C₂-symmetric Bissulfoximines as Ligands in Copper-catalyzed Enantioselective Diels-Alder-Reactions

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General remarks

All manipulations except workup and purification were conducted under an inert atmosphere of argon using standard Schlenk techniques. Toluene was distilled from sodium/benzophenone ketyl radical prior to use. ¹H- and ¹³C-NMR spectra were recorded on a Varian Unity 400 spectrometer at 400 and 100 MHz, respectively, chemical shifts are given in ppm with internal referencing to the solvent peaks. IR spectra were measured on a Perkin Elmer 1760 FT spectrometer, MS spectra on a Varian MAT 212 and a Finnigan MAT 95 mass spectrometer, both with EI ionization. Optical rotations were determined on Perkin-Elmer PE-241 (d = 1 dm, c in g/100 mL). Elemental analyses were carried out at the Institute of Organic Chemistry at the RWTH Aachen on a Heraeus CHNO-Rapid apparatus.

[Pd₂(dba)₃] was obtained from the dmc2; 1,2-dibromo-4-nitrobenzene,¹ (*R*)-*S*-methyl-*S*-(*o*-methoxyphenyl)-sulfoximine,² and **4a-g**³ were prepared according to literature procedures. All other chemicals were commercially available and have been used without further purification: *rac*-BINAP (Strem), 1,2-dibromo-4,5-difluorobenzene (Aldrich), 1,2-dibromo-4,5-dimethylbenzene (Lancaster), NaO-*t*Bu (Acros).

General procedure for the sulfoximine coupling to aryl dibromides:

In a typical experiment [Pd₂(dba)₃] (36.0 mg, 0.04 mmol) and *rac*-BINAP (50.0 mg, 0.08 mmol) were dissolved in toluene (20 mL) under an argon atmosphere and refluxed for 10 min. After cooling of the resulting red solution to room temperature, NaO-*t*Bu (384 mg, 4.06 mmol), the sulfoximine (5.0 mmol), and the 1,2-dibromoarene (1.0 mmol) were added and stirring was continued under reflux for additional 20 h. At room temperature the suspension was diluted with diethyl ether and filtered through a plug of celite. After removing the volatile compounds, the product was directly purified by column chromatography (silica gel). All solid products could be recrystallized in ethylacetate.

(*S,S*)-*N,N'*-1,2-bis[*S*-methyl-*S*-phenylsulfonimidoyl]-benzene (**5a**):⁴

yield: 275 mg (70 %); white crystals; mp: 156-157 °C; [α]_D = -181.6 (c = 1, CHCl₃)

¹H NMR (400 MHz, CDCl₃): δ 3.37 (s, 6H, S-CH₃), 6.70 (d, *J* = 6.1 Hz, 1H, CH_{aryl}), 6.71 (d, *J* = 6.1 Hz, 1H, CH_{aryl}), 7.03 (d, *J* = 6.1 Hz, 1H, CH_{aryl}), 7.04 (d, *J* = 6.1 Hz, 1H, CH_{aryl}), 7.48-7.60 (m, 6H, CH_{aryl}), 8.12-8.15 (m, 4H, CH_{aryl})

¹³C NMR (100 MHz, CDCl₃): δ 46.1, 122.9, 124.4, 128.9, 129.5, 133.2, 138.7, 140.5

MS: m/z = 384.0 (M^+ , 100), 181.0 (17), 140.0 (71), 125.0 (46), 77.0 (10)

IR (KBr): 3052, 3018, 3001, 2918, 1584, 1563, 1490, 1444, 1339, 1298, 1286, 1250, 1195, 1120, 1096, 1055, 1031, 1021, 998, 974, 944, 789, 755, 743, 730, 687, 586, 523

Anal. calcd. for: $C_{20}H_{19}N_3O_4S_2$: C, 62.47; H, 5.24; N, 7.29; found: C, 62.37; H, 5.39; N, 7.24

