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Efficient synthesis of β-hydroxy thiocyanates from epoxides and ammonium thiocyanates using tetraarylporphyrins as new catalysts

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Abstract

The reaction of some oxiranes with ammonium thiocyanates in the presence of catalytic amounts of meso-tetraarylporpherins was carried out with high yields and regioselectivity under mild reaction conditions. Thus, several 2-hydroxyethyl thiocyanates useful synthetic intermediates towards the synthesis of many biologically active compounds are easily obtained in high yields.

Keywords: Thiocyanohydrin; Epoxide; Ring opening; Tetraarylporphyrin

1. Introduction

Epoxides are considered to be on the main muscles of organic synthesis [1] because of the fact that they are easily prepared from a variety of substrates and are easily opened under a broad range of conditions giving a wide spectrum of products. One very favorable aspect of the ring opening reactions of epoxides is that they are usually stereospecific, proceeding with inversion of configuration at the site of the opening via a S_N2 mechanism. However, opening of epoxides with nucleophiles often requires presence of promoters [2]. In continuation of our interest on the chemistry of 2-hydroxyethyl thiocyanates [3], we desired to develop a straightforward method for preparation of β-hydroxyethyl thiocyanates, which are considered as an important class of compounds often used as key intermediates in agricultural and pharmaceutical chemistry. 2-Hydroxyethyl thiocyanates represent an interesting subclass having multiple modes of reactivity. Synthetic access of β-hydroxy thiocyanates by oxirane ring opening with thiocyanate ion has been limited by further reaction to give thiiranes [4,5]. Although the reagents such as HSCN [6], DDQ [7], $Pd(PPh_3)_4$ [8], Ti $(O\text{-}^iPr)_4$ [9], $TiCl_3$ (or $ZnCl_2$) [10], $Ph_3P(SCN)_2$ [11], and TMSNCS (Cat. TBAF) [12], are useful, they are limited to specific oxiranes and are not applicable as versatile reagents in preparation of 2-hydroxyethyl thiocyanates [12]. However, we have observed that when a variety of epoxides were treated with a system consisting of 5,10,15,20-tetrakis(4-hydroxyphenyl)-porphyrin [T(4-OH P)P] in CH_3CN under reflux condition, the corresponding 2-hydroxyethyl thiocyanates were formed in good to excellent yields.

2. Results and discussion

We have already presented a new synthetic strategy for preparing tetraarylporphyrins under mild conditions at room temperature that should greatly expand synthetic entries into porphyrin containing

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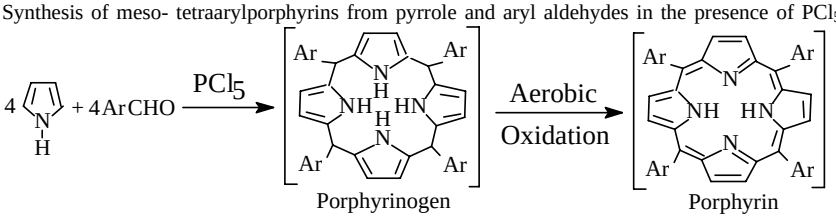
Table 1
Synthesis of meso- tetraarylporphyrins from pyrrole and aryl aldehydes in the presence of PCl_5, at room temperature using air as oxidant



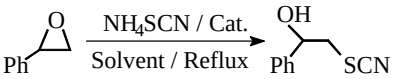
Entry	Ar	Product	Reaction time (h)	Yield (%)
1	Ph	TPP	5	56
2	4-Me C_6H_4	T(4-Me P)P	5	65
3	4-OH C_6H_4	T(4-OH P)P	5	28
5	4-Cl C_6H_4	T(4-Cl P)P	5	48
7	4-NO_2 C_6H_4	T(4-NO_2 P)P	5.5	45

model systems [13]. Pyrrole and the desired arylaldehyde in the presence of PCl_5 react to form tetraarylporphyrins in one pot without the need of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) as oxidant. Under these reaction conditions tetraarylporphyrins are formed in 28–65% yield (Table 1) [13].

