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Three-Component Procedure for the Synthesis Chiral Spirooxindolopyrrolizidines via Catalytic Highly Enantioselective 1,3-Dipolar Cycloaddition of Azomethineylides and 3-(2-Alkenoyl)-1,3-Oxazolidin-2-ones

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ABSTRACT

The catalytic highly regio- diastereo-, and enantioselective synthesis of a small library of spiropyrrolizidineoxindoles via a four-component 1,3-dipolar cycloaddition reaction of azomethineylides, derived from isatin, with electron-deficient dipolarophile was described. The process occurs at room temperature in aqueous ethanol as a green solvent and in the presence of a bidendatebis(imine)–Cu(II)triflate complex as catalyst. The reaction mechanism is discussed on the basis of the assignment of the absolute configuration of the cycloadducts.

Keyword: Chiral spiro-oxindolopyrrolizidines; Asymmetric 1,3-dipolar; Chiral auxiliaries; Azomethineylide; Three-component reaction; Proline; Sarcosine.

1. INTRODUCTION

Catalytic asymmetric multicomponent reaction (CAMCR) is one of the most efficient processes in terms of chirality economy and environmental benignity. In addition, this strategy has manifested as a powerful tool for the rapid introduction and expansion of molecular diversity [1]. It is therefore desirable to utilize and develop this method for the synthesis of important heterocycles such as chiral spirooxindolpyrrolizidines and spirooxindolprolines like horsfiline [2], elacomine [3], rychnophyline exhibit significant biological activities [4] (Figure 1). Asymmetric multicomponent 1,3 dipolar cycloaddition of azomethineylides with alkenes can be a great interest and useful strategies for stereoselective synthesis and develop of these class of molecules and compounds having similar structure [5].

We recently reported the enantiomerically pure novel

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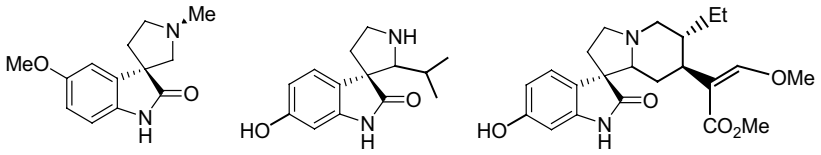


(-) horsfiline (+) elacomine richnophiline

Figure 1: *Spiro pyrrolidineoxindole alkaloids.*

spirooxindolpyrrolizidines [6] by applying optically active cinnamoyloxazolidinone as chiral auxiliary and the enantioselectivities were exceptionally high. However, it requires the use of at least one equivalent of enantiopure auxiliary. To resolve this problem and in continuation of our previous work on the synthesis of spirooxindoles [7], we applied copper complex of cyclohexane-1,2-bis(arylmethyleneamine) ligands (1) as a catalyst to synthesis of a small library of this important class of spirooxindols [8] (Figure 2). Herein, we wish to report a highly exo- and enantioselective

