Heterogeneous Permanganate Oxidation of Thiols

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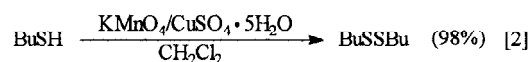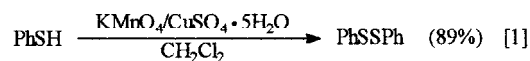*Received 10 February 1998*

Abstract: The products that may be obtained from the oxidation of thiols by permanganate under heterogeneous conditions have been compared with those that are known to be produced by use of the same oxidant under homogeneous conditions. The products obtained from the oxidation of thiols under homogeneous and heterogeneous conditions are distinctively different. Sulfonic acids are obtained under homogeneous conditions, while disulfides are the only detectable products when the reactions are carried out heterogeneously. For example, a quantitative yield of dibutyl disulfide is obtained from the oxidation of butane-1-thiol, and oxidation of pentane-1,5-dithiol gives the corresponding cyclic disulfide, 1,2-dithiepane.

Key words: heterogeneous permanganate oxidation, thiols, disulfides, cyclic disulfides

There is an accumulation of evidence which indicates that heterogeneous permanganate oxidations yield significantly different products from those obtained under homogeneous conditions. For example, alkenes readily react with permanganate in homogeneous solutions to yield diols, ketols, epoxides, diones or products derived from the oxidative cleavage of carbon–carbon double bonds.[1] However, under heterogeneous conditions, where permanganate is adsorbed on a solid support, a very different selectivity is observed.[2, 3]
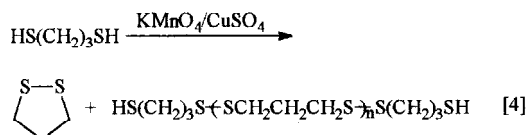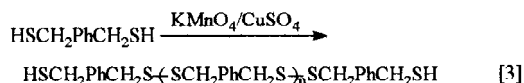
In this paper we wish to describe a method for the oxidation of thiols by permanganate under heterogeneous conditions, to note the remarkable difference between the products obtained under heterogeneous and homogeneous conditions, and to comment on the potential synthetic usefulness of the heterogeneous reactions.

Although sulfides are oxidized to similar products by permanganate under both heterogeneous and homogeneous conditions,[4, 5] the results obtained from the oxidation of thiols are dramatically different. Under homogeneous conditions, thiols are converted into sulfonic acids.[6, 7] However, under heterogeneous conditions, thiols are oxidized to the corresponding disulfides. As illustrated by the reactions depicted in Equations 1 and 2, both aromatic and aliphatic thiols are converted into disulfides in good yields.

$$PhSH \xrightarrow[CH_2Cl_2]{KMnO_4/CuSO_4 \cdot 5H_2O} PhSSPh \quad (89\%) \quad [1]$$

$$BuSH \xrightarrow[CH_2Cl_2]{KMnO_4/CuSO_4 \cdot 5H_2O} BuSSBu \quad (98\%) \quad [2]$$
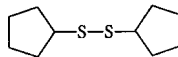
The oxidation of dithiols results in the formation of cyclic disulfides and/or polymers. The polymers result from intermolecular oxidations, while the cyclic disulfides arise from intramolecular oxidations. For example, the oxidation of 1,4-benzenedimethanethiol gives only polymeric

material (Equation 3) and propane-1,3-dithiol gives about 50% cyclic disulfides and 50% polymeric material (Equation 4), while butane-1,4-dithiol gives only the cyclic disulfide in 97% yield. In the case of 1,4-benzenedimethanethiol, intramolecular oxidation to a cyclic disulfide is obviously not possible, resulting in the formation of only polymer, while for butane-1,4-thiol intramolecular oxidation takes place preferentially. For propane-1,3-thiol, intramolecular and intermolecular oxidations appear to be of approximately equal probability.

$$HSCH_2PhCH_2SH \xrightarrow{KMnO_4/CuSO_4}$$

$$HSCH_2PhCH_2S\!-\!(SCH_2PhCH_2S)_n\!-\!SCH_2PhCH_2SH \quad [3]$$

$$HS(CH_2)_3SH \xrightarrow{KMnO_4/CuSO_4}$$

$+ \ HS(CH_2)_3S\!-\!(SCH_2CH_2CH_2S)_n\!-\!S(CH_2)_3SH \quad [4]$

A summary of the disulfides that have been prepared to illustrate the scope of this reaction is presented in the Table.

Table. Isolated Yields of Disulfides Obtained from the Oxidation of Thiols and Dithiols by Potassium Permanganate Adsorbed on Copper Sulfate Pentahydrate.

