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Diastereoselective and Enantioselective Desymmetrization of α-Substituted Cyclohexadienones via Intramolecular Stetter Reaction

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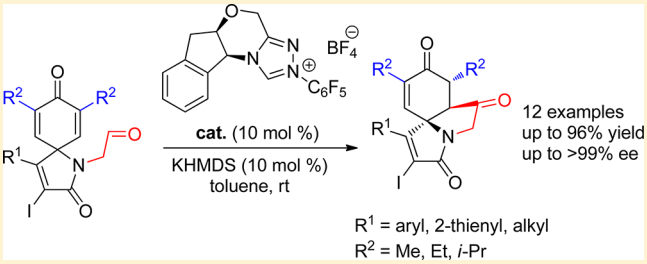
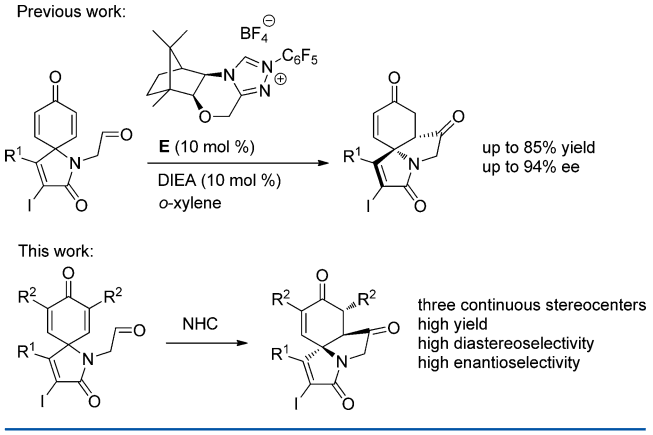
Supporting Information

ABSTRACT: Highly diastereoselective and enantioselective desymmetrization of α-substituted cyclohexadienones via NHC-catalyzed intramolecular Stetter reaction was realized. Amino-indanol derived triazolium salt bearing a C_6F_5 group was found to be the optimal catalyst precursor in the intramolecular Stetter reaction furnishing tricyclic products bearing multi-stereocenters in up to 96% yield and >99% ee.



N-Heterocyclic carbenes (NHCs) as organocatalysts have witnessed rapid development since the first isolation of stable carbene in 1991.[1] Reversing the reactivity (umpolung) of aldehyde functionality opens a new area for organic chemists.[2] The Stetter reaction is a powerful tool that takes advantage of umpolung reactivity of aldehyde, in which aldehyde adds to a Michael acceptor to construct a bisfunctionalized backbone.[3] When an α-substituent is introduced in the Michael acceptor, an additional stereocenter will be generated.[4] To our knowledge, NHC-catalyzed diastereoselective Stetter reactions from enantioselective protonation have been rarely explored.[5−8] Rovis et al. reported the first highly diastereoselective and enantioselective Stetter reaction in 2005 by introducing an α-substituent.[5] In 2006 Rovis et al. reported another highly diastereoselective and enantioselective Stetter type desymmetrization of cyclohexadienones to afford the bicyclic compounds.[6,7] The same group also reported the intermolecular Stetter reaction in good to excellent yields, enantioselectivity and diastereoselectivity in 2009 with glyoxamide as substrate.[8] On the basis of these elegant works and our interest in NHC-catalyzed desymmetrization of cyclohexadienones, we recently reported the enantioselective desymmetrization of cyclohexadienones via D-camphor-derived triazolium salts catalyzed intramolecular Stetter reaction to construct novel tricyclic structures.[9,10] However, α-methyl substituted cyclohexadienone aldehyde reacted poorly under the standard conditions. After extensive efforts toward catalyst screening, amino-indanol derived NHC was found to be highly efficient for this type of substrate (Scheme 1). Herein, we report our detailed results on this subject.

Scheme 1. Diastereoselective and Enantioselective Desymmetrization of Cyclohexadienones



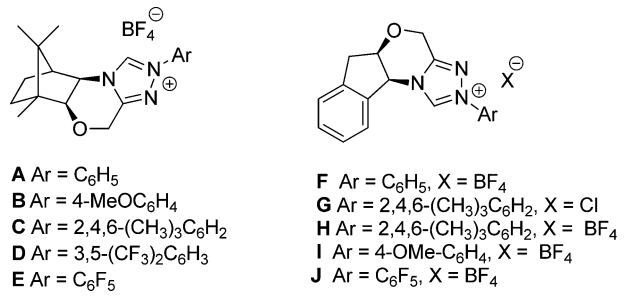


Figure 1. Several readily available chiral NHC precursors.

To begin our study, dimethyl substituted cyclohexadienone **1a** was used as a model substrate under NHC catalysis to optimize the reaction conditions. Several readily available chiral NHC precursors (Figure 1) were examined in the desymmetrization of cyclohexadienone **1a** via an intramolecular Stetter reaction. The results are summarized in Table 1. With 10 mol % of triazolium salt **E** bearing a C_6F_5 group and 10 mol % of DIEA in *o*-xylene, the desired intramolecular Stetter reaction

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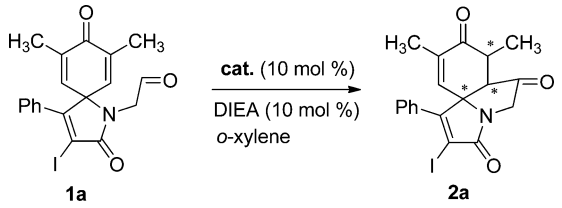
Table 1. Screening of the Chiral NHC Catalysts[a]



entry	catalyst	yield (%)	ee (%)[b]
1	**A**	NR	
2	**B**	NR	
3	**C**	NR	
4	**D**	trace	
5	**E**	9	−99
6	**F**	NR	
7	**G**	NR	
8	**H**	NR	
9	**I**	NR	
10	**J**	72	>99

