4a-methyl-4a,5-dihydronaphthalen-2(8*H*)-one (3). A solution of 0.250 g (1.65 mmol) of quinone 1 in 5 mL of absolute methanol and 3.5 mL of 1,3-butadiene was heated in a sealed glass tube at 100 °C for 20 h. The color changed from red-orange to light yellow during this time. Evaporation of the volatiles left a residue which was *rapidly* chromatographed on 30 g of Florisil. Elution with 3:1 hexane–ethyl acetate afforded 0.214 g (63%) of adduct **3.** Washing with pentane gave analytically pure material: mp 103.5–104 °C; λ_{max} ($CHCl_3$) 2.86, 6.20 μ; δ ($CDCl_3$, 250 MHz) 1.38 (s, 3), 2.11 (d, J = 17.5 Hz, 1), 2.56 (dd, J = 17.5, 4 Hz, 1), 2.86 (d, J = 20 Hz, 1), 3.45 (d, J = 20 Hz, 1), 3.78 (s, 3), 5.66 (s, 1), 5.67–5.75 (m, 2), 6.70 (s, 1 exchanges with D_2O).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.62; H, 6.74.

Diels–Alder Reaction of Quinone (1) with 1-Methoxy-1, 3-butadiene in Absolute Methanol. Preparation of *dl*-4aα-Methyl-8aα-4,8β-dimethoxy-1,2,4a,5,8,8a-hexahydronaphthalene-1,2-dione (7). To a solution of 0.200 g (1.32 mmol) of quinone 1 in 5 mL of absolute methanol was added 0.331 g (3.95 mmol] of 1-methoxy-1,3-butadiene (Aldrich). The orange solution was heated under reflux under a nitrogen atmosphere for 6 h. During this time the color became yellow. The solution was cooled and the volatiles removed in vacuo to afford a brown solid which upon trituration with pentane containing a small amount of ether gave 0.206 g (67%) of adduct (7), as an off-white crystalline solid: mp 118.5–119.5 °C; λ_{max} ($CHCl_3$) 5.80, 6.06, 6.23 μ; δ ($CDCl_3$, 250 MHz) 1.34 (s, 3), 1.71 (d, J = 15 Hz, 1), 2.85 (d,d J = 15, 6 Hz, 1), 3.09 (d, J = 9 Hz, 1), 3.23 (s, 3), 3.81 (s, 3), 4.00 (d, J = 9 Hz, 1), 5.78 (s, 1), 5.80–5.99 (m, 2).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.07; H, 6.78.

Diels–Alder Reaction of Quinone (1) with 1-Methoxy-1,3-butadiene in Benzene. Formation of Spiro Adduct (6). To a solution of 0.150 g (0.99 mmol) of quinone (1) in 6 mL of benzene was added 0.250 g (2.96 mmol) of 1-methoxy-1,3-butadiene. The solution was heated under reflux for 6 h. The reaction mixture was cooled and the volatiles evaporated in vacuo to give an oil. This was *rapidly* chromatographed on 20 g of Florisil. Elution with 3:1 hexane–ethyl acetate afforded 0.087 g (37%) of spiro adduct (6): mp 110–111 °C; λ_{max} ($CHCl_3$) 6.11, 6.38 μ; δ ($CDCl_3$, 60 MHz) 1.8–3.0 (m, 5), 3.4 (s, 3), 3.9 (s, 3), 5.1 (m, 1) 5.6 (s, 1), 5.9–6.1 (m, 2), 6.8 (q, 1).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.96; H, 6.81.

Diels–Alder Reaction of Quinone (1) with 1,3-Butadiene in 1:1 Molar Ratio Benzene–Absolute Methanol. A solution of 0.100 g (0.66 mmol) of quinone (1), 2 mL of 1,3-butadiene, and 2 mL of a 1:1 molar ratio solution of benzene–absolute methanol was heated at 100 °C in a sealed glass tube for 20 h. The color changed from red-orange to a light yellow during this time. Evaporation of the volatiles gave an oil which was *rapidly* chromatographed on 12 g of Florisil. Elution with 3:1 hexane–ethyl acetate afforded 0.075 g (56%) of adduct **3.**

Diels–Alder Reaction of Quinone (1) with 1-Methoxy-1,3-butadiene in 1:1 Molar Ratio Benzene–Absolute Methanol. To a solution of 0.100 g (0.66 mmol) of quinone (1) in 2 mL of 1:1 molar ratio solution of benzene–methanol was added 0.175 g (3.16 equiv, 2.08 mmol) of 1-methoxy-1,3-butadiene. The solution was heated under reflux under N_2 for 6 h. The volatiles were removed completely in vacuo to give an oil which could not be crystallized. The crude NMR spectra of this material showed it to be a mixture of adduct **7** and spiro adduct 6 in a ratio of approximately 1:1.

