Highly Enantioselective Synthesis of Secondary Alcohols using Triphenylborane

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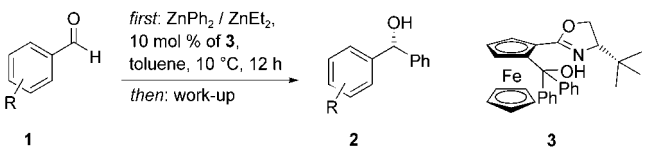
Dedicated to Joe P. Richmond on the occasion of his 60th birthday.

Abstract: Asymmetric phenyl transfer reactions with triphenylborane as aryl source and a ferrocene-based catalyst give secondary alcohols in high yields and excellent enantioselectivities.

Keywords: C–C bond formation; diarylmethanol; enantioselective catalysis; iron; triphenylborane; zinc organyls

Due to the high biological activity of various derivatives, enantiopure diarylmethanols are important compounds for the pharmaceutical industry. For example, neobenodine, orphenadrine, and carbinoxamine show strong antihistaminic properties.[1] More recently, enantiopure diarylmethanols have been used as key intermediates for the synthesis of diarylalkylmethanes which are antimuscarinics, antidepressants, and endothelin antagonists.[2] For their large-scale preparation the application of highly efficient catalytic and enantioselective methods employing inexpensive starting materials would be most desirable. Previous approaches towards enantiopure diarylmethanols involved asymmetric reductions of prochiral ketones[3] or phenyl transfer reactions to aryl aldehydes.[4] For the latter transformation we developed a protocol which utilized ferrocene-based catalyst **3** and diphenylzinc (in combination with diethylzinc) as aryl source.[5,6] Enantiomerically enriched diarylmethanols with excellent enantiomeric excesses (up to 99% ee) were thus obtained in a straightforward manner (Scheme 1).

Subsequently, the applicability of air-stable arylboronic acids as aryl source was demonstrated.[7] This



Scheme 1. Phenyl transfer to aromatic aldehydes with a mixture of $ZnPh_2$ and $ZnEt_2$.

broadened the substrate scope significantly, and now almost any diarylmethanol is accessible by this aryl transfer method.

With the intention to reduce the catalyst loading (of commonly 10 mol %) we also explored additive effects in the phenyl transfer to aldehydes. Within these studies we found triphenylborane to be an interesting alternative phenyl source.[8] This boron reagent is (commercially) available in large quantities and rather inexpensive compared to diphenylzinc. The initial studies revealed that good results in terms of yield and enantioselectivity could be achieved in the phenyl transfer from BPh_3 to 4-chlorobenzaldehyde (**1a**) and 4-methylbenzaldehyde (**1b**). Questionable at that point was whether BPh_3 could also be employed in the phenyl transfer to higher functionalized or heterocyclic aldehydes. Since the resulting products are of interest for pharmaceutical purposes,[1] we decided to initiate a more detailed investigation of the catalytic aryl transfer from BPh_3 to aldehydes. The results of these studies, which revealed BPh_3 as a cheap and versatile phenyl source for the synthesis of optically active secondary alcohols including diarylmethanols, are summarized in Table 1. For comparison literature data[5b] obtained with the original $ZnPh_2/ZnEt_2$ system are listed as well.

Gratifyingly, the BPh_3-based system worked rather well for a wide range of substrates. In many cases similar or even better results (yields and ee values) were obtained compared to the original system using $ZnPh_2$ as phenyl source. For example, (4-chlorophenyl)phenylmethanol (**2a**) had 97% ee in both reactions, and the yield increased from 95 to 98%, when applying BPh_3 instead of $ZnPh_2$ (Table 1, entry 1). In the catalysis starting from 4-phenylbenzaldehyde (**1d**), the BPh_3-based system afforded diarylmethanol **2d** with 98% ee in 88% yield, which, in this case, corresponds to a higher ee but reduced yield compared to the reaction with $ZnPh_2$ (Table 1, entry 4). Mesityl aldehyde (**1g**) reacted also well and gave **2g** with 91% ee in 84% yield. In contrast to these overall positive data, a significantly decreased enantioselectivity was observed in phenyl additions from BPh_3 to 4-methoxybenzaldehyde (**1c**) and 2-bromobenzaldehyde (**1e**), which both were formed with

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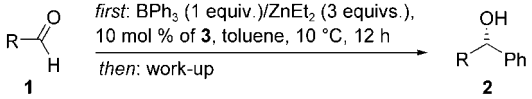
Table 1. Catalyzed asymmetric phenyl transfer to various aldehydes.

