Regioselective Synthesis of Nitrofuran Containing Novel Spiropyrrolidine Library through 1,3-Dipolar Cycloaddition Reactions

Sahana Mallya,[a] Balakrishna Kalluraya,[a]* and K. S. Girisha[b]

[a]Department of Studies in Chemistry, Mangalore University, Mangalagangothri 574 199, Karnataka, India
[b]Solid State and Structural Chemistry Unit, Indian Institute of Science, Bangalore 560 012, India
*E-mail: bkalluraya@gmail.com

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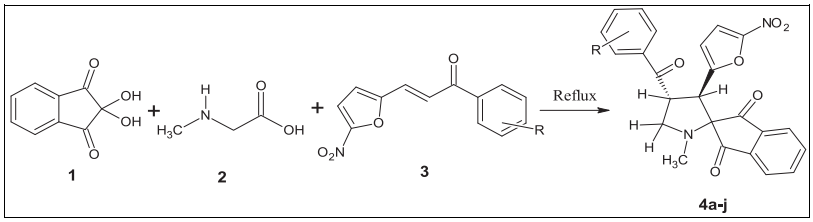

A novel series of nitrofuran containing spiropyrrolidines has been synthesized with high regioselectivity in moderate to excellent yields via 1,3-dipolar cycloaddition reaction of azomethine ylides with various substituted chalcones.

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INTRODUCTION

The chemistry of azomethine ylides has been investigated intensively in recent years, as it serves as a significant route for the construction of nitrogen containing five-membered heterocycles [1]. The 1,3-dipolar cycloaddition of azomethine ylides with olefinic dipolarophiles offers an excellent route for the construction of substituted pyrrolidine derivatives [2]. The spiropyrrolidine ring systems form the core structure of numerous natural products [3] and alkaloids [4], and are also elegant precursors in organic synthesis due to their significant pharmacological and biological activities [5].

Nitrofurans find an important place in the field of heterocyclic chemistry because of a good profile of varied types of pharmacological activities associated with them [6]. It is reported that the incorporation of nitrofuran ring in the molecule could alter the biological properties, thus retaining nitrofurans as an area of active research interest.

In our endeavor to synthesize novel bioactive nitrofuran derivatives, which may enhance the biocidal profile or create molecules with new medicinal properties [7], herein, we report the facile synthesis of a novel class of spiropyrrolidine derivatives in a highly regioselective and stereoselective manner through one-pot, three-component 1,3-dipolar cycloaddition of nitrofuran containing chalcones as dipolarophiles with 1,3-dipole generated from 1,2-diketone and secondary amino acids. The presence of nitro group on dipolarophile reverses the reactivity of α and β positions, making the 5-nitro-2-furyl chalcone position β electron rich, which results in the regioselective synthesis of compounds **4** in this case.

RESULTS AND DISCUSSION

Initially, in order to obtain optimal reaction conditions for the synthesis of (3′*R*,4′*R*)-4′-(4-substituted benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione **4a–j** derivatives, we investigated the one-pot, three-component reaction between ninnhydrin **1**, sarcosine **2**, and 1-(*p*-tolyl)-3-(5-nitrofuryl) prop-2-en-1-one **3a** using different solvents under a refluxing condition. It is found that the reaction in ethanol furnished an excellent yield of 87% in short reaction time compared with other solvents (Table 1). Ethanol even gave a remarkable advantage in the product separation compared with other solvents. Even the reaction was performed with the excess of reagents with an increase in reaction time as an attempt to increase the yield of the cycloadduct, but no change in the yield of cycloadducts was observed.

As per the results of solvent optimization, for all further reactions, we used ethanol as solvent, and all the reactants were used in equimolar ratio to obtain the optimum yield (Table 2).

As described in Scheme 1, the 1,3-dipole generated *in situ* from decarboxylative cyclocondensation of ninhydrin **1** and sarcosine **2** reacted readily with the dipolarophiles **3a–j** under refluxing conditions in absolute ethanol medium to give only one regioisomer as cycloadducts **4a–j** as indicated by TLC. The required dipolarophiles, 1-aryl-3-(5-nitrofuryl) propenones **3a–j**, were prepared according to literature procedure by acid catalyzed Claisen–Schmidt condensation of 5-nitro furfuraldehyde diacetate with substituted acetophenones [8].

