Pergamon

TETRAHEDRON

Tetrahedron 58 (2002) 5179–5184

Dinitrogen tetroxide supported on polyvinylpyrrolidone (PVP–N_2O_4): a new nitrosating and coupling agent for thiols and a selective oxidant for sulfides and disulfides

Nasser Iranpoor,* Habib Firouzabadi* and Ali-Reza Pourali

Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

Received 4 December 2001; accepted 5 April 2002

Abstract—Gaseous N_2O_4 was immobilized on polyvinylpyrrolidone to give a stable polymeric reagent. Thiols were converted to *S*-nitrosothiols (thionitrites) using this new nitrosating agent in *n*-hexane or $CHCl_3$ at 10°C. With this reagent, thiols were also converted into their corresponding disulfides. Selective oxidation of sulfides to sulfoxides and disulfides to thiosulfonates can also be achieved by this reagent at room temperature. By using an excess of the reagent, the selective one-pot synthesis of thiosulfonates from thiols at room temperature was also performed. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Over the last decade, close attention has been paid to the potent chemical and biological properties of compounds possessing the *S*-nitroso, disulfide, and thiosulfonate functional groups, which are synthetically useful sulfenylating agents[1–4] and photolytic sources of thiyl radicals.[5] *S*-Nitrosothiols have attracted increasing attention because of having a potential medical use as nitric oxide donors,[6–9] and were used in many useful organic syntheses such as the synthesis of α-alkylthio oximes[5a] (or *C*-nitroso compounds)[10] from alkenes, decarboxylative nitrosation of Barton esters,[5b,c] direct conversion of amines to the corresponding halides,[11] fluorination of heterocyclic amines,[11c] α-oximation of methylene groups in ketones or α-haloketones,[11c,12,13] facile cleavage of C=N bond to ketones;[11c] desulfurization of thioacetals, thioketals[11c] and thiocarbonyls,[14] reductive deimination of sulfoximides and sulfimides,[15] and nitrosation of metal centers or addition to metalloporphyrins.[16]

The use of gaseous N_2O_4 in an inert solvent at low temperature has been reported to convert thiols into their corresponding *S*-nitrosothiols.[3,17] However, the reaction is very heat sensitive and should be carefully controlled to avoid overoxidation reactions.[18]

The supported nitrosation reagents on inorganic K10 montmorillonite clay such as 'claycop' and 'clayfen' (clay impregnated with copper nitrate and ferric nitrate, respectively) have also been used for nitrosation of thiols.[19] However, the produced thionitrite is immediately oxidized into the corresponding disulfides by the copper and iron ions present in the reagents.

Recently, we have used inorganic and organic complexes of N_2O_4 such as $Cu(NO_3)_2{\cdot}N_2O_4$[20] and $[NO^+{\cdot}18\text{-crown-}6{\cdot}H(NO_3)_2^-]$[21] instead of gaseous N_2O_4 for nitrosation of thiols. In the case of using $Cu(NO_3)_2{\cdot}N_2O_4$, similar to the reaction with claycop and clayfen, the generated thionitrites were immediately oxidized into disulfide due to the presence of Cu(II) in the nitrosating agent. In the case of using $[NO^+{\cdot}18\text{-crown-}6{\cdot}H(NO_3)_2^-]$, the reagent was soluble and its separation from the solution of thionitrite was not possible. Similar disadvantages could be considered for the preparation of thionitrites using oxalic acid and sodium nitrite in *tert*-butanol.[22]

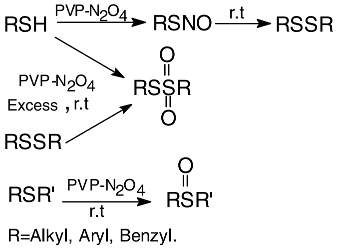
In order to overcome the problem of high reactivity of gaseous N_2O_4 and also to be able to produce pure solution of thionitrites under hetergenous conditions, we decided to prepare polyvinylpyrrolidone (PVP) supported N_2O_4 as a heterogeneous reagent. The choice of PVP for this purpose is due to its high complexing ability with gaseous NO_2.[23] In comparison with the recently reported reagents for nitrosation of thiols, such as $[NO^+{\cdot}18\text{-crown-}6{\cdot}H(NO_3)_2^-]$[21] and oxalic acid/sodium nitrite,[22] the use of this polymer supported N_2O_4 provides the possibility of having a pure solution of thionitrites by a simple filtration. The other attractive aspect of this polymeric reagent is that toxic and noxious N_2O_4 gas could be immobilized, thereby improving its general acceptability, safety, handling, and utility under mild reaction conditions.[24] We report here on the use of

---

Keywords: *S*-nitrosothiol; thiol; sulfide; sulfoxide; thiosulfonate; dinitrogen tetroxide; polyvinylpyrrolidone; oxidant.

