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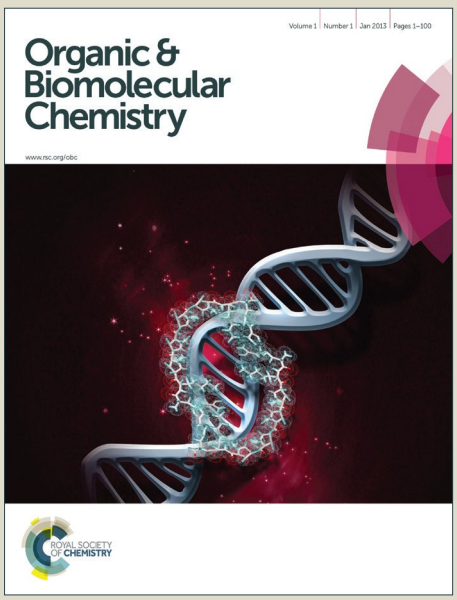

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Copper(I) catalyzed diastereoselective multicomponent synthesis of spiroindolo-pyrrolidines/-imidazolidines/-triazolidines from diazoamides via azomethine ylides

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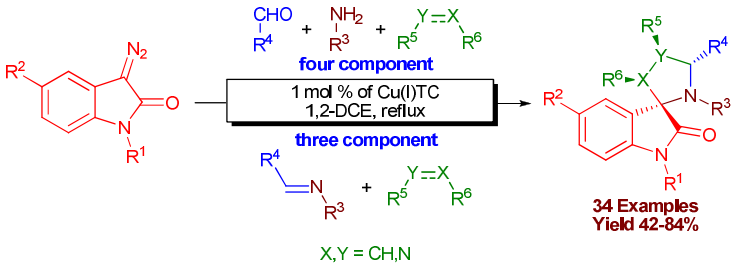
TOC: Investigations of regio-, chemo- and diastereoselective studies on three- / four-component reactions in the presence of copper(I) thiophene-2-carboxylate as a catalyst are described to afford spiroindolo-pyrrolidines/-imidazolidines/-triazolidines in good yields.



Keywords: Azomethine ylides / Copper(I) catalyst / Diastereoselectivity / Diazoamides / Multicomponent / Spiroheterocycles

Abstract: Investigations of regio-, chemo- and diastereoselective studies on three- as well as four-component reactions using diazooxindoles, imines, aldehydes, amines, alkenes, alkynes or diazenes in the presence of copper(I) thiophene-2-carboxylate are described to furnish spiroindolo-pyrrolidine/-imidazolidine/-triazolidine ring systems in good yields. A mixture of products was obtained when unsymmetrical alkenes used as dipolarophiles. This study demonstrates that the successful generation of intermolecular azomethine ylides from copper(I) carbenoids and their subsequent 1,3-dipolar cycloaddition reactions with various dipolarophiles, such as olefins (C=C), imines (C=N), diazenes (N=N) in a stereoselective manner. The single-crystal X-ray analyses were performed to establish unambiguously the structure and stereochemistry of spiroheterocyclic ring systems.

Introduction

The chemistry of diazo compounds has been widely explored and established useful applications in organic synthesis.[1] Organic transformations utilizing the reactive carbene intermediates, generated from thermolysis or photolysis of diazo compounds, found narrow synthetic applications due to the formation of a mixture of products.[2] In contrast, metallo-carbenoid species, generated from the transition metal-catalyzed reactions of diazo compounds, can undergo diverse reactions[3] such as X–H (X = C, Si, N, O etc.) insertion, cyclopropanation, ylide formation and 1,2-migration. Catalytic 1,3-dipolar cycloaddition reactions of ylides are among the most powerful tools for the efficient assembly of complex molecules. Among available methods to generate ylides from diazo compounds, dirhodium catalysts are found to be good based on their selectivity in obtaining products.[4] However, copper catalyzed decomposition of diazo compounds has a longer history, which has actually conquered in the literature[5] before the advent of the dirhodium catalysis reactions. Copper catalysts have obvious advantages due to their lower cost but occasionally less selective for reactions involving diazo compounds.[6] Among copper catalysts, the application of copper(I) thiophene-2-carboxylate (CuTC) as a catalyst have less focus[7] on diazo-mediated metal carbenoid chemistry. Multicomponent reaction (MCR) from simple starting materials is a very powerful method for the formation of carbon-carbon and carbon-heteroatom bonds in stereo-controlled manner and many variants have been developed in the past.[8] The generation of azomethine ylides and their 1,3-dipolar cycloaddition methodology have been shown as an important tool to construct nitrogen containing heterocycles with a high degree of regio- and stereocontrol.[9] Generally, azomethine ylides are being generated *via* thermolysis or photolysis of aziridines,[10a] deprotanation/desilylation/destannylation of imines,[10b] nucleophilic addition to oxazolium salts[10c] and decarboxylation of amino acids.[10d] Additionally, diazo compounds are also known to be useful in generating azomethine ylides for the construction of nitrogen

heterocyclic systems.[11] The spirooxindole moiety is present in a number of natural products such as horsfiline,[12a] elacomine,[12b] alstonisine,[12c] strychnofoline[12d] and spirotryprostatins A and B,[12e,f] as well as pharmaceutically and medically relevant compounds. The representative biologically active[13] spirooxindoloheterocycles are shown in Figure 1. In continuation of our interest on the chemistry[14] of ylides from cyclic diazoamides, we herein demonstrate three- as well as four-component reactions involving diazoamides for the construction of spiroindolo-pyrrolidine/-imidazolidine/-triazolidine ring systems *via* the generation of azomethine ylides in a diastereoselective manner.

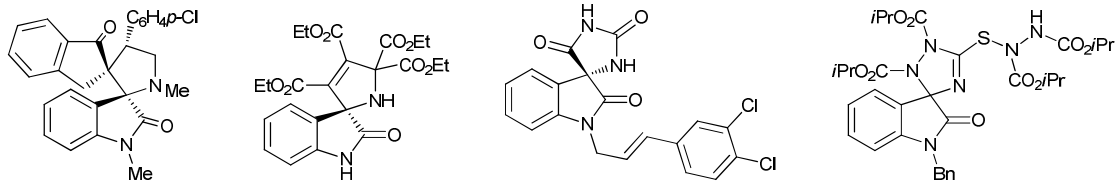


Figure 1. Selected biologically active spirooxindoloheterocycles

Results and discussion

To develop the multi-component reactions for spiroheterocycles, the required diazoamides **1** were assembled from isatin based on the literature[15] procedure. Multi-component reaction of 3-diazooxindole **1a** was initially studied to optimize with benzaldehyde, aniline and *N*-phenylmaleimide (NPM) in the presence of various metal catalysts (Table 1). Rhodium(II) acetate catalyzed reactions of cyclic diazoamides were well demonstrated[14] by us. Initial study on the feasibility of a 1,2-dichloroethane (1,2-DCE) solution containing an equimolar mixture of α-diazoamide **1a**, benzaldehyde, aniline and *N*-phenylmaleimide (NPM) in the presence of 1 mol % of rhodium(II) acetate at reflux for 1 hour afforded highly substituted spiroindolopyrrolidine **5a** in 72% yield (Table 1, entry 1) in a tandem manner. On the other hand, a low product yield was observed when the reaction performed in dichloromethane or toluene (Table 1, entries 2 and 3). The reaction was also performed in the presence of $Sc(OTf)_3$ or $Zn(OTf)_2$ but did not yield the desired product **5a** (Table 1, entries 4 and 5). The

reaction was also screened with various copper(I) and (II) catalysts (Table 1, entries 6-13). Reaction in the presence of copper(II) triflate furnished the less yield of product **5a** (Table 1, entry 6). Similarly, a low yield of the product was observed when the reaction performed in the presence of copper(I) catalysts such as CuOTf, CuI, CuCl, CuBr (Table 1, entries 7-10). Reaction at low or room temperature did not improve the product yield (Table 1, entries 11 and 12). Reaction in the presence of copper(I) thiophene-2-carboxylate as a catalyst in 1,2-DCE at reflux conditions furnished **5a** in 85% yield. Thus, the optimized reaction conditions were found to be the slow addition of diazoamide in the presence of 1 mol % of Cu(I)TC for the formation of **5a** (Table 1, entry 13). The ^{1}H NMR analysis of the crude reaction mixture shows **5a** as a single diastereomer under the above experimental conditions.

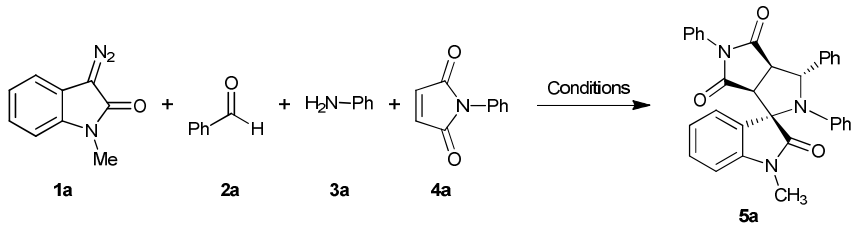


Table 1. Catalyst screening for the synthesis of spiroindolopyrrolidine **5a**[a]

entry	catalyst	solvent	time (hrs)	yield (%)
1	$Rh_2(OAc)_4$	1,2-DCE	3	72
2	$Rh_2(OAc)_4$	DCM	3	43
3	$Rh_2(OAc)_4$	toluene	2	48
4	$Sc(OTf)_3$	1,2-DCE	6	Nr
5	$Zn(OTf)_2$	1,2-DCE	6	Nr
6	$Cu(OTf)_2$	1,2-DCE	4	28
7	CuOTf	1,2-DCE	3	42
8	CuI	1,2-DCE	4	46
9	CuCl	1,2-DCE	5	39
10	CuBr	1,2-DCE	4	42
11	Cu(I)TC[b]	1,2-DCE	4	68
12	Cu(I)TC[c]	1,2-DCE	4	32
13	Cu(I)TC	1,2-DCE	2	85

[a]The reaction was carried out by adding a solution of diazo compound (1 mmol) over a period of 1 h via syringe pump with the flow rate of 2 mL/h to a mixture of aldehyde (1.1 mmol), amine (1.1 mmol), NPM (1.2 mmol) in the presence of 1 mol % of catalyst under an argon atmosphere at reflux conditions. [b]The reaction was carried out at room temperature. [c]The reaction was carried out at 0 °C. Nr = No reaction

To investigate the scope of this methodology, reactions involving various diazoamides, aldehydes, amines and olefins were carried out (Table 2) under the above optimized reaction conditions. Imines, generated *in situ* from aldehydes **2** and amines **3** with varying substituents

(R^3, R^4 = H, OMe, Cl, Me), were allowed to react with substituted diazomides **1** to produce azomethine ylides. Subsequent [3+2]-cycloaddition reaction with alkenes such as NPM, dimethyl maleate yielded spiroindolopyrrolidines **5a,b**. Reaction with alkynes such as DMAD afforded spirodihydropyrrolidine **5c** in good yield. The effect of electron-donating substituents such as methoxy, dimethoxy or naphthyl group on aldehydes was examined to result a facile access to spiroindolopyrrolidines **5d-f** in good yield. However, reaction of aldehydes having electron-withdrawing groups such as nitro- or bromo-substituent provided the corresponding products **5g,h** in moderate to good yield. The incorporation of electron-donating or -withdrawing group on amines provided the corresponding spiroindolopyrrolidines **5i,j** in good yields with complete diastereoselectivity. But, the reaction involving 4-nitroaniline did not provide the corresponding product. The structure and stereochemistry of product **5j** were confirmed using single-crystal X-ray analysis (Figure 2) and similar stereochemistry was tentatively assigned for other spiroindolopyrrolidines **5**.