Dramatic change in the regiochemistry of product **4** during cycloaddition was found than expected, pointing to the importance of the electronegative nitrofuran moiety

Table 1

Solvent optimization for the synthesis of **4a**.

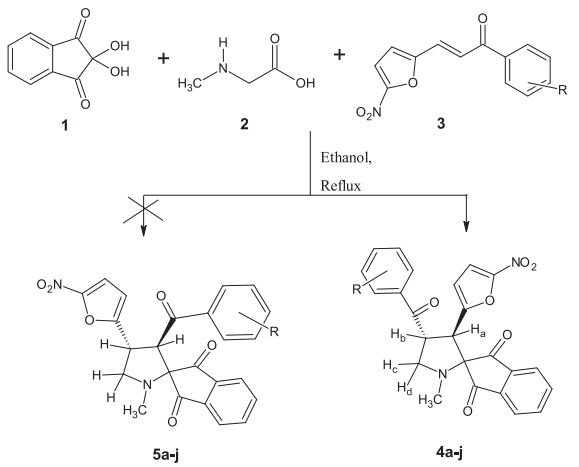
Sl no.	Solvent	Reaction time (h)	Yield (%)
1	Methanol	4	86
2	Ethanol	4	87
3	Propanol	5	83
4	Butan-2-ol	5	80
5	Acetonitrile	5	82
6	DMF	4	84
7	1,4-Dioxane	6	48
8	Water	6	12
9	DMSO	4	85
10	Toluene	7	67

Table 2

Comparison of the reaction time and yields for thermal [3 + 2]-cycloaddition reactions of pyrrolidine derivatives **4a–j**.

Compound	R	Time (h)	Yield (%)
4a	p-CH3	4	87
4b	H	5	84
4c	p-Cl	2.5	87
4d	p-OMe	3.5	81
4e	p-Br	3	85
4f	p-F	2	88
4g	p-OH	6	73
4h	m-Br	3.2	89
4i	m-OH	4	87
4j	o-Cl	2	88

Scheme 1. Synthesis of novel spiropyrrolidines.

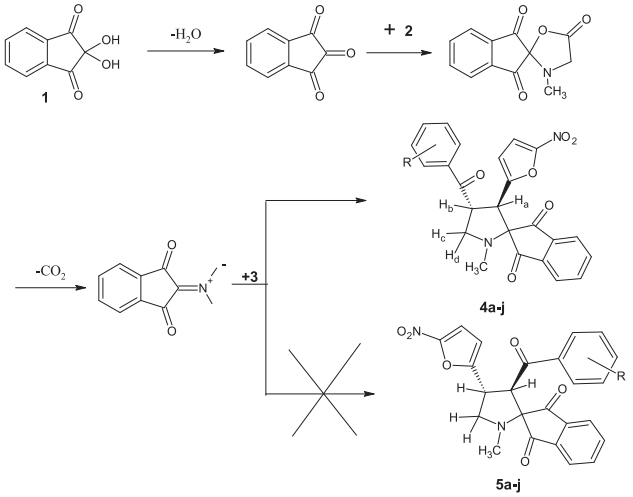


R = p-CH_3(a), H(b), p-Cl(c), p-OMe(d), p-Br(e), p-F(f), p-OH(g), m-Br(h), m-OH(i), o-Cl(j)

in the vicinity of the C=C double bond of chalcone. In the presence of 5-nitro-2-furyl group, chalcone position β becomes electron rich because of the presence of electron withdrawing a nitro group attached to a furan ring, which results in the formation of compounds **4**.

