Tetrahedron 69 (2013) 10369–10374

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Aminocatalytic asymmetric Diels–Alder reaction of phosphorus dienophiles and 2,4-dienals

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ARTICLE INFO

Article history:
Received 12 August 2013
Received in revised form 29 September 2013
Accepted 3 October 2013
Available online 7 October 2013

Keywords:
Phosphonate
Phosphine oxide
Dienophile
Diels–Alder cycloaddition
Trienamine

ABSTRACT

Chiral compounds bearing a phosphorus functional group are valuable because of their wide application in biological studies and asymmetric catalysis. Here we present an asymmetric Diels–Alder cycloaddition between phosphor-containing dienophiles and 2,4-dienals under the catalysis of chiral amine **1** via the intermediacy of trienamine species (trienamine catalysis). A spectrum of densely functionalized phosphonocyclohexene derivatives was efficiently constructed in excellent enantioselectivity (up to 99% ee) and with good to high diastereoselectivity (up to >19:1).

1. Introduction

Phosphorus-containing motifs are the key structural features in a large number of enzyme inhibitors, antibiotics, antiviral agents, agrochemicals, and haptens of catalytic antibodies.[1] In addition, the chiral phosphines or their oxides have been extensively used as ligands for metal catalysts or as catalysts in organocatalysis.[2] Thus, the synthesis of chiral organophosphorus compounds has generated much interest in synthetic communities.[3] Among them, the enantioselective addition of phosphorus nucleophiles provides a straightforward protocol to access chiral organophosphorus materials through a new P–C bond formation.[4] Another way to construct these motifs is to employ asymmetric addition reactions with prochiral phosphorous-containing nucleophiles or electrophiles used as substrates, through which stereogenic centers adjacent or remote to the phosphorous atom could be generated.[3e,5]

Asymmetric Diels–Alder cycloaddition is one of the most powerful methodologies to construct six-membered chiral carbo- or heterocycles.[6] In fact, this tool has also been applied to phosphorus dienophiles or dienes to obtain valuable phosphonocyclohexene derivatives.[7] Although such asymmetric variants have been reported by using chiral auxiliary strategy,[8] to the best of our knowledge, there are still very scare examples of catalytic Diels–Alder reaction with phosphorus dienophiles. Encouraged by our recent success in the asymmetric Diels–Alder cycloadditions with HOMO-activated trienamine species,[9] here we would like to present the aminocatalytic and highly stereoselective Diels–Alder reaction of phosphorus dienophiles and 2,4-dienals, giving an efficient and convenient approach to synthesize complex cyclohexenes containing a phosphonate or phosphine oxide moiety.

2. Results and discussion

We initially selected 3-(phosphorylmethylene)-oxindole[10] **2a** as the model dienophile in the reaction with 2,4-hexadienal **3a** under the catalysis of chiral amine **1** and *o*-fluorobenzoic acid (OFBA) in chloroform at room temperature, since the analogous 3-(oxycarbonylmethylene)oxindoles[9a] exhibited high reactivity, and useful spirocyclic oxindoles could be generated.[11] To our delight, the cycloadduct **4a** was smoothly obtained as a single regio- and *endo*-diastereomer in high yield (94%) in 2 h, and with excellent enantioselectivity (96% ee) (Table 1, entry 1). In this case, oxindole moiety still showed stronger electron-withdrawing property than that of phosphonate group. We also briefly screened a series of solvents, such as toluene, THF, 1,4-dioxane, but generally producing inferior results.[12] Consequently, we investigated the substrate scope and limitations under the above established catalytic conditions. For the cycloadditions with 2,4-hexadienal **3a**, 3-

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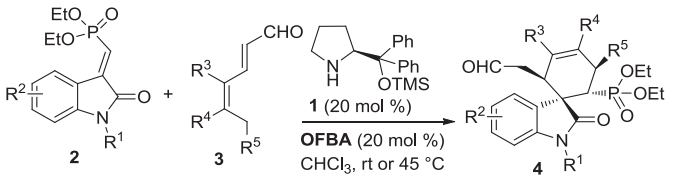
http://dx.doi.org/10.1016/j.tet.2013.10.001

Table 1
Asymmetric Diels–Alder reaction of 3-(phosphorylmethylene)oxindoles **2** and 2,4-dienals **3**[a]



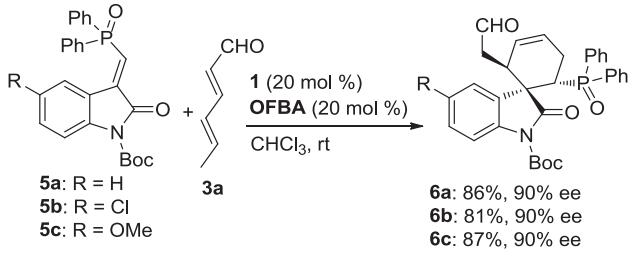
Entry	R^2	R^3, R^4, R^5	Yield[b] (%)	dr[c]	ee[d] (%)
1	H	H, H, H	**4a**, 94	>19:1	96
2[e]	5-F	H, H, H	**4b**, 77	10:1	97
3[e]	5-Cl	H, H, H	**4c**, 95	>19:1	90[f]
4[e]	5-Br	H, H, H	**4d**, 80	9:1	94
5	5-CF_3O	H, H, H	**4e**, 81	>19:1	98
6[e]	5-MeO	H, H, H	**4f**, 91	>19:1	94
7	5,7-Me_2	H, H, H	**4g**, 87	15:1	96
8	H	H, Me, H	**4h**, 94	>19:1	96
9	H	Me, H, H	**4i**, 94	>19:1	99
10	H	Et, H, H	**4j**, 91	10:1	99
11	H	Ph, H, H	**4k**, 92	15:1	98
12	H	Ph, H, Me	**4l**, 92	12:1	98
13[e]	H	H, $(CH_2)_3$	**4m**, 52	8:1	94
14[e,g]	H	H, H, H	**4n**, 90	>19:1	95
15[h]	H	H, H, H	—	—	—

[a] Unless noted otherwise, reactions were performed with dienophile **2** (0.1 mmol, R^1=Boc), 2,4-dienal **3** (0.12 mmol), amine **1** (20 mol %), and *o*-fluorobenzoic acid (OFBA, 20 mol %) in chloroform (1.0 mL) at room temperature.
[b] Yield of isolated major diastereomer.
[c] By ^{1}H NMR analysis of crude mixture.
[d] Determined by chiral HPLC analysis after conversion to the corresponding alcohol.
[e] At 45 °C.
[f] The absolute configuration of **4c** was determined by X-ray analysis after conversion to 2,4-dinitrobenzenehydrazone, see the SD.[13] The other products were assigned by analogy.
[g] R^1=Cbz.
[h] R^1=Me.

