First Organocatalyzed Asymmetric Michael Addition of Aldehydes to Vinyl Sulfones

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Supporting Information

General Remarks. All reactions were carried out under a nitrogen atmosphere with oven dried glassware. Concerning ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra, chemical shift (δ) are given in ppm relative to tetramethylsilane (0 ppm). Multiplicity is indicated as follows : s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants are reported in Hz. GC/MS were recorded with Electronic Impact EI (70 eV) as source; m/z (%). Mass spectra (MS) were obtained by EI (70 eV) and High resolution mass spectra HRMS by Electrospray Ionisation (ESI). Optical rotations were measured at 25°C in a 10 cm cell in the stated solvent ; $[\alpha]_D$ values are given in $10^{-1} \text{ deg.cm}^2 \text{ g}^{-1}$ (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral Super Fluid Chromatography (SFC), with appropriated program using a gradient of methanol or by chiral Gas Chromatography (GC), with appropriated program using a gradient of temperature. Temperature programs are described as follows: initial temperature (°C) – initial time (min) – temperature gradient (°C/min) – final temperature (°C); retention times (R_T) are given in min. Flash chromatography was performed using florisil® 100-200 mesh or silicagel 32-63 μm , 60 Å.

Evolution of reaction was followed by TLC. Chloroform, extra dry, with molecular sieves was purchased from Acros and dried by filtration over basic alumina. Pyrrolidine used in organocatalysis was distilled at atmosphere pressure prior to use. phenylvinyl sulfone **1** was purchased from Fluka and used as received. 1,1-bis(benzenesulfonyl)ethylene **2** was purchased from Fluka or synthesized by known experimental procedures¹ starting from commercially available thiophenol and dichloromethane. Diamine *i*PBP **4c** was prepared according to the literature procedure.²

Aldehydes **3a-b,d-h** and L-proline were purchased from Fluka and used as received. (S)-(+)-(1-pyrrolidinylmethyl)pyrrolidine **4g** diamine was purchased from Aldrich and used as received. 2-cyclohexylacetaldehyde **3c** was prepared according to the literature procedure.³

THF and dichloromethane were dried by filtration over activated alumina. Acetonitrile was distilled over CaH_2 prior to use. Methanol was used without previous distillation.

¹ Preparation of bis(phenylthio)methane, see Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713. Preparation of bis(phenylsulfonyl)methane, see Nantz, M. H.; Radisson, X.; Fuchs, P. L. *Synth. Commun.* **1987**, *17*, 55. Preparation of 1,1-bis(benzenesulfonyl)ethylene **2** : for the 1st step Setter, see H.; Steinbeck, K. *Liebigs Ann. Chem.* **1974**, 1315. And for the 2nd step, see Carpino, L. A. *J. Org. Chem.*, **1973**, *38*, 2600.

² (a) Alexakis, A.; Andrey, O. *Org. Lett.* **2002**, *4*, 3611. (b) Andrey, O.; Alexakis, A.; Tomassini, A.; Bernardinelli, G. *Adv. Synth. Catal.* **2004**, *346*, 1147.

³ Rumbolt, G.; Rigbi, G. *J. Org. Chem.*, **1996**, *61*, 3557.

(*S,S*)-*N*-3-pentyl-2,2'-bipyrrolidine (**4e**)

To a solution of 2*S*,2'*S*-bipyrrolidine⁴ (435 mg, 3 mmol, 1 eq.) in pentan-3-one (5 mL) was added para-toluenesulfonic acid (1.14 g, 6 mmol, 2 eq.). After current procedure for hydrogenation, platinum oxide was introduced (34 mg, 0.15 mmol, 0.05 eq.), then the reaction was conducted under hydrogen atmosphere (1 atm). The mixture was filtered on celite after 2 days. The filtrate was diluted with Et₂O (10 mL) and hydrolyzed with NaOH_{aq.} 30% (5 mL) and water (3 mL). The solution was decanted, the aqueous phase was extracted three times with Et₂O. The combined organic phases were dried over MgSO₄, filtered, concentrated under reduced pressure and purified by bulb to bulb distillation (P = 0.3 mbar, θ = 140°C) to give the diamine **4e** (121 mg, 20%). [α]_D = -52.35 (CHCl₃, c = 0.96 g/100mL).

