Study of Regiochemical Trends During the Synthesis of Furan and 5-(*p*-chlorophenyl)Furan Containing Novel Spiropyrrolidine Library Through 1,3-dipolar Cycloaddition Reactions

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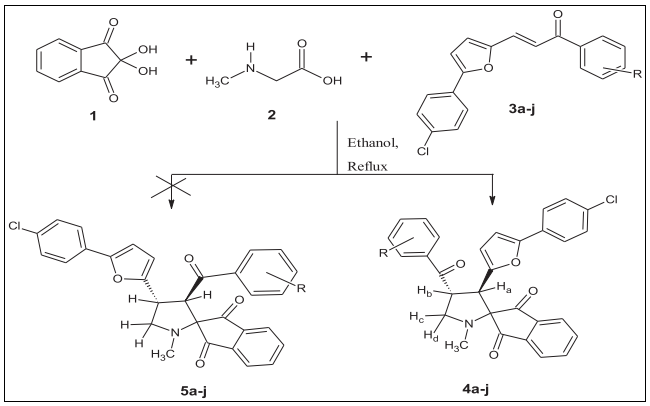

A new class of functionalized furan and 5-(*p*-chlorophenyl)furan containing spiropyrrolidines has been synthesized in moderate to excellent yields by the one-pot, three-component 1,3-dipolar cycloaddition reaction of in situ generated azomethine ylides with various furan/aryl furan-substituted chalcones as dipolarophiles. The effect of electron deficient substituents at the fifth position of the furan ring in the chalcone on the regiochemistry of the cycloaddition formed was studied. The structures of the newly synthesized cycloaddicts were proved by analytical and spectral data.

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INTRODUCTION

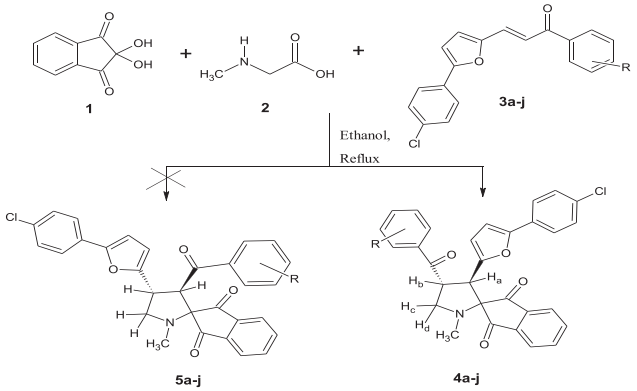
Spiropyrrolidine ring systems form the core structure of numerous natural products and alkaloids and are also elegant precursors in organic synthesis due to their significant pharmacological and biological activities [1–9]. A number of strategies have been devised to provide access to the synthesis of spiropyrrolidine core. The 1,3-dipolar cycloaddition of azomethine ylides with olefinic dipolarophiles offers an excellent route for the construction of nitrogen containing five membered substituted pyrrolidine derivatives [10]. Although highly substituted spiropyrrolidines are known [10], there seems to be a very sparse report on the study of substituent effect on the regioselectivity of spiropyrrolidines [11,12]. The regiochemistry and stereochemistry of spiropyrrolidine formed by 1,3-dipolar cycloaddition may be controlled either by choosing the appropriate dipole and dipolarophile or by controlling the reaction using a catalyst. The steric and electronic effects are two major factors that can influence the selectivity of these reactions.

Our group had recently reported a novel regioselectivity trend during the reaction of 1-(substituted benzyl)-3-(5-nitrofuryl) prop-2-en-1-one were employed as dipolarophiles to react with azomethine ylides [12]. The presence of strong electron withdrawing nitro substituents on the substrates significantly affected the regioselectivity of the 1,3-dipolar cycloaddition, which allowed the formation of (3′R,4′R)-4′-(4-substituted benzoyl)-1′-methyl-3′-(5-nitro-2-furfuryl) spiro[indene-2,2′-pyrrolidine]-1,3-dione in good regioselectivity. Our continued interest in further exploring the effect of electron withdrawing groups on the regioselectivity trends prompted us to study the mode of addition during the 1,3-dipolar cycloaddition of azomethine ylides to unsubstituted furfuryl chalcones and aryl furfuryl chalcones. Moreover, as we envisioned that the strong electron-withdrawing nature of substituents like nitro group on the furan ring effectively tunes the regioselectivity of a 1,3-dipolar cycloaddition of azomethine ylide in our previous work [12], herein, we reported the regioselectivity trends observed during the one-pot, three-component 1,3-dipolar cycloaddition of azomethine ylides, generated in situ from ninhydrin and sarcosine, with α,β-unsaturated enones having furyl moiety and aryl furyl moiety, with weaker electron withdrawing *p*-chlorophenyl substituent at the fifth position of the furan ring.

RESULT AND DISCUSSION

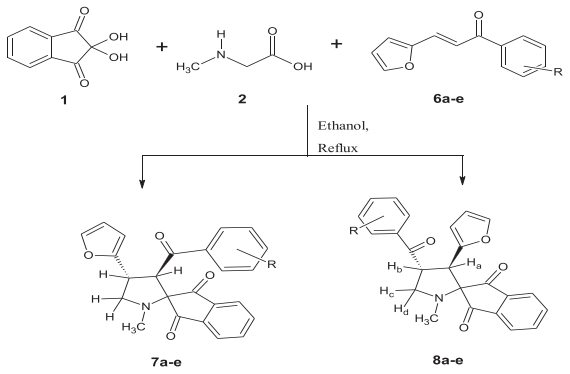
As described in Scheme 1, the 1,3-dipole generated in situ from decarboxylative cyclocondensation of ninhydrin

Scheme 1. Synthesis of aryl furan containing spiropyrrolidines.



