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Atroposelective synthesis of axially chiral P,S-ligands based on Arynes

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Introduction

The importance of biaryls in natural products, drugs, catalysis, and organic materials has led to the development of numerous strategies for their synthesis, especially in the case of atropo-enriched biaryls. In our laboratory, we developed the potential of the old reaction of an aryllithium and an ortho-dihaloarene bearing at least one exchangeable halogen, leading to functionalizable 2-haloarbiyli. We studied its regioselectivity and applied it to the synthesis of various C-symmetric phosphorus ligands. Recently, we described the use of this so-called ‘ARYNE coupling’ in the modular synthesis of highly atropo-enriched biphenyls (Scheme 1), following Clayden’s ‘traceless resolving agent’ method based on sulfoxides. We started from achiral or racemic polychalobiphenyls obtained by ‘ARYNE coupling’, which were then desymmetrized or deracemized. We showed that 2,2’,6,6’-tribromo-1,1’-biphenyl could serve as a platform for accessing atropo-enriched biphenyls, variously derivatizable in positions 2, 2’ and 6. In the present paper, we report now on an improved alternative method, where axial stereoenrichment is installed during the ary-aryl coupling step by means of a covalently attached chiral sulfoxide auxiliary, i.e. an atropodiastereoselective ‘ARYNE coupling’.

Results and discussion

In the target transformation, the position of the chiral auxiliary would be key for an efficient atropo-selective coupling. On the one hand, the auxiliary could be located on the aryllithium nucleophile, closest to the reacting center, namely ortho to lithium. Using a chiral coordinating group in ortho position would produce a more rigid metallacycle, increasing the chances for a high stereoinduction. On the other hand, if the arylene bears the auxiliary ortho to the triple bond, complex regioselectivity issues could arise due to steric and electronic effects of the arylene substituents, including the chiral auxiliary. In particular, a lithium-coordinating auxiliary could favor addition of the nucleophile alternately on both termini of the triple bond depending on the reaction conditions, as shown by Meyers leading to competing kinetic and thermodynamic controls. Consequently, we chose to locate the chiral auxiliary on the nucleophile. The already proposed mechanism would be modified as depicted in Scheme 2. Diastereoselection would proceed either by a favored approach of the arylene to the chiral nucleophile, or by formation of the more stable atropodiastereomer of the resulting biaryl lithium, depending on the early or late nature of the transition state. Arynes being high energy intermediates, and considering the successful prediction of the regioselectivity of nucleophilic addition onto arynes based on the ground state distortion model, it is much probable that the transition state would be early. This implies in our case that atropo-diastereoselection arises from the dissymmetric approach of the arylmetal to the arylene.

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Due to the successful results obtained in the literature using sulfoxides as chiral auxiliaries in directed lithiation-diastereoselective trapping sequences on aromatic compounds,25-34 as well as in our precedent work,35-40 and due to the robustness of the tert-butyl sulfinyl group, we chose the latter as stereoinducer in our targeted transformation.

Atropo-diastereoselective ‘ARYNE coupling’ with aryl tert-butyl sulfoxides

Aryl tert-butyl sulfoxides 1a-c were therefore prepared following Ellman’s method,41, 42 after enantioselective oxidation of di-tert-butyl disulfide and treatment with the desired aryllithium reagents (Scheme 3). Sulfoxide 1a was chosen as test substrate in the ‘ARYNE coupling’ with 1,2-dibromobenzene due to its easy access, its completely regioselective lithiation with nBuLi,43, 44 and the ease of detection of its derivatives by 1H and 13C NMR thanks to the OMe signals. Preliminary experiments showed that in the previously reported conditions (treatment of the pronucleophile with nBuLi at -78 °C, followed by addition of 1,2-dibromobenzene at -78 °C and stirring while warming up to room temperature no coupling product was obtained (Table 1, entry 1). We suspected a lack of reactivity of the lithiated arylsulfoxide in the halogen/lithium exchange with 1,2-dibromobenzene (stage (I) in Scheme 2). Accordingly, 0.2 equivalents of nBuLi were added after introduction of the benzyne precursor so as to trigger the generation of ortho-bromo-lithiobenzene and the chain reaction (Table 1, entry 2). Here again, the formation of the coupling product was not observed, and only the starting sulfoxide, 1,2-dibromobenzene and its homocoupling product, 2,2'-dibromobiphenyl, were recovered. Increasing the temperature before introduction of 1,2-dibromobenzene for a facile elimination of LiBr did not lead to the desired biarylsulfoxide either (entry 3). Finally, in

