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Synthesis of the functionalized spiro[indoline-3,5′-pyrroline]-2,2′-diones via three-component reactions of arylamines, acetylenedicarboxylates, and isatins

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ABSTRACT

In the presence of *p*-toluenesulfonic acid as the catalyst the three-component reactions of arylamines, acetylenedicarboxylates, and isatins showed very interesting molecular diversity. When equal amount of arylamine was used, the three-component reaction resulted in the high yields of functionalized 3′-hydroxyspiro[indoline-3,5′-pyrroline]-2,2′-dione derivatives. On the other hand the functionalized 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-diones were also successfully prepared in satisfactory yields by using 2 M arylamine in the reaction.

1. Introduction

Spiro compounds represent an important class of naturally occurring substances characterized by highly pronounced biological properties. Spirocyclic oxindole systems are found in a number of alkaloids.[1,2] As a consequence, versatile efficient methods have been reported for the preparation of spirooxindole-fused heterocycles.[3,4] Recent synthetic methods to access spirocyclic oxindoles include formal cycloaddition,[5–7] Morita–Baylis–Hillman reaction,[7a,8,9] and other cyclization reactions.[10] Isatin derivatives are useful precursors in the synthesis of wide number of spirocyclic oxindoles.[11,12] In the past few years the multicomponent reactions or domino reactions based on the versatile reactivity of isatin derivatives have become the most widely efficient synthetic methods for various spirooxindoles.[13–16] It has been known that the domino reactions of isatins with Huisgen's zwitterions formed in situ from the reaction of pyridine, quinoline or isoquinoline with electron-deficient alkynes have become the efficient synthetic procedures for constructing versatile spirooxindole systems.[17,18] Perumal and co-workers successfully reported the synthesis of spiro[indole-3,4′-pyridines] by the four-component reaction of arylamine, acetylenedicarboxylate, malononitrile, and isatin.[19] We found that the four-component reactions of arylamines, dimethyl acetylenedicarboxylate, isatins, and dimedone in acetic acid gave novel spiro[indoline-3,2′-quinoline] derivatives.[20] Each of the aforementioned methods resulted in a different class of spirocycles that may show promise as biologically active compounds. As part of our program on the study of developing new multicomponent reactions for the synthesis of heterocyclic compounds,[21] herein we wish to report the efficient synthesis of the hydroxyl and arylamino substituted functionalized spiro[indoline-3,5′-pyrroline]-2,2′-diones from the three-component reactions of arylamines, acetylenedicarboxylate, and isatins.

2. Results and discussions

Very recently we reported that the three-component reaction of arylamines, aromatic aldehydes, and acetylenedicarboxylates to give the novel polysubstituted 3-hydroxy-2-pyrrolidinones.[21d] We envisioned that a spiro compound would be formed if isatin was utilized in the reaction to replace aromatic aldehydes. Thus our investigation began with the reaction of *p*-methoxyaniline, dimethyl acetylenedicarboxylate, and isatin in ethanol with a catalytic amount of *p*-toluensulfonic acid according to the previously established reaction conditions. After workup we are pleased to find that the reaction resulted in a functionalized 3′-hydroxyspiro[indoline-3,5′-pyrroline]-2,2′-dione **1a** in 83% yield. This result clearly indicated that isatin can be used as the third component to provide a three-component reaction for the synthesis of spiro compounds. Then under similar reaction conditions various arylamines and 5-methyl, 5-chloro, 5-fluoroisatins were successfully used in the three-component reaction to give the corresponding polysubstituted 3′-hydroxyspiro[indoline-3,5′-pyrroline]-2,2′-diones

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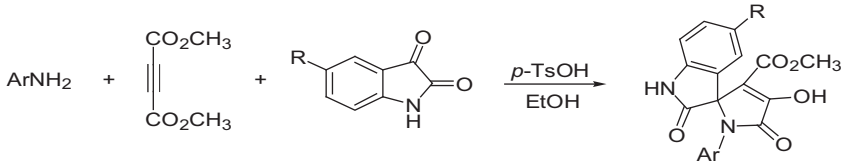
1b–**1j** in good yields (Table 1). The structures of the prepared spiro[indole-3,5′-pyrrole] **1a**–**1j** were fully characterized by ^{1}H and ^{13}C NMR, HRMS, IR spectra and were further confirmed by single-crystal X-ray diffraction study performed for compound **1g** (Fig. 1). In the ^{1}H NMR spectra of the spiro compounds **1a**–**1j** the hydroxyl group displays a broad singlet at about 12.40 ppm and the cyclic NH unit showed a singlet at about 10.60 ppm.

Analyzing the molecular structures of spiro compounds **1a**–**1j**, it is very clearly seen that the amino group of arylamine unit was bridged between the molecules of isatin and carbonyl group of acetylenedicaroboxylate, which indicates arylamine did not react with acetylenedicarboxylate to give the expected active intermediate β-enamino ester in the reaction. Thus further reaction of dimethyl acetylenedicarboxylate, isatin, and 2 M equiv of *p*-toluidine in ethanol with *p*-toluensulfonic acid as acid catalyst was carried out. After workup, we found that instead of isolating the hydroxyl substituted spiro compound, a 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione was successfully obtained as main product. In order to increase the yields and selectivity the reaction conditions of this acid-catalyzed three-component reaction were carefully examined. It is better to let isatin react with 2 M *p*-toluidine in ethanol at room temperature with 20% molar ratio of *p*-toluensulfonic acid as acid catalyst for about 1 h. Then dimethyl acetylenedicarboxylate was introduced and the reaction was furnished on reflux in 6 h to give the expected 3′-*N*-*p*-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione **2a** in 86% yield (Table 2). Afterward, with the optimized conditions in hand, we turned our attention to examine the scope of the reaction. Under this optimized reaction conditions, other arylamines and 5-methyl, 5-chloro, 5-fluoroisatins reacted smoothly with dimethyl or diethyl acetylenedicarboxylate to give the corresponding 3′-*N*-*p*-

Table 1
Synthesis of 3′-hydroxyspiro[indoline-3,5′-pyrroline]-2,2′-diones **1a**–**1j**



