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1,3-Dipolar Cycloaddition Reaction of Dibenzalaceton with Non-stabilized Azomethinylides: Synthesis of New Spiro-oxindolo(pyrrolizidines/ pyrrolidines)

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ABSTRACT

1,3-dipolar cycloaddition reaction of 1 mol or 2 mol of dibenzalaceton with 1 mol of non-stabilized azomethinylides generated in situ by decarboxylative condensation of isatin and proline or sarcosine give the novel new spiro-oxindolo(pyrrolizidines/ pyrrolidines) instead of bis-spirooxindolo(pyrrolizidines/ pyrrolidines).

Keyword: 1,3-Dipolar cycloaddition; Azomethinylides; Spiro-oxindolo(pyrrolizidines/ pyrrolidines); Isatin; Proline; Sarcosine.

1. INTRODUCTION

1,3-Dipolarcycloaddition of azomethineylides is a fesible protocol for the synthesis of highly functionalised five-membered ring heterocycles [1]. Azomethineylides, generated in situ from isatin and sarcosine, add to α,β-unsaturated carbonyl compounds to afford spiropyrrolidines [2-4].

Some spiropyrrolidines are potential antileukemic and anticonvulsant agents [5] and possess antiviral [6] and local anaesthetic [7] activities. They are found in a number of biologically active compounds [8, 9]. Isatin and its derivatives have interesting biological activities and are widely used as precursors for many natural products [10-14]. Spiropyrrolidinyloxindoles are also found in a number of alkaloids of biological importance [15]. Gelsemine is representatives of the alkaloids, which incorporate spiro-oxindole ring systems [16-18]. Here in we will report the synthesise a series of new spirooxindoles using a three-component reaction involving 1,3-dipolar cycloadditions of appropriate azomethineylides with diolefins which makes possible the simultaneous

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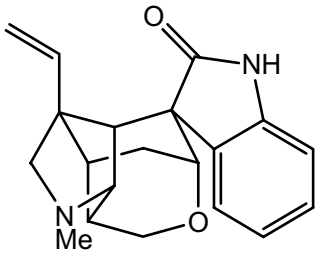
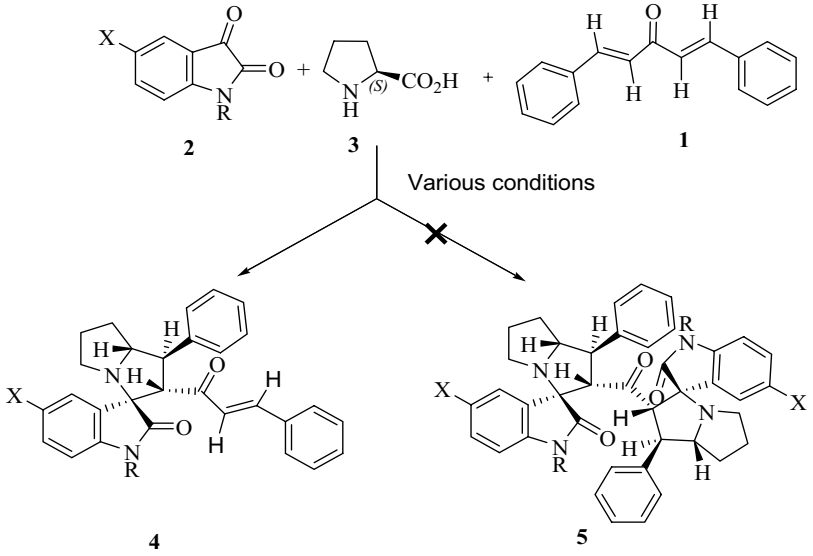
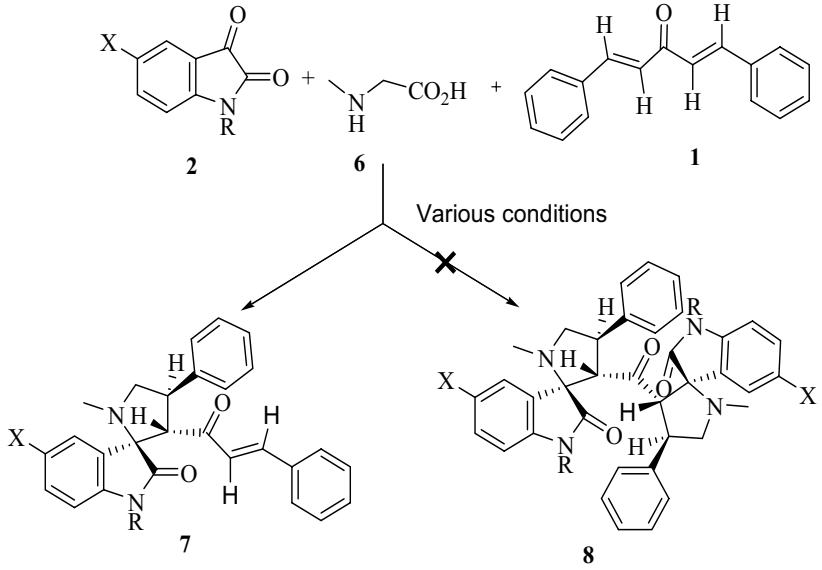
formation of up to four stereocenters in cycloadduct. Afterwards, the reactions were carried out in various conditions, but only at room temperature, in aqueous ethanol and in the absence of any bidentate chelating Lewis acids through a one-pot three-component 1,3-dipolar cycloaddition reaction of the dipolarophiles 1 with non-stabilized azomethineylides which was generated in situ by the decarboxylative condensation of isatins 2 with proline 3 or sarcosine 6 (Scheme 1 and 2).



