Organic & Biomolecular Chemistry

Accepted Manuscript

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Cite this: DOI: 10.1039/c0xx00000x

FULL PAPER

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Facile synthesis of spirooxindole-pyrazolines and spirobenzofuranone-pyrazolines and their fungicidal activity

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

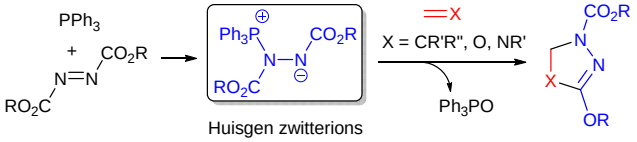
Novel spirooxindole-pyrazolines and spirobenzofuranone-pyrazolines have been synthesized in good to excellent yields via the annulation reactions of the corresponding 3-alkylideneoxindoles and 3-alkylidenebenzofuranones with Huisgen zwitterions. The preliminary bioassay has demonstrated that some of the spiropyrazolines possess good in vitro fungicidal activity against several crop fungi at the concentration of 50 μg/mL.

Introduction

Spirooxindoles are prevalent molecular architectures frequently found in a diverse range of natural products and pharmaceutical molecules.[1] As one category of these spirocyclic motifs, spirooxindole-heterocycles have gained increasing interest due to their broad spectrum of bioactivities.[2] In this context, spirooxindolyl azaheterocycles, particularly spirooxindole-pyrrolidines, have received much attention from organic chemists and biologists since the spirooxindole-pyrrolidine core represents a privileged skeleton that is featured in a number of natural alkaloids and artificial compounds with promising biological activities.[2d,2e] Given their structural similarity to spirooxindole-pyrrolidines and the prevalence of the pyrazoline scaffold in bioactive molecules,[3] spirooxindole-pyrazolines have also aroused considerable interest in their synthesis and bioactivity.[4] In the syntheses of different types of spirooxindoles, 3-alkylidene oxindoles have emerged as the versatile substrates.[5] Recently, highly efficient and stereoselective syntheses of spirooxindole-pyrazolines have been realized by Roth[4c] and Feng[4d] via a [3 + 2]cycloaddition reaction of 3-alkylidene oxindoles with nitrile imines.

The Huisgen zwitterions, readily generated from Ph_3P and dialkyl azodicarboxylates, are the key intermediates in the famous Mitsunobu reaction and early reported annulation reactions.[6] Recently, the renewed interest has revealed that the Huisgen zwitterions could undergo a series of annulation reactions with electron-deficient alkenes, carbonyls or imines to give nitrogen-containing heterocycles such as pyrazolines, oxadiazoles and triazoles (Scheme 1).[2g,7] In the cyclizations, elimination of by-product Ph_3PO is the common step.

Intrigued by the attractive reactivity of Huisgen zwitterions, and also motivated by the potential bioactivity of spirooxindole-pyrazolines, we intended to investigate the feasibility of the annulation reaction between 3-alkylidene oxindoles and Huisgen zwitterions as a new route to spirooxindole-pyrazolines. Considering the structural resemblance and the diverse biological activities of spirocyclic benzofuranones,[8] the possible annulation reaction of 3-alkylidene benzofuran-2-ones and Huisgen zwitterions was also explored in this study. Herein, we wish to report the results from the relevant investigations in detail.



Scheme 1 The annulation reactions of Huisgen zwitterions with electron-deficient alkenes, carbonyls and imines.

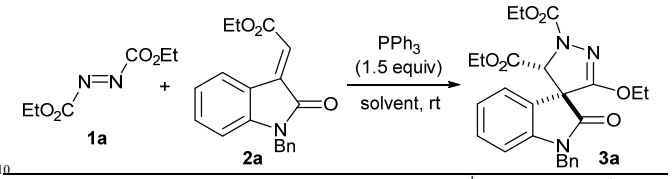
Results and discussion

Synthesis of spiropyrazolines

We initiated our research with the substrates diethyl azodicarboxylate (DEAD) **1a** and (*E*)-1-benzyl-3-ethoxycarbonylmethylidene oxindole **2a** (Table 1). Under predetermined conditions, a model reaction of **1a** (0.3 mmol), **2a** (0.2 mmol) and PPh_3 (0.3 mmol) in CH_2Cl_2 (2.0 mL) was stirred at rt for 48 h. To our delight, the expected spirooxindole-pyrazoline **3a** was obtained in 49% yield and high diastereoselectivity after column chromatographic isolation (Table 1, entry 1). The structure and relative configuration of **3a** was confirmed by X-ray diffraction analysis (Fig. 1). This initial result revealed a highly diastereoselective annulation of 3-alkylideneoxindoles with in situ generated Huisgen zwitterions and a new approach to spirooxindole-pyrazolines as well. To further improve the reaction efficiency, a brief survey on the model reaction conditions was carried out (Table 1). Elevating the temperature to 40°C only led to a slight improvement of the yield (entry 2). Run in $CHCl_3$ for an elongated time, the reaction gave a significantly enhanced yield (entry 3). Non-halogenated solvents THF and toluene both furnished even better yields of **3a**

in a shortened reaction time (entries 4 and 5). However, the protic solvent ethanol was harmful to the reaction and no desired product was formed (entry 6). Finally, THF was selected as the preferred solvent with regard to the yield and diastereoselectivity although solvents $CHCl_3$ and toluene also gave comparable results (entries 3–5). Thus, the optimized conditions for the annulation reaction between 3-alkylidene oxindoles like **2a** and in situ generated Huisgen zwitterions were established.

Table 1 A brief survey on the model reaction conditions[a]



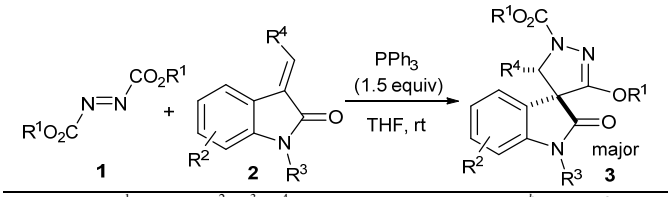
Entry	Solvent	Time [h]	Yield[b] [%]	dr[c]
1	CH_2Cl_2	48	49	>20:1
2[d]	CH_2Cl_2	48	53	>20:1
3	$CHCl_3$	72	96	>20:1
4	THF	24	99	>20:1
5	toluene	24	98	>20:1
6	ethanol	96	–	–

[a] Typical conditions: under a N_2 atmosphere, to a mixture of **1a** (52 mg, 0.3 mmol) and **2a** (61 mg, 0.2 mmol) in solvent (2.0 mL) was added PPh_3 (79 mg, 0.3 mmol), and the resulting mixture was then stirred at rt for a specified time. [b] Isolated yield. [c] Determined by the ^{1}H NMR assay of the crude product. [d] The reaction was run at 40°C.