Entry	Compd	Ar′	R	Yield (%)
1	**1a**	*p*-$CH_3OC_6H_4$	H	83
2	**1b**	*p*-$CH_3C_6H_4$	Me	79
3	**1c**	*p*-$CH_3OC_6H_4$	Me	86
4	**1d**	*p*-$C_2H_5OC_6H_4$	Me	84
5	**1e**	*p*-ClC_6H_4	Me	74
6	**1f**	*p*-$CH_3C_6H_4$	F	81
7	**1g**	*p*-$CH_3OC_6H_4$	F	84
8	**1h**	*p*-ClC_6H_4	F	71
9	**1i**	*p*-BrC_6H_4	F	73
10	**1j**	*p*-ClC_6H_4	Cl	70

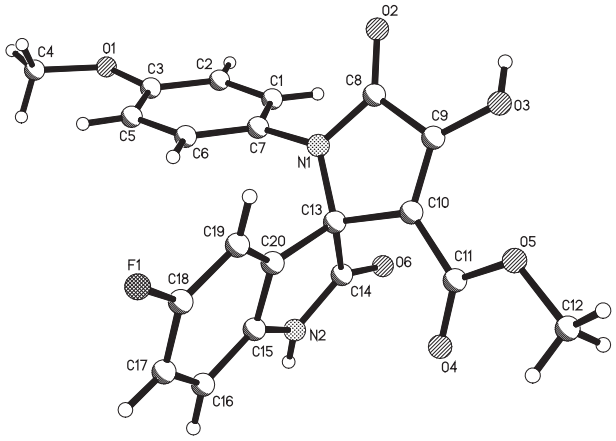
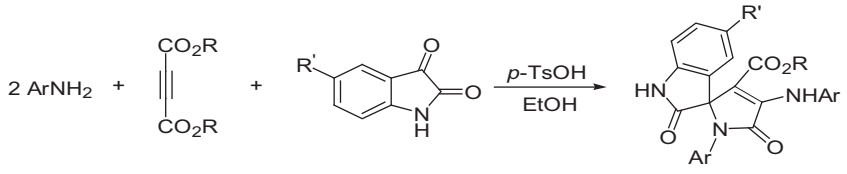


Fig. 1. Molecular structure of spiro[indoline-3,5′-pyrroline]-2,2′-dione **1g**.

Table 2
Synthesis of 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-diones **2a**–**2j**



Entry	Compd	Ar′	R	R′	Yield (%)
1	**2a**	*p*-$CH_3C_6H_4$	Me	H	86
2	**2b**	*m*-$NO_2C_6H_4$	Me	H	89
3	**2c**	α-Naph	Me	H	72
4	**2d**	*p*-$CH_3C_6H_4$	Me	Me	85
5	**2e**	*m*-$NO_2C_6H_4$	Me	Me	87
6	**2f**	*p*-$CH_3C_6H_4$	Me	F	84
7	**2g**	*p*-$CH_3C_6H_4$	Me	Cl	81
8	**2h**	*p*-$CH_3OC_6H_4$	Me	Cl	82
9	**2i**	*p*-$CH_3C_6H_4$	Et	Me	69
10	**2j**	*p*-$CH_3C_6H_4$	Et	Cl	64

methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-diones **2b**–**2j** in good yields (Table 2, entries 2–10). The structures of the prepared 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-diones **2a**–**2j** were established by ^{1}H and ^{13}C NMR, HRMS, IR spectra. The molecular structure of spiro compound **2f** was successfully determined by X-ray single-crystal diffraction method (Fig. 2). In ^{1}H NMR spectra of 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-diones **2a**–**2j** the amino group usually show a singlet at about 9.20 ppm and the cyclic NH unit displays a singlet at about 10.60 ppm.

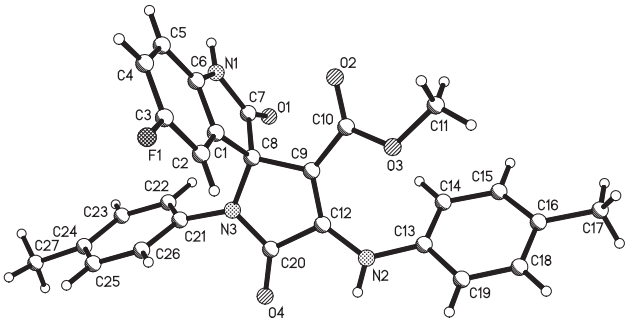


Fig. 2. Molecular structure of spiro[indoline-3,5′-pyrroline]-2,2′-dione **2f**.