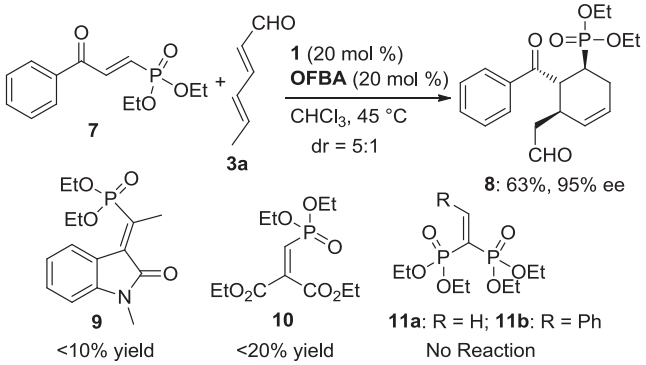
(phosphorylmethylene)oxindoles **2** bearing either electron-withdrawing or donating substituents could be well tolerated, generally exhibiting high to outstanding diastereo- and enantioselectivity. The corresponding cycloadducts **4b–g** could be isolated in a diastereopure form in good to excellent yield (entries 2–7). On the other hand, we explored a variety of 2,4-dienals with diverse substituted patterns in the reactions with dienophile **2a**. As summarized in Table 1, entries 8–12, the similar excellent enantioselectivity and high isolated yields were obtained for products **4h–l**, though a small amount of *exo*-diastereomers were detected in some cases. Nevertheless, a 2,4-dienal with a cyclopentylene motif exhibited lower reactivity, and product **4m** was obtained in a moderate yield but still with good stereocontrol (entry 13). A dienophile with an *N*-Cbz group could be efficiently used, and remarkable data was afforded (entry 14). However, an *N*-methyl 3-olefinic oxindole demonstrated to be inert in the cycloaddition due to lower electrophilicity (entry 15).

With the delightful results in hand, we further designed another type of 3-methyleneoxindoles **5** bearing a phosphine oxide moiety, and tested their reactions with 2,4-dienal **3a**. As outlined in Scheme 1, all the cycloadditions took place smoothly under the same catalytic conditions, and products **6a–c** were produced in exclusive diastereoselectivity and with high enantioselectivity. Thus, the chiral phosphine compounds, which might be used as potential metal ligands or in organocatalysis could be attainable after reducing P=O bond.[14]

In order to introduce more structural diversity into phosphonocyclohexene derivatives, more dienophiles containing a phosphonate group was investigated. As illustrated in Scheme 2, diethyl



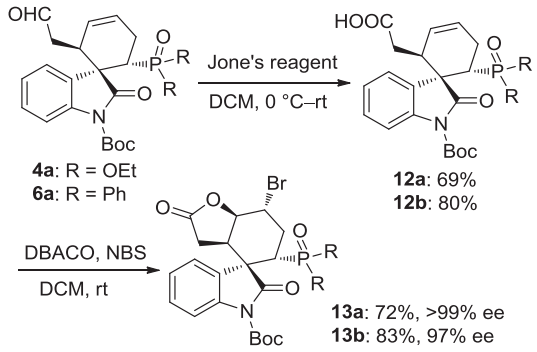
Scheme 1. Asymmetric Diels–Alder reaction of 3-methyleneoxindoles **5** with a phosphine oxide moiety.



Scheme 2. Exploration with more phosphono dienophiles.

(3-oxo-3-phenylprop-1-en-1-yl)-phosphonate **7** exhibited considerable reactivity with 2,4-hexadienal under the above catalytic conditions. In contrast to what's observed using substrate **2**, this reaction is *exo*-selective with respect to the carbonyl group, probably due to the bulkiness of benzoyl moiety.[15] Cycloadduct **8** was isolated in a moderate yield, while the enantioselectivity was also outstanding (95% ee). Unfortunately, much lower or inert reactivity were observed for dienophiles **9–11** in the reactions with **3a** or other 2,4-dienals.

As outlined in Scheme 3, the multifunctional spirocyclic oxindoles **4a** and **6a** could be used to construct more complex frameworks. The aldehyde group was firstly oxidized by Jone's reagent in DCM with good yield. Then an intramolecular bromolactonization reaction with the obtained acids **12** was conducted with *N*-bromosuccinimide (NBS) catalyzed by 1,4-diazabicyclo[2.2.2]octane (DABCO),[16] and the corresponding products **13a** and **13b** were isolated in 72% and 83% yield, respectively, both with excellent diastereo- and enantiopurity.



Scheme 3. Synthetic transformations to access more complex framework.

3. Conclusion

In conclusion, we have developed an asymmetric Diels–Alder cycloaddition of diverse phosphorus dienophiles with 2,4-dienals under the catalysis of a chiral secondary amine, which provides an efficient and straightforward approach to construct densely functionalized phosphonocyclohexene derivatives in excellent enantioselectivity and with good to high diastereoselectivity. These chiral frameworks with a phosphonate or phosphine oxide group might find applications in medicinal chemistry or asymmetric catalysis.

4. Experimental

4.1. General comments

NMR data were obtained for ^{1}H at 400 MHz, and for ^{13}C at 100 MHz. Chemical shifts were reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution. ESI–HRMS was recorded on a Waters SYNAPT G2. In each case, enantiomeric ratio was determined by HPLC analysis on a chiral column in comparison with authentic racemate. UV detection was monitored at 220 or 254 nm. Optical rotation data were examined at 589 nm in $CHCl_3$ solution at 25 °C.

