Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gsrp20

Green preparation of disulfides from corresponding thiols by poly(4-vinylpyridinium nitrate) as recoverable and new polymeric reagent

Arash Ghorbani-Choghamarani [a] & Sara Sardari [b]

[a] Department of Chemistry, Faculty of Science, Ilam University, PO Box 69315516, Ilam, Iran

[b] Islamic Azad University, Branch-Omidiyeh, Ahvaz, Iran

Version of record first published: 21 Dec 2010.

To cite this article: Arash Ghorbani-Choghamarani & Sara Sardari (2011): Green preparation of disulfides from corresponding thiols by poly(4-vinylpyridinium nitrate) as recoverable and new polymeric reagent, Journal of Sulfur Chemistry, 32:1, 63-69

To link to this article: http://dx.doi.org/10.1080/17415993.2010.541462

Journal of Sulfur Chemistry
Vol. 32, No. 1, February 2011, 63–69

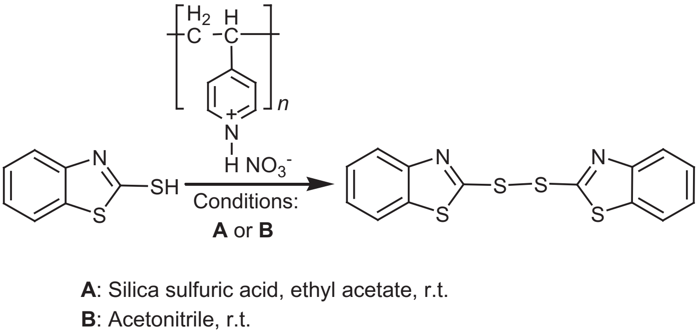
Green preparation of disulfides from corresponding thiols by poly(4-vinylpyridinium nitrate) as recoverable and new polymeric reagent

Arash Ghorbani-Choghamarani[a]* and Sara Sardari[b]

[a]*Department of Chemistry, Faculty of Science, Ilam University, PO Box 69315516, Ilam, Iran;* [b]*Islamic Azad University, Branch-Omidiyeh, Ahvaz, Iran*

(*Received 26 September 2010; final version received 16 November 2010*)

Poly(4-vinylpyridinium nitrate) was found to be a recyclable and highly efficient oxidizing polymer for the oxidative coupling of a variety of aliphatic or aromatic thiols to the corresponding disulfides. Poly(4-vinylpyridinium nitrate) is an extremely mild agent, which gave no other oxidized side products.



Keywords: thiols; disulfides; poly(4-vinylpyridine); poly(4-vinylpyridinium nitrate); coupling

1. Introduction

In the last few years, supported reagents on polymers have become increasingly applied in organic synthesis (*1–5*), because the reactions are carried out under mild conditions. Disulfide bonds play crucial roles in biology and chemistry (*6*). Oxidation of thiols is the most exploited method for disulfide synthesis mainly because a large number of thiols are commercially available and/or are easily synthesized (*7*). The controlled oxidative coupling of thiols to disulfides is of great interest and oxidative coupling of thiols to disulfides under mild conditions is of practical importance

---

*Corresponding author. Email: arashghch58@yahoo.com or a.ghorbani@mail.ilam.ac.ir

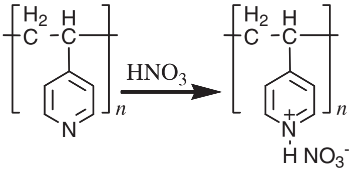
ISSN 1741-5993 print/ISSN 1741-6000 online

DOI: 10.1080/17415993.2010.541462
http://www.informaworld.com

in synthetic methodology. In the last decade, variable methodologies have been studied for the conversion of thiols into disulfides (*8–20*), but some of these methods have several disadvantages such as overoxidation, tedious work-up, low yields of products, heavy metal contamination, harsh conditions, and expensive reagents or catalysts. Therefore, to improve the mentioned limitations, we decided to design a new system for this transfromation.

