

**Electronic Supplementary Information for:****Enantiomerically pure  $\beta$ -phenylalanine analogues from  $\alpha/\beta$ -phenylalanine mixtures in a single reactive extraction step****Bastiaan J.V. Verkuijl, Wiktor Szymański, Bian Wu, Adriaan J. Minnaard,  
Dick B. Janssen, Johannes G. de Vries and Ben L. Feringa****Extraction experiments and chemical analysis**

All extraction experiments were carried out in 1.5 mL screw capped vials. In a standard experiment, a 1.0 mM solution of the host in the organic phase was combined with a 2.0 mM solution of the substrate in the buffered aqueous solution in equivolumous amounts (0.40 mL). Reactions were carried out *in duplo* and with a simultaneous blank extraction ( $c(\text{host}) = 0.0 \text{ mM}$ ) to determine the physical partition of the substrate. Physical partitions were found to be not significant in this study. The two phase systems were stirred overnight at  $T = 6 \text{ }^\circ\text{C}$  and subsequently allowed to settle for at least 30 min. The aqueous phase was analyzed by RP-HPLC, using Shimadzu CC-20AD pumps, a Chirobiotic T column (Sigma-Aldrich) equipped with a SPD-M20A diode array detector. A calibration curve was prepared in the concentration range employed for the determination of the distribution. Error margins were typically between 0.5-2.0 %. A buffer of triethylamine (0.05 v-%) and acetic acid (0.05 v-%) was diluted with double distilled water ( $130 \text{ mL L}^{-1}$ ). MeOH was used with the buffer in a 20:80 ratio as an eluent at a flow rate of  $0.30 \text{ mL min}^{-1}$ .

**Chemicals**

Triphenylphosphine and all organic solvents were obtained from Acros.  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  was obtained from Strem. All Phe analogues were obtained from PepTech. Water used in this study was doubly distilled prior to use. All buffers were prepared using  $\text{NaH}_2\text{PO}_4$ , obtained from Merck at a concentration of 100 mM and subsequent addition of HCl (aq) or NaOH (aq). The pH was measured using a Hanna Instruments pH 213 Microprocessor pH meter.

 **$\text{PdCl}_2(\text{triphenylphosphine})_2$** 

$\text{PdCl}_2(\text{triphenylphosphine})_2$  was made according to a modified procedure by Robert *et al.*<sup>1</sup> In a Schlenk tube under nitrogen, 100 mg (0.28 mmol) triphenylphosphine and 36 mg (0.14 mmol)  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  were dissolved in 10 mL dichloromethane. The solution was stirred overnight and the solvent was evaporated *in vacuo*. The crude product was triturated with ether and dried in a vacuum oven overnight, yielding  $\text{PdCl}_2(\text{tpp})_2$  (82 mg, 84 %) as a yellow solid. <sup>1</sup>H NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 – 7.60 (m,  $J = 12.3, 6.7, 10\text{H}$ ), 7.51 – 7.27 (m, 20H). <sup>13</sup>C NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  135.4, 135.3, 135.1, 130.7, 130.7, 130.3, 129.8, 129.4, 128.4, 128.3, 128.16. <sup>31</sup>P NMR (80 MHz,  $\text{CDCl}_3$ )  $\delta$  24.3. MS (ES)  $m/z$ : 666.4 ( $\text{M}^+ - \text{Cl}$ ). Anal. Calcd for  $\text{C}_{36}\text{H}_{30}\text{P}_2\text{Cl}_2$ : C, 61.60; H, 4.31; Found: C, 61.52 H, 4.31.

**General procedure for the recovery of palladium complex from the extraction mixture (recycling of the host):**

After extraction, the organic and aqueous layer were separated. A 0.100 M HCl aqueous solution was added in equivolumous amounts to the organic layer containing the palladium phosphine complex. The mixture was stirred for 3h. After settling, the layers were separated and the organic phase containing the palladium phosphine complex could be re-used in extraction, giving similar results.

Reference List

1. R. A. Michelin, L. Zanutto, D. Braga, P. Sabatino, and R. J. Angelici, *Inorganic Chemistry*, 1988, **27**, 85.