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Bismuth(III) Nitrate Pentahydrate $Bi(NO_3)_3 \cdot 5H_2O$: An Inexpensive and Mild Reagent for the Efficient and Clean Oxidation of Thiols to Disulfides

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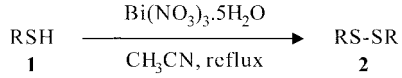
Oxidation of thiols to their disulfides is an important transformation from both biological and synthetic points of views.[1,2] Disulfides are important reagents in organic synthesis and can be used for the preparation of sulfinyl and sulfenyl compounds.[3] A variety of reagents have already been used for the conversion of thiols to disulfides.[4] However, some of these reagents suffer from disadvantages such as long reaction times, availability, toxicity, difficult work-up, preparation and instability. Consequently, there is still a need for introducing readily available, safe, stable and cheap reagents for the oxidation of thiols to disulfides.

The applications of bismuth compounds to organic transformations have been extensively investigated.[5] Recently we introduced Bi(III) salts as efficient reagents for different organic transformations including the conversion of epoxides to thiiranes,[6a,b] deprotection of 1,1-diacetates,[6c] alcoholysis, hydrolysis and acetolysis of epoxides,[6d] deprotection of silyl and tetrahydropyranyl ethers,[6e,f] conversion of epoxides to 1,3-dioxolanes,[6g] acetylation, benzoylation and formylation of alcohols, phenols, trimethylsilyl and tetrahydropyranyl ethers,[6h-j] and conversion of thiocarbonyls to their carbonyl compounds.[6k] In continuation of our ongoing work on Bi(III) catalysis, we now report an efficient and environmentally benign procedure for the oxidative coupling of thiols to their corresponding disulfides using bismuth(III) nitrate pentahydrate (Scheme 1).



Scheme 1

Bismuth(III) nitrate pentahydrate is an inexpensive, crystalline solid and commercially available reagent and requires no special handling. Oxidation of thiols to their disulfides was performed efficiently in the presence of 30 mol% of this reagent. The results of this study are summarized in Table 1. Aromatic thiols such as benzenethiol (**1a**), 4-methylbenzenethiol (**1b**), 4-bromobenzenethiol (**1c**), 4-chlorobenzenethiol (**1d**) and 2-naphthalenethiol (**1e**) exhibited a similar reactivity, leading to the corresponding disulfides **2a-2e** in excellent yields. Heteroaromatic thiol such as 2-pyridinethiol (**1f**) underwent oxidative coupling with $Bi(NO_3)_3.5H_2O$, to afford 2,2'-dipyridine disulfide (**2f**) in 93% yield. Under the same reaction conditions, benzylthiol (**1g**) and aliphatic thiols **1h-1l** were oxidized to their disulfides **2g-2l** in excellent yields. The selectivity of the present method is evident by the oxidation of 2-mercaptoethanol (**1h**), where only mercaptan functionality is converted to the disulfide **2h**.

In conclusion, the paper describes a facile synthesis of disulfides using catalytic amounts of $Bi(NO_3)_3.5H_2O$. The method offers several advantages including high yields of the products, short reaction times, ease of isolation of the products, and stable, inexpensive and relatively non-toxic reagent which make the reaction process convenient and environmentally benign.

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Table 1. Catalytic oxidation of thiols to disulfides with $Bi(NO_3)_3 \cdot 5H_2O$

Thiol	R	Disulfide[a]	Time (min)	Isolated Yield %	mp (°C)	Lit. mp (°C)
1a	C_6H_5	**2a**	20	93	59-60	58-59[4t]
1b	4-MeC_6H_4	**2b**	5	96	44-45	45-46[4e]
1c	4-BrC_6H_4	**2c**	5	97	91-93	91-92[4t]
1d	4-ClC_6H_4	**2d**	10	98	70-71	72-74[4q]
1e	2-Naphthyl	**2e**	45	97	142-144	144-145[4q]
1f	2-Pyridyl	**2f**	40	93	55-57	55-57[4t]
1g	$C_6H_5CH_2$	**2g**	40	93	70-71	69-70[4t]
1h	$HOCH_2CH_2$	**2h**	40	98	oil[4t]	
1i	*n*-C_4H_9	**2i**	25	93	oil[4q]	
1j	*n*-C_8H_{17}	**2j**	35	93	oil[4l]	
1k	$(CH_3)_2CHCH_2$	**2k**	20	96	oil[4g]	
1l	*c*-C_6H_{11}	**2l**	40	94	oil[4g]	

[a]All products were identified by comparison of their physical and spectral data with those of authentic samples.

Experimental Section

General procedure: To a solution of thiol (1 mmol) in acetonitrile (10 mL) was added $Bi(NO_3)_3 \cdot 5H_2O$ (0.3 mmol) and the mixture was refluxed for the indicated time according to Table 1. The reaction mixture was filtered and the solid material was washed with acetonitrile (10 mL). Evaporation of the solvent followed by recrystallization or chromatography on silica gel afforded the pure disulfide in 93-98% Yields (Table 1).

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