tained with the 6-fluoro analogue probably is related to the inherent instability of 6-fluorouracil.[4] As was found in the dealkylation of esters by iodotrimethylsilane,[5] debenzylation in the pyrimidine series is much more facile than either demethylation or deethylation. The order of dealkylation appears to be benzyl > methyl > ethyl. 2,4-Diethoxy-6-chloropyrimidine (not listed in Table I) was dealkylated only to the extent of ca. 20% after 1 week under conditions that effected quantitative dealkylation of 2,4-dibenzyloxy-6-chloropyrimidine in less than 15 min. We have not investigated the mechanism of the hydrolysis, but it is most likely similar to that proposed by Jung and Lyster[5,6] for the hydrolysis of esters and ethers by iodotrimethylsilane. An alternate mechanism would involve initial attack of the pyrimidine nitrogens instead of the alkoxyl oxygens on iodotrimethylsilane.

Experimental Section

Melting points were determined on a Hoover-Thomas Unimelt melting point apparatus. Infrared spectra were obtained on a Perkin-Elmer 283 infrared spectrophotometer, and nuclear magnetic resonance (NMR) spectra were recorded on either a Hitachi Perkin-Elmer R20B or a Varian T-60 60 MHz spectrometer.

Sulfolane (Eastman) was dried by distillation from calcium hydride after pretreatment with sodium hydroxide pellets. The following compounds were synthesized according to the literature procedures and had physical and spectral properties consistent with their assigned structures: **1a**,[1] **1b**,[3] **1c**,[2] **1d**,[2,8] **1e**,[2] **1f**,[9] **1g**,[10] **2c**,[2,11] and **2e**.[4] 6-Methyluracil and uracil were purchased from Sigma Chemical Co.

General Procedure for the Hydrolysis of 2,4-Dialkoxy-6-substituted Pyrimidines. To a solution (or mixture) of the 2,4-dialkoxy-6-substituted pyrimidine (1.0 mmol) in dry sulfolane (2 mL) under nitrogen was syringed iodotrimethylsilane[6] (315 μL, 2.2 mmol). This was incubated at 40–45 °C[12] until the NMR resonance of the alkoxyl protons adjacent to the oxygens disappeared.[13] Water (10 mL) was added to the yellow to orange-red solution, and the cloudy solution was washed with 4 × 15 mL of methylene chloride or chloroform. The colorless aqueous layer was evaporated in vacuo to a white or off-white solid which was triturated with ether and collected by filtration. Spectral data were consistent with the assigned structures.

Uracil-6-sulfonic Acid (2a). The general procedure was followed, starting with 2,4-dimethoxy-6-pyrimidinesulfonic acid (1 mmol) which yielded uracil-6-sulfonic acid as an off-white solid (193 mg, quantitative). This was converted into the disodium salt[14] by adding 10 M NaOH to an ethanolic solution of this compound until no more solid precipitated. The precipitate was recrystallized from H_2O–EtOH to give white crystals. Physical and chemical properties of the product corresponded to those reported.[2] Anal. Calcd for $C_4H_2N_2O_5SNa_2 \cdot H_2O$: C, 18.91; H, 1.59; N, 11.02; S, 12.62. Found: C, 18.82; H, 1.64; N, 11.01; S, 12.61.

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Registry No. **1a**, 71885-70-6; **1b**, 21378-96-1; **1c**, 6320-15-6; **1d**, 7781-23-9; **1e**, 658-87-7; **1f**, 20461-60-3; **1g**, 71885-71-7; **2a**, 5807-21-6; **2b**, 5338-86-3; **2c**, 4270-27-3; **2d**, 626-48-2; **2e**, 591-36-6; **2f**, 66-22-8.

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(12) The reaction can be run at a higher temperature to increase the rate.
(13) At this concentration the sulfolane resonances do not interfere with the alkoxyl protons adjacent to the oxygen.
(14) It was found easier to purify this particular compound by first converting it to the disodium salt.

