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Effective and Diastereoselective Preparation of Dispiro[cyclopent-3′-ene]bisoxindoles via Novel [3 + 2] Annulation of Isoindigos and MBH Carbonates

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A novel and diastereoselective [3 + 2] annulation of isoindigos and Morita−Baylis−Hillman carbonates has been developed for the highly efficient and one-step preparation of highly steric dispiro[cyclopent-3'-ene]bisoxindoles with two all-carbon quaternary spirocenters and three adjacent cycles in excellent yields (up to >99%) and diastereoselectivities(up to >20:1) under mild conditions within a few minutes. A series of dispiro[cyclopent-3′-ene]bisoxindoles were obtained and scale-up experiment was conducted with excellent results demonstrating the potential applications of this protocol.

Introduction

The spirooxindole scaffold, widely existed in huge numbers of bioactive natural products, such as Coerulescine,[1a] Horsfiline,[1b] Welwitindolinone A,[1c] Spirotryprostatin A[1d] and Alstonisine,[1e] is an important structural motif with highly pronounced pharmacological activities, which made spirooxindoles and their derivatives unusual attractive synthetic targets.[2] Bispirooxindoles, fusing two oxindole rings into one cyclic molecule, may exhibit enhanced bioactivities compared with mono-spirooxindoles.[3] However, the catalytic approaches for bispirooxindoles construction were inadequate, probably due to the more constrained structure of bispirooxindole with at least two quaternary spirocenters.[4] Except for the syntheses of bispirooxindoles from oxindole derivatives,[5] the reported methods directly from isoindigos are limited, which may attribute to the less reactivity of isoindigos caused by extremely steric congestion and big π bond conjugation. Overman has reported a diastereoselective preparation of meso-bispyrrolidinoindoline alkaloids by samarium-mediated reductive dialkylation of isoindigo in high yields.[6a] A Diels−Alder reaction between readily available N-Ts isoindigo and 1,3-butadiene to form the cyclohexene cycloadduct was reported by Peter's group.[7] Dispiro(indoline-3,3'-pyrrolidine) fragments were prepared by S. V. Kurbatov from cycloaddition of isoindigo derivatives and in situ generated azomethineylide from sarcosine and paraformaldehyde.[8] We[3] have also successfully developed a sulfa-Michael/aldol cascade reaction between 1,4-dithiane-2,5-diol and isoindigos to afford the highly congested bispirooxindoletetrahydrothiophenes with two vicinal quaternary spirocenters.

Scheme 1 Related studies concerning with isoindigo

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On the other hand, Morita–Baylis–Hillman(MBH) carbonate is particularly useful synthon in organic syntheses, for [2 + 1],[9] [4 + 1],[10] [3 + 2],[11] [3 + 3],[12] [4 + 3],[13] [6 + 3][14] annulations, alkylations[15] and domino reactions[16], which are generally catalyzed by organic phosphines or amines. Especially, the in situ generated 1,3-dipole from MBH carbonates in the presence of tertiary phosphine is usually used for [3 + 2] annulations.[11b]

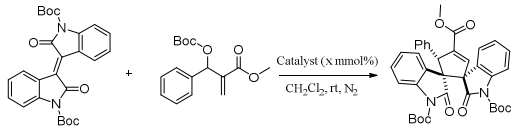
In recent years, we have successfully developed some annulations of methyleneindolinone for the constructions of mono- and bispirooxindoles, such as [2 + 2],[17] [3 + 2][18] and domino reactions[19]. We[20] also reported a new isatin N,N'-cyclic azomethine imine synthon and its unexpected abnormal [3 + 2] cycloaddition with maleimide catalyzed by 1, 4-diazabicyclo-[2.2.2]-octane (DABCO) to construct mono-spirooxindoles. Based on our series of work in spirooxindole syntheses[3, 17-21] and related work in MBH carbonates[22], herein, we wish to report a novel and highly effective diastereoselective organocatalytic [3 + 2] annulation of isoindigos and MBH carbonates to stepwise construct the dispiro[cyclopent-3'-ene]bisoxindoles with two all-carbon quaternary spirocenters and three adjacent cycles in excellent yields and diastereoselectivities (up to >99% yield and >20:1 dr).

Results and discussion

Our studies were conducted with N-Boc isoindigo **1a** and MBH carbonate **2a** in CH_2Cl_2 in the presence of 20 mol% organic phosphines or amines as catalysts (Table 1). No reaction was observed without catalyst, while sorts of phosphines can smoothly catalyze the reaction with good results (Entries 1-5, Table 1). Compared with less nucleophilic phosphines, the more nucleophilic Bu_3P displayed higher catalytic activity with excellent yield (up to 93%) and diastereoselectivity (up to >20:1) (Entry 5, Table 1). For Chiral phosphines (*S*)-BINAP and (*R*)-BINAP, the reaction did not occur without observable result (Entry 6, 7, Table 1). Comparatively, when amine was used as catalyst, less or no desired product was observed (Entries 8-11, Table 1). So, Bu_3P was chosen as the candidate catalyst. When increasing the load of Bu_3P to 30 mol%, no better result was obtained (Entry 12, Table 1). Decreasing the load to 10 mol% or 5 mol%, the yields were sharply reduced with untouched diastereoselectivities (Entries 13-14, Table 1).