¹H NMR (400 MHz, C₆D₆) : δ = 2.96-2.82 (m, 3H); 2.81-2.72 (m, 3H); 2.67-2.43 (m, 1H); 1.70-1.66 (m, 8H); 1.45-1.31 (m, 5H); 1.08 (t, 3H; J = 10.9 Hz); 0.85 (t, 3H, J = 7.6 Hz).

¹³C NMR (100 MHz, C₆D₆) : δ = 63.48 (CH); 63.11 (CH); 61.88 (CH); 45.48 (CH₂); 44.21 (CH₂); 27.96 (CH₂); 26.93 (CH₂); 24.69 (CH₂); 24.12 (CH₂); 23.67 (CH₂); 20.14 (CH₂); 11.03 (CH₃); 10.71 (CH₃).

IR (CHCl₃) : 2956 (s); 2924 (s); 2870 (s); 2814 (m); 1460 (m); 1446 (m); 1376 (w); 1261 (w); 1198 (w); 1159 (w); 1092 (m); 1067 (m); 921 (m); 851 (m).

MS (EI mode) *m/z* (%) : 211 (1); 141 (38); 140 (100); 112 (16); 70 (84).

HRMS (ESI) calcd for C₁₃H₂₆N₂ [M+H]⁺ 211.2167880, found 211.21679.

GC/MS (80-1-20-270-3) : R_T = 7.91 min.

Addition of unmodified aldehydes to 1,1-bis(benzenesulfonyl)ethylene 2 catalysed by amines. *General Procedure 1* : To a solution of pyrrolidine **4a** (0.16 mmol, 50 mol%) or diamine *i*PBP **4c** (0.08 mmol, 25 mol%) in dry chloroform filtered on basic alumina (3 mL) was added 1,1-bis(benzenesulfonyl)ethylene **2** (0.103 g, 0.335 mmol, 1 eq.). Then the aldehyde (3.35 mmol, 10 eq) was introduced at the appropriate temperature. The evolution of the reaction was controlled by TLC until completion. The solution was hydrolysed with NH₄Cl aq. sat. (2 mL). The layers were separated and the aqueous phase was extracted with CH₂Cl₂ (3 x 3 mL). The combined organic phases were dried over Na₂SO₄, filtered, concentrated and purified by flash column chromatography on Florisil® using a mixture of cyclohexane (c-Hex) and ethylacetate (AcOEt) as eluent.

Bis(phenylsulfonyl)ethyl-3-methylbutanal (5a)

From 3-methyl-butyraldehyde **3a** (3.35 mmol, 10 eq., 0.36 mL), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq., 0.103 g) and *i*PBP (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (164 mg) as crude which is purified by column chromatography on Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (94 mg, 71%). The enantiomeric excess was determined by chiral SFC (chiralcel OJ column, 2 mL/min, 200

⁴ a) Alexakis, A.; Tomassini, A.; Chouillet, C.; Roland, S.; Mangeney, P.; Bernardinelli, G., *Angew. Chem. Int. Ed.* **2000**, 39, 4093. b) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, 123, 9488.

bar, MeOH 10%-2-1-25%, 30°C, R_T : 4.14 (*S*), 5.80 (*R*). $[\alpha]_D = +36.41$ (CHCl_3 , $c = 0.93$ g/100mL).

^1H NMR (400 MHz, CDCl_3) : $\delta = 9.59$ (s, 1H), 7.96-7.88 (dd, 4H, $J_1 = 24.1$ Hz, $J_2 = 7.4$ Hz), 7.73-7.67 (m, 2H), 7.60-7.53 (m, 4H), 4.71-4.68 (dd, 1H, $J_1 = 9.1$ Hz, $J_2 = 3.1$ Hz), 2.94-2.90 (m, 1H), 2.54-2.47 (m, 1H), 2.17-2.11 (m, 2H), 0.99 (d, 3H, $J = 7.1$ Hz), 0.94 (d, 3H, $J = 6.8$ Hz).

^{13}C NMR (100 MHz, CDCl_3) : $\delta = 203.99$ (1 CHO), 137.89 (1C_{quat.}), 137.74 (1C_{quat.}), 134.75 (1CH), 134.57 (1CH), 129.78 (1CH), 129.37 (1CH), 129.186 (1CH), 129.14 (1CH), 80.55 (1CH), 54.67 (CH), 28.62 (1CH), 21.51 (1CH₂), 19.84 (1CH₃), 19.04 (1CH₃).

