

Graphical Abstract

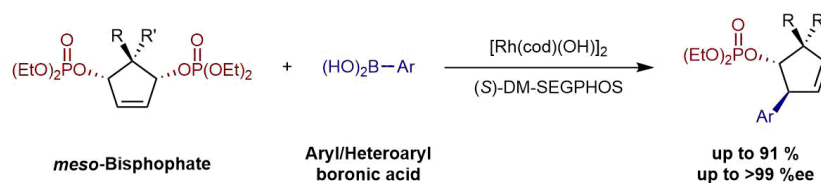
Desymmetrization of *meso*-bisphosphates via rhodium catalyzed asymmetric allylic arylation

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Desymmetrization of *meso*-bisphosphates via rhodium catalyzed asymmetric allylic arylation

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The desymmetrization of *meso*-compounds allows for the unmasking of previously installed stereogenic centers, and quaternary centers are of special interest as they are frequently challenging to form with control in synthesis. Here, we report the desymmetrization of highly functionalized cyclic *meso*-bisphosphates via Rhodium-catalyzed enantioselective allylic arylation. The highly enantioselective introduction of functionalized (hetero)aryl moieties to a prostereogenic quaternary center generates three continuous stereogenic centers. Typical (hetero)arylboronic acids are tolerated in synthetically useful yields and excellent enantioselectivity.

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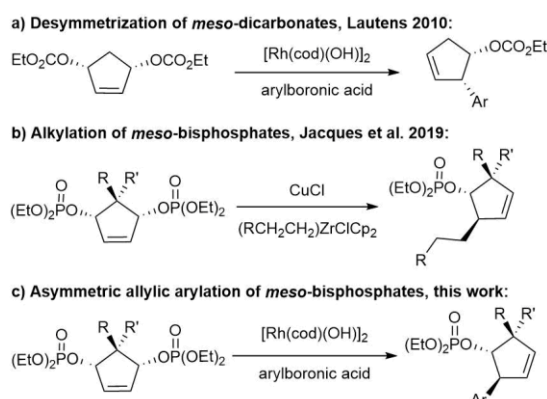
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1. Introduction

Desymmetrization is a powerful tool to exploit prostereogenic centers in *meso*-compounds and rapidly generate multiple stereogenic centers, from the synthesis of small molecule building blocks to the late stage functionalization of complex natural products.^[1] Consequently, this strategy has attracted considerable attention resulting in a range of transition metal catalyzed desymmetrization protocols.^[2,3] In particular, Pd-catalyzed asymmetric allylic additions (AAAs) have been studied extensively and several natural product syntheses incorporate a Pd-catalyzed desymmetrization step,^[4] however these processes commonly rely on stabilized nucleophiles with pKa's <15. Although different metal catalysts allow non-stabilized nucleophiles to be applied in desymmetrizations, these procedures are currently limited in comparison to methods using stabilized nucleophiles. Lautens and coworkers used Rhodium catalysis to successfully desymmetrize cyclic *meso*-1,4-dicarbonates using arylboronic acids (Scheme 1).^[5,6] Cu-catalyzed methods have also been developed with Gennari and coworkers demonstrating addition of dimethyl and diethyl zinc to unfunctionalized bisphosphates,^[7,8] and more recently Sawamura and coworkers using allylboronic ester nucleophiles,^[9] while Feringa and coworkers used this strategy in the desymmetrization of cyclic *meso*-dibromides.^[10] We have shown that Cu-catalyzed AAA can be applied to the desymmetrization of highly functionalized cyclic *meso*-bisphosphates using a wide variety of alkylzirconocene nucleophiles.^[11-13]

The enantioselective generation of all-carbon quaternary centers is a well-recognized challenge in both the synthesis of small molecules and bioactive compounds.^[14-22] The desymmetrization of suitable *meso*-compounds bearing a quaternary prostereogenic center through an enantioselective reaction is an elegant way of "revealing" this stereocenter and incorporating it in a synthetic strategy.^[23] This approach allows access to scaffolds with an array of well-defined stereocenters, particularly if the desymmetrization step introduces a new substituent.^[24]

Given our recently developed Cu-catalyzed desymmetrization of cyclic *meso*-bisphosphates and our experience with Rh-catalyzed AAAs,^[25-27] we reasoned that the desymmetrization of cyclic 1,4-bisphosphates using Rh-catalysis would yield the complementary desymmetrized arylation products. This would enable the use of non-stabilized nucleophiles from readily available arylboronic acids, allowing access to structures containing (hetero)aryl moieties.



Scheme 1 a) Rh-catalyzed desymmetrization of unfunctionalized *meso*-1,4-dicarbonates; b) Cu-catalyzed asymmetric allylic alkylation of *meso*-bisphosphates; c) This work: Rh-catalyzed arylation to desymmetrize *meso*-bisphosphates

Herein, we report the desymmetrization of *meso*-1,4-bisphosphates using a Rh-catalyzed allylic arylation strategy to access highly functionalized cyclopentene derivatives in an enantioselective fashion.