A Novel Synthesis of 2*H*-1,3-Benzoxathiol-2-ones

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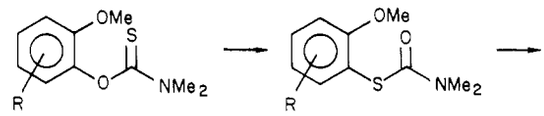
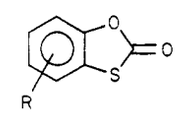
The synthesis of 2*H*-1,3-benzoxathiol-2-ones usually[1] is carried out either by thiocyanation of a substituted phenol,[2,3] by treatment of a 2-mercaptophenol with phosgene[2] or carbonyl sulfide,[4] or by hydrolysis of a 2-hydroxythiuronium salt,[5] the latter probably also involving an intermediate thiocyanate. These methods have the important disadvantage that the substitution pattern of the product is limited by the requirement of a substituent para to the phenolic hydroxyl to prevent para-directed thiocyanation. Further, in cases in which 2-mercaptophenols are used as starting materials, the use of phosgene or carbonyl sulfide presents a significant hazard in laboratories not equipped to deal with these materials. In view of these difficulties, an alternative method of preparation was desirable.

This report discusses the preparation of 2*H*-1,3-benzoxathiol-2-ones (**3**) by cyclization of the corresponding *S*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamates (**2**) which are conveniently available by means of the thione–carbamate rearrangement[6-8] of the corresponding *O*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamates (**1**) as indicated in the equation. This rearrangement has been of



1a, R = H
b, R = 4-Me
c, R = 4-Cl
d, R = 3-OMe
e, R = 6-OMe

2a, R = H
b, R = 4-Me
c, R = 4-Cl
d, R = 3-OMe
e, R = 6-OMe



3a, R = H
b, R = 6-Me
c, R = 6-Cl
d, R = 7-OH
e, R = 4-OMe
f, R = 4-OH

considerable utility for the preparation of a variety of substituted mercaptobenzenes[9-15] and thus represents a

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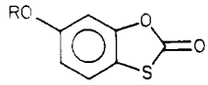
versatile method for the preparation of starting materials for cyclization to 2*H*-1,3-benzoxathiol-2-ones as indicated. Suitable substituted *S*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamates are also available by treatment of the corresponding 2-methoxythiophenols with *N*,*N*-dimethylcarbamoyl chloride, but the synthesis of substituted thiophenols is frequently a multistep procedure.[16]

Results and Discussion

The *O*-aryl *N*,*N*-dimethylthiocarbamates (**1**) prepared in this work are listed in Table I, together with the corresponding *S*-aryl *N*,*N*-dimethylthiocarbamates (**2**) obtained by rearrangement. Compounds **1** are prepared in the usual fashion[6] by treatment of the corresponding anhydrous sodium phenoxide with *N*,*N*-dimethylthiocarbamoyl chloride. Rearrangements of the *O*-aryl thiocarbamates were carried out without solvent under nitrogen at the indicated temperatures, with two exceptions. In the case of **1b** and **1c**, TLC indicated a multiplicity of materials in the reaction mixture, and IR indicated the presence of the desired product (i.e., **2b** and **2c**) in only minor amounts in several attempts at temperatures from 260 to 300 °C. Use of sulfolane as a solvent gave satisfactory yields of rearrangement product **2** in the latter two cases.

The 2*H*-1,3-benzoxathiol-2-ones **3** prepared by cyclization of *S*-aryl *N*,*N*-dimethylthiocarbamates **2** also are listed in Table I. The cyclizations were carried out either with 47% hydriodic acid or with pyridine hydrochloride. In the case of **2e**, where both reagents were investigated, use of hydriodic acid gave a product mixture with an odor of hydrogen sulfide from which resorcinol (identified by TLC) and 4-methoxy-2*H*-1,3-benzoxathiol-2-one (**3e**) were isolated, the latter in 44% yield. Use of pyridine hydrochloride gave 4-hydroxy-2*H*-1,3-benzoxathiol-2-one (**3f**) in 67% yield.

The availability of **3f**, and thus an unequivocal route to 2-mercaptoresorcinols, presented an opportunity to clarify a point of confusion in the literature. The claim that reaction of resorcinol with cuprous thiocyanate produces 4-hydroxy-2*H*-1,3-benzoxathiol-2-one (**3f**) was made many years ago, without unequivocal structure proof,[17] and subsequently this material found significant application in the treatment of various malfunctions and diseases of the skin.[1] Pantlitschko and Benger,[18] in a further investigation of this reaction, claimed agreement with the earlier conclusion on the basis of the chemistry of the product (nitration, hydrolysis). Later authors, notably Urushibara and Kogo[19] and Fiedler,[20] by establishing the structure of the hydrolysis and oxidation[19] and bromination[20] products of **4a**, showed that reaction of resorcinol with cuprous thiocyanate under similar conditions gives 6-hydroxy-2*H*-1,3-benzoxathiol-2-one (**4a**).



