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Enantioselective Construction of Spiro[indoline-3,2′-pyrrole] Framework via Catalytic Asymmetric 1,3-Dipolar Cycloadditions Using Allenes as Equivalents of Alkynes

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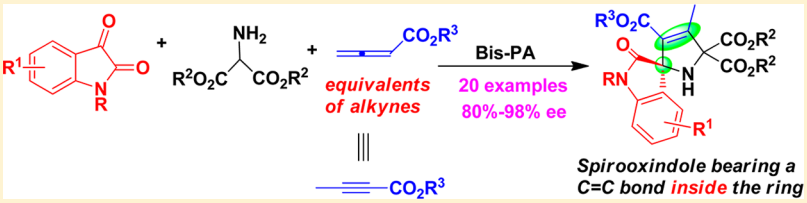
Supporting Information

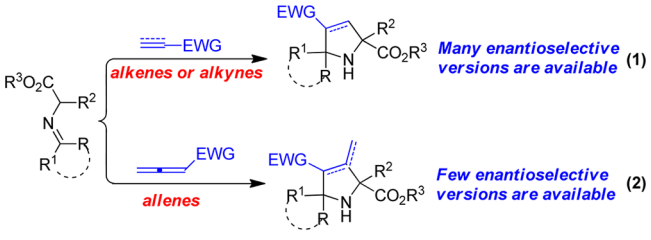


ABSTRACT: The first catalytic asymmetric 1,3-dipolar cycloadditions (1,3-DCs) of isatin-derived azomethine ylide with allenes have been established, which efficiently assembly isatins, amino-esters and 2,3-allenoate into enantioenriched spiro[indoline-3,2′-pyrrole] derivatives with a quaternary stereogenic center in generally high enantioselectivities (80−98% *ee*). In this allene-involved 1,3-DC, an unexpected spirooxindole framework bearing an intra-annular C═C double bond was generated, which is quite different from previously reported 1,3-DCs of allenes. This approach not only confronted the great challenge in using allenes as dipolarophiles of 1,3-DCs, but also provided a unique strategy of using allenes as equivalents of alkynes to construct spiro[indoline-3,2′-pyrrole] structure. Besides, this reaction also represents the first catalytic asymmetric ketone-involved 1,3-DCs of allenes, which will also greatly enrich the research contents of 1,3-DCs, the chemistry of allenes as well as the synthetic methods of spirooxindoles.

INTRODUCTION

Catalytic enantioselective 1,3-dipolar cycloadditions (1,3-DCs) of azomethine ylide with unsaturated carbon−carbon bonds have proven to be powerful tools to construct chiral five-membered nitrogenous heterocyclic frameworks (Scheme 1), which constitute the core structures of numerous natural alkaloids and bioactive compounds.[1] As a result, elegant developments have been achieved in this research area by using electron-deficient alkenes[1] and alkynes[2] as dipolarophiles in the presence of either metal[1,3] or organocatalysts[1,4] (eq 1). However, in sharp contrast, allenes as a unique type of unsaturated compounds have rarely been employed as dipolarophiles to react with azomethine ylide (eq 2).[5]

Scheme 1. Profile of Enantioselective 1,3-DCs of Azomethine Ylide



Survey of the literature revealed that Gong and co-workers established an enantioselective 1,3-DC of 2,3-allenoates with aldehyde-derived azomethine ylide catalyzed by a chiral bisphosphoric acid[6] (Bis-PA), which afforded chiral pyrrolidines bearing a C═C double bond outside the five-membered ring (eq 3).[5a] In spite of this pioneer work, the investigation on allene-involved catalytic asymmetric 1,3-DCs is still rather limited and full of challenge.

In view of the challenge in using allenes as dipolarophiles and as a continuation of our efforts in constructing spirooxindole scaffolds via isatin-involved reactions,[7] we tried the 1,3-DC of 2,3-allenoates with isatin-derived azomethine ylide in the presence of the same catalyst (eq 4). Interestingly, a chiral spirooxindole motif was constructed with the concomitant generation of the C═C double bond inside the five-membered ring, which is very different from the reaction of aldehyde-derived azomethine ylide. In this transformation, allenes served as equivalents of alkynes to participate in the catalytic asymmetric isatin-involved 1,3-DCs, offering enantioselective spiro[indoline-3,2′-pyrrole] derivatives with a quaternary stereogenic center.

On the other hand, spiro[indoline-3,2′-pyrrole] derivatives as one of the most important class of spirooxindoles,[8] exhibited

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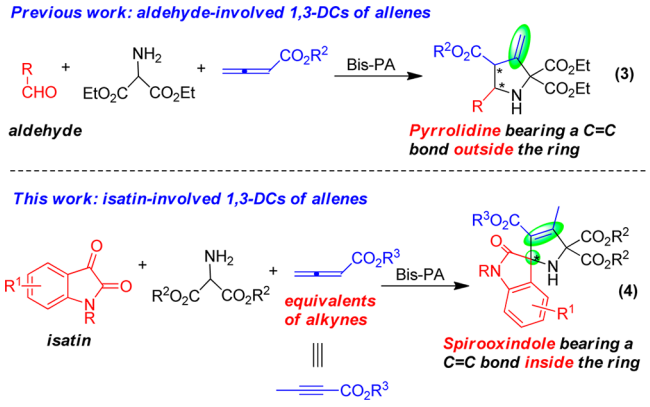


promising pharmaceutical activities[9] such as antimicrobial,[9a] anticancer[9b] and cytotoxic to MCF-7 cells[9c] (Figure 1).

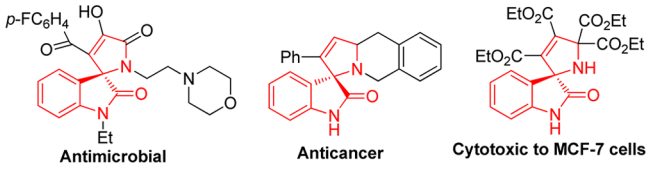


Figure 1. Selected bioactive spiro[indoline-3,2′-pyrrole] derivatives.

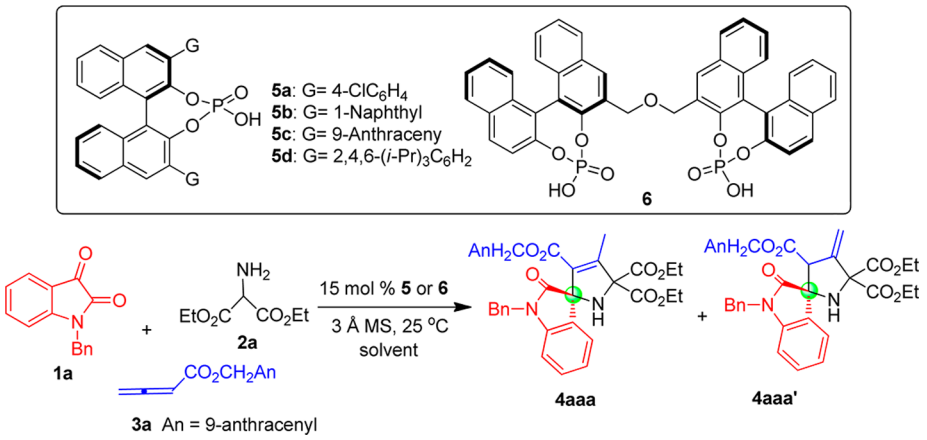
Consequently, the construction of this intriguing scaffold, especially with high optical purity, is also an important issue in the organic community.[10−12] Nevertheless, most of the approaches were in racemic manners[9d,e,10] or employed chiral starting materials,[11] and the catalytic asymmetric transformations to obtain this framework have sporadically been described in the literature.[2d,12]

Herein, we report the first catalytic asymmetric 1,3-dipolar cycloadditions of isatin-derived azomethine ylide with allenes, which utilize allenes as equivalents of alkynes to construct biologically important spiro[indoline-3,2′-pyrrole] framework in a highly enantioselective fashion (up to 98% *ee*).