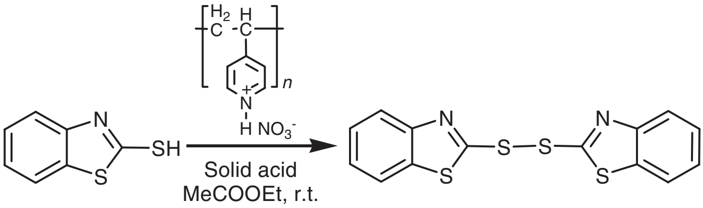
2. Results and discussion

In continuation of our studies on the application of new reagents or reagent systems in organic reactions (*21–27*), we became interested to explore a new methodology for the fine and selective conversion of thiols into disulfides. In this light, we decided to prepare a mild oxidizing agent based on oxidizing properties of nitric acid. Therefore, we prepared a polymeric nitrate salt via a reaction of nitric acid (65%) with poly(4-vinylpyridine) (Scheme 1).



Scheme 1. Preparation of poly(4-vinylpyridinium nitrate).

Based on our previous studies, we assumed that the oxidizing properties of this polymeric nitrate salt could be increased in the presence of an acid. Consequently, we have examined a variety of solid acids for this purpose (Scheme 2 and Table 1).



Scheme 2. Oxidative coupling of 2-mercaptobenzothiazole in the presence of different solid acids.

As the results show, all of the mentioned solid acids in Table 1 are applicable for the coupling reaction, but we decided to use silica sulfuric acid because of (a) shorter reaction time, (b) higher purity of produced disulfide (based on resulting melting points), and (c) metal-free content of this acid.

Certainly, solvent plays a critical role in the reactions; therefore, we decided to investigate the solvent effect and select an appropriate solvent for the oxidative coupling of thiols into disulfides. Therefore, we screened different solvents for the preparation of 1,2-bis(2-benzoxazol)disulfane, as a typical example, by poly(4-vinylpyridinium nitrate) and silica sulfuric acid in different solvents at room temperature (Table 2).

Consequently, Table 2 shows that the best solvent for the oxidative coupling of thiols (by poly(4-vinylpyridinium nitrate) and silica sulfuric acid) is ethyl acetate in terms of reaction kinetics.

Table 1. Oxidative coupling of 2-mercaptobenzothiazole with poly(4-vinylpyridinium nitrate) and solid acids in ethyl acetate at room temperature.[a]

Entry	Solid acid	Time (min)	Yield (%)[b]	Mp (°C)[c]
1	$Zn(HSO_4)_2$	10	99	160–164
2	$Ca(HSO_4)_2$	10	99	160–165
3	$Fe(HSO_4)_2$	10	96	168
4	Citric acid	40	99	163–168
5	L-Alanine	40	99	171–174
6	NH_2SO_3H	25	99	160–165
7	$Al(HSO_4)_3$	5	99	165–168
8	$KHSO_4$	35	99	175–179
9	$NaHSO_4$	45	96	170–171
10	SiO_2-OSO_3H	10	97	176–178

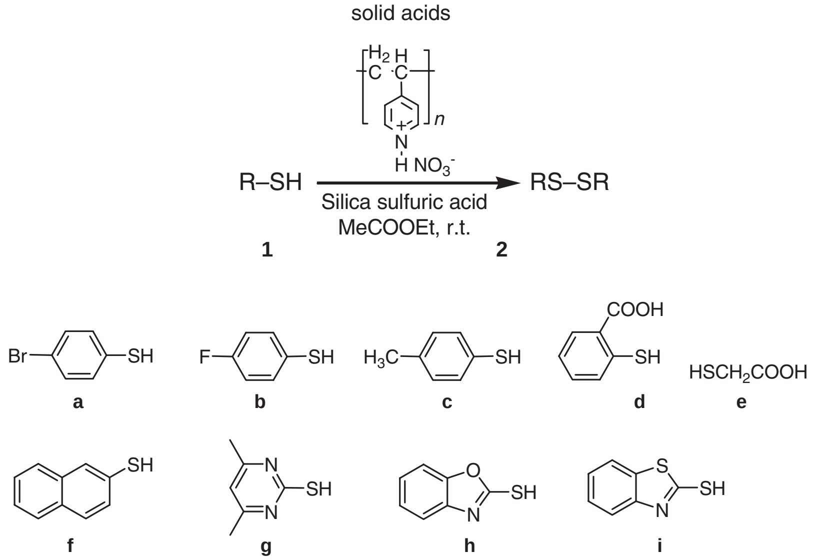
Notes: [a]Substrate/poly(4-vinylpyridinium nitrate)/acid for Entries 1–9 (1 mmol/0.338 g/2 mmol) for Entry 10 (1 mmol/0.338 g/0.2 g). [b]Isolated yield. [c]Reported mp (177–179) (*8*).

