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Synthesis of new sulfur-containing oxazoline ligands and their use in palladium-catalyzed allylic substitution

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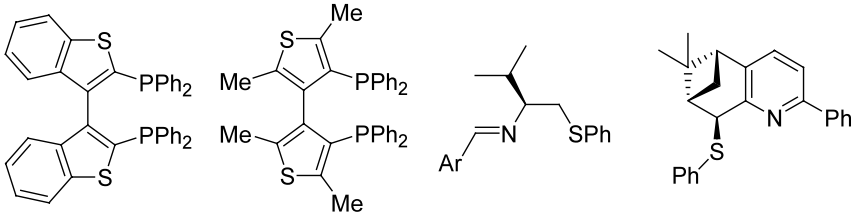
Abstract—New chiral sulfur-containing ligands have been prepared and fully characterized. Their structure includes a dibenzothiophene or benzothiophene ring as backbone, where the sulfur atom is enclosed in a strong π-donor structure. The chirality was introduced by oxazoline moieties placed near the sulfur atom. These ligands have been successfully tested in asymmetric palladium-catalyzed allylic substitutions leading to products with ee of up to 77%. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

The preparation of new and efficient enantiopure ligands providing a chiral environment to metals for asymmetric catalysis is nowadays a great concern in modern organic chemistry. Highly selective and active catalysts have already been prepared, some of them being used at the industrial scale, mostly in hydrogenation reactions.[1] A lot of work has already been published and is still in progress to optimize transformations involving C–C bond formations. Recent reviews[2,3] clearly show that nitrogen-containing ligands (and especially those with oxazoline moieties) are particularly good candidates to achieve, for example, allylic substitutions, cyclopropanations, Diels–Alder reactions, aldol or Michael-type additions.

Furthermore, the efficient use of sulfur-containing ligands has been recently reported in numerous asymmetric catalytic C–C bond formations. For example, Sannicolò et al. have described the preparation of ligands based on chiral atropoisomeric structures ((*R*)-(+)-BITIANP **1**,[4] and (+)-TMBTP **2**,[5] Scheme 1) and their use in enantioselective Heck reactions.[6,7]

Pd-catalyzed allylic substitutions, i.e. Tsuji–Trost reactions,[8] have been intensively studied with sulfur-containing ligands over the past few years. Anderson et al.[9,10] developed a series of sulfur–imine mixed donor chiral ligands (see structure **3**, Scheme 1) which gave up to 94% enantiomeric excess in this reaction. Sulfur-pyridine compounds (**4**, Scheme 1) were prepared by Chelucci[11] and enantioselectivities of up to 83% were obtained. Williams prepared various *S*,*N*-ligands (structures **5**[12]–**7**, Scheme 2) containing oxazoline functionalities and sulfur as an auxiliary donor ligand, providing enantioselectivities of 40–96% ee.[13] Bryce synthesized chiral oxazolines linked to tetrathiaful-



Scheme 1.

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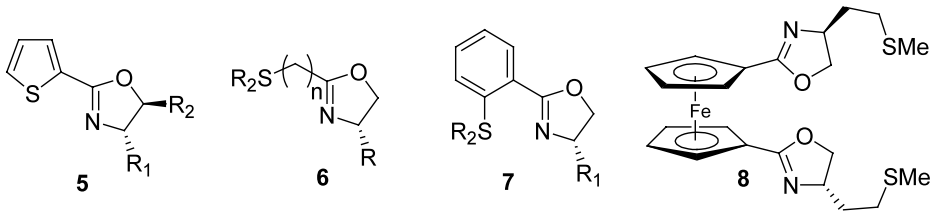


Scheme 2.

valene[14] and chiral ferrocenyl-oxazolines incorporating thioether units (see structure **8**, Scheme 2).[15] These redox-active liganding systems were successfully used in palladium-catalyzed allylic substitution reactions (up to 93% ee).

Based upon the previous work, we attempted to introduce new sulfur-containing oxazoline compounds as ligands for asymmetric catalysis. We report herein their synthesis as well as our first promising results with these chiral ligands for the enantioselective palladium-catalyzed allylic substitution.[16]

2. Results and discussion

We have chosen dibenzothiophene and benzothiophene as backbones, where the sulfur atom is part of a strong π-donor structure. These skeletons are of particular interest since their aromatic structure opens the door to a great variety of synthetic transformations, on various positions of the aromatic rings, according to the procedure used.

