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A one pot cobalt catalyzed regio- and stereoselective synthesis of oxazolidin-2-thiones from alkenes and trimethylsilylisothiocyanate

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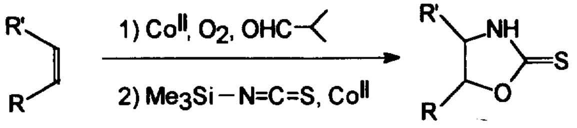
Abstract: *Efficient synthesis of Oxazolidin-2-thiones can be achieved from alkenes by employing a one pot Cobalt complex 1 catalyzed aerobic epoxidation followed by its cleavage with trimethylsilylisothiocyanate.* Copyright © 1996 Published by Elsevier Science Ltd

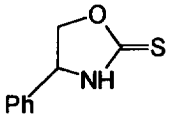
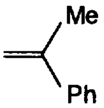
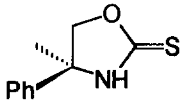
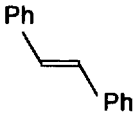
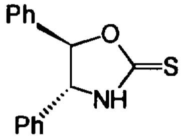
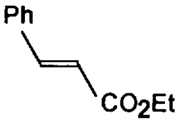
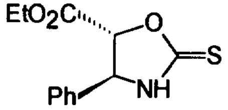
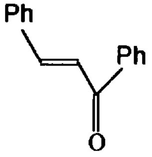
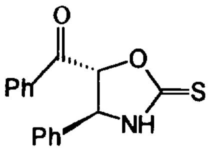
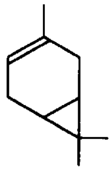
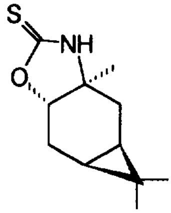
Oxazolidin-2-thiones are very useful chiral auxillaries[1] and they show interesting biological activity[2], however, there are no direct methods available for their syntheses from alkenes or epoxides. We have recently demonstrated that Co(II) catalyzes the epoxidation of a wide range of alkenes by using a combination of dioxygen and 2-methyl propanal[3]. In an earlier study, we have also shown that Co(II) catalyzes the cleavage of epoxides with anilines to give the corresponding amino alcohols[4]. We now demonstrate the synthesis of oxazolidin-2-thiones from alkenes by employing one pot Co(II) catalyzed epoxidation followed by its cleavage with trimethylsilylisothiocyanate (eqn.1).



eq. 1

Typically, alkene (10 mmol) is added to a solution of catalyst 1[5] (5 mol%) and 2-methylpropanal (20 mmol) in acetonitrile (20 mL) and the reaction is stirred under an oxygen atmosphere at ambient temperature for 10-15 h. Freshly prepared trimethylsilylisothiocyanate (12.5 mmol) is then added dropwise at ambient temperature to this mixture and the resulting solution is heated at 70° C for 12-16 h. Removal of solvent gave a residue which was chromatographed on silica gel to afford the corresponding oxazolidin-2-thiones. According to this protocol, styrene, 2-methylstyrene and *trans*-stilbene were converted to the corresponding oxazolidin-2-thiones in modest yields (Table 1; Entry 1-3). Similarly, ethyl cinnamate and chalcone were transformed in one pot to the corresponding *trans*-oxazolidin-2-thiones in modest yields (Table 1; Entry 4

Table 1 : Cobalt complex 1 catalyzed one pot synthesis of oxazolidin-2-thiones from alkenes

Entry	Alkene	Product	(Yield)[a]
1.			23%
2.			24%
3.			56%
4.			24%
5.			29%
6.			20%

a) Yield of the product purified by silica gel chromatography and 5). Interestingly, 3-carene underwent transformation to the corresponding tricyclic system (Table 1: Entry 6) and it is noteworthy that the ring junction stereochemistry of oxazolidin-2-thione is trans as evidenced from the X-ray crystal structure (Fig. 1a). These reactions are highly regio and stereoselective as only one isomer was obtained in all cases and the careful analysis of the reaction mixture indicated the absence of the other regioisomer. The double bond geometry is also retained during this process as observed in the case of *trans*-stilbene and ethyl cinnamate. This was confirmed by the X-ray crystal structure of the product derived from ethyl cinnamate, which clearly illustrates the trans stereochemistry of the major product (Fig. 1b).

