the pmr spectra of amides upon addition of pyridine,[23] shifts in the electronic spectrum of pyridazine in the presence of benzophenone,[24] and the rapid rate of which β-keto alcohols effect displacement of halide from 2-halopyridines.[25] As a test of this mechanism we examined the rates of hydrogen evolution accompanying acylations of **1** with methyl *p*-chlorobenzoate and ethyl trifluoroacetate, anticipating that the more positive carbonyl groups of these two esters would favor complex formation. If this occurred, the rates of hydrogen release should exceed the rate observed with methyl benzoate. The indeed proved to be the case, as shown in Figure 2, where it may be seen that the reaction with trifluoroacetate was greater than 60% complete after only 1 hr. It should also be noted that excess methyl benzoate should favor formation of complex **13**, thereby increasing the rate of hydrogen evolution as is observed. Thus, the course of the sodium hydride promoted benzoylation of **1** *via* complex **13** appears to be consistent with our experimental findings. It is also possible that acylations of β-diketone monoenolates in the presence of excess sodium hydride might also involve similar complex formation prior to removal of a terminal methyl proton, since the rates of such reactions are dependent on ester concentration.[20]

Registry No.—**1**, 91-63-4; **6a**, 1531-38-0; **6b**, 51425-11-7; **6c**, 7543-20-6; **6d**, 1620-53-7; **6e**, 1620-55-9; **6f**, 40061-45-8; **6g**, 16310-38-6; **6h**, 51425-12-8; **6i**, 51425-13-9; **6j**, 51425-14-0; **6k**, 7248-83-1; **6l**, 13119-79-4; **7a**, 51425-15-1; **7b**, 51425-16-2; **8**, 1083-25-6; **9**, 51425-17-3; **10d**, 51425-18-4; **10f**, 51425-19-5; **10g**, 51425-20-8; 4-methylquinoline, 491-35-0; 2-methylpyridine, 109-06-8; 4-methylpyridine, 108-89-4; 2-methylpyrazine, 109-08-0; 2-methylquinoxaline, 7251-61-8; 2,3-dimethylquinoxaline, 2379-55-7; methyl benzoate, 93-58-3; methyl *p*-chlorobenzoate, 1126-46-1; ethyl nicotinate, 614-18-6; ethyl trifluoroacetate, 383-63-1; diethyl oxalate, 95-92-1; diethyl phthalate, 84-66-2; 2,6-lutidine, 108-48-5; 2-methylbenzoxazole, 95-21-6.

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References and Notes

(1) (a) Taken in part from the Ph.D. dissertation of D. E. P., Virginia Polytechnic Institute and State University, 1972. (b) Supported by Public Health Service Research Grants GM 14340 and NS-10197.
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Chemistry of 2-Tetrahydropyranthiol

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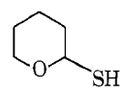
Hydrogen sulfide reacts with 2,3-dihydropyran to form 2-tetrahydropyranthiol (1). 1 has been shown to be a useful reagent for direct introduction of a protected mercaptan into a variety of organic compounds. Addition reactions under ionic and free-radical conditions and displacement reactions have been studied. Subsequent facile cleavage utilizing neutral aqueous silver nitrate followed by treatment of the mercaptide with hydrogen chloride gave the desired mercaptans.

2,3-Dihydropyran reacts with aliphatic and aromatic hydroxyl or sulfhydryl groups under acidic conditions to form alkyl or aryl tetrahydropyranyl ethers[2] or sulfides,[3] respectively. These cyclic acetals and monothioacetals are readily hydrolyzed, in most instances, under mild acid conditions to yield the free alcohol or mercaptan.

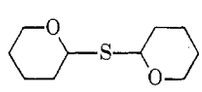
It seemed possible that the same protected thiol function might be prepared directly by addition of 2-tetrahydropyranthiol (1) to multiple bonds or by appropriate displacement reactions. Of perhaps greatest interest was the possibility of preparing derivatives of otherwise unstable tautomers such as enethiols or thioimidates. Although our

original efforts[4] in the latter direction were inconclusive, there were, nevertheless, indications of potential utility.

