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Highly Regio- and Diastereoselective Construction of Spirocyclopenteneoxindole Phosphonates Through Phosphine-catalyzed [3+2] Annulation Reaction

Chengbin Yu,[a] Weiping Zheng,[a] Junchen Zhan,[a] Yuchao Sun,[a] and Zhiwei Miao*[a,b]

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A phosphine-catalyzed [3+2] annulation of MBH phosphonates with isatylidene malononitriles is developed. The described method, which is different from most traditional phosphorus ylide intermediate reaction mode of the MBH carbonates with isatylidene malononitriles, represents a novel approach to highly regioselective and diastereoselective synthesis of spirocyclopenteneoxindole phosphonates.

Introduction

The spirocyclic oxindoles bearing a tetrasubstituted carbon stereocenter at the 3-position is featured in a large number of natural products and medicinally relevant compounds (Figure 1).[1] Among many spirooxindole cores, the regioselective and stereoselective preparation of 3-spirocyclopentane-2-oxindoles containing two adjacent quaternary centers is challenging and has been addressed formidable synthetic tasks.[2] Although many synthetic methods have been developed for the stereoselective synthesis of spirooxindoles, but their high-yielding synthesis with multiple stereocenters and a spiro-quaternary carbon is a still demanding task.[3]

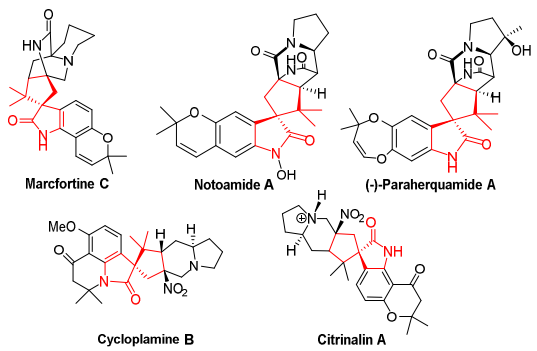
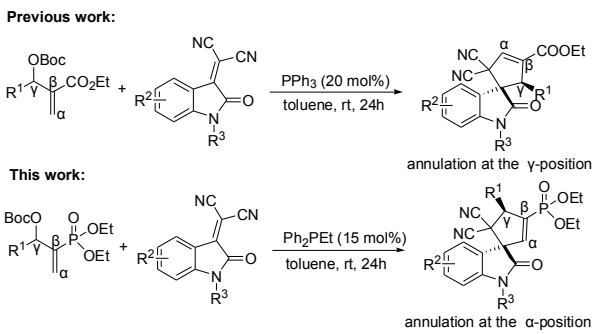


Figure 1. Spirocyclicpentane oxindole structures having two contiguous quaternary centers.

The annulation of Morita–Baylis–Hillman acetates and carbonates with electron-deficient olefins is an extremely useful synthetic method to construct multifunctional cyclic compounds.[4] In this context, Lu and co-workers first reported annulation reactions of MBH carbonates as a reactive functionalized 1,3-dipoles with various electron-deficient olefins catalyzed by tertiary phosphine, affording the corresponding cycloadducts in good yields.[4d-i] Trost and co-workers reported an enantioselective construction of spirocyclic oxindolic cyclopentanes by using a palladium catalysed [3+2] cycloaddition of trimethylenemethane.[5] Recently, Barbas and his co-workers reported a novel asymmetric [3+2] cycloaddition of MBH carbonates with methyleneindolinones in the presence of a chiral phosphine to give the corresponding spirocyclopentaneoxindoles in good yields and high *ee* values.[6] Lu disclosed an L-threonine-derived phosphines catalytic asymmetric [3+2] annulation of MBH adducts for the synthesis of 3-spirocyclopentene-2-oxindoles.[2h] In contrast, the direct catalytic asymmetric construction of the spirocyclopententene oxindole scaffold has remained an important challenge.

For the construction of five-membered ring systems, phosphine-mediated [3+2] annulation represents one of the most efficient approaches. However, the asymmetric cyclo-addition employing the MBH adducts is rare reported.[7] Compared with allenes and alkynes, the MBH adducts are much more challenging substrates for such annulations. Their lower reactivity makes the development of an asy mmetric catalytic annulation process particularly difficult. Furthermore, the previous researchers found that the transformations of MBH acetates and carbonates have been directed toward the annulation at the γ-position with electron-deficient olefins in the presence of tertiary phosphine (Scheme 1).[4d-s]



Scheme 1. Phosphine-catalyzed [3+2] annulations of isatylidenenalononitirle to construct spirocyclopentene oxindoles.