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Registry No.—1, 13523-09-6; **3**, 62006-21-7; **6**, 62006-22-8; **7**, 62006-23-9; 1,3-butadiene, 106-99-0; methanol, 67-56-1; 1-methoxy-1,3-butadiene, 3036-66-6; benzene, 71-43-2.

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(5) Cf. inter alia (a) L. F. Fieser and C. K. Bradsher, *J. Am. Chem. Soc.*, **61**, 417 (1939); (b) L. F. Fieser and M. Fieser, *ibid.*, **61**, 596 (1939); (c) W. Brown, J. W. A. Findlay, and A. B. Turner, *Chem. Commun.*, 10 (1968); (d) S. M. Ali and A. B. Turner, *J. Chem. Soc., Perkin Trans. 1*, 2225 (1974).
(6) As previously observed[4] the normal adducts of orthoquinones with 1,3-butadiene exist as the diosphenols while those derived from *trans*-1-methoxy-1,3-butadiene exist in the α-diketone form.
(7) Unfortunately, in our hands, these products are unstable to column or gas chromatography. Only the major components are isolated after substantial loss by rapid chromatography on Florisil. Product ratios are thus approximate and are based on integration of the angular methyl signal of the normal adducts relative to the methoxy signals of both compounds.
(8) For a report indicating that Diels–Alder cycloaddition to quinones (though not acid catalyzed) occurs faster in ethanol than in benzene see A. Wasserman, *J. Chem. Soc.*, 828 (1935).
(9) The stereochemistry of the secondary methoxyl group is unassigned. Apparently only a single isomer is produced in the "normal" mode.
(10) Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded in chloroform solution using sodium chloride optics on either a Perkin-Elmer 137 infrared spectrophotometer or a Perkin-Elmer 247 infrared spectrophotometer. The polystyrene absorption at 6.238 μ was used as a reference. Only selected high intensity absorptions are reported. The NMR spectra were measured in $CDCl_3$ with tetramethylsilane as an internal reference. Chemical shifts are reported in parts per million (δ) relative to Me_4Si. Elemental analyses were conducted by Galbraith Laboratories, Inc., Knoxville, Tenn.

Studies on *N*-Alkyl-2(1*H*)-pyridothione. 1. A New Synthetic Method for Thiols

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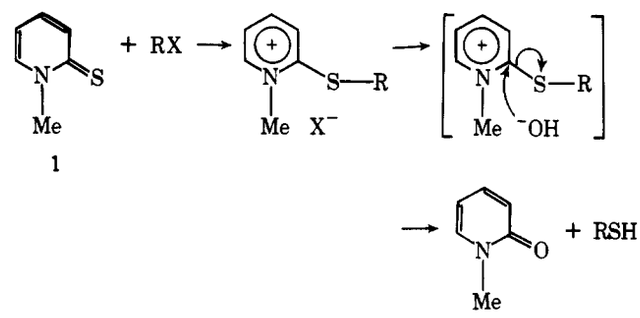
Widely used laboratory methods for the preparation of thiols are the reaction of alkyl halides with sodium hydrosulfide[1] or thiourea with subsequent alkaline hydrolysis,[2] and the direct alkylation of free sulfur with aryllithium[3] or Grignard reagents.[4] Although the thiourea method has been generally employed in preparative scale, α-mercaptocarbonyl compounds cannot be obtained because of thiazole formation.[5]

In this laboratory, the chemistry of *N*-methyl-2-alkylthiopyridinium salts has been investigated as an extension of studies on *N*-(ω-haloalkyl)pyridinium salts.[6] It was found in preliminary experiments that *N*-methyl-2(1*H*)-pyridothione

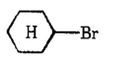
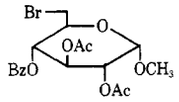


(1) reacted readily with alkyl halides to give the corresponding 2-alkylthiopyridinium salts, which were very labile under alkaline conditions.

We now wish to describe briefly a new preparative method for various kinds of thiol by alkaline hydrolysis of these salts, which are activated intermediates similar to *S*-thiouronium salts.[2] Primary and secondary halide, α-halo ketone, α- and β-halocarboxylic ester, and halo sugar were employed as alkyl halide for quaternization.