The structures of newly synthesized spiropyrrolidines were elucidated using ^{1}H NMR, ^{13}C NMR, HMBC, CHN analysis, mass spectroscopy, and X-ray analysis. The analytical and spectral data are in consistency with the proposed structure. The ^{1}H NMR spectrum of compound **4c** showed a doublet at δ = 4.64 ppm for H_a, a multiplet at δ = 4.75 ppm for H_b, and a doublet of doublet at δ = 3.35 and 3.92 ppm for H_c and H_d, respectively. The aromatic protons appeared around δ = 7.5–8.1 ppm as multiplet, the protons of nitrofuryl ring appeared at δ = 6.4 and 7.1 ppm, respectively, as doublets, and N-CH_3 protons of spioropyrrolidine ring appeared at δ = 2.1 ppm as singlet. The ^{13}C NMR spectrum of **4c** showed a peak at δ = 76.8 ppm because of spirocarbon, and the two C=O of ninhydrin ring appears at δ = 199 and 202 ppm, whereas C=O of benzoyl group appears at δ = 195 ppm. Furthermore, the molecular ion peak at *m/z* 465.2 and 467.2 [M^+ + 1] (3:1 ratio) confirms the formation of product **4c** (Scheme 2).

Scheme 2. Mechanism for regioselective formation of spiropyrrolidines.



The regiochemistry of the product was established from the HMBC spectra. As indicated in the HMBC data of **4c** (Figure 1), the benzoyl C=O group at δ = 195 ppm correlates with all the four protons attached to the pyrrolidine ring (H_a, H_b, H_c, and H_d), showing that the correct regiochemistry of the product is as shown in structure. 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.

The regiochemical and stereochemical outcome of the cycloaddition reaction was unambiguously ascertained by single crystal X-ray analysis of **4g** [9]. The ORTEP view of single crystal X-ray analysis of **4g** is shown in Figure 2. The crystal structure of **4g** reflects the *trans* geometry of chalcone, clearly defines the relative configurations at all the four chiral centers, and establishes the regiochemistry of the chalcone addition, a result that supports a concerted bond-forming process. X-ray diffraction measurements also showed that the configuration of the five-membered

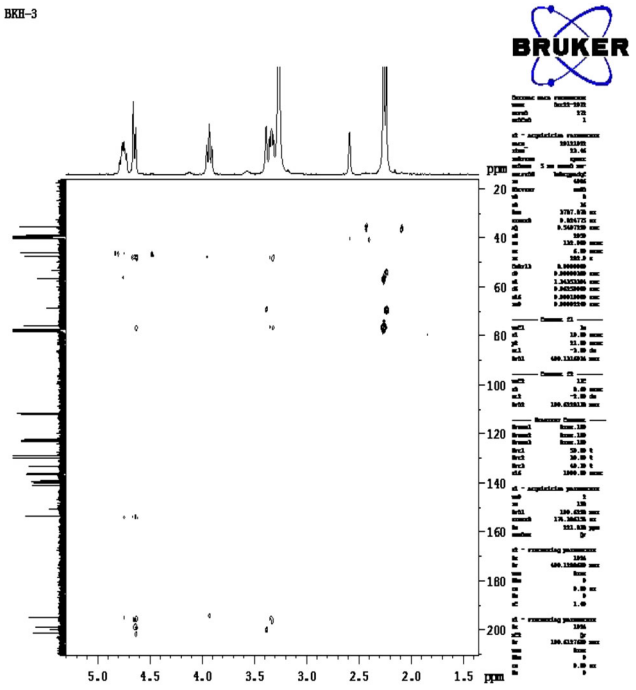


Figure 1. HMBC of **4c**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.].

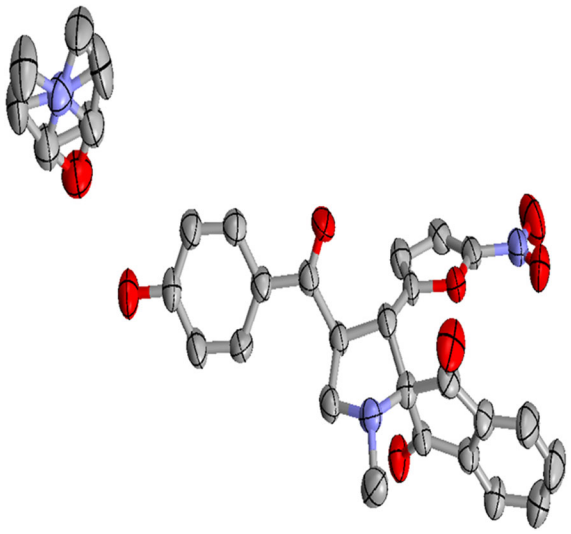


Figure 2. ORTEP of **4g** associated with solvent molecule (DMF). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.].

