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

The Action of Heat on S-Crotylthiosalicylic Acid and Related Compounds

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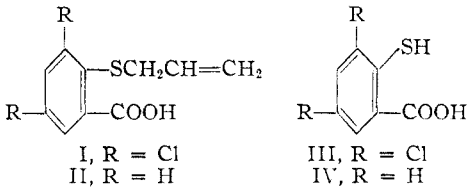
The behavior of allyl and crotyl aryl sulfides on heating is very different from that of the oxygen analogs. S-Allyl-3,5-dichlorothiosalicylic acid (I) is converted in part to dichlorothiosalicylic acid and to bis-(carboxydichlorophenyl) sulfide by heating to 275°. S-Crotylthiosalicylic acid (VII) yields 2-ethyl-2,3-dihydrobenzothiophene (IX) and the 7-carboxy derivative of this compound (VIII) when heated at 260°. The structures were proved by degradation and synthesis. The decarboxylation involved is simultaneous with the rearrangement and the crotyl group must rearrange without inversion, followed by cyclization to form VIII and IX. The following new compounds, isomeric with IX, have been synthesized during the identification of IX: 4-methylthiochroman, 3-ethyl-2,3-dihydrobenzothiophene-1,1-dioxide, 2-methylthiochroman and 3-methylthiochroman.

In a preceding paper,[2a] the reasons were given for undertaking a study of the pyrolysis of allyl sulfides derived from thiosalicylic acid. The present article shows that S-crotylthiosalicylic acid does undergo a thermal rearrangement, but that the results are markedly different from those obtained with the corresponding oxygen compounds.[3]

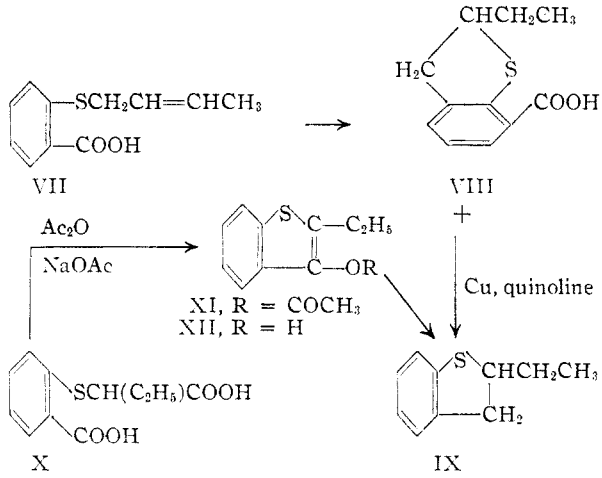
Earlier work[4] has shown that allyl phenyl and allyl *p*-tolyl sulfide did rearrange thermally to form O-allylthiophenols, but the yields were poorer and the reactions were much slower than those with the corresponding ethers. In the first example, there appeared to be some 2-methyl-2,3-dihydrobenzothiophene formed also.

It was known that the rearrangement of O-allyl-3,5-dichlorosalicylic acid (I, O instead of S) to give the allylphenol, with loss of carbon dioxide, occurred at a much faster rate than the rearrangement of the ether lacking the carboxyl group[5] and we therefore examined the behavior of I.



Pyrolysis of I at 250–275° gave only half of the theoretical volume of gas, assuming that one mole of carbon dioxide should be evolved. Neither of the two products isolated were the result of a rearrangement of the Claisen type; one was 3,5-dichlorothiosalicylic acid (III), and the other, from its composition and properties, was considered to be bis-(2,4-dichloro-5-carboxyphenyl) sulfide (V).[6]

It is known[5,7] that crotyl aryl ethers rearrange more rapidly than the allyl ethers and the crotyl sulfide VII was next studied. Pyrolysis of VII at 250–260° yielded 11% of thiosalicylic acid (IV), 17% of 2-ethyl-2,3-dihydro-7-benzothiophenecarboxylic acid (VIII) and 16% of 2-ethyl-2,3-dihydrobenzothiophene (IX). The relationship between VIII and IX was shown by the formation of IX by decarboxylation of VIII. The presence of a hetero ring containing sulfur in VIII and IX was shown by Raney nickel desulfuration of VIII to *m*-butylbenzoic acid, which was oxidized by permanganate to isophthalic acid. IX formed a crystalline sulfilimine and neither VIII or IX was reduced by hydrogen and palladium–charcoal.[2a]



The structure of IX and hence of VIII was established by the following synthesis. Thiosalicylic acid was alkylated with α-bromobutyric acid to give X which was cyclized to XI by acetic anhydride and sodium acetate.[8] Saponification of XI produced XII, which was reduced to 2-ethyl-1,2-dihydrobenzothiophene (IX) by the modified Wolff–Kishner procedure[9] and the synthetic product was shown to be identical with the pyrolysis product by a mixed

(1) Abbott Laboratories Fellow, 1951–1952.

