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Facile synthesis of 3-spiropyrrolizidine oxindoles and 3-spirotetrahydroquinoline oxindoles via [3+2] and [4+2] cycloaddition reactions

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ABSTRACT

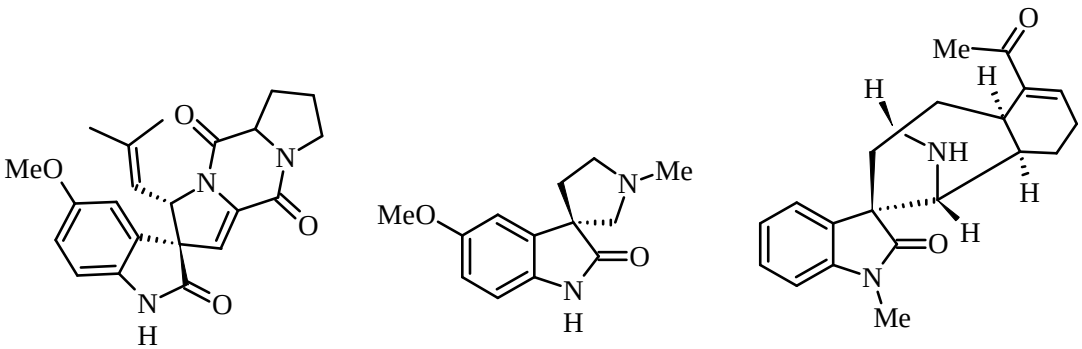
A rapid and efficient synthesis of a number of functionalized 3-spiropyrrolizidine oxindoles from [3+2] cycloaddition of azomethine ylide and 3-spirotetrahydroquinoline oxindoles from [4+2] imino Diels-Alder reaction; catalyzed by Antimony(III)chloride in excellent yields are reported.

KEYWORDS

Isatin;
Imino Diels-Alder;
Antimony(III)chloride;
Spiropyrrolizidine oxindoles;
Spirotetrahydroquinoline-oxindoles.

INTRODUCTION

Heterocyclic compounds containing isatin (1*H*-indole-2, 3-dione) scaffold have a wide range of biological activities[1] and also serves as an important precursor for the synthesis of biologically active indole derivatives and natural products[2]. The Spirooxindoles core is featured in a number of natural products and recently has been the subject of significant synthetic interest[3]. Oxindoles derivatized like Spirotryprostatin B, Horsfiline



Spirotryprostatin B **Horsfiline** **Alstonisine**

Spirooxindole alkaloid natural products

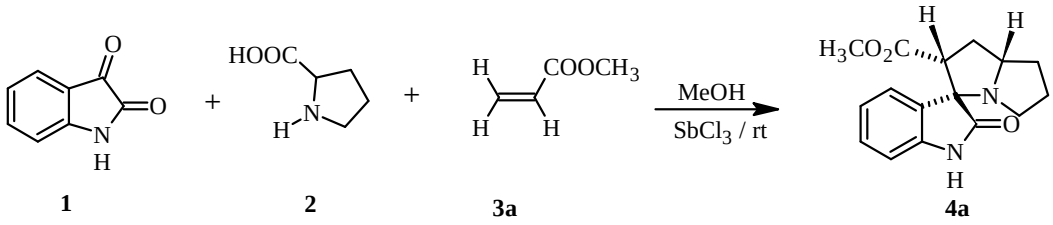
Figure 1 : Spirotryprostatin B, horsfiline and alstonisine are alkaloids present in nature and are elegant targets in the organic synthesis due to their significant biological activities.

and Alstonisine are alkaloids present in nature and are elegant targets in the organic synthesis due to their significant biological activities[4,5] (Figure 1).

Classical preparations of oxindoles have involved carboline oxidative rearrangement[6], intramolecular Mannich and radical cyclization approach[7,8]. The transition metal catalyst mediated methods have also been developed and have become the part of elegant total synthesis of oxindole derivatized at C_3 as spirocarbo and heterocyclics, spirolactones and spirocyclic ethers are main targets in organic synthesis due to their significant biological activities[9]. These derivatives have been served as potential synthons for the synthesis of alkaloids, drug intermediates and clinical pharmaceuticals. Azomethine ylides are a class of powerful reagents to utilized in the dipolar cycloaddition reactions[4,10], which generally afford a range of pharmacologically important heterocyclic compounds[11]. The synthetic versatility of isatin and its derivatives has led to the extensive use of this compound in synthetic organic chemistry[12,13]. With the ongoing discovery of new natural compounds containing Spirocenters, the synthesis of these structures will remain an active area of research. As part of our research in the area of novel synthesis of bioactive heterocycles[14-24], we have explored the [3+2] cycloaddition reaction of azomethine ylide derived from decarboxylative condensation between isatin and proline. And [4+2] imino Diels-Alder cycloaddition reaction was also been studied to obtain structurally diversified spirotetrahydroquinoline oxindoles. Our work in cycloaddition reaction in the synthesis of nitrogen heterocycles catalysed by Antimony(III)chloride[24], prompted us to use Antimony(III)chloride as a catalyst in the synthesis of spiropyrrolizidine oxindoles and spirotetrahydroquinoline oxindoles. Thus the current method provides a rapid route for access to stereo chemically distinct spirooxindoles and this method will lead to library synthesis for biological evaluation. Herewith we are reporting our findings.