With the optical catalyst, other parameters were furtherly screened (Table 2). Due to the excellent results afforded by CH_2Cl_2, other halogenated hydrocarbon solvents were also tested. However, no better result was obtained (Entries 1-6, Table 2). When other aprotic solvents, such as THF, CH_3CN, DMF, DMAc and DMSO, were used, the yields decreased slightly (Entries 7, 8, Table 2) or seriously (Entries 9-11, Table 2). Protic solvent of EtOH gave only moderate yield (Entry 12, Table 2). However, the best result was obtained in toluene (up to >99% yield and >20:1 dr, Entry 13, Table 2). When changing the substrate ratio of **1a** and **2a** to 1:1.1, 1:1 or even 1.2:1, the reaction was still not accomplished after 120 h and the yields were observed to decrease slightly (Entries 14-16, Table 2), and the optimal reaction conditions were established as： 1.0 eq. **1a** and 1.2 eq. **2a** in toluene at room temperature under N_2 atmosphere in the presence of 20 mol% Bu_3P for 10 mins (0.17 hour).

Table 1 Screening of catalysts[a]



1a 2a 3a

Entry	Catalyst	Reaction time (h)	Yield[b] (%)	Dr[c]
1	None	120	NR	-
2	Ph_3P	12	90	4.2:1
3	$MePh_2P$	8	70	2:1
4[d]	DPPB	6	62	3:1
5	Bu_3P	0.17	93	>20:1
6	(*S*)-BINAP	120	NR	--
7	(*R*)-BINAP	120	NR	--
8	DBACO	120	NR	-
9	Et_3N	120	Trace	-
10	DMAP	120	13	9:1
11	DBU	120	NR	-
12[e]	Bu_3P	0.17	92	>20:1
13[f]	Bu_3P	48	78	>20:1
14[g]	Bu_3P	120	45	>20:1

[a] Unless otherwise specified, the reaction was performed with 0.1 mmol **1a**, 0.12 mmol **2a** and 20 mol% catalyst in 1 mL CH_2Cl_2 at room temperature under N_2 atmosphere. [b] Isolated yields. [c] Determined by HPLC. [d] The reaction was conducted with 10 mol% DPPB (DPPB was the abbreviation of 1, 4-Bis(diphenylphosphino)butane). [e] 30 mol% Bu_3P used; [f] 10 mol% Bu_3P used. [g] 5 mol% Bu_3P used.

Under the optimized conditions, the generality of the annulation was broadened, and the results were summarized in Table 3. In general, the reaction could successfully occur with different substituted isoindigos **1** and MBH carbonates **2**, providing corresponding products in excellent yields and diastereoselectivities. Notably, MBH carbonates **2** with no matter ortho-, meta-, or para-substituted phenyl group (R^3) as the reactants, the reaction finished almost spontaneously with excellent yields and diastereoselectivities (Entries 2-13, Table 3). When the aromatic ring of the MBH carbonates bearing an electron-donating group such as methyl, excellent yields and diastereoselectivities (Entries 9, 10, Table 3) were obtained. When bearing a strong electron-withdrawing group of F or

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NO_2, almost no decreasing yield or diastereoselectivity was observed (Entries 2, 3, 12, 13, Table 3). For hetereocyclic 2-furyl MBH carbonate (Entry14, Table 3), excellent results were still achieved. Alternatively, when changing the methyl ester to butyl ester in MBH carbonates, equally excellent result was obtained (Entry 15, Table 3). Furtherly, the reaction still worked well for substrate isoindigos **1** with different substitutions on N or aromatic ring (Entries 16–21, Table 3) with both excellent yields and diastereoselectivities. For less electron-withdrawing group or even electron-donnating groups on Nitrogen atom in isoindigos **1**, prolonged reaction time was required with slightly reduced yields, which may attribute to the relative lower reactivity of the less electron-deficiency double bond caused by the electron-withdrawing deficient substitutions on Nitrogen atom (Entries 20, 21, Table 3). The configuration of the annulation products was determined by X-ray crystal structural analysis of the representative product **3f** (see the Supporting Information for details).

Table 2 Effect of solvent and substrate loadings[a]

Entry	Solvent	Reaction time (h)	Yield[b] (%)	Dr[c]
1[d]	$CHCl_3$	120	66	>20:1
2	$ClCH_2CH_2Cl$	120	58	>20:1
3	Cl_2CHCH_3	120	72	>20:1
4	Cl_2CHCH_2Cl	120	65	>20:1
5	$Cl_2CHCHCl_2$	120	33	>20:1
6	1-Chlorobutane	120	49	>20:1
7	THF	0.25	87	>20:1
8	CH_3CN	0.17	88	>20:1
9	DMF	120	49	>20:1
10	DMAc	120	38	>20:1
11	DMSO	72	47	>20:1
12	EtOH	24	52	>20:1
13	Toluene	0.17	>99[h]	>20:1
14[d,e]	Toluene	120	87	>20:1
15[d, f]	Toluene	120	85	>20:1
16[d, g]	Toluene	120	80	>20:1

[a] Unless otherwise specified, the reaction was performed with 0.1 mmol **1a**, 0.12 mmol **2a** and 20 mol% Bu_3P in 1 mL solvent at room temperature under N_2 atmosphere. [b] Isolated yields. [c] Determined by HPLC. [d] After 120 h, the reaction was still not accomplished completely. [e] The ratio of **1a** and **2a** was 1:1.1. [f] The ratio of **1a** and **2a** was 1:1. [g] The ratio of **1a** and **2a** was 1.2:1. [h] quantitative yield.