(*R,R*)-*N,N'*-1,2-bis[*S*-methyl-*S*-(*o*-methoxy-phenyl)-sulfonimidoyl]-benzene (5b):

yield: 330 mg (75 %); white crystals; mp: 60-62 °C; $[\alpha]_D = +186.2$ ($c = 1$, $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$): δ 3.46 (s, 6H, S- CH_3), 3.92 (s, 6H, OCH_3), 6.66 (d, $J = 5.8$ Hz, 1H, CH_{aryl}), 6.67 (d, $J = 5.8$ Hz, 1H, CH_{aryl}), 6.94-7.04 (m, 6H, CH_{aryl}), 7.49 (dd, 7H, $J = 7.4$, 1.7 Hz, 1H, CH_{aryl}), 7.51 (dd, 7H, $J = 7.4$, 1.7 Hz, 1H, CH_{aryl}), 8.13 (dd, 7H, $J = 7.7$, 1.7 Hz, 2H, CH_{aryl})

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.8, 56.5, 112.7, 120.7, 122.3, 123.9, 128.6, 131.6, 134.9, 139.2, 157.4.

MS: m/z = 444.0 (M^+ , 100), 211.0 (23), 153.0 (99), 125 (25)

IR (KBr): 3015, 2936, 2839, 1589, 1479, 1436, 1321, 1279, 1250, 1185, 1135, 1120, 1070, 1019, 967, 801, 758

Anal. calcd. for: $C_{22}H_{24}N_2O_4S_2$: C, 59.44; H, 5.44; N, 6.30; found: C, 59.22; H, 5.46; N, 6.01

(*S,S*)-*N,N'*-1,2-bis[*S*-methyl-*S*-phenylsulfonimidoyl]-4-nitrobenzene (5c):

yield: 360 mg (84 %); yellow crystals; mp: 166 °C; $[\alpha]_D = -93.2$ ($c = 1$, $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$): δ 3.36 (s, 3H, S- CH_3), 3.39 (s, 3H, CH_3), 6.92 (d, $J = 8.8$ Hz, 1H, CH_{aryl}), 7.50-7.75 (m, 7H, CH_{aryl}), 7.85 (d, $J = 2.8$ Hz, 1H, CH_{aryl}), 8.00-8.06 (m, 2H, CH_{aryl}), 8.06-8.10 (m, 2H, CH_{aryl})

^{13}C NMR (100 MHz, $CDCl_3$): δ 46.4, 46.7, 118.1, 118.7, 122.1, 128.3, 128.3, 129.3, 129.4, 133.2, 133.4, 138.7, 139.1, 139.6, 141.9, 146.0

MS: m/z = 429.1 (M^+ , 100), 140.1 (70), 125.1 (66), 97.1 (13)

IR (KBr): 3011, 2925, 1564, 1507, 1484, 1325, 1274, 1253, 1194, 1100, 744

Anal. calcd. for: $C_{20}H_{19}N_3O_4S_2$: C, 55.93; H, 4.46; N, 9.78; found: C, 55.34; H, 4.29; N, 9.75

(*S,S*)-*N,N'*-1,2-bis[*S*-methyl-*S*-phenylsulfonimidoyl]-3,4-difluorobenzene (5d):

yield: 240 mg (57 %); white crystals; mp: 122 °C; $[\alpha]_D = -164.4$ ($c = 1$, $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$): δ 3.35 (s, 6H, S- CH_3), 6.84 (t, $J = 10$ Hz, 2H, CH_{aryl}), 7.50-7.65 (m, 6H, CH_{aryl}), 8.04-8.14 (m, 4H, CH_{aryl})

^{13}C NMR (100 MHz, $CDCl_3$): δ 45.9, 111.7, 111.8, 111.9, 128.5, 129.3, 133.0, 139.6

^{19}F NMR (376 MHz, $CDCl_3$): δ 145.62

MS: m/z = 420.1 (M^+ , 100), 265.1 (15), 217.1 (26), 140.1 (82), 125.1 (62)

IR (KBr): 502, 516, 687, 731, 746, 873, 990, 1039, 1096, 1179, 1200, 1217, 1244, 1282, 1378, 1400, 1503, 1600, 2921, 3003, 3020, 3061