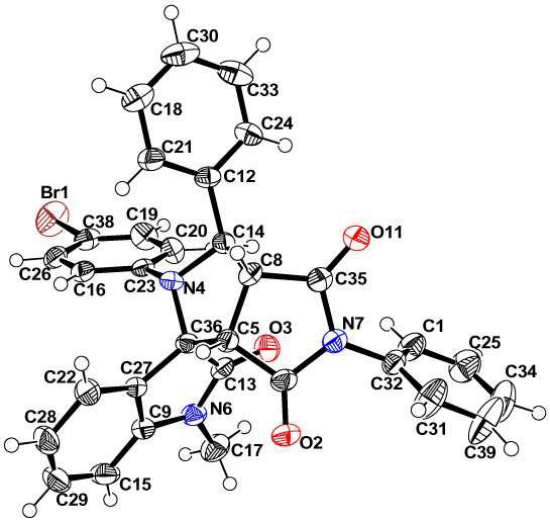
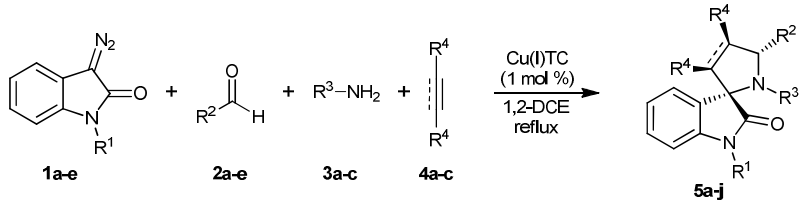
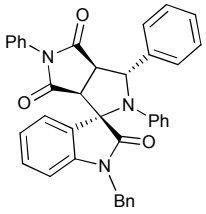


Figure 2. ORTEP view of **5j** with 50% probability ellipsoids.

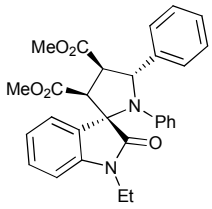
Table 2. Diastereoselective synthesis of spiro-indolopyrrolidines **5** *via* four-component reactions



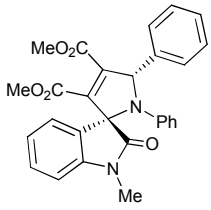
1a-e **2a-e** **3a-c** **4a-c** **5a-j**



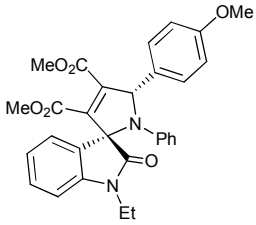
5a, 79%



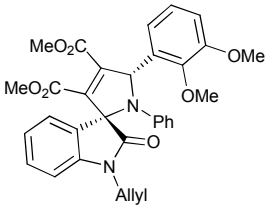
5b, 76%



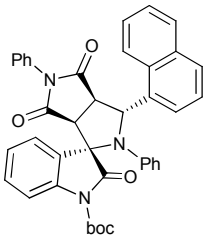
5c, 77%



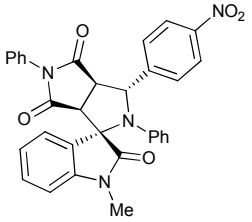
5d, 82%



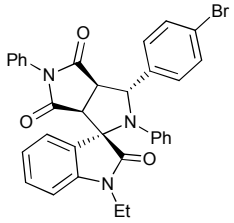
5e, 76%



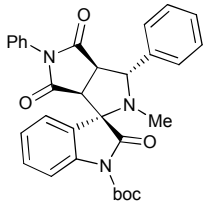
5f, 79%



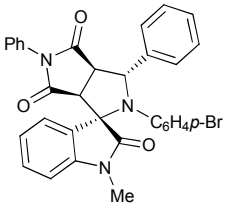
5g, 42%



5h, 73%



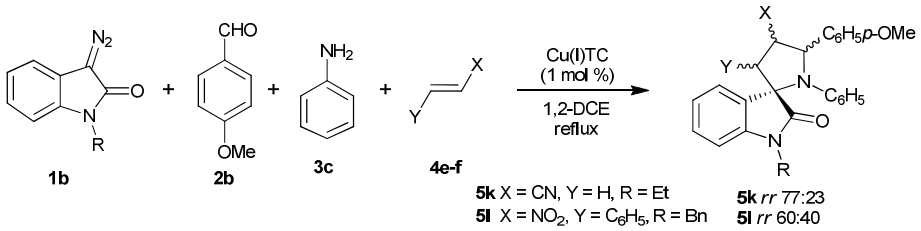
5i, 78%



5j, 73%

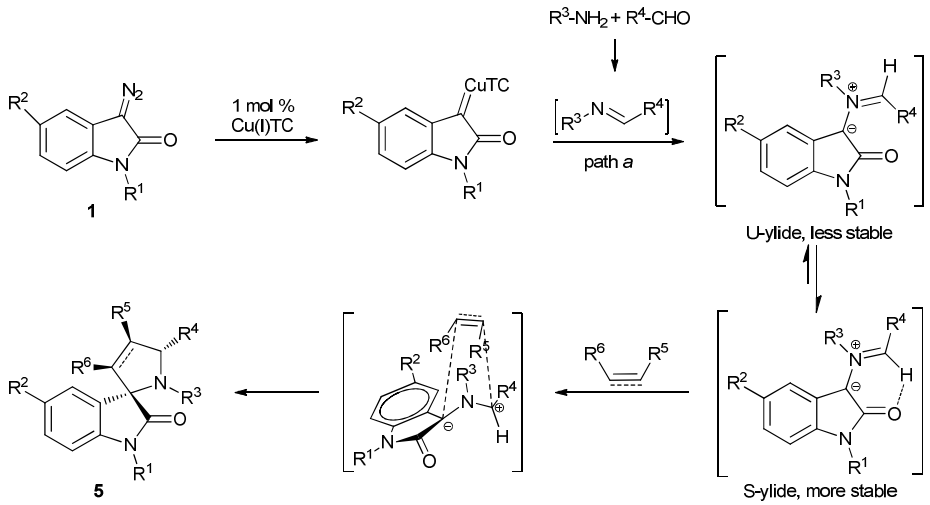
Reaction with unsymmetrical dipolarophiles such as acrylonitrile, nitrostyrene furnished a mixture of isomers (Scheme 1). The ratio could not be determined based on NMR studies of the crude reaction mixture but the HPLC analyses revealed the ratio of 77:23. The above four component reaction (4-CR) can be switched into three component (3-CR) by utilizing the already prepared imines, from amines **2** and aldehydes **3**, as one of the starting materials. Thus, the three-component reaction of 1 mmol of diazoamide **1a**, 1.1 mmol of imine, 1.2

mmol of alkene **4a** in the presence of 1 mol % of Cu(I)TC provided spiroindolopyrrolidine **5a** in 82% yield with complete diastereoselectivity. To study the scope of three component reaction, similar reaction was performed to furnish spiroindolopyrrolidines **5b-e** (Table 5).



Scheme 1. Synthesis of spiro-indolopyrrolidines **5** with unsymmetrical alkenes

A plausible mechanism for the formation of spiroindolopyrrolidines is illustrated in Scheme 2. The initially generated copper(I) carbenoids, generated from the reaction of diazoamides with a catalytic amount of Cu(I)TC, react with imines, generated from aldehydes and amines, providing azomethine ylide intermediates. The subsequent intermolecular 1,3-dipolar cycloaddition reaction of azomethine ylides with symmetrical alkenes/alkynes furnished the corresponding cycloadducts **5** with complete diastereoselectivity. The azomethine ylide dipoles can have both S- or U-shaped conformations. Out of these, S-shaped conformation is relatively more stable than U-shaped due to the presence of possible hydrogen bond[14g] between amide carbonyl and imine proton affording a single diastereomer. The stereochemistry and diastereoselectivity of spiroindolopyrrolidine **5j** were unequivocally corroborated based on the single crystal X-ray analysis (Fig. 2). Similar stereochemistry was tentatively assigned for other spiropyrrolidines **5**. We did not observe any other side-products due to the reaction of diazoamides **1** with aromatic aldehydes (carbonyl ylides)[14a] and anilines (N-H insertion)[14b] in the presence of rhodium catalyst.