Table 3 Generality of substrate scope[a]

Entry	**1**/R^1/R^2	**2**/R^3/R^4	**3**	Yield[b] (%)	Dr[c]
1	**1a**/Boc/H	**2a**/Ph/Me	**3a**	>99[e]	>20:1
2	**1a**/Boc/H	**2b**/2-FC_6H_4/Me	**3b**	>99[e]	>20:1
3	**1a**/Boc/H	**2c**/4-FC_6H_4/Me	**3c**	98	>20:1
4	**1a**/Boc/H	**2d**/2-ClC_6H_4/Me	**3d**	>99[e]	>20:1
5	**1a**/Boc/H	**2e**/3-ClC_6H_4/Me	**3e**	>99[e]	>20:1
6	**1a**/Boc/H	**2f**/4-ClC_6H_4/Me	**3f**	>99[e]	>20:1
7	**1a**/Boc/H	**2g**/2-BrC_6H_4/Me	**3g**	98	>20:1
8	**1a**/Boc/H	**2h**/3-BrC_6H_4/Me	**3h**	>99[e]	>20:1
9	**1a**/Boc/H	**2i**/2-$CH_3C_6H_4$/Me	**3i**	>99[e]	>20:1
10	**1a**/Boc/H	**2j**/4-$CH_3C_6H_4$/Me	**3j**	95	>20:1
11	**1a**/Boc/H	**2k**/3-$OBocC_6H_4$/Me	**3k**	>99[e]	>20:1
12	**1a**/Boc/H	**2l**/3-$NO_2C_6H_4$/Me	**3l**	>99[e]	>20:1
13	**1a**/Boc/H	**2m**/4-$NO_2C_6H_4$/Me	**3m**	97	>20:1
14	**1a**/Boc/H	**2n**/2-Furyl/Me	**3n**	92	>20:1
15	**1a**/Boc/H	**2o** /Ph/Bu	**3o**	>99[e]	>20:1
16	**1b**/Boc/5,5'-2F	**2a**/Ph/Me	**3p**	95	>20:1
17	**1c**/Boc/7,7'-2F	**2a**/Ph/Me	**3q**	92	>20:1
18	**1d**/Boc/5,5'-2Cl	**2a**/Ph/Me	**3r**	92	>20:1
19	**1e**/Boc/6,6'-2Cl	**2a**/Ph/Me	**3s**	>99[e]	>20:1
20[d]	**1f**/Et/H	**2a**/Ph/Me	**3t**	89	>20:1
21[d]	**1g**/Allyl/H	**2a**/Ph/Me	**3w**	85	>20:1

[a] Unless otherwise specified, the reaction was performed with 0.1 mmol **1**, 0.12 mmol **2** and 20 mol% Bu_3P in 1 mL toluene at room temperature for 10 mins under N_2 atmosphere. [b] Isolated yields. [c] Determined by HPLC. [d] After 120 hours, the reactants were still not consumed completely. [e] quantitative yield.

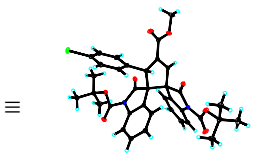

Fig. 1 Representative X-ray crystallographic structure of product **3f**

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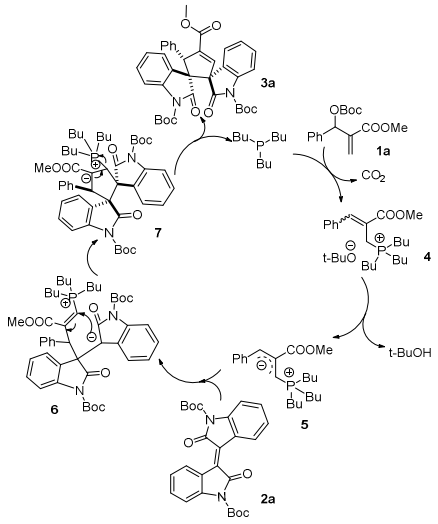
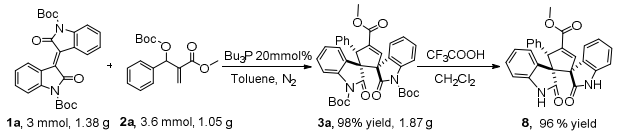
Based on previous reports on phosphine-catalyzed annulations of MBH carbonates[9-12], we proposed a plausible mechanism (Scheme 2) for the present protocol. The reaction was initiated by nucleophilic attack of Bu_3P to form quaternary salt **4**, CO_2 and *tert*-butoxide anion. The 1, 3-dipole **5** was formed after the deprotonation of **4** by *tert*-butoxide anion, and the double bond in isoindigo **1a** was attacked by the nucleophilic site of **5** to form intermediate **6** with one nucleophilic site and electron-deficient double bond. **6** took the intramolecular addition from less steric hindrance to realize the construction of bispiro-adductive **7**. The elimination of phosphine completed the catalytic cycle, yielding the product and setting the catalyst free.

To demonstrate the synthetic potential of this new [3 + 2] annulation protocol, scale-up experiment was conducted on gram scale, almost equal result (98% yield and >20:1 dr) was still achieved, which may lead to a further potential scale-up. When product **3a** was treated with CF_3COOH in CH_2Cl_2 at room temperature, two Boc groups were deprotected to form the N-H dispiro[cyclopent-3'-ene]bisoxindoles **8** in 96% yield.



Scheme 2 Plausible reaction mechanism



Scheme 3 Scale-up preparation and the deprotection of [3 + 2] product **3a**

Conclusions

In summary, we have developed a highly efficient organocatalytic [3 + 2] annulation reaction of isoindigos and MBH carbonates in the presence of Bu_3P for the direct construction of highly steric dispiro[cyclopent-3'-ene]bisoxindole derivatives with two all-carbon quaternary spirocenters and three adjacent cycles in excellent yields and diastereoselectivities (up to >99% yield and >20:1 dr) under mild conditions within a few minutes. A series of isoindigos and MBH carbonates are compatible with this protocol. The synthetic potential of this novel [3 + 2] annulation protocol was demonstrated on a gram scale experiment. This strategy will be useful in medicinal chemistry and diversity-oriented synthesis and may also find potential applications in further scale-up preparations.