Under the optimized conditions, the generality of this annulation was investigated (Table 2). With azodicarboxylate **1a** employed as a representative reactant, a variety of 3-alkylidene oxindoles **2** were explored. Different substituents R^2 on the aromatic ring of the oxindole framework were first examined. Both electron-withdrawing and -donating substituents R^2 of substrates **2** were well tolerated. In the cases examined, the substrates **2a-i** smoothly afforded their corresponding annulation products **3** in good to excellent yields and high diastereoselectivity (entries 1–9). The substituents R^3 at the nitrogen atom of the indole ring in **2** were further checked. All the examined substrates **2j-n** with a substituent R^3 other than benzyl were capable of delivering their normal annulation products in good yields, although the allyl-, *tert*-butoxycarbonyl-, and acetyl-substituted oxindoles **2l-n** gave a relatively lower diastereoselectivity (entries 10–14). The electron-withdrawing group R^4 in **2** was also surveyed. Substrates **2o** and **2p** with a bulky ester group uneventfully afforded their corresponding annulation products in excellent yields and diastereoselectivity (entries 15 and 16). Cyano-substituted substrate **2q** readily gave its corresponding product **3q** in a modest yield and high diastereoselectivity (entry 17). Phenyl-substituted **2r** could also furnish the normal annulation product in a moderate yield but in a low stereoselectvity (entry 18).

Selected dialkyl azodicarboxylates **1** were further examined in the annulation reaction with representative 3-alkylidene oxindoles **2**. Under the standard conditions, diisopropyl and dibenzyl azodicarboxylates **1b** and **1c** smoothly afforded their corresponding annulation products **3** in good to excellent yields and moderate to high diastereoselectivity (entries 19–24). Thus, the annulation reaction of 3-alkylidene oxindoles **2** and in situ generated Huisgen zwitterions has a broad substrate scope and accordingly provides a facile and new access to spirooxindole-pyrazolines.

Table 2 Synthesis of spirooxindole-pyrazolines **3**[a]



Entry	R^1 in **1**	R^2, R^3, R^4 in **2**	Time [h]	Yield[b] [%]	dr[c]
1	Et (**1a**)	H, Bn, CO_2Et (**2a**)	24	**3a**, 99	>20:1
2	**1a**	4-Br, Bn, CO_2Et (**2b**)	24	**3b**, 95	>20:1
3	**1a**	5-F, Bn, CO_2Et (**2c**)	48	**3c**, 88	>20:1
4	**1a**	5-Cl, Bn, CO_2Et (**2d**)	24	**3d**, 97	>20:1
5	**1a**	5-Br, Bn, CO_2Et (**2e**)	24	**3e**, 99	>20:1
6	**1a**	5-Me, Bn, CO_2Et (**2f**)	30	**3f**, 91	>20:1
7	**1a**	5-MeO, Bn, CO_2Et (**2g**)	24	**3g**, 99	>20:1
8	**1a**	6-Br, Bn, CO_2Et (**2h**)	48	**3h**, 87	>20:1
9	**1a**	7-Cl, Bn, CO_2Et (**2i**)	48	**3i**, 80	>20:1
10	**1a**	H, Me, CO_2Et (**2j**)	24	**3j**, 95	>20:1
11	**1a**	5-Me, Me, CO_2Et (**2k**)	24	**3k**, 91	>20:1
12	**1a**	H, Allyl, CO_2Et (**2l**)	24	**3l**, 97	7:1
13	**1a**	H, Boc, CO_2Et (**2m**)	24	**3m**, 77	5:1
14	**1a**	H, Ac, CO_2Et (**2n**)	48	**3n**, 87	10:1
15	**1a**	H, Bn, CO_2Bn (**2o**)	24	**3o**, 96	>20:1
16	**1a**	H, Bn, $CO_2{}^tBu$ (**2p**)	24	**3p**, 98	10:1
17	**1a**	H, Bn, CN (**2q**)	48	**3q**, 45	>20:1
18	**1a**	H, Bn, Ph (**2r**)	72	**3r**, 56	2:1
19	^{i}Pr (**1b**)	**2a**	24	**3s**, 95	5:1
20	**1b**	**2j**	24	**3t**, 78	>20:1
21	**1b**	**2l**	48	**3u**, 88	10:1
22	**1b**	**2o**	24	**3v**, 90	6:1
23	**1b**	**2p**	48	**3w**, 95	20:1
24	Bn (**1c**)	**2a**	48	**3x**, 82	>20:1

[a] For a typical procedure, see Experimental Section. [b] Isolated yield. [c] Determined by the ^{1}H NMR assay of the crude product.

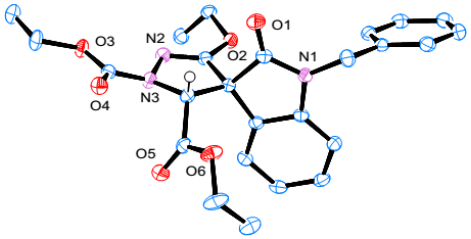


Fig. 1 ORTEP drawing for **3a**.

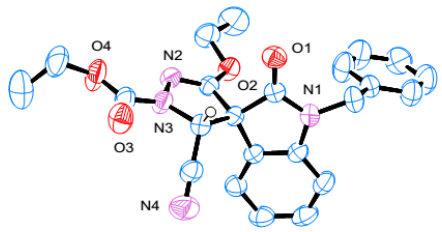
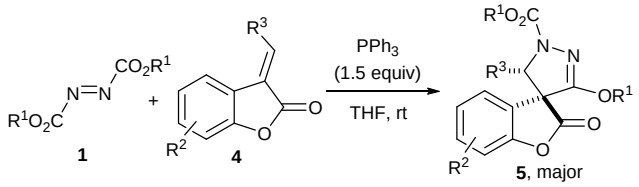


Fig. 2 ORTEP drawing for **3q**.

The scope of the Huisgen zwitterions-involving annulation reaction could be even extended to 3-alkylidene benzofuranones **4**. As shown in Table 3, under the standard conditions, representative 3-alkylidene benzofuranones **4** bearing variable substituents readily furnished the expected annulation products **5** with all of three selected dialkyl azodicarboxylates **1** in moderate to good yields (entries 1–7). The diastereoselectivity of the annulation reaction was apparently affected by the ester group R^3 in **4;** the substrates **4c–e** with a bulky ester group *tert*-butoxycarbonyl all gave their spirocyclic products in higher diastereoselectivity (entries 3–7). These results accordingly unveiled a facile synthetic method for spirobenzofuranone-pyrazolines. To the best of our knowledge, this also represents the first synthesis of the spirobenzofuranone-pyrazoline core.

