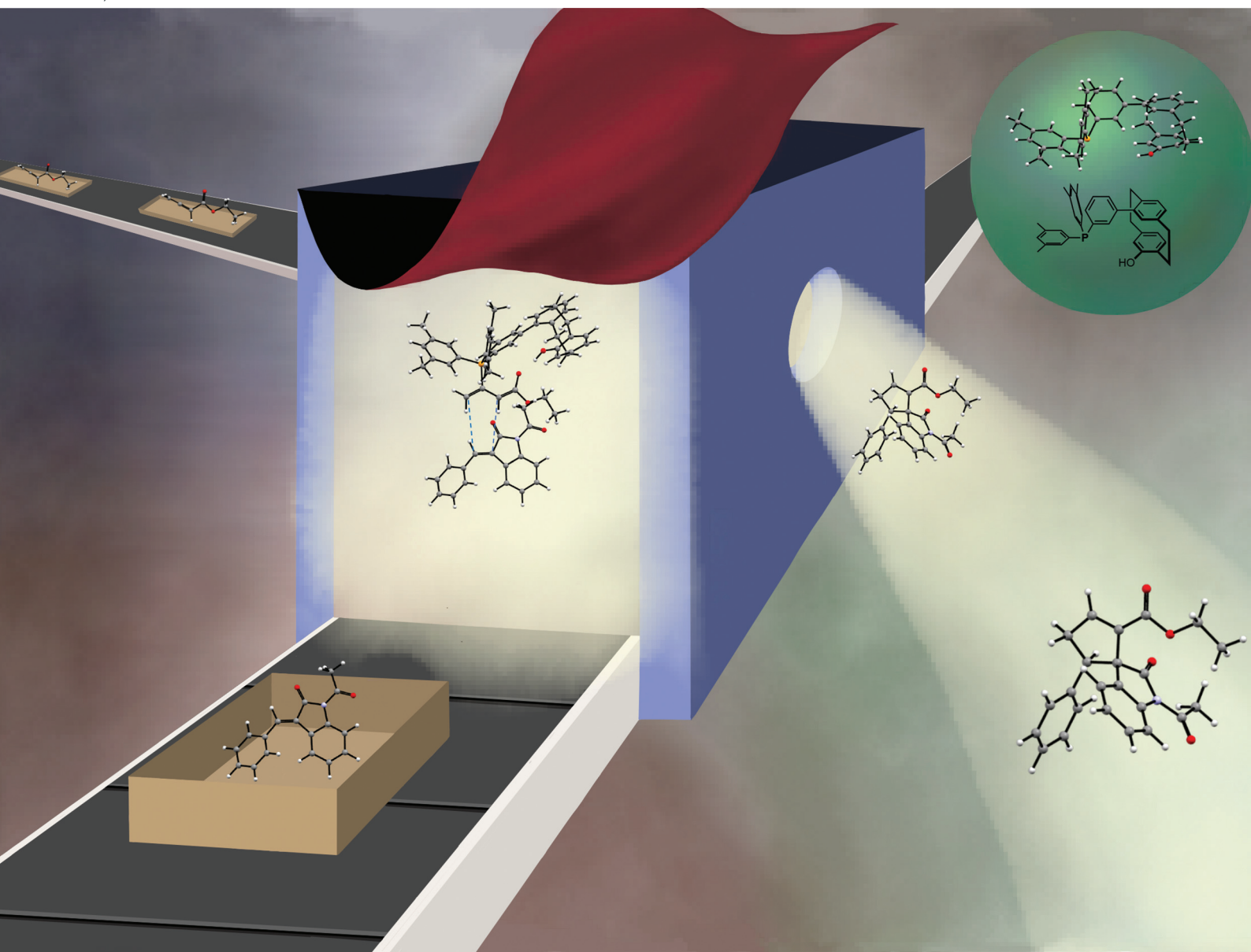


Organic & Biomolecular Chemistry

rsc.li/obc

Volume 22
Number 38
14 October 2024
Pages 7745-7906



ISSN 1477-0520

PAPER

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Cite this: *Org. Biomol. Chem.*, 2024, **22**, 7817

Highly regio- and stereoselective (3 + 2) annulation reaction of allenates with 3-methyleneindolin-2-ones catalyzed by a planar chiral [2.2]paracyclophane-based bifunctional phosphine–phenol catalyst†

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A planar chiral [2.2]paracyclophane-based phosphine–phenol catalyst catalyzed the (3 + 2) annulation reaction of ethyl 2,3-butadienoate with 3-methyleneindolin-2-ones to produce 2,5-disubstituted cyclopentene-fused C3-spirooxindoles in high yields with high regio-, diastereo-, and enantioselectivities. This catalyst was suitable for reactions of not only benzylideneindolinones but also alkylideneindolinones, the chiral phosphine-catalyzed reactions of which have not yet been reported. Density functional theory calculations suggested that the formation of hydrogen bonds between the phenolic OH group of the catalyst and the allenate carbonyl group, rather than between the OH group and the carbonyl group of indolinone, contributed to the formation of an efficient reaction space at the enantiodetermining step.

Received 20th May 2024,
 Accepted 4th July 2024
 DOI: 10.1039/d4ob00831f

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Introduction

Phosphine catalysts perform nucleophilic attacks on activated alkynes, alkenes, and allenes, and thus these catalysts have been used for a variety of transformations.¹ Lu and colleagues reported the first phosphine-catalyzed (3 + 2) annulation reactions between allenates or alkynoates^{2a} or Morita–Baylis–Hillman (MBH) adduct analogues^{2b} as three-carbon synthons and electron-deficient alkenes as two-carbon synthons. Since then, this type of reaction has been one of the most reliable methods for constructing highly substituted cyclopentane

derivatives, and the asymmetric variants of this reaction have been thoroughly studied. Substituents on the phosphorus atom enable efficient control of the reactivity and chemo-, regio-, and stereoselectivities in the phosphine-catalyzed reactions. Chiral phosphine molecules produce enantiomerically enriched compounds by forming a proper asymmetric environment based on a chiral phosphorus center or a chiral backbone.³ Hybridized phosphine catalysts with an acid functionality have expanded the reaction to produce the desired regio- and stereoisomer exclusively through the multiple recognition of the substrates and reactants. Many chiral phosphines, such as axially chiral binaphthyl,⁴ spirocyclic SITCP,⁵ planar chiral FerroPHANE,⁶ and amino acid-derived multifunctional phosphines (Fig. 1),⁷ have been reported as excellent catalysts for various useful reactions. However, the development of new types of phosphine catalyst is still highly desirable because of the diversity of phosphine catalysis.

Spirocycles are produced by annulation with three-carbon synthons, using *exo*-methylenecycles as the two-carbon synthons. Chiral cyclopentane-fused C3-spirooxindoles with multiple stereocenters are found in many natural products and biologically active compounds (Fig. 2).⁸ Several organocatalytic and metal complex-catalyzed methods for the simultaneous creation of spiro centers and other chiral centers on this privileged structure have been developed.⁹ The phosphine-catalyzed (3 + 2) annulation reaction of three-carbon synthons and

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† Electronic supplementary information (ESI) available: Experimental details, ¹H, ¹H–¹H COSY and ¹³C NMR spectra, HPLC data, computational methods, and X-ray data. CCDC 2343919, 2343921, and 2343914. Xyz cartesian coordinates format. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d4ob00831f>

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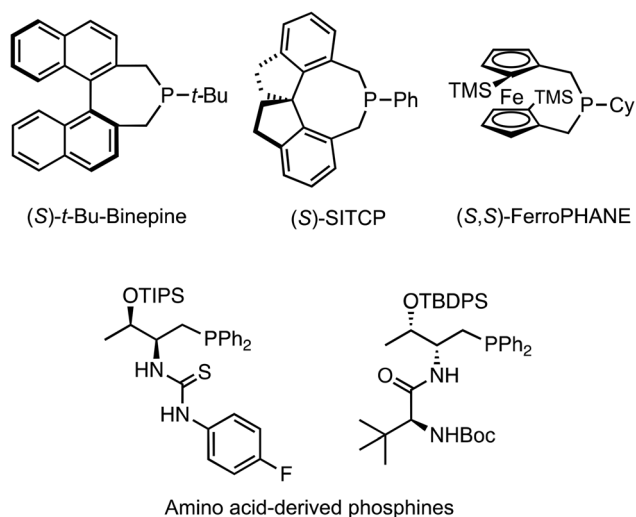


Fig. 1 Chiral phosphine catalysts.

3-methyleneindolin-2-ones is one of the most efficient synthetic methods for accessing cyclopentane-spirooxindoles.¹⁰ Marinetti and colleagues^{11a,b,d} first reported the highly enantioselective (3 + 2) annulation reaction of allenates with 3-methyleneindolinones catalyzed by chiral phosphines (Scheme 1a).¹¹ A similar reaction was developed independently using MBH carbonates¹² (Scheme 1b). Reactions using alkynates (Scheme 1a)¹³ as three-carbon synthons and a Rauhut-Currier reaction with diene derivatives¹⁴ have also been

reported. However, in the syntheses of cyclopentene-spirooxindoles, the substituent on the methylene carbon in the substrates is limited to an aryl group (Type A in Scheme 1) or electron-withdrawing group (Type B in Scheme 1). This limitation is probably caused by the low reactivity of alkyl-substituted methyleneindolinones¹⁵ for the Michael addition reaction of the phosphonium enolates or phosphonium ylides, which is the first step of (3 + 2) annulation. For allenates, Marinetti and colleagues' (3 + 2) annulation method using *t*-Bu-binepine or FerroPHANE is suitable for reactions of ethyl 2,3-butadienoate and benzylideneindolinones containing various types of aromatic groups on the methylene carbon. The reaction efficiently gives 5-aryl-substituted cyclopentene-spirooxindoles (γ -adduct), which are obtained *via* γ -addition of the phosphonium enolate to the β -position of methyleneindolinone, in high yields with high γ/α (regio)- and stereoselectivities (Scheme 1a).^{11a} However, product yields and regioselectivities are moderate in some cases, especially the reaction of furyl- and alkynyl-substituted methyleneindolinones. Reactions of alkylideneindolinones are not found in the literature. Wang *et al.* also reported SITCP-catalyzed (3 + 2) cyclization of allenates with oxindoles, but the substrates used were methyleneindolinones with a phenyl or naphthyl group.^{11c} To the best of our knowledge, only one example of a reaction of hexylideneindolinone with 4-phenyl-2,3-butadienoate catalyzed by Ph_3P has been reported.^{11b,16} In searching for attractive bioactive compounds, there is a need to develop new catalysts that activate both allenes and alkenes, allowing access to greater structural diversity.

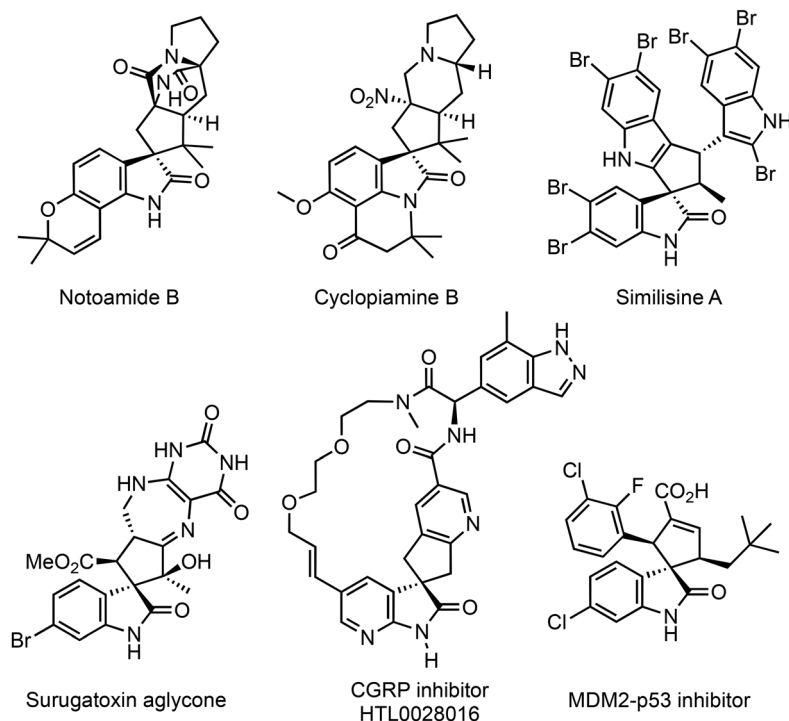
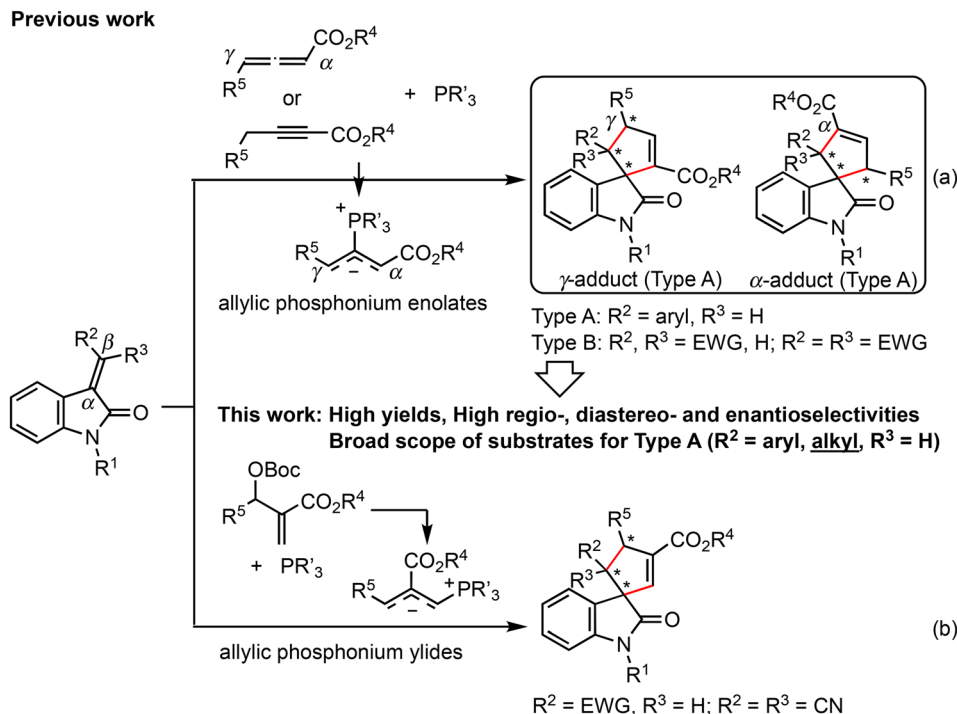


Fig. 2 Examples of natural products and biologically active compounds containing the cyclopentane-spirooxindole scaffold.