RESULTS AND DISCUSSION

Initially, the three-component 1,3-dipolar cycloaddition of *N*-benzyl isatin **1a**, amino-ester **2a** and 2,3-allenoate **3a** was employed as a model reaction to optimize the reaction conditions (Table 1). Notably, 9-anthracenylmethyl buta-2,3-dienoate **3a** was chosen as a preferred substrate because previous report revealed that the introduction of a bulky substituent to the ester moiety of buta-2,3-dienoate was helpful to the enantioselective control.[5a] In the presence of chiral phosphoric acids **5**−**6**, all the reactions afforded the unexpected spirooxindole product **4aaa** bearing an intra-annular C═C double bond rather than the anticipated spiro-product linking an exocyclic C═C double bond in high selectivity (entries 1−

Table 1. Optimization of Reaction Conditions[a]



entry	solvent	cat.	yield (%)[b]	4aaa:4aaa′[c]	ee (%)[d]
1	toluene	**5a**	31	95:5	20
2	toluene	**5b**	25	>95:5	14
3	toluene	**5c**	37	93:7	28
4	toluene	**5d**	23	>95:5	32
5	toluene	**6**	63	>95:5	91
6	DCE	**6**	39	95:5	74
7	THF	**6**	trace	–	–
8	CH_3CN	**6**	trace	–	–
9	*o*-xylene	**6**	49	91:9	71
10	*m*-xylene	**6**	55	83:17	80
11	*p*-xylene	**6**	51	78:22	80
12[e]	toluene	**6**	58	86:14	89
13[f]	toluene	**6**	49	84:16	92
14[g]	toluene	**6**	65	83:17	91

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in a solvent (1 mL) with 3 Å MS (100 mg) at 25 °C for 48 h, and the mole ratio of **1a**:**2a**:**3a** was 1.2:1:1.2. [b]Isolated yield. [c]The ratio of **4aaa**:**4aaa**′ was determined by HPLC. [d]The enantiomeric excess (*ee*) was determined by HPLC. [e]5 Å MS was used as additives instead of 3 Å MS. [f]Performed at 65 °C. [g]The mole ratio of **1a**:**2a**:**3a** was 1.2:1:2.4.

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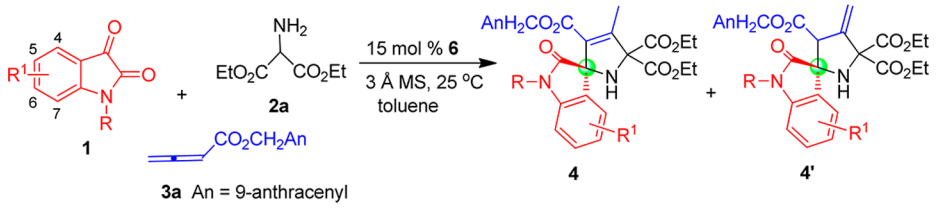
Table 2. Substrate Scope of the Isatin-Involved 1,3-DCs of Allenes[a]



entry	4	R\R^1 (1)	yield (%)[b]	4:4′[c]	ee (%)[d]
1	**4aaa**	Bn\H (**1a**)	63	>95:5	91
2	**4baa**	*p*-Me$C_6H_4CH_2$\H (**1b**)	55	90:10	90
3	**4caa**	*m*-Me$C_6H_4CH_2$\H (**1c**)	54	93:7	86
4	**4daa**	*o*-Me$C_6H_4CH_2$\H (**1d**)	57	87:13	86
5	**4eaa**	*p*-*t*Bu$C_6H_4CH_2$\H (**1e**)	58	>95:5	80
6	**4faa**	*p*-Br$C_6H_4CH_2$\H (**1f**)	40	>95:5	92
7	**4gaa**	*m*-Cl$C_6H_4CH_2$\H (**1g**)	53	>95:5	86
8	**4haa**	*o*-Cl$C_6H_4CH_2$\H (**1h**)	49	93:7	85
9	**4iaa**	Ph\H (**1i**)	65	91:9	93
10	**4jaa**	Bn\5-Me (**1j**)	51	90:10	98
11	**4kaa**	Bn\5,6-F_2 (**1k**)	59	>95:5	92
12	**4laa**	Bn\6-Br (**1l**)	60	>95:5	95
13	**4maa**	Bn\6-Cl (**1m**)	60	>95:5	84
14	**4naa**	Bn\7-Me (**1n**)	55	88:12	80
15	**4oaa**	Bn\7-F (**1o**)	56	87:13	92
16	**4paa**	Bn\7-CF_3 (**1p**)	59	>95:5	91

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in toluene (1 mL) with 3 Å MS (100 mg) at 25 °C for 48 h, and the mole ratio of **1**:**2a**:**3a** was 1.2:1:1.2. [b]Isolated yield. [c]The ratio of **4**:**4′** was determined by ^{1}H NMR. [d]The enantiomeric excess (*ee*) was determined by HPLC.

5). However, bisphosphoric acid (Bis-PA) **6** exhibited much higher catalytic activity than monophosphoric acid **5a**−**5d** both in reactivity and in enantioselectivity (entry 5 vs 1−4), which afforded the product **4aaa** in a good yield of 63% and high enantioselectivity of 91% *ee* (entry 5). This phenomenon demonstrated again the superiority of Bis-PA in catalytic asymmetric 1,3-DCs of azomethine ylide.[5a,b,6a−c] Then, in the presence of Bis-PA **6**, different types of solvents including arene, haloalkane, ether and nitrile were evaluated by the model reaction (entries 5−8), which revealed that the reaction could hardly occur in solvents of ether and nitrile (entries 7−8). Due to the good performance of toluene, xylenes as analogues of toluene were then tested, but none of them showed higher catalytic activity than toluene (entries 9−11 vs 5). So, toluene was selected as the most suitable solvent for further condition optimization. Changing the molecular sieves (MS) from 3 to5 Å could not benefit the reaction in terms of yield, chemoselectivity and enantioselectivity (entry 5 vs 12). Besides, raising the reaction temperature from 25 to 65 °C was detrimental to the yield albeit with a slightly improved enantioselectivity (entry 5 vs 13). Finally, increasing the stoichiometry of 2,3-allenoate **3a** had no obvious effect on the yield and the enantioselectivity (entry 5 vs 14). Thus, the optimal conditions were set as what entry 5 illustrated for subsequent investigation on the substrate scope. It should be mentioned that the moderate yield of the reaction should be ascribed to the relatively lower reactivity of isatin-derived azomethine ylide compared with aldehyde-derived azomethine ylide, because TLC revealed that a plenty of isatin-derived azomethine ylides were remained intact at the end of the reaction apart from the formation of product **4**. Besides, during the course of condition optimization, we identified the structure of compound **4aaa′** by crude ^{1}H NMR, but this compound could hardly be isolated as a pure product because it was very easily transformed into more stable product **4aaa**.

With the optimal reaction conditions known, we then investigated the substrate scope of this catalytic asymmetric isatin-involved 1,3-DCs of allenes by the reactions of different isatins **1** with amino-ester **2a** and 2,3-allenoate **3a**. As shown in Table 2, this approach is applicable to a wide range of isatins with various R\R^1 groups, delivering structurally diverse spiro[indoline-3,2′-pyrrole] derivatives **4** in generally acceptable yields, high selectivity and excellent enantioselectivities (80−98% *ee*).