The structures of spiropyrazolines **3** and **5** listed in Tables 2 and 3 were identified by ^{1}H, ^{13}C NMR and HRMS-ESI measurements, and further confirmed by X-ray crystallographic analyses for representative compounds (Fig. 1 and 2, CCDC number for **3a**: CCDC 1046817, for **3q**: CCDC 1046823, also see ESI†). The copies of ^{1}H and ^{13}C NMR spectra for all new compounds are available in ESI.†

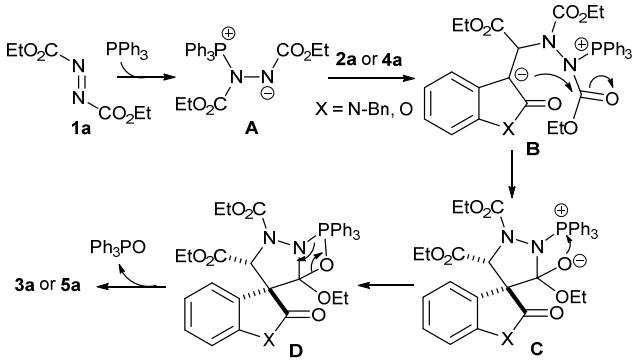
Table 3 Synthesis of spirobenzofuranone-pyrazolines **5**[a]



Entry	R^1 in **1**	R^2, R^3 in **2**	Time [h]	Yield[b] [%]	dr[c]
1	Et (**1a**)	H, CO_2Et (**4a**)	1	**5a**, 79	3:1
2	**1a**	H, CO_2Bn (**4b**)	6	**5b**, 59	2:1
3	**1a**	H, $CO_2{}^t$Bu (**4c**)	1	**5c**, 85	7:1
4	**1a**	5-Me, $CO_2{}^t$Bu (**4d**)	8	**5d**, 70	>20:1
5	**1a**	6-MeO, $CO_2{}^t$Bu (**4e**)	9	**5e**, 78	>20:1
6	^{i}Pr (**1b**)	**4c**	1	**5f**, 85	20:1
7	Bn (**1c**)	**4c**	24	**5g**, 56	6:1

[a] For a typical procedure, see Experimental Section. [b] Isolated yield. [c] Determined by the ^{1}H NMR assay of the crude product.

Although a precise mechanism of this annulation reaction remains elusive, according to the closely related reports,[7c,7f,7h] a rationale for the formation of spiropyrazolines **3** and **5** is exemplified in Scheme 2. The annulation sequence is presumably initiated with the formation of Huisgen zwitterions **A** through nucleophilic addition of triphenylphosphine to dialkyl azodicarboxylates **1**. Subsequent conjugate addition of zwitterions **A** to 3-alkylidene oxindoles **2** or 3-alkylidene benzofuranones **4** brings about intermediate **B**, which engages in an intramolecular addition of the carbanion centre to the ester carbonyl to generate intermediate **C**. Finally intermediate C eliminates triphenylphosphine oxide via betaine **D** to produce spirooxindole-pyrazolines **3** or spirobenzofuranone-pyrazolines **5** (Scheme 2).



Scheme 2 A rationale for the formation of spiropyrazolines **3** and **5**.

Fungicidal activity

The in vitro fungicidal activities of selected spiropyrazolines **3** and **5** were preliminarily evaluated against 9 fungi often occurring in the China agro-ecosystem including AS (*Alternaria solani*), CA (*Cercosporaarachidicola*), GZ (*Gibberellazeae*), PP (*Physalos-pora piricola*), BC (*Botrytis cinerea*), SS (*Sclerotinia sclerotiorum*), RC (*Rhizoctonia cerealis*), PS (*Pellicularia sasakii*), and PI (*Phytophthora infestans (Mont) de Bary*). The results are shown in Table 4. All of the examined spiropyrazolines **3** and **5** showed some certain degrees of fungicidal activities at the concentration of 50 μg/mL. Particularly, all of the selected spirobenzofuranone-pyrazolines **5** exhibited higher fungicidal activities against all the selected fungi. Their activities are comparable to those of the positive control fungicide azoxystrobin. This encouraging result should inspire further investigations into the structure-activity relationship of the spirobenzofuranone-pyrazolines **5** as the potential fungicides.

Table 4 The in vitro fungicidal activity of selected compounds **3** and **5**[a,b]

Compound	AS	CA	GZ	PP	BC	SS	RC	PS	PI
3a	7	12	83	50	44	59	59	95	17
3b	18	24	76	52	44	66	55	92	7
3c	4	29	76	50	35	79	54	73	10
3d	11	24	79	41	28	52	57	92	7
3e	4	6	69	48	42	59	62	77	20
3g	7	12	72	57	35	69	52	88	10
3h	14	18	79	52	37	76	64	85	13
3i	18	47	72	57	42	83	70	83	10
3q	4	29	72	45	53	66	57	90	17
3r	4	24	69	34	44	14	54	75	7
5a	50	47	76	72	60	90	81	92	53
5c	64	65	86	60	70	93	77	100	57
5d	54	59	72	86	72	97	87	98	53
5e	50	59	45	57	63	93	83	95	50
5f	54	71	76	53	60	93	62	100	50
Azoxystrobin	63	56	75	85	71	100	88	70	88

[a] Each compound was evaluated at the concentration of 50 μg/mL and the activity is expressed by the fungus growth inhibition percentage. [b] AS: *Alternaria solani*; CA: *Cercosporaarachidicola*; GZ: *Gibberellazeae*; PP: *Physalospora piricola*; BC: *Botrytis cinerea*; SS: *Sclerotinia sclerotiorum*; RC: *Rhizoctonia cerealis*; PS: *Pellicularia sasakii*; PI: *Phytophthora infestans (Mont) de Bary*.

Conclusions

In summary, we have successfully realized a facile synthesis of spirooxindole-pyrazolines and spirobenzofuranone-pyrazolines through the annulation reaction of 3-alkylidene oxindoles and 3-alkylidene benzofuranones with in situ generated Huisgen zwitterions. Under very mild conditions, novel spirooxindole-pyrazolines and spirobenzofuranone-pyrazolines have been readily prepared in good yields and diastereoselectivity. This synthetic method further strengthens the effectiveness and versatility of the phosphorus reagent-mediated annulation strategy in organic synthesis.[9] Furthermore, some of the spiropyrazoline compounds obtained in this work have exhibited good in vitro fungicidal activity in the preliminary bioassay, and therefore provide valuable candidates for the development of new agricultural fungicides.

Experimental section

General information

Unless otherwise noted, all reactions were carried out in a nitrogen atmosphere. Solvents were purified prior to use according to conventional procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard. HRMS spectra were acquired in the ESI mode (positive ion) with the mass analyzer of TOF used. Column chromatography was performed on silica gel (200–300 mesh) using a mixture of petroleum ether/ethyl acetate as eluant. Dialkyl azodicarboxylates **1** were purchased from commercial sources. 3-Alkylidene oxindoles **2** and 3-alkylidene benzofuranones **4** were prepared according to the reported procedures from isatins and benzofuran-2,3-diones, respectively.[10]

General procedure for synthesis of spiropyrazolines 3 and 5 (Table 2 and 3)

Under a N_2 atmosphere, to a solution of dialkyl azodicarboxylate **1** (0.3 mmol) and 3-alkylidene oxindole **2** or 3-alkylidene benzofuranone **4** (0.2 mmol) in THF (2.0 mL) was added PPh_3 (79 mg, 0.3 mmol). The resulting mixture was stirred at room temperature for a specified time (Table 2 and 3) till substrate **2** or **4** was completely consumed, as monitored by TLC. The solvent was then removed on a rotary evaporator under reduced pressure and the residue was subjected to column chromatographic isolation on silica gel (gradient eluant, petroleum ether/ ethyl acetate 20:1–10:1) to give the annulation product **3** or **5**.