Reactant	Product	Yield (%)
PhSH	PhSSPh	89
4-MeC$_6$H$_4$SH	4-MeSC$_6$H$_4$SSC$_6$H$_4$Me-4	78
4-NO$_2$C$_6$H$_4$SH	4-NO$_2$C$_6$H$_4$SSC$_6$H$_4$NO$_2$-4	97
BuSH	BuSSBu	98
CH$_3$(CH$_2$)$_3$CH$_2$SH	CH$_3$(CH$_2$)$_3$CH$_2$SSCH$_2$(CH$_2$)$_3$CH$_3$	86
CH$_3$(CH$_2$)$_7$CH$_2$SH	CH$_3$(CH$_2$)$_7$CH$_2$SSCH$_2$(CH$_2$)$_7$CH$_3$	83
⬡—SH	⬡—S–S—⬡	98
HS(CH$_2$)$_5$SH	(cyclic disulfide)	73
HS(CH$_2$)$_4$SH	(cyclic disulfide)	97
HS(CH$_2$)$_3$SH	(cyclic disulfide)	45

An attempt was also made to use heterogeneous permanganate oxidations to prepare unsymmetrical disulfides, but with limited success. For example, the oxidation of an equimolar mixture of pentane-1-thiol and *p*-thiocresol resulted in the formation of three products, dipentyl disul-

fide, *pentyl p-tolyl disulfide* and *di-p-tolyl disulfide* in a molar ratio of 1:2:1.5.

Delaude and Laszlo have recently reported that the heterogeneous oxidation of thiols by potassium tetraoxoferrate(VI), K_2FeO_4, adsorbed on K10 montmorillonite clay, also results in the formation of disulfides in quantitative yields.[8] Although both experimental methods are similar, the use of potassium permanganate offers one practical advantage; it is an inexpensive, commercially available product while ferrate(VI) must be prepared and purified prior to use. On the other hand, the use of iron-based oxidants is attractive from an environmental viewpoint because iron, unlike most other transition metals, including manganese, is considered to be nontoxic.[8, 9]

Possible mechanisms for these and other heterogeneous permanganate oxidations have been previously considered.[4, 10]

The oxidant used in these experiments was prepared by placing equal amounts (typically 5 g) of $KMnO_4$ and $CuSO_4 \cdot 5\,H_2O$ in a mortar and grinding until homogeneous. The solvent, CH_2Cl_2, was purified by stirring over $KMnO_4$, using a small amount of phase transfer agent (Bu_4NBr) to solubilize the oxidant, and distilled. The purity of the solvent treated in this way was confirmed, by use of GC, to be 99.9% or better. The thiols and sulfides were obtained from the Aldrich Chemical Co. The liquids were distilled before use to ensure that no alkene impurities were present. The products were identified by comparison of spectroscopic data with published data for the same compounds. Purity was confirmed by mp, refractive indices and/or GC analysis.

Oxidation of Thiols; General Procedure:
Thiol (2.5 mmol) was placed in a 50-mL round-bottomed flask. CH_2Cl_2 (20 mL) and oxidant (0.8 g) were added and the heterogeneous mixture was stirred at r.t. for several hours. The progress of the reaction was monitored by TLC or GC until no thiol was detected. The contents of the flask were then filtered through Celite and washed with CH_2Cl_2 (2×10 mL) and Et_2O (10 mL). The product was isolated by evaporation of the solvent under reduced pressure, and identified from spectroscopic analysis. Although the yields determined by GC analysis were usually quantitative, isolated yields were somewhat less. It was found that the reaction time could be decreased without any reduction in yield by using more oxidant and/or by refluxing the solution.

Diphenyl Disulfide:
Oxidation of thiophenol (0.275 g, 2.5 mmol) following the general procedure gave diphenyl disulfide (0.242 g, 89%). The reaction was complete in 33 min; mp 60.7–60.9 °C (lit.[11] 61–62 °C).
^1H NMR: $\delta = 7.63–7.49$ (m, 4H), 7.42–7.20 (m, 6H).
IR (KBr): $\nu = 1573, 1474, 1436, 736, 686, 471, 461$ cm^{-1}.
MS: m/z (%) = 218 (M$^+$, 82), 185 (20), 154 (27), 109 (100), 65 (48).

p-Ditolyl Disulfide:
Oxidation of *p*-thiocresol (0.313 g, 2.52 mmol) following the general procedure gave a partially soluble, faintly yellow product after 32 min. Because of the insolubility of the product in CH_2Cl_2, several Et_2O washes of the Celite were required to obtain a yield of 0.241 g (78%); mp 44.5–44.8 °C (lit.[11] 47–48 °C).
^1H NMR: $\delta = 7.60–7.35$ (m, 4H), 7.25–7.07 (m, 4H), 2.33 (s, 6H).
IR (KBr): $\nu = 3029, 2913, 1488, 1396, 800, 489, 480$ cm^{-1}.
MS: m/z (%) = 246 (M$^+$, 77), 123 (100), 91 (17), 79 (26), 77 (26), 45 (47).