Scheme 2. Plausible mechanism

After studying the synthesis of spiroindolopyrrolidines with alkenes/alkynes, reactions of azomethine ylides were planned with two equivalents of imines having electronic differences to furnish spiroindoloimidazolidines. Towards this, the four-component reaction of diazoamide **1a**, electron-withdrawing tosyl-substituted imine **6a**, electron-donating aldehyde **2a** and amine **3a** in the presence of Cu(I)TC provided spiroindoloimidazolidine **7a** in 74% yield with complete chemo- and regioselectivity (Table 3). The initially generated azomethine ylide from diazoamide and imine, formed from electron-donating aldehyde and amine, underwent [3+2]-cycloaddition with electron-withdrawing tosyl-substituted imine furnished spiroindoloimidazolidine in a chemo- and diastereoselective manner. In order to study the scope of this reaction, electron-withdrawing nitro-substituted imine was utilized to synthesize spiroindoloimidazolidines **7c-d** in good yield. Similar reaction with methoxy-substituted benzaldehydes or naphthaldehyde with electron-withdrawing nitro-substituted imine furnished the corresponding spiroindoloimidazolidines **7e-g** in good yield. Interestingly, the heteroaryl aldehyde such as thiophene-2-aldehyde furnished the corresponding spiroimidazolidine **7h** in better yield. For example, electron-withdrawing bromo- or nitro-substituents on aromatic aldehyde afforded good yield of spiro compounds

7i,j. The utilization of methyl- or bromo-substituted amine also provided products **7k,l** in good yield with complete diastereoselectivity (Table 3). The spectral data evidently confirm the proposed structure of spiroindoloimidazolidines **7** in a chemo- and diastereoselective manner. The structure and stereochemistry of spiroindoloimidazolidine **7a** were determined on the basis of X-ray crystallographic analysis (Figure 3) and similar stereochemistry was tentatively assigned for other spiro products **7**. Representative three component of reaction of diazoamides **1** was also carried out with two equivalents of already synthesized imines having electron-donating and -withdrawing substituents in the presence of Cu(I)TC also furnished spiroindoloimidazolidines **7a-e** in good yield (Table 5).

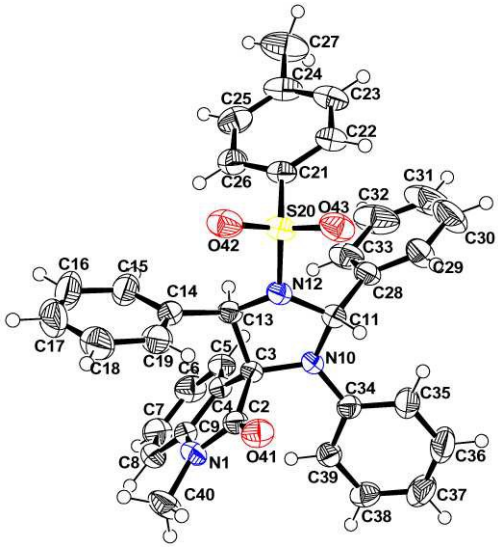
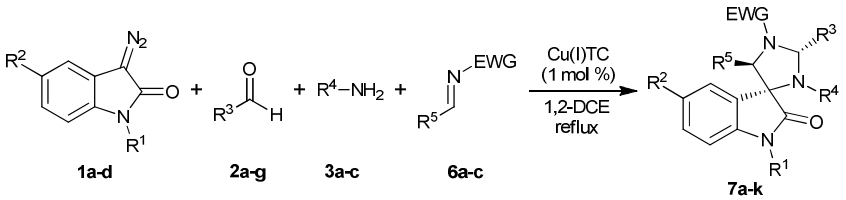
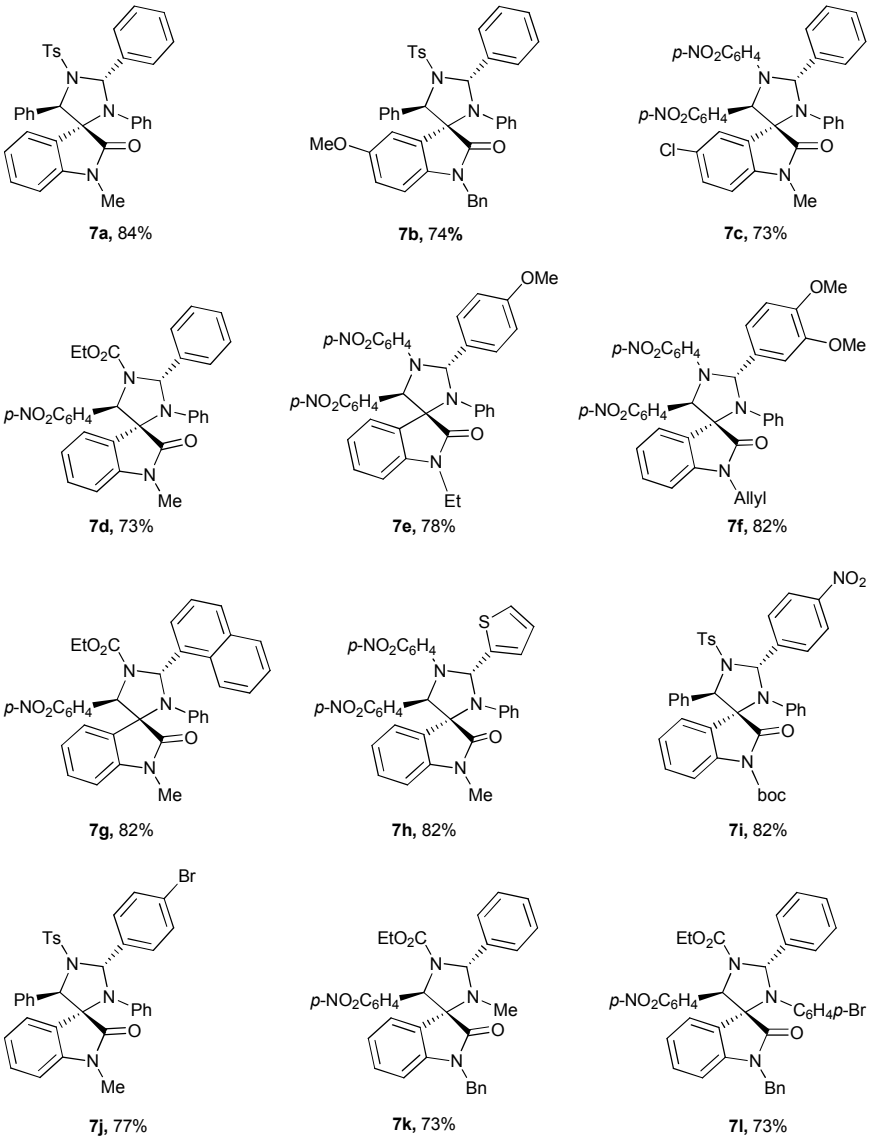


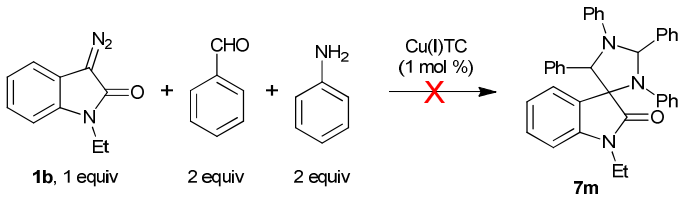
Figure 3. ORTEP view of **7a** with 50% probability ellipsoids.

Table 3. Regio- and chemoselective synthesis of spiro-indoloimidazolidines **7** with imines





Next, the above reaction was repeated as an equivalent to five component reaction with 1 equiv of diazoamide **1b** and 2.2 equiv of benzaldehyde and aniline in the presence of Cu(I)TC to furnish a complex mixture instead of the corresponding spiroindoloimidazolidine **7m**. The reason might be the formation of the corresponding azomethine ylide, derived from **1b** and *in situ* generated imine, could not undergo [3+2]-cycloaddition as there was no difference in the electronic property between imines (Scheme 3).



Scheme 3. Reaction of diazoamide **1b** with an excess amount of aldehyde and amine

Encouraged by the above results of copper-catalyzed intermolecular [3+2]-cycloaddition of azomethine ylide intermediates with alkenes/alkynes/imines, exploration of the reaction of azomethine ylides with diazenes **8** was planned to construct spiroindolotriazolidines **9** with stereoselectivity. Thus, the four-component reaction of diazoamide **1a**, triazole-3,5-dione **8a**, electron-donating aldehyde **2a** and amine **3a** in the presence of Cu(I)TC provided spiroindolotriazolidine **9a** in 74% yield with complete diastereoselectivity (Table 4). Further, the substrate scope was examined with varying substitutents on starting materials. The electronic effect of aromatic aldehydes was examined with substituents such as methoxy or dimethoxy groups. Reaction of the electron-donating aromatic aldehydes with triazole-3,5-dione or DEAD afforded the desired spiroindolotriazolidines **9b-d** in good yields with complete diastereoselectivity. Similar reaction with naphthaldehyde furnished the corresponding spirotriazolidine **9e** in better yield. Reaction with electron-withdrawing groups such as nitro- or bromo-substituent on aromatic aldehyde provided the corresponding products **9f,g**. These results indicate that electron-donating or -withdrawing substituent on aldehydes gave comparable yield of spiroindolotriazolidines. Reaction of diazoamide **1** with electron-donating or -withdrawing substituents on amine part was performed to furnish products **9h-j** with good diastereoselectivity. In order to demonstrate the above reaction via three component reaction (3-CR), reaction of diazoamides **1**, imines and diazenes **8** was carried out to afford spiroindolotriazolidines **9a-f** with the comparable yield obtained from four component reactions (Table 5).