MS (EI mode) m/z (%) : 396 (1), 225 (28), 169 (12), 145 (14), 143 (25), 141 (11), 134 (13), 125 (49), 97 (15), 91 (17), 83 (19), 81 (10), 79 (12), 78 (25), 77 (100), 69 (13), 67 (10), 55 (35), 51 (35).

IR (CHCl_3) : 3065w, 3020w, 2964w, 2928w, 2873w, 1724s, 1585m, 1448m, 1331s, 1311m, 1157s, 1079s cm^{-1} .

HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{22}\text{O}_5\text{S}_2$ $[\text{M}+\text{Na}]^+$ 417.08046, found 417.08063.

2-(2,2-bis(phenylsulfonyl)ethyl)-3,3-dimethylbutanal (**5b**)

From 3,3-dimethyl butyraldehyde **3b** (0.41 mL, 3.35 mmol, 10 eq), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and **iPBP** (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (202 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (106 mg, 78%). The enantiomeric excess was determined by SFC (chiralcel OB-H column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, R_T : 3.05 (*S*), 3.46 (*R*)). $[\alpha]_D = +36.74$ (CHCl_3 , $c = 0.92$ g/100mL). ^1H NMR (400 MHz, CDCl_3) : $\delta = 9.71$ (s, 1H); 7.96-7.86 (m, 4H); 7.73-7.68 (m, 2H); 7.59-7.53 (m, 4H); 4.57-4.54 (dd, 1H, $J = 9.3, 2.5$ Hz); 2.79-2.76 (m, 1H); 2.58-2.51 (m, 1H); 2.28-2.21 (m, 1H); 1.02 (s, 9H).

^{13}C NMR (100 MHz, CDCl_3) : δ = 204.91 (CHO), 137.83 (2C_{quat}); 134.74 (CH), 134.57 (CH), 129.73 (2CH), 129.35 (2CH), 129.19 (2CH), 129.14 (2CH), 80.92 (CH), 58.70 (CH), 33.93 (C_{quat}), 27.81 (3 CH_3); 20.96 (CH_2).

IR (CHCl_3) : 3029 (m), 2967 (s), 2871 (w), 2849 (w), 1716 (s), 1585 (w), 1448 (s), 1373 (m), 1331 (s), 1156 (s), 1079 (s).

MS (EI mode) m/z (%) : 380 (2), 240 (15), 239 (100), 174 (11), 169 (12), 143 (47), 141 (15), 125 (63), 97m (41), 91 (14), 81 (11), 79 (12), 78 (20), 77 (73), 70 (14), 69 (21), 57 (45), 55 (52), 51 (19).

Microanalysis : calcd for $\text{C}_{20}\text{H}_{24}\text{O}_5$ S_2 : C (58.80%), H (5.92%), found C (58.80%), H (5.97%).

2-cyclohexyl-4,4-bis(phenylsulfonyl)butanal (**5c**)

From 2-cyclohexylacetaldehyde **3c** (0.422 g, 3.35 mmol, 10 eq.), 1,1-bis (benzenesulfonyl) ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and *i*PBP (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (268 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (103 mg, 71%). The enantiomeric excess was determined by SFC (chiralcel OJ column or chiralpak AS column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C , R_T : 4.18 (*R*), 5.08 (*S*)). $[\alpha]_D = +22.11$ (CHCl_3 , $c = 1.01$ g/100mL).

^1H NMR (400 MHz, CDCl_3) : δ = 9.57 (s, 1H); 7.95-7.87 (dd, 4H, $J = 22.0, 8.6$ Hz); 7.72-7.66 (m, 2H); 7.59-7.54 (m, 4H); 4.67-4.64 (dd, 1H, $J = 9.1, 3.3$ Hz); 2.91-2.87 (m, 1H); 2.55-2.48 (m, 1H); 2.19-2.12 (m, 1H); 1.76-1.54 (m, 5H), 1.28-1.01 (m, 5H).