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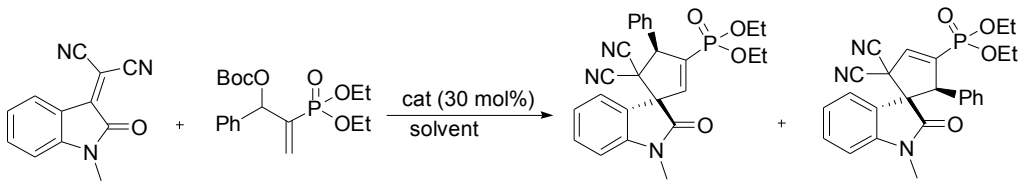
The annulation of MBH adducts at the α-position with electron-deficient olefins is yet to be developed. Herein, we document the first highly regio- and diastereoselective [3+2] cyclo-addition between the MBH phosphonates and electron-deficient olefins. The electron-deficient alkene components necessary for the annulation reactions can be conveniently derived from isatins. Such tetrasubstituted activated alkenes are explored substrates in the asymmetric [3+2] cyclization processes, thereby creating 3-spirocyclopentene-2-oxindoles containing two contiguous quaternary centers.

Results and discussioin

We initiated our studies by evaluating the reaction between isatin-derived α,α-dicyanoalkene **1a**[8] and the MBH phosphonate **2a**[9] using triphenylphosphine as the catalyst in toluene at room temperature (Table 1, entry 1). No product was obtained after 24h, and **1a** was completely recovered. We assumed that the lack of reaction was due to steric hindrance and the weak nucleophilic ability of the phosphine. Therefore, we turned our attention to more active phosphine catalysts (Table 1, entries 2-4). With tributylphosphine (Bu_3P) as the catalyst, the desired cycloaddition product **3a** was obtained in good yield with excellent diastereoselectivity (Table 1, entry 2). To further improve the reaction efficiency, a brief survey on the reaction conditions was conducted by using the reaction of **1a** and **2a** as a model. Among several phosphine catalysts tested, ethyldiphenylphosphine (Ph_2PEt) emerged as the preferred catalyst in terms of the yield and diastereoselectivity (Table 1, entries 3-4). This result implied that the nucleophilicity of the phosphines had a significant influence on the outcome of the reaction.

With Ph_2PEt chosen as the catalyst, other parameters for the reaction conditions were further examined. An elevated temperature (50 ºC) brought about a better yield of **3a** with a ratio of **3a**/**3a'** 99:1 (Table 1, entry 5). A solvent screening was subsequently performed, and toluene was identified to be the best solvent for the reaction, whereas other solvent, such as CH_2Cl_2, THF, methyl *tert*-butyl ether (MTBE), and CH_3CN, could readily afford the desired product in inferior yields (Table 1, entries 6-9).

Table 1. Optimization of conditions of the [3+2] cycloaddition of **1a** and **2a**.[a]



1a **2a** α addition product **3a** γ addition product **3a'**

Entry	Catalyst	Solvent	Temp. (ºC)	Time (h)	**3a**/**3a'**[b]	d.r.[b]	Yield (%)[c]
1	Ph_3P	toluene	25	24	—	—	—
2	Bu_3P	toluene	25	15	>99:1	>99:1	83
3	Ph_2PEt	toluene	25	35	>99:1	>99:1	88
4	$PhPMe_2$	toluene	25	35	>99:1	>99:1	80
5	Ph_2PEt	toluene	50	10	>99:1	>99:1	98
6	Ph_2PEt	CH_2Cl_2	30	20	>99:1	>99:1	95
7	Ph_2PEt	THF	50	30	>99:1	>99:1	91
8	Ph_2PEt	MTBE[d]	50	48	>99:1	>99:1	85
9	Ph_2PEt	CH_3CN	50	15	>99:1	>99:1	93
10[e]	Ph_2PEt	toluene	50	15	>99:1	>99:1	99

[a] Unless otherwise noted, all reactions were carried out using isatylidenemalononitrile **1a** (0.10 mmol, 1 equiv), MBH phosphonate **2a** (0.13 mmol) in 2 mL solvent with 30 mol% of catalyst at 25 °C. [b] The ratio of the **3a**/**3a'** and d.r. was determined by ^{31}P NMR analysis of the crude product. [c] Yield of the isolated product. [d] MTBE = methyl *tert*-butyl ether. [e] 15% Ph_2PEt was used.

