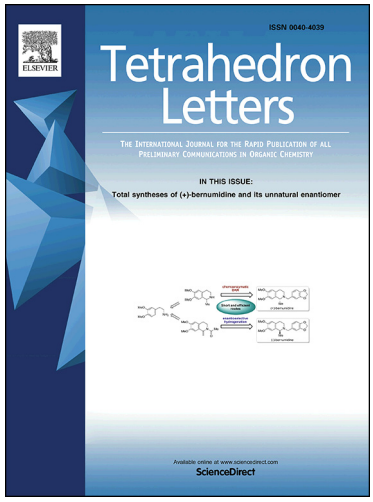

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PII: S0040-4039(18)31100-6
DOI: https://doi.org/10.1016/j.tetlet.2018.09.019
Reference: TETL 50258

To appear in: *Tetrahedron Letters*

Received Date: 24 July 2018
Revised Date: 4 September 2018
Accepted Date: 7 September 2018

Please cite this article as: Peng, C., Liu, Y., Guo, X., Liu, W., Li, Q., Zhao, Z.K., Selective carboxylation of substituted phenols with engineered *Escherichia coli* whole-cells, *Tetrahedron Letters* (2018), doi: https://doi.org/10.1016/j.tetlet.2018.09.019

Tetrahedron Letters
journal homepage: www.elsevier.com

Selective carboxylation of substituted phenols with engineered *Escherichia coli* whole-cells

Chang Peng[†,a,b], Yuxue Liu[†,a,b], Xiaojia Guo,[a,b] Wujun Liu,[a] Qing Li,[a,b] and Zongbao K. Zhao*[a,c]

[a.] *Division of Biotechnology, Dalian Institute of Chemical Physicals, Chinese Academy of Sciences, Dalian 116023, China.*
[b.] *University of Chinese Academy of Sciences, Beijing, 100049, China.*
[c.] *State Key Laboratory of Catalysis, Dalian Institute of Chemical Physicals, CAS, Dalian 116023, China.*
† These authors contributed equally to the study.

ARTICLE INFO

Article history:
Received
Revised
Accepted
Available online

Keywords:
carboxylation
5-carboxyvanillate decarboxylase
lignin-derived phenols
decarboxylase
whole-cell biocatalyst

ABSTRACT

Selective carboxylation of substituted phenols is realized in the presence of bicarbonate under ambient pressure by engineered *Escherichia coli* whole-cells expressing various hydroxybenzoate decarboxylases, leading to their corresponding *ortho*-hydroxybenzoates. This process may be further developed as an efficient route to upgrade lignin-derived phenolic compounds as valuable building blocks.

Introduction

In the past few decades, the growing demand for energy associated with dwindling fossil resources has created tremendous surge in interests for efficient transformation of lignocellulosic biomass into fuels and chemicals.[1-3] Lignin is an aromatic-rich polymer in nature and therefore represents a potential feedstock for the production of aromatic chemicals. At present, much effort has been devoted to selective depolymerization of lignin into monomeric aromatics, such as 4-substituted phenol, 4-substituted-2-methoxy phenol, or 4-substituted-2,6-dimethoxy phenol,[3-6] of which many resemble *p*-coumaroyl, coniferyl and sinapyl alcohol that bear a hydroxyphenyl (H), guaiacyl (G), and syringyl (S) fragment, respectively (Figure 1). It is thus important to convert these compounds into value-added products by exploiting their functionality.[7-10] To date, chemical approaches are playing a dominant role in the field of lignin chemistry. For example, acetylation of ferulic acid, followed by UV-catalyzed 2+2 cycloaddition led to diacids, which were then polymerized with diamines to afford the corresponding polyamides.[8] Cinnamyl alcohol and 4-(3-hydroxypropyl)phenol were converted into different products using dimethyl carbonate as the solvent/reagent.[10] Yet many of these methods use toxic organic solvents and require relatively harsh conditions. Driven by ever-growing ecological and environmental concerns, it is appealing to develop greener and sustainable approaches to upgrade lignin-derived building blocks.

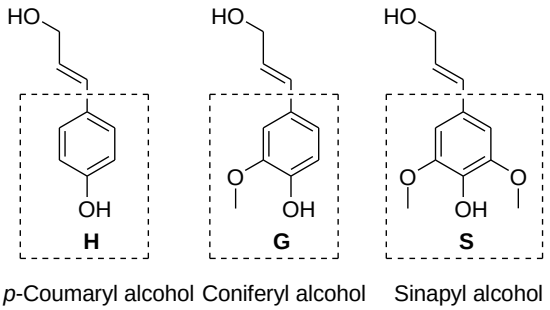

Figure 1. Chemical structures of representative lignin alcohols.

Kolbe-Schmitt reaction has been known for carboxylation of phenols to hydroxybenzoates in the presence of CO_2 and a strong base under high pressure and elevated temperatures.[11] Recently, the biological version of Kolbe-Schmitt reaction has been established, where enzymatic carboxylation of phenols proceeds in an aqueous environment under ambient conditions. A number of phenols have been converted into their corresponding hydroxybenzoates by biocatalysts, such as 2,3-dihydroxybenzoate decarboxylase form *Aspergillus oryzae* (2,3-DHBD_Ao),[12] salicylic acid decarboxylase from *Trichosporon moniliiforme* (SAD_Tm)[13] and 2,6-dihydroxybenzoate decarboxylase from *Rhizobium* sp. (2,6-DHBD_Rs).[14, 15] Moreover, structurally diverse phenols[16, 17] and complex polyphenols[18, 19] were regioselectively carboxylated by