Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 1291–1293
Tetrahedron Letters

Selectfluor™: a novel and efficient reagent for the synthesis of β-hydroxy thiocyanates

J. S. Yadav,* B. V. S. Reddy and Ch. Srinivas Reddy

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500-007, India

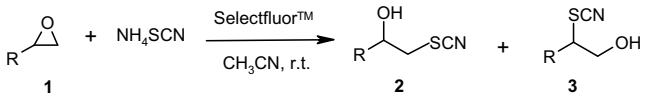
Received 13 August 2003; revised 10 November 2003; accepted 21 November 2003

Abstract—A variety of epoxides undergo rapid ring opening with ammonium thiocyanate in the presence of 10 mol% Selectfluor™ in acetonitrile at room temperature to afford the corresponding β-hydroxy thiocyanates in excellent yields with high regioselectivity.
© 2003 Elsevier Ltd. All rights reserved.

Oxiranes are well-known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo regioselective ring opening reactions contributes largely to their synthetic value.[1] Consequently, several methods have been developed for the regioselective ring opening of epoxides with various nucleophiles to produce ring-opened products.[2] The ring opening of epoxides with thiocyanates is a widely used method for the preparation of thiiranes.[3] The formation of thiiranes from oxiranes and thiocyanates has been explained by the intermediacy of the corresponding β-hydroxy thiocyanate. However, β-hydroxy thiocyanates have not been isolated due to rapid conversion into the corresponding thiiranes.[4] Thus, very few methods are reported for the preparation of β-hydroxy thiocyanates.[5,6] Most of these methods involve high temperature reaction conditions to obtain ring-opened products, which are not only detrimental to certain functional groups, but also to the control of regioselectivity. Polymeric phase-transfer catalysts have been reported to perform the epoxide ring opening with thiocyanates under mild conditions.[7] Since organo-sulfur compounds are useful and important in organic synthesis, the development of simple, convenient and efficient catalytic systems for the preparation of β-hydroxy thiocyanates especially those which carry acid labile functional groups, are desirable. Recently, Selectfluor™ has been introduced commercially as a user-friendly electrophilic fluorinating agent. Selectfluor™ is readily available at low cost and is easy to handle and also retains its activity even in the presence of amines.[8] More recently, Selectfluor™ has been employed as an efficient Lewis acid catalyst for the one-pot allylation reactions of imines and for the hydrolysis of acetals, dithia-acetals and tetrahydropyranyl ethers.[9] However, there are no examples of the use of Selectfluor™ as a catalyst for the cleavage of epoxides with thiocyanates.

Herein we report the use of Selectfluor™ as a novel and efficient catalyst for the preparation of β-hydroxy thiocyanates by a regioselective ring opening of epoxides with ammonium thiocyanate under mild conditions[10] (Scheme 1).

Treatment of styrene oxide with ammonium thiocyanate in the presence of 10 mol% Selectfluor™ in acetonitrile afforded β-hydroxy thiocyanates **2** and **3** as a mixture in 80% and 15% yields, respectively. Aryl substituted epoxides underwent cleavage by thiocyanate in a regioselective manner with preferential attack at the less hindered position (Table 1, entries a, c and d). Glycidyl aryl ethers and esters also gave the corresponding β-hydroxy thiocyanate **2** in high yields (Table 1, entries h–o) with high regioselectivity. No trace of the other regioisomers of **3** were observed during the cleavage of glycidyl aryl ethers with ammonium thiocyanate under the reaction conditions. Similarly, hexene oxide

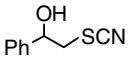
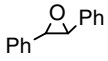
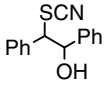
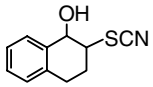
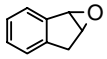
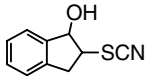
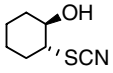
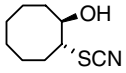
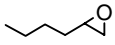
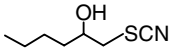
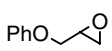
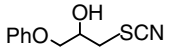
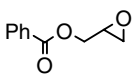
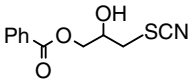
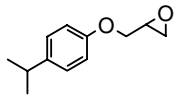
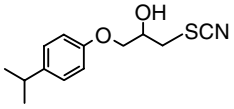
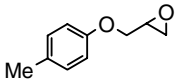
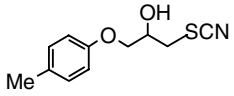
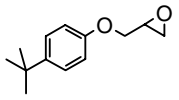
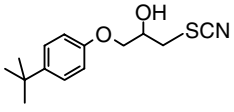
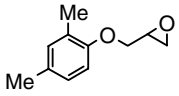
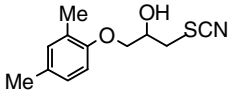
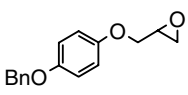
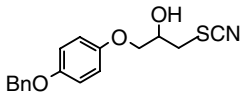
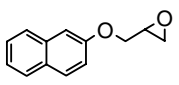
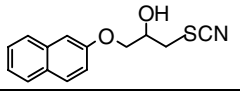


Scheme 1.