2. Results

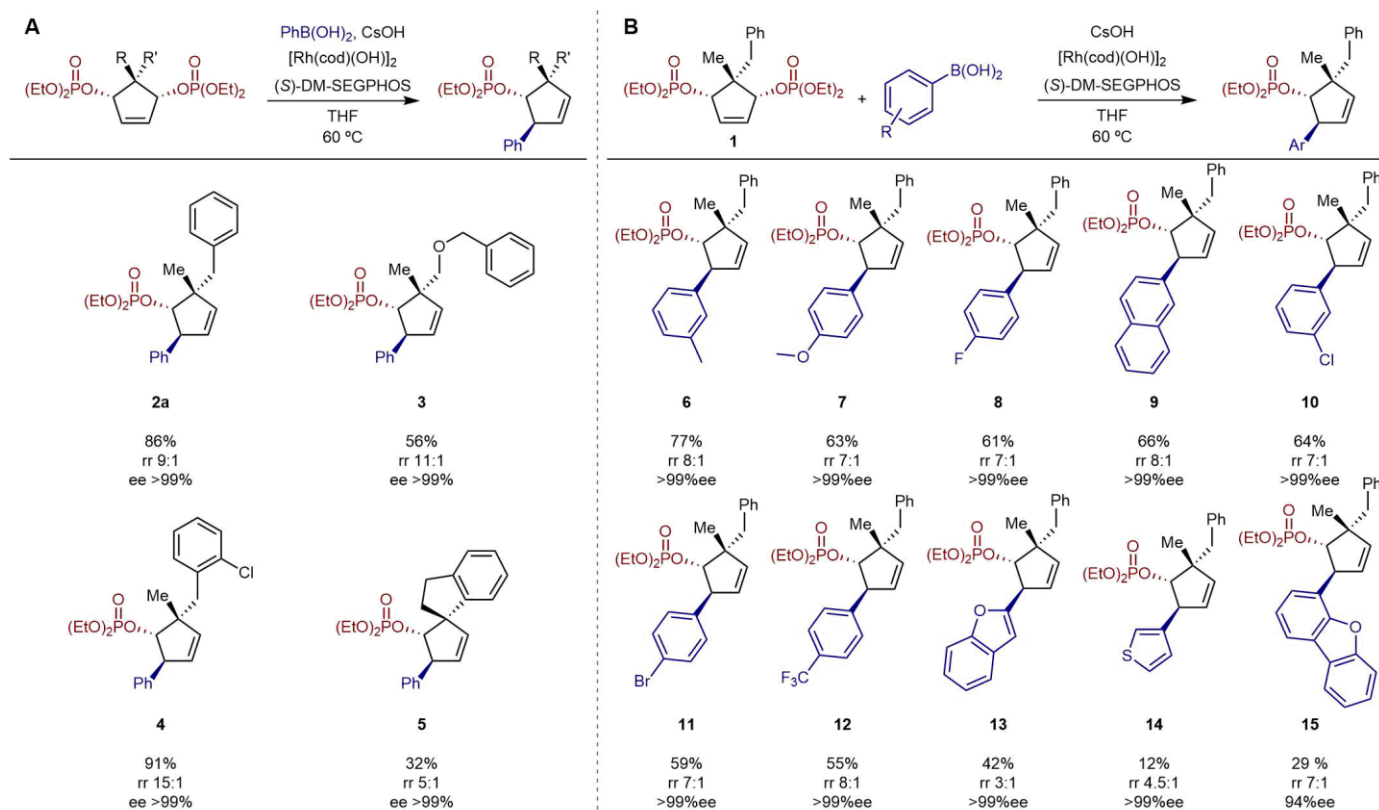
2.1. Optimization

As starting point for initial optimization studies, conditions known to be generally applicable in Rh-catalyzed AAAs were examined,^[25-27] giving ~40% conversion and complete enantioselectivity of the desired *anti*-S_N2' product (Table 1, entry 1). However, the 4.3:1 ratio of allylic arylation product (**2a**) and undesired S_N2 regioisomer (**2b**) required our attention. Raising the reaction temperature to 80 °C (entry 2) in both THF and 2- MeTHF (entries 3 and 4) gave only marginal improvement in the conversion. Investigating the effect of ligands showed an effect on the regioselectivity in favor of the desired product when (*S*)-P-PHOS (15.5:1) and (*S*)-Xylyl-P-PHOS (9.1:1) were used, while the conversion also improved slightly (entries 6 and 7). Higher conversion was observed using SEGPHOS-ligands (entries 8-10), in particular (*S*)-DM-SEGPHOS provided excellent (90%) conversion while maintaining a regioisomeric ratio of 8.7:1 (entry 9). Eventually, conditions to give 86% isolated yield, a regioisomeric ratio of 8.9:1, and an ee of >99% were identified at a concentration of 0.2 M (table 1, entry 12). The isolated yield refers only to the desired allylic arylation product as the S_N2 regioisomer is removed during purification. The absolute configuration of all compounds in this study are assigned by comparing signs of optical rotation to previously reported alkyl-substituted compounds with similar substitution patterns.^[11]

Table 1 Optimization of reaction conditions based on conversion, enantiomeric excess, and regioisomeric ratio of **2a:2b**.^a

Entry	Ligand	T [°C]	Conv. [%] ^b	ee [%] ^c	2a:2b ^b
1	(<i>S</i>)-BINAP	60	40	>99	4.3:1
2	(<i>S</i>)-BINAP	80	36	>99	4:1
3 ^d	(<i>S</i>)-BINAP	60	36	>99	6.3:1
4 ^d	(<i>S</i>)-BINAP	80	49	>99	4.3:1
5	(<i>R</i>)-TOL-BINAP	60	51	>99	3.3:1
6	(<i>S</i>)-P-Phos	60	60	>99	15.5:1
7	(<i>S</i>)-Xylyl-P-Phos	60	55	>99	9.1:1
8	(<i>S</i>)-SEGPHOS	60	79	>99	7.6:1
9	(<i>S</i>)-DM-SEGPHOS	60	90	>99	8.7:1
10	(<i>S</i>)-DTBM-SEGPHOS	60	2	-	4:1
11	(<i>S</i>)-(-)-Cl-MeO-BIPHEP	60	70	53	2.7:1
12 ^{e,f}	(<i>S</i>)-DM-SEGPHOS	60	91	>99	8.9:1

^a Conditions: 0.2 mmol **1** (1.0 equiv.), 0.4 mmol phenylboronic acid (2.0 equiv.), 5 μmol [Rh(cod)(OH)]₂ (0.025 equiv., 5 mol% Rh), 0.012 mmol ligand (0.06 equiv.), 0.2 mmol CsOH (1.0 equiv.) in 2 mL THF (0.1 M); ^b Determined by ¹H-NMR spectroscopy; ^c Determined by SFC (see SI for conditions); ^d 2-Methyltetrahydrofuran used as solvent; ^e reaction concentration increased to 0.2 M; ^f Isolated yield of 86%.



Scheme 2 A) Influence of different pro-quaternary center substitution; B) Scope of aryl and heteroaryl boronic acids. The yields refer to the isolated $\text{S}_{\text{N}}2'$ product, crude regioisomeric ratios determined by $^1\text{H-NMR}$ spectroscopy prior to purification.

2.2. Scope

The influence of substitution on the prostereogenic quaternary center α to the phosphate moieties was examined (Scheme 2 A). Replacing the benzyl moiety of **2a** with a methyl benzyl ether (**3**) gave 11:1 regioselectivity and 56% yield. A chlorobenzyl substituent showed both high yield (91%) and regioisomeric ratio (15:1). Incorporating a spirocycle (**5**) gave 32% yield with moderate regioselectivity (5:1). To our delight, the enantioselectivity of these reactions was not affected and all products were obtained in >99% ee. While the substituent on the quaternary center is important in terms of yield and regioselectivity, exactly why is not yet clear.

