Air Oxidative Coupling of Thiols to Disulfides Catalyzed by Fe(III) / NaI

N. Iranpoor,* B. Zeynizadeh

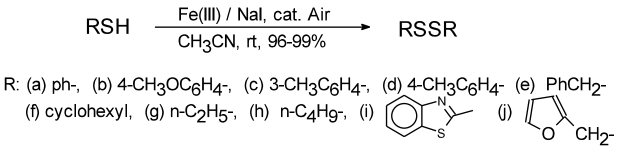
Chemistry Department, Shiraz University, Shiraz 71454, Iran
Fax: +98 71 20027; E-mail: iranpoor@chem.susc.ac.ir

Received 17 April 1998; revised 3 June 1998

Abstract: A very simple and mild reaction is described for the efficient coupling of thiols at room temperature catalyzed by Fe (III)/NaI in the presence of air.

Key words: thiols, oxidative coupling, Fe(III) catalysis, sodium iodide

Controlled oxidation of thiols to disulfides is important in organic synthesis and wide range of reagents have been used for this transformation.[1–9] Recently, the catalytic coupling of thiols has been the subject of some investigation and new methods have been reported. These methods employ Fe(III)/montmorillonite/water/phosphate buffer[10] and $Ca(OCl)_2$/montmorillonite/water[11] systems under aqueous conditions. In this context, we have already reported two catalytic methods for coupling of thiols using tris(trinitrato)cerium(IV)para-periodate[12] or $Cu(NO_3)_2 \cdot N_2O_4$[13] as the catalyst. In both of these reagents, two oxidizing agents come together to show this catalytic activity. In the course of our studies on some reactions of Fe(III), it was observed that the oxidative dimerization of thiols with sodium iodide can be catalyzed efficiently at room temperature with Fe(III) under air atmosphere and the corresponding disulfides are formed rapidly in excellent yields (Scheme).



Scheme

The possibility of using different Fe(III) species such as anhydrous $FeCl_3$, $FeCl_3 \cdot 6H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$ and $NH_4Fe(SO_4)_2 \cdot 12H_2O$ in the reaction of thiophenol with NaI were studied. It was observed that among these compounds, anhydrous $FeCl_3$ is more efficient than others.

The possibility of performing this coupling reaction with catalytic amounts of NaI was also studied. It was observed that 0.2 molar equivalent of NaI is enough to complete the dimerization of thiols in the presence of 0.1 molar equivalent of Fe(III). The effect of air oxygen on the progress of this reaction is shown in Table 2.The results obtained from the reaction of different thiols with catalytic amounts of anhydrous $FeCl_3$ and NaI in acetonitrile at room temperature are listed in Table 1.

Table 1 Catalytic Coupling of Thiols with NaI/Anhydrous $FeCl_3$ in Acetonitrile at Room Temperature

R[a]	Molar Equivalent		Time (min)	Yield (%)	mp (°C) or bp (°C)/Torr	
	Fe(III)	NaI			found	reported
a	0.1	0.2	15	97	59–60	60[14,17]
b	0.1	0.2	35	97	43	43–44[15a,17]
c	0.1	0.2	30	96	–21	–22[16a]
d	0.1	0.2	30	98	45–46	45–46[15a,17]
e	0.1	0.2	10	99	71–72	72[15a,17]
f	0.1	0.2	20	98	124–129	125–130[16b]
g	0.1	0.2	7	98	153–154	154/760[17]
h	0.1	0.2	7	97	116–118/20	114–115/18[15a,17]
i	0.2	0.3	40	98	183–184	182–183.5[16c]
j	0.1	0.2	12	96	119–121/1	112–115/0.5[15b]

[a] For R, see Scheme.
[b] Isolated yield.