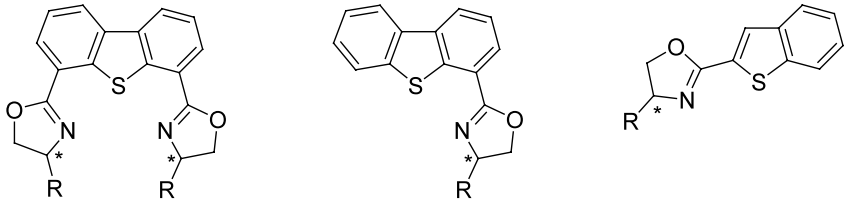
Furthermore different possible sites of chelation are offered by these ligands, i.e., *N*,*N*′- or *N*,*S*-type ligation. C_2-symmetric bis(oxazolines) based on the dibenzothiophene structure, (DBT-BOx, **9**, Scheme 3),[17] have also been synthesized to allow potential *trans*-chelating tridentate ligands. DBT-MOx **10** and BT-MOx **11** (Scheme 3) provide different possibilities: the former can afford a six-membered chelate with the metal, whereas the latter may yield a five-membered chelate. Moreover, the structural differences of both heteroaromatic rings were supposed to induce various electronic effects on the complexes. Kanemasa et al.[18] have described an analogous ligand derived from dibenzofuran and substituted by two (*R*)-phenyl-bis(oxazolines) (DBFOX/Ph). With various transition-metal(II) perchlorates, this ligand proved to be particularly efficient and enantioselective in Diels–Alder reactions.[19] Such complexes promoted moreover asymmetric nitrone cycloadditions[20] and 1,3-dipolar cycloadditions of diazoalkane.[21] Only recently, DBFOX/Ph was tested as a chiral ligand to prepare a palladium complex and its catalytic performance was studied in allylic substitution reactions.[22] This system proved to be inactive and the authors assumed that the steric hindrance between the chiral ligand and the allyl group was responsible for the instability of the complex. The well-known affinity of palladium towards sulfur justified the choice of testing DBT-BOx's and their derivatives in Pd-catalyzed allylic substitutions.

2.1. Synthesis of 4,6-dibenzothiophenediyl-2,2′-bis(4-alkyloxazolines)—DBT-BOx's

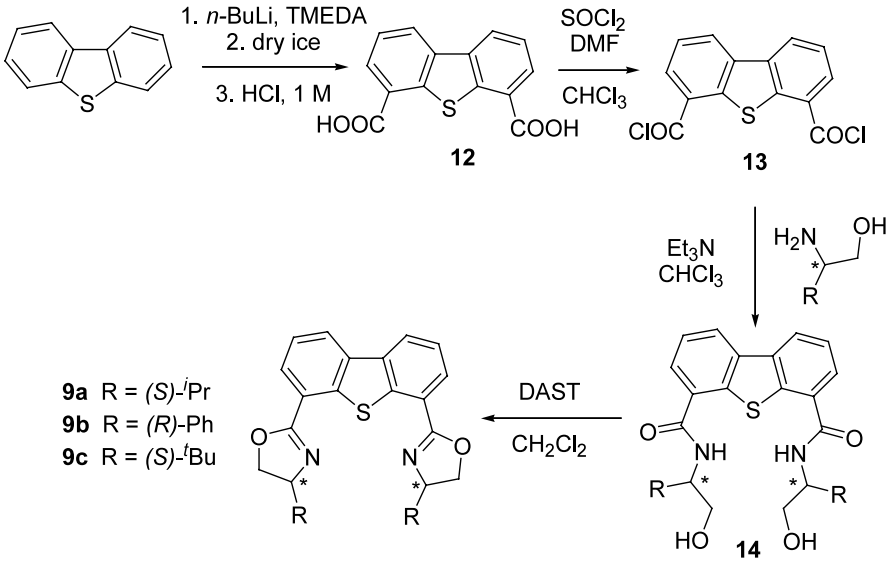
DBT-BOx ligands have been prepared following classical procedures to obtain bis(oxazolines) (Scheme 4). Dibenzothiophene was bislithiated[23] using 4 equiv. of *n*-butyllithium and tetramethylethylenediamine (TMEDA) in refluxing cyclohexane and subsequently dicarboxylated[24] with dry ice to give 4,6-dibenzothiophenedicarboxylic acid **12** with 88% yield. The corresponding diamide **14** was obtained via the acid dichloride **13**, and cyclization was then performed by activation with diethylaminosulfur trifluoride (DAST).[25] The use of (*S*)-(+)-2-amino-3-methyl-1-butanol (L-valinol) allowed the preparation of DBT-BOx(*i*Pr) **9a** in 52% yield for the whole procedure starting from dicarboxylic acid **12**. DBT-BOx(Ph) **9b** was similarly synthesized in 41% yield from (*R*)-(−)-2-phenylglycinol and DBT-BOx(*t*Bu) **9c** was obtained in 37% yield from (*S*)-*tert*-leucinol.

2.2. Synthesis of 4-dibenzothiophenyl-2-(4-alkyloxazolines)—DBT-MOx's

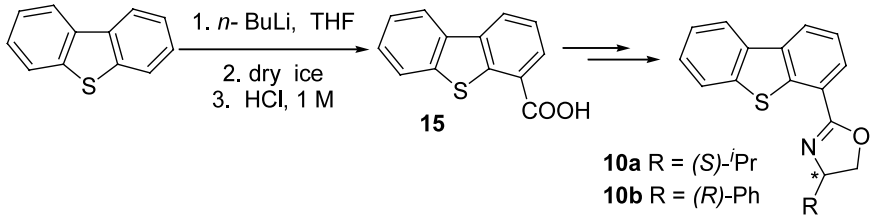
A similar strategy was used to obtain different DBT-MOx derivatives (Scheme 5). The synthesis of 4-diben



Scheme 3.