A series of functionalized aryl and heteroaryl boronic acids were tested in combination with bisphosphate **1** (Scheme 2 B). As a general trend, *meta*- and *para*-substituted arylboronic acids (**6-12**) gave good yields with excellent enantioselectivity, tolerating different electronic properties of the substituents, while heteroaryl boronic acids (**13-15**) provided more moderate yields. However, *ortho*-substitution of arylboronic acids was less well accommodated, resulting in unsatisfactory yields. Equally, the non-aromatic boronic acids tested, and those with complex substitution patterns, were not tolerated here. A methyl substituent in *meta*-position (**6**) resulted in a yield of 77% and a rr of 8:1 in favor of the desired regioisomer. *Para*-fluoro substitution (**8**) was similarly well tolerated, giving a yield of 61%, as were other halogen functionalities such as *meta*-chloride (**10**) and *para*-bromide (**11**), giving 64% and 59% yield respectively. The AAA product of 2-naphthyl-boronic acid was obtained in 66% yield (**9**). *Para*-methoxy (**7**) and *para*-trifluoromethyl (**12**) boronic acids gave products in 63% and 55% yield, demonstrating that electron donating and withdrawing groups are tolerated. All examples **6-12** displayed a relative regio-isomeric ratio between 7:1 and 8:1 without any specific

trends to be identified. While this system did not accommodate the nitro-gen-containing substrates we examined, it tolerated benzofuran-2-ylboronic acid, giving **13** in 42% yield, with a rr of 3:1. With thiophen-3-ylboronic acid only 12% yield of **14** was obtained. It should be emphasized that the ee remains excellent and is not affected by the choice of boronic acid. The only exception to this trend occurred when introducing a 4-dibenzo- $[b,d]$ furan moiety (**15**) where 29% yield and 94% ee were obtained.

3. Conclusion

In summary, we reported a Rh-catalyzed asymmetric allylic arylation strategy to desymmetrize cyclic *meso*-bisphosphates featuring a prostereogenic quaternary center. The reaction displays excellent enantioselectivity in moderate to good yields over a range of both aryl and heteroarylboronic acids and *meso*-bisphosphates. This transformation is complementary to our recently reported Cu-catalyzed AAA and expands the toolkit for enantioselective desymmetrization reactions.

4. Experimental section

4.1. General procedure 1 for the synthesis of racemic reference compounds

Flask A: A flame-dried 5 mL round-bottomed-flask was charged with (*rac*)-SEGPHOS (7.3 mg, 0.012 mmol, 0.06 equiv.) and then $[\text{Rh(cod)(OH)}]_2$ (2.3 mg, 0.005 mmol, 0.025 equiv.), and the solids were dissolved in 1.0 mL dry THF. An aqueous solution (50 wt.% in H_2O) of CsOH (35 μL , 0.2 mmol, 1.0 equiv.) was added to this mixture which was then stirred at 60°C for 30 min.

Flask B: A flame-dried 5 mL round-bottomed-flask was charged with bisphosphate (0.2 mmol, 1.0 equiv.) and then a

boronic acid (0.4 mmol, 2.0 equiv.), 0.8 mL of dry THF was then added and the mixture was stirred for 30 min at room temperature.

After the mixtures in both Flask A and B were stirred for 30 min, the contents of flask B were transferred into flask A via syringe. Flask B was rinsed with 0.2 mL dry THF which was transferred into flask A in the same way. The reaction was stirred at 60 °C overnight and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography using silica gel (eluent system specified below) to give the racemic product.

4.2. General procedure 2 for the synthesis of compounds 2a-15

Flask A: A flame-dried 5 mL round-bottomed-flask was charged with (*S*)-DM-SEGPPOS (17.3 mg, 0.024 mmol, 0.06 equiv.) and then [Rh(cod)(OH)]₂ (4.6 mg, 0.010 mmol, 0.025 equiv.), and the solids were dissolved in 1.0 mL dry THF. An aqueous solution (50 wt.% in H₂O) of CsOH (70 µL, 0.4 mmol, 1.0 equiv.) was added to this mixture which was then stirred at 60 °C for 30 min.

Flask B: A flame-dried 5 mL round-bottomed-flask was charged with bisphosphate (0.4 mmol, 1.0 equiv.) and then a boronic acid (0.8 mmol, 2.0 equiv.), 0.8 mL of dry THF was then added and the mixture was stirred for 30 min at room temperature.

After the mixtures in both Flask A and B were stirred for 30 min, the contents of flask B were transferred into flask A via syringe. Flask B was rinsed with 0.2 mL dry THF which was transferred into flask A in the same way. The reaction was stirred at 60 °C for 4 hours and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (eluent system specified below) using silica gel to give the product.

4.3. (1*R*,2*S*,3*S*)-2-Benzyl-2-methylcyclopent-4-ene-1,3-bis(diethyl phosphate) (**1**)

A solution of (1*R*,2*S*,3*S*)-2-benzyl-2-methylcyclopent-4-ene-1,3-diol (14.3 mmol, 1.0 equiv.) in THF (86 mL) and TMEDA (22 mL) was cooled to -40 °C using a MeCN/CO₂ bath before *n*BuLi (2.5 M in hexane, 12.60 mL, 31.5 mmol, 2.2 equiv.) was added dropwise. The resulting solution was left to stir for 10 minutes at -40 °C before dialkyl chlorophosphate (35.8 mmol, 2.5 equiv.) was added dropwise. The resulting mixture was left to stir at -40 °C for 2 hours and then warmed to 0 °C. Brine (10 mL) was added slowly to the mixture which was then poured over H₂O (80 mL) and extracted with CH₂Cl₂ (3 x 80 mL). The organic extracts were combined, washed with brine (100 mL), dried (MgSO₄) and evaporated *in vacuo*. The crude material was purified by flash column chromatography on silica (1-2-3% MeOH in EtOAc) to give **1** in 93% yield as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.35 – 7.30 (m, 2H), 7.27 – 7.22 (m, 2H), 7.17 (tt, *J* = 7.2, 1.4 Hz, 1H), 6.33 (s, 2H), 4.66 – 4.63 (m, 2H), 4.16 – 4.03 (m, 8H), 2.98 (s, 2H), 1.31 (qd, *J* = 7.1, 1.0 Hz, 12H), 0.81 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ_C/ppm: 138.3, 136.0, 130.7, 128.2, 126.2, 86.2, 63.9, 48.6, 36.2, 24.0, 16.3; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -2.00; HRMS (ESI) *m/z* calcd for C₁₇H₃₅O₈P₂ [M+H]⁺: 477.17291, found: 477.17285; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2985.8 (w), 1368.0 (w), 1260.7 (m), 1162.4 (w), 1021.5 (s), 987.6 (s), 911.1