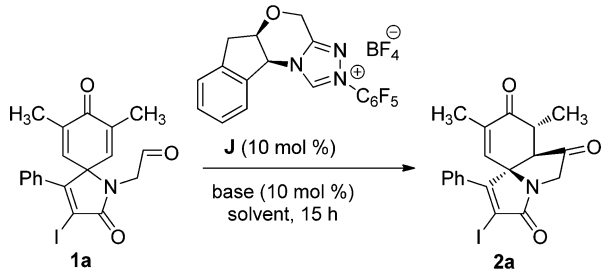
[a]Reaction conditions: **1a** (0.1 mmol), 10 mol % of catalyst, 10 mol % of DIEA in *o*-xylene (1.0 mL) at room temperature. [b]Determined by HPLC.

proceeded sluggishly affording the desymmetrization product **2a** with 99% ee but in only 9% yield (entry 5, Table 1).[10] However, other camphor-derived triazolium salts **A**–**D**[11] were found almost ineffective in this intramolecular Stetter reaction (entries 1–4, Table 1). Then, amino-indanol derived triazolium salts **F**–**J**[12] were screened under otherwise identical conditions. To our great delight, with 10 mol % amino-indanol derived triazolium salt **J** bearing a C_6F_5 group, the desired intramolecular Stetter reaction proceeded smoothly affording desymmetrization product **2a** in 72% yield with >99% ee (entry 10, Table 1). However, other substituted amino-indanol derived triazolium salts **F**–**I** failed to catalyze the reaction.

Other reaction parameters were further examined with 10 mol % of triazolium salt **J** as the optimal catalyst precursor. The results are summarized in Table 2. Various solvents were first examined in the model reaction. All tested solvents such as toluene, CH_2Cl_2, $CHCl_3$, and dioxane were well tolerated, affording the desired product with excellent ee, although reaction activity varied slightly (entries 1–6, Table 2). Reaction in *o*-xylene and toluene gave the highest ees. Compared with *o*-xylene, reaction in toluene was much faster, and the reaction proceeded to completion in 15 h (82% yield, 99% ee, entry 2, Table 2). With toluene as the optimal solvent, several bases such as DBU, Et_3N, Cs_2CO_3, and KHMDS were further examined (entries 7–10, Table 2). All bases screened gave excellent ees, and the reaction with KHMDS (0.5 M in toluene) led to an elevated yield and excellent enantioselectivity (92% yield, >99% ee, entry 10, Table 2). The substrate concentration of reaction was further optimized (entries 11–13, Table 2). When the substrate concentration was 0.05 mol/L, slightly higher yield (95%) was obtained. The catalyst loading could be reduced to 5 mol % (85% yield, >99% ee, entry 14, Table 2).

To investigate the generality of the reaction, various substrates were tested under the optimized conditions [10 mol % of **J**, 10 mol % of KHMDS (0.5 M in toluene), 0.05 M of substrate in toluene, rt, 15 h]. The results are summarized in Table 3. For substrates bearing a tolyl group (R^1), the position of methyl substituent had almost no influence on the

Table 2. Optimization of the Reaction Conditions[a]



entry	base	solvent	concentration (mol/L)	yield (%)	ee (%)[b]
1[c]	DIEA	*o*-xylene	0.1	72	>99
2	DIEA	toluene	0.1	82	>99
3	DIEA	CH_2Cl_2	0.1	71	95
4	DIEA	$CHCl_3$	0.1	86	91
5	DIEA	THF	0.1	55	99
6	DIEA	dioxane	0.1	59	99
7	DBU	toluene	0.1	54	>99
8	Et_3N	toluene	0.1	55	>99
9	Cs_2CO_3	toluene	0.1	70	>99
10	KHMDS	toluene	0.1	92	>99
11	KHMDS	toluene	0.2	88	>99
12	KHMDS	toluene	0.05	95	>99
13	KHMDS	toluene	0.025	80	>99
14[d]	KHMDS	toluene	0.1	85	>99

[a]Reaction conditions: **1** (0.1 mmol), 10 mol % of **J**, 10 mol % of KHMDS (0.5 M in toluene) in solvent (1.0 mL) at room temperature. KHMDS = potassium bis(trimethylsilyl)amide. [b]Determined by HPLC. [c]Reaction time: 72 h. [d]With 5 mol % of **J** and 5 mol % of KHMDS.

Table 3. NHC-Catalyzed Desymmetrization of Cyclohexadienones via Intramolecular Stetter Reaction[a]

entry	R^1	R^2	product	yield (%)	ee (%)[b]
1	Ph	Me	**2a**	95	>99
2	4-Me-C_6H_4	Me	**2b**	90	99
3[c]	3-Me-C_6H_4	Me	**2c**	85	98
4[c,d]	2-Me-C_6H_4	Me	**2d**	80	98/87
5	4-F-C_6H_4	Me	**2e**	86	98
6	4-Cl-C_6H_4	Me	**2f**	86	99
7	2-thienyl	Me	**2g**	91	99
8[e]	Me	Me	**2h**	90	87
9	*n*-Pr	Me	**2i**	96	>99
10	cyclopropyl	Me	**2j**	92	98
11	Ph	Et	**2k**	96	99
12[f]	Ph	*i*-Pr	**2l**	70	>99

[a]Reaction conditions: **1** (0.2 mmol), 10 mol % of **J**, 10 mol % of KHMDS (0.5 M in toluene) in toluene (4.0 mL) at room temperature, unless noted otherwise. [b]Determined by HPLC. [c]Reaction time: 40 h. [d]dr: 5/1. [e]dr: 10/1. [f]Reaction time: 60 h. Concentration: 0.02 mol/L. Intermolecular benzoin product **2l′** was observed.