2-Tetrahydropyranthiol (1) can be prepared in 40–60% yield by treating a four- to fivefold excess of hydrogen sulfide with dihydropyran in the presence of an acid catalyst. A mixture of *p*-toluenesulfonic acid and trifluoroacetic acid gave the best results. The other product in significant quantities appears to be the bis(2-tetrahydropyranyl) sulfide (**2**). **1** is relatively stable but undergoes gradual dis-



1



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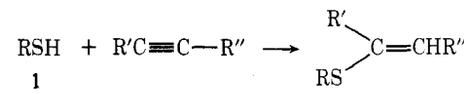
proportionation to **2** and decomposition to polymeric material. The thiol **1** is stable when stored under nitrogen in the cold for several weeks.

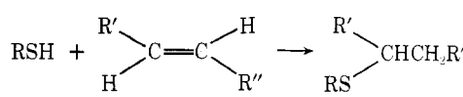
With the potential reagent in hand a study of its addition reactions under ionic and free-radical conditions was undertaken. The addition products of **1** and acetylenes are the corresponding substituted vinyl 2-tetrahydropyranyl sulfides (**3, 4, and 5**). All base-catalyzed additions of **1** to the acetylenes gave predominantly the product from trans



3, R′ = H; R″ = CO_2Et
4, R′ = R″ = CO_2Me
5, R′ = H; R″ = Ph

addition, as anticipated from the work of Truce[5] on similar reactions with simpler thiols. The cis/trans ratios were determined for both ionic and free-radical additions by analysis of the nmr spectra which was in some cases confirmed by glc analysis.

Addition reactions of the thiol **1** were also studied with diethyl maleate and styrene as representative olefins. The expected tetrahydropyranyl derivatives of diethyl 2-mercaptosuccinate (**6**) and β-phenylethanethiol (**7**) were obtained in good yield.



6, R′ = R″ = CO_2Et
7, R′ = H; R″ = Ph

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EXPERIMENTAL[10]

2-Tetrahydropyranthiol (1). Hydrogen sulfide (90 g) was liquefied in a 200 ml stainless steel cylinder placed in an acetone-dry ice bath. 2,3-Dihydropyran (30 g) was added dropwise to the cylinder over a period of 10 min. Five to ten drops of trifluoroacetic acid and 50 mg of *p*-toluenesulfonic acid were added, the cylinder valve was closed and the reaction mixture was allowed to attain and remain at ambient temperature for 12 hr. The unreacted H_2S was released slowly and the resulting liquid distilled at reduced pressure to yield 26 g (57%) of the desired product, bp 58° (15 mm) n_D^{26} 1.4973; nmr δ 5.02 (m, 1, CH), 3.78 (m, 2, CH_2O), 2.17 (d, 1, SH), 1.65 (br, 6 $(CH_2)_3$); ir 2565 cm^{-1} (SH).

Anal. Calcd for $C_5H_{10}OS$: C, 50.80; H, 8.53; S, 27.13
Found: C, 50.82; H, 8.58; S, 27.28.

A second fraction, presumed to be bis-2-tetrahydropyranyl sulfide (**2**) was obtained, bp 108° (1.5 mm), n_D^{26} 1.5107; nmr δ 5.05 (q, 1, CH), 3.72 (m, 2, CH_2O), 1.6 (m, 6, $(CH_2)_3$).

Anal. Calcd for $C_{10}H_{18}O_2S$: C, 59.36; H, 8.97; S, 15.85
Found: C, 58.79; H, 8.82; S, 14.14.

