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PAPER

Acetic Acid Promoted Tandem Cyclization of *in situ* Generated 1,3-Dipoles: Setereoselective Synthesis of Dispiroimidazolidinyl and Dispiropyrrolidinyl Oxindoles with Multiple Chiral Stereocenters

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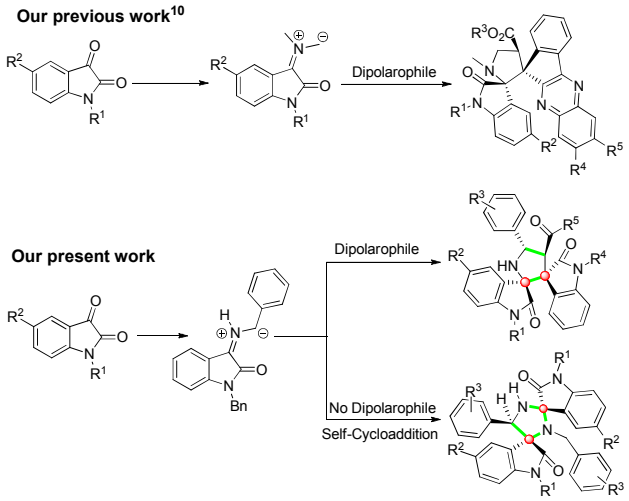
Abstract: We report acetic acid promoted *in situ* generation of ketimine and 1,3-dipole that results in regio- and diastereoselective formation of dispiropyrrolidineoxindoles and dispiroimidazolidineoxindoles *via* tandem cycloaddition. This novel one-pot reaction generates four chiral centres with two contiguous spirostereocenters in dispiropyrrolidineoxindoles, and three chiral centres with two distal spirostereocenters in dispiroimidazolidineoxindoles.

The unique structural features of the spirocyclic oxindole moiety, found in many alkaloids and biologically active natural products,[1] has been the center of attraction for the past several decades as they possess highly pronounced biological activities.[2] Consequently, a variety of methods for the synthesis of spirooxindoles containing all carbon quaternary chiral stereocentre at C-3 position of oxindole moiety have been reported recently.[3-6] As the 1,3-dipolar cycloaddition of azomethine ylide with olefinic dipolarophiles is a convenient method for the construction of highly functionalized pyrrolidineoxindoles,[2,7,8] the scope of this reaction has been broadened using various substituted dipolarophiles.[9]

In our previous attempts to broaden the scope of 1,3-dipolar cycloadditions, we utilized variously substituted electron deficient dipolarophiles,[10] for the construction of dispiropyrrolidineoxindoles. When we looked at other methods for *in situ* generation of new 1,3-dipoles, the ketimine derived from benzylamine and isatin seemed appropriate.[11-13] Surprisingly, we observed the formation of a highly substituted imidazolidine ring system,[14,15] while preparing the ketimine using benzylamine and isatin. We further explored the scope of this reaction, and report herein acetic acid mediated single step construction of densely functionalized dispiroimidazolidinoxindoles and dispiropyrrolidinoxindoles. Unlike the previously described method,[16] a single regiosomer is formed under acetic acid catalysed conditions. Use of dicarboxylic acid also furnished a single regiosomer with comparable yields.



Scheme 1 Synthetic cascade approach to dispiroimidazolidinyl and dispiropyrrolidinyl oxindoles

Results and Discussion

With the idea of generating ketimines, we carried out a reaction using 0.5 mmol quantities of N-benzylisatin and benzylamine in ethanol (10 mL) containing 5 mol % acetic acid, and the mixture was stirred at room temperature for about 3.0 h until the disappearance of starting materials as monitored by using TLC. The white precipitate formed (product **3a**; 65% yield) showed a higher mass value than expected for the corresponding ketimine. To our delight, the white precipitate turned out to be dispiroimidazolidineoxindole derivative. While the ^{1}H NMR spectrum of the product showed six doublets at δ 4.80 (d, J = 15.8 Hz, 1H), 4.74 (d, J = 15.8 Hz, 1H), 4.40 (d, J = 15.8 Hz, 1H), 3.84 (d, J = 4.6 Hz, 1H), 3.82 (d, J = 12.8 Hz,

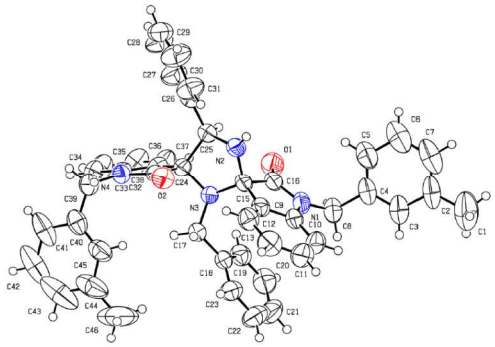


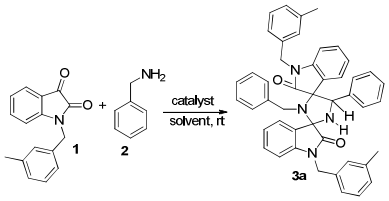
Fig1. Ortep-diagram of Compound **3a**

1H) and 3.52 (d, J = 13.0 Hz, 1H) ppm arising from three benzylic groups, the ^{13}C NMR spectrum displayed two peaks at δ 177.43, 177.36 ppm indicating presence of two amide carbonyl peaks. These results and the mass spectral data together were convincing enough to arrive at an imidazolidine ring system with two N-benzylisatin moieties. Finally, the weak ^{1}H resonance at 5.63 (s, 1H) ppm corresponding to the hydrogen atom at the imidazolidine ring, and the observation of [M+H] peak in the HRMS indicated the existence of the imidazolidine derivative **3a**. Further, the single crystal-XRD studies of **3a** confirmed the presence of the dispiroimidazolidineoxindole derivative.

After establishing the identity of the imidazolidine derivative **3a**, we set out to optimize the yield and generality of this reaction by using equimolar quantities of N-benzylisatin and benzylamine and various Lewis-acid catalysts (5 mol %) in different solvents at room temperature. Among the different catalysts used, acetic acid in methanol turned out to be suitable for better yields (Table 1).

Significant improvement in the yield of the reaction was achieved by increasing the amount of catalyst to 10 mol % (Table 1, entry 11). However, formation of the imidazolidine system was not observed in aprotic solvents and in the absence of a catalyst. The generality of this reaction as well as the substrate scope was assessed by varying the substituents on **1** and **2** (Table 2). Good yields were obtained in almost all the cases regardless of the position of substituents on **1** and **2**. Interestingly, the presence of electron withdrawing as well as electron releasing groups on the substrates do not seem to significantly alter the yield of the products. In all the 16 examples tested under the optimized conditions, the corresponding imidazolidine derivative (**3a-p**) was formed in good yields. An analysis of HRMS, ^{1}H and ^{13}C NMR data of compounds **3a-p**, and the chemical shift value of the

Table 1 Optimization of reaction conditions



Entry	Catalyst (mol%)[a]	Solvent	Time (h)	Yield (%)[b]
1	Acetic acid	water	6.2	n.r[c]
2	Acetic acid	EtOH	3.0	65
3	Et_3N	EtOH	6.0	n.r
4	$InCl_3$	EtOH	5.4	42
5	$In(OTf)_3$	EtOH	6.0	48
6	$Bi(OTf)_3$	EtOH	6.2	50
7	$Sc(OTf)_3$	EtOH	6.0	54
8	$Yb(OTf)_3$	EtOH	6.4	55
9	$Cu(OTf)_2$	EtOH	6.3	52
10	Acetic acid	MeOH	3.4	71
11[d]	**Acetic acid**	**MeOH**	**3.0**	**83**
12	Acetic acid	THF	6.2	n.r
13	Acetic acid	CAN	6.4	n.r
14	Acetic acid	DMF	6.5	n.r
15[d]	Oxalic acid	MeOH	3.0	82

[a]Unless otherwise noted, 1 mmol of 1, 1 mmol 2 and 5 mol % catalyst were used at room temperature. [b]Isolated yield. [c]Insoluble in water. [d]10 mol % of catalyst was used.