1 and sarcosine **2** reacted readily with the aryl furan containing chalcones **3a-j** as dipolarophiles under refluxing conditions in absolute ethanol medium to give only one regioisomer as cycloadducts **4a-j** in high yield, in which the benzoyl group was connected to C-4 of the newly constructed pyrrolidine, thus showing that when strong electron-withdrawing nitro group was replaced by weaker electron-withdrawing group such as *p*-chlorophenyl, we were still able to reproduce the regiochemical trends similar to those of nitrofuran [12]. But in the case of cycloaddition of azomethine ylides to furfuryl chalcone derivatives, **6a-e** (Scheme 2), a pair of regioisomers **7a-e** and **8a-e** were obtained with a modest yield and a poor regioisomeric ratio.

Scheme 2. Synthesis of furan containing spiropyrrolidines.



It is interesting to note that in the case of electron-withdrawing aryl substituents on the fifth position of furan ring in the chalcone, unusual cycloadduct is formed easily with regioselectivity. A plausible mechanism for the regioselectivity in this transformation can be proposed as the presence of electron-withdrawing *p*-chlorophenyl attached to the fifth position of furfuryl ring of the chalcone generates the electron-deficient α-carbon of aryl furfuryl chalcone (Fig. 1), which adds up with the nucleophilic carbon center of azomethine ylides generated from the reaction of ninhydrin with sarcosine during the cycloaddition, leading to single regioisomer. In the case of furfuryl chalcones, due to the absence of electron withdrawing group, there was no polarity in the alkenyl bond of chalcone (Fig. 1). Thus, the nucleophilic center of the azomethine ylide adds to α as well as β carbon of the olefinic portion of furfuryl chalcone. Even when efforts were given to study the reaction of 5-methyl furyl chalcones with azomethine ylides, a pair of regioisomers were obtained as product. The regioseparation was not observed in cases of electron donating groups.

Thus, it can be summarized that the presence of electron-withdrawing groups significantly changed the regiochemistry and yield of this reaction, whereas removal of electron withdrawing group makes the reaction to loose regiospecificity. More importantly, the regioselectivity of the 1,3-dipolar cycloaddition of azomethine ylide can be changed by the presence of electron withdrawing groups in the dipolarophiles, which lead to the formation of spirooxindoles with novel regiochemical trends.

The structures of newly synthesized spiropyrrolidines were elucidated using ^{1}H NMR, ^{13}C NMR, HMBC, mass spectra, and elemental analysis data. The analytical and spectral data are in consistency with the proposed structure.

Thus, in the IR spectrum of **4a**, the three carbonyl absorption bands of furfuryl containing spiropyrrolidine moiety were observed at 1638, 1680, and 1741 cm^{-1}, respectively, thus providing proof for the formation of spiropyrrolidines. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **4a** shows a doublet at δ = 4.66 ppm for proton H_a, a multiplet

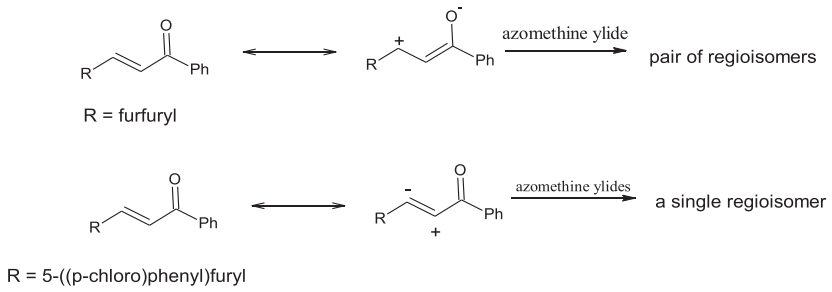


Figure 1. Mechanism for the formation of polarity in the chalcones.

at δ = 4.72 ppm for proton H_b, a doublet of doublet at δ = 3.44 ppm for proton H_c, and a doublet of doublet at 3.86 ppm for proton H_d of spiropyrrolidine, respectively. The aromatic protons came into resonance at δ = 6.80–8.02 ppm as multiplet, the protons of aryl furfuryl ring appeared at δ = 5.99 and 6.19 ppm respectively as two doublets, and N-CH_3 protons of spioropyrrolidine ring appeared at δ = 2.61 ppm as a singlet. Similarly, the ^{13}C NMR spectrum of **4a** shows the peak at δ = 78.41 ppm due to spirocarbon, whereas two C=O carbons of ninhydrin ring appeared at 200.04 and 202.25 ppm, while C=O carbon of benzoyl group appears at δ = 195.59 ppm.

The regiochemistry of the product was established from the HMBC data of **4a**; the benzoyl C=O group at δ = 195.59 ppm correlates with all the four protons attached to the pyrrolidine ring (H_a, H_b, H_c, and H_d) protons, showing that the correct regiochemistry of the product is as shown previously. If the other possible regioisomer had formed, a long-range coupling between the benzoyl C=O group and H_c would not have been observed.

Furthermore, the support for the formation of the spiropyrrolidines has been obtained by mass spectral studies. All the compounds showed the molecular ion peak ($M^+ + 1$) there by indicating the stability of spiropyrrolidines. In the mass spectrum of compound **4f**, the molecular ion ($M^+ + 1$) peak was observed at m/z 526.2:528.2 at 3:1 ratio, which is in agreement with the molecular formula (M. F.: $C_{31}H_{24}ClNO_5$) and confirms the formation of the product **4f**.

In the IR spectrum of compound **7d**, the carbonyl absorption bands were observed in the range of 1699, 1709, and 1741 cm^{-1}, respectively, whereas in the IR spectrum of compound **8d**, the carbonyl absorption bands were observed in the range of 1684, 1701, and 1733 cm^{-1}, respectively, thus showing the formation of regioisomeric cycloadducts.