* Corresponding authors. Tel.: +98-711-2284822; fax: +98-711-2280926; e-mail: iranpoor@chem.susc.ac.ir; firouzabadi@chem.susc.ac.ir

PII: S0040-4020(02)00390-3



Scheme 1.

PVP–N_2O_4 as a new, efficient, and easy to handle reagent for mild nitrosation of thiols at 10°C. This reagent can also be used for coupling of thiols to disulfides, selective oxidation of sulfides to sulfoxides and disulfides to thiosulfonates at room temperature. By using an excess of this reagent, the selective synthesis of thiosulfonates from thiols under mild reaction conditions can also be performed (Scheme 1).

2. Results and discussion

Polyvinylpyrrolidone-supported N_2O_4, (PVP–N_2O_4) is a safe, cheap and easily prepared source of N_2O_4. This reagent was simply prepared by dissolving polyvinylpyrrolidone (PVP) in dichloromethane and adding liquid N_2O_4 at 0°C while the solution was gently stirred. After 1 h, bubbling of N_2 gas into the solution extrudes the excess of N_2O_4 as NO_2 and then the solvent was evaporated.

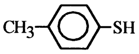
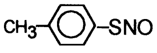
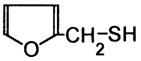
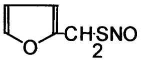
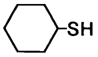
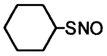
The obtained polymeric reagent was dried under vacuum and the resulting solid mass was ground in a mortar to produce a pale green powder. On the basis of the obtained weight of the PVP–N_2O_4, the capacity of this polymeric reagent was found to be 5 mmol of N_2O_4 per each gram of the reagent.

Based on the amount of absorbed N_2O_4 per each unit of polymer, a 1:1 addition compound (PVP–N_2O_4) is probable. This kind of addition compound has already been proposed for different ethers (or amines) and N_2O_4.[25] The IR spectrum of a dilute solution of PVP–N_2O_4 in CH_2Cl_2 showed a strong absorption band centered at 1355 cm^{-1} similar to that which we observed for its ether or amine complexes at 1360 cm^{-1}. The observed decrease in the frequency of carbonyl band of the PVP–N_2O_4, (KBr disk, 1645 cm^{-1}) in comparison with the band for PVP, (KBr disk, 1665 cm^{-1}) could account for the interaction of N_2O_4 with the oxygen atom of the amide group in this polymeric reagent. This polymeric reagent is stable below 0°C and could be stored in the refrigerator for several months without loss of its weight or activity.

When a solution of thiol (1 mmol in 2 mL of $CHCl_3$ or *n*-hexane) was treated with 0.2 g of the reagent at 10°C in the dark, an immediate change in the color of reaction occurred and the mixture became bright red or reddish green, characteristic color of thionitrites, except for *tert*-butyl thionitrite,[11b,17a,b] which became dark green. The advantage of using this reagent is that by a simple filtration the solution of pure thionitrite is obtained which could be used for further synthetic purposes. In addition, the released polymer acts as an acid scavenger and removes the produced nitric acid from the reaction mixture. The filtered polymer, which was found by comparison with a known sample to be PVP–HNO_3, was easily recycled.[26] In Table 1, the reaction times for conversion of various thiols to their corresponding thionitrites and the spectral data of the products are shown. The UV–visible spectra of thionitrites showed the characteristic bands at 330–350 nm region (ε around 10^3 M^{-1} cm^{-1}, $n_0 \rightarrow \sigma^*$) and at 550–600 nm (ε around 20 M^{-1} cm^{-1}, $n_N \rightarrow \sigma^* >$).[3,8a,17b,27]

Due to the steric hindrance of the tertiary alkyl group, the reaction of *tert*-butyl mercaptan with this reagent did not proceed at room temperature and was performed under reflux (Table 1). The remarkably stable *tert*-butyl thionitrite was further oxidized to the colorless and stable thionitrate [$(CH_3)_3CSNO_2$],[11b,17a,b,28] when it was refluxed with 3 molar equiv. of the reagent in $CHCl_3$ for 6 h.