Gelsemine



Scheme1: *Synthesis of spirooxindolopyrrolidines (4a-i).*



Scheme 2: *Synthesis of spirooxindolopyrrolizidines (7a-i).*

2. RESULTS AND DISCUSSION

The dibenzalaceton 1 was prepared based on the literature procedure [19, 20]. Three component reactions between dipolarophile 1, isatin derivatives 2 and L-proline 3 or sarcosine 6 carried out in ethanol at room temperature. As shown in Scheme 1 and 2, condensation of compounds 2 and 3 after decarboxylation leading to the non-stabilized azomethineylides stereogenic centers in one step. We expected by this method a bis-spirooxindolo (pyrrolizidines/ pyrrolidines) 5 and 8 products would be prepared, but by using the 1 mmol or 2 mmol of the dipolarophileonly the diastereoisomers 4 and 7 were obtained purely in high total yield (Scheme 1 and 2). After this, other derivatives of this new spirooxindolo(pyrrolizidines/ pyrrolidines) were also synthesized. The results are summarized in Table1.

The structures of cycloaducts were assigned by IR, ^{1}HNMR, ^{13}CNMR Observation of three characteristic singlet at about (52.5, 66.5 and 72.6) in the ^{13}CNMR spectra of 4 and two characteristic singlet at about (60.8 and 65.4) in the ^{13}CNMR spectra of 7 is consistent with formation new pyrrolidine cyclic. The stereochemistry and the correct structure of this isomer andother derivatives were determined by ^{1}HNMR, For example, the ^{1}HNMR spectrum of 4g exhibits a triplet signal at δ= 3.83 ppm, a multiple at δ= 4.19 and a doublet at δ= 4.57 ppm which are related to H*b*, Hcand H*a* protons respectively. The ^{1}HNMR spectrum of 7g exhibits a triplet signal at δ= 3.64 ppm and a doublet at δ= 4.14 ppm which are related to H*b* and H*a* protons respectively. Stereochemistryand absolute configuration of spirooxindoles 7g was determined by singlecrystal X-ray analysis (Figure 1).