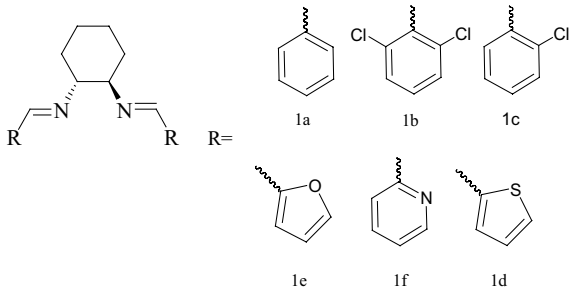
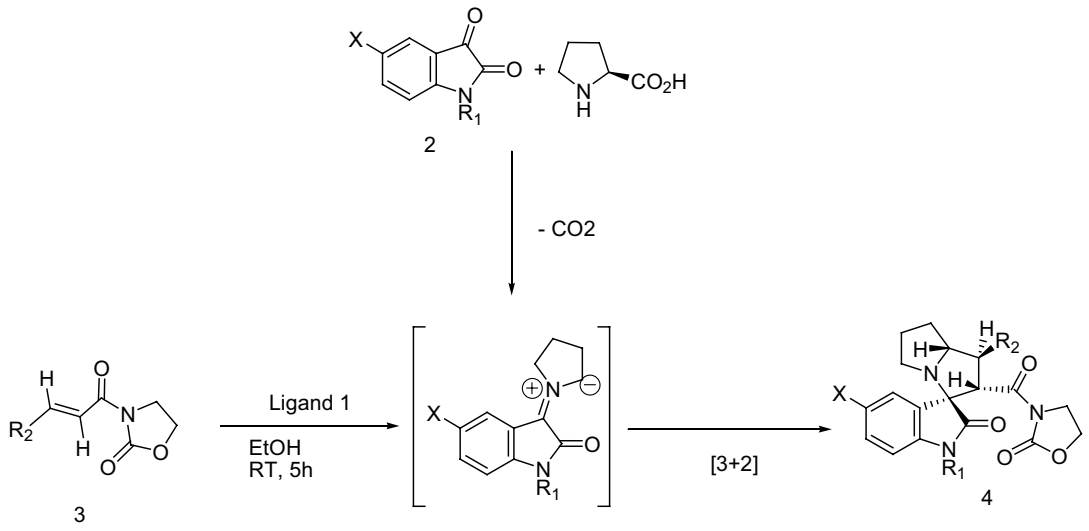


Figure 2: *Cyclohexane-1,2-bis(arylmethyleneamine) ligands 1(a-f).*

1,3-dipolar cycloaddition reaction of azomethineylides, derived from isatin, with electron-deficient dipolarophile by using bidendate bis(imine)-Cu(II) complex 1, that can be readily assembled from commercially available trans1,2-cyclohexanediamine and a variety of suitable aldehyde precursors, in optimized reaction condition. Based on experiences in our previous works and literature survey [9], Initially, the effects of substituents of bis(imines) ligands were examined using 10 mol% [$Cu(OTf)_2$] as catalyst in a typical reaction of azomethineylide 2a with dipolarophile 3a at room temperature in aqueous ethanol as a solvent (Scheme 1). The results are summarized in Table 1.

2. RESULTS AND DISCUSSION

The ligands 1b and 1c bearing the electron-withdrawing and relatively bulky Cl substituents at the 2- or/ and 6-positions of the benzene ring resulted in considerably higher yields and enantioselectivities in



Scheme 1: *Asymmetric synthesis of new chiral spirooxindolopyrrolizidines 4 with ligand of 1.*

Table 1: *Asymmetric synthesis of new chiral spirooxindolopyrrolizidines with ligand of 1(a- f).*

Entry	Ligand	T (°C)	Time (h)	4[a]	
				Yield (%)[b]	Ee (%)[c]
1	1a	25	24	84	55
2	1b	25	22	93	95
3	1c	25	20	89	63
4	1d	25	29	79	Race
5	1e	25	29	73	Race
6	1f	25	32	83	Race
7	1b	0	35	35	93
8	1b	-40	48	<10	n.d

[(a)] Reaction of 2a (0.22 mmol) with 3a (0.20 mmol) was carried out in 3 ml of EtOH at room temperature in the presence of 10% catalyst [$Cu(OTf)_2$ -1=1.0: 1.1], unless otherwise noted; [(b)] Isolated yield; [(c)] Determined by chiral HPLC analysis.

comparison with the other ligands [10]. The highest enantioselectivity (95%) and yield in high selectivitywere achieved by employing ligand 1b. The yields and enantiomeric ratios of the products showed the temperature dependence of this process. A decrease in the reaction temperature from 25°C to -40°C greatly decreased the reaction yield and enantioselectivity (entries 2, 7, 8). Considering the 1b as the best ligand, we tested the effect of Cu salts (Table 2). In all cases, $Cu(OTf)_2$ proved to be the best copper source while other Cu salts led to a decrease in the ee by 34-90% and longer reaction times (entries 3-4 vs.2). The use of $Zn(OTf)_2$ instead of $Cu(OTf)_2$ gave worse result in term of enantioselectivity (entry1). The effects of catalyst loading were also investigated and the best results were obtained when 10 mol % catalysts loading was used in the reaction. The ligand-to-metal ratio of 1.1:1 using 20 mol % of ligand was investigated under the similar conditions and the isolated yields and enantioselectivity remained the same at 95% respectively. Lowering the catalyst loading to less than 10 mol % led to a sharp decrease in the results. It should be noted, the addition of additives such as MS 4A, 3A did not give any observable changes in the results of the reaction and even lead to decreasing yields.