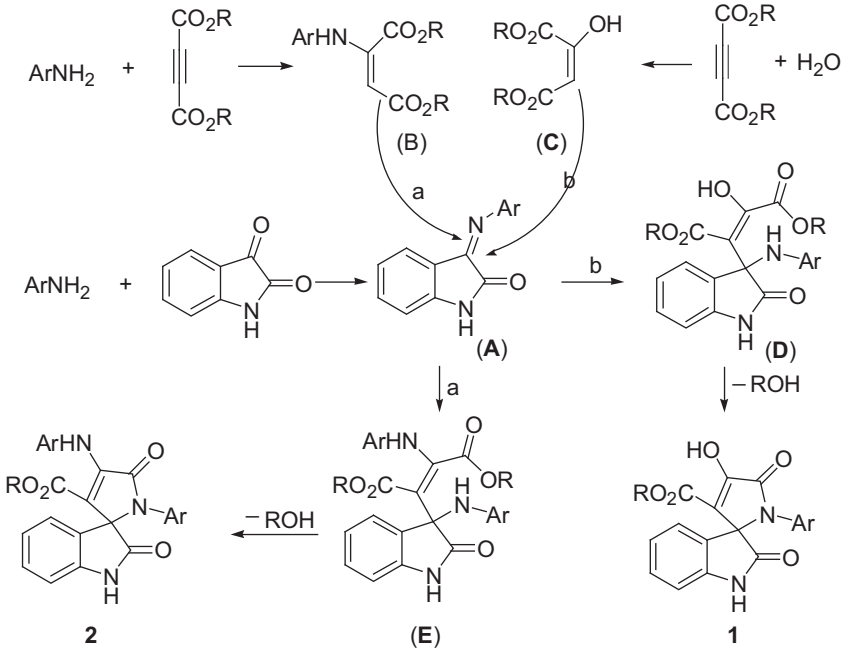
On the basis of the above experimental results together with the related reactions,[20–22] a plausible reaction mechanism for this three-component reaction to give the two kinds of spiro[indoline-3,5′-pyrroline]-2,2′-diones is outlined in Scheme 1. The first step in the reaction is the formation of 3-*N*-aryliminoisatin (**A**) from the condensation of arylamine and isatin with the catalysis of *p*-toluenesulfonic acid. When 2 M arylamine was used, the second step is the reaction of remaining arylamine with acetylenedicarboxylate to form the active intermediate β-enamino ester (**B**). Then the addition of β-enamino ester (**B**) to 3-*N*-aryliminoisatin (**A**) resulted in an adduct (**E**). The intramolecular reaction of arylamino group with the ester group with the elimination of methanol gave the final 3′-*N*-arylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione **2**. On the other hand if only 1 M arylamine was used, it is believed that water in the system as the nucleophile adds to acetylenedicarboxylate to give a 1,3-dipolar intermediate (**C**).[21d] Then the 1,3-dipolar intermediate (**C**) reacts with 3-*N*-aryliminoisatin (**A**) to give an addition intermediate (**D**). The intramolecular ammonolysis of one esteric carbonyl group forms the final 3′-hydroxyspiro[indoline-3,5′-pyrroline]-2,2′-dione **1**. In this reaction process the key step is the formation of active β-enamino ester (**B**) and its hydroxyl analog (**C**), which controls the selective formation of the arylamino and hydroxyl substituted spiro[indoline-3,5′-pyrroline] derivatives. It should be pointed out that the in situ formation of β-enamino ester (**B**) is supported by many reactions containing arylamine and acetylenedicarboxylate,[17–20] while at present the generation of its hydroxyl analog (**C**) from the addition of water to acetylenedicarboxylate was only our tentative proposal based on the previous similar reaction[21d] and more stronger experimental supports are needed.

In summary we have developed the efficient procedures for the selective synthesis of two kinds of the functionalized [indoline-3,5′-pyrroline]-2,2′-diones via acid-catalyzed three-component reactions of arylamine, acetylenedicarboxylate, and isatin under different conditions. The advantages of the reactions are using common starting material, mild reaction conditions, operational simplicity, and wide variety of substrates. The potential uses of the reaction in synthetic and medicinal chemistry might be quite significant. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

3. Experimental section

3.1. Reagents and apparatus

Reagents and solvents were commercial available with analytical grade. Melting points were determined on a hot-plate microscope apparatus and were uncorrected. Analytical thin-layer chromatography (TLC) was performed on silica gel plates with GF-254 indicator, visualized by irradiation with UV light. IR spectra were obtained on a Bruker Tensor27 spectrometer (KBr disc). ^{1}H NMR and ^{13}C NMR spectra were measured with a Bruker



Scheme 1. Proposed formation mechanism of spiro[indoline-3,5′-pyrroline]-2,2′-dione.

AV-600 spectrometer. High-resolution mass (ESI) spectra were obtained with a Bruker MicroTOF spectrometer. X-ray data were collected on a Bruker Smart APEX-2 CCD diffractometer.

3.2. General procedure for the synthesis of the functionalized spiro[indoline-3,5′-pyrroline]-2,2′-diones 1a–1j

A solution of arylamine (2.0 mmol) and acetylenedicarboxylate (2.0 mmol, 0.284 g) in 10 mL ethanol was stirred at room temperature for 10 min. Then isatin (2.0 mmol) and *p*-toluenesulfonic acid (2.0 mmol) were added to it and the mixture was stirred at about 40–50 °C for about 24 h. The solution was then concentrated to half the volume. The resulting precipitates were collected and washed with ethanol to give the pure product for analysis.

*3.2.1. 3′-Hydroxy-4′-methoxycarbonyl-1′-p-methoxyphenylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1a**).* Yellow solid, 83%, mp 222–224 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.40 (br s, 1H, OH), 10.77 (s, 1H, NH), 7.30 (d, J=7.8 Hz, 1H, ArH), 7.18 (t, J=7.8 Hz, 1H, ArH), 6.93 (t, J=7.2 Hz, 1H, ArH), 6.88 (d, J=9.0 Hz, 2H, ArH), 6.82 (d, J=9.0 Hz, 2H, ArH), 6.75 (d, J=7.2 Hz, 1H, ArH), 3.66 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.5, 165.4, 161.8, 158.7, 154.9, 143.3, 130.1, 128.6, 127.0, 124.9, 124.4, 122.1, 114.2, 110.2, 109.4, 70.0, 55.1, 51.2; IR (KBr) ν: 3290, 2956, 2844, 1721, 1619, 1585, 1516, 1459, 1419, 1360, 1331, 1302, 1280, 1256, 1205, 1179, 1160, 1132, 1112, 1089, 1027, 943, 924, 881, 790, 765, 755 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{15}N_2O_6$ ([M−H]$^-$): 379.0936. Found: 379.0936.

*3.2.2. 3′-hydroxy-4′-methoxycarbonyl-5-methyl-1′-p-methylphenylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1b**).* white solid, 79%, mp 239–241 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.39 (br s, 1H, OH), 10.68 (s, 1H, NH), 7.10–6.98 (m, 4H, ArH), 6.87 (s, 2H, ArH), 6.65 (s, 1H, ArH), 3.55 (s, 3H, OCH_3), 2.19 (s, 6H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.4, 165.2, 161.7, 154.8, 140.8, 137.5, 132.2, 131.1, 130.4, 129.5, 126.6, 124.9, 124.7, 109.9, 109.5, 69.8, 51.2, 20.5; IR(KBr) ν: 3281, 2957, 2923, 1735, 1653, 1625, 1515, 1495, 1458, 1417, 1353, 1267, 1239, 1201, 1151, 1093, 1025, 1014, 967, 946, 936, 924, 886, 846, 826, 811, 764 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}N_2O_5$ ([M−H]$^-$): 377.1143. Found: 377.1141.

