was distilled under reduced pressure below 50°. The cooled liquid residue was taken up in 1.5*N* hydrochloric acid and washed with ether. Neutralization of the aqueous acid solution with sodium bicarbonate precipitated a yellowish oil which solidified in a short time. Recrystallization from methanol gave 10.0 g. (41%) of cream-colored crystals, m.p. 109–110°. The colorless analytical sample was obtained from heptane, m.p. 109–110° (reported[6b] m.p. 110°). The carbonyl band occurred at 1644 cm.$^{-1}$ in the infrared spectrum.

Extraction of the resin with 1.5*N* hydrochloric acid and cooling of the extract gave the hydrochloride of II, m.p. 170–171° dec. Upon neutralization with sodium bicarbonate the aqueous acid solution gave an additional 1.5 g. of the ketol, m.p. 108–110°.

2-Hydroxy-β-(2-pyridyl)acrylophenone (IIa). A solution of 2.0 g. of the ketol (II) in 10 ml. of concd. hydrochloric acid was refluxed for 3 min., cooled, and neutralized with sodium bicarbonate. The deep yellow precipitated oil gradually solidified. Recrystallization of the crude product (1.8 g., m.p. 80–84°) from aqueous methanol gave 1.4 g. (76%) of fine, bright yellow needles, m.p. 99–100° (reported[11] m.p. 101–102°). The ultraviolet spectrum exhibited a maximum at 309 mμ (ε 21,600) and in the infrared the carbonyl band occurred at 1635 cm.$^{-1}$

2',3-Dihydroxy-3-(4-pyridyl)propiophenone (III). The condensation of 5.4 g. (0.05 mole) of 4-pyridinecarboxaldehyde and 7.5 g. (0.055 mole) of *o*-hydroxyacetophenone in the presence of 10 g. of the resin by the method employed for compound II gave 5.5 g. (45%) of almost colorless crystals, m.p. 143–146°. The analytical sample melted at 148–149° (from ethanol; reported[6b] m.p. 152°). The carbonyl band occurred at 1638 cm.$^{-1}$ in the infrared spectrum.

Approximately the same yield of the ketol (III) was obtained when the reaction was carried out in 60% ethanol. When the recovered resin was extracted with 1.5*N* hydrochloric acid an additional 1.0 g. of III separated in the form of its colorless hydrochloride, m.p. 206–207° (dec., from ethanol). Upon neutralization with sodium bicarbonate an aqueous solution of the latter gave III, m.p. 148–149° (from ethanol).

2-Hydroxy-β-(4-pyridyl)acrylophenone (IIIa). (a) A solution of 2.0 g. of the ketol (III) in 20 ml. of concentrated hydrochloric acid was dehydrated by procedure (a) for the preparation of compound IIa. Recrystallization of the crude product (1.7 g., m.p. 114–121°) from aqueous ethanol gave 1.1 g. of long, yellow needles, m.p. 124–125°. The ultraviolet spectrum exhibited a maximum at 292 mμ (ε 23,650); in the infrared the carbonyl band occurred at 1640 cm.$^{-1}$

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.68; H, 4.94; N, 6.08.

(b) One gram of the ketol (III) and 25 g. of polyphosphoric acid were heated at 100° with stirring for 5 min. The colorless solid dissolved with the formation of a deep orange solution and upon dilution with water and neutralization with sodium hydroxide it precipitated a yellow solid. Recrystallization of the crude product from ethanol gave 0.25 g. of bright yellow needles, m.p. 124–125°.

2',3-Dihydroxy-3'-methoxy-3-(3-pyridyl)propiophenone (IV). A solution of 5.5 g. of 2-hydroxy-3-methoxyacetophenone[18] and 3.6 g. of 3-pyridinecarboxaldehyde was condensed in the presence of Amberlite IRA-400 (OH^-) and ethanol by the procedure employed for the preparation of compound II. The colorless solid which separated (1.8 g., m.p. 170–173° dec.) was obtained from aqueous ethanol as fine colorless needles, m.p. 173–175° dec.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.75; H, 5.06; N, 5.42.