Scheme 1 Typical organocatalytic (3 + 2) annulations of 3-methyleneindolin-2-ones. Type A: Annulation reaction proceeds via Michael addition of phosphonium enolates at the β -position of methyleneindolinones. Type B: Michael reaction occurs at the α -position of methyleneindolinones.

Planar chiral ligands with a [2.2]paracyclophane (pCp) backbone are effective in many asymmetric catalysis reactions.¹⁷ However, the potential of pCp as a planar chiral organocatalyst backbone has yet to be investigated sufficiently.¹⁸ There are few examples of highly enantioselective reactions catalyzed by pCp-based chiral molecules.¹⁹ Therefore, we developed pCp-based bifunctional phosphine-phenol catalysts, in which one of the aryl groups on the phosphorus atom of the triarylphosphine has a pseudo-*ortho*-hydroxy-substituted pCp group at the *meta* position (Fig. 3). In other words, one of the aryl groups in the triarylphosphine serves as a spacer, which offers conformational flexibility and makes the distance between the two functional groups suitable for performing dual activation of the substance and reactant. Catalyst (S_p)-**1a** (R^1 = H, R^2 = Me) showed exceptionally high reactivity and good enantioselectivity in the aza-MBH reaction of *N*-tosylaldimines with various vinyl ketones.²⁰

The importance of the phenolic OH group at the pseudo-*ortho* position for the reactivity and enantioselectivity of the reaction has been demonstrated by comparison with the results using methylated (S_p)-**1b** (R^1 = R^2 = Me).^{20b} Catalyst **1a** also worked well in the (3 + 2) annulation reaction of allenates with *N*-tosylaldimines²¹ and of MBH carbonates with dicyanomethyleneindolinones.^{12e}

Here, we report that pCp-phosphine-phenol (S_p)-**1c** (R^1 = H, R^2 = *t*-Bu)²¹ efficiently catalyzes the (3 + 2) annulation of allenates with not only benzyldeneoxindoles but also alkylideneoxindoles to produce 2,5-disubstituted cyclopentene-fused C3-spirooxindoles in a highly regio-, diastereo-, and enantioselective manner (Scheme 1a). Density functional theory (DFT) studies elucidate the origin of the enantioselectivity and the role of the phenolic OH group on the chiral pCp backbone in the (3 + 2) annulation.

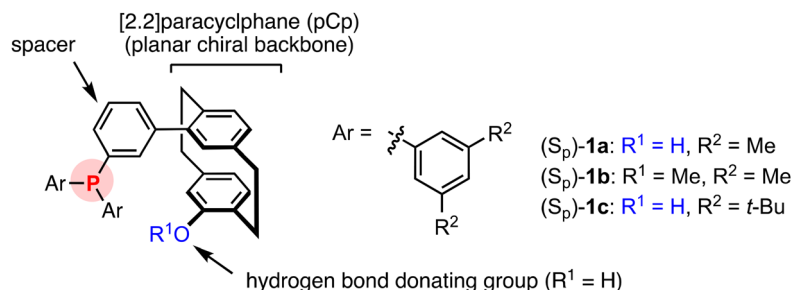


Fig. 3 [2.2]Paracyclophane-based planar chiral triarylphosphine catalysts.



Results and discussion

We started by evaluating pCp-phosphine-phenol catalyst (S_p)-**1a** with two xylyl groups in the reaction of (*E*)-enriched *N*-acetyl-3-benzylideneindolinone (*E/Z* = >20/1) (**2a**) and ethyl 2,3-butadienoate (**3**) (Table 1). A reaction with 5 mol% (S_p)-**1a** in dichloromethane at room temperature was complete within 30 min to provide a 8.1 : 1 mixture of γ - and α -adducts *trans*-**4a** in quantitative yield with 51% and 3% enantiomeric excess (ee), respectively (entry 1). Their diastereomers were not detected in the reaction mixture. Using a more polar solvent, such as THF or acetonitrile, slowed the reaction rate and decreased the enantioselectivity (entries 2–4). Among the solvents examined, toluene gave the highest reactivity and enantioselectivity (entry 6). Masked hydroxy group catalyst (S_p)-**1b** resulted in markedly lower reactivity and enantioselectivity, which suggested that the hydroxy group is an important feature of catalyst (S_p)-**1a** (entry 7). Catalyst (S_p)-**1c** with two bulky *tert*-butyl groups²¹ improved the γ -selectivity and the ee of the major product. Lowering the reaction temperature increased the enantioselectivity (up to 93% ee), although a catalyst loading of 10 mol% was needed for a smooth reaction (entries 10 and 11).

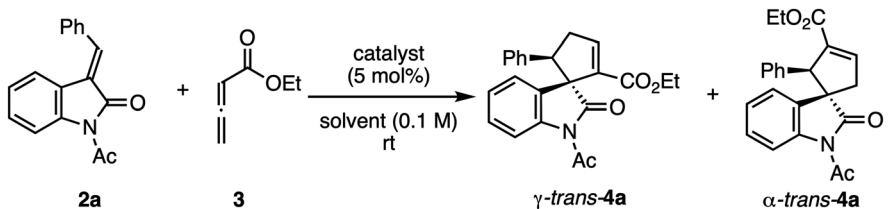
To increase the enantioselectivity, we performed simple protecting group manipulations of the benzylideneindolinone and allenolate using 5 mol% (S_p)-**1a** in toluene at room temperature (Table S1, see ESI†). However, replacing the acetyl group in **2a** with a Boc or alkyl group decreased the regio- and enantioselectivities, whereas a Ts group gave a similar yield and enantioselectivity but much lower regioselectivity.

Increased steric bulk of alkoxy group or installation of γ -substituents on the allenates gave poor results.

Having ascertained the effectiveness of the combination of *N*-acetylindolinone **2a** and ethyl 2,3-butadienoate (**3**), we investigated the scope of the reaction with respect to the substituent on the benzene ring of the benzylidene group of *N*-acetyl-3-benzylideneindolinones **2** (*E/Z* = 7.3/1 to >20/1) with the optimal reaction conditions and catalyst (S_p)-**1c** (Scheme 2). Both electron-withdrawing and -donating substituents at the *para* position on the benzene ring were compatible with the reaction conditions (Scheme 2, *trans*-**4b–4f**). The position of the substituent did not affect the product yield and selectivities (Scheme 2, *trans*-**4g, 4h**). The naphthyl and heteroaryl-substituted methyleneindolinones also reacted smoothly to give the desired products in excellent yields and high regio- and stereoselectivities (Scheme 2, *trans*-**4i–4k**).

The structural determination of the minor product of this reaction using γ -unsubstituted allenolate has not yet been reported. Therefore, we conducted the triphenylphosphine-catalyzed (3 + 2) cyclization reaction of **2a** and **3**^{11a,c} on a large scale and purified the crude products using column chromatography and preparative thin-layer chromatography to separate the two cyclized products (Scheme 3). The structures of the two isolated products were determined by NMR analysis, including ¹H–¹H COSY, and substantiated further by X-ray structural analysis of both compounds. The major product was γ -*trans* adduct **4a**, as reported in the literature,^{11a,c} and the minor product, not specified in the literature, was α -*trans* adduct **4a** (Fig. 4).²² In addition, the absolute configuration of γ -*trans*-**4a** was (1*S*,5*R*) based on comparing the optical rotation

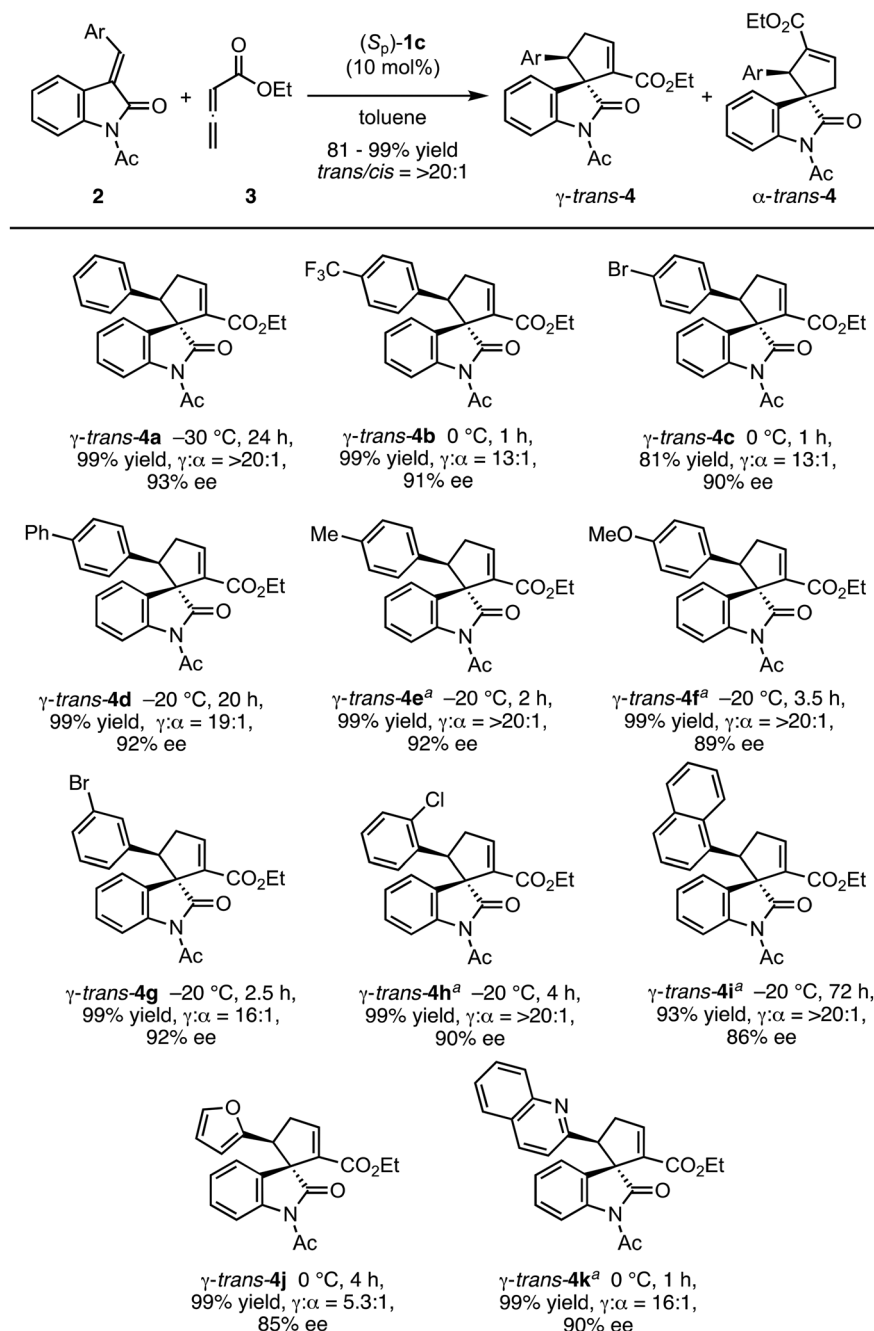
Table 1 Optimization of reaction conditions^a



Entry	Catalyst	Solvent	Time (h)	Yield ^b (%)	γ/α^c	ee of γ^d (%)
1	(S_p)- 1a	CH ₂ Cl ₂	0.5	>99	8.1 : 1	51
2	(S_p)- 1a	THF	3.5	98	16 : 1	32
3	(S_p)- 1a	CPME ^e	1	>99	9 : 1	47
4	(S_p)- 1a	MeCN	20	20 ^f	6.7 : 1	23
5	(S_p)- 1a	CF ₃ C ₆ H ₅	2.5	93	9 : 1	57
6	(S_p)- 1a	Toluene	0.25	>99	10 : 1	64
7	(S_p)- 1b	Toluene	24	66 ^g	12 : 1	8
8	(S_p)- 1c	Toluene	1.5	91	19 : 1	80
9 ^h	(S_p)- 1c	Toluene	2.5	>99	>20 : 1	87
10 ^{i,j}	(S_p)- 1c	Toluene	5.5	>99	>20 : 1	92
11 ^{j,k}	(S_p)- 1c	Toluene	24	99	>20 : 1	93

^a Reaction conditions: 0.05 mmol **2a**, 0.1 mmol **3**, and 5 mol% catalyst (S_p)-**1** in the suggested solvent (0.1 M) at room temperature and for the specified time. ^b Isolated yield of a γ/α mixture. ^c Determined by ¹H NMR of the crude product. ^d Determined by HPLC. ^e CPME = cyclopentyl methyl ether. ^f SM (71%) was recovered. ^g SM (19%) was recovered. ^h Reaction was performed at 0 °C. ⁱ Reaction was performed at –20 °C. ^j Reaction was performed in 0.05 M solution with 10 mol% catalyst. ^k Reaction was performed at –30 °C.





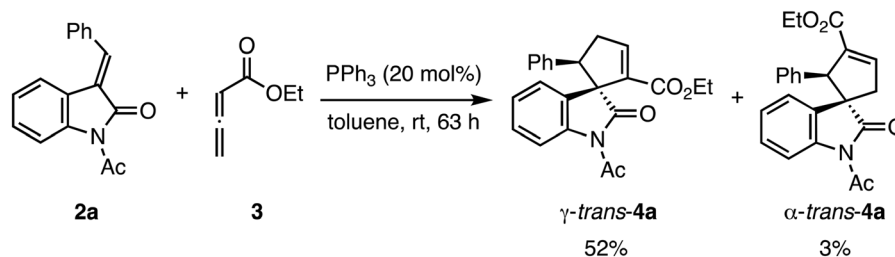
Scheme 2 Substrate scope (benzylideneindolinones). Reaction conditions: 0.05 mmol **2**, 0.1 mmol **3**, and 10 mol% catalyst (S_P) -**1c** in toluene (0.05 M) at the suggested temperature and for the specified time. Yields were of a γ/α mixture after column chromatography. The diastereomer ratio was determined by ^1H NMR of the crude product. Enantiomeric excess was determined by chiral HPLC analysis. ^a Performed at a concentration of 0.03 M.

with literature data.^{11a} We assigned the other products by analogy.