Considering the optimized reaction conditions, we next examined the scope and generality of this reaction with various types of azomethine ylides and numerous 3-(2-alkenoyl)-1,3-oxazolidin-2-ones (3) and synthesized a small library of new chiral spirooxindo-

Table 2: *Dependence of reaction with Lewis acid.*

Entry	Lewis acid	Time (h)	4[a]	
			Yield (%)[b]	Ee (%)[c]
1	$Zn(OAc)_2$	12	>99	Race
2	$Cu(OTf)_2$	22	93	95
3	$Cu(OAc)_2$	23	92	66
4	$Cu(Cl)_2$	28	76	Race
5	$Cu(OTf)_2$[d]	22	96	90

[(a)] Reaction of 2a (0.22 mmol) with 3a (0.20 mmol) was carried out in 3 ml of $EtOH/CH_2Cl_2$ at room temperature in the presence of 10% catalyst [Lewisacid-1=1.0:1.1], unless otherwise noted; [(b)] Isolated yield; [(c)] Determined by chiral HPLC analysis; [(d)] 20% catalyst is used.

Table 3: *Asymmetric synthesis of new chiral spirooxindolopyrrolizidines derivaitives 4.*

Entry	X	R_1	R_2	Product	Yield	Ee
1	H	H	Me	4a	93	95
2	H	H	Ph	4b	95	93
3	H	Me	Me	4c	93	89
4	H	Et	Ph	4d	92	87
5	H	Bn	Me	4e	92	91
6	Br	H	Me	4f	99	89
7	Br	Me	Me	4g	92	87
8	Br	Et	Me	4h	94	90
10	Br	Me	Ph	4i	91	89
11	NO_2	H	Me	4j	88	83

lopyrrolizidines 4a-j (Table 3).

The structures of cycloadducts were assigned from their elemental and spectroscopic analyses including IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data. The observation of two characteristic triplets and one doublet in the ^{1}H NMR spectra of products 4 confirmed unambiguously the formation of a new pyrrolizidine ring. We also were able to obtain suitable crystals of the 4g for crystallography to confirm the assigned stereochemistry of products 4 that was carried out here using several NMR spectroscopy techniques. The ORTEP view of single crystal X-ray analysis of 4g with atomic numbering is shown in Figure 3. On the basis of X-ray structure of 4, we can now assign the four chiral centers in spiropyrrolizidineoxindole 4g to be5R (spiro carbon C7), 6S (C21), 7R (C14), 8R (C13). X-ray crystallographic analysis of compound 4g also confirmed this absolute configuration.

Because reactions of most non-stabilized azomethineylides with electron-deficient dipolarophiles are HOMO(dipole)-LUMO(dipolarophile)controlled[11], thus, in order to obtain an increased reaction rate, the 3-Cu(OTf)$_2$ was coordinated to the electron-deficient dipolarophileto form square planner geometry [12]. On the other hand, condensation of isatin derivative 1 and (S)-proline, after decarboxylation, led to the non- stabilized azomethineylide 2. The [3+2] cycloaddition of activated dipolarophileswithazomethineylide 2 resulted in the formation of chiral spirooxindolopyrrolizidine 4 which contain contiguous stereogenic centers. Despite the fact that sixteen different stereoisomers could be prepared theoretically, only diaste-

