NBS as a Powerful Catalyst for the Synthesis of β-Hydroxysulphides with Thiolysis of Epoxides under Mild Reaction Conditions

Amin Rostami[a*] and Hadi Jafari[b]

[a]*Department of Chemistry, Faculty of Science, University of Kurdistan, Sanandaj 66177-15143, Iran.*
[b]*Faculty of Science, Islamic Azad University of Sanandaj, Sanandaj, Iran.*

Received 24 April 2008, revised 16 September 2008, accepted 19 September 2008.

ABSTRACT

***N*-Bromosuccinimide (NBS) catalyses the ring opening of various epoxides with different thiols in CH_3CN at room temperature under mild reaction conditions. The corresponding β-hydroxysulphides are obtained in short reaction times and in good to high yields with nearly complete regioselectivity. The catalyst was compared with previously reported catalysts and only one that we have found [$B(C_6F_5)_3$] gave the same regioselectivity, but the reaction time was much longer (4 h *versus* 5 min) and the yield was considerably lower. $Zn(ClO_4)_2{\cdot}6H_2O$ gave slightly lower selectivity but higher yields. The reaction time was about 12 times longer.**

KEYWORDS

***N*-Bromosuccinimide, thiols, ring opening, epoxides, β-hydroxysulphides.**

1. Introduction

β-Hydroxysulphides are valuable intermediates that have been used for the synthesis of allyl alcohols,[1] cyclic sulphides,[2] a number of important natural products,[3] and a variety of compounds with pharmacological and/or biological activity.[4,5]

The ring opening of 1,2-epoxides by sulphur-containing nucleophiles (thiolates, thiols and disulphides) is a convenient, practical and widely employed strategy for the synthesis of β-hydroxysulphides. Thiolysis of 1,2-epoxides with thiols to yield β-hydroxysulphides has been promoted in the presence of some activating agents such as Et_3N,[6] $(n\text{-}Bu)_4NF$,[7] $B(C_6F_5)_3$,[8] $InCl_3$,[9] *p*-TsOH,[9] $LiClO_4$,[9] CsF-celite,[10] $AlPW_{12}O_{40}$,[11] Zn(II),[12] $LiClO_4{\cdot}3H_2O$,[13] [Emim]BF_4,[14] HBF_4-SiO_2,[15] $Zn(ClO_4)_2{\cdot}6H_2O$,[16] $Sc(OTf)_3$,[17] 1,5,7-triazabicyclo[4.4.0]dec-5-ene (PS-TBD),[18] indium-bipyridine,[19] montmorillonite K-10,[20] Sn(IV)(TPP)$(BF_4)_2$,[21] $MgBr_2{\cdot}OEt_2$,[22] cyanuric chloride[23] and additive-free.[24] However, some of these reagents suffer from disadvantages such as the use of stoichiometric amounts of the reagents, requirement of excess thiols, drastic reaction conditions, prolonged reaction times, elevated temperatures, moisture sensitive/hazardous/costly reagents, poor regioselectivity and low yields. Thus there is a need for the development of protocols using readily available reagents under mild conditions to overcome the above limitations.

In the last decade organocatalysis has became a field of great interest.[25] Organocatalysts are usually robust, inexpensive, readily available, non-toxic and inert towards moisture and oxygen. Because of the absence of transition metals, organocatalytic methods seem to be especially attractive for the preparation of compounds that do not tolerate metal contamination such as pharmaceutical products.

2. Results and Discussion

In continuation of our interest in the application of *N*-halo compounds in organic synthesis,[26] we have found that NBS is an inexpensive, commercially available and versatile reagent.[27] This reagent has recently been used as an effective catalyst for the acetalization of carbonyl compounds,[28] the conversion of aldehydes to 1,1-diacetates,[29] and acylation of alcohols[30] under mild and nearly neutral reaction conditions. In this paper we present the catalytic application of NBS as a selective reagent for the efficient ring opening of various epoxides with different thiols in CH_3CN.

At first the effect of different ratios of RSH/catalyst was examined. A ratio of 1:0.05 for thiols gave the best result and produced β-hydroxysulphides in good to high yields (see Table 1).