^{13}C NMR (100 MHz, CDCl_3) : δ = 204.01 (CHO), 137.85 (C_{quat}); 134.72 (C_{quat}), 134.67 (CH), 134.50 (CH), 129.71 (2CH), 129.33 (2CH), 129.13 (2CH), 129.08 (2CH), 80.91 (CH), 54.40 (CH), 38.69 (CH), 30.39 (CH_2), 29.51 (CH_2), 26.33 (CH_2), 26.29 (CH_2), 25.95 (CH_2), 21.74 (CH_2).

IR (CHCl_3) : 2923 (m), 2852 (w), 1721 (m), 1584 (w), 1446 (s), 1325 (s), 1310 (s), 1151 (s), 1142 (s), 1077 (s).

MS (EI mode) m/z (%) : 435 (<1), 353 (1), 266 (18), 265 (100), 211 (12), 200 (22), 174 (21), 169 (20), 143 (53), 141 (14), 125 (62), 123 (20), 122 (15), 121 (10), 118 (10), 107 (10), 91 (19), 83 (10), 81 (53), 79 (19), 78 (15), 77 (51), 69 (14), 67 (29), 55 (31).

HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{26}\text{O}_5\text{S}_2$ $[\text{M}+\text{H}]^+$ 435.1292890, found 435.12929.

2-(2,2-bis(phenylsulfonyl)ethyl)pentanal (**5d**)

From valeraldehyde **3d** (3.35 mmol, 10 eq, 0.35 mL), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and *i*PBP (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (157 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (101 mg, 76%). The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, *R_T*: 9.19 (*S*), 11.49 (*R*)). [α]_D = +15.30 (CHCl₃, c = 1.02 g/100mL).

¹H NMR (400 MHz, CDCl₃) : δ = 9.52 (s, 1H), 7.96-7.88 (dd, 4H, *J*₁ = 20.2 Hz, *J*₂ = 8Hz), 7.73-7.67 (m, 2H), 7.59-7.54 (m, 4H), 4.74-4.72 (dd, 1H, *J*₁ = 8 Hz, *J*₂ = 4Hz), 3.00-2.97 (m, 1H), 2.51-2.45 (m, 1H), 2.22-2.16 (m, 1H), 1.72-1.66 (m, 1H), 1.45-1.43 (m, 1H), 1.58-1.26 (m, 2H), 0.94-0.90 (t, 2H, *J* = 7.2 Hz).

¹³C NMR (100 MHz, CDCl₃) : δ = 203.41 (1 CHO), 137.75 (C_{quat.}), 137.74 (C_{quat.}), 134.71 (1CH), 134.57 (1CH), 129.69 (2CH), 129.43 (2CH), 129.21 (2CH), 129.17 (2CH), 80.60 (1CH), 48.75 (1CH), 34.91 (1CH₂), 26.90 (1CH₂), 19.74 (1CH₂), 14.18 (1CH₃).

IR (CHCl₃) : 3028w, 2967w, 2929w, 2874w, 2854w, 2726w, 1724s, 1584m, 1465w, 1448m, 1331s, 1312m, 1156s, 1079s cm⁻¹.

MS (EI mode) *m/z* (%) : 395 (1), 296 (10), 226 (10), 225 (67), 169 (39), 160 (32), 143 (61), 141 (27), 134 (70), 125 (85), 111 (10), 109 (12), 97 (12), 91 (20), 83 (17), 81 (13), 79 (11), 78 (25), 77 (100), 55 (45), 51 (22).

2-methyl-4,4-bis(phenylsulfonyl)butanal (**5e**)

From propionaldehyde **3e** (0.24 mL, 3.35 mmol, 10 eq.), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and pyrrolidine **4a** (0.16 mmol, 0.5 eq., 14 μ L) according to *General Procedure 1* (1 hour, 25°C) to give a yellow oil (231 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (87 mg, 71%). The enantiomers couldn't be separated by SFC.

¹H NMR (400 MHz, CDCl₃) : δ = 9.56 (s, 1H); 7.95-7.90 (m, 4H); 7.73-7.69 (m, 2H); 7.60-7.56 (m, 4H); 4.77-4.74 (dd, 1H, J = 7.6, 4.6 Hz); 3.14-3.05 (m, 1H); 2.57-2.49 (m, 1H); 2.16-2.08 (m, 1H), 1.17-1.16 (d, 3H, J = 7.3 Hz).

