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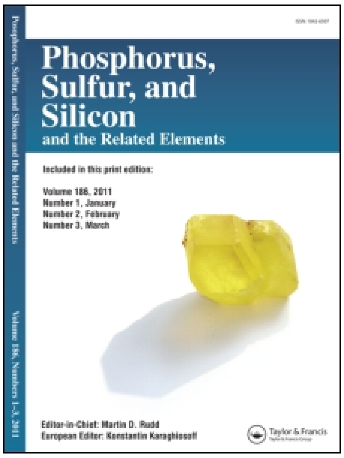

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2-Phenyl-2-(2-pyridyl)imidazolidine (PPI) as New Catalyst in the Efficient, Mild, and Regioselective Conversion of Epoxides to Thiocyanohydrines with Ammonium Thiocyanate

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2-PHENYL-2-(2-PYRIDYL)IMIDAZOLIDINE (PPI) AS NEW CATALYST IN THE EFFICIENT, MILD, AND REGIOSELECTIVE CONVERSION OF EPOXIDES TO THIOCYANOHYDRINES WITH AMMONIUM THIOCYANATE

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2-Phenyl-2-(2-pyridyl)imidazolidine (PPI) catalysis the addition of thiocyanate ion to epoxides to afford β-hydroxy thiocyanate in high yields, mild conditions, and regioselectivity. Thus, several 2-hydroxyethyl thiocyanates, which are useful intermediates toward biological active molecules, are obtained easily in very good yields.

Keywords: Epoxide; β-hydroxy thiocyanate; 2-Phenyl-2-(2-pyridyl) imidazolidine (PPI)

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Thiocyanates are important intermediates in agricultural and pharmaceutical chemistry. Beta-hydroxy thiocyanates represent an interesting subclass because they have multiple modes of reactivity. Synthetic access by epoxides opening with thiocyanate ion have been limited by further reaction to give thiiranes.[1,2] There are two methods reported in the literature for the synthesis of β-hydroxy thiocyanates. In one method, thiocyanohydrines are prepared by opening of a cyclic sulfate with NH_4SCN to form the corresponding β-sulfate, which is hydrolyzed to the thiocyanohydrines. A second method employed the addition to the epoxide of thiocyanic acid generated in situ at a low temperature.[3] For these syntheses, it has been reported that the presence of some hydroquinone or DDQ are required to stabilize the produced β-hydroxy thiocyanate and inhibit its conversion to thiirane.[4] Although the reagents such as Ti $(O\text{-}^{i}Pr)_4$.[5] $Ph_3P(SCN)_2$,[6] $TiCl_3$(or

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$ZnCl_2$),[7] and $Pd(PPh_3)_4$[8] are useful, they are limited to specific oxiranes and are not applicable as versatile reagents in preparation of β-hydroxy thiocyanates.[9]

RESULTS AND DISCUSSION

We already have reported the use of 2-phenyl-2-(2-pyridyl)imidazolidine (PPI) as a catalyst for conversion of epoxide into corresponding vicinal halohydrin with elemental halogen.[10] In conjunction with the ongoing work in our laboratory on the catalytic activities of PPI, we found out that PPI efficiently catalyzed the addition of ammonium thiocyanate to epoxide to form β-hydroxy thiocyanate in high yields under mild reaction conditions. DBU, DABCO, and Et_3N also were used as catalysts in these reactions. The results of the reaction of styrene oxide with thiocyanate ion in the presence of the above catalysts are summarized in Table I. In each case, cleavage of the epoxide ring occurs, and on workup, the corresponding thiocyanohydrin was obtained. The catalyst easily was recovered and could be reused several times. The optimum amount of the catalyst was found to be 0.02 equiv versus

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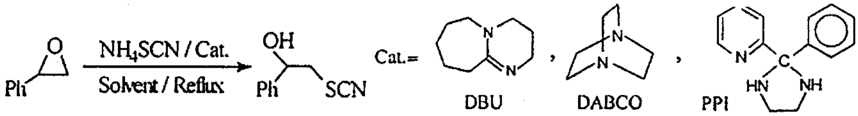
TABLE I Thiocyanative Cleavage of Styrene Oxide with NH_4SCN in the Presence of PPI, DBU, DABCO, and Et_3N in Different Solvents under Reflux Condition



Entry	Catalyst[a]	Solvent	Time (min)	Yield[b](%)
1	PPI	CH_3CN	45	95
2	DBU	CH_3CN	120	75
3	DABCO	CH_3CN	90	50
4	Et_3N	CH_3CN	150	45
5	—[c]	CH_3CN	190	d
6	PPI	$CHCl_3$	100	25
7	PPI	THF	110	70
8	PPI	Et_2O	100	<15
9	PPI	EtOH	95	30
10	PPI	C_6H_{12}	120	<10
11	PPI	CH_3COCH_3	100	35

[a] 0.02 mol%.

[b] Determined by GC.

[c] In the presence of excess of NH_4SCN.