Scheme 4.

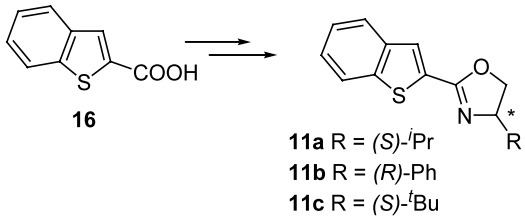


Scheme 5.

zothiophene carboxylic acid could be performed under less severe conditions than those used to synthesize the corresponding diacid. The monoacid **15** was indeed obtained in 75% yield by preparing the monolithiated species with *n*-BuLi (2 equiv.) in THF at 0°C and subsequently quenching the solution with dry ice.[26] The formation of mono-oxazoline dibenzothiophene derivatives followed then the above-mentioned procedure by using 1.1 equiv. of the desired amino-alcohol. Starting from 4-dibenzothiophene carboxylic acid, DBT-MOx(*i*Pr) **10a** was thus obtained in 22% yield for the total steps. DBT-MOx(Ph) **10b** was similarly synthesized in 34% yield.

2.3. Synthesis of 2-benzothiophenyl-2-(4-alkyloxazoline)s—BT-MOx's

Interested in testing five-membered chelating *N*,*S*-ligands, we chose the commercially available thianaphthene-2-carboxylic acid **16** as precursor. From this backbone, BT-MOx(*i*Pr) **11a** could be analogously obtained in 54% yield, BT-MOx(Ph) **11b** in 64% yield and BT-MOx(*t*Bu) **11c** was prepared in 74% yield (Scheme 6).

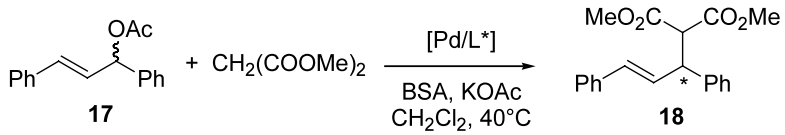


Scheme 6.

2.4. Pd-catalyzed allylic substitution

To evaluate the selectivity of a new chiral ligand for allylic substitutions, the reaction usually performed is the transformation of the 1,3-diphenylallyl system with dimethyl malonate (Scheme 7). This reaction allows indeed an easy comparison and analysis of the results due to the symmetry of the substrate. Allylic substitution of *rac*-1,3-diphenyl-2-propenyl acetate **17** was firstly investigated under various reaction conditions with DBT-BOx(*i*Pr) **9a** as chiral ligand. The C_2-symmetry of this ligand resulted in catalytic systems with restricted numbers of diastereomeric transition states and the analysis of the interactions responsible for enantioselection was thus facilitated.

We have previously reported[16] that DBT-BOx **9a**, contrary to its dibenzofuran analogue,[22] induced a high level of enantioselectivity (77% e.e., Table 1, entry 1) and activity in the transformation of *rac*-**17**, when the nucleophile was prepared in refluxing dichloromethane from BSA (*N*,*O*-bis(trimethylsilyl)acetamide) using



Scheme 7.

allylpalladium chloride dimer as catalyst precursor. Under these conditions, (*R*)-**18** was isolated in 90% yield.

Analogous ligands **9b** and **9c** (Table 1, entries 2 and 3) were both less efficient and selective when the transformation was performed under these optimized conditions. Furthermore, we noticed that DBT-BOx **9a** containing chiral fragments with (*S*)-configuration led to the substitution-product **18** with (*R*)-configuration as the major isomer. This is in contrast with results obtained by using other C_2-symmetric bis(oxazolines),[28–30] where (*S*)-configuration in the chiral ligand led to the (*S*)-**18** product as the major product. Our DBT-BOx system, as potential tridentate chelate, may also act as a bidentate or monodentate ligand, which complicates the explanation of the results obtained. However, compared with the inefficiency of the dibenzofuran analogue to perform this palladium-catalyzed reaction, we assume a probable participation of the sulfur atom for stabilizing the complex involved in the selective transformation.

DBT-MOx compounds were then tested as ligands for the palladium-catalyzed allylic substitution of *rac*-**17** under the same conditions as those used for DBT-BOx (Table 2). These *N*,*S*-chelating ligands do not contain a C_2-symmetry axis and are able to form six-membered chelates with the palladium atom.

The transformation of *rac*-**17** was first realized with **10a** in dichloromethane, with a ligand:palladium ratio of 1:1. This catalytic system allowed the preparation of the desired product **18**, with a lower activity than that of the analogous bis(oxazoline) system **9a**. Furthermore, it was noticed that, contrary to DBT-BOx(*i*Pr) **9a**, the monooxazoline **10a** led predominantly to the (*S*)-enantiomer of **18**, with 30% ee (Table 2, entry 1). We assumed both steric and electronic effects to be responsible for the observed configuration. Regarding the steric hindrance generated by the isopropyl-substituent on the oxazoline group, the substrate was thus placed on the square-planar palladium complex, as depicted in Scheme 8. In such a context, the intermediate **A** would be favored over the alternative **B**, where the steric hindrance is greater between the substituent of the oxazoline ring and the phenyl group of the substrate.

