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Saccharomyces Cerevisiae as a Biocatalyst for Different Carbonyl Group under Green Condition

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In this research *saccharomyces cerevisiae* (baker's yeast) was used as a cheap, readily accessible, selective, efficient, and green bio-catalyst in a chemo selective reduction of carbonyl group to hydroxyl group. In this green procedure three substrates *e.g.* (3-(3-nitrophenyl)aziridin-2-yl)-1-phenyl-methanone, pyruvate ester, and 2-acetyl-γ-butyrolactone were reduced to their corresponding reduced compounds in the presence of *saccharomyces cerevisiae* at ambient temperature in aqueous media. It was worthy to note that ketone groups were chemo-selectively reduced, while ester and lactone groups remained unchanged. Moreover, in this procedure, chemo selective bio-reduction of ketone group to hydroxyl group can be performed by coenzyme NADPH in *saccharomyces cerevisiae* (baker's yeast) which is recyclable in water, as a green solvent, while this recyclization cannot occur in non-aqueous systems. The structure of products was confirmed by IR and ^{1}H NMR spectra.

Keywords: *Saccharomyces cerevisiae*, Baker's yeast, Bio-reduction, (3-(3-Nitrophenyl)aziridin-2-yl)-1-phenyl-methanone, Pyruvate ester, 2-Acetyl-γ-butyrolactone

INTRODUCTION

Synthesis of chiral compounds has attracted great attention due to their wide applications as chemical and pharmaceutical compounds. Chiral compounds have been used in chemical catalysts, flavors, liquid crystals, agrochemicals, fine chemical and drugs [1]. Green chemistry involves design and development of chemical processes to reduce or eliminate the use of hazardous materials such as solvent or catalyst harmful for the human health and environment. One of the ways approaching to green chemistry is using microorganisms as catalyst. *Saccharomyces cerevisiae* (baker's yeast) is a cheap, readily accessible, and stable microorganism used as catalyst in many reduction or synthesis reactions.

Lopchuk [2] and co-workers reported that enantioselective reduction of bruceolline E with *β*-chloro-diisopinocampheylborane as biocatalyst yielded to unnatural enantiomer of bruceolline in 98% ee, both the natural and unnatural enantiomers of bruceolline were prepared while using baker's yeast. Enantioselective reduction of some ketoesters with *S. cerevisiae* and chiral ruthenium catalysts in aqueous media was carried out. The highest enantiomeric excesses for the reduction of *α*- and *β*-ketoesters have been obtained by *S. cerevisiae* [3]. Recently, asymmetric reduction of C=C bond of unsaturated ketones or esters has been the subject of extensive studies [4-6]. Also, regioisomeric bio-reduction of both C=C and C=O groups of *α,β*-unsaturated compounds using baker's yeast has been reported [7,8,9,10].

S. cerevisiae has been used in synthesis of many

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chemical compounds such as 3*H*-isobenzofuran [11], 1,4-benzothiazines [12], benzothiazoles [13], 3,4-dihydro-pyrimidin-2-(1*H*)-ones [14], polyhydroquinoline derivatives [15], polyfunctionalized 4*H*-pyrans [16], isoindolo[2,1-a] quinazoline [17] and 2,3-diaryl-4-thiazolidinones [18]. In contribution to our previous efforts regarding the use of *S. cerevisiae* as a green reducing reagent, here we reports bio-reductions of compounds 1, 3 and 5, respectively [19-22].

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR-470 spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded in ppm (δ) on a Bruker 500 MHz spectrometer using solvent as internal standard ($CDCl_3$ at 7.31 ppm).