One of the most important synthetic utilities of these meso-tetraarylporphyrins was explored by examining the reaction of epoxides with ammonium thiocyanate for preparation of β-hydroxy thiocyanates. As catalysts, five meso-tetraarylporphyrins (tetraphenylporphyrin [TPP], 5,10,15,20-tetrakis(4-hydroxyphenyl)-porphyrin [T(4-OH P)P], 5,10,15,20-tetrakis(4-methylphenyl)porphyrin [T(4-Me P)P], 5,10,15,20-tetrakis-(4-chlorophenyl)porphyrin [T(4-Cl P)P] and 5,10,15, 20-tetrakis(4-nitrophenyl)porphyrin [T(4-NO_2P)P]) that were synthesized according to above method (Table 1) were used. The results of the reaction of styrene oxide with thiocyanate ion in the presence of the above catalysts are summarized in Table 2. In each case, cleavage of the epoxide ring occurs and upon work up, the corresponding thiocyanohydrin was obtained. The catalyst was easily recovered and could be reused several times. By comparison, the cleavage of the styrene oxide with ammonium thiocyanate in the absence of catalyst is given in entry 6 of Table 2. As shown in Table 2, yields of thiocyanation with this new methodology were quite good and reaction times are very short. Without the catalyst the reaction required a much longer time, moreover, undesirable thiirane-formation predominated. T(4-OH P)P was the most effective catalyst and the reaction was completed in 20 min. In the presence of other derivatives TPP as catalysts, the reaction times for thiocyanation are in the rang 35–50 min. In these reactions a 3–5% of the corresponding thiiranes was also formed, which could easily isolated by column chromatography.

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 2.

Table 2
Thiocyanative cleavage of styrene oxide with NH_4SCN in the presence of some meso-tetraarylporphyrins in different solvents under reflux condition



Entry	Catalyst 0.01 mol%	Solvent	Time (min)	Yield[a] (%)
1	TPP	CH_3CN	40	85
2	T(4-MeP)P	CH_3CN	35	88
3	T(4-Cl P)P	CH_3CN	45	85
4	T(4-NO_2P)P	CH_3CN	50	90
5	T(4-OH P)P	CH_3CN	20	96
6	–	CH_3CN	190	–[b]
7	T(4-OH P)P	$CHCl_3$	120	45
8	//	THF	70	75
9	//	Et_2O	120	Trace
10	//	EtOH	55	35
11	//	C_6H_{12}	120	15
12	//	CH_3COCH_3	110	40

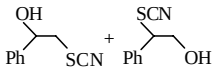
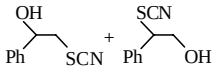
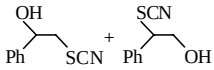
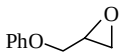
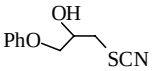
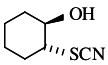
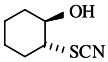
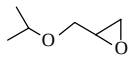
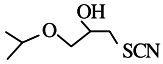
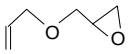
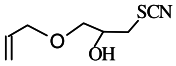
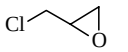
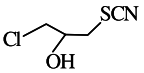
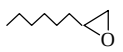
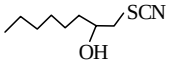
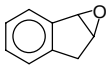
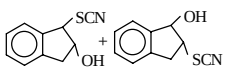
[a] Determined by GC.
[b] In the presence of excess of NH_4SCN, 35% of the corresponding thiirane was obtained (see [3]).

As found out that, the above reactions appeared to be largely dependent on the nature of solvent.

To ascertain the scope and limitation of the present reaction, several oxiranes were examined using catalyst T(4-OH P)P and these results were summarized in Table 3. By comparison, numbers of methods [7–10] for the conversion of oxiranes to the corresponding 2-hydroxyethyl thiocyanates are given in entries 2–5 and 8 (Table 3). In all cases listed, when epoxides were allowed to react in the presence of our catalyst, the yields were increased and regioselectivities were also enhanced and the optimum amount of the catalyst was found to be 0.01 equiv versus oxiranes. However, other factors can exert a controlling influence, such as (1) steric hindrance of oxiranes, (2) the nature of solvent, and (3) electron-donating or withdrawing groups bonded to the oxiranes. Each one can have a pronounced effect on the observed ratio of 2-hydroxyethyl thiocyanate isomers and overall yield.