Scheme 1 Post-‘ARYNE coupling’ desymmetrization (X = Br) or deracemization (X = Cl) and functionalization of biphenyls.

Scheme 2 Proposed mechanism of the atropo-diastereoselective ‘ARYNE coupling’ (Aux* = coordinating chiral auxiliary).
order to facilitate further the formation of the arylene, in both stages (I) and (III) of the mechanism (Scheme 2), 1,2-dibromobenzene was replaced with 1-bromo-2-iodobenzene, since halogen/lithium exchanges are faster with iodine than with bromine. In that case, starting from sulfoxides 1a–c, the corresponding coupling products 2b–d were indeed obtained, in various yields and atropo-selectivities (Table 1, entries 4–6). Only one diastereomer of 2b could be isolated in 20% yield from the complex mixture, although formation of the other diastereomers starting from (±)-di-tert-butyl-thiosulfinate, confirming the configurational stability of the sulfinyl auxiliary during the ‘ARYNE coupling’. The absolute configuration of the major atropo-diastereomer could not be ascertained; formation of the other atropo-diastereomers could not be ruled out (entry 4). The benzodioxole analogue 2d was obtained in a ca. 1:1 diastereomeric ratio, yet with a good 82% yield (entry 6). Most interestingly, biaryl 2c could be obtained with a promising diastereomeric ratio of 79:21, and the atropo-diastereomers could be separated by column chromatography with respective yields of 40% and 11% (entry 5). After recrystallization from ethyl acetate, the absolute configuration of the major isomer could be determined by X-ray diffraction crystallography and was shown to be (S,S,S) (Figure 1). We could moreover show that each atropo-diastereomer of 2c was obtained with high enantiomeric enrichment (e.r. = 97:3 for (S,S,S)-2c; 99:1 for (S,S,R)-2c) by chiral SFC analysis after synthesis of both racemic diastereomers starting from (±)-di-tert-butyl-thiosulfinate, confirming the configurational stability of the sulfinyl auxiliary during the ‘ARYNE coupling’.

Table 1 Atropo-diastereoselective ‘ARYNE coupling’ of aryl tert-butyl sulfoxides.

<table>
<thead>
<tr>
<th>Entry</th>
<th>S.M.</th>
<th>R^1</th>
<th>R^2</th>
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<th>X</th>
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<th>n</th>
<th>Yield (%)</th>
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<tr>
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<td>OCH_3</td>
<td>H</td>
<td>-78</td>
<td>I</td>
<td>2d</td>
<td>0.2</td>
<td>82</td>
<td>54:46</td>
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</table>