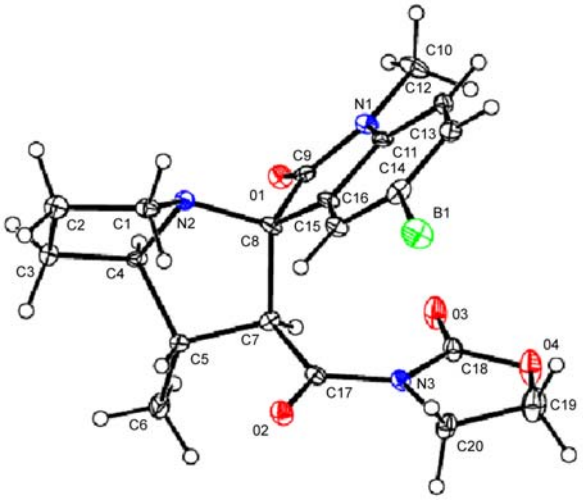
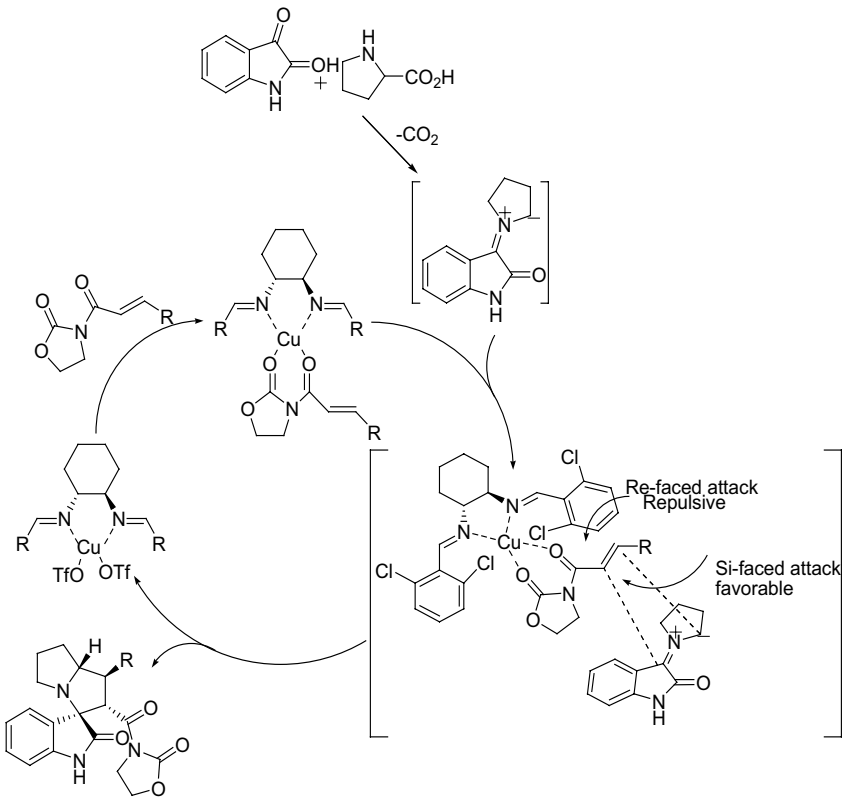


Figure 3: *ORTEP diagram of one of the four crystallographic independent molecules in the asymmetric unit of 4g. Thermal ellipsoids are at 30% probability level.*



Scheme 2: *Propose of the transition state and the reaction pathway.*

reoisomer 4 was obtained in high yield in all the cases that we present in this article (Scheme 2). Based on the stereochemistry of the cycloadduct that clarified by single-crystal X-ray analysis and 2D NMR spectroscopic techniques, the transition state and the reaction pathway were proposed as below:

3. EXPERIMENTAL

General procedure: To a magnetically stirred solution of an isatin derivatives (1 mmol), proline (1 mmol) and chiral oxazolidinone (1 mmol) as dipolarophile in 10 mL EtOH was added dropwise at room temperature. Then, the reaction mixture was stirred for 12 h. The solvent was then removed under reduced pressure and the residue was separated by recrystalization in $CHCl_3$.