First, the effect of *N*-substituents (R group) of isatins on the reaction was studied (entries 1−9), which disclosed that *N*-phenyl group was superior to a series of *N*-benzyl groups with regard to the yield and the enantioselectivity (entry 9 vs 1−8). As to *N*-benzyl groups, the position of the substituents on the benzyl moiety seemed to have some influence on the enantioselectivity. For instance, *para*-methyl substituted substrate **1b** afforded higher enantioselectivity than its *meta*- and *ortho*-substituted counterparts **1c**−**1d** (entry 2 vs 3−4), while there was no difference between substrates **1c** and **1d** in terms of enantioselectivity (entry 3 vs 4). Besides, the electronic nature of the substituents linked to the benzyl group had no obvious impact on the enantioselectivity, since either electron-donating group or electron-withdrawing group at the same position offered the spiro-products in similar enantioselectivities (entry 2 vs 6, entries 3−4 vs 7−8). However, the size of the substituents seemed to affect the enantioselectivity to some extent, because *tert*-butyl as a bulky group exhibited much lower capability than methyl group in enantioselective control (entry 5 vs 2).

Second, the impact of the substituents linked to the phenyl ring of isatin motif (R^1 group) was also investigated by using

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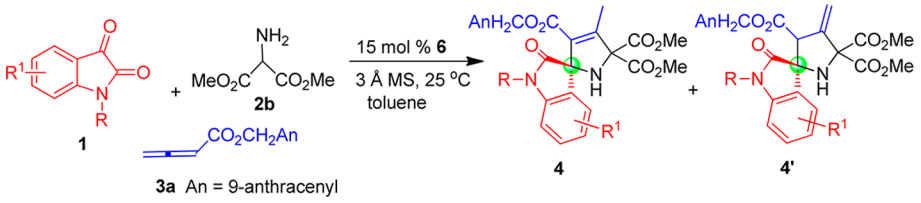
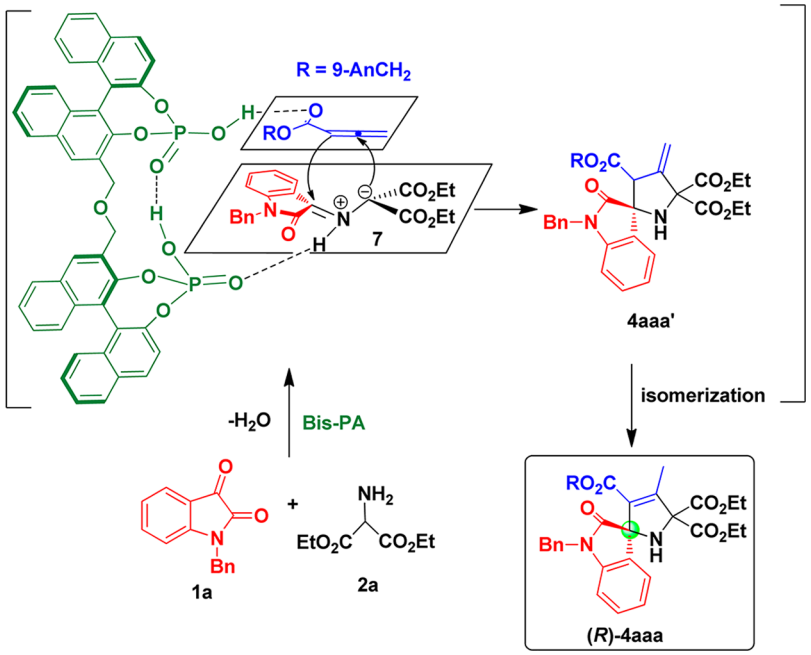
Table 3. Isatin-Involved 1,3-DCs of Allenes Using Amino-Ester 2b as a Substrate[a]



entry	4	R\ R^1 (1)	yield (%)[b]	4:4′[c]	ee (%)[d]
1	**4aba**	Bn\H (**1a**)	50	91:9	92
2	**4iba**	Ph\H (**1i**)	59	>95:5	92
3	**4lba**	Bn\6-Br (**1l**)	46	90:10	95
4	**4oba**	Bn\7-F (**1o**)	52	92:8	95

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in toluene (1 mL) with 3 Å MS (100 mg) at 25 °C for 48 h, and the mole ratio of **1**:**2b**:**3a** was 1.2:1:1.2. [b]Isolated yield. [c]The ratio of **4**:**4′** was determined by ^{1}H NMR. [d]The enantiomeric excess (*ee*) was determined by HPLC.

Scheme 2. Proposed Reaction Pathway and Transition State



isatins **1j**−**1p** with various substituents at different position of the phenyl ring (entries 10−16). Among the tested substrates, C5-methyl substituted isatin **1j** showed the highest capacity in offering the spiro-product in the best enantioselectivity of 98% *ee* (entry 10). This result also demonstrated that the position of the substituents imposed an obvious effect on the enantioselectivity because C7-methyl substituted isatin **1n** was much inferior to its C5-methyl substituted counterpart **1j** in enantioselective control (entry 14 vs 10). For C7-substituted isatins, electronically poor substituents delivered better *ee* value than electronically rich ones (entries 15−16 vs 14), which indicated that the electronic nature of the substituents also affected the enantioselectivity. Notably, these electron-withdrawing groups (F and CF_3) are fluorine-contained ones, the superior enantioselectivity delivered by these substituents might have some correlation with the fluorine effect.[13] Besides, disubstituted substrate **1k** could smoothly take part in the 1,3-DC reaction with an excellent enantioselectivity of 92% *ee* (entry 11).

Then, we examined the generality of this catalytic asymmetric 1,3-DCs of allenes by using amino-ester **2b** as a substrate to react with several representative isatins. As illustrated in Table 3, dimethyl 2-aminomalonate **2b** proved to be a suitable reactant, which successfully participated in the 1,3-DCs of isatins **1** with 2,3-allenoate **3a**, affording the spirooxindole products **4** bearing a quaternary stereogenic center in high enantioselectivities (92−95% *ee*). Thus, this three-component 1,3-DCs provided a good opportunity for the synthesis of chiral spiro[indoline-3,2′-pyrrole] derivatives with structural diversity.

The absolute configuration of spiro-product **4aaa** was unambiguously determined to be *R* by X-ray single crystal analysis (>99% *ee* after recrystallization).[14] The configurations of other spiro-products **4** were assigned by analogy.

Based on the experimental results and previous theoretical calculations on Bis-PA catalyzed 1,3-DCs,[6b,c] we suggested a possible reaction pathway and transition state (Scheme 2). As exemplified by the formation of spiro-product **4aaa**, the condensation of isatin **1a** with amino-ester **2a** afforded the corresponding azomethine ylide **7** in the presence of Bis-PA.

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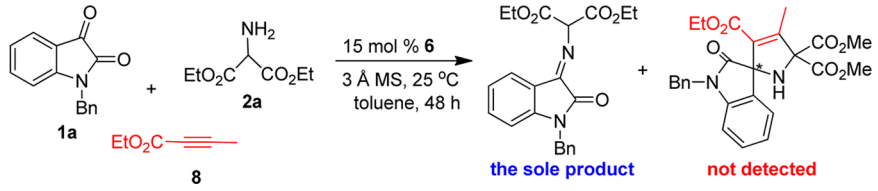
Scheme 3. Control Experiment Using Alkyne 8 as a Substrate



Then, Bis-PA simultaneously activated the two substrates of azomethine ylide **7** and 2,3-allenoate **3a** by forming dual hydrogen-bonds, thus facilitating an enantioselective [3 + 2] cycloaddition to generate an intermediate product **4aaa′** linking an exocyclic C═C double bond, which quickly isomerized into the final spiro-product **4aaa** bearing an intra-annular C═C double bond. In the suggested transition state, Bis-PA formed an intramolecular hydrogen-bond[6b,c] and acted as a Lewis base/Brønsted acid bifunctional catalyst to activate both of the dipole and dipolarophile via dual hydrogen-bonding activation mode. So, this activation mode along with the chiral environment created by (*R*)-bis-BINOL backbone of the catalyst contributed to the experimentally observed high enantioselectivity and the (*R*)-configuration of the spiro-product.