A series of the key intermediates, *N*-methyl-2-alkylthiopyridinium salts, was synthesized in refluxing ethanol in yields of 81–84% (see Table I). A little higher temperature (in

Table I. Reaction of 1 with Alkyl Halides and Hydrolysis of the Salts

Run	RX		Solvent	Time, h	Yield, %, of the salt		Yield, %, of thiol[b]	
1	$PhCH_2Br$	2a	CH_3CN	0.5	2b	83	2c	90
2	$PhCH_2CH_2Br$	3a	EtOH	4	3b	84	3c	82
3		4a	*n*-PrOH	16	4b	*a*	4c	70
4	$ClCH_2COPh$	5a	EtOH	4	5b	81	5c	72[c]
5	$ClCH_2COOEt$	6a	EtOH	4	6b	83	6c	65[d]
6		7a	*n*-PrOH	8	7b	*a*	7c	71[c]
7	$BrCH_2CH_2COOCH_2CH_2Ph$	8a	EtOH	4	8b	*a*	8c	0[e]

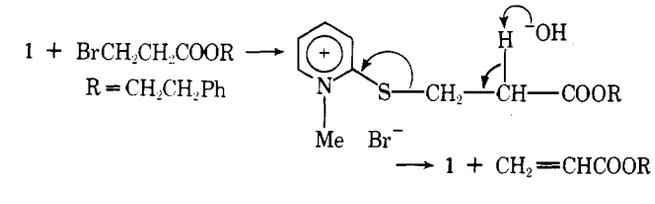
[a] Too hygroscopic to isolate. [b] Calculated from disulfide. [c] Isolated as thiol.[9] [d] Obtained after reesterification. [e] β-Elimination product only was isolated.

1-propanol) was more effective in the case of more hindered cyclohexyl bromide (**4a**) and methyl 4-*O*-benzoyl-6-bromo-6-deoxy-2,3-di-*O*-acetyl-α-D-glucopyranoside[7] (**7a**) prepared by NBS reaction.[8]

Hydrolytic cleavage of the C–S bond of the salts proceeded smoothly (within 30 min) in aqueous sodium hydroxide at room temperature. Acidification with hydrochloric acid gave the corresponding thiols, which in runs 1–3 and 5 were isolated as the odorless disulfides with iodine treatment. These reactions were performed without isolation of the quaternary salts. Although, at the hydrolysis step, blocking groups acetyl, benzoyl, and phenethyl were not affected in runs 6 and 7, the ethyl acetate derivative (**6b**) was saponified under the same conditions to give α-mercaptoacetic acid which was reesterified for isolation (run 5). The structure of the syrupy methyl 4-*O*-benzoyl-2,3-di-*O*-acetyl-6-thio-α-D-glucopyranoside (**7c**) was determined by microanalysis and ^1H NMR data in which SH appears at 1.20 ppm as a triplet.

It is particularly noteworthy that this method is nicely applicable to preparation of α-mercaptocarbonyl compounds (**5c, 6c**) and thio sugar **7c** with yields of 72, 65, and 71%, respectively.

However, when this method was applied to phenethyl β-bromopropionate (run 7), the intermediary salt (**8a**) underwent β-elimination under the hydrolysis conditions to give phenethyl acrylate in 68% yield with recovery of **1**.



Experimental Section[10]

Preparation of the Quaternary Salts. A mixture of *N*-methyl-2(1*H*)-pyridothione (1, 1.25 g, 0.01 mol) and a series of alkyl halides (0.01 mol) was refluxed in the solvent for a suitable time (see Table I). After removal of solvent, the crude solid was recrystallized from the solvent described below.

2b (CH_3CN), mp 183–184 °C.

Anal. Calcd for $C_{13}H_{14}NSBr$: C, 52.72; H, 4.76; N 4.73; S, 10.80. Found: C, 52.47; H, 4.68; N, 4.56; S, 10.54.

3b (*i*-PrOH), mp 148–150 °C.

Anal. Calcd for $C_{14}H_{16}NSBr$: C, 54.20; H, 5.20; N, 4.52; S, 10.32. Found: C, 54.56; H, 5.20; N, 4.58; S, 10.23.

5b (*i*-PrOH) did not show a clear melting point.

Anal. Calcd for $C_{14}H_{14}OSCl$: C, 60.11; H, 5.05; N, 5.01; S, 11.44. Found: C, 59.98; H, 5.01; N, 4.94; S, 11.21.

6b (*i*-PrOH) did not show a clear melting point.

Anal. Calcd for $C_{10}H_{14}O_2NSCl$: C, 48.49; H, 5.70; N, 5.66; S, 12.92. Found: C, 48.24; H, 5.45; N, 5.53; S, 12.78.

Other salts were too hygroscopic to isolate.