In order to understand the scope and limitations of NBS as a catalyst for the preparation of β-hydroxysulphides, various epoxides were treated with aromatic, benzylic, heterocyclic, cyclic and aliphatic (primary, secondary and tertiary) thiols. The results are shown in Table 2.

Interestingly, the reaction of tert-butyl thiol (as a model for tertiary thiols) and 2-mercapto benzimidazolyl (as a model for heterocyclic thiols) with different epoxides gave the corresponding β-hydroxysulphides in good to excellent yield at room temperature.

Unsymmetrical epoxides underwent cleavage by a variety of thiols with preferential attack at the less substituted carbon atom, except for styrene epoxide, for which the thiol attack is driven predominantly, as expected, at the benzylic carbon by electronic effects. Complete regio- and chemoselectivity were observed for the reaction of thiols with epichlorohydrin. This reaction gives the corresponding β-hydroxysulphides via nucleophilic attack of thiols at the less substituted carbon atom of the epoxide.

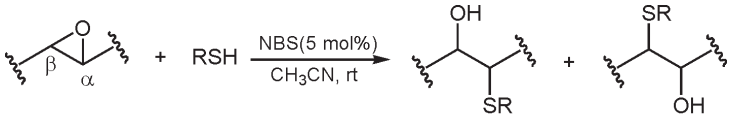
In order to study the catalytic activity of NBS, we compared our results for the reaction of styrene epoxide with thiophenol, with the best of the well-known data from literature (Table 3). As shown in Table 3, NBS, as catalyst, shows higher regioselectivity for the ring-opening of styrene epoxide with thiophenol in a shorter reaction time.

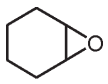
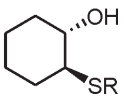
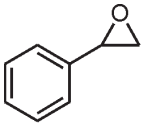
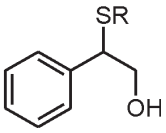
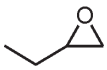
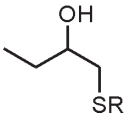
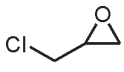
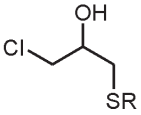
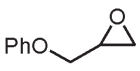
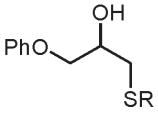
* To whom correspondence should be addressed. E-mail:a_rostami372@yahoo.com, a.rostami@uok.ac.ir

Table 1 The effect of different ratios of RSH/catalyst for ring opening of epoxides.

Entry	Epoxide	Thiol	Ratio RSH:NBS	Time/min	Yield/%
1	styrene epoxide	PhSH	1:0.01	5	50
2	styrene epoxide	PhSH	1:0.03	5	100
3	styrene epoxide	PhSH	1:0.04	5	100
4	styrene epoxide	PhSH	1:0.05	5	100
5	1,2- butane epoxide	PhSH	1:0.01	5	trace
6	1,2- butane epoxide	PhSH	1:0.03	5	50
7	1,2- butane epoxide	PhSH	1:0.04	5	70
8	1,2- butane epoxide	PhSH	1:0.05	5	85
9	styrene epoxide	t-butylthiol	1:0.01	5	trace
10	styrene epoxide	t-butylthiol	1:0.03	5	50
11	styrene epoxide	t-butylthiol	1:0.04	5	60
12	styrene epoxide	t-butylthiol	1:0.05	5	80

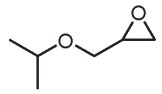
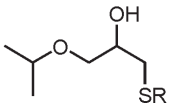
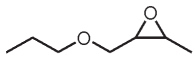
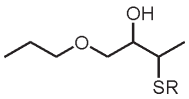
Table 2 NBS-catalysed ring opening of epoxides by thiols in CH_3CN at room temperature.