Finally, we tried the catalytic asymmetric 1,3-DC using alkyne **8** as a substrate instead of allene **3a** under the standard conditions (Scheme 3). However, only an imine as the precursor of isatin-derived azomethine ylide was generated, and no other products including the desired spirooxindole were formed at all. This result indicated that ethyl but-2-ynoate **8** had much lower reactivity than 2,3-allenoate **3a** to participate in the isatin-involved 1,3-DC under the current conditions. So, 2,3-allenoate can serve as an equivalent or surrogate of the corresponding but-2-ynoate to undergo the catalytic asymmetric 1,3-DCs with isatin-derived azomethine ylides in excellent enantioselectivities, leading to biologically important spiro[indoline-3,2′-pyrrole] scaffold.

■ CONCLUSIONS

In summary, we have established the first catalytic asymmetric 1,3-dipolar cycloadditions (1,3-DCs) of isatin-derived azomethine ylide with allenes, which efficiently assembly isatins, amino-esters and 2,3-allenoate into enantioenriched spiro[indoline-3,2′-pyrrole] derivatives with a quaternary stereogenic center in generally excellent enantioselectivities (80−98% *ee*). In this allene-involved 1,3-DC, an unexpected spirooxindole framework bearing an intra-annular C═C double bond was generated, which is quite different from previously reported 1,3-DCs of allenes. Thus, allenes could act as equivalents of alkynes to construct biologically important spiro[indoline-3,2′-pyrrole] scaffold in a highly enantioselective fashion. This approach not only confronted the great challenge in using allenes as dipolarophiles of 1,3-DCs, but also provided a unique strategy of using allenes as equivalents of alkynes to construct spiro[indoline-3,2′-pyrrole] structure. Besides, this reaction also represents the first catalytic asymmetric ketone-involved 1,3-DCs of allenes, which will also greatly enrich the research contents of 1,3-DCs, the chemistry of allenes as well as the synthetic methods of spirooxindoles.

■ EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra were measured respectively at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS spectra were recorded on a LTQ-Orbitrap mass spectrometer. Enantiomeric excesses (*ee*) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral column used for the determination of enantiomeric excesses by chiral HPLC was Chiralpak AD-H and IA columns. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at the temperatures indicated. The single crystal X-ray diffraction analysis of compound **4aaa** was performed on Bruker Apex Duo and the X-ray source was Cu Kα (λ = 1.54178). Analytical grade solvents for the column chromatography and commercially available reagents were used as received. All starting materials commercially available were used directly. Substrates **1** and **3a** were synthesized according to the literature methods.[6c,5a] Catalyst **6** was prepared according to the procedures reported in the literature.[6a,b]

Typical Procedure for the Catalytic Asymmetric Isatin-Involved 1,3-DCs of Allenes. After a solution of isatins **1** (0.12 mmol), amino-esters **2** (0.1 mmol), the catalyst **6** (0.015 mmol), and 3 Å molecular sieves (100 mg) in toluene (0.5 mL) was stirred at 25 °C for 30 min, the solution of 2,3-allenoate **2a** (0.12 mmol) in toluene (0.5 mL) was added. After being stirred at 25 °C for 48 h, the reaction mixture was filtered to remove the molecular sieves and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified through flash column chromatography on silica gel and preparative thin layer chromatography to afford pure products **4**.

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4aaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 63% (42.1 mg); >95:5 **4aaa:4aaa′**; white solid; mp 78−80 °C; $[\alpha]_D^{20}$ = −76.5 (c 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.55−7.50 (m, 2H), 7.50−7.43 (m, 2H), 7.18−7.11 (m, 3H), 7.02−6.99 (m, 1H), 6.83−6.78 (m, 2H), 6.59 (t, *J* = 7.5 Hz, 1H), 6.36−6.31 (m, 1H), 6.06 (d, *J* = 12.5 Hz, 1H), 5.79 (d, *J* = 12.5 Hz, 1H), 5.16 (d, *J* = 7.8 Hz, 1H), 4.41−4.28 (m, 4H), 4.18 (d, *J* = 16.1 Hz, 1H), 3.69 (s, 1H), 2.55 (s, 3H), 2.08 (d, *J* = 16.1 Hz, 1H), 1.37−1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 169.3, 168.2, 162.4, 153.6, 142.3, 135.5, 131.3, 131.1, 130.9, 130.0, 128.9, 128.8, 128.4, 128.3, 127.1, 126.9, 126.7, 125.2, 124.9, 123.5, 123.1, 122.2, 107.8, 81.9, 74.1, 62.7, 62.5, 58.5, 42.4, 14.2, 14.1, 14.0; IR (KBr) 3336, 2963, 2924, 2852, 2360, 2341, 1733, 1651, 1613, 1540, 1488, 1468, 1363, 1261, 1182, 1095, 1023, 801, 733, 695; ESI FTMS exact mass calcd for $(C_{41}H_{36}N_2O_7+Na)^+$ requires *m*/*z* 691.2421, found *m*/*z* 691.2380; Enantiomeric excess 91%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 21.58 min (major), t_R = 12.03 min (minor).

Compound 4aaa′. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.04 (d, *J* = 8.5, Hz, 2H), 7.95 (d, *J* = 8.6 Hz, 2H), 7.50−7.43 (m, 4H), 7.12−7.09 (m, 3H), 6.99 (d, *J* = 7.4, Hz, 1H), 6.86−6.84 (m, 2H), 6.47 (t, *J* = 8.0 Hz, 1H), 6.34 (t, *J* = 8.0 Hz, 1H), 6.25 (d, *J* = 12.5 Hz, 1H), 6.17 (d, *J* = 2.8 Hz, 1H), 5.98 (d, *J* = 2.8 Hz, 1H), 5.54 (d, *J* = 12.5 Hz, 1H), 5.36 (d, *J* = 7.7 Hz, 1H), 4.31−4.18 (m, 6H), 3.68 (s, 1H), 2.40 (d, *J* = 15.9 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 4′-methyl-1-(4-methylbenzyl)-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4baa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/