4. CONCLUSIONS

Simple cyclohexane-1,2-bis(arylmethyleneamine) ligands with copper(II) triflate catalyzed 1,3-dipolar cycloaddition reaction of azomethineylides with electron-deficient dipolarophile to give spiropyrrolizidineoxindoles in good yield with high regio-, diastereo-, and enantioselectivity (up to 93% ee) in optimized condition. The reaction was accomplished with 10% catalyst at room temperature in environmentally friendly aqueous ethanol. The structures of the products were elucidated using IR, mass, one and two dimensional NMR techniques, and X-ray single crystal diffraction. The reaction mechanism is briefly discussed on the basis of the assignment of the absolute configuration of the cycloadduct.

3-((1'S,2'S,3R,7a'R)-1'-methyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4a): white powder, mp 125-128°C, yield 93%, [α]D+267.5 (c 0.01, CH_2Cl_2), IR(KBr)(υ_{max}, cm^{-1}): 1694(C=O), 1723(C=O), 1745 (C=O), 3430(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.17 (3H, d, $^3J_{HH}$=6.3 Hz, CH_3), 1.73-1.93 (4H, m, $2CH_2$), 2.07-2.16 (1H, m, CH), 2.56 (1H, m, CH), 2.83-3.00 (2H, m, CH_2), 3.53-3.62 (1H, m, CH), 3.87-3.96 (3H,

m, CH and CH_2), 4.13-4.21 (1H, m, CH), 4.31 (1H, d, $^3J_{HH}$=9.6 Hz, CH), 6.83-7.23 (4H, m, Ar-H), 7.55 (1H, s, NH); ^{13}CNMR (300.1 MHz, $CDCl_3$); 15.9(1C, CH_3), 24.8, 27.6, 41.3, 42.7, 62.1 (5C, 5CH_2), 49.3, 59.9, 69.4 (3C, 3CH), 71.9(1C), 110.5, 121.1, 126.0, 129.8 (4C, 4CH), 125.6, 142.7 (2C) 153.0, 172.3, 179.7 (3C, 3C=O); MS, 352 (M^+ ,20), 69 (100), 131 (40).

3-((1'R,2'S,3R,7a'R)-2-oxo-1'-phenyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4b): white powder, mp 125-128°C, yield 95%, [α]D+247.2 (c 0.01, CH_2Cl_2), IR(KBr)(υ_{max}, cm^{-1}): 1616(C=O), 1716(C=O), 1782 (C=O), 3430(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.77-2.02 (4H, m, 2CH_2), 2.67 (1H, m, CH), 3.15 (1H, m, CH), 3.62 (1H, m, CH), 3.80-4.11 (4H, m, OCH_2, 2CH), 4.46 (1H, m, CH), 4.81 (1H, d, $^3J_{HH}$=9.3 Hz, CH), 6.87-7.63 (9H, m, Ar-H), 7.68 (1H, s, NH); ^{13}CNMR (300.1 MHz, $CDCl_3$); 24.4, 27.4, 29.7, 42.7 (4C, 4CH_2), 49.3, 53.3, 61.8 (3C, 3CH), 57.9 (1C, OCH_2), 72.1(1C), 110.6, 121.1, 126.1, 126.8, 129.8 (5C, 5CH), 128.7, 129.1 (4C, 4CH), 125.8, 138.2, 143.0 (3C), 153.0, 172.2, 179.9 (3C, 3C=O); MS, 417 (M^+,7), 200 (100), 131 (70).