^1H NMR (400 Hz, $CDCl_3$) spectrum of compound **7a** shows a doublet at δ = 4.66 ppm for H_a, a multiplet at δ = 4.74–4.82 ppm for H_b, a doublet of doublet at δ = 3.43 and 3.87 ppm for H_c and H_d, respectively. The aromatic protons appeared around δ = 7.26–7.98 ppm as multiplet, the α and γ protons of furyl ring appeared at δ = 5.89 and 6.92 ppm as doublets and β proton appeared at 5.93 ppm respectively as a doublet of doublet and N-CH_3 protons of spioropyrrolidine ring appeared at δ = 2.33 ppm as singlet and methyl group of benzoyl substituent is found at δ = 2.41 ppm as singlet.

Further ^1H NMR (400 MHz, $CDCl_3$) spectrum of compound **8a** showed a doublet at δ = 4.55 ppm for H_a, a multiplet at δ = 4.68 ppm for H_b, a doublet of doublet at δ = 3.36 and 3.78 ppm for H_c and H_d, respectively. The aromatic protons appeared around δ = 7.18–7.90 ppm as multiplet; the protons of furyl ring appeared at δ = 5.80 ppm(d), 5.86 ppm(dd), and 6.84 ppm(d), respectively; N-CH_3 protons of spioropyrrolidine ring appeared at δ = 2.25 ppm as a singlet; and methyl group of benzoyl substituent is found at δ = 2.33 ppm as singlet.

The ^{13}C NMR spectrum of **7d** showed a peak at δ = 77.06 ppm due to spirocarbon, whereas the two C=O of ninhydrin ring appear at δ = 202.87 and 200.39 ppm, while C=O of benzoyl group appears at δ = 196.15 ppm.

The ^{13}C NMR spectrum of **8d** showed a peak at δ = 77.39 ppm due to spirocarbon, whereas the two C=O of ninhydrin ring appears at δ = 200.35 and 202.83 ppm, while C=O of benzoyl group appears at δ = 196.35 ppm.

As indicated in the HMBC data of **8d**, the benzoyl C=O group at δ = 196.35 ppm correlates with all the four protons attached to the pyrrolidine ring (H_a, H_b, H_c, and H_d) protons, showing that the correct regiochemistry of the product is as shown in structure. Similarly, as indicated in the HMBC data of **7d**, the benzoyl C=O group at δ = 196.15 ppm correlates with only two protons of pyrrolidine ring (H_a and H_b), and a long-range coupling between the benzoyl C=O group and H_c would not have been observed, showing that the correct regiochemistry of the product is as shown in structure.

The mass spectrum of the compound **7d** shows the molecular ion ($M^+ + 1$) peak at m/z 464.1 and 466.1 [$M^+ + 1$] (1:1 ratio), which is in agreement with the molecular formula there by confirming the formation of the product **7d**. Similarly, the mass spectrum of the compound **8d** shows the molecular ion (M^++1) peak at m/z 464.8 and 467.2 [$M^+ + 1$] (1:1 ratio), which is in agreement with the molecular formula that confirms the formation of the product **8d**. Here, although compounds had same molecular formula, their formula weight did differ, providing a hint for the formation of isomers.

During the cycloaddition reaction of ninhydrin, sarcosine, and aryl furfuryl chalcone, only a single regioisomer was formed, whereas a pair of regioisomers was obtained in poor regioselectivities when the cycloaddition of ninhydrin, sarcosine, and furfuryl chalcone derivatives were carried out, in which the benzoyl group was connected to the C-4 of the newly constructed pyrrolidine in one regioisomer, whereas the benzoyl group was connected to the C-3 of the newly constructed pyrrolidine in another regioisomer. It was found that the presence of electron-withdrawing groups can significantly changed the regiochemistry and yield of this reaction in the previous cases, whereas the absence of electron-withdrawing group in furfuryl chalcones resulted in a pair of regioisomers. More importantly, the regioselectivity of the 1,3-dipolar cycloaddition of azomethine ylide was changed by the presence of electron withdrawing groups, which led to the formation of spirooxindoles with novel regiochemical trends.

In summary, we have successfully synthesized a new class of functionalised aryl furan containing spiropyrrolidines **4a-j** and furan containing spiropyrrolidines **7a-e** and **8a-e** containing furan moiety by one-pot, three-component 1,3-dipolar

cycloaddition of in situ generated azomethine ylides with chalcones. It was found that the presence of electron withdrawing groups can significantly changed the regiochemistry and yield of this reaction in the previous case of nitrofuran and aryl furan, whereas the absence of electron withdrawing group in furfuryl chalcones resulted in a pair of regioisomers.

MATERIALS AND METHODS

The melting points of the newly synthesized compounds were determined in open capillaries and are uncorrected. IR spectra were obtained in KBr discs on a Shimadzu-8400 FTIR spectrophotometer (Kyoto, Japan), ^{1}H NMR spectra were recorded on Bruker spectrometer (400 MHz) (Billerica, MA, USA) in $CDCl_3$ using TMS as an internal standard, and ^{13}C NMR spectra were recorded on Bruker spectrometer (100 MHz) in $CDCl_3$ as solvent. All the chemical shift values are expressed in δ scale downfield from TMS, and proton signals are indicated as s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartlet, and m = multiplet. Mass spectra were recorded on Waters Micromass Q-Tof Micro mass spectrometer (Milford, MA, USA). Elemental analyses were carried out on Elementar Vario-EL-Elementar III model analyzer. The purity of the compounds was confirmed by TLC using silica gel plates (Merck, Kenilworth, NJ, USA) using hexane:ethyl acetate (6:4) as mobile phase.

The required dipolarophiles, 1-aryl-3-[5-(*p*-chlorophenyl) furfuryl] propenones **3a-j**/1-aryl-3-furyl propenones **6a-e**, were prepared according to literature procedure by base-catalyzed Claisen–Schmidt condensation of 5-(*p*-chlorophenyl) furfuraldehyde[13]/furfuraldehyde with substituted acetophenones [13].