Typical procedure for fungicidal activity evaluation (Table 4)

Preliminary fungicidal activity of compounds **3** and **5** was evaluated by measuring fungi growth inhibition percentage according to a conventional method using potato dextrose agar (PDA) as the cultivation medium.[11] A stock solution of each compound was prepared at 500 μg/mL using *N*,*N*-dimethylformamide (DMF) as a solvent. A working solution (50 μg/mL) was prepared by diluting the stock solution (0.1 mL) with sterilized water (0.9 mL) in a 10 cm diameter of Petri dish. PDA (9 mL) was then added to prepare the plate containing the test compound. Before the plate solidified, the PDA was thoroughly mixed by turning around the Petri dish in the sterilized operation desk 5 times to scatter the compound in PDA evenly. Then, 4 mm of diameter of fungi cake was inoculated on the plate and cultured in the culture tank at 24−26 °C for 48 h. The diameter of fungi spread was measured, and growth inhibition percentage was then calculated by using the corresponding negative control. For the purpose of comparison, fungicide azoxystrobin was used as the positive control.

Analytical data of compounds 4c–e, 3 and 5

New compounds **4c**–**e** were prepared according to a reported procedure.[10c]

(*E*)-*tert*-butyl 2-(2-oxobenzofuran-3(2*H*)-ylidene)acetate (4c): yellow solid, mp 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 8.4 Hz, 1H), 7.48–7.44 (m, 1H), 7.23–7.19 (m, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.87 (s, 1H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 164.1, 155.9, 133.5, 132.5, 128.8, 127.8, 124.5, 120.7, 110.9, 82.5, 28.0; HRMS-ESI calcd for $C_{14}H_{14}NaO_4$ $[M + Na]^+$ 269.0784, found 269.0787.

(*E*)-*tert*-butyl 2-(5-methyl-2-oxobenzofuran-3(2*H*)-ylidene) acetate (4d): yellow solid, mp 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.84 (s, 1H), 2.40 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 164.1, 154.0, 134.1, 132.7, 126.4, 128.9, 127.3, 120.5, 110.4, 82.4, 28.0, 21.2; HRMS-ESI calcd for $C_{15}H_{16}NaO_4$ $[M + Na]^+$ 283.0941, found 283.0945.

(*E*)-*tert*-butyl 2-(6-methoxy-2-oxobenzofuran-3(2*H*)-ylidene) acetate (4e): yellow solid, mp 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.8 Hz, 1H), 6.71 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.68 (s, 1H), 6.65 (d, *J* = 2.4 Hz, 1H), 3.88 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 164.7, 164.1, 157.8, 132.3, 130.3, 123.9, 113.8, 110.6, 96.9, 82.0, 55.8, 28.1; HRMS-ESI calcd for $C_{15}H_{16}NaO_5$ $[M + Na]^+$ 299.0890, found 299.0896.

Diethyl 1-benzyl-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole] -1',5'(5'*H*)-dicarboxylate (3a): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2a** (61 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 24 h to afford **3a**, 92 mg, 99% yield, > 20:1 dr; as a slightly yellow solid, mp 114–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.34–7.27 (m, 5H), 7.25–7.17 (m, 2H), 7.03–7.00 (m, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.34 (s, 1H), 5.03 (d, *J* = 15.9 Hz, 1H), 4.96 (d, *J* = 15.9 Hz, 1H), 4.37–4.17 (m, 4H), 3.89–3.75 (m, 2H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.67 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 165.6, 159.4, 153.5, 143.0, 134.8, 130.2, 128.8, 127.8, 126.9, 125.0, 124.0, 123.2, 109.7, 68.5, 67.2, 62.6, 61.5, 61.4, 44.2, 14.6, 14.0, 13.5; HRMS-ESI calcd for $C_{25}H_{28}N_3O_6$ $[M + H]^+$ 466.1973, found 466.1981.

Diethyl 1-benzyl-4-bromo-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3b): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2b** (77 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3b**, 103 mg, 95% yield, > 20:1 dr; as a white solid, mp 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.26 (m, 5H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.14–7.10 (m, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 5.44 (s, 1H), 5.05 (d, *J* = 16.0 Hz, 1H), 4.81 (d, *J* = 16.0 Hz, 1H), 4.40–4.29 (m, 4H), 4.23–4.17 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.26–1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 166.9, 157.1, 153.6, 144.6, 134.34, 131.4, 128.8, 127.9, 127.2, 126.9, 125.2, 119.1, 109.0, 67.4, 66.2, 62.4, 62.2, 62.1, 44.2, 14.7, 14.1, 14.0; HRMS-ESI calcd for $C_{25}H_{27}BrN_3O_6$ $[M + H]^+$ 544.1078, found 544.1075.

Diethyl 1-benzyl-3'-ethoxy-5-fluoro-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3c): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2c** (65 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3c**, 85 mg, 88% yield, > 20:1 dr; as a

white solid, mp 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.26 (m, 5H), 7.00–6.91 (m, 2H), 6.62 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.34 (s, 1H), 4.98 (s, 2H), 4.38–4.18 (m, 4H), 3.98–3.83 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.78 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 165.4, 159.0 (d, *J* = 243.2 Hz), 158.7, 153.3, 138.9 (d, *J* = 2.1 Hz), 134.3, 128.8, 127.9, 126.8, 125.1 (d, *J* = 8.4 Hz), 116.6 (d, *J* = 23.5 Hz), 113.2 (d, *J* = 25.7 Hz), 110.4 (d, *J* = 7.9 Hz), 68.3, 67.3, 62.6, 61.6, 61.5, 44.3, 14.5, 14.0, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -118.6; HRMS-ESI calcd for $C_{25}H_{27}FN_3O_6$ $[M + H]^+$ 484.1878, found 484.1882.

Diethyl 1-benzyl-5-chloro-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (**3d**): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2d** (68 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3d**, 97 mg, 97% yield, > 20:1 dr; as a white solid, mp 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.23 (m, 5H), 7.22–7.18 (m, 2H), 6.61 (d, *J* = 8.2 Hz, 1H), 5.32 (s, 1H), 5.01 (d, *J* = 16.0 Hz, 1H), 4.95 (d, *J* = 16.0 Hz, 1H), 4.38–4.18 (m, 4H), 3.99–3.85 (m, 2H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 165.4, 158.6, 153.3, 141.5, 134.2, 130.1, 128.8, 128.6, 127.9, 126.8, 125.3, 125.3, 110.7, 68.3, 67.3, 62.6, 61.7, 61.3, 44.2, 14.5, 13.9, 13.5; HRMS-ESI calcd for $C_{25}H_{27}ClN_3O_6$ $[M + H]^+$ 500.1583, found 500.1585.

Diethyl 1-benzyl-5-bromo-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3e): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2e** (77 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 24 h to afford **3e**, 108 mg, 99% yield, > 20:1 dr; as a white solid, mp 148–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 5H), 7.28–7.24 (m, 2H), 6.57 (d, *J* = 8.8 Hz, 1H), 5.32 (s, 1H), 5.01 (d, *J* = 15.9 Hz, 1H), 4.94 (d, *J* = 15.9 Hz, 1H), 4.37–4.19 (m, 4H), 4.01–3.84 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 165.5, 158.7, 153.4, 142.1, 134.2, 133.1, 128.9, 128.1, 128.0, 126.8, 125.7, 115.8, 111.2, 68.4, 67.4, 62.6, 61.7, 61.3, 44.3, 14.6, 14.0, 13.6; HRMS-ESI calcd for $C_{25}H_{27}BrN_3O_6$ $[M + H]^+$ 544.1078, found 544.1075.