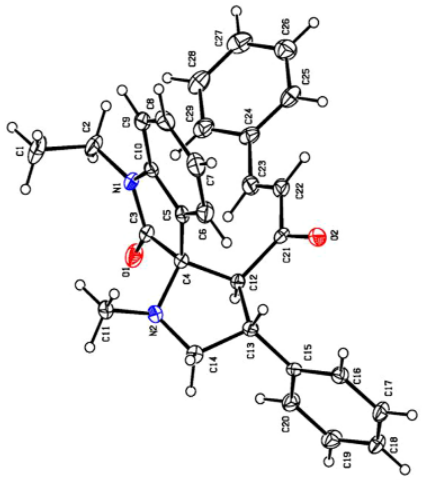


Figure 1: *Molecular structure of compound 7g (thermal ellipsoids at 50% probability level).*

3. EXPERIMENTAL

General melting points were recorded on an electrothermal digital melting point apparatus. Infrared spectra were recorded on a mattson 1000

Table 1: *Yield of spirooxindolo(pyrrolizidines/ pyrrolidines) (4a-i) and (7a-i).*

Entry	R	X	Product	4	7
				Yield (%)	Yield (%)
1	H	H	a	95	85
2	H	Br	b	90	83
3	H	NO_2	c	93	80
4	Me	H	d	95	83
5	Me	Br	e	93	80
6	Me	NO_2	f	90	85
7	Et	H	g	90	87
8	Et	Br	h	93	85
9	Et	NO_2	i	90	83

FTIR. ^{1}H, $^{13}CNMR$ spectra were measured with a Bruker DRX-250 AVANCE instrument with $CDCl_3$ as solvent at 250.1 MHz. Mass spectra were recorded on a Finnigan MAT 8430 mass spectrometer operating at an electron energy of 70 eV. Isatin derivatives, proline, and sarcosine were obtained from Fluka (Buchs, Switzerland) and were used without further purification, and dibenzalaceton were obtained via synthesized.

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

4. CONCLUSIONS

Because of wide distribution in nature and variegated biological activities, pyrrolizidines alkaloids are very attractive synthetic targets. For the reason that a pyrrolizidine can be viewed as a fused pyrrolidine, thus method employed for the formation of pyrrolidine rings can be used to construct the pyrrolizidine ring system. So, the 1,3-Dipolar cycloaddition reaction of azomethine ylides, including pyrrolidine derivatives, with olefins can be useful method for the synthesis of pyrrolizidines. In result of we have found a tri-component synthetic method for the prepration of some oxindoles derivatives of potential synthetic interest. The present method carries the advantage that not only is the reaction performed under neutral conditions, but also the starting materials and reagents can be mixed without any activation or modification.

2'-cinnamoyl-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7a): yellow powder, yield 95%; IR(KBr)(ν_{max}, cm^{-1}): 1614(C=C), 1692(C=O), 1722(C=O), 3440(NH); $^{1}HNMR$ (300.1 MHz, $CDCl_3$); 1.27-2.06 (4H, m, $2CH_2$), 2.58-2.63 (2H, m, CH_2), 3.86 (1H, t, $^{3}J_{HH}$=9 Hz, CH), 4.19 (1H, m, CH), 4.58 (1H, d, $^{3}J_{HH}$=9Hz, CH), 6.27 (1H, d, $^{3}J_{HH}$=12.5 Hz, CH), 6.83-7.49 (15H, m, Ar-H), 9.04 (1H, s, NH); $^{13}CNMR$ (75 MHz, $CDCl_3$); 27.7, 31.2, 48.0 (3C, $3CH_2$), 52.5, 66.5, 72.6 (3C, 3CH), 74.1(1C),110.7(1C, 1CH), 125.4, 125.5, 127.0, 127.4, 129.6, 130.5 (6C, 6CH), 128.0, 128.3, 128.6, 128.8 (4C, 8CH), 122.5, 134.2, 139.8, 140.8 (4C), 143.6 (1C, 1CH), 181.7, 195.0 (2C, 2C=O); MS, 434 (M+, 5), 200 (100), 131 (70).