ring is envelope with the nitrogen atom being out of plane from the rest of the ring atoms and the *N*-methyl occupying the axial position. Also, the X-ray structure of the molecule reveals that the H-3 proton and oxoindene ring at spirocarbon are *cis* to each other in the pyrrolidine ring.

In summary, we have successfully synthesized a new class of functionalized spiropyrrolidines **4a–j** containing nitrofuran moiety with high stereoselectivity and regioselectivity in good to excellent yields, by one-pot, three-component 1,3-dipolar cycloaddition of *in situ* generated azomethine ylides with 1-aryl-3-(5-nitrofuryl) prop-2-en-1-ones **3a–j**. This process is capable of generating spiropyrrolidines containing nitrofuran moiety with novel regiochemistry in a single reaction that may create a new molecule with interesting pharmacological properties.

EXPERIMENTAL

Thin layer chromatography was used to analyze the reaction progress and purity of the compounds synthesized. Melting points were determined by open glass capillary method and were uncorrected. IR spectra were obtained in KBr discs on a Shimadzu-8400 FTIR spectrophotometer, ^{1}H NMR spectra were recorded on Bruker spectrometer (400 MHz) in $CDCl_3$ using TMS as an internal standard, ^{13}C NMR spectra were recorded on Bruker spectrometer (100 MHz) in $CDCl_3$, and ^{19}F NMR spectra were recorded on a Bruker spectrophotometer (376 MHz) in $CDCl_3$ as solvent. Mass spectra were recorded on Waters Micromass Q-Tof Micro mass spectrometer. CHN analysis was carried out on an Elementar Vario-EL III model analyzer.

The required dipolarophiles, 1-aryl-3-(5-nitrofuryl) propenones **3a–j**, were prepared according to the method described previously [8].

General procedure for the synthesis of (3′*R*,4′*R*)-4′-(4-substituted benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione 4a–j. A mixture of chalcone (1 mmol), ninhydrin (1 mmol), and sarcosine (1.1 mmol) was refluxed in ethanol (10 mL) at 100–120°C until the disappearance of the starting materials as evidenced by the TLC. After the completion of reaction, the reaction mixture was concentrated *in vacuo*, and the residue was subjected to column chromatography using hexane : ethyl acetate (6:4) as eluent and recrystallized from ethanol : DMF (2:1) to give the products.

(3′*R*,4′*R*)-4′-(4-Methyl benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4a). Orange yellow crystals (87%), mp: 209–210°C; IR (KBr) cm^{-1}: 1672 (C=O), 1707 (C=O), 1743 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.50 (d, 1H, H_a, $J = 9.4$ Hz), 4.75 (m, 1H, H_b), 3.15 (dd, 1H, H_c, $J = 5.72$ Hz, $J = 9.1$ Hz), 3.85 (dd, 1H, H_d, $J = 9.3$ Hz, $J = 5.4$ Hz), 2.17 (s, 3H, N-CH_3), 2.39 (s, 3H, *p*-methyl) 6.75 (d, 1H, nitrofuryl-3H, 3.7 Hz), 7.75 (d, 1H, nitrofuryl-4H, 3.8 Hz), 7.30–8.10 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 21.69, 29.68, 36.02 (N-CH_3), 47.25, 57.4, 76.99 (spirocarbon), 111.31, 122.69, 128.72, 133.21, 136.21, 140.66, 144.89, 154.21, 196.01, 199.69, 202.33; *m/z*: 445.2 ($M^+ + 1$); Anal. calcd $C_{25}H_{20}N_2O_6$: C, 67.56; H, 4.54; N, 6.30. Found: C, 67.74; H, 4.57; N, 6.32.