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ethyl acetate = 10/1); Reaction time = 48 h; yield 55% (37.5 mg); 90:10 **4baa:4baa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −77.9 (c 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.07 (t, J = 7.6 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H), 7.54−7.44 (m, 4H), 6.99 (d, J = 6.8 Hz, 1H), 6.95 (d, J = 7.8 Hz, 2H), 6.70 (d, J = 7.9 Hz, 2H), 6.57 (t, J = 7.3 Hz, 1H), 6.33 (t, J = 7.7, 1.0 Hz, 1H), 6.06 (d, J = 12.5 Hz, 1H), 5.78 (d, J = 12.5 Hz, 1H), 5.17 (d, J = 7.8 Hz, 1H), 4.38−4.29 (m, 4H), 4.15 (d, J = 15.9 Hz, 1H), 2.54 (s, 3H), 2.22 (s, 3H), 2.07 (d, J = 15.9 Hz, 1H), 1.36−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.3, 168.2, 162.4, 153.5, 142.3, 136.7, 132.4, 131.3, 131.21, 130.9, 130.0, 129.1, 129.0, 128.8, 128.7, 128.6, 127.0, 126.8, 126.7, 125.2, 125.1, 124.9, 123.5, 123.1, 122.2, 107.9, 81.9, 74.1, 62.7, 62.5, 58.5, 42.2, 20.9, 14.2, 14.0; IR (KBr) 3338, 2963, 2922, 2360, 2341, 1734, 1651, 1612, 1540, 1515, 1488, 1467, 1363, 1260, 1182, 1094, 1036, 955, 800, 754, 732, 692; ESI FTMS exact mass calcd for $(C_{42}H_{38}N_2O_7+Na)^+$ requires m/z 705.2577, found m/z 705.2587; Enantiomeric excess 90%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 27.47 min (major), t_R = 12.06 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 4′-methyl-1-(3-methylbenzyl)-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4caa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 54% (36.9 mg); 93:7 **4caa:4caa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −12.1 (c 0.74, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 7.55−7.50 (m, 2H), 7.49−7.44 (m, 2H), 7.05−6.99 (m, 2H), 6.92 (d, J = 7.6 Hz, 1H), 6.63−6.57 (m, 3H), 6.35 (td, J = 7.7, 1.2 Hz, 1H), 6.06 (d, J = 12.5 Hz, 1H), 5.79 (d, J = 12.5 Hz, 1H), 5.20 (d, J = 7.7 Hz, 1H), 4.39−4.29 (m, 4H), 4.14 (d, J = 16.0 Hz, 1H), 3.69 (s, 1H), 2.54 (s, 3H), 2.22 (s, 3H), 2.09 (d, J = 16.0 Hz, 1H), 1.37−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 169.3, 168.2, 162.4, 153.5, 142.4, 138.0, 135.4, 131.3, 131.0, 130.9, 130.0, 128.9, 128.8, 128.2, 127.9, 127.3, 126.9, 125.2, 124.9, 123.8, 123.5, 123.1, 122.2, 107.9, 81.9, 74.1, 62.7, 62.5, 58.5, 42.5, 21.1, 14.2, 14.1, 14.0; IR (KBr) 3381, 2974, 2925, 2853, 2360, 2341, 1704, 1655, 1613, 1541, 1490, 1467, 1445, 1377, 1358, 1297, 1229, 1093, 1035, 956, 937, 874, 856, 771, 753, 733, 694; ESI FTMS exact mass calcd for $(C_{42}H_{38}N_2O_7+Na)^+$ requires m/z 705.2577, found m/z 705.2512; Enantiomeric excess 86%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 14.70 min (major), t_R = 10.95 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 4′-methyl-1-(2-methylbenzyl)-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4daa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 57% (38.6 mg); 87:13 **4daa:4daa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −39.6 (c 0.77, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.05 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.7 Hz, 2H), 7.56−7.44 (m, 4H), 7.05 (d, J = 7.4 Hz, 1H), 7.04−6.96 (m, 2H), 6.93−6.87 (m, 1H), 6.63 (t, J = 7.5 Hz, 1H), 6.57 (d, J = 7.8 Hz, 1H), 6.34 (t, J = 7.7 Hz, 1H), 6.02 (d, J = 12.5 Hz, 1H), 5.80 (d, J = 12.5 Hz, 1H), 5.07 (d, J = 7.8 Hz, 1H), 4.44−4.28 (m, 4H), 4.07 (d, J = 16.7 Hz, 1H), 3.70 (s, 1H), 2.58 (s, 3H), 2.06 (d, J = 16.7 Hz, 1H), 1.93 (s, 3H), 1.37−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.3, 168.2, 162.5, 153.9, 142.5, 135.1, 132.9, 131.2, 131.1, 130.9, 130.1, 130.0, 128.9, 128.8, 126.9, 126.8, 125.9, 125.7, 125.3, 124.9, 123.9, 123.5, 123.2, 122.3, 107.8, 81.9, 74.1, 62.7, 62.5, 58.6, 40.3, 19.1, 14.2, 14.0, 13.9; IR (KBr) 3338, 2978, 2924, 2852, 2360, 2341, 1734, 1651, 1612, 1557, 1540, 1488, 1466, 1446, 1364, 1254, 1223, 1186, 1094, 1038, 955, 855, 802, 733, 689; ESI FTMS exact mass calcd for $(C_{42}H_{38}N_2O_7+Na)^+$ requires m/z 705.2577, found m/z 705.2527; Enantiomeric excess 86%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 14.96 min (major), t_R = 9.76 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-(4-(*tert*-butyl)-benzyl)-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4eaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 58% (41.7 mg); >95:5 **4eaa:4eaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −10.2 (c 0.83, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.08 (d, J = 8.2 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 7.54−7.43 (m, 4H), 7.16 (d, J = 8.3 Hz, 2H), 7.01−6.98 (m, 1H), 6.76 (d, J = 8.3 Hz, 2H), 6.58 (d, J = 7.4 Hz, 1H), 6.35 (td, J = 7.7, 1.2 Hz, 1H), 6.06 (d, J = 12.5 Hz, 1H), 5.78 (d, J = 12.5 Hz, 1H), 5.22 (d, J = 7.7 Hz, 1H), 4.41−4.27 (m, 4H), 4.10 (d, J = 15.9 Hz, 1H), 3.66 (s, 1H), 2.54 (s, 3H), 2.09 (d, J = 15.9 Hz, 1H), 1.36−1.32 (m, 6H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.3, 168.1, 162.4, 153.5, 150.0, 142.4, 132.5, 131.3, 131.2, 130.9, 130.1, 128.8, 128.7, 126.8, 126.5, 125.2, 125.2, 124.95, 123.5, 123.1, 122.2, 107.8, 81.9, 74.1, 62.7, 62.5, 58.5, 42.1, 34.3, 31.2, 14.2, 14.1; IR (KBr) 3363, 2963, 2360, 2341, 1734, 1652, 1612, 1541, 1516, 1488, 1467, 1363, 1261, 1181, 1095, 1019, 955, 799, 751, 732, 669; ESI FTMS exact mass calcd for $(C_{45}H_{44}N_2O_7+Na)^+$ requires m/z 747.3047, found m/z 747.3043; Enantiomeric excess 86%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 17.07 min (major), t_R = 8.96 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-(4-bromobenzyl)-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4faa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 40% (29.8 mg); >95:5 **4faa:4faa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −25.5 (c 0.58, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.57−7.44 (m, 4H), 7.14−7.09 (m, 2H), 7.01 (d, J = 6.6 Hz, 1H), 6.74 (d, J = 8.4 Hz, 2H), 6.61 (t, J = 7.5 Hz, 1H), 6.36 (t, J = 7.7, 1H), 6.06 (d, J = 12.5 Hz, 1H), 5.80 (d, J = 12.5 Hz, 1H), 5.13 (d, J = 7.1 Hz, 1H), 4.42−4.27 (m, 4H), 4.12 (d, J = 16.2 Hz, 1H), 3.66 (s, 1H), 2.53 (s, 3H), 2.09 (d, J = 16.2 Hz, 1H), 1.38−1.29 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 169.2, 162.3, 153.7, 142.0, 134.0, 132.9, 131.3, 131.0, 130.9, 129.99, 128.8, 128.7, 128.5, 128.1, 126.9, 125.2, 124.9, 123.5, 123.2, 122.4, 107.7, 81.9, 74.1, 62.7, 62.5, 58.5, 41.8, 14.2, 14.0; IR (KBr) 3363, 2963, 2360, 2341, 1734, 1652, 1612, 1541, 1516, 1488, 1467, 1363, 1261, 1181, 1095, 1019, 955, 799, 751, 732, 669; ESI FTMS exact mass calcd for $(C_{41}H_{35}BrN_2O_7+Na)^+$ requires m/z 769.1526, found m/z 769.1516; Enantiomeric excess 92%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 27.28 min (major), t_R = 14.93 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-(3-chlorobenzyl)-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4gaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 53% (37.1 mg); >95:5 **4gaa:4gaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −25.5 (c 0.74, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.10 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.55−7.52 (m, 2H), 7.50−7.44 (m, 2H), 7.12−7.06 (m, 2H), 7.03−7.01 (m, 1H), 6.79 (s, 1H), 6.69 (d, J = 7.1 Hz, 1H), 6.62 (t, J = 7.2 Hz, 1H), 6.38 (t, J = 7.7 Hz, 1H), 6.06 (d, J = 12.5 Hz, 1H), 5.80 (d, J = 12.5 Hz, 1H), 5.16 (d, J = 7.8 Hz, 1H), 4.40−4.30 (m, 4H), 4.11 (d, J = 16.2 Hz, 1H), 3.67 (s, 1H), 2.53 (s, 3H), 2.09 (d, J = 16.2 Hz, 1H), 1.38−1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 169.2, 162.0, 153.2, 147.1, 142.4, 140.1, 134.0, 131.3, 130.9, 128.8, 128.7, 128.5, 128.1, 126.9, 125.2, 124.9, 123.5, 123.2, 122.4, 107.7, 81.9, 74.1, 62.7, 62.5, 58.5, 41.8, 14.2, 14.0; IR (KBr) 3055, 3055, 2962, 2924, 2852, 2360, 2341, 1733, 1651, 1613, 1575, 1557, 1488, 1468, 1377, 1362, 1260, 1224, 1183, 1095, 1037, 954, 860, 801, 751, 733, 680, 669; ESI FTMS exact mass calcd for $(C_{41}H_{35}ClN_2O_7+Na)^+$ requires m/z 725.2031, found m/z 725.2009; Enantiomeric excess 86%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 19.75 min (major), t_R = 12.56 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-(2-chlorobenzyl)-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4haa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 49% (34.7 mg); 93:7 **4haa:4haa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −50.3 (c 0.69, $CHCl_3$);