(m), 821.3 (w), 756.2 (w). Consistent with data in the literature.^[11]

4.4. (1*S*,2*R*,5*S*)-2-benzyl-2-methyl-5-phenylcyclopent-3-en-1-yl diethyl phosphate (**2a**)

Synthesized according to general procedure 2 using **1**. Purified by flash chromatography (10-30-40% EtOAc in petroleum ether) to give **2a** in 86% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IA; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, *t_R* = 2.443 min; major enantiomer, *t_R* = 2.591 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.34 – 7.18 (m, 10H), 5.61 (ddd, *J* = 6.2, 1.6, 1.1 Hz, 1H), 5.53 (dd, *J* = 6.2, 2.5 Hz, 1H), 4.56 (dd, *J* = 8.6, 7.8 Hz, 1H), 4.08 – 3.99 (m, 1H), 3.97 (dt, *J* = 7.8, 2.2 Hz, 1H), 3.91 – 3.70 (m, 3H), 2.99 (d, *J* = 13.0 Hz, 1H), 2.75 (d, *J* = 13.0 Hz, 1H), 1.22 (td, *J* = 7.1, 1.1 Hz, 3H), 1.21 (s, 3H), 1.11 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 142.0, 139.0, 138.7, 131.0, 130.0, 129.6, 128.2, 127.8, 127.1, 126.1, 93.7, 63.7, 56.2, 50.9, 41.0, 24.2, 16.1; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.84; HRMS (ESI) *m/z* calcd for C₂₃H₃₉O₄NaP [M+Na]⁺: 423.16957, found: 423.16941; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2981.0 (w), 1494.7 (w), 1453.9 (w), 1264.3 (w), 1025.9 (s), 974.1 (m), 750.4 (w), 701.7 (w); [α]_D²⁵₅₈₉ = -169.4 (c=1.0 in CHCl₃, >99% ee).

4.5. (1*S*,2*S*,5*S*)-2-((Benzyloxy)methyl)-2-methyl-5-phenylcyclopent-3-en-1-yl diethyl phosphate (**3**)

Synthesised according to general procedure 2 using (1*R*,2*S*,3*S*)-2-((benzyloxy)methyl)-2-methylcyclopent-4-ene-1,3-bis(diethyl phosphate) (**17**, see SI). Purified by flash chromatography (10-30-40% EtOAc in petroleum ether) to give **3** in 56% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IA; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, *t_R* = 3.090 min; major enantiomer, *t_R* = 3.179 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.27 – 7.24 (m, 2H), 7.24 – 7.10 (m, 7H), 5.69 (dd, *J* = 6.1, 2.3 Hz, 1H), 5.63 – 5.55 (m, 1H), 4.47 (d, *J* = 5.6 Hz, 2H), 4.43 (dd, *J* = 8.7, 7.2 Hz, 1H), 4.06 – 4.02 (m, 1H), 3.84 (m, 1H), 3.72 – 3.59 (m, 3H), 3.56 (d, *J* = 9.0 Hz, 1H), 3.38 (d, *J* = 9.0 Hz, 1H), 1.18 (s, 3H), 1.04 (td, *J* = 7.1, 1.1 Hz, 3H), 0.98 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 142.3, 138.9, 137.4, 131.2, 128.6, 128.4, 128.1, 127.5, 127.5, 127.0, 92.9, 74.1, 73.6, 63.7, 57.3, 51.7, 22.7, 16.1; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.76; HRMS (ESI) *m/z* calcd for C₂₄H₃₂O₅P [M+H]⁺: 431.19819, found: 431.19799; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2980.6 (w), 1453.9 (w), 1264.0 (w), 1100.0 (w), 1029.7 (s), 974.2 (m), 746.8 (w), 699.9 (w); [α]_D²⁵₅₈₉ = -115.2 (c=1.0 in CHCl₃, >99% ee).

4.6. (1*S*,2*R*,5*S*)-2-(2-Chlorobenzyl)-2-methyl-5-phenylcyclopent-3-en-1-yl diethyl phosphate (**4**)

Synthesised according to general procedure 2 using (1*R*,2*S*,3*S*)-2-(2-chlorobenzyl)-2-methylcyclopent-4-ene-1,3-bis(diethyl phosphate) (**16**, see SI). Purified by flash chromatography (10-30-40% EtOAc in petroleum ether) to give **4** in a 91% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IA; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ =

210 nm; minor enantiomer, t_R = 2.755 min; major enantiomer, t_R = 2.936 min].

^1H NMR (400 MHz, CDCl_3) δ_{H} /ppm: 7.36 – 7.33 (m, 1H), 7.33 – 7.28 (m, 3H), 7.27 – 7.22 (m, 3H), 7.20 – 7.11 (m, 2H), 5.58 (s, 2H), 4.56 (dd, J = 8.8, 7.8 Hz, 1H), 4.06 – 3.97 (m, 2H), 3.90 – 3.69 (m, 3H), 3.09 (s, 2H), 1.25 (s, 3H), 1.20 (td, J = 7.1, 1.1 Hz, 3H), 1.11 (td, J = 7.1, 1.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ_{C} /ppm: 141.9, 138.6, 136.8, 135.4, 132.9, 130.1, 129.8, 128.6, 128.2, 127.7, 127.1, 126.2, 93.7, 63.7, 56.2, 51.7, 36.9, 24.6, 16.2; ^{31}P NMR (162 MHz, CDCl_3) δ_{P} /ppm: –1.78; HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{29}\text{O}_4^{35}\text{ClP}$ $[\text{M}+\text{H}]^+$: 435.14865, found: 435.14863; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2980.8 (w), 1442.1 (w), 1265.0 (w), 1024.3 (s), 973.1 (m), 754.0 (w), 700.7 (w); $[\alpha]^{25}_{589}$ = –153.0 (c = 1.0 in CHCl_3 , >99% ee).