Experimental section

General information

Commercial grade solvent was dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance (300 MHz for ^{1}H NMR, 75 MHz for ^{13}C NMR) instrument. Data for ^{1}H NMR are reported as chemical shift (ppm, tetramethylsilane as the internal standard), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet), coupling constant (Hz). Data for ^{13}C NMR are reported as chemical shift. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. Reactions were monitored by TLC and visualized with ultraviolet light.

General procedure for [3 + 2] annulation

The mixture of 0.1 mmol **1**, 0.12 mmol **2** and 20 mol% Bu_3P in 1 mL toluene was stirred at room temperature under N_2 atmosphere, and the reaction was detected by TLC. After the reaction was completed, the crude product was directly purified by silica gel chromatography to give the desired [3 + 2] product **3**.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3a).** >99% yield, dr >20:1, white solid, mp 141.2 °C (decomposition); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.70 (d, J = 7.2 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.32–7.27 (m, 5H), 7.09-7.14 (m, 4H), 6.86 (d, J = 2.5 Hz, 1H), 6.79 (dd, J = 6.7, 2.8 Hz, 2H), 5.22 (d, J = 2.6 Hz, 1H), 3.67 (s, 3H), 1.55 (s, 9H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.5, 170.3,

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164.1, 147.9, 147.4, 141.7, 141.1, 139.5, 139.4, 135.2, 130.1, 129.9, 128.6, 127.7, 127.2, 125.8, 124.6, 124.5, 124.4, 124.1, 122.5, 114.2, 114.1, 84.2, 83.9, 68.4, 66.3, 55.5, 51.9, 27.6, 27.4; HRMS-ESI (m/z): Calcd for $C_{37}H_{36}N_2O_8$, $(M + H)^+$: 637.25444, found: 637.25458.