(3′*R*,4′*R*)-4′-(Benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4b). Dark yellow amorphous (84%), mp: 204–205°C; IR (KBr) cm^{-1}: 1637 (C=O), 1676 (C=O), 1708 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.73 (m, 2H, H_a, H_b), 3.45 (dd, 1H, H_c, $J = 4.8$ Hz, $J = 9.2$ Hz), 3.85 (m, 1H, H_d), 2.32 (s, 3H, N-CH_3), 6.20 (d, 1H, nitrofuryl 3H, $J = 3.6$ Hz), 6.90 (d, 1H, nitrofuryl 4H, $J = 3.6$ Hz), 7.50–8.10 (m, 9H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.99 (N-CH_3), 47.16, 48.49, 57.24, 77.00 (spirocarbon), 111.33, 122.68, 128.68, 133.85, 136.59, 140.63, 151.26, 154.08, 196.41, 199.62, 202.26; *m/z*: 431.2 ($M^+ + 1$);

Anal. calcd $C_{24}H_{18}N_2O_6$: C, 66.97; H, 4.22; N, 6.51. Found: C, 66.94; H, 4.28; N, 6.53.

(3′*R*,4′*R*)-4′-(4-Chloro benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4c). Yellow crystals (87%), mp: 200–202°C; IR (KBr) cm^{-1}: 1654 (C=O), 1674 (C=O), 1705 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.64 (d, 1H, H_a, $J = 9.6$ Hz), 4.75 (m, 1H, H_b), 3.35 (dd, 1H, H_c, $J = 6.4$ Hz, $J = 14.0$ Hz), 3.92 (dd, 1H, H_d, $J = 7.0$ Hz, $J = 10.16$ Hz), 2.10 (s, 3H, N-CH_3), 6.40 (d, 1H, nitrofuryl-3H, $J = 3.2$ Hz), 7.10 (d, 1H, nitrofuryl-4H, $J = 3.2$ Hz), 7.50–8.10 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.98 (N-CH_3), 40.18,47.11, 54.15, 57.11, 76.8 (spirocarbon), 111.39, 122.74,123.46, 129.31, 129.97, 133.95, 136.24, 139.93, 140.48, 141.57, 153.82, 195.36, 199.49, 202.21; *m/z*: 465.2:467.2 (3:1) ($M^+ + 1$); Anal. calcd $C_{24}H_{17}ClN_2O_6$: C, 62.00; H, 3.69; N, 6.03. Found: C, 62.06; H, 3.64; N, 6.07.

(3′*R*,4′*R*)-4′-(4-Methoxy benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4d). Yellowish brown crystals (81%), mp: 193°C; IR (KBr) cm^{-1}: 1639 (C=O), 1669 (C=O), 1703 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.54 (d, 1H, H_a, $J = 13.6$ Hz), 4.68 (m, 1H, H_b), 3.24 (dd, 1H, H_c, $J = 6.8$ Hz, $J = 12.8$ Hz), 3.81 (dd, 1H, H_d, $J = 7.0$ Hz, $J = 12.8$ Hz), 2.18 (s, 3H, N-CH_3), 3.87 (s, 3H, OMe), 6.41 (d, 1H, nitrofuryl 3H, $J = 3.4$ Hz), 7.10 (d, 1H, nitrofuryl-4H, $J = 3.4$ Hz), 6.90–8.10 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 36.02 (N-CH_3), 47.06, 55.56, 57.53, 76.78 (spirocarbon), 111.31, 114.11, 122.67, 128.69, 130.92, 136.55, 140.65, 151.26, 154.25, 164.10, 194.82, 199.71, 202.33; *m/z*: 466.2:461.2 ($M^+ + 1$); Anal. calcd $C_{25}H_{20}N_2O_7$: C, 65.21; H, 4.38; N, 6.08. Found: C, 65.24; H, 4.40; N, 6.11.