General Procedure for Thiols. The above crude solid was dissolved in water (10 mL) and then treated with 1 N sodium hydroxide (15 mL) for 30 min at room temperature. Thiol generated by acidification with 1 N hydrochloric acid (10 mL) was extracted with chloroform. The extract contained practically pure thiol.

α-Mercaptoacetophenone 5c (1.1 g, 72%): bp 95 °C (0.7 mm) [lit.[9] bp 87–90 °C (0.5 mm)]; ^1H NMR δ 3.90 (2 H, d, J = 8.0 Hz, CH_2S) and 2.10 (1 H, t, J = 8.0 Hz, SH).

Methyl 4-*O*-Benzoyl-2,3-di-*O*-acetyl-6-thio-α-D-glucopyranoside (7c). The syrup obtained by removal of the chloroform extract was chromatographed to give syrup **7c** (2.8 g, 71%): $[\alpha]^{22}_D$ +175° (*c* 2.2, ethanol); ^1H NMR δ 1.20 (1 H, t, J = 8.0 Hz, SH).

Anal. Calcd for $C_{18}H_{22}O_8S$: C, 54.27; H, 5.33; S, 8.04. Found: C, 54.43; H, 5.72; S, 7.88.

Isolation as Disulfides. Phenylmethanethiol (2c), 2-Phenylethanethiol (3c), and Cyclohexanethiol (4c). The chloroform solution was treated with iodine (1.5 g)–1 N sodium hydroxide (15 mL) and then washed with aqueous sodium hyposulfide to remove excess iodine. After evaporation, the residue was purified by column chromatography (2.5 × 10 cm). The disulfide of **2c** (1.1 g, 90%) was crystallized from ethanol (5 mL): mp 70–71 °C (lit.[11] mp 72 °C); ^1H NMR δ 3.63 (4 H, s, CH_2).

Disulfide of **3c** (1.1 g, 82%): bp 180 °C (0.7 mm) [lit.[12] bp 172–175 °C (0.8 mm)]; ^1H NMR δ 3.43 (8 H, s, CH_2CH_2).

Disulfide of **4c** (0.81 g, 72%): bp 125 °C (0.2 mm) [lit.[13] bp 130–131 °C (0.35 mm)]; ^1H NMR δ 2.67 (2 H, m, SCH).

Ethyl α-Mercaptoacetate (6c). After iodine oxidation, the product was esterified in refluxing ethanol containing a catalytic amount of concentrated sulfuric acid for 2 h. To the mixture was added barium carbonate and then the mixture was filtered. After evaporation, the liquid was distilled to give **6c** (0.78 g, 65%): bp 165 °C (12 mm) [lit.[14] bp 164 °C (14 mm)]; δ 3.63 (4 H, s, CH_2).

Registry No.—1, 2044-27-1; **2a**, 100-39-0; **2b**, 62058-65-5; **2c** disulfide, 150-60-7; **3a**, 103-63-9; **3b**, 62058-66-6; **3c** disulfide, 27846-22-6; **4a**, 108-85-0; **4c** disulfide, 2550-40-5; **5a**, 532-27-4; **5b**, 62058-67-7; **5c**, 2462-02-4; **6a**, 105-39-5; **6b**, 62058-68-8; **6c**, 623-51-8; **7a**, 56543-19-2; **7c**, 62058,69-9; **8a**, 62058-70-2.

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T-60 spectrometer using tetramethylsilane as internal standard in chloroform-d_1. Satisfactory analytical data (±0.3%) were obtained on all products. Column chromatography was performed on silica gel (Wako C300, Japan) using chloroform for elution.

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Chemisorbed Chromyl Chloride as a Selective Oxidant

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Selective oxidation is one of the most important of all chemical transformation. Many oxidants, however, remain too vigorous for such application. In this regard, one of the distinct advantages which heterogeneous reactions offer is the ability to isolate and moderate reactive species by chemisorption. Such procedures frequently have the additional virtue that intermediate products which under homogeneous conditions would prove difficult or impossible to isolate, for a variety of reasons become readily isolable under heterogeneous conditions. We have explored the possibility of moderating the reactivity of several strong oxidants by employing them as chemisorbed reagents on a high-surface, inert support. Here we report the results of one such investigation: specifically, the utility of chromyl chloride adsorbed on silica–alumina as a convenient, efficient, economical reagent for the oxidation of alcohols under neutral, nonaqueous conditions.

$$RCH_2OH \xrightarrow[CH_2Cl_2,\ 25\ ^\circ C]{CrO_2Cl_2/SiO_2\text{–}Al_2O_3} RCHO$$

$$RR'CHOH \xrightarrow[CH_2Cl_2,\ 25\ ^\circ C]{CrO_2Cl_2/SiO_2\text{–}Al_2O_3} RR'CO$$