*3.2.3. 3′-Hydroxy-4′-methoxycarbonyl-1′-p-methoxyphenyl-5-methylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1c**).* White solid, 86%, mp 241–242 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.34 (br s, 1H, OH), 10.63 (s, 1H, NH), 7.12 (s, 1H, ArH), 6.99 (d, J=7.8 Hz, 1H, ArH), 6.87–6.82 (m, 4H, ArH), 6.63 (d, J=7.8 Hz, 1H, ArH), 3.68 (s, 3H, OCH_3), 3.56 (s, 3H, OCH_3), 2.21 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.4, 165.3, 161.7, 158.6, 154.8, 140.8, 131.1, 130.4, 128.5, 127.1, 124.9, 124.8, 114.2, 109.9, 109.4, 70.0, 55.2, 51.2, 20.5; IR (KBr) ν: 3296, 2960, 2842, 1720, 1651, 1625, 1611, 1584, 1514, 1495, 1457, 1418, 1361, 1255, 1206, 1173, 1150, 1112, 1095, 1028, 970, 953, 942, 932, 885, 848, 822, 791, 763 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}N_2O_6$ ([M−H]$^-$): 393.1092. Found: 393.1092.

*3.2.4. 1′-p-Ethoxyphenyl-3′-hydroxy-4′-methoxycarbonyl-5-methylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1d**).* Yellow solid, 84%, mp 239–240 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.33 (br s, 1H, OH), 10.63 (s, 1H, NH), 7.11 (s, 1H, ArH), 6.99 (d, J=6.6 Hz, 1H, ArH), 6.86–6.81 (m, 4H, ArH), 6.64 (d, J=6.6 Hz, 1H, ArH), 3.93 (br s, 2H, OCH_2), 3.55 (s, 3H, OCH_3), 2.20 (s, 3H, CH_3), 1.26 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.4, 165.3, 161.7, 158.0, 154.9, 140.8, 131.1, 130.4, 128.4, 127.0, 124.9, 124.8, 114.6, 114.5, 109.9, 109.4, 70.0, 63.1, 51.2, 20.5, 14.5; IR (KBr) ν: 3359, 2988, 2956, 2906, 1724, 1650, 1624, 1610, 1586, 1513, 1493, 1457, 1421, 1366, 1310, 1236, 1198, 1175, 1146, 1113, 1095, 1044, 1018, 968, 952, 927, 902, 890, 845, 827, 817, 799, 781, 767 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}N_2O_6$ ([M−H]$^-$): 407.1249. Found: 407.1248.

*3.2.5. 1′-p-Chlororphenyl-3′-hydroxy-4′-methoxycarbonyl-5-methylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1e**).* White solid, 74%, mp 242–244 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.48 (br s, 1H, OH), 10.77 (s, 1H, NH), 7.38 (d, J=8.4 Hz, 2H, ArH), 7.14 (s, 1H, ArH), 7.02–7.00 (m, 3H, ArH), 6.68 (d, J=7.8 Hz, 1H, ArH), 3.56 (s, 3H, OCH_3), 2.18 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.2, 165.3, 161.6, 154.5, 140.7, 133.8, 132.4, 131.3, 130.6, 129.2, 128.2, 124.8, 124.6, 110.1, 109.8, 69.7, 51.3, 20.5; IR(KBr) ν: 3276, 2992, 2948, 1725, 1625, 1496, 1463, 1419, 1355, 1322, 1238, 1197, 1149, 1089, 1019, 966, 951, 891, 848, 817, 797, 767, 752 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{14}ClN_2O_5$ ([M−H]$^-$): 397.0597. Found: 397.0593.

*3.2.6. 5-Fluoro-3′-hydroxy-4′-methoxycarbonyl-1′-p-methylphenylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1f**).* White solid, 81%, mp 246–248 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.46 (br s, 1H, OH), 10.80 (s, 1H, NH), 7.37 (d, J=6.0 Hz, 1H, ArH), 7.10 (d, J=7.8 Hz, 2H, ArH), 7.00 (t, J=7.8 Hz, 1H, ArH), 6.90 (d, J=7.8 Hz, 2H, ArH), 6.74–6.72 (m, 1H, ArH), 3.57 (s, 3H, OCH_3), 2.21 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.6, 165.2, 161.8, 158.9, 157.3, 155.2, 139.4, 137.8, 132.0, 129.6, 126.9, 126.8, 126.7, 116.5, 116.4, 112.6, 112.5, 111.0, 110.9, 109.0, 69.9, 51.3, 20.5; IR (KBr) ν: 3259, 3045, 2962, 1722, 1629, 1515, 1490, 1463, 1421, 1351, 1319, 1266, 1244, 1210, 1172, 1130, 1083, 1025, 1015, 979, 948, 937, 882, 858, 844, 825, 805, 765 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{14}FN_2O_5$ ([M−H]$^-$): 381.0892. Found: 381.0891.

*3.2.7. 5-Fluoro-3′-hydroxy-4′-methoxycarbonyl-1′-p-methoxyphenylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1g**).* Yellow solid, 84%, mp 250–252 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.47 (br s, 1H, OH), 10.79 (s, 1H, NH), 7.39 (d, J=7.8 Hz, 1H, ArH), 7.03–6.99 (m, 1H, ArH), 6.93 (d, J=8.4 Hz, 2H, ArH), 6.86 (d, J=8.4 Hz, 2H, ArH), 6.74–6.72 (m, 1H, ArH), 3.68 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.6, 165.3, 161.8, 158.9, 158.8, 157.3, 155.2, 139.4, 128.7, 126.9, 126.8, 116.5, 116.4, 114.3, 112.7, 112.5, 110.9, 110.8, 108.9, 70.1, 55.1, 51.3; IR (KBr) ν: 3273, 3046, 2962, 2842, 1720, 1628, 1612, 1584, 1515, 1490, 1461, 1446, 1421, 1360, 1325, 1303, 1281, 1257, 1208, 1172, 1128, 1084, 1028, 982, 952, 933, 890, 881, 846, 822, 804, 765 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{14}FN_2O_6$([M−H]$^-$): 397.0841. Found: 397.0840.