Entry	Epoxide	Product [a,b]	R	Ratio α/β [c]	Time/min	Yield(isolated) [d,e]/%
1			a) R =phenyl		5	92(82)
			b) R = benzyl		10	90(84)
			c) R = furfuryl		90	50
			d) R =benzimidazol		10	90(80)
			e) R = cyclohexyl		25	84(73)
			f) R = n-butyl		35	90(85)
			g) R = t-butyl		30	90(83)
2			a) R =phenyl	0/100	5	100(93)
			b) R = benzyl	5/95	10	100(95)
			c) R = furfuryl	10/90	45	83(76)
			d) R =benzimidazol	0/100	5	90(83)
			e) R = cyclohexyl	0/100	15	85(70)
			f) R = n-butyl	10/90	20	92(83)
			g) R = t-butyl	10/90	15	90(80)
3			a) R =phenyl	100/0	5	85(80)
			b) R = benzyl	95/5	10	94(86)
			c) R = furfuryl	90/10	90	50
			d) R =benzimidazol	90/10	15	90(82)
			e) R = cyclohexyl	80/20	45	85(74)
			f) R = n-butyl	90/10	45	80(74)
			g) R = t-butyl	90/10	30	87(80)
4			a) R =phenyl	100/0	5	90(83)
			b) R = benzyl	100/0	10	92(86)
			c) R = furfuryl	100/0	90	trace
			d) R =benzimidazol	100/0	15	85(82)
			e) R = cyclohexyl	100/0	50	93(84)
			f) R = n-butyl	100/0	60	90(84)
			g) R = t-butyl	100/0	35	90(85)
5			a) R =phenyl	95/5	5	91(85)
			b) R = benzyl	95/5	10	90(85)
			c) R = furfuryl	50/50	90	93(85)
			d) R =benzimidazol	90/10	10	91(83)
			e) R = cyclohexyl	85/15	20	90(85)
			f) R = n-butyl	80/20	30	92(85
			g) R = t-butyl	80/20	35	90(85)

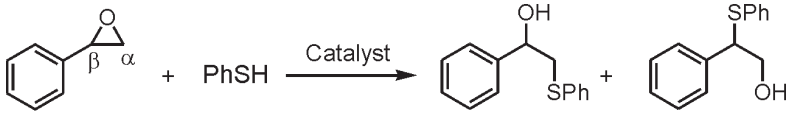
Continued on p. 117

Table 2 — *continued*.

6			a) R =phenyl	100/0	5	100(97)
			b) R = benzyl	100/0	10	100(97)
			c) R = furfuryl	100/0	90	trace
			d)R =benzimidazol	85/15	15	95(89)
			e) R = cyclohexyl	90/10	35	90(86)
			f) R = n-butyl	70/30	40	96(86)
			g) R = t-butyl	70/30	40	91(85)
7			a) R =phenyl	100/0	5	90(81)
			b) R = benzyl	100/0	10	91(82)
			c) R = furfuryl	100/0	90	trace
			d)R =benzimidazol	90/10	20	90(82)
			e) R = cyclohexyl	90/10	30	83(76)
			f) R = n-butyl	80/20	40	82(75)
			g) R = t-butyl	90/10	40	90(84)

[a] All the compounds were characterized by IR and NMR spectroscopy and compared with authentic samples.[12–15]
[b] All the 1,2-epoxides considered in this paper gave only *anti*-oxirane ring opening.
[c] Regioselectivity was determined by GC and ^{1}H-NMR.
[d] Conversion.
[e] Refer to the sum of both products.

Table 3 Comparison of the activity of various catalysts for ring opening of styrene epoxide with thiophenol at room temperature.



(C-α) (C-β)