Diethyl 1-benzyl-3'-ethoxy-5-methyl-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3f): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2f** (64 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 30 h to afford **3f**, 86 mg, 91% yield, > 20:1 dr; as a white solid, mp 117–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.18 (m, 5H), 6.95–6.92 (m, 2H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.25 (s, 1H), 4.89 (s, 2H), 4.28–4.09 (m, 4H), 3.87–3.67 (m, 2H), 2.18 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 0.62 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 165.6, 159.6, 153.5, 140.6, 134.9, 132.9, 130.4, 128.7, 127.7, 126.9, 125.7, 123.9, 109.4, 68.4, 67.1, 62.5, 61.5, 61.4, 44.2, 20.9, 14.6, 14.0, 13.4; HRMS-ESI calcd for $C_{26}H_{30}N_3O_6$ $[M + H]^+$ 480.2129, found 480.2136.

Diethyl 1-benzyl-3'-ethoxy-5-methoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3g): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2g** (67 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 24 h to afford **3g,** 98 mg, 99% yield, > 20:1 dr; as a slightly red solid, mp 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.23 (m, 5H), 6.81 (d, *J* = 2.5 Hz, 1H), 6.74 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.58 (d, *J* = 8.6 Hz, 1H), 5.33 (s, 1H), 4.96 (s, 2H), 4.36–4.16 (m, 4H), 3.88–3.81 (m, 2H), 3.71 (s, 3H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 165.6, 159.5, 156.2, 153.5, 136.2, 134.9, 128.8, 127.8, 126.9, 124.9, 115.5, 111.4, 110.3, 68.4, 67.2, 62.6, 61.9, 61.4, 55.9, 44.3, 14.6, 14.0, 13.5; HRMS-ESI calcd for $C_{26}H_{30}N_3O_7$ $[M + H]^+$ 496.2078, found 496.2078.

Diethyl 1-benzyl-6-bromo-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3h): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2h** (77 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3h,** 95 mg, 87% yield, > 20:1 dr; as yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.38–7.25 (m, 5H), 7.17 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 1.6 Hz, 1H), 5.31 (s, 1H), 4.98 (d, *J* = 16.3 Hz, 1H), 4.94 (d, *J* = 16.3 Hz, 1H), 4.36–4.18 (m, 4H), 3.87 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.78 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 165.5, 158.7, 153.4, 144.4, 134.2, 129.0, 128.1, 126.8, 126.3, 126.2, 124.0, 122.8, 113.1, 68.3, 67.3, 62.7, 61.6, 61.2, 44.3, 14.6, 14.0, 13.6; HRMS-ESI calcd for $C_{25}H_{27}BrN_3O_6$ $[M + H]^+$ 544.1078, found 544.1086.

Diethyl 1-benzyl-7-chloro-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3i): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2i** (68 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 48 h to afford **3i,** 80 mg, 80% yield, > 20:1 dr; as a white solid, mp 155–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.24 (m, 5H), 7.21 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.13 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.00–6.96 (m, 1H), 5.42 (s, 2H), 5.33 (s, 1H), 4.40–4.16 (m, 4H), 3.98–3.79 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 165.3, 158.8, 153.4, 139.1, 136.4, 132.7, 128.5, 127.3, 126.6, 126.1, 124.1, 123.6, 115.9, 68.7, 67.3, 62.6, 61.5, 61.1, 45.5, 14.5, 14.0, 13.6; HRMS-ESI calcd for $C_{25}H_{27}ClN_3O_6$ $[M + H]^+$ 500.1583, found 500.1589.

Diethyl 3'-ethoxy-1-methyl-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3j): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2j** (46 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3j,** 74 mg, 95% yield, > 20:1 dr; as a slightly yellow solid, mp 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (m, 1H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.08–7.04 (m, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 5.21 (s, 1H), 4.35–4.19 (m, 4H), 3.84 (q, *J* = 7.1 Hz, 2H), 3.29 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 165.7, 159.4, 153.4, 144.1, 130.3, 124.9, 123.8, 123.2, 108.6, 68.5, 67.1, 62.5, 62.2, 61.3, 27.0, 14.6, 14.0, 13.6; HRMS-ESI calcd for $C_{19}H_{24}N_3O_6$ $[M + H]^+$ 390.1660, found 390.1659.

Diethyl 3'-ethoxy-1,5-dimethyl-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3k): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2k** (49 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3k,** 74 mg, 91% yield, > 20:1 dr; as a slightly yellow solid, mp 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (d, *J* = 8.0 Hz, 1H), 7.00 (s, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.20 (s, 1H), 4.37–4.12 (m, 4H), 3.92–3.79 (m, 2H), 3.26 (s, 3H), 2.30 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 165.8, 159.6, 153.4, 141.7, 132.8, 130.5, 125.7, 123.7, 108.3, 68.5, 67.1, 62.5, 61.4, 61.3, 27.1, 21.0, 14.6, 14.0, 13.6; HRMS-ESI calcd for $C_{20}H_{26}N_3O_6$ $[M + H]^+$ 404.1816, found 404.1820.

Diethyl 1-allyl-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3l): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2l** (51 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 24 h to afford **3l,** 80 mg, 97% yield, 7:1 dr; as a white solid, mp

112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.34 (m, 1H), 7.20 (d, *J* = 7.5, 1H), 7.07–7.03 (m, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 5.89–5.80 (m, 1H), 5.26 (s, 1H), 5.24–5.16 (m, 2H), 4.43–4.37 (m, 2H), 4.34–4.18 (m, 4H), 3.85 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz,, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 165.6, 159.3, 153.3, 143.2, 130.1, 125.0, 123.9, 123.1, 117.2, 117.1, 109.5, 68.4, 67.1, 64.1, 62.5, 61.4, 42.6, 14.6, 13.9, 13.6; HRMS-ESI calcd for $C_{21}H_{26}N_3O_6$ $[M + H]^+$ 416.1816, found 416.1821.

1-*tert*-Butyl 1',5'-diethyl 3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1,1',5'(5'*H*)-tricarboxylate (3m): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2m** (63 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3m,** 73 mg, 77% yield, 5:1 dr; as a yellow semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.38–7.34 (m, 2H), 7.08 (dd, *J* = 7.6, 0.7 Hz, 1H), 5.63 (s, 1H), 4.33 (q, 7.1 Hz, 2H), 4.18–3.88 (m, 4H), 1.66 (s, 9H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 166.0, 156.6, 150.6, 148.8, 146.2, 130.6, 125.8, 124.0, 122.3, 116.1, 84.5, 68.0, 64.3, 63.2, 62.9, 61.8, 28.1, 14.1, 13.9, 13.7; HRMS-ESI calcd for $C_{23}H_{30}N_3O_8$ $[M + H]^+$ 476.2027, found 476.2031.