The incoming nucleophile is supposed to attack on the opposite face of the π-allyl system, i.e. on the less-sterically hindered face. The regiochemistry of attack has been demonstrated to be influenced by electronic factors with bidentate ligands containing donor atoms with different properties.[10,12,31] Dibenzothiophene is an electron-rich compound, and thus acts as a π-donor.[32] It is assumed that this electronic information would be transferred via the *trans* effect to the allyl moiety. In our particular case, the nucleophile would thus preferentially attack the allylic system on the carbon possessing a greater positive charge character, i.e. on the carbon situated *trans* to the nitrogen atom of the oxazoline moiety (see Scheme 8, for DBT-MOx **10a**). DBT-MOx **10a** led indeed to (*S*)-**18** as the major enantiomer. On the contrary, and as expected by the above-mentioned mechanism, DBT-MOx **10b** possessing a phenyl group with (*R*)-configuration on the oxazoline, allowed the preparation of **18** with a similar enantiomeric excess (34%, Table 2, entry 5) but with (*R*)-configuration. Furthermore, we tested the influence of the ratio ligand versus palladium on the enantiomeric excess, and we observed in the case of **10a** an increase in the ee value with the quantity of ligand introduced, accompanied with a maximum activity for a ratio of 2:1. This indicated that this ligand was probably not strongly bounded to the metal. However, when present in a large excess (Table 2, entry 4) DBT-MOx **10a** acted to poison the catalyst, since the conversion only reached 56% in nearly 5 days.

Finally, the Tsuji–Trost reaction was tested in the presence of the BT-Mox ligands **11** as sulfur-nitrogen-chelates, leading to a five-membered ring on coordination with the palladium centre, in an attempt to achieve selectivity control by reducing the chelate ring-size. The results are summarized in Table 3. However, the use of ligands **11** lead to catalysts with slightly lower activity than DBT-MOx's.

Again, it could be demonstrated that these *N*,*S*-ligands are not strongly bound to the metal centre, since the enantioselectivity value increased with the ratio ligand **11a**/palladium introduced at the beginning of the reaction, from 0% for a 1/1 ratio to a maximum of 35% ee for a 4/1 ratio (Table 3, entries 1–3).

Table 1. Allylic substitution of *rac*-**17** in the presence of DBT-BOx ligands[a]

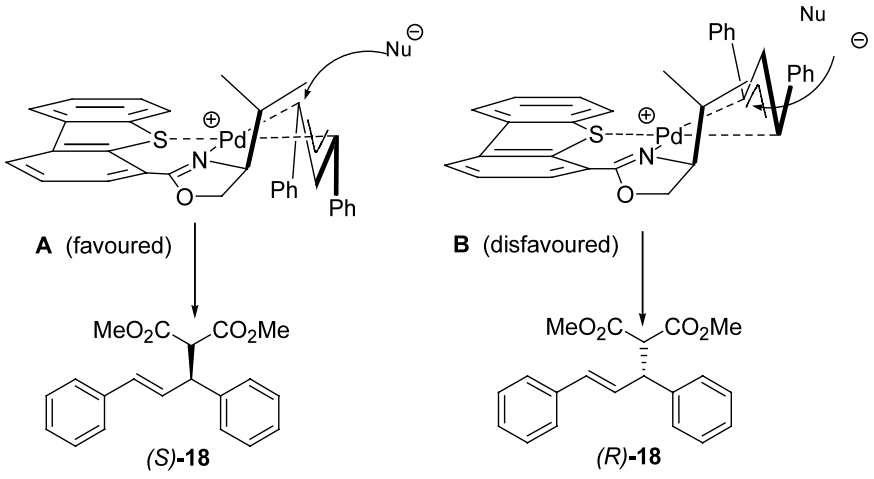
Entry	Ligand	t (h)	Conversion[b] (% of **18**)	e.e.[c] (% of **18**)
1	**9a**	70	100	77 (*R*)
2	**9b**	120	39	28 (*S*)
3	**9c**	70	50	51 (*R*)

[a] 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$, 3 equiv. of dimethylmalonate, 3 equiv. of BSA, 2 mol% of KOAc, CH_2Cl_2, 40°C.
[b] Determined by GC analysis.
[c] Determined by HPLC (Whelk O1) and absolute configuration determined by comparison with literature values.[27]

Table 2. Allylic substitution of *rac*-**17** in the presence of DBT-MOx ligands[a]

Entry	Ligand	L*/Pd	t (h)	Conversion[b] (% of **18**)	e.e.[c] (% of **18**)
1	**10a**	1/1	111	54	30 (*S*)
2	**10a**	2/1	88	100	32 (*S*)
3	**10a**	4/1	98	100	37 (*S*)
4	**10a**	6/1	117	56	41 (*S*)
5	**10b**	2/1	112	80	34 (*R*)

[a] 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$, 3 equiv. of dimethyl malonate, 3 equiv. of BSA, 2 mol% of KOAc, CH_2Cl_2, 40°C.
[b] Determined by GC analysis.
[c] Determined by HPLC (Whelk O1) and absolute configuration determined by comparison with literature values.[27]



Scheme 8.