2'-cinnamoyl-5-nitro-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2- one (7b): yellow powder, yield 90%; IR(KBr)(ν_{max}, cm^{-1}): 1610(C=C), 1712(C=O), 3395(NH); $^{1}HNMR$ (300.1 MHz, CDCl3); 1.26-2.05 (4H, m, 2CH2), 2.57-2.63 (2H, m, CH2), 3.85 (1H, t, $^{3}J_{HH}$=9 Hz, CH), 4.19 (1H, m, CH), 4.59 (1H, d, $^{3}J_{HH}$=9Hz, CH), 6.27 (1H, d, $^{3}J_{HH}$=12.5 Hz, CH) 6.83-7.56 (14H, m, Ar-H), 8.84 (1H, s, NH); $^{13}CNMR$ (75 MHz, $CDCl_3$); 27.8, 31.1, 47.9 (3C, $3CH_2$), 52.5, 66.4, 72.6 (3C, 3CH), 74.1 (1C), 110.7 (1C, 1CH), 125.4, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.0, 128.3, 128.6, 128.8 (4C, 8CH), 122.5, 134.2, 137.8, 139.8, 140.8 (5C), 143.5 (1C, 1CH), 180.5, 195.0 (2C, 2C=O); MS, 479 (M^{+}, 6), 245 (100), 176 (75).

2'-cinnamoyl-5-bromo-3'-phenyl-3', 3a', 4', 5', 6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7c): yellow powder, yield 93%; IR(KBr)(ν_{max}, cm^{-1}): 1603(C=C), 1719(C=O), 3422(NH); $^{1}HNMR$ (300.1 MHz, $CDCl_3$); 1.28-2.06 (4H, m, 2CH2), 2.57-2.63 (2H, m, CH_2), 3.85 (1H, t, $^{3}J_{HH}$=9 Hz, CH), 4.21 (1H, m, CH), 4.58 (1H, d, $^{3}J_{HH}$=9Hz, CH), 6.27 (1H, d, $^{3}J_{HH}$=12.5 Hz, CH) 6.75-7.49 (14H, m, Ar-H), 8.38(1H, s, NH); $^{13}CNMR$ (75 MHz, $CDCl_3$); 27.7, 31.2, 48.0 (3C, $3CH_2$), 52.5, 66.5, 72.6 (3C, 3CH), 74.0 (1C), 110.7 (1C, 1CH), 125.4, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.0, 128.3, 128.6, 128.8 (4C, 8CH), 122.4, 134.2, 137.4, 139.7, 140.8 (5C), 143.6 (1C, 1CH), 181.6, 195.1 (2C, 2C=O); MS, 513, 515 (M+, M++2, 5), 278, 280 (100), 131 (40).

2'-cinnamoyl-1-methyl-3'-phenyl-3',3a',4', 5', 6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7d): yellow powder, yield 95%; IR(KBr)(ν_{max}, cm^{-1}):1609(C=C), 1703(C=O), 1726(C=O); $^{1}HNMR$ (300.1 MHz, $CDCl_3$); 1.28-

2.06 (4H, m, $2CH_2$), 2.57-2.63 (2H, m, CH_2), 3.58 (3H, s, NMe), 3.85 (1H, t, $^3J_{HH}$=9 Hz, CH), 4.06 (1H, m, CH), 4.41 (1H, d, $^3J_{HH}$=9Hz, CH), 6.07 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.82-7.49 (15H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 27.7, 31.2, 48.0 (3C, $3CH_2$), 42.4 (1c, NMe), 52.5, 66.4, 72.6 (3C, 3CH), 74.1 (1C), 111.2 (1C, 1CH), 125.4, 125.5, 127.1, 127.4, 129.6, 130.5 (6C, 6CH), 128.0, 128.3, 128.6, 128.8 (4C, 8CH), 122.4, 134.2, 139.7, 140.8 (4C), 143.6(1C, 1CH), 181.4, 195.1 (2C, 2C=O); MS, 448 (M^+, 8), 214 (100), 131 (77).