Ethyl cis and trans-3-(2′-Tetrahydropyranylthio)propenoate (**3**). A. Base Catalyzed Addition. A mixture of 5.8 g (50 mmol) of ethyl propiolate, 5 g anhydrous K_2CO_3, and 300 ml THF distilled from $LiAlH_4$ was placed in a 3-neck 500 ml round bottom flask equipped with a magnetic stirrer, a nitrogen inlet tube, and a pressure equalizing dropping funnel. To this reaction mixture was added 5.9 g (50 mmol) of **1** dissolved in 50 ml of THF over a period of 1 hr. The mixture was stirred for 6 hr at ambient temperature, washed with 3 volumes of saturated NaCl solution, and dried with $MgSO_4$. The THF was evaporated and the remaining yellow oil was chromatographed on silica gel using $CHCl_3$ as solvent to afford 10.9 g (100%) of a cis/trans (70%:30% calculated from pmr and glc data) mixture of the addition products. Separation of the isomers was accomplished by preparative glc using a column temp of 175°, a detector and injector temp of 225°, and a collector temp of 230°. Bp trans 98–100° (5 μ) and cis 134–138° (25 μ); nmr δ trans 7.97 and 6.15 (2d, 2, olefinic, J = 16 Hz), 5.45 (m, 1, CH-O), 4.32 and 1.33 (q and t, 2 and 3, C_2H_5), 4.03 (m, 2, CH_2O), 1.80 (m, 6 $(CH_2)_3$); cis 7.51 and 6.09 (2d, 2, olefinic, J = 10 Hz), 5.23 (m, 1, CH-O), 4.33 and 1.33 (q and t, 2 and 3, C_2H_5), 4.04 (m, 2, CH_2-O), 1.80 (m, 6, $(CH_2)_3$). The elemental analysis was obtained on the cis/trans mixture.

Anal. Calcd for $C_{10}H_{16}O_3S$: C, 55.55; H, 7.46; S, 14.80
Found: C, 55.47; H, 7.21; S, 14.74.

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B. Radical Initiated Addition. A mixture of 5.8 g (50 mmol) of ethyl propiolate, 5.9 g (50 mmol) of **1**, 0.135 g (1 mmol) azobisisobutyronitrile, and 10 ml of THF distilled from $LiAlH_4$ was sealed in a 20 ml ampoule which had been flushed with nitrogen. The ampoule was placed in an oil bath at 50°. At the end of 1 hr the ampoule was opened, the THF evaporated, and the contents distilled at reduced pressure to afford 6 g (55%) of a 20%/80% cis/trans mixture (calculated from the pmr spectrum).

cis- and trans-Dimethyl (2-Tetrahydropyranylthio)butenedioate (**4**). A. Base Catalyzed Addition. A mixture of 7.1 g (50 mmol) of freshly distilled dimethyl acetylenedicarboxylate, 7 g of anhydrous K_2CO_3, and 300 ml of THF distilled from $LiAlH_4$ was placed in a 3-necked 500 ml round bottom flask equipped with nitrogen inlet tube, a magnetic stirrer, and a pressure equalizing dropping funnel. To this mixture was added dropwise 5.9 g (50 mmol) of **1** in 50 ml of THF at −10 to −15° over a period of 30 min. The mixture was stirred for 8 hr, washed with saturated NaCl solution, dried (Na_2SO_4), and chromatographed on a silica gel column using 50–50 ether-petroleum ether (30–70°) for elution. The column afforded 8.5 g (64%) of a 35%/65% cis/trans mixture.

Anal. Calcd for $C_{11}H_{16}O_5S$: C, 50.77; H, 6.20; S, 12.29
Found: C, 50.86; H, 6.07; S, 12.28.

Separation was accomplished on a silica gel (60–200 mesh) column using $CHCl_3$ as a solvent. The cis isomer gave nmr δ 6.08 (s, 1, CH), 5.45 (m, 1, CH-O), 3.68 (s, 3, CH_3), 3.02 (s, 3, CH_3), 3.85 (m, 2, OCH_2), 1.77 (m, 6, $(CH_2)_3$); ir 1651, 795 cm^{-1}. The trans isomer gave nmr δ 6.34 (s, 1, CH), 5.50 (m, 1, CH-O), 3.75 (s, 3, CH_3), 3.80 (s, 3, CH_3), 3.78 (m, 2, CH_2-O), 1.73 (m, 6, $(CH_2)_3$); ir 1356, 1005 cm^{-1}.