Table 1. Reaction of thiols with equimolar amount of PVP–N_2O_4 at 10°C

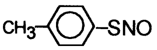
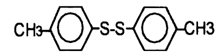
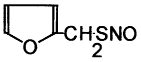
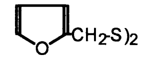
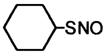
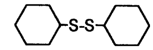
Thiol	Thionitrite	Time in $CHCl_3$ (*n*-hexane) (min)	Spectral data (in *n*-hexane) λ_{max} (nm) (ε)[a]
iso-C_3H_7SH	*iso*-C_3H_7SNO	10 (60)	341 (750), 518 (12), 557 (25)
n-C_4H_9SH	*n*-C_4H_9SNO	14 (40)	340 (820), 519 (12), 550 (28)
sec-C_4H_9SH	*sec*-C_4H_9SNO	60 (120)	342 (900), 517 (14), 553 (25)
n-$C_8H_{17}SH$	*n*-$C_8H_{17}SNO$	15 (200)	340 (750), 515 (12), 549 (18)
C_6H_5SH	C_6H_5–SNO	15 (8)	261, 380, 530 (27), 570 (42)
$C_6H_5CH_2$–SH	$C_6H_5CH_2$–SNO	35 (14)	340 (1030), 530 (18), 560 (26)
		4 (10)	261, 382 (265), 532 (27), 575 (50)
		12 (8)	266, 378 (138), 545 (29)
		100 (250)	336 (890), 521 (15), 550 (21)
t-C_4H_9SH	*t*-C_4H_9SNO[b,c]	300	345 (675), 562 (7), 552 (6), 598 (17), 605 (16)

[a] Reference to the products.[3]

[b] The reaction was refluxed in $CHCl_3$.

[c] The reaction with 3 molar equiv. of PVP–N_2O_4 produced S-nitro thiol (*tert*-$C_4H_9SNO_2$) after 6 h under reflux in $CHCl_3$.

Table 2. Preparation of disulfides from thionitrites

Thionitrite	Product[a]	Solvent	Time (min)	Yield[b] %
iso-C_3H_7SNO	(*iso*-$C_3H_7S)_2$	$CHCl_3$	10	95
n-C_4H_9SNO	(*n*-$C_4H_9S)_2$	*n*-Hexane	5	90
sec-C_4H_9SNO	(*sec*-$C_4H_9S)_2$	$CHCl_3$	15	88
n-$C_8H_{17}SNO$	(*n*-$C_8H_{17}S)_2$	$CHCl_3$	7	90
C_6H_5SNO	$(C_6H_5S)_2$	$CHCl_3$	10	92
$C_6H_5–CH_2SNO$	$(C_6H_5–CH_2S)_2$	$CHCl_3$	15	80
		*n*-Hexane	5	92
		*n*-Hexane	5	82
		$CHCl_3$	25	80
tert-C_4H_9SNO[c]	(*tert*-$C_4H_9S)_2$	$CHCl_3$	120	0

All *S*-nitrosothiol solutions were prepared at similar concentration (0.5 mol l^{-1}) and stirred in the presence of air.

[a] Reference to the products.[20,42]

[b] Isolated yield.

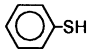
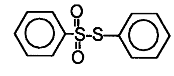
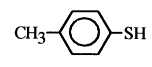
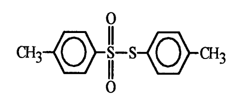
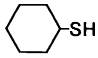
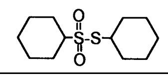
[c] The reaction was performed under reflux for 2 h.

Most of the thionitrites are thermally[3,29] and photochemically[3,30] unstable, especially in the presence of O_2.[31,32] We observed that if the reaction of thiols with PVP-supported N_2O_4 was stirred for a longer period of time in the presence of air at room temperature, the thionitrite intermediate could be converted into the corresponding disulfides with high yields without adding any extra reagent. The results obtained for the conversion of thiols into disulfides are shown in Table 2.

Thiosulfonates (thiosulfonic *S*-esters) have been reported to be strong sulfenylating agents, which react even faster than disulfides.[1,33a,b] In addition, as source of sulfenylating agent, they are considered to be more stable than sulfinyl chlorides and their handling is much easier and safer. They are also used for temporary blocking of mercapto groups in protein chemistry.[34]

Thiosulfonates are the intermediary compounds in the reduction of sulfonyl chlorides to disulfides with Me_3SiI,[35] or tetrathiotungstates.[36] There are also other routes reported in the literature for their preparation.[37] However, their one-pot synthesis from thiols by use of excess N_2O_4 at low temperatures (ca. −20°C) has been considered as a synthetically useful approach.[18a] This latter method suffers from over oxidation of thiosulfonates into sulfonic acids as by products. In this reaction, the intermediacy of RS(O)NO or $RS(O)NO_2$ followed by their conversion into α-disulfoxide is proposed for the formation of thiosulfonates.