2'-cinnamoyl-1-methyl-5-nitro-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7e): yellow powder, yield 93%; IR(KBr)(ν_{max}, cm^{-1}): 1603(C=C), 1720(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.28-2.06 (4H, m, $2CH_2$), 2.57-2.63 (2H, m, CH_2), 3.57 (3H, s, NMe), 3.85 (1H, t, $^3J_{HH}$=9 Hz, CH), 4.07 (1H, m, CH), 4.41 (1H, d, $^3J_{HH}$=9Hz, CH), 6.06 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.82-7.49 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 27.7, 31.2, 48.0 (3C, $3CH_2$), 42.4 (1c, NMe), 52.5, 66.4, 72.7 (3C, 3CH), 74.1 (1C), 110.9 (1C,1CH), 125.4, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.0, 128.3, 128.6, 128.8 (4C, 8CH), 122.4, 134.2, 137.2, 139.7, 140.8 (5C), 143.6 (1C, 1CH), 181.4, 195.0 (2C, 2C=O); MS, 493 (M^+, 3), 259 (100), 190 (70).

5-bromo-2'-cinnamoyl-1-methyl-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7f): yellow powder, yield 90%; IR(KBr)(ν_{max}, cm^{-1}): 1615(C=C), 1717(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.27-2.05 (4H, m, $2CH_2$), 2.57-2.64 (2H, m, CH_2), 3.50 (3H, s, NMe), 3.73 (1H, t, $^3J_{HH}$=9 Hz, CH), 4.09 (1H, m, CH), 4.36 (1H, d, $^3J_{HH}$=9Hz, CH), 6.19 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.76-7.47 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 26.3, 27.3, 30.0 (3C, $3CH_2$), 42.9 (1c, NMe), 48.3, 51.0, 63.4 (3C, 3CH), 71.4 (1C), 110.7 (1C, 1CH), 125.3, 125.5, 127.3, 129.6, 130.5 (5C, 5CH), 128.1, 128.3, 128.6, 128.8 (4C, 8CH), 122.4, 134.2, 137.2, 139.7, 140.8 (5C), 143.6 (1C, 1CH), 181.4, 194.9 (2C, 2C=O); MS, 527, 529 (M^+, M^++2, 7), 292, 294 (100), 131 (49).

2'-cinnamoyl-1-ethyl-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7g): yellow powder, yield 90%; IR(KBr)(ν_{max}, cm^{-1}): 1615(C=C), 1716(C=O); ^{1}HNMR (300.1 MHz, CDCl3); 1.06 (3H, t, $^3J^{HH}$=7.5 Hz, CH3), 1.67-2.03 (4H, m, $2CH_2$), 2.55-2.60 (2H, m, CH_2), 3.66 (2H, q, $^3J_{HH}$=7.5 Hz, CH_2), 3.83 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.19 (1H, m, CH), 4.57 (1H, d, $^3J_{HH}$=10Hz, CH), 6.22 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.69-7.50 (15H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 12.3 (1C, CH_3), 27.1, 30.2, 31.3 (3C, $3CH_2$), 35.4 (1C, NCH_2), 47.2, 51.4, 65.2 (3C, 3CH), 72.4(1C), 108.6 (1C,1CH), 125.5, 125.6, 127.1, 127.4, 129.6, 130.5 (6C, 6CH), 128.2, 128.5, 128.8, 129.0 (4C, 8CH), 122.4, 134.2, 139.7, 140.8 (4C), 142.7 (1C, 1CH), 178.4, 194.7 (2C, 2C=O); MS, 462 (M^+, 9), 228 (100), 159 (68).

2'-cinnamoyl-1-ethyl-5-nitro-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7h): yellow powder, yield 93%; IR(KBr)(ν_{max}, cm^{-1}): 1613(C=C), 1720(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.07 (3H, t, $^3J_{HH}$=7.5 Hz, CH_3), 1.69-2.03 (4H, m, $2CH_2$), 2.53-2.60 (2H, m, CH_2), 3.66 (2H, q, $^3J_{HH}$=7.5 Hz, CH_2), 3.83 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.19 (1H, m, CH), 4.57 (1H, d, $^3J_{HH}$=10Hz, CH), 6.19 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.69-7.50 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 12.3 (1C, CH_3), 27.1, 30.2, 31.6 (3C, $3CH_2$), 35.4 (1C, NCH_2), 47.1, 51.4, 65.2 (3C, 3CH), 72.1(1C), 108.6 (1C,1CH), 125.5, 125.6, 127.4, 129.6, 130.5 (5C, 5CH), 128.2, 128.5, 128.8, 129.0 (4C, 8CH), 122.3, 134.1, 137.9, 139.7, 140.3 (5C), 142.7 (1C, 1CH), 178.4, 194.9 (2C, 2C=O); MS, 507 (M^+, 4), 273 (100), 158 (73).