RESULTS AND DISCUSSION

The synthetic strategy for the construction of spiropyrrolizidine oxindoles is as shown in Scheme 1. Accordingly, the spiropyrrolizidine oxindoles derivative **(4a)** could be synthesized from [3+2] cycloaddition reaction of isatin **(1)**, proline **(2)** and various unsymmetrical dipolarophiles **(3a-g)** (TABLE 3) in one pot.



1 **2** **3a** **4a**

Scheme 1 : The synthetic strategy for the construction of spiropyrrolizidine oxindoles.

In a typical experiment, the three component one pot reaction of isatin **(1)**, proline **(2)** and methyl acrylate **(3a)** in methanol proceeds smoothly at room temperature for 1hr in presence of Antimony(III)chloride (20 mol%) to afford the corresponding spiropyrrolizidineoxindole derivative **(4a)** in >90% yield (TABLE 3, entry 1). Thus the reaction of proline, isatin, and methyl acrylate occur regio and stereo specifically to give **(4a)**[9,26] in good yield. The relative stereo chemistry of the 2'-H and 7a'-H, protons was established by NOE studies and stereo chemical assignment at C_2' was later confirmed by a single crystal X-ray structure[25].

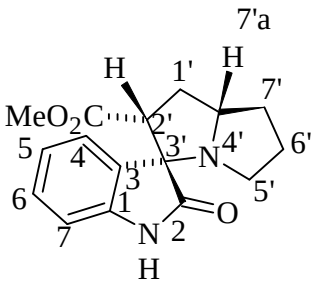
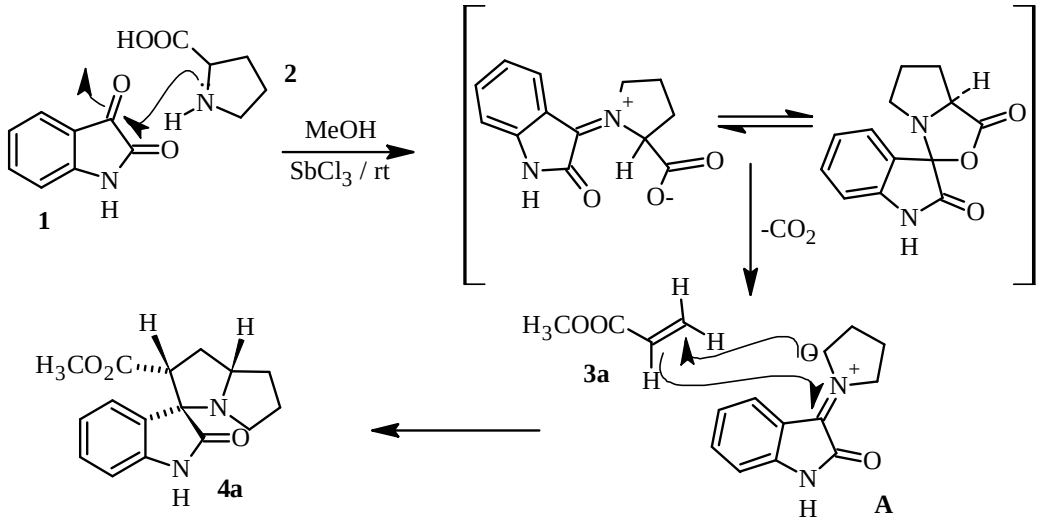


Figure 2 : Structure 1

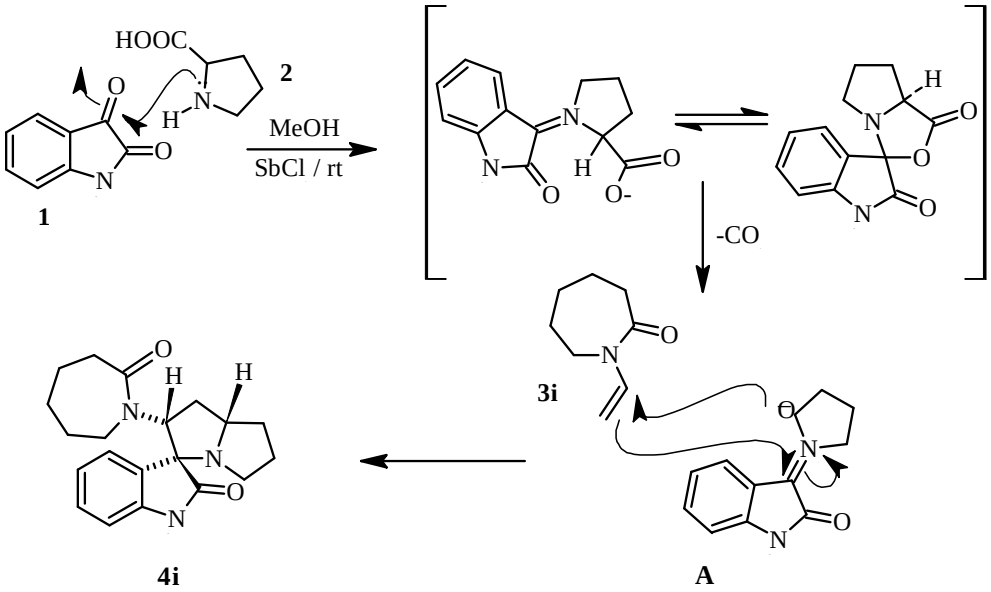
Hence, based on the spectral analysis such as ^{1}H NMR and Mass spectral analysis and in comparison of these results with earlier report[26], the regio and stereochemistry of the products have been established