Table 3. Reaction of thiols with 3 molar equiv. of $PVP–N_2O_4$

Entry	Thiol	Product[a]	Isolated yield (%)
1	*n*-C_4H_9SH	$^nC_4H_9–SO_2–S–^nC_4H_9$	85
2	*n*-$C_8H_{17}SH$	$^nC_8H_{17}–SO_2–S–^nC_8H_{17}$	80
3			88
4			92
5			90

All the reactions were performed in $CHCl_3$ at room temperature for 4 h.

[a] Reference to the products.[18a,33b]

We observed that thiosulfonates were the only product of the reaction of thiols when 3 molar equiv. of $PVP–N_2O_4$ were used in chloroform at room temperature. The results of the reaction of thiols with $PVP–N_2O_4$ are shown in Table 3. This reaction proceeded via disulfide intermediate since the disulfide was isolated when the reaction was stopped at early stage (Scheme 2, Eq. 1). The produced disulfide from the reaction of thiol with $PVP–N_2O_4$ reacts with excess of the reagent to form the unstable α-disulfoxide (Scheme 2, Eq. 2), which in the subsequent step oxygen transfer[38] occurs to form the stable thiosulfonate (Scheme 2, Eq. 3).

$$\text{RSH} \xrightarrow{\text{PVP-N}_2\text{O}_4} \text{RSSR} \qquad \text{Eq. 1}$$

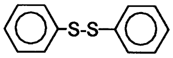
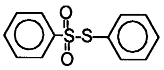
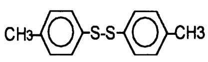
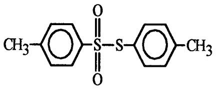
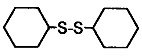
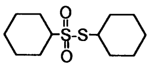
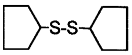
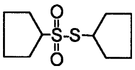
$$\text{RSSR} \xrightarrow[\text{(Excess)}]{\text{PVP-N}_2\text{O}_4} [\text{RS(O)S(O)R}] \qquad \text{Eq. 2}$$

$$[\text{RS(O)S(O)R}] \longrightarrow \text{RSO}_2\text{SR} \qquad \text{Eq. 3}$$

Scheme 2.

In order to have more evidence in support of the intermediacy of disulfide in this reaction, we performed a reaction between diphenyl disulfide and $PVP–N_2O_4$ in chloroform at room temperature. The reaction furnished *S*-phenyl benzenethiosulfonate in 90% yield after 3 h. Since the reaction of disulfides with reactive gaseous N_2O_4 in CCl_4 has been reported to produce sulfonic acid anhydrides,[39] we therefore extended our studies and performed the reaction of different disulfides with 4 molar equiv. of the polymeric reagent in $CHCl_3$ at room temperature to obtain their corresponding thiosulfonates.

Table 4. Reaction of disulfides with PVP–N_2O_4

Entry	Disulfide	Product[a]	Isolated yield (%)
1	$^nC_4H_9$–S–S–$^nC_4H_9$	$^nC_4H_9$–SO_2–S–$^nC_4H_9$	88
2			93
3			95
4			92
5			80

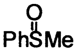
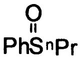
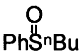
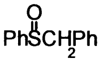
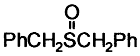
All reactions were performed in $CHCl_3$ for 3 h at room temperature.

[a] The products were identified by comparison of their spectral data with known samples.[18a,33b]

The results obtained from these reactions are shown in Table 4.

Gaseous dinitrogen tetroxide was also known to be a good reagent for the oxidation of sulfides to sulfoxides.[40,41] We therefore studied the applicability of PVP–N_2O_4 for this oxidation at room temperature. By use of this polymeric reagent, different sulfides were smoothly converted into their corresponding sulfoxides without the need for temperature control to avoid over oxidation into sulfones. The results are shown in Table 5.

Table 5. Reaction of sulfides with PVP–N_2O_4

Entry	Sulfide	Product[a]	Isolated yield (%)
1	CH_3–S–CH_3	$(CH_3)_2S{=}O$	85
2	$^nC_4H_9$–S–$^nC_4H_9$	$(^nC_4H_9)_2S{=}O$	80
3	PhSMe	 $Ph\overset{O}{\overset{\|}{S}}Me$	82
4	PhSEt	 $Ph\overset{O}{\overset{\|}{S}}Et$	91
5	PhS–^{n}Pr	 $Ph\overset{O}{\overset{\|}{S}}{}^nPr$	89
6	PhS–^{n}Bu	 $Ph\overset{O}{\overset{\|}{S}}{}^nBu$	95
7	$PhSCH_2Ph$	 $Ph\overset{O}{\overset{\|}{S}}CH_2Ph$	85
8	$PhCH_2SCH_2Ph$	 $PhCH_2\overset{O}{\overset{\|}{S}}CH_2Ph$	91

All reactions were performed in $CHCl_3$ for 2 h at room temperature.