B. Radical Initiated Addition. A mixture of 5.9 g (50 mmol) of **1**, 1.42 g (10 mmol) dimethyl acetylenedicarboxylate, and 0.13 g (1 mmol) of azobisisobutyronitrile was placed in a 20 ml ampoule, flushed with nitrogen, and sealed. The ampoule was placed in an oil bath at 60° and heated for 10 min. The yellow material was then chromatographed on a silica gel column using 50–50 ether-petroleum ether (30–70°) for elution. The column afforded 3.6 g (84%) of a 50%/50% cis/trans mixture.

2-Phenylvinyl 2-Tetrahydropyranyl Sulfide (**5**). A. Base Catalyzed Addition. Freshly distilled phenylacetylene (5.1 g, 50 mmol), **1** (5.9 g, 50 mmol) and K_2CO_3 (1.36 g, 10 mmol) were stirred in 250 ml THF for 6 hr. After washing (saturated NaCl), drying (Na_2SO_4), concentration, and distillation (250 μ, 128–130°) there

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was obtained 6.1 g (56%) of an 80/20 cis/trans mixture. Attempts to separate the isomers were not successful. Nmr δ cis 6.57, 6.44 (2d, 2, vinylic H, J = 10.5 Hz), 4.38 (t, 1, CH-O); trans 6.97, 6.71 (2d, 2, vinylic H, J = 15.7 Hz), 5.12 (t, 1, CH-O).

Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32; S, 14.52
Found: C, 70.97; H, 7.28; S, 14.49.

B. Photolytic Addition. Phenylacetylene (5.1 g, 50 mmol) and **1** (5.9 g, 50 mmol) sealed in a nitrogen flushed ampoule at 0° was allowed to remain at 25° for 3 days. Volatile materials were removed under vacuum (20°) and the residue was taken up in $CHCl_3$ and washed with 5% NaOH, 5% HCl and saturated NaCl. After drying and evaporation there was obtained 4 g (40%) of a 80/20 cis/trans mixture. Variations in reactant ratios has very little effect on the yield.

cis- and trans-Ethyl 3-Mercaptopropenoate. To 4.32 g (20 mmol) cis-trans **3** in 20 ml CH_3OH was added 3.6 g (20 mmol) $AgNO_3$ in 40 ml of water. The precipitate was removed by filtration, suspended in 10 ml $CHCl_3$, and cooled to 0°. Excess HCl was bubbled into the suspension. This mixture was filtered through filter aid and the $CHCl_3$ filtrate was washed with saturated $KHCO_3$ and concentrated to give 2.6 g (99%) of an oil which could not be distilled or chromatographed on silica gel without decomposition. Ir data: 2552, 2517 (SH); 1751, 1712 (C=O); 965 (CH-trans) and 762 cm^{-1} (CH-cis); nmr δ 7.08 (m, 1, SH, exchanged with D_2O), 5.88 (m, 2, olefinic), 4.28 and 4.27 (2q, 4, CH_2), 1.30 and 1.28 (2t, 6, CH_3).

Anal. Calcd for $C_5H_8O_2S$: C, 45.45; H, 6.10; S, 24.22
Found: C, 45.69; H, 5.96; S, 24.04.

Dimethyl Mercaptofumarate. To 5.2 g (20 mmol) of a mixture of 35% cis/65% trans **4** in 25 ml MeOH was added 3.4 g (20 mmol) of $AgNO_3$ in 50 ml of water. The precipitate was collected and suspended in 100 ml $CHCl_3$ at 0°. Excess HCl was bubbled through the suspension and the precipitate (AgCl) was removed by filtration. The $CHCl_3$ was washed with water until the washings became neutral, dried (Na_2SO_4) and evaporated. The resulting liquid sublimed to form a colorless solid upon distillation at reduced pressure thus affording 1.5 g (43%) of the desired product. Subsequent attempts to resublime the product provided an oil, bp 80–82° (15 mm); nmr δ 6.82 (s, 1, CH), 6.32 (s, 1, SH, exchanged with D_2O), 3.90 (s, 3, CH_3), 3.80 (s, 3, CH_3); ir 2468, 1733, 1694 cm^{-1}.