This reaction seems to be applicable to the oxidation of primary and secondary alcohols to the respective aldehyde and ketone. A preliminary examination of the functional group compatibility of this reagent indicates that halocarbons, esters, lactones, nitriles, and ethers appear inert. Olefins, on the other hand, undergo oxidative cleavage. Thus, the same reagent will, for example, convert stilbene to benzaldehyde in 71% yield.[2]

Chromyl chloride is a vigorous oxidant whose action on organic substrates generally produces complex mixtures of products.[3] Recently, Sharpless and co-workers have demonstrated that a substantial moderation of this reactivity toward certain substrates (specifically olefins) can be achieved if these reactions are carried out at low temperatures.[4a] Further moderation can be achieved by employing a reagent derived by admixing chromyl chloride with *tert*-butyl alcohol and pyridine in methylene chloride at low temperatures.[4b] The resulting reagent is useful for the homogeneous oxidation of alcohols to aldehydes and ketones.

It is clear from the results in Table I that the chromyl chloride chemisorbed on silica–alumina is a great deal more selective than the homogeneous reagent. It is not apparent, however, whether this enhanced selectivity is a result of the inherently reduced reactivity of the chemisorbed species relative to that of chromyl chloride, or to the ability of the rigid support to immobilize a highly reactive species [e.g., Cr(IV)] so as to prevent its further possible reactions,[13a] reactions which could ultimately lead to a complex mixture of reaction products such as observed under homogeneous conditions.

Several investigators have recently employed the concept of utilizing reagents adsorbed on inert inorganic supports for organic synthesis.[5–7] Of these, three in particular bear brief comparison.[8] Lalancette and co-workers[9] have reported that primary but not secondary alcohols are oxidized to the corresponding aldehydes by a reagent purported to be CrO_3–graphite.[10] Complementing this activity are the results of Posner and co-workers,[6] who found that secondary but not primary alcohols are effectively oxidized by trichloroacetaldehyde when carried out over highly activated alumina. In contrast, the reactivity of chemisorbed chromyl chloride compares to that of the more standard reagents for alcohol oxidation[13] with the distinct advantages of preparative and manipulative convenience, similar to those recently reported

Table I. Reaction of Alcohols with Chromyl Chloride Adsorbed on Silica–Alumina[a]

Substrate	Registry no.	Product (%)[b]	Registry no.	Reaction time, h
1-Octanol	111-87-5	1-Octanal (94)	124-13-0	5
2-Octanol	123-96-6	2-Octanone (94)	111-13-7	24
2,2-Dimethylpropanol	75-84-3	2,2-Dimethylpropanal (78)	630-19-3	24
4-*tert*-Butylcyclohexanol	98-52-2	4-*tert*-Butylcyclohexanone (89)	98-53-3	6
exo-2-Norbornanol	497-37-0	2-Norbornanone (87)	497-38-1	24
1-Phenylethanol	60-12-8	Acetophenone (100)	98-86-2	5
Methyl mandelate	771-90-4	Methyl (2-keto-2-phenyl)acetate (77)	15206-55-0	
		Benzaldehyde (14)	100-52-7	3
Benzoin	119-53-9	Benzil (89)[c]	134-81-6	
		Benzaldehyde (6)		24
3-β-Cholestanol	17608-41-2	Cholestan-3-one (89)[c]	15600-08-5	5
Benzyl alcohol	100-51-6	Benzaldehyde (94)		5
4-Nitrobenzyl alcohol	619-73-8	4-Nitrobenzaldehyde (87) (83)[c]	555-16-8	5
4-Cyanobenzyl alcohol	874-89-5	4-Cyanobenzaldehyde (85)	105-07-7	5
4-Methylbenzyl alcohol	589-18-4	4-Methylbenzaldehyde (100)	104-87-0	4
2-Chlorocyclohexanol	1561-86-0	2-Chlorocyclohexanone (87)	822-87-7	24
2-Bromocyclohexanol	24796-87-0	2-Bromocyclohexanone (95)	822-85-5	24
2-Bromo-1-indanol	5400-80-6	2-Bromo-1-indanone (77)	1775-27-5	12

[a] Reactions carried out at 25 °C in methylene chloride solvent. Substrate to oxidant ratio: 0.10 mol to ~180 g of CrO_2Cl_2–SiO_2–Al_2O_3 reagent (2.92% Cr by weight[15]). [b] Yields, unless otherwise indicated, were determined by GLC or HPLC. Products were identified by comparison of their IR and mass spectra with those of authentic samples as well as GLC retention times and melting points where applicable. [c] Value based on isolated yield.