Diethyl 1-acetyl-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3n): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2n** (52 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3n,** 73 mg, 87% yield, 10:1 dr; as a colorless solid, mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.2 Hz, 1H), 7.46–7.38 (m, 1H), 7.24–7.19 (m, 2H), 5.25 (s, 1H), 4.38–4.18 (m, 4H), 3.84 (q, *J* = 6.9 Hz, 2H), 2.73 (s, 3H), 1.34 (t, *J* = 6.9 Hz, 3H), 1.19 (t, *J* = 6.9 Hz, 3H), 0.79 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 170.2, 165.0, 158.2, 153.3, 140.5, 130.5, 125.5, 124.4, 122.6, 116.7, 69.3, 67.4, 62.6, 62.2, 61.6, 26.6, 14.5, 13.8, 13.5; HRMS-ESI calcd for $C_{20}H_{24}N_3O_7$ $[M + H]^+$ 418.1609, found 418.1612.

5'-Benzyl 1'-ethyl 1-benzyl-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3o): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2o** (74 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 24 h to afford **3o,** 102 mg, 96% yield, > 20:1 dr; as a white solid, mp 129–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.15 (m, 10H), 6.98–6.93 (m, 1H), 6.88–6.86 (m, 2H), 6.63 (d, *J* = 7.7 Hz, 1H), 5.38 (s, 1H), 5.00 (d, *J* = 16.0 Hz, 1H), 4.85 (d, *J* = 12.1 Hz, 1H), 4.79 (d, *J* = 16.0 Hz, 1H), 4.72 (d, *J* = 12.1 Hz, 1H), 4.35–4.17 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 172.4 , 165.7 , 159.4 , 153.4, 143.0, 134.7, 134.6, 134.5, 130.2, 128.8, 128.4, 128.3, 127.7, 126.7, 124.9, 123.6, 123.3, 109.8, 68.3, 67.2, 67.2, 62.6, 61.5, 44.1, 14.6, 14.0; HRMS-ESI calcd for $C_{30}H_{30}N_3O_6$ $[M + H]^+$ 528.2129, found 528.2135.

5'-*tert*-Butyl 1'-ethyl 1-benzyl-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3p): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2p** (67 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 24 h to afford **3p,** 96 mg, 98% yield, 10:1 dr; as a slightly yellow solid, mp 171–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.25 (m, 5H), 7.25–7.19 (m, 2H), 7.04 (d, *J* = 7.7, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.22 (s, 1H), 5.03 (d, *J* = 15.8 Hz, 1H), 4.94 (d, *J* = 15.8 Hz, 1H), 4.39–4.14 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 164.3, 159.4, 153.6, 143.1, 134.9, 130.0, 128.8, 127.8, 127.0, 125.8, 124.1, 123.2, 109.4, 82.4, 68.7, 67.0, 62.4, 61.6, 44.3, 27.5, 14.6, 14.0; HRMS-ESI calcd for $C_{27}H_{32}N_3O_6$ $[M + H]^+$ 494.2286, found 494.2291.

Ethyl 1-benzyl-5'-cyano-3'-ethoxy-2-oxospiro[indoline-3,4'-pyrazole]-1'(5'*H*)-carboxylate (3q): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2q** (52 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3q,** 38 mg, 45% yield, > 20:1 dr; as an orange solid, mp 172–174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.5 Hz, 1H), 7.35–7.27 (m, 6H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 5.48 (s, 1H), 5.22 (d, *J* = 15.9 Hz, 1H), 4.73 (d, *J* = 15.9 Hz, 1H), 4.44–4.36 (m, 2H), 4.35–4.28 (m, 1H), 4.27–4.17 (m, 1H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 160.0, 153.1, 142.8, 134.3, 131.0, 128.9, 127.9, 126.8, 125.3, 124.0, 122.8, 113.4, 110.3, 67.7, 63.4, 61.7, 56.4, 44.4, 14.5, 13.9; HRMS-ESI calcd for $C_{23}H_{23}N_4O_4$ $[M + H]^+$ 419.1714, found 419.1720.

Ethyl 1-benzyl-3'-ethoxy-2-oxo-5'-phenylspiro[indoline-3,4'-pyrazole]-1'(5'*H*)-carboxylate (3r): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **2r** (63 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 72 h to afford **3r** as an inseparable diastereomeric mixture (dr 2:1), 53 mg, 56% yield, as a white powder; NMR data for the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.3 Hz, 1H), 7.34–7.28 (m, 5H), 7.19–7.11 (m, 5H), 6.62–6.56 (m, 2H), 6.47 (d, *J* = 7.5 Hz, 1H), 5.88 (s, 1H), 4.91 (d, *J* = 9.8 Hz, 1H), 4.87 (d, *J* = 9.8 Hz, 1H), 4.41–4.28 (m, 4H), 1.30–1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 160.5, 154.2, 143.1, 135.9, 134.9, 129.8, 128.8, 128.2, 127.9, 127.5, 127.0, 126.8, 126.3, 123.5, 122.5, 109.5, 74.1, 66.9, 64.5, 62.2, 44.1, 14.5, 14.1; Selected NMR data for the minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.21 (m), 7.02 (t, *J* = 7.7 Hz), 6.74–6.71 (m), 6.68 (t, *J* = 7.6 Hz), 5.61 (s), 5.03 (d, *J* = 15.8 Hz), 4.28–4.16 (m), 1.20–1.14 (m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 160.3, 154.2, 129.2, 128.6, 127.8, 127.3, 126.9, 126.0, 123.8, 123.4, 109.3, 71.3, 66.8, 64.6, 62.2, 14.4; HRMS-ESI calcd for $C_{28}H_{28}N_3O_4$ $[M + H]^+$ 470.2074, found 470.2077.

5'-Ethyl 1'-isopropyl 1-benzyl-3'-isopropoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3s): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **2a** (61 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3s** as an inseparable diastereomeric mixture (dr 5:1)**,** 93 mg, 95% yield, as colorless oil; NMR data for the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) :δ 7.34–7.28 (m, 5H), 7.21–7.14 (m, 2H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.29 (s, 1H), 5.09–5.03 (m, 2H), 4.98 (d, *J* = 6.4 Hz, 1H), 4.97 (d, *J* = 6.4 Hz, 1H), 3.82 (q, *J* = 7.1 Hz, 2H), 1.27 (d, *J* = 6.4 Hz, 12H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 165.9, 158.4, 156.4, 143.0, 134.8, 130.0, 128.8, 128.6, 127.8, 126.9, 125.0, 124.1, 123.1, 121.1, 109.6, 74.6, 70.0, 68.3, 61.6, 61.3, 44.1, 22.2, 22.0, 21.5, 21.2, 13.5; Selected NMR data for the minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.2 Hz), 7.28–7.25 (m), 7.26–7.22 (m), 6.87 (d, *J* = 7.6 Hz), 6.57 (d, *J* = 7.6 Hz), 5.63 (s), 5.24 (d, *J* = 16.4 Hz), 4.61 (d, *J* = 16.4 Hz), 4.15–3.95 (m), 1.13 (d, *J* = 6.1 Hz), 1.06 (t, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.3, 127.5, 123.8, 122.9, 22.0, 21.4, 13.9; HRMS-ESI calcd for $C_{27}H_{32}N_3O_6$ $[M + H]^+$ 494.2286, found 494.2289.