4.7. Diethyl ((1*S*,4*S*,5*S*)-4-phenyl-2',3'-dihydrospiro[cyclopentane-1,1'-inden]-2-en-5-yl) phosphate (5)

Synthesised according to general procedure 2 using (1*S*,2*R*,5*S*)-2',3'-dihydrospiro[cyclopentane-1,1'-inden]-3-ene-2,5-bis(diethyl phosphate) (**18**, see SI) on a 0.4 mmol scale. Purified by flash chromatography (10-30-40% EtOAc in petroleum ether) to give **5** in 32% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.300 min; major enantiomer, t_R = 3.517 min].

^1H NMR (400 MHz, CDCl_3) δ_{H} /ppm: 7.29 – 7.23 (m, 4H), 7.21 – 7.16 (m, 2H), 7.15 – 7.08 (m, 3H), 5.80 (s, 2H), 4.70 (dd, J = 8.7, 4.8 Hz), 4.18 (d, J = 4.8 Hz), 3.59 (m, 1H), 3.48 – 3.37 (m, 1H), 3.36 – 3.21 (m, 2H), 3.05 – 2.94 (m, 1H), 2.76 (ddd, J = 15.9, 7.9, 3.9 Hz, 1H), 2.18 – 2.09 (m, 2H), 0.95 (td, J = 7.1, 1.1 Hz, 3H), 0.88 (td, J = 7.1, 1.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ_{C} /ppm: 144.9, 143.5, 141.9, 138.5, 131.1, 128.6, 128.1, 127.3, 127.1, 126.0 (2C), 124.5, 90.7, 64.7, 63.3, 58.2, 38.5, 31.0, 15.9; ^{31}P NMR (162 MHz, CDCl_3) δ_{P} /ppm: –2.12; HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{O}_4\text{P}$ $[\text{M}+\text{H}]^+$: 399.17197, found: 399.17191; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2981.0 (w), 1477.3 (w), 1455.3 (w), 1257.2 (m), 1029.8 (s), 969.9 (m), 757.7 (w), 701.3 (w); $[\alpha]^{25}_{589}$ = –269.8 (c = 1.0 in CHCl_3 , >99% ee).

4.8. (1*S*,2*R*,5*S*)-2-benzyl-2-methyl-5-(*m*-tolyl)cyclopent-3-en-1-yl diethyl phosphate (6)

Synthesised according to general procedure 2, using **1** and 3-methylphenylboronic acid (108.8 mg, 0.8 mmol, 2.0 equiv.) to give **6** in 77% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IF; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.151 min, major enantiomer, t_R = 3.250 min].

^1H NMR (400 MHz, CDCl_3) δ_{H} /ppm: 7.31 – 7.26 (m, 2H), 7.25 – 7.17 (m, 4H), 7.07 – 7.02 (m, 3H), 5.61 (dt, J = 6.2, 1.4 Hz, 1H), 5.52 (dd, J = 6.2, 2.5 Hz, 1H), 4.55 (dd, J = 8.6, 7.8 Hz, 1H), 4.11 – 3.98 (m, 1H), 3.93 (dt, J = 7.8, 2.1 Hz, 1H), 3.90 – 3.70 (m, 3H), 2.99 (d, J = 13.0 Hz, 1H), 2.74 (d, J = 13.0 Hz, 1H), 2.33 (s, 3H), 1.26 – 1.22 (m, 3H), 1.21 (s, 3H), 1.12 (td, J = 7.1, 1.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ_{C} /ppm: 141.9, 138.9, 138.8, 138.1, 131.0, 130.1, 128.9, 128.5, 127.9, 127.8, 126.1, 125.3, 93.7, 63.80, 63.75, 63.67, 63.61, 56.1, 50.9, 41.0, 24.4, 21.5, 16.2, 16.0; ^{31}P NMR (162 MHz, CDCl_3) δ_{P} /ppm: –1.85; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{32}\text{O}_4\text{P}$ $[\text{M}+\text{H}]^+$: 415.20437,

found: 415.20340; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2980.3 (w), 1606.1 (w), 1494.0 (w), 1453.6 (w), 1369.2 (w), 1264.5 (m), 1165.5 (w), 1025.3 (s), 973.8 (m), 901.3 (w), 786.0 (w), 749.6 (m), 702.7 (m); $[\alpha]^{25}_{589}$ = –159.5 (c = 1.0 in CHCl_3 , >99% ee).

4.9. (1*S*,2*R*,5*S*)-2-benzyl-5-(4-methoxyphenyl)-2-methylcyclopent-3-en-1-yl diethyl phosphate (7)

Synthesised according to general procedure 2, using **1** and (4-methoxyphenyl)boronic acid (121.6 mg, 0.8 mmol, 2.0 equiv.) to give **7** in 63% yield as a yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.547 min, major enantiomer, t_R = 3.709 min].

^1H NMR (400 MHz, CDCl_3) δ_{H} /ppm: 7.30 – 7.12 (m, 7H), 6.88 – 6.82 (m, 2H), 5.59 (dt, J = 6.3, 1.3 Hz, 1H), 5.51 (dd, J = 6.2, 2.5 Hz, 1H), 4.52 (dd, J = 8.6, 7.7 Hz, 1H), 4.08 – 3.99 (m, 1H), 3.93 (dt, J = 7.3, 2.4, 1.7 Hz, 1H), 3.91 – 3.80 (m, 2H), 3.79 (s, 3H), 3.78 – 3.74 (m, 1H), 2.98 (d, J = 13.0 Hz), 2.74 (d, J = 13.0 Hz, 1H), 1.27 – 1.22 (m, 3H), 1.20 (s, 3H), 1.14 (td, J = 7.1, 1.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ_{C} /ppm: 158.8, 138.8, 134.1, 131.0, 130.26, 129.1, 127.8, 126.14, 114.0, 93.78, 63.82, 63.76, 63.70, 63.64, 55.5, 55.4, 50.8, 41.0, 24.4, 16.29, 16.22, 16.16, 16.09; ^{31}P NMR (162 MHz, CDCl_3) δ_{P} /ppm: –1.78; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{32}\text{O}_5\text{P}$ $[\text{M}+\text{H}]^+$: 431.19819, found: 431.19830; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 3281.6 (w), 2982.8 (w), 2849.9 (w), 2360.3 (w), 1587.9 (m), 1513.2 (m), 1492.0 (m), 1479.1 (m), 1371.7 (w), 1257.7 (s), 1140.5 (m), 1082.3 (m), 1026.8 (s), 976.7 (m), 840.7 (m), 741.5 (m), 715.8 (m), 645.9 (w); $[\alpha]^{25}_{589}$ = –133.0 (c = 1.0 in CHCl_3 , >99% ee).