Table 3. Allylic substitution of *rac*-**17** in the presence of BT-MOx ligands[a]

Entry	Ligand	L*/Pd	t (h)	Conversion[b] (% of **18**)	e.e.[c] (% of **18**)
1	**11a**	1/1	111	74	0
2	**11a**	2/1	115	100	13 (*R*)
3	**11a**	4/1	118	30	35 (*R*)
4	**11b**	2/1	111	71	30 (*S*)
5	**11c**	2/1	115	78	13 (*S*)

[a] 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$, 3 equiv. of dimethylmalonate, 3 equiv. of BSA, 2 mol% of KOAc, CH_2Cl_2, 40°C.
[b] Determined by GC analysis.
[c] Determined by HPLC (Whelk O1) and absolute configuration determined by comparison with literature values.[27]

The direction of the enantioselectivity was more difficult to describe and rationalize since BT-MOx **11a** and BT-MOx **11c**, possessing both a substituent with (*S*)-configuration on the oxazoline moiety, led to (*R*)-**18** (or (*S*)-**18**)), respectively, as the major enantiomer, albeit with low enantioselectivity (Table 3, entries 2 and 5). We assume that the ability of (*S*)-BT-MOx(^{t}Bu) **11c** to preferentially stabilize one of the diastereomeric complexes is too low to allow predominant stereodifferention. (*R*)-BT-MOx **11b** led also to (*S*)-**18** as major enantiomer (Table 3, entry 4). The enantioselectivity of the reaction performed with these ligands is not explainable by a mechanism as proposed in Scheme 8. Such effects have already been reported by Chelucci et al.[33] who described the use of oxazolinylpyridines and acridininyloxazolines as ligands for the same transformation. The introduction of a benzo-fused substituent on the pyridine ring not containing the chiral backbone resulted, also in their case, in the switch of the expected chiral sense of enantioselection.

3. Conclusion

We have prepared a variety of new sulfur-containing oxazoline(s) with benzothiophene or dibenzothiophene as backbones. The compounds have been fully characterized and tested as ligands in the asymmetric palladium-catalyzed substitution of *rac*-1,3-diphenyl-2-propenyl acetate with dimethylmalonate. (*S*,*S*)-DBT-BOx(^{i}Pr) **9a**, as the most active and selective ligand of this series, allowed the preparation of (*R*)-**18** with 77% e.e. It is worth mentioning that the analogous dibenzofuran–bisoxazoline ligand was not successfully used for

this transformation. Furthermore, and to the best of our knowledge, other reported bisoxazolines led to reversal selectivities as those here obtained. We thus assume that the sulfur atom of the dibenzothiophene backbone probably participates in the stabilization of the sterically favored Pd-complex. DBT-MOx's, as six-membered chelate ring-forming ligands proved to be more active and selective than their five-membered chelate ring-forming counterparts of the BT-MOx series. These ligands displayed lower efficiency and selectivity than the DBT-BOx's. Other catalytic enantioselective reactions using these ligands are currently in progress in our laboratory.

4. Experimental

Solvents were purified by standard techniques: CH_2Cl_2, $CHCl_3$, cyclohexane and diethylether were dried over CaH_2 and THF over sodium and benzophenone. ^1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Brucker AM-200 and a AC-250 Fourier Transform spectrometer and obtained in chloroform-*d*. Chemical shifts are reported in parts per million (ppm), and coupling constants are reported in Hertz (Hz). Optical rotations were measured with a Perkin–Elmer 341 Polarimeter. Conversions were determined by GC analysis (DB-1 column, 10 m×0.32 mm Ø). Enantiomeric excesses were measured by HPLC (Whelk 01 column, hexane/*iso*propanol: 98/2, flow rate = 1 mL/min, $\lambda = 254$ nm). High Resolution Mass Spectra were obtained with a Finningan-MAT-95-5-S apparatus. The amino-alcohols were purchased from Acros and thianaphthene-2-carboxylic acid **16** is commercially available from Aldrich.

4.1. General synthesis of DBT-BOx ligands, 9

Dibenzothiophene-4,6-dicarboxylic acid **12** was prepared according to a procedure described by Macaud et al.[24] and obtained in 88% yield: ^1H NMR (250 MHz, DMSO-d_6) δ 8.71 (d, 2H, $J = 7.8$ Hz), 8.20 (d, 2H, $J = 7.3$ Hz), 7.67 (dd, 2H, $J = 7.3$ Hz, 7.8 Hz); ^{13}C NMR (62.5 MHz, DMSO-d_6) δ 167.3, 141.7, 135.6, 129.5, 126.3, 125.0, 124.8.