4a, R = H
b, R = Me
c, R = Ac

The preparation of Pantlitshko and Benger[18] therefore was repeated as exactly as possible to give an hydroxybenzoxathiolone (mp 154–156 °C, 79% crude yield, homogeneous by TLC (lit. mp 160 °C,[18] 154.5–155 °C,[19] 158–158.5 °C[20])) which was not identical with 4-hydroxy-2*H*-1,3-benzoxathiol-2-one (**3f**, mp 155–157 °C) by TLC, IR, or mixture melting point. Hydrolysis of the former thiocyanation product yielded 94% of a mercaptoresorcinol, mp 109–111 °C, in agreement with the literature[19] melting point for 4-mercaptoresorcinol, which was not identical by TLC or IR with 2-mercaptoresorcinol (mp 75–78 °C) prepared by hydrolysis of **3f**. Pantlitshko and Benger[18] indicate mp 83–84 °C for a similarly prepared material. Further, these authors methylated their hydroxybenzoxathiolone to give a product with mp 72 °C; similar treatment of the duplicate thiocyanation product in our laboratories gave mp 61–62 °C, in agreement with the literature[21,22] melting point for 6-methoxy-2*H*-1,3-benzoxathiol-2-one (**4b**). 4-Methoxy-2*H*-1,3-benzoxathiol-2-one (**3e**) has mp 83–85 °C. In addition, 6-acetoxy-2*H*-1,3-benzoxathiol-2-one (**4c**) has mp 93–96 °C,[21] while the acetoxybenzoxathiolone prepared by Pantlitschko and Benger[18] had mp 100 °C. An explanation for the anomalous results obtained by these workers is not apparent, but it would seem that 4-hydroxy-2*H*-1,3-benzoxathiol-2-one (**3f**) and its derivatives, as well as 2-mercaptoresorcinol, have not heretofore appeared in the literature.

Experimental Section

Melting points were determined with a Hershberg apparatus and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 727B spectrophotometer, and NMR spectra were obtained with a Perkin-Elmer R24 instrument (60 MHz). CHN analyses were carried out by the Velsicol Analytical Department under the direction of Z. Srnak.

Reactions routinely were followed by IR [$\nu_{C=O}$ for *O*-aryl *N*,*N*-dimethylthiocarbamates[6,11] ca. 1530 cm^{-1}; $\nu_{C=O}$ for *S*-aryl *N*,*N*-dimethylthiocarbamates[11] ca. 1660 cm^{-1}; and $\nu_{C=O}$ for 2*H*-1,3-benzoxathiol-2-ones[9] 1750 cm^{-1}] and by TLC on Gelman ITLC sheets (silica gel), usually by development with 1:1 benzene–hexane and with iodine visualization. NMR occasionally was used for structural verification[11,12] of the *O*- and *S*-aryl *N*,*N*-dimethylthiocarbamates.

Starting materials were used as received from the chemical supply houses unless otherwise indicated. The 4-chloro-2-methoxyphenol was prepared in 77% yield by chlorination of guaiacol.[23] The *O*- and *S*-aryl *N*,*N*-dimethylthiocarbamates were prepared by the usual methods,[6,11] as indicated earlier.

General Procedure for the Preparation of 2*H*-1,3-benzoxathiol-2-ones. The *S*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamate (2.5 mmol) was heated in 2 mL of 47% HI or in three times its weight of previously fused pyridine hydrochloride at reflux or at 200 °C, respectively, until TLC (preferably) or IR indicated the absence of starting material. The reaction mixture was cooled, added to 2–3 volumes of water, and extracted with ether. The ether solution was washed with water, dilute $Na_2S_2O_3$ solution (for HI cyclizations), and water, dried, and concentrated. The residue was recrystallized, usually from aqueous or anhydrous methanol or diisopropyl ether, to give the 2*H*-1,3-benzoxathiol-2-one.

