

**Supplementary Information for**

**Deciphering the molecular interactions of binaphthyl compounds with  
*Penicillium expansum* lipase: prediction of the lipase enantioselectivity  
and reactivity**

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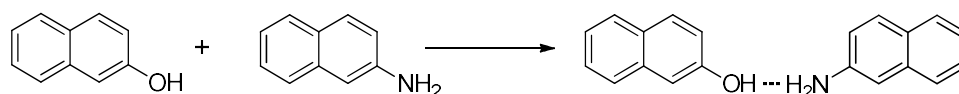
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## 1. General Procedures

Reagents and solvents were purchased from common commercial sources and used as received or purified by distillation over appropriate drying agents.

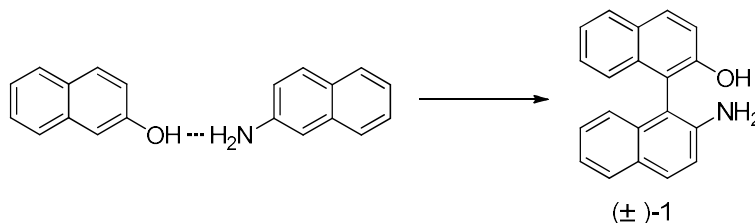
## 2. Preparation of substrates for the enzymatic reaction

### 2.1 Synthesis of the molecular crystal (the precursor of NB)



An equimolar solution of 2-naphthol (10 g, 69.8 mmol) and 2-naphthylamine (10 g, 69.8 mmol) in toluene was refluxed at 80 °C for 1 h under nitrogen atmosphere. Then the reaction mixture was filtered with toluene after cooling to room temperature. A two-component molecular crystal composed of equimolar solution of 2-naphthol and 2-naphthylamine was obtained by the slow evaporation of toluene (14.45 g, 72% yield).

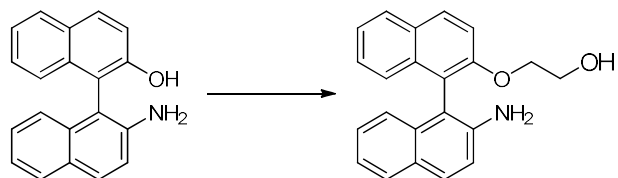
### 2.2 Synthesis of racemic NB (2-amino-2'-hydroxy-1,1'-binaphthyl)



Racemic 2-amino-2'-hydroxy-1,1'-binaphthyl was prepared as follows: a suspension of molecular crystal (8 g, 27.84 mmol) in water containing  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  (30 g, 111.36 mmol) was stirred at 55 °C for 6 h under a nitrogen atmosphere. After cooling, the solid material was collected quantitatively by filtration and washed with distilled water to remove  $\text{Fe}^{3+}$  and  $\text{Fe}^{2+}$ . The solid was chromatographed on an activated charcoal column (100×18 mm, 100 g of activated charcoal) using acetone as eluent. The solvent was then removed in

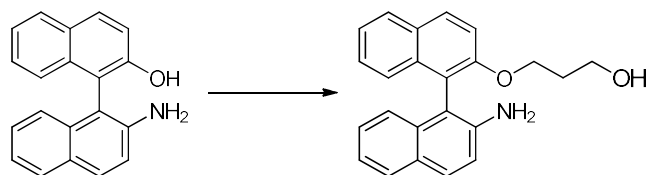
vacuo, and white crystals of NB were obtained by recrystallisation in benzene (5.32 g, 67% yield).

### 2.3 Synthesis of racemic ENB (2-amino-2'-(2-hydroxy)-ethoxy-1,1'-binaphthyl)



Potassium carbonate (1.94 g; 14.06 mmol) was added to the solution of 2-amino-2'-hydroxy-1,1'-binaphthyl (2 g, 7.01 mmol) in 20 mL dry dimethylformamide. The reaction mixture was stirred at 110 °C for 1 h. 2-chloroethanol (0.56 mL; 8.42 mmol) was then dropwisely added and the reaction mixture was stirred at 110 °C for another 24 h. At the end of reaction, the mixture was cooled to room temperature and extracted with ethyl acetate (3×20 mL). The combined organic phases were dried under Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was then removed under vacuum leaving oil. Purification by column chromatography (eluent: petroleum ether/ethyl acetate = 70/ 30) gave the racemic hydroxyethyl-NOBIN as a oily solid (2.10 g, 91% yield). (Found: C, 79.94; H, 5.91; N, 4.24; O, 9.91). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>, δ =7.26): δ = 3.57 – 3.67 (2H, m, ArOCH<sub>2</sub>CH<sub>2</sub>), 4.13-4.26 (2H, m, ArOCH<sub>2</sub>CH<sub>2</sub>), 6.96-7.46 (8H, m, aromatic protons), 7.77-8.04 (4H, m, aromatic protons); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>, δ =77.0): δ = 61.06, 71.44, 114.66, 115.35, 118.36, 119.12, 122.64, 124.17, 124.34, 125.18, 126.60, 126.99, 128.17, 128.18, 128.63, 129.20, 129.65, 130.21, 133.63, 133.93, 141.20, 154.41). ESI/MS Calcd. for C<sub>22</sub>H<sub>20</sub>NO<sub>2</sub> [M+H]<sup>+</sup> : 330.2. Found 330.5.