a Combined yield of both atropo-diastereomers. b Diastereomeric ratio measured by ^1H NMR of the crude mixture. c Only one atropo-diastereomer could be isolated, whose configuration could not be ascertained; formation of the other atropo-isomer could not be ruled out. d The absolute configuration of the major atropo-diastereomer was shown to be (S,S,S) (see text).
The stereochemical outcome of the ‘ARYNE coupling’ could be explained by the following considerations (Scheme 4). During the attack of the aryllithium nucleophile onto the aryne, both aromatic rings should be perpendicular to minimize steric interactions. Due to the strong lithium-coordinating property of sulfinyl groups, the ortho-lithioaryl sulfoxide intermediate forms a metallacycle, where the tert-butyl substituent and the non-bonding electron pair point away from each side of the benzene ring, respectively towards the top and the bottom in Scheme 4. If the aryne approaches the carbon-lithium bond anti to the tBu group, i.e. from the bottom face, the sulfinyl group is forced to rotate “clockwise” in the transition state, thus pushing the tert-butyl towards the ortho-proton. This 1,3-allylic-type repulsion would hence defavor the anti transition state. On the other hand, in the syn approach, the rotation of the sulfinyl moiety would be “counter-clockwise”, pushing the tBu group into a pseudo-axial position. Despite the flatness of the aryne positioned perpendicularly to the aryllithium, the tBu/aryne steric repulsion would dramatically increase the energy of the syn transition state. A weak stabilizing electrostatic interaction between the π cloud of the aryne and the C–H bonds of the tBu group, whose electron density is affected by the electron-withdrawing sulfinyl function, could be expected and would oppose to the steric repulsion. Given the unambiguous absolute configuration of the major atropo-diastereomer (Figure 1), it appears that both potential stabilizing C–H–π interaction and the 1,3-allylic-type repulsion of the anti approach are overpowered by the tBu/aryne repulsion in the syn approach. Nevertheless, the imperfect stereoselectivity observed in this reaction may be due to a delicate balance between these various steric and stereoelectronic parameters. This could be also suggested by the poor stereoselectivity of the coupling leading to 2d, which could be ascribed to a competitive coordination of lithium to the oxygen atoms of the dioxole motif, thus upsetting the relative weight of stabilizing or destabilizing interactions discussed above.

**Scheme 4** Stereochemical rationale for the atropo-diastereoselective ‘ARYNE coupling’ of aryl tert-butyl sulfoxides (R = tBu).

**Synthesis of P,S ligands and evaluation in catalysis**

As 2c bears a functionalisable iodo substituent *ortho* to the biphenyl junction, and as both of its atropo-diastereomers are separable by column chromatography, we reasoned that it could be easily converted into a set of enantiomeric P,S ligands. Indeed, the strong affinity of phosphorus and sulfur for transition metals has motivated the synthesis of many phosphine-thioether bidentate ligands. Yet, among them, very few are based on an atropo-enriched 1,1'-biaryl-2,2'-diyl...
phosphine-thioether backbone, and the latter are exclusively binaphthyl-derived ligands.\textsuperscript{49-58} We were hence interested in the properties of atropo-enriched biphenyl-linked phosphine-thioethers derived from 2c. Each atropomer of sulfoxide 2c was therefore converted into the corresponding thioether, before undergoing iodine/lithium exchange with tBuLi and trapping with chlorodiphenyl- or chlorodicyclohexylphosphine (Scheme 5). Gratifyingly, the corresponding biarylphosphines were obtained without loss of atropo-enrichment. The enantiomeric purity of sulfides 3 and of P,S ligands 4a,b was determined by SFC by comparison with the racemic counterparts obtained by a similar synthesis starting from racemic di-tert-butyl thiosulfinate. The retention of axial configuration was confirmed by X-ray diffraction analysis of monocrystals of compound (aS)-4a (Figure 2).\textsuperscript{45}