***Syn*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3a').** ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.49 (ddd, J = 9.2, 7.8, 1.1 Hz, 2H), 7.38 (t, J = 8.5 Hz, 2H), 7.31–7.24 (m, 1H), 7.15 (d, J = 1.3 Hz, 1H), 7.07 (dd, J = 3.6, 2.4 Hz, 4H), 6.83–6.72 (m, 3H), 6.66 (d, J = 7.6 Hz, 1H), 5.19 (d, J = 2.6 Hz, 1H), 3.66 (s, 3H), 1.39 (s, 9H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.9, 168.6, 164.1, 148.0, 147.9, 141.3, 139.4, 139.3, 138.8, 134.9, 130.2, 129.5, 129.2, 127.4, 127.1, 125.5, 124.6, 124.4, 123.4, 122.6, 114.6, 113.7, 83.7, 83.4, 67.9, 66.3, 55.1, 51.9, 27.6, 27.5. HRMS-ESI (m/z): Calcd for $C_{37}H_{36}N_2O_8$, $(M + H)^+$: 637.25444, found: 637.25456.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1'-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*o*-fluorobenzene-1-ene (3b).** >99% yield, dr >20:1, white solid, mp 171.2 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.77 (dt, J = 7.7, 1.5 Hz, 1H), 7.67–7.64 (m, 1H), 7.54 (dd, J = 7.7, 1.4 Hz, 1H), 7.46 (dd, J = 8.1, 1.2 Hz, 1H), 7.29–7.24 (m, 3H), 7.16–7.10 (m, 3H), 6.75–6.9 (m, 1H), 6.81 (ddd, J = 9.6, 8.3, 1.3 Hz, 1H), 6.75 (d, J = 2.6 Hz, 1H), 5.71 (d, J = 2.2 Hz, 1H), 3.72 (s, 3H), 1.64 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 172.6, 170.6, 163.9, 148.3, 148.1, 142.0, 141.1, 140.2, 139.8, 135.3 (J = 282.67 Hz), 129.9, 128.9, 128.9, 127.5, 127.2, 126.8, 124.7, 124.4, 124.2, 123.9, 122.7, 114.7, 114.6, 84.6, 84.1, 68.9, 66.2, 56.6, 51.8, 28.0, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}FN_2O_8$, $(M + H)^+$: 655.24502, found: 655.24536.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindolespiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*p*-fluorobenzene-1-ene (3c).** 98% yield, dr >20:1, white solid, mp 183.6 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.63 (dd, J = 7.4, 1.5 Hz, 1H), 7.60 (dt, J = 8.2, 0.8 Hz, 1H), 7.47–7.46 (m, 1H), 7.42–7.42(m, 1H), 7.25–7.23 (m, 2H), 7.15 (dd, J = 7.6, 1.3 Hz, 1H), 7.08 (dd, J = 7.6, 1.1 Hz, 1H), 6.82–6.67 (m, 5H), 5.30 (d, J = 2.6 Hz, 1H), 3.69 (s, 3H), 1.59 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 172.6, 170.8, 164.1, 162.1 (J = 257.45 Hz), 160.3, 148.3, 140.7, 140.2, 139.8, 130.8, 130.8, 130.5, 130.4, 129.8, 129.8, 126.7, 124.6, 124.3, 124.2, 124.0, 122.8, 114.7, 114.6, 114.5, 114.4, 84.6, 84.0, 68.9, 66.1, 56.2, 51.8, 27.9, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}FN_2O_8$, $(M + H)^+$: 655.24502, found: 655.24457.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*o*-chlorobenzene-1-ene (3d).** >99 % yield, dr >20:1, white solid, mp 189.3 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.80 (dd, J = 7.6, 1.4 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.52–7.48 (m, 2H), 7.41 (d, J = 8.2 Hz, 1H), 7.26–7.20 (m, 3H), 7.09–7.06 (m, 5H), 6.76 (d, J = 2.6 Hz, 1H), 5.97 (d, J = 2.6 Hz, 1H), 3.63 (s, 3H), 1.61 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 172.7, 170.5, 163.8, 148.4, 148.1, 143.2, 140.7, 139.9, 139.8, 134.1, 133.3, 132.6, 129.9, 129.6, 129.2, 128.5, 127.1, 126.4, 126.0, 124.6, 123.9, 123.7, 122.3, 114.5, 114.1, 84.5, 83.9, 68.9, 66.7, 52.1, 51.7, 28.0, 27.9, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}ClN_2O_8$, $(M + H)^+$: 671.21547, found: 671.21503.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3'']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*m*-chlorobenzene-1-ene (3e).** >99% yield, dr >20:1, white solid, mp 181.8 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.74–7.69 (d, J = 7.9 Hz, 1H), 7.63 (dd, J = 8.1, 1.0 Hz, 1H), 7.48 (td, J = 7.9, 1.2 Hz, 2H), 7.29–7.21 (m, 3H), 7.18 (dd, J = 7.6, 1.3 Hz, 1H), 7.15–6.98 (m, 3H), 6.85 (s, 1H), 6.78–6.70 (m, 2H), 5.28 (d, J = 2.6 Hz, 1H), 3.71 (s, 3H), 1.60 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 142.0, 141.1, 140.2, 139.8, 137.2, 133.4, 129.9, 128.9, 128.9, 127.4, 127.2, 126.8, 124.7, 124.4, 124.2, 123.9, 122.7, 114.7, 114.6, 84.6, 84.1, 68.8, 56.6, 51.8, 28.0, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}ClN_2O_8$, $(M + H)^+$: 671.21547, found: 671.21509.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*p*-chlorobenzene-1-ene (3f).** >99% yield, dr >20:1, white solid, mp 195.7 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.70 (dd, J = 7.5, 1.6 Hz, 1H), 7.66 (d, J = 8.2 Hz, 1H), 7.45 (td, J = 8.1, 1.2 Hz, 2H), 7.29–7.20 (m, 2H), 7.15 (td, J = 7.6, 1.3 Hz, 1H), 7.12–7.03 (m, 3H), 6.85–6.77 (m, 2H), 6.74 (d, J = 2.6 Hz, 1H), 5.29 (d, J = 2.6 Hz, 1H), 3.71 (s, 3H), 1.60 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 172.6, 170.7, 164.0, 148.3, 148.0, 142.2, 141.0, 140.2, 139.8, 133.7, 133.1, 130.2, 130.0, 129.9, 127.9, 126.8, 124.7, 124.4, 124.2, 124.0, 122.8, 114.7, 114.6, 84.6, 84.1, 68.84, 66.2, 56.3, 51.8, 28.0, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}ClN_2O_8$, $(M + H)^+$: 671.21547, found: 671.21545.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*o*-bromolbenzene-1-ene (3g).** 98% yield, dr >20:1, white solid, mp 190.5 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.84 (dd, J = 7.7, 1.3 Hz, 1H), 7.68–7.59 (m, 1H), 7.52 (ddd, J = 7.9, 3.6, 1.5 Hz, 2H), 7.41 (dd, J = 8.3, 1.1 Hz, 1H), 7.31 (dd, J = 8.0, 1.4 Hz, 1H), 7.29–7.14 (m, 3H), 7.08 (tt, J = 7.6, 1.3 Hz, 2H), 6.99 (d, J = 1.7 Hz, 1H), 6.76 (d, J = 2.6 Hz, 1H), 5.96 (d, J = 2.6 Hz, 1H), 3.62 (s, 3H), 1.61 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 172.9, 170.5, 163.8, 148.4, 148.1, 143.3, 140.7, 140.0, 135.1, 132.7, 132.7, 129.9, 129.7, 128.8, 127.3, 126.9, 126.7, 124.8, 124.6, 124.0, 123.7, 122.1, 114.6, 114.1, 84.6, 84.0, 69.2, 66.7, 54.6, 51.8, 28.0, 27.9, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}BrN_2O_8$, $(M + H)^+$: 715.16496, found: 715.16559.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*m*-bromolbenzene-1-ene (3h).** >99% yield, dr >20:1, white solid, mp 176.8 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.71 (dd, J = 7.5, 1.5 Hz, 1H), 7.63 (dd, J = 8.1, 1.0 Hz, 1H), 7.48 (td, J = 7.3, 1.2 Hz, 2H), 7.29–7.20 (m, 3H),