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^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.05 (d, J = 7.8 Hz, 2H), 7.85 (d, J = 8.6 Hz, 2H), 7.53−7.43 (m, 4H), 7.21 (dd, J = 7.9, 1.0 Hz, 1H), 7.07−7.03 (m, 2H), 6.98 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 7.0 Hz, 1H), 6.62 (t, J = 7.3 Hz, 1H), 6.39 (t, J = 7.7 Hz, 1H), 6.05 (d, J = 12.5 Hz, 1H), 5.81 (d, J = 12.5 Hz, 1H), 5.20 (d, J = 7.8 Hz, 1H), 4.37−4.31 (m, 4H), 4.14 (d, J = 17.0 Hz, 1H), 2.56 (s, 3H), 1.40−1.28 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 169.3, 168.2, 162.4, 153.7, 141.9, 132.7, 132.4, 131.2, 130.9, 130.8, 129.9, 129.1, 129.0, 129.0, 128.3, 127.6, 126.9, 125.2, 124.6, 123.3, 123.2, 122.4, 107.6, 81.9, 74.2, 62.8, 62.5, 58.7, 39.8, 14.2, 14.1, 14.0; IR (KBr) 3338, 2963, 2924, 2360, 2341, 1734, 1651, 1613, 1540, 1488, 1444, 1363, 1260, 1183, 1094, 1038, 955, 860, 751, 732, 669; ESI FTMS exact mass calcd for $(C_{41}H_{35}ClN_2O_7+Na)^+$ requires m/z 725.2031, found m/z 725.2025; Enantiomeric excess 85%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 14.44 min (major), t_R = 9.99 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 4′-methyl-2-oxo-1-phenylspiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4iaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 65% (42.5 mg); 91:9 **4iaa:4iaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −23.3 (c 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.8 Hz, 2H), 7.46−7.35 (m, 4H), 7.18 (d, J = 7.4 Hz, 1H), 7.12 (d, J = 7.4 Hz, 1H), 7.03 (d, J = 7.3 Hz, 2H), 6.85 (t, J = 7.4 Hz, 1H), 6.73 (t, J = 7.4 Hz, 1H), 6.46 (d, J = 7.5 Hz, 2H), 6.00 (s, 2H), 5.87 (d, J = 7.9 Hz, 1H), 4.38−4.28 (m, 4H), 3.76 (s, 1H), 2.53 (s, 3H), 1.39−1.28 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 169.2, 168.1, 162.8, 154.2, 143.4, 133.7, 131.1, 131.0, 129.9, 129.5, 129.3, 129.2, 129.0, 128.9, 128.8, 128.7, 127.1, 126.8, 126.7, 126.1, 125.6, 125.4, 125.0, 124.9, 124.7, 123.7, 123.5, 123.0, 108.7, 81.8, 74.1, 62.8, 62.5, 59.1, 14.5, 14.0, 13.9; IR (KBr) 3340, 3056, 2963, 2926, 2853, 2359, 1734, 1650, 1611, 1594, 1525, 1499, 1466, 1367, 1324, 1260, 1205, 1095, 1033, 957, 934, 855, 801, 751, 732, 698; ESI FTMS exact mass calcd for $(C_{40}H_{34}N_2O_7+Na)^+$ requires m/z 677.2264, found m/z 677.2271; Enantiomeric excess 93%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 18.52 min (major), t_R = 13.88 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-4′,5-dimethyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4jaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 51% (35 mg); 90:10 **4jaa:4jaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −51.1 (c 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.57−7.51 (m, 2H), 7.50−7.45 (m, 2H), 7.21−6.97 (m, 4H), 6.78 (d, J = 6.5 Hz, 2H), 6.14 (d, J = 12.4 Hz, 1H), 6.04−5.94 (m, 1H), 5.73 (d, J = 12.4 Hz, 1H), 4.93 (d, J = 7.9 Hz, 1H), 4.43−4.23 (m, 5H), 3.65 (s, 1H), 2.55 (s, 3H), 2.07−1.99 (m, 4H), 1.37−1.33 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 169.3, 168.2, 168.1, 149.7, 140.7, 139.8, 139.7, 135.5, 131.5, 131.3, 130.9, 129.9, 129.0, 128.83, 128.4, 128.3, 127.0, 126.7, 125.1, 123.7, 123.5, 107.5, 81.8, 74.2, 62.7, 62.5, 58.3, 42.4, 20.8, 14.2, 14.0; IR (KBr) 3339, 2962, 2924, 2853, 2359, 1734, 1651, 1623, 1603, 1497, 1455, 1376, 1345, 1261, 1184, 1096, 1023, 863, 733, 696; ESI FTMS exact mass calcd for $(C_{42}H_{38}N_2O_7+Na)^+$ requires m/z 705.2577, found m/z 705.2546; Enantiomeric excess 98%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 15.21 min (major), t_R = 12.93 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-5,6-difluoro-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate(4kaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 59% (41.3 mg); >95:5 **4kaa:4kaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −55.2 (c 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.12 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.59−7.49 (m, 4H), 7.16−7.13 (m, 3H), 6.83 (t, J = 8.0 Hz, 1H), 6.72−6.68 (m, 2H), 6.16 (d, J = 12.5 Hz, 1H), 5.78 (d, J = 12.5 Hz, 1H), 4.40−4.30 (m, 4H), 4.20 (d, J = 16.1 Hz, 1H), 3.64 (s, 1H), 2.57 (s, 3H), 1.73 (d, J = 16.1 Hz, 1H), 1.38−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 169.2, 167.8, 161.9, 154.6, 138.4, 134.5, 131.2, 130.7, 130.3, 128.9, 128.9, 128.5, 127.4, 127.0, 126.6, 125.5, 124.7, 123.1, 113.1, 112.9, 98.2, 98.0, 81.7, 73.8, 62.9, 62.7, 58.5, 42.6, 14.2, 14.0; IR (KBr) 3348, 2961, 2922, 1754, 1655,1650, 1489, 1440, 1379, 1299, 1185, 1099, 1011, 957, 876, 800, 711, 689; ESI FTMS exact mass calcd for $(C_{41}H_{34}F_2N_2O_7+Na)^+$ requires m/z 727.2232, found m/z 727.2201; Enantiomeric excess 92%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 16.48 min (major), t_R = 9.87 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-6-bromo-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4laa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 60% (44.6 mg); >95:5 **4laa:4laa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −38.6 (c 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 8.7 Hz, 2H), 7.63−7.48 (m, 4H), 7.22−7.10 (m, 3H), 6.86 (d, J = 7.9 Hz, 1H), 6.80−6.71 (m, 3H), 6.09 (d, J = 12.4 Hz, 1H), 5.82 (d, J = 12.4 Hz, 1H), 5.35 (d, J = 1.6 Hz, 1H), 4.40−4.25 (m, 4H), 4.06 (d, J = 16.1 Hz, 1H), 3.62 (s, 1H), 2.56 (s, 3H), 1.98 (d, J = 16.1 Hz, 1H), 1.37−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 153.8, 143.3, 135.4, 135.0, 131.1, 131.0, 130.5, 129.5, 128.4, 128.2, 127.7, 126.4, 120.9, 120.4, 118.1, 116.2, 110.8, 106.9, 60.5, 51.2, 21.0, 14.2, 11.4, 8.4; IR (KBr) 3355, 2962, 2921, 1752, 1656, 1608, 1485, 1426, 1376, 1347, 1297, 1228, 1184, 1095, 1039, 956, 875, 803, 730, 689; ESI FTMS exact mass calcd for $(C_{41}H_{35}BrN_2O_7+Na)^+$ requires m/z 769.1526, found m/z 769.1506; Enantiomeric excess 95%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 21.13 min (major), t_R = 10.89 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-6-chloro-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4maa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 60% (42.3 mg); >95:5 **4maa:4maa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −69.7 (c 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H), 7.60−7.53 (m, 2H), 7.52−7.47 (m, 2H), 7.21−7.11 (m, 3H), 6.90 (d, J = 7.9 Hz, 1H), 6.78−6.74 (m, 2H), 6.55 (dd, J = 7.9, 1.7 Hz, 1H), 6.09 (d, J = 12.5 Hz, 1H), 5.80 (d, J = 12.5 Hz, 1H), 5.15 (d, J = 1.6 Hz, 1H), 4.39−4.27 (m, 4H), 4.08 (d, J = 16.1 Hz, 1H), 3.63 (s, 1H), 2.56 (s, 3H), 1.92 (d, J = 16.1 Hz, 1H), 1.36−1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.2, 168.0, 162.1, 154.1, 143.5, 134.9, 134.5, 131.2, 130.7, 130.6, 129.0, 128.9, 128.7, 128.7, 128.5, 127.3, 126.9, 126.6, 125.4, 124.7, 124.2, 123.2, 122.2, 108.6, 81.8, 73.6, 62.8, 62.6, 58.6, 42.5, 14.2, 14.0, 13.9; IR (KBr) 3337, 2962, 2922, 2851, 2359, 2340, 1736, 1715, 1651, 1575, 1540, 1472, 1371, 1347, 1261, 1227, 1177, 1073, 1037, 946, 910, 881, 842, 804, 730, 698; ESI FTMS exact mass calcd for $(C_{41}H_{35}ClN_2O_7+Na)^-$ requires m/z 725.2031, found m/z 725.1990; Enantiomeric excess 84%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 19.75 min (major), t_R = 10.58 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-4′,7-dimethyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4naa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 55% (37.8 mg); 88:12 **4naa:4naa′** colorless sticky oil; $[\alpha]_D^{20}$ = −53.1 (c 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.08 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 7.56−7.51 (m, 2H), 7.49−7.45 (m, 2H), 7.18−7.07 (m, 3H), 6.93 (d, J = 7.2 Hz, 1H), 6.69 (d, J = 7.2 Hz, 2H), 6.58 (t, J = 7.5 Hz, 1H), 6.19 (d, J = 7.6 Hz, 1H), 6.04 (d, J = 12.5 Hz, 1H), 5.79 (d, J = 12.5 Hz, 1H), 4.39−4.31 (m, 4H), 4.20 (d, J = 17.2 Hz, 1H), 3.72 (s, 1H), 2.57 (s, 3H), 2.49 (d, J = 17.2 Hz, 1H), 1.37−1.31(m, 6H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 169.3, 168.2, 162.5, 153.7, 140.4, 137.5, 132.9, 131.4, 131.3, 131.0, 131.0, 128.9, 128.7, 128.4, 126.9, 126.6, 125.3, 125.3, 124.9, 123.9, 123.5, 122.4, 121.3, 119.1, 81.8, 73.5, 62.7, 62.5, 58.8, 44.0, 17.3, 14.2,