Table 4. Synthesis of spiroindolotriazolidines **9** with diazenes

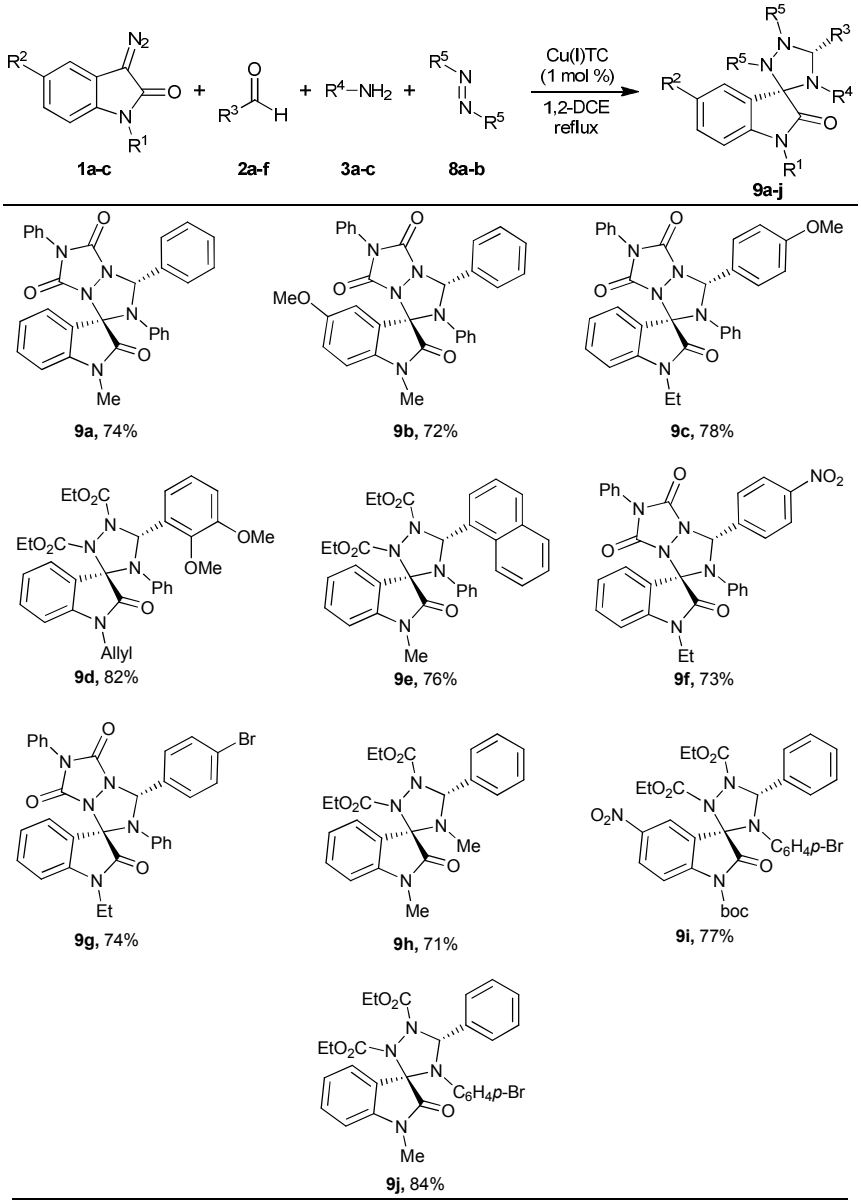
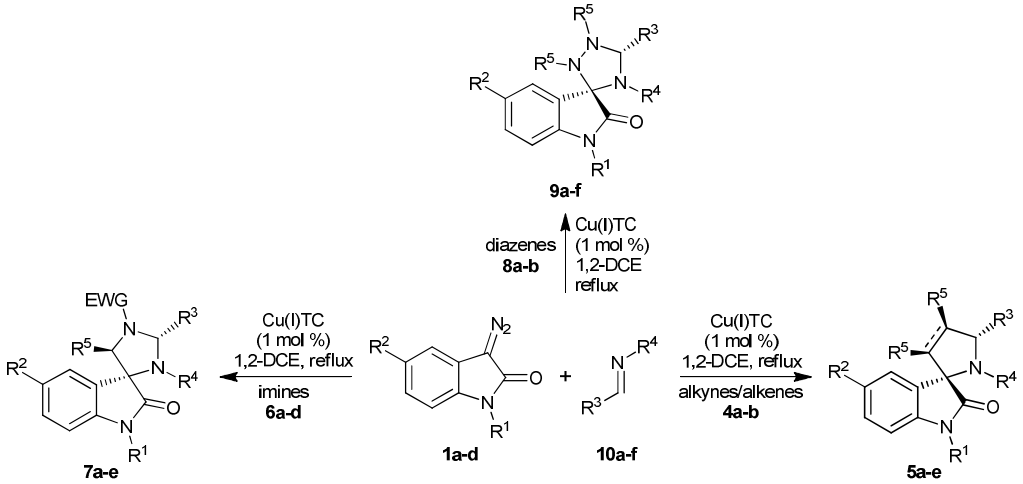


Table 5. Yield comparison of four (4-CR) and three component reactions (3-CR)



s.no	compound	yield (%) from 4-CR	yield (%) from 3-CR
1	**5a**	79	82
2	**5b**	76	81
3	**5c**	77	79
4	**5d**	82	74
5	**5e**	76	43
6	**7a**	84	76
7	**7b**	74	79
8	**7c**	73	83
9	**7d**	73	76
10	**7e**	78	81
11	**9a**	74	75
12	**9b**	72	77
13	**9c**	78	84
14	**9d**	82	82
15	**9e**	76	77
16	**9f**	73	78

Conclusion

In conclusion, an efficient Cu(I)TC catalyzed synthesis of highly substituted spiroindolo-pyrrolidines/-imidazolidines/-triazolidines *via* azomethine ylide intermediates, generated from aldehydes, amines and diazoamides, followed by their 1,3-dipolar cycloaddition reaction with alkenes/alkynes/imines/diazenes was demonstrated. The Cu(I)TC catalyzed synthesis of spiroindoloheterocycles *via* four-component (4-CR) as well as three-component reaction (3-CR) was also demonstrated and up to four chemical bonds were formed in a single-step with complete regio-, chemo- and diasteroselectivity. The biological activity of these synthesized interesting spiroindoloheterocycles is in progress.

Experimental Section

All reagents were from commercial sources and were used as received. All solvents were distilled and dried according to standard procedures. Thin layer chromatography was carried out on aluminium sheets coated with silica gel (40−63 μm). Compound detection was achieved by exposure to iodine or UV light (254 nm). The melting points are uncorrected. Infrared spectra were recorded using ATR technique. All samples were analyzed in $CDCl_3$ on ^1H NMR at 400 MHz and ^{13}C NMR at 100 MHz at 25 ºC. Chemical shifts were expressed in ppm with TMS as an internal standard (δ = 0 ppm) for NMR. Abbreviations used for multiplicities of coupled signals were designated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet signal and are given in hertz. HR-MS spectra were recorded on a mass spectrometer equipped for ESI+ experiments.

All air sensitive reactions were conducted in oven-dried glassware under a positive pressure of an argon or nitrogen with magnetic stirring. Imines and CuTC were prepared using the literature methods.

General experimental procedure for the synthesis for spiroindoloheterocycles

Method A (Four component reaction): Under an argon atmosphere, a mixture of aldehyde (1.1 mmol), amine (1.1 mmol), dipolarophile (1.2 mmol) and copper(I) thiophenecarboxylate (1 mol %) was taken in dichloroethane (15 mL) with stirring for 5 minutes and then N-substituted 3-diazooxindole (1 mmol) in dichloroethane (3 mL) was slowly added using syringe pump with the flow rate of 3 mL/h (0.05 mL/min) at reflux conditions and continued until the reaction completed (monitored using TLC). The reaction mixture was concentrated and the resulting residue subjected to column chromatography using silica gel (100-200 mesh) to give the corresponding spiroindoloheterocycles.

Method B (Three component reaction): Under an argon atmosphere, a mixture of imine (1.1 mmol), dipolarophile (1.2 mmol) and copper(I) thiophenecarboxylate (1 mol %) was taken in dichloroethane (15 mL) with stirring and then N-substituted 3-diazooxindole (1 mmol) in

dichloroethane (3 mL) was added using syringe pump with the flow rate of 3 mL/h (0.05 mL/min) at reflux conditions and continued until the reaction completed (monitored using TLC). The reaction mixture was purified as described in Method A.

1-Benzyl-2',3',5'-triphenyl-3',3a'-dihydro-2'H-spiro[indoline-3,1'-pyrrolo[3,4-c]pyrrole]-2,4',6'(5'H,6a'H)-trione (**5a**). According to the general procedure, to a solution of aldehyde **2a** (45 mg, 0.42 mmol), amine **3a** (40 mg, 0.43 mmol), *N*-phenylmaleimide **4a** (85 mg, 0.49 mmol) and copper(I) thiophenecarboxylate (0.8 mg, 1 mol %) in dichloroethane was transferred diazoamide **1a** (100 mg, 0.4 mmol). Purification gave the corresponding spiroindolopyrrolidine **5a** as a white solid; yield: 196 mg (79%); Eluent: hexane/EtOAc, 90:10. R_f = 0.42 (hexane/EtOAc, 9:1); mp 153-154 ºC; IR (neat): ν_{max} 3062, 2923, 2854, 1780, 1713, 1613, 1597, 1492, 1380, 1261, 1176, 1075, 1103, 732, 693, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.78-7.76 (m, 1H, ArH), 7.59 (d, J = 7.6 Hz, 2H, ArH), 7.18-7.48 (m, 10H, ArH), 7.06-7.13 (m, 3H, ArH), 6.90-6.95 (m, 3H, ArH), 6.77-6.79 (m, 2H, ArH), 6.63 (d, J = 7.2 Hz, 2H, ArH), 6.47-6.49 (m, 1H, ArH), 5.98 (d, J = 6.4 Hz, 1H, CH), 4.93 (d, J = 16 Hz, 1H, CH), 4.42 (d, J = 16 Hz, 1H, CH), 4.12 (d, J = 10 Hz, 1H, CH), 3.69-3.73 (dd, J_1 = 6.5 Hz, J_2 = 10 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.47 (*C*=O), 176.93 (*C*=O), 175.92 (*C*=O), 156.07 (*quat-C*), 154.84 (*quat-C*), 152.83 (*quat-C*), 144.49 (*C*H), 143.83 (*quat-C*), 142.28 (*quat-C*), 141.22 (*C*H), 133.67 (*C*H), 132.13 (*C*H), 131.07 (*C*H), 130.95 (*C*H), 130.60 (*C*H), 130.57 (*C*H), 130.12 (*quat-C*), 129.53 (*C*H), 128.81 (*C*H), 128.74 (*C*H), 125.95 (*C*H), 125.77 (*C*H), 125.31 (*C*H), 125.03 (*C*H), 110.84 (*C*H), 76.31 (*quat-C*), 67.44 (*C*H), 54.89 (*C*H), 54.09 (*C*H), 31.51 (CH_2); HRMS (ESI) Calcd for $C_{38}H_{29}N_3O_3$ [$(M+H)^+$] 576.2287, found 576.2281.