Except for the reactions of styrene oxide (Table 3, entry 1) and indene oxide (Table 3, entry 13), which produce a smal1 percentage of the other regioisomer,

Table 3
Reaction of various epoxides with ammonium thiocyanate in the presence of the representative catalyst

Entry	Epoxide	Catalyst (0.01)	Reaction conditions	Product(s)	Reaction time (min)	Yield (%)[a]
1		T(4-OH P)P	NH_4SCN/CH_3CN reflux		20	96
2		$Pd(PPh_3)_4$ [8]	$NH_4SCN/N_2/THF$/reflux		120	35
3		$Ti(O\text{-}^iPr)_4$ [9]	NH_4SCN THF/reflux		240	30
4		$ZnCl_2$ [10]	KSCN/THF/reflux		180	60
5		DDQ	NH_4SCN/CH_3CN reflux		50	91 (1:8) [7b]
6		T(4-OH P)P	NH_4SCN/CH_3CN reflux		30	95
7		T(4-OH P)P	NH_4SCN/CH_3CN reflux		35	95
8		H_2Q[b]	$KSCN/H_3PO_4/H_2O/Et_2O$		–	48 [7a]
9		T(4-OH P)P	NH_4SCN/CH_3CN reflux		45	90
10		T(4-OH P)P	NH_4SCN/CH_3CN reflux		40	90
11		T(4-OH P)P	NH_4SCN/CH_3CN reflux		50	65
12		T(4-OH P)P	NH_4SCN/CH_3CN reflux		45	90
13		T(4-OH P)P	NH_4SCN/CH_3CN reflux		55	95

[a] Determined by GC.
[b] Hydroquinone has been used to stabilize 2-hydroxycyclohexyl thiocyanate (see [7a]).

the reaction of other oxiranes were found to be highly regioselective, and only one isomer was obtained. Also in case of cyclohexene oxide (Table 3, entry 7) *trans* products were obtained. Obviously, in these reactions, the nucleophilic attack by thiocyanate ion appears to be largely, if not entirely, at the primary carbon atom of the epoxide ring. The direction of ring opening is that characteristically observed for reactions of monoalkyl-substituted epoxides under S_N2 conditions and is probably dictated by steric and electronic factors.

In conjunction with our previous studies on the ring opening of oxiranes with different nucleophiles [3,14] and on the basis of our study on the complexation of tetraarylporphyrins with ammonium thiocyanate it seems that in these reactions free thiocyanate ion, SCN^-, was formed and used as an active nucleophile. A supporting evidence for the formation of free SCN^- in non aqueous media was obtained by studying the complexation reaction of T(4-OH P)P with NH_4SCN in acetonitrile increasing amount of NH_4SCN in acetonitrile solution are shown in Fig. 1. As is obvious, the addition of ammonium thiocyanate to the porphyrin derivative solution results in a considerable decrease in the porphyrin absorption bands at 516, 554 and 595 nm, accompanied by the creation of new absorption bands at 625 and 695 nm, through a distinct isobestic point at 610 nm. Such a spectral behavior can be presumably related to the complexation of T(4-OH P)P with NH_4^+ ion in solution which is associated with an activated SCN^- ion suitable to

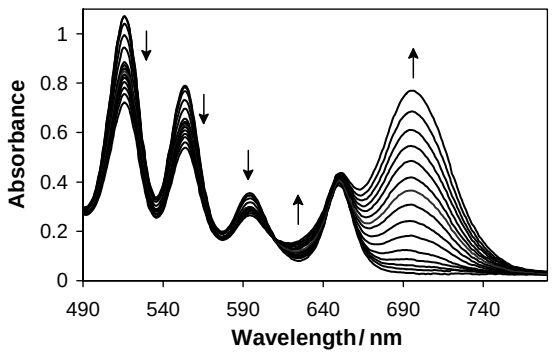
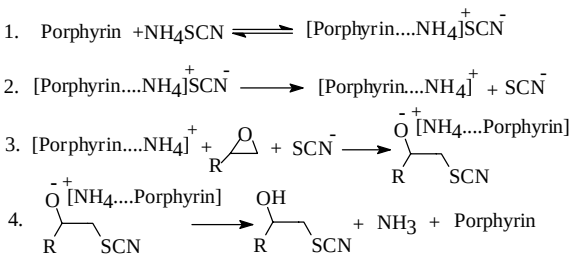


Fig. 1. Absorption spectra from bottom to top refer to T(4-OH P)P in the presence of different concentrations of NH_4SCN at 25 °C in acetonitrile.