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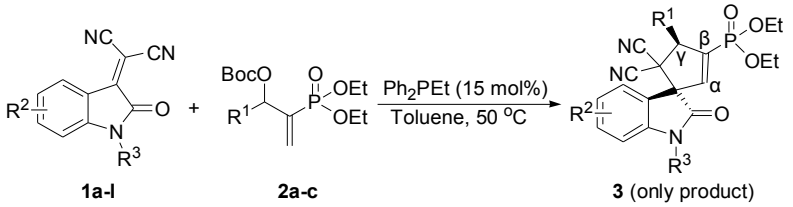
Table 2. Substrate scope of the reaction[a]



1a-l **2a-c** **3** (only product)

Entry	R^1	R^2	R^3	Time (h)	d.r.[b]	Yield (%)[c]
1	**2a**, Ph	**1a**, H	Me	15	>99:1	**3a**, 99
2	Ph	**1b**, 5-Br	Me	15	>99:1	**3b**, 87
3	Ph	**1c**, 5-Cl	Me	30	>99:1	**3c**, 95
4	Ph	**1d**, 5-Me	Me	11	>99:1	**3d**, 95
5	Ph	**1e**, 5-OMe	Me	8	>99:1	**3e**, 99
6	Ph	**1f**, 6-OMe	Me	50	>99:1	**3f**, 85
7	Ph	**1g**, 6-Me	Me	30	>99:1	**3g**, 93
8	Ph	**1h**, 7-Me	Me	8	>99:1	**3h**, 99
9	Ph	**1i**, 5-Me-7-Me	Me	7	>99:1	**3i**, 99
10[d]	**2b**, *n*-Pr	H	Me	50	>99:1	**3j**, 99
11[d]	*n*-Pr	5-Me	Me	44	>99:1	**3k**, 95
12[d]	*n*-Pr	7-Me	Me	44	>99:1	**3l**, 98
13[d]	*n*-Pr	5-Me-7-Me	Me	44	>99:1	**3m**, 98
14	**2c**, furan	H	Me	8	>99:1	**3n**, 98
15	furan	**1j**, H	Bn	13	>99:1	**3o**, 95
16	furan	5-OMe	Me	8	>99:1	**3p**, 91
17	furan	6-OMe	Me	44	>99:1	**3q**, 97
18	furan	7-Me	Me	11	>99:1	**3r**, 98
19	furan	5-Br	Me	13	>99:1	**3s**, 85
20	furan	6-Me	Me	33	>99:1	**3t**, 88
21	Ph	**1k**, H	H	72	>99:1	**3u**, 68
22	Ph	H	Bn	11	>99:1	**3v**, 88
23	Ph	**1l**, H	Ac	72	>99:1	**3w**, <15

[a] Reaction conditions: isatylidenemalononitrile **1** (0.10 mmol), MBH phosphonate **2** (0.13 mmol) in 2 mL of toluene at 50°C in the presence of 15 mol% of Ph_2PEt. [b] The d.r. was determined by ^{31}P NMR analysis of the crude product. [c] Yield of the isolated product. [d] 30% Ph_2PEt was used.

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It is worthwhile noting that the regioselectivity and diastereoselectivity of this reaction was excellence and the catalyst loading could be further reduced to 15 mol% with Ph_2PEt (Table 1, entry 10). Thus, the optimal reaction conditions for this transformation were determined to be 0.1 mmol isatylidenemalononitrile **1a**, 0.13 mmol MBH phosphonate **2a**, and 15 mol% of Ph_2PEt as a catalyst in 2 mL toluene as a solvent at 50 ºC. The diastereomeric ratio of product was determined by ^{31}P NMR spectroscopy of the crude product. In order to determine the relative configuration of the major diastereomer **3a**, a single crystal X-ray diffraction study of **3a** was performed.[10] The molecular structure of **3a** is shown in Figure 2, and the structure showed that the relative configuration of the main product was assigned as *threo*.