¹³C NMR (100 MHz, CDCl₃) : δ = 202.9 (CHO), 137.68 (C_{quat}); 137.64 (C_{quat}), 134.78 (CH), 134.67 (CH), 129.70 (2CH), 129.47 (2CH), 129.22 (2CH), 129.18 (2CH), 80.57 (CH), 43.74 (CH), 26.38 (CH₂), 14.11 (CH₃).

IR (CHCl₃) : 2927 (m), 1723 (s), 1584 (w), 1447 (s), 1326 (s), 1311 (s), 1141 (s), 1077 (m).

MS (EI mode) *m/z* (%) : 367 (2), 197 (46), 169 (75), 143 (58), 141 (52), 132 (25), 126 (13), 125 (84), 109 (15), 107 (15), 106 (70), 97 (24), 91 (26), 83 (17), 79 (14), 78 (48), 77 (100), 65 (10), 55 (64), 53 (15), 51 (65), 50 (12).

2,2-dimethyl-4,4-bis(phenylsulfonyl)butanal (**5f**)

From isobutyraldehyde **3f** (3.35 mmol, 10 eq, 0.30 mL), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and pyrrolidine **4a** (0.16 mmol, 0.5 eq., 14 μ L) according to *General Procedure 1* (1 hour, 25°C) to give a yellow oil (148 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (93 mg, 73%).

¹H NMR (400 MHz, CDCl₃) : δ = 9.44 (s, 1H), 7.80-7.76 (m, 4H), 7.63-7.58 (m, 2H), 7.49-7.44 (m, 4H), 4.43 (t, 1H, J = 4.3 Hz), 2.48 (d, 2H, J = 4.5 Hz), 1.06 (s, 6H).

¹³C NMR (100 MHz, CDCl₃) : δ = 203.86 (1 CHO), 138.94 (C_{quat}), 136.56 (1CH), 128.66 (1CH), 128.16 (1CH), 79.59 (1CH), 43.96 (C_{quat}), 30.69 (1CH₂), 21.35 (2CH₃).

MS (EI mode) *m/z* (%) : 381 (1), 296 (12), 211 (59), 143 (57), 125 (100), 77 (91), 69 (91).

IR (CHCl₃) : 2969 (w), 2928 (w), 1721 (s), 1584 (w), 1471 (w), 1448 (s), 1372 (w), 1327 (s), 1312 (s), 1243 (m), 1150 (s), 1079 (s), 1045 (m).

HRMS (ESI) calcd for C₁₈H₂₀O₅S₂ [M+H]⁺ 381.4883, found 381.0819.

2-(2,2-bis(phenylsulfonyl)ethyl)-2-methylbutanal (**5g**)

From 2-methyl-butylaldehyde **3g** (3.35 mmol, 10 eq, 0.36 mL), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and **iPBP** (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (4 hours, 25°C) to give a yellow oil (173 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (79 mg, 59%). The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, *R*_T: 5.51 (*R*), 6.28 (*S*)). [α]_D = +70.08 (CHCl₃, c

= 1.2 g/100mL).

^1H NMR (400 MHz, CDCl_3) : δ = 9.51 (s, 1H), 7.87-7.83 (m, 4H), 7.69-7.65 (m, 2H), 7.55-7.51 (m, 4H), 4.46-4.44 (dd, 1H, J_1 = 3.7 Hz, J_2 = 5.1 Hz), 2.6-2.54 (dd, 1H, J_1 = 5.1 Hz, J_2 = 16.4 Hz), 2.35-2.30 (dd, 1H, J_1 = 3.5 Hz, J_2 = 16.4 Hz), 1.82-1.73 (q, 1H, J_1 = 7.3 Hz, J_2 = 6.8 Hz), 1.51-1.44 (q, 1H, J_1 = 7.3 Hz, J_2 = 6.8 Hz), 0.95 (s, 3H), 0.85 (t, 3H, J_1 = 7.3).

^{13}C NMR (100 MHz, CDCl_3) : δ = 205.95 (1 CHO), 137.9 (C_{quat}), 137.36 (1CH), 134.71 (1CH), 134.56 (1CH), 79.40 (1CH), 48.39 (C_{quat}), 30.64 (1CH₂), 29.47 (CH₂), 17.05 (1CH₃), 8.37 (1CH₃).