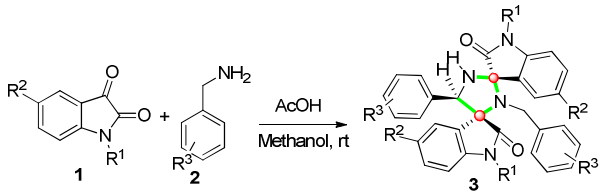
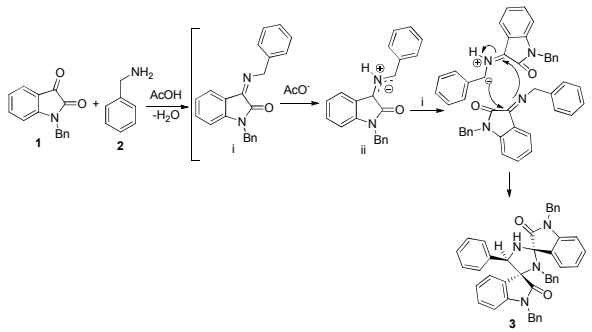


Table 2 Substrate scope[a]

Entry	R^1	R^2	R^3	Product	Yield(%)[b]
1	3-Me-Bn	H	H	**3a**	83
2	Bn	H	H	**3b**	79
3	Bn	F	H	**3c**	81
4	Bn	Cl	H	**3d**	78
5	Bn	Me	H	**3e**	82
6	H	I	H	**3f**	68
7	H	H	H	**3g**	73
8	Me	H	H	**3h**	82
9	4-*t*-Butyl-Bn	H	H	**3i**	75
10	4-CN-Bn	Cl	H	**3j**	73
11	Bn	H	2-Me	**3k**	72
12	Bn	H	4-Me	**3l**	73
13	Bn	H	4-OMe	**3m**	70
14	Bn	H	4-Cl	**3n**	82
15	Bn	H	3,4-di methoxy	**3o**	65
16	Bn	H	3,4,5-tri methoxy	**3p**	65

[a]Unless otherwise noted, 1 mmol of **1**, 1 mmol of **2**, 10 mol % of acetic acid in 5 mL of methanol at room temp. [b]Isolated yield.

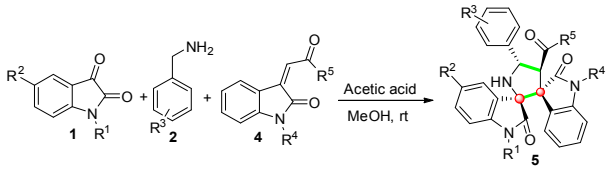
lone hydrogen in the imidazolidine ring, and the exchangeable nature of NH protons together revealed the existence of imidazolidine system in all the cases.



Scheme 2 Plausible mechanism

The imidazolidine derivatives obtained in the present investigation appear to have resulted from a tandem cycloaddition reaction. The ketimine generated *in situ* from the reaction between N-alkylisatin **1** and benzylamine **2** can act as a precursor for generating 1,3-dipole *in situ* (Scheme 2) as well as a substrate for cycloaddition with the 1,3-dipole generated *in situ*, leading to the formation imidazolidine ring system.

Table 3 Substrate Scope[a]



Entry	R^1	R^2	R^3	R^4	R^5	5	Yield (%)[b]
1	Bn	H	H	Bn	-OMe	**5a**	78
2	Bn	H	H	Bn	-OEt	**5b**	70
3	Bn	F	H	Bn	-OMe	**5c**	69
4	Me	H	H	Bn	-OMe	**5d**	68
5	Propargyl	H	H	Bn	-OMe	**5e**	65
6	Bn	F	H	Bn	-OEt	**5f**	69
7	Bn	H	2,4-dichloro	Bn	-OMe	**5g**	62

[a]Reaction carried out with 1 mmol of **1,** 1 mmol of **2**, 1 mmol of **4,** 10 mol % of acetic acid in 5 mL of methanol at room temp. [b]Isolated yield.

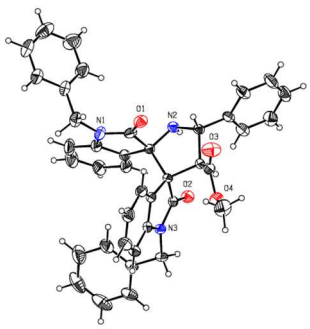
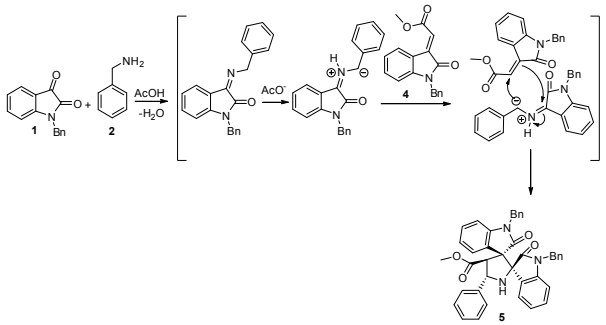


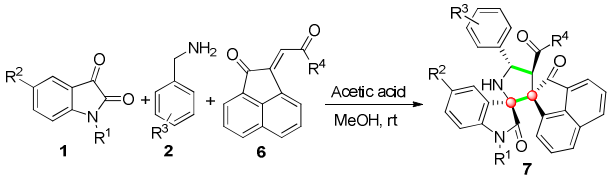
Fig. 2 Ortep diagram of Compound **5a**

In order to explore the generality of the developed method, we attempted to trap the *in situ* generated 1,3-dipole by adding preformed electron deficient dipolarophiles. To our delight, we observed the diastereoselective formation of dispiropyrrolidinyl oxindole as a single isomer, unlike the formation of a mixture of regioisomers in non-catalysed condition.[15] Interestingly, we did not observe the formation of imidazoline oxindoles. With this, we concluded that the *in situ* generated 1,3-dipole undergoes rapid cycloaddition with the added electron deficient dipolarophile and results in the formation of dispiropyrrolidines. However, in the absence of an activated dipolarophile, the 1,3-dipole generated *in situ* undergoes cycloaddition with the ketimine generated *in situ* and results in the formation of dispiroimidazolidines. In separate experiments, we used **4** and **6** as substrates for the *in situ* generated 1,3-dipoles, which resulted in the formation of dispiropyrrolidinyl oxindoles **5** and **7**. Good yields were obtained in almost all the cases regardless of the electronic nature, bulkiness or the position of the substituents on the reactants (Table 3 and 4). Analysis of HRMS, ^{1}H and ^{13}C NMR data of compounds **5a-g** and **7a-g**, and the exchangeable nature of NH proton indicated the existence of pyrrolidine ring structure in all the cases. The very formation of dispiropyrrolidine systems confirmed the intermediary of 1,3-dipole, and the tandem cycloaddition.



Scheme 3. Plausible mechanism

Table 4 Substrate Scope with dipolarophile **6**[a]



Entry	R^1	R^2	R^3	R^4	7	Yield(%)[b]
1	Bn	H	H	-4-Brphenyl	**7a**	73
2	Bn	H	H	-4-OMephenyl	**7b**	70
3	Bn	Cl	H	-4-Brphenyl	**7c**	65
4	Bn	H	H	-4-Biphenyl	**7d**	77
5	Bn	H	4-Cl	-4-Brphenyl	**7e**	65
6	Bn	H	3,4-dimethoxy	-4-Brphenyl	**7f**	62
7	Bn	H	2,4-dichloro	-4-Brphenyl	**7g**	63

[a]Reaction carried out with 1 mmol of **1,** 1 mmol of **2**, 1 mmol of **6,** 10 mol % of acetic acid in 5 mL of methanol at room temp. [b]Isolated yield.

The XRD analyses of dispiroimidazolidine and disypiropyrrolidine oxindole analogues (**3a** and **5a**)[12] revealed the *syn* and *anti* π-facial selectivity responsible for the regioselective outcome of the reaction (Scheme 2 and 3). The inherent facial bias stemming from the difference in polarizability of imine and olefinic double bonds (dipolarophiles) appear to govern the regioselectivity and diastereoselectivity observed in the present study.

Conclusions

In summary, tandem cycloaddition of *in situ* generated 1,3-dipole with dienophiles resulting in rapid formation of densely functionalized dispiroimidazolidine and dispiropyrrolidine ring systems is reported. The unique advantages of this one-pot methodology are: 1) Single-step construction of imidazolidine ring with three chiral centers including two non-contiguous spiro-quaternary stereocenters *via* the formation of one new C−C and three new C−N bonds, 2) Construction of pyrrolidine ring with four chiral centers including two contiguous spiro-quaternary stereocenters *via* the formation of two new C−C bonds, and 3) Regio- and diastereoselective formation of highly stable single isomer. Further, oxalic acid is also found to efficiently catalyse this tandem cycloaddition. We believe that the imidazolidine and pyrrolidine ring systems described in this report would help in the future construction of biologically important highly functionalized dispiroimidazolidineoxindoles and dispiropyrrolidinyloxindoles with high stereoselectivity.

Experimental Section

General methods

All the reagents were purchased from Sigma-Aldrich and used without further purification. Pre-coated plates (Merck, silica gel 60 GF_{254}, 0.25 mm) were used for TLC analysis. The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 400 and 500 MHz Spectrometers. The DEPT-135 experiments were carried out on Bruker Avance 400 MHz Spectrometer. Mass fragmentation was obtained using JEOL GCMATE II GC-MS. The ^1H and ^{13}C chemical shift values (δ) are given in ppm with reference to TMS as internal standard (zero ppm). Coupling constants are given in Hertz.

2. General procedures

Procedure (A): Benzyl isatin **1** (1 mmol), benzylamine **2** (1 mmol) and acetic acid (10 mol %) were taken in an oven-dried 50 mL round-bottom-flask containing 5-10 mL methanol, and the contents of the flask were stirred at room temperature until the starting materials were consumed. Only a single product was obtained as solid. The crude product was separated by filtration, and washed with 10-15 mL of methanol to obtain pure white solid that did not require further purification.