4.10. (1*S*,2*R*,5*S*)-2-benzyl-5-(4-fluorophenyl)-2-methylcyclopent-3-en-1-yl diethyl phosphate (8)

Synthesised according to general procedure 2, using **1** and 4-fluorophenylboronic acid (111.9 mg, 0.8 mmol, 2.0 equiv.) to give **8** in 61% yield as colourless crystals.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 1.0 mL/min; MeOH/CO₂: 0% isocratic for 3 min, 0% to 10% over 5 min, 10% to 50% over 1 min; λ = 210 nm; minor enantiomer, t_R = 8.675 min, major enantiomer, t_R = 8.911 min].

^1H NMR (400 MHz, CDCl_3) δ_{H} /ppm: 7.31 – 7.17 (m, 7H), 7.04 – 6.97 (m, 2H), 5.58 (dt, J = 6.4, 1.2 Hz, 1H), 5.54 (dd, J = 6.3, 2.5 Hz, 1H), 4.50 (dd, J = 8.7, 7.7 Hz, 1H), 4.11 – 4.00 (m, 1H), 3.98 – 3.75 (m, 4H), 2.98 (d, J = 13.0 Hz, 1H), 2.73 (d, J = 13.0 Hz, 1H), 1.26 (td, J = 7.0, 1.1 Hz, 3H), 1.20 (s, 3H), 1.15 (td, J = 7.1, 1.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ_{C} /ppm: 148.0, 139.3, 138.6, 131.0, 129.73, 129.64, 129.57, 127.9, 126.2, 115.5, 115.2, 93.6, 63.83, 63.75, 63.69, 63.64, 55.5, 41.0, 51.0, 24.4, 16.29, 16.21, 16.15, 16.08; ^{31}P NMR (162 MHz, CDCl_3) δ_{P} /ppm: –1.72; ^{19}F NMR (376 MHz, CDCl_3) δ_{F} /ppm: –116.22; HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{29}\text{O}_4\text{FP}$ $[\text{M}+\text{H}]^+$: 419.17820, found: 419.17913; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2981.5 (w), 1603.8 (w), 1509.7 (m), 1454.1 (w), 1369.7 (w), 1265.0 (m), 1223.9 (m), 1159.2 (w), 1025.3 (s), 973.5 (m), 903.7 (w), 863.0 (w), 831.4 (w), 750.1 (m), 704.1 (m), 626.2 (w); $[\alpha]^{25}_{589}$ = –139.1 (c = 1.0 in CHCl_3 , >99% ee); Melting Point: 74.9 °C.

4.11. (1*S*,2*R*,5*S*)-2-benzyl-2-methyl-5-(naphthalen-2-yl)cyclopent-3-en-1-yl diethyl phosphate (**9**)

Synthesised according to general procedure 2, using **1** and naphthalen-2-ylboronic acid (137.6 mg, 0.8 mmol, 2.0 equiv.) to give **9** in 66% yield as colourless crystals.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IA; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.236 min, major enantiomer, t_R = 3.409 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.87 – 7.74 (m, 3H), 7.70 (s, 1H), 7.51 – 7.36 (m, 3H), 7.32 – 7.27 (m, 2H), 7.26 – 7.20 (m, 3H), 5.70 (dt, *J* = 6.2, 1.3 Hz, 1H), 5.60 (dd, *J* = 6.3, 2.5 Hz, 1H), 4.67 (dd, *J* = 8.7, 7.7 Hz, 1H), 4.14 (dt, *J* = 7.7, 2.1 Hz, 1H), 4.07 – 3.92 (m, 1H), 3.89 – 3.78 (m, 1H), 3.78 – 3.60 (m, 2H), 3.04 (d, *J* = 13.0 Hz, 1H), 2.78 (d, *J* = 13.0 Hz, 1H), 1.25 (s, 3H), 1.13 (td, *J* = 7.1, 1.1 Hz, 3H), 0.95 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 139.3, 139.2, 138.7, 133.6, 132.8, 131.0, 129.9, 128.4, 127.9, 127.8, 127.7, 126.9, 126.24, 126.21, 126.19, 125.7, 93.4, 63.84, 63.78, 63.68, 63.62, 56.4, 51.1, 41.0, 24.4, 16.15, 16.08, 15.94, 15.86; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.79; HRMS (ESI) *m/z* calcd for C₂₇H₃₁O₄²³NaP [M+Na]⁺: 473.18631, found: 473.18524; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2980.7 (w), 1602.1 (w), 1495.1 (w), 1453.7 (w), 1370.0 (w), 1264.3 (m), 1165.3 (w), 1025.7 (s), 974.3 (m), 900.6 (w), 818.9 (m), 748.7 (m), 704.0 (m), [α]_D²⁵₅₈₉ = -201.0 (c=1.0 in CHCl₃, >99% ee); Melting Point: 79.5 °C.

4.12. (1*S*,2*R*,5*S*)-2-benzyl-5-(3-chlorophenyl)-2-methylcyclopent-3-en-1-yl diethyl phosphate (**10**)

Synthesised according to general procedure 2, using **1** and 3-chlorophenylboronic acid (125.1 mg, 0.8 mmol, 2.0 equiv.) to give **10** in 64% yield as a dark yellow oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.204 min, major enantiomer, t_R = 3.397 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.31 – 7.11 (m, 9H), 5.63 – 5.54 (m, 2H), 4.51 (dd, *J* = 8.7, 7.8 Hz, 1H), 4.13 – 4.00 (m, 1H), 4.00 – 3.77 (m, 4H), 2.97 (d, *J* = 13.0 Hz, 1H), 2.74 (d, *J* = 13.0 Hz, 1H), 1.26 (td, *J* = 7.1, 1.1 Hz, 3H), 1.21 (s, 3H), 1.16 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 144.2, 139.7, 138.5, 134.4, 131.0, 129.9, 129.2, 128.4, 127.9, 127.2, 126.3, 126.2, 93.33, 63.95, 63.89, 63.82, 63.77, 55.9, 51.1, 41.0, 24.4, 16.28, 16.21, 16.14, 16.07; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.75; HRMS (ESI) *m/z* calcd for C₂₃H₂₉O₄³⁵ClP [M+H]⁺: 435.14865, found: 435.14816; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2980.9 (w), 1597.7 (w), 1454.0 (w), 1393.3 (w), 1265.0 (m), 1165.1 (w), 1026.4 (s), 972.7 (m), 785.9 (w), 750.3 (m), 722.1 (w), 703.4 (w); [α]_D²⁵₅₈₉ = -84.2 (c=1.0 in CHCl₃, >99% ee).