The coordination of (aS)-4a with a transition metal was then studied by reacting it with bis(benzonitrile)dichloropalladium (Scheme 6). The expected complex ((aS)-4a)PdCl\textsubscript{2} (5) was indeed obtained and characterized by \textsuperscript{1}H, \textsuperscript{13}C and \textsuperscript{31}P NMR as well as HRMS. A clear shift in \textsuperscript{31}P NMR from -14.1 ppm (free ligand 4a) to +29.4 ppm in 5 attested the coordination of the phosphine moiety to palladium. Similarly, the singlet corresponding to the protons of the tert-butyl group moved downfield, from 1.12 to 1.63 ppm, indicative of electron depletion at sulfur and hence of coordination of the thioether to the metal. Additionally, the \textsuperscript{13}C NMR signal of the quaternary carbons in the tBu group moved upfield from 47.4 ppm in 4a to 30.4 ppm in 5, which is coherent with back-donation from the metal. The structure of complex 5 was further unambiguously determined by X-ray diffraction analysis of single crystals of 5 (Figure 5).\textsuperscript{45} The metal is effectively chelated by the bidentate ligand, affording a distorted square-planar geometry. The Cl-Pd-Cl angle is almost equal to 90° (89.60°), but other angles deviate from the ideal case; the P-Pd-S and P-Pd-Cl3 angles are smaller than 90° (respectively 87.61° and 87.97°), while the S-
Pd-Cl2 angle is 95.59°, i.e. wider than a right angle. These distortions are explained in part by the difference in trans influence between the phosphine and thioether moieties; indeed, the Pd-Cl bond measures 2.339 Å and the Pd-Cl one 2.316 Å, demonstrating the stronger trans influence of the phosphine. Last but not least, the axial configuration of the free ligand is preserved in complex 5, and coordination of sulfur to palladium is effected so as to place the tBu group in an equatorial position, away from the phenyl substituents at phosphorus.

Scheme 6 Synthesis of a palladium complex from atropo-enantiopure P,S ligand (aS)-4a.

As palladium-catalyzed asymmetric allylic substitution constitutes a benchmark reaction for the assessment of chiral bidentate ligands, compounds 4a,b were evaluated in the reaction of 1,3-diphenylallyl acetate with dimethyl malonate and indole (Table 2). In the reaction with dimethyl malonate, ligands (aS)-4a and (aS)-4b gave similar results in terms of yield and enantioselectivity (entries 1–2), indicating negligible influence of the phosphorus substituents. Both enantiomers of ligand 4b also gave similar results as expected (entries 2–3). Running the reaction at higher temperature (25 °C instead of 10 °C) did not bring any improvement (entry 4), but a slight increase in enantioselectivity was observed when diminishing the reaction temperature to -25 °C (entry 5). On the other hand, switching from potassium to lithium in the acetate salt proved markedly advantageous, as it increased the e.r. from 90:10 (80% ee) to 97:3 (94% ee) at 25 °C, and from 93:7 (86% ee) to 99:1 (98% ee) at -25 °C (entries 4–7). For comparison purposes, binaphthyl-derived phosphine-thioether ligands afforded 68–96% yield and 7-96% ee in the same reaction. Ligand (aS)-4a was also evaluated in the reaction with indole, using Hoshi and Hajiwara et al.’s conditions developed for related Sulfur-MOP ligands. In our case (entry 8), 83% yield and 92:8 e.r. (i.e. 84% ee) were achieved, which compares honorably with the cited Sulfur-MOP ligands (58–89% yield and 48–92% ee).

Table 2 Evaluation of ligands 4a,b in palladium-catalyzed asymmetric allylic substitution.
Conclusions

This work describes the first attempt at developing an unprecedented asymmetric version of the so-called 'ARYNE coupling', i.e. the coupling of an aryllithium and an aryne generated in situ from an ortho-dihaloarene by halogen/lithium exchange in a chain reaction. A tert-butylsulfinyl group was used as chiral auxiliary on the aryllithium nucleophile. In one case, both atropo-diastereomers of the resulting 2-(tert-butylsulfinyl)-6-chloro-2-ido-1,1'-biphenyl could be separated by column chromatography, and derivatized into atropoenantiopure biphenyl-based phosphine-thioether ligands. The latter are the first of their kind in the family of phosphine-thioethers, where congeners had been built up to now from a binaphthyl scaffold. The new P,S heterodonor ligands were assessed in model palladium-catalyzed allylic substitution reactions, where they showed comparable efficiency with regard to their binaphthyl homologues of the literature. Other developments of the atropo-diastereoselective 'ARYNE coupling' will soon be reported.