Table 2. Oxidative coupling of 2-mercaptobenzothiazole using poly(4-vinylpyridinium nitrate) and silica sulfuric acid in different solvents at room temperature.[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	Acetonitrile	45	99
2	Acetone	270	90
3	Chloroform	145	95
4	Dichloromethane	45	91
5	Ethyl acetate	10	97
6	Ethanol	360	–[c]

Notes: [a]Substrate/poly(4-vinylpyridinium nitrate)/silica sulfuric acid (1mmol/0.338 g/0.2 g). [b]Isolated yield. [c]No reaction.

With optimal conditions in hand, we investigated the coupling of a variety of aliphatic and aromatic thiols into disulfides using poly(4-vinylpyridinium nitrate) and silica sulfuric acid in ethyl acetate at room temperature (Scheme 3 and Table 3).



Scheme 3. Coupling of thiols by poly(4-vinylpyridinium nitrate) and silica sulfuric acid.

Table 3. Oxidative coupling of thiols into disulfides by poly(4-vinylpyridinium nitrate) I and silica sulfuric acid II in ethyl acetate at room temperature.

			Substrate/reagents (mmol)[a]						
Entry	Substrate	Product	I	II	Time (min)	Yield (%)[b]	Mp (°C) found	Mp (°C) reported	Reference
1	**1a**	**2a**	0.338	0.2	95	97	89–92	90–92	(*8*)
2	**1b**	**2b**	0.338	0.4	25	99	Oil	Oil	(*22*)
3	**1c**	**2c**	0.338	0.2	10	99	39–42	43–44	(*8*)
4	**1d**	**2d**	0.338	0.4	80	95	273–285	278–280	(*22*)
5	**1e**	**2e**	0.338	0.4	60	90	Oil	Oil	(*22*)
6	**1f**	**2f**	0.338	0.4	75	91	141–144	144–146	(*8*)
7	**1g**	**2g**	0.338	0.4	105	99	164–166	167–169	(*12*)
8	**1h**	**2h**	0.338	0.4	20 h	87	84–88	77.5–79	(*22*)
9	**1i**	**2i**	0.338	0.2	10	97	176–178	177–179	(*8*)
10	**1i**	**2i**	0.338	0.0	55	90[c]	176–178	177–179	(*8*)

Notes: [a] I and II refer to grams of poly(4-vinylpyridinium nitrate) and silica sulfuric acid. [b] Isolated yield. [c] In the absence of silica sulfuric acid.

Reactions were carried out under completely heterogeneous conditions. After reaction completion, pure product was easily obtained by simple filtration, washing by ethyl acetate, and evaporating the solvent.

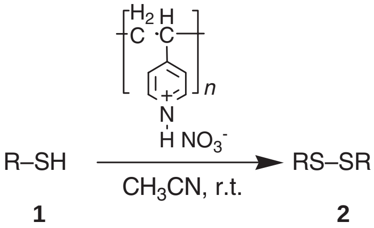
In order to study the role of silica sulfuric acid, 2-mercaptobenzothiazole was subjected to oxidative coupling by poly(4-vinylpyridinium nitrate) in the absence of silica sulfuric acid (as a typical example). Interestingly, we observed that the reaction time increased to 55 min (Table 3, Entry 10). Although silica sulfuric acid increases the rate of the reaction, fortunately this increased time is not too much. Consequently, we decided to run all of the coupling reactions in the absence of acid.

