

ected peptide resin (1a) was reacted with L-Met-Co (III) complex (3)¹⁰ in the presence of acetic acid as catalyst. After 19 hours, IR spectrum of the resin showed the disappearance of the oxime ester peak at 1775 cm^{-1} , which indicates the cleavage of the peptide from the resin and the formation of 1b. The pentapeptide-Co (III) complex (1b) was recovered as pink solids after filtration and evaporation of the solvent in vacuo (70% yield based on Boc-L-Phe-oxime resin). The unreacted 3 was easily removed from the reaction mixture by washing with methanol.

As previously reported, Co (III) group was selectively removed from 1b by briefly treating with sodium borohydride.¹⁰ Gel filtration and crystallization of the crude product in methanol afforded 1c in white crystals.¹¹ One of the advantages of this reaction scheme is that both conditions employed for the recovery of the peptide from the resin and for the removal of Co (III) complex are very mild and there is no danger of racemization during these steps.^{6,10} Furthermore, simple purification without any complicate chromatographic work has

ensured high yield.

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- (11) Yield, 50% from Boc-Phe-oxime resin; M.P. 178–180°C; TLC, R_f 0.75 (silica gel; n-butanol-acetic acid- H_2O , 40:4:12); Amino acid anal., Gly 2.19, Tyr 0.78, Phe 1.10 (Met could not be detected because of oxidation during hydrolysis); $^1\text{H NMR}$ ($\text{DMSO}-d_6$) δ : 2.04 (3H, s, S- CH_3), 2.40–4.90 (19H, m, 5 methines and 6 methylenes), 5.08 and 5.20 (4H, s, 2-O CH_2Ph), 6.90–7.80 (21H, m, 4 aromatics and 2 amides), 7.80–8.90 (3H, m, 3 amides).

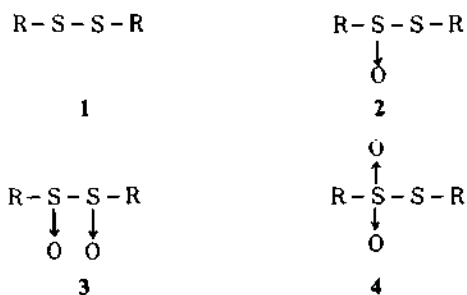
Unusually Stable Thiolsulfinate: *o*-Hydroxyphenyl-*o*-hydroxybenzene-thiolsulfinate

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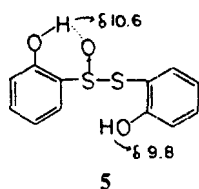
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Considerable interest has focused on thiolsulfates, 2¹ which are unstable, but an important precursor of unstable intermediate, α -disulfoxides, 3² thiolsulfonates, 4^{1b,3} being well used for the synthetic utility for organosulfur compounds. Although thiolsulfates are known to be unstable, only a few exceptionally stable thiolsulfates such as *trans*- and *cis*-1,2-dithiane-4,5-dioldiacetate⁴ and 2,4,6-triisopropylphenyl-2,4,6-triisopropylbenzene thiolsulfinate⁵ have been

reported without any detailed evidence or suitable explanation for their stability. During the course of our studies on the oxidations of disulfide reated compounds we have found that *o*-hydroxyphenyl-*o*-hydroxybenzene disulfide⁶ was readily mono-oxidized with equimolar amount of *m*-chloroperbenzoic acid at -45°C to give the corresponding unusually stable thiolsulfinate which showed no change after more than two years at room temperature.⁷

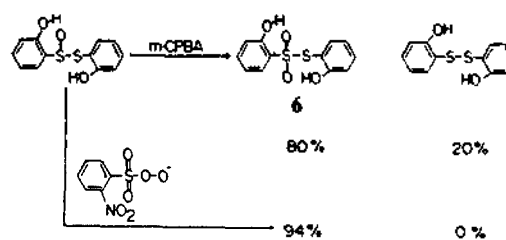


m-chloroperbenzoic acid solution (121 mg, 0.704 mmol, CH₂Cl₂: 5 ml) was slowly added to *o*-hydroxyphenyl-*o*-hydroxybenzene disulfide solution (176 mg, 0.704 mmol, CH₂Cl₂: 3 ml) at -45°C. Pale yellow solid immediately appeared. After being stirred at -45°C for 10 min, the solid was filtered, washed 3 times with ether (10 ml × 3), and then dried to give **5** (170 mg, 91%) mp. 96–97°C, ¹H NMR (DMSO-*d*₆) δ 6.8–7.8 (m, 8H), 9.8, 10.6 (s, -OH); IR (KBr) ν_{max} 1090 cm⁻¹ (S=O), 3400 cm⁻¹ (OH); m/e (rel. intensity), 125 (100), 141 (39), 250 (-S-S-, 34)⁺, 157 (22), 282 (-S-SO₂-, 15)⁺. Thiolsulfinate (**2**) has been known usually to be unstable, and easily to be decomposed to **1** and **4**.^{9–11} For instance, *p*-tolyl benzenethiolsulfinate which is stable for a few months under normal atmospheric condition was observed to undergo rapid decomposition under high vacuum by Backer and Kloosterziel.¹² Similar decomposition took place after longer periods of storage over phosphoric oxide, suggesting that in each case the stringent drying was responsible for the instability: stability is probably owing to some interaction between thiolsulfinate and the hydroxyl group of moisture. Our compound, **5** is stable even under high vacuum (10⁻¹ torr) for several days. It can be best explained that the thiolsulfinate, **5** containing hydroxyl groups at ortho position is exceptionally stable owing to its strong intramolecular hydrogen bond between the hydrogen of hydroxyl group and the oxygen of the highly polarized S^{δ+}-O^{δ-} group in **5** (cf. chemical shifts of ¹H NMR and IR for OH in **5** and in ref. 6).



It is noteworthy that though **5** was further oxidized to the corresponding thiolsulfonate (**6**, 80%) together with disulfide (20%) by *m*-chloroperbenzoic acid (*m*-CPBA) at -30°C in methylene chloride it was selectively oxidized to only **6** (94%) by a peroxysulfur intermediate at -45°C in acetonitrile which was generated from *o*-nitrobenzenesulfonyl chloride and potassium superoxide.¹³ In contrast to the electrophilic oxidation agent, *m*-CPBA,¹⁴ the latter appears to be nucleophilic oxidation agent

because only oxygenation of the sulfinylsulfur of **5** might take place affording the corresponding thiolsulfonate, **6** as shown in Scheme 1.



Scheme 1.

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- (6) *o*-hydroxyphenyl *o*-hydroxybenzenedisulfide was prepared by the reaction of 2-hydroxybenzenethiol with I₂ in the presence of NaOH in aqueous ethanol (¹H NMR (DMSO-*d*₆) δ 6.8–7.8 (m, ArH), 9.9 (s, OH); IR (film) ν_{max} 3450 cm⁻¹ (OH); m/e (rel. intensity), 250 (M⁺, 100%), 251 (M⁺, 16%), 125 (86%).
- (7) The thiolsulfinate is exceptionally still stable after being kept in a decicator at room temperature for more than two years: mp. 96–97°C.
- (8) It is well known that thiolsulfinate (**2**) is readily decomposed to **1** and **4**. The thiolsulfinate, **5** should decompose to disulfide (MW = 250) and thiolsulfonate, **6** (MW = 282).
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