Procedure (B): Benzyl isatin **1** (1 mmol), benzylamine **2** (1 mmol), (*E*)-alkyl 2-(1-benzyl-2-oxoindolin-3-ylidene)acetate **4** (1 mmol) and acetic acid (10 mol %) were taken in an oven-dried 50 mL round-bottom-flask containing 5-10 mL methanol, and the contents of the flask were stirred at room temperature until the starting materials were consumed. The single product obtained (crude product) was separated by filtration, and washed with 10-15 mL methanol to obtain a pure white solid that did not require further purification.

Procedure (C): Benzyl isatin **1** (1 mmol), benzylamine **2** (1 mmol), (*E*)-2-(2-oxo-2-phenylethylidene)acenaphthylen-1(2H)-one derivatives **6** (1 mmol) and acetic acid (10 mol %) were taken in an oven-dried 50 mL round-bottom-flask containing 5-10 mL methanol, and the contents of the flask were stirred at room temperature until the starting materials were consumed. The crude product obtained was separated by filtration, and washed with 10-15 mL methanol to obtain a pure white solid that did not require further purification.

(3S, 4'R, 5'R)-3'-benzyl-1,1''-bis[(3-methylphenyl)methyl]-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3a): The title compound was prepared according to the general procedure (**A**) as a white solid in 83% yield; mp = 188-190 °C; IR (KBr): 3055, 3026, 2915, 2845, 1728, 1699, 1610, 1485, 1466, 1345, 1179, 1093, 965, 943, 755, 739, 694, 560 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.6 Hz, 1H), 8.06 (d, *J* = 7.1 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 4H), 7.14 (t, *J* = 7.3 Hz, 4H), 7.09 (s, 1H), 6.98 (qd, *J* = 13.7, 5.4 Hz, 8H), 6.93 – 6.87 (m, 2H), 6.68 (d, *J* = 7.1 Hz, 1H), 6.65 (d, *J* = 18.1 Hz, 1H), 6.54 (d, *J* = 7.2 Hz, 1H), 6.31 (d, *J* = 7.6 Hz, 1H), 5.98 (d, *J* = 7.0 Hz, 1H), 5.63 (s, 1H), 4.80 (d, *J* = 15.8 Hz, 1H), 4.74 (d, *J* = 15.8 Hz, 1H), 4.40 (d, *J* = 15.8 Hz, 1H), 3.84 (d, *J* = 4.6 Hz, 1H), 3.82 (d, *J* = 12.8 Hz, 1H), 3.52 (d, *J* = 13.0 Hz, 1H), 2.28 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.43, 177.36, 143.89, 143.61, 138.41, 137.94, 136.96, 135.64, 135.29, 133.89, 130.40, 129.16, 128.93, 128.66, 128.54, 128.27, 128.13, 127.97, 127.91, 127.88, 127.41, 127.38, 127.06, 126.81, 126.65, 126.45, 125.81, 125.18, 124.17, 123.49, 123.04, 122.89, 109.32, 109.14, 81.76, 74.43, 69.76, 49.44, 43.67, 43.47, 21.41, 21.39; HRMS (EI) Calcd for $[C_{46}H_{40}N_4O_2+H]$: 681.3230; found : 681.3226.

(3S, 4'R, 5'R)-1,1'',3'-tribenzyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3b):

The title compound was prepared according to the general procedure (**A**) as a white solid in 79% yield; mp = 204-206 °C; IR (KBr): 3045, 3028, 2926, 2840, 1721, 1610, 1482, 1444, 1340, 1256, 1178, 1072, 1025, 962, 880, 811, 735, 697, 604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.6 Hz, 1H), 8.08 (d, *J* = 6.6 Hz, 1H), 7.28 – 7.18 (m, 9H), 7.13 (dd, *J* = 14.4, 6.7 Hz, 4H), 7.04 (dd, *J* = 6.9, 6.0 Hz, 3H), 7.00 – 6.94 (m, 4H), 6.70 (d, *J* = 7.1 Hz, 2H), 6.52 (d, *J* = 6.9 Hz, 1H), 6.38 (d, *J* = 7.3 Hz, 2H), 6.29 (d, *J* =

7.7 Hz, 1H), 5.63 (s, 1H), 4.83 (d, *J* = 8.8 Hz, 1H), 4.79 (d, *J* = 8.9 Hz, 1H), 4.48 (d, *J* = 15.8 Hz, 1H), 3.88 (d, *J* = 16.0 Hz, 1H), 3.84 (d, *J* = 13.2 Hz, 1H), 3.53 (d, *J* = 13.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.41, 177.24, 143.80, 143.43, 136.96, 135.66, 135.22, 133.78, 130.41, 129.17, 128.97, 128.76, 128.50, 128.21, 127.95, 127.45, 127.09, 126.99, 126.76, 126.69, 126.51, 126.39, 125.86, 125.18, 123.07, 122.95, 109.29, 109.06, 81.74, 74.63, 69.82, 49.42, 43.63, 43.31; HRMS (EI) Calcd for $[C_{44}H_{36}N_4O_2+H]$: 653.2917; found : 653.2913.

(3S, 4'R, 5'R)-1,1'',3'-tribenzyl-5,5''-difluoro-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3c):

The title compound was prepared according to the general procedure (**A**) as a white solid in 81% yield; mp = 232-234 °C; IR (KBr): 3060, 3030, 2925, 2850, 1724, 1611, 1488, 1454, 1342, 1263, 1177, 1076, 1031, 967, 881, 818, 739, 698, 608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.4 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.27 (dd, *J* = 15.4, 7.8 Hz, 4H), 7.19 (t, *J* = 7.5 Hz, 4H), 7.13 (d, *J* = 6.8 Hz, 1H), 7.10 – 7.04 (m, 3H), 7.04 – 6.96 (m, 3H), 6.94 (t, *J* = 8.8 Hz, 1H), 6.84 (t, *J* = 8.8 Hz, 1H), 6.77 (d, *J* = 7.2 Hz, 2H), 6.43 (dd, *J* = 8.3, 3.4 Hz, 1H), 6.36 (d, *J* = 7.4 Hz, 2H), 6.19 (dd, *J* = 8.4, 3.6 Hz, 1H), 5.57 (d, *J* = 9.8 Hz, 1H), 4.85 (d, *J* = 4.2 Hz, 1H), 4.81 (d, *J* = 4.4 Hz, 1H), 4.44 (d, *J* = 15.8 Hz, 1H), 4.00 (d, *J* = 11.2 Hz, 1H), 3.86 (t, *J* = 14.5 Hz, 2H), 3.56 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.18, 176.91, 159.62 (*J* = 240.0 Hz), 159.57 (*J* = 241.0 Hz), 139.70, 139.32, 136.39, 135.30, 134.83, 133.27, 128.99, 128.87, 128.61, 128.37, 128.27, 127.65, 127.19, 127.09, 127.01, 126.57, 126.39, 116.70 (*J* = 23.0 Hz), 115.65 (*J* = 23.0 Hz), 113.93 (*J* = 25.0 Hz), 112.94 (*J* = 24.0 Hz), 110.05 (*J* = 8.0 Hz), 109.79 (*J* = 8.0 Hz), 81.78, 74.95, 70.10, 49.62, 43.81, 43.53; HRMS (EI) Calcd for $[C_{44}H_{34}F_2N_4O_2]$: 689.2728; found: 689.2725.

(3S, 4'R, 5'R)-1,1'',3'-tribenzyl-5,5''-dichloro-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3d):

The title compound was prepared according to the general procedure (**A**) as a white solid in 78% yield; mp = 240-242 °C; IR (KBr): 3064, 3030, 2925, 2850, 1731, 1608, 1484, 1454, 1338, 1181, 1110, 1076, 1031, 960, 814, 743, 694, 574 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.97 (s, 1H), 7.25 – 7.18 (m, 5H), 7.12 (dd, *J* = 12.8, 7.2 Hz, 6H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.99 (t, *J* = 8.3 Hz, 4H), 6.92 (d, *J* = 7.4 Hz, 2H), 6.69 (d, *J* = 6.8 Hz, 2H), 6.36 (d, *J* = 8.2 Hz, 1H), 6.27 (d, *J* = 7.3 Hz, 2H), 6.12 (d, *J* = 8.3 Hz, 1H), 5.50 (s, 1H), 4.78 (d, *J* = 15.8 Hz, 2H), 4.36 (d, *J* = 15.9 Hz, 1H), 3.84 – 3.73 (m, 2H), 3.49 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.91, 176.67, 142.34, 141.95, 136.31, 135.14, 134.67, 133.16, 130.51, 129.78, 129.34, 129.06, 128.92, 128.82, 128.65, 128.42, 128.34, 127.71, 127.25, 127.07, 126.60, 126.37, 126.21, 125.24, 110.45, 110.19, 81.68, 74.80, 70.05, 49.71, 43.77, 43.51; HRMS (EI) Calcd for $[C_{44}H_{34}Cl_2N_4O_2+H]$: 721.2137; found: 721.2135.