[d] 35% of the corresponding thiirane was obtained (see Sharghi et al.[11]).

epoxides. By comparison, the cleavage of the styrene oxide with ammonium thiocyanate in the absence of catalyst is given in entry 5 of Table I. As shown in Table I, yields of thiocyanation with this new methodology were quite good and the reaction times are very low. PPI was the most effective, and the reaction was completed in 45 min. In the presence of other catalysts the reaction times for thiocyanation at 80°C are in the rang 90–150 min. However, the reaction of the styrene oxide with an excess of ammonium thiocyanate in the absence of catalyst afforded the corresponding thiirane in 35% yield, when refluxing the reaction mixture for 3 h.[11]

In order to ascertain the effect of nature of solvent, these reactions on the styrene oxide in various solvents were carried out. The results are shown in Table I. The above reactions appeared largely to be dependent on the nature of solvent.

The results obtained with some representative epoxides in the presence of PPI as catalyst are summarized in Table II. On the other hand, some other methods for conversion of epoxides into the corresponding thiocyanohydrins are given in Table II (entries 2, 3, 4, 5, and 8). When epoxides were allowed to react in the presence of our catalysts, the yield and the regioselectivity were higher to the observed in all of the reactions conditions studied.

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As indicated in Table 2, entry 7 only the trans isomer is obtained, and the reactions are completely anti-stereoselective. The regiochemical mode of epoxide cleavage by ammonium thiocyanate in the presence of PPI can be viewed as occurring via nucleophilic attack by thiocyanate ion on the less sterically hindered epoxide carbon. This mechanism closely resembles the S_N2 model for aliphatic nucleophilic displacement. On the basis of our study on the complexation of PPI with ammonium thiocyanate, it seems that in these reactions thiocyanate ion, ^{-}SCN, was formed and used as a nucleophile. The electronic absorption spectra of NH_4SCN, PPI, and PPI in the presence of NH_4SCN in CH_3CN solution are shown in Figure 1. As we can see, addition of ammonium thiocyanate to PPI has shown strong increasing on maximum absorption at 313 nm. As it is obvious, the PPI/NH_4SCN interaction results in a strong hyperchromic effect, presumably due to the complex formation of this ligand with ammonium thiocyanate.

In conclusion, the simplicity of this new method by using ammonium thiocyanate and PPI as catalyst, high yield, chemoselectivity and regioselectivity and the possibility of performing the reaction with different epoxide make this procedure a novel method for the synthesis of alkyl and functionalized alkyl thiocyanate.

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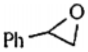
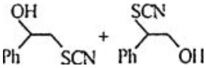
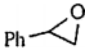
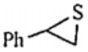
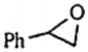
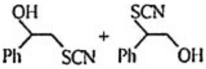
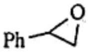
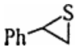
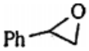
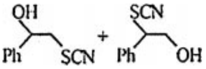
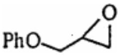
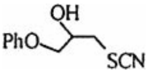
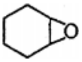
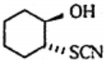
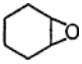
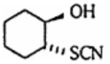
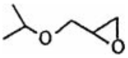
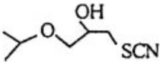
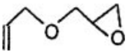
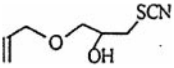
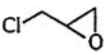
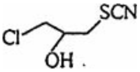
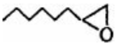
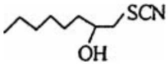
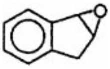
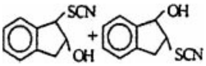
TABLE II Reaction of Various Epoxides with Ammonium Thiocyanate in the Presence of the Representative Catalyst

Entry	Epoxide	Catalyst (0.02)	Reaction conditions	Product(s)	Reaction time (min)	Yield%[a]
1		PPI	NH_4SCN/CH_3CN Reflux		45	95 (5:1)
2		$Pd(PPh_3)_4$[8]	NH_4SCN/N_2 THF/Reflux		120	35
3		$Ti(O\text{-}^iPr)_4$[5]	NH_4SCN THF/Reflux		240	30
4		$ZnCl_2$[7]	KSCN THF/Reflux		180	60
5		DDQ	NH_4SCN/CH_3CN Reflux		50	91 (1:8)[4b]
6		PPI	NH_4SCN/CH_3CN Reflux		55	93
7		PPI	NH_4SCN/CH_3CN Reflux		55	95
8		H_2Q[b]	$KSCN/H_3PO_4$ H_2O/Et_2O		—	48[3a]
9		PPI	NH_4SCN/CH_3CN Reflux		70	80
10		PPI	NH_4SCN/CH_3CN Reflux		65	83
11		PPI	NH_4SCN/CH_3CN Reflux		60	75
12		PPI	NH_4SCN/CH_3CN Reflux		65	85
13		PPI	NH_4SCN/CH_3CN Reflux		80	92

[a] Determined by GC.