General procedure for the synthesis of spiropyrrolidines 4a-j. A mixture of chalcone **3a-j** (1 m mol), ninhydrin (1 m mol), and sarcosine (1.1 m mol) was refluxed in ethanol (10 mL) at 100–120°C until the disappearance of the starting materials (5–6 h) as evidenced by the TLC. After the completion of reaction, the reaction mixture was concentrated in vacuum, and the resulting crude mass was diluted with water (30 mL) and extracted with ethyl acetate (3 × 15 mL) and dried over anhydrous, Na_2SO_4. The organic layers were concentrated and purified by flash chromatography (SiO_2) with progressive increase in polarity (hexane:ethyl acetate as eluent from 95:5 to 60:40). The pure products **4a-j** thus obtained were recrystallized from ethanol:DMF (2:1).

4′-(4-bromobenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4a). Brownish yellow amorphous (79%), mp 170–172°C; IR (KBr): 1638 (C=O), 1680 (C=O), 1741 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.66 (d, 1H, H_a, J = 9.7 Hz), 4.72 (m, 1H, H_b), 3.44 (dd, 1H, H_c, J = 6.1 Hz, J = 9.0Hz), 3.86 (dd, 1H, H_d, J = 9.9 Hz, J = 10.8), 2.61 (s, 3H, N-CH_3), 5.99 (d, 1H, arylfuryl-3H, 3.2 Hz), 6.19 (d, 1H, arylfuryl-4H, 3.2 Hz), 6.80–8.02 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.57, 38.94, 47.55, 47.09, 55.41, 57.25, 76.87, 78.41, 78.74, 79.07, 106.44, 109.59, 113.96, 122.11, 122.75, 124.27, 128.17, 128.40, 128.46, 130.70, 131.75, 136.45, 140.07, 141.18, 149.97, 151.09, 163.51, 195.59, 200.04, 202.25; ms: m/z 574.6 ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{21}BrClNO_4$: C, 62.68; H, 3.68; N, 2.44. Found: C, 62.70; H, 3.70; N, 2.40.

4′-(benzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4b). Orange crystalline (78%), mp 125–127°C; IR (KBr): 1641 (C=O), 1681 (C=O), 1740 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.69 (d, 1H, H_a, J = 10.0 Hz), 4.73 (m, 1H, H_b), 3.39 (dd, 1H, H_c, J = 5.9 Hz, J = 8.9 Hz), 3.82 (dd, 1H, H_d, J = 9.1 Hz, J = 10.6 Hz), 2.73 (s, 3H, N-CH_3), 5.72 (d, 1H, aryl furfuryl α-H, J = 3.2 Hz) 6.03 (d, 1H, aryl furfuryl β-H, J = 3.3 Hz), 6.92–8.01 (m, 13H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.24, 47.62, 56.41, 76.72 (spirocarbon), 104.36, 106.52, 111.31, 117.54, 120.13, 121.89, 123.56, 125.91, 126.72, 127.23,, 128.93, 129.62, 129.98, 130.31, 131.12, 133.54, 136.98, 138.20, 139.84, 141.63, 144.52, 150.62, 152.39, 153.27, 156.93, 196.38, 199.97, 201.89; ms: m/z 496.5:498.6 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{22}ClNO_4$: C, 72.65; H, 4.47; N, 2.82. Found: C, 72.60; H, 4.50; N, 2.80.

4′-(4-chlorobenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4c). Yellowish brown crystalline (80%), mp 120–122°C; IR (KBr): 1643 (C=O), 1687 (C=O), 1742 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.72 (d, 1H, H_a, J = 9.92 Hz), 4.81 (m, 1H, H_b), 3.47 (dd, 1H, H_c, J = 5.6 Hz, J = 8.8 Hz), 3.87 (dd, 1H, H_d, J = 8.9 Hz, J = 10.5 Hz), 2.26 (s, 3H, N-CH_3), 6.01 (d, 1H, aryl furfuryl 3H, J = 3.1 Hz), 6.25 (d, 1H, aryl furfuryl β-H, J = 3.5 Hz), 7.01–8.28 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.62, 44.56, 49.71, 54.65, 76.81 (spirocarbon), 104.81, 107.84, 109.63, 111.42, 115.79, 120.53, 123.74, 123.98, 125.97, 127.86, 128.35, 129.37, 131.62, 132.21, 132.43, 132.75, 133.68, 135.93, 136.29, 139.68, 140.71, 147.45, 149.76, 151.68, 154.32, 187.68, 195.98, 200.03, 202.31; ms: m/z 530.3:532.2:534.4 (1:2:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{21}Cl_2NO_4$: C, 67.93; H, 3.99; N, 2.64. Found: C, 67.90; H, 4.00; N, 2.60.

4′-(4-methylbenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4d). Dark brown amorphous (75%), mp 180–184°C; IR (KBr): 1642 (C=O), 1689 (C=O), 1744 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47 (d, 1H, H_a, J = 10.0 Hz), 4.58 (m, 1H, H_b), 3.21 (dd, 1H, H_c, J = 5.8 Hz, J = 8.7 Hz), 3.79 (dd, 1H, H_d, J = 8.9 Hz, J = 10.5 Hz), 2.71 (s, 3H, N-CH_3), 3.28(s, 3H, CH_3), 6.14 (d, 1H, aryl furfuryl α-H, J = 3.2 Hz), 6.48 (d, 1H, aryl furfuryl β-H, J = 3.4 Hz), 7.08–8.17 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.86, 41.97, 47.53, 56.89, 76.73 (spirocarbon), 103.95, 106.38, 107.91, 112.35, 115.68, 118.74, 121.58, 123.46, 125.43, 126.58, 128.93, 129.17, 129.37, 130.35, 131.43, 133.58, 134.81, 135.79, 136.38,

139.68, 144.56, 148.39, 152.36, 153.89, 155.76, 196.47, 200.08, 202.76; ms: m/z 510.4:512.3 (3:1) ($M^+ + 1$). *Anal.* Calcd. for $C_{31}H_{24}ClNO_4$: C, 73.01; H, 4.74; N, 2.75. Found: C, 73.10; H, 4.80; N, 2.70.