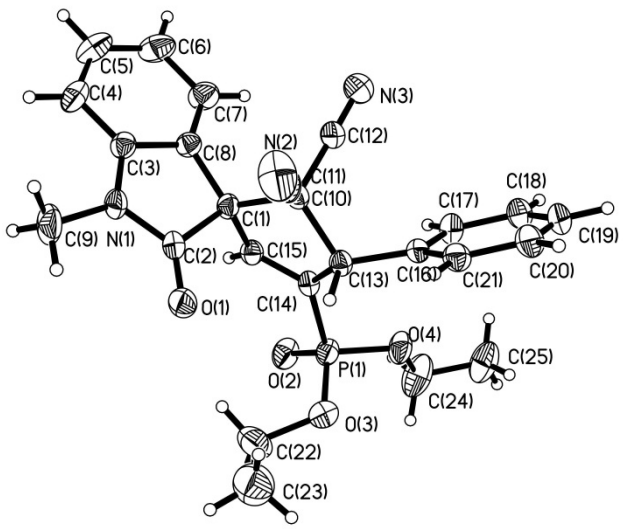


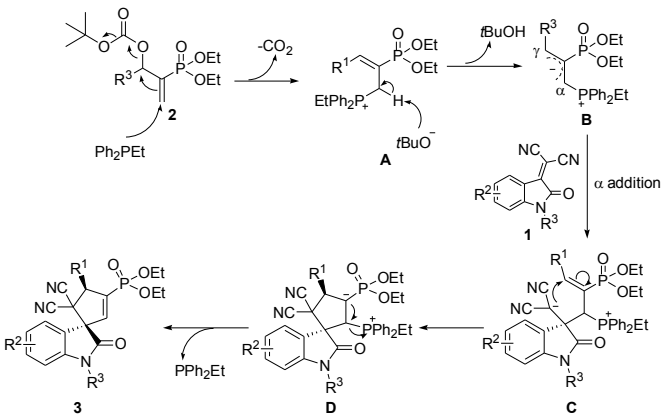
Figure 2. The X-ray crystal structure of **3a**.

Under the optimized reaction conditions, we set out to examine the scope and limitations of this reaction between isatylidenemalononitriles **1a-l** and MBH phosphonates **2a-c** (Table 2). Firstly, the annulation reactions of **1a-i** and **2a** proceeded smoothly to afford the desired products **3a-i** in 85-99% yield with >99% d.r., irrespective of the variation in the electronic and steric properties of the substituents attached to the phenyl rings of the oxindole backbones (Table 2, entries 1-9). Notably, the reaction proceeded slowly when electron-withdrawing substituents were at the 5-position and electron-donating substituents at the 6-position on the aromatic ring (Table 2, entries 3 and 6).

Substrate **2b** was ineffective for this transformation under the identical conditions (Table 2, entries 10-13). The reactions of (2-BocO-1-methylene-pentyl)-phosphonate **2b**, which bear straight-chain alkane substitutent at the MBH phosphonate, proceeded sluggishly in the presence of 15 mol% of catalyst loading to give less than 40% yield of the desired products with 24h. Consequently, the catalyst loading was increased to 30 mol%, which afforded the desired products **3j-m** in good yields with almost perfect regio- and stereocontrol (up to 99:1) within 50h (Table 2, entries 10-13). The reaction tolerated different substitute moieties in the MBH phosphonates **2**. Notably, the presence of 3-furyl in **2c** resulted in good to excellent yields and stereoselectivities (Table 2, entries 14-20).

We further demonstrated the electronic factor of *N*-substitution in the 2-(2-oxindolin-3-ylidene)malononitriles **1**. Reaction of **2a** with *N*-H olefin 1k under the catalysis of Ph_2PEt in toluene at 60 ºC for 72h furnished **3u** in 68% yield (Table 2, entry 21). In a similar manner, the annulation reaction of **2a** with *N*-Me or *N*-Bn olefins 1a/1j under Ph_2PEt catalysis within 15h furnished **3a** and **3v** in 99/88% yield with >99% stereoselectivity (Table 2, entries 1 and 22). Surprisingly, when *N*-acetyl protected olefin 1l was employed as the substrate the reaction proceeded exclusively in lower yield (15%) despite a long reaction time (Table 2, entry 23). This result clearly shows that the single directional electrophilicity of olefin **1** is crucial to achieving high yields in this reaction.