(2) Recent papers in this series: (a) D. S. Tarbell and M. A. McCall, THIS JOURNAL, **74**, 49 (1952); (b) B. C. Morse and D. S. Tarbell, *ibid.*, **74**, 417 (1952); (c) D. S. Tarbell and J. C. Petropoulos, *ibid.*, **74**, 244, 1249 (1952); (d) D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 1 (1951).

(3) For a summary of the allyl ether rearrangement, see "Organic Reactions," Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1.

(4) C. D. Hurd and H. Greengard, THIS JOURNAL, **52**, 3356 (1930).

(5) D. S. Tarbell and J. W. Wilson, *ibid.*, **64**, 607 (1942).

(6) The formation of VI, the chlorine-free analog of V, by heating thiosalicylic acid (IV) at 280° has been reported (O. Hinsberg, *Ber.*, **43**, 1877 (1910)).

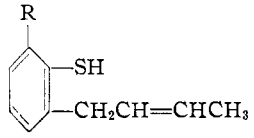
(7) W. R. Nummy and D. S. Tarbell, THIS JOURNAL, **73**, 1500 (1951).

(8) *Cf.* C. Hansch and H. G. Lindwall, *J. Org. Chem.*, **10**, 381 (1945).

(9) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

m.p. determination with the crystalline sulfilimine derivative.

In separate experiments, it was shown that the carboxylic acid VIII was *not* converted to IX by heating at 260° for 1.5 hr., 95% of VIII being recovered; furthermore, crotyl phenyl sulfide was recovered in 90% yield after 2 hr. at 255°, along with 4.4% of diphenyl disulfide. These observations show conclusively that the formation of the decarboxylated product IX must be the result of a simultaneous rearrangement and expulsion of carbon dioxide from VII; the decarboxylation does not occur either before or after rearrangement. The heterocyclic ring in VIII and IX must be due to cyclization of the initially formed crotylthiophenol XIII by heat.



XIII, (a) R = COOH, (b) R = H

Attempts to carry out the rearrangement under milder conditions with the hope of avoiding the cyclization of XIII to VIII or IX, were unsuccessful; the starting material was either recovered unchanged or was converted to the mixture of VIII and IX.

The results thus show very marked difference between the sulfur and the oxygen analogs. The most striking is the very much slower rate of rearrangement of the sulfides compared to the ethers; thus the oxygen analog of I rearranges in high yield at 140°, and the allyl ether of salicylic acid (II, O instead of S) gives the rearrangement at 170-180° with partial decarboxylation.[5] Furthermore, the crotyl ethers studied rearrange (to the ortho position) with attachment of the γ-carbon to the ring ("inversion"), giving the α-methylallylphenols.[10]

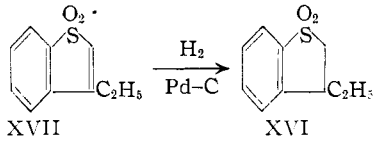
The slow rate of rearrangement of the sulfides may be due in part to the deactivating effect of sulfur on electrophilic attack on the aromatic nucleus,[11] since the rearrangement of allyl ethers is best regarded[5,12] as an electrophilic attack by the γ-carbon atom of the allyl group on the nucleus. The second reason, which would apply only to O-carboxy derivatives, is that with the ethers, the rearrangement may be favored by a high degree of hydrogen bonding between the carboxyl group and the ether oxygen. This would be absent in the sulfides, due to the very small tendency of sulfur to participate in hydrogen bonding.[2d]

Before the final identification of IX by synthesis, several isomeric compounds, which were considered *a priori* to be more likely structures for the rearrangement product, were synthesized in turn and found to give solid derivatives different from those obtained from the rearrangement product.

The first of these was 4-methylthiochroman (XIV), which was prepared by treatment of thiochromanone (XV) with methylmagnesium iodide, followed by dehydration of the carbinol and catalytic reduction of the resulting thiochromene with hydrogen and platinum. The second was 3-ethyl-

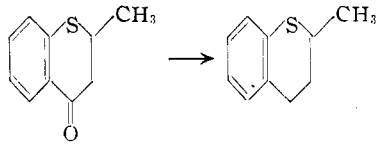
XIV XV

dihydrobenzothiophene, which was obtained, as the crystalline sulfone XVI, by the reduction with hydrogen and palladium–charcoal, of 3-ethylbenzothiophene-1,1-dioxide XVII; catalytic reduction of 3-ethylbenzothiophene itself could not be made to take place, even in the presence of a large amount of platinum or palladium catalyst.