General procedure for preparation of compounds 2, 4 and 6. To a two-necked flask was added glucose (27.75 mmol), $CaCO_3$ (0.99 mmol), $MgSO_4$ (0.83 mmol) and K_2HPO_4 (3 ml, 0.1 M, pH = 7). The mixture was dissolved in warm H_2O (60 °C, 150 ml), then *S. cerevisiae* (5 g) was added. The flask was connected to a trap containing $Ba(OH)_2$ solution. This mixture was stirred for 20 min in 25 °C. Then (3-(3-nitrophenyl)aziridin-2-yl)-1-phenyl-methanone 1 or pyruvate ester 3 or 2-acetyl-γ-butyrolactone 5 (1 mmol) was added dropwise within 2 hours to the mixture. The progress of the reaction was monitored by TLC (EtOAC: ether 3:1). After 3 days, 50 ml of EtOAC was added to the reaction mixture, and then was stirred for 10 min; the mixture was filtered on celite. Saturated solution of NaCl (50 ml) was added to the filtrate, and the filtrate was extracted by EtOAC (5 × 20 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum.

(3-(3-Nitrophenyl)aziridin-2-yl)(phenyl)methanol (2). Yield 25%, IR (KBr, cm^{-1}): 3400 (OH stretch), 3270 (NH stretch), 1590 (C=C stretch), 1570 (NO_2 asymmetric stretch), 1525 (C=C stretch), 1350 (NO_2 symmetric stretch), 1120 (C-O stretch). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.8 (1H), 2.21 (s, br, 1H), 2.3 (1H), 2.5 (1H), 7.5-8.3 (m, 9H) ppm.

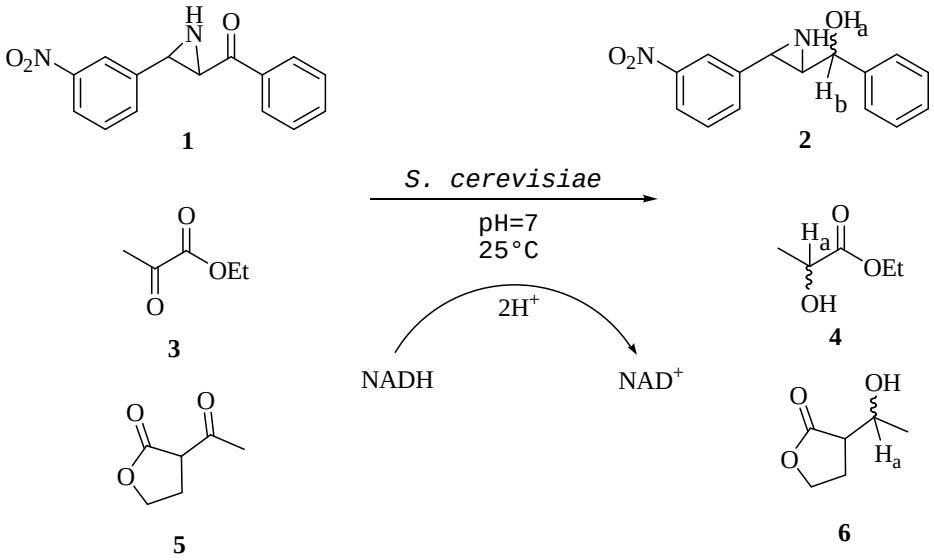
2-Hydroxy propionic acid ethyl ester (4). Colorless liquid, yield: 51%, $[\alpha]_D^{25}$ = -4.65° (c = 2 g/100 ml, EtOH). IR (KBr, cm^{-1}): 3448 (OH stretch), 2984, 2939 (C-H stretch), 1735 (C=O ester stretch), 1215, 1131 (C-O stretch). ^{1}H NMR (500 MHz, $CDCl_3$): δ; 1.26 (t, J = 7.1 Hz, 3H), 1.38 (d, J = 6.8 Hz, 3H), 3.2 (d, J = 3.9 Hz, 1H), 4.17-4.21 (q, J = 7.1 Hz, 2H), 4.23 (m, 1H) ppm.

