

Communications

Magtrieve™: A New Reagent for the Oxidation of Thiols to Disulfides under a Neutral and Anhydrous Condition

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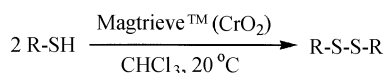
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The oxidative conversion of thiols to disulfides is a useful transformation in organic synthesis as well as biochemistry.¹ This oxidation has been carried out using a variety of reagents² including halogens,³ periodate,⁴ calcium hypochlorite,⁵ peroxodisulfate,⁶ *N*-hydroxy-*o*-benzenedisulfonimide,⁷ sodium chlorite,⁸ thallium(III) acetate,⁹ enzyme,¹⁰ CCl₄,¹¹ transition metals such as Fe(III),¹² Cu(II),^{12b} active MnO₂,¹³ potassium ferrate(VI),¹⁴ rhenium catalyst,¹⁵ and tellurite,¹⁶ trichloronitromethane,¹⁷ and Caros acid (H₂SO₅)¹⁸ among others. However, some reagents mentioned above suffer from disadvantages such as incompatibility with certain functional groups, toxic nature of reagents, strong acidic conditions, or nonavailability of reagents.

Magtrieve™ is Dupont's trademark for its magnetically retrievable oxidant based on chromium dioxide (CrO₂).¹⁹ This reagent was first used for the mild oxidation of alcohols.²⁰ Since only the surface of Magtrieve™ is reduced during the oxidation process, this oxidant is still ferromagnetic and can be conveniently removed by magnet, after use. Because Magtrieve™ can be recycled by simple heating in air, this reagent can serve as a mild and environment-friendly oxidant.

We recently reported that Magtrieve™ can be used as an oxidant for the aromatization of 1,4-dihydropyridines to pyridines²¹ and the generation of diphenyldiazomethane from benzophenone hydrazone.²² Our experience with Magtrieve™ prompted us to investigate the possibility of using this reagent as a new oxidant for thiols. In this communication, we report that Magtrieve™ can serve as a new oxidant for the heterogeneous oxidation of thiols to disulfides under a neutral and anhydrous condition, as shown in Table 1.



The oxidation was performed by stirring a mixture of thiol and Magtrieve™ in chloroform at 20 °C under nitrogen, except for dodecanethiol and benzyl mercaptan. For the aromatic thiols, the oxidation was complete within a few hours. In contrast, the oxidation of aliphatic long-chain thiol such

Table 1. Oxidation^a of Thiols to Disulfides with Magtrieve™

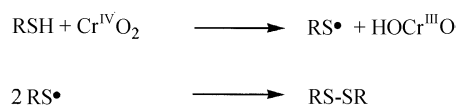
2 R-SH		Magtrieve™ (CrO ₂)		R-S-S-R	
		CHCl ₃ , 20 °C			
Entries	Thiols (R-SH)	Time (h)	Yield (%) ^b	mp (°C)	Lit. mp (°C)
1	2-mercaptobenzothiazole	1	91	180-182	183-184 ^c
2	2,6-(CH ₃) ₂ C ₆ H ₃ SH	6	93	104-105	105-106 ^d
3	2,5-(CH ₃) ₂ C ₆ H ₃ SH	3	92	48-49	46.5-48 ^e
4	C ₆ H ₅ SH	2	92	58-59	59-60 ^f
5	4-BrC ₆ H ₄ SH	1	96	91-92	92-94 ^f
6	2-mercaptopyridine	1	98	55-57	56-58 ^g
7	HSCH ₂ CH ₂ OH	2	93	oil	26-28 ^h
8a	<i>n</i> -C ₁₁ H ₂₃ CH ₂ SH	120	73 ⁱ	31-32	30-31 ^j
8b		48 ^k	99		
9a	PhCH ₂ SH	24	50 ^l	69-70	71-72 ^c
9b		8 ^l	91		
10	1,2-(HSCH ₂) ₂ C ₆ H ₄	2	87	76-77	77-78 ^f
11	8-mercaptomenthone	24	trace ^m		
12	Ph ₃ CSH	24	trace ^m		

^aAll reactions were conducted at 20 °C, using 1 mmol of thiol and 1.51 g of Magtrieve™ in chloroform (20 mL) under nitrogen, unless noted otherwise. ^bYield refers to the pure isolated product. ^cRef. 12a. ^dBeilstein E IV 6, 3125. ^eBeilstein E IV 6, 3171. ^fDictionary of Organic Compounds; Chapman and Hall: London, 6th Ed., 1996. ^gRef. 6. ^hBeilstein E IV 1, 2442. ⁱThe rest is the starting thiol. ^jBeilstein E IV 1, 1853. ^kin refluxing toluene. ^lin refluxing chloroform. ^mInertness of tertiary thiols to oxidation may be ascribed to the poor absorption on Magtrieve™ surface due to the unfavorable steric strain.²³

as dodecanethiol required higher reaction temperature and longer time (entry 8). The higher reactivity of aromatic thiols toward Magtrieve™ may be ascribed to the more acidic nature of aromatic thiols.²³ Tertiary thiols (entries 11, 12) were inert to oxidation. Although Magtrieve™ is known to oxidize unactivated alcohols to carbonyl compounds in refluxing toluene,²⁰ the chemoselective oxidation of thiol containing a primary hydroxyl group was achieved at 20 °C (entry 7).

Oxidation of 2-mercaptopyridine (entry 6) is representative. To a solution of 2-mercaptopyridine (110 mg, 1.0 mmol) in chloroform (20 mL) was added Magtrieve™ (1.51 g) all at once at 20 °C. The mixture was stirred under nitrogen atmosphere for 1 h, until TLC showed the absence of the starting material (R_f of thiol = 0.15, R_f of disulfide = 0.55 in EtOAc : hexanes = 1 : 1). A magnet was placed on one side of the flask and the solution was decanted. The oxidant was rinsed with EtOAc (3 × 20 mL) and this solution was combined with the decantate. The whole solution was dried with Na₂SO₄ and concentrated to give 108 mg (98%) of the pure product (¹H NMR and TLC) as a pale yellow solid, mp 55–57 °C (Lit.⁶ mp 56–58 °C).

A previous study of the oxidation of thiols by transition metal oxides showed that disulfides are formed by the coupling of thiyl radicals (RS•).²³ Similar mechanism for thiol oxidation on Magtrieve™ can be suggested as follows:^{20,24}



In conclusion, the easy work-up, the recyclability of the used reagent, the neutral and anhydrous reaction condition, the chemoselectivity, the commercial availability, and high yields make the use of Magtrieve™ attractive for the lab-scale oxidation of thiols to disulfides.

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