XVII XVI

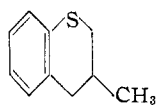
The next isomer was 2-methylthiochroman (XVIII), prepared by Clemmensen reduction of the corresponding thiochromanone XIX. The latter



XIX XVIII

was very readily obtained by heating crotonic acid to reflux with thiophenol;[13] a strong exothermic reaction ensued, with the formation in 72% yield, of β-(phenylmercapto)-butyric acid, $C_6H_5SCH(CH_3)CH_2COOH$, which could be cyclized, without isolation, to the ketone XIX.

The possibility that the rearrangement product might have been 3-methylthiochroman (XX) was very remote; however, in view of the relative ease of synthesis, it was prepared by the addition of thiophenol to methyl methacrylate, followed by saponification, cyclization to the thiochromanone, and Clemmensen reduction.



XX

Experimental[14]

Effect of Heat on S-Allyl-3,5-dichlorothiosalicylic Acid (II).—This compound[2a] (2.0 g.) was heated for 45 min. at 200–275°; gas evolution was first observed at about 230°. The gas was collected over a saturated sodium chloride

(10) A few exceptions to the rule that rearrangement of allyl ethers involves attachment of the γ-carbon to the nucleus are known (*e.g.*, W. M. Lauer and W. F. Filbert, THIS JOURNAL, **58**, 1388 (1936); C. D. Hurd and M. A. Pollak, *J. Org. Chem.*, **3**, 550 (1939)) but in no case does the substituted allyl group appear as a straight-chain group after rearrangement to the ortho position. The only analogous example is the rearrangement of the 9-phenanthrylmethyl ether of 3,5-dichlorosalicylic acid (D. S. Tarbell and V. P. Wystrach, THIS JOURNAL, **65**, 2149 (1943); D. S. Tarbell and Y. Sato, *ibid.*, **68**, 1091 (1946)).

(11) *Cf.* a discussion of this in ref. 2c; also G. B. Bachman and C. L. Carlson, *ibid.*, **73**, 2857 (1951), and D. S. Tarbell and A. H. Herz, *ibid.*, in press.

(12) A. C. Cope and E. M. Hardy, *ibid.*, **62**, 441 (1940).

(13) The addition of thiophenol to β-alkylacrylonitriles and to cyclohexenyl cyanide is favored by piperidine–Triton B as catalyst (R. M. Rose, *ibid.*, **71**, 3458 (1949); **73**, 129 (1951)). Possibly these reactions would proceed without catalyst at higher temperatures.

(14) All m.ps. corrected; analyses by Miss Claire King.

solution and heating was continued until the volume remained constant for a 15-min. period; the volume of gas (87 cc., N.T.P) corresponded to 51% yield, assuming complete decarboxylation.

The product was dissolved in ether, extracted with 5% bicarbonate and the extract acidified. The precipitated acidic material (1.7 g.) melted in the range 163–205°; it gave a negative test for the mercapto group with iodine. It was chromatographed on Florisil and eluted with benzene containing 10% methanol; this yielded material melting at 153–156°; the m.p. was not changed appreciably by sublimation at 1 mm.

Anal. Calcd. for $C_{14}H_6Cl_4O_4S$ (bis-(2,4-dichloro-6-carboxyphenyl) sulfide): C, 40.81; H, 1.45. Found: C, 40.85; H, 1.88.

The ether solution of the pyrolyzed material yielded after extraction with Claisen alkali, 0.6 g. of material, which, after reduction with zinc dust in 75% acetic acid for 1.5 hr., followed by digestion for a few minutes with hydrochloric acid, was recrystallized from methanol–water. Its m.p. was 206.5–207.5°, and it was shown to be 3,5-dichlorothiosalicylic acid by mixed m.p. with an authentic sample.

Pyrolysis of Crotyl Phenyl Sulfide.—Crotyl phenyl sulfide[15] was converted to the **sulfilimine** by treatment with Chloramine-T in aqueous alcohol[16] in 64% yield, m.p. 69–71°.

Anal. Calcd. for $C_{17}H_{19}NS_2O_2$: C, 61.23; H, 5.74. Found: C, 61.14; H, 5.69.

Pyrolysis of 5.15 g. of crotyl phenyl sulfide at 250–255° for 2 hr. in nitrogen leads to the formation of thiophenol isolated in 4.4% yield as the disulfide; the only other product which could be isolated was 90% of the starting material, identified as the sulfilimine.