Initially, to find an appropriate solvent for this new condition, we screened different solvents for the oxidative coupling of 2-mercaptobenzothiazole using poly(4-vinylpyridinium nitrate) as a typical example (Table 4).

Table 4. Oxidative coupling of 2-mercaptobenzothiazole using poly(4-vinylpyridinium nitrate) in the absence of silica sulfuric acid in different solvents at room temperature.[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	Acetonitrile	15	98
2	Acetone	175	99
3	Chloroform	52	99
4	Dichloromethane	30	98
5	Ethyl acetate	55	90
6	Ethanol	360	–[c]

Notes: [a] Substrate/poly(4-vinylpyridinium nitrate): (1 mmol/0.338 g). [b] Isolated yield. [c] No reaction.



Scheme 4. Coupling of thiols with poly(4-vinylpyridinium nitrate) in the absence of acid.

Table 5. Oxidative coupling of thiols to corresponding disulfides with poly(4-vinylpyridinium nitrate) in acetonitrile at room temperature.[a]

Entry	Substrate	Product	Time (Min)	Yield (%)[b]	Mp (°C) found	Mp (°C) reported	Reference
1	**1a**	**2a**	150	99	88–93	90–92	(*8*)
2	**1b**	**2b**	230	91	Oil	Oil	(*22*)
3	**1c**	**2c**	110	99	40–42	43–44	(*8*)
4	**1d**	**2d**	160	90	277–285	278–280	(*22*)
5	**1e**	**2e**	70	87	Oil	Oil	(*22*)
6	**1f**	**2f**	150	95	139–142	144–146	(*8*)
7	**1g**	**2g**	380	Sluggish	–	–	–
8	**1h**	**2h**	25	97	84–90	77.5–79	(*22*)
9	**1i**	**2i**	15	98	177–180	177–179	(*8*)

Notes: [a] Substrate/poly(4-vinylpyridinium nitrate) for Entries 1–5 and 7–9 (1 mmol/0.338 g); for Entry 6 (1 mmol/0.507 g). [b] Isolated yield.

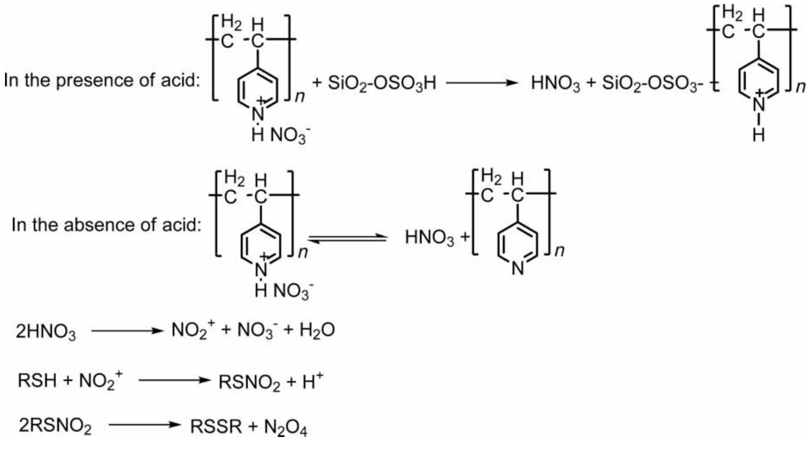
Table 6. Recoverability of poly(4-vinylpyridinium nitrate) for the coupling of 2-mercaptobenzothiazole.

Run no.	Time (min)	Yield (%)[a]
1	15	99
2	10	95
3	9	97
4	12	98
5	11	98

Note: [a] Isolated yield.

The results show that the appropriate solvent for the oxidative coupling of thiols by poly(4-vinylpyridinium nitrate) in the absence of solid acids is different from the reaction in the presence of acid. Therefore, the best choice for the new conditions is acetonitrile. Eventually, all of the thiols were subjected to the oxidative coupling by poly(4-vinylpyridinium nitrate) in the absence of any acid (Scheme 4 and Table 5).