5-bromo-2'-cinnamoyl-1-ethyl-3'-phenyl-3',3a',4',5',6',6a'-hexahydro-2'H-spiro[indoline-3,1'-pentalen]-2-one (7i): yellow powder, yield 90%; IR(KBr)(ν_{max}, cm^{-1}): 1612(C=C), 1715(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.06 (3H, t, $^3J_{HH}$=7.5 Hz, CH_3), 1.67-2.03 (4H, m, $2CH_2$), 2.55-2.60 (2H, m, CH_2), 3.64 (2H, q, $^3J_{HH}$=7.5 Hz, CH_2), 3.83 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.19 (1H, m, CH), 4.57 (1H, d, $^3J_{HH}$=10Hz, CH), 6.22 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.69-7.49 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 12.3 (1C, CH_3), 27.1, 30.2, 31.3 (3C, $3CH_2$), 35.5 (1C, NCH_2), 47.2, 51.4, 65.2 (3C, 3CH), 72.4 (1C), 108.6 (1C,1CH), 125.5, 125.6, 127.4, 129.6, 130.5 (5C, 5CH), 128.2, 128.4, 128.8, 129.0 (4C, 8CH), 122.4, 134.1, 137.6,

139.7, 140.7 (5C), 142.7 (1C, 1CH), 179.7, 194.7 (2C, 2C=O); MS, 541, 543 (M^+, M^++2, 8), 306, 308 (100), 131 (70).

3'-cinnamoyl-1'-methyl-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4a): yellow powder, yield 85%; IR(KBr)(ν_{max}, cm^{-1}): 1609(C=C), 1711(C=O), 3430(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 2.16 (3H, s, NMe), 3.43 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.14 (1H, d, $^3J_{HH}$=10Hz, CH), 4.43 (1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.55 (15H, m, Ar-H), 8.84 (1H, s, NH); 13CNMR (75 MHz, $CDCl_3$); 35.2 (1C, NCH_3), 43.9 (1C, $1CH_2$), 60.8, 65.4, (2C, 2CH), 74.2 (1C), 110.1 (1C, 1CH), 125.3, 125.5, 127.1, 127.4, 129.6, 130.5 (6C, 6CH), 128.2, 128.7, 128.8, 129.4 (4C, 8CH), 122.5, 134.2, 139.8, 140.8 (4C), 143.0 (1C, 1CH), 180.6, 195.9 (2C, 2C=O); MS, 408 (M^+, 5), 147 (100), 131 (68).

3'-cinnamoyl-1'-methyl-5-nitro-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4b): yellow powder, yield 83%; IR(KBr)(ν_{max}, cm^{-1}): 1615(C=C), 1721(C=O), 3420(NH); 1HNMR (300.1 MHz, $CDCl_3$); 2.16 (3H, s, NMe), 3.43(1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.43(1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.55 (14H, m, Ar-H), 8.84 (1H, s, NH); 13CNMR (75 MHz, $CDCl_3$); 35.2 (1C, NCH_3), 43.9 (1C, 1CH2), 60.8, 65.4, (2C, 2CH), 74.2 (1C), 110.1 (1C, 1CH), 125.3, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.2, 128.7, 128.8, 129.4 (4C, 8CH), 122.5, 134.2,137.6, 139.8, 140.8 (5C), 143.0 (1C, 1CH), 180.6, 195.9 (2C, 2C=O); MS, 453 (M^+, 5), 219 (100), 131 (72).