Scheme 2 : Regio and stereochemistry of the products

(TABLE 3, Scheme 2).

Further by adopting established reaction condition we attempted to carry out analogous reactions of azomethine ylide with various dipolarophiles i.e. acrylates **(3a-g)** and electron rich dienophiles such as 3,4-dihydro-2*H*-pyran, *N*-vinyl pyrrolidin-2-one (NVP) and *N*-vinyl caprolactum (NVC) (TABLE 3). The predominate products (85-90%) arise from azomethine ylide via an endo-transition state with regiospecificity is as shown in Scheme 3 and products are summarize in



Scheme 3 : The predominate products (85-90%) arise from azomethine ylide via an endo-transition state with regiospecificity

TABLE 3.

Initially the one pot reaction carried out as a model reaction in various solvents to investigate the solvent effect. The results are summarized in TABLE 1. Methanol, ethanol and acetonitrile were found to be better solvents for this transformation. However, the best results were achieved by carrying out the reaction in MeOH at room temperature to afford spiropyrrolizidineoxindole in 85-90% yield respectively. Further we set out to establish the optimal amount of Antimony(III) chloride, finding that reaction with a 10 mol% catalyst loading gave a 75% yield after 1.5 hr (entry 1), however the best result (90%) was found which corresponds to the use of 20 mol% catalyst (entry 2) and the reaction time reduced to 1hr. The increasing amount of the catalyst did not change the re-

TABLE 1 : Screening of the catalytic activity in various solvents for the synthesis of 3-spiroxindoles

Entry	Solvent	Catalyst[a] Load mol%	Time/hr	Yield[b] (%)
1	MeOH	10	1.5	75
2	MeOH	20	1.0	90
3	EtOH	20	1.3	80
4	CH_3CN	20	4.0	80
5	DMF	20	12	38
6	Ether	20	14	30
7	Toluene	20	24	Trace
8	Hexane	20	24	No reaction
8	EtOAc	20	9	25
9	CH_2Cl_2	20	7	30

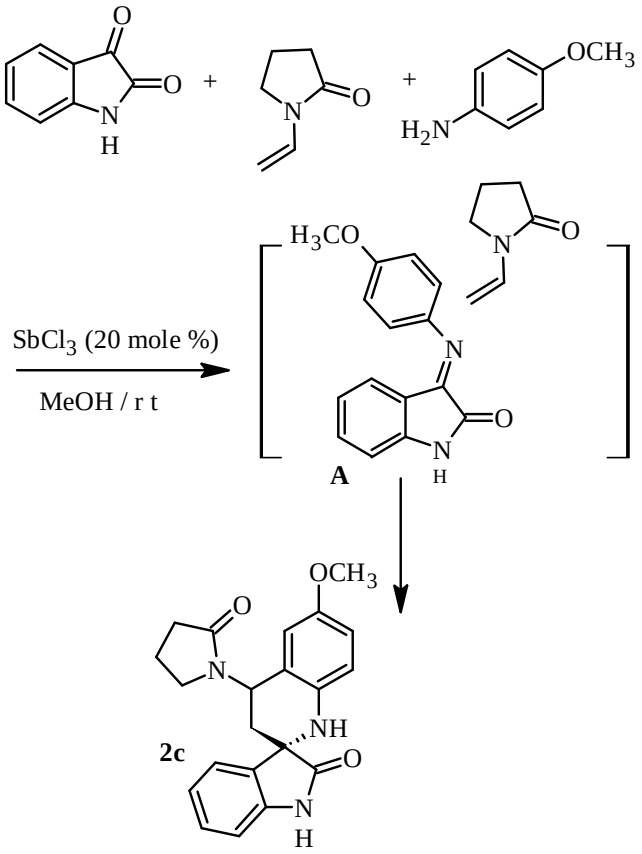
[a]20 mol % of catalyst used; [b]Isolated yield.

action time whereas isolated yield was found to be less in nature.