[a] Reference to the products.[42,43]

3. Conclusion

Formation of 1,1-adduct of polyvinylpyrrolidone with N_2O_4 gives a stable polymeric reagent. The use of this polymeric reagent provides the possibility of preparing pure solution of thionitrites under heterogeneous condition.

Due to the lower reactivity of this polymeric reagent compared to dinitrogen tetroxide, thiols can be selectively converted into their corresponding thionitrites, disulfides or thiosulfonates using different quantities of the reagent and reaction conditions. In addition, the conversion of disulfides into thiosulfonates and sulfides into sulfoxides can be simply achieved with this reagent without over oxidation. The mildness of the reaction conditions, easy and safe handling of the reagent and easy work-up of the reaction mixtures make this polymeric reagent a new and safe source of dinitrogen tetroxide in organic synthesis.

4. Experimental

Chemicals were purchased from Fluka, Aldrich and Merck chemical companies. All the solvents were dried and redistilled. Polyvinylpyrrolidone K-30 (average M_w 40,000) was purchased from Fluka Company. Liquid N_2O_4 prepared from 98% H_2SO_4 and fuming 100% HNO_3 in the presence of Arsenious oxide and condensed by a salt-ice bath as the Brook's procedure.[44] Disulfides (Table 4) were prepared by standard methods.[45] Thin layer chromatography (TLC) on commercial plates of silica gel 60 F_{254} and GLC by a Shimadzu GC-14A instrument was used to monitor the progress of the reactions and to determine the purity of substrates. Column chromatography was carried out using silica gel 60. Yields refer to isolated pure products after column chromatography. Products were characterized by comparison with authentic samples (mp, bp, UV, IR, ^1H NMR). UV spectra were recorded on an Ultraspec 3000 Pharmacia Biotech spectrophotometer. IR and ^1H NMR spectra were recorded on Perkin–Elmer 781 and Bruker DPX 250 instruments, respectively.

4.1. Preparation of polyvinylpyrrolidone-supported N_2O_4 (PVP–N_2O_4)

To a solution of PVP (10 g) in dichloromethane (250 mL) at 0°C, was added 8 mL of liquid N_2O_4 (liquefied in a salt-ice bath) by a pipette while the solution was gently stirred. After 1 h, bubbling of dry N_2 gas was performed through the solution in order to extrude the excess of NO_2 and then the solvent was evaporated. The obtained solid was dried under vacuum and was powdered in a mortar to give PVP supported N_2O_4 (18 g) as a pale green powder material. The capacity of the reagent was determined to be 5 mmol of N_2O_4 per gram of the polymer. The reagent could be stored in the refrigerator for several months without loss of its weight or activity.

4.1.1. Typical procedure for the preparation of *S*-nitrosothiols. To a stirred solution of thiophenol (0.11 g, 1 mmol) in $CHCl_3$ (2 mL), 0.2 g of the reagent was added at 10°C in the dark and under atmosphere of argon. The mixture became immediately bright red to reddish green, characteristic of thionitrites. The reaction mixture was monitored by GLC and TLC until thiol was consumed. The reaction mixture was filtered after 15 min. Evaporation of the solvent under reduced pressure and at low temperatures (<10°C) in the dark, yielded *S*-nitroso thiophenol quantitatively. UV (*n*-hexane): 261, 380, 530 (27), 570 (42) nm (ε) [lit.,[3] 261, 380, 530 (27), 570 (42) nm (ε)]. The solution of thionitrite in *tert*-butanol can be stored in the refrigerator.

4.1.2. Procedure for the preparation of *tert*-butyl thionitrate. To a solution of 2-methyl-2-propane thiol (0.09 g, 1 mmol) in $CHCl_3$ (5 mL), the reagent (0.6 g) was added and the reaction mixture was refluxed for 6 h. TLC monitored the reaction mixture until the obtained thionitrite was consumed. The reaction mixture was then filtered. Evaporation of the solvent under reduced pressure gave 0.107 g (90%) *S*-nitroso 2-methyl-2-propane thiol (*tert*-butyl thionitrate) as colorless oil: bp 40–42°C/6 mmHg (lit.,[46] 55°C/13 mmHg). IR (neat): 2950, 1515 (NO), 1300, 1260, 1156, 820 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.58 (s) ppm. UV (*n*-hexane): 201 (5700), 268 (3400) nm (ε).