4.2. General procedure for asymmetric Diels–Alder reaction of phosphono dienophiles and 2,4-dienals via trienamine activation

Phosphono dienophile **2** or **5** or **7** (0.1 mmol), 2,4-dienal **3** (0.12 mmol), *o*-fluorobenzoic acid (0.02 mmol), and secondary amine catalyst **1** (0.02 mmol) were dissolved in $CHCl_3$ (1.0 mL) and the solution was stirred at room temperature or at 45 °C. After completion, the mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc) to give the Diels–Alder cycloadduct **4** or **6** or **8**.

*4.2.1. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4a**).* 2 h, 94% yield; colorless oil; R_f=0.32 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −14.3 (*c* 0.14 in $CHCl_3$); 96% ee, determined by HPLC analysis after **4a** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AS-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=8.16 min, *t* (major)=13.48 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.68 (s, 1H), 7.86 (d, *J*=8.4 Hz, 1H), 7.32–7.29 (m, 2H), 7.08 (dt, *J*=7.6, 0.8 Hz, 1H), 6.01–5.99 (m, 1H), 5.78–5.75 (m, 1H), 3.84–3.70 (m, 3H), 3.61–3.55 (m, 1H), 3.36 (dd, *J*=18.4, 8 Hz, 1H), 2.78–2.68 (m, 4H), 2.35 (dd, *J*=18.4, 4.8 Hz, 1H), 1.63 (s, 9H), 1.10 (t, *J*=7.2 Hz, 3H), 0.98 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.4, 176.3, 148.5, 128.3, 128.3, 128.0, 125.7, 125.6, 124.6, 123.9, 114.8, 83.9, 62.2 (d, J_{COP}=6.3 Hz), 61.2 (d, J_{COP}=6.8 Hz), 45.8, 37.4 (d, J_{CP}=12.1 Hz), 34.3, 32.9, 29.6, 23.0 (d, J_{CCCP}=3.8 Hz), 16.0 (d, J_{CCOP}=6.0 Hz), 15.8 (d, J_{CCOP}=6.6 Hz) ppm; ESI–HRMS: calcd for $C_{24}H_{32}NO_7P+Na^+$ 500.1809, found:500.1814.

*4.2.2. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-5′-fluoro-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′ carboxylate (**4b**).* 7 h, 77% yield; yellow semisolid; R_f=0.34 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −9.4 (*c* 0.13 in $CHCl_3$); 97% ee, determined by HPLC analysis after **4b** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=9.32 min, *t* (major)=13.92 min]; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.68 (s, 1H), 7.86 (dd, *J*=8.4, 4.8 Hz, 1H), 7.04–6.99 (m, 2H), 6.02–6.00 (m, 1H), 5.79–5.75 (m, 1H), 3.91–3.62 (m, 4H), 3.37 (dd, *J*=18.8, 8.0 Hz, 1H), 2.90–2.89 (m, 1H), 2.77–2.69 (m, 3H), 2.39–2.33 (m, 1H), 1.62 (s, 9H), 1.12 (t, *J*=7.2 Hz, 3H), 1.01 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 174.5, 159.5 (d, $J_{C,F}$=24.0 Hz), 148.9, 127.8, 125.7 (d, $J_{C,F}$=13.1 Hz), 116.0 (d, $J_{C,F}$=8.0 Hz), 114.7, 114.5, 112.3, 112.1, 84.1, 62.3 (d, J_{COP}=6.3 Hz), 61.3 (d, J_{COP}=7.1 Hz), 45.6, 37.2 (d, J_{CP}=11.9 Hz), 34.1, 32.7, 28.0, 22.9 (d, J_{CCCP}=3.8 Hz), 16.0 (d, J_{CCOP}=5.9 Hz), 15.8 (d, J_{CCOP}=6.6 Hz) ppm; ESI–HRMS: calcd for $C_{24}H_{31}FNO_7P+Na^+$ 518.1714, found: 518.1721.

*4.2.3. (1S,2S,6S)-tert-Butyl-5′-chloro-6 (diethoxyphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′ carboxylate (**4c**).* 4 h, 95% yield; orange oil; R_f=0.31 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −19.5 (*c* 0.42 in $CHCl_3$); 90% ee, determined by HPLC analysis after **4c** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=80:20, 1.0 mL/min, λ=254 nm, *t* (major)=5.62 min, *t* (minor)=6.53 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.67 (s, 1H), 7.85 (d, *J*=8.8 Hz, 1H), 7.30–7.25 (m, 2H), 6.03–6.01 (m, 1H), 5.79–5.75 (m, 1H), 3.86–3.72 (m, 3H), 3.65–3.59 (m, 1H), 3.35 (dd, *J*=18.4, 8.4 Hz, 1H), 2.89–2.88 (m, 1H), 2.72–2.68 (m, 3H), 2.35 (dd, *J*=18.4, 4.0 Hz, 1H), 1.62 (s, 9H), 1.11 (t, *J*=7.2 Hz, 3H), 1.02 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 171.8, 148.8, 137.5, 129.3, 128.2, 127.8, 125.8, 125.7, 124.8, 116.1, 84.3, 62.3 (d, J_{COP}=6.4 Hz), 61.3 (d, J_{COP}=6.1 Hz), 45.7, 37.1 (d, J_{CP}=12.0 Hz), 34.1, 32.7, 28.0, 22.9 (d, J_{CCCP}=3.7 Hz), 16.0 (d, J_{CCOP}=6.0 Hz), 15.8 (d, J_{CCOP}=6.7 Hz) ppm; ESI–HRMS: calcd for $C_{24}H_{31}Cl^{35}NO_7P+Na^+$ 534.1419, found: 534.1424 (Cl^{35}), 536.1431 (Cl^{37}).