Table 2 Oxidative Coupling of Thiophenol Under Different Reaction Conditions in Acetonitrile

Entry	Reaction Components	Molar Ratio	Temp/Time (h)	Conversion[a]
1	thiol/NaI	1:1	r.t./10	0
2	thiol/$FeCl_3$/NaI	1:0.05:1	r.t./1.5	100
3	thiol/$FeCl_3$/NaI[b]	1:0.1:1	r.t./0.1	100
4	thiol/$FeCl_3$/NaI	1:0.1:0.2	r.t./0.25	100
5	thiol/I_2/NaI	1:0.5:1	r.t./2	50
6	thiol/I_2	1.1	reflux	50
7	thiol/$FeCl_3$/I_2	1:0.1:0.2	r.t./1.25	100

[a] GC yield.
[b] When this reaction was performed in oxygen-free solvent under argon atmosphere, only 4–7% of conversion to disulfide was observed after 2 h.

In order to show the necessity of Fe(III), the role of NaI and air oxygen in this transformation, a set of experiments was undertaken by performing the coupling reaction of thiophenol under different reaction conditions (Table 2). These results show that Fe(III) in the presence of air oxygen can catalyze the coupling of thiophenol with catalytic amounts of NaI (Table 2, Entries 2–4), or iodine (Table 2, Entry 7) but the reaction time with NaI is shorter.

Although oxidative coupling of thiols has been widely studied with different reagents, due to the ready polymerization reactions, the reported results on coupling of dithiols are rare.[18] We studied the possibility of coupling of 1,3-propanedithiol to 1,2-dithiacyclopentane with our method under high dilution conditions.[19] The reaction was found to give some polymeric materials, but 1,2-dithiacyclopentane was also obtained in 55% yield.

In order to see the efficiency of other Lewis acids for this catalytic transformation, coupling of thiophenol with different metal halides were studied. The results are tabulated in Table 3.

Table 3 The Effect of 0.1 Molar Equivalents of Different Lewis Acids for Coupling of Thiophenol with Equimolar of NaI in Acetonitrile at Room Temperature.

Entry	Lewis Acid[a]	Time (h)	Conversion (%)[b]
1	$FeCl_3$	0.1	100
3	$CrCl_3$	6	50
4	$CoCl_2{\cdot}6\,H_2O$	5	30
5	$SnCl_2{\cdot}2\,H_2O$	1	90
	$ZrCl_4$	10	10
	$TiCl_4$	10	40

[a] The conversion yield was found to be 0%, when chloride of Ni, Zn, Al, Ce(III), Pb(II), Mn(II), Hg(I), Nb(V), Cd(II) and Mg(II) were used as catalyst.

[b] GC Yield.

In conclusion, this catalytic method is very simple and efficient for coupling of thiols. The easy procedure and simple workup, simplicity, availability of reagents, short reaction times and excellent yield of the products make this method a useful addition to the present methodologies.

Products were characterized by comparison of their physical data with those of known samples. All yields refer to isolated products. IR spectra were recorded on a Perkin Elmer 781 and Pye Unicam 8725 spectrometers. NMR spectra were recorded on a Bruker DPX 250 spectrometer. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates or by GC on a Shimadzu GC-14A instrument.

Oxidative Coupling of Thiophenol with $FeCl_3$, Phenyl Disulfide; Typical Procedure

To a solution of thiophenol (1.1 g, 10 mmol) in MeCN (30 mL) were added NaI (0.299 g , 2 mmol) and $FeCl_3$ (0.162 g, 1 mmol). The resulting mixture was stirred at r. t. for 6 min. After completion of the reaction, the solvent was evaporated and 1% aq solution of $Na_2S_2O_3$ (30 mL) was added. The mixture was then extracted with CH_2Cl_2 (3 × 40 mL) and dried (Na_2SO_4). The solvent was evaporated and the residue was chromatographed on a short column of silica gel using CCl_4 as the eluent. The pure product was obtained as colorless crystals (1.06 g, 97%).

Acknowledgement

We are grateful to Shiraz University Research Council for partial support of this work and Professor H. Firouzabadi for discussion and assistance.

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(19) The reaction was performed between 1,3-propanedithiol (0.216 g, 2 mmol), $FeCl_3$ (0.048 g, 0.3 mmol) and NaI (0.3g, 2 mmol) in MeCN (100 mL) at r.t. After 20 min the product was isolated according to the procedure and identified by its ^1H, ^{13}C NMR and mass spectral data.