4.13. (1*S*,2*R*,5*S*)-2-benzyl-5-(4-bromophenyl)-2-methylcyclopent-3-en-1-yl diethyl phosphate (**11**)

Synthesised according to general procedure 2, using **1** and 4-bromophenylboronic acid (160.7 mg, 0.8 mmol, 2.0 equiv.) to give **11** in 59% yield as yellow crystals.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 0.5 mL/min; MeOH/CO₂: 1% to 30%; λ =

210 nm; minor enantiomer, t_R = 9.411 min, major enantiomer, t_R = 9.664 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.47 – 7.40 (m, 2H), 7.31 – 7.11 (m, 7H), 5.60 – 5.53 (m, 2H), 4.50 (dd, *J* = 8.7, 7.7 Hz, 1H), 4.11 – 4.00 (m, 1H), 3.98 – 3.75 (m, 4H), 2.97 (d, *J* = 13.0 Hz, 1H), 2.73 (d, *J* = 13.1 Hz, 1H), 1.25 (td, *J* = 7.1, 1.1 Hz, 3H), 1.20 (s, 3H), 1.15 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 141.1, 139.6, 138.5, 131.6, 131.0, 129.9, 129.4, 127.9, 126.2, 120.9, 93.34, 63.94, 63.88, 63.81, 63.75, 55.7, 51.1, 41.0, 24.40, 16.27, 16.20, 16.14, 16.06; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.74; HRMS (ESI) *m/z* calcd for C₂₃H₂₉O₄⁷⁹BrP [M+H]⁺: 479.09813, found: 479.09805; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2980.7 (w), 1489.2 (w), 1453.8 (w), 1393.2 (w), 1264.6 (m), 1165.3 (w), 1025.2 (s), 973.2 (m), 903.4 (w), 817.7 (m), 749.8 (m), 704.0 (m); [α]_D²⁵₅₈₉ = -146.6 (c=1.0 in CHCl₃, >99% ee); Melting Point: 78.6 °C.

4.14. (1*S*,2*R*,5*S*)-2-benzyl-2-methyl-5-(4-(trifluoromethyl)phenyl)cyclopent-3-en-1-yl diethyl phosphate (**12**)

Synthesised according to general procedure 2, using **1** and (4-(trifluoromethyl)phenyl)boronic acid (151.9 mg, 0.8 mmol, 2.0 equiv.) to **12** in 55% yield as a dark red crystals.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IC; flow: 0.5 mL/min; MeOH/CO₂: 1% isocratic for 4 min, 1% to 5% in 1 min, 5% isocratic for 8 min, then 5% to 30% in 5 min; λ = 210 nm; minor enantiomer, t_R = 10.704 min, major enantiomer, t_R = 11.062 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.58 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.32 – 7.17 (m, 5H), 5.60 (d, *J* = 0.9 Hz, 2H), 4.54 (dd, *J* = 8.7, 7.8 Hz, 1H), 4.10 – 3.99 (m, 2H), 3.96 – 3.72 (m, 3H), 2.99 (d, *J* = 13.0 Hz, 1H), 2.74 (d, *J* = 13.0 Hz, 1H), 1.28 – 1.20 (m, 6H), 1.11 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 146.2, 139.9, 138.4, 131.0, 129.6, 129.0, 128.6, 127.9, 126.3, 125.52, 125.48, 93.24, 63.96, 63.90, 63.80, 63.74, 56.0, 51.1, 41.0, 24.4, 16.23, 16.16, 16.05, 15.98; ³¹P NMR (162 MHz, CDCl₃) δ_P/ppm: -1.74; ¹⁹F NMR (376 MHz, CDCl₃) δ_F/ppm: -62.47; HRMS (ESI) *m/z* calcd for C₂₄H₂₉O₄F₃P [M+H]⁺: 469.17501, found: 469.17484; IR (ATR) ν (cm⁻¹) thin film, CHCl₃: 2981.4 (w), 1619.3 (w), 1454.2 (w), 1421.2 (w), 1325.7 (s), 1266.0 (m), 1164.7 (m), 1124.4 (m), 1068.2 (m), 1026.2 (s), 973.2 (m), 904.7 (w), 832.0 (w), 750.5 (m), 704.1 (m); [α]_D²⁵₅₈₉ = -113.8 (c=1.0 in CHCl₃, >99% ee); Melting Point: 58.2 °C.

4.15. (1*R*,2*R*,5*R*)-5-(benzofuran-2-yl)-2-benzyl-2-methylcyclopent-3-en-1-yl diethyl phosphate (**13**)

Synthesised according to general procedure 2, using **1** and benzofuran-2-ylboronic acid (129.6 mg, 0.8 mmol, 2.0 equiv.) to give **13** in 42% yield as colourless crystals.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IG; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; λ = 210 nm; minor enantiomer, t_R = 3.606 min, major enantiomer, t_R = 3.913 min].

¹H NMR (400 MHz, CDCl₃) δ_H/ppm: 7.55 – 7.50 (m, 1H), 7.46 – 7.41 (m, 1H), 7.34 – 7.18 (m, 7H), 6.62 (s, 1H), 5.72 (dt, *J* = 6.3, 1.3 Hz, 1H), 5.61 (dd, *J* = 6.2, 2.6 Hz, 1H), 4.94 (dd, *J* = 8.8, 7.6 Hz, 1H), 4.21 – 4.16 (m, 1H), 4.15 – 3.91 (m, 4H), 3.01 (d, *J* = 13.1 Hz, 1H), 2.79 (d, *J* = 13.1 Hz, 1H), 1.30 – 1.23 (m, 6H), 1.14 (td, *J* = 7.1, 1.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ_C/ppm: 157.7, 155.1, 139.5, 138.4, 131.0, 128.8, 127.9, 127.0,

126.3, 123.8, 122.8, 120.8, 111.1, 103.3, 89.4, 64.05, 63.99, 63.94, 63.88, 51.0, 50.4, 41.0, 24.4, 16.21, 16.14, 16.06, 15.98; ^{31}P NMR (162 MHz, CDCl_3) $\delta_{\text{P}}/\text{ppm}$: -1.73; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{30}\text{O}_5\text{P}$ $[\text{M}+\text{H}]^+$: 441.18254, found: 441.18256; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2980.7 (w), 1601.8 (w), 1454.7 (m), 1256.4 (m), 1166.3 (w), 1025.2 (s), 972.8 (m), 901.0 (w), 803.1 (w), 749.5 (m), 703.9 (m); $[\alpha]^{25}_{589} = -214.8$ ($c=1.0$ in CHCl_3 , >99% ee); Melting Point: 81.3 °C.

