N-(1-Methylbutan-2-onyl)propionamide (IIIb). The procedure for the preparation of 3-acetamido-2-butanone[12] was utilized. Treatment of 20 g. (0.224 mole) of DL-alanine with 95 g. (1.2 moles) of pyridine and 174.8 g. (1.344 moles) of propionic anhydride yielded 20.2 g. (58.5%) of IIIb, b.p. 79–81° (0.1 mm.), n_D^{25} 1.4547, d^{25} 1.016.

Anal. Calcd. for $C_8H_{15}NO_2$: C, 61.11; H, 9.61. Found: C, 61.30; H, 9.48.

N-(2-Hydroxy-1-methylbutyl)propionamide, propionate ester (IIb). To 4 g. (0.0254 mole) of IIIb in methanol was added slowly with swirling 750 mg. of sodium borohydride. The reaction mixture was allowed to stand overnight. Ammonium hydroxide was added to the solution. The solution was extracted with ether and the ether extracts dried over anhydrous sodium sulfate, filtered, and evaporated to leave a white solid. Recrystallization of the solid from petroleum ether–acetone yielded 2.663 g. (66%) of *N*-(2-hydroxy-1-methylbutyl)-propionamide, m.p. 113–114°. A solution of 2.563 g. of this alcohol in pyridine was added to an excess of propionyl chloride in pyridine and the mixture was allowed to stand overnight, then poured onto cracked ice. The aqueous mixture was extracted with ether and the ether extract was washed successively with dilute hydrochloric acid, water, sodium bicarbonate, and water. The ether solution was dried and then distilled to yield 1.752 g. (51%) of IIb, b.p. 101–103° (0.1 mm.), n_D^{25} 1.4523, d^{25} 1.004. The infrared spectrum of this compound was in agreement with the assigned structure.

Anal. Calcd. for $C_{11}H_{21}NO_3$: C, 61.36; H, 9.83; N, 6.51. Found: C, 61.12; H, 9.80; N, 6.45.

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Derivatives of Sulfenic Acids. XXIV. Synthesis of Certain Thiophenols by Cleavage of Unsymmetrical Disulfides[1]

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In a preceding paper of this series[3] a new synthesis of thiophenols was recorded, involving alkaline cleavage of aryl 2,4-dinitrophenol sulfides:

$$(NO_2)_2C_6H_3SAr + OCH_3^- \longrightarrow ArS^- + (NO_2)_2C_6H_3{-}OCH_3 \quad (1)$$

We now wish to describe another new method for preparing certain thiophenols, which was an outgrowth of our interests in the mechanisms of scission of the sulfur-sulfur bond.

It is well known[4] that many disulfides are cleaved by nucleophilic reagents such as CN^-, RS^-, SO_3^{--}, $(C_6H_5)_3P$, AsH_5, $S_2O_3^{--}$, *etc.* These reactions are simply nucleophilic displacements from bivalent sulfur, of a mercaptide ion, by a base with more affinity for sulfur. The reactions involve equilibria, which may be represented as in (2), where B^- is a base such as those above, and R and R′ are any groups (not necessarily different), which form a covalent bond with sulfur which is less susceptible to cleavage than the =S—S—bond.

$$R{-}S{-}S{-}R' + B^- \rightleftharpoons RS^- + R'S{-}B \quad (2)$$

In many cases, equilibrium *b* lies well to the left because of the high affinity of RS^- for sulfur, and, in other cases, the alternate scission (3) may compete with (2). If, however, B^- is a strong

$$R{-}S{-}S{-}R' + B^- \rightleftharpoons RS{-}B + R'S^- \quad (3)$$

displacing anion, and R is a strong electron withdrawing group (such as 2,4-dinitrophenyl or 2-nitro-4-chlororophenyl), the reactivity of RS^- in reaction (2) will be less than that of B^- and this will cause equilibrium (*b*) to lie to the right. Also, if R is considerably more electron withdrawing than R′, RS^- will be the more easily displaced mercaptide group, so that primarily reaction (2) and not (3), will occur. With these conditions in mind, reaction (2) can be adapted to a convenient synthesis of certain thiophenols, RSH, starting with sulfenyl chlorides, RSCl, in which R is a strong electronegative group, and choosing a less electronegative group, R′, so that R′SB, or its decomposition products, are readily soluble in water, or are volatile.

We selected 2-mercaptosuccinic acid (thiomalic acid) as the source for the group R′S, and hydroxide ion as the nucleophilic reagent for general use; ethyl mercaptan, mercaptoacetic acid, and β-mercaptoethanol are equally effective sources of the R′S group. It is also known[4] that cyanide ion and triphenylphosphine are much more powerful displacing nucleophiles for reaction (1) than is hydroxide ion, and—although less convenient—should be chosen when cleaving disulfides (RSSR′) in which R is not as strongly electron withdrawing as it is in the case of 2,4-dinitrophenyl or 2-nitro-4-chlorophenyl. In one reaction (R = 2-nitrophenyl), the use of cyanide ion as the displacing anion increased the yield of 2-nitrothiophenol by 35% over that obtained with hydroxide ion as nucleophile.