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enantioselectivity, and products **2b−d** were obtained in excellent yields and ee (80−90% yields, 98−99% ee, entries 2−4, Table 3). It should be noted that substrate **1d** bearing a 2-Me-C_6H_4 group resulted in a product with 5/1 dr originated from an observed atropisomer. Electron-withdrawing groups such as F or Cl were tolerated in this reaction, and only one diastereomer was observed in both cases by ^{1}H NMR analysis. When 4-F-C_6H_4 group was introduced, the corresponding product **2e** was obtained in 86% yield and 98% ee (entry 5, Table 3). The substrate bearing 4-Cl-C_6H_4 group also led to the desired product **2f** in good yield with excellent ee (86% yield, 99% ee, entry 6, Table 3). Moreover, heteroaryl group was also well tolerated. The reaction of 2-thienyl bearing substrate provided the desired tricyclic product **2g** in 91% yield with 99% ee (entry 7, Table 3). Various alkyl substituents such as methyl, *n*-propyl, cyclopropyl were also demonstrated as suitable substrates (entries 8−10, Table 3). When methyl group was introduced, a dr value of 10/1 was observed by ^{1}H NMR analysis (90% yield, 87% ee, entry 8, Table 3). *n*-Propyl, cyclopropyl substituted substrates led to the products with excellent yields and ee (92−96% yields, 98 to >99% ee, entry 9−10, Table 3). Other substrates bearing Et or *i*-Pr at the α-position of the ketone were also investigated. The reaction of substrate **1k** bearing an ethyl group ran smoothly affording product in high yield with excellent ee (96% yield, 99% ee, entry 11, Table 3). When *i*-Pr bearing substrate **1l** was used, the reaction proceeded with excellent ee albeit slightly lower yield because of intermolecular benzoin reaction. The intermolecular benzoin condensation could be suppressed by running the reaction with a lower substrate concentration (70% yield, >99% ee, entry 12, Table 3). The absolute configuration of the product was determined by a single crystal X-ray analysis of enantiopure **2a** as (6a*R*,7*R*,10a*S*).[13]

A postulated model of transition state is depicted in Figure 2. The exceptional enantioselectivity is rationalized by avoiding the steric collision with amino-indanol backbone in the favored transition state.

In summary, highly diastereoselective and enantioselective desymmetrization of cyclohexadienones via NHC-catalyzed intramolecular Stetter reaction was realized. Amino-indanol derived triazolium salt **J** bearing a C_6F_5 group was found to be the optimal catalyst precursor for the intramolecular Stetter reaction (up to 96% yield, >99% ee). Highly enantioenriched functionalized tricyclic structures containing a quaternary stereogenic center and three contiguous stereocenters could be formed efficiently in one step under mild reaction conditions.

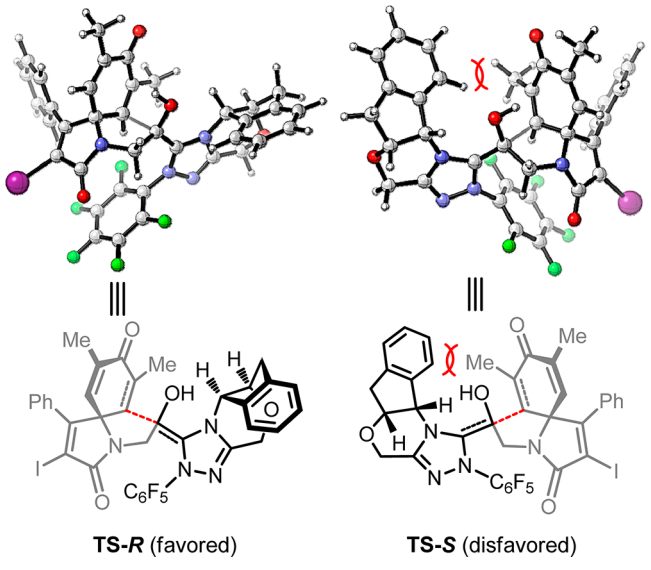

Figure 2. Postulated model of transition states.