(3S, 4'R, 5'R)-1,1'',3'-tribenzyl-5,5''-dimethyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3e): The title compound was prepared according to the general procedure (**A**) as a white solid in 82% yield; mp = 210-212 °C; IR (KBr): 3052, 3022, 2905, 2840, 1721, 1690, 1608, 1484, 1460, 1341, 1165, 1090, 961, 936, 755, 734, 690, 564 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.88 (s, 1H), 7.23 (m, 5H), 7.21 – 7.08 (m, 5H), 7.08 – 6.90 (m, 10H), 6.73 (d, *J* = 7.1 Hz, 2H), 6.39 (t, *J* = 8.4 Hz, 2H), 6.18 (d, *J* = 7.9 Hz, 1H), 5.61 (d, *J* = 11.3 Hz, 1H), 4.81 (d, *J* = 15.8 Hz, 2H), 4.47 (d, *J* = 15.9 Hz, 1H), 3.87 (t, *J* = 14.1 Hz, 2H), 3.55 (d, *J* = 13.2 Hz, 1H), 2.46 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.47, 177.26, 141.38, 141.08, 137.23, 135.80, 135.35, 133.96, 132.74, 132.60, 130.63, 129.48, 129.00, 128.73, 128.48, 128.18, 127.88, 127.44, 127.38, 127.15, 127.07, 126.94, 126.78, 126.63, 126.51, 126.49, 126.42, 125.76, 109.10, 108.81, 81.91, 74.83, 69.74, 49.51, 43.64, 43.37, 21.33, 21.29; HRMS (EI) Calcd for $[C_{46}H_{40}N_4O_2+H]$: 681.3230; found : 681.3230.

(3S, 4'R, 5'R)-3'-benzyl-5,5''-diiodo-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3f): The title compound was prepared according to the general procedure (**A**) as a white solid in 68% yield; mp = 224-226 °C; IR (KBr): 3326, 3180, 3030, 2848, 1722, 1613, 1473, 1300, 1189, 1103, 972, 895, 812, 748, 697, 535 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.19 (s, 1H), 7.88 (s, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.55 (s, 1H), 7.26 (s, 1H), 7.16 (d, *J* = 6.9 Hz, 2H), 6.99 (d, *J* = 6.6 Hz, 2H), 6.92 (d, *J* = 7.2 Hz, 2H), 6.72 (d, *J* = 7.0 Hz, 2H), 6.55 (d, *J* = 8.2 Hz, 1H), 6.46 (d, *J* = 8.1 Hz, 1H), 5.39 (d, *J* = 11.2 Hz, 1H), 3.80 (d, *J* = 12.4 Hz, 1H), 3.71 (d, *J* = 13.3 Hz, 1H), 3.54 (d, *J* = 13.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.38, 178.00, 141.50, 140.98, 139.44, 138.28, 136.40, 134.94, 133.91, 133.23, 130.06, 129.16, 129.02, 128.22, 127.77, 127.12, 126.02, 112.22, 111.92, 85.59, 85.20, 81.48, 75.08, 69.86, 49.79; HRMS (EI) Calcd for $[C_{30}H_{22}I_2N_4O_2+H]$: 724.9910; found : 724.9905.

(3S, 4'R, 5'R)-3'-benzyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3g): The title compound was prepared according to the general procedure (**A**) as a white solid in 75% yield; mp = 158-160 °C; IR (KBr): 3195, 3030, 2892, 2843, 1720, 1619, 1469, 1334, 1278, 1196, 1117, 1020, 967, 750, 698, 567 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.3 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.68 (s, 1H), 7.61 – 7.50 (m, 1H), 7.33 (s, 1H), 7.31 – 7.27 (m, 1H), 7.25 (d, *J* = 4.4 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.16 – 7.07 (m, 3H), 6.99 – 6.87 (m, 5H), 6.68 (d, *J* = 7.6 Hz, 2H), 6.63 – 6.57 (m, 1H), 5.49 (s, 1H), 3.76 (d, *J* = 13.3 Hz, 1H), 3.53 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.48, 179.18, 141.93, 141.43, 138.55, 137.08, 134.49, 133.94, 130.48, 129.77, 129.28, 128.95, 128.04, 127.86, 127.78, 127.48, 127.01, 126.75, 126.25, 125.96, 125.64, 125.45, 123.77, 123.04, 122.86, 112.58, 110.12, 109.86, 81.73, 77.35,

77.03, 76.72, 75.05, 69.60, 49.37; HRMS (EI) Calcd for $[C_{30}H_{24}N_4O_2+H]$: 473.1978; found : 473.1975.

(3S,4'R,5'R)-3'-benzyl-1,1''-dimethyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3h): The title compound was prepared according to the general procedure (**A**) as a white solid in 82% yield; mp = 200-202 °C; IR (KBr): 3058, 3026, 2928, 2886, 2854, 1728, 1706, 1610, 1489, 1466, 1367, 1336, 1253, 1214, 1119, 1083, 1023, 972, 879, 803, 752, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.2 Hz, 1H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.34 – 7.28 (m, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 4.9 Hz, 1H), 6.85 (d, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 5.8 Hz, 1H), 6.56 (d, *J* = 7.4 Hz, 1H), 5.52 (s, 1H), 3.71 (d, *J* = 13.0 Hz, 1H), 3.46 (d, *J* = 13.0 Hz, 1H), 2.87 (s, 1H), 2.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.47, 176.86, 144.65, 144.24, 136.84, 133.98, 130.42, 129.26, 128.96, 127.83, 127.72, 127.48, 127.28, 126.50, 126.34, 125.92, 125.81, 124.86, 123.09, 122.78, 108.07, 107.90, 81.10, 75.25, 69.61, 49.42, 25.62, 25.35; HRMS (EI) Calcd for $[C_{32}H_{28}N_4O_2+H]$: 501.2291; found : 501.2290.

(3S, 4'R, 5'R)-3'-benzyl-1,1''-bis[(4-tert-butylphenyl)methyl]-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3i): The title compound was prepared according to the general procedure (**A**) as a white solid in 76% yield; mp = 182-184 °C; IR (KBr): 3055, 3030, 2963, 2861, 1734, 1706, 1610, 1489,1470, 1361, 1176, 969, 940, 758, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.24 – 7.19 (m, 3H), 7.19 – 7.11 (m, 5H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 7.0 Hz, 1H), 6.96 (dd, *J* = 15.4, 7.7 Hz, 4H), 6.69 (d, *J* = 7.3 Hz, 2H), 6.57 (d, *J* = 7.6 Hz, 1H), 6.37 (d, *J* = 7.9 Hz, 2H), 6.34 (d, *J* = 7.7 Hz, 1H), 5.62 (s, 1H), 4.79 (d, *J* = 15.8 Hz, 1H), 4.71 (d, *J* = 15.7 Hz, 1H), 4.44 (d, *J* = 15.8 Hz, 1H), 4.06 (s, 1H), 3.89 (d, *J* = 15.8 Hz, 1H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 1.25 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.37, 177.23, 150.34, 149.79, 143.94, 143.61, 137.02, 133.89, 132.68, 132.24, 130.38, 129.12, 128.97, 128.17, 127.83, 127.42, 127.15, 126.91, 126.84, 126.64, 126.49, 126.19, 125.85, 125.68, 125.37, 125.21, 123.00, 122.85, 109.29, 109.09, 81.77, 77.34, 77.02, 76.70, 74.56, 69.81, 49.46, 43.29, 42.97, 34.45, 34.34, 31.29; HRMS (EI) Calcd for $[C_{52}H_{52}N_4O_2+H]$: 765.4169; found : 765.4165.

(3S, 4'R, 5'R)-3'-benzyl-5,5''-dichloro-1,1''-bis[(4-cyanophenyl)methyl]-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3j): The title compound was prepared according to the general procedure (**A**) as a white solid in 73% yield; mp = 176-178 °C; IR (KBr): 3064, 2922, 2850, 2229, 1731, 1709, 1608, 1480, 1338, 1173, 1110, 1031, 949, 814, 750, 698, 563 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.05 (s, 1H), 7.58 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 3H), 7.29 – 7.15 (m, 7H), 7.06 (dt, *J* = 13.8, 6.9 Hz, 3H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.75 (d, *J* = 7.1 Hz, 2H), 6.37 (d, *J* = 8.0 Hz, 3H), 6.15 (d, *J* = 8.3 Hz, 1H), 5.53 (s, 1H), 4.93 (dd, *J* = 31.3, 14.9 Hz, 2H), 4.45 (d, *J* = 16.5 Hz, 1H), 3.91 (d, *J* = 16.7 Hz, 1H), 3.81 (d, *J* = 13.1 Hz, 1H), 3.56 (d, *J* = 13.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.88, 176.60, 141.71, 141.30, 140.56, 140.14, 136.02, 132.94, 132.78, 132.52, 130.72, 129.60, 129.20, 129.17, 129.09, 128.66, 128.53, 128.07, 127.78, 127.62, 127.19, 126.89, 126.66, 126.50, 125.44, 118.42, 111.81, 111.32, 110.02, 109.74, 81.53, 74.92, 70.07, 49.63, 43.34, 43.12; HRMS (EI) Calcd for $[C_{46}H_{32}Cl_2N_{46}O_2+H]$: 771.2042; found : 771.2040.