S-Crotylthiosalicylic Acid (VII).—Thiosalicylic acid (38.5 g.) in 300 cc. of methanol containing 0.5 mole of sodium methoxide was treated dropwise with 81.0 g. of crotyl bromide[17] and the solution was refluxed with stirring for three hours. The solvent was distilled off, the oily residue was washed twice with water and then heated with 10% alkali on the steam-bath to hydrolyze the ester. The solution was refluxed with a little Darco, filtered and acidified with hydrochloric acid. The crude acid (49.4 g., m.p. 125–128°) yielded, after two recrystallizations from benzene, 26.4 g. (51%) of material of m.p. 138.5–139.5°.

Anal. Calcd. for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81. Found: C, 63.40; H, 5.70.

The structure was indicated by reduction with palladium-on-charcoal, in the manner previously described, to S-*n*-butylthiosalicylic acid, m.p. 97.5–98.5°, which gave no depression on mixed m.p. with an authentic sample of this compound,[18] prepared by the alkylation of thiosalicylic acid with *n*-butyl bromide.

Thermal Rearrangement of S-Crotylthiosalicylic Acid (VII).—This compound (20 g.) was heated in an atmosphere of nitrogen for 2 hr., until the gas volume became constant. The gas evolved amounted to 10% of the theoretical (219 cc., N.T.P.), calculated for complete decarboxylation; however, analysis[19] of the gas showed 39% of carbon dioxide, 25% of unsaturated hydrocarbons (C_3 or higher), no ethylene or carbon monoxide leaving 35% unaccounted for, possibly saturated hydrocarbons. The nitrogen gas present at the beginning was taken into account in the calculation.

The pyrolyzed material (19.0 g.) was dissolved in benzene, was extracted seven times with 5% bicarbonate, the extract was acidified, taken up in ether, re-extracted with bicarbonate, heated with Darco, and acidified. The solid acid was treated with hot heptane and filtered to remove the heptane-insoluble material which was not characterized (probably polymeric material). On cooling, the heptane gave 3.23 g. (17%) of solid of m.p. 137–141°. Several recrystallizations from methanol–water produced needles which melted at 147–148°. It was isomeric but not identical with S-crotylthiosalicylic acid, as shown by analysis and mixed m.p., and it was unaffected by treatment with hydrogen and palladium on charcoal.

Anal. Calcd. for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81; S, 15.37. Found: C, 63.73; H, 5.72; S, 15.42.

The benzene solution, after the bicarbonate extraction described above, was extracted four times with Claisen alkali. From the extract, 2.9 g. (20%) of impure thiosalicylic acid was recovered, which after several recrystallizations, and treatment with zinc and acetic acid (to reduce any disulfide present) melted at 163–164°, and gave no depression on mixed m.p. with thiosalicylic acid. The material is apparently not extracted readily from benzene by bicarbonate.

2-Ethyl-1,2-dihydrobenzothiophene (IX).—The benzene solution above, from which the acidic materials had been removed by bicarbonate and Claisen alkali, yielded 2.0 g. (16%) of neutral material, b.p. 69–72° (0.7–0.8 mm.), $n^{20}D$ 1.5714. It did not decolorize an iodine solution or give a precipitate with lead acetate.

Anal. Calcd. for $C_{10}H_{12}S$: C, 73.12; H, 7.37. Found: C, 73.18; H, 7.40.

The sulfilimine melted at 129–129.5° showing that the compound was not crotyl phenyl sulfide.

Anal. Calcd. for $C_{17}H_{19}NS_2O_2$: C, 61.23; H, 5.74. Found: C, 61.11; H, 5.66.

The dihydrobenzothiophene was unaffected by hydrogen and palladium–charcoal; the recovered material was converted to the 2-ethyl-2,3-dihydrobenzothiophene-1,1-dioxide of m.p. 71–73° using 30% hydrogen peroxide.[20]

Anal. Calcd. for $C_{10}H_{12}O_2S$: C, 61.19; H, 6.17. Found: C, 61.34; H, 6.24.

Desulfuration of 2-Ethyl-7-carboxy-1,2-dihydrobenzothiophene (VIII).—The material obtained from the bicarbonate extraction (3.0 g.) was desulfurated with Raney nickel in sodium carbonate solution.[21] Analysis showed that the material still contained sulfur and the desulfuration process was repeated. The liquid product (1.9 g.) would not crystallize, even at low temperatures, and hence was distilled, after first subliming some crystalline material, probably benzoic acid. The product boiled at 130–132° (1.0 mm.).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.24; H, 7.96.