*3.2.8. 1′-p-Chlorophenyl-5-fluoro-3′-hydroxy-4′-methoxycarbonylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1h**).* White solid, 71%, mp 216–218 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.59 (br s, 1H, OH), 10.90 (s, 1H, NH), 7.41 (d, J=9.0 Hz, 3H, ArH), 7.06–7.01 (m, 3H, ArH), 6.77–6.75 (m, 1H, ArH), 3.57 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.4, 165.2, 161.7, 157.3, 154.9, 139.4, 133.6, 132.6, 129.3, 128.6, 126.5, 116.8, 116.6, 112.7, 112.6, 111.1, 111.0, 109.2, 69.8, 51.4; IR(KBr) ν: 3256, 2961, 1731, 1491, 1465, 1423, 1351, 1318, 1265, 1212, 1171, 1127, 1093, 1048, 1019, 980, 947, 935, 890, 877, 847, 827, 804, 766, 753 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{11}ClFN_2O_5$ ([M−H]$^-$): 401.0346. Found: 401.0345.

*3.2.9. 1′-p-Bromophenyl-5-fluoro-3′-hydroxy-4′-methoxycarbonylspiro[indoline-3,5′-pyrroline]-2,3′-dione (**1i**).* White solid, 73%, mp 230–232 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 12.59 (br s, 1H, OH), 10.92 (s, 1H, NH), 7.53 (d, J=8.4 Hz, 2H, ArH), 7.41 (d, J=8.4 Hz, 1H, ArH), 7.02 (d, J=8.4 Hz, 3H, ArH), 6.78 (d, J=8.4 Hz, 1H, ArH), 3.57 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.5, 165.2, 161.7, 158.9, 157.3, 154.9, 139.4, 134.0, 132.2, 128.8, 126.5, 126.4, 121.2, 116.8, 116.6, 112.7, 112.5, 111.1, 111.0, 109.3, 69.7, 51.3; IR (KBr) ν: 3256, 3092, 2961, 1722, 1490, 1465, 1423, 1350, 1317, 1266, 1211, 1171, 1127, 1074, 1047, 1017, 980, 947, 934, 890, 877, 846, 826,

814, 804, 766 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{11}BrFN_2O_5$ ($[M-H]^-$): 444.9841. Found: 444.9841.

*3.2.10. 5-Chloro-1′-p-chlorophenyl-3′-hydroxy-4′-methoxycarbonylspiro[indoline-3,5′-pyrroline]-2,2′-dione (**1j**).* Yellow solid, 70%, mp 248–250 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 12.60 (br s, 1H, OH), 11.03 (s, 1H, NH), 7.57–6.81 (m, 7H, ArH), 3.57 (br s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.3, 165.2, 161.7, 155.0, 142.1, 133.6, 132.6, 130.2, 129.3, 128.3, 126.8, 126.4, 124.9, 111.7, 109.2, 69.5, 51.3; IR(KBr) ν: 3259, 2972, 1723, 1620, 1496, 1480, 1460, 1419, 1354, 1316, 1231, 1208, 1159, 1092, 1041, 1017, 964, 949, 919, 883, 835, 818, 767, 752 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{11}Cl_2N_2O_5$ ($[M-H]^-$): 417.0051. Found: 417.0049.

3.3. General procedure for the synthesis of the functionalized spiro[indoline-3,5′-pyrroline]-2,2′-dione

A solution of arylamine (4.0 mmol) and isatin (2.0 mmol) and *p*-toluenesulfonic acid (0.5 mmol) in 10 mL ethanol was stirred at room temperature for about 2 h. Then acetylenedicarboxylate (2.0 mmol) was added to it and the whole mixture was refluxed for about 6 h. After cooling to room temperature, the resulting precipitates were collected and washed with ethanol to give the pure product for analysis.

*3.3.1. 4′-Methoxycarbonyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2a**).* Yellow solid, 86%, mp 229–231 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.74 (s, 1H, NH), 9.08 (s, 1H, NH), 7.31 (d, J=7.2 Hz, 1H, ArH), 7.18 (t, J=7.8 Hz, 1H, ArH), 7.11–7.07 (m, 4H, ArH), 7.02 (d, J=8.4 Hz, 2H, ArH), 6.94 (t, J=7.8 Hz, 1H, ArH), 6.87 (d, J=8.4 Hz, 2H, ArH), 6.74 (d, J=7.8 Hz, 1H, ArH), 3.19 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3), 2.21 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.1, 165.6, 162.2, 143.2, 141.7, 137.5, 137.2, 132.9, 132.3, 129.9, 129.5, 128.5, 127.0, 125.7, 124.3, 122.1, 122.0, 110.1, 105.7, 71.0, 50.6, 20.5; IR (KBr) ν: 3298, 3195, 3092, 2949, 1718, 1676, 1625, 1515, 1472, 1417, 1384, 1357, 1330, 1305, 1247, 1215, 1160, 1128, 1110, 1031, 966, 951, 936, 920, 886, 866, 824, 811, 789, 762 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{22}N_3O_4$ ($[M-H]^-$): 452.1616. Found: 452.1613.

*3.3.2. 4′-Methoxycarbonyl-1′-m-nitrophenyl-3′-N-m-nitrophenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2b**).* Yellow solid, 89%, mp 238–240 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 11.07 (s, 1H, NH), 9.71 (s, 1H, NH), 8.10 (d, J=8.4 Hz, 1H, ArH), 7.99–7.91 (m, 3H, ArH), 7.65 (t, J=8.4 Hz, 1H, ArH), 7.59–7.52 (m, 4H, ArH), 7.24 (t, J=7.8 Hz, 1H, ArH), 6.97 (t, J=7.8 Hz, 1H, ArH), 6.84 (d, J=7.8 Hz, 1H, ArH), 3.31 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.5, 165.5, 161.7, 147.9, 147.6, 143.2, 141.0, 140.5, 136.0, 132.5, 130.7, 130.6, 129.2, 127.8, 124.8, 124.5, 122.5, 120.6, 117.9, 115.8, 110.5, 109.8, 70.9, 51.2; IR (KBr) ν: 3342, 3271, 3110, 2949, 1723, 1694, 1650, 1619, 1596, 1527, 1484, 1470, 1437, 1392, 1347, 1266, 1222, 1197, 1159, 1141, 1094, 1030, 981, 934, 914, 892, 848, 802, 764 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{16}N_5O_8$ ($[M-H]^-$): 514.1004. Found: 514.1004.