*4.2.4. (1S,2S,6S)-tert-Butyl-5′-bromo-6-(diethoxyphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4d**).* 8 h, 80% yield; orange oil; R_f=0.33 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −24.5 (*c* 0.29 in $CHCl_3$); 94% ee, determined by HPLC analysis after **4d** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AS-H Column, *n*-hexane/*i*-PrOH=80:20, 1.0 mL/min, λ=254 nm, *t* (minor)=4.86 min, *t* (major)=6.57 min]; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.67 (s, 1H), 7.79 (d, *J*=8.4 Hz, 1H), 7.44 (dd, *J*=8.4, 2.0 Hz, 1H), 7.37 (d, *J*=2.0 Hz, 1H), 6.03–6.01 (m, 1H), 5.79–5.75 (m, 1H), 3.86–3.64 (m, 3H), 3.62–3.56 (m, 1H), 3.34 (dd, *J*=18.8, 8.4 Hz, 1H), 2.89–2.88 (m, 1H), 2.71–2.67 (m, 3H), 2.38–2.32 (m, 1H), 1.62 (s, 9H), 1.11 (t, *J*=7.2 Hz, 3H), 1.03 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.1, 175.6, 148.9, 138.0, 131.1, 127.8, 127.5, 125.8, 125.7, 116.9, 116.5, 84.3, 62.3 (d, J_{COP}=6.4 Hz), 61.3 (d, J_{COP}=6.9 Hz), 45.6, 37.1 (d, J_{CP}=12.0 Hz), 34.2, 32.7, 28.0, 22.9 (d, *J*=3.8 Hz), 16.0 (d, J_{CCOP}=5.9 Hz), 15.8 (d, J_{CCOP}=6.8 Hz) ppm; ESI–HRMS: calcd for $C_{24}H_{31}Br^{79}NO_7P+Na^+$ 578.0914, found: 578.0920 (Br^{79}), 580.0919 (Br^{81}).

*4.2.5. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-2′-oxo-2-(2-oxoethyl)-5′-(trifluoromethoxy)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4e**).* 4 h, 81% yield; orange oil; R_f=0.35 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −16.7 (*c* 0.31 in $CHCl_3$); 98% ee, determined by HPLC analysis after **4e** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (major)=8.86 min, *t* (minor)=15.04 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.68 (s, 1H), 7.93 (d, *J*=8.8 Hz, 1H), 7.20–7.17 (m, 2H), 6.04–6.02 (m, 1H), 5.79–5.76 (m, 1H), 3.88–3.72 (m, 3H), 3.68–3.58 (m, 1H), 3.38 (dd, *J*=18.8, 8.4 Hz, 1H), 2.91–2.90 (m, 1H), 2.72–2.68 (m, 3H), 2.36 (dd, *J*=18.8, 3.6 Hz, 1H), 1.63 (s, 9H), 1.11 (t, *J*=7.2 Hz, 3H), 1.00 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 175.8, 148.8, 145.4, 137.5, 132.4, 127.8, 125.8 (d, d, $J_{C,F}$=13.3 Hz), 121.0, 118.0, 115.8, 84.4, 62.3 (d, J_{COP}=6.5 Hz), 61.3 (d, J_{COP}=7.0 Hz), 45.5, 37.1 (d, J_{CP}=11.7 Hz), 34.2, 32.8, 29.6, 28.0, 22.9 (d, J_{CCCP}=3.9 Hz), 15.9 (d, J_{CCOP}=5.8 Hz), 15.7 (d, J_{CCOP}=6.5 Hz) ppm;

ESI–HRMS: calcd for $C_{25}H_{31}F_3NO_8P+Na^+$ 584.1632, found: 584.1639.

*4.2.6. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-5′-methoxy-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4f**).* 4 h, 91% yield; orange semisolid; R_f=0.32 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −29.7 (*c* 0.20 in $CHCl_3$); 94% ee, determined by HPLC analysis after **4f** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (major)=12.87 min, *t* (minor)=19.70 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.68 (s, 1H), 7.79 (d, *J*=8.8 Hz, 1H), 6.90 (d, *J*=2.4 Hz, 1H), 6.82 (dd, *J*=9.2, 2.4 Hz, 1H), 6.00–5.98 (m, 1H), 5.78–5.75 (m, 1H), 3.89–3.85 (m, 1H), 3.77 (s, 3H), 3.74–3.67 (m, 2H), 3.65–3.57 (m, 1H), 3.36 (dd, *J*=18.8, 8.0 Hz, 1H), 2.89–2.69 (m, 3H), 2.52–2.32 (m, 2H), 1.62 (s, 9H), 1.11 (t, *J*=6.8 Hz, 3H), 1.00 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.4, 156.4, 149.0, 132.4, 132.1, 128.1, 125.7, 125.6, 115.5, 112.1, 111.9, 83.8, 62.2 (d, J_{COP}=6.4 Hz), 61.2 (d, J_{COP}=7.0 Hz), 55.6, 45.8, 37.4 (d, J_{CP}=12.1 Hz), 34.3, 32.9, 28.1, 23.1, 16.0 (d, J_{CCOP}=6.1 Hz), 15.8 (d, J_{CCOP}=6.6 Hz) ppm; ESI–HRMS: calcd for $C_{25}H_{34}NO_8P+Na^+$ 530.1914, found: 530.1921.

*4.2.7. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-5′,7′-dimethyl-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4g**).* 3 h, 87% yield; colorless oil; R_f=0.33 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −15.4 (*c* 0.13 in $CHCl_3$); 96% ee, determined by HPLC analysis after **4g** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AS-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=6.78 min, *t* (major)=8.89 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.73 (s, 1H), 7.00 (s, 1H), 6.98 (s, 1H), 6.06–6.63 (m, 1H), 5.83–5.80 (m, 1H), 3.93–3.74 (m, 3H), 3.64–3.57 (m, 1H), 3.65–3.61 (m, 1H), 3.39 (dd, *J*=18.4, 8.0 Hz, 1H), 2.93–2.84 (m, 1H), 2.80–2.74 (m, 3H), 2.43 (dd, *J*=18.4, 4.8 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 1.67 (s, 9H), 1.15 (t, *J*=6.8 Hz, 3H), 1.05 (t, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.4, 177.1, 148.9133.2, 131.7, 128.2, 125.7, 125.6, 123.0, 122.8, 110.7, 84.0, 62.1 (d, J_{COP}=6.3 Hz), 61.1 (d, J_{COP}=7.1 Hz), 45.9, 37.3 (d, J_{CP}=11.8 Hz), 34.4, 32.9, 27.7, 23.1 (d, J_{CCCP}=3.4 Hz), 21.1, 19.7, 16.0 (d, J_{CCOP}=5.7 Hz), 15.7 (d, J_{CCOP}=6.6 Hz) ppm; ESI–HRMS: calcd for $C_{26}H_{36}NO_7P+Na^+$ 528.2122, found: 528.2126.