2-(3-Pyridyl)-8-methoxy-4-chromanone hydrochloride (IVb). When a solution of 100 mg. of compound IV in 2 ml. of concd. hydrochloric acid was refluxed for 1 min. and allowed to evaporate there remained a mass of colorless crystals, m.p. 235–236° (dec., from ethanol). The carbonyl band occurred at 1690 cm.$^{-1}$ in the infrared.

Anal. Calcd. for $C_{15}H_{14}NO_3Cl$: C, 61.75; H, 4.84. Found: C, 61.80; H, 5.04.

2-Hydroxy-3,6-dimethoxy-β-(3-pyridyl)acrylophenone hydrochloride (Va). A solution of 0.65 g. of 3-pyridinecarboxaldehyde and 1.0 g. of 2-hydroxy-3,6-dimethoxyacetophenone[19] in 10 ml. of ethanol was stirred gently for 24 hr. with 2.0 g. of Amberlite IRA-400 (OH^-). The resin was filtered from the orange solution and washed with ethanol. Distillation of the combined filtrates under reduced pressure on the steam bath left a deep orange liquid which was taken up in dilute hydrochloric acid and washed with ether. Neutralization of the aqueous acid solution precipitated an orange semisolid which was dissolved in ether. The ether phase was dried by shaking briefly with anhydrous magnesium sulfate and acidified slightly by passing a stream of anhydrous hydrogen chloride over the surface of the solution. The dense, deep red precipitate which separated (0.99 g., m.p. 229–231° dec.) was recrystallized from ethanol, m.p. 233–234° dec. The carbonyl band occurred in the infrared at 1642 cm.$^{-1}$

Anal. Calcd. for $C_{16}H_{16}NO_4Cl$: C, 59.54; H, 5.31; N, 4.34. Found: C, 59.47; H, 5.07; N, 4.41.

When the reaction time was extended to 72 hr., compound Va and a colorless by-product were obtained in approximately equal yields. The colorless material [2-(3-pyridyl)-5,8-dimethoxy-4-chromanone, Vb] melted at 173–174° (dec., from ether). It was insoluble in dilute sodium hydroxide solution and the carbonyl band occurred at 1695 cm.$^{-1}$ in the infrared.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.17; H, 5.44; N, 4.76.

2',3-Dihydroxy-3',6'-dimethoxy-3-(4-pyridyl)propiophenone (VI). The condensation of 2.6 g. of 4-pyridinecarboxaldehyde and 4.9 g. of 2-hydroxy-3,6-dimethoxyacetophenone by the procedure employed for compound II gave 0.5 g. of colorless crystals, m.p. 124–125° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.30; H, 5.53; N, 4.75.

4-Hydroxy-4-(2-pyridyl)-2-butanone. A solution of 5.2 g (0.05 mole) of 2-pyridinecarboxaldehyde in 100 ml. of acetone was cooled in a Dry Ice bath and 10 g. of the resin was added. The suspension was stirred gently for 24 hr. in the cold and allowed to warm to room temperature. The resin was filtered off and the filtrate was concentrated under reduced pressure on the steam bath. The residue of pale orange liquid, which solidified to an oily crystalline mass (8.7 g.), was recrystallized from heptane to yield 5.4 g. (70%) of colorless crystals, m.p. 75–76° (reported[5] m.p. 75.5–76°).

The hydrochloride melted at 120–121° (from ethanol–ethyl acetate).

Anal. Calcd. for $C_9H_{12}NO_2Cl$: C, 53.34; H, 5.97; N, 6.91. Found: C, 53.09; H, 6.00; N, 7.06.