Diacid **12** (4.0 g, 14.7 mmol) was suspended in dry $CHCl_3$ (55 ml), thionyl chloride (32 mL, 0.4 mol, 30 equiv.) and DMF (1 drop) were added at rt. The mixture was refluxed 2.5 h, and then stirred at rt overnight. The resulting mixture was filtered, and the solid washed with $CHCl_3$. After drying in vacuum, dibenzothiophene-4,6-dicarbonyl dichloride **13** was obtained as a white powder (3.8 g, 13.5 mmol, 92%). This compound was used in the following reaction without further purification.

To a suspension of **13** (2.0 g, 6.5 mmol) in dry $CHCl_3$ (50 mL) at 0°C, was slowly added a solution containing the commercially available chiral amino-alcohol (14.9 mmol, 2.3 equiv.) and triethylamine (2.0 mL, 14.3 mmol, 2.2 equiv.) in dry $CHCl_3$ (15 mL). This mixture was stirred at rt overnight. Usual work up procedure (aq. NH_4Cl and CH_2Cl_2) yielded dibenzothiophene-4,6-diamide **14** as a brown solid, used in the cyclization step without purification.

To **14** (3.8 mmol) in dry CH_2Cl_2 (40 mL) at −78°C, was slowly added (diethylamino)sulfur trifluoride DAST (10.0 mol, 2.6 equiv.). After stirring 4 h at −78°C and overnight at rt, a solution of 14% aq. NH_4OH was added. Usual work up (CH_2Cl_2) yielded DBT-BOx ligands **9** as solids, which were recrystallized several times in cold pentane.

4.1.1. (*S*,*S*)-4,6-Dibenzothiophenediyl-2,2′-bis(4-isopropyloxazoline) (DBT-BOx(*i*Pr)), 9a. Obtained from (*S*)-(+)-2-amino-3-methyl-1-butanol (L-Valinol) in 52% yield from dibenzothiophene-4,6-dicarboxylic acid **12** as a light brown solid: mp 194–196°C; $[\alpha]_D^{20} = -74.3$ (*c* 2.28, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 8.27 (dd, 2H, $J = 7.8$ Hz, 1.0 Hz), 7.99 (dd, 2H, $J = 7.3$ Hz, 1.0 Hz), 7.50 (dd, 2H, $J = 7.8$ Hz, 7.3 Hz), 4.51 (m, 2H), 4.19 (m, 4H), 1.84 (m, 2H), 1.17 (d, 6H, $J = 6.8$ Hz), 1.03 (d, 6H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.1, 141.7, 135.9, 127.2, 123.9 123.7, 122.5, 73.4, 70.8, 33.5, 19.1, 19.0; HRMS calcd for $C_{24}H_{26}N_2O_2S$ 406.1704, found 406.1715.

4.1.2. (*R*,*R*)-4,6-Dibenzothiophenediyl-2,2′-bis(4-phenyloxazoline) (DBT-BOx(Ph)), 9b. Obtained from (*R*)-(−)-2-phenylglycinol (2-amino-2-phenylethanol) in 41% yield from **12** as a light brown solid: mp 230–232°C; $[\alpha]_D^{20} = -247.7$ (*c* 1.29, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 8.36 (dd, 2H, $J = 7.8$ Hz, 1.0 Hz), 8.18 (dd, 2H, $J = 7.3$ Hz, 1.0 Hz), 7.58 (dd, 2H, $J = 7.8$ Hz, 7.3 Hz), 7.50–7.20 (m, 10H), 5.59 (dd, 2H, $J = 8.3$ Hz, 8.3 Hz), 4.89 (dd, 2H, $J = 8.3$ Hz, 8.3 Hz), 4.33 (dd, 2H, $J = 8.3$ Hz, 8.3 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 163.8, 142.4, 141.4, 136.0, 128.6, 128.0, 127.4, 126.7, 124.2, 124.1, 122.3, 74.9, 70.1; HRMS calcd for $C_{30}H_{22}N_2O_2S$ 474.1402, found 474.1402.

4.1.3. (*S*,*S*)-4,6-Dibenzothiophenediyl-2,2′-bis(4-*tert*-butyloxazoline) (DBT-BOx(*t*Bu)), 9c. Obtained from (*S*)-*tert*-Leucinol (2-amino-3,3-dimethyl-1-butanol) in 37% yield from **12** as a yellow solid: mp 183–185°C; $[\alpha]_D^{20} = -49.4$ (*c* 1.06, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 8.27 (dd, 2H, $J = 7.8$ Hz, 1.0 Hz), 7.98 (dd, 2H, $J = 7.3$ Hz, 1.0 Hz), 7.50 (dd, 2H, $J = 7.8$ Hz, 7.3 Hz), 4.41 (m, 2H), 4.26 (m, 4H), 1.03 (s, 18H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.4, 142.4, 136.4, 127.6, 124.3, 124.1, 123.0, 77.3, 69.0, 34.4, 26.4; HRMS calcd for $C_{26}H_{30}N_2O_2S$ 434.2029, found 434.2028.