Similarly, the spiropyrrolizidineoxindole derivatives **(4a-j)** could be synthesized from the three component one pot reaction between isatin **(1)**, proline **(2a)** and dipolarophiles **(3a-g)**. The dipole azomethine ylide **(A)** could be generated *in situ* from isatin and proline by thermal decarboxylation reaction which immediately underwent [3+2] cycloaddition reaction with dipolarophiles as shown in Scheme 2.

In order to test the scope of this [3+2] cycloaddition reaction, various dipolarophiles (TABLE 3) have been examined. In addition to these dipolarophiles, electron rich dienophiles such as 3,4-dihydro-2*H*-pyran, *N*-vinyl pyrrolidin-2-one (NVP) and *N*-vinyl caprolactum were also tested along with dipolarophiles. The results are summarized in TABLE 3, the treatment of electron rich dienophiles with azomethine ylide **(A)**, underwent smooth [3+2] cycloaddition reaction similar to dipolarophiles affording the corresponding products **(4h-j)** in 80,90,85% yield respectively (TABLE 3). This results suggested that the electron donating heteroatom (i.e., O, N) present in the dienophiles such as 3,4-dihydro-2*H*-pyran, *N*-vinyl pyrrolidin-2-one (NVP) and *N*-vinyl caprolactum (NVC) facilitates the [3+2] cycloaddition reaction much faster than the dipolarophiles. Thus the present method could be applied successfully to various types of cyclic and acyclic dienophiles and dipolarophiles to provide Spiropyrrolizidineoxindoles **(4a-j)** in good yields.

Since, we are interested to identify various spirooxindolyl compounds and impressed by the success in synthesizing various spiropyrrolizidineoxindoles **(4a-j)**, further we thought to exploit the utilization of C=O group of isatin in [4+2] cycloaddition reaction to obtain various structurally diversified spirotetrahydroquinolineoxindole compounds **(2a-c)**. Similarly, the isatin underwent smooth condensation with 4-methoxyaniline to produce corresponding imines in an excellent yield. Since the imines are known to undergo imino Diels-Alder reaction with electron rich dienophiles[24], the imine thus generated was subsequently made to react with 2,3-dihydro furan/3,4-dihydro-2*H*-pyran, and *N*-vinyl pyrrolidin-2-one (NVP) dienophiles to obtain various spirotetrahydroquinolineoxindole derivatives **(2a)**, **(2b)**[27], **(2c)**



Scheme 4 : The synthetic strategy for the construction of spiro tetrahydro quinoline

in good yield (Scheme 4, TABLE 2).

In this case, the reaction proceeded well with dienophiles such as 2, 3-dihydrofuran/3,4-dihydro-2*H*-pyran, *N*-vinyl pyrrolidin-2-one (NVP) furnishing 2a-c in good yield (TABLE 2). Further it was observed that the Antimony(III)chloride catalyst is quite effective for

azo methine ylide [3+2] cycloaddition reaction with wide variety of dienophiles and dipolarophiles, whereas during [4+2] cycloaddition reactions, aniline bearing electron withdrawing substituents such Cl, Br, F, NO_2 groups did not give the expected products under similar reaction conditions.

Hence, the plausible reaction pathway involves the initial imine formation in the reaction between isatin and aniline, in presence of Antimony(III)chloride, which immediately undergoes imino-Diels alder reaction with dienophiles in one pot to give the desired products is as shown in Scheme 4. The similar reaction mechanism was also suggested in our earlier studies[14].

EXPERIMENTAL

Products were identified by their physical and spectroscopic data all the melting points were recorded in open capillaries. The purity of the compounds were checked by TLC on silica gel. ^{1}H NMR spectra were recorded on a Bruker-400Hz spectrometer using DMSO-d_6 as an internal standard. Mass spectra were recorded on a JEOL

TABLE 2 : Antimony(III)chloride catalyzed synthesis of 3-spirotetra hydroquinoline oxindoles in MeOH at room temperature.