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Reactions of *N*-Chloromethylphthalimide with Nucleophilic Divalent Sulfur Compounds

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The reactions of *N*-bromomethylphthalimide with various nucleophilic reagents have been re-

ported in the literature.[1-7] Of these nucleophiles only two (potassium thiocyanate[2] and thiourea[7]) are divalent sulfur compounds.[8] Although *N*-chloromethylphthalimide was known at the same time with the bromomethyl compound, its reaction with thiourea[7] appears to be the only one recorded.[9] This paper reports the reactions of this highly reactive chloromethyl compound with several types of mercapto compounds including the salts of xanthic acids, dithiocarbamic acids, thiosulfonic acid, thiophenol, 2-mercaptobenzothiazole, and so forth.

When a suspension of *N*-chloromethylphthalimide in acetone was mixed at room temperature[10] with an aqueous solution of the salt of the mercapto compound, the corresponding *N*-(substituted mercaptomethyl)phthalimide separated almost instantaneously. In the case of xanthates and dialkyldithiocarbamates the crude products of the expected structure, which melted sharply and usually within one or two degrees of that of the pure compound, were obtained in 86–95 % yield. (Crude products from unsubstituted dithiocarbamate and ethylenebisdithiocarbamate, however, are less pure and are difficult to purify.) The ease of formation of these compounds in high yield and purity suggests the possible use of *N*-chloromethylphthalimide as a reagent for the identification of xanthates and dialkyldithiocarbamates. On the other hand the reactions of *N*-chloromethylphthalimide with other nucleophilic divalent sulfur compounds, such as thiosulfonate and thiophenol, are less straightforward as evidenced by the lower yield and wider melting range of the crude product obtained under similar conditions. The cause of the side reaction and the nature of the by-product(s) are not known.

The eleven new *N*-(substituted mercaptomethyl)phthalimides synthesized in the present work were evaluated as fungicides. Preliminary tests[11] against *Stemphylium sarcinaeforme* and *Monilinia fructicola* indicated that none of these has sufficient activity to be of interest.

EXPERIMENTAL[12]

N-Chloromethylphthalimide was prepared from *N*-hydroxymethylphthalimide[3,13] by the method of Gabriel.[14,15] The yield of the crude product (m.p. 128–131°) was 90%. It was used in subsequent reactions without further purification. The recrystallized product (from ethylene dichloride) has a melting point of 133–134°.[16]

Preparation of N-(substituted mercaptomethyl)phthalimides. General procedure. A suspension of *N*-chloromethylphthalimide (19.6 g., 0.1 mole) in acetone (100 ml.) was mixed with stirring with a solution of the soluble salt of the mercapto compound (0.11–0.12 mole) in water (50 ml.). The latter solution was obtained by dissolving the preformed salt of the unstable acids, such as xanthic, dithiocarbamic, thiosulfonic acid, in water, or the more accessible mercapto compound like thiophenol and 2-mercaptobenzothiazole in a stoichiometric amount of 10% sodium hydroxide and a proper amount of water. The mixture was stirred at room temperature for 0.5 hr. Water (200 ml.) was added and the mixture was cooled to complete the separation of the product. The solid was collected, washed with water, and air dried. The product was recrystallized from ethanol or acetone.

The pertinent data of the eleven *N*-(substituted mercaptomethyl)phthalimides thus prepared are given below.

Phthalimidomethyl ethylxanthate was prepared from potassium ethylxanthate; crude yield 93% (m.p. 94–96°); m.p. 95–96°.[17]

Anal. Calcd. for $C_{12}H_{11}NO_3S_2$: N, 4.98; S, 22.79. Found[18]: N, 4.98; S, 22.54.

Phthalimidomethyl n-butylxanthate was prepared from potassium *n*-butylxanthate; crude yield 95% (m.p. 77–78°); m.p. 77–78°.[17]

Anal. Calcd. for $C_{14}H_{15}NO_3S_2$: N, 4.53; S, 20.73. Found[18]: N, 4.54; S, 20.97.

Phthalimidomethyl dimethyldithiocarbamate was prepared from sodium dimethyldithiocarbamate; crude yield 89% (m.p. 167–169°); m.p. 168–170°.[19]

Anal. Calcd. for $C_{12}H_{12}N_2O_2S_2$: N, 10.00; S, 22.91. Found[18]: N, 10.00; S, 23.00.