*3.3.3. 4′-Methoxycarbonyl-1′-α-naphthyl-3′-N-α-naphthylaminospiro[indoline-3,5′-pyrroline]-2,3′-dione (**2c**).* Yellow solid, 72%, mp 258–260 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 11.22 (s, 1H, NH), 9.26 (s, 1H, NH), 8.55 (d, J=8.4 Hz, 1H, ArH), 8.26 (d, J=7.8 Hz, 1H, ArH), 7.93 (d, J=8.4 Hz, 1H, ArH), 7.77 (d, J=7.8 Hz, 1H, ArH), 7.63–7.51 (m, 6H, ArH), 7.39 (d, J=8.4 Hz, 1H, ArH), 7.20–7.14 (m, 4H, ArH), 6.70 (t, J=7.2 Hz, 1H, ArH), 6.54 (d, J=8.4 Hz, 1H, ArH), 6.49 (d, J=7.2 Hz, 1H, ArH), 3.36 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 181.7, 138.7, 137.2, 134.2, 133.3, 133.2, 133.1, 128.5, 128.1, 128.0, 127.1, 126.2, 126.0, 125.3, 125.2, 122.6, 122.5, 121.9, 121.6, 120.7, 119.6, 119.3, 119.2, 115.7, 112.7, 56.4; IR (KBr) ν: 3356, 3192, 3060, 1683, 1639, 1607, 1574, 1526, 1493, 1469, 1449, 1412, 1375, 1308, 1254, 1194, 1173, 1128, 1096, 1074, 1037, 898, 881, 847, 808, 795 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{24}N_3O_4$ ($[M-H]^-$): 526.1761. Found: 526.1760.

*3.3.4. 4′-methoxycarbonyl-5-methyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2d**).* Yellow solid, 85%, mp 249–250 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.62 (s, 1H, NH), 9.05 (s, 1H, NH), 7.14 (s, 1H, ArH), 7.11–7.07 (m, 4H, ArH), 7.03 (d, J=7.8 Hz, 2H, ArH), 6.98 (d, J=7.8 Hz, 1H, ArH), 6.87 (d, J=7.8 Hz, 2H, ArH), 6.64 (d, J=7.8 Hz, 1H, ArH), 3.22 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3), 2.21 (s, 6H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.0, 165.5, 162.3, 141.8, 140.8, 137.4, 137.1, 132.9, 132.4, 131.1, 130.3, 129.5, 128.5, 126.8, 125.7, 124.7, 122.1, 109.8, 105.9, 71.0, 50.7, 20.5, 20.4; IR (KBr) ν: 3365, 3278, 3028, 2951, 2918, 1671, 1638, 1544, 1514, 1495, 1439, 1395, 1355, 1294, 1253, 1230, 1196, 1101, 1034, 972, 932, 888, 852, 813, 780, 766 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{24}N_3O_4$ ($[M-H]^-$): 466.1772. Found: 466.1770.

*3.3.5. 4′-Methoxycarbonyl-5-methyl-1′-m-nitrophenyl-3′-N-m-nitrophenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2e**).* Yellow solid, 87%, mp 221–223 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.96 (s, 1H, NH), 9.67 (s, 1H, NH), 8.10 (d, J=7.8 Hz, 1H, ArH), 7.99–7.92 (m, 3H, ArH), 7.66–7.53 (m, 4H, ArH), 7.35 (s, 1H, ArH), 7.04 (d, J=7.8 Hz, 1H, ArH), 6.73 (d, J=7.8 Hz, 1H, ArH), 3.33 (s, 3H, OCH_3), 2.21 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 173.4, 165.4, 161.7, 147.8, 147.6, 140.9, 140.7, 140.4, 136.1, 132.2, 131.6, 130.9, 130.7, 129.2, 127.9, 125.2, 124.5, 122.4, 120.3, 117.9, 115.9, 110.3, 110.0, 70.9, 51.2, 20.5; IR (KBr) ν: 3360, 3269, 2958, 1727, 1630, 1513, 1489, 1462, 1421, 1359, 1301, 1252, 1212, 1171, 1123, 1085, 1031, 933, 890, 824, 803, 764 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{18}N_5O_8$ ($[M-H]^-$): 528.1161. Found: 528.1156.

*3.3.6. 5-Fluoro-4′-methoxycarbonyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2f**).* Yellow solid, 84%, mp 264–266 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 9.11 (s, 1H, NH), 7.41 (d, J=8.4 Hz, 1H, ArH), 7.11–6.98 (m, 7H, ArH), 6.91 (d, J=8.4 Hz, 2H, ArH), 6.72 (d, J=8.4 Hz, 1H, ArH), 3.22 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.3, 165.4, 162.2, 158.9, 157.3, 142.1, 139.4, 137.6, 137.0, 133.0, 132.2, 129.6, 129.5, 128.4, 127.7, 127.6, 127.1, 126.9, 122.3, 116.3, 116.2, 112.5, 112.4, 110.8, 110.7, 105.0, 71.1, 50.7, 20.5; IR (KBr) ν: 3352, 3267, 3035, 2956, 1743, 1706, 1667, 1639, 1609, 1546, 1514, 1489, 1443, 1399, 1361, 1296, 1277, 1258, 1234, 1203, 1174, 1121, 1089, 1034, 981, 969, 934, 892, 869, 850, 815, 801, 782, 768 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{21}FN_3O_4$ ($[M-H]^-$): 470.1522. Found: 470.1514.