Dimethyl 1-ethyl-2-oxo-1',5'-diphenylspiro[indoline-3,2'-pyrrolidine]-3',4'-dicarboxylate (**5b**). According to the general procedure, to a solution of aldehyde **2a** (60 mg, 0.57 mmol), amine **3a** (55 mg, 0.59 mmol), dimethyl maleate **4b** (90 mg, 0.63 mmol) and copper(I)

thiophenecarboxylate (1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1b** (100 mg, 0.53 mmol). Purification furnished the corresponding spiroindolopyrrolidine **5b** as a white solid; yield : 195 mg (76%): R_f = 0.42 (hexane/EtOAc, 9:1); mp 167-169 ºC; IR (neat): ν_{max} 3042, 2894, 2874, 1748, 1735, 1628, 1567, 1475, 1428, 1442, 1358, 1276, 1059, 732, 693, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88-7.93 (m, 3H, ArH), 7.46-7.76 (m, 5H, ArH), 7.20-7.28 (m, 3H, ArH), 6.94 (t, *J* = 7.2 Hz, 1H, ArH), 6.57-6.61 (m, 3H, ArH), 3.64-3.87 (m, 5H, OCH_3 & NCH_2), 3.57 (s, 3H, OCH_3), 2.40 (d, *J* = 10 Hz, 1H, CH), 2.14-2.09 (dd, J_1 = 6.4 Hz, J_2 = 9.6 Hz, 1H, CH) 1.24 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.14 (*C*=O), 169.88 (*C*=O), 167.83 (*C*=O), 150.91 (*quat-C*), 150.39 (*quat-C*), 150.23 (*quat-C*), 144.77 (*quat-C*), 139.53 (*quat-C*), 137.05 (*C*H), 135.60 (*C*H), 135.55 (*C*H), 135.48 (*quat-C*), 135.10 (*C*H), 133.61 (*C*H), 131.24 (*C*H), 130.08 (*C*H), 126.11 (*C*H), 121.63 (*C*H), 115.54 (*C*H), 84.28 (*quat-C*), 77.74 (*C*H), 58.96 (CH_2), 53.66 (O*C*H_3), 52.63 (O*C*H_3), 35.06 (*C*H), 33.26 (*C*H), 12.17 (*C*H_3); HRMS (ESI) Calcd for $C_{29}H_{28}N_2O_5$ [$(M+H)^+$] 485.2076, found 485.2087.

Dimethyl 1-methyl-2-oxo-1',5'-diphenyl-1',5'-dihydrospiro[indoline-3,2'-pyrrole]-3',4'-dicarboxylate (**5c**). According to the general procedure, to a solution of aldehyde **2a** (65 mg, 0.61 mmol), amine **3a** (60 mg, 0.64 mmol), DMAD **4c** (100 mg, 0.70 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dicholoroethane was transferred a solution of diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindolodihydropyrrole **5c** as a white solid; yield: 209 mg (77%). R_f = 0.54 (hexane/EtOAc, 8:2); mp 144-146 ºC; IR (neat): ν_{max} 3052, 2904, 2854, 1780, 1711, 1613, 1597, 1492, 1455, 1435, 1379, 1310, 1261, 1176, 1029, 732, 693, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.58-7.63 (m, 3H, ArH), 7.28-7.47 (m, 5H, ArH), 7.19 (t, *J* = 7.5 Hz, 1H, ArH), 6.82 (d, *J* = 7.6 Hz, 1H, ArH), 6.92 (t, *J* = 7.8 Hz, 1H, ArH), 6.64 (t, *J* = 7.1 Hz, 1H, ArH), 6.32-6.28 (m, 3H, ArH), 3.65 (s, 3H, OCH_3), 3.51 (s, 3H, OCH_3), 3.26 (s, 3H, NCH_3); ^{13}C

NMR ($CDCl_3$, 100 MHz) δ 173.52 (*C*=O), 163.26 (*C*=O), 161.22 (*C*=O), 144.29 (*quat-C*), 143.77 (*quat-C*), 143.61 (*quat-C*), 138.15 (*quat-C*), 132.91 (*quat-C*), 130.43 (*quat-C*), 128.98 (*quat-C*), 128.93 (*C*H), 128.86 (*quat-C*), 128.48 (*C*H), 126.99 (*C*H), 124.62 (*C*H), 123.46 (*C*H), 119.49 (*C*H), 115.01 (*C*H), 108.92 (*C*H), 77.66 (*quat-C*), 71.1 (O*C*H_3), 52.34 (O*C*H_3), 26.64 (N*C*H_3); HRMS (ESI) Calcd for $C_{28}H_{24}N_2O_5$ [$(M+H)^+$] 469.1763, found 469.1758.

Dimethyl 1-ethyl-5'-(4-methoxyphenyl)-2-oxo-1'-phenyl-1',5'-dihydrospiro[indoline-3,2'-pyrrole]-3',4'-dicarboxylate (**5d**). According to the general procedure, to a solution of aldehyde **2b** (80 mg, 0.59 mmol), amine **3a** (55 mg, 0.59 mmol), DMAD **4c** (90 mg, 0.63 mmol) and copper(I) thiophenecarboxylate (1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1b** (100 mg, 0.53 mmol). Purification furnished the corresponding spiroindolodihydropyrrole **5d** as a white solid; yield: 223 mg (82%): R_f = 0.42 (hexane/EtOAc, 9:1); mp 163-165 ºC; IR (neat): ν_{max} 3062, 2924, 2854, 1780, 1711, 1613, 1597, 1492, 1455, 1435, 1379, 1310, 1261, 1176, 1029, 732, 693, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.62 (d, *J* = 6.8 Hz, 1H, ArH), 7.51 (d, *J* = 8.8 Hz, 2H, ArH), 7.43 (td, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.15-7.19 (m, 1H, ArH), 6.89-6.99 (m, 5H, ArH), 6.39 (t, *J* = 7.2 Hz, 1H, ArH), 6.34 (d, *J* = 8.4 Hz, 2H, ArH), 6.23 (s, 1H, CH), 3.70-3.87 (m, 5H), 3.66 (s, 3H, OCH_3), 3.5 (s, 3H, OCH_3), 1.24 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.99 (*C*=O), 163.31 (*C*=O), 161.34 (*C*=O), 159.59 (*quat-C*), 144.21 (*quat-C*), 143.71 (*quat-C*), 142.77 (*quat-C*), 133.02 (*quat-C*), 130.32 (*quat-C*), 130.15 (*quat-C*), 129.12 (*quat-C*), 129.02 (*quat-C*), 128.83 (*C*H), 128.26 (*C*H), 124.84 (*C*H), 123.2 (*C*H), 119.53 (*C*H), 115.41 (*C*H), 114.28 (*C*H), 114.16 (*C*H), 109.01 (*C*H), 77.54 (*quat-C*), 70.47 (O*C*H_3), 55.2 (*C*H), 52.33 (*C*H_3), 52.2 (*C*H_3), 35.06 (*C*H_2), 12.17 (*C*H_3); HRMS (ESI) Calcd for $C_{30}H_{28}N_2O_6$ [$(M+H)^+$] 513.2026 , found 513.2037.

5'-(4-Bromophenyl)-1-methyl-2',3'-diphenyl-3',3a'-dihydro-2'H-spiro[indoline-3,1'-pyrrolo[3,4-c]pyrrole]-2,4',6'(5'H,6a'H)-trione (**5j**). According to the general procedure, to a

solution of aldehyde **2a** (65 mg, 0.61 mmol), amine **3c** (110 mg, 0.64 mmol), *N*-phenylmaleimide **4a** (120 mg, 0.69 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindolopyrrolidine **5j** as a white solid; yield : 244 mg (73%): R_f = 0.27 (hexane/EtOAc, 6:4); mp 167-169 ºC; IR (neat): ν_{max} 3059, 2832, 2844, 1758, 1701, 1633, 1577, 1472, 1448, 1398, 1276, 1186, 1095, 1123, 728, 639, 668 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69 (d, *J* = 7.2 Hz, 1H, ArH), 7.53 (d, *J* = 7.6 Hz, 2H, ArH), 7.45-7.49 (m, 2H, ArH), 7.21-7.42 (m, 8H, ArH), 7.01 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.53-6.57 (m, 2H), 5.82 (d, *J* = 6.0 Hz, 1H), 4.04 (d, *J* = 10.4 Hz, 1H), 3.69-3.65 (dd, J_1 = 6.0 Hz, J_2 = 10.4 Hz, 1H, CH), 2.95 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.8 (*C*=O), 176.26 (*C*=O), 175.23 (*C*=O), 145.24 (*quat-C*), 143.32 (*quat-C*), 141.53 (*quat-C*), 132.98 (*quat-C*), 132.60 (*quat-C*), 131.75 (*C*H), 130.35 (*C*H), 130.11 (*C*H), 130.00 (*quat-C*), 129.14 (*C*H), 128.12 (*C*H), 128.07 (*C*H), 126.06 (*C*H), 125.26 (*C*H), 124.84 (*C*H), 118.36 (*C*H), 110.48 (*quat-C*), 75.57 (*C*H), 66.98 (*C*H), 54.33 (*C*H), 53.34 (*C*H), 27.10 (CH_3); HRMS (ESI) Calcd for $C_{32}H_{24}BrN_3O_3$ [$(M+Na)^+$] 600.0899, found 600.0889.

Crystal data for compound 5j: (CCDC 1432259) $C_{32}H_{24}BrN_3O_3$, colourless, plates, *M* = 578.45, 0.31 × 0.22 × 0.14 mm, Triclinic, space group P-1 with *a* = 9.6198(8) Å, *b* = 11.1689(9) Å, *c* = 13.4682(6)Å, *α* = 113.744(6)°, β = 93.929(5)°, *γ* = 90.612(7)°, *V* = *1320.30(16)Å^3,* T = *251(18) K, R_1 = 0.0513, wR_2* = 0.1299 on observed data, z = 2, D_{calcd} = 2.910 mg cm^{-3}, *F(000)* = 592.0, Absorption coefficient = 1.596 mm^{-1}, *λ* = 0.7107 Å, 4868 reflections were collected on asmart apex CCD single crystal diffractometer 3260 observed reflections (*I*≥2σ (*I*)). The largest difference peak and hole = 0.398 and -0.550 $eÅ^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL–97 software.