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14.0, 13.9; IR (KBr) 3359, 2980, 2924, 2851, 1712, 1644, 1602, 1524, 1496, 1470, 1367, 1352, 1254, 1176, 1031, 957, 890, 856, 775, 730, 695; ESI FTMS exact mass calcd for $(C_{42}H_{38}N_2O_7+Na)^+$ requires m/z 705.2577, found m/z 705.2525; Enantiomeric excess 80%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 19.17 min (major), t_R = 9.45 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-7-fluoro-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4oaa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 56% (38.7 mg); 87:13 **4oaa:4oaa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −69.4 (c 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.10 (d, J = 8.2 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.54−7.45 (m, 4H), 7.15−7.11 (m, 3H), 6.88 (d, J = 7.5 Hz, 2H), 6.79 (d, J = 7.3 Hz, 1H), 6.51 (t, J = 7.9, 4.3 Hz, 1H), 6.13−6.05 (m, 2H), 5.79 (d, J = 12.5 Hz, 1H), 4.40−4.26 (m, 4H), 4.14 (d, J = 15.7 Hz, 1H), 3.66 (s, 1H), 2.55 (s, 3H), 2.50 (d, J = 15.9 Hz, 1H), 1.43−1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 169.2, 168.0, 162.2, 154.0, 136.7, 131.3, 130.8, 129.3, 129.0, 128.4, 128.2, 127.0, 126.9, 125.1, 124.4, 123.3, 123.0, 122.9, 119.1, 117.0, 116.9, 81.8, 74.1, 62.7, 62.6, 58.6, 44.1, 14.2, 14.0, 13.9; IR (KBr) 3345, 2963, 2925, 2360, 1742, 1714, 1647, 1557, 1541, 1488, 1474, 1344, 1260, 1182, 1027, 858, 803, 730, 668; ESI FTMS exact mass calcd for $(C_{41}H_{35}FN_2O_7+Na)^+$ requires m/z 709.2326, found m/z 709.2328; Enantiomeric excess 92%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 20.89 min (major), t_R = 9.80 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-diethyl 1-benzyl-4′-methyl-2-oxo-7-(trifluoromethyl)spiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4paa). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 59% (43.5 mg); >95:5 **4paa:4paa′**; colorless sticky oil; $[\alpha]_D^{20}$ = −53.1 (c 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.08−8.05 (m, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.54−7.42 (m, 4H), 7.32 (dd, J = 7.2, 0.9 Hz, 1H), 7.22−7.09 (m, 3H), 7.02−6.96 (m, 1H), 6.86−6.82 (m, 3H), 6.09 (d, J = 12.6 Hz, 1H), 5.85 (d, J = 12.6 Hz, 1H), 4.46−4.23 (m, 5H), 3.72 (s, 1H), 3.51 (d, J = 17.2 Hz, 1H), 2.52 (s, 3H), 1.36−1.28 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 169.1, 167.8, 162.3, 154.7, 136.2, 133.6, 131.3, 130.9, 130.5, 129.5, 129.0, 128.0, 127.2, 126.7, 126.4, 125.4, 124.9, 124.2, 123.2, 122.1, 81.7, 72.1, 62.8, 62.6, 59.3, 45.4, 14.4, 14.0, 13.9; IR (KBr) 3337, 2963, 2924, 2852, 2360, 2341, 1733, 1651, 1595, 1540, 1455, 1336, 1261, 1159, 1095, 1019, 800, 731, 694; ESI FTMS exact mass calcd for $(C_{42}H_{35}F_3N_2O_7+Na)^+$ requires m/z 759.2294, found m/z 759.2254; Enantiomeric excess 91%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 14.57 min (major), t_R = 7.11 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-dimethyl 1-benzyl-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4aba). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 50% (32.2 mg); 91:9 **4aba:4aba′**; colorless sticky oil; $[\alpha]_D^{20}$ = −35.8 (c 0.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 7.56−7.50 (m, 2H), 7.49−7.44 (m, 2H), 7.20−7.09 (m, 3H), 6.99 (d, J = 7.3 Hz, 1H), 6.83−6.76 (m, 2H), 6.60 (t, J = 7.5 Hz, 1H), 6.36−6.32 (m, 1H), 6.07 (d, J = 12.5 Hz, 1H), 5.79 (d, J = 12.5 Hz, 1H), 5.17 (d, J = 7.8 Hz, 1H), 4.18 (d, J = 16.1 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.67 (s, 1H), 2.52 (s, 3H), 2.09 (d, J = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.8, 168.7, 162.3, 153.2, 142.3, 135.4, 131.3, 130.9, 129.8, 128.9, 128.9, 128.8, 128.3, 127.1, 126.9, 126.7, 125.2, 124.9, 123.5, 123.1, 122.3, 107.9, 81.8, 74.2, 58.6, 53.5, 42.4, 14.1; IR (KBr) 3352, 2962, 2924, 2852, 2359, 2340, 1739, 1651, 1613, 1540, 1468, 1434, 1361, 1261, 1096, 1023, 870, 801, 732, 694; ESI FTMS exact mass calcd for $(C_{39}H_{32}N_2O_7+Na)^+$ requires m/z 663.2108, found m/z 663.2092; Enantiomeric excess 92%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 28.47 min (major), t_R = 15.60 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-dimethyl 4′-methyl-2-oxo-1-phenylspiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4iba). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 59% (36.9 mg); >95:5 **4iba:4iba′**; colorless sticky oil; $[\alpha]_D^{20}$ = −16.5 (c 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 7.47−7.41 (m, 2H), 7.41−7.34 (m, 2H), 7.17 (dd, J = 7.4, 0.9 Hz, 1H), 7.13−7.11 (m, 1H), 7.05 (t, J = 7.6 Hz, 2H), 6.85 (td, J = 7.5, 0.8 Hz, 1H), 6.74 (td, J = 7.7, 1.3 Hz, 1H), 6.51−6.45 (m, 2H), 6.00 (s, 2H), 5.88 (d, J = 7.8 Hz, 1H), 3.90 (s, 3H), 3.85 (s, 3H), 3.74 (s, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 169.7, 168.7, 162.8, 153.8, 143.4, 133.6, 131.2, 131.1, 131.0, 129.7, 129.3, 129.1, 128.8, 128.8, 127.0, 126.9, 125.4, 124.9, 124.6, 123.7, 123.5, 123.0, 108.8, 81.7, 74.1, 59.1, 53.6, 53.4, 14.4; IR (KBr) 3344, 2961, 2923, 2852, 2360, 2341, 1740, 1650, 1612, 1540, 1498, 1465, 1434, 1371, 1326, 1261, 1098, 1026, 935, 888, 801, 752, 733, 698; ESI FTMS exact mass calcd for $(C_{38}H_{30}N_2O_7+Na)^+$ requires m/z 649.1951, found m/z 649.1977; Enantiomeric excess 92%, determined by HPLC (Daicel Chirapak IA, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 22.83 min (major), t_R = 17.93 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-dimethyl 1-benzyl-6-bromo-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4lba). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 46% (33.3 mg); 90:10 **4lba:4lba′**; colorless sticky oil; $[\alpha]_D^{20}$ = −28.7 (c 0.67, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.12 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.59−7.54 (m, 2H), 7.53−7.48 (m, 2H), 7.21−7.10 (m, 3H), 6.85 (d, J = 7.9 Hz, 1H), 6.80−6.73 (m, 3H), 6.09 (d, J = 12.5 Hz, 1H), 5.82 (d, J = 12.4 Hz, 1H), 5.36 (d, J = 1.6 Hz, 1H), 4.06 (d, J = 16.1 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.61 (s, 1H), 2.54 (s, 3H), 1.99 (d, J = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 169.7, 168.5, 162.0, 153.8, 143.7, 134.8, 131.2, 130.7, 130.7, 129.1, 129.0, 129.0, 128.5, 127.3, 127.0, 126.6, 125.5, 125.2, 124.6, 124.6, 123.1, 122.8, 111.4, 81.7, 73.7, 58.6, 53.6, 53.5, 42.5, 14.1; IR (KBr) 3342, 2962, 2923, 2851, 2360, 2341, 1740, 1653, 1604, 1541, 1486, 1435, 1372, 1338, 1261, 1180, 1098, 1022, 955, 873, 801, 732, 696; ESI FTMS exact mass calcd for $(C_{39}H_{31}BrN_2O_7+Na)^+$ requires m/z 741.1213, found m/z 741.1193; Enantiomeric excess 95%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 28.56 min (major), t_R = 14.56 min (minor).