Phthalimidomethyl diethyldithiocarbamate was prepared from sodium diethyldithiocarbamate; crude yield 94% (m.p. 124–126°); m.p. 124–125°.[17]

Anal. Calcd. for $C_{14}H_{16}N_2O_2S_2$: N, 9.09; S, 20.79. Found[18]: N, 8.84; S, 20.71.

Phthalimodomethyl (diisopropyl)dithiocarbamate was prepared from sodium (diisopropyl)dithiocarbamate; crude yield 86% (m.p. 120–122°); m.p. 122.5–123.5°.[17]

Anal. Calcd. for $C_{16}H_{20}N_2O_2S_2$: N, 8.38; S, 19.17. Found[18]: N, 8.19; S, 19.11.

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(8) The reaction of *N*-bromomethylphthalimide with another sulfur compound, sodium sulfite, to form phthalimidomethanesulfonic acid in low yield has been reported by Balaban (ref. 4). In this case, the sulfur is tetravalent, however.

(9) The reaction of *N*-chloromethylphthalimide with β-dioxo compounds which are substituted in the methylene group has been reported recently. H. Böhme, R. Broese, and F. Eiden, *Chem. Ber.*, **92**, 1258 (1959).

(10) Both *N*-bromomethyl- (ref. 1) and *N*-chloromethylphthalimide are sensitive to hot water, being hydrolyzed to *N*-hydroxymethylphthalimide. The effect of water on *N*-chloromethylphthalimide at various temperatures was studied by R. S. Cook of these Laboratories. There were 80% and 60% conversion to *N*-hydroxymethylphthalimide at 90° and 75° (in 15 min.), respectively. The author is grateful to Mr. Cook for this information.

(11) Tested by the slide-germination method published by the American Phytopathological Society, *Phytopathology*, **33**, 627 (1943).

(12) All melting points are uncorrected.

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(16) Lit. value: 133–134° (ref. 14), 136.5° (ref. 15), 134–135° (ref. 9).

(17) Recrystallized from ethanol.

(18) On the crude product which had the m.p. shown in the parentheses.

(19) Recrystallized from acetone.

Di(phthalimidomethyl) ethylenebisdithiocarbamate was prepared from disodium ethylenebisdithiocarbamate; crude yield 92.5% (m.p. 188–191°).[20]

Anal. Calcd. for $C_{22}H_{18}N_4O_4S_4$: N, 10.56; S, 24.17. Found[18]: N, 10.20; S, 24.20.

Phthalimidomethyl dithiocarbamate was prepared from ammonium dithiocarbamate; crude yield 93%; m.p. 182–185°.[21]

Anal. Calcd. for $C_{10}H_8N_2O_2S_2$: N, 11.11; S, 25.42. Found: N, 10.71; S, 24.52.

Phthalimidomethyl p-toluenethiolsulfonate was prepared from sodium *p*-toluenethiolsulfonate; yield 56%; m.p. 158.5–160°.[17]

Anal. Calcd. for $C_{16}H_{13}NO_4S$: N, 4.03; S, 18.46. Found: N, 3.96; S, 18.56.

Ethyl phthalimidomethylmercaptoacetate was prepared from ethyl mercaptoacetate; yield 71%; m.p. 106–109°.[17]

Anal. Calcd. for $C_{13}H_{13}NO_4S$: N, 5.02; S, 11.48. Found: N, 5.08; S, 11.36.

N-(p-Chlorophenylthiomethyl)phthalimide was prepared from *p*-chlorobenzenethiol; yield 57%; m.p. 99–101°.[17]

Anal. Calcd. for $C_{15}H_{10}ClNO_2S$: N, 4.61; S, 10.46. Found: N, 4.55; S, 10.45.

2-Phthalimidomethylmercaptobenzothiazole was prepared from 2-mercaptobenzothiazole; yield 86%, m.p. 139–140°.[17]

Anal. Calcd. for $C_{16}H_{10}N_2O_2S_2$: N, 8.64; S, 19.77. Found: 8.46; S, 19.65.