The reactions of various methyleneindolinones **2** bearing carbon substituents other than aryl groups on the methylene carbon ($E/Z > 20/1$) with allenoate **3** and 10 mol% (S_P) -**1c** were examined (Scheme 4). Phenethyl-substituted methyleneindolinone **2l** reacted with **3** at room temperature to produce γ -*trans*-adduct **4l** as a 10:1 mixture of *trans/cis*

diastereomers in 65% yield with 91% ee for the *trans*-isomer. The structure of minor product **4l** was determined to be the γ -*cis*-adduct by ^1H NMR analysis. The corresponding α -isomer was not detected in the crude reaction product. Using (S) -SITCP in the reaction of **2l** gave **4l** in low yield, low regio- and diastereoselectivity, and moderate enantioselectivity under the reported^{11c} conditions (Scheme 5). The effects of the geometry of alkylidene group were investigated using hexyl-substituted





Scheme 3 Preparation of racemic products **4a** for X-ray crystallographic analysis.

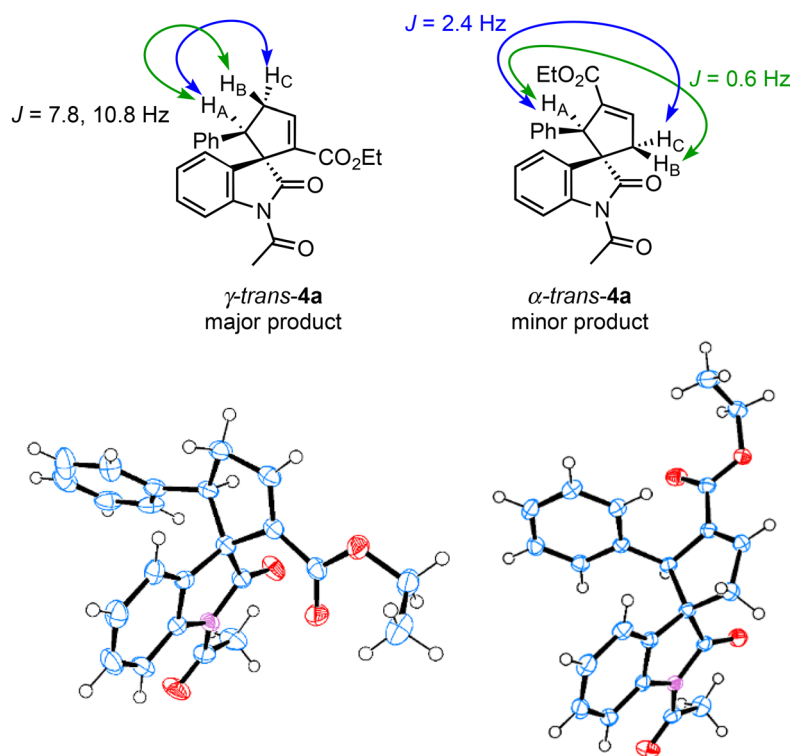


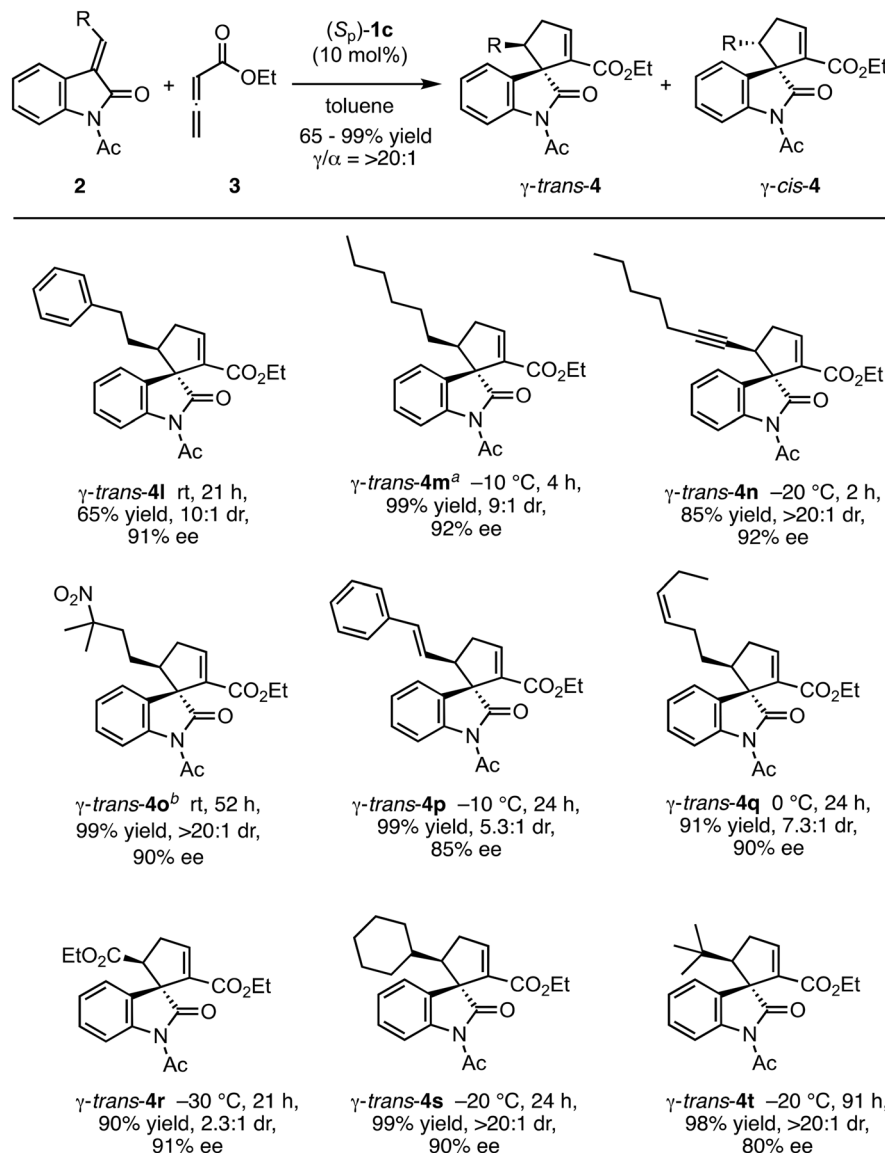
Fig. 4 X-ray crystal structures of γ -trans-4a and α -trans-4a.

substrate **2m** because the *E/Z*-isomers of **2m** were separated easily by column chromatography. Reaction of (*E*)-**2m** with **3** in toluene at -10 °C was complete after 4 h and yielded γ -**4m** quantitatively as a 9:1 mixture of *trans/cis* isomers with 92% ee for the *trans*-isomer (Scheme 4). In contrast, the reaction of (*Z*)-**2m** under the same conditions gave γ -adduct **4m** in only 21% yield, even after 18 h, and starting material **2m** was recovered as an *E/Z* mixture (Scheme 6). Thus, the γ -adduct was obtained as a 4:1 mixture of *trans/cis* isomers and the ee of the major *trans*-isomer was 91%, which was similar to that of the reaction product of (*E*)-**2m**. This result suggested that in the (*S_P*)-**1c**-catalyzed reaction of methyleneindolinones **2** with **3**, the *Z*-isomer of **2** was less reactive than the *E*-isomer, and the *E*-isomer, which was produced by the isomerization of the *Z*-isomer under the conditions,^{11b} mainly reacted with **3** to give γ -*trans*-adduct **4**. In this reaction, alkene, nitro, and ester groups were tolerated (Scheme 4, **4o–4r**). Sterically demanding

cyclohexyl and *tert*-butyl group-substituted substrates **2s** and **2t**, respectively, also exhibited high reactivity for the (3 + 2) annulation reaction to give corresponding γ -*trans*-adducts **4s** and **4t** in excellent yields with high regio- and stereoselectivity.

Scheme 7 shows the five-step catalytic cycle for the (3 + 2) annulation of allenates and electron-deficient alkenes proposed in earlier reports.^{11,6b,23} The catalyst–allenoate complex is first formed by nucleophilic attack of the catalyst phosphorus on the sp-hybridized allenolate carbon (step 1). The cycloaddition proceeds stepwise to afford the ylide intermediate (steps 2 and 3), and the following proton transfer and elimination of the catalyst gives the final product (steps 4 and 5). The 1,4-addition of the γ -carbon of the anionic complex during step 2 gives the γ -adduct and the reaction of the α -anion produces the α -adduct. To establish the origin of the stereoselectivity, the DFT calculations were performed on the reaction pathway of steps 2 and 3 in the reaction of **2a**





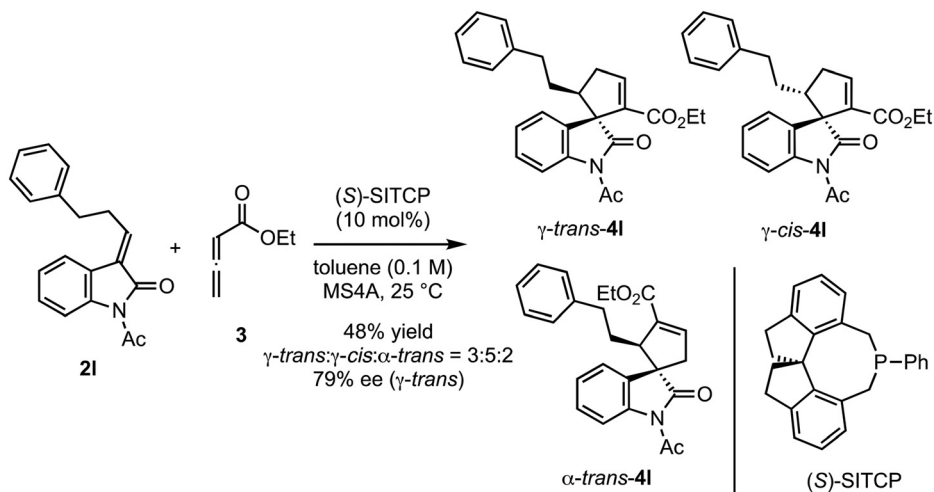
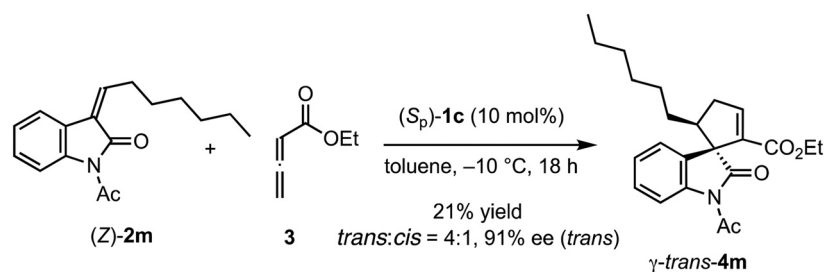
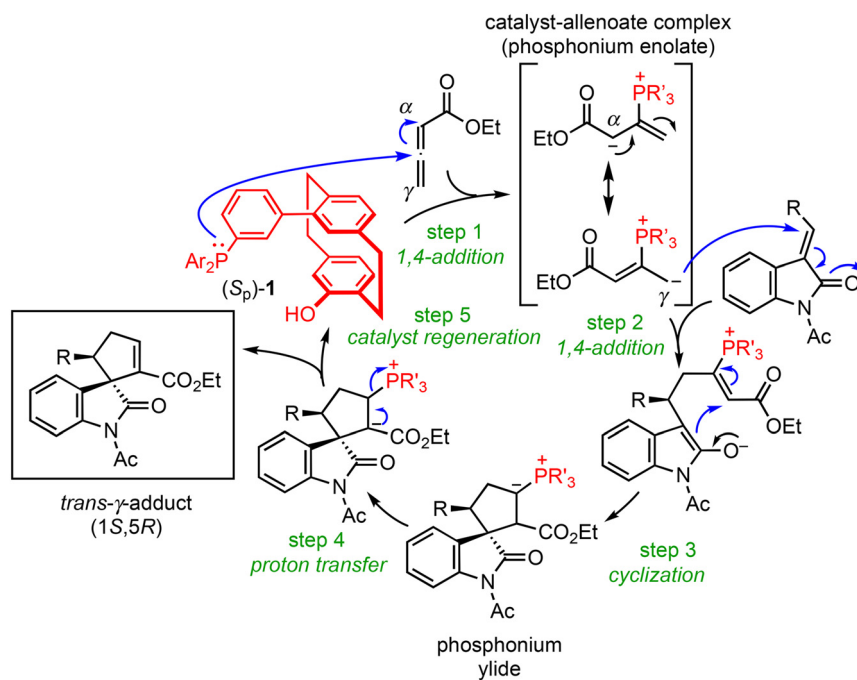
Scheme 4 Substrate scope (alkylideneindolinones). Reaction conditions: 0.05 mmol **2**, 0.1 mmol **3**, and 10 mol% catalyst (S_P) -**1c** in toluene (0.05 M) at the suggested temperature and for the specified time. Yields were of a *trans/cis* mixture after column chromatography. The diastereomer ratio was determined by ^1H NMR of the crude product. Enantiomeric excess was determined by chiral HPLC analysis. ^a Performed at a concentration of 0.03 M. ^b Further catalyst (10 mol%) was added after 24 h.

(Scheme 7, R = Ph)²⁴ because previous studies by other groups showed that the enantiodetermining step was step 2.^{23i,l} Because we had obtained crystals of catalyst **1a** suitable for X-ray diffraction (Fig. 5),²⁵ the X-ray data of **1a** were used as a reference for the initial structure for the catalyst conformation.