The reactions are easy to perform and lead to the desired thiophenols quickly. The sulfenyl chloride is converted almost quantitatively to the thiomalic acid derivative (Equation 4), which is a stable, odorless, crystalline disulfide. Like the aryl 2,4-dinitrophenyl sulfides of Equation (1), these disulfides cleaved rapidly to yield the thiophenol.

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(2) Australian Commonwealth Scientific and Industrial Research Organization post-doctoral fellow at the University of Southern California, 1958–1959.

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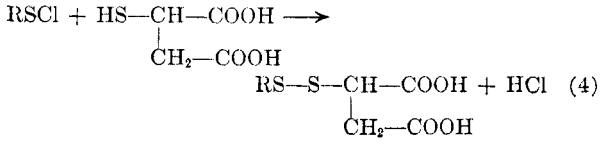
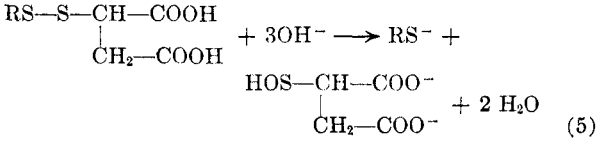


Addition of alkali, followed by warming in some cases, dissolves the disulfide and displaces RS^- (Equation 5). Filtration and acidification of the



filtrate precipitates the thiophenol, leaving the other reaction products in solution.

The general procedure, described below, was used to prepare 2,4-dinitrothiophenol, m.p. 128–130°, in 95% yield; 2-nitrothiophenol, m.p. 56°, in 50% yield (with alkali) and in 85% yield (with cyanide as nucleophile); 4-chloro-2-nitrothiophenol, m.p. 122°, in 60% yield; and pentachlorothiophenol, m.p. 232–233°, in 55% yield. The yields are based on the amount of sulfenyl chloride used.

It is, of course, recognized that the required sulfenyl chlorides can, themselves, often best be prepared from thiophenols,[5] so that the conversion $ArSCl \rightarrow ArSH$ is not always important for synthetic use; and, of course, other routes to the thiophenols listed are available.[6] Nevertheless, the present method is quite convenient, especially when stocks of the stable intermediate disulfides are available, for preparing—as required—quantities of reactive thiols. For example, 2,4-dinitrothiophenol is frequently desired as a reagent for characterizing halides,[7] and it is convenient to prepare it in small amounts, as described above, because of its great tendency to oxidize to the very insoluble disulfide, if not stored quite properly.

The mechanistic factors involved in nucleophilic scission of unsymmetrical disulfides have been discussed at some length in ref. (4). It may be noted that the yields of thiophenols (RSH) recorded agree with the expected effect of electron withdrawing substituents in R on the relative affinities of RS^- and B^- for sulfur (Equation 2), and, hence, on the ease of displacement of RS^-.

EXPERIMENTAL

General procedure. The sulfenyl chloride RSCl (0.1 mole) was dissolved in 100 ml. dry acetic and 0.1 mole of thiomalic acid, suspended in 50 ml. acetic acid, was added, with stirring. The solution was warmed to 70–80° for a few minutes and the acetic acid then removed under reduced pressure to yield the crude disulfide of Equation 4. Without further purification, the thiol was displaced from the above disulfide, by adding an excess of the appropriate nucleophile, as described below.

(a) *Displacement by alkali.* The solid residue was dissolved in 100 ml. 4*N* alkali and refluxed, preferably under nitrogen, for 30 min. The reaction mixture was filtered, cooled, the filtrate acidified with hydrochloric acid and the precipitated thiol collected immediately and recrystallized from ligroin. Thorough drying, and storage under nitrogen, permits the thiols to be stored for long periods without oxidation to disulfide. If considerably stronger alkali is used for the displacement, refluxing is not necessary and a purer product results on acidification. It is probable that some redox reactions of the nitrothiophenoxide ions can occur on heating.

(b) *Displacement by cyanide.* The disulfide obtained by reaction of the sulfenyl chloride and thiomalic acid, by the general procedure above, was dissolved in dilute alkali and 0.1 mole of solid sodium cyanide was added. The reaction mixture was warmed for a few minutes, filtered, and the filtrate acidified (CAUTION: HCN) with hydrochloric acid. The precipitated thiol was purified as described above.

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A Vinyl Azlactone

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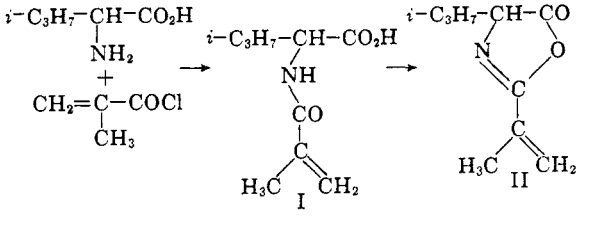
A novel vinyl-polymerizable azlactone, 2-isopropenyl-4-isopropyl-2-oxazolin-5-one (II), was prepared by the cyclodehydration of 2-methacrylamido-3-methylbutyric acid (I), which was prepared by acylation of *dl*-valine with methacrylyl chloride.



Both in homopolymerization and in copolymerization with vinylidene chloride II proved to be a very reactive vinyl monomer. Copolymers of II possess a pendant azlactone group which may provide a site for crosslinking or chemical modification of a resin.