(3′*R*,4′*R*)-4′-(4-Bromo benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4e). Dark yellow crystals (85%), mp: 209–211°C; IR (KBr) cm^{-1}: 1658 (C=O), 1675 (C=O), 1705 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.53 (d, 1H, H_a, $J = 9.5$ Hz), 4.74 (m, 1H, H_b), 3.21 (dd, 1H, H_c, $J = 5.8$ Hz, $J = 9.0$ Hz), 3.86 (dd, 1H, H_d, $J = 6.0$ Hz, $J = 9.5$ Hz), 2.17 (s, 3H, N-CH_3), 6.50 (d, 1H, nitrofuryl 3H, $J = 3.48$ Hz), 7.10 (d, 1H, nitrofuryl 4H, $J = 3.5$ Hz), 7.60–8.00 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.96 (N-CH_3), 47.07, 48.44, 57.07, 77.0 (spirocarbon), 111.85,122.74, 123.51, 129.22, 130.04, 132.30, 134.32, 136.66, 140.61, 141.54, 153.78, 195.60,199.49, 202.20; *m/z*: 509.1:511.1 (1:1) ($M^+ + 1$)/($M^+ + 3$); Anal. calcd $C_{24}H_{17}BrN_2O_6$: C, 56.60; H, 3.36; N, 5.50. Found: C, 56.61; H, 3.40; N, 5.52.

(3′*R*,4′*R*)-4′-(4-Fluoro benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4f). Yellow crystals (88%), mp: 197–198°C; IR (KBr) cm^{-1}: 1658 (C=O), 1674 (C=O), 1703 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.60 (d, 1H, H_a, $J = 10.0$ Hz), 4.75 (m, 1H, H_b), 3.45 (dd, 1H, H_c, $J = 4.4$ Hz, $J = 9.2$ Hz), 3.85 (dd, 1H, H_d, $J = 7.6$ Hz, $J = 9.6$ Hz), 2.30 (s, 3H, N-CH_3), 6.10 (d, 1H, nitrofuryl 3H, $J = 3.6$ Hz), 6.90 (d, 1H, nitrofuryl 4H, $J = 3.6$ Hz), 7.00–8.00 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.99 (N-CH_3), 40.17, 47.16, 54.13, 57.19, 77.0 (spirocarbon), 111.38, 116.04, 122.73, 131.25, 136.24, 139.92, 140.63, 141.57, 153.87, 194.91, 199.53, 202.23; ^{19}F NMR (400 MHz, $CDCl_3$) δ_F: −103.453; *m/z*: 449.2 ($M^+ + 1$); Anal. calcd $C_{24}H_{17}FN_2O_6$: C, 64.29; H, 3.82; F, 4.24; N, 6.25. Found: C, 64.27; H, 4.27; N, 6.31.

(3′*R*,4′*R*)-4′-(4-Hydroxy benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4g). Dark brown crystals (73%), mp: 177–178°C; IR (KBr) cm^{-1}: 1646 (C=O), 1664 (C=O), 1706 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.60 (d, 1H, H_a, $J = 10.4$ Hz), 4.73 (m, 1H, H_b), 3.40 (dd, 1H, H_c, $J = 6.0$ Hz, $J = 8.8$ Hz), 3.80 (dd, 1H, H_d, $J = 6.4$ Hz, $J = 9.6$ Hz), 2.32 (s, 3H, N-CH_3), 6.20 (d, 1H, C-H nitrofuryl 3H, $J = 3.6$ Hz), 6.90 (d, 1H, nitrofuryl 4H, $J = 3.6$ Hz), 6.96 (br s, 1H, ArOH), 7.00–7.90 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 31.76, 36.03 (N-CH_3), 47.44, 57.60, 77.0 (spirocarbon), 111.38, 115.84, 123.53, 122.72, 128.23, 131.24, 136.66, 140.64, 141.55, 151.26, 154.20, 161.72, 163.01, 194.94, 199.89, 202.44; *m/z*: 447.2 ($M^+ + 1$); Anal. calcd $C_{24}H_{18}N_2O_7$: C, 64.57; H, 4.06; N, 6.28. Found: C, 64.60; H, 4.09; N, 6.31.