Oxidation of the *m*-*n*-Butylbenzoic Acid to Isophthalic Acid.—The liquid (0.24 g.) obtained by desulfuration was oxidized in 10% sodium hydroxide solution by slowly adding 3% permanganate over a period of several days as it was used up, until further oxidizing agent was not discharged. The manganese dioxide was reduced with sulfur dioxide and the solution on acidification yielded 0.1 g. of isophthalic acid. Esterification of 60 mg. of this material with diazomethane yielded 40 mg. of dimethyl isophthalate,[22] m.p. 64–65.5°, giving no depression on mixed m.p. with an authentic sample.

Thermal Treatment of 2-Ethyl-2,3-dihydro-7-benzothiophenecarboxylic Acid (VIII).—This compound (616 mg.) was heated in an atmosphere of nitrogen for 1.5 hr. at 250–260°. During this period no carbon dioxide was detected. After cooling the solid product was dissolved in benzene and extracted with aqueous sodium bicarbonate solution. Acidification of the combined extracts gave 585 mg. (95%) of starting material, identified by a mixed melting point. Evaporation of the benzene solution gave less than 5 mg. of a non-acidic oily material which was not identified.

Decarboxylation.—To 447 mg. of VIII was added 2 cc. of quinoline and 300 mg. of copper powder. The mixture was refluxed (bath temperature 235°) for 30 min. During this period carbon dioxide (identified as barium carbonate) was evolved. The cooled mixture was dissolved in ether and extracted with dilute hydrochloric acid to remove the quinoline. Sodium bicarbonate extraction of the ether solution removed only a trace of acidic material. Evaporation of the ether left an oily residue which was distilled to

(15) A. C. Cope, D. E. Morrison and L. Field, THIS JOURNAL, **72**, 66 (1950).

(16) *Cf.* M. A. McCall, D. S. Tarbell and M. A. Havill, *ibid.*, **73**, 4476 (1951).

(17) W. G. Young and J. F. Lane, *ibid.*, **59**, 2051 (1937). The crotyl alcohol was prepared by lithium aluminum hydride reduction of crotonaldehyde (R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197 (1947)).

(18) J. J. Donleavy and J. English, Jr., *ibid.*, **62**, 220 (1940).

(19) We are indebted to Dr. William Barry for the analysis.

(20) A. Pomerantz and R. Connor, THIS JOURNAL, **61**, 3386 (1939).

(21) Using the procedure of F. F. Blicke and D. G. Sheets, *ibid.*, **70**, 3768 (1948).

(22) O. Aschan, *Ann.*, **387**, 36 (1912), reports a m.p. of 64–65°.

give 250 mg. (79%) of a colorless oil (IX), b.p. 135–140° (pot temperature) (10 mm.), $n^{20}D$ 1.5798.

The solid sulfilimine derivative of the above oil was identical in all respects with the sulfilimine of an authentic sample of IX.

α-(O-Carboxyphenylmercapto)-butyric acid (X) was prepared by condensing for one hour at reflux temperature 15.4 g. (0.1 mole) of thiosalicylic acid with 18.3 g. (0.11 mole) of α-bromobutyric acid in the presence of 45 g. (0.33 mole) of anhydrous potassium carbonate in 200 cc. of acetone. Addition of water to the reaction mixture caused the precipitation of 22.0 g. (91%) of crude product, m.p. 172–173.5°. Several recrystallizations from hot water gave clusters of needles of m.p. 173.5–174°.

Anal. Calcd. for $C_{11}H_{12}O_4S$: C, 54.99; H, 5.04. Found: C, 55.20; H, 5.16.

2-Ethyl-3-acetoxybenzothiophene (XI).[8]—A mixture of 4.0 g. of the above acid X, 9.0 cc. of acetic anhydride and 2.0 g. of anhydrous sodium acetate was heated on a steam-bath until the evolution of carbon dioxide had ceased after which time the mixture was refluxed for 20 minutes. Addition of water to the cooled reaction mixture gave an oil, which was dissolved in ether and washed with an aqueous solution of sodium bicarbonate and water. Evaporation of the dried ether and distillation of the oily residue gave 2.5 g. (60%) of a light yellow oil, b.p. 172–174° (pot temperature) (14 mm.), $n^{20}D$ 1.5770.

Anal. Calcd. for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found: C, 65.78; H, 5.54.

2-Ethyl-3-hydroxybenzothiophene (XII).—Crude XI, prepared from 15 g. of X by the above method, was hydrolyzed for 2.5 hr. at reflux temperature with 100 cc. of 10% aqueous sodium hydroxide. The cooled mixture was acidified to congo red with hydrochloric acid and extracted with ether. Evaporation of the ether from the combined dried ether extracts gave an orange oily residue, which was distilled to give 7.8 g. (70%) of a yellow oil, b.p. 166–168° (pot temperature) (14 mm.), $n^{20}D$ 1.6062. This oil gave a positive purple ferric chloride test and a precipitate with dinitrophenylhydrazine reagent.