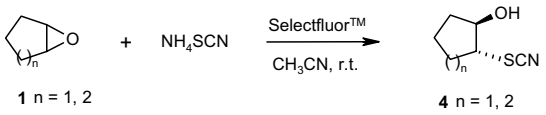
Keywords: Selectfluor™; Epoxides; β-Hydroxy thiocyanates.
* Corresponding author. Tel.: +91-402-7193434; fax: +91-402-7160-512; e-mail: yadav@iict.ap.nic.in

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.11.102

Table 1. Selectfluor™ promoted synthesis of β-hydroxy thiocyanates from epoxides

Entry	Epoxide	β-Hydroxy thiocyanate[a]	Reaction time (h)	Yield (%)[b]
a			2.5	80(15)[c]
b			3.5	92
c			4.0	75(20)[c]
d			3.0	70(15)[c]
e			4.5	89
f			6.0	85
g			4.5	75(10)[c]
h			3.5	90
i			5.0	86
j			4.0	91
k			3.0	95
l			3.5	89
m			4.0	94
n			3.5	92
o			5.0	90

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Isolated and unoptimized yields.
[c] Yield in parenthesis refers to the other regioisomer.



Scheme 2.

underwent cleavage by thiocyanate in a regioselective manner with preferential attack at the terminal position (Table 1, entry g). The structures and the regiochemical ratios of products were determined by ^{1}H NMR spectroscopy and also by comparison with authentic compounds.[6,7] In all cases, the reactions proceeded rapidly at room temperature with high efficiency. The β-hydroxy thiocyanates were obtained in excellent yields without the formation of corresponding thiiranes. Furthermore, cycloalkyl epoxides such as cyclohexene oxide and cyclopentene oxide reacted smoothly with ammonium thiocyanate to produce the corresponding β-hydroxy thiocyanates **4** under similar conditions (Scheme 2).

Except for the reactions of styrene oxide, hexene oxide, indene oxide and tetrahydronaphtho[1,2-*b*]oxirane, which gave minor amounts of the other regioisomer, the reactions of other epoxides were found to be highly regioselective affording a single product in good to excellent yields. In the case of cyclic epoxides, the stereochemistry of the ring opened products was found to be *trans* from the coupling constants of the ring hydrogens as has been observed in most the epoxide ring-opening reactions.[5–7] The direction of ring opening is that characteristically observed for terminal epoxides under S_N2 conditions, and is probably dictated by steric and electronic factors. The reactivity of several epoxides with ammonium thiocyanate was examined using various Lewis acids such as $CeCl_3{\cdot}7H_2O$, YCl_3, $TaCl_5$, $InCl_3$, $InBr_3$, $In(OTf)_3$, $Bi(OTf)_3$ and $Sc(OTf)_3$. In most of these cases, thiiranes were obtained exclusively and no β-hydroxy thiocyanate was isolated. Acetonitrile appears to be the solvent of choice giving the best results. The scope and generality of this process is illustrated with respect to various epoxides and ammonium thiocyanate and the results are presented in Table 1.

In summary, we describe a novel and efficient protocol for the synthesis of β-hydroxy thiocyanates by the regioselective ring opening of epoxides with ammonium thiocyanate using Selectfluor™ as a novel catalyst. This method offers several advantages including mild reaction conditions, high conversions, greater regioselectivity, short reaction times, clean reaction profiles, ease of handling and ready availability of the catalyst at low cost, which makes it a useful and attractive process for the synthesis of β-hydroxy thiocyanates.

Acknowledgements

B.V.S., Ch.S.R. thank CSIR New Delhi for the award of fellowships.