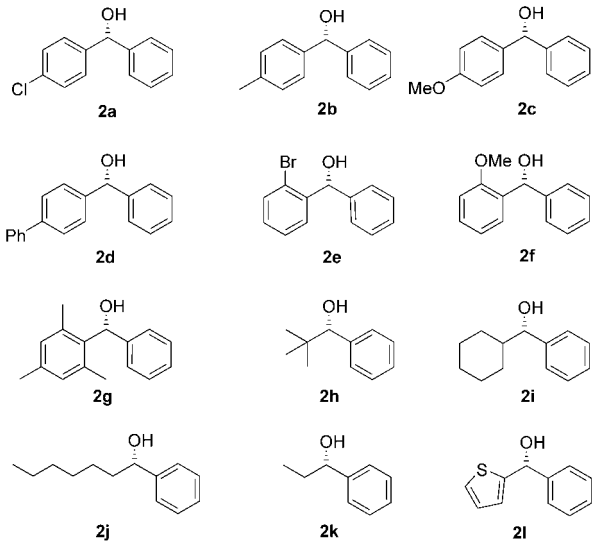


Entry	Aldehyde	Product	$ZnPh_2/ZnEt_2$ protocol[a]		$BPh_3/ZnEt_2$ protocol	
			Yield [%][b]	ee [%][c]	Yield [%][b]	ee [%][c]
1	4-Chlorobenzaldehyde (**1a**)	**2a**	95	97	98	97 (*R*)
2	4-Methylbenzaldehyde (**1b**)	**2b**	99	98	97	98 (*R*)
3	4-Methoxybenzaldehyde (**1c**)	**2c**	82	98	91	87 (*R*)
4	4-Phenylbenzaldehyde (**1d**)	**2d**	95	95	88	98 (*R*)
5	2-Bromobenzaldehyde (**1e**)	**2e**	99	96	56	87 (*R*)
6	2-Methoxybenzaldehyde (**1f**)	**2f**	–	–	89	87 (*R*)
7	2,4,6-Trimethylbenzaldehyde (**1g**)	**2g**	99	92	84	91 (*R*)
8	2,2-Dimethyl-1-propanal (**1h**)	**2h**	68	94	51	97 (*S*)
9	Cyclohexylcarbaldehyde (**1i**)	**2i**	–	–	99	89 (*S*)
10	Heptanal (**1j**)	**2j**	–	–	97	80 (*S*)
11	Propanal (**1k**)	**2k**	–	–	97	85 (*S*)
12	2-Thiophenecarbaldehyde (**1l**)	**2l**	–	–	87	91 (*R*)

[a] Data taken from Ref.[5b]; – indicates that no data were given.
[b] After column chromatography.
[c] The enantiomeric ratios were determined by HPLC using a chiral column. For details see experimental section. The assignment of the absolute configuration is based on previous studies (Ref.[5b]) under the assumption of a similar reaction pathway.

87% ee (Table 1, entries 3 and 5). For the latter substrate steric reasons or a potential chelating effect with the *ortho*-bromo substituent might be responsible for this relatively low ee. The same argument could be relevant in the conversion of the 2-methoxy-substituted benzaldehyde **1f**, which gave **2f** with 87% ee in 89% yield. Furthermore, this product appeared to be somewhat unstable, and decomposition could only be avoided by rapid work-up.

A very striking result was obtained with pivaldehyde (**1h**). Generally, aliphatic aldehydes are difficult substrates in catalyzed organozinc additions,[9–11] and thus the 91% ee for **2h** achieved in the phenyl transfer to **1h** were remarkable. To our delight we found that other aliphatic substrates (**1i**–**k**) reacted well, too, affording the corresponding secondary alcohols **2i**–**k** with ee values in the range of 85–89% in excellent yield (Table 1, entries 9–11).



These positive results with BPh_3 as phenyl source became also possible because a modified work-up was used, which allowed the removal of residual boron compounds from the crude product by extraction with diluted acetic acid and avoids any tedious chromatographic separation of **2** from those by-products. Furthermore, ferrocene **3** could be recovered in almost quantitative yield by simple flash chromatography. Its reuse in the catalyzed aryl transfer revealed its retained catalytic activity and enantioselectivity.