4′-(4-hydroxybenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4e). Yellowish brown crystalline (72%), mp 203–204°C; IR (KBr): 1640 (C=O), 1687 (C=O), 1742 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.64 (d, 1H, H_a, J = 9.8 Hz), 4.69 (m, 1H, H_b), 3.39 (dd, 1H, H_c, J = 5.6 Hz, J = 8.9 Hz), 3.85 (dd, 1H, H_d, J = 9.0 Hz, J = 10.5 Hz), 2.78 (s, 3H, N-CH_3), 6.08 (d, 1H, aryl furfuryl α-H, J = 3.1Hz), 6.57 (d, 1H, aryl furfuryl β-H, J = 3.3 Hz), 6.81(s, br, 1H, Ar-OH), 7.04–7.90 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.69, 41.82, 47.63, 53.68, 77.21 (spirocarbon), 103.27, 105.68, 107.89, 109.37, 112.37, 117.93, 120.29, 121.58, 123.76, 126.39, 128.46, 129.37, 131.48, 131.52, 136.47, 136.67, 137.75, 137.89, 137.95, 140.37, 141.38, 147.68, 150.37, 151.81, 154.88, 156.74, 196.11, 200.82, 202.32; ms: m/z 512.6:514.5 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{22}ClNO_5$: C, 70.38; H, 4.33; N, 2.74. Found: C, 70.40; H, 4.30; N, 2.80.

4′-(4-methoxybenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4f). Yellow amorphous (81%), mp 198–199°C; IR (KBr): 1643 (C=O), 1689 (C=O), 1743 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.50 (d, 1H, H_a, J = 9.92 Hz), 4.67 (m, 1H, H_b), 3.25 (dd, 1H, H_c, J = 5.84 Hz, J = 8.88 Hz), 3.82 (dd, 1H, H_d, J = 9.32 Hz, J = 10.72 Hz), 2.22 (s, 3H, N-CH_3), 3.89(s, 3H, OCH_3), 6.12 (d, 1H, aryl furfuryl α-H, J = 3.12 Hz), 6.49 (d, 1H, aryl furfuryl β-H, J = 3.40 Hz), 7.04–8.20 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.19, 40.97, 48.51, 57.23, 76.77 (spirocarbon), 105.78, 108.73, 110.24, 118.22, 119.29, 122.41, 124.49, 125.68, 127.81, 129.11, 129.92, 130.00, 130.72, 131.88, 132.81, 134.42, 136.00, 136.92, 140.72, 141.69, 149.28, 151.18, 152.18, 155.39, 188.47, 196.19, 200.28, 202.92; ms: m/z 526.2:528.2 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{31}H_{24}ClNO_5$: C, 70.79; H, 4.60; N, 2.66. Found: C, 70.80; H, 4.60; N, 2.70.

4′-(4-fluorobenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4g). Reddish brown crystalline (73%), mp 203–204°C; IR (KBr): 1641 (C=O), 1687 (C=O), 1739 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.74 (d, 1H, H_a, J = 9.92Hz), 4.82 (m, 1H, H_b), 3.52 (dd, 1H, H_c, J = 5.9Hz, J = 9.0 Hz), 3.89 (dd, 1H, H_d, J = 9.3 Hz, J = 10.8 Hz), 2.36 (s, 3H, N-CH_3), 5.76 (d, 1H, aryl furfuryl α-H, J = 3.3 Hz), 6.07 (d, 1H, aryl furfuryl β-H, J = 3.5 Hz), 7.01–7.90 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 38.67, 41.86, 47.69, 56.36, 76.86 (spirocarbon), 105.58, 107.83, 109.73, 110.85, 117.89, 118.37, 121.69, 123.73, 125.41, 126.95, 127.68, 128.59, 129.36, 130.19, 131.58, 131.75, 132.36, 133.39, 135.89, 136.43, 141.32, 141.67, 147.56, 150.65, 151.79, 154.69, 162.32, 196.15, 200.03, 202.43; ms: m/z 514.3:516.2 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{21}FClNO_4$: C, 70.11; H, 4.12; N, 2.73. Found: C, 70.10; H, 4.10; N, 2.70.

4′-(2-chlorobenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4h). Dark yellow crystalline (82%), mp 201–203°C; IR (KBr): 1644 (C=O), 1685 (C=O), 1742 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.67 (d, 1H, H_a, J = 10.0 Hz), 4.89 (m, 1H, H_b), 3.43 (dd, 1H, H_c, J = 5.7 Hz, J = 9.1 Hz), 3.68 (dd, 1H, H_d, J = 9.1 Hz, J = 10.7 Hz), 2.36 (s, 3H, N-CH_3), 5.76 (d, 1H, aryl furfuryl α-H, J = 3.2 Hz), 6.08 (d, 1H, aryl furfuryl β-H, J = 3.3 Hz), 7.10–8.12 (m, 12H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.46, 41.53, 47.61, 55.18, 76.68 (spirocarbon), 104.78, 106.37, 107.57, 111.56, 113.59, 117.89, 119.57, 121.75, 124.46, 126.73, 127.79, 128.85, 129.56, 130.32, 132.27, 134.78, 140.48, 142.56, 144.45, 146.76, 147.07, 148.87, 149.91, 195.98, 200.13, 202.61; ms: m/z 530.3:532.2:534.4 (1:2:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{21}Cl_2NO_4$: C, 67.93; H, 3.99; N, 2.64. Found: C, 67.90; H, 4.00; N, 2.60.