(3S, 4'R, 5'R)-1,1''-dibenzyl-5'-(2-methylphenyl)-3'-[(2-methylphenyl)methyl]-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3k): The title compound was prepared according to the general procedure (**A**) as a white solid in 75 % yield; mp = 138-140 °C; IR (KBr): 3058, 2975, 2905, 2867, 1718, 1648, 1604, 1460, 1380, 1351, 1179, 1103, 1010, 937, 870, 752, 704, 640, 614, 551 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 6.5 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 1H), 7.61 (s, 1H), 7.28 – 7.12 (m, 10H), 7.09 (dd, *J* = 21.7, 14.5 Hz, 5H), 6.98 (s, 1H), 6.90 (d, *J* = 6.7 Hz, 3H), 6.79 (d, *J* = 5.6 Hz, 1H), 6.55 (d, *J* = 6.9 Hz, 2H), 6.36 (d, *J* = 7.0 Hz, 1H), 6.20 (d, *J* = 7.4 Hz, 1H), 5.93 (s, 1H), 4.90 (d, *J* = 16.6 Hz, 1H), 4.85 (d, *J* = 16.5 Hz, 1H), 4.62 (d, *J* = 15.9 Hz, 1H), 4.01 (d, *J* = 13.3 Hz, 1H), 3.90 (d, *J* = 16.2 Hz, 1H), 3.47 (d, *J* = 13.2 Hz, 1H), 1.92 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.37, 177.00, 143.69, 143.07, 137.71, 137.37, 135.72, 135.32, 134.46, 132.06, 130.49, 130.39, 130.27, 129.42, 129.03, 128.79, 128.55, 127.86, 127.49, 127.20, 127.14, 126.99, 126.94, 126.82, 126.77, 126.27, 125.95, 125.91, 124.75, 123.09, 122.47, 109.35, 109.05, 82.06, 75.03, 65.79, 47.35, 43.70, 43.32, 19.70, 19.22; HRMS (EI) Calcd for $[C_{46}H_{40}N_4O_2+H]$: 681.3230; found : 681.3230.

(3S, 4'R, 5'R)-1,1''-dibenzyl-5'-(4-methylphenyl)-3'-[(4-methylphenyl)methyl]-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3l): The title compound was prepared according to the general procedure (**A**) as a white solid in 73 % yield; mp = 208-210 °C; IR (KBr): 3058, 3030, 2918, 2851, 1728, 1699, 1613, 1517, 1489, 1470, 1358, 1182, 1042, 965, 758, 729,697, 554 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.7 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.29 – 7.17 (m, 9H), 7.13 (t, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.79 (d, *J* = 7.6 Hz, 2H), 6.57 (d, *J* = 7.6 Hz, 2H), 6.51 (d, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 7.5 Hz, 2H), 6.29 (d, *J* = 7.7 Hz, 1H), 5.57 (s, 1H), 4.84 (d, *J* = 10.8 Hz, 1H), 4.80 (d, *J* = 10.8 Hz, 1H), 4.47 (d, *J* = 15.8 Hz, 1H), 3.88 (d, *J* = 15.9 Hz, 1H), 3.79 (d, *J* = 13.1 Hz, 1H), 3.48 (d, *J* = 13.0 Hz, 1H), 2.30 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.54, 177.37, 143.83, 143.46, 137.44, 136.09, 135.74, 135.35, 134.06, 130.84, 130.32, 129.04, 128.96, 128.87, 128.75, 128.34, 128.09, 127.44, 127.37, 127.13, 127.00, 126.55, 126.45, 125.91, 125.19, 123.03, 122.90, 109.28, 109.01, 81.74, 74.74, 69.80, 49.06, 43.69, 43.38, 21.25, 21.06;

HRMS (EI) Calcd for $[C_{46}H_{40}N_4O_2+H]+$: 681.3230; found : 681.3230.

(3S, 4'R, 5'R)-1,1''-dibenzyl-5'-(4-methoxyphenyl)-3'-[(4-methoxyphenyl)methyl]-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3m): The title compound was prepared according to the general procedure (**A**) as a white solid in 70% yield; mp = 202-204 °C; IR (KBr): 3058, 3030, 2928, 2835, 1725, 1699, 1613, 1514, 1466, 1355, 1300, 1253, 1179, 1036,962, 828, 758, 732, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.8 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.28 – 7.16 (m, 9H), 7.15 – 7.11 (m, 2H), 7.07 (t, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.67 (d, *J* = 8.3 Hz, 2H), 6.60 (d, *J* = 8.2 Hz, 2H), 6.53 (d, *J* = 8.0 Hz, 3H), 6.42 (d, *J* = 7.4 Hz, 2H), 6.33 (d, *J* = 7.6 Hz, 1H), 5.55 (s, 1H), 4.86 (d, *J* = 15.9 Hz, 1H), 4.80 (d, *J* = 15.9 Hz, 1H), 4.54 (d, *J* = 15.8 Hz, 1H), 3.95 (d, *J* = 15.9 Hz, 1H), 3.78 (d, *J* = 13.0 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.46 (d, *J* = 13.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.57, 177.38, 159.37, 158.40, 143.83, 143.42, 135.69, 135.27, 130.34, 130.22, 129.23, 129.08, 128.75, 128.38, 127.74, 127.46, 127.09, 126.97, 126.50, 125.86, 125.07, 123.02, 122.93, 113.56, 112.90, 109.31, 109.00, 81.62, 69.61, 55.21, 55.04, 48.69, 43.69, 43.34; HRMS (EI) Calcd for $[C_{46}H_{40}N_4O_4+H]$: 713.3128; found : 713.3125.

(3S, 4'R, 5'R)-1,1''-dibenzyl-5'-(4-chlorophenyl)-3'-[(4-chlorophenyl)methyl]-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3n): The title compound was prepared according to the general procedure (**A**) as a white solid in 82 % yield; mp = 218-220 °C; IR (KBr): 3056, 2972, 2901, 2868, 1712, 1640, 1609, 1461, 1380, 1350, 1175, 1101, 1015, 934, 870, 750, 704, 648, 612, 550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.4 Hz, 1H), 8.03 (d, *J* = 6.2 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.27 – 7.24 (m, 3H), 7.22 (dd, *J* = 7.0, 4.4 Hz, 4H), 7.17 (d, *J* = 7.0 Hz, 3H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.61 (d, *J* = 8.3 Hz, 2H), 6.57 (d, *J* = 7.4 Hz, 1H), 6.49 – 6.42 (m, 2H), 6.38 (d, *J* = 7.5 Hz, 1H), 5.58 (s, 1H), 4.86 (d, *J* = 3.0 Hz, 1H), 4.82 (d, *J* = 3.1 Hz, 1H), 4.54 (d, *J* = 15.8 Hz, 1H), 3.91 (d, *J* = 15.8 Hz, 1H), 3.80 (d, *J* = 13.2 Hz, 1H), 3.46 (d, *J* = 13.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.21, 176.95, 143.76, 143.39, 135.56, 135.48, 134.99, 133.96, 132.47, 132.37, 130.67, 130.37, 129.54, 128.84, 128.58, 128.44, 127.91, 127.59, 127.38, 127.11, 126.59, 126.50, 126.45, 125.82, 125.16, 123.25, 123.17, 109.49, 109.25, 81.70, 77.35, 77.03, 76.71, 74.36, 69.10, 48.79, 43.74, 43.48; HRMS (EI) Calcd for $[C_{44}H_{34}Cl_2N_4O_2+H]$: 721.2137; found : 721.2135.

(3S, 4'R, 5'R)-1,1''-dibenzyl-5'-(3,4-dimethoxyphenyl)-3'-[(3,4-dimethoxyphenyl)methyl]-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3o): The title compound was prepared according to the general procedure (**A**) as a white solid in 68 % yield; mp = 176-178 °C; IR (KBr): 3055, 3030, 2937, 2835, 1709, 1610, 1517, 1466, 1355, 1259, 1179, 1138, 1026, 965, 857, 796, 761, 732, 697, 554 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.1 Hz, 1H), 8.06 (d, *J* = 7.3 Hz, 1H), 7.30 – 7.18 (m, 9H), 7.15 (t, *J* = 7.7 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 2H), 6.67 (q, *J* = 8.6 Hz, 2H), 6.56 (d, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 6.45 (d, *J* = 7.5 Hz, 2H), 6.36 (d, *J* = 7.8 Hz, 1H), 6.33 (s, 1H), 6.25 (d, *J* = 8.2 Hz, 1H), 6.18 (s, 1H), 5.57 (s, 1H), 4.87 (d, *J* = 10.9 Hz, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 4.60 (d, *J* = 15.8 Hz, 1H), 4.02 (s, 1H), 3.94 (d, *J* = 15.8 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.69 (s, 3H), 3.51 (d, J = 13.1 Hz, 1H), 3.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.44, 177.43, 148.69, 148.37, 147.99, 147.56, 143.87, 143.64, 135.59, 135.08, 130.43, 129.75, 129.06, 128.79, 128.45, 127.54, 127.33, 127.05, 126.97, 126.43, 126.28, 125.71, 125.06, 123.03, 122.90, 120.99, 117.92, 111.95, 110.61, 110.29, 109.72, 109.36, 109.02, 81.72, 74.50, 69.60, 55.90, 55.63, 55.42, 55.30, 49.03, 43.67, 43.37; HRMS (EI) Calcd for $[C_{48}H_{44}N_4O_6+H]$: 773.3339; found : 773.3335.

