Effect of Additive Concentration on Asymmetric Reduction of Fluorine-containing Ketones Using Cyanobacterium *Synechocystis* sp. PCC 6803

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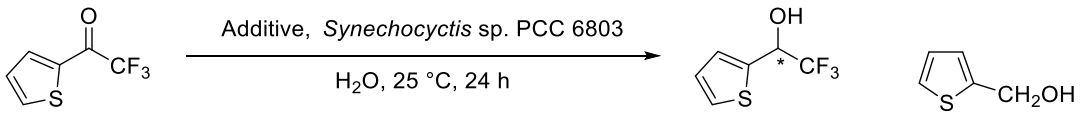
Optically active alcohols are important as chiral building blocks in the synthesis of pharmaceuticals and agrochemicals. Whole-cell biotransformation through the asymmetric reduction of prochiral ketones is a useful method for producing such optically active alcohols as the reducing cofactors (e.g., NADPH and NADH) are available and recycled inside the cells. We have previously studied the asymmetric reduction of *β*-keto esters using cyanobacterial cells.[1,2] In this report, we investigate the effect of additive concentrations on the asymmetric reduction of fluorine-containing ketones using the cyanobacterium *Synechocystis* sp. PCC 6803.

Synechocystis sp. PCC 6803 strains were grown in BG-11 medium under illumination (fluorescent light, 20 μmol m^{-2} s^{-1}) at 25 °C for 10 days. Asymmetric reduction of ketone **1** (0.1 mg/mL) to chiral alcohol **2** using the cyanobacterial strain was performed in the presence of an additive under illumination with red LED light (660 nm, 10 μmol m^{-2} s^{-1}) or in the dark at 25 °C for 24 h. For example, 2-thiophenemethanol (**3**) was added to the reaction mixture. The yields of **2** were slightly increased by the addition of **3**, regardless of light conditions. Moreover, we found that the higher the concentration of **3**, the greater the *R*-selectivity (Table 1).



1 **2** **3**

Table 1.

Entry	Light cond.	Additive (mg/mL)	Yield/%	**2**/%ee (config.)
1	light	−	34	19 (*S*)
2	dark	−	5	1 (*R*)
3	light	**3** (0.1)	46	13 (*S*)
4	dark	**3** (0.1)	14	5 (*R*)
5	light	**3** (0.5)	41	0
6	dark	**3** (0.5)	17	15 (*R*)

1) S. Tanaka, H. Kojima, S. Takeda, R. Yamanaka, T. Takemura, *Tetrahedron Lett.*, **2020**, *61*, 151973.
2) S. Tanaka, H. Kojima, S. Takeda, R. Yamanaka, T. Takemura, *Tetrahedron Lett.*, **2021**, *77*, 153249.