4′-(3-bromobenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4i). Yellowish brown amorphous (78%), mp 126–128°C; IR (KBr): 1638 (C=O), 1686 (C=O), 1740 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.61 (d, 1H, H_a, J = 9.8 Hz), 4.74 (m, 1H, H_b), 3.42 (dd, 1H, H_c, J = 5.8 Hz, J = 8.9 Hz), 3.85 (dd, 1H, H_d, J = 9.1 Hz, J = 10.6 Hz), 2.39 (s, 3H, N-CH_3), 5.83 (d, 1H, aryl furfuryl α-H, J = 3.1 Hz), 6.06 (d, 1H, aryl furfuryl β-H, J = 3.3 Hz), 7.20–8.10 (m, 12H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.76, 38.87, 41.18, 55.78, 76.68 (spirocarbon), 104.67, 107.78, 109.95, 114.43, 117.89, 121.36, 122.37, 123.65, 125.83, 127.62, 128.37, 129.53, 129.37, 130.15, 132.56, 132.78, 133.54, 135.78, 136.39, 141.43, 141.57, 145.57, 150.38, 151.78, 153.57, 157.86, 196.47, 200.39, 202.76; ms: m/z 574.7 ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{21}BrClNO_4$: C, 62.68; H, 3.68; N, 2.44. Found: C, 62.70; H, 3.70; N, 2.40.

4′-(3-hydroxybenzoyl)-1′-methyl-3′-(5-(p-chlorophenyl)-2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (4j). Brown crystals (81%), mp 123–126°C; IR (KBr): 1639 (C=O), 1682 (C=O), 1741(C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.58 (d, 1H, H_a, J = 9.8 Hz), 4.76 (m, 1H, H_b), 3.36 (dd, 1H, H_c, J = 5.8 Hz, J = 8.9 Hz), 3.78 (dd, 1H, H_d, J = 9.2 Hz, J = 10.4 Hz), 2.37 (s, 3H, N-CH_3), 5.84 (d, 1H, aryl furfuryl α-H, J = 3.2 Hz), 6.15 (d, 1H, aryl furfuryl β-H, J = 3.3 Hz), 7.01–8.03 (m, 12H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.68, 40.37, 47.58, 49.38, 57.68, 76.69 (spirocarbon), 104.65, 1 07.54, 109.68, 114.67, 116.37, 121.38, 123.37, 124.57, 127.38, 128.89, 129.39, 129.98, 130.56, 131.23, 132.12, 132.34, 134.39, 136.37, 135.78, 141.16,149.03, 150.95, 151.27, 153.05, 196.27, 200.01, 202.17; ms: m/z 512.3:514.2 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{30}H_{22}ClNO_5$: C, 70.38; H, 4.33; N, 2.74. Found: C, 70.40; H, 4.30; N, 2.80.

General procedure for the synthesis of spiropyrrolidines 7a-e and 8a-e. A mixture of chalcone **6a-e** (1 m mol), ninhydrin (1 m mol), and sarcosine (1.1 m mol) was refluxed in ethanol (10 mL) at 100–120°C until the disappearance of the starting materials (6–8 h) as evidenced by the TLC. After

the completion of reaction, the reaction mixture was concentrated *in vacuo*, and the resulting crude mass was diluted with water (30 mL) and extracted with ethyl acetate (3 × 15 mL) and dried over anhy, Na_2SO_4. The organic layers were concentrated and purified by flash chromatography (SiO_2) with progressive increase in polarity (hexane:ethyl acetate as eluent from 95:5 to 70:30). The separated regioisomers **7a-e** and **8a-e** were recrystallised from ethanol:DMF (2:1) to give the products.

3′-(4-methylbenzoyl)-1′-methyl-4′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (7a). Creamish yellow amorphous (32%), mp 208–209°C; IR (KBr): 1701 (C=O), 1707 (C=O), 1741 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.66 (d, 1H, H_a, J = 10.2 Hz), 4.78 (m, 1H, H_b), 3.43 (dd, 1H, H_c, J = 6.5 Hz, J = 8.9 Hz), 3.87 (dd, 1H, H_d, J = 9.1 Hz, J = 10.6 Hz), 2.33 (s, 3H, N-CH_3), 2.41(s, 3H, CH_3), 5.89 (d, 1H, furyl α-H, J = 3.16 Hz), 5.93 (dd, 1H, furyl β-H, J = 1.8 Hz, J = 5.0 Hz), 6.92 (d, 1H, furyl γ-H, J = 1.56 Hz), 7.26–7.98 (m, 8H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.87, 36.58, 48.63, 48.92, 55.79, 76.98, 77.07, 77.18, 77.52, 104.38, 105.98, 108.37, 117.45, 120.54, 127.61, 128.09, 131.12, 133.25, 135.49, 136.94, 138.87, 140.38, 140.08, 143.35, 193.38, 199.55, 201.07; ms: m/z 400.3 ($M^+ + 1$). *Anal*. Calcd. for $C_{25}H_{21}NO_4$: C, 75.17; H, 5.30; N, 3.51. Found: C, 75.10; H, 5.30; N, 3.60.

3′-(benzoyl)-1′-methyl-4′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (7b). Golden yellow crystalline (29%), mp 201–203°C; IR (KBr): 1698 (C=O), 1707 (C=O), 1743 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.63 (d, 1H, H_a, J = 10.1 Hz), 4.78 (m, 1H, H_b), 3.42 (dd, 1H, H_c, J = 6.6 Hz, J = 9.0 Hz), 3.83 (dd, 1H, H_d, J = 9.2 Hz, J = 10.7 Hz), 2.31 (s, 3H, N-CH_3), 5.85 (d, 1H, furyl α-H, J = 3.2 Hz), 5.93 (dd, 1H, furyl β-H, J = 1.8 Hz, J = 4.9 Hz), 6.83 (d, 1H, furyl γ-H, J = 1.6 Hz), 7.03–7.86 (m, 9H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.87, 49.01, 49.65, 57.61, 76.82, 77.12, 77.23, 77.98, 105.96, 107.94, 109.68, 118.97, 121.35, 128.74, 129.16, 133.68, 135.07, 136.11, 138.87, 140.88, 141.54, 142.07, 149.16, 195.93, 200.08, 202.25; ms: m/z 386.3 ($M^+ + 1$). *Anal*. Calcd. $C_{24}H_{19}NO_4$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.80; H, 5.00; N, 3.70.