4.16. (1*S*,2*R*,5*S*)-2-benzyl-2-methyl-5-(thiophen-3-yl)cyclopent-3-en-1-yl diethyl phosphate (**14**)

Synthesised according to general procedure 2, using **1** and thiophen-3-ylboronic acid (102.4 mg, 0.8 mmol, 2.0 equiv.) to give **14** in 12% yield as an orange oil.

SFC analysis indicated an enantiomeric excess of >99% [Chiralpak® IF; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; $\lambda = 210$ nm; minor enantiomer, $t_{\text{R}} = 3.310$ min, major enantiomer, $t_{\text{R}} = 3.420$ min].

^1H NMR (400 MHz, CDCl_3) $\delta_{\text{H}}/\text{ppm}$: 7.31 – 7.15 (m, 6H), 7.11 (dd, $J = 3.0, 1.2$ Hz, 1H), 7.03 (dd, $J = 5.0, 1.3$ Hz, 1H), 5.64 (dt, $J = 6.2, 1.3$ Hz, 1H), 5.50 (dd, $J = 6.2, 2.5$ Hz, 1H), 4.61 (dd, $J = 8.5, 7.5$ Hz, 1H), 4.15 – 4.03 (m, 2H), 4.02 – 3.83 (m, 3H), 2.97 (d, $J = 13.0$ Hz, 1H), 2.73 (d, $J = 13.0$ Hz, 1H), 1.29 (td, $J = 7.1, 1.1$ Hz, 3H), 1.24 – 1.16 (m, 6H); ^{13}C NMR (126 MHz, CDCl_3) $\delta_{\text{C}}/\text{ppm}$: 142.7, 138.63, 138.57, 131.0, 129.6, 127.9, 127.4, 126.2, 125.9, 121.4, 92.6, 63.91, 63.85, 63.81, 63.75, 51.54, 50.90, 40.9, 24.5, 16.34, 16.27, 16.22, 16.15; ^{31}P NMR (162 MHz, CDCl_3) $\delta_{\text{P}}/\text{ppm}$: -1.71; HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{27}\text{O}_4^{23}\text{NaP}^{32}\text{S}$ $[\text{M}+\text{Na}]^+$: 429.12599, found: 429.12607; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2980.6 (w), 1495.6 (w), 1454.0 (w), 1392.4 (w), 1259.7 (m), 1165.5 (w), 1030.7 (s), 987.3 (s), 777.4 (w), 753.3 (w), 704.4 (m); $[\alpha]^{25}_{589} = -36.3$ ($c=1.0$ in CHCl_3 , >99% ee).

4.17. (1*S*,2*R*,5*S*)-2-benzyl-5-(dibenzo[*b,d*]furan-4-yl)-2-methylcyclopent-3-en-1-yl diethyl phosphate (**15**)

Synthesised according to general procedure 2, using **1** and dibenzo[*b,d*]furan-4-ylboronic acid (169.6 mg, 0.8 mmol, 2.0 equiv.) to give **15** in 29% yield as an orange oil.

SFC analysis indicated an enantiomeric excess of 94% [Chiralpak® ID; flow: 1.5 mL/min; MeOH/CO₂: 1% to 30%; $\lambda = 210$ nm; minor enantiomer, $t_{\text{R}} = 4.325$ min, major enantiomer, $t_{\text{R}} = 3.995$ min].

^1H NMR (400 MHz, CDCl_3) $\delta_{\text{H}}/\text{ppm}$: 7.95 (ddd, $J = 7.7, 1.4, 0.7$ Hz, 1H), 7.85 (dd, $J = 7.0, 2.0$ Hz, 1H), 7.58 (dt, $J = 8.2, 0.9$ Hz, 1H), 7.46 (ddd, $J = 8.4, 7.3, 1.4$ Hz, 1H), 7.39 – 7.22 (m, 8H), 5.71 (dt, $J = 6.1, 1.6$ Hz, 1H), 5.59 (dt, $J = 6.2, 2.6$ Hz, 1H), 4.90 (dd, $J = 8.8, 8.1$ Hz, 1H), 4.72 (dt, $J = 8.1, 2.6, 1.7$ Hz, 1H), 4.04 – 3.92 (m, 1H), 3.87 – 3.76 (m, 1H), 3.63 – 3.45 (m, 2H), 3.12 (d, $J = 12.9$ Hz, 1H), 2.83 (d, $J = 12.9$ Hz, 1H), 1.30 (s, 3H), 1.15 (td, $J = 7.1, 1.1$ Hz, 3H), 0.79 (td, $J = 7.1, 1.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) $\delta_{\text{C}}/\text{ppm}$: 156.2, 155.0, 139.2, 138.8, 131.0, 129.5, 127.9, 127.3, 126.22, 126.20, 126.07, 124.5, 124.2, 123.3, 122.8, 120.9, 119.2, 111.8, 92.4, 63.84, 63.78, 63.47, 63.41, 50.9, 50.0, 41.0, 24.17, 16.16, 16.09, 15.72, 15.65; ^{31}P NMR (162 MHz, CDCl_3) $\delta_{\text{P}}/\text{ppm}$: -1.86; HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{32}\text{O}_5\text{P}$ $[\text{M}+\text{H}]^+$: 491.19819, found: 491.19809; IR (ATR) ν (cm^{-1}) thin film, CHCl_3 : 2979.1 (w), 1494.9 (w), 1451.8 (m), 1425.0 (w), 1268.5 (m), 1186.3 (m), 1025.3 (s), 973.4 (m), 899.3

(w), 845.3 (w), 754.2 (m), 703.9 (m); $[\alpha]^{25}_{589} = -114.9$ ($c=1.0$ in CHCl_3 , 94% ee).

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Supplementary Material

Supplementary Data is provided.

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