3-((1'S,2'S,3R,7a'R)-1,1'-dimethyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4c): white powder, mp 189°C, yield 93%, [α]D+223.1 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1686(C=O), 1716(C=O), 1778 (C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.16 (3H, d, $^3J_{HH}$=6.3 Hz, CH_3), 1.72-2.13 (4H, m, 2CH_2), 2.57 (1H, m, CH), 2.88 (1H, m, CH), 2.99 (1H, m, CH), 3.16 (3H, s, NCH_3), 3.55 (1H, m, CH), 3.80-3.98 (3H, m, CH and CH_2), 4.11 (1H, m, CH), 4.21 (1H, m, $^3J_{HH}$=9.3 Hz, CH), 6.78 (1H, d, $^3J_{HH}$=7.8 Hz, CH), 6.92 (1H, m, CH), 7.14 (1H, d, $^3J_{HH}$=7.8 Hz, CH), 7.28 (1H, m, CH); ^{13}CNMR (300.1 MHz, $CDCl_3$); 16.4 (1C, CH_3), 24.7, 26.4, 27.6, 43.1, 62.7 (5C, 5CH_2), 41.2 (1C, NCH_3), 49.3, 60.0, 69.2 (3C, 3CH), 71.5(1C), 108.9, 121.6, 125.7, 130.1 (4C, 4CH), 125.5, 145.4 (2C) 153.3, 172.2, 178.1 (3C, 3C=O); MS: 269 (M^+, 9), 214 (100), 131 (59).

3-((1'R,2'S,3R,7a'R)-1-ethyl-2-oxo-1'-phenyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4d): Yellow powder, mp 103°C, yield 92%, [α]D+224.5 (c 0.01, CH_2Cl_2) IR(KBr) (υ_{max}, cm^{-1}): 1613(C=O), 1711(C=O), 1781(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.38 (3H, t, $^3J_{HH}$=7.2 Hz, CH_3), 1.76-2.01 (4H, m, 2CH_2), 2.67 (1H, m, CH), 3.13 (1H, m, CH), 3.61 (1H, m, CH), 3.78-4.11 (6H, m, 2CH, 2CH_2), 4.46 (1H, m, CH), 4.81 (1H, d, $^3J_{HH}$=9 Hz, CH), 6.87-7.68 (9H, m, Ar-H); ^{13}CNMR (300.1 MHz, $CDCl_3$); 11.9 (1C, CH_3), 24.4, 27.4, 29.7, 42.7 (4C, 4CH_2), 35.0 (1C, NCH_2), 49.3, 53.3, 61.8 (3C, 3CH), 57.9 (1C, OCH_2), 72.1(1C), 110.6, 121.1, 126.1, 126.8, 129.8 (5C, 5CH), 128.7, 129.1 (4C, 4CH), 125.8, 138.2, 143.0 (3C), 153.0, 172.2, 179.9 (3C, 3C=O); MS, 443 (M^+, 7), 227 (100), 131 (90).

3-((1'S,2'S,3R,7a'R)-1-benzyl-1'-methyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4e): white powder, mp 125-128°C, yield 92%, [α]D+253.9 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1616(C=O), 1716(C=O), 1782(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.15 (3H, d, $^3J_{HH}$=6.6 Hz, CH_3), 1.80-2.04 (4H, m, 2CH_2), 2.65(1H, m, CH), 3.16 (1H, m, CH), 3.57 (1H, m, CH), 3.76-3.89 (2H, m, CH_2), 3.99-4.11(2H, m, CH_2), 4.52(1H, m, CH), 4.76 (1H, d, $^3J_{HH}$=15.9 Hz, CH), 4.88 (1H, d, $^3J_{HH}$=9.3 Hz, CH), 5.13 (1H, d, $^3J_{HH}$=15.9 Hz, CH), 6.65-7.99 (9H, m, Ar-H); ^{13}CNMR (300.1 MHz, $CDCl_3$); 15.5(1C, CH_3), 24.4, 27.4, 29.7, 42.7 (4C, 4CH_2), 49.3, 53.3, 61.8 (3C, 3CH), 54.3 (1C, NCH_2), 57.9 (1C, OCH_2), 72.1(1C), 110.6, 121.1, 126.1, 126.8, 129.8 (5C, 5CH), 127.7, 129.9 (4C, 4CH), 125.5, 139.8, 143.4 (3C), 153.1, 172.9, 181.2 (3C, 3C=O); MS, 445 (M^+,9), 290 (100), 131 (65), 91 (58).