Experimental section

General information

Starting materials, if commercially available, were purchased and used as received after check of the purity. When known compounds had to be prepared according to literature procedures, pertinent references are given. Air and moisture sensitive materials were stored in Schlenk tubes under argon. Et₂O, 1,4-dioxane and THF were dried by distillation over sodium/benzophenone after the characteristic blue color of sodium diphenyl ketyl (benzophenone so sensitive materials were stored in Schlenk tubes under argon. When known reactions, where they showed comparable efficiency with regard to their binaphthyl homologues of the literature. Other developments of the atropo-diastereoselective 'ARYNE coupling' will soon be reported.

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* Isolated yield. ** Enantiomeric ratio measured by chiral SFC analysis. ** When possible, absolute configuration was assigned by comparison with literature data.

General procedure for the synthesis of tert-butylsulfinyl benzene derivatives

At -78 °C, n-butyllithium (1.6 M in hexanes, 1.1 equiv., 12.5 mL, 20.0 mmol) was added dropwise to a solution of the substrate (1 equiv., 20.0 mmol) in THF (100 mL, C = 0.2 mol/L). The resulting mixture was stirred for 30 min at -78 °C and a solution of (S)-tert-butyl-tert-butamidemethanesulfonate (1 equiv., 3.89 g, 20.0 mmol) in THF (18 mL, C = 1.1 mol/L) was added. The resulting mixture was stirred for 2 h at -78 °C and then MeOH was added (100 mL) at -78 °C, followed by water (100 mL) at 25 °C. The aqueous and organic layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over Na₂SO₄, filtered and evaporated to dryness.
The product was prepared according to the general procedure and starting from 1-bromo-3-methoxybenzene (1 equiv., 3.74 g, 20.0 mmol). Purification by column chromatography on silica gel (eluent: cyclohexane/AcOEt (7/3)) afforded (S)-1-(tert-butysulfinyl)-3-methoxybenzene 1a as a colorless solid (2.12 g, 10.0 mmol, 50%). Mp = 79-81 °C; 1H NMR (CDCl3, 300 MHz): δ = 7.38 (app. t, J = 7.9 Hz, 1 H), 7.21-7.17 (m, 1 H), 7.10 (d, J = 7.9 Hz, 1 H), 7.02 (dd, J = 8.3, 2.3 Hz, 1 H), 3.86 (s, 3 H, OMe), 1.18 (s, 9 H, S(O)CMe3) ppm; 13C NMR (CDCl3, 75 MHz): δ = 159.8 (C6, CMe3), 141.4 (C4v, C(O)Me3), 129.2, 118.7, 117.5, 110.7, 56.0 (Cv, Si(O)CMe3), 55.6 (Ome), 22.9 (3 C, S(O)Me3). Elemental analysis calcld. (%) C 58.32, H 6.23. Found C 58.72, H 6.23. αR = -151.7 (c 1, CHCl3). ee > 99% (SFC, CHIRALCEL OD-H).

The product was prepared according to the general procedure and starting from 5-bromobenzyl[1,3]dioxole (1 equiv., 2.41 g, 20.0 mmol). Purification by column chromatography on silica gel (eluent: cyclohexane/AcOEt (7/3)) afforded (S)-5-(tert-butysulfinyl)benzyl[1,3]dioxole 1c as a colorless solid (2.31 g, 10.2 mmol, 51%). Mp = 67-69 °C; 1H NMR (CDCl3, 300 MHz): δ = 7.04 (d, J = 1.5 Hz, 1 H), 6.97 (dd, J = 8.1, 1.5 Hz, 1 H), 6.82 (d, J = 8.1 Hz, 1 H), 5.98 (s, 2 H, OCH2), 1.09 (s, 9 H, S(O)CMe3) ppm; 13C NMR (CDCl3, 75 MHz): δ = 150.3 (Cv), 148.1 (C1v), 133.1 (C3v, COSiMe3), 121.1, 108.1, 106.4, 101.8 (C2v, OCH2O), 55.9 (C3v, S(O)Me3), 22.8 (3 C, S(O)CMe3) ppm; Elemental analysis calcld. (%) C 58.38, H 6.24; found C 58.32, H 6.23. αR = -39.4 (c 1, CHCl3).

