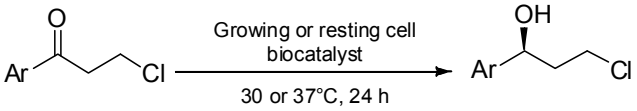
# Supplementary Materials: Stereoselective Chemoenzymatic Synthesis of Optically Active Aryl-Substituted Oxygen-Containing Heterocycles

**Paola Vitale, Antonia Digeo, Filippo Maria Perna, Gennaro Agrimi, Antonio Salomone, Antonio Scilimati, Cosimo Cardellicchio and Vito Capriati**

**Table S1.** Screening of biocatalysts for the stereoselective reduction of 3-chloro-1-aryl-propanones [a].

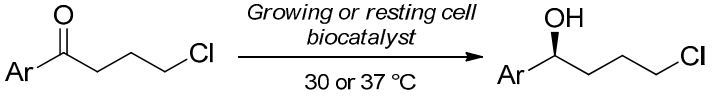



**1a-d** **2a-d**

| Entry | Biocatayst | Ar (1a–d) | Product 2 (Yield %) [b] | Conversion % | er [c] | Abs. Conf. [d] |
|---|---|---|---|---|---|---|
| 1 | *Baker's yeast* (RC) | $C_6H_5$ (**1a**) | **2a** (44) | 50 | 94:6 | *S* |
| 2 | *Saccharomyces cerevisiae* (GC) [e] | $C_6H_5$ (**1a**) | **2a** (48) | 55 | 75:25 | *S* |
| 3 | *Kluyveromyces marxianus* (GC) [f] | $C_6H_5$ (**1a**) | **2a** (31) [g] | 70 | 58:42 | *S* |
| 4 | *Lactobacillus reuteri* (RC) [h,i] | $C_6H_5$ (**1a**) | **2a** (–) [j] | 40 | ND [k] | ND [k] |
| 5 | *Baker's yeast* (RC) | 4-$FC_6H_4$ (**1b**) | **2b** (13) | 15 | 63:37 | *S* |
| 6 | *Lactobacillus reuteri* (RC) [h,i] | 4-$FC_6H_4$ (**1b**) | **2b** (–) [l] | 28 | ND [k] | ND [k] |
| 7 | *Baker's yeast* (RC) | 4-$BrC_6H_4$ (**1c**) | **2c** (5) [m] | 85 | 95:5 | *S* |
| 8 | *Lactobacillus reuteri* (RC) [h,i] | 4-$BrC_6H_4$ (**1c**) | **2c** (–) [n] | 12 | ND [k] | ND [k] |
| 9 | *Baker's yeast* (RC) | 4-$MeOC_6H_4$ (**1d**) | **2d** (–) [o] | 12 | ND [k] | ND [k] |

[a] Typical reaction conditions: orbital incubator (200 rpm); temperature: 30 °C; (GC): inoculum after 24 h growth in a sterile medium containing glucose (1%), peptone (0.5%), yeast extract (0.3%), and malt extract (0.3%) in sterile water; (RC): 0.1 g/L of cell wet mass in 0.1 M $KH_2PO_4$ buffer (pH = 7.4) enriched with 1% glucose, halo-ketone (2 mM final concentration); [b] Isolated yield after column chromatography; [c] Enantiomeric ratio (er) determined by HPLC analysis; [d] Absolute configuration (abs. conf.) of halohydrins (**2a–d**) determined by comparing optical rotation sign and retention time (HPLC analysis) with known data; [e] CBS 7536; [f] CBS 6556; [g] Propiophenone (35%) and 1-phenylpropan-1-ol (33%) have been detected by $^1$H NMR analysis of the reaction crude; [h] DSM 20016; [i] Typical reaction conditions: cells were suspended in PBS at pH 7.4 supplemented with 1% glucose; then, ketone was added at the final concentration of 1 g/L (50 mL total volume), anaerobiosis; temperature: 37 °C; orbital incubator: 200 rpm; [j] 1-Phenylprop-2-en-1-one (24%), 1-phenylprop-2-en-1-ol (5%), propiophenone (3%) and 3-hydroxypropiophenone (7%) have been detected by $^1$H NMR analysis of the reaction crude; [k] ND means not determined because of the trace content; [l] 1-(4-Fluorophenyl)prop-2-en-1-one (17%), 1-(4-fluorophenyl)prop-2-en-1-ol (5%), 1-(4-fluorophenyl)propanone (1%), and 3-hydroxy-1-(4-fluorophenyl)propanone (4%) have been detected by $^1$H NMR analysis of the reaction crude; [m] Propiophenone (75%) was isolated as the main product, together with 4-bromophenyloxetane (9%, er = 96:4%); [n] 1-(4-Bromophenyl)prop-2-en-1-one (5%), 1-(4-bromophenyl)prop-2-en-1-ol (5%), and 3-hydroxy-1-(4-bromophenyl)propanone (1%) have been detected by $^1$H NMR analysis of the reaction crude; [o] Propiophenone (5%) has also been detected together with the starting material (88%) in the reaction crude.