### 2.4 Synthesis of racemic PNB (2-amino-2'-(3-hydroxy)-propyloxy-1,1'-binaphthyl)



Potassium carbonate (0.97 g; 7.03 mmol) was added to the solution of 2-amino-2'-hydroxy-1,1'-binaphthyl (1 g, 3.50 mmol) in 20 ml dry dimethylformamide. The reaction mixture was stirred at 110°C for 1 h. 3-chloro-1-propanol (0.36 ml; 4.21 mmol) was then dropwisely added and the reaction mixture was stirred at 110°C for another 24 h. Work up and purification were carried out according to the methods mentioned above. The racemic hydroxypropyl-NOBIN as a oily solid (1.21 g, 90% yield) was obtained finally. (Found: C, 80.14; H, 6.16; N, 4.08; O, 9.62). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>, δ = 7.26): δ = 1.62-1.80 (2H, m, ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.24 - 3.34 (2H, m, ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 4.11-4.21 (2H, m, ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 6.97-7.53 (8H, m, aromatic protons), 7.77-8.05 (4H, m, aromatic protons); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>, δ = 77.0): δ = 31.61, 59.68, 67.59, 114.37, 115.73, 118.26, 119.47, 122.53, 124.21, 124.28, 125.08, 126.48, 126.98, 128.15, 128.48, 129.21, 129.81, 130.15, 133.55, 134.03, 141.58, 154.86. ESI/MS Calcd. for C<sub>23</sub>H<sub>22</sub>NO<sub>2</sub> [M+H]<sup>+</sup> : 344.2. Found 344.5.

## 2.5 (*S*)-enriched monoacetyl-hydroxyethyl-NOBIN (2-amino-2'-(2-acyloxy)ethyloxy-1,1'-binaphthyl)

(*S*)-enriched monoacetyl-hydroxyethyl-NOBIN (0.11 g, 31% yield, 74% ee) was obtained at 30% conversion. (Found: C, 77.41; H, 5.91; N, 3.87; O, 12.81). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>, δ = 7.26): δ = 1.77 (3H, s, COCH<sub>3</sub>), 3.98-4.20 (4H, m, OCH<sub>2</sub>CH<sub>2</sub>O), 6.94-7.49 (8H, m, aromatic protons), 7.74-8.04 (4H, m, aromatic protons); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>, δ = 77.0): δ = 20.53, 62.83, 68.13, 113.47, 117.21, 118.20, 121.08, 122.10,

124.24, 124.49, 125.29, 126.31, 126.98, 127.97, 128.12, 128.15, 129.07, 129.98, 130.26, 133.66, 134.21, 142.20, 154.49, 170.80. ESI/MS Calcd. for  $C_{24}H_{21}NO_3K$   $[M+K]^+$  : 410.1. Found 410.5. The same procedure was applied in PEL-catalyzed esterification of (*R,S*)-NOBIN and (*R,S*)-hydroxypropyl-NOBIN.

## **2.6 (S)-enriched monoacetyl-hydroxypropyl-NOBIN (2-amino-2'-(3-acyloxy)-propyloxy-1,1'-binaphthyl)**

(*S*)-enriched monoacetyl-hydroxypropyl-NOBIN (0.27 g, 46% yield, 17% ee) was obtained at 70% conversion. (Found: C, 77.62; H, 6.12; N, 3.68; O, 12.60).  $^1H$ -NMR (400 MHz,  $CDCl_3$ ,  $\delta = 7.26$ ):  $\delta = 1.69-1.83$  (2H, m,  $ArOCH_2CH_2CH_2$ ), 1.92 (3H, s,  $COCH_3$ ), 3.63-3.72 (1H, m,  $CH_2OAc$ ), 3.78-3.87 (1H, m,  $CH_2OAc$ ), 3.96-4.17 (2H, m,  $ArOCH_2CH_2CH_2$ ), 6.93-7.48 (8H, m, aromatic protons), 7.75-8.02 (4H, m, aromatic protons);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ,  $\delta = 77.0$ ):  $\delta = 20.86, 28.74, 60.99, 66.36, 113.90, 116.34, 118.20, 120.29, 122.14, 124.21, 125.21, 126.22, 126.92, 127.98, 128.06, 128.24, 129.01, 129.93, 133.68, 134.16, 141.81, 154.62, 170.81$ . ESI/MS Calcd. for  $C_{25}H_{24}NO_3$   $[M+H]^+$  : 386.2. Found 386.5.

## **2.7 General procedure for PEL catalyzed esterification of NBs**

The PEL catalyzed esterification was initiated by adding free PEL (20 U/mL) to the mixed solvent  $CH_3CN/H_2O=9/1$  containing NBs and 10 eq. vinyl acetate at 180 rpm and 35 °C. The procedure was monitored by TLC and HPLC analysis, stopped when designated amount of substrate was converted to product. Then, the product was extracted with separatory funnel and then concentrated under vacuum. The remaining substrate and acetylated product were obtained through silica gel column chromatography eluting with

ethyl acetate / petroleum ether =1/2 (v/v).

## **2.8 General procedure for PEL catalyzed hydrolysis of NBs**

The acetylated NBs was added into Gly-NaOH buffer (pH 9.5) containing free PEL (20 U/mL) at 180 rpm and 35 °C. The reaction was stopped when designated amount of substrate was converted to product. Then, the product was extracted with separatory funnel and then concentrated under vacuum. The remaining substrate and deacetylated product were obtained through silica gel column chromatography eluting with ethyl acetate / petroleum ether =1/2 (v/v).