The mechanism of this [3+2] annulation reaction is proposed on the basis of previous literatures[2h,4f,s] as shown in Scheme 2. The first step involves the nucleophilic attack of the phosphine on the MBH phosphonate **2** to yield the phosphonium salt **A**. The *in situ* generated *tert*-butoxide anion deprotonates **A** to generate ylide **B**, which then undergoes α addition to alkene **1** to give the intermediate **C**. Subsequent Michael addition at the α-position of phosphorus cation to generate intermediate **D**. The elimination of the phosphine moiety along with the double bond formation furnishes the corresponding product **3** and then regenerates the catalyst. The observed α selectivity maybe attributed to the steric hindrance effects and electronic repulsions between the phosphonate group and ethyl-diphenyl-phosphonium.



Scheme 2. Plausible reaction mechanism.

Conclusions

In conclusion, we have developed a phosphine-catalyzed highly regio- and diastereoselective [3+2] annulation of MBH phosphonates **2** with isatylidene malononitriles **1**, affording the corresponding functionalized spirocyclopenteneoxindole

phosphonates **3** in good to excellent yields. This is the first time for MBH phosphonates as C_3 synthons in [3+2] annulation reactions. Compared with MBH carbonates, MBH phosphonates undergoes α addition to alkene from the ylide **B**. A plausible reaction mechanism has also been proposed on the basis of previous literature. Further investigations on the enantioselective phosphine-catalyzed annulation reaction are currently underway.

Acknowledgements

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Experimental section

General methods

Solvents were dried and distilled prior to use according to the standard methods. Unless otherwise indicated, all materials were obtained from commercial sources, and used as purchased without dehydration. Flash column chromatography was performed on silica gel (particle size 10-40 μm, Ocean Chemical Factory of Qingdao, China). Nitrogen gas (99.999%) was purchased from Boc Gas Inc. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were recorded in $CDCl_3$ at Bruker 400 MHz spectrometers, TMS served as internal standard (δ = 0 ppm) for ^{1}H NM R and ^{13}C NMR, H_3PO_4 served as internal standard (δ = 0 ppm) for ^{31}P NMR. The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer. Melting points were determined on a T-4 melting point apparatus (uncorrected). Optical rotations were recorded on a Perkin Elemer 241 Polarimeter.

General procedure for the preparation of 3:

A solution of MBH phosphonates **2** (0.13 mmol), isatylidene malononitrile **1** (0.1 mmol) and catalyst Ph_2PEt (0.015 mmol) in toluene (2.0 mL) was stirred at 50°C under N_2 atmosphere. After isatylidene malononitrile **1** was completely consumed (monitored by TLC), the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 1:1) to afford product **3** as a white solid.

Diethyl(5,5-dicyano-1'-methyl-2'-oxo-4-phenylspiro [cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3a). White solid; mp 233 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 4.5 Hz, 2H), 7.50 (dd, *J* = 16.7, 5.7 Hz, 4H), 7.25 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.57 (dd, *J* = 11.0, 2.2 Hz, 1H), 5.51 (s, 1H), 4.00-4.17 (m, 2H), 3.80-4.01 (m, 2H), 3.34 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.00, 145.82 (d, *J* = 12.4 Hz), 144.08, 140.18 (d, *J* = 190.8 Hz), 132.51, 131.46, 130.18, 129.74, 128.55, 126.93, 123.95, 123.09, 112.73, 111.84, 109.19, 65.58 (d, *J* = 18.7 Hz), 62.85 (d, *J* = 5.9 Hz), 62.74 (d, *J* = 6.5 Hz), 60.81 (d, *J* = 15.1 Hz), 52.87 (d, *J* = 13.0 Hz), 27.13, 16.23 (d, *J* = 6.5 Hz), 16.03 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.41; HRMS calculated $[M+Na]^+$ for $C_{25}H_{24}N_3O_4P$: 484.1402, found: 484.1399.