**Table S2.** Screening of biocatalysts for the stereoselective reduction of 4-chloro-1-aryl-1-butanones [a].




**1e-h** **2e-h**

| Entry | Biocatayst | Ar (1e–h) | Product 2 (yield %) [b] | Conversion (%) | er [c] | Abs. Config. [d] |
|---|---|---|---|---|---|---|
| 1 | *Baker's yeast* (RC) | $C_6H_5$ (**1e**) | **2e** (44) | 49 | 95:5 | S |
| 2 | *Saccharomyces cerevisiae* (GC) [e] | $C_6H_5$ (**1e**) | **2e** (65) | 70 | 49:51 | S |
| 3 | *Kluyveromyces marxianus* (GC) [f] | $C_6H_5$ (**1e**) | **2e** (4) | 7 | 42:58 | S |
| 4 | *Lactobacillus reuteri* (RC) [g,h] | $C_6H_5$ (**1e**) | **2e** (–) [i] | 15 | ND [j] | ND [j] |
| 5 | *Baker's yeast* (RC) | 4-$FC_6H_4$ (**1f**) | **2f** (–) [k] | 40 | ND [j] | ND [j] |
| 6 | *Lactobacillus reuteri* (RC) [g,h] | 4-$FC_6H_4$ (**1f**) | **2f** (–) [l] | 14 | ND [j] | ND [j] |
| 7 | *Baker's yeast* (RC) | 4-$BrC_6H_4$ (**1g**) | **2g** (–) [m] | – [m] | ND [j] | ND [j] |
| 8 | *Baker's yeast* (RC) | 4-$CH_3OC_6H_4$ (**1h**) | **2h** (–) [n] | 5 | ND [j] | ND [j] |
| 9 | *Lactobacillus reuteri* (RC) [g,h] | 4-$CH_3OC_6H_4$ (**1h**) | **2h** (–) [o] | 42 | ND [j] | ND [j] |

[a] Typical reaction conditions: orbital incubator at 200 rpm; temperature: 30 °C; (GC): inoculum after 24 h cell growth in a sterile medium containing glucose (1%), peptone (0.5%), yeast extract (0.3%), and malt extract (0.3%) in sterile water; (RC): 0.1 g/L of cell wet mass in 0.1 M $KH_2PO_4$ buffer (pH = 7.4) enriched with 1% glucose, haloketone (2 mM final concentration); [b] Isolated yield after column chromatography; [c] Enantiomeric ratio (er) determined by HPLC analysis; [d] Absolute configuration (abs. conf.) of halohydrins (**2e–h**) determined both by comparing optical rotation sign and retention time (HPLC analysis) with known data; [e] CBS 7336; [f] CBS 6556; [g] DSM 20016; [h] Typical reaction conditions: cells were suspended in PBS at pH 7.4 supplemented with 1% glucose; then, ketone was added at the final concentration of 1 g/L (50 mL total volume), anaerobiosis; temperature: 37 °C; orbital incubator: 200 rpm; [i] 4-Hydroxy-1-phenylbutan-1-one (13%) has been detected by $^1$H NMR analysis of the reaction crude; [j] ND means not determined because of the trace content; [k] The corresponding butyrophenone (37%) has been detected by $^1$H NMR analysis of the reaction crude; [l] 4-Hydroxy-1-(4-fluorophenyl)butan-1-one (13%) has been detected by GC-MS and $^1$H NMR analysis of the reaction crude; [m] No reaction. [n] Chlorohydrin **2h** (5%) has been detected by GC-MS analysis of the reaction crude; [o] 4-Hydroxy-1-(4-methoxyphenyl)butan-1-one (32%) and 4-(4-methoxyphenyl)butan-2-one (9%) have been detected by $^1$H NMR analysis of the reaction crude.