*4.2.8. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-4-methyl-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4h**).* 3 h, 94% yield; colorless oil; R_f=0.34 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −17.9 (*c* 0.21 in $CHCl_3$); 96% ee, determined by HPLC analysis after **4h** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AD-H Column, *n*-hexane *i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (major)=10.52 min, *t* (minor)=11.99 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.68 (s, 1H), 7.86 (d, *J*=8.4 Hz, 1H), 7.31–7.27 (m, 1H), 7.13–7.05 (m, 2H), 5.46–5.45 (m, 1H), 3.86–3.68 (m, 3H), 3.63–3.57 (m, 1H), 3.33 (dd, *J*=18.4, 8.0 Hz, 1H), 2.87–2.82 (m, 2H), 2.73–2.48 (m, 2H), 2.37–2.31 (m, 1H), 1.84 (s, 3H), 1.63 (s, 9H), 1.11 (t, *J*=7.2 Hz, 3H), 0.98 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.7, 176.5, 148.9, 138.8, 133.0, 132.9, 128.2, 124.4, 123.9, 122.3, 114.8, 84.9, 62.2 (d, J_{COP}=6.3 Hz), 61.2 (d, J_{COP}=7.3 Hz), 46.0, 37.9 (d, J_{CP}=12.7 Hz), 34.9, 33.5, 28.0, 27.6 (d, J_{CCCP}=3.7 Hz), 23.0, 16.0 (d, J_{CCOP}=6.0 Hz), 15.7 (d, J_{CCOP}=6.6 Hz) ppm; ESI–HRMS: calcd for $C_{25}H_{34}NO_7P+Na^+$ 514.1965, found: 514.1973.

*4.2.9. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-3-methyl-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4i**).* 3 h, 94% yield; colorless oil; R_f=0.34 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −58.1 (*c* 0.13 in $CHCl_3$); >99% ee, determined by HPLC analysis after **4i** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=7.67 min, *t* (major)=9.65 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.64 (s, 1H), 7.80 (d, *J*=8.0 Hz, 1H), 7.24–7.16 (m, 2H), 7.00–6.97 (m, 1H), 5.65 (s, 1H), 3.79–3.55 (m, 3H), 3.53–3.47 (m, 1H), 3.34 (dd, *J*=18.8, 8.8 Hz, 1H), 2.72–2.59 (m, 4H), 2.29–2.24 (m, 1H), 1.58 (s, 3H), 1.55 (s, 9H), 1.03 (t, *J*=7.2 Hz, 3H), 0.90 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.5, 176.5, 148.9, 138.8, 133.7, 130.5, 128.2, 124.5, 123.9, 120.9 (d, J_{CP}=13.2 Hz), 114.8, 83.8, 62.1 (d, J_{COP}=6.3 Hz), 61.2 (d, J_{COP}=7.1 Hz), 43.8, 41.4 (d, J_{CP}=12.5 Hz), 33.4, 32.0, 28.0, 23.2 (d, J_{CCCP}=3.5 Hz), 22.6, 16.0 (d, J_{CCOP}=5.9 Hz), 15.7 (d, J_{CCOP}=6.5 Hz) ppm; ESI–HRMS: calcd for $C_{25}H_{34}NO_7P+Na^+$ 514.1965, found: 514.1971.

*4.2.10. (1S,2S,6S)-tert-Butyl-6-(diethoxyphosphoryl)-3-ethyl-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4j**).* 6 h, 95% yield; colorless oil; R_f=0.34 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −41.0 (*c* 0.23 in $CHCl_3$); 99% ee, determined by HPLC analysis after **4j** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=6.71 min, *t* (major)=8.84 min]; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.70 (s, 1H), 7.87 (d, *J*=8.4 Hz, 1H), 7.31–7.27 (m, 1H), 7.21 (d, *J*=7.6 Hz, 1H), 7.05 (t, *J*=7.6 Hz, 1H), 5.71 (s, 1H), 3.84–3.55 (m, 4H), 3.42 (dd, *J*=18.8, 9.2 Hz, 1H), 2.86–2.69 (m, 3H), 2.23 (dd, *J*=18.8, 1.6 Hz, 1H), 2.06–2.00 (m, 2H), 1.80–1.77 (m, 1H), 1.62 (s, 9H), 1.10 (t, *J*=7.2 Hz, 3H), 0.98 (t, *J*=7.2 Hz, 3H), 0.89 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.4, 176.7, 149.0, 139.4, 138.9, 128.2, 124.8, 123.7, 119.4, 119.2, 114.8, 83.9, 62.1 (d, J_{COP}=6.4 Hz), 61.2 (d, J_{COP}=7.3 Hz), 44.4, 39.8 (d, *J*=12.5 Hz), 33.6, 32.2, 28.3, 28.0, 23.0, 16.1 (d, J_{CCOP}=5.9 Hz), 15.8 (d, J_{CCOP}=6.6 Hz), 12.2 ppm; ESI–HRMS: calcd for $C_{26}H_{36}NO_7P+Na^+$ 528.2122, found 528.2129.