Anal. Calcd for $C_6H_8O_4S$: C, 40.90; H, 4.58; S, 18.16
Found: C, 41.18; H, 4.50; S, 18.08.

2-Phenylethanethiol. Cleavage of **5** with $AgNO_3$ as described for **4** afforded 59% of a cis-trans mixutre, n_D^{24} = 1.6367, bp 57–60° (0.3 mm); nmr δ 7.25 (m, 5, C_6H_5), 6.32 (m, 2, vinyl), 2.39 (m, 1, SH, exchanged with D_2O); ir 2555 cm^{-1} (SH). There was no evidence for a trifluoroacetyl group.

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Anal. Calcd for C_8H_8S: C, 70.58; H, 5.92; S, 23.50
Found: C, 70.48; H, 6.03; S, 23.32.

Diethyl 2-(2′-Tetrahydropyranylthio)succinate (**6**). To 8.6 g (50 mmol) of freshly distilled diethyl maleate, 5 g anhydrous K_2CO_3, and 200 ml of THF distilled from $LiAlH_4$ in a 500 ml three-necked round bottom flask equipped with a nitrogen inlet tube, pressure equalizing dropping funnel, and magnetic stirrer was added 5.9 g (50 mmol) of **1** in 50 ml of THF dropwise into the reaction mixture over a period of 15 min. This mixture was stirred for 8 hr at ambient temperature. It was then extracted with 3 volumes of saturated NaCl solution and the THF dried with anhydrous Na_2SO_4. The THF was evaporated and the resulting liquid distilled at reduced pressure to afford 10.3 g (72%) of a colorless liquid, bp 128–130° (100 μ); n_D^{23} 1.4586; nmr δ 6.16 (m, 1, CH-O), 4.16 (2q, 4, OCH_2), 3.83 (m, 2, CH_2O), 3.92 (m, 1, CH), 2.90 (m, 2, CH_2), 1.67 (m, 6, $(CH_2)_3$), 1.23 (2t, 6, CH_3).

Anal. Calcd for $C_{13}H_{22}O_5S$: C, 53.77; H, 7.64; S, 11.04.
Found: C, 53.55; H, 7.69; S, 10.97.

2-Phenylethyl 2-Tetrahydropyranyl Sulfide (**7**). Styrene (5.2 g, 50 mmol), **1** (5.9 g, 50 mmol), benzene (250 ml), and azobisisobutyronitrile (0.25 g, 1 mmol) in a 500 ml flask was flushed with nitrogen and heated in an oil bath for 5 min at 50°. The reaction mixture was allowed to stand at 25° for 4 days and then distilled to give 10 g (90%) of the addition product, bp 124–125° (250 μ), nmr δ 7.18 (m, 5, Ph), 4.92 (m, 1, CH-O), 3.75 (m, 2, CH_2-O), 2.82 (m, 4, $(CH_2)_2$), 1.68 (m, 6, $(CH_2)_3$).

Anal. Calcd for $C_{13}H_{18}OS$: C, 70.24; H, 8.16; S, 14.39
Found: C, 69.99; H, 8.09; S, 14.68.

Diethyl Mercaptosuccinate. To 5.8 g (20 mmol) of **6** in 20 ml CH_3OH was added 3.4 g (20 mmol) $AgNO_3$ dissolved in water. The silver mercaptide was collected, suspended in 100 ml $CHCl_3$, and cooled to 0°. Excess HCl was bubbled into the suspension and the solid (AgCl) was removed by filtration. The $CHCl_3$ was dried (Na_2SO_4), evaporated, and the resulting liquid was distilled at reduced pressure to afford 3.6 g (85%) of the desired product, bp 62–64° (50 μ), n_D^{26} 1.4581 (lit.[11] b_{20} 130°–135°), nmr δ 4.16 (2q, 4, CH_2), 3.72 (t, 1, CH), 2.86 (m, 2, CH_2), 2.72 (d, 1, SH, exchanges with D_2O), 1.27 (2t, 6, CH_3); ir 2562 cm^{-1} (SH).