4.1.3. Typical procedure for the preparation of disulfides. To a stirred solution of thiophenol (0.11 g, 1 mmol) in $CHCl_3$ (2 mL), the reagent (0.2 g) was added at room temperature. The reaction mixture was stirred for 25 min until the color changed from dark red to pale yellow. The reaction mixture was filtered. Evaporation of the solvent followed by purification of the product by chromatography on a short column of silica gel eluted with *n*-hexane, afforded diphenyl disulfide (0.10 g, 92%), mp 58–60°C; (lit.,[37a] mp 58°C); IR(KBr): 3070, 3050, 1575, 1475, 1430, 1070, 1020, 995, 740 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.49 (4H), 7.27 (4H), 7.20 (2H) ppm.

4.1.4. Typical procedure for the preparation of thiosulfonates from thiols. To the solution of *p*-thiocresole (0.124 g, 1 mmol) in $CHCl_3$ (5 mL), the reagent (0.6 g) was added with stirring at room temperature. After 4 h, the reaction mixture was filtered. The filtrate was washed with aqueous solution of $NaHCO_3$ (5%) and then with water. The organic layer was separated and dried over $MgSO_4$ Evaporation of the solvent followed by chromatography on a short column of silica gel eluted with *n*-hexane–EtOAc 5:1 gave *S*-(4-methylphenyl)4-methylbenzenethiosulfonate (0.13 g, 92%); mp 72–74°C (lit.,[33b] mp 73–75°C).

4.1.5. Typical procedure for the oxidation of disulfides to thiosulfonates. Di (*p*-tolyl) disulfide (0.246 g, 1 mmol) was dissolved in $CHCl_3$ (5 mL). To this solution, the reagent (0.8 g) was added with stirring at room temperature. After 3 h, the reaction mixture was worked up as preceding procedure to afford *S*-(4-methylphenyl)4-methylbenzenethiosulfonate (0.26 g, 95%); mp 72–74°C (lit.,[33b] mp 73–75°C).

4.1.6. Typical procedure for the oxidation of sulfides to sulfoxides. To a solution of benzyl sulfide (0.214 g, 1 mmol) in $CHCl_3$ (4 mL), the reagent (0.4 g) was added with stirring at room temperature. After 2 h, the reaction mixture was filtered. Evaporation of the solvent followed by chromatography on a short column of silica gel (eluted with *n*-hexane followed by Et_2O) afforded benzyl sulfoxide (0.21 g, 91%); mp 133–134°C (lit.,[47] mp 135–136°C).

Acknowledgement

The authors are thankful to Shiraz University Research Council for the partial support of this work.

References

1. (a) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363–382. (b) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405–4412. (c) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887–4902.
2. Hart, T. W. *Tetrahedron Lett.* **1985**, *26*, 2013–2016.
3. Oae, S.; Kim, Y. H.; Fukushima, D.; Shinhama, K. *J. Chem. Soc., Perkin Trans. 1* **1978**, 913–917.
4. Oae, S.; Kim, Y. H.; Shinhama, K. *Bull. Chem. Soc. Jpn* **1980**, *53*, 1771–1772.
5. (a) Cavero, M.; Motherwell, W. B.; Potier, P. *Tetrahedron Lett.* **2001**, *42*, 4377–4379. (b) Girard, P.; Guillot, N.; Motherwell, W. B.; Hay-Motherwell, R. S.; Potier, P. *Tetrahedron* **1999**, *55*, 3573–3584. (c) Girard, P.; Guillot, N.; Motherwell, W. B.; Potier, P. *J. Chem. Soc., Chem. Commun.* **1995**, 2385–2386. (d) Oae, S.; Kim, Y. H.; Fukushima, D.; Takata, T. *Chem. Lett.* **1977**, 893–896.
6. (a) Jia, L.; Bonaventura, C.; Bonaventura, J.; Stamler, J. S. *Nature* **1996**, *380*, 221–226. (b) Feldman, P. L.; Griffith, O. W.; Stuehr, D. J. *Chem. Engng News* **1993**, *20*, 26–37. (c) Ignarro, L. J. *Angew. Chem. Int. Ed.* **1999**, *38*, 1882–1892. (d) Kown, S.; George, S. C. *Nitric Oxide: Biol. Chem.* **1999**, *3*, 348–357.
7. (a) Roy, B.; d'Hardemare, A. duM.; Fontecave, M. *J. Org. Chem.* **1994**, *59*, 7019–7026. (b) Petit, C.; Hoffmann, P.; Souchard, J.-P.; Labidalle, S. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1997**, *129*, 59–68.
8. (a) Williams, D. L. H. *Acc. Chem. Res.* **1999**, *32*, 869–876. (b) Williams, D. L. H. *Chem. Commun.* **1996**, 1085–1091. (c) Noble, D. R.; Swift, H. R.; Williams, D. L. H. *Chem. Commun.* **1999**, 2317–2318. (d) Askew, S. C.; Barnett, D. J.; McAninly, J.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1995**, 741–745. (e) Butler, A. R.; Williams, D. L. H. *Chem. Soc. Rev.* **1993**, *22*, 233–241.
9. (a) Hou, Y.; Wu, X.; Xie, W.; Braunschweiger, P. G.; Wang, P. G. *Tetrahedron Lett.* **2001**, *42*, 825–829. (b) Goto, K.; Hino, Y.; Kawashima, T.; Kaminaga, M.; Yano, E.; Yamamoto, G.; Takagi, N.; Nagase, S. *Tetrahedron Lett.* **2000**, *41*, 8479–8483. (c) deFallois, L. L. H.; D'ecout, J.-L.;