*4.2.11. (1S,2S,3S)-tert-Butyl-1-(diethoxyphosphoryl)-2′-oxo-3-(2-oxoethyl)-4-phenylspiro[cyclohex[4]ene-2,3′-indoline]-1′-carboxylate (**4k**).* 3 h, 92% yield; white semisolid; R_f=0.36 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ +5.1 (*c* 0.46 in $CHCl_3$); 98% ee, determined by HPLC analysis after **4k** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AD-H Column, *n*-hexane/*i*-PrOH=80:20, 1.0 mL/min, λ=254 nm, *t* (major)=5.45 min, *t* (minor)=7.70 min]; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.56 (s, 1H), 7.94 (d, *J*=8.0 Hz, 1H), 7.35–7.24 (m, 4H), 7.19–7.17 (m, 2H), 7.07–7.03 (m, 1H), 6.25–6.24 (m, 1H), 3.89–3.65 (m, 3H), 3.63–3.52 (m, 2H), 3.41 (dd, *J*=18.4, 9.2 Hz, 1H), 3.03–2.85 (m, 3H), 2.18 (d, *J*=18.4 Hz, 1H), 1.64 (s, 9H), 1.12 (t, *J*=7.2 Hz, 3H), 1.01 (t, *J*=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.0, 176.5, 149.0, 140.0, 139.0, 138.6, 130.5, 128.6, 128.4, 127.7, 126.1, 124.4, 124.1, 123.8 (d, J_{CP}=13.4 Hz), 115.0, 83.9, 62.2 (d, J_{COP}=6.3 Hz), 61.3 (d, J_{COP}=7.1 Hz), 44.4, 39.6 (d, J_{CP}=12.6 Hz), 33.7, 32.2, 28.0, 24.0 (d, J_{CCCP}=3.6 Hz), 16.1 (d, J_{CCOP}=5.9 Hz), 15.8 (d, J_{CCOP}=6.5 Hz) ppm; ESI–HRMS: calcd for $C_{30}H_{36}NO_7P+Na^+$ 576.2122, found: 576.2129.

*4.2.12. (1S,2S,3S)-tert-Butyl-1-(diethoxyphosphoryl)-6-methyl-2′-oxo-3-(2-oxoethyl)-4-phenylspiro[cyclohex[4]ene-2,3′-indoline]-1′-carboxylate (**4l**).* 4 h, 92% yield; semisolid; R_f=0.36 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −32.5 (*c* 0.21 in $CHCl_3$); 98% ee, determined by HPLC analysis after **4l** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=254 nm, *t* (minor)=7.72 min, *t* (major)=10.06 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.55 (s, 1H), 7.93 (d, *J*=8.4 Hz, 1H), 7.32–7.20 (m, 5H), 7.15–7.13 (m, 2H), 7.01 (t, *J*=7.6 Hz, 1H), 6.12–6.10 (m, 1H), 3.87–3.62 (m, 4H), 3.44–3.24 (m, 2H), 2.62 (dd, *J*=20.8, 9.6 Hz, 1H),

2.36–2.32 (m, 1H), 2.17 (dd, J=18.8, 1.6 Hz, 1H), 1.64 (s, 9H), 1.47 (d, J=6.8 Hz, 3H), 1.13 (t, J=6.8 Hz, 3H), 1.05 (t, J=6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=198.7, 177.0, 149.0, 139.6, 139.1, 136.9, 130.7, 130.6, 128.5, 128.3, 127.7, 126.0, 124.7, 123.8, 114.9, 83.8, 62.0 (d, J_{COP}=5.9 Hz), 61.4 (d, J_{COP}=7.2 Hz), 53.4, 44.8, 39.9 (d, J=9.9 Hz), 29.9, 28.0, 22.1, 16.1 (d, J_{CCOP}=5.9 Hz), 15.8 (d, J_{CCOP}=6.3 Hz) ppm; ESI–HRMS: calcd for $C_{31}H_{38}NO_7P+Na^+$ 590.2278, found: 590.2286.

*4.2.13. (3′S,4S,6S)-tert-Butyl-4-(diethoxyphosphoryl)-2′-oxo-6-(2-oxoethyl)-1,2,3,3a,4,6-hexahydrospiro[indene-5,3′-indoline]-1′-carboxylate (**4m**).* 20 h, 52% yield; orange oil; R_f=0.35 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −9.8 (*c* 0.42 in $CHCl_3$); 94% ee, determined by HPLC analysis after **4m** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AD-H Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=220 nm, *t* (major)=10.39 min, *t* (minor)=17.30 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.59 (s, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.24–7.14 (m, 2H), 7.00 (t, J=7.6 Hz, 1H), 5.29 (s, 1H), 3.73–3.63 (m, 3H), 3.54–3.44 (m, 1H), 3.14 (dd, J=18.4, 8.4 Hz, 1H), 2.92–2.71 (m, 2H), 2.34–2.31 (m, 1H), 2.29–2.25 (m, 4H), 1.80–1.68 (m, 3H), 1.56 (s, 9H), 1.01 (t, J=6.8 Hz, 3H), 0.96 (t, J=6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=200.6, 177.3, 149.2, 144.4, 144.2, 139.4, 128.5, 124.7, 124.2, 118.6, 115.2, 84.1, 62.2 (d, J_{COP}=6.3 Hz), 61.4 (d, J_{COP}=7.6 Hz), 47.1, 41.6, 41.2, 39.6, 38.8, 33.7 (d, J_{CCCP}=2.7 Hz), 29.6, 28.4, 22.6, 16.4 (d, J_{CCOP}=5.7 Hz), 16.2 (d, J_{CCOP}=6.4 Hz) ppm; ESI–HRMS: calcd for $C_{27}H_{36}NO_7P+Na^+$ 540.2122, found: 540.2129.

*4.2.14. (1S,2S,6S)-Benzyl-6-(diethoxyphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**4n**).* 4 h, 90% yield; white semisolid; R_f=0.37 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −27.8 (*c* 0.26 in $CHCl_3$); 95% ee, determined by HPLC analysis after **4n** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Daicel Chiralcel OD-H Column, *n*-hexane/*i*-PrOH=80:20, 1.0 mL/min, λ=220 nm, *t* (minor)=11.42 min, *t* (major)=13.71 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.74 (s, 1H), 8.00 (d, J=8.4 Hz, 1H), 7.57–7.55 (m, 2H), 7.45–7.33 (m, 5H), 7.16 (t, J=7.6 Hz, 1H), 6.07–6.05 (m, 1H), 5.84–5.81 (m, 1H), 5.50–5.49 (m, 2H), 3.84–3.73 (m, 3H), 3.51–3.41 (m, 2H), 2.94–2.81 (m, 1H), 2.76–2.72 (m, 3H), 2.44 (dd, J=18.8, 4.0 Hz, 1H), 1.03 (t, J=7.2 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 176.0, 150.4, 138.2, 134.9, 128.3, 128.2, 128.0, 127.8, 127.7, 125.5, 124.3, 124.1, 114.9, 68.2, 61.9 (d, J_{COP}=6.1 Hz), 61.0 (d, J_{COP}=7.0 Hz), 45.6, 37.1 (d, J_{CP}=11.8 Hz), 34.5, 33.1, 22.8 (d, J=3.7 Hz), 15.8 (d, J_{CCOP}=6.0 Hz), 15.6 (d, J_{CCOP}=6.3 Hz) ppm; ESI–HRMS: calcd for $C_{27}H_{30}NO_7P+Na^+$ 534.1652, found: 534.1657.