(3S, 4'R, 5'R)-1,1''-dibenzyl-2,2''-dioxo-5'-(3,4,5-trimethoxyphenyl)-3'-[(3,4,5-trimethoxyphenyl)methyl]-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-imidazolidine-4',3''-indol]-1'-ide (3p): The title compound was prepared according to the general procedure (A) as a white solid in 65 % yield; mp = 170-172 °C; IR (KBr): 3062, 3023, 2934, 2838, 1725, 1610, 1591, 1505, 1470, 1422, 1358, 1240, 1179, 1122, 1010, 841, 761, 732, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 6.4 Hz, 1H), 8.03 (d, *J* = 7.0 Hz, 1H), 7.25 (dt, *J* = 13.8, 6.8 Hz, 9H), 7.17 (s, 4H), 6.58 (d, *J* = 7.5 Hz, 1H), 6.55 (s, 2H), 6.38 (d, *J* = 7.5 Hz, 1H), 6.10 (s, 2H), 6.00 (s, 2H), 5.62 (s, 1H), 4.94 (d, *J* = 9.9 Hz, 1H), 4.90 (d, *J* = 9.7 Hz, 1H), 4.57 (d, *J* = 15.9 Hz, 1H), 3.95 (d, *J* = 15.7 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.67 (s, 6H), 3.52 (d, *J* = 13.0 Hz, 1H), 3.43 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.52, 177.23, 152.88, 152.29, 143.90, 137.64, 136.19, 135.53, 134.94, 132.72, 130.55, 129.57, 129.19, 128.85, 128.70, 127.62, 127.55, 127.40, 127.05, 126.84, 126.40, 125.65, 125.04, 123.04, 122.88, 109.40, 109.14, 105.41, 103.02, 81.71, 73.90, 69.42, 60.88, 60.76, 55.72, 55.65, 49.62, 43.60, 43.52; HRMS (EI) Calcd for $[C_{50}H_{48}N_4O_8+H]$: 833.3550; found : 833.3555.

Methyl (3S,3'R,4'S,5'S)-1,1''-dibenzyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5a): The title compound was prepared according to the general procedure (**B**) as a white solid in 78 % yield; mp = 182-184 °C; IR (KBr): 3318, 3060, 3030, 2933, 2835, 1716, 1679, 1600, 1488, 1364, 1304, 1256, 1173, 1027, 967, 840, 750, 698, 552 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.1 Hz, 2H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.51 – 7.38 (m, 3H), 7.33 (d, *J* = 6.8 Hz, 1H), 7.15 – 6.99 (m, 8H), 6.86 (d, *J* = 6.8 Hz, 2H), 6.67 (d, *J* = 7.0 Hz, 2H), 6.59 (d, *J* = 7.0 Hz, 2H), 6.45 (d, *J* = 7.6 Hz, 1H), 6.36 (d, *J* = 7.5 Hz, 1H), 6.14 (d, *J* = 9.0 Hz, 1H), 5.05 (t, *J* = 17.0 Hz, 2H), 4.57 (d, *J* = 16.0 Hz, 1H), 4.27 (d, *J* = 15.9 Hz, 1H), 4.06 (d, *J* = 9.0 Hz, 1H), 3.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.59, 143.33, 140.57, 134.98, 134.90, 129.85, 128.84, 128.75,

128.61, 128.55, 128.05, 127.96, 127.18, 127.11, 126.76, 126.60, 126.50, 126.26, 125.42, 122.88, 122.71, 109.13, 108.99, 77.35, 77.03, 76.72, 75.21, 63.56, 63.05, 60.88, 51.41, 43.83, 43.32; HRMS (EI) Calcd for $[C_{40}H_{33}N_3O_4+H]$: 620.2549; found : 620.2545.

Ethyl (3S,3'R,4'S,5'S)-1,1''-dibenzyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5b): The title compound was prepared according to the general procedure (**B**) as a white solid in 70 % yield; mp = 162-164 °C; IR (KBr): 3318, 3060, 3030, 2907, 2835, 1716, 1679, 1596, 1507, 1492, 1462, 1364, 1301, 1259, 1173, 1031, 840, 754, 732, 698, 597, 552 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.4 Hz, 2H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.17 – 6.97 (m, 7H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.85 (t, *J* = 7.7 Hz, 1H), 6.69 (d, *J* = 7.4 Hz, 2H), 6.58 (d, *J* = 7.5 Hz, 2H), 6.45 (d, *J* = 7.8 Hz, 1H), 6.36 (d, *J* = 7.8 Hz, 1H), 6.12 (d, *J* = 9.3 Hz, 1H), 5.09 (d, *J* = 16.0 Hz, 1H), 4.97 (d, *J* = 16.1 Hz, 1H), 4.61 (d, *J* = 16.1 Hz, 1H), 4.26 (d, *J* = 16.0 Hz, 1H), 4.05 (d, *J* = 9.3 Hz, 1H), 3.70 (q, *J* = 7.2 Hz, 2H), 0.61 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.44, 176.62, 169.48, 143.59, 143.40, 140.65, 135.00, 134.91, 129.82, 128.78, 128.71, 128.60, 128.54, 127.99, 127.20, 127.09, 127.02, 126.60, 126.45, 126.38, 125.61, 122.82, 122.72, 108.97, 75.08, 63.42, 63.04, 60.88, 60.35, 43.73, 43.34, 13.43; HRMS (EI) Calcd for $[C_{41}H_{35}N_3O_4+H]$: 634.2706; found : 634.2700.

Methyl (3S,3'R,4'S,5'S)-1,1''-dibenzyl-5-fluoro-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5c): The title compound was prepared according to the general procedure (**B**) as a white solid in 73 % yield; mp = 209-211 °C; IR (KBr): 3314, 3050, 3028, 2930, 2832, 1710, 1675, 1605, 1484, 1360, 1302, 1254, 1170, 1024, 962, 836, 750, 695, 550 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 2.1 Hz, 1H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.12 (dd, *J* = 13.1, 5.7 Hz, 2H), 7.08 (t, *J* = 7.2 Hz, 3H), 7.06 – 7.02 (m, 2H), 7.01 (t, *J* = 7.7 Hz, 2H), 6.85 (q, *J* = 7.0 Hz, 2H), 6.67 (t, *J* = 9.3 Hz, 3H), 6.56 (d, *J* = 7.5 Hz, 2H), 6.46 (d, *J* = 7.8 Hz, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 5.11 (d, *J* = 16.0 Hz, 1H), 5.04 (d, *J* = 16.1 Hz, 1H), 4.56 (d, *J* = 16.1 Hz, 1H), 4.23 (d, *J* = 16.0 Hz, 1H), 4.13 (d, *J* = 9.3 Hz, 1H), 3.26 (s, 3H), 2.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.16, 176.32, 169.82, 159.04 (*J* = 240.0 Hz), 143.38, 140.42, 139.42, 134.88, 134.67, 129.00, 128.86, 128.76, 128.64, 128.62, 128.11, 127.95, 127.63, 127.32, 127.26, 127.14, 126.81, 126.71, 126.64, 126.59, 126.44, 125.18, 122.79, 116.15 (*J* = 24.0 Hz), 114.77 (*J* = 26.0 Hz), 109.45 (*J* = 8.0 Hz), 74.91, 63.41, 62.75, 60.77, 51.41, 43.85, 43.45; HRMS (EI) Calcd for $[C_{40}H_{32}FN_3O_4+H]$: 638.2455; found : 638.2450.

Methyl (3S,3'R,4'S,5'S)-1''-benzyl-1-methyl-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5d): The title compound was prepared according to the general procedure (**B**) as a white solid in 68% yield; mp = 152-154 °C; IR (KBr): 3060, 3034, 2925, 1764, 1720, 1697, 1608, 1492, 1462, 1432, 1372, 1245, 1177, 1121, 1031, 923, 758, 702, 541 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 12.5, 5.2 Hz, 3H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.16 (dd, *J* = 15.9, 8.5 Hz, 3H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.94 – 6.83 (m, 2H), 6.78 (d, *J* = 7.0 Hz, 2H), 6.57 (d, *J* = 7.7 Hz, 1H), 6.41 (d, *J* = 7.7 Hz, 1H), 6.16 (d, *J* = 8.6 Hz, 1H), 4.99 (d, *J* = 16.0 Hz, 1H), 4.60 (d, *J* = 16.0 Hz, 1H), 3.97 (d, *J* = 8.7 Hz, 1H), 3.25 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.72, 175.96, 170.05, 144.26, 143.13, 140.76, 135.00, 129.84, 128.81, 128.76, 128.63, 127.97, 127.29, 126.66, 125.99, 125.69, 125.02, 124.90, 122.81, 122.28, 109.05, 107.77, 75.32, 63.68, 62.87, 60.87, 51.41, 43.79, 25.57; HRMS (EI) Calcd for $[C_{34}H_{29}N_3O_4+H]$: 544.2236; found : 544.2232.