[b] Hydroquinone has been used to stabilize 2-hydroxycyclohexyl thiocyanate (see Tamelen[3a]).

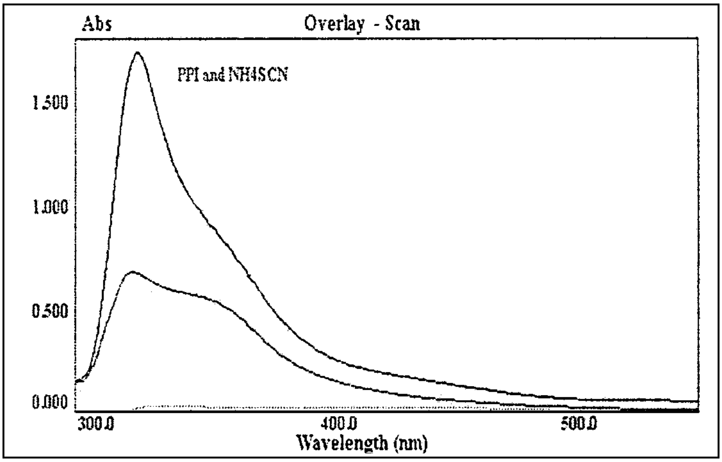


FIGURE 1 Absorption spectra from bottom to top refer to NH_4SCN, PPI, and PPI in the presence of NH_4SCN, in CH_3CN solution.

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EXPERIMENTAL

General

Epoxides and other chemical materials were purchased from Fluka and Merck in high purity. All of the thiocyanohydrin compounds were prepared by our procedure and their spectroscopic and physical data were compared with the literature.[4,6,7,11] NMR spectra were recorded in $CDCl_3$ on a Brucker Advanced Dpx-250 (^1H NMR 250 MHz and ^{13}C NMR 62.9 MHz) spectrophotometer using TMS as internal standard. UV-vis spectra were obtained with a Philips PU8750 spectrometer. GC spectra were recorded on a Shimadzu GC-14A. Infrared spectra were recorded on a Perkin Elmer IR-157G and a Perkin Elmer 781 spectrometer.

Typical Procedures

General Procedure for the Synthesis of Catalyst

Ethylenediamine (0.240 g, 4 mmol) was added to a solution of phenyl-2-pyridyl ketone (0.733 g, 4 mmol) in methanol. The reaction mixture was refluxed with stirring for about 16 h. The solvent then was evaporated to give a solid product. The crude product was recrystallized from dichloromethane (see Sharghi and Naeimi[10]).

General Procedure for Conversion of Epoxides to β-Hydroxy Thiocyanate Using PPI as Catalyst

To a mixture of epoxide (10 mmol) and NH_4SCN (10 mmol, 0.76 g) in acetonitrile (30 ml), a solution of catalyst (0.2 mmol) in CH_2Cl_2 (5 ml) was added and the mixture was stirred on the reflux condition for 45–80 min. The reaction was monitored by TLC or GC. After completion of the reaction, the mixture was filtered and the solvent was evaporated. Chromatography of the crude product was performed on a column of silica gel eluted first with n-hexane for separation of thiirane followed by using C_6H_{12}/CH_2Cl_2 (1:1) for the separation of β-hydroxy thiocyanate as a pale yellow liquid.

Selected Spectral Data for 2-Hydroxyethyl Thiocyanates[11]

3-Phenoxy-2-hydroxypropyl thiocyanate. IR (neat): ν SCN (2163 cm^{-1}); ^{1}HNMR ($CDCl_3$, 250 MHz) $\delta = 7.27$(2H, m), 6.92(3H, m), 5.0(1H, m), 4.2(2H, d), 3.64(2H, d). ^{13}CNMR ($CDCl_3$, 62.9 MHz) $\delta = 158.0$, 130.0, 122.0, 115.1, 114.9, 78.2, 67.2, 33.6.

2-Hydroxy-3-isopropoxypropyl thiocyanate. IR (neat): ν SCN (2170 cm^{-1}); ^{1}HNMR ($CDCl_3$, 250 MHz) $\delta = 3.74$(1H, m), 3.57(3H, m), 3.33(2H, d), 3.17(1H, brs), 1.1(6H, d, J = 6 Hz). ^{13}CNMR ($CDCl_3$, 62.9 MHz) $\delta = 114.5$, 79.4, 73.2, 67.6, 38.2, 23.0, 22.0.

2-Hydroxy-1-indanyl thiocyanate. IR (neat): ν SCN (2160 cm^{-1}); ^{1}HNMR ($CDCl_3$, 250 MHz) $\delta = 7.2$–7.5(4H, m), 5.0(1H, d), 4.8(1H, m), 3.55(2H, d), 3.2–3.5(1H, brs). ^{13}CNMR ($CDCl_3$, 62.9 MHz) $\delta = 139.0$, 130.0, 128.0, 126.0, 124.0, 120.0, 112.4, 83.7, 50.1, 39.4.

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