*4.2.15. (1S,2S,6S)-tert-Butyl-6-(diphenylphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**6a**).* 1.5 h, 86% yield; white semisolid; R_f=0.38 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −88.9 (*c* 0.51 in $CHCl_3$); 90% ee, determined by HPLC analysis after **6a** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak AD-H Column, *n*-hexane/*i*-PrOH=70:30, 1.0 mL/min, λ=220 nm, *t* (major)=7.04 min, *t* (minor)=17.28 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.63 (s, 1H), 7.72–7.51 (m, 3H), 7.49–7.22 (m, 11H), 7.21–7.04 (m, 1H), 6.02–5.99 (m, 1H), 5.76–5.73 (m, 1H), 3.43–3.37 (m, 1H), 3.16 (dd, J=18.4, 7.2 Hz, 1H), 3.06–2.95 (m, 1H), 2.89–2.78 (m, 1H), 2.40–2.35 (m, 2H), 1.56 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 176.8, 148.3, 138.7, 131.9, 131.8, 131.4, 131.3, 128.5, 128.3, 127.8, 127.7, 125.9, 125.8, 125.3, 114.7, 83.7, 45.7, 38.8 (d, J_{CP}=8.3 Hz), 35.9, 35.3, 28.0, 23.1 ppm; ESI–HRMS: calcd for $C_{32}H_{32}NO_5P+Na^+$ 564.1910, found: 564.1917.

*4.2.16. (1S,2S,6S)-tert-Butyl-5′-chloro-6-(diphenylphosphoryl)-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**6b**).* 3 h, 81% yield; orange semisolid; R_f=0.37 (petroleum ether/ethyl acetate, 1:1); $[\alpha]_D^{20}$ −63.3 (*c* 0.33 in $CHCl_3$); 90% ee, determined by HPLC analysis after **6b** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak IC Column, *n*-hexane/*i*-PrOH=70:30, 1.0 mL/min, λ=220 nm, *t* (minor)=16.48 min, *t* (major)=19.33 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.55 (s, 1H), 7.87 (d, J=8.8 Hz, 1H), 7.42–7.41 (m, 2H), 7.30–7.26 (m, 9H), 6.80 (d, J=2.0 Hz, 1H), 5.93–5.91 (m, 1H), 5.63–5.61 (m, 1H), 3.67 (dt, J=15.2, 6.4 Hz, 1H), 3.48–3.45 (m, 1H), 2.64–2.41 (m, 2H), 1.97 (dd, J=17.2, 3.2 Hz, 1H), 1.79 (ddd, J=17.2, 10.8, 2.0 Hz, 1H), 1.62 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.4, 176.4, 148.4, 139.0, 131.7, 131.6, 131.4, 131.3, 128.9, 128.4, 128.3, 128.0, 127.9, 127.4, 125.9, 125.8, 125.3, 116.5, 84.5, 50.0 (d, J_{CP}=2.9 Hz), 43.1, 40.1, 39.4 (d, J_{CP}=4.6 Hz), 28.0, 24.4 ppm; ESI–HRMS: calcd for $C_{32}H_{31}Cl^{35}NO_8P+Na^+$ 598.1521, found: 598.1527 (Cl^{35}), 600.1503 (Cl^{37}).

*4.2.17. (1S,2S,6S)-tert-Butyl-6-(diphenylphosphoryl)-5′-methoxy-2′-oxo-2-(2-oxoethyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**6c**).* 2 h, 87% yield; white semisolid; R_f=0.39 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −84.4 (*c* 0.24 in $CHCl_3$); 90% ee, determined by HPLC analysis after **6c** was converted to the corresponding alcohol [$NaBH_4$ in DCM and EtOH at −5 °C in ice salt bath] [Chiralpak IC Column, *n*-hexane/*i*-PrOH=70:30, 1.0 mL/min, λ=220 nm, *t* (minor)=19.65 min, *t* (major)=24.09 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.63 (s, 1H), 7.68–7.60 (m, 3H), 7.51–7.27 (m, 6H), 7.26–7.21 (m 2H), 6.87–6.80 (m, 2H), 6.00–5.98 (m, 1H), 5.76–5.73 (m, 1H), 3.75 (s, 3H), 3.41–3.39 (m, 1H), 3.14 (dd, J=18.8, 7.2 Hz, 1H), 2.99–2.85 (m, 2H), 2.43–2.35 (m, 1H), 1.56 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.2, 176.7, 156.2, 148.3, 131.8, 131.7, 131.6, 131.5, 131.4, 128.4, 128.3, 127.9, 127.8, 127.7, 126.3, 126.2, 115.5, 113.1, 112.0, 83.5, 55.5, 45.6, 38.7 (d, J_{CP}=8.0 Hz), 36.1, 35.4, 28.0, 23.2 ppm; ESI–HRMS: calcd for $C_{33}H_{34}NO_6P+Na^+$ 594.2016, found: 594.2021.