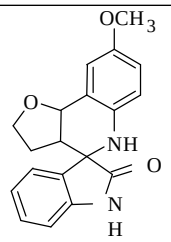
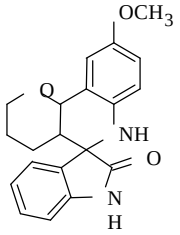
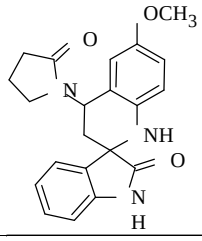
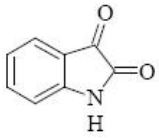
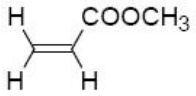
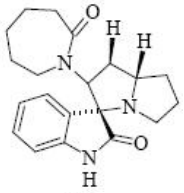
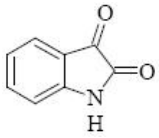
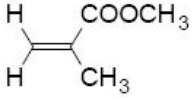
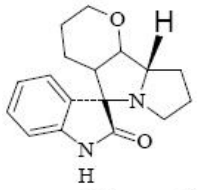
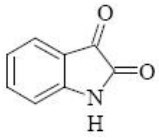
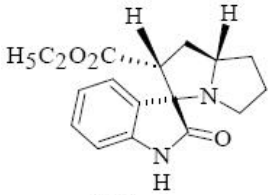
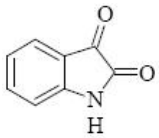
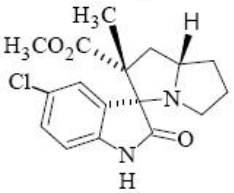
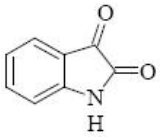
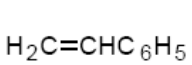
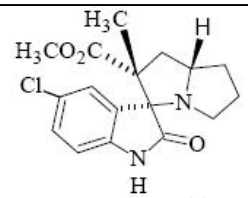
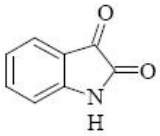
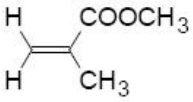
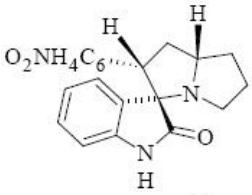
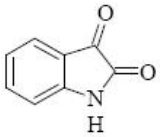
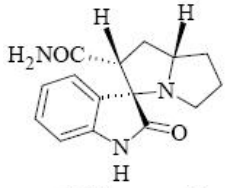
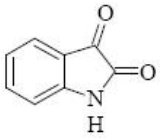
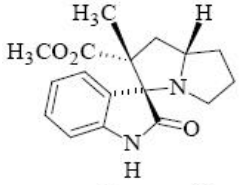
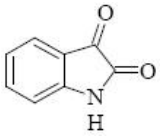
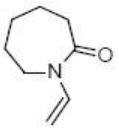
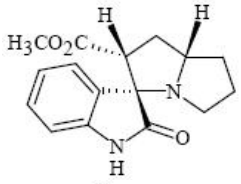
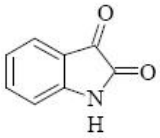
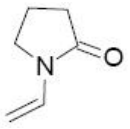
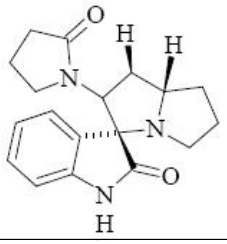
Entry	Products	Time/hr	Yield %	Mp °C
2a		1.50	90	187-189
2b[27]		2.00	88	171-173
2c		2.50	90	178-180

TABLE 3 : Antimony(III)chloride catalysed synthesis of 3-spiro pyrrolizidine oxindoles

Entry	Isatin	Dipolarophiles (3a-j)	Products	Time/hr	Yield %
4a				1	90
4b				6	90
4c		$H_2C{=}CHCONH_2$		10	80
4d		$CH_2{=}CHC_6H_4NO_2$		10	65

Entry	Isatin	Dipolarophiles (3a-j)	Products	Time/hr	Yield %
4e				09	80
4f				05	90
4g				06	80
4h				04	80
4i				04	80
4j				04	85

SX 102=DA-6000 (10kV) FAB mass spectrometer. Solvents, chemicals and reagents were purchased from Merck chemical company in high-grade quality.

General procedure for the synthesis compound ($C_{21}H_{21}N_3O_3$) (2c)

Antimony(III)chloride [(20 mol%) 0.031 g] was added to a mixture of Isatin [0.5g (3.3984 mmol)] and 4-methoxyaniline [0.42 g (3.3984 mmol] in MeOH (20 ml). The reaction mixture was stirred at room temperature for 2h, produce corresponding imines in an excellent yield. Then it is treated with [*N*-Vinyl pyrrolidone [0.38 g (3.3984 mmol)], under similar condition. The reaction completion was monitored by TLC, after the completion of the reaction; the reaction mixture was poured into water (100 ml) and the crude product was extracted with ethyl acetate (2x50 ml). The combined ethylacetate extracts were washed with brine, followed by water and dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to provide a crude solid. The solid thus obtained was further purified by column chromatography using silica gel (60-120 mesh) and eluted with petroleum ether: ethyl acetate to afford corresponding 3-Spiro tetrahydroquinolineoxindoles.

General procedure for the synthesis compound ($C_{16}H_{18}N_2O_3$) (4a)

The Isatin 1 [0.5g (3.3984 mmol)] L-Proline 2 [0.39

g (3.3984 mmol)] and methyl acrylate [0.03g (3.3984 mmol)] were dissolved in MeOH (20 ml). To this reaction mixture was added Antimony(III)chloride [(20 mole %) 0.031 g] and placed at room temperature stirring for 1h. The reaction completion was monitored by TLC, after the completion of the reaction, the reaction mixture was poured into water (100ml) and the crude product was extracted with ethylacetate (2x50 ml). The combined ethyl acetate extracts were washed with brine, followed by water and dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to provide a crude solid. The solid thus obtained was further purified by column chromatography using silica gel (60-120 mesh) and eluted with petroleumether: ethyleacetate to afford corresponding 3-Spiropyrrolizidine oxindoles.