5'-Ethyl 1'-isopropyl 3'-isopropoxy-1-methyl-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3t): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **2j** (46 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3t,** 65 mg, 78% yield, > 20:1 dr; as a slightly yellow solid, mp 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.05 (dd, *J* = 7.6, 7.4 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 5.08–4.97 (m, 2H), 3.82 (q, *J* = 7.1 Hz,

2H), 3.28 (s, 3H), 1.30 (d, J = 6.0 Hz, 3H), 1.27 (d, J = 6.2 Hz, 3H), 1.21 (d, J = 6.2 Hz, 3H), 1.10 (d, J = 6.2 Hz, 3H), 0.82 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 166.0, 158.4, 152.9, 144.1, 130.1, 124.9, 124.0, 123.1, 108.5, 74.6, 70.0, 68.4, 61.8, 61.2, 27.0, 22.2, 21.9, 21.4, 21.2, 13.7; HRMS-ESI calcd for $C_{21}H_{28}N_3O_6$ $[M + H]^+$ 418.1973, found 416.1979.

5'-Ethyl 1'-isopropyl 1-allyl-3'-isopropoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3u): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **2l** (51 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 48 h to afford **3u,** 77 mg, 88% yield, 10:1 dr; as a white solid, mp 144–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (dd, J = 7.8, 7.6 Hz, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.04 (dd, J = 7.6, 7.3 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 5.92–5.76 (m, 1H), 5.22 (s, 1H), 5.22–5.14 (m, 2H), 5.08–5.03 (m, 1H), 5.01–4.96 (m, 1H), 4.45–4.36 (m, 2H), 3.84 (q, J = 7.1 Hz, 2H), 1.27 (d, J = 6.2 Hz, 6H), 1.20 (d, J = 6.2 Hz, 3H), 1.11 (d, J = 6.1 Hz, 3H), 0.81 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 165.9, 158.4, 152.8, 143.1, 130.1, 130.0, 125.0, 124.0, 123.0, 117.0, 109.4, 74.6, 70.1, 68.2, 61.8, 61.3, 42.5, 22.2, 22.0, 21.4, 21.2, 13.6; HRMS-ESI calcd for $C_{23}H_{30}N_3O_6$ $[M + H]^+$ 444.2129, found 444.2137.

5'-Benzyl 1'-isopropyl 1-benzyl-3'-isopropoxy-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3v): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **2o** (74 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **3v,** 100 mg, 90% yield, 6:1 dr; as a slightly yellow solid, mp 106–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.15 (m, 10H), 6.95 (d, J = 7.6 Hz, 1H), 6.92–6.90 (m, 2H), 6.62 (d, J = 7.8 Hz, 1H), 5.34 (s, 1H), 5.05 (d, J = 16.0 Hz, 1H), 5.03–4.93 (m, 2H), 4.85 (d, J = 12.1 Hz, 1H), 4.76 (d, J = 16.0 Hz, 1H), 4.70 (d, J = 12.1 Hz, 1H), 1.26 (d, J = 6.2 Hz, 6H), 1.24 (d, J = 6.2 Hz, 3H), 1.12 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 165.9, 158.5, 152.8, 143.0, 134.7, 134.6, 130.1, 128.8, 128.4, 128.3, 128.3, 127.7, 126.7, 124.8, 123.9, 123.2, 109.7, 74.7, 70.2, 68.0, 67.1, 61.9, 44.1, 22.1, 22.0, 21.5, 21.2; HRMS-ESI calcd for $C_{32}H_{34}N_3O_6$ $[M + H]^+$ 556.2442, found 556.2451.

5'-*tert*-Butyl 1'-isopropyl 1-benzyl-3'-isopropoxy-2-oxospiro [indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3w): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **2p** (67 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3w,** 99 mg, 95% yield, 20:1 dr; as a slightly yellow solid, mp 143–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (m, 5H), 7.24–7.19 (m, 2H), 7.02–6.98 (m, 1H), 6.71 (d, J = 7.7 Hz, 1H), 5.18 (s, 1H), 5.07 (d, J = 15.8 Hz, 1H), 5.08–4.98 (m, 2H), 4.89 (d, J = 15.8 Hz, 1H), 1.31 (d, J = 6.1 Hz, 3H), 1.28 (d, J = 6.0 Hz, 3H), 1.24 (d, J = 6.1 Hz, 3H), 1.12 (d, J = 6.0 Hz, 3H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 164.5, 158.4, 153.0, 143.0, 134.9, 129.9, 128.8, 127.8, 127.0, 125.7, 124.3, 123.2, 109.3, 82.2, 74.5, 70.0, 68.3, 62.1, 44.2, 27.5, 22.2, 22.0, 21.6, 21.2; HRMS-ESI calcd for $C_{29}H_{36}N_3O_6$ $[M + H]^+$ 522.2599, found 522.2606.

1'-Benzyl 5'-ethyl 1-benzyl-3'-(benzyloxy)-2-oxospiro[indoline-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (3x): Following the general procedure, the reaction of **1c** (93 mg, 0.3 mmol), **2a** (61 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 48 h to afford **3x,** 96 mg, 82% yield, > 20:1 dr; as yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.37 (m, 2H), 7.35–7.30 (m, 3H), 7.28–7.25 (m, 2H), 7.24–7.14 (m, 10H), 6.98 (d, J = 7.4 Hz, 1H), 6.64 (d, J = 7.7 Hz, 1H), 5.40 (s, 1H), 5.34 (d, J = 12.3 Hz, 1H), 5.28 (d, J = 12.3 Hz, 1H), 5.24 (d, J = 14.1 Hz, 1H), 5.16 (d, J = 14.1 Hz, 1H), 4.99 (d, J = 15.9 Hz, 1H), 4.88 (d, J = 15.9 Hz, 1H), 3.76 (q, J = 7.1 Hz, 2H), 0.63 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 165.5, 159.6, 153.2, 143.0, 136.0, 134.8, 134.6, 130.3, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 126.8, 125.1, 123.6, 123.3, 109.8, 72.8, 68.7, 68.1, 61.5, 44.2, 13.4; HRMS-ESI calcd for $C_{35}H_{23}N_3O_6$ $[M + H]^+$ 590.2286, found 590.2292.

Diethyl 3'-ethoxy-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5a): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **4a** (44 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was run for 1 h to afford **5a** as an inseparable diastereomeric mixture (dr 3:1)**,** 60 mg, 79% yield; as colorless oil; NMR data for the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.5 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.19–7.14 (m, 2H), 4.94 (s, 1H), 4.39–4.32 (m, 2H), 4.31–4.26 (m, 2H), 4.16–4.07 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 166.3, 165.5, 160.9, 155.5, 131.2, 126.2, 124.7, 123.5, 112.0, 73.2, 64.1, 63.3, 63.2, 62.3, 14.4, 14.1, 13.7; Selected NMR data for the minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) :δ 7.39–7.36 (m), 7.20 (d, J = 7.6 Hz), 7.12 (d, J = 7.6 Hz), 5.67 (s), 4.46–4.40 (m), 4.22–4.18 (m), 4.03–3.94 (m), 1.16 (t, J = 7.1 Hz), 1.16 (t, J = 7.1 Hz), 1.08 (t, J = 6.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$):167.6, 162.1, 131.4, 126.4, 124.1, 121.6, 112.1, 70.0, 63.2, 62.0, 14.5, 13.9; HRMS-ESI calcd for $C_{18}H_{21}N_2O_7$ $[M + H]^+$ 377.1343, found 377.1350.