2-Phenylethanethiol. Cleavage of **7** with $AgNO_3$ gave 90% of the desired product, bp 41° (125 μ) (lit.[12] 95–98° at 12 mm), nmr δ 7.15 (m, 5, C_6H_5), 2.75 (m, 4, $(CH_2)_2$), 1.17 (m, 1, SH, exchanged with D_2O); ir 2551 cm^{-1}.

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Ethyl 2-(2′-Tetrahydropyranylthio)propionate (**8**). A mixture of 5.9 g (50 mmol) of **1**, 9.05 g (50 mmol) of ethyl 2-bromopropionate, 3.5 g (25 mmol) K_2CO_3, and 100 ml acetone were placed in a 200 ml round bottom flask equipped with a magnetic stirrer and a condenser. This mixture was refluxed for 12 hr. The KBr which formed was removed by filtration, the acetone evaporated, and the resulting liquid distilled at reduced pressure to afford 7 g (64%) of the desired product, bp 78–80° (100 μ). nmr δ 5.09 (m, 1, CH-O), 4.11 (q, 2, CH_2), 3.73 (m, 2, CH_2-O), 3.43 (q, 1, CH-S), 1.68 (m, 6, $(CH_2)_3$), 1.32 (m, 6, CH_3).

Anal. Calcd for $C_{10}H_{18}O_3S$: C, 55.03; H, 8.31; S, 14.46
Found: C, 54.82; H, 8.11; S, 14.52.

n-Butyl 2-Tetrahydropyranyl Sulfide (**9**). To a solution of 2.7 g (50 mmol) of CH_3ONa and 5.9 g (50 mmol) of **1** in 100 ml CH_3OH was added, with stirring, 6.85 g (50 mmol) of 1-bromobutane in 50 ml CH_3OH. After heating under reflux for 6 hr the mixture was diluted with 200 ml of saturated NaCl and extracted with ether-benzene (3:1). The extract was dried ($MgSO_4$) and evaporated and the residue distilled to give 5.6 g (63%), bp 48° (250 μ), nmr δ 4.98 (t), 3.92 (2), 2.72 (2), 1.67 (10), 0.96 (3).

Anal. Calcd for $C_9H_{18}OS$: C, 62.04; H, 10.41; S, 18.37
Found: C, 61.97; H, 10.37; S, 18.41.

Benzyl 2-Tetrahydropyranyl Sulfide (**10**). α-Chlorotoluene (3.1 g, 24 mmol), **1** (2.8 g, 24 mmol), and K_2CO_3 (1.65 g, 12 mmol) in 50 ml acetone was stirred under reflux for 14 hr. Removal of KCl and acetone followed by distillation gave 2.3 g (47%) of the substitution product, bp 109–111° (250 μ), nmr δ 7.44 (5), 4.8 (1), 3.92 (2), 3.87 and 3.84 (2), 1.68 (6).

Anal. Calcd for $C_{12}H_{16}OS$: C, 69.21; H, 7.74; S, 15.37
Found: C, 69.16; H, 7.61; S, 15.42.

Ethyl 2-Mercaptopropionate. To 4.4 g (20 mmol) of **8** dissolved in 20 ml of CH_3OH was added 3.4 g (20 mmol) of $AgNO_3$ dissolved in 50 ml of water. The precipitate was collected, suspended in 100 ml $CHCl_3$, and cooled to 0°. Excess HCl was bubbled through the suspension and the precipitate (AgCl) was removed by filtration. The $CHCl_3$ layer was washed with water until the washings became neutral, dried (Na_2SO_4) and evaporated. The resulting liquid distilled at reduced pressure to afford 2.5 g (92%) of the desired product, bp 90° (60 mm), lit.[13] 34° (6 mm), identical in all respects to an authentic sample.

1-Butanethiol. Cleavage of **9** with $AgNO_3$ gave 94% of the butanethiol identical in all respects to an authentic sample.