*3.3.7. 5-Chloro-4′-methoxycarbonyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2g**).* Yellow solid, 81%, mp 258–260 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.87 (s, 1H, NH), 9.11 (s, 1H, NH), 7.58 (br s, 1H, ArH), 7.22 (d, J=8.4 Hz, 1H, ArH), 7.11–7.05 (m, 6H, ArH), 6.90 (d, J=8.4 Hz, 2H, ArH), 6.75 (d, J=7.8 Hz, 1H, ArH), 3.24 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.1, 165.3, 162.3, 142.2, 142.1, 137.6, 137.0, 133.1, 132.2, 129.8, 129.7, 129.6, 128.4, 128.0, 126.9, 126.2, 124.7, 122.4, 111.4, 104.8, 70.8, 50.7, 20.5; IR (KBr) ν: 3353, 3276, 3033, 2953, 2919, 1705, 1545, 1514, 1478, 1441, 1357, 1291, 1256, 1197, 1158, 1108, 1065, 1034, 971, 956, 931, 876, 851, 815, 771 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{21}ClN_3O_4$ ($[M-H]^-$): 486.1226. Found: 486.1223.

*3.3.8. 5-Chloro-4′-methoxycarbonyl-1′-p-methoxyphenyl-3′-N-p-methoxyphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2h**).* Yellow solid, 82%, mp 254–256 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.83 (s, 1H, NH), 9.04 (s, 1H, NH), 7.59 (s, 1H, ArH),

7.23 (s, 1H, ArH), 7.13 (br s, 2H, ArH), 6.92–6.87 (m, 6H, ArH), 6.75 (s, 1H, ArH), 3.74 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.26 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.2, 165.4, 162.4, 158.7, 156.3, 142.7, 142.1, 132.4, 129.8, 128.7, 128.6, 128.2, 127.2, 126.2, 124.7, 124.4, 114.3, 114.2, 113.2, 111.4, 103.5, 70.8, 55.2, 55.1, 50.8; IR (KBr) ν: 3333, 3251, 2955, 2838, 1731, 1627, 1512, 1477, 1363, 1300, 1248, 1107, 1067, 1032, 960, 932, 918, 890, 861, 824, 789, 765 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{21}ClN_3O_6$ ($[M-H]^-$): 518.1124. Found: 518.1123.

*3.3.9. 4′-Ethoxycarbonyl-5-methyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2i**).* Yellow solid, 69%, mp 235–237 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.61 (s, 1H, NH), 9.05 (s, 1H, NH), 7.14 (s, 1H, ArH), 7.09 (d, J=7.2 Hz, 4H, ArH), 7.02–6.98 (m, 3H, ArH), 6.88–6.85 (m, 2H, ArH), 6.63 (d, J=7.8 Hz, 1H, ArH), 3.72–3.64 (m, 2H, OCH_2), 2.27 (s, 3H, CH_3), 2.21 (s, 6H, CH_3), 0.66 (t, J=7.2 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 179.3, 170.9, 167.1, 146.6, 146.1, 142.6, 142.4, 137.8, 137.7, 136.3, 135.4, 134.8, 134.7, 133.7, 132.0, 131.9, 131.1, 130.0, 126.8, 115.0, 111.4, 76.4, 64.7, 61.3, 25.8, 25.7, 23.8, 18.9, 18.2; IR (KBr) ν: 3349, 3289, 2918, 1736, 1698, 1666, 1640, 1611, 1545, 1515, 1495, 1473, 1449, 1374, 1343, 1293, 1251, 1230, 1186, 1099, 1034, 967, 872, 853, 813, 763 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}N_3O_4$ ($[M-H]^-$): 480.1929. Found: 480.1924.

*3.3.10. 5-Chloro-4′-ethoxycarbonyl-1′-p-methylphenyl-3′-N-p-methylphenylaminospiro[indoline-3,5′-pyrroline]-2,2′-dione (**2j**).* Yellow solid, 64%, mp 247–249 °C; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.88 (s, 1H, NH), 9.13 (s, 1H, NH), 7.59 (s, 1H, ArH), 7.23 (d, J=8.4 Hz, 1H, ArH), 7.12–7.04 (m, 6H, ArH), 6.92 (d, J=8.4 Hz, 2H, ArH), 6.75 (d, J=8.4 Hz, 1H, ArH), 3.73–3.67 (m, 2H, OCH_2), 2.27 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 0.67 (t, J=7.2 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 174.1, 165.5, 161.8, 142.2, 142.0, 137.6, 137.0, 132.8, 132.3, 129.8, 129.6, 128.4, 128.1, 126.9, 126.1, 124.7, 121.9, 111.4, 105.1, 70.9, 59.6, 20.5, 20.4, 13.0; IR (KBr) ν: 3338, 3287, 3035, 2919, 1701, 1545, 1514, 1477, 1441, 1374, 1344, 1291, 1253, 1191, 1106, 1065, 1033, 1006, 962, 885, 868, 853, 813, 773 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{23}ClN_3O_4$ ($[M-H]^-$): 500.1383. Found: 500.1381.

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Supplementary data

NMR spectra (^1H and ^{13}C) for all products. This material is available free of charge. Crystallographic data of **1g** (CCDC 879517) and **2f** (CCDC 879518) have been deposited at the Cambridge Crystallographic Database Centre. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.08.030.