3-((1'S,2'S,3R,7a'R)-5-bromo-1'-methyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4f): Yellow powder, mp 128°C, yield 99%, [α]D+227.5 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1614(C=O), 1720(C=O), 1779(C=O), 3420(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.15 (3H, d, $^3J_{HH}$=6.7 Hz, CH_3), 1.76-1.96 (4H, m, 2CH_2), 2.07-2.17 (1H, m, CH_2), 2.57 (1H, m, CH), 2.83-3.05 (2H, m, CH_2), 3.56 (1H, dt, $^2J_{HH}$=12 Hz, $^3J_{HH}$=6 Hz, CH), 3.88-3.96 (3H, m, CH and CH_2),

4.16 (1H, dt, $^2J_{HH}$=12 Hz, $^3J_{HH}$=6 Hz, CH), 4.31 (1H, d, $^3J_{HH}$=9 Hz, CH), 6.67 (1H, d, $^3J_{HH}$=8.0 Hz, Ar-H), 7.27 (1H, m, Ar-H), 7.47 (1H, d, $^3J_{HH}$=8.0 Hz, Ar-H), 8.06 (1H, s, NH); ^{13}CNMR (300.1 MHz, $CDCl_3$); 16.1(1C, CH_3), 24.2, 27.4, 41.2, 42.7, 62.5 (5C, $5CH_2$), 49.3, 59.9, 69.4 (3C, 3CH), 72.1(1C), 108.5, 122.3, 129.8 (3C, 3CH), 125.9, 142.3, 144.9 (3C) 153.1, 172.9, 179.9 (3C, 3C=O); MS, 434, 436 (M^+, M^++2, 6), 278, 280 (75), 131 (100).

3-((1'S,2'S,3R,7a'R)-5-bromo-1,1'-dimethyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4g): white powder, mp 122°C, yield 92%, [α]D+262.5 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1614(C=O), 1711(C=O), 1785(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.16 (3H, d, $^3J_{HH}$=5.1 Hz, CH_3), 1.76-2.17 (4H, m, $2CH_2$), 2.56 (1H, m, CH), 2.93 (2H, m, CH_2), 3.14(3H, s, NCH_3), 3.66 (1H, m, CH), 3.04 (3H, m, CH and CH_2), 4.17 (1H, m, CH), 4.37 (1H, d, $^3J_{HH}$=9 Hz, CH), 6.67 (1H, d, $^3J_{HH}$=8.1 Hz, Ar-H), 7.27 (1H, s, Ar-H), 7.43 (1H, d, $^3J_{HH}$=8.1 Hz, Ar-H); ^{13}CNMR (300.1 MHz, $CDCl_3$); 16.4(1C, CH_3), 24.5, 27.7, 41.3, 42.9, 61.8 (5C, $5CH_2$), 42.4(1C, NCH_3), 49.3, 59.9, 69.8 (3C, 3CH), 72.8(1C), 109.9, 121.3, 130.5 (3C, 3CH), 125.7, 142.6, 144.2 (3C) 153.1, 172.9, 179.8 (3C, 3C=O); MS, 448, 450 (M^+, M^++2, 6), 292, 294 (M^+, M^++2, 67), 131 (100).

3-((1'S,2'S,3R,7a'R)-5-bromo-1-ethyl-1'-methyl-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4h): Yellow powder, mp 135°C, yield 94%, [α]D+237.8 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1611(C=O), 1711(C=O), 1781(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.15 (3H, d, $^3J_{HH}$=6.8 Hz, CH_3), 1.39 (3H, t, $^3J_{HH}$=7 Hz, CH_3),1.76-1.96 (4H, m, $2CH_2$), 2.09-2.17 (1H, m, CH_2), 2.56 (1H, m, CH), 2.83-3.05 (2H, m, CH_2), 3.80 (2H, q, $^3J_{HH}$=7 Hz, CH_2), 3.56 (1H, dt, $^2J_{HH}$=12 Hz, $^3J_{HH}$=6 Hz, CH), 3.88-3.96 (3H, m, CH and CH_2), 4.16 (1H, dt, $^2J_{HH}$=12 Hz, $^3J_{HH}$=6 Hz, CH), 4.31 (1H, d, $^3J_{HH}$=9 Hz, CH), 6.67 (1H, d, $^3J_{HH}$=8.0 Hz, Ar-H), 7.27 (1H, m, Ar-H), 7.47 (1H, d, $^3J_{HH}$=8.0 Hz, Ar-H); ^{13}CNMR (300.1 MHz, $CDCl_3$); 12.4 (1C, CH3), 16.1(1C, CH_3), 24.6, 27.7, 41.3, 42.7, 62.8 (5C, $5CH_2$), 35.1 (1C, NCH_2), 49.2, 59.9, 69.4 (3C, 3CH), 72.1(1C), 108.7, 121.1, 129.9 (3C, 3CH), 125.8, 142.8, 144.7 (3C) 153.1, 172.9, 179.9 (3C, 3C=O); MS, 462, 464 (M^+, M^++2, 5), 305, 307 (M^+, M^++2, 60), 131 (100).