Bis(p-nitrophenyl) Disulfide:
p-Nitrothiophenol is sparingly soluble in CH_2Cl_2. Oxidation was achieved by stirring a finely powdered suspension of somewhat impure *p*-nitrothiophenol (0.615 g, 2.5 mmol) with oxidant, as in the general procedure, for 140 min. The product precipitated; yield: 0.373 g (97%); mp 177–178 °C (lit.[11] 182 °C).
^1H NMR: $\delta = 8.25–8.13$ (m, 4H), 7.70–7.56 (m, 4H).
MS: m/z (%) = 308 (M$^+$, 100), 171 (14), 155 (07), 138 (15), 124 (14), 108 (26), 69 (27).

Dibutyl Disulfide:
Oxidation of butane-1-thiol (0.271 g, 3.01 mmol) following the general procedure gave dibutyl disulfide (0.263 g, 98%) in 21 min; η_D 1.4938 (lit.[11] 1.4926).
^1H NMR: $\delta = 2.66$ (t, 4H, $J = 7$ Hz), 1.73–1.54 (m, 4H), 1.51–1.32 (m, 4H), 0.98–0.88 (m, 6H).
IR (neat): $\nu = 2957, 2929, 2872, 1464, 1413, 1378, 1272, 1217, 1131, 1089, 912, 743$ cm^{-1}.
MS: m/z (%) = 178 (M$^+$, 31), 122 (26), 57 (100), 41 (63), 29 (57).

Dipentyl Disulfide:
Oxidation of pentane-1-thiol (0.315 g, 3.02 mmol) following the general procedure gave dipentyl disulfide (0.267 g, 86%) in 2 h; η_D 1.4888 (lit.[11] 1.4889).
^1H NMR: $\delta = 2.61$ (t, 4H, $J = 7$ Hz), 1.71–1.52 (m, 4H), 1.41–1.20 (m, 8H), 0.92–0.77 (m, 6H).
IR (neat): $\nu = 2956, 2925, 2958, 1465, 1412, 1378, 1329, 1271, 1209, 1131, 729, 502, 488, 474$ cm^{-1}.
MS: m/z (%) = 206 (M$^+$, 19), 136 (15), 103 (14), 71 (39), 43 (100), 39 (12).

Dinonyl Disulfide:
Oxidation of nonane-1-thiol (0.393 g, 2.39 mmol) following the general procedure gave dinonyl disulfide (0.317 g, 83%) in 3 h; η_D 1.4773.
^1H NMR: $\delta = 2.62$ (t, 4H, $J = 7$ Hz), 1.70–1.50 (m, 4H), 1.50–1.15 (m, 24H), 0.990–0.75 (m, 6H).
IR (neat): $\nu = 2918, 2851, 1465, 1412, 1377, 1333, 1300, 1262, 1228, 1132, 722, 520, 488, 454$ cm^{-1}.
MS: m/z (%) = 318 (M$^+$, 20), 192 (18), 159 (22), 85 (37), 71 (66), 57 (64), 43 (100), 41 (62), 29 (34).

1,2-Dithiolane:
Oxidation of propane-1,3-dithiol (0.283 g, 2.61 mmol) following the general procedure gave 1,2-dithiolane (0.124 g, 45%) in 30 min.
^1H NMR: $\delta = 2.89–2.67$ (m, 4H), 2.18–1.95 (m, 2H).
IR (KBr): $\nu = 2918, 1440, 1410, 1331, 1290, 1234, 825, 753$ cm^{-1}.
MS: m/z (%) = 106 (M$^+$, 100), 78 (37), 64 (52), 45 (53), 41 (95).
The remainder of the product was an insoluble, polymeric sheet on the inside of the reaction flask.

1,2-Dithiane:
The oxidation of butane-1,4-dithiol (0.303 g, 2.48 mmol) following the general procedure gave 1,2-dithiane (0.289 g, 97%) in 80 min.
^1H NMR: $\delta = 2.90–2.62$ (m, 4H), 2.05–1.71 (m, 4H).
IR (neat): $\nu = 2924, 2846, 1432, 1407, 1323, 1302, 1279, 1225, 1131, 912, 731, 712, 514, 450$ cm^{-1}.
MS: m/z (%) = 120 (M$^+$, 61), 64 (21), 55 (100), 45 (27).

1,2-Dithiepane:
The oxidation of pentane-1,5-dithiol (0.332 g, 2.44 mmol) following the general procedure gave 1,2-dithiepane (0.239 g, 73%) in 1 h.
^1H NMR: $\delta = 2.70$ (t, 4H, $J = 6.4$ Hz), 1.82–1.64 (m, 4H), 1.61–1.44 (m, 2H).
IR (neat): $\nu = 2925, 2849, 1654, 1636, 1458, 669, 486, 458$ cm^{-1}.
MS: m/z (%) = 134 (M$^+$, 56), 101 (8), 87 (18), 69 (56), 45 (27), 41 (100), 27 (25).

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