The important advantage of the coupling reaction using poly(4-vinylpyridinium nitrate) without any additive is the recoverability of the poly(4-vinylpyridinium nitrate). After reaction completion, poly(4-vinylpyridine) can be easily isolated by simple filtration. It could be converted into poly(4-vinylpyridinium nitrate) by reaction with nitric acid again. As is evident from Table 6, recycled



Scheme 5. Mechanism of the oxidative coupling of thiols.

poly(4-vinylpyridinium nitrate) is reusable for five times and its activity dose not show any significant decrease.

The proposed mechanism for the oxidative coupling of thiols into disulfides by described systems is outlined in Scheme 5.

3. Conclusion

In summary, in this research, a new oxidizing polymer has been introduced for the preparation of disulfides in the presence of solid acids in the absence of any acid under mild and heterogeneous conditions. Poly(4-vinylpyridinium nitrate) is a recoverable, metal-free and non-toxic polymeric oxidizing agent, which could be recognized as a new and green organic agent.

4. Experimental

The chemicals and solvents were purchased from Fluka, Merck, and Aldrich chemical companies without further purifications. All products are known and were characterized by comparison of their spectral (IR, ^{1}H NMR, or ^{13}C NMR) and physical data with authentic samples.

4.1. *Preparation of poly(4-vinylpyridinium nitrate)*

In a 50 ml round-bottomed flask, 2 ml of HNO_3 (65%) and 3.03 g of poly(4-vinylpyridine) was stirred for 1 h, then kept at 50°C for 48 h to obtain dry poly(4-vinylpyridinium nitrate) as a white crystalline solid quantitatively.

4.2. *Oxidative coupling of 2-mercaptobenzoxazole into 1,2-bis(2-benzoxazol)disulfane using poly(4-vinylpyridinium nitrate) and silica sulfuric acid: as a typical procedure*

Poly(4-vinylpyridinium nitrate) (0.338 g) and silica sulfuric acid (0.2 g) was added to a solution of 2-mercaptobenzoxazole (0.167 g, 1 mmol) in ethyl acetate (10 ml). The resulting mixture was stirred at room temperature for 10 min (the reaction progress was monitored by TLC) and then filtered. The residue was washed with ethyl acetate (4 × 5 ml). Finally, the solvent was removed and 1,2-bis(2-benzoxazol)disulfane was obtained in 97% yield (0.323 g) as a crystalline white solid; mp 176–178°C (Lit. (*8*) 177–179°C).

4.3. *Oxidative coupling of 2-mercaptobenzoxazole using poly(4-vinylpyridinium nitrate) without solid acid: as a typical procedure*

Poly(4-vinylpyridinium nitrate) (0.338 g) was added to a solution of 2-mercaptobenzoxazole (0.167 g, 1 mmol) in acetonitrile (10 ml). The resulting mixture was stirred at room temperature for 15 min (the reaction progress was monitored by TLC) and then filtered. The residue was washed with acetonitrile (4 × 5 ml). Finally, the solvent was evaporated and 1,2-bis(2-benzoxazol)disulfane was obtained in 98% yield (0.326 g) as a crystalline white solid; mp 177–180°C (Lit. (*8*) 177–179°C).

Acknowledgement

This work was supported by the research facilities of Ilam University, Ilam, Iran.