1-(tert-Butylsulfinyl)-2-iodo-6-methoxy-1,1'-biphenyl (2b), n-Butyllithium (1.6 M in hexanes, 1 equiv., 688 µL, 1.10 mmol) was added to a solution of (S)-1-(tert-butylsulfinyl)-3-methoxybenzene 1a (1 equiv., 234 mg, 1.10 mmol) in THF (5.5 mL, C = 0.2 mol/L) at -78 °C. 1-Bromo-2-iodobenzene (1 equiv., 141 µL, 1.10 mmol) was added at -78 °C, followed by n-butyllithium (1.6 M in hexanes, 0.2 equiv., 138 µL, 0.220 mmol). The reaction mixture was allowed to reach 25 °C during 12 h. Water was added (2 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 2 mL). The combined organic layers were dried over Na2SO4, filtered and evaporated to dryness. The crude mixture was purified by column chromatography on silica gel (eluent: pentane/AcOEt (7/3)) (235 mg, 0.561 mmol, 51%). Elemental analysis calcld. (%) C 47.67, H 4.00; found C 47.99, H 4.22.

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The organic and aqueous layers were separated and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic layers were dried over Na2SO4, filtered and evaporated to dryness. The crude mixture was purified by column chromatography on silica gel (elucent: cyclohexane): Mp = 55-57 °C; 1H NMR (CDCl3, 300 MHz): δ = 7.93 (dd, J = 7.5, 0.6 Hz, 1 H), 7.64 (dd, J = 7.5, 0.9 Hz, 1 H), 7.49-7.37 (m, 2 H), 7.31 (app. t, J = 8.1 Hz, 1 H), 7.17 (dd, J = 7.5, 1.5 Hz, 1 H), 7.08 (app. dd, J = 7.8, 1.5 Hz, 1 H), 1.26 (s, 9 H, SCMe3) ppm; 13C NMR (CDCl3, 75 MHz): δ = 147.1 (CIV), 143.9 (CV), 138.6, 135.9 (CV), 135.1, 134.3 (CIV), 130.9, 129.3, 129.0, 128.5, 127.4, 101.2 (CIV, CI), 47.6 (CIV, SCMe3), 31.7 (3 C, SCMe3) ppm; Elemental analysis calcd. (%) C 72.95, H 5.68; found C 72.52, H 5.48. 

Synthesis of (aS)-3: The product was prepared according to the general procedure and starting from (aS)-2-(6-chloro-2'-iodo-1',1'-biphenyl) (SαS)2a,2c. Purification by column chromatography afforded (aS)-3 as a colorless solid (191 mg, 0.474 mmol, 99%). 1H NMR (CDCl3, 500 MHz): δ = 7.58 (dd, J = 7.8, 1.2 Hz, 1 H), 7.56-7.52 (m, 1 H), 7.41 (dd, J = 7.8, 1.2 Hz, 1 H), 7.38-7.34 (m, 2 H), 7.28-7.24 (m, 1 H), 7.21-7.15 (m, 1 H), 1.85-1.45 (m, 11 H), 1.39-0.96 (m, 11 H), 1.18 (s, 9 H, SCMe3) ppm; 13C NMR (CDCl3, 75 MHz): δ = 145.8 (CIV, d, J = 29.3 Hz), 145.3 (CV, d, J = 5.6 Hz), 136.8 (CIV, d, J = 18.9 Hz), 136.0 (CV, d, J = 2.1 Hz), 134.8, 134.6 (CIV, d, J = 0.9 Hz), 132.0 (d, J = 2.9 Hz), 131.4 (d, J = 6.0 Hz), 129.1, 127.8, 127.3, 126.7, 47.3 (CV, d, J = 3.1 Hz, SCMe3), 34.7 (d, J = 15.2 Hz), 33.3 (d, J = 13.7 Hz), 31.5 (3 C, SCMe3), 30.6 (CIV, d, J = 13.2 Hz), 29.8-29.6 (CII, m), 27.7-27.3 (CII, m), 26.5 (CIV, d, J = 8.2 Hz) ppm; 31P NMR (161 MHz, CDCl3): δ = -9.89 ppm; Elemental analysis calcd. (%) C 71.09, H 8.10; found C 71.01, H 8.19.