Spectral data

8-methoxy-1',2',3,3a,5,9b-hexahydro-2H-spiro[3,2-c]quinoline-4,3'-indo le]-2'-one (2a)

Crystalline yellow solid : ^{1}H NMR (400 MHz DMSO-d_6): 10.4 (br, s, NH), 7.2 (t, *J*=5.4Hz, 1H), 6.7 (d, *J*=2.3 Hz, 1H), 6.7 (q, *J*= 3.7Hz, 3H), 6.5 (d, *J*=13.1Hz, 1H), 6.0(d, *J*=15.1Hz, 1H) 5.01 (s, NH),3.7(s,3H,OCH_3), 3.6 (t, *J*=4.5 Hz, 1H), 3.3(d, *J*=6, 1H), 2.2(d, *J*=4.2 Hz, 1H), 1.9(t, *J*=9 Hz, 2H), 1.8(d, *J*=5.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 28.4, 30.1, 55.1, 80.1, 90.1, 112.1, 113.1, 113.9, 120.1, 123.1, 123.6, 125.4, 128.1, 131.1, 135.1, 140.2, 150.2, 172.0. MS (EI 70 eV): m/z (%): 322 (M^+)

9'-methoxy-1,2,2',3',4',4'a,6',10'b-octahydospiro [indole-3,5'-pyrano [3,2-c] quinoline]-2-one (2b)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): 10.3 (br, s, NH), 7.2(t, *J*=14.1Hz, 1H), 6.9(s, 1H), 6.8(m, 3H), 6.6(d, *J*=2.1Hz, 1H), 6.0(d, *J*=6.9Hz, 1H), 5.0(br, s, NH), 3.6(s, 3H), 3.5(d, *J*=5.7, 1H), 1.7(t, *J*=4.2Hz, 2H), 1.4(d, *J*=6.6Hz, 3H), 1.3(d, *J*=6.1, 2H), 1.2(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 18.1, 24.9, 46.8, 56.1, 67.1, 67.2, 76.2, 112.1, 113.6, 114.1, 120.0, 123.5,123.9, 124.8, 128.5, 130.5, 135.1, 140.5, 149.5, 172.1. MS (EI 70 eV): m/z (%): 337 (M+1)

6'-methoxy-4'-(2-oxopyrrolidin-1-yl)1,2,3',4'-tetrahydro-1'H-spiro [indo le-3,2'quinoline]2-one (2c)

Crystalline yellow solid; ^{1}H NMR (400 MHz DMSO-d_6): 10.2(br, s, NH), 7.3(d, *J*=5.49Hz, 1H), 7.2(t, *J*=7.64Hz, 1H), 7.0(t, *J*=7.44Hz, 1H), 6.8(d, *J*=7.72Hz, 1H), 6.6(q, *J*=8 Hz, 1H), 6.5(d, *J*=8.64, 1H), 6.2(s, 1H), 6.1(s, 1H), 5.1 (br, s, NH),3.6(s, 3H), 3.3(t, *J*=7.16 Hz, 1H), 3.1(d, *J*=5.6Hz, 1H), 2.3(d,*J*=3H), 2.34(q, *J*=4.68, 2H), 3.14(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 21.6, 36.2, 37.1, 39.8, 43.1, 50.2, 71.8, 112.4, 114.5, 116.2, 121.1, 123.1, 124.5, 126.1, 128.1, 138.3, 139.7, 149.1, 152.0, 171.1,173.4: MS (EI 70eV): m/z (%): 363 (M^+)

(2'R,3S,7'aS)-2'-[(methylperoxy)methyl-1,1',2,2',5',6'7',7'a-octahydrospiro(indole-3,3'-pyr rolizine]-2-one (4a)

Crystalline yellow solid : ^{1}H NMR (400 MHz DMSO-d_6): δ 10.3(br, s, NH),7.2(t, *J*=7.62Hz, 1H), 7.1(d, *J*=7.4Hz, 1H), 6.9(t, *J*=7.62Hz, 1H), 6.8 (d, *J*=7.7Hz, 1H), 3.7(q, *J*=6.8Hz, 1H), 3.58(q, *J*=6.3Hz, 1H), 3.09(s, 3H (-$OOCH_3$), 2.3(m, *J*=4.81 Hz, 3H), 2.1(t, *J*=10.8 Hz, 1H), 1.9(t, *J*=5.6 Hz, 1H), 1.7(q, *J*=4.8, 2H), 1.5(q, *J*=6.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 176.1, 172.0, 140.8, 131.4, 128.1, 125.4, 123.7, 120.2, 55.1, 50.7, 43.1, 34.2, 28.4, 24.3, 20.5. MS (EI 70 eV): m/z (%): 286 (M^+); M.p:142-144 ^{o}C.