(3′*R*,4′*R*)-4′-(3-Bromo benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4h). Brown crystals (89%), mp: 186–188°C; IR (KBr) cm^{-1}: 1658 (C=O), 1684 (C=O), 1704 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.64 (d, 1H, H_a, $J = 10.0$ Hz), 4.72 (m, 1H, H_b), 3.45 (dd, 1H, H_c, $J = 3.2$ Hz, $J = 10.4$ Hz), 3.85 (dd, 1H, H_d, $J = 3.0$ Hz, $J = 9.2$ Hz), 2.32 (s, 3H, N-CH_3), 6.20 (d, 1H, nitrofuryl-3H, $J = 3.6$ Hz), 6.90 (d, 1H, nitrofuryl-4H, $J = 3.6$ Hz), 7.20–8.00 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.96 (N-CH_3), 47.06, 56.96, 77.0 (spirocarbon), 111.42, 122.74,123.33, 124.49, 130.50, 131.52, 136.65, 137.34, 140.62, 141.53, 151.32, 153.71, 195.25, 199.44, 202.16; *m/z*: 509.1:511.1 (1:1) ($M^+ + 1$); Anal. calcd $C_{24}H_{17}BrN_2O_6$: C, 56.60; H, 3.36; N, 5.50. Found: C, 56.62; H, 3.40; N, 5.52.

(3′*R*,4′*R*)-4′-(3-Hydroxy benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4i). Yellowish brown crystals (87%), mp: 203–204°C; IR (KBr) cm^{-1}: 1671 (C=O), 1685 (C=O), 1701 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 3.94 (d, 1H, H_a, $J = 10$ Hz), 4.68 (m, 1H, H_b), 3.4 (dd, 1H, H_c, $J = 2.8$ Hz, $J = 8.0$ Hz), 3.86 (dd, 1H, H_d, $J = 6.4$ Hz, $J = 10.8$ Hz), 2.30 (s, 3H, N-CH_3), 5.81 (br s, 1H, ArOH), 6.19 (d, 1H, nitrofuryl-3H, $J = 3.6$ Hz), 6.92 (d, 1H, nitrofuryl-4H, $J = 3.6$ Hz), 7.10–8.10 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 36.01 (N-CH_3), 47.29, 48.60, 57.30, 77.0 (spirocarbon), 111.43, 115.12, 121.20, 122.77, 123.57, 130.25, 137.13, 140.63, 141.59, 153.96, 156.36. 196.29, 199.68, 202.52; *m/z*: 447.2 ($M^+ + 1$); Anal. calcd $C_{24}H_{18}N_2O_7$: C, 64.57; H, 4.06; N, 6.28. Found: C, 64.61; H, 4.03; N, 6.30.

(3′*R*,4′*R*)-4′-(2-Chloro benzoyl)-1′-methyl-3′-(5-nitro-2-furyl) spiro [indene-2,2′-pyrrolidine]-1,3-dione (4j). Yellow amorphous (88%), mp: 196–198°C; IR (KBr) cm^{-1}: 1641 (C=O), 1687 (C=O), 1708 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.50 (d, 1H, H_a, $J = 10.0$ Hz), 4.75 (m, 1H, H_b), 3.40 (dd, 1H, H_c, $J = 6.4$ Hz, $J = 9.2$ Hz), 3.70 (dd, 1H, H_d, $J = 6.2$ Hz, $J = 9.2$ Hz), 2.25 (s, 3H, N-CH_3), 6.20 (d, 1H, nitrofuryl-3H, $J = 3.6$ Hz), 6.90 (d, 1H, nitrofuryl-4H, $J = 3.6$ Hz), 7.20–8.10 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_c: 35.99 (N-CH_3), 47.58, 51.80, 55.86, 77.0 (spirocarbon), 111.41, 122.71, 123.52, 127.16, 129.42, 130.72, 132.34, 136.63, 137.88, 140.65, 141.42, 153.95, 199.61, 199.70, 201.77; *m/z*: 465.2:467.1 (3:1) ($M^+ + 1$); Anal. calcd $C_{24}H_{17}ClN_2O_6$: C, 62.0; H, 3.69; N, 6.03. Found: C, 62.07; H, 3.64; N, 6.06.

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[9] Crystallographic data (excluding structure factors) for the structure of **4g** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 924427. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).