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(20) Attempts to recrystallize this product resulted in excessive decomposition.

(21) Recrystallized from acetone and then from ethanol. Further recrystallization from ethanol yielded a product m.p. 184–186°, of lower sulfur analysis (Found: N, 10.70; S, 23.85).

β-(2-Thioxo-1-imidazolidyl)ethyl Isothiocyanate and Related Compounds

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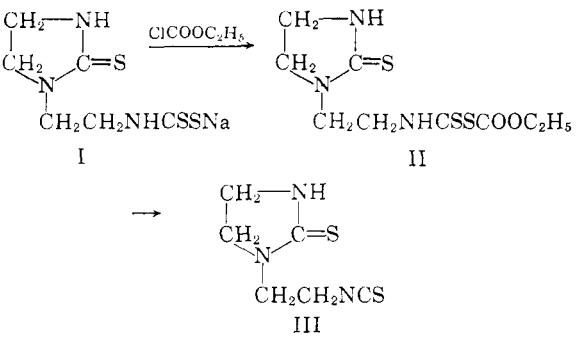
In the general method of preparation of isothiocyanates from monosubstituted dithiocarbamates and alkyl chlorocarbonates,[1-3] the intermediate alkoxycarbonyl dithiocarbamates[4] were not isolated because of their instability. The alkoxycarbonyl derivatives of alkylenebisdithiocarbamic acids, $(CH_2)_n(NHCSSCOOR)_2$ (type A), appear to be more stable than those of the alkyldithiocarbamic acids, R'NHCSSCOOR (type B). Most alkoxycarbonyl monosubstituted dithiocarbamates reported belong to the type A[5-7] and few of the type B have ever been isolated in pure state and characterized.[8] This paper reports the isolation of a solid ethoxycarbonyl β-(2-thioxo-1-imidazolidyl)ethyldithiocarbamate (II) and its conversion to β-(2-thioxo-1-imidazolidyl)ethyl isothiocyanate (III).



I II III

When sodium β-(2-thioxo-1-imidazolidyl)ethyldithiocarbamate (I) was allowed to react with ethyl chlorocarbonate in the cold, compound II was isolated as a crystalline solid. Decomposition of II in boiling ethanol yielded III and carbon oxysulfide which was identified by the formation of cyclohexylammonium cyclohexylthiocarbamate. Reaction of I with other chlorocarbonates such as 2-chloroethyl, isopropy *n*-butyl chlorocarbonate, at room temperature yielded III directly. The isothiocyanate III is a stable solid which can be recrystallized from alcohol. It reacts normally with amines to form the expected thioureas. The thiourea IV obtained from III and aniline is identical with that formed by the reaction of phenyl isothiocyanate and 1-β-aminoethyl-2-imidazolidinethione (V). Reaction of III with dimethylamine yielded 1-[β-(2-thioxo-1-imidazolidyl)ethyl]-3,3-dimethyl-2-thiourea (VI).

(1) For a general discussion and early references, see Houben-Weyl, *Methoden der organischen Chemie*, vol. 9, p. 870, George Thieme Verlag, Stuttgart, 1955.

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(4) The alkoxycarbonyl dithiocarbamates have the general structure of $NH_2CSSCOOR$. According to Chemical Abstracts nomenclature these compounds should be named as the thioanhydrides of dithiocarbamic acid and monoalkylcarbonic acid.

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(8) For example: (a) methoxycarbonyl β-hydroxyethyldithiocarbamate was reported by P. G. Sergeev and S. N. Ivanova, *J. Gen. Chem. (U.S.S.R.)*, **7**, 1495 (1937) [*Chem. Abstr.*, **32**, 2534 (1938)]; (b) ethoxycarbonyl phenyldithiocarbamate by O. E. Schultz and E. Barthold, *Arch. Pharm.*, **285**, 267 (1952) [*Chem. Abstr.*, **48**, 5129 (1954)].