3′-(4-chlorobenzoyl)-1′-methyl-4′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (7c). Creamish yellow crystalline (38%), mp 196–197°C; IR (KBr): 1700 (C=O), 1708 (C=O), 1742 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.38 (d, 1H, H_a, J = 10.2 Hz), 4.59 (m, 1H, H_b), 3.25 (dd, 1H, H_c, J = 6.7 Hz, J = 8.9 Hz), 3.68 (dd, 1H, H_d, J = 9.0 Hz, J = 10.5 Hz), 2.13 (s, 3H, N-CH_3), 5.69 (d, 1H, furyl α-H, J = 3.1 Hz), 5.75 (dd, 1H, furyl β-H, J = 1.9 Hz, J = 4.8 Hz), 6.68 (d, 1H, furyl γ-H, J = 1.7 Hz), 7.15–7.98 (m, 8H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.34, 41.56, 47.53, 48.39, 55.48, 74.38, 75.91, 76.32, 75.49, 107.51, 107.83, 109.87, 115.53, 119.80, 124.56, 128.96, 131.79, 133.25, 136.58, 138.86, 139.97, 142.23, 142.39, 148.71, 195.98, 200.09, 202.63; ms: m/z 420.2:422.1 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{24}H_{18}ClNO_4$: C, 68.66; H, 4.32; N, 3.34. Found: C, 68.60; H, 4.30; N, 3.30.

3′-(4-bromobenzoyl)-1′-methyl-4′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (7d). Yellowish crystalline (43%), mp 204–205°C; IR (KBr): 1699 (C=O), 1709 (C=O), 1741 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.50 (d, 1H, H_a, J = 10.1 Hz), 4.64–4.70 (m, 1H, H_b), 3.35 (dd, 1H, H_c, J = 15.08 Hz, J = 8.36 Hz), 3.75 (dd, 1H, H_d, J = 10.0 Hz, J = 9.6 Hz), 2.25 (s, 3H, N-CH_3), 5.80 (d, 1H, furyl α-H, J = 3.7 Hz), 5.86 (dd, 1H, furyl β-H, J = 1.3 Hz, J = 3.7 Hz), 6.87 (d, 1H, furyl γ-H, J = 1.6 Hz), 7.20–7.90 (m, 8H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.20, 48.22, 48.50, 57.15, 76.74, 77.06, 77.37, 78.03, 108.25, 110.16, 122.43, 123.11, 129.93, 129.08, 134.53, 135.97, 136.22, 139.95, 140.77, 141.77, 142.15, 149.16, 196.15, 200.39, 202.87; ms: m/z 464.1:466.1 (1:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{24}H_{18}BrNO_4$: C, 62.08; H, 3.91; N, 3.02. Found: C, 62.10; H, 3.90; N, 3.00.

3′-(4-methoxybenzoyl)-1′-methyl-4′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (7e). Golden yellow crystalline (34%), mp 204–205°C; IR (KBr): 1697 (C=O), 1708 (C=O), 1740 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.58 (d, 1H, H_a, J = 10.1 Hz), 4.68 (m, 1H, H_b), 3.28 (dd, 1H, H_c, J = 6.8 Hz, J = 9.0 Hz), 3.65 (dd, 1H, H_d, J = 9.0 Hz, J = 10.6 Hz), 2.36 (s, 3H, N-CH_3), 3.97(s, 3H, OCH_3), 5.77 (d, 1H, furyl α-H, J = 3.6 Hz), 5.89 (dd, 1H, furyl β-H, J = 1.7 Hz, J = 5.1 Hz), 6.75 (d, 1H, furyl γ-H, J = 1.7 Hz), 7.17–7.95 (m, 8H, Ar-H); **7d** (Fig. 3.2.9): ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.98, 35.98, 47.62, 48.38, 56.98, 76.89, 77.13, 77.45, 77.91, 107.93, 108.98, 109.76, 121.13, 123.08, 127.73, 128.81, 133.39, 136.04, 136.51, 138.89, 141.13, 141.34, 142.12, 146.65, 196.06, 200.03, 202.17; ms: m/z 416.3 ($M^+ + 1$). *Anal*. Calcd. for $C_{25}H_{21}NO_5$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.30; H, 5.20; N, 3.40.

4′-(4-methylbenzoyl)-1′-methyl-3′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (8a). Yellowish brown crystalline (68%), mp 178-179°C; IR (KBr): 1683 (C=O), 1702 (C=O), 1735 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.55 (d, 1H, H_a, J = 10.2 Hz), 4.68 (m, 1H, H_b), 3.36 (dd, 1H, H_c, J = 6.6 Hz, J = 8.9 Hz), 3.78 (dd, 1H, H_d, J = 9.0 Hz, J = 10.7 Hz), 2.25 (s, 3H, N-CH_3), 2.33 (s, 3H, CH_3), 5.80 (d, 1H, furyl α-H, J = 3.2 Hz), 5.86 (dd, 1H, furyl β-H, J = 1.8 Hz, J = 5.1 Hz), 6.84 (d, 1H, furyl γ-H, J = 1.7 Hz), 7.18–7.90 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.65, 29.68, 30.20, 31.43, 36.22, 48.10, 48.51, 57.48, 77.06, 108.06, 110.08, 122.38, 123.06, 128.66, 129.42, 133.79, 135.88, 136.11, 140.81, 141.81, 142.01, 144.33, 149.53, 196.76, 200.57, 202.95; ms: m/z 400.2 ($M^+ + 1$). *Anal*. Calcd. for $C_{25}H_{21}NO_5$: C, 75.17; H, 5.30; N, 3.51. Found: C, 75.20; H, 5.20; N, 3.50.