IR (CHCl_3) : 3029 (w), 2972 (w), 2929 (w), 1718 (s), 1585 (w), 1459 (w), 1448 (s), 1331 (s), 1316 (s), 1155 (s), 1079 (s).

MS (EI mode) m/z (%) : 395 (1), 347 (1), 296 (10), 226 (10), 225 (65), 223 (18), 169 (11), 143 (54), 141 (17), 134 (37), 126 (10), 125 (86), 97 (16), 91 (25), 83 (71), 82 (36), 81 (24), 79 (16), 78 (27), 77 (100), 67 (24), 55 (64), 53 (14), 51 (32).

Microanalysis : calcd for $\text{C}_{19}\text{H}_{22}\text{O}_5\text{S}_2$: C (57.85%), H (5.62%), found C (58.06%), H (5.86%).

2-methyl-2-phenyl-4,4-bis(phenylsulfonyl)butanal (**5h**)

From 2-phenylpropionaldehyde **3h** (0.44 mL, 3.35 mmol, 10 eq.), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and *i*PBP (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (7 hours, 25°C) to give a yellow oil (452 mg) as crude which is purified by column chromatography Florisil® (c-Hex/AcOEt 2:1) to obtain a pale yellow oil (10 mg, 14%). The enantiomeric excess was determined by SFC (chiralcel OJ column or chiralcel OB-H column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, R_T : 5.03, 6.84).

^1H NMR (400 MHz, CDCl_3) : δ = 9.60 (s, 1H); 7.88-7.85 (m, 2H); 7.68-7.41 (m, 12H); 7.28-7.27 (m, 1H); 4.42-4.40 (dd, 1H, J = 8.1, 3.1 Hz); 2.96-2.92 (dd, 1H, J = 16, 3.1 Hz); 2.84-2.80 (dd, 1H, J = 17.7, 4.6 Hz); 1.46 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) : δ = 201.32 (CHO), 138.35 (C_{quat}); 137.85 (C_{quat}), 137.40 (C_{quat}), 134.54 (CH), 134.52 (CH), 129.80 (2CH), 129.76 (2CH), 129.25 (2CH), 129.05 (2CH), 129.04 (2CH), 128.09 (CH), 127.61 (2CH), 80.24 (CH), 53.10 (C_{quat}), 30.91 (CH₂), 19.60 (CH₃).

IR (CHCl_3) : 3029 (m), 1723 (s), 1600 (w), 1448 (s), 1331 (s), 1313 (s), 1158 (s), 1079 (m).

MS (EI mode) m/z (%) : 443 (<1), 395 (1), 273 (18), 143 (12), 134 (11), 131 (100), 130 (23), 129 (84), 125 (24), 121 (15), 119 (29), 105 (41), 103 (26), 91 (30), 79 (10), 78 (14), 77 (72), 51 (15).

HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{22}\text{O}_5\text{S}_2$ [$\text{M}+\text{H}$]⁺ 443.0990760, found 443.09908.

2-methyl-4,4-bis(phenylsulfonyl)butan-1-ol (**7e**)

From propionaldehyde **3e** (0.24 mL, 3.35 mmol, 10 eq.), 1,1-bis(benzenesulfonyl)ethylene **2** (0.335 mmol, 1 eq, 0.103 g) and **iPBP** (0.08 mmol, 0.25 eq., 15 mg) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (173 mg) as crude. Then, it was diluted in MeOH (3 mL), cooled to 0°C, and NaBH₄ was added by portion (17 mg, 0.435 mmol, 1.3 eq.). After 1 h at 0°C, the conversion was completed. The solution was hydrolysed with NH₄Cl aq. sat. (3 mL).

The layers were separated and the aqueous phase was extracted with EtOAc (2 x 4 mL). The combined organic phases were dried over Na₂SO₄, filtered, concentrated and purified by flash column chromatography on silica gel (c-Hex/EtOAc 1:1) to obtain a yellow pale oil **7e** (89 mg, 72%). The enantiomeric excess was determined by SFC (chiralpak AD column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, *R*_T: 8.85, 9.75)

¹H NMR (400 MHz, CDCl₃) : δ = 8.01-7.97 (m, 4H); 7.76-7.72 (m, 2H); 7.64-7.60 (m, 4H); 5.02-4.99 (t, 1H, J = 5.56 Hz); 3.67-3.64 (m, 1H); 3.45-3.41 (m, 1H); 2.37-2.30 (m, 1H), 2.15-2.10 (m, 1H), 1.57-1.50 (m, 2H), 0.89-0.87 (d, J = 6.56 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) : δ = 138.00 (C_{quat}); 137.76 (C_{quat}), 134.81 (CH), 129.78 (CH), 129.97 (2CH), 129.79 (2CH), 129.33 (2CH), 129.27 (2CH), 81.72 (CH), 68.04 (CH₂), 34.38 (CH), 30.16 (CH₂), 17.00 (CH₃).