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7.17 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.08 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.02–6.91 (m, 2H), 6.80 (dt, *J* = 7.8, 1.4 Hz, 1H), 6.74 (d, *J* = 2.6 Hz, 1H), 5.27 (d, *J* = 2.6 Hz, 1H), 3.71 (s, 3H), 1.60 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.5, 170.6, 163.9, 148.3,148.1, 142.0, 141.1, 140.2, 139.8, 137.4, 131.8, 130.3, 129.9, 129.2, 127.6, 126.8, 124.7, 124.4, 124.1, 123.9, 122.6, 121.6, 114.7, 114.6, 84.6, 84.1, 68.9, 66.2, 56.5, 51.8, 28.0, 27.8. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}BrN_2O_8$, $(M + H)^+$: 715.16496, found: 715.16534.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*o*-methylbenzene-1-ene (3i).** >99% yield, dr >20:1, white solid, mp 192.3 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.78 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.61–7.54 (m, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.35 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.26(m, 2H), 7.13–6.95 (m, 4H), 6.91–6.83 (m, 1H), 6.73 (dd, *J* = 2.6, 1.0 Hz, 1H), 5.64 (d, *J* = 2.6 Hz, 1H), 3.62 (s, 3H), 1.69 (s, 3H), 1.63 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 173.4, 170.3, 164.2, 148.4, 140.2, 139.8, 136.6, 133.5, 130.9, 129.9, 129.8, 129.7, 127.6, 127.0, 125.3, 125.1, 124.6, 124.4, 123.9, 123.3, 114.6, 114.5, 84.6, 83.9, 69.1, 66.3, 53.4, 51.7, 28.0, 27.8, 19.7. HRMS-ESI (m/z): Calcd for $C_{38}H_{38}N_2O_8$, $(M + H)^+$: 651.27009, found: 651.27051.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*p*-methylbenzene-1-ene (3j).** 95% yield, dr >20:1, white solid, mp 194.4 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.72 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.50 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.44 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.30–7.11 (m, 3H), 7.07 (td, *J* = 7.6, 1.1 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 2H), 6.74 (dd, *J* = 8.5, 2.3 Hz, 2H), 6.70 (d, *J* = 2.6 Hz, 1H), 5.29 (d, *J* = 2.7 Hz, 1H), 3.70 (s, 3H), 2.20 (s, 3H), 1.60 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.8, 170.8, 164.3, 148.4, 148.2, 142.9, 140.3, 139.8, 136.6, 131.9, 129.8, 129.6, 128.7, 128.4, 126.9, 124.6, 124.3, 124.2, 123.2, 114.6, 114.5, 84.5, 83.8, 69.0, 66.2, 56.7, 51.7, 28.0, 27.8, 21.0. HRMS-ESI (m/z): Calcd for $C_{38}H_{38}N_2O_8$, $(M + H)^+$: 651.27009, found: 651.26990.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*m*-OBoc-benzene-1-ene (3k).** >99% yield, dr >20:1, white solid, mp 174.8 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.76–7.66 (m, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.46 (dd, *J* = 7.7, 4.4 Hz, 2H), 7.29–7.13 (m, 3H), 7.11–6.99 (m, 2H), 6.97–6.87 (m, 1H), 6.74–6.60 (m, 3H), 5.32 (d, *J* = 2.6 Hz, 1H), 3.67 (s, 3H), 1.58 (s, 9H), 1.48 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.5, 170.5, 164.1, 151.3, 150.3, 148.2, 148.0, 142.6, 140.5, 140.2, 139.7, 136.8, 129.8, 129.7, 128.4, 126.7, 126.1, 124.5, 124.2, 124.1, 123.9, 122.8, 121.8, 119.9, 114.7, 114.5, 84.5, 83.8, 83.0, 68.7, 66.3, 56.2, 51.7, 27.9, 27.7, 27.5. HRMS-ESI (m/z): Calcd for $C_{42}H_{44}N_2O_{11}$, $(M + Na)^+$: 775.28373, found: 775.28373.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*m*-NO_2-benzene-1-ene (3l).** >99% yield, dr >20:1, white solid, mp 174.2 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.99 (d, *J* = 6.9 Hz, 1H), 7.80–7.73 (m, 1H), 7.73–7.69 (m, 1H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.47 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.26 (m, 5H), 7.07 (td, *J* = 7.6, 1.2 Hz, 1H), 6.81 (d, *J* = 2.5 Hz, 1H), 5.42 (d, *J* = 2.6 Hz, 1H), 3.72 (s, 3H), 1.60 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.2, 170.7, 163.6, 148.2, 147.8, 147.6, 141.7, 141.3, 140.0, 139.8, 137.3, 135.2, 130.2, 130.1, 128.6, 126.6, 124.7, 124.6, 124.2, 124.0, 123.6, 122.3, 122.1, 114.7, 114.7, 84.7, 84.3, 68.7, 66.4, 56.1, 51.9, 27.9, 27.7. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}N_3O_{10}$, $(M + H)^+$: 704.22147, found: 704.22168.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-*p*-NO_2-benzene-1-ene (3m)** 97% yield, dr >20:1, white solid, mp 206.9 °C (decomposition); ^{1}H NMR (300 MHz, DMSO-d_6) *δ* 8.03–7.87 (m, 2H), 7.72 (dd, *J* = 7.1, 1.3 Hz, 1H), 7.61–7.50 (m, 1H), 7.41–7.15 (m, 5H), 7.14–6.99 (m, 3H), 6.88 (d, *J* = 2.5 Hz, 1H), 5.37 (d, *J* = 2.5 Hz, 1H), 3.69 (s, 3H), 1.54 (s, 9H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) *δ* 171.2, 170.1, 163.4, 147.7, 147.1, 146.6, 142.9, 141.8, 140.7, 139.5, 139.3, 130.0, 129.9, 129.8, 125.7, 124.4, 124.3, 124.2, 123.4, 122.5, 121.6, 114.2, 114.2, 84.0, 83.8, 79.1, 78.9, 78.7, 78.2, 68.2, 66.2, 55.0, 51.7, 27.5, 27.3. HRMS-ESI (m/z): Calcd for $C_{37}H_{35}N_3O_{10}$, $(M + Na)^+$: 704.22147, found: 704.22119.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-methoxycarbonyl-3-fruyl-1-ene (3n).** 92% yield, dr >20:1, red solid, mp 146.8 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.62 (ddd, *J* = 8.1, 3.3, 1.2 Hz, 2H), 7.52 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.29–7.21 (m, 2H), 7.18 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.09 (dtd, *J* = 12.5, 7.6, 1.2 Hz, 2H), 6.64 (d, *J* = 2.8 Hz, 1H), 6.16 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.01–5.81 (m, 1H), 5.41 (d, *J* = 2.8 Hz, 1H), 3.73 (s, 3H), 1.58 (s, 9H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.3, 171.0, 163.6, 149.5, 148.4,148.2, 141.7, 141.4, 140.2, 139.8, 139.4, 129.9, 129.8, 126.5, 124.6, 124.3, 124.2, 123.7, 122.9, 114.6, 114.5, 110.3, 108.4, 84.5, 84.0, 67.6, 66.2, 51.8, 50.3, 27.9, 27.9. HRMS-ESI (m/z): Calcd for $C_{35}H_{34}N_2O_9$, $(M + H)^+$: 649.21565, found: 649.21594.