4-Methoxy-2*H*-1,3-benzoxathiol-2-one (3e). A solution of 1.0 g (4.1 mmol) of *S*-(2,6-dimethoxyphenyl) *N*,*N*-dimethylthiocarbamate (**2e**) in 5 mL of 47% HI was heated for 62 h at ca. 70 °C, cooled to 25 °C, and extracted with benzene. The benzene extract was washed with water, 5% $Na_2S_2O_3$, and water to give, after being dried with phase separation paper and concentrated on a rotary evaporator at 60 °C, 0.30 g (43.5%) of light yellow

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Table I. Yields and Physical Properties of Substituted *O*- and *S*-(2-Methoxyphenyl) *N,N*-Dimethylthiocarbamates and 2*H*-1,3-Benzoxathiol-2-ones[a]

			anal.					
			% calcd			% found		
compd	mp, °C	yield, %	C	H	N	C	H	N
		O-(2-Methoxyphenyl) *N,N*-Dimethylthiocarbamates						
1a	52-56[b]	42						
1b	86-88	49	58.65	6.71	6.22	58.57	6.61	6.14
1c	58-60	42	48.89	4.89	5.70	48.97	4.88	5.72
1d	66-68	51	54.75	6.27	5.81	55.09	6.41	5.96
1e	144-146	39	54.75	6.27	5.81	54.86	6.46	5.77
		S-(2-Methoxyphenyl) *N,N*-Dimethylthiocarbamates						
2a	89-91[c]	72[d]						
2b	67-69	56[d,e]	58.65	6.71	6.22	58.70	6.84	6.18
2c	104-106	21[f]	48.89	4.89	5.70	48.88	4.91	5.73
2d	84-86	55[f,e]	54.75	6.27	5.81	54.89	6.38	5.88
2e	122-127	75[d]	54.75	6.27	5.81	54.62	6.38	5.73
		2*H*-1,3-Benzoxathiol-2-ones						
3a	[g]	88						
3b	71-73	100	57.81	3.64		57.70	3.76	
3c	87-89	81	45.04	1.62		45.28	1.77	
3d	142-144	87	50.00	2.40		50.10	2.39	
3e	83-85[h]	44	52.74	3.32		52.82	3.28	
3f	155-157[h]	67	50.00	2.40		50.25	2.60	

[a] Satisfactory analytical data (±0.4% for C, H, N on **1b-e** and **2b-e**; ±0.3% for C, H on **3b-f**) were reported. [b] Lit.[6] mp 61-62 °C. [c] Lit.[6] mp 93-95 °C. [d] Rearrangement *T*, 280 °C. [e] Rearrangement in sulfolane. [f] Rearrangement *T*, 260 °C. [g] Bp 85-90 °C (0.4 mm) [Lit.[9] bp 72 °C (0.25 mm)]. [h] Obtained from **2e**; see Discussion and Experimental Sections.

oil which crystallized to sticky yellow crystals which were shown by TLC to contain two components, one of which was identified by comparison with resorcinol. Recrystallization from diisopropyl ether gave colorless needles, mp 80–82 °C. Sublimation at 65 °C (5 μm) gave an analytical sample; mp 83–85 °C (see Table I); IR (Nujol) 1750, 755, 700 cm^{-1}.

4-Hydroxy-2*H*-1,3-benzoxathiol-2-one (3f). To a melt of 16 g of pyridine hydrochloride at 200 °C under N_2 was added 5.5 g (22.7 mmol) of **2e**, and the yellow-brown solution was magnetically stirred at 200 °C for 1.25 h, cooled to 25 °C, and added to 30 mL of water. The mixture was extracted with ether, which was washed with water, dried superficially with phase separation paper, and concentrated on a rotary evaporator to give 3.0 g (78.8%) of solid, mp 136–152 °C, which was recrystallized from benzene to give mp 155–157 °C (see Table I): IR (Nujol) 3250, 1700, 760, 700 cm^{-1}.