IR : 3540 (br OH), 2964 (m), 2929 (m), 2876 (m), 1732 (m), 1584(w), 1447 (s), 1326 (s), 1310 (s), 1244 (m), 1144 (s), 1078 (s), 1043 (s), 731 (s), 686 (s).

MS (EI mode) *m/z* (%) : 338 (3), 209 (30), 197 (14), 169 (57), 143 (31), 141 (26), 132 (14), 125 (67), 106 (29), 97 (11), 85 (100), 78 (25), 77 (91), 69 (15), 67 (15), 59 (13), 57 (18), 55 (30), 51 (23).

HRMS (ESI) calcd C₁₇H₂₀O₅S₂ [M+H]⁺ 369.0824, found 369.0847.

Determination of absolute configuration of 1,4-adducts :

2-(2,2-bis(phenylsulfonyl)ethyl)-3-methylbutan-1-ol (**7a**)

From isovaleraldehyde **3a** (1.08 mL, 10.05 mmol, 10 eq.), 1,1-bis(benzenesulfonyl)ethylene **2** (0.309 g, 1.005 mmol, 1 eq.) and *i*PBP (45 mg, 0.251 mmol, 0.25 eq.) according to *General Procedure 1* (2 hours, -60°C) to give a yellow oil (476 mg) as crude. Then, it was diluted in MeOH (9 mL), cooled to 0°C, and NaBH₄ was added by portion (50 mg, 1.306 mmol, 1.3 eq.). After 1 h, the conversion was completed. The solution was hydrolysed with NH₄Cl aq. sat. (9 mL).

The layers were separated and the aqueous phase was extracted with EtOAc (2 x 3 mL). The combined organic phases were dried over Na₂SO₄, filtered, concentrated and purified by flash column chromatography on silica gel (c-Hex/EtOAc 1:1) to obtain a yellow pale oil **7a** (275 mg, 69%). The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, *R*_T: 5.28 (*R*), 5.84 (*S*)). [α]_D = -19.82 (CHCl₃, c = 1.025 g/100mL).

¹H NMR (400 MHz, CDCl₃) : δ = 7.97-7.93 (m, 4H); 7.69-7.67 (m, 2H); 7.59-7.55 (m, 4H); 5.22-5.20 (dd, 1H, J = 7.3, 3.3 Hz); 3.75-3.71 (m, 1H), ; 3.54-3.49 (m, 1H); 2.33-2.26 (m, 1H), 2.22-2.16 (m, 1H), 1.76-1.60 (m, 2H), 0.85-0.82 (m, 6H).

¹³C NMR (100 MHz, CDCl₃) : δ = 137.96 (C_{quat}); 137.73 (C_{quat}), 134.55 (C_{quat}), 134.52 (CH), 129.72 (2CH), 129.59 (2CH), 129.12 (2CH), 129.05 (2CH), 81.63 (CH), 64.80 (CH₂), 44.46 (CH), 29.84 (CH), 26.14 (CH₂), 19.47 (CH₃), 19.27 (CH₃).

IR : 3545 (br OH), 2958 (m), 2928 (m), 1732 (m), 1584(w), 1447 (s), 1326 (s), 1310 (s), 1244 (m), 1144 (s), 1078 (s), 731 (s), 686 (s).

MS (EI mode) *m/z* (%) : 366 (3), 237 (29), 225 (51), 169 (36), 160 (25), 149 (15), 143 (44), 141 (17), 134 (23), 125 (69), 113 (41), 97 (17), 95 (59), 94 (19), 91 (13), 83 (21), 81 (14), 79 (20), 78 (31), 77 (100), 71 (15), 70 (10), 69 (23), 67 (15), 57 (11), 55 (38), 53 (12), 51 (28).

