound with bromine in the ring was studied.

3,4-Dimethoxy-6-bromocinnamic Acid Dibromide, $(CH_3O)_2C_6H_2BrCHBrCHBrCOOH$.—This tribromo acid was prepared under the same conditions as for the dibromide, a second molecular proportion of bromine being added to the reaction mixture. The second mole of bromine was decolorized very slowly, with copious evolution of hydrogen bromide. After standing for twenty-four hours the solvent was drawn off by a current of dry air. The residue, a pasty solid, was washed with benzene which left very hard, granular buff-colored crystals melting at about 147° with slow loss of hydrogen bromide. This decomposition takes place spontaneously and in all the solvents used, a behavior strikingly different from that of 2,4-dimethoxy-5-bromocinnamic acid dibromide from which it was not found possible to eliminate hydrogen bromide, either by heating or by the use of the usual reagents, in the latter case, the β-bromine atom being quantitatively replaced by hydroxyl or alkoxyl groups. The 3,4-dimethoxytribromo acid separates from boiling benzene in firm white crystals the analysis of which showed that about 8% of the bromine had been lost as hydrogen bromide. The compound melts, with slow effervescence, at about 149°. The clear yellow liquid then solidifies and the new solid, the unsaturated acid, melts well above 200°. This behavior led to the preparation of the unsaturated acid as follows.

α-Bromo-3,4-dimethoxy-6-bromocinnamic Acid, $(CH_3O)_2BrC_6H_2CH{=\!=}CBrCOOH$ (233°).—A sample of the crude tribromo acid was heated in a sulfuric acid bath to 150° for five minutes. After effervescence had ceased, the solidified residue was ground to a powder, washed with warm benzene and crystallized repeatedly from boiling benzene from which it separated when pure in fine cream colored needles melting at 233° without effervescence. The acid is only slightly soluble in boiling benzene and ether, very readily soluble in alcohols, acetone and chloroform.

Anal. Calcd. for $C_{11}H_{10}O_4Br_2$: C, 36.07; H, 2.73. Found: C, 36.15; H, 2.64.

When precipitated by dilute acid from its alkaline solution the acid comes down as a white jelly.

The methyl ester was formed by action of diazomethane on a suspension of the acid in ether to which a little methyl alcohol had been added. The mixture was allowed to stand for several hours. The solid left after evaporation of the solvent separated from boiling methyl alcohol in brilliantly shining white needles, melting at 139°.

Anal. Calcd. for $C_{12}H_{12}O_4Br_2$: C, 37.89; H, 3.15. Found: C, 38.25; H, 3.00.

The position of the nuclear bromine atom in these compounds was determined by oxidation of the tribromo acid in alkaline solution with potassium permanganate. The

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(8) Van Duin, *Rec. trav. chim.*, **45**, 349 (1926).

acid product, crystallized from water, melted at 183–184°, the melting point of 3,4-dimethoxy-6-bromobenzoic acid (6-bromoveratric acid). It was identified as this acid by a mixed melting point with the acid formed by oxidation of 6-bromoveratric aldehyde made by bromination of veratric aldehyde according to the directions of Pschorr.[9]

When the tribromo acid was treated with alcoholic potassium hydroxide an isomeric unsaturated bromo acid was obtained, and a small amount of a styrene derivative.

α-Bromo-3,4-dimethoxy-6-bromocinnamic Acid (198°).—Four grams of tribromo acid, finely pulverized, was stirred rapidly into 25 cc. of a 25% solution of potassium hydroxide in methyl alcohol. A colorless potassium salt began to separate at once. After ten minutes this was filtered out and dissolved in about 100 cc. of water. The solution deposited a small amount of solid, a styrene, which was filtered out and the solution cooled and acidified. The gelatinous precipitate was air dried and crystallized from boiling benzene from which it separates in fine pale lemon-yellow needles melting at 198°. The acid is readily soluble in acetone, boiling benzene and methyl alcohol, insoluble in ether.

Anal. Calcd. for $C_{11}H_{10}O_4Br_2$: C, 36.07; H, 2.73. Found: C, 36.16; H, 2.96.

The acid changes slowly to the higher melting isomeric acid (233°) on heating. It is, then, the less stable of the two isomers. The alcoholic filtrate from the separation of the potassium salt of the lower melting acid deposited, on acidification, a small amount of the impure high-melting acid.