Phenyl additions to heteroaromatic aldehydes proved to be more challenging. Among the tested substrates, which also included 2-furylcarbaldehyde and all positional isomers of pyridinecarbaldehyde, only 2-thiophenecarbaldehyde (**1l**) was a suitable starting material, and the corresponding diarylmethanol **2l** was obtained with 91% ee in 87% yield (Table 1, entry 12). Noteworthy, a rapid work-up was essential to avoid decomposition of the rather unstable product. In all other cases, no conversion (presumably due to complexation of BPh_3) or product decomposition was observed, which did not allow an adequate NMR or HPLC analysis.

A larger scale application of the newly developed protocol with low cost BPh_3 as phenyl source was investigated with three different aldehydes (Table 2).

Table 2. Gram-scale synthesis of diarylmethanols with BPh_3 as phenyl source.[a]

Entry	Aldehyde	Yield [%][b]	ee [%][c]
1	4-chlorobenzaldehyde (**1a**)	97	97 (*R*)
2	4-methylbenzaldehyde (**1b**)	98	95 (*R*)
3	2-bromobenzaldehyde (**1e**)	97	82 (*R*)

[a] A mixture of 1 equiv. of BPh_3 and 3 equivs. of $ZnEt_2$ in toluene (at 10 °C for 12 h) was used in all experiments.
[b] After column chromatography.
[c] Enantiomer ratios were determined by HPLC analysis using a chiral column.

The larger-scale protocol proved highly efficient in terms of the product yield. Even the *ortho*-substituted diarylmethanol **2e**, which had been difficult to prepare in good yield before, was obtained in 97% yield.[12] With respect to the extent of the asymmetric induction, we noted a slight ee decrease in the larger-scale reactions for **1b**, since the corresponding alcohol was obtained in 95% ee, whereas the 0.25 mmol scale protocol provided it with 98% ee. Since we can exclude solvent and concentration effects, the reason for this decrease in enantioselectivity still needs to be elucidated.

With the goal to improve the efficiency of the catalyzed aryl transfer reaction, we also investigated the possibility to reduce the overall reagent amount by increasing the aldehyde-to-triphenylborane ratio. Thus, with 3 equivs. of **1a** (and 1 equiv. of BPh_3) **2a** was obtained in 62% yield. This value corresponds to a borane-based yield of **2a** of 185% and indicates that about two-thirds of all phenyl groups of the boron reagent can be activated in this process. Under these conditions, the ee of **2a** was 87%, which corresponds well to an aryl transfer reaction catalyzed by 3.3 mol % of ferrocene **3**.

In summary, we have developed a new protocol for the catalyzed, highly enantioselective phenyl transfer to aldehydes. Inexpensive and readily available triphenylborane serves as phenyl source, and the method allows the versatile synthesis of a broad range of secondary alcohols with high enantioselectivities in good to excellent yields with a good atom economy for BPh_3. Additionally, remarkable enantioselectivities have also been achieved in conversions of aliphatic aldehydes.

Experimental Section

All air sensitive manipulations were carried out under an inert atmosphere of Ar using standard Schlenk techniques or sealed vials. Toluene was distilled under nitrogen from sodium/benzophenone ketyl radical. Diethyl ether and pentane for column chromatograpy were distilled before use. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer (300 MHz and 75 MHz) and on a Varian Inova 400 spectrometer (400 MHz and 100 MHz). HPLC measurements were performed on a Dionex HPLC system (previously Gynkotek) with autosampler (Gina 50), UV detector (UVD 170S), degasser (DG 503) and gradient pump (M480G). As stationary phase chiral HPLC columns from Chiral Technologies were used.