EXPERIMENTAL SECTION

General Methods. Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a 300 or 400 MHz spectrometer and internally referenced to tetramethylsilane signal or residual protic solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Substrates **1a−l**[10] were synthesized according to reported procedure.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-trien-1-yl)acetaldehyde (1a). White solid, 920 mg, 47% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (4.5 mmol scale): mp 214−216 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.41−7.34 (m, 3H), 7.27−7.22 (m, 2H), 6.33 (s, 2H), 4.13 (s, 2H), 1.86 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 185.0, 167.5, 160.4, 140.2, 137.7, 132.0, 130.0, 128.5, 127.5, 96.0, 70.6, 50.5, 16.0; IR (thin film) ν_{max} (cm^{-1}) = 2920, 2838, 1729, 1692, 1668, 1638, 1388, 1037, 913, 756, 699; MS (ESI-TOF) 434 ([M + H]$^+$); HRMS (MALDI-TOF) mass calcd. for $C_{19}H_{17}INO_3$ ([M + H]$^+$) 434.0248, found 434.0255.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-(*p*-tolyl)-1-azaspiro[4.5]-deca-3,6,9-trien-1-yl)acetaldehyde (1b). White solid, 244 mg, 21% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (2.6 mmol scale): mp 204−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 7.16 (d, J = 3.9 Hz, 4H), 6.34 (s, 2H), 4.12 (s, 2H), 2.35 (s, 3H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 185.1, 167.5, 160.3, 140.1, 139.9, 137.9, 129.2, 128.9, 127.3, 95.4, 70.5, 50.4, 21.3, 16.0; IR (thin film) ν_{max} (cm^{-1}) = 2925, 2833, 1732, 1692, 1640, 1384, 1346, 823, 760; MS (ESI-TOF) 448 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0395.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-(*m*-tolyl)-1-azaspiro-[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1c). White solid, 661 mg, 48% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (3.1 mmol scale): mp 203−205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.26−7.19 (m, 2H), 7.07−7.00 (m, 2H), 6.34 (s, 2H), 4.14 (s, 2H), 2.34 (s, 3H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 185.0, 167.5, 160.6, 140.0, 138.1, 137.7, 131.9, 130.6, 128.3, 128.1, 124.5, 95.7, 70.6, 50.4, 21.3, 15.9; IR (thin film) ν_{max} (cm^{-1}) = 2921, 1733, 1691, 1643, 1602, 1383, 1218, 1161, 805, 757, 706; MS (ESI-TOF) 448 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0394.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-(*o*-tolyl)-1-azaspiro[4.5]-deca-3,6,9-trien-1-yl)acetaldehyde (1d). White solid, 837 mg, 41% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (4.6 mmol scale): mp 177−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.32−7.18 (m, 2H), 7.17−7.09 (m, 1H), 6.82 (d, J = 7.2 Hz, 1H), 6.45 (q, J = 1.6 Hz, 1H), 6.37 (q, J = 1.6 Hz, 1H), 4.20 (s, 2H), 2.23 (s, 3H), 1.88 (d, J = 1.6 Hz, 3H), 1.75 (d, J = 1.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 184.7, 167.2, 161.8, 140.4, 139.5, 137.3, 137.2, 135.4, 130.7, 130.5, 129.5, 127.8, 125.1, 104.9, 97.9, 72.2, 50.9, 19.8, 15.86, 15.84; IR (thin film) ν_{max} (cm^{-1}) = 2925, 1734, 1701, 1671, 1642, 1378, 1339, 1299, 1017, 841, 801, 754; MS (ESI-TOF) 448 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0402.

2-(4-(4-Fluorophenyl)-3-iodo-7,9-dimethyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1e). White solid, 356 mg, 33% overall yield in four steps starting from 5-iodo-2-

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methoxy-1,3-dimethylbenzene (2.4 mmol scale): mp 173−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.32−7.22 (m, 2H), 7.12−6.97 (m, 2H), 6.34 (s, 2H), 4.14 (s, 2H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 184.9, 167.3, 163.3 (d, J = 249.9 Hz), 159.3, 140.2, 137.6, 129.6 (d, J = 8.5 Hz), 127.9 (d, J = 3.4 Hz), 115.9 (d, J = 21.7 Hz), 96.5, 70.6, 50.5, 16.0; IR (thin film) ν_{max} (cm^{-1}) = 2936, 2831, 1733, 1693, 1641, 1601, 1503, 1383, 1233, 1158, 840, 802, 760, 690; MS (ESI-TOF) 452 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{19}H_{16}FINO_3$ ([M + H]$^+$) 452.0153, found 452.0152.

2-(4-(4-Chlorophenyl)-3-iodo-7,9-dimethyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1f). White solid, 260 mg, 23% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (2.4 mmol scale): mp 184−186 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 6.37 (s, 2H), 4.16 (s, 2H), 1.86 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.3, 184.7, 167.0, 159.0, 140.1, 137.3, 135.8, 130.2, 128.8, 96.6, 70.3, 50.3, 15.9. IR (thin film) ν_{max} (cm^{-1}) = 2926, 1683, 1602, 1392, 1215, 1155, 743, 692; MS (ESI-TOF) 468 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{19}H_{16}ClINO_3$ ([M + H]$^+$) 467.9858, found 467.9858.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-(thiophen-2-yl)-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1g). Pale yellow solid, 130 mg, 13% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (2.3 mmol scale): mp 201−203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.75 (dd, J = 4.0, 1.2 Hz, 1H), 7.53 (dd, J = 4.8, 0.8 Hz, 1H), 7.12 (dd, J = 4.8, 3.6 Hz, 1H), 6.34 (s, 2H), 4.10 (s, 2H), 1.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 185.3, 167.7, 151.4, 140.3, 138.8, 132.5, 130.1, 129.7, 127.5, 91.3, 69.5, 49.9, 16.10, 16.08; IR (thin film) ν_{max} (cm^{-1}) = 2924, 1734, 1688, 1634, 1599, 1387, 1345, 796, 729; MS (ESI-TOF) 440 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{17}H_{15}INO_3S$ ([M + H]$^+$) 439.9812, found 439.9801.

2-(3-Iodo-4,7,9-trimethyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1h). White solid, 530 mg, 37% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (3.9 mmol scale): mp 173−175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 6.21 (s, 2H), 4.10 (s, 2H), 1.94 (s, 6H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 185.1, 167.4, 159.1, 140.1, 138.2, 93.9, 70.3, 50.5, 16.0, 15.5; IR (thin film) ν_{max} (cm^{-1}) = 2888, 1741, 1686, 1637, 1490, 1391, 1159, 748, 691; MS (ESI-TOF) 372 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{14}H_{14}INO_3$ ([M + H]$^+$) 372.0091, found 372.0081.