The optimized geometries of three assumed reactant complexes, RC-A, RC-B, and RC-C, stabilized by an intramolecular or intermolecular hydrogen bond are presented in Fig. 6a, b, and c, respectively. RC-A and RC-B are reactant complexes on the major enantiomer formation pathway, and RC-C is the reactant complex on the minor enantiomer formation pathway. The catalyst-allenoate complex was arranged on the *re*-face side of **2a** in RC-A and RC-B, and on the *si*-face side of

2a in RC-C, leading to different enantiomer formation. The reaction pathways initiated by RC-A, RC-B, and RC-C were defined as pathways A, B, and C, respectively. The phenolic OH group intramolecularly formed hydrogen bonds with the carbonyl groups of the allenoate moiety (1.751 and 1.760 Å, respectively) in RC-A and RC-C, and intermolecularly formed hydrogen bonds with the carbonyl groups of **2a** (1.749 Å) in RC-B. In these conformations, the phosphonium is near to the carbonyl oxygen of the allenoate moiety (3.038, 2.572, and 2.968 Å in RC-A, RC-B, and RC-C, respectively), allowing the formation of an electrostatic interaction between the two, which helps to stabilize the conformation of the catalyst-allenoate complex.²³ In RC-A, RC-B, and RC-C, the distances



Scheme 5 Reaction of **2l** with **3** in the presence of **(S)-SITCP**.Scheme 6 Reaction of **(Z)-2m** with **3** in the presence of **(S_p)-1c**.Scheme 7 Plausible mechanism for the **(3 + 2)** cyclization.

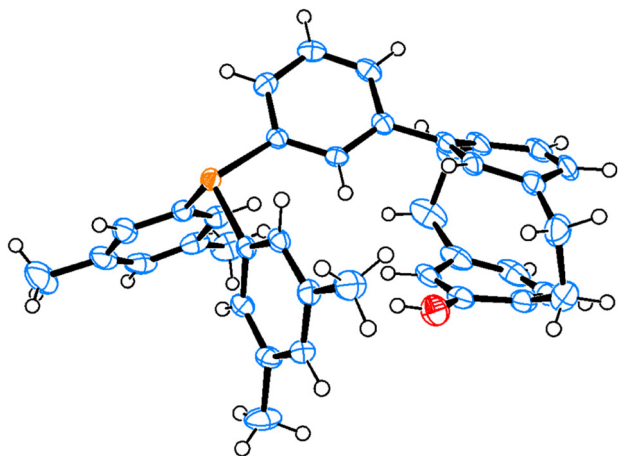


Fig. 5 X-ray crystal structure of **1a**.

between the γ carbon of the allenolate moiety in the catalyst-allenolate complex and the β carbon in **2a** were 3.464, 3.359, and 3.793 Å, respectively. In RC-A, a weak CH \cdots O hydrogen bond was observed between an acidic hydrogen of a xylyl group in the catalyst-allenolate complex and the carbonyl oxygen of **2a** (3.042 Å). In RC-B, the carbonyl oxygen of **2a** formed the CH \cdots O hydrogen bonds with the spacer aryl group CH of the catalyst-allenolate complex in addition to the phenolic OH group. In contrast, the carbonyl oxygen of **2a** did not form hydrogen bonds with the catalyst-allenolate complex in RC-C.

The calculated energy profile is presented in Fig. 7. The energy of RC-B was 6.09 kcal mol $^{-1}$ higher than that of RC-A, and that of RC-C was 3.82 kcal mol $^{-1}$ lower than that of RC-A. The energies of the transition states (TSs) of step 2 (TS1) were higher than those of the TSs of step 3 (TS2) for all pathways. The relative energies of TSs of pathways A-C (TS1-A, TS1-B, and TS1-C) with respect to RC-A were 5.99, 12.9, and 8.68 kcal mol $^{-1}$, respectively.

Optimized geometries of TS1-A, TS1-B, and TS1-C are presented in Fig. 6d, e, and f, respectively. In TS1-A, TS1-B, and TS1-C, the distances between the γ carbon of the allenolate moiety in the catalyst-allenolate complex and the β carbon in **2a** were 2.190, 2.285, and 2.110 Å, respectively. During the formation of TS1-A and TS1-B from RC-A and RC-B, respectively, hydrogen bonds between the catalyst-allenolate complex and **2a** were strengthened and formed. In general, the formation and strengthening of hydrogen bonds stabilizes the TS. In TS1-A, the CH \cdots O hydrogen bond between the xylyl acidic hydrogen of catalyst-allenolate complex and carbonyl oxygen of **2a** was strengthened, and the hydrogen bond distance was shortened to 2.350 Å. Additionally, a weak CH \cdots O hydrogen bond was newly formed between the spacer aryl moiety of the catalyst-allenolate complex and carbonyl group of **2a** (2.770 Å). In TS1-B, the two hydrogen bonds between the phenolic OH group of the catalyst-allenolate complex and the carbonyl group of **2a** and between the spacer aryl moiety and carbonyl group of **2a** were strengthened, with hydrogen bond distances of 1.712 and 2.235 Å, respectively. In contrast, during the for-

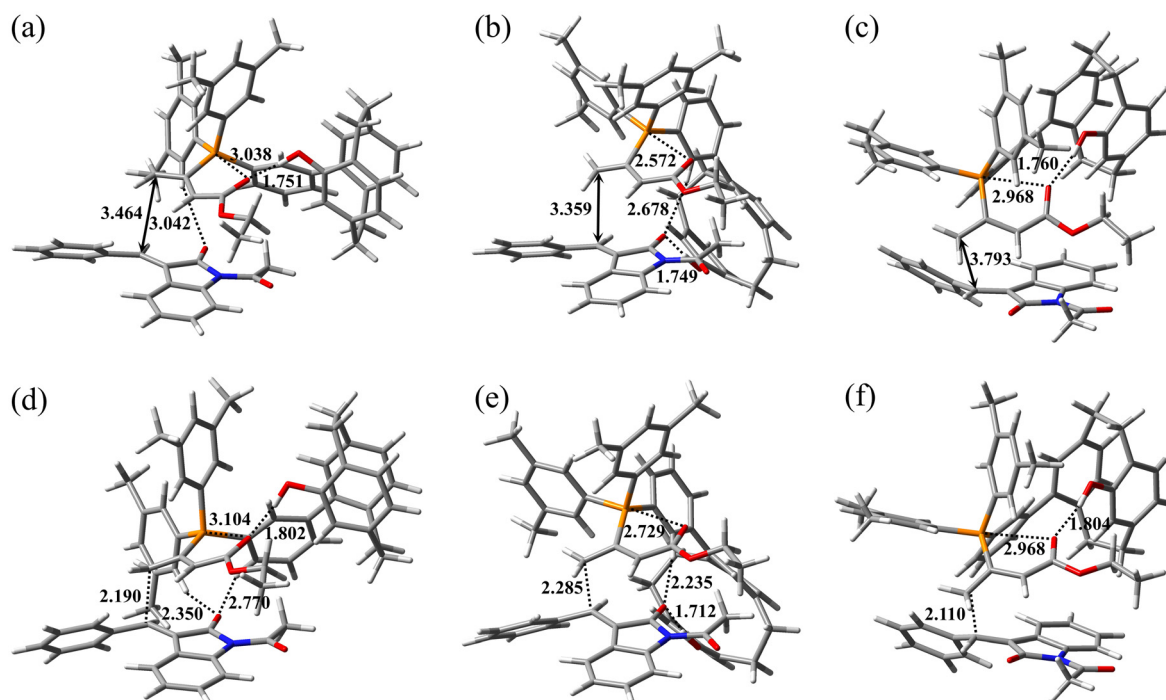


Fig. 6 Optimized geometries of (a) RC-A, (b) RC-B, (c) RC-C, (d) TS1-A, (e) TS1-B, and (f) TS1-C. Selected interatomic distances are shown in angstroms. The carbon, hydrogen, nitrogen, oxygen, and phosphorus atoms are shown in gray, white, blue, red, and orange, respectively. The cartesian coordinates of the atoms in these geometries are provided in separated xyz format file.



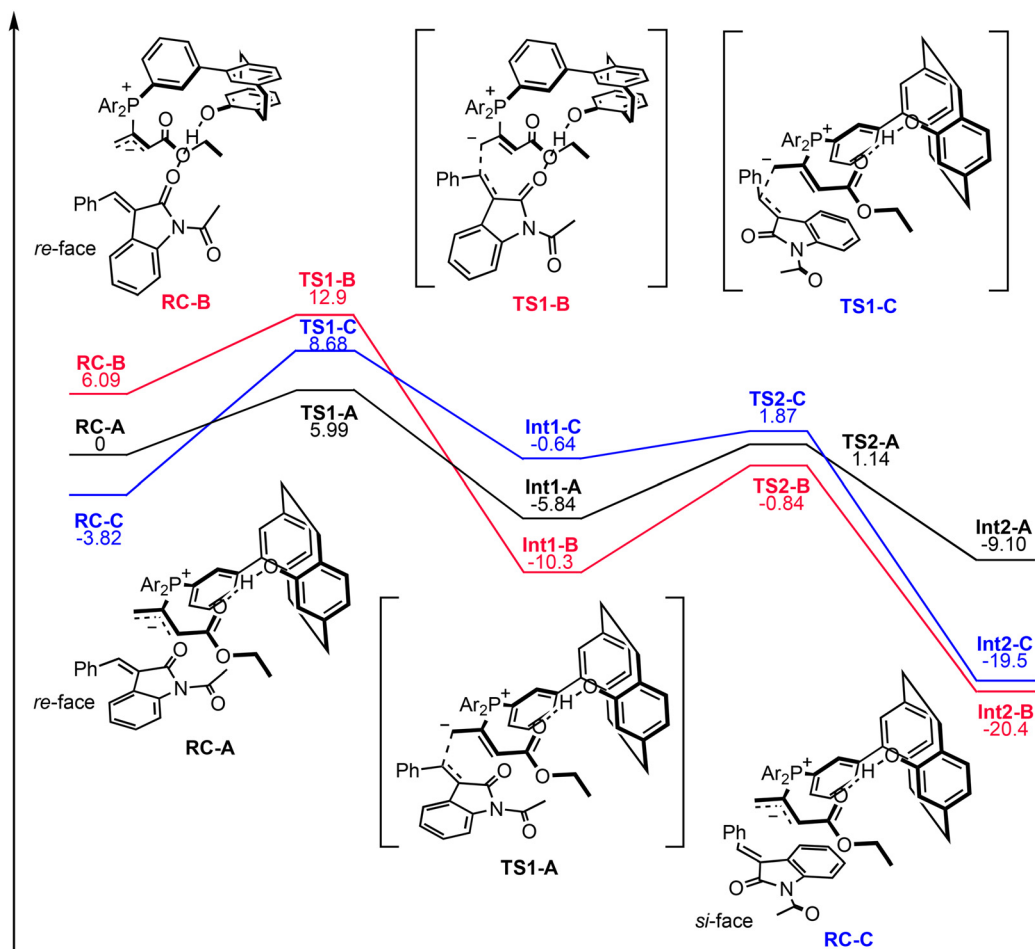


Fig. 7 Calculated energy profiles for pathways A–C. Pathways A, B, and C are shown in black, red, and blue, respectively. Relative energies are shown in kilocalories per mole (M06-2X/6-311+G(d)//B3LYP/6-31G(d)).

mation of TS1-C from RC-C, no new hydrogen-bond formation occurred and the indolinone approached the pCp moiety, suggesting that steric repulsion between the two destabilizes TS1-C.

The energy of TS1-A was substantially lower than that of TS1-C ($2.69 \text{ kcal mol}^{-1}$), which could explain the experimentally observed enantioselectivity (82% ee at 0°C , data not shown). Two strengthened $\text{CH}\cdots\text{O}$ hydrogen bonds were observed between the catalyst–allenoate complex and **2a** in TS1-A; however no strengthened hydrogen bonds were observed in TS1-C. The importance of the strengthened hydrogen bonds between the catalyst–allenoate complex and substrate in controlling the enantioselectivities is noted in previous studies by other groups.^{23i,l} However, the energy of TS1-B was substantially larger than those of TS1-A and TS1-C despite the strengthening of the two hydrogen bonds (one of which was a $\text{CH}\cdots\text{O}$ hydrogen bond). This computational result suggests that the formation of hydrogen bonds between the phenolic OH group and carbonyl group of **2a** did not contribute greatly to the TS stabilization in our reaction system. The catalyst–allenoate complex was paced on the

re-face side of **2a** in TS1-A and TS1-B, and the carbonyl oxygen atom of the *N*-acetyl group in **2a** faces in the opposite direction of the phenolic OH group of catalyst–allenoate complex. Conformational isomers with the carbonyl oxygen atom facing the phenolic OH group are also possible, and the formation of an additional hydrogen bond between the two was expected to contribute to stabilizing the TS. However, contrary to our intention, the energy of this TS was greater than that of TS1-A, and the additional hydrogen-bond formation did not dramatically stabilize the TS. Therefore, the main role of the phenolic OH group was probably to create the proper structure for substrate binding by forming an intramolecular hydrogen bond with the allenoate moiety^{23l} to anchor the pCp in the appropriate position. As shown in Fig. 6, **2a** was placed on the lower side of the catalyst–allenoate complex. The xyl groups of catalyst–allenoate complex were on the upper side, and the steric hindrance of the xyl groups prevented **2a** from being placed on the upper side. That is, the xyl groups could be involved in facilitating proper substrate binding to the catalyst–allenoate complex.



Conclusions

pCp-phosphine-phenol (S_p)-**1c** ($R^1 = H$, $R^2 = t\text{-Bu}$) catalyzed the (3 + 2) annulation of ethyl 2,3-butadienoate with various 3-methyleneindolinones to produce 2,5-disubstituted cyclopentene-fused C3-spirooxindoles in a highly regio-, diastereo-, and enantioselective manner. This catalyst could be applied to the reaction of not only benzylideneoxindoles but also alkylideneoxindoles, the enantioselective reaction of which has not been reported previously. DFT studies suggested that a phenolic OH group on the chiral pCp backbone interacted intramolecularly with the anionic oxygen atom of the phosphonium enolate by hydrogen bonding, creating a reaction space that resulted in high selectivities.