Anal. calcd. for: $C_{20}H_{18}F_2N_2O_2S_2$: C, 57.13; H, 4.32; N, 6.66; found: C, 57.26; H, 4.38; N, 6.54

(*S,S*)-*N,N'*-1,2-bis[*S*-methyl-*S*-phenylsulfonimidoyl]-3,4-dimethylbenzene (5e**):**

yield: 295 mg (72 %); white crystals; mp: 188 °C; $[\alpha]_D = -54.0$ ($c = 1$, $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, 6H, Ar- CH_3), 3.32 (s, 6H, S- CH_3), 6.86 (s, 2H, CH_{aryl}), 7.50-7.60 (m, 6H, CH_{aryl}), 8.10-8.18 (m, 4H, CH_{aryl})

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.0, 45.4, 125.4, 128.6, 129.0, 130.4, 132.6, 135.8, 140.6

MS: $m/z = 412$ (M^+ , 100), 411 (8), 257 (18), 209 (28), 140 (94), 125 (84), 125 (85), 97 (20), 77 (22)

IR (KBr): 1499, 1581, 1602, 2914, 2929, 3025, 3057

Anal. calcd. for: $C_{22}H_{24}N_2O_2S_2$: C, 64.05; H, 5.86; N, 6.79; found: C, 64.21; H, 6.07; N, 6.73

(*R,R*)-*N,N'*-1,2-bis[*S*-methyl-*S*-(*o*-methoxy-phenyl)-sulfonimidoyl]-3,4-dimethylbenzene (5f**):**

yield: 320 mg (68 %), colorless oil; $[\alpha]_D = -52.0$ ($c = 1$, $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$): δ 1.93 (d, $J = 1.6$ Hz, 6H, Ar- CH_3), 3.34 (d, $J = 2.2$ Hz, 6H, S- CH_3), 3.84 (d, $J = 2.4$ Hz, 6H, OMe), 6.71 (s, 2H, CH_{aryl}), 6.80-7.00 (m, 4H, CH_{aryl}), 7.35-7.45 (m, 2H, CH_{aryl}), 8.07 (d, $J = 7.7$ Hz, 2H, CH_{aryl})

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.1, 43.2, 56.1, 112.2, 120.3, 125.0, 129.0, 129.8, 131.2, 134.3, 136.3, 157.0

MS: $m/z = 472.2$ (M^+ , 100), 239.1 (32), 153.0 (81)

IR (KBr): 3013, 2938, 1590, 1478, 1278, 1248, 756

Anal. calcd. for: $C_{24}H_{28}N_2O_4S_2$: C, 61.00; H, 5.97; N, 5.93; found: C, 60.92; H, 6.15; N, 5.31

General procedure for the Diels-Alder reaction:

In a typical experiment $[Cu(OTf)_2]$ or $[CuCl_2]$ (0.05 mmol; 10 mol%) and ligand (0.05 mmol; 10 mol%) were dissolved in the given solvent (5 mL) under an argon atmosphere and stirred for 60 min. In the case of the counter anion screening, silver salts (0.10 mmol) were added to the precursor complex synthesized from $[CuCl_2]$. Stirring was continued for 30 min. The catalysis was started by adding the dienophile (0.50 mmol), cooling to the given temperature and injecting of cyclopentadiene (0.10 mL). The reaction was monitored by TLC and stopped by filtration through a plug of silica gel using dichloromethane as solvent. After removal of the volatile compounds, the product was purified by flash-chromatography. The enantiomeric excess was determined by HPLC using a chiral column (**3a**: Chiralcel OD, *i*-PrOH:heptane = 5:95, 0.5 mL/min; **3b**: Chiralcel OD EtOH:heptane = 4:96, 1.0 mL/min; **3c**: Chiralcel OD, *i*-PrOH:heptane = 5:95 to 1:99 gradient, 0.5 mL/min). NMR was used to determine the diastereomeric ratio by integration of the olefinic protons.

References

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