2-(3-Iodo-7,9-dimethyl-2,8-dioxo-4-propyl-1-azaspiro[4.5]-deca-3,6,9-trien-1-yl)acetaldehyde (1i). White solid, 250 mg, 28% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (2.2 mmol scale): mp 177−179 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.46 (s, 1H), 6.13 (s, 2H), 4.02 (s, 2H), 2.12−1.98 (m, 2H), 1.86 (s, 6H), 1.50−1.35 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.7, 185.1, 167.4, 162.1, 139.8, 138.1, 94.2, 70.5, 50.4, 31.4, 21.6, 15.9, 14.1; IR (thin film) ν_{max} (cm^{-1}) = 2926, 1734, 1692, 1642, 1383, 804, 758, 690; MS (ESI-TOF) 400 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{16}H_{19}INO_3$ ([M + H]$^+$) 400.0404, found 400.0398.

2-(4-Cyclopropyl-3-iodo-7,9-dimethyl-2,8-dioxo-1-azaspiro-[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1j). White solid, 305 mg, 28% overall yield in four steps starting from 5-iodo-2-methoxy-1,3-dimethylbenzene (2.7 mmol scale): mp 181−183 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (s, 1H), 6.25 (s, 2H), 4.05 (s, 2H), 1.94 (s, 6H), 1.42−1.21 (m, 3H), 1.02−0.86 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.7, 185.4, 167.7, 161.1, 139.8, 138.6, 87.1, 70.8, 50.1, 16.0, 11.9, 7.8; IR (thin film) ν_{max} (cm^{-1}) = 2831, 2719, 1734, 1689, 1637, 1600, 1406, 1387, 830, 756, 682; MS (ESI-TOF) 398 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{16}H_{17}INO_3$ ([M + H]$^+$) 398.0248, found 398.0240.

2-(7,9-Diethyl-3-iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-trien-1-yl)acetaldehyde (1k). White solid, 700 mg, 41% overall yield in four steps starting from 1,3-diethyl-5-iodo-2-methoxybenzene (3.7 mmol scale): mp 203−205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.45−7.30 (m, 3H), 7.22 (d, J = 7.2 Hz, 2H), 6.27 (s, 2H), 4.13 (s, 2H), 2.41−2.13 (m, 4H), 0.96 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 184.1, 167.5, 160.8, 145.6, 136.0, 132.1, 129.9, 128.4, 127.5, 95.8, 70.7, 50.5, 22.3, 12.2; IR (thin film) ν_{max} (cm^{-1}) = 2970, 2856, 1729, 1702, 1668, 1639, 1458, 1375, 834, 752, 703; MS (ESI-TOF) 462 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{21}H_{21}INO_3$ ([M + H]$^+$) 462.0561, found 462.0553.

2-(3-Iodo-7,9-diisopropyl-2,8-dioxo-4-phenyl-1-azaspiro-[4.5]deca-3,6,9-trien-1-yl)acetaldehyde (1l). White solid, 630 mg, 39% overall yield in four steps starting from 5-iodo-1,3-diisopropyl-2-methoxybenzene (3.3 mmol scale): mp 179−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 7.42−7.30 (m, 3H), 7.22−7.17 (m, 2H), 6.24 (s, 2H), 4.11 (s, 2H), 2.91 (q, J = 6.8 Hz, 2H), 1.00 (t, J = 6.4 Hz, 6H), 0.91 (t, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 183.1, 167.5, 160.9, 150.1, 134.4, 132.0, 129.8, 128.3, 127.5, 95.6, 70.5, 50.4, 26.6, 21.6, 21.3; IR (thin film) ν_{max} (cm^{-1}) = 2970, 2838, 1739, 1701, 1664, 1640, 1464, 1394, 1374, 1248, 828, 702; MS (ESI-TOF) 490 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{23}H_{25}INO_3$ ([M + H]$^+$) 490.0874, found 490.0864.