Experimental section

General information

Infrared spectra (IR) were measured in CHCl_3 using a JASCO FT/IR-4100 spectrometer; absorptions are reported in reciprocal centimeters (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance III 600 spectrometer operating at 600 MHz (150 MHz for ^{13}C NMR) at 25 °C with tetramethylsilane ($\delta = 0.0$ ppm) as an internal standard. The data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet), integration, and coupling constant (Hz). ^{31}P NMR spectra were recorded with 85% H_3PO_4 ($\delta = 0.0$ ppm) as an external standard. High-resolution mass spectra were measured with a Thermo Scientific Exactive Plus Orbitrap. Analytical thin-layer chromatography was performed on MERCK silica gel, grade 60 F_{254} . The spots and bands were detected under UV light (254 nm) and/or by staining with 5% phosphomolybdic acid followed by heating. Products were isolated by column chromatography using KANTO Sillica Gel 60 (230–400 mesh). HPLC analyses were performed using JASCO UV-2075 Plus and UV-4075 Intelligent UV/VIS detectors. The chiral columns used included Chiralpak IA-3, IB-3, and IC-3 (Daicel Chemical Industries, Ltd, 0.46 $\Phi \times 25$ cm). Optical rotations were measured on a JASCO P-2200 polarimeter.

Experimental details

General procedure for (3 + 2) annulation (Table 1: entry 11)

The following reaction was carried out under N_2 . Compound **3** (13.4 mg, 13.8 μL , 0.12 mmol) was added to a cooled (-30 °C) stirred solution of **2a** (15.8 mg, 0.0601 mmol) and (S_p)-**1c** (4.3 mg, 6.0×10^{-3} mmol) in toluene (1.2 mL). After stirring at -30 °C for 24 h, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:10) to provide **4a** (22.4 mg, 99%, $\gamma/\alpha = >20:1$) as slightly yellow solid.

Ethyl (1*S*,5*R*)-1'-acetyl-2'-oxo-5-phenylspiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-**4a**)^{11a}

$[\alpha]_{\text{D}}^{25} = -95.6$ ($c = 0.425$ in CHCl_3) (lit.: $[\alpha]_{\text{D}}^{25} = -113$ ($c = 2.0$ in CHCl_3) for (1*S*,5*R*)-**4a**, >99% ee, $\gamma/\alpha = >95:5$). IR 3031, 2940, 1753, 1708, 1635, 1606 cm^{-1} . ^1H NMR (600 MHz, C_6D_6): δ 0.68 (t, 3H, $J = 7.2$ Hz), 2.34 (ddd, 1H, $J = 3.0, 7.8, 18.0$ Hz), 2.67 (s, 3H), 2.69 (ddd, 1H, $J = 1.8, 10.8, 18.0$ Hz), 3.61–3.71 (m, 2H), 4.38 (dd, 1H, $J = 7.8, 10.8$ Hz), 6.66 (dd, 1H, $J = 1.2, 7.8$ Hz), 6.72 (dt, 1H, $J = 1.2, 7.8$ Hz), 6.77 (m, 1H), 6.82–6.87 (m, 5H), 6.97 (t, 1H, $J = 2.4$ Hz), 8.36 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.9, 26.8, 36.4, 56.3, 60.9, 65.2, 116.3, 123.9, 124.5, 127.4, 127.7 (2C), 127.9, 128.2 (2C), 128.7, 136.4, 138.4, 139.6, 146.6, 162.5, 170.8, 180.1. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 376.1543; found, 376.1542. HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 10:90, flow rate = 1.0 mL min^{-1}): $\lambda = 230$ nm, t_{R} (min) = 13.6 (major: γ -*trans*-**4a**), 42.0 (minor: *ent*- γ -*trans*-**4a**). Compound γ -*trans*-**4a** was determined to have 93% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-2'-oxo-5-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-**4b**)^{11a}

Yellowish oil (99%, $\gamma/\alpha = 13:1$): $[\alpha]_{\text{D}}^{25} = -72.9$ ($c = 0.995$ in CHCl_3) (lit.: $[\alpha]_{\text{D}}^{25} = -76$ ($c = 0.9$ in CHCl_3) for (1*S*,5*R*)-**4b**, 99% ee, $\gamma/\alpha = 85:15$). IR 3032, 2991, 1751, 1715, 1647, 1620 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 1.07 (t, 3H, $J = 7.0$ Hz), 2.72 (s, 3H), 3.08 (ddd, 1H, $J = 3.0, 7.8, 18.0$ Hz), 3.26 (ddd, 1H, $J = 1.8, 10.8, 18.0$ Hz), 4.00 (q, 2H, $J = 7.2$ Hz), 4.36 (dd, 1H, $J = 7.8, 10.8$ Hz), 6.95 (dd, 1H, $J = 1.2, 7.8$ Hz), 7.01 (t, 1H, $J = 7.2$ Hz), 7.08 (d, 2H, $J = 7.8$ Hz), 7.16 (dt, 1H, $J = 1.8, 7.2$ Hz), 7.31–7.33 (m, 3H), 8.01 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 26.7, 36.4, 55.5, 60.9, 64.9, 116.5, 123.6, 123.8 ($J = 271$ Hz), 124.6, 125.1 (2C, $J = 4$ Hz), 127.3, 128.1 (2C), 129.1, 129.6 ($J = 32$ Hz), 138.5, 139.5, 140.6, 145.9, 162.2, 170.6, 179.7. HRMS (DART) calcd for $\text{C}_{24}\text{H}_{21}\text{F}_3\text{NO}_4$ $[\text{M} + \text{H}]^+$, 444.1417; found, 444.1418; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 5:95, flow rate = 0.5 mL min^{-1}): $\lambda = 220$ nm, t_{R} (min) = 17.9 (major), 22.9 (minor). Compound γ -*trans*-**4b** was determined to have 91% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(4-bromophenyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-**4c**)^{11a}

Yellowish oil (81%, $\gamma/\alpha = 13:1$): $[\alpha]_{\text{D}}^{25} = -67.4$ ($c = 0.93$ in CHCl_3) (lit.: $[\alpha]_{\text{D}}^{25} = -60$ ($c = 1.1$ in CHCl_3) for (1*S*,5*R*)-**4c**, >99% ee, $\gamma/\alpha = 90:10$). IR 3033, 2992, 1750, 1715, 1635 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 1.06 (t, 3H, $J = 7.2$ Hz), 2.71 (s, 3H), 3.03 (ddd, 1H, $J = 3.0, 7.8, 18.0$ Hz), 3.19 (ddd, 1H, $J = 2.4, 10.8, 18.0$ Hz), 4.00 (q, 2H, $J = 7.2$ Hz), 4.26 (dd, 1H, $J = 7.8, 10.8$ Hz), 6.83 (d, 2H, $J = 8.4$ Hz), 6.94 (dd, 1H, $J = 1.2, 7.8$ Hz), 7.03 (dt, 1H, $J = 1.2, 7.8$ Hz), 7.14–7.18 (m, 3H), 7.31 (dd, 1H, $J = 1.8, 3.0$ Hz), 8.01 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 26.7, 36.5, 55.5, 60.9, 64.9, 116.5, 121.3, 123.7, 124.6, 127.5, 129.0, 129.4 (2C), 131.3 (2C), 135.5, 138.5, 139.5, 146.1, 162.3, 170.6, 179.8. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{21}\text{BrNO}_4$ $[\text{M} + \text{H}]^+$, 454.0648; found, 454.0649; HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 2:98, flow rate = 1.0 mL min^{-1}): $\lambda = 220$ nm, t_{R} (min) = 17.9 (major), 22.9 (minor).



min⁻¹): λ = 230 nm, t_R (min) = 28.5 (major), 80.6 (minor). Compound γ -*trans*-4c was determined to have 90% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(biphenyl-4-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4d)^{11a}

Yellow solid (99%, γ/α = 19:1): $[\alpha]_D^{25}$ = -50.4 (c = 0.128 in CHCl₃) (lit.: $[\alpha]_D^{22}$ = -159 (c = 0.5 in CHCl₃) for (1*S*,5*R*)-4d, 99% ee, γ/α = 90:10). IR 3028, 2995, 2948, 1750, 1715, 1603 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.08 (t, 3H, J = 7.2 Hz), 2.75 (s, 3H), 3.07 (ddd, 1H, J = 3.0, 7.8, 18.0 Hz), 3.29 (ddd, 1H, J = 1.8, 10.2, 18.0 Hz), 4.01 (q, 2H, J = 7.2 Hz), 4.37 (dd, 1H, J = 7.8, 10.2 Hz), 6.98–7.02 (m, 2H), 7.03 (d, 2H, J = 8.4 Hz), 7.12 (dt, 1H, J = 1.8, 8.4 Hz), 7.27–7.37 (m, 6H), 7.45 (d, 2H, J = 8.4 Hz), 8.01 (d, 1H, J = 7.8 Hz). ¹³C NMR (150 MHz, CDCl₃): δ 13.8, 26.7, 36.6, 55.9, 60.8, 65.0, 116.3, 123.8, 124.4, 126.7, 126.8, 127.3, 127.8, 128.1, 128.6, 128.7, 135.4, 138.4, 139.6, 140.0, 140.3, 146.4, 162.3, 170.7, 180.0. HRMS (DART) calcd for C₂₉H₂₆NO₄ [M + H]⁺, 452.1856; found, 452.1859; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 5:95, flow rate = 1.0 mL min⁻¹): λ = 230 nm, t_R (min) = 16.9 (minor), 18.0 (major). Compound γ -*trans*-4d was determined to have 92% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-2'-oxo-5-(*p*-tolyl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4e)^{11a}

Yellowish oil (99%, γ/α = >20:1): $[\alpha]_D^{25}$ = -144 (c = 0.152 in CHCl₃) (lit.: $[\alpha]_D^{22}$ = -102 (c = 2.0 in CHCl₃) for (1*S*,5*R*)-4e, 97% ee, γ/α = 90:10). IR 3030, 2946, 1750, 1707, 1603 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.06 (t, 3H, J = 7.2 Hz), 2.15 (s, 3H), 2.71 (s, 3H), 3.00 (ddd, 1H, J = 3.0, 7.8, 18.0 Hz), 3.22 (ddd, 1H, J = 2.4, 10.2, 18.0 Hz), 3.99 (q, 2H, J = 7.2 Hz), 4.29 (dd, 1H, J = 7.8, 10.2 Hz), 6.82–6.85 (m, 4H), 6.96 (dd, 1H, J = 1.2, 7.8 Hz), 7.00 (dt, 1H, J = 1.2, 7.8 Hz), 7.12 (dt, 1H, J = 1.2, 7.8 Hz), 7.32 (dd, 1H, J = 2.4, 3.0 Hz), 7.99 (d, 1H, J = 8.4 Hz). ¹³C NMR (150 MHz, CDCl₃): δ 13.8, 20.9, 26.7, 36.6, 56.0, 60.7, 65.0, 116.2, 123.8, 124.3, 127.6 (2C), 127.9, 128.6, 128.8 (2C), 133.2, 136.9, 138.4, 139.5, 146.5, 162.4, 170.7, 180.1. HRMS (DART) calcd for C₂₄H₂₄NO₄ [M + H]⁺, 390.1700; found, 390.1698; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 2:98, flow rate = 1.0 mL min⁻¹): λ = 230 nm, t_R (min) = 9.6 (major), 11.9 (minor). Compound γ -*trans*-4e was determined to have 92% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-2'-oxo-5-(*p*-anisyl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4f)

Yellowish oil (99%, γ/α = >20:1): $[\alpha]_D^{25}$ = -87.8 (c = 0.934 in CHCl₃). IR 3033, 2939, 1750, 1706, 1653, 1635 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.06 (t, 3H, J = 7.2 Hz), 2.71 (s, 3H), 3.00 (ddd, 1H, J = 3.0, 8.4, 18.6 Hz), 3.18 (ddd, 1H, J = 2.4, 10.8, 18.6 Hz), 3.65 (s, 3H), 3.99 (q, 2H, J = 7.2 Hz), 4.26 (dd, 1H, J = 8.4, 10.8 Hz), 6.57 (d, 2H, J = 8.4 Hz), 6.87 (d, 1H, J = 8.4 Hz), 6.95 (dd, 2H, J = 1.2, 7.8 Hz), 7.01 (dt, 1H, J = 0.6, 7.8 Hz), 7.14 (dt, 1H, J = 1.2, 8.4 Hz), 7.32 (dd, 1H, J = 2.4, 3.0 Hz), 7.99 (d, 1H, J = 7.8 Hz). ¹³C NMR (150 MHz, CDCl₃): δ 13.8, 26.7, 36.7, 55.0, 55.7, 60.7, 65.0, 113.4 (2C), 116.2, 123.7, 124.4, 127.9, 128.3, 128.6, 128.7 (2C), 138.3, 139.5, 146.5, 158.6, 162.4, 170.7,

180.1. HRMS (DART) calcd for C₂₄H₂₄NO₅ [M + H]⁺, 406.1649; found, 406.1649; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 2:98, flow rate = 1.0 mL min⁻¹): λ = 230 nm, t_R (min) = 15.5 (major), 18.2 (minor). Compound γ -*trans*-4f was determined to have 89% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(3-bromophenyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4g)^{11a}

Yellowish oil (99%, γ/α = 16:1): $[\alpha]_D^{25}$ = -62.6 (c = 1.20 in CHCl₃) (lit.: $[\alpha]_D^{25}$ = -56 (c = 1.2 in CHCl₃) for (1*S*,5*R*)-4g, >99% ee, γ/α = 85:15). IR 3034, 2941, 1750, 1715, 1653, 1635 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.07 (t, 3H, J = 7.2 Hz), 2.72 (s, 3H), 3.03 (ddd, 1H, J = 3.0, 7.8, 18.0 Hz), 3.20 (ddd, 1H, J = 2.4, 10.2, 18.0 Hz), 4.00 (q, 2H, J = 7.2 Hz), 4.26 (dd, 1H, J = 7.8, 10.2 Hz), 6.84 (d, 1H, J = 7.8 Hz), 6.91 (t, 1H, J = 7.8 Hz), 6.94 (dd, 1H, J = 1.2, 7.8 Hz), 7.05 (dt, 1H, J = 1.0, 7.5 Hz), 7.12–7.14 (m, 1H), 7.16 (dt, 2H, J = 1.0, 7.8 Hz), 7.31 (t, 1H, J = 2.4 Hz), 8.01 (d, 1H, J = 7.8 Hz). ¹³C NMR (150 MHz, CDCl₃): δ 13.8, 26.7, 36.3, 55.6, 60.9, 65.0, 116.4, 122.2, 123.7, 124.6, 126.4, 127.3, 129.0, 129.7, 130.5, 130.9, 138.3, 138.8, 139.5, 146.1, 162.2, 170.6, 179.7. HRMS (DART) calcd for C₂₃H₂₁BrNO₄ [M + H]⁺, 454.0648; found, 454.0645; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 5:95, flow rate = 1.0 mL min⁻¹): λ = 230 nm, t_R (min) = 12.4 (major), 16.6 (minor). Compound γ -*trans*-4g was determined to have 92% ee.