3-((1'R,2'S,3R,7a'R)-5-bromo-1-methyl-2-oxo-1'-phenyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4i): white powder, mp 122°C, yield 91%, [α]D+227.5 (c 0.01, CH_2Cl_2), IR(KBr) (υ_{max}, cm^{-1}): 1614(C=O), 1711(C=O), 1785(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.77-2.02 (4H, m, $2CH_2$), 2.67 (1H, m, CH), 3.15 (1H, m, CH), 3.24 (3H, s, NMe), 3.61 (1H, m, CH), 3.78-4.06 (4H, m, OCH_2, 2CH), 4.46 (1H, m, CH), 4.81 (1H, d, $^3J_{HH}$=9 Hz, CH), 6.87-7.68 (8H, m, Ar-H); ^{13}CNMR (300.1 MHz, $CDCl_3$); 24.4, 27.4, 29.7, 42.7 (4C, $4CH_2$), 42.1 (1C, NCH_3), 49.3, 53.3, 61.8 (3C, 3CH), 57.9 (1C, OCH_2), 72.1(1C), 110.6, 121.1, 126.1, 129.8 (4C, 4CH), 128.7, 129.1 (4C, 4CH), 125.8, 138.2, 141.5, 144.1 (4C), 153.0, 172.2, 179.9 (3C, 3C=O); MS, 508, 510 (M^+, M^++2, 6), 292, 294 (M^+, M^++2, 69), 131 (100).

3-((1'S,2'S,3R,7a'R)-1'-methyl-5-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizine]-2'-ylcarbonyl)oxazolidin-2-one (4j): Yellow powder, mp 120-123°C, yield 88%, [α]D+243.7 (c 0.01, CH_2Cl_2), IR(KBr)(υ_{max}, cm^{-1}): 1615(C=O), 1719(C=O), 1780(C=O), 3431(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.19 (3H, d, $^3J_{HH}$=6.6 Hz, CH_3), 1.67-1.83 (2H, m, CH_2), 1.87-2.18 (2H, m, CH_2) 2.52 (1H, m, CH), 2.66 (2H, m, CH_2), 3.70 (1H, m, CH), 3.86 (1H, m, CH), 3.97-4.08 (1H, m, CH) 4.23 (2H, m, CH_2), 6.96 (1H, d, $^3J_{HH}$=8.4 Hz, CH), 8.00 (1H, d, $^4J_{HH}$=3 Hz, CH), 8.22 (1H, dd, $^3J_{HH}$=8.4 Hz, $^4J_{HH}$=3 Hz, CH), 8.32 (1H, s, NH); ^{13}CNMR (300.1 MHz, $CDCl_3$); 15.9(1C, CH_3), 24.6, 27.7, 41.3, 42.8, 62.9 (5C, $5CH_2$), 49.3, 59.9, 69.4 (3C, 3CH), 71.9(1C), 110.5, 121.1, 129.8 (3C, 3CH), 125.9, 142.7, 144.8 (3C) 153.0, 172.3, 179.7 (3C, 3C=O); MS, 400 (M^+, 8), 244 (100), 131 (57).

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