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# Bioreduction of methyl heteroaryl and aryl heteroaryl ketones in high enantiomeric excess with newly isolated fungal strains

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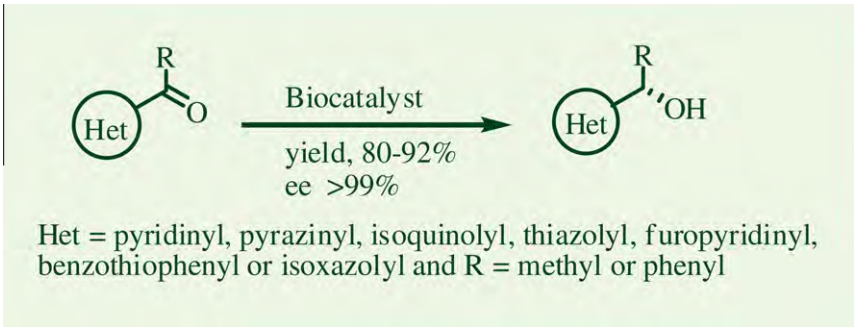
## HIGHLIGHTS

- Three newly isolated fungal strains including new species of *Penicillium* described.
- Heteroaryl ethanols and aryl heteroarylmethanols obtained in >99% ee; 80–92% yield.
- Intermediate of HIV-1 reverse transcriptase inhibitor PNU142721 prepared in >99% ee.
- Enantiopure (*S*)-phenyl(pyridin-2-yl)methanol, an analgesic obtained in 88% yield.
- Chiral building block (*S*,*S*)-2,6-bis(1-hydroxyethyl)pyridine obtained in >99% ee.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Enantioenriched heteroaryl ethanols and aryl heteroarylmethanols are important intermediates and structural motifs in medicinal chemistry. Asymmetric biocatalytic reduction of corresponding ketones provides a straightforward approach for preparation of these compounds. Accordingly, three newly isolated fungal strains have been described, which produced the desired heteroaryl alcohols in high enantiomeric excess (ee). A broad substrate specificity was observed within these limited number of biocatalysts as demonstrated by preparation of a variety of heteroaryl alcohols, including (*S*)-5-(1-hydroxyethyl)furo[2,3-c]pyridine, a key intermediate for HIV-1 reverse transcriptase inhibitor, (*S*)-phenyl(pyridin-2-yl)methanol, an analgesic and (*S*,*S*)-2,6-bis(1-hydroxyethyl)pyridine, a chiral building block, mostly in >99% ee and 80–92% yield. Micro-morphologically, one of the isolate was found to be similar to *Penicillium funiculosum*. However, its β-tubulin sequence showed only 88% sequence identity with the known β-tubulin sequences of *Penicillium*. It may, therefore, represent a new species of *Penicillium*. The other biocatalysts were identified as *Alternaria alternata* and *Talaromyces flavus*.



## 1. Introduction

Enantioenriched heteroaryl ethanols and aryl heteroarylmethanols are important intermediates and structural motifs for various biologically active compounds, such as (*R*)-neobenodine, (*R*)-orphenadrine, (*S*)-cetrazine (Salvi et al., 2009), (*S*)-carbinoxamine (Clistin, Palgic), (*S*)-duloxetine (Kamal et al., 2009), (1*R*,2*S*)-mefloquine (Knight et al., 2011), HIV reverse-transcriptase inhibitor furo[2,3-c]pyridine thiopyrimidine ether (Wishka et al., 1998), β-blocker 2-(2-*tert*-butylamino-1-hydroxyethyl)benzofuran (Machin et al., 1985) and analgetic (*S*)-phenyl(pyridin-2-yl)methanol (Gearien et al., 1971). Similarly, aryl benzofurans have been used as intermediates for synthesis of azole derivatives, which are indicated in the treatment of hormone-dependent breast cancer (Buzdar, 2002). Optically pure 1-heteroaryl-1-alkanols also act as

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