Synthesis of (aS)-4b: The product was prepared according to the general procedure and starting from (aS)-4a. Purification by column chromatography afforded (aS)-4b as a colorless solid (92.2 mg, 0.200 mmol, 80%). ee > 99% (SFC, CHIRALPAK AD).

**(2′-tart-Butylthio)-6′-chloro-(1′,1′-biphenyl)-2′-ydicyclohexylphosphine ((aS)-4b and (aR)-4b).** tart-Butylthiolum (1.7 M in pentane, 2 equiv., 294 µL, 0.500 mmol) was added to a solution of the substrate (1 equiv., 100 µg, 0.250 mmol) in THF (0.5 mL, C = 0.5 mol/L) at -100 °C. After 5 min, a solution of chlorodicyclohexylphosphine (1 equiv., 44.9 µL, 0.250 mmol) in toluene (0.25 mL, C = 1 mol/L) was added. The reaction mixture was allowed to reach 25 °C and was stirred for 5 minutes. The organic and aqueous layers were separated and the aqueous layer was extracted with dichloromethane (3 × 1 mL). The combined organic layers were dried over Na2SO4, filtered and evaporated to dryness. The crude mixture was purified by column chromatography on silica gel (elucent: cyclohexane): Mp = 55-57 °C; 1H NMR (CDCl3, 300 MHz): δ = 7.93 (dd, J = 7.5, 0.6 Hz, 1 H), 7.64 (dd, J = 7.5, 0.9 Hz, 1 H), 7.49-7.37 (m, 2 H), 7.31 (app. t, J = 8.1 Hz, 1 H), 7.17 (dd, J = 7.5, 1.5 Hz, 1 H), 7.08 (app. dd, J = 7.8, 1.5 Hz, 1 H), 1.26 (s, 9 H, SCMe3) ppm; 13C NMR (CDCl3, 75 MHz): δ = 147.1 (CIV), 143.9 (CV), 138.6, 135.9 (CV), 135.1, 134.3 (CIV), 130.9, 129.3, 129.0, 128.5, 127.4, 101.2 (CIV, CI), 47.6 (CIV, SCMe3), 31.7 (3 C, SCMe3) ppm; Elemental analysis calcd. (%) C 72.95, H 4.00; found C 72.78, H 4.10.
Complex [\((\text{a}-4\text{a})\text{PdCl}_2\)] (5). Ligand (\(a\)-4a) (1 equiv., 46.1 mg, 0.100 mmol) and bis(benzonitrile)palladium dichloride (1 equiv., 38.4 mg, 0.100 mmol) were dissolved in dichloromethane (1 mL) under an argon atmosphere and the reaction mixture was stirred for 1 h at 25 °C. Degassed hexane (5 mL) was then slowly added, which led to the precipitation of 5. The precipitate was filtered and washed with hexane to afford 5 as an orange powder. The single crystals for X-ray diffraction were obtained by recrystallization from dichloromethane and toluene (1:4). Complex 5 and one molecule of toluene crystallize in the same packing: \(^1\)H NMR (CDCl\(_3\), 400 MHz) (Complex 5 + toluene, 400 MHz, \(\delta = 8.07\) (d, J = 7.6 Hz, 1 H), 7.83-7.71 (m, 4 H), 7.67 (app. t, J = 7.6 Hz, 1 H), 7.54-7.36 (m, 5 H), 7.35 (dd, J = 7.2, 3.6 Hz, 1 H), 7.30-7.22 (m, 4 H), 7.21-7.13 (m, 4 H), 7.00-6.93 (m, 2 H), 2.36 (s, 3 H, Me of toluene), 1.63 (s, 9 H, SCMe\(_3\)) ppm; \(^{13}\)C NMR (CDCl\(_3\), 101 MHz) (Complex 5 + toluene): \(\delta = 141.25\) (C\(_{\text{v}}\)), \(\delta = 7.1\) Hz, 137.9 (C\(_{\text{v}}\) of toluene), 136.9 (C\(_{\text{v}}\), d, J = 2.0 Hz), 136.2, 136.0, 134.6 (d, J = 11.2 Hz), 134.3 (C\(_{\text{v}}\)), 134.1 (d, J = 7.1 Hz), 132.6, 131.8-131.7 (m), 131.5-131.4 (m), 130.2, 129.6, 129.5, 129.0, 128.7, 128.5, 128.4, 128.6, 127.4 (C\(_{\text{v}}\), d, J = 9.9 Hz), 127.2, 125.3, 123.5 (C\(_{\text{v}}\)), 122.9 (C\(_{\text{v}}\)), 30.4 (SCMe\(_3\)), 21.5 (Me of toluene) ppm; \(^{13}\)P NMR (CDCl\(_3\), 161 MHz) (CDCl\(_3\), 5%): \(\delta = +29.35\); HRMS [M + Na]\(^+\) for C\(_{32}\)H\(_{22}\)Cl\(_2\)PdNa calc. 658.949; found 658.949.