General Procedure for Intramolecular Stetter Reaction. A flame-dried Schlenk tube was cooled to room temperature and filled with argon. To this flask were added triazolium salt **J** (9.4 mg, 0.02 mmol, 10 mol %), toluene (4.0 mL), KHMDS (0.5 M in toluene) (40.0 μL, 0.02 mmol, 10 mol %). The reaction mixture was stirred at 25 °C for 30 min. The aldehyde substrate (0.2 mmol) was then added. The reaction mixture was stirred at room temperature for 15 h unless noted otherwise. All the volatiles were removed under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (eluent:ethyl acetate/petroleum ether = 1/4) to afford the product.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-phenyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2a). White solid, 82.0 mg, 95% yield, >99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 26.7 min, t (major) = 34.4 min]: $[\alpha]_D^{20}$ = −37.5 (c = 0.2, $CHCl_3$); mp 215−217 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.35 (m, 3H), 7.28−7.20 (m, 2H), 6.49 (s, 1H), 4.49 (AB, J_{AB} = 19.2 Hz, 1H), 3.64 (AB, J_{BA} = 19.2 Hz, 1H), 3.08 (q, J = 7.8 Hz, 1H), 2.52 (s, 1H), 1.91 (s, 3H), 0.41 (d, J = 8.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.4, 196.6, 169.4, 165.1, 140.5, 137.5, 133.4, 130.2, 129.0, 127.8, 98.4, 73.7, 57.6, 49.8, 37.9, 17.7, 16.7; IR (thin film) ν_{max} (cm^{-1}) = 2925, 2853, 1768, 1703, 1680, 1362, 1007, 846, 797, 752, 693; MS (ESI-TOF) 434 ([M + H]$^+$); HRMS (MALDI-TOF) calcd. for $C_{19}H_{17}INO_3$ ([M + H]$^+$) 434.0248, found 434.0256.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-(*p*-tolyl)-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2b). White solid, 80.3 mg, 90% yield, 99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 25.1 min, t (major) = 33.5 min]: $[\alpha]_D^{20}$ = −18.1 (c = 0.2, $CHCl_3$); mp >240 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 6.49 (s, 1H), 4.48 (AB, J_{AB} = 18.9 Hz, 1H), 3.62 (AB, J_{BA} = 18.9 Hz, 1H), 3.07 (q, J = 7.8 Hz, 1H), 2.53 (s, 1H), 2.39 (s, 3H), 1.90 (s, 3H), 0.44 (d, J = 8.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.6, 196.7, 169.5, 165.2, 140.4, 137.6, 130.3, 129.6, 127.7, 97.8, 73.6, 57.6, 49.8, 37.9, 21.3, 17.8, 16.6; IR (thin film) ν_{max} (cm^{-1}) = 2926, 1765, 1700, 1679, 1371, 824, 747, 703; MS (ESI-TOF) 448 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0391.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-(*m*-tolyl)-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2c). White solid, 76.2 mg, 85% yield, 98% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 23.3 min, t (major) = 31.0 min]: $[\alpha]_D^{20}$ = −54.9 (c = 0.2, $CHCl_3$); mp 234−235 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.17 (m, 2H), 7.05−7.02 (m, 2H), 6.50−6.45 (m, 1H), 4.48 (dd, J = 19.2, 1.2 Hz, 1H), 3.63 (d, J = 19.2 Hz, 1H), 3.07 (qd, J = 8.0, 1.2 Hz, 1H), 2.52 (d, J = 1.2 Hz, 1H), 2.37 (s, 3H), 1.90 (d, J = 1.6 Hz, 3H), 0.43 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5, 196.6, 169.5, 165.2, 140.4, 138.7, 137.6, 133.2, 130.8, 128.8, 128.4, 124.9, 97.9, 73.6, 57.5, 49.8, 37.9, 21.4, 17.6, 16.6; IR (thin film) ν_{max} (cm^{-1}) = 2957, 2919, 1761, 1716, 1663, 1348, 798, 758, 696; MS (ESI-TOF) 448 ([M +

H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0404.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-(*o*-tolyl)-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2d). White solid, 71.2 mg, 80% yield, 98% ee (major diastereomer)/87% ee (minor diastereomer) [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, major diastereomer t (minor) = 22.1 min, t (major) = 29.9 min; minor diastereomer t (minor) = 28.0 min, t (major) = 33.1 min]: $[\alpha]_D^{20}$ = −51.2 (c = 0.2, $CHCl_3$); mp >240 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.29 (m, 2H), 7.25−7.20 (m, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.42 (s, 1H), 4.48 (AB, J_{AB} = 19.2 Hz, 1H), 3.64 (AB, J_{BA} = 19.2 Hz, 1H), 3.10 (q, J = 8.0 Hz, 1H), 2.60 (s, 1H), 2.34 (s, 3H), 1.85 (s, 3H), 0.51 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 196.6, 168.8, 165.1, 139.9, 138.0, 135.7, 132.4, 131.1, 129.8, 126.9, 125.8, 100.8, 74.4, 56.6, 49.6, 38.1, 20.3, 16.9, 16.6; IR (thin film) ν_{max} (cm^{-1}) = 2925, 1759, 1678, 1453, 1373, 852, 758, 734; MS (ESI-TOF) 448 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{20}H_{19}INO_3$ ([M + H]$^+$) 448.0404, found 448.0378.

(6a*R*,7*R*,10a*S*)-1-(4-Fluorophenyl)-2-iodo-7,9-dimethyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2e). White solid, 77.4 mg, 86% yield, 98% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 21.3 min, t (major) = 26.6 min]: $[\alpha]_D^{20}$ = −43.2 (c = 0.2, $CHCl_3$); mp 235−237 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.22 (m, 2H), 7.17 (t, J = 8.4 Hz, 2H), 6.48 (s, 1H), 4.49 (AB, J_{AB} = 19.2 Hz, 1H), 3.64 (AB, J_{BA} = 19.2 Hz, 1H), 3.10 (q, J = 7.8 Hz, 1H), 2.53 (s, 1H), 1.91 (d, J = 0.9 Hz, 3H), 0.48 (d, J = 8.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 196.4, 169.2, 164.0, 163.6 (d, J = 250.7 Hz), 140.7, 137.2, 130.0 (d, J = 1.6 Hz), 129.3 (d, J = 3.5 Hz), 116.3 (d, J = 21.8 Hz), 99.0, 73.6, 57.6, 49.8, 37.8, 17.9, 16.7; IR (thin film) ν_{max} (cm^{-1}) = 2918, 1757, 1702, 1677, 1504, 1370, 1228, 846, 798, 748, 697; MS (ESI-TOF) 452 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{19}H_{16}FINO_3$ ([M + H]$^+$) 452.0153, found 452.0143.