Anal. Calcd. for $C_{10}H_{10}OS$: C, 67.38; H, 5.66. Found: C, 67.18; H, 5.54.

2-Ethyl-2,3-dihydrobenzothiophene (IX).[9]—To a mixture of 4.0 g. of XII, 5.0 cc. of 85% hydrazine hydrate and 25 cc. of triethylene glycol at 125° was added 2.5 g. of potassium hydroxide. The temperature of the clear yellow reaction mixture was maintained for 1.5 hr. at 125–130° and then was allowed to climb to 215° by removing the water from the reflux condenser. After 4.5 hr. at 215°, the mixture was cooled and diluted with 75 cc. of water and extracted with ether. Removal of the ether from the combined dried ether extracts gave an oily residue, which was distilled to give 1.60 g. (44%) of a colorless oil, b.p. 130–133° (pot temperature) (14 mm.), $n^{20}D$ 1.5840.

The sulfilimine derivative of synthetic IX melted at 129–129.5° and gave no depression on mixed melting with the same derivative prepared from IX which was isolated from the rearrangement.

β-(Phenylmercapto)-propionic Acid.—A mixture of 128 cc. (1.45 moles) of methyl acrylate, 118 cc. (1.15 moles) of thiophenol and 5 drops of dry piperidine was refluxed on a steam-bath for 22 hr. The excess methyl acrylate was removed by distillation and the condensation product was hydrolyzed with 300 cc. of dilute hydrochloric acid in 600 cc. of acetone for 15 hr. at reflux temperature. The mixture was diluted with water, extracted with ether and the combined ether extracts were washed with saturated aqueous sodium bicarbonate solution. Acidification gave the solid acid which, when crystallized from heptane, melted at 60.5°, over-all yield 67%. The reported m.p. is 59°.[23]

Thiochromanone (XV) was prepared by a concentrated sulfuric acid cyclization of the above acid.[23]

4-Methylthiochroman (XIV).—The addition of methyl Grignard reagent to thiochromanone by a previously described method[24] produced **4-hydroxy-4-methyl-thiochroman.** The carbinol (5 g.) was dehydrated at 150° with a crystal of iodine as the catalyst. The resulting olefin was dissolved in ether and washed with sodium bisulfite solution to remove the iodine. Evaporation of the dried ether and distillation of the residue gave 3.22 g. of a light yellow oil, b.p. 138–140° (pot temperature) (15 mm.). The olefin[24] on exposure to air turns green.

XIV was obtained by a platinum oxide (300 mg.) catalyzed reduction of 2.2 g. of the above olefin in 15 cc. of glacial acetic acid. The reduction required 19 hr. for the theoretical uptake of hydrogen. The product was isolated as a colorless oil by distillation b.p. 134–136° (pot temperature) (14 mm.), $n^{20}D$ 1.6008, yield 2.02 g. (90%).

Anal. Calcd. for $C_{10}H_{12}S$: C, 73.12; H, 7.37. Found: C, 73.13; H, 7.11.

The sulfilimine derivative of XIV melted at 142–143° and gave a marked depression on mixed melting point with the sulfilimine derivative of IX.

Anal. Calcd. for $C_{17}H_{19}NO_2S_2$: C, 61.23; H, 5.74. Found: C, 61.40; H, 5.90.

3-Ethyldihydrobenzothiophene-1,1-dioxide.—3-Acetylbenzothiophene (6.0 g.) prepared by a previously described method,[8] was reduced with 25 g. of amalgamated zinc, 25 cc. of concentrated hydrochloric acid, 10 cc. of water and 10 cc. of toluene, for 48 hr. at reflux temperature.[25] The steam-volatile product, 3-ethylbenzothiophene, was purified by distillation, b.p. 130–131° (pot temperature) (10 mm.), $n^{20}D$ 1.6028, yield 3.0 g. (54%).

Attempts to reduce 3-ethylbenzothiophene in the presence of large amounts of platinum and palladium catalyst were unsuccessful.

3-Ethylbenzothiophene (1.2 g.) was treated with 4 cc. of "Superoxol" and 15 cc. of glacial acetic acid at 80–85° for 6 hr.[26] After cooling, the mixture was diluted with water and neutralized with potassium carbonate which caused the precipitation of 420 mg. (30%) of product (XVII), m.p. 125–127°. Several crystallizations from methanol–water raised the m.p. to 130–131°.

Anal. Calcd. for $C_{10}H_{10}O_2S$: C, 61.83; H, 5.19. Found: C, 62.22; H, 5.29.