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α-Toluenethiol. Cleavage of **10** with $AgNO_3$ gave 89% of α-toluenethiol, bp 60–61° (2mm) identical in all respects to an authentic sample.

bis-2-Tetrahydropyranyl Dithiooxaldiimidate (**11**). Into 3.0 g (26 mmol) of freshly distilled **1** and two drops of butylamine in 250 ml of heptane at −80° was passed 1.44 g (30 mmol) of cyanogen gas. Vigorous stirring was maintained throughout the addition, which required about 30 min and for two additional hrs at −80°. After settling, the solvent was decanted, leaving a white solid in the reaction flask to be used immediately in the next reaction.

In a previous experiment an effort was made to isolate the diimidate. After standing three hrs at −80° the reaction mixture was permitted to warm to room temperature. A portion of the solid material was collected on a filter and washed with heptane, which caused the material to liquify. A portion of the oil was crystallized using a mixture of heptane and benzene, to give colorless needles, mp 102–104°. Further attempts to recrystallize the product gave only cinnioxa-tice.

5-Benzylideneamino-2-phenyl-4(2-tetrahydropyranyl-mercapto)oxazole (**12**). **11** prepared from 3.0 g (26 mmol) of **1** was refluxed for 3 hr with 7 g (66 mmol) of benzaldehyde in 50 ml of dry benzene in a flask equipped with a Dean-Stark trap. A dark brown oil collected in the trap and on the base of the reflux condenser. The benzene was evaporated from the reaction mixture leaving a dark brown, viscous oil. The oil was crystallized from ethanol to give yellow rosettes, mp 152–155°. Additional material was obtained from the mother liquor. Four recrystallizations, two from ethanol followed by two from acetone, gave yellow needles, mp 157–158°. The yield was 2.75 g (59% based on **1**). Nmr δ 8.67 (s, 1, N=CH), 7.94 and 7.40 (m, 10, Ph), 5.91 (t, 1, CH), 3.4 and 3.6 (m, 2, CH_2O), 1.8 (m, 6, $(CH_2)_3$).

Anal. Calcd for $C_{21}H_{20}N_2O_2S$: C, 69.20; H, 6.53; N, 7.59; S, 8.80
Found: C, 69.13; H, 6.53; N, 7.69; S, 8.13.

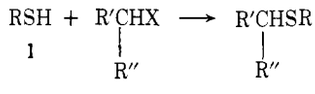
10. Elemental analyses were performed at the Microanalytical Laboratory, Department of Chemistry, University of California, Berkeley. All nmr spectra for analysis of cis/trans ratios were obtained on a Varian model A-60A spectrometer using $CDCl_3$ with TMS as internal standard except for the analysis of cis and trans **3** which was carried out on a Jeolco Model JNM 4H-100 MHz spectrometer. Glc analysis of cis and trans **3** was accomplished using a 10′ × 1/4″ aluminum column packed with 10% polyethylene glycol succinate on Chromosorb W 40/60 mesh.

11. A. Emr and F. Roubinek, Chem. Listy, 50, 664 (1956).

12. M. Kulka, Can.J.Chem., 34, 1093 (1956).

13. M. M. Kreevoy, B. E. Eichinger, F. E. Story, E. A. Katz, and J. H. Elstedt, J.Org.Chem., 29, 1641 (1964).

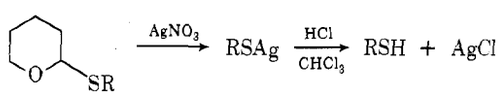
Substitution reactions using **1** with ethyl 2-bromopropionate, *n*-butyl bromide, and benzyl chloride provided the expected products **8**, **9**, and **10**, respectively.