*4.2.18. Diethyl ((1S,5R,6R)-6-benzoyl-5-(2-oxoethyl)cyclohex-3-en-1-yl)phosphonate (**8**).* 10 h, 63% yield; colorless oil; R_f=0.31 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ +55.2 (*c* 0.56 in $CHCl_3$); 95% ee, determined by HPLC analysis after **8** was converted to the corresponding alcohol [$NaBH_4$ in DCM and MeOH at 0 °C] Chiralpak IC Column, *n*-hexane/*i*-PrOH=70:30, 1.0 mL/min, λ=254 nm, *t* (major)=20.75 min, *t* (minor)=28.99 min]; ^{1}H NMR of the corresponding alcohol: (400 MHz, $CDCl_3$): δ=8.08 (d, J=7.2 Hz, 2H), 7.57 (t, J=7.2 Hz, 1H), 7.49–7.46 (m, 2H), 5.81–5.73 (m, 2H), 3.92–3.90 (m, 2H), 3.88–3.69 (m, 1H), 3.67–3.59 (m, 3H), 2.78–2.69 (m, 1H), 2.56–2.44 (m, 3H), 1.82–1.70 (m, 1H), 1.54–1.41 (m, 2H), 1.14 (t, J=7.2 Hz, 3H), 1.05 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=203.7, 133.1, 129.4, 128.6, 128.4, 124.5, 124.4, 61.8 (d, J_{COP}=6.4 Hz), 61.2 (d, J_{COP}=7.1 Hz), 60.0, 45.6, 44.5 (d, J_{CP}=3.8 Hz), 37.5 (d, J_{CP}=13.3 Hz), 36.1, 33.9, 24.8 (d, J_{CP}=3.8 Hz), 15.9 (d, J_{CCOP}=6.3 Hz), 15.8 (d, J_{CCOP}=6.1 Hz) ppm; ESI–HRMS: calcd for $C_{19}H_{25}O_5P+Na^+$ 387.1332, found: 387.1354.

4.3. General procedure for the synthetic transformations

To a stirred solution of **4a** or **6a** (0.1 mmol) in DCM was added Jone's reagent (0.1 mmol) at 0 °C. After 2 h, the mixture was stirred at room temperature for 10 h. After completion, the mixture was purified by flash chromatography on silica gel (petroleum ether/EtOAc) to give acid products **12a** or **12b** in 69% and 80% yield, respectively. To a solution of acid (0.1 mmol) and DBACO (0.02 mmol) in DCM (1 mL) was added *N*-bromosuccinimide (0.2 mmol) at room temperature. After 2 h, the mixture was purified by flash chromatography on silica gel (petroleum ether/EtOAc) to give the products **13a** or **13b** in 72% and 83% yield, respectively.

*4.3.1. (3aR,3′S,5S,7R,7aR)-tert-Butyl-7-bromo-5-(diethoxyphosphoryl)-2,2′-dioxo-3,3a,5,6,7,7a-hexahydro-2H-spiro[benzofuran-4,3′-indoline]-1′-carboxylate (**13a**).* White semisolid; R_f=0.58 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −2.7 (*c* 0.23 in $CHCl_3$); >99% ee, determined by HPLC analysis [Chiralpak IA Column, *n*-hexane/*i*-PrOH=90:10, 1.0 mL/min, λ=220 nm, *t* (major)=24.41 min, *t* (minor)=29.78 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.98 (d, *J*=8.4 Hz, 1H), 7.52–7.44 (m, 2H), 7.32–7.26 (m, 1H), 4.97 (dd, *J*=9.6, 7.2 Hz, 1H), 4.12–4.08 (m, 1H), 3.89–3.79 (m, 3H), 3.62–3.58 (m, 1H), 3.09 (dd, *J*=17.6, 6.4 Hz, 1H), 2.88–2.67 (m, 4H), 2.32 (dd, *J*=17.6, 8.4 Hz, 1H), 1.69 (s, 9H), 1.13 (q, *J*=6.8 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=173.8, 173.3, 148.4, 139.0, 129.4, 124.3, 124.2, 115.7, 84.9, 81.4, 62.6 (d, J_{COP}=6.7 Hz), 61.8 (d, J_{COP}=7.1 Hz), 47.6 (d, J_{CP}=20.4 Hz), 45.1 (d, J_{CCP}=15.2 Hz), 38.6, 37.1, 31.6, 29.5 (d, J_{CP}=20.3 Hz), 28.0, 16.1 (d, J_{CCOP}=5.5 Hz), 15.9 (d, J_{CCOP}=6.5 Hz) ppm; ESI–HRMS: calcd for $C_{24}H_{31}Br^{79}NO_8P+Na^+$ 594.0863, found: 594.0869 (Br^{79}), 596.0864 (Br^{81}).

*4.3.2. (3aR,3′S,5S,7R,7aR)-tert-Butyl-7-bromo-5-(diphenylphosphoryl)-2,2′-dioxo-3,3a,5,6,7,7a-hexahydro-2H-spiro[benzofuran-4,3′-indoline]-1′-carboxylate (**13b**).* White semisolid; R_f=0.63 (petroleum ether/ethyl acetate=1:1); $[\alpha]_D^{20}$ −74.8 (*c* 0.83 in $CHCl_3$); 97% ee, determined by HPLC analysis [Chiralpak IB Column, *n*-hexane/*i*-PrOH=60:40, 1.0 mL/min, λ=220 nm, *t* (minor)=10.62 min, *t* (major)=22.05 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.73–7.63 (m, 3H), 7.56–7.53 (m, 1H), 7.47–7.36 (m, 5H), 7.32–7.25 (m, 4H), 7.15–7.11 (m, 1H), 4.84 (dd, *J*=10.0, 7.2 Hz, 1H), 4.14–4.07 (m, 1H), 3.47–3.40 (m, 1H), 3.08 (dd, *J*=17.6, 14.0 Hz, 1H), 2.92 (dq, *J*=20.8, 7.2 Hz, 1H) 2.58–2.50 (m, 2H), 2.32 (dd, *J*=17.6, 7.6 Hz, 1H), 1.68 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=174.3, 173.0, 147.9, 138.8, 132.0, 131.2, 131.1, 129.4, 128.8, 128.7, 128.1, 128.0, 124.8, 115.5, 84.6, 81.2, 47.8 (d, J_{CP}=12.9 Hz), 46.5 (d, J_{CCP}=10.6 Hz), 39.5, 38.8, 32.1, 29.9, 28.0 ppm; ESI–HRMS: calcd for $C_{32}H_{31}Br^{79}NO_6P+Na^+$ 658.0965, found: 658.0971 (Br^{79}), 660.0966 (Br^{81}).

Acknowledgements

We are grateful for financial support from the NSFC (21125206 and 21021001), and the National Basic Research Program of China (973 Program, 2010CB833300).

Supplementary data

Crystal data for enantiopure 2,4-dinitrobenzenehydrazone of **4c**, NMR spectra, and HPLC chromatograms are provided in the Supplementary data. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.10.001.

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