4.2. General synthesis of DBT-MOx ligands, 10

Dibenzothiophene-4-carboxylic acid **15** was prepared according to a procedure described by Tye et al.[26] and obtained in 75% yield, mp 257–259°C. (lit. mp (AcOH) 261–263°C, 75% yield). This monoacid **15** (2.0 g, 8.8 mmol) was suspended in dry $CHCl_3$ (35 mL), thionyl

chloride (19.2 mL, 0.3 mol, 30 equiv.) and DMF (1 drop) were added at rt. The mixture was refluxed 2.5 h, and then stirred at rt overnight. The resulting mixture was filtered, and the solid washed with $CHCl_3$. After drying in vacuum, dibenzothiophene-4-carbonyl chloride was obtained as a white powder (2.01 g, 8.1 mmol, 93%). This compound was used in the following reaction without further purification.

To a suspension of the monoacid chloride (1.0 g, 4.1 mmol) in dry $CHCl_3$ (30 mL) at 0°C, was slowly added a solution containing the commercially available chiral amino-alcohol (4.5 mmol, 1.1 equiv.) and triethylamine (0.6 mL, 4.5 mmol, 1.1 equiv.) in dry $CHCl_3$ (10 mL). This mixture was stirred overnight at rt. Usual work up procedure (aq. NH_4Cl and CH_2Cl_2) yielded dibenzothiophene-4-amide as a brown solid, used directly in the cyclization step without purification.

To the monoamide (1.2 g, 3.5 mmol) in dry CH_2Cl_2 (35 mL) at −78°C, was slowly added (diethylamino)sulfur trifluoride DAST (0.6 mL, 4.5 mmol, 1.3 equiv.). After stirring 4 h at −78°C and overnight at rt, a solution of 14% aq. NH_4OH was added. Usual work up (CH_2Cl_2) yielded DBT-MOx ligands **10** as brown solids, which were recrystallized several times in cold pentane.

4.2.1. (*S*)-2-Dibenzothiophen-4-yl-4-isopropyloxazoline (DBT-MOx(^{i}Pr)), 10a. Obtained from (*S*)-(+)-2-amino-3-methyl-1-butanol (L-Valinol) in 22% yield from dibenzothiophene-4-carboxylic acid **15** as a light brown solid: mp 88–90°C; $[\alpha]_D^{20} = -28.3$ (*c* 0.86, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.26 (dd, 1H, $J = 7.8$ Hz, 1.0 Hz), 8.16 (m, 1H), 7.98 (dd, 1H, $J = 7.3$ Hz, 1.0 Hz), 7.89 (m, 1H), 7.52 (dd, 1H, $J = 7.8$ Hz, 7.3 Hz), 7.48–7.40 (m, 2H), 4.48 (m, 1H), 4.21 (m, 2H), 1.88 (m, 1H), 1.13 (d, 3H, $J = 6.5$ Hz), 1.01 (d, 3H, $J = 6.5$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.8, 142.3, 140.2, 137.2, 135.5, 127.7, 127.6, 124.9, 124.7, 124.6, 123.3, 123.0, 122.1, 73.8, 71.1, 34.0, 19.6, 19.2; HRMS calcd for $C_{18}H_{17}NOS$ 295.1027, found 295.1031.

4.2.2. (*R*)-2-Dibenzothiophen-4-yl-4-phenyloxazoline (DBT-MOx(Ph)), 10b. Obtained from (*R*)-(−)-2-phenylglycinol (2-amino-2-phenylethanol) in 34% yield from **15** as a brown solid: mp 110–112°C; $[\alpha]_D^{20} = -190.1$ (*c* 1.03, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.29 (d, 1H, $J = 7.8$ Hz), 8.16 (m, 1H), 8.10 (d, 1H, $J = 7.8$ Hz), 7.90 (m, 1H), 7.60–7.30 (m, 8H), 5.64 (dd, 1H, $J = 8.3$ Hz, 8.3 Hz), 4.86 (dd, 1H, $J = 8.3$ Hz, 8.3 Hz), 4.31 (dd, 1H, $J = 8.3$ Hz, 8.3 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 164.4, 143.1, 142.1, 140.3, 137.3, 135.4, 129.4, 128.2, 128.0, 127.6, 127.2, 125.0, 124.9, 124.7, 123.3, 122.6, 122.1, 75.5, 70.9; HRMS calcd for $C_{21}H_{15}NOS$ 329.0875, found 329.0874.

4.3. General synthesis of BT-MOx ligands, 11

Thianaphthene-2-carboxylic acid **16** (1.5 g, 8.4 mmol) was suspended in dry $CHCl_3$ (30 mL), thionyl chloride (18.5 mL, 0.25 mol, 30 equiv.) and DMF (1 drop) were added at rt. The mixture was refluxed 2.5 h, and then stirred at rt overnight. The resulting mixture was filtered, and the solid washed with $CHCl_3$. After drying in vacuum, thianaphtene-2-carbonyl chloride was obtained as a white powder (1.6 g, 8.1 mmol, 97%). This compound was used in the following reaction without further purification.