(2'R,3R,7'aS)-2'methyl-2'[(methylperoxy)methyl-1,1',2,2',5',6'7',7'a-octahydrospiro(indol e-3,3'-pyrrolizine)]-2-one (4b)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.2 (br, s, NH),7.1 (q, *J*=7.65Hz, 2H), 6.9 (t, *J*=5.3Hz, 1H), 6.7 (d, *J*=7.59Hz, 1H), 3.8 (q, *J*=6.3Hz, 1H), 3.3 (s, 3H), 2.4 (t, *J*=10.23, 2H), 2.2 (q, *J*=9.06,1H), 1.9 (d, *J*=6.03, 2H), 1.7 (d, *J*=10.12,2H), 1.5 (s, 3H). ^{13}C NMR (75 MHz,$CDCl_3$): 14.9, 21.2, 22.0, 35.8, 38.1, 43.1, 51.1, 62.8, 68.1, 120.1, 123.2, 125.1, 128.6, 131.1, 141.1, 172.1, 176.2. MS (EI 70 eV): m/z (%): 300 (M^+); M.p:204-206 ^{o}C.

(2'R,3S,7'aS)-2'-[(aminooxy)methyl]-1,1',2,2',5',6',7',7'a-octahydrospiro[indole-3,3'-pyrro lizine]-2-one (4c)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.3(br, s, NH), 7.2 (t, *J*=7.62Hz, 1H), 7.1(d, *J*=7.4Hz, 1H), 6.9(t, *J*=7.62Hz, 1H), 6.8(d, *J*=7.7Hz, 1H), 3.7(q, *J*=6.8Hz, 1H), 3.58(q, *J*=6.3Hz, 1H), 4.8(br, NH, 2H), 2.3(m, *J*=4.81Hz, 3H), 2.1(t,

J=10.8Hz, 1H), 1.9(t, *J*=5.6 Hz, 1H), 1.7(q, *J*=4.8, 2H), 1.5(q, *J*=6.8Hz, 1H). MS (EI 70 eV): m/z (%):271.1 (M^+); M.p:156-158 °C.

(2'S,3S,7'aS)-2'-(4-nitrophenyl)-1,1',2,2',5',6',7',7'a-octahydrospiro [indole-3,3'-pyrrolizin e]-2-one (4d)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.2(br, s, NH), 7.8(d, *J*=7.26Hz, 1H), 7.5(d, *J*=7.6Hz, 1H), 7.3(d, *J*= 7.59Hz, 1H), 7.2 (d, *J*=6.96Hz, 1H), 7.1(d, *J*=12.01Hz 1H), 7.0(t, *J*=7.83Hz, 1H),6.6(d, *J*=8.1Hz,1H), 6.3(s,1H) and 4.6(q, *J*=8.67Hz, 1H), 4.2(d, J=8.2Hz, 1H), 3.7(d, *J*=7.68Hz, 1H) 2.9(s 1H,), 2.5(t, *J*=2.68Hz, 1H), 2.05(m, 2H), 1.9 (m,2H), 1.8 (d, *J*=9.06 Hz,1H),MS (EI 70 eV): m/z (%): 349 (M^+); M.p:163-165 °C.

(2'S,3S,7'aS)-2'-phenyl-1,1',2,2',5',6',7',7'a-octahydrospiro[indole-3,3'-pyrrolizine]-2-one (4e)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.1(br, s, NH),7.59(d, *J*=7.6Hz, 1H), 7.16(d,*J*=6.91Hz,1H), 7.18(t, *J*=7.6Hz, 1H), 7.13(d, *J*=6.1Hz, 1H), 7.14(d, *J*=6.7Hz, 1H), 7.10(d *J*=8.12Hz,1H), 7.08(d, *J*=7.23Hz, 1H), 7.06 (t,*J*=7.6Hz,1H), 6.95(t,*J*=5.9Hz,1H), 3.47 (s,1H), 2.25 (t, *J*=2.1Hz,2H), 2.24(s,1H)1.84(t,*J*=1.8 2H), 1.59(m,2H),1.55(q, *J*=9,02, 2H). MS (EI 70 eV): m/z (%): 305.15 (M+1); M.p:151-153 °C.

(1'S)-5-chloro-1'-methyl-1'-[(methylperoxy)methyl]-1,1'2,2',5',6',7',7'a-octahydrospiro [in dole-3,3'-pyrrolizine]-2-one (4f)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.2 (br, s, NH),6.9(d, *J*=7.65Hz, 1H), 6.7(s, 1H), 6.5(d, *J*=7.59Hz, 1H), 3.3(s, 3H), 2.4 (t, *J*=10.23Hz, 2H), 2.2(q, *J*=9.06Hz, 1H), 2.0(d, *J*=8.1Hz, 2H),1.9(d, *J*=6.03Hz, 2H), 1.7 (d, *J*=10.12Hz, 2H), 1.5(s, 3H). ^{13}C NMR (75 MHz,$CDCl_3$):14.9, 21.2, 22.0, 35.8, 38.1, 43.1, 51.1, 68.1, 120.1, 123.2, 125.1, 128.6, 131.1, 141.1, 172.1, 176.2. MS (EI 70 eV): m/z (%): 336 (M+2); M.p:120-122 °C.