5-bromo-3'-cinnamoyl-1'-methyl-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4c):
yellow powder, yield 80%; IR(KBr)(ν_{max}, cm^{-1}): 1612(C=C), 1707(C=O), 3427(NH); ^{1}HNMR (300.1 MHz, $CDCl_3$); 2.16 (3H, s, NMe), 3.43 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.43(1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.63-7.55 (14H, m, Ar-H), 8.84(1H, s, NH); ^{13}CNMR (75 MHz, $CDCl_3$); 35.2 (1C, NCH_3), 43.9 (1C, 1CH2), 60.8, 65.4, (2C, 2CH), 74.2 (1C), 110.1 (1C, 1CH), 125.3, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.2, 128.7, 128.8, 129.4 (4C, 8CH), 122.5, 134.2,137.4, 139.8, 140.8 (5C), 143.0(1C, 1CH), 180.6, 195.9 (2C, 2C=O); MS, 483, 485 (M^+, M^++2, 6), 251, 253 (100), 131 (70).

3'-cinnamoyl-1,1'-dimethyl-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4d): yellow powder, yield 83%; IR(KBr)(ν_{max}, cm^{-1}): 1609(C=C), 1703(C=O), 1725(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 2.16 (3H, s, NMe), 3.14 (3H, s, NMe), 3.43 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.43 (1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.55 (15H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 26.2 (1C, NCH_3), 35.2 (1C, NCH_3), 43.9 (1C, $1CH_2$), 60.8, 65.4, (2C, 2CH), 74.2 (1C), 110.1 (1C, 1CH), 125.3, 125.5, 127.1, 127.4, 129.6, 130.5 (6C, 6CH), 128.2, 128.7, 128.8, 129.4 (4C, 8CH), 122.5, 134.2, 139.8, 140.8 (4C), 143.0 (1C, 1CH), 180.6, 195.9 (2C, 2C=O); MS, 422 (M^+, 3), 188 (100), 131 (78).

3'-cinnamoyl-1,1'-dimethyl-5-nitro-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4e):
yellow powder, yield 80%; IR(KBr)(ν_{max}, cm^{-1}): 1603(C=C), 1717(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 2.16(3H, s, NMe), 3.15 (3H, s, NMe), 3.43 (1H, m, CH), 3.65 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.45(1H, m, CH), 6.12 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.63-7.55 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 26.3 (1C, NCH_3), 35.1 (1C, NCH_3), 43.9 (1C, $1CH_2$), 60.9, 65.3, (2C, 2CH), 73.8(1C), 107.9 (1C, 1CH), 125.3, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.0, 128.2, 128.6, 128.8 (4C, 8CH), 123.2, 134.2, 137.6, 139.8, 141.9 (5C), 142.5 (1C, 1CH), 177.9, 196.1 (2C, 2C=O); MS, 467 (M^+, 6), 233 (100), 131 (81).

5-bromo-3'-cinnamoyl-1,1'-dimethyl-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4f):
yellow powder, yield 85%; IR(KBr)(ν_{max}, cm^{-1}): 1613(C=C), 1714(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 2.16(3H, s, NMe), 3.14(3H, s, NMe), 3.43 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 4.15 (1H, d, $^3J_{HH}$=10Hz CH), 4.43 (1H, m, CH), 6.09 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.50 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 26.2 (1C, NCH_3), 35.2 (1C, NCH_3), 43.9 (1C, $1CH_2$), 60.8, 65.4, (2C, 2CH), 74.2 (1C), 110.1 (1C, 1CH), 125.3, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.1,

128.6, 128.8, 129.4 (4C, 8CH), 122.4, 134.2, 137.4, 139.8, 140.8 (5C), 143.1(1C, 1CH), 181.6, 195.8 (2C, 2C=O); MS, 501, 503 (M^+, M^++2, 4), 266, 268 (100), 131 (75).