XVII (97 mg.), dissolved in 5 cc. of glacial acetic acid, was reduced in a hydrogen atmosphere over 200 mg. of prereduced palladium catalyst. Removal of the catalyst and acetic acid gave a solid (XVI) which, when recrystallized from methanol–water melted at 37.5–38°; yield 53 mg. (55%).

Anal. Calcd. for $C_{10}H_{12}O_2S$: C, 61.20; H, 6.17. Found: C, 61.30; H, 6.11.

An admixture of XVI with 2-ethyldihydrobenzothiophene-1,1-dioxide melted on mixing.

2-Methylthiochroman.—A mixture of 26 g. (0.3 mole) of crotonic acid, 33 g. (0.3 mole) of thiophenol and five drops of dry piperidine was heated on a steam-bath for 5 hr. At the end of this period no reaction had occurred; therefore, the mixture was heated to higher temperatures. At 180° an exothermic reaction occurred and the temperature increased to 245° where it remained constant. After 3 min. at 245° the reaction was cooled and 35 g. of the crude product was distilled to give 25 g. (72%) of β-(phenylmercapto)-butyric acid as a light yellow oil, b.p. 182° (9 mm.), $n^{20}D$ 1.5590. The reported b.p. is 183° (10 mm.).[24]

The remaining 23 g. of crude acid was cyclized in the presence of 230 g. of concentrated sulfuric acid[23] to give 8.4 g. (40% over-all yield) of **2-methylthiochromanone,** b.p. 146–147° (9 mm.), $n^{20}D$ 1.6125; the reported b.p. is 152° (13 mm.).[24] The semicarbazone of the ketone melted at 168–169°. The reported m.p. is 167–168°.[24]

The above ketone (6.0 g.) was reduced with 25 g. of amalgamated zinc, 25 cc. of concentrated hydrochloric acid, 10 cc. of water and 10 cc. of toluene for 48 hr. at reflux temperature. The mixture was made alkaline with sodium hydroxide and then was steam distilled. Ether extraction of the distillate gave, after the ether was evaporated, 2.93 g. (53%) of 2-methylthiochroman as a colorless oil, b.p. 125–127° (pot temperature) (9 mm.), $n^{20}D$ 1.5878.

Anal. Calcd. for $C_{10}H_{13}S$: C, 73.12; H, 7.37. Found: C, 73.26; H, 7.28.

The sulfilimine prepared by the usual method melted at 139–140° and gave a depression on mixed melting with the sulfilimine of 2-ethyldihydrobenzothiophene.

(23) F. Krollpfeiffer and H. Schultze, *Ber.*, **56**, 1821 (1923).

(24) F. Krollpfeiffer, *et al.*, *ibid.*, **58**, 1654 (1925).

(25) Ng. Ph. Buu-Hoi and P. Cagniant, *ibid.*, **76B**, 1272 (1943).

(26) D. S. Tarbell, D. K. Fukushima and H. Dam, THIS JOURNAL, **67**, 1643 (1945).

Anal. Calcd. for $C_{17}H_{19}NO_2S_2$: C, 61.23; H, 5.74. Found: C, 61.48; H, 6.03.

3-Methylthiochroman.—A solution of 14.5 cc. (0.14 mole) of thiophenol, 14 g. (0.14 mole) of methyl methacrylate and 3 drops of dry piperidine was heated until the reflux temperature increased from 130 to 250°; about 10 hr. was required. On cooling, the crude ester was hydrolyzed with 100 cc. of dilute hydrochloric acid in 150 cc. of acetone for 12 hr. at reflux temperature. The mixture was diluted with water, extracted with ether and the combined ether extracts were washed with saturated aqueous sodium bicarbonate solution. Acidification caused the separation of an oil which was collected by ether extraction. Evaporation of the ether from the dried ether extracts gave a residue which was distilled to give 11.5 g. (42%) of **α-methyl-β-(phenylmercapto)-propionic acid,** b.p. 188–190° (pot temperature) (12 mm.). The oil slowly solidified and melted, after crystallization from pentane, at 31.5–32°.

Anal. Calcd. for $C_{10}H_{12}O_2S$: C, 61.20; H, 6.17. Found: C, 61.47; H, 6.13.

The above acid (10 g.) was cyclized in the presence of 100 g. of concentrated sulfuric acid by a previous described method[23] to give 5.3 g. (59%) of 3-methylthiochromanone as a colorless oil, b.p. 146–150° (pot temperature) (10 mm.). The oil slowly solidified and was recrystallized from pentane to give needles of m.p. 41–42°.

Anal. Calcd. for $C_{10}H_{10}OS$: C, 67.38; H, 5.66. Found: C, 67.37; H, 5.50.