Methyl (3S,3'R,4'S,5'S)-1''-benzyl-2,2''-dioxo-5'-phenyl-1-(prop-2-yn-1-yl)-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5e):

The title compound was prepared according to the general procedure (**B**) as a white solid in 65 % yield; mp = 184-186 °C; IR (KBr): 3288, 3060, 3030, 2951, 2929, 1739, 1709, 1611, 1492, 1465, 1435, 1349, 1177, 1012, 762, 702, 642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.20 – 7.10 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 7.3 Hz, 2H), 6.78 (d, *J* = 4.8 Hz, 3H), 6.40 (d, *J* = 7.7 Hz, 1H), 6.13 (d, *J* = 8.7 Hz, 1H), 4.94 (d, *J* = 16.1 Hz, 1H), 4.61 (d, *J* = 16.1 Hz, 1H), 4.29 (d, *J* = 17.6 Hz, 1H), 4.10 (d, *J* = 17.7 Hz, 1H), 3.97 (d, *J* = 8.7 Hz, 1H), 3.24 (s, 3H), 1.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.51, 175.25, 170.06, 143.09, 142.29, 140.72, 135.03, 129.88, 128.84, 128.79, 128.66, 128.03, 128.00, 127.32, 126.68, 126.05, 125.93, 124.90, 124.79, 123.19, 122.56, 109.07, 108.67, 76.30, 75.30, 72.11, 63.68, 62.98, 60.65, 51.46, 43.84, 28.72; HRMS (EI) Calcd for $[C_{36}H_{29}N_3O_4+H]$: 568.2236; found : 568.2233.

Ethyl (3S,3'R,4'S,5'S)-1,1''-dibenzyl-5-fluoro-2,2''-dioxo-5'-phenyl-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5f): The title compound was prepared according to the general procedure (**B**) as a white solid in 69 % yield; mp = 176-178 °C; IR (KBr): 3330, 3064, 3030, 2981, 2914, 1724, 1611, 1492, 1454, 1364, 1267, 1264, 1177, 1046, 967, 878, 818, 754, 698, 559 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 6.8 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 6.8 Hz, 2H), 7.34 (d, *J* = 6.7 Hz, 1H), 7.17 – 7.01 (m, 7H), 6.88 (t, *J* = 7.0 Hz, 1H), 6.79 (d, *J* = 6.4 Hz, 3H), 6.57 (d, *J* = 6.8 Hz, 2H), 6.52 (d, *J* = 7.5 Hz, 1H), 6.26 (d, *J* = 3.8 Hz, 1H), 6.12 (d, *J* = 9.0 Hz, 1H), 5.08 (d, *J* = 15.7 Hz, 1H), 4.96 (d, *J* = 16.0 Hz, 1H), 4.68 (d, *J* = 16.0 Hz, 1H), 4.23 (d, *J* = 15.9 Hz, 1H), 4.02 (d, *J* = 9.1 Hz, 1H), 3.76 – 3.63 (m, 2H), 0.60 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.17,

176.50, 169.30, 143.47, 140.54, 139.46, 134.91, 134.73, 128.96, 128.74, 128.65, 128.00, 127.35, 127.10, 126.62, 126.45, 125.42, 122.82, 116.12 (J = 23.0 Hz), 114.89 (J = 26.0 Hz), 109.41 (J = 7.0 Hz), 109.03, 74.82, 63.31, 62.78, 60.78, 60.40, 43.78, 43.50, 13.43; HRMS (EI) Calcd for [$C_{41}H_{34}FN_3O_4$+H] : 652.2612; found : 652.2610.

Methyl (3S,3'R,4'S,5'S)-1,1''-dibenzyl-5'-(2,4-dichlorophenyl)-2,2''-dioxo-1,1'',2,2''-tetrahydrodispiro[indole-3,2'-pyrrolidine-3',3''-indole]-4'-carboxylate (5g):

The title compound was prepared according to the general procedure (**B**) as a white solid in 65 % yield; mp = 184-186 °C; IR (KBr): cm^{-1}; 3286, 3050, 3028, 2950, 2925, 1736, 1705, 1610, 1495, 1460, 1434, 1345, 1175, 1018, 760, 705, 640 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.47 (dd, J = 22.7, 1.8 Hz, 2H), 7.42 – 7.34 (m, 1H), 7.21 – 7.04 (m, 9H), 6.87 (t, J = 7.6 Hz, 1H), 6.75 (d, J = 7.4 Hz, 2H), 6.69 (d, J = 7.0 Hz, 3H), 6.45 (d, J = 7.7 Hz, 1H), 6.35 (d, J = 8.3 Hz, 1H), 5.14 (d, J = 15.9 Hz, 1H), 4.99 (d, J = 16.2 Hz, 1H), 4.59 (d, J = 16.1 Hz, 1H), 4.30 (d, J = 15.9 Hz, 1H), 4.09 (d, J = 9.1 Hz, 1H), 3.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.17, 175.92, 169.23, 143.75, 141.84, 135.56, 134.95, 134.31, 130.57, 130.21, 129.62, 128.99, 128.76, 128.69, 128.45, 127.96, 127.48, 127.36, 127.20, 126.69, 126.48, 126.09, 124.59, 123.06, 110.17, 109.19, 75.02, 62.31, 60.02, 58.68, 51.81, 44.00, 43.59; HRMS (EI) Calcd for [$C_{40}H_{31}Cl_2N_3O_4$+H] : 688.1770; found : 688.1770.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-bromobenzoyl)-5'-phenyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7a): The title compound was prepared according to the general procedure (**C**) as a white solid in 73 % yield; mp = 180-182 °C; IR (KBr): 2922, 2850, 1742, 1720, 1608, 1585, 1492, 1465, 1353, 1177, 1114, 1069, 1012, 833, 784, 750, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 6.6 Hz, 1H), 7.85 – 7.81 (m, 2H), 7.64 – 7.57 (m, 4H), 7.54 (d, J = 7.0 Hz, 1H), 7.46 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.24 (dd, J = 19.1, 8.8 Hz, 3H), 7.16 – 7.12 (m, 1H), 7.03 – 6.98 (m, 1H), 6.93 (t, J = 7.4 Hz, 3H), 6.88 (d, J = 8.4 Hz, 1H), 6.79 (t, J = 7.5 Hz, 3H), 6.72 (d, J = 7.7 Hz, 1H), 6.11 (s, 1H), 5.24 (d, J = 8.6 Hz, 1H), 5.22 (d, J = 7.2 Hz, 1H), 5.09 (d, J = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.25, 196.60, 178.95, 143.78, 141.44, 138.56, 136.21, 136.11, 135.54, 132.79, 131.61, 130.89, 130.50, 129.83, 129.75, 129.07, 128.82, 128.45, 128.27, 127.95, 127.72, 127.67, 127.58, 127.48, 127.39, 126.71, 126.61, 124.42, 123.61, 123.30, 122.75, 121.17, 109.52, 71.51, 68.13, 66.86, 66.05, 44.03; HRMS (EI) Calcd for [$C_{42}H_{29}BrN_2O_3$+H]: 689.1440; found: 689.1440.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-methoxybenzoyl)-5'-phenyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7b): The title compound was prepared according to the general procedure (**C**) as a white solid in 70 % yield; mp = 197-199 °C; IR (KBr): 3330, 3056, 2951, 2835, 1720, 1671, 1600, 1495, 1469, 1432, 1346, 1267, 1170, 1027, 971, 840, 788, 754, 702, 604, 548 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 2H), 7.84 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.0 Hz, 1H), 7.51 (d, J = 7.1 Hz, 4H), 7.41 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 7.2 Hz, 1H), 7.25 (d, J = 7.3 Hz, 2H), 7.19 (t, J = 7.7 Hz, 1H), 7.09 (d, J = 7.2 Hz, 1H), 7.02 (t, J = 7.4 Hz, 2H), 6.88 (dd, J = 5.3, 3.2 Hz, 2H), 6.61 (d, J = 8.6 Hz, 1H), 6.48 (d, J = 7.4 Hz, 2H), 6.27 (d, J = 8.7 Hz, 2H), 6.11 (dd, J = 5.2, 3.2 Hz, 1H), 4.92 (d, J = 15.9 Hz, 1H), 4.84 (d, J = 8.7 Hz, 1H), 4.18 (d, J = 15.9 Hz, 1H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.76, 195.25, 176.58, 162.56, 143.36, 141.84, 141.62, 135.03, 134.07, 131.95, 131.75, 130.64, 129.86, 129.63, 129.52, 128.66, 128.53, 128.43, 127.96, 127.71, 127.64, 127.10, 126.60, 126.45, 125.20, 124.81, 124.48, 122.32, 121.63, 112.85, 108.69, 76.30, 67.61, 62.92, 61.24, 55.13, 43.25; HRMS (EI) Calcd for [$C_{43}H_{32}N_2O_4$+H]: 641.2440; found : 641.2440.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-bromobenzoyl)-5''-fluoro-5'-phenyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7c): The title compound was prepared according to the general procedure (**C**) as a white solid in 68 % yield; mp = 162-164 °C; IR (KBr): 3303, 2229, 1716, 1675, 1611, 1581, 1488, 1432, 1338, 1170, 1072, 1012, 840, 780, 698, 567 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 6.6 Hz, 1H), 7.89 (d, J = 18.9 Hz, 2H), 7.72 (dd, J = 20.7, 7.5 Hz, 4H), 7.64 (d, J = 8.2 Hz, 1H), 7.57 (d, J = 6.8 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 7.02 (d, J = 6.9 Hz, 1H), 6.95 (t, J = 7.0 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 7.7 Hz, 4H), 6.53 (d, J = 8.1 Hz, 1H), 6.03 (s, 1H), 5.42 (d, J = 16.6 Hz, 1H), 5.19 (s, 1H), 4.93 (d, J = 16.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.81, 196.74, 178.62, 141.70, 141.46, 141.27, 138.22, 135.83, 135.17, 132.79, 132.65, 131.77, 130.62, 129.89, 129.79, 128.99, 128.67, 128.29, 128.02, 127.83, 127.04, 126.71, 124.65, 123.04, 121.42, 118.66, 111.69, 110.06, 71.46, 68.03, 67.08, 65.78, 43.74; HRMS (EI) Calcd for [$C_{42}H_{28}BrClN_2O_3$+H]: 723.1050; found : 723.1048.