Diethyl(5'-bromo-5,5-dicyano-1'-methyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3b). White solid; mp 185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.64 (dt, *J* = 9.8, 4.9 Hz, 1H), 7.55-7.61 (m, 2H), 7.40-7.53 (m, 3H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.54 (dd, *J* = 10.9, 2.5 Hz, 1H), 5.49 (s, 1H), 4.01-4.19 (m, 2H), 3.82-4.00 (m, 2H), 3.31 (s, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.47, 144.86 (d, *J* = 12.7 Hz), 143.14, 140.87 (d, *J* = 190.6 Hz), 134.40, 132.26, 130.17, 130.10, 129.85, 128.59, 124.96, 116.54, 112.47, 111.63, 110.59, 65.31 (d, *J* = 19.2 Hz), 62.85 (t, *J* = 5.9 Hz), 60.89 (d, *J* = 14.7 Hz), 52.73 (d, *J* = 13.0 Hz), 27.24, 16.22 (d, *J* = 6.4 Hz), 16.05 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.02. HRMS calculated $[M+Na]^+$ for $C_{25}H_{23}BrN_3O_4P$: 562.0507, found: 562.0504.

Diethyl(5'-chloro-5,5-dicyano-1'-methyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3c). White solid; mp 225 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 1.7 Hz, 1H), 7.59 (dd, *J* = 6.2, 2.7 Hz, 2H), 7.44-7.53 (m, 4H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.54 (dd, *J* = 11.0, 2.6 Hz, 1H), 5.50 (s, 1H), 4.02-4.18 (m, 2H), 3.85-4.01 (m, 2H), 3.32 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.57 (d, *J* = 2.3 Hz), 144.89 (d, *J* = 12.8 Hz), 142.64, 140.82 (d, *J* = 190.6 Hz), 132.25, 131.50, 130.17, 129.86, 129.47, 128.59, 127.36, 124.60, 112.47, 111.64, 110.17, 65.37 (d, *J* = 19.0 Hz), 62.86 (t, *J* = 6.0 Hz), 60.87 (d, *J* = 14.9 Hz), 52.70 (d, *J* = 12.9 Hz), 27.27, 16.23 (d, *J* = 6.4 Hz), 16.05 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.05. HRMS calculated $[M+Na]^+$ for $C_{25}H_{23}ClN_3O_4P$: 518.1012, found: 518.1005.

Diethyl(5,5-dicyano-1',5'-dimethyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3d). White solid; mp 195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 6.5, 2.8 Hz, 2H), 7.49 (dd, *J* = 8.7, 4.7 Hz, 4H), 7.30 (d, *J* = 8.2 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.56 (dd, *J* = 11.0, 2.7 Hz, 1H), 5.51 (t, *J* = 2.2 Hz, 1H), 4.01-4.18 (m, 2H), 3.82-4.00 (m, 2H), 3.31 (s, 3H), 2.42 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.93, 146.02 (d, *J* = 12.4 Hz), 141.67, 139.99 (d, *J* = 190.7 Hz), 133.73, 132.61, 131.68, 130.20, 129.70, 128.51, 127.68, 123.13, 112.79, 111.88, 108.87, 65.65 (d, *J* = 19.1 Hz), 62.81 (d, *J* = 6.0 Hz), 62.69 (d, *J* = 6.3 Hz), 60.85 (d, *J* = 15.0 Hz), 52.89 (d, *J* = 13.0 Hz), 27.12, 21.15, 16.22 (d, *J* = 6.4 Hz), 16.02 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.49. HRMS calculated $[M+Na]^+$ for $C_{26}H_{26}N_3O_4P$: 498.1559, found: 498.1561.

Diethyl(5,5-dicyano-5'-methoxy-1'-methyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3e). White solid; mp 205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 4.4 Hz, 2H), 7.48 (d, *J* = 3.8 Hz, 3H), 7.30 (s, 1H), 7.04 (d, *J* = 8.6 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.53-6.63 (m, 1H), 5.52 (s, 1H), 4.03-4.15 (m, 2H), 3.88-3.97 (m, 2H), 3.85 (s, 3H), 3.31 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.71, 156.72, 145.79 (d,

J = 12.7 Hz), 140.18 (d, *J* = 190.9 Hz), 137.24, 132.56, 130.18, 129.72, 128.53, 124.04, 116.86, 113.30, 112.70, 111.90, 109.74, 65.92 (d, *J* = 19.1 Hz), 62.86 (d, *J* = 5.9 Hz), 62.73 (d, *J* = 6.4 Hz), 60.83 (d, *J* = 14.9 Hz), 55.98, 52.95 (d, *J* = 13.0 Hz), 27.17, 16.22 (d, *J* = 6.4 Hz), 16.01 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.47. HRMS calculated $[M+Na]^+$ for $C_{26}H_{26}N_3O_5P$: 514.1508, found: 514.1503.