References

(1) Ghorbani-Choghamarani, A.; Chenani, Z.; Mallakpour, S. *Synthetic Commun.* **2009,** *39,* 4264–4270.
(2) Evangelisti, C.; Panziera, N.; Pertici, P.; Vitulli, G.; Salvadori, P.; Battocchio, C.; Polzonetti, G. *J. Catal.* **2009,** *262,* 287–293.
(3) Chari, M.A.; Syamasundar, K. *Catal. Commun.* **2005,** *6,* 67–70.
(4) Iranpoor, N.; Tamami, B.; Niknam, K. *Can. J. Chem.* **1997,** *75,* 1913–1919.
(5) Lakouraj, M.M.; Mokhtary, M. *Monatsh. Chem.* **2009,** *140,* 53–56.
(6) Akdag, A.; Webb, T.; Worley, S.D. *Tetrahedron Lett.* **2006,** *47,* 3509–3510.
(7) Alam, A.; Takaguchi, Y.; Tsuboi, S. *Synth. Commun.* **2005,** *35,* 1329–1333.
(8) Montazerozohori, M.; Karami, B.; Azizi, M. *Arkivoc* **2007,** 99–104.
(9) Hosseinzadeh, R.; Tajbakhsh, M.; Khaledi, H.; Ghodrati, K. *Monatsh. Chem.* **2007,** *138,* 871–873.
(10) Imanieh, H.; Ghamami, S.; Mohammadi, M.K.; Jangjoo, A. *Russ. J. Gen. Chem.* **2007,** *77,* 282–284.
(11) Golchoubian, H.; Hosseinpoor, F. *Catal. Commun.* **2007,** *8,* 697–700.
(12) Silveira, C.C.; Mendes, S.R. *Tetrahedron Lett.* **2007,** *48,* 7469–7471.
(13) Joshi, G.; Bhadra, S.; Ghosh, S.; Agrawal, M.K.; Ganguly, B.; Adimurthy, S.; Ghosh, P.K.; Ranu, B.C. *Ind. Eng. Chem. Res.* **2010,** *49,* 1236–1241.
(14) Ghafuri, H.; Hashemi, M.M. *J. Sulfur Chem.* **2009,** *30,* 578–580.
(15) Yan, J.; Tao, H.; Zeng, M.; Tao, J.; Mang, S.; Yan, Z.; Wang, W.; Wang, J. *Chin. J. Catal.* **2009,** *30,* 856–858.
(16) Witt, D. *Synthesis* **2008,** 2491–2509.
(17) Zolfigol, M.A.; Shirini, F.; Zamani, K.; Ghofrani, E.; Ebrahimi, S. *Phosphorus Sulfur Silicon Relat. Elem.* **2004,** *179,* 2177–2182.
(18) Zolfigol, M.A. *Tetrahedron* **2001,** *57,* 9509–9511.
(19) Iranpoor, N.; Firouzabadi, H.; Pourali, A.R. *Synlett* **2004,** 347–349.
(20) Misra, A.K.; Agnihotri, G. *Synth. Commun.* **2004,** *34,* 1079–1085.
(21) Khodaei, M.M.; Mohammadpoor-Baltork, I.; Nikoofar, K. *Bull. Korean Chem. Soc.* **2003,** *24,* 885–886.
(22) Ghorbani-Choghamarani, A.; Hajjami, M.; Goudarziafshar, H.; Nikoorazm, M.; Mallakpour, S.; Sadeghizadeh, F.; Azadi, G. *Monatsh. Chem.* **2009,** *140,* 607–610.
(23) Ghorbani-Choghamarani, A.; Zolfigol, M.A.; Rastegar, T. *Chin. J. Catal.* **2009,** *30,* 273–275.
(24) Goudarziafshar, H.; Ghorbani-Choghamarani, A.; Nikoorazm, M.; Naserifar, Z. *Chin. J. Chem.* **2009,** *27,* 1801–1804.
(25) Ghorbani-Choghamarani, A.; Nikoorazm, M.; Goudarziafshar, H.; Shiri, L.; Chenani, Z. *Bull. Korean Chem. Soc.* **2009,** *30,* 972–974.
(26) Ghorbani-Choghamarani, A.; Goudarziafshar, H.; Rezaee, S.; Mortazavi, S.S. *Chin. Chem. Lett.* **2009,** *20,* 415–419.
(27) Ghorbani-Choghamarani, A.; Zolfigol, M.A.; Hajjami, M.; Rastgoo, S.; Mallakpour, S. *Lett. Org. Chem.* **2010,** *7,* 249–254.