(1R,2'S,4'S,5'S)-1''-benzyl-5'-phenyl-4'-(4-phenylbenzoyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7d): The title compound was prepared according to the general procedure (**C**) as a white solid in 77 % yield; mp = 162-164 °C; IR (KBr): 3034, 2925, 2850, 1720, 1649, 1600, 1488, 1462, 1353, 1293, 1252, 1177, 1005, 840, 825, 788, 739, 694 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.2 Hz, 2H), 7.97 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 6.9 Hz, 2H), 7.84 (d, J = 6.9 Hz, 2H), 7.74 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.4 Hz, 2H), 7.29 (d, J = 6.8 Hz, 2H), 7.13 (d, J = 7.5 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 6.99 (d, J = 7.1 Hz, 1H), 6.93 (t, J = 7.3 Hz, 2H), 6.88 – 6.81 (m, 3H), 6.73 (d, J = 7.7 Hz, 1H), 6.13 (d, J = 14.8 Hz, 1H), 5.33 (s, 1H), 5.24 (d, J = 15.9 Hz, 1H), 5.13 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.36, 195.41, 176.43,

144.84, 141.92, 139.42, 137.38, 135.82, 135.42, 134.52, 134.19, 133.40, 132.09, 131.72, 131.06, 129.93, 129.57, 128.73, 128.54, 127.95, 127.91, 127.33, 127.12, 126.94, 126.61, 126.32, 125.50, 124.85, 122.11, 109.74, 75.62, 66.65, 60.58, 58.30, 43.46; HRMS (EI) Calcd for $[C_{48}H_{34}N_2O_3+H]$: 687.2648; found : 687.2645.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-bromobenzoyl)-5'-(4-chlorophenyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7e): The title compound was prepared according to the general procedure (**C**) as a white solid in 65 % yield; mp = 148-150 °C; IR (KBr): 3318, 3053, 2922, 1716, 1611, 1518, 1492, 1469, 1353, 1282, 1177, 1069, 1009, 900, 840, 784, 758, 664, 548 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.4 Hz, 3H), 7.81 (d, *J* = 6.8 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.21 – 7.15 (m, 1H), 7.05 (dt, *J* = 14.0, 8.2 Hz, 5H), 6.91 (d, *J* = 8.9 Hz, 4H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 7.1 Hz, 2H), 6.13 (s, 1H), 4.89 (d, *J* = 15.9 Hz, 1H), 4.70 (d, *J* = 8.4 Hz, 1H), 4.20 (d, *J* = 15.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.18, 195.87, 176.86, 143.33, 141.80, 140.13, 135.97, 134.91, 133.62, 133.56, 132.01, 131.79, 130.96, 129.92, 129.72, 129.39, 128.86, 128.78, 128.48, 127.92, 127.41, 127.21, 126.61, 125.11, 124.84, 124.61, 122.49, 121.93, 108.80, 75.92, 66.89, 61.73, 61.60, 43.31, 29.70; HRMS (EI) Calcd for $[C_{42}H_{28}BrClN_2O_3+H]$: 723.1050; found : 723.1048.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-bromobenzoyl)-5'-(3,4-dimethoxyphenyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7f): The title compound was prepared according to the general procedure (**C**) as a white solid in 62 % yield; mp = 224-226 °C; IR (KBr): 3303, 2925, 2854, 1716, 1611, 1589, 1514, 1462, 1353, 1271, 1233, 1173, 1140, 1005, 833, 788, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 6.6 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.54 (m, 5H), 7.53 – 7.45 (m, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.23 (td, *J* = 7.8, 1.0 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.52 (d, *J* = 2.8 Hz, 2H), 6.05 (d, *J* = 2.5 Hz, 2H), 5.25 (d, *J* = 9.5 Hz, 1H), 5.23 (d, *J* = 6.4 Hz, 1H), 5.09 (d, *J* = 15.9 Hz, 1H), 3.70 (s, 3H), 3.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.32, 196.55, 178.92, 148.19, 147.90, 143.78, 141.45, 138.77, 136.10, 135.56, 132.90, 131.46, 130.56, 129.84, 129.71, 129.12, 128.83, 128.78, 128.69, 128.33, 127.82, 127.49, 127.40, 126.75, 124.30, 123.61, 123.24, 122.75, 121.32, 118.59, 110.33, 109.90, 109.54, 71.37, 68.11, 66.60, 66.03, 55.59, 55.11, 44.04, 29.26; HRMS (EI) Calcd for $[C_{44}H_{33}BrN_2O_5+H]$: 749.1651; found : 749.1650.

(1R,2'S,4'S,5'S)-1''-benzyl-4'-(4-bromobenzoyl)-5'-(2,4-dichlorophenyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,3'-pyrrolidine-2',3''-indole]-2,2''-dione (7g): The title compound was prepared according to the general procedure (**C**) as a white solid in 67 % yield; mp = 242-244 °C; IR (KBr): 3301, 2227, 1706, 1670, 1610, 1584, 1482, 1430, 1338, 1170, 1074, 1015, 840, 780, 694, 563 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 9.1 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.0 Hz, 1H), 7.59 (d, *J* = 7.3 Hz, 1H), 7.58 (d, *J* = 4.1 Hz, 1H), 7.56 (d, *J* = 4.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.30 – 7.24 (m, 2H), 7.20 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.09 (t, *J* = 8.5 Hz, 4H), 7.02 (t, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.60 (t, *J* = 8.7 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 2H), 6.03 (dd, *J* = 8.5, 4.2 Hz, 1H), 4.96 (d, *J* = 15.9 Hz, 1H), 4.88 (d, *J* = 8.6 Hz, 1H), 4.15 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.24, 194.95, 176.62, 160.01, 141.89, 139.29, 137.24, 135.81, 135.37, 134.62, 134.28, 133.21, 132.29, 131.54, 131.03, 129.95, 129.61, 128.79, 128.54, 128.07, 127.92, 127.52, 127.32, 126.61, 126.28, 125.48, 125.03, 122.26, 115.99, 115.02, 114.77, 109.44, 75.70, 66.48, 60.53, 58.22, 43.51; HRMS (EI) Calcd for $[C_{42}H_{27}BrCl_2N_2O_3+H]$: 757.0660; found : 757.0660.

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Notes and references

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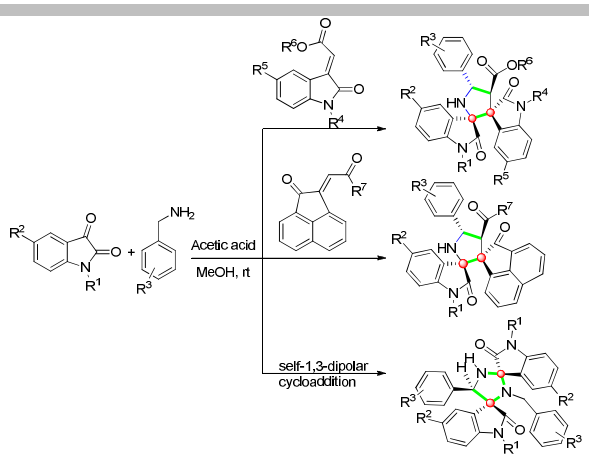
Advantages:
1) Acetic acid catalysed *in situ* generation of 1,3-dipole.
2) Single-step construction of imidazolidine ring with three chiral centers including two-non-contiguous spiro-quaternary stereocenters *via* formation of one new C-C and three new C-N bonds.
3) Construction of pyrrolidine ring with four chiral centers including two contiguous spiro-quaternary stereocenters *via* formation of one new C-N and two new C-C bonds.



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Acetic Acid Promoted Tandem Cyclization of *in situ* Generated 1,3-Dipoles: Setereoselective Synthesis of Dispiroimidazolidinyl and Dispiropyrrolidinyl Oxindoles with Multiple Chiral Stereocenters