1-Ethyl-5'-(4-methoxyphenyl)-2-oxo-1'-phenylspiro[indoline-3,2'-pyrrolidine]-4'-carbonitrile (**5k**). According to the general procedure, to a solution of aldehyde **2b** (80 mg, 0.59 mmol), amine **3a** (55 mg, 0.59 mmol), acrylonitrile **4d** (35 mg, 0.64 mmol) and copper(I) thiophenecarboxylate (1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1b** (100 mg, 0.53 mmol). Purification furnished the corresponding mixture of spiroindolopyrrolidines **5k** as a white solid; yield : 186 mg (83%); *rr* : 77:23; R_f = 0.41 (hexane/EtOAc, 8:2); mp 157-159 ºC; IR (neat): ν_{max} 3068, 2876, 2676, 1758, 1698, 1676, 1652, 1487, 1298, 1098, 1035, 727 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (for major isomer) δ 7.76 (d, *J* = 8.4 Hz, 1H, ArH), 7.60 (t, *J* = 8 Hz, 2H, ArH), 7.53 (s, 1H, ArH), 7.32 (d, *J* = 8.4 Hz, 3H, ArH), 7.24 (d, *J* = 8.0 Hz, 3H, ArH), 7.09 (d, *J* = 7.6 Hz, 3H, ArH), 6.41 (s, 1H, CH), 4.12-4.18 (m, 5H), 2.58 (t, *J* = 8 Hz, 1H), 2.46 (t, *J* = 7.2 Hz, 1H), 2.22-2.25 (dd, J_1 = 5.2 Hz, J_2 = 9.2 Hz, 1H), 1.60 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.06 (*C*=O), 155.35 (*quat-C*), 152.58 (*quat-C*), 143.23 (*quat-C*), 128.79 (CH), 126.29 (*C*H), 125.55 (*C*H), 122.33 (*C*H), 119.02 (*C*H), 115.91 (*C*H), 112.32 (*C*H), 111.99 (*C*H), 108.88 (*C*H), 100.89 (*C*H), 55.77 (*C*H), 35.42 (CH), 31.80 (CH), 21.21 (CH), 15.12 (*C*H), 12.82 (*C*H). HRMS (ESI) Calculated for $C_{27}H_{25}N_3O_2$ [$(M+H)^+$]: 424.2025 found: 424.2031.

1-Benzyl-5'-(4-methoxyphenyl)-4'-nitro-1',3'-diphenylspiro[indoline-3,2'-pyrrolidin]-2-one (**5l**). According to the general procedure, to a solution of aldehyde **2b** (60 mg, 0.44 mmol), amine **3a** (40 mg, 0.43 mmol), *trans*-β-nitrostyrene **4e** (70 mg, 0.47 mmol) and copper(I) thiophenecarboxylate (0.8 mg, 1 mol %) in dichloroethane was transferred diazoamide **1a** (100 mg, 0.4 mmol). Purification furnished the corresponding mixture of spiroindolopyrrolidines **5l** as a white solid; yield : 184 mg (79%); *rr* : 80:20: R_f = 0.41 (hexane/EtOAc, 8:2); mp 157-159 ºC; IR (neat): ν_{max} 3038, 2918, 2799, 1758, 1728, 1652, 1622, 1398, 1250, 1075, 1025, 732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (for major isomer) δ 7.83 (s, 1H, ArH), 7.60 (s, 2H, ArH), 7.20 (d, *J* = 20.8 Hz, 6H, ArH), 6.83-6.97 (m, 6H,

ArH), 6.65-6.72 (m, 6H, ArH), 6.52 (s, 1H, ArH), 6.28 (s, 2H, ArH), 5.79 (d, J = 8.4 Hz, 1H, CH), 4.57-4.65 (dd, J_1 = 12.4 Hz, J_2 = 20.8 Hz, 3H, CH), 3.79 (d, J = 36.8 Hz, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.66 (*C*=O), 160.11 (*quat-C*), 159.87 (*quat-C*), 144.75 (*quat-C*), 142.39 (*quat-C*), 134.84 (*quat-C*), 130.02 (*quat-C*), 129.18 (*C*H), 128.97 (*quat-C*), 128.59 (*C*H), 128.10 (*C*H), 127.55 (*C*H), 127.05 (*C*H), 123.65 (*C*H), 123.60 (*C*H), 122.18 (CH), 119.73 (CH), 115.48 (CH), 114.49 (*C*H), 114.03 (*C*H), 110.32 (*C*H), 85.65 (*C*H), 73.92 (CH), 65.09 (*C*H), 55.25 (*C*H), 54.54 (*C*H), 43.90 (CH). HRMS (ESI) Calculated for $C_{37}H_{31}N_3O_4$ [$(M+H)^+$]: 582.2393 found: 582.2402.

1'-Methyl-2,3,5-triphenyl-1-tosylspiro[imidazolidine-4,3'-indolin]-2'-one (**7a**). According to the general procedure, to a solution of aldehyde **2a** (70 mg, 0.63 mmol), amine **3a** (60 mg, 0. 64 mmol), *N*-benzylidene benzenesulfonamide **6a** (180 mg, 0.69 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindoloimidazolidine **7a** as a white solid. Eluent: hexane/EtOAc, 90:10. R_f = 0.39 (hexane/EtOAc, 9:1); yield: 285 mg (84%); mp 163-164 ºC; IR (neat): ν_{max} 3162, 2852, 2835, 1722, 1712, 1625, 1542, 1422, 1261, 1152, 1063, 752, 632 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, J = 2 Hz, 1H, ArH), 7.94 (d, J = 7.2 Hz, 3H, ArH), 7.73 (d, J = 6.8 Hz, 2H, ArH), 7.59 (s, 1H, ArH), 7.47 -7. 58 (m, 7H, ArH), 7.34 -7. 42 (m, 3H, ArH), 6.96 (t, J = 8.4 Hz, 2H, ArH), 6.64-6.73 (m, 3H, ArH), 6.13 (d, J = 8 Hz, 2H, ArH), 5.31 (s, 1H, ArH), 2.68 (s, 3H, NCH_3), 2.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.91 (*C*=O), 149.63 (*quat-C*), 147.44 (*quat-C*), 144.77 (*quat-C*), 143.58 (*quat-C*), 143.12 (*quat-C*), 139.40 (*C*H), 135.21 (*quat-C*), 132.33 (*C*H), 130.58 (*C*H), 129.29 (*C*H), 129.18 (*C*H),129.05 (CH), 128.95 (*C*H), 127.81 (*C*H), 127.21 (*C*H), 127.04 (*C*H), 123.72 (*C*H), 123.53 (CH), 121.24 (CH), 119.26 (*quat-C*), 114.13 (*C*H), 109.03 (*C*H), 93.44 (*C*H), 85.38 (*C*H), 74.44 (*quat-C*), 25.78 (N*C*H_3), 16.89 (CH_3); HRMS (ESI) Calcd for $C_{36}H_{31}N_3O_3S$ [$(M+H)^+$] 586.2164, found 586.2177.

Crystal data for compound 7a: (CCDC 1432260) $C_{36}H_{31}N_3O_3S$, white, diamond, M = 585.70, 0.28 × 0.19 × 0.11 mm, Monoclinic, space group $P2_1/c$ with a = 13.4366 (9) Å, b = 9.3183 (6) Å, c = 23.8673 (16) Å, α = 90.00°, β = 91.5620° (10), γ = 90.00°, V = 2987.2(3) $Å^3$, T = 295 (2) K, R_1 = 0.0500, wR_2 = 0.1323 on observed data, z = 4, D_{calcd} = 1.302 mg cm^{-3}, $F(000)$ = 1232, Absorption coefficient = 0.150 mm^{-1}, λ = 0.71073 Å, 6849 reflections were collected on a smart apex CCD single crystal diffractometer 5427 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 0.388 and -0.255 $eÅ^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL–97 software.

1'-Benzyl-5'-methoxy-2,3,5-triphenyl-1-tosylspiro[imidazolidine-4,3'-indolin]-2'-one (**7b**). According to the general procedure, to a solution of aldehyde **2a** (40 mg, 0.38 mmol), amine **3a** (35 mg, 0. 38 mmol), *N*-benzylidene benzenesulfonamide **6a** (110 mg, 0.42 mmol) and copper(I) thiophenecarboxylate (0.7 mg, 1 mol %) in dichloroethane was transferred diazoamide **1f** (100 mg, 0.36 mmol). Purification furnished the corresponding spiroindoloimidazolidine **7b** as a white solid. Eluent: hexane/EtOAc, 90:10. R_f = 0.39 (hexane/EtOAc, 9:1); yield: 183 mg (74%); mp 153-154 ºC; IR (neat): ν_{max} 3162, 2852, 2835, 1722, 1712, 1625, 1542, 1422, 1261, 1152, 1063, 752, 632 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.67-7.62 (m, 3H, ArH), 7.26-7.28 (m, 3H, ArH), 7.08-6.22 (m, 9H, ArH), 6.99 (s, 1H, ArH), 6.86-6.90 (m, 4H, ArH), 6.63-6.78 (m, 3H, ArH), 6.48 (d, J = 7.2 Hz, 2H, ArH), 6.50 (d, J = 8 Hz, 2H, ArH), 6.31-6.33 (m, 1H, ArH), 5.28 (s, 1H, CH), 4.61 (d, J = 16 Hz, 1H, NCH_2), 4.09 (d, J = 16 Hz, 1H, CH_3), 3.56 (s, 3H, CH), 2.32 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.99 (*C*=O), 150.52 (*quat-C*), 146.66 (*quat-C*), 146.20 (*quat-C*), 142.48 (*quat-C*), 138.28 (*quat-C*), 135.4 (*quat-C*), 133.65 (*quat-C*), 132.37 (*C*H), 132.26 (*quat-C*),132.13 (*C*H), 132.02 (*C*H), 131.88 (*C*H), 130.18 (*C*H), 128.12 (*C*H), 126. 8 (*C*H), 126.61 (*C*H), 124.32 (*C*H), 122.34 (*C*H), 117.21 (*C*H), 112.1 (*C*H), 96.52 (*C*H), 88.44 (*C*H), 79.76 (*quat-*

C), 77.51 (*C*H), 28.85 (*C*H), 26.96 (*C*H), 16.86 (*C*H). HRMS (ESI) Calcd for $C_{42}H_{37}N_3O_4S[(M+H)^+]$ 692.2583, found 692.2596.