Fontecave, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2587–2595.

10. Chandra, H.; Gowenlock, B. G.; Pfab, J. *J. Chem. Soc., Chem. Commun.* **1979**, 392–393.
11. (a) Oae, S.; Shinhama, K.; Kim, Y. H. *Tetrahedron Lett.* **1978**, *19*, 4519–4522. (b) Oae, S.; Shinhama, K.; Kim, Y. H. *Bull. Chem. Soc. Jpn* **1980**, *53*, 1065–1069. (c) Kim, Y. H. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1993**, *74*, 249–260.
12. Kim, Y. H.; Park, Y. J.; Kim, K. *Tetrahedron Lett.* **1989**, *30*, 2833–2836.
13. Kim, Y. H.; Jung, S. H. *Tetrahedron Lett.* **1981**, *22*, 2371–2372.
14. Kim, H. J.; Kim, Y. H. *Tetrahedron Lett.* **1987**, *28*, 1669–1670.
15. Oae, S.; Iida, K.; Takata, T. *Phosphorus Sulfur* **1981**, *12*, 103–114.
16. (a) Yi, G.-B.; Khan, M. A.; Richter-Addo, G. B. *Chem. Commun.* **1996**, 2045–2046. (b) Bladon, P.; Dekker, M.; Knox, G. R.; Willison, D.; Jaffari, G. A.; Doedens, R. J.; Muir, K. W. *Organometallics* **1993**, *12*, 1725–1741.
17. (a) Oae, S.; Kim, Y. H.; Fukushima, D. *J. Chem. Soc., Chem. Commun.* **1977**, 407–408. (b) Oae, S.; Shinhama, K.; Fujimori, K.; Kim, Y. H. *Bull. Chem. Soc. Jpn* **1980**, *53*, 775–784. (c) Oae, S.; Shinhama, K. *Org. Prep. Proced. Int.* **1983**, *15*, 165–198.
18. (a) Kim, Y. H.; Shinhama, K.; Fukushima, D.; Oae, S. *Tetrahedron Lett.* **1978**, 1211–1212. (b) Capozzi, G.; Modena, G. In *Chemistry of the Thiol Group*, Patai, S., Ed.; Wiely: New York, 1974; pp 785–786 Chapter 17.
19. (a) Cornelis, A.; Depaye, N.; Gerstmans, A.; Laszlo, P. *Tetrahedron Lett.* **1983**, *24*, 3103–3106. (b) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909–918. (c) Cornelis, A.; Laszlo, P. *Synlett* **1994**, 155–161.
20. Iranpoor, N.; Firouzabadi, H.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 367–375.
21. Iranpoor, N.; Firouzabadi, H.; Heydari, R. *J. Chem. Res. (S)* **1999**, 668–669.
22. Zolfigol, M. A.; Nematollahi, D.; Mallekpour, S. *Synth. Commun.* **1999**, *29*, 2277–2280.
23. Davydov, E. Y. A.; Pustoshnyi, V. P.; Pariyskii, G. B.; Zaikov, G. E. *Int. J. Polym. Mater.* **2000**, *46*, 107–120.
24. (a) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815–4195. (b) Sherrington, D. C. *J. Polym. Sci. Part A: Polym. Chem.* **2001**, *39*, 2364–2377.
25. (a) Rubin, B.; Sisler, H. H.; Shechter, H. *J. Am. Chem. Soc.* **1952**, *74*, 877–882. (b) Davenport, D. A.; Burkhardt, H. J.; Sisler, H. H. *J. Am. Chem. Soc.* **1953**, *75*, 4175–4178. (c) Whanger, J. G.; Sisler, H. H. *J. Am. Chem. Soc.* **1953**, *75*, 5188–5191.
26. The IR spectrum of the filtered polymer was found to be exactly similar to the polymer which was obtained from the reaction of PVP and nitric acid. To regenerate the PVP–N_2O_4, the filtered polymer (0.5 g) was stirred in CH_2Cl_2 (10 mL) in the presence of basic alumina (1.0 g) for 15 min. The filtered solution was then reacted with N_2O_4 as described for the preparation of the reagent.