**Dimethyl (1,3-diphenyl-2-propen-1-yl)malonate (6). General procedure.** To a solution of allylpyridinium chloride dimer [Pd\(\eta^2\)-C\(_6\)H\(_4\)Cl\(_2\)] (2 mol%, 0.100 mmol) in chloroform (1.6 mL) was added the ligand (6 mol%, 0.0240 mmol) under an argon atmosphere, and the reaction mixture was stirred at 25 °C for 30 min. A solution of 1,3-diphenylpropenyl acetate (1.27 mL, 1.20 mmol) in chloroform (0.8 mL, C = 0.5 mol/L) was added, followed by the addition of the base (10 mol%, 0.0400 mmol) at temperature T. The reaction mixture was then stirred for a further 5 min under the temperature T. Afterwards, dimethyl malonate (3 equiv., 137 µL, 1.20 mmol) and N,N-bis(trimethylsilyl) acetamide (BSA) (3 equiv., 294 µL, 1.20 mmol) were added. The reaction mixture was stirred for 48 h at the temperature T. The reaction mixture was then quenched by the addition of a saturated aqueous solution of NH\(_4\)Cl (2 mL) and the product extracted with dichloromethane (3 × 2 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo to yield the crude product, which was purified by flash chromatography (eluent: pentane/AcOEt (8:2)); \(\delta = 48.51\) °C; \(^{1}H\) NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.35-7.17\) (m, 10 H), 6.48 (d, J = 15.6 Hz, 1 H), 6.33 (dd, J = 15.6, 8.4 Hz, 1 H), 4.27 (dd, J = 10.8, 8.8 Hz, 1 H), 3.96 (d, J = 10.8 Hz, 1 H), 3.71 (s, 3 H, OMe), 3.52 (s, 3 H, OMe) ppm; \(^{13}\)C NMR (CDCl\(_3\), 101 MHz): \(\delta = 168.2\) (C\(_{\text{v}}\)), \(\delta = 167.8\) (C\(_{\text{v}}\), C=C), 140.2 (C\(_{\text{v}}\)), 136.8 (C\(_{\text{v}}\)), 131.9, 129.1, 128.7, 128.5, 127.9, 127.6, 127.2, 126.4, 57.7, 52.6, 52.5, 49.2 ppm. Determination of enantioenrichment by chiral SFC (CHIRALPAK AD column).

**Notes and references**

The structures of products were determined by single crystal X-ray diffraction (see ESI†).

Summary of data: CCDC 1051048, determined by single crystal X-ray diffraction (see ESI†).

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