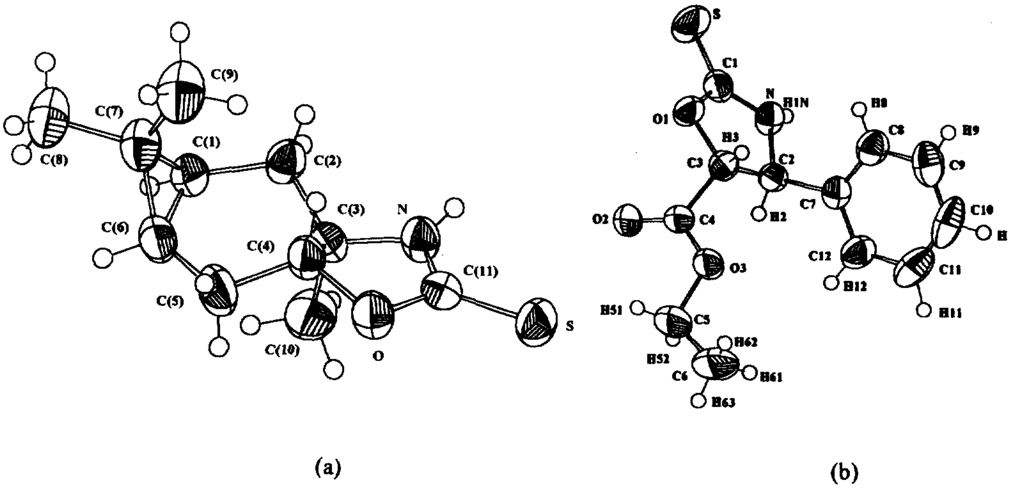
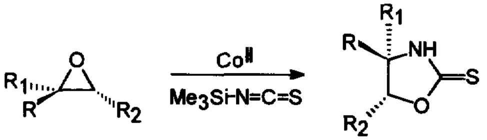


Fig.1 ORTEP stereoview of (a) oxazolidin-2-thione from 3-carene (b) oxazolidin-2-thione from ethylcinnamate

That these reactions are occurring via epoxides is confirmed by carrying out the transformation on epoxides, that are rapidly cleaved by trimethylsilylisothiocyanate at 70°C in the presence of catalytic amount of complex **1** to afford the corresponding oxazolidin-2-thione. *It is also noteworthy that the yield of oxazolidin-2-thiones are improved considerably by using the epoxide instead of the alkene.* Accordingly, epoxides from styrene, α-methylstyrene, trans-stilbene and ethyl cinnamate were smoothly transformed to the corresponding oxazolidin-2-thione in good yields (Scheme 1). The stereochemistry of the product in the case of *trans*-stilbene is anti as evidenced by coupling constant in the proton NMR.

Scheme 1



a)	$R = C_6H_5$; $R_1 = H$; $R_2 = H$	52%
b)	$R = C_6H_5$; $R_1 = Me$; $R_2 = H$	48%
c)	$R = C_6H_5$; $R_1 = H$; $R_2 = C_6H_5$	68%
d)	$R = C_6H_5$; $R_1 = H$; $R_2 = CO_2Et$	65%

In conclusion, Co complex **1** catalyzed conversion of alkenes or epoxides by trimethylsilyl-isothiocyanate provides a novel route to the corresponding oxazollidin-2-thiones.

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5. To a solution of the Schiff's base ligand derived from Pyridine-2-carboxaldehyde and ethylene-di-amine in dry acetonitrile, anhydrous $CoCl_2$ was added. Upon stirring for 2-3h, a pinkish brown powder precipitated from which the solvent was removed, dried and stored in desiccator. (See ref 3).

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