27. Barrett, J.; Fitzgibbons, L. J.; Glauser, J.; Still, R. H.; Young, P. N. W. *Nature* **1966**, *211*, 848.
28. Oae, S.; Shinhama, K.; Kim, Y. H. *Chem. Lett.* **1979**, 1077–1081 See also Refs. 11b, 17b, 18.
29. Van Zwet, H.; Kooyman, E. C. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 45–48.
30. Barrett, J.; Debenham, D. F.; Glauser, J. *J. Chem. Soc., Chem. Commun.* **1965**, 248–249.
31. Ignarro, L. J.; Lippton, H.; Edwards, J. C.; Baricos, W. H.; Hyman, A. L.; Kadowitz, P. J.; Gruetter, C. A. *J. Pharmacol. Exp. Ther.* **1981**, *218*, 739–749.
32. (a) Pryor, W. A.; Church, D. F.; Govindan, C. K.; Crank, G. *J. Org. Chem.* **1982**, *47*, 156–159. (b) Josephy, P. D.; Rehorek, D.; Janzen, E. G. *Tetrahedron Lett.* **1984**, *25*, 1685–1688. (c) Lu, J.-M.; Wittbrodt, J. M.; Wang, K.; Wen, Z.; Schlegel, H. B.; Wang, P. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **2001**, *123*, 2903–2904.
33. (a) Rajca, A.; Wiessler, M. *Tetrahedron Lett.* **1990**, *31*, 6075–6076. (b) Palumbo, G.; Caputo, R. *Synthesis* **1981**, 888–889.
34. Smith, D. J.; Maggio, E. T.; Kenyon, G. L. *Biochemistry* **1975**, *14*, 766–771.
35. Kielbasinski, P.; Drabowicz, J.; Mikolajczyk, M. *J. Org. Chem.* **1982**, *47*, 4806–4808.
36. Dhar, P.; Ranjan, R.; Chandrasekaran, S. *J. Org. Chem.* **1990**, *55*, 3728–3729.
37. (a) Mahieu, J.-P.; Gosselet, M.; Sebille, B.; Beuzard, Y. *Synth. Commun.* **1986**, *16*, 1709–1722. (b) Field, L.; Parsons, T. F. *J. Org. Chem.* **1965**, *30*, 657–659. (c) Field, L.; Barbee, R. B. *J. Org. Chem.* **1969**, *34*, 1792–1798. (d) Cipris, D.; Pouli, D. *Synth. Commun.* **1979**, *9*, 207–212. (e) Vara Prasad, J. V. N.; Panapoulous, A.; Rubin, J. R. *Tetrahedron Lett.* **2000**, *41*, 4065–4068.
38. (a) Oae, S.; Kim, Y. H.; Takata, T.; Fukushima, D. *Tetrahedron Lett.* **1977**, 1195–1198. (b) Chau, M.; Kice, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 7711–7714. (c) Oae, S.; Takata, T. *Tetrahedron Lett.* **1980**, *21*, 3213–3216.
39. Kunieda, N.; Oae, S. *Bull. Chem. Soc. Jpn* **1968**, *41*, 233–234.
40. Madesclaire, M. *Tetrahedron* **1986**, *42*, 5459–5495.
41. (a) Oae, S.; Kunieda, N.; Tagaki, W. *Chem. Ind.* **1965**, *23*, 1790–1791. (b) Luk'yanitsa, V. G.; Gal'pern, G. D. *Neftekhimiya* **1985**, *25*, 103–109 *Chem. Abstr.* **1985**, *102*, 169342y. (c) Addison, C. C.; Sheldon, J. C. *J. Chem. Soc.* **1956**, 2705–2708.
42. Firouzabadi, H.; Iranpoor, N.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 1179–1187.
43. Yang, R.-Y.; Dai, L.-X. *Synth. Commun.* **1994**, *24*, 2229–2236.
44. Brook, A. G. *J. Chem. Soc.* **1952**, 5040–5041.
45. *Organic Functional Group Preparations*, Sandler, S. R., Karo, W., Eds.; Academic: New York, 1968; pp 489–490.
46. Kresze, G.; Uhlich, U. *Chem. Ber.* **1959**, *92*, 1048–1051.
47. Johnson, C. R.; Keiser, J. E. *Org. Synth.* **1966**, *46*, 78–80.