***Anti*-1'-*tert*-butoxycarbonyloxy-spiro[4.3']oxindole-spiro [5.3'']1''-*tert*-butoxycarbonyloxy-oxindole-cyclopent-2-butyloxycarbonyl-3-benzene-1-ene (3o).** >99% yield, dr >20:1, white solid, mp 143.2 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) *δ* 7.74 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.68–7.57 (m, 1H), 7.52 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.44 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.30–7.14 (m, 3H), 7.13–7.01 (m, 4H), 6.94–6.79 (m, 2H), 6.71 (dd, *J* = 2.7, 0.9 Hz, 1H), 5.32 (d, *J* = 2.6 Hz, 1H), 4.15 (dt, *J* = 11.1, 6.6 Hz, 1H), 4.07–3.90 (m, 1H), 1.61 (s, 9H), 1.41 (m, 11H), 1.15–0.98 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) *δ* 172.8, 170.7, 163.9, 148.4, 148.1, 143.3, 140.2, 140.0, 139.8, 135.2, 129.8, 129.6, 128.9, 127.6, 127.0, 126.9, 124.6, 124.3, 124.2, 123.2, 114.6, 114.5, 84.5, 83.8, 69.0, 66.2, 64.4, 57.0,

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30.4, 28.0, 27.8, 18.9, 13.6. HRMS-ESI (m/z): Calcd for $C_{40}H_{42}N_2O_8$, $(M + Na)^+$: 701.28334, found: 701.28363.

***Anti*-1'-*tert*-butoxycarbonyloxy-5'-fluoro-spiro[4.3'] oxindole-spiro[5.3'']1''-*tert*-butoxycarbonyloxy-5''-fluoro-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3p).** 95% yield, dr >20:1, white solid, mp 198.3 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 9.0, 4.7 Hz, 1H), 7.59–7.41 (m, 2H), 7.32–7.22 (m, 1H), 7.18–7.05 (m, 3H), 6.97 (tdd, *J* = 8.8, 4.0, 2.8 Hz, 2H), 6.90–6.80 (m, 2H), 6.69 (dd, *J* = 2.7, 0.9 Hz, 1H), 5.28 (d, *J* = 2.7 Hz, 1H), 3.69 (s, 3H), 1.62 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 172.1, 170.1, 163.9, 159.6(*J*= 242.6 Hz), 159.6(*J* = 214.9 Hz), 161.2, 161.2, 158.0, 148.4, 148.2, 143.1, 139.6, 134.5, 134.50, 128.8, 127.8, 127.4, 116.7, 116.6, 116.4, 116.3, 116.1, 116.0, 116.00, 115.9, 114.7, 114.4, 112.0, 111.7, 85.2, 84.4, 68.8, 66.0, 57.2, 51.8, 27.8, 27.6. HRMS-ESI (m/z): Calcd for $C_{37}H_{34}F_2N_2O_8$, $(M + Na)^+$: 695.21754, found: 695.21814.

***Anti*-1'-*tert*-butoxycarbonyloxy-7'-fluoro-spiro[4.3'] oxindole-spiro[5.3'']1''-*tert*-butoxycarbonyloxy-7''-fluoro-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3q).** 92% yield, dr >20:1, white solid, mp 165.4 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.52 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.34–7.25 (m, 1H), 7.23–6.97 (m, 7H), 6.91–6.77 (m, 2H), 6.70 (d, *J* = 2.6 Hz, 1H), 5.32 (d, *J* = 2.6 Hz, 1H), 3.69 (s, 3H), 1.52 (s, 9H), 1.31 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 172.0, 170.3, 164.0, 149.8, 146.5, 142.9, 139.5, 134.5, 128.7, 127.8, 127.5, 127.2, 126.3, 126.1, 126.0, 125.7, 125.6, 121.5 (*J* = 195.3Hz),121.5 (*J* = 198.8 Hz), 118.4, 118.1, 118.1, 117.8, 85.2, 84.3, 69.7, 66.7, 57.1, 51.8, 27.5, 27.4. HRMS-ESI (m/z): Calcd for $C_{37}H_{34}F_2N_2O_8$, $(M + Na)^+$: 695.21754, found: 673.23560.