Ethyl (1*S*,5*S*)-1'-acetyl-5-(2-chlorophenyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4h)

Yellowish oil (99%, γ/α = >20:1): $[\alpha]_D^{25}$ = -60.8 (c = 0.178 in CHCl₃). IR 3025, 2948, 1760, 1714, 1603 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.00 (t, 3H, J = 7.2 Hz), 2.70 (s, 3H), 3.17 (ddd, 1H, J = 2.4, 10.2, 19.2 Hz), 3.22 (ddd, 1H, J = 3.0, 9.0, 19.2 Hz), 3.94–3.99 (m, 2H), 4.81 (t, 1H, J = 8.4 Hz), 6.68 (dd, 1H, J = 1.2, 7.8 Hz), 6.88 (dt, 1H, J = 1.2, 7.8 Hz), 6.99 (dt, 1H, J = 1.8, 7.8 Hz), 7.02 (dt, 1H, J = 1.8, 7.8 Hz), 7.10–7.13 (m, 2H), 7.19 (dd, 1H, J = 1.2, 7.8 Hz), 7.36 (dd, 1H, J = 2.4, 3.0 Hz), 8.03 (d, 1H, J = 8.4 Hz). ¹³C NMR (150 MHz, CDCl₃): δ 12.7, 25.6, 37.0, 49.4, 59.7, 63.7, 115.2, 122.9, 123.2, 125.1, 126.7, 127.4, 127.6, 128.5 (2C), 133.7, 134.3, 136.0, 139.2, 145.9, 161.4, 169.8, 178.6. HRMS (DART) calcd for C₂₃H₂₁ClNO₄ [M + H]⁺, 410.1154; found, 410.1153; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 2:98, flow rate = 1.0 mL min⁻¹): λ = 230 nm, t_R (min) = 13.4 (major), 15.8 (minor). Compound γ -*trans*-4h was determined to have 90% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(naphthalene-1-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4i)^{11a,c}

White solid (93%, γ/α = >20:1): $[\alpha]_D^{25}$ = -373 (c = 0.215 in CHCl₃) (lit.: ref. 11a, $[\alpha]_D^{25}$ = -445 (c = 1.3 in CHCl₃) for (1*S*,5*R*)-4i, >99% ee, γ/α = >95:5; ref. 11c, $[\alpha]_D^{25}$ = +211.9 (c = 0.5 in CHCl₃) for 98% ee with use of (*R*)-SITCP). IR 3055, 2941, 1749, 1715, 1653, 1636 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 1.04 (t, 3H, J = 7.2 Hz), 2.58 (s, 3H), 3.19 (ddd, 1H, J = 3.0, 8.4, 18.6 Hz), 3.43 (ddd, 1H, J = 1.8, 9.6, 18.6 Hz), 4.00 (q, 2H, J = 7.2 Hz), 5.22 (dd, 1H, J = 8.4, 9.0 Hz), 6.94 (d, 2H, J = 4.2 Hz), 6.98–7.01



(m, 1H), 7.17 (t, 1H, $J = 7.8$ Hz), 7.31 (d, 1H, $J = 7.2$ Hz), 7.37 (t, 1H, $J = 7.2$ Hz), 7.41–7.45 (m, 2H), 7.54 (d, 1H, $J = 7.8$ Hz), 7.69 (dd, 1H, $J = 1.2, 8.4$ Hz), 7.76 (d, 1H, $J = 8.4$ Hz), 8.03 (d, 1H, $J = 9.0$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 12.7, 25.5, 37.2, 49.0, 59.7, 64.2, 115.1, 121.6, 123.09, 123.13, 123.3, 124.5, 125.06, 125.08, 126.9, 127.1, 127.4, 127.9, 130.9, 131.4, 132.5, 136.5, 138.4, 146.0, 161.5, 169.3, 179.4. HRMS (DART) calcd for $\text{C}_{27}\text{H}_{24}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 426.1700; found, 426.1702; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 2:98, flow rate = 1.0 mL min $^{-1}$): λ = 230 nm, t_{R} (min) = 18.3 (major), 23.9 (minor). Compound γ -trans-4i was determined to have 86% ee.

Ethyl (1S,5S)-1'-acetyl-5-(furan-2-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -trans-4j) 11a

Yellow oil (99%, $\gamma/\alpha = 5.3:1$): $[\alpha]_{\text{D}}^{25} = -67.2$ ($c = 1.12$ in CHCl_3). IR 3032, 2987, 1751, 1708, 1635 cm $^{-1}$. ^1H NMR (CDCl_3 , 600 MHz): δ 1.06 (t, 3H, $J = 7.2$ Hz), 2.75 (s, 3H), 3.10 (ddd, 1H, $J = 3.0, 9.0, 18.0$ Hz), 3.16 (ddd, 1H, $J = 2.4, 10.2, 18.0$ Hz), 3.98 (q, 2H, $J = 7.2$ Hz), 4.32 (dd, 1H, $J = 9.0, 9.6$ Hz), 5.90 (dd, 1H, $J = 1.2, 2.4$ Hz), 6.01 (dd, 1H, $J = 2.4, 3.0$ Hz), 6.88 (dd, 1H, $J = 1.2, 7.2$ Hz), 6.95–6.98 (m, 2H), 7.18 (dt, 1H, $J = 1.2, 7.8$ Hz), 7.24 (t, 1H, $J = 2.4$ Hz), 8.11 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 26.7, 35.6, 49.0, 60.8, 63.8, 106.9, 109.8, 116.1, 123.6, 124.4, 127.6, 128.7, 138.3, 139.9, 142.0, 145.8, 151.7, 162.2, 170.9, 179.7. HRMS (DART) calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_5$ $[\text{M} + \text{H}]^+$, 366.1336; found, 366.1338; HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 10:90, flow rate = 1.0 mL min $^{-1}$): λ = 230 nm, t_{R} (min) = 11.9 (major), 25.8 (minor). Compound γ -trans-4j was determined to have 85% ee.

Ethyl (1S,5S)-1'-acetyl-2'-oxo-5-(quinolin-2-yl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -trans-4k) 11a

Yellowish oil (99%, $\gamma/\alpha = 16:1$): $[\alpha]_{\text{D}}^{25} = -37.0$ ($c = 1.27$ in CHCl_3) (lit.: $[\alpha]_{\text{D}}^{25} = -15$ ($c = 0.6$ in CHCl_3) for (1S,5S)-4k, 97% ee, $\gamma/\alpha = 90:10$). IR 3020, 2989, 1750, 1705, 1635, 1600 cm $^{-1}$. ^1H NMR (600 MHz, CDCl_3): δ 1.09 (t, 3H, $J = 7.0$ Hz), 2.85 (s, 3H), 3.21 (ddd, 1H, $J = 3.6, 8.4, 18.6$ Hz), 3.81 (ddd, 1H, $J = 1.8, 10.2, 18.6$ Hz), 4.02 (q, 2H, $J = 7.2$ Hz), 4.70 (dd, 1H, $J = 8.4, 10.2$ Hz), 6.74 (dt, 1H, $J = 1.2, 7.8$ Hz), 6.81 (dd, 1H, $J = 1.2, 7.2$ Hz), 6.95–6.98 (m, 2H), 7.37–7.41 (m, 2H), 7.58 (dt, 1H, $J = 1.2, 8.4$ Hz), 7.61 (d, 1H, $J = 8.4$ Hz), 7.74 (d, 1H, $J = 8.4$ Hz), 7.85 (d, 1H, $J = 8.4$ Hz), 8.02 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 26.8, 34.8, 57.3, 60.8, 64.1, 115.9, 119.3, 123.6, 124.2, 126.1, 126.5, 127.3, 128.2, 128.3, 129.0, 129.5, 136.2, 138.4, 140.1, 146.5, 147.3, 157.1, 162.4, 171.1, 180.5. HRMS (DART) calcd for $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$, 427.1652; found, 427.1650; HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 10:90, flow rate = 1.0 mL min $^{-1}$): λ = 230 nm, t_{R} (min) = 17.0 (major), 41.5 (minor). Compound γ -trans-4k was determined to have 90% ee.

Ethyl (1S,5S)-1'-acetyl-2'-oxo-5-(3-phenylpropyl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -trans-4l)

Yellow oil: $[\alpha]_{\text{D}}^{24} = -48.2$ ($c = 0.106$ in CHCl_3). IR 3030, 2938, 1755, 1707, 1604 cm $^{-1}$. ^1H NMR (600 MHz, CDCl_3): δ 1.06 (t,

3H, $J = 7.2$ Hz), 1.40 (m, 1H), 1.55 (m, 1H), 2.25 (ddd, 1H, $J = 5.4, 10.8, 13.8$ Hz), 2.43 (ddd, 1H, $J = 5.4, 10.8, 13.2$ Hz), 2.51 (ddd, 1H, $J = 1.8, 9.6, 18.0$ Hz), 2.71 (s, 3H), 2.93 (ddd, 1H, $J = 3.0, 8.4, 18.0$ Hz), 3.06 (m, 1H), 3.98 (q, 2H, $J = 7.2$ Hz), 6.88 (d, 2H, $J = 7.2$ Hz), 7.01 (dd, 1H, $J = 0.6, 7.2$ Hz), 7.12 (t, 1H, $J = 7.8$ Hz), 7.15–7.19 (m, 4H), 7.34 (dt, 1H, $J = 1.2, 7.8$ Hz), 8.28 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 14.2, 26.9, 31.2, 34.6, 44.8, 55.8, 56.9, 60.6, 116.4, 121.4, 125.89, 125.92, 128.29 (2C), 128.31, 128.5, 135.5, 138.1, 138.2, 140.4 (2C), 141.3, 163.9, 170.8, 179.3. HRMS (DART) calcd for $\text{C}_{25}\text{H}_{26}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 404.1856; found, 404.1855; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 1.5:98.5, flow rate = 1.0 mL min $^{-1}$): λ = 230 nm, t_{R} (min) = 12.4 (major), 17.9 (minor). Compound γ -trans-4l was determined to have 91% ee.

γ -cis-4l. Yellow oil: IR 3030, 2938, 1753, 1711, 1634, 1605 cm $^{-1}$. ^1H NMR (600 MHz, CDCl_3): δ 1.32 (t, 3H, $J = 7.2$ Hz), 1.52–1.59 (m, 1H), 1.86 (ddd, 1H, $J = 4.8, 12.0, 13.2$ Hz), 2.15 (ddd, 1H, $J = 6.6, 7.2, 13.2$ Hz), 2.35 (m, 1H), 2.68 (s, 3H), 2.77 (td, 1H, $J = 2.4, 18.6$ Hz), 3.12 (td, 1H, $J = 2.4, 18.6$ Hz), 3.59 (m, 1H), 4.18–4.27 (m, 2H), 6.72 (d, 2H, $J = 7.8$ Hz), 6.82 (q, 1H, $J = 2.4$ Hz), 7.08 (t, 1H, $J = 7.8$ Hz), 7.13 (t, 2H, $J = 7.8$ Hz), 7.23 (dt, 1H, $J = 0.6, 7.2$ Hz), 7.32 (dd, 1H, $J = 0.6, 7.2$ Hz), 7.41 (dt, 1H, $J = 1.2, 7.8$ Hz), 8.31 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 14.3, 26.7, 31.1, 33.8, 45.4, 53.9, 57.0, 60.6, 116.7, 123.8, 125.2, 125.9, 128.16 (2C), 128.24 (2C), 128.8, 130.8, 138.1, 139.5, 140.0, 141.1, 164.2, 170.9, 181.7. HRMS (DART) calcd for $\text{C}_{25}\text{H}_{26}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 404.1856; found, 404.1855.

α -trans-4l. Yellow oil: IR 3026, 2928, 1753, 1710, 1639, 1604 cm $^{-1}$. ^1H NMR (600 MHz, CDCl_3): δ 1.30 (t, 3H, $J = 7.2$ Hz), 2.12–2.19 (m, 2H), 2.36–2.41 (m, 2H), 2.72 (s, 3H), 2.76 (dd, 1H, $J = 3.0, 18.0$ Hz), 3.25 (td, 1H, $J = 3.0, 18.0$ Hz), 3.27–3.29 (m, 1H), 4.19–4.26 (m, 2H), 6.90 (m, 1H), 7.00 (d, 2H, $J = 7.8$ Hz), 7.12 (t, 1H, $J = 7.8$ Hz), 7.16–7.23 (m, 4H), 7.33 (dt, 1H, $J = 1.8, 7.8$ Hz), 8.24 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 14.2, 26.9, 31.2, 34.6, 44.8, 55.8, 56.9, 60.6, 116.4, 121.4, 125.89, 125.93, 128.29 (2C), 128.32 (2C), 128.5, 135.5, 138.1, 138.2, 140.4, 141.3, 163.9, 170.8, 179.3. HRMS (DART) calcd for $\text{C}_{25}\text{H}_{26}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 404.1856; found, 404.1857.