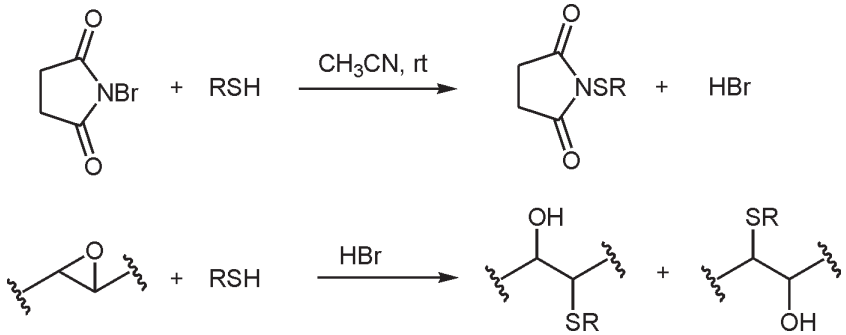
Entry	Catalyst	Conditions	Catalyst/mol%	Time/min	Yield/%	Ratio α/β	Ref.
1	NBS	CH_3CN, rt	5	5	90	0/100	–
2	$AlPW_{12}O_{40}$	CH_3CN, rt	2	10	90	15/85	11
3	$LiClO_4 \cdot 3H_2O$	solvent-free, rt	12.5	20	98	17/83	13
4	Zn(II)	H_2O, rt	10	20	100	16/84	12
5	*p*-TsOH	solvent-free, rt	5	2880	73	5/95	9
6	$InCl_3$	solvent-free, rt	1	10	85	5/95	9
7	$B(C_6F_5)_3$	CH_2Cl_2, rt	5	240	84	0/100	8
8	$Zn(ClO_4)_2 \cdot 6H_2O$	solvent-free, rt	2.5	60	99	2/98	16
9	Et_3N	MeOH, rt	100	240	99	55/45	6

At this stage the precise role of NBS is not clear. However, on the basis of previous reports of the catalytic application of NBS,[22] one hypothesis about the role of NBS for this process is that NBS probably generates small quantities of HBr *in situ*, which may be the actual catalyst for the ring-opening reaction (Scheme 1). The actual role of this catalyst should be further studied in detail.

3. Conclusion

In conclusion, notable features of this methodology are as follows:

NBS is an inexpensive organocatalyst, commercially available, moisture-insensitive, non-metallic, with low toxicity, corrosive and air stable. The reactions take place in short reaction times, under mild conditions and in good to high yields with nearly complete regioselectivity. In this method, the use of protic acids and metallic Lewis acids is avoided. Therefore, the reaction conditions are mild and are not sufficiently acidic to cause side reactions. Comparison of the results obtained using NBS as catalyst with recently reported methods indicate the superiority of the present protocol in terms of reaction time, yields and regioselectivity.



Scheme 1

4. Experimental

4.1. General Procedure for the Synthesis of β-Hydroxysulphides

To a mixture of epoxide (5 mmol) and NBS (0.25 mmol) in CH_3CN (5 mL), thiol (5 mmol) was added and the mixture was stirred at room temperature for the specified time (see Table 2). The progress of the reaction was monitored by TLC. On completion of the reaction, the solvent was removed under reduced pressure and the crude products (where necessary) were purified through simple plate chromatography (ethyl acetate: *n*-hexane, 1:4) to obtain pure β-hydroxysulphides.

Selected spectral data for 1-chloro-3-phenylsulphanyl-propan-2-ol (Table 2, entry 4a) are:

IR(Neat): 3630-3220, 1570, 1475, 740 and 690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.88 (br, 1H, OH), 3.05–3.18 (m, 2H, CH_2S), 3.72 (d, 2H, J = 8.00 Hz, $ClCH_2$), 3.90–4.10 (m, 1H, OCH) and 7.20–7.50 ppm (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): δ 38.60, 48.40, 69.90, 127.30, 129,70, 130.50 and 135.10 ppm.

Acknowledgements

The authors thank the University of Kurdistan Research Councils for partial support of this work.