6-Methoxy-2*H*-1,3-benzoxathiol-2-one. The sodium salt was prepared by treating 6.35 g (0.037 mol) of 6-hydroxy-2*H*-1,3-benzoxathiol-2-one (from resorcinol and CuSCN[18]) in 30 mL of ethylene glycol–dimethyl ether (dried with 4A molecular sieves) with 0.89 g (0.037 mol) of NaH under N_2 at 20 °C. To a yellow suspension was then added 5.25 g (0.037 mol) of MeI in 10 mL of ethylene glycol–dimethyl ether at 10 °C, and the cloudy solution was stirred overnight at 25 °C. The reaction mixture was added to 75 mL of ice water containing 0.5 mL of concentrated HCl to give a yellow-brown semisolid, which was extracted with ether, washed with water, dried with phase separation paper, and concentrated on a rotary evaporator to give a yellow-brown oil which partly solidified. The product was recrystallized from methanol to give yellow crystals, mp 57–59 °C [3.40 g (50.5%)]. Recrystallization from diisopropyl ether gave white crystals: mp 61–62 °C (lit. mp 62–64 °C,[21] 61–62 °C[22]); IR (Nujol) 1725, 860, 780 cm^{-1}.

Anal. Calcd for $C_8H_6O_3S$: C, 52.74; H, 3.32. Found: C, 52.78; H, 3.34.

2-Mercaptoresorcinol. To a nitrogen-blanketed slurry of 0.5 g (3 mmol) of 4-hydroxy-2*H*-1,3-benzoxathiol-2-one (**3f**) in an equal volume of water was added 5.1 mL of 2 N NaOH. The mixture was stirred without heating (exotherm to ca. 30 °C) for 20 min and acidified with concentrated HCl with ice bath cooling to pH ca. 3. The resulting suspension was extracted with ether, and the ether layer was washed once with a small volume of water, dried with phase separation paper, and concentrated on a rotary evaporator at 60 °C to give a yellow oil (0.40 g, 95%) which partly solidified. The product was purified by sublimation at 60 °C (8 μm) to give the following: mp 75–78 °C; IR (Nujol) 3380, 2500, 770, 695 cm^{-1}.

Anal. Calcd for $C_6H_6O_2S$: C, 50.68; H, 4.26. Found: C, 50.74; H, 4.32.

After 10 days at 25 °C, this material had mp 70–127 °C.

4-Mercaptoresorcinol. The hydrolysis of 2.5 g (14.9 mmol) of 6-hydroxy-2*H*-1,3-benzoxathiol-2-one (mp 154–156 °C, from resorcinol and CuSCN) in 25 mL of 2 N NaOH was carried out as described above for 2-mercaptoresorcinol to give 1.95 g (94%) of yellow oil which solidified: mp 106–110 °C. Sublimation at 60 °C (5 μm) gave white crystals: mp 109–111 °C (lit.[19] mp 110–111 °C); IR (Nujol) 3380, 2495, 900, 835, 795, 690 cm^{-1}.

Anal. Calcd for $C_6H_6O_2S$: C, 50.68; H, 4.26. Found: C, 50.55; H, 4.21.

After 10 days at 25 °C, this material had mp 106–110 °C.

Registry No. **1a**, 13522-62-8; **1b**, 71912-75-9; **1c**, 71912-76-0; **1d**, 71912-77-1; **1e**, 71912-78-2; **2a**, 13511-97-2; **2b**, 71912-79-3; **2c**, 71912-80-6; **2d**, 71912-81-7; **2e**, 71912-82-8; **3a**, 7735-53-7; **3b**, 71912-83-9; **3c**, 71912-84-0; **3d**, 71912-85-1; **3e**, 71912-86-2; **3f**, 95-18-1; 4-chloro-2-methoxyphenol, 16766-30-6; guaiacol, 90-05-1; 6-methoxy-2*H*-1,3-benzoxathiol-2-one, 6074-48-2; 6-hydroxy-2*H*-1,3-benzoxathiol-2-one sodium salt, 71912-87-3; 6-hydroxy-2*H*-1,3-benzoxathiol-2-one, 4991-65-5; 2-mercaptoresorcinol, 2103-60-8; 4-mercaptoresorcinol, 2553-70-0; sodium 2-methoxyphenoxide, 13052-77-2; sodium 2-methoxy-4-methylphenoxide, 71912-88-4; sodium 2-methoxy-4-chlorophenoxide, 71912-89-5; sodium 2,4-dimethoxyphenoxide, 35471-47-7; sodium 2,6-dimethoxyphenoxide, 71912-90-8; *N,N*-dimethylthiocarbamoyl chloride, 16420-13-6.

Regiospecific 2β-Chloro-3-tropinone Preparation. A Synthesis of Tropinone and Pseudopelletierine

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Recent synthetic work on tropane alkaloids has focused on schemes which allow specific and diverse tropane structural modification.[2-4] We now report a route to the

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