***Anti*-1'-*tert*-butoxycarbonyloxy-5'-chloro-spiro[4.3']oxindole-spiro[5.3'']1''-*tert*-butoxycarbonyloxy-5''-chloro-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3r)** 92% yield, dr >20:1, white solid, mp 180.1 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 0.9 Hz, 1H), 7.71 (d, *J* = 5.7 Hz, 1H), 7.50 (d, *J* = 2.3 Hz, 1H), 7.49 (d, *J* = 4.3 Hz, 1H), 7.31–7.18 (m, 2H), 7.16–7.01 (m, 3H), 6.93–6.76 (m, 2H), 6.68 (d, *J* = 2.6 Hz, 1H), 5.29 (d, *J* = 2.6 Hz, 1H), 3.68 (s, 3H), 1.65 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 171.9, 169.8, 163.9, 148.3, 148.1, 143.0, 139.7, 138.9, 138.5, 134.4, 130.2, 130.1, 130.0, 129.9, 128.7, 127.8, 127.4, 127.0, 125.7, 124.9, 124.4, 116.1, 116.0, 85.4, 84.6, 68.6, 65.8, 57.5, 51.8, 27.9, 27.7. HRMS-ESI (m/z): Calcd for $C_{37}H_{34}Cl_2N_2O_8$, $(M + Na)^+$: 727.15844, found: 727.15857.

***Anti*-1'-*tert*-butoxycarbonyloxy-6'-chloro-spiro[4.3'] oxindole-spiro[5.3'']1''-*tert*-butoxycarbonyloxy-6''-chloro-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3s).** >99% yield, dr >20:1, white solid, mp 149.5 °C (decomposition); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.12 (s, 5H), 6.83-6.81 (m, 2H), 6.67 (d, *J* = 2.6 Hz, 1H), 5.26 (d, *J* = 2.6 Hz, 1H), 3.69 (s, 3H), 1.62 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 172.3, 170.2, 164.0, 148.0, 147.7, 142.9, 141.2, 140.6, 139.8, 135.9, 135.7, 134.5, 128.6, 127.8, 127.4, 125.2, 124.8, 124.4, 122.4, 121.4, 115.5, 85.3, 84.6, 68.6, 65.7, 57.2, 51.8, 27.9, 27.7. HRMS-ESI (m/z): Calcd for $C_{37}H_{34}Cl_2N_2O_8$, $(M + Na)^+$: 727.15844, found : 727.15936.

***Anti*-1'-ethyl-spiro[4.3']oxindole-spiro[5.3'']1''-ethyl-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3t).** 89% yield, dr >20:1, white solid, mp 244.3-245.7 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.79 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.60 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.17 (dtd, *J* = 9.2, 7.7, 1.3 Hz, 2H), 7.08–6.97 (m, 4H), 6.93 (td, *J* = 7.6, 1.1 Hz, 1H), 6.81 (dt, *J* = 8.6, 2.1 Hz, 3H), 6.64 (d, *J* = 7.9 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 5.42 (d, *J* = 2.6 Hz, 1H), 3.85 (dq, *J* = 14.5, 7.3 Hz, 1H), 3.68 (s, 3H), 3.51 (dq, *J* = 14.2, 7.2 Hz, 1H), 3.28 (dt, *J* = 14.4, 7.2 Hz, 1H), 3.04 (dq, J = 14.3, 7.1 Hz, 1H), 1.10 (t, *J* = 7.2 Hz, 3H), 0.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 174.2,172.6, 164.6, 143.2, 143.1, 142.9, 141.6, 135.7, 129.1, 129.0, 128.5, 128.2, 127.4, 127.2, 126.9, 126.7, 126.6, 125.3, 125.1, 122.6, 122.1, 121.2, 107.9, 107.5, 107.0, 67.5, 64.4, 57.3, 57.0, 51.6, 34.8, 34.4, 33.5, 12.5, 11.4. HRMS-ESI (m/z): Calcd for $C_{31}H_{28}N_2O_4$, $(M + Na)^+$: 515.19413, found: 515.19458.

***Anti*-1'-allyl-spiro[4.3']oxindole-spiro[5.3'']1''-allyl-oxindole-cyclopent-2-methoxycarbonyl-3-benzene-1-ene (3w).** 85% yield, dr >20:1, white solid, mp 177.1-178.0 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.57 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.22–6.97 (m, 6H), 6.93 (td, *J* = 7.7, 1.1 Hz, 1H), 6.89–6.82 (m, 2H), 6.80 (d, *J* = 2.6 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 6.35 (d, *J* = 7.7 Hz, 1H), 5.59 (ddt, *J* = 17.0, 10.3, 5.1 Hz, 1H), 5.47 (d, *J* = 2.6 Hz, 1H), 5.12–4.92 (m, 2H), 4.82 (d, *J* = 17.1 Hz, 1H), 4.73–4.60 (m, 1H), 4.50 (ddt, *J* = 16.6, 4.6, 2.0 Hz, 1H), 4.20–4.07 (m, 1H), 4.08–3.95 (m, 1H), 3.87 (ddt, *J* = 16.7, 4.3, 2.0 Hz, 1H), 3.78–3.56 (m, 4H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 174.3, 172.7, 164.5, 143.3, 143.2, 142.6, 141.9, 135.8, 130.6, 130.2, 129.2, 129.0, 128.7, 127.4, 127.2, 126.8, 126.2, 125.1, 125.0, 122.8, 122.4, 117.7, 116.3, 108.8, 108.4, 67.9, 57.0, 51.6, 42.5, 41.1. HRMS-ESI (m/z): Calcd for $C_{33}H_{28}N_2O_4$, $(M + Na)^+$: 539.19413, found: 539.19458.

Conflicts of interest

There are no conflicts to declare.

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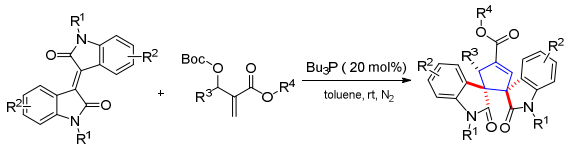

Effective and Diastereoselective Preparation of Dispiro[cyclopent-3′-ene]bisoxindoles via Novel [3 + 2] Annulation of Isoindigos and MBH Carbonates