References

1 V. Kesavan, D. Bonnet-Delpon and J.-P. Begue, *Tetrahedron Lett.,* 2000, **41**, 2895–2898.

2 S. Ozaki, E. Matsui, H. Yoshinaga and S. Kitagawa, *Tetrahedron Lett.,* 2000, **41**, 2621–2624.

3 T. Hashiyama, *Med. Res. Rev.,* 2000, **20**, 485–501.

4 M.J. Martinelly, R. Vaidyanathan, V.V. Khaun and M.A. Staszak, *Tetrahedron Lett.,* 2002, **43**, 3365–3367.

5 T. Furutani, R. Imashiro, M. Hatsuda and M. Seki, *J. Org. Chem.,* 2002, **67**, 4599–4601.

6 M. Chini, P. Crotti, E. Giovanni, F. Macchia and M. Pineschi, *Synlett,* 1992, 303–305.

7 D. Albanese, D. Landini and M. Penso, *Synthesis,* 1994, 34–36.

8 S. Chandrasekhar, C.R. Reddy, B.N. Babu and G. Chandrashekar, *Tetrahedron Lett.,* 2002, **43**, 3801–3803.

9 M.M. Mojtahedi, H. Abassi, M. Saeed Abaee and B. Mohebali, *Monatsh. Chem.*, 2006, **137**, 455–458.

10 V. Polshettiwar and M. P. Kaushik, *Catal. Commun.,* 2004, **5**, 515–518.

11 H. Firouzabadi, N. Iranpoor, A.A. Jafari and S. Makarem, *J. Mol. Catal. A: Chem.,* 2006, **250**, 237–242.

12 F. Fringuelli, F. Pizzo, S. Tortoioli and L. Vaccaro, *J. Org. Chem.,* 2003, **68**, 8248–8251.

13 N. Azizi and M.R. Saidi, *Catal. Commun.,* 2006, **7**, 224–227.

14 J.X. Chen, H.Y. Wu, C. Jin, X.X. Zhang, Y.Y. Xie and W.K. Su, *Green Chem.,* 2006, **8**, 330–332.

15 B.P. Bandgar, A.V. Patil, O.S. Chavan and V.T. Kamble, *Catal. Commun.,* 2007, **8**, 1065–1069.

16 Shivani and A.K. Chakraborti, *J. Mol. Catal. A: Chem.,* 2007, **263**, 137–142.

17 C. Ogawa, N. Wang and S. Kobayashi, *Chem. Lett.,* 2007, **36**, 34–35.

18 F. Fringuelli, F. Pizzo, C. Vittoriani and L. Vaccaro, *Eur. J. Org. Chem.,* 2006, 1231–1236.

19 M.V. Nandakumar, A. Tschop, H. Krautscheid and C. Schneider, *Chem. Commun.,* 2007, 2756–2758.

20 M.M. Mojtahedi, M.H. Ghasemi, M. Saeed Abaee and M. Bolourtchian, *Arkivoc,* 2005, 68–73.

21 M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork and S.A. Taghavi, *Catal Commun.*, 2007, **8**, 2087–2095.

22 M.M. Mojtahedi, M.S. Abaee, M. Bolourtchian and H. Abbasi, *Phosphorus, Sulfur,* 2007, **182**, 905–910.

23 B.P. Bandgar, N.S. Joshi, V.T. Kamble and S.S. Sawant, *Aust. J. Chem.*, 2008, **61**, 231–234.

24 S.M. Abaee, M.M. Mojtahedi, H. Abbasi and E.R. Fatemi, *Synthetic Commun.*, 2008, **38**, 282–289.

25 (a) P.I. Dalko and L. Moisan, *Angew. Chem. Int. Ed. Engl.,* 2004, **43**, 5138–5175; (b) R.O. Duthaler, *Angew. Chem. Int. Ed. Engl.,* 2003, **42**, 975–978.

26 (a) A. Khazaei, A.A. Manesh and A. Rostami, *J. Chem. Res – S*, 2004, 695–696; (b) A. Khazaei, A. Rostami, Z. Tanbakochian and Z. Zinati, *J. Braz. Chem. Soc.,* 2006, **17**, 206–208; (c) A. Khazaei, A. Rostami and M. Mahboubifar, *Catal. Commun.,* 2007, **8**, 383–388; (d) A. Khazaei, A. Rostami, A. Raiatzadeh and M. Mahboubifar, *Can. J. Chem.,* 2007, **85**, 336–340; (e) A. Rostami, M. Mahboubifar and A. Khazaei, *S. Afr. J. Chem.,* 2008, **61**, 9–12.

27 K. Taraknath, *Synlett,* 2006, 496–497.

28 B. Karimi, G.R. Ebrahimian and H. Seradj, *Org. Lett.,* 1999, **1**, 1737–1739.

29 B. Karimi, H. Seradj and G.R. Ebrahimian, *Synlett,* 2000, 623–624.

30 B. Karimi and H. Seradj, *Synlett,* 2001, 519–520.