4′-(benzoyl)-1′-methyl-3′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (8b). Brownish crystals (71%), mp 165–167°C; IR (KBr): 1683 (C=O), 1702 (C=O), 1734 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.63 (d, 1H, H_a, J = 10.2 Hz), 4.78 (m, 1H, H_b), 3.47 (dd, 1H, H_c, J = 6.5 Hz, J = 8.9 Hz), 3.77 (dd, 1H, H_d, J = 9.0 Hz, J = 10.5 Hz), 2.28 (s, 3H,

N-CH_3), 5.79 (d, 1H, furyl α-H, J = 3.3 Hz), 5.99 (dd, 1H, furyl β-H, J = 1.8 Hz, J = 3.3 Hz), 6.86 (d, 1H, furyl γ-H, J = 1.3 Hz), 7.15–8.03 (m, 9H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.21, 48.01, 48.17, 56.38, 76.77, 77.05, 77.34, 78.07, 106.59, 108.67, 110.56, 121.67, 122.56, 127.39, 129.08, 131.36, 134.08, 135.39, 136.08, 140.05, 141.48, 141.97, 148.87, 196.08, 200.14, 202.49; ms: m/z 386.6 ($M^+ + 1$). *Anal*. Calcd. for $C_{24}H_{19}NO_4$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.80; H, 5.00; N, 3.60.

4′-(4-chlorobenzoyl)-1′-methyl-3′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (8c). Yellowish brown powder (62%), mp 169–170°C; IR (KBr): 1682 (C=O), 1700 (C=O), 1731 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.51 (d, 1H, H_a, J = 10.1 Hz), 4.69 (m, 1H, H_b), 3.42 (dd, 1H, H_c, J = 6.5 Hz, J = 8.9 Hz), 3.79 (dd, 1H, H_d, J = 9.0 Hz, J = 10.7 Hz), 2.27 (s, 3H, N-CH_3), 5.83 (d, 1H, furyl α-H, J = 3.3 Hz), 5.97 (dd, 1H, furyl β-H, J = 1.7 Hz, J = 3.2 Hz), 6.95 (d, 1H, furyl γ-H, J = 1.4 Hz), 7.32–8.56 (m, 8H ,Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.56, 40.39, 47.64, 56.84, 76.89, 77.04, 77.31, 77.89, 107.84, 109.96, 120.49, 122.67, 127.58, 130.19, 131.93, 134.37, 135.15, 136.85, 140.09, 141.73, 141.98, 148.89, 196.08, 200.18, 202.45; ms: m/z 420.1:422.3 (3:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{24}H_{18}ClNO_4$: C, 68.66; H, 4.32; N, 3.34. Found: C, 68.70; H, 4.30; N, 3.40.

4′-(4-bromobenzoyl)-1′-methyl-3′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (8d). Brown crystalline (57%), mp 181–182°C; IR (KBr): 1684 (C=O), 1701 (C=O), 1733 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.58 (d, 1H, H_a, J = 10.2 Hz), 4.74 (m, 1H, H_b), 3.44 (dd, 1H, H_c, J = 6.4 Hz, J = 8.9 Hz), 3.86 (dd, 1H, H_d, J = 9.1 Hz, J = 10.6 Hz), 2.33 (s, 3H, N-CH_3), 5.88 (d, 1H, furyl α-H, J = 3.2 Hz), 5.95 (dd, 1H, furyl β-H, J = 1.8 Hz, J = 3.1 Hz), 6.95 (d, 1H, furyl γ-H, J = 1.1 Hz), 7.28–7.98 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.18, 48.21, 48.49, 57.13, 76.75, 77.07, 77.39, 78.01, 108.23, 110.16, 122.42, 123.09, 128.69, 130.01, 132.06, 134.95, 135.96, 136.21, 140.78, 141.77, 142.13, 149.17, 196.35, 200.35, 202.83; ms: m/z 464.8:467.2 (1:1) ($M^+ + 1$). *Anal*. Calcd. for $C_{24}H_{18}BrNO_4$: C, 62.08; H, 3.91; N, 3.02. Found: C, 62.10; H, 3.90; N, 3.00.

4′-(4-methoxybenzoyl)-1′-methyl-3′-(2-furyl) spiro[indene-2,2′-pyrrolidine]-1,3-dione (8e). Creamish yellow crystals (66%), mp 164–165°C; IR (KBr): 1685 (C=O), 1702 (C=O), 1732 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.51 (d, 1H, H_a, J = 10.1 Hz), 4.72 (m, 1H, H_b), 3.40 (dd, 1H, H_c, J = 6.3 Hz, J = 9.0 Hz), 3.85 (dd, 1H, H_d, J = 9.1 Hz, J = 10.5 Hz), 2.27 (s, 3H, N-CH_3), 3.91 (s, 3H, OCH_3), 5.83 (d, 1H, furyl α-H, J = 3.3 Hz), 5.94 (dd, 1H, furyl β-H, J = 1.5 Hz, J = 3.2 Hz), 6.96 (d, 1H, furyl γ-H, J = 1.4 Hz), 7.15–8.02 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.48, 38.89, 40.36, 47.58, 47.91, 56.35, 76.89, 77.04, 77.35, 78.04, 107.58, 111.37, 121.53, 122.97, 127.87, 129.56, 131.71, 134.85, 135.09, 135.98, 140.51, 142.39, 142.70, 148.95, 196.29, 200.41, 202.76; ms: m/z 416.5 ($M^+ + 1$). *Anal*. Calcd. for $C_{25}H_{21}NO_5$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.30; H, 5.10; N, 3.40.

CONCLUSION

In summary, we studied the effect of the presence of electron–withdrawing groups on the regiochemical trends during the 1,3-dipolar cycloaddition reaction of azomethine ylides with propenones carrying furan/5-aryl-substituted furan to give the novel series of spiropyrrolidines in good to excellent yields. It was observed that the regioselectivity can be conveniently tuned and reversed by the presence of electron-withdrawing groups attached to the furan ring, which provides a facile approach to access a wide range of spiropyrrolidine ring systems with novel substitution patterns.

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