References and notes

1. (a) Sundberg, R. J. *The Chemistry of Indoles*; Academic: New York, NY, 1996; (b) Abdel-Rahman, A. H.; Keshk, E. M.; Hanna, M. A.; El-Bady, Sh. M *Bioorg. Med. Chem.* **2004**, *12*, 2483–2488.
2. (a) Marti, C.; Carreia, E. M. *Eur. J. Org. Chem.* **2003**, 2209–2219; (b) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6477–6487.
3. (a) Zhu, S. L.; Jia, S. J.; Zhang, Y. *Tetrahedron* **2007**, *63*, 9365–9372; (b) Kumar, R. S.; Perumal, S. *Tetrahedron Lett.* **2007**, *48*, 7164–7168.
4. (a) Shanthi, G.; Subbulakshmi, G.; Perumal, P. T. *Tetrahedron* **2007**, *63*, 2057–2063; (b) Mohammadi, A. A.; Dabiri, M.; Qaraat, H. *Tetrahedron* **2009**, *65*, 3804–3808.
5. (a) Basavaiah, D.; Reddy, R. K. *Org. Lett.* **2007**, *9*, 57–60; (b) Kumar, R. R.; Perumal, S.; Senthilkumar, P.; Yogeeswari, P.; Sriram, D. *Eur. J. Med. Chem.* **2009**, *44*, 3821–3829.
6. (a) Liu, H.; Dou, D. L.; Shi, D. Q. *J. Comb. Chem.* **2010**, *12*, 633–637; (b) Liu, H.; Dou, G. L.; Shi, D. Q. *J. Comb. Chem.* **2010**, *12*, 292–294.
7. (a) Shanmugam, P.; Viswambharan, B.; Madhavan, S. *Org. Lett.* **2007**, *9*, 4095–4098; (b) Badillo, J. J.; Arevalo, G. E.; Fettinger, J. C.; Franz, A. K. *Org. Lett.* **2011**, *13*, 418–421.
8. Shanmugam, P.; Viswambharan, B.; Selvakumar, K.; Madhavan, S. *Tetrahedron Lett.* **2008**, *49*, 2611–2615.
9. (a) Zhang, X. C.; Cao, S. H.; Wei, Y.; Shi, M. *Org. Lett.* **2011**, *13*, 1142–1145; (b) Deng, H. P.; Wei, Y.; Shi, M. *Org. Lett.* **2011**, *13*, 3348–3351.
10. (a) Wang, L.; Zhang, Y.; Hu, H. Y.; Fun, H. K.; Xu, J. H. *J. Org. Chem.* **2005**, *70*, 3850–3858; (b) Viswambharan, B.; Selvakumar, K.; Madhavan, S.; Shanmugam, P. *Org. Lett.* **2010**, *12*, 2108–2111.
11. (a) Bazgir, A.; Noroozi Tisseh, Z.; Mirzaei, P. *Tetrahedron Lett.* **2008**, *49*, 5165–5168; (b) Jadidi, K.; Ghahremanzadeh, R.; Bazgir, A. *Tetrahedron* **2009**, *65*, 2005–2009.
12. (a) Gao, S. J.; Tsai, C. H.; Tseng, C.; Yao, C. F. *Tetrahedron* **2008**, *64*, 9143–9149; (b) Chen, W. B.; Wu, Z. J.; Pei, Q. L.; Cun, N. F.; Zhang, X. M.; Yuan, W. C. *Org. Lett.* **2010**, *12*, 3132–3135.
13. (a) Mokhtari, J.; Alizadeh, A. *Helv. Chim. Acta* **2011**, *94*, 1315–1319; (b) Quiroga, J.; Portillo, S.; Pérez, A.; Gálvez, J.; Abonia, R.; Insuasty, B. *Tetrahedron Lett.* **2011**, *52*, 2664–2666.
14. (a) Ghahremanzadeh, R.; Sayyafi, M.; Ahadi, S.; Bazgir, A. *J. Comb. Chem.* **2009**, *11*, 393–396; (b) Shakibaei, G. I.; Feiz, A.; Khavasi, H. R.; Soorki, A. A.; Bazgir, A. *ACS Comb. Sci.* **2011**, *13*, 96–99.
15. (a) Nair, V.; Menon, R. S.; Sreekanth, A.; Abhilash, N.; Biju, A. T. *Acc. Chem. Res.* **2006**, *39*, 520–530; (b) Shaabani, A.; Maleki, A.; Rezayan, A. H.; Sarvary, A. *Mol. Divers.* **2011**, *15*, 41–68.
16. (a) Yadav, J. S.; Reddy, B. V. S.; Yadav, N. N.; Gupta, M. K.; Sridhar, B. *J. Org. Chem.* **2008**, *73*, 6857–6859; (b) Alizadeh, A.; Rostamnia, S.; Zhu, L. G. *Tetrahedron Lett.* **2010**, *51*, 4750–4754.
17. (a) Esmaili, A. A.; Bodaghi, A. *Tetrahedron* **2003**, *59*, 1169–1171; (b) Esmaeili, A. A.; Darbanian, M. *Tetrahedron* **2003**, *59*, 5545–5548; (c) Nair, V.; Vinod, A. U.; Abhilash, N.; Menon, R. S.; Santhi, V.; Varma, R. L.; Viji, S.; Mathewa, S.; Srinivas, R. *Tetrahedron* **2003**, *59*, 10279–10286; (d) Nair, V.; Devipriya, S.; Suresh, E. *Tetrahedron* **2008**, *64*, 3567–3577.
18. (a) Esmaelli, A. A.; Nazer, M. *Synlett* **2009**, 2119–2122; (b) Esmaeili, A. A.; Vesalipoor, H.; Hosseinabadi, R.; Zavareh, A. F.; Naseri, N. A.; Ghiamati, E. *Tetrahedron Lett.* **2011**, *52*, 4865–4867.
19. Kiruthika, S. E.; Lakshmi, N. V.; Banu, B. R.; Perumal, P. T. *Tetrahedron Lett.* **2011**, *52*, 6508–6511.
20. Sun, J.; Sun, Y.; Xia, E. Y.; Yan, C. G. *Eur. J. Org. Chem.* **2012**, 1976–1983.
21. (a) Sun, J.; Xia, E. Y.; Wu, Q.; Yan, C. G. *Org. Lett.* **2010**, *12*, 3678–3681; (b) Sun, J.; Xia, E. Y.; Wu, Q.; Yan, C. G. *ACS Comb. Sci.* **2011**, *13*, 421–426; (c) Sun, J.; Sun, Y.; Xia, E. Y.; Yan, C. G. *ACS Comb. Sci.* **2011**, *13*, 436–441; (d) Sun, J.; Wu, Q.; Xia, E. Y.; Yan, C. G. *Eur. J. Org. Chem.* **2011**, 2981–2986.
22. Zhu, Q.; Jiang, H. F.; Li, J.; Liu, S.; Xia, C.; Zhang, M. *J. Comb. Chem.* **2009**, *11*, 685–696.