General Procedure for the Synthesis of Secondary Alcohols 2a–l

In a glove-box a 10 mL vial was charged with triphenylborane (60.5 mg, 0.25 mmol). The vial was sealed with a septum and removed from the glove-box. Freshly distilled toluene was added (1.25 mL). After the addition of $ZnEt_2$ (1 M in heptane, 0.75 mL, 0.75 mmol), the mixture was stirred for 45 min at room temperature. Another vial was charged with ferrocene **3** (12.5 mg, 0.025 mmol), sealed with a septum, and flushed with argon. Toluene (1 mL) was added to dissolve **3** and the solution was transferred *via* a syringe into the first vial. The resulting mixture was stirred for 30 min at room temperature, then cooled to 10 °C and stirred for an additional 10 min at this temperature. A third vial was charged with aldehyde **1a–l** (0.25 mmol, 1 equiv.), closed with a septum, flushed with argon, and the substrate was dissolved in toluene (1 mL). After cooling to 10 °C the solution was transferred *via* syringe into the other reaction vial. The resulting mixture was stirred for 12 h at 10 °C. Then the reaction was quenched with water. Diluted acetic acid (20% in water, 30 mL) was added and the mixture extracted with dichloromethane. The organic layer was washed with water, dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, eluents: pentane/diethyl ether, 8:2) to give the desired alcohol **2**.

General Procedure for the Larger Scale Preparation of Diarylmethanols 2a, 2b, and 2e

The protocol was identical to the one described for the 0.25-mmol scale reactions with the following exceptions: A well-dried Schlenk flask was charged with triphenylborane (1.614 g, 6.67 mmol). Freshly distilled toluene (60 mL), $ZnEt_2$ (1 M in heptane, 20 mL, 20 mmol), ferrocene **3** (329 mg, 0.67 mmol), toluene (65 mL), and aldehyde **1** (6.67 mmol, 1 equiv.) were used. After the 12 h reaction time (at 10 °C) the mixture was quenched with water and acetic acid (20% in water, 100 mL) was added. The subsequent work-up was performed as described above.

(*R*)-(4-Chlorophenyl)phenylmethanol (2a)[13]

Obtained yield from 4-chlorobenzaldehyde (**1a**) (35 mg, 0.25 mmol) according to the general procedure as a white solid; yield: 54 mg (99%, 0.25 mmol, 97% ee); ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.23$ (sbr, 1H, OH), 5.78 (s, 1H, CH), 7.23–7.45 (m, 9H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 75.7$ (CH), 126.6 (2CH), 127.9 (3CH), 128.7 (2CH), 128.7 (2CH), 133.3 (C), 142.3 (C), 143.5 (C); HPLC – separation conditions: Chiralcel OB-H, 30 °C, 230 nm, 90:10 heptane/*i*-PrOH, 0.5 mL/min; $t_R = 25.7$ min (*R*), 33.6 min (*S*).

(*R*)-(4-Methylphenyl)phenylmethanol (2b)[14]

Obtained from 4-methylbenzaldehyde (**1b**) (29 μL, 0.25 mmol) according to the general procedure as a white solid; yield: 48 mg (96%, 0.24 mmol, 98% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.04 (s, 1H, OH), 2.31 (s, 3H CH_3), 5.76 (s, 1H, CH), 7.08–7.37 (m, 9H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.2 (CH_3), 76.2 (CH), 126.6 (2CH), 126.7 (2CH), 127.5 (CH), 128.5 (2CH), 129.3 (2CH), 137.3 (C), 141.0 (C), 144.0 (CH); HPLC – separation conditions: Chiralcel OD, 30 °C, 230 nm, 98:2 heptane/*i*-PrOH, 0.9 mL/min; t_R = 28.1 min (*S*), 31.3 min (*R*).

(*R*)-(4-Methoxyphenyl)phenylmethanol (2c)[4e,15]

Obtained from 4-methoxybenzaldehyde (**1c**) (34 mg, 30 μL, 0.25 mmol) according to the general procedure as a clear liquid; yield: 49 mg (91%, 0.23 mmol, 87% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.19 (sbr, 1H, OH), 3.78 (s, 3H, CH_3), 5.80 (s, 1H, CH), 6.84–6.89 (m, 2H, H_{ar}), 7.24–7.39 (m, 7H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 55.2 (CH_3), 75.6 (CH), 113.7 (2CH), 126.2 (2CH), 127.2 (CH), 127.7 (2CH), 128.2 (2CH), 136.0 (C), 143.8 (C), 158.8 (C); HPLC – separation conditions: Chiralcel OJ, 25 °C, 254 nm, 90:10 heptane/*i*-PrOH, 1.0 mL/min; t_R = 31.8 min (*R*), 37.7 min (*S*).