Ethyl (1S,5S)-1'-acetyl-5-hexyl-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -trans-4m)

Yellow oil: $[\alpha]_{\text{D}}^{24} = -72.1$ ($c = 0.876$ in CHCl_3). IR 3032, 2930, 1755, 1707 cm $^{-1}$. ^1H NMR (600 MHz, CDCl_3): δ 0.79 (t, 3H, $J = 7.2$ Hz), 0.95–1.17 (m, 13H), 2.47 (ddd, 1H, $J = 2.4, 10.2, 18.6$ Hz), 2.71 (s, 3H), 2.89 (ddd, 1H, $J = 3.0, 7.8, 18.6$ Hz), 2.99 (quint, 1H, $J = 7.8$ Hz), 3.97 (q, 2H, $J = 7.2$ Hz), 6.98 (dd, 1H, $J = 1.2, 7.8$ Hz), 7.14 (dt, 1H, $J = 1.2, 7.8$ Hz), 7.18 (t, 1H, $J = 2.4$ Hz), 7.32 (dt, 1H, $J = 1.2, 7.8$ Hz), 8.26 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.7, 13.9, 22.3, 26.6, 27.6, 29.0, 30.6, 31.4, 38.6, 50.4, 60.6, 63.0, 116.6, 123.7, 124.6, 128.3, 128.7, 139.0, 139.9, 146.7, 162.5, 171.0, 180.5. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{30}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 384.2169; found, 384.2169; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 1:99, flow rate = 1.0 mL min $^{-1}$): λ = 220 nm, t_{R} (min)



= 11.3 (major), 19.1 (minor). Compound γ -*trans*-**4m** was determined to have 92% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(hept-1-yn-1-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4n**)^{11a}**

Yellow oil: $[\alpha]_{\text{D}}^{24} = -23.1$ ($c = 0.609$ in CHCl_3) (lit.: $[\alpha]_{\text{D}}^{25} = -19$ ($c = 1.7$ in CHCl_3) for (1*S*,5*R*)-**4n**, 86% ee, $\gamma/\alpha = 80:20$). IR 2934, 1756, 1708, 1635 cm^{-1} . ^1H NMR (CDCl_3 , 600 MHz): δ 0.80 (t, 3H, $J = 7.2$ Hz), 0.95–0.99 (m, 2H), 1.02–1.08 (m, 5H), 1.11–1.15 (m, 2H), 1.82–1.84 (m, 2H), 2.71 (s, 3H), 2.86 (ddd, 1H, $J = 1.8$, 10.2, 18.0 Hz), 3.07 (ddd, 1H, $J = 3.0$, 8.4, 18.0 Hz), 3.77 (m, 1H), 3.95–4.10 (m, 2H), 7.06 (dd, 1H, $J = 1.2$, 7.8 Hz), 7.12–7.18 (m, 2H), 7.31 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.26 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 13.9, 18.3, 22.1, 26.7, 28.0, 30.5, 39.6, 41.7, 60.8, 64.0, 76.4, 86.2, 116.4, 123.7, 124.6, 128.5, 128.8, 138.1, 140.0, 145.7, 162.2, 170.9, 179.4. HRMS (DART) calcd for $\text{C}_{24}\text{H}_{28}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 394.2013; found, 394.2013; HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 1:99, flow rate = 1.0 mL min^{-1}): $\lambda = 205$ nm, t_{R} (min) = 16.4 (major), 39.8 (minor). Compound γ -*trans*-**4n** was determined to have 92% ee.

Ethyl (1*S*,5*S*)-1'-acetyl-5-(3-methyl-3-nitrobutyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4o**)**

Yellow oil: $[\alpha]_{\text{D}}^{24} = -89.5$ ($c = 0.74$ in CHCl_3). IR 3031, 2934, 1756, 1706, 1635, 1541 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 1.07 (t, 3H, $J = 7.2$ Hz), 1.09–1.36 (m, 9H), 1.85 (dt, 1H, $J = 4.2$, 13.2 Hz), 2.49 (m, 1H), 2.72 (s, 3H), 2.90–2.98 (m, 2H), 3.98 (q, 2H, $J = 7.2$ Hz), 6.97 (d, 1H, $J = 7.2$ Hz), 7.15–7.18 (m, 2H), 7.35 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.27 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 24.4, 25.3, 26.6, 31.3, 38.6, 38.7, 49.4, 60.8, 62.8, 87.4, 116.7, 123.8, 124.9, 127.6, 129.1, 139.0, 139.9, 146.1, 162.3, 170.9, 180.2. HRMS (DART) calcd for $\text{C}_{22}\text{H}_{27}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$, 415.1864; found, 415.1865; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 1.5:98.5, flow rate = 1.0 mL min^{-1}): $\lambda = 230$ nm, t_{R} (min) = 15.2 (major), 23.9 (minor). Compound γ -*trans*-**4o** was determined to have 90% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-2'-oxo-5-((*E*)-styryl)spiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4p**)**

Yellow oil (99%, *trans/cis* = 5:1): $[\alpha]_{\text{D}}^{24} = 22.5$ ($c = 0.584$ in CHCl_3). IR 3032, 2986, 1750, 1708, 1635 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 1.08 (t, 3H, $J = 7.2$ Hz), 2.70 (s, 3H), 2.86 (ddd, 1H, $J = 1.8$, 9.6, 18.6 Hz), 2.97 (ddd, 1H, $J = 2.4$, 7.8, 18.0 Hz), 3.79 (q, 1H, $J = 9.0$ Hz), 4.00 (m, 2H), 5.71 (dd, 1H, $J = 9.0$, 15.6 Hz), 6.38 (d, 1H, $J = 15.6$ Hz), 7.02 (d, 2H, $J = 6.6$ Hz), 7.08 (dd, 1H, $J = 1.2$, 7.8 Hz), 7.15–7.20 (m, 4H), 7.24 (t, 1H, $J = 2.4$ Hz), 7.31 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.22 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 26.7, 38.5, 53.9, 60.8, 64.2, 116.8, 123.3, 124.8, 126.27, 126.34, 126.4, 127.7, 128.5, 129.0, 132.7, 136.4, 138.8, 139.8, 146.4, 162.3, 170.8, 179.7. HRMS (DART) calcd for $\text{C}_{25}\text{H}_{24}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 402.1700; found, 402.1699; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 1.5:98.5, flow rate = 1.0 mL min^{-1}): $\lambda =$

230 nm, t_{R} (min) = 15.2 (major), 22.7 (minor). Compound γ -*trans*-**4p** was determined to have 85% ee.

Ethyl (1*S*,5*S*)-1'-acetyl-5-((*Z*)-hex-3-en-1-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4q**)**

Yellow oil: $[\alpha]_{\text{D}}^{24} = -89.8$ ($c = 0.299$ in CHCl_3). IR 3019, 1749, 1706, 1653, 1636 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 0.84 (t, 3H, $J = 7.2$ Hz), 1.06 (t, 3H, $J = 7.2$ Hz), 1.08–1.14 (m, 1H), 1.24–1.30 (m, 1H), 1.72–1.84 (m, 4H), 2.50 (ddd, 1H, $J = 2.4$, 10.2, 18.6 Hz), 2.71 (s, 3H), 2.91 (ddd, 1H, $J = 3.0$, 7.8, 18.6 Hz), 3.02 (m, 1H), 3.98 (q, 2H, $J = 7.2$ Hz), 5.10 (m, 1H), 5.27 (m, 1H), 6.99 (dd, 1H, $J = 1.2$, 7.8 Hz), 7.15 (dt, 1H, $J = 1.2$, 7.2 Hz), 7.18 (t, 1H, $J = 2.4$ Hz), 7.32 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.27 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.8, 14.2, 20.2, 25.3, 26.7, 30.9, 38.6, 50.1, 60.7, 63.0, 116.6, 123.7, 124.7, 127.5, 128.2, 128.8, 132.4, 139.0, 140.0, 146.6, 162.4, 171.0, 180.4. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 382.2013; found, 382.2012; HPLC analysis (column, Daicel Chiralpak IB-3, 2-propanol/hexane = 1.5:98.5, flow rate = 1.0 mL min^{-1}): $\lambda = 230$ nm, t_{R} (min) = 7.6 (major), 13.5 (minor). Compound γ -*trans*-**4q** was determined to have 92% ee.

Diethyl (1*S*,5*S*)-1'-acetyl-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2,5-dicarboxylate (γ -*trans*-4r**)**

White solid (90%, *trans/cis* = 2.3:1): $[\alpha]_{\text{D}}^{26} = -59.2$ ($c = 0.603$ in CHCl_3). IR 3033, 2986, 1714, 1636 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 0.71 (t, 3H, $J = 7.2$ Hz), 1.08 (t, 3H, $J = 7.2$ Hz), 2.74 (s, 3H), 2.92 (ddd, 1H, $J = 3.0$, 9.0, 19.2 Hz), 3.33 (ddd, 1H, $J = 2.4$, 9.6, 19.2 Hz), 3.60–3.71 (m, 2H), 3.93 (t, 1H, $J = 9.6$ Hz), 3.99 (q, 2H, $J = 7.2$ Hz), 6.99 (dd, 1H, $J = 1.2$, 7.8 Hz), 7.11 (dt, 1H, $J = 1.2$, 7.8 Hz), 7.16 (t, 1H, $J = 2.4$ Hz), 7.31 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.23 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.3, 13.8, 26.6, 33.5, 54.0, 60.8, 60.9, 61.0, 116.4, 122.9, 125.0, 129.2, 129.3, 137.3, 140.4, 145.8, 161.9, 169.6, 170.9, 179.3. HRMS (DART) calcd for $\text{C}_{20}\text{H}_{22}\text{NO}_6$ $[\text{M} + \text{H}]^+$, 372.1442; found, 372.1443; HPLC analysis (column, Daicel Chiralpak IC-3, 2-propanol/hexane = 3:97, flow rate = 0.5 mL min^{-1}): $\lambda = 230$ nm, t_{R} (min) = 13.1 (major), 14.6 (minor). Compound γ -*trans*-**4r** was determined to have 91% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-cyclohexyl-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4s**)**

Yellow oil: $[\alpha]_{\text{D}}^{23} = -98.3$ ($c = 0.596$ in CHCl_3). IR 3030, 2933, 1756, 1706, 1635 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 0.66–0.75 (m, 2H), 0.92–1.12 (m, 7H), 1.22 (m, 1H), 1.40 (m, 1H), 1.49 (m, 1H), 1.64–1.70 (m, 2H), 2.56 (ddd, 1H, $J = 2.4$, 9.6, 17.4 Hz), 2.71 (s, 3H), 2.78–2.89 (m, 2H), 3.96 (dq, 2H, $J = 1.2$, 7.2 Hz), 7.02 (dd, 1H, $J = 1.2$, 7.8 Hz), 7.13–7.16 (m, 2H), 7.32 (dt, 1H, $J = 1.2$, 7.8 Hz), 8.26 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.7, 25.4, 25.7, 25.9, 26.7, 30.7, 31.6, 37.2, 38.8, 56.2, 60.6, 62.0, 116.5, 123.8, 124.6, 128.3, 128.7, 139.6, 140.0, 146.0, 162.4, 171.2, 180.6. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 382.2013; found, 382.2015; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 1.5:98.5, flow rate = 1.0 mL min^{-1}): $\lambda = 230$ nm, t_{R} (min) = 8.5



(major), 12.7 (minor). Compound γ -*trans*-4s was determined to have 90% ee.

Ethyl (1*S*,5*R*)-1'-acetyl-5-(*tert*-butyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate (γ -*trans*-4t)

Yellow oil: $[\alpha]_D^{25} = -71.7$ ($c = 0.165$ in CHCl_3). IR 3024, 2951, 1758, 1705, 1603 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 0.73 (s, 9H), 1.03 (t, 3H, $J = 7.2$ Hz), 2.71 (s, 3H), 2.74 (ddd, 1H, $J = 3.0, 7.8, 18.0$ Hz), 2.82 (ddd, 1H, $J = 2.4, 11.4, 18.0$ Hz), 2.99 (dd, 1H, $J = 7.8, 11.4$ Hz), 3.94 (dq, 2H, $J = 2.4, 7.2$ Hz), 7.05 (dd, 1H, $J = 1.2, 7.2$ Hz), 7.09 (dt, 1H, $J = 1.2, 7.2$ Hz), 7.23 (t, 1H, $J = 2.4$ Hz), 7.31 (dt, 1H, $J = 1.8, 7.8$ Hz), 8.26 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 13.9, 26.9, 28.8 (3C), 33.4, 33.9, 60.7, 61.8, 62.2, 116.8, 124.4, 125.7, 128.8, 129.0, 139.8, 140.1, 146.2, 162.4, 171.2, 181.1. HRMS (DART) calcd for $\text{C}_{21}\text{H}_{26}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 356.1856; found, 356.1857; HPLC analysis (column, Daicel Chiralpak IA-3, 2-propanol/hexane = 1.5 : 98.5, flow rate = 1.0 mL min^{-1}): $\lambda = 230$ nm, t_R (min) = 8.42 (major), 12.4 (minor). Compound γ -*trans*-4t was determined to have 80% ee.

Preparation of racemic γ -*trans*-4a and α -*trans*-4a for X-ray crystallographic analysis

The following reaction was carried out under N_2 . Compound 3 (0.410 mL, 3.56 mmol) was added to a stirred solution of 2a (500 mg, 1.90 mmol) and PPh_3 (100 mg, 0.380 mmol) in toluene (5.9 mL). After stirring at room temperature for 63 h, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel twice (EtOAc /hexane, 1 : 10) and preparative thin-layer chromatography (CH_2Cl_2) to provide γ -*trans*-4a (368 mg, 52%) as slightly yellow crystals and α -*trans*-4a (24.6 mg, 3%) as slightly yellow crystals.

Ethyl (1*R**,2*R**)-1'-acetyl-2'-oxo-2-phenylspiro[cyclopentane-1,3'-indolin]-3-ene-3-carboxylate (α -*trans*-4a)

IR 3031, 2933, 1749, 1714, 1647 cm^{-1} . ^1H NMR (600 MHz, acetone- d_6): δ 1.12 (t, 3H, $J = 7.2$ Hz), 2.65 (s, 3H), 3.00 (dt, 1H, $J = 2.4, 18.6$ Hz), 3.16 (ddd, 1H, $J = 0.6, 3.0, 18.6$ Hz), 4.03–4.13 (m, 2H), 4.64 (s, 1H), 6.42 (dd, 1H, $J = 1.2, 7.8$ Hz), 6.75 (dt, 1H, $J = 1.2, 7.8$ Hz), 6.93 (m, 2H), 7.09–7.14 (m, 4H), 7.20 (q, 1H, $J = 2.4$ Hz), 8.05 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (150 MHz, CDCl_3): δ 14.0, 26.7, 43.1, 58.2, 60.0, 60.5, 115.8, 124.39, 124.42, 127.4, 128.0, 128.2, 128.3, 129.1, 137.0, 137.3, 139.3, 142.3, 163.8, 170.8, 181.3. HRMS (DART) calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_4$ $[\text{M} + \text{H}]^+$, 376.1543; found, 376.1544.

Data availability

The data supporting this article have been included as part of the ESI† Experimental details, ^1H , ^1H - ^1H COSY and ^{13}C NMR spectra, HPLC data, computational methods, and X-ray data. CCDC 2343919, 2343921, and 2343914.† Xyz cartesian coordinates format. For ESI and crystallographic data in CIF or other electronic format, see.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This research was supported in part by JSPS KAKENHI Grant Number 15K07875 and the Hoansha Foundation. We also acknowledge We thank Ms M. Kawamura and Y. Sugiura for their technical assistance.