3'-cinnamoyl-1-ethyl-1'-methyl-4'-phenylspiro [indoline-3,2'-pyrrolidin]-2-one (4g): yellow powder, yield 87%; IR(KBr)(ν_{max}, cm^{-1}): 1609(C=C), 1714(2C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.07 (3H, t, $^3J_{HH}$=7.5 Hz, CH3), 2.15 (3H, s, NMe), 3.44 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 3.68 (2H, q, $^3J_{HH}$=7.5 Hz, CH_2), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.44 (1H, m, CH), 6.11 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.55 (15H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 12.3 (1C, CH_3), 35.2 (1C, NCH_3), 35.5 (1C, NCH_2), 43.7 (1C, $1CH_2$), 60.8, 65.3, (2C, 2CH), 74.1 (1C), 110.2 (1C, 1CH), 125.3, 125.5, 127.3, 127.4, 129.6, 130.5 (6C, 6CH), 128.2, 128.5, 128.7, 128.9 (4C, 8CH), 122.4, 134.2, 139.8, 140.8 (4C), 143.1 (1C, 1CH), 180.6, 195.7 (2C, 2C=O); MS, 436 (M^+, 4), 202 (100), 131 (65).

3'-cinnamoyl-1-ethyl-1'-methyl-5-nitro-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4h): yellow powder, yield 85%; IR(KBr)(ν_{max}, cm^{-1}): 1609(C=C), 1717(C=O); ^{1}HNMR (300.1 MHz, $CDCl_3$); 1.06 (3H, t, $^3J_{HH}$=7.5 Hz, CH_3), 2.16 (3H, s, NMe), 3.43(1H, m, CH), 3.63 (1H, t, 3JHH=10 Hz, CH), 3.69 (2H, q, $^3J_{HH}$=7.5 Hz, CH_2), 4.13 (1H, d, $^3J_{HH}$=10Hz CH), 4.43(1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH) 6.65-7.49 (14H, m, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$); 12.3 (1C, CH_3), 35.2 (1C, NCH_3), 35.4 (1C, NCH_2), 43.9 (1C, $1CH_2$), 61.3, 65.4, (2C, 2CH), 74.2(1C), 110.1(1C, 1CH), 125.3, 125.5, 127.4, 129.6, 130.5 (5C, 5CH), 128.2, 128.6, 128.8, 129.3 (4C, 8CH), 122.5, 134.2,137.6, 139.8, 140.8 (5C), 143.0 (1C, 1CH), 178.9, 195.4 (2C, 2C=O); MS, 481 (M^+, 6), 247 (100), 131 (73).

5-bromo-3'-cinnamoyl-1-ethyl-1'-methyl-4'-phenylspiro[indoline-3,2'-pyrrolidin]-2-one (4i): yellow powder, yield 83%; IR(KBr)(ν_{max}, cm^{-1}): 1612(C=C), 1719(C=O); 1HNMR (300.1 MHz, CDCl3); 1.06 (3H, t, $^3J_{HH}$=7.5 Hz, CH_3), 2.16 (3H, s, NMe), 3.43 (1H, m, CH), 3.64 (1H, t, $^3J_{HH}$=10 Hz, CH), 3.64 (2H, q, $^3J_{HH}$=7.5 Hz, CH2), 4.14 (1H, d, $^3J_{HH}$=10Hz CH), 4.43(1H, m, CH), 6.08 (1H, d, $^3J_{HH}$=12.5 Hz, CH), 6.63-7.55 (14H, m, Ar-H), 8.84 (1H, s, NH); ^{13}CNMR (75 MHz, $CDCl_3$); 12.1 (1C, CH_3), 35.2 (1C, NCH_3), 35.5 (1C, NCH_2), 43.9 (1C, $1CH_2$), 60.7, 65.4, (2C, 2CH), 74.1(1C), 110.1 (1C, 1CH), 125.4, 125.5, 127.2, 129.6, 131.2 (5C, 5CH), 128.2, 128.7, 128.8, 129.4 (4C, 8CH), 122.5, 134.2,137.4, 139.7, 140.7 (5C), 143.0 (1C, 1CH), 181.2, 195.9 (2C, 2C=O); MS, 515, 517 (M^+, M^++2, 7), 280, 282 (100), 131 (70).

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