To a suspension of the monoacid chloride (1.6 g, 8.1 mmol) in dry $CHCl_3$ (50 mL) at 0°C, was slowly added a solution containing the commercially available chiral amino-alcohol (9.0 mmol, 1.1 equiv.) and triethylamine (1.25 mL, 9.0 mmol, 1.1 equiv.) in dry $CHCl_3$ (15 mL). This mixture was stirred overnight at rt. Usual work up procedure (aq. NH_4Cl and CH_2Cl_2) yielded thianaphtene-4-amide as a brown solid, used in the cyclization step without purification.

To the monoamide (8.1 mmol) in dry CH_2Cl_2 (80 mL) at −78°C, was slowly added (diethylamino)sulfur trifluoride DAST (0.01 mol, 1.3 equiv.). After stirring 4 h at −78°C and overnight at rt, a solution of 14% aq. NH_4OH was added. Usual work up (CH_2Cl_2) yielded BT-MOx ligands **11** as solids, which were recrystallized several times in cold pentane.

4.3.1. (*S*)-2-Benzo[*b*]thiophen-2-yl-4-isopropyloxazoline (BT-MOx(^{i}Pr)), 11a. Obtained from (*S*)-(+)-2-amino-3-methyl-1-butanol (L-Valinol) in 54% yield from thianaphthene-2-carboxylic acid **16** as a white solid; mp 80–82°C; $[\alpha]_D^{20} = -57.6$ (*c* 0.99, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.85–7.72 (m, 3H), 7.45–7.38 (m, 2H), 4.50–4.35 (m, 1H), 4.20–4.05 (m, 2H), 1.96–1.79 (m, 1H), 1.02 (d, 3H, $J = 6.8$ Hz), 0.92 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 160.1, 141.9, 139.8, 131.2, 127.8, 126.7, 125.4, 125.4, 123.2, 73.6, 71.3, 33.4, 19.6, 18.7; HRMS (ESI) calcd for $C_{14}H_{15}NOS$ (M+H$^+$) 246.0949, found 246.0953.

4.3.2. (*R*)-2-Benzo[*b*]thiophen-2-yl-4-phenyloxazoline (BT-MOx(Ph)), 11b. Obtained from (*R*)-(−)-2-phenylglycinol (2-amino-2-phenylethanol) in 64% yield from **16** as a white solid; mp 90–92°C; $[\alpha]_D^{20} = +6.6$ (*c* 0.99, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.95–7.75 (m, 3H), 7.50–7.25 (m, 7H), 5.40 (dd, 1H, $J = 9.8$ Hz, 8.3 Hz), 4.82 (dd, 1H, $J = 8.3$ Hz, 9.8 Hz), 4.30 (dd, 1H, $J = 8.3$ Hz, 8.3 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 161.4, 142.5, 142.0, 139.7, 130.7, 129.4, 128.4, 127.4, 126.9, 125.5, 125.4, 123.2, 76.1, 71.0; HRMS (ESI) calcd for $C_{17}H_{14}NOS$ (M+H$^+$) 280.0801, found 280.0796.

4.3.3. (*S*)-2-Benzo[*b*]thiophen-2-yl-4-*tert*-butyloxazoline (BT-MOx(^{t}Bu)), 11c. Obtained from (*S*)-*tert*-Leucinol (2-amino-3,3-dimethyl-1-butanol) in 74% yield from **16** as a light brown solid; mp 75°C; $[\alpha]_D^{20} = -58.7$ (*c* 1.01, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.85–7.70 (m, 3H), 7.40–7.25 (m, 2H), 4.40–4.20 (m, 2H), 4.05 (m, 1H), 0.95 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 160.3, 141.8, 139.5, 130.2, 128.4, 126.7, 125.4, 125.2, 122.9, 76.3, 70.1, 34.6, 26.3; HRMS calcd for $C_{15}H_{17}NOS$ 259.1026, found 259.1030.

4.4. General procedure for palladium-catalyzed allylic alkylation of *rac*-(*E*)-1,3-diphenyl-prop-2-enyl acetate

The ligand (10 mol%), $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (2.5 mol%) and KOAc (2 mol%) were dissolved in dry CH_2Cl_2 (1.5 mL). The reaction mixture was degassed in three freeze-evacuate-thaw cycles and stirred at 40°C for 15 min under argon atmosphere. BSA (*N*,*O*-bis(trimethylsilyl)acetamide) (3 equiv.) and dimethyl malonate (3 equiv.) were added, and the resultant solution was stirred at 40°C for 15 min. Whereupon, *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate (1 equiv.) was added, and the reaction mixture was degassed in three freeze–evacuate–thaw cycles before the reaction vessel was sealed, and stirred at 40°C under argon atmosphere for 3 days. It was then diluted with diethyl ether and washed with a saturated aqueous NH_4Cl solution. The organic phase was separated, dried ($MgSO_4$) and the solvent removed in vacuo. Purification by column chromatography (cyclohexane/ethyl acetate: 9/1), resulted in a clear oil. The enantiomeric excess was determined by chiral HPLC (Whelk 01 column). The absolute configuration was determined by polarometric measurements and compared to the literature values.[27]

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