References

- For selected reviews: (a) H. Guo, Y. C. Fan, Z. Sun, Y. Wu and O. Kwon, *Chem. Rev.*, 2018, **118**, 10049; (b) S. B. Nallapati and S.-C. Chuang, *Asian J. Org. Chem.*, 2018, **7**, 1743.
- (a) C. Zhang and X. Lu, *J. Org. Chem.*, 1995, **60**, 2906; (b) Y. Du, X. Lu and C. Zhang, *Angew. Chem., Int. Ed.*, 2003, **42**, 1035.
- For selected reviews: (a) Y. Xiao, Z. Sun, H. Guo and O. Kwon, *Beilstein J. Org. Chem.*, 2014, **10**, 2089; (b) H. Ni, W.-L. Chan and Y. Lu, *Chem. Rev.*, 2018, **118**, 9344.
- S. Gladiali, E. Alberico, K. Junge and M. Beller, *Chem. Soc. Rev.*, 2011, **40**, 3744.
- For selected examples: (a) D. Wang, Z.-F. Song, W.-J. Wang and T. Xu, *Org. Lett.*, 2019, **21**, 3963; (b) D. Wang, W. Liu, Y. Hong and X. Tong, *Org. Lett.*, 2018, **20**, 5002.
- For selected examples: (a) A. Voituriez, A. Panossian, N. Fleury-Brégeot, P. Retailleau and A. Marinetti, *J. Am. Chem. Soc.*, 2008, **130**, 14030; (b) N. Pinto, M. Neel, A. Panossian, P. Retailleau, G. Frison, A. Voituriez and A. Marinetti, *Chem. – Eur. J.*, 2010, **16**, 1033.
- For selected examples of amino acid-derived phosphine catalysts: (a) T. Wang, X. Han, F. Zhong, W. Yao and Y. Lu, *Acc. Chem. Res.*, 2016, **49**, 1369; (b) B. J. Cowen and S. J. Miller, *J. Am. Chem. Soc.*, 2007, **129**, 10988; (c) H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang and G. Zhao, *Angew. Chem., Int. Ed.*, 2010, **49**, 4467. For other phosphine catalysts, see ref. 3.
- For selected reviews: (a) S. S. Panda, A. S. Girgis, M. N. Aziz and M. S. Bekheit, *Molecules*, 2023, **28**, 618; (b) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748.
- For selected reviews: (a) M. Ganesh and S. Suraj, *Org. Biomol. Chem.*, 2022, **20**, 5651; (b) Y. Wang, A. A. Cobo and A. K. Franz, *Org. Chem. Front.*, 2021, **8**, 4315; (c) A. J. Boddy and J. A. Bull, *Org. Chem. Front.*, 2021, **8**, 1026; (d) P.-W. Xu, J.-S. Yu, C. Chen, Z.-Y. Cao, F. Zhou and J. Zhou, *ACS Catal.*, 2019, **9**, 1820; (e) G.-J. Mei and F. Shi, *Chem. Commun.*, 2018, **54**, 6607; (f) A. Ding, M. Meazza, H. Guo, J. W. Yang and R. Rios, *Chem. Soc. Rev.*, 2018, **47**, 5946; (g) L. Hong and R. Wang, *Adv. Synth. Catal.*, 2013, **355**, 1023.



- 10 For selected reviews: (a) Q.-F. Li, J. Ma, J. Meng and E.-Q. Li, *Adv. Synth. Catal.*, 2023, **365**, 4412; (b) R. Saeed, A. P. Sakla and N. Shankaraiah, *Org. Biomol. Chem.*, 2021, **19**, 7768; (c) G. Molteni and A. Silvani, *Eur. J. Org. Chem.*, 2021, 1653; (d) A. Voituriez, A. Marinetti and M. Gicquel, *Synlett*, 2015, 142; (e) H. Li and Y. Lu, *Asian J. Org. Chem.*, 2017, **6**, 1130.
- 11 (a) A. Voituriez, N. Pinto, M. Neel, P. Retailleau and A. Marinetti, *Chem. – Eur. J.*, 2010, **16**, 12541; (b) C. Gomez, M. Gicquel, J.-C. Carry, L. Schio, P. Retailleau, A. Voituriez and A. Marinetti, *J. Org. Chem.*, 2013, **78**, 1488; (c) D. Wang, G.-P. Wang, Y.-L. Sun, S.-F. Zhu, Y. Wei, Q.-L. Zhou and M. Shi, *Chem. Sci.*, 2015, **6**, 7319; (d) M. Gicquel, C. Gomez, M. C. G. Alvarez, O. Pamard, V. Guérineau, E. Jacquet, J. Bignon, A. Voituriez and A. Marinetti, *J. Med. Chem.*, 2018, **61**, 9386 For reactions of (2-oxoalkylidene)indolinones: (e) X.-C. Zhang, S.-H. Cao, Y. Wei and M. Shi, *Chem. Commun.*, 2011, **47**, 1548 For reactions of bis (alkoxycarbonyl)methyleneindolinones: (f) X.-C. Zhang, S.-H. Cao, Y. Wei and M. Shi, *Org. Lett.*, 2011, **13**, 1142 For reactions of dicyanomethylideneindolinones: (g) S. Guo, R. Wang, J. Li, C. Li, H. Deng and X. Jia, *Synlett*, 2011, 2256 For reactions of pyrazoloneyldiene oxindoles: (h) W. Luo, B. Shao, J. Li, X. Xiao, D. Song, F. Ling and W. Zhong, *Org. Chem. Front.*, 2020, **7**, 1016 For reactions of isoindigos: (i) W.-L. Chan, X. Tang, F. Zhang, G. Quek, G.-J. Mei and Y. Lu, *Angew. Chem., Int. Ed.*, 2019, **58**, 6260.
- 12 (a) B. Tan, N. R. Candeias and C. F. Barbas III, *J. Am. Chem. Soc.*, 2011, **133**, 4672; (b) Z. Lu, Y. Jia, X. Chen and P. Li, *J. Org. Chem.*, 2022, **87**, 3184 For reactions of dicyanomethylideneindolinone and its analogues: (c) F. Zhong, X. Han, Y. Wang and Y. Lu, *Angew. Chem., Int. Ed.*, 2011, **50**, 7837; (d) H.-P. Deng, Y. Wei and M. Shi, *Org. Lett.*, 2011, **13**, 3348; (e) S. Kitagaki, M. Tsuji, H. Teramoto, N. Takenaga and K. Yoshida, *Heterocycles*, 2020, **101**, 127 For reactions of pyrazoloneyldiene oxindoles: (f) J. Zhang, W.-L. Chan, L. Chen, N. Ullah and Y. Lu, *Org. Chem. Front.*, 2019, **6**, 2210.
- 13 J. Zhang, C. Cheng, D. Wang and Z. Miao, *J. Org. Chem.*, 2017, **82**, 10121.
- 14 C. Hu, Q. Zhang and Y. Huang, *Chem. – Asian J.*, 2013, **8**, 1981.
- 15 The vinylogous reactions using 3-alkylideneoxindole as a nucleophile have been reported. For selected examples: (a) Y.-J. Tsou, N. Sathishkumar, I.-T. Chen, T.-A. Lee, H.-T. Chen and J.-L. Han, *J. Org. Chem.*, 2022, **87**, 2520; (b) J.-X. Xu, Y.-S. Jiang, C.-H. Chen, N. Sathishkumar, K.-T. Chu, M.-H. Chiang, H.-T. Chen and J.-L. Han, *J. Org. Chem.*, 2022, **87**, 197; (c) N. D. Iorio, P. Righi, S. Ranieri, A. Mazzanti, R. G. Margutta and G. Bencivenni, *J. Org. Chem.*, 2015, **80**, 7158.
- 16 (a) One example of reaction of 3-methylenebenzofuranone bearing an alkyl substituent on the methylene carbon has been reported. See ref. 11c (b) Chiral phosphine-catalyzed (4 + 2) cyclization of γ -benzyl-substituted allenates also includes only use of benzyldieneindolinones. S. Jia, M. Ma, E.-Q. Li, Z. Duan and F. Mathey, *Org. Lett.*, 2021, **23**, 3337.
- 17 (a) S. E. Gibson and J. D. Knight, *Org. Biomol. Chem.*, 2003, **1**, 1256; (b) V. Rosenberg, E. Sergeeva and H. Hopf, in *Modern Cyclophane Chemistry*, ed. R. Gleiter and H. Hopf, Wiley-VCH, Weinheim, Germany, 2004, p. 435; (c) A. A. Aly and A. B. Brown, *Tetrahedron*, 2009, **65**, 8055; (d) J. Paradies, *Synthesis*, 2011, 3749; (e) Special Issue: Cyclophanes, *Isr. J. Chem.*, 2012, **52**, 1 (f) Z. Hassan, E. Spuling, D. M. Knoll, J. Lahann and S. Bräse, *Chem. Soc. Rev.*, 2018, **47**, 6947.
- 18 S. Felder, S. Wu, J. Brom, L. Micouin and E. Benedetti, *Chirality*, 2021, **33**, 506.
- 19 Phosphines: (a) T. G. Driver, J. R. Harris and K. A. Woerpel, *J. Am. Chem. Soc.*, 2007, **129**, 3836; (b) T.-Z. Zhang, L.-X. Dai and X.-L. Hou, *Tetrahedron: Asymmetry*, 2007, **18**, 1990 Phosphoric acids: (c) E. Xie, S. Huang and X. Lin, *Org. Lett.*, 2019, **21**, 3682 Thioureas: (d) Y. Lu, Y. Ma, S. Yang, M. Ma, H. Chu and C. Song, *Tetrahedron: Asymmetry*, 2013, **24**, 1082; (e) S. Kitagaki, T. Ueda and C. Mukai, *Chem. Commun.*, 2013, **49**, 4030; (f) S. Kitagaki, E. Shimo, S. Takeda, R. Fukai, N. Kojima, S. Yoshioka, N. Takenaga and K. Yoshida, *Heterocycles*, 2021, **103**, 678 N-Heterocyclic carbenes: (g) L. Wang, Z. Chen, M. Ma, W. Duan, C. Song and Y. Ma, *Org. Biomol. Chem.*, 2015, **13**, 10691; (h) P. An, Y. Huo, Z. Chen, C. Song and Y. Ma, *Org. Biomol. Chem.*, 2017, **15**, 3202 Imines: (i) M. Negru, D. Schollmeyer and H. Kunz, *Angew. Chem., Int. Ed.*, 2007, **46**, 9339 Hypervalent iodines: (j) Y. Wang, H. Yuan, H. Lu and W.-H. Zheng, *Org. Lett.*, 2018, **20**, 2555; (k) Y. Wang, C.-Y. Zhao, Y.-P. Wang and W.-H. Zheng, *Synthesis*, 2019, 3675 NAD(P)H models: (l) Z.-H. Zhu, Y.-X. Ding, B. Wu and Y.-G. Zhou, *Chem. Sci.*, 2020, **11**, 10220; (m) Z.-B. Zhao, J. Wang, Z.-H. Zhu, M.-W. Chen and Y.-G. Zhou, *Org. Lett.*, 2021, **23**, 9112; (n) Z.-H. Zhu, Y.-X. Ding and Y.-G. Zhou, *Chem. Commun.*, 2022, **58**, 3973 Isothioureas: (o) S. Yuan, C. Liao and W.-H. Zheng, *Org. Lett.*, 2021, **23**, 4142.
- 20 (a) S. Kitagaki, Y. Ohta, R. Takahashi, M. Komizu and C. Mukai, *Tetrahedron Lett.*, 2013, **54**, 384; (b) N. Takenaga, S. Adachi, A. Furusawa, K. Nakamura, N. Suzuki, Y. Ohta, M. Komizu, C. Mukai and S. Kitagaki, *Tetrahedron*, 2016, **72**, 6892.
- 21 S. Kitagaki, K. Nakamura, C. Kawabata, A. Ishikawa, N. Takenaga and K. Yoshida, *Org. Biomol. Chem.*, 2018, **16**, 1770.
- 22 (a) CCDC 2343919.†; (b) CCDC 2343921.†
- 23 For mechanistic studies: (a) T. Dudding, O. Kwon and E. Mercier, *Org. Lett.*, 2006, **8**, 3643; (b) E. Mercier, B. Fonovic, C. Henry, O. Kwon and T. Dudding, *Tetrahedron Lett.*, 2007, **48**, 3617; (c) Y. Xia, Y. Liang, Y. Chen, M. Wang, L. Jiao, F. Huang, S. Liu, Y. Li and Z.-X. Yu, *J. Am. Chem. Soc.*, 2007, **129**, 3470; (d) X.-F. Zhu, C. E. Henry and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 6722; (e) Y. Liang, S. Liu, Y. Xia, Y. Li and Z.-X. Yu, *Chem. – Eur. J.*, 2008, **14**, 4361; (f) Y. Liang, S. Liu and Z.-X. Yu, *Synlett*, 2009, 905; (g) G.-T. Huang, T. Lankau and C.-H. Yu, *J. Org. Chem.*,



- 2014, **79**, 1700; (h) G.-T. Huang, T. Lankau and C.-H. Yu, *Org. Biomol. Chem.*, 2014, **12**, 7297; (i) M. C. Holland, R. Gilmour and K. N. Houk, *Angew. Chem., Int. Ed.*, 2016, **55**, 2022; (j) H. Ni, Z. Yu, W. Yao, Y. Lan, N. Ullah and Y. Lu, *Chem. Sci.*, 2017, **8**, 5699; (k) C.-X. Cui, C. Shan, Y.-P. Zhang, X.-L. Chen, L.-B. Qu and Y. Lan, *Chem. – Asian J.*, 2018, **13**, 1076; (l) Z. Yu, Z. Jin, M. Duan, R. Bai, Y. Lu and Y. Lan, *J. Org. Chem.*, 2018, **83**, 9729; (m) S. Anwar, L.-T. Lin, V. Srinivasadesikan, V. B. Gudise and K. Chen, *RSC Adv.*, 2021, **11**, 38648.
- 24 See the ESI† for details of computational methods.
- 25 CCDC 2343914.†