(1'S,3S,7'aS)-1'-[(ethylperoxy)metyl]-1,1'2,2',5',6',7',7'a-octahydro[indole-3,3'-pyrrolizine]-2-one (4g)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.2(br, s, NH), 7.5 (d, *J*=7.65Hz, 1H), 7.10(d, *J*=7.45Hz, 1H), 7.06(t, *J*=7.59Hz, 1H), 6.95(t, *J*=6.12Hz, 1H), 4.12(q, *J*=10.23Hz, 2H),3.10(s,1H), 2.25 (t, *J*=6.03Hz, 2H), 2.24(s, 1H),1.90(t, *J*=9.1Hz, 2H), 1.59 (m, 2H),1.55(q, *J*=9.16Hz, 2H),1.30(t, *J*=9.3Hz, 3H). MS (EI 70 eV): m/z (%): 300.15 (M^+); M.p:156-159°C.

(3S,9'aS)-1,2,3',4',4'a,7',8',9',9'a,9'b-decahydro-2'H-spiro[indole-3,5'-pyrano[2,3-a] pyrro lizine]-2-one (4h)

Crystalline yellow solid: ^{1}H NMR (400 MHz DMSO-d_6): δ 10.2(br, s, NH),7.59(d, *J*=7.6Hz, 1H), 7.10(q, *J*=7.57Hz, 1H), 7.06(t, *J*=8.1Hz, 1H), 6.95(t, *J*=6.2Hz,1H), 3.60(t, *J*=7.6Hz, 2H), 2.92 (d, *J*=8.6Hz,1H), 2.56(s, 1H), 2.50(t, *J*=8.6Hz, 1H), 2.25(t, *J*=9.16Hz, 2H), 1.59(m, 2H), 1.60 (m,2H), 1.56(d, *J*=9.56Hz, 2H), 1.55(t, *J*=9.6Hz, 2H) MS (EI 70 eV): m/z (%): 285.15 (M+1); M.p:105-107 °C.

(3R,7'aS)-2'-(2-oxoazepan-1-yl)-1,1',2,2',5',6',7',7'a-octahydrospiro [indole-3,3'-pyrrolizin e]-2-one;1-ethenylazepan-2-one (4i)

^{1}H NMR (400 MHz, DMSO-*d6*): δ 10.2 (br, s, NH), 7.2(t, *J*=7.62Hz, 1H), 7.0 (d, *J*=7.4Hz, 1H), 6.8(t, *J*=7.62Hz, 1H), 6.6(d, *J*=7.7Hz, 1H), 3.60(t, *J*=6.3Hz, 1H), 2.7(q, *J*=12.4Hz, 1H), 2.8(d, *J*=9.8Hz, 1H), 3.2(m, *J* = 10.36Hz, 1H), 3.4(m, *J*=6.28Hz, 1H), 2.4(m, *J*=7.76Hz, 1H), 2.3(m, *J*=4.81Hz, 3H), 2.2(t, *J*=10.8Hz, 1H), 2.1(m, *J*=5.3Hz, 4H), 2.1(t, *J*=5.6Hz, 1H),1.9(m, *J*=10.2 Hz, 3H), 1.6(q, *J*=4.8Hz, 2H). MS (EI 70 eV): m/z (%): 340.4 (M+1);M.p:168-170 °C.

(3R,7'aS)-2'-(2-oxopyrrolidin-1-yl)-1,1',2,2',5',6',7',7'a-octahydrospiro[indole3,3'-pyrrolizi ne]-2-one (4j)

^{1}H NMR (400 MHz DMSO-d_6): δ 10.2(br, s, NH), 7.2(q, *J*=7.65Hz, 2H), 6.8(t, *J*=5.3Hz, 1H), 6.6(d, *J*=7.59Hz, 1H), 3.6(q, *J*=6.3Hz, 1H), 2.4(t, *J*=10.23Hz, 2H), 2.2(q, *J*=9.06Hz,1H), 1.9(d, *J*=6.03Hz, 2H), 2.6(d, *J*=10.12Hz, 2H), 2.4(t, *J*=7.2Hz, 2H), 2.9(t, *J*=7.16Hz, 1H), 3.1(d, *J*=5.6 Hz, 1H), 2.3(m, 2H), 2.1(q, *J*=4.68, 2H), MS (EI 70 eV): m/z (%): 312.3 (M+1); M.p: 110-112 °C.

CONCLUSION

In summary we have developed a facile synthetic

route for the construction of functionalized 3-spiropyrrolizidineoxindoles and 3-Spirotetrahydroquinolineoxindoles starting from azomethine ylide via [3+2] cycloaddition and isatin Schiff base via [4+2] cycloaddition reaction. The synthe tic versatility of this protocol which leads to structurally diversified spirooxindolyl derivatives is under progress in our laboratory.

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