Scheme 1.

attack the corresponding oxirane ring. On the basis of above evidence, a general mechanism was suggested for ring opening of oxiranes with a thiocyanato group, as shown in Scheme 1.

The first step involves the formation of a molecular complex between porphyrin and NH_4SCN in which thiocyanate ion (SCN^-) exists as a contact ion pair. In the second step, this complex is further decomposed to release the SCN^- ion into the solution. Therefore, in this way, the SCN^- ion is produced as a nucleophilic species in the presence of a suitable porphyrin and, in the third step, this ion participates in the ring-opening reaction of oxiranes. Finally, in step (4) the catalyst is reproduced and is used in the first step again. These steps occur continuously until all of the epoxides and ammonium thiocyanate are consumed and, after work up, the catalyst can be recovered easily and thiocyanohydrin was obtained. Moreover, based on the experimental results, it can be concluded that the reaction rate in the present reaction should be affected not only by complexation of NH_4SCN with porphyrin, but also by dissociation of the SCN^- anion from the adduct and the solubility of porphyrin or the adduct in acetonitrile.

3. Summary

In conclusion, we have found that TPP derivative compounds can catalyze ring opening of epoxides by ammonium thiocyanate under mild reaction conditions wherein high yields and regioselectivity. It is noteworthy that the operation is quite simple and the reaction conditions are sufficiently mild to operate several sensitive functionalities and that the porphyrin catalysts can be recycled and reusable.

4. Experimental section

Methylene chloride and chloroform (Merck) were distilled from K_2CO_3. Pyrrole was distilled from calcium hydride and stored samples were discarded when discoloration occurred. Benzaldehyde was distilled under reduced pressure. Epoxides, substituted benzaldehydes and other chemical materials were purchased from Fluka and Merck in high purity. All of the meso-tetraarylporphyrins and thiocyanohydrin compounds were prepared by our procedures and their spectroscopic and physical data were compared with the literature [3,7b,11–13].

4.1. General procedure for synthesis of meso-tetraarylporphyrins [13]

Standard reaction was performed at a 150 ml, three-necked, round bottomed flask fitted with a septum port, a reflux condenser, and a gas inlet port. The inlet port consisted of a glass disk immersed in the solution, with N_2 flow rates maintained at ca. 2 ml per min. The flask was charged with 100 ml of distilled arylaldehyde in CH_2Cl_2 (1 mmol) and pyrrole (0.07 ml, 1 mmol, 10^{-2} M). The resulting solution was magnetically stirred at RT. After stirring the solution for 10–15 min, an appropriate amount of PCl_5 (0.04 g, 0.2 mmol) was added. After 1 h, the yield of porphyrinogen was maximum. Then the gas inlet line was switched to filtered house air and the mixture was aerated for 4 h (39 °C), during this time the mixture became dark purple and porphyrinogen under aerobic oxidation was converted to porphyrin. The solution was concentrated by rotary evaporation and chromatographed on silica gel with CH_2Cl_2/petroleum ether (1:1) to give tetraarylporphyrins.

4.2. General procedure for conversion of epoxides to β-hydroxy thiocyanate using TPP derivatives 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 (0.1 mmol) in CH_3CN (5 ml) was added and the mixture was stirred under reflux condition for 20–50 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 hexane for separation of thiirane followed by using C_6H_{14}/CH_2Cl_2 (1:1) for the separation of β-hydroxy thiocyanate as a pale yellow liquid. Then, the catalyst was recovered by elution with $CHCl_3$.

Acknowledgements

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