(6a*R*,7*R*,10a*S*)-1-(4-Chlorophenyl)-2-iodo-7,9-dimethyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2f). White solid, 80.4 mg, 86% yield, 99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 21.2 min, t (major) = 25.4 min]: $[\alpha]_D^{20}$ = −41.9 (c = 0.2, $CHCl_3$); mp >240 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.8 Hz, 2H), 6.48 (t, J = 1.4 Hz,1H), 4.74 (AB, J_{AB} = 19.0 Hz, 1H), 3.63 (AB, J_{BA} = 19.0 Hz, 1H), 3.10 (qd, J = 8.0, 1.2 Hz, 1H), 2.56 (s, 1H), 1.90 (d, J = 1.2 Hz, 3H), 0.50 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 196.3, 169.0, 163.7, 140.7, 137.1, 136.3, 131.7, 129.29, 129.21, 99.2, 73.5, 57.6, 49.7, 37.8, 18.0, 16.7; IR (thin film) ν_{max} (cm^{-1}) = 2927, 1767, 1699, 1681, 1484, 1368, 1146, 1008, 835, 747, 708; MS (ESI-TOF) 468 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{19}H_{16}ClINO_3$ ([M + H]$^+$) 467.9858, found 467.9848.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-(thiophen-2-yl)-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2g). White solid, 70.5 mg, 91% yield, 99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 25.9 min, t (major) = 32.9 min]: $[\alpha]_D^{20}$ = +62.2 (c = 0.2, $CHCl_3$); mp 216−218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.50 (m, 2H), 7.18 (dd, J = 4.8, 4.0 Hz, 1H), 6.47 (s, 1H), 4.52 (AB, J_{AB} = 18.8 Hz, 1H), 3.64 (AB, J_{BA} = 18.8 Hz, 1H), 3.14 (q, J = 8.0 Hz, 1H), 2.62 (s, 1H), 1.95 (d, J = 0.8 Hz, 3H), 0.65 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.4, 196.6, 169.5, 157.7, 142.9, 136.9, 132.8, 130.2, 129.4, 127.7, 97.1, 73.2, 58.3, 49.8, 37.4, 17.6, 16.8; IR (thin film) ν_{max} (cm^{-1}) = 2924, 1766, 1680, 1598, 1378, 748, 706; MS (ESI-TOF) 440 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{17}H_{15}INO_3S$ ([M + H]$^+$) 439.9812, found 439.9817.

(6a*R*,7*R*,10a*S*)-2-Iodo-1,7,9-trimethyl-6a,7-dihydropyrrolo-[2,1-i]indole-3,6,8(5*H*)-trione (2h). White solid, 66.5 mg, 90% yield, 87% ee (major diastereomer) [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 28.1 min, t (major) = 30.4 min]: $[\alpha]_D^{20}$ = −207.0 (c = 0.2, $CHCl_3$); mp 169−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22−6.10 (m, 1H), 4.43 (dd, J = 19.2, 1.0 Hz, 1H), 3.56 (d, J = 19.2 Hz, 1H), 3.27 (qd, J = 8.0, 1.2 Hz, 1H), 2.55 (d, J = 1.2 Hz, 1H), 2.16 (s, 3H), 1.87 (d, J = 1.6 Hz, 3H), 1.44 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 196.9, 169.6, 163.5, 140.2, 138.8, 96.8, 72.6, 57.1, 49.7, 37.7, 19.3, 18.2, 16.7; IR (thin film) ν_{max} (cm^{-1}) = 2924, 1760, 1701, 1668, 1429, 1380, 1354, 1037, 750, 705; MS (ESI-TOF) 372 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{14}H_{15}INO_3$ ([M + H]$^+$) 372.0091, found 372.0088.

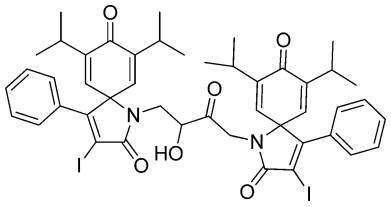
(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-dimethyl-1-propyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2i). White solid, 79.0 mg, 96% yield, >99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 19.2 min, t (major) = 22.3 min]: $[\alpha]_D^{20}$ = −171.0 (c = 0.2, $CHCl_3$); mp 109−111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.16 (s, 1H), 4.42 (AB, J_{AB} = 19.2 Hz, 1H), 3.56 (AB, J_{BA} = 19.2 Hz, 1H), 3.25 (q, J = 7.8 Hz, 1H), 2.48 (s, 1H), 2.46−2.38 (m, 1H), 2.37−2.23 (m, 1H), 1.86 (s, 3H), 1.75−1.52 (m, 2H), 1.43 (d, J = 7.8 Hz, 3H), 1.00 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.8, 196.9, 169.8, 167.1, 140.1, 138.7, 96.2, 72.8, 57.1, 49.6, 37.7, 33.0, 21.3, 19.0, 16.7, 14.2; IR (thin film) ν_{max} (cm^{-1}) = 2923, 1765, 1671, 1602, 1461, 803, 751; MS (ESI-TOF) 400 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{16}H_{19}INO_3$ ([M + H]$^+$) 400.0404, found 400.0392.

(6a*R*,7*R*,10a*S*)-1-Cyclopropyl-2-iodo-7,9-dimethyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2j). White solid, 73.3 mg, 92% yield, 98% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (minor) = 30.5 min, t (major) = 33.5 min]: $[\alpha]_D^{20}$ = −190.4 (c = 0.2, $CHCl_3$); mp 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25−6.20 (m, 1H), 4.43 (dd, J = 18.8, 0.8 Hz, 1H), 3.56 (d, J = 18.8 Hz, 1H), 3.26 (qd, J = 8.0, 1.2 Hz, 1H), 2.56 (d, J = 1.2 Hz, 1H), 1.87 (d, J = 1.2 Hz, 3H), 1.74−1.66 (m, 1H), 1.58−1.51 (m, 1H), 1.49 (d, J = 8.0 Hz, 3H), 1.43−1.35 (m, 1H), 1.18−1.08 (m, 1H), 1.07−0.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.8, 197.2, 170.3, 165.6, 140.7, 139.3, 86.8, 74.0, 58.0, 49.9, 37.6, 19.0, 16.8, 12.4, 9.0, 8.2; IR (thin film) ν_{max} (cm^{-1}) = 2929, 1767, 1693, 1666, 1593, 1348, 840, 753, 691; MS (ESI-TOF) 398 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{16}H_{17}INO_3$ ([M + H]$^+$) 398.0248, found 398.0236.