(*R*)-(4-Biphenyl)phenylmethanol (2d)[16]

Obtained from 4-biphenylylaldehyde (**1d**) (45 mg, 0.25 mmol) according to the general procedure as a white solid; yield: 57 mg (88%, 0.22 mmol, 98% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.39 (sbr, 1H, OH), 5.83 (s, 1H, CH), 7.22–7.44 (m, 10H, H_{ar}), 7.51–7.58 (m, 4H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 76.1 (CH), 126.7 (2CH), 127.1 (2CH), 127.2 (2CH), 127.3 (2CH), 127.4 (CH), 127.7 (CH), 128.7 (2CH), 128.8 (2CH), 140.6 (C), 140.9 (C), 142.9 (C), 143.9 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 230 nm, 98:2 heptane/*i*-PrOH, 1.0 mL/min; t_R = 65.9 min (*R*), 75.5 min (*S*).

(*R*)-(2-Bromophenyl)phenylmethanol (2e)[17]

Obtained from 2-bromobenzaldehyde (**1e**) (29 mL, 0.25 mmol) according to the general procedure as a pale yellow solid; yield: 37 mg (56%, 0.14 mmol, 97% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.47 (s, 1H, OH), 6.17 (s, 1H, CH), 7.20–7.42 (m, 7H, H_{ar}), 7.50–7.59 (m, 2H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 74.9 (CH), 122.9 (C), 127.1 (2CH), 127.8 (CH), 127.9 (CH), 128.6 (2CH), 129.2 (CH), 129.7 (CH), 132.9 (CH), 142.2 (C), 142.6 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 90:10 heptane/*i*-PrOH, 0.8 mL/min; t_R = 11.6 min (*R*), 14.9 min (*S*).

(*R*)-(2-Methoxyphenyl)phenylmethanol (2f)[18]

Obtained from 2-methoxybenzaldehyde (**1f**) (34 mg, 27 μL, 0.25 mmol) according to the general procedure as a clear liquid; yield: 48 mg (89%, 0.22 mmol, 87% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.10 (sbr, 1H, OH), 3.79 (s, 3H, CH_3), 6.05 (s, 1H, CH), 6.88 (d, 1H, *J* = 8.3 Hz, H_{ar}), 6.92–6.96 (m, 1H, H_{ar}), 7.22–7.33 (m, 5H, H_{ar}), 7.37–7.40 (m, 2H, H_{ar}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 55.7 (CH_3), 72.5 (CH), 111.0 (CH), 121.0 (CH), 126.8 (2CH), 127.3 (CH), 128.1 (CH), 128.4 (2CH), 128.9 (CH), 132.2 (C), 143.5 (C), 156.9 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 97:3 heptane/*i*-PrOH, 0.8 mL/min; t_R = 33.4 min (*S*), 38.1 min (*R*).

(*R*)-Mesitylphenylmethanol (2g)[19]

Obtained from 2,4,6-trimethylbenzaldehyde (**1g**) (37 μL, 0.25 mmol) according to the general procedure as a white solid; yield: 48 mg (84%, 0.21 mmol, 91% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.13 (sbr, 1H, OH), 2.23 (s, 6H, CH_3), 2.28 (s, 3H, CH_3), 6.32 (s, 1H, CH), 6.85 (2H, H_{ar}), 7.17–7.33 (m, 5H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.6 ($2CH_3$), 20.9 (CH_3), 71.1 (CH), 125.5 (2CH), 126.6 (CH), 128.2 (2CH), 130.1 (2CH), 136.6 (C), 137.1 (2C), 137.4 (C), 143.2 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 95:5 heptane/*i*-PrOH, 0.7 mL/min; t_R = 13.9 min (*R*), 16.2 min (*S*).

(*S*)-2,2-Dimethyl-1-phenyl-1-propanol (2h)[20]

Obtained from 2,2-dimethyl-1-propanal (**1h**) (27 μL, 0.25 mmol) according to the general procedure as a pale white solid; yield: 21 mg (51%, 0.13 mmol, 99% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.93 (s, 9H, CH_3), 1.85 (s, 1H, OH), 4.40 (s, 1H, CH), 7.23–7.34 (m, 5H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.0 ($3CH_3$), 35.7 (C), 82.5 (CH), 127.3 (CH), 127.6 (2CH), 127.7 (2CH), 142.2 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 97:3 heptane/*i*-PrOH, 1.0 mL/min; t_R = 18.8 min (*S*), 20.3 min (*R*). Due to deviation in the retention times, the HPLC analysis of **2 h** proved to be difficult. Only a strict sequential injection of the racemate and the sample to be analyzed allowed us to obtain reliable data for the enantiomer ratio determination.