5'-Benzyl 1'-ethyl 3'-ethoxy-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5b): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **4b** (56 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was conducted for 6 h to afford **5b** as an inseparable diastereomeric mixture (dr 2:1)**,** 52 mg, 59% yield; as yellow oil; NMR data for the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.45 (m, 1H), 7.44–7.36 (m, 5H), 7.30–7.27 (m, 1H), 7.16–7.11 (m, 2H), 5.36 (d, J = 12.1 Hz, 1H), 5.29 (d, J = 12.1 Hz, 1H), 5.00 (s, 1H), 4.32–4.23 (m, 2H), 4.10–3.99 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 166.2, 165.5, 160.8, 155.4, 134.8, 131.2, 128.6, 128.6, 126.1, 124.7, 124.2, 123.3, 111.9, 73.1, 68.0, 64.1, 63.3, 63.2, 14.3, 13.7; Selected NMR data for the minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01–6.90 (m), 5.73 (s), 5.04 (d, J = 12.0 Hz), 4.96 (d, J = 12.0 Hz), 4.21–4.12 (m), 1.36 (t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 162.0, 134.4, 131.3, 128.5, 126.4, 112.0, 67.7, 63.4, 14.4; HRMS-ESI calcd for $C_{23}H_{23}N_2O_7$ $[M + H]^+$ 439.1500, found 439.1497.

5'-*tert*-Butyl 1'-ethyl 3'-ethoxy-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5c): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **4c** (50 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 1 h to afford **5c,** 70 mg, 85% yield, 7:1 dr; as colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.5 Hz, 1H), 7.42–7.37 (m, 1H), 7.19 (dd, J = 7.5, 7.1 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 4.84 (s, 1H), 4.35–4.25 (m, 2H), 4.25–4.06 (m, 2H), 1.60 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 165.4, 164.9, 160.8, 155.5, 131.0, 126.2, 124.6, 123.7, 111.8, 83.2, 73.8, 63.9, 63.3, 63.1, 27.9, 14.4, 13.7; HRMS-ESI calcd for $C_{20}H_{25}N_2O_7$ $[M + H]^+$ 405.1656, found 405.1654.

5'-*tert*-Butyl 1'-ethyl 3'-ethoxy-5-methyl-2-oxo-2*H*-spiro [benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5d): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **4d** (52 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 8 h to afford **5d,** 59 mg, 70% yield, > 20:1 dr; as colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ

7.33 (s, 1H), 7.17 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 4.81 (s, 1H), 4.34–4.25 (m, 2H), 4.23–4.17 (m, 1H), 4.15–4.07 (m, 1H), 2.37 (s, 3H), 1.60 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 165.6, 165.0, 158.8, 155.5, 134.4, 131.5, 126.5, 123.5, 111.4, 83.2, 73.8, 64.0, 63.1, 63.0, 27.9, 21.0, 14.4, 13.8; HRMS-ESI calcd for $C_{21}H_{27}N_2O_7$ $[M + H]^+$ 419.1813, found 419.1813.

5'-*tert*-Butyl 1'-ethyl 3'-ethoxy-6-methoxy-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5e): Following the general procedure, the reaction of **1a** (52 mg, 0.3 mmol), **4e** (55 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 9 h to afford **5e,** 67 mg, 78% yield, > 20:1 dr; as slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.4 Hz, 1H), 6.72(d, J = 8.4 Hz, 1H), 6.70 (s, 1H), 4.79 (s, 1H), 4.34–4.24 (m, 2H), 4.23–4.17(m, 1H), 4.13–4.05 (m, 1H), 3.82 (s, 3H), 1.58 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 165.7, 164.9, 162.1, 161.9, 155.4, 126.5, 115.4, 110.5, 98.3, 83.1, 74.1, 63.4, 63.0, 62.9, 55.7, 27.9, 14.4, 13.8; HRMS-ESI calcd for $C_{21}H_{27}N_2O_8$ $[M + H]^+$ 435.1762, found 435.1761.

5'-*tert*-Butyl 1'-isopropyl 3'-isopropoxy-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5f): Following the general procedure, the reaction of **1b** (61 mg, 0.3 mmol), **4c** (50 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 1 h to afford **5f,** 75 mg, 85% yield, 20:1 dr; as yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.54 (d, J = 7.5 Hz, 1H), 7.41–7.36 (m, 1H), 7.20–7.16 (m, 1H), 7.14 (d, J = 8.3 Hz, 1H), 5.10–5.03 (m, 1H), 4.95–4.88 (m, 1H), 4.83 (s, 1H), 1.60 (s, 9H), 1.34 (d, J = 6.3 Hz, 3H), 1.32 (d, J = 6.3 Hz, 3H), 1.27 (d, J = 6.3 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 165.1, 164.8, 160.8, 155.2, 130.9, 126.1, 124.5, 124.1, 111.8, 83.1, 73.7, 71.5, 71.0, 63.9, 28.0, 21.9, 21.9, 21.5, 21.2; HRMS-ESI calcd for $C_{22}H_{29}N_2O_7$ $[M + H]^+$ 433.1969, found 433.1974.

1'-Benzyl 5'-*tert*-butyl 3'-(benzyloxy)-2-oxo-2*H*-spiro[benzofuran-3,4'-pyrazole]-1',5'(5'*H*)-dicarboxylate (5g): Following the general procedure, the reaction of **1c** (93 mg, 0.3 mmol), **4c** (50 mg, 0.2 mmol), and PPh_3 (79 mg, 0.3 mmol) in THF (2.0 mL) was performed for 24 h to afford **5g,** 60 mg, 56% yield, 10:1 dr; as colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 7.6 Hz, 1H), 7.41–7.39 (m, 3H), 7.36–7.30 (m, 5H), 7.26–7.24 (m, 2H), 7.18–7.16 (m, 2H), 7.12 (d, J = 8.2 Hz, 1H), 5.30 (d, J = 12.2 Hz, 1H), 5.24 (d, J = 12.2 Hz, 1H), 5.16 (d, J = 12.6 Hz, 1H), 5.08 (d, J = 12.6 Hz, 1H), 4.88 (s, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 165.3, 164.8, 160.9, 155.3, 135.5, 134.4, 131.2, 128.5, 128.5, 128.4, 127.6, 127.3, 126.3, 124.7, 123.6, 121.6, 112.0, 83.5, 74.0, 68.5, 68.3, 64.1, 27.9; HRMS-ESI calcd for $C_{30}H_{29}N_2O_7$ $[M + H]^+$ 529.1969, found 529.1976.

Acknowledgements

Financial support from National Natural Science Foundation of China (Grant no. 21272119; 21472096; 21121002; J1103306) and the Natural Science Foundation of Shanxi (Grant no. 2014021015-3) is gratefully acknowledged. The authors also thank professor Zhi-Jin Fan at Nankai University for his kind assistance with the bioassay.

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† Electronic Supplementary Information (ESI) available: X-ray crystal structure data and ORTEP drawings for **3a** (CCDC 1046817) and **3q** (CCDC 1046823); copies of NMR spectra for **4c–e**, **3** and **5**. See DOI: 10.1039/b000000x/

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