5'-Chloro-1'-methyl-1,5-bis(4-nitrophenyl)-2,3-diphenylspiro[imidazolidine-4,3'-indolin]-2'-one (**7c**). According to the general procedure, to a solution of aldehyde **2a** (55 mg, 0.52 mmol), amine **3a** (50 mg, 0. 54 mmol), (*E*)-4-nitro-*N*-(4-nitrobenzylidene)aniline **6b** (155 mg, 0.58 mmol) and copper(I) thiophenecarboxylate (0.9 mg, 1 mol %) in dichloroethane was transferred diazoamide **1g** (100 mg, 0.48 mmol). Purification furnished the corresponding spiroindoloimidazolidine **7c** as a white solid; yield: 222 mg (73 %): R_f = 0.27 (hexane/EtOAc, 9:1); mp 167-169 ºC. IR (neat): ν_{max} 3059, 2962, 1768, 1732, 1693, 1563, 1452, 1425, 1252, 1196, 1003, 762, 663 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, *J* = 2 Hz, 1H, ArH), 7.73 (d, *J* = 7.2 Hz, 2H, ArH), 7.59 (d, *J* = 6.8 Hz, 1H, ArH), 7.53 (s, 1H, ArH), 7.38-7.47 (m, 7H, ArH), 7.19-7.34 (m, 3H, ArH), 6.94 (t, *J* = 8.4 Hz, 2H, ArH), 6.63-6.72 (m, 3H, ArH), 6.13 (d, *J* = 8 Hz, 2H, ArH), 5.31 (s, 1H, ArH), 2.67 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.92 (*C*=O), 148.63 (*quat-C*), 147.45 (*quat-C*), 144.76 (*quat-C*), 143.59 (*quat-C*), 143.13 (*quat-C*), 139.4 (*C*H), 135.21 (*quat-C*), 132.33 (*C*H), 130.58 (*C*H), 129.29 (*C*H), 129.18 (*C*H),129.05 (CH), 128.95 (*C*H), 128.81 (*C*H), 127.11 (*C*H), 127.05 (*C*H), 123.73 (*C*H), 123.54 (-CH), 121.25 (-CH), 119.27 (*quat-C*), 114.14 (*C*H), 109.03 (*C*H), 93.45 (*C*H), 85.37 (*C*H), 74.44 (*quat-C*), 25.78 (NCH_3). HRMS (ESI) Calcd for $C_{35}H_{26}ClN_5O_5$ $[(M+H)^+]$ 632.1701, found 632.1718.

Ethyl 1'-methyl-5-(4-nitrophenyl)-2'-oxo-2,3-diphenylspiro[imidazolidine-4,3'-indoline]-1-carboxylate (**7d**). According to the general procedure, to a solution of aldehyde **2a** (65 mg, 0.61 mmol), amine **3a** (60 mg, 0. 64 mmol), (*E*)-ethyl 4-nitrobenzylidenecarbamate **6c** (155 mg, 0.7 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindoloimidazolidine **7d** as a white solid; yield: 232 mg (73 %): R_f = 0.44

(hexane/EtOAc, 9:1); mp 167-169 ºC; IR (neat): ν_{max} 3062, 2912, 2901, 1760, 1702, 1662, 1602, 1493, 1392, 1128, 1085, 1098, 732, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41 (t, *J* = 7.6 Hz, 4H, ArH), 7.34 (t, *J* = 7.6 Hz, 3H, ArH), 7.22 (t, *J* = 7.6 Hz, 2H, ArH), 6.98 (d, *J* = 7.6 Hz, 5H, ArH), 6.85 (d, *J* = 8 Hz, 2H, ArH), 6.73 (t, *J* = 7.6 Hz, 2H, ArH), 6.60 (d, *J* = 8 Hz, 2H, ArH), 4.1 (q, *J* = 7.2 Hz, 2H, CH_2), 3.27 (s, 3H, OCH_3), 1.24 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.98 (*C*=O), 163.17 (*C*=O), 154.36 (*C*=O), 150.27 (*quat-C*), 147.92 (*quat-C*), 146.64 (*quat-C*), 145.74 (*C*H), 145.05 (*quat-C*), 134.16 (*C*H), 133.82 (*C*H), 129.37 (*C*H), 128.45 (*C*H), 125.98 (*C*H), 125.24 (*C*H), 125.08 (*C*H), 123.16 (*C*H), 122.86 (*C*H), 122.61 (*C*H), 121.19 (*C*H), 118.92 (*C*H), 117.71 (CH), 115.51 (*C*H), 109.31 (*C*H), 60.28 (CH_2), 26.28 (CH_3), 14.16 (*CH₃*); HRMS (ESI) Calcd for $C_{32}H_{28}N_4O_5$ [$(M+Na)^+$] 571.1957, found 571.1969.

1'-Ethyl-2-(4-methoxyphenyl)-1,5-bis(4-nitrophenyl)-3-phenylspiro[imidazolidine-4,3'-indolin]-2'-one (**7e**). According to the general procedure, to a solution of aldehyde **2b** (80 mg, 0.59 mmol), amine **3a** (55 mg, 0. 59 mmol), (*E*)-4-nitro-*N*-(4-nitrobenzylidene)aniline **6b** (175 mg, 0.64 mmol), copper(I) thiophenecarboxylate (1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1b** (100 mg, 0.53 mmol). Purification furnished the corresponding spiroindoloimidazolidine **7e** as a white solid. Eluent: hexane/EtOAc, 80:20. R_f = 0.32 (hexane/EtOAc, 8:2); yield: 265 mg (78%). mp 144-146 ºC; IR (neat): ν_{max} 3102, 2932, 2872, 1794, 1724, 1625, 1605, 1468, 1455, 1379, 1261, 1029, 732, 662 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, *J* = 7.2 Hz, 1H, ArH), 7.42-7.44 (m, 2H, ArH), 7.24-7.30 (m, 6H, ArH), 7.11-7.21 (m, 4H, ArH), 7.00-7.04 (m, 1H, ArH), 6.83-6.87 (m, 2H, ArH), 6.58-6.73 (m, 6H, ArH), 5.81 (d, *J* = 9.2 Hz, 1H, CH), 4.28 (d, *J* = 9.2 Hz, 1H, CH), 3.72-3.63 (m, 4H), 0.89 (t, *J* = 9.2, 3H, NCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.88 (*C*=O), 158.57 (*C*=O), 143.73 (*C*=O), 142.24 (*quat-C*), 136.49 (*quat-C*), 135.94 (*quat-C*), 135.32 (*quat-C*), 133.75 (*quat-C*), 132.92 (*quat-C*), 132.88 (*quat-C*), 132.22 (*C*H), 132.16 (*C*H), 131.39 (*C*H), 129.61 (*C*H),

128.89 (*C*H), 128.64 (CH), 128.47 (CH), 128.32 (CH), 127.89 (CH), 127.34 (*C*H), 123.94 (*quat-C*), 123.13 (*C*H), 122.46 (*C*H), 113.64 (CH), 108.13 (*C*H), 68.94 (*quat-C*), 63.81 (*C*H), 58.61 (*C*H), 55.01 (*C*H), 34.36 (*C*H), 11.99 (N*C*H$_3$). HRMS (ESI) Calcd for $C_{37}H_{31}N_5O_6$ [(M+H)$^+$] 642.2353, found 642.2365.

1'-Methyl-2,3,6-triphenyl-2H-spiro[[1,2,4]triazolo[1,2-a][1,2,4]triazole-1,3'-indoline]-2',5,7(3H,6H)-trione (**9a**). According to the general procedure, to a solution of aldehyde **2a** (70 mg, 0.65 mmol), amine **3a** (60 mg, 0.64 mmol), 4-phenyl-[1,2,4]-triazole-3,5-dione **8a** (120 mg, 0.69 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindolotriazolidine **9a** as a white solid; yield: 215 mg (74%); R_f = 0.39 (hexane/EtOAc, 9:1); mp 153-154 ºC; IR (neat): ν_{max} 3042, 2826, 1774, 1702, 1652, 1597, 1467, 1355, 1205, 1152, 1002, 732, 677 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58-7.63 (m, 3H, ArH), 7.43-7.47 (m, 2H, ArH), 7.36-7.39 (m, 3H, ArH), 7.25-7.2 (m, 2H, ArH), 7.17-7.21 (m, 1H, ArH), 6.95-6.99 (m, 1H, ArH), 6.91-6.92 (m, 3H, ArH), 6.65 (t, *J* = 7.2 Hz, 1H, ArH), 6.29-6.33 (m, 4H, CH), 3.26 (s, 3H, NCH$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.53 (*C*=O), 163.26 (*C*=O), 161.22 (*C*=O), 144.29 (*quat-C*), 143.77 (*quat-C*), 143.61 (*quat-C*), 138.15 (*quat-C*), 132.91 (*quat-C*), 130.43 (*C*H), 128.98 (*C*H),128.93 (*C*H), 128.86 (*C*H), 128.49 (*C*H), 127.00 (*C*H), 124.64 (*C*H), 123.46 (*C*H), 119.49 (*C*H), 115.01 (*C*H), 108.92 (*C*H), 77.66 (*quat-C*), 71.12 (*C*H), 26.34 (O*C*H$_3$); HRMS (ESI) Calcd for $C_{30}H_{23}N_5O_3$ [(M+H)$^+$] 502.1879, found 502.1892.