(*R*)-3′-(Anthracen-9-ylmethyl) 5′,5′-dimethyl 1-benzyl-7-fluoro-4′-methyl-2-oxospiro[indoline-3,2′-pyrrole]-3′,5′,5′(1′*H*)-tricarboxylate (4oba). (Flash column chromatography eluent followed by preparative thin layer chromatography, petroleum ether/ethyl acetate = 10/1); Reaction time = 48 h; yield 52% (34.0 mg); 92:8 **4oba:4oba′**; colorless sticky oil; $[\alpha]_D^{20}$ = −17.8 (c 0.68, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.10 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.58−7.43 (m, 4H), 7.17−7.09 (m, 3H), 6.87 (d, J = 6.6 Hz, 2H), 6.78 (dd, J = 7.4, 0.8 Hz, 1H), 6.55−6.50 (m, 1H), 6.15−6.02 (m, 2H), 5.79 (d, J = 12.5 Hz, 1H), 4.13 (d, J = 15.7 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.65 (s, 1H), 2.53−2.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 169.6, 168.5, 162.0, 153.6, 145.0, 136.7, 132.9, 131.3, 131.0, 130.8, 129.3, 129.0, 128.9, 128.2, 127.0, 126.9, 126.8, 125.1, 124.4, 123.2, 123.1, 123.0, 119.2, 119.1, 117.2, 117.0, 81.7, 74.2, 58.7, 53.5, 44.1, 44.0, 14.1; IR (KBr) 3343, 2962, 2924, 2851, 2360, 2341, 1736, 1646, 1616, 1541, 1488, 1473, 1435, 1347, 1261, 1180, 1096, 1022, 867, 801, 731, 693, 669; ESI FTMS exact mass calcd for $(C_{39}H_{31}FN_2O_7+Na)^+$ requires m/z 681.2013, found m/z 681.2053; Enantiomeric excess 95%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 27.56 min (major), t_R = 12.32 min (minor).

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■ ASSOCIATED CONTENT

Supporting Information

Characterization data (including ^{1}H, ^{13}C NMR and HPLC spectra) for all products **4**, crystal data of compound **4aaa** and crude ^{1}H NMR spectrum of compound **4aaa′**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(14) CCDC 1031911 for compound **4aaa**. See the Supporting Information for details.