References and notes

1. (a) Bonini, C.; Righi, G. *Synthesis* **1994**, 225–238; (b) Shimizu, M.; Yoshida, A.; Fujisawa, T. *Synlett* **1992**, 204–206; (c) Smith, J. G. *Synthesis* **1984**, 629–656.
2. (a) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737–799; (b) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323–2367; (c) Hirose, T.; Sunazuka, T.; Zhi-ming, T.; Handa, M.; Vchida, R.; Shiomi, K.; Harigaya, Y.; Omura, S. *Heterocycles* **2000**, *53*, 777–784.
3. (a) Jankowski, K.; Harvey, R. *Synthesis* **1972**, 627; (b) Iranpoor, N.; Kazemi, F. *Synthesis* **1996**, 821–822; (c) Tamami, B.; Kiasat, A. R. *Synth. Commun.* **1996**, *26*, 3953–3958; (d) Brimeyer, M. O.; Mehrota, A.; Quici, S.; Nigam, A.; Regen, S. L. *J. Org. Chem.* **1980**, *45*, 4254–4255.
4. (a) Sander, M. *Chem. Rev.* **1966**, *66*, 297–339; (b) Vedejs, E.; Krafft, G. A. *Tetrahedron* **1982**, *38*, 2857–2881; (c) Iranpoor, N.; Kazemi, F. *Tetrahedron* **1997**, *53*, 11377–11382.
5. (a) Van Tamelen, E. E. *J. Am. Chem. Soc.* **1951**, *73*, 3444–3448; (b) Kawashima, K.; Eshiguro, T. *Chem. Pharm. Bull.* **1978**, *26*, 951–955; (c) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538–7539.
6. Sharghi, H.; Nasseri, M. A.; Niknam, K. *J. Org. Chem.* **2001**, *66*, 7287–7293.
7. Tamami, B.; Mahdavi, H. *Tetrahedron Lett.* **2002**, *43*, 6225–6228.
8. (a) Shibata, N.; Suzuki, E.; Asahi, T.; Shiro, M. *J. Am. Chem. Soc.* **2001**, *123*, 7001–7009; (b) Burkart, M. D.; Zhang, Z.; Hung, S.-C.; Wong, C.-H. *J. Am. Chem. Soc.* **1997**, *119*, 11743–11746.
9. (a) Liu, J.; Wong, C.-H. *Tetrahedron Lett.* **2002**, *43*, 3915–3917; (b) Liu, J.; Wong, C.-H. *Tetrahedron Lett.* **2002**, *43*, 4037–4039.
10. Experimental procedure: A mixture of epoxide (1 mmol) and ammonium thiocyanate (1 mmol) and Selectfluor™ (10 mol%) in acetonitrile (10 mL) was stirred at room temperature for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the solvent was evaporated under reduced pressure. Then the resulting product was directly charged onto a small silica gel column and eluted with a mixture of ethyl acetate: *n*-hexane (2:8) to afford pure β-hydroxy thiocyanate. Spectral data for selected products: *2-Hydroxy-2-phenylethyl thiocyanate* **3a**: Liquid, IR (neat): ν 2165, 1600, 1453, 1319, 1270, 1165, 1105, 1025, 710 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.80 (br s, OH, 1H), 3.05–3.25 (m, 2H), 4.95–5.05 (m, 1H), 7.25–7.45 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$): 42.5, 73.1, 113.0, 126.3, 128.4, 129.6, 135.7. EIMS: m/z: 179 M$^+$, 153, 140, 131, 119, 105, 91, 77, 45. *3-Phenoxy-2-hydroxypropyl thiocyanate* **3h**: Liquid, IR (neat): ν 2160, 1605, 1450, 1316, 1271, 1160, 1109, 1027, 711 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.95 (br s, OH, 1H), 3.05–3.15 (m, 1H), 3.20–3.29 (m, 1H), 4.05–4.10 (m, 2H), 4.25–4.30 (m, 1H), 6.80 (d, 2H, $J = 8.0$ Hz), 6.95 (t, 1H, $J = 7.9$ Hz), 7.20–7.30 (m, 2H). EIMS: m/z: 209 M$^+$, 170, 154, 139, 133, 117, 103, 80, 69, 56, 44. *1-(4-Isopropylphenoxy)-3-thiocyanato-2-propanol* **3j**: Liquid, IR (neat): ν 2167, 1601, 1457, 1311, 1278, 1165, 1101, 1030, 714 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20 (d, 6H, $J = 6.9$ Hz), 2.80–2.95 (m, 1H), 3.05–3.15 (m, 1H), 3.20–3.27 (m, 1H), 4.0–4.05 (m, 2H), 4.20–4.30 (m, 1H), 6.80 (d, 2H, $J = 8.1$ Hz), 7.15 (d, 2H, $J = 8.1$ Hz). EIMS: m/z: 251 M$^+$, 239, 207, 175, 161, 149, 133, 121, 107, 95, 81, 73, 55.