HRMS (ESI) calcd C₁₉H₂₄O₅S₂ [M+Na]⁺ 396.10652, found 419.09563.

(*S*)-2-ethyl-3-methyl-1-butanol (**8**)

To Mg turnings (0.568 g, 23.4 mmol, 45 eq.) activated by TMSCl (1 drop) and 1,2-dibromoethane (1 drop) was added dropwise a solution of alcohol **7a** (206 mg, 0.52 mmol, 1 eq.) in MeOH (8 mL) at 0°C. After 1 h at 0°C, the reaction mixture was allowed to reflux overnight. Then, after cooling at room temperature, it was diluted in Et₂O (10 mL) and hydrolyzed with HCl 1N (10 mL). The layers were separated and the aqueous phase was extracted with Et₂O

(4 x 10 mL). The combined organic phases were washed by H₂O and dried over Na₂SO₄, filtered, concentrated and purified by flash column chromatography on silica gel (Et₂O/pentane 4:1) to obtain a yellow pale oil **8** (27 mg, 45%). The enantiomeric excess was determined by GC (CHIRASIL-DEX-CB column : 50°C-0-1-170-0, *R*_T: 37.97 (S), 38.73 (R)). $[\alpha]_{\text{D}}^{25}$ = -6.79 (CHCl₃, *c* = 0.118 g/100mL) compared to literature data⁵ $[\alpha]_{\text{D}}^{20}$ = -9.47(*c*=2.126, CHCl₃).

GC/MS (EI) (50°C-2-10-270-5) : *R*_T=6.27 min (100%) : 98 (10), 85 (100), 83 (15), 69 (55), 56 (60).

¹H NMR (400 MHz, CDCl₃) : δ = 3.66-3.56 (m, 2H), 1.84-1.76 (m, 1H), 1.44-1.45 (m, 1H), 1.23-1.25 (m, 2H), 0.93-0.88 (m, 9H).

Spectroscopic data are in agreement with published data.⁵

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	37.977	MM	0.1454	52.61903	6.03150	86.92489
2	38.736	MM	0.1284	7.91487	1.02703	13.07511
Totals :				60.53390	7.05853	

⁵ (a) Gao, L.-J.; Zhao, X.-Y.; Vandewalle, M.; De Clercq, P. *Eur. J. Org. Chem.* **2000**, 2755. (b) Tsuda, K.; Kishida, Y.; Hayatsu, R. *J. Am. Chem. Soc.* **1960**, 82, 3396.

¹H (C6D6, 400 MHz)

¹³C (C6D6, 100 MHz)

¹H (CDCl₃, 400MHz)

¹³C (CDCl₃, 100 MHz)

¹H (CDCl₃, 400 MHz)

¹³C (CDCl₃, 100 MHz)

¹³C (CDCl₃, 125 MHz)

¹H (CDCl₃, 400 MHz)

^{13}C (CDCl₃, 125 MHz)

^1H (CDCl₃, 400 MHz)

¹H (CDCl₃, 400 MHz)

¹³C (CDCl₃, 100 MHz)

¹H (CDCl₃, 400 MHz)

¹³C (CDCl₃, 100 MHz)

¹H (CDCl₃, 400 MHz)

¹³C (CDCl₃, 100 MHz)

Chemical structure of **5h** is shown in the inset. The structure is a benzene ring attached to a quaternary carbon, which is also bonded to a hydrogen, a carbonyl group, and a 1,1-diphenyl-2,2-dimethylpropan-1-ylidene group. The quaternary carbon is also bonded to a hydrogen and a carbonyl group.

¹³C NMR spectrum (CDCl₃) of **5h**. The x-axis represents chemical shift in ppm, ranging from -30 to 210. The spectrum shows several peaks, with the following chemical shifts (ppm) labeled above the peaks:

- 201.3217
- 138.3536
- 137.8521
- 137.4043
- 136.5522
- 134.5257
- 129.8085
- 129.7652
- 129.2576
- 129.0574
- 128.9971
- 129.0988
- 127.6109
- 80.2429
- 53.1077
- 30.9187
- 19.6044

¹H (CDCl₃, 400 MHz)

¹³C (CDCl₃, 100 MHz)

¹H Spectrum

¹³C (CDCl₃, 100 MHz)

¹H (CDCl₃, 400 MHz)