(*S*)-Cyclohexylphenylmethanol (2i)[21]

Obtained from cyclohexylcarbaldehyde (**1i**) (33 μL, 0.25 mmol) according to the general procedure as a pale yellow solid; yield: 47 mg (99%, 0.25 mmol, 89% ee); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.85–1.42 (m, 6H, H_{al}), 1.54–1.81 (m, 4H, H_{al}), 1.89 (s, 1H, OH), 1.92–2.03 (m, 1H, H_{al}),. 4.35 (d, *J* = 7.2 Hz, CH), 7.22–7.36 (m, 5H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.1 (CH_2), 26.2 (CH_2), 26.5 (CH_2), 28.9 (CH_2), 29.4 (CH_2), 45.0 (CH), 79.4 (CH), 126.7 (2CH), 127.5 (CH), 128.2 (2CH), 143.7 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 95:5 heptane/*i*-PrOH, 0.7 mL/min; t_R = 8.8 min (*S*), 10.9 min (*R*).

(*S*)-1-Phenylheptanol (2j)[22]

Obtained from heptanal (**1j**) (35 μL, 0.25 mmol) according to the general procedure as a pale white solid; yield: 47 mg 97%, 0.24 mmol, 80% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.87 (t, *J* = 7.2 Hz, 3H, CH_3), 1.10–1.45 (m, 7H, H_{al}), 1.65–

1.95 (m, $3H_{al}$), 4.66 (dd, $J=6.0$ Hz, $J=7.4$ Hz, 1H, CH), 7.24–7.36 (m, 5H, H_{ar}); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=14.2$ (CH_3), 22.7 (CH_2), 26.0 (CH_2), 29.4 (CH_2), 31.9 (CH_2), 39.3 (CH_2), 74.8 (CH), 125.9 (2CH), 127.5 (CH), 128.4 (2CH), 144.9 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 98:2 heptane/*i*-PrOH, 1.0 mL/min; $t_R=$ 21.1 min (*R*), 24.9 min (*S*).

(*S*)-1-Phenylpropanol (2k)[23]

Obtained from 1-propanal (**1k**) (18 μL, 0.25 mmol) according to the general procedure as a pale clear oil; yield: 33 mg (97%, 0.24 mmol, 85% ee);^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=$ 0.90 (t, $J=7.4$ Hz, 3H, H_{al}), 1.65–1.89 (m, 2H, H_{al}), 2.02 (sbr, 1H, OH), 4.58 (t, $J=6.9$ Hz, CH), 7.26–7.37 (m, 5H, H_{ar}); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=10.2$ (CH_3), 31.9 (CH_2), 76.1 (CH), 126.0 (2CH), 127.5 (CH), 128.5 (2CH), 144.7 (C); HPLC – separation conditions: Chiralcel OD, 20 °C, 254 nm, 98:2 heptane/*i*-PrOH, 0.5 mL/min; $t_R=15.5$ min (*R*), 17.7 min (*S*).

(*R*)-Phenyl-(2-thienyl)methanol (2l)[24]

Obtained from 2-thiophenecarbaldehyde (**1l**) (23 μL, 0.25 mmol) according to the general procedure as a white solid; yield: 41 mg (87%, 0.22 mmol, 91% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=2.26$ (d, $J=3.9$ Hz, 1H, OH), 5.89 (d, $J=$ 3.6 Hz, 1H, CH), 6.95–7.04 (m, 1H, H_{ar}), 7.16–7.19 (m, 1H, H_{ar}), 7.24–7.41 (m, 6H, H_{ar}); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=72.7$ (CH), 121.5 (CH), 126.0 (CH), 126.2 (CH), 126.3 (2CH), 127.6 (CH), 128.3 (2CH), 143.1 (C), 145.1 (C); HPLC – separation conditions: Chiralcel OD, 25 °C, 254 nm, 99:1 heptane/*i*-PrOH, 0.9 mL/min; $t_R=42.6$ min (*S*), 47.7 min (*R*).

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