Dihydro-3-(1-hydroxyethyl)furan-2(3*H*)-one (6). Colorless liquid, yield: 30%, IR (KBr, cm^{-1}): 3450 (OH stretch), 2990, 2900 (C-H stretch), 1760 (C=O ester stretch), 1250, 1040 (C-O stretch). ^{1}H NMR (400 MHz, $CDCl_3$): δ; 1.21, 1.16 (d, J = 5.6, 9.6 Hz, 4H), 2.04 (m, 2H), 2.32-2.36 (m, 3H), 2.78-2.82 (m, 2H), 3.53-3.57 (m, 1H), 3.73 (dd, J = 6.8 Hz, 1H), 4.21-4.29 (m, 1H), 4.37-4.44 (m, 2H) ppm.

RESULTS AND DISCUSSION

Bio-reduction of (3-(3-nitrophenyl)aziridin-2-yl)-1-phenyl-methanone 1, pyruvate ester 3 and 2-acetyl-γ-butyrolactone 5 were performed at 25 °C in the presence of *S. cerevisiae*. The reaction condition was optimized by addition of glucose, $MgSO_4$, $CaCO_3$ and potassium phosphate (pH = 7) (Scheme 1).

3-((3-Nitrophenyl)aziridin-2-yl)-1-phenyl-methanone 1 was reduced to corresponding (3-(3-nitrophenyl) aziridin-2-yl)(phenyl)methanol 2. IR and ^{1}H NMR spectra of the corresponding (3-(3-nitrophenyl) aziridin-2-yl)(phenyl) methanol 2 were recorded as a mixture of 1 and 2. IR spectrum of compound 2 revealed the absorbances of hydroxyl (OH) and C-O at 3400 and 1120 cm^{-1}, respectively. In ^{1}H NMR spectrum recorded in $CDCl_3$, presence of a singlet in 5.4 ppm (H_b) and a multiple in 1.8 ppm (OH) confirmed reduction of carbonyl group. Selective bio-reduction of pyruvate ester 3 yielded 2-hydroxy propionic acid ethyl ester 4 in 51% yield. Baker's yeast reduced ketone group in a reasonable yield, despite the presence of ester group. In IR spectrum of 4, the absorbance at 3448 cm^{-1} is related to hydroxyl group. ^{1}H NMR spectrum revealed diagnostic resonances for hydroxyl and H_a protons at 3.21 ppm as a doublet and 4.22-4.24 ppm as a multiplet, respectively. Optical rotation of the product 4 was measured as $[\alpha]_D^{25}$ = -4.65°.



Scheme 1. Bio-reduction of compounds 1, 3 and 5 using baker's yeast

2-Acetyl-γ-butyrolactone 5 was reduced selectively to dihydro-3-(1-hydroxyethyl)furan-2(3*H*)-one 6. IR and ^{1}H NMR spectra were recorded as a mixture of 2-acetyl-γ-butyrolactone and dihydro-3-(1-hydroxyethyl)furan-2(3*H*)-one 6. IR spectrum revealed the absorbance of hydroxyl group (OH) at 3450 cm^{-1}. In accordance with ^{1}H NMR recorded in $CDCl_3$, two doublets appeared at 1.20 and 1.22 ppm which are related to CH_3 group and are indicative of reduction of ketone group. Appearance of two doublets in these chemical shifts is related to the corresponding diastereoisomers. Singlet at 2.47 ppm is related to CH_3 group in 2-acetyl-γ-butyrolactone 5. Consistent with average integrations of ^{1}H NMR the ratio of diastereoisomers 6 to 2-acetyl-γ-butyrolactone 5 was calculated ~75:25. For two diastereomers of 6 at δ = 1.15-1.23 ppm the same ratio was confirmed.

CONCLUSIONS

(3-(3-Nitrophenyl)aziridin-2-yl)-1-phenyl-methanone, pyruvate ester, and 2-acetyl-γ-butyrolactone were reduced selectively using *Saccharomyces cerevisiae* at room temperature.

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