The ketone (4.0 g.) was reduced by the exact method used above for the reduction of 2-methylthiochromanone. **2-Methylthiochroman** was isolated in 63% yield (2.38 g.) as a colorless oil, b.p. 132–134° (pot temperature) (10 mm.), $n^{20}D$ 1.6020.

Anal. Calcd. for $C_{10}H_{12}S$: C, 73.12; H, 7.37. Found: C, 73.34; H, 6.97.

The sulfilimine melted at 142–143° and gave a depression on mixed melting with the sulfilimine of 2-ethyldihydrobenzothiophene.

Anal. Calcd. for $C_{17}H_{19}NO_2S_2$: C, 61.33; H, 5.74. Found: C, 61.38; H, 5.85.

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[CONTRIBUTION FROM THE FULMER LABORATORY, DEPARTMENT OF CHEMISTRY, THE STATE COLLEGE OF WASHINGTON]

Preparation of Ketones and their Enol Esters by the Base-catalyzed Condensation of Acids and Acid Derivatives with Anhydrides[1,2]

BY GRANT GILL SMITH

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The condensation of phenylacetic acid with anhydrides in the presence of pyridine to produce benzyl ketones has been shown to be general for a number of aliphatic acid anhydrides, but not for aromatic acid anhydrides. Enol esters of the ketones were isolated as secondary products. Although condensation was slow with phenylacetic acid, the reaction rate was considerably increased by use of phenylacetic anhydride, phenylacetyl chloride or acids with more reactive α-hydrogens, such as *p*-nitrophenylacetic acid. Under the same conditions ethyl phenylacetate and cinnamic acid did not condense.

When phenylacetic acid reacts with an excess of an aliphatic acid anhydride in the presence of pyridine at elevated temperatures, benzyl alkyl ketones are formed.[3] Since this first report by Dakin and West, the reaction has been studied by several investigators.[4] In this investigation phenylacetic acid, phenylacetyl chloride, phenylacetic anhydride, *p*-nitrophenylacetic acid and *o*-chlorophenoxyacetic acid were condensed with acetic anhydride. The first two were also condensed with propionic, butyric and phenylacetic anhydride. The ketones (I) and their enol esters (II) which resulted from this condensation were isolated directly by fractional vacuum distillation.

$$ARCH_2COX + (RCO)_2O \xrightarrow[100\text{–}145^\circ]{\text{pyridine}} ARCH_2COR + ARCH{=}C(OCOR){-}R + RCOOH + CO_2$$

I II

X = OH, Cl, $OCOCH_2C_6H_5$
R = CH_3, C_2H_5, C_3H_7, $C_6H_5CH_2$
AR = C_6H_5, *p*-$NO_2C_6H_4$, *o*-Cl-C_6H_4-O-

The ketones (I) were characterized by conversion to their semicarbazide and 2,4-dinitrophenylhydrazine derivatives. The structure of the enol esters (II) was established by elementary analysis, their unreactivity to sodium bisulfite, and by the comparison of the infrared curve of the enol acetate of *p*-nitrophenyl-2-propanone with those of isopropenyl acetate (III) and acetylacetone (IV). If O-acylation took place the product would show infrared absorption bands in the ester and olefin regions similar to those found in isopropenyl acetate. If on the other hand C-alkylation occurred, a 1,3-diketone would have resulted whose infrared bands would correspond to those of acetylacetone in the ketone region.

$CH_2{=}C(OCOCH_3){-}CH_3$ (III) $\qquad CH_3{-}C(=O){-}CH_2{-}C(=O){-}CH_3$ (IV)

Infrared spectra are given in Fig. 1. The enol acetate of *p*-nitrophenyl-2-propanone and isopropenyl acetate have strong absorption bands near 1755 and 1672 mμ and no absorption between these figures. For acetylacetone these bands do not appear; however, it shows a characteristic ketone band at 1710 mμ.[5] The characteristic bands for esters are near 1750 mμ[5]; olefins have characteristic bands at 1620 to 1680 mμ.[5] Another typical example of an unsaturated ester similar to isopropenyl acetate is vinyl acetate which has a band at 1660 and 1760 mμ.[5] Hence, it appears quite evi-

(1) Presented before the Division of Organic Chemistry, 119th Meeting of the American Chemical Society, Boston, Mass., April 4, 1951.

(2) This work was completed prior to the publication by J. A. King and F. H. MacMillan, THIS JOURNAL, **73**, 4911 (1951), and since the work was done independently is being published independently.

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(5) R. B. Barnes, R. C. Gove, U. Liddel and V. E. Williams, "Infrared Spectroscopy," Reinhold Publ. Corp., New York, N. Y., 1944.