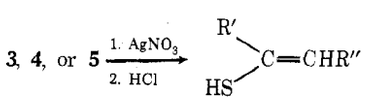
8, $R' = CH_3$; $R'' = CO_2Et$; $X = Br$
9, $R' = n\text{-}C_3H_7$; $R'' = H$; $X = Br$
10, $R' = Ph$; $R'' = H$; $X = Cl$

Having established that the thiol reacts in the expected ways to provide a series of thio ethers, it was then necessary to demonstrate that cleavage to the free mercaptan could be accomplished in satisfactory yield. In contrast to the facile cleavage of acetals by hydrochloric acid, mercaptals and monothioacetals are generally more resistant to this acid.[6,7] The use of silver nitrate to form the mercaptide of a monothioacetal has been reported.[8]

During our preliminary attempts to cleave the 2-tetrahydropyranyl sulfides, including the heterocyclic system discussed below, this resistance to mild acid treatment was borne out. Most systems were resistant to aqueous, ethanolic or gaseous hydrogen chloride and aqueous or ethanolic *p*-toluenesulfonic acid. However, the silver salts of the mercaptans are easily obtained by addition of an equivalent amount of aqueous silver nitrate to a methanolic solution of the sulfide. The precipitated mercaptide is then suspended in chloroform through which excess gaseous hydrogen chloride is passed. After filtration of silver chloride the mercaptan is recovered from the chloroform.

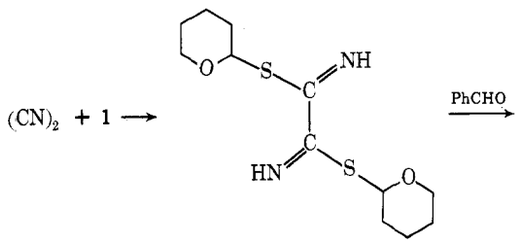


In the case of enethiols derived from cleavage of the addition of **1** and acetylenic compounds there was no evidence



for the formation of tautomeric thioketones or thio aldehydes. With these substances, all of which contain substituents expected to stabilize the enethiol tautomer, this is not surprising. Since preparation of protected enethiols appears to be one of the more useful applications of **1** we plan to conduct a more complete study of such substances and their cleavage products.

The potential use of the reagent is further illustrated by preparation of the protected mercapto oxazole **12**. Previous reactions with dialkyl and diaryl dithiooxaldiimidates[9] provided alkyl- or arylmercaptooxazoles which could not possibly provide the free thiol. Reaction of **1** with cyanogen provided the expected thioimidate **11**, which was too unstable to be characterized completely. However, it reacted with benzaldehyde in the usual way to give the fully characterized heterocyclic product **12**. This and other uses of the reagent are the subject of continuing studies.



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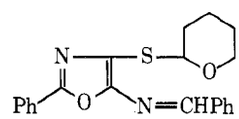

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Registry No.—**1**, 40446-64-8; **2**, 51380-90-6; *cis*-**3**, 51380-91-7; *trans*-**3**, 51380-92-8; *cis*-**4**, 51380-93-9; *trans*-**4**, 51380-94-0; *cis*-**5**, 51380-95-1; *trans*-**5**, 51380-96-2; **6**, 51380-97-3; **7**, 51380-98-4; **8**, 51380-99-5; **9**, 16315-52-9; **10**, 1927-50-0; **11**, 51464-54-1; **12**, 51381-00-1; hydrogen sulfide, 7783-06-4; 2,3-dihydropyran, 110-87-2; ethyl propiolate, 623-47-2; dimethyl acetylenedicarboxylate, 762-42-5; phenylacetylene, 536-74-3; dimethyl mercaptofumarate, 51381-01-2; *cis*-ethyl 3-mercaptopropenoate, 51381-02-3; *trans*-ethyl 3-mercaptopropenoate, 51381-03-4; *cis*-2-phenylethenethiol, 51381-05-6; *trans*-2-phenylethenethiol, 51381-04-5; styrene, 100-42-5; diethyl mercaptosuccinate, 23060-14-2; 2-phenylethanethiol, 4410-99-5; ethyl 2-bromopropionate, 535-11-5; 1-bromobutane, 109-65-9; α-chlorotoluene, 100-44-7.

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References and Notes

(1) Taken, in part, from the Ph.D. Thesis of M. G. M., June 1972. Supported by U. S. Public Health Service Training Grant GM-00728-09. Presented at the 4th International Congress of Heterocyclic Chemistry, Salt Lake City, Utah, July 1973.
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