(6a*R*,7*R*,10a*S*)-7,9-Diethyl-2-iodo-1-phenyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2k). White solid, 89.6 mg, 96% yield, 99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (major) = 17.8 min, t (minor) = 19.8 min]: $[\alpha]_D^{20}$ = −37.2 (c = 0.2, $CHCl_3$); mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.39 (m, 3H), 7.30−7.24 (m, 2H), 6.41 (s, 1H), 4.49 (AB, J_{AB} = 19.2 Hz, 1H), 3.61 (AB, J_{BA} = 19.2 Hz, 1H), 2.79 (dd, J = 10.0, 6.8 Hz, 1H), 2.68 (s, 1H), 2.41−2.32 (m, 1H), 2.30−2.20 (m, 1H), 1.07 (t, J = 7.6 Hz, 3H), 1.03−0.94 (m, 1H), 0.62 (t, J = 7.2 Hz, 3H), 0.27−0.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.0, 195.8, 169.3, 165.1, 145.4, 135.5, 133.4, 130.1, 128.7, 127.7, 98.5, 73.8, 54.2, 49.8, 45.9, 23.8, 23.0, 12.3, 11.9; IR (thin film) ν_{max} (cm^{-1}) = 2962, 1765, 1707, 1669, 1366, 1219, 784, 758, 704; MS (ESI-TOF) 462 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. for $C_{21}H_{21}INO_3$ ([M + H]$^+$) 462.0561, found 462.0552.

(6a*R*,7*R*,10a*S*)-2-Iodo-7,9-diisopropyl-1-phenyl-6a,7-dihydropyrrolo[2,1-i]indole-3,6,8(5*H*)-trione (2l). White solid, 68.0 mg, 70% yield, >99% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 80/20, v = 0.8 mL·min^{-1}, λ = 254 nm, t (major) = 22.8 min, t (minor) = 26.2 min]: $[\alpha]_D^{20}$ = −28.5 (c = 0.2, $CHCl_3$); mp 185−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.39 (m, 3H), 7.34−7.32 (m, 2H), 6.33−6.30 (m, 1H), 4.47 (dd, J = 19.2, 1.0 Hz, 1H), 3.53 (d, J = 19.2 Hz, 1H), 3.04−2.92 (m, 1H), 2.84 (s, 1H), 2.51 (d, J = 8.4 Hz, 1H), 1.11 (d, J = 7.2 Hz, 3H), 1.05 (d, J = 7.2 Hz, 3H), 0.63 − 0.36 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 195.7, 169.3, 164.9, 149.8, 133.6, 133.3, 130.1, 128.5, 127.9, 99.0, 74.1, 54.1, 53.2, 49.6, 29.6, 27.0, 26.8, 21.5, 21.3, 21.0, 20.6; IR (thin film) ν_{max} (cm^{-1}) = 2924, 1764, 1702, 1669, 1464, 1373, 1344, 806, 764, 703; MS (ESI-TOF) 490 ([M + H]$^+$); HRMS (ESI-TOF) mass calcd. For $C_{23}H_{25}INO_3$ ([M + H]$^+$) 490.0874, found 490.0864.

Benzoin Product 2l′. Pale yellow solid, 16.2 mg, 17% yield, 0% ee [Daicel Chiralpak IC, *n*-hexane/2-propanol = 60/40, v = 0.8 mL·min^{-1}, λ = 254 nm, t (major) = 15.1 min, t (minor) = 20.8 min]: mp 226−228 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 6H), 7.25−7.28 (m, 4H), 6.35−6.10 (m, 4H), 4.69 (AB, J_{AB} = 18.8 Hz,



1H), 4.31 (t, J = 5.6 Hz, 1H), 4.17 (AB, J_{BA} = 18.8 Hz, 1H), 3.66−3.50 (m, 2H), 3.05−2.80 (m, 4H), 1.10 (d, J = 6.8 Hz, 3H), 1.06−1.01 (m, 6H), 0.97 (d, J = 7.2 Hz, 3H), 0.92−0.87 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 183.3, 183.2, 171.1, 167.4, 162.5, 161.1, 150.8, 150.2, 149.9, 149.2, 134.9, 134.5, 134.4, 132.2, 132.1, 129.79, 129.75, 128.3, 127.7, 127.6, 95.7, 94.8, 72.5, 70.8, 48.0, 47.0, 29.7, 26.9, 26.8, 26.7, 26.5, 21.8, 21.68, 21.65, 21.63, 21.5, 21.3, 20.9, 14.1; IR (thin film) ν_{max} (cm^{-1}) = 2963, 2921, 1733, 1696, 1667, 1643, 1463, 1390, 843, 755, 697; MS (ESI-TOF) 979 ($[M + H]^+$); HRMS (ESI-TOF) mass calcd. for $C_{46}H_{49}I_2N_2O_6$ ($[M + H]^+$) 979.1674, found 979.1657.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR, ^{13}C NMR of all the new compounds, HPLC spectra of **2a**−**2l′** and crystal data (CIF) for **2a**. 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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(13) See the Supporting Information for details.