5'-Methoxy-1'-methyl-2,3,6-triphenyl-2H-spiro[[1,2,4]triazolo[1,2-a][1,2,4]triazole-1,3'-indoline]-2',5,7(3H,6H)-trione (**9b**). According to the general procedure, to a solution of aldehyde **2a** (55 mg, 0.52 mmol), amine **3a** (50 mg, 0.54 mmol), 4-phenyl-[1,2,4]-triazole-3,5-dione **8a** (105 mg, 0.60 mmol) and copper(I) thiophenecarboxylate (0.9 mg, 1 mol %) in dichloroethane was transferred diazoamide **1h** (100 mg, 0.49 mmol). Purification furnished

the corresponding spiroindolotriazolidine **9b** as a white solid; yield: 188 mg (72 %): R_f = 0.32 (hexane/EtOAc, 8:2); mp 144-146 ºC; IR (neat): ν_{max} 3092, 2924, 2854, 1780, 1711, 1613, 1597, 1492, 1455, 1435, 1379, 1310, 1261, 1176, 1029, 732, 693, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.64-7.58 (m, 3H, ArH), 7.34-7.47 (m, 1H, ArH), 7.36-7.4 (m, 3H, ArH), 7.25-7.2 (m, 2H, ArH), 7.17-7.21 (m, 1H, ArH), 6.95-6.99 (m, 1H, ArH), 6.91-6.92 (m, 3H, ArH), 6.64 (t, *J* = 6.8 Hz, 1H, ArH), 6.28-6.32 (m, 4H, CH), 3.65 (s, 3H, OCH_3), 3.26 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.52 (*C*=O), 163.26 (*C*=O), 161.22 (*C*=O), 144.29 (*quat-C*), 143.77 (*quat-C*), 143.61 (*quat-C*), 138.15 (*quat-C*), 132.91 (*quat-C*), 130.43 (*C*H), 128.98 (*C*H),128.93 (*C*H), 128.86 (*C*H), 128.49 (*C*H), 127.00 (*C*H), 124.62 (*C*H), 123.46 (*C*H), 119.49 (*C*H), 115.01 (*C*H), 108.92 (*C*H), 77.66 (*quat-C*), 71.12 (*C*H), 52.34 (O*C*H_3), 26.34 (O*C*H_3); HRMS (ESI) Calcd for $C_{31}H_{25}N_5O_4$ [$(M+H)^+$] 532.1985, found 532.1987.

1'-Ethyl-3-(4-methoxyphenyl)-2,6-diphenyl-2H-spiro[[1,2,4]triazolo[1,2-a][1,2,4]triazole-1,3'-indoline]-2',5,7(3H,6H)-trione (**9c**). According to the general procedure, to a solution of aldehyde **2b** (80 mg, 0.59 mmol), amine **3a** (55 mg, 0.59 mmol), 4-phenyl-[1,2,4]-triazole-3,5-dione **8a** (110 mg, 0.63 mmol) and copper(I) thiophenecarboxylate (1 mg, 1 mol %) catalyst in dichloroethane was transferred solution of diazoamide **1b** (100 mg, 0.53 mmol). Purification furnished the corresponding spiroindolotriazolidine **9c** as a white solid; yield: 225 mg (78 %). R_f = 0.32 (hexane/EtOAc, 8:2); mp167-169 ºC; IR (neat): ν_{max} 3059, 2931, 2863, 1776, 1716, 1654, 1568, 1498, 1432, 1379, 1256, 1075, 1102, 730, 661 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, *J*= 6.8 Hz, 1H, ArH), 7.51 (d, *J*= 8.8 Hz, 3H, ArH), 7.41-7.53 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 2H, ArH), 7.25 (s, 1H, ArH), 7.19-7.15 (m, 1H, ArH), 6.92-6.89 (m, 6H, ArH), 6.64 (d, *J*= 7.2 Hz, 1H, ArH), 6.62-6.33 (m, 3H, ArH), 6.23 (s, 1H, ArH), 3.71-3.89 (m, 5H), 1.24 (t, *J*= 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.99 (*C*=O), 163.30 (*C*=O), 161.34 (*C*=O), 160.34 (*quat-C*), 159.59 (*quat-C*), 144.20 (*quat-C*),

143.70 (*quat-C*), 142.77 (*quat-C*), 133.02 (*C*H), 130.94 (*C*H), 130.32 (*C*H), 130.15 (*C*H), 129.12 (*C*H), 129.02 (*C*H), 128.82 (*C*H), 128.26 (*C*H), 125.20 (*C*H), 124.83 (*C*H), 123.19 (*C*H), 122.98 (*C*H), 119.52 (*C*H), 115.41 (*C*H), 114.28 (*C*H), 109.01 (*C*H), 77.54 (*quat-C*), 76.77 (CH), 70.47 (*C*H), 35.06 (CH_2), 12.17 (CH_3); HRMS (ESI) Calcd for $C_{32}H_{27}N_5O_4$ [$(M+H)^+$] 546.2141, found 546.2153.

Diethyl 1-allyl-5'-(2,3-dimethoxyphenyl)-2-oxo-4'-phenylspiro[indoline-3,3'-[1,2,4]triazolidine]-1',2'-dicarboxylate (**9d**). According to the general procedure, to a solution of aldehyde **2c** (90 mg, 0.54 mmol), amine **3a** (50 mg, 0.54 mmol), DEAD **8b** (105 mg, 0.6 mmol) and copper(I) thiophenecarboxylate (1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1d** (100 mg, 0.50 mmol). Purification furnished the corresponding spiroindoltriazolidine **9d** as a white solid; yield: 240 mg (82 %); R_f = 0.41 (hexane/EtOAc, 9:1). mp 153-154 ºC. IR (neat): ν_{max} 3062, 2923, 2854, 1780, 1713, 1613, 1264, 1166, 1025, 1003, 731, 690, 687 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.64-7.66 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.39-7.43 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H, ArH), 7.26 (d, J_1 = 1.2 Hz, 1H, ArH), 7.16-7.20 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H, ArH), 7.07 (t, J = 8 Hz, 1H, ArH), 7.94-7.99 (m, 3H, ArH), 6.90-6.99 (m, 1H, ArH), 6.73 (s, 1H, ArH), 6.71 (t, J = 7.2 Hz, 1H, ArH), 6.46 (d, J = 8.0 Hz, 2H, ArH), 5.77-5.84 (m, 1H, CH), 5.29 (ddt, 2H, J_1 = 17.2 Hz, J_2 = 10.4 Hz, J_3 = 1.2 Hz, CH_2), 4.43 (ddt, 2H, J_1 = 17.2 Hz, J_2 = 10.4 Hz, J_3 = 1.2 Hz, CH_2), 4.39 (s, 3H, OCH_3), 4.36 (s, 3H, OCH_3), 4.07 (q, J = 7.2 Hz, 2H, NCH_2), 3.84-3.89 (m, 1H, CH_2), 3.56-361 (m, 1H, OCH_2), 1.27 (t, J = 7.6 Hz, 3H, CH_3), 1.17 (t, J = 7.2 Hz, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.60 (*C*=O), 163.66 (*C*=O), 161.62 (*C*=O), 152.66 (*quat-C*), 147.24 (*quat-C*), 144.96 (*quat-C*), 144.05 (*quat-C*), 143.37 (*quat-C*), 133.32 (*C*H), 131.85 (*C*H), 131.66 (*C*H), 130.42 (*C*H), 129.41 (*quat-C*), 129.22 (*C*H), 124.98 (*C*H), 124.54 (*C*H), 123.57 (*C*H), 119.96 (*C*H), 119.78 (CH_2), 118.56 (*C*H), 115.77 (*C*H), 112.65 (*C*H), 110.11 (*C*H), 64.62 (*C*H), 61.19 (*C*H), 56.04 (*C*H), 52.66 (OCH_3), 52.54 (OCH_3), 43.36 (NCH_2),

14.64 (*C*H), 13.27 (*C*H); HRMS (ESI) Calcd for $C_{32}H_{34}N_4O_7$ [$(M+H)^+$] 587.2506, found 587.2519.

Diethyl-1-methyl-5'-(naphthalen-1-yl)-2-oxo-4'-phenylspiro[indoline-3,3'-[1,2,4]triazolidine]-1',2'-dicarboxylate (**9e**). According to the general procedure, to a solution of aldehyde **2d** (100 mg, 0.64 mmol), amine **3a** (60 mg, 0.64 mmol), DEAD **8b** (120 mg, 0.69 mmol) and copper(I) thiophenecarboxylate (1.1 mg, 1 mol %) in dichloroethane was transferred diazoamide **1c** (100 mg, 0.58 mmol). Purification furnished the corresponding spiroindolotriazolidine **9e** as a white solid: yield: 243 mg (76 %): R_f = 0.42 (hexane/EtOAc, 9:1); mp 167-169 ºC. IR (neat): ν_{max} 3059, 2932, 2864, 1778, 1721, 1653, 1587, 1492, 1468, 1380, 1261, 1176, 1075, 1103, 732, 693, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.16 (s, 1H, ArH), 7.16-7.40 (m, 12H, ArH), 6.82 (t, *J* = 7.5 Hz, 2H, ArH), 6.64-6.71 (m, 1H, ArH), 5.90 (d, *J* = 6.0 Hz, 1H, CH), 3.66 (q, *J* = 7.2 Hz, 2H, CH), 3.63-3.65 (m, 1H, CH), 3.60-3.62 (m, 1H, CH), 2.96 (s, 3H, CH_3), 1.27 (t, *J* = 0.8 Hz, 3H, CH_3), 1.11 (t, *J* = 0.8 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.61 (*C*=O), 174.45 (*C*=O), 173.83 (*C*=O), 148.19 (*quat-C*), 142.28 (*quat-C*), 140.53 (*quat-C*), 137.95 (*quat-C*), 133.37 (*quat-C*), 133.11 (*C*H), 131.82 (*quat-C*), 130.59 (*C*H), 129.08 (*C*H), 128.89 (*C*H), 128.8 (*C*H), 128.52 (*C*H), 128.09 (*C*H), 128.03 (*C*H), 127.64 (*C*H), 126.98 (*C*H), 126.5 (*C*H), 126.17 (*C*H), 126.0 (*C*H), 125.32 (*C*H), 124.38 (*C*H), 124.14 (*C*H), 123.36 (CH), 115.98 (*C*H), 66.04 (*quat-C*), 53.92 (CH_2), 52.08 (CH_2), 27.88 (*C*H), 14.64 (CH_3), 13.27 (CH_3); HRMS (ESI) Calcd for $C_{32}H_{30}N_4O_5$ [$(M+H)^+$] 551.2294, found 551.2308.

Supporting Information

Experimental data for compounds **5e-i, 7f-l, 9f-j**. Copies of ^1H and ^{13}C NMR spectra data for all new products and the crystallographic data of **5j,7a** (CIF). For ESI and crystallographic data in CIF or other electronic format see DOI:

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(16) See ESI† for characterization of compounds **5e-i, 7f-l, 9f-j** details.