The methyl ester of the acid (198°) was prepared by the usual procedure with diazomethane. It crystallizes from ether and from boiling methyl alcohol in fine white needles melting at 92°.

Anal. Calcd. for $C_{12}H_{12}O_4Br_2$: C, 37.89; H, 3.15. Found: C, 38.00; H, 3.24.

α-Bromo-3,4-dimethoxy-6-bromostyrene, $(CH_3O)_2C_6H_2\text{-}BrCH{=}CHBr$.—The styrene derivative mentioned above separates from methyl alcohol in fine cream colored needles melting at 100°.

Anal. Calcd. for $C_{10}H_{10}O_2Br_2$: C, 37.26; H, 3.10. Found: C, 37.45; H, 3.67.

Concentrated sulfuric acid dissolves all these cinnamic acids, the solutions being of a pale yellow color as with other cinnamic acids studied. In the present case, however, the yellow solutions take on slowly a pale green or blue color which readily fades out.

Summary

3,4-Dimethoxybenzalpyruvic acid and its bromination products have been prepared for purposes of comparison with other substituted benzalpyruvic acids. 3,4-Dimethoxycinnamic acid and its bromination products have also been studied and contrasted with 3-methoxy- and with 2,4-dimethoxycinnamic acids.

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[9] Pschorr, *Ann.*, **391**, 32 (1912).

[CONTRIBUTION FROM THE HENRY LESTER INSTITUTE OF MEDICAL RESEARCH, SHANGHAI, CHINA]

Researches on Pyrimidines. The Molecular Rearrangement of 2-Ethylmercapto-5-ethyl-6-thiocyanopyrimidine[1,2]

BY YUOH-FONG CHI AND YÜ-LIN T'IEN[3]

This paper describes the conditions of the molecular rearrangement of 2-ethylmercapto-5-ethyl-6-thiocyanopyrimidine (III) which is another example in our thiocyanate researches.[4,5,6,7,8,9,10] The thiocyanate (III) which is obtained from the corresponding chloropyrimidine (II)[11] prepared by the action of phosphorus chloride on the oxypyrimidine (I)[12] exhibits all the properties of a rhodanide, the structure of which is established by its interaction with thio-acetic acid[5,7,9,10,13] to give a dithiourethan (V). This thiocyanopyrimidine (III) is stable at its boiling point, and exhibits a similar behavior to 2-ethylmercapto-5-carbethoxy-6-thiocyanopyrimidine,[7] 2-ethylmercapto-4-methyl-6-thiocyanopyrimidine[8] and 2-ethylmercapto-5-phenyl-6-thiocyanopyrimidine.[9] It can be distilled at 158–160° under 5 mm. pressure without decomposition and without its conversion into its isomeric isothiocyanate (IV). Nevertheless, the stability of thiocyanopyrimidine (III) is greatly influenced by the presence of other reagents, and a molecular re-

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[1] This paper is a report of one phase of a research program dealing with the chemistry of certain pyrimidine thiocyanates, which was started originally in the Sterling Chemistry Laboratory of Yale University under the direction of Professor Treat B. Johnson.

[2] The authors desire to express their sincere thanks to The Lester Institute for their permission to undertake this research in their laboratories. They also wish to acknowledge help and criticisms from Professor Bernard E. Read.

[3] Holder of Fellowship from the China Foundation.

[4] Wheeler and Bristol, *Am. Chem. J.*, **33**, 448 (1905).

[5] Johnson and McCollum, *ibid.*, **36**, 136 (1906).

[6] Johnson and Storey, *ibid.*, **40**, 131 (1908).

[7] Johnson and Chi, THIS JOURNAL, **52**, 1580 (1930).

[8] Chi and Chen, *ibid.*, **54**, 2056 (1932).

[9] Chi and Tien, *ibid.*, **55**, 4181 (1933).

[10] Chi and Ma, *ibid.*, **55**, 4655 (1933).

[11] Johnson and Menge, *J. Biol. Chem.*, 3, 105 (1906).

[12] Johnson and Menge, *loc. cit.*, p. 1508.

[13] Wheeler and Merriam, THIS JOURNAL, **23**, 283 (1901).