Diethyl(5,5-dicyano-6'-methoxy-1'-methyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3f). White solid; mp 155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.64 (m, 3H), 7.42-7.52 (m, 3H), 6.72 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.55 (dd, *J* = 11.0, 2.4 Hz, 2H), 5.46 (s, 1H), 4.02-4.16 (m, 2H), 3.83-3.97 (m, 5H), 3.31 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.55, 162.60, 146.32 (d, *J* = 12.4 Hz), 145.51, 139.77 (d, *J* = 191.1 Hz), 132.67, 130.15, 129.66, 128.52, 127.87, 114.74, 112.84, 112.02, 107.51, 97.31, 65.52 (d, *J* = 19.3 Hz), 62.82 (d, *J* = 5.8 Hz), 62.70 (d, *J* = 6.3 Hz), 60.62 (d, *J* = 15.0 Hz), 55.73, 53.08 (d, *J* = 12.7 Hz), 27.11, 16.21 (d, *J* = 6.4 Hz), 16.01 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.56. HRMS calculated $[M+Na]^+$ for $C_{26}H_{26}N_3O_5P$: 514.1508, found: 514.1508.

Diethyl(5,5-dicyano-1',6'-dimethyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3g). White solid; mp 181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 4.0 Hz, 2H), 7.49 (dd, *J* = 10.7, 5.7 Hz, 4H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 11.0 Hz, 1H), 5.50 (s, 1H), 4.00-4.15 (m, 2H), 3.83-3.98 (m, 2H), 3.60 (s, 3H), 2.64 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.77 (d, *J* = 2.4 Hz), 146.05 (d, *J* = 12.6 Hz), 141.79, 139.94 (d, *J* = 190.8 Hz), 135.21, 132.58, 130.19, 129.70, 128.52, 124.84, 123.73, 123.69, 120.85, 112.88, 111.76, 65.17 (d, *J* = 18.9 Hz), 62.84 (d, *J* = 6.0 Hz), 62.72 (d, *J* = 6.3 Hz), 60.79 (d, *J* = 15.0 Hz), 53.28 (d, *J* = 12.8 Hz), 30.60, 19.06, 16.22 (d, *J* = 6.4 Hz), 16.03 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.49. HRMS calculated $[M+Na]^+$ for $C_{26}H_{26}N_3O_4P$: 498.1559, found: 498.1558.

Diethyl(5,5-dicyano-1',7'-dimethyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3h). White solid; mp 183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 19.9 Hz, 2H), 7.49 (d, *J* = 16.5 Hz, 4H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 11.0 Hz, 1H), 5.50 (s, 1H), 4.02-4.17 (m, 2H), 3.82-3.99 (m, 2H), 3.60 (s, 3H), 2.64 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.77, 146.01 (d, *J* = 12.5 Hz), 141.80, 140.00 (d, *J* = 190.7 Hz), 135.21, 132.60, 130.19, 129.69, 128.51, 124.84, 123.72, 120.83, 112.88, 111.76, 65.18 (d, *J* = 18.8 Hz), 62.81 (d, *J* = 6.1 Hz), 62.70 (d, *J* = 6.2 Hz), 60.81 (d, *J* = 15.0 Hz), 53.30 (d, *J* = 12.8 Hz), 30.60, 19.05, 16.22 (d, *J* = 6.3 Hz), 16.02 (d, *J* = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.49. HRMS calculated $[M+Na]^+$ for $C_{26}H_{26}N_3O_4P$: 498.1559, found: 498.1555.

Diethyl(5,5-dicyano-1',5',7'-trimethyl-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3i). White solid; mp 183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 3.8 Hz, 2H), 7.47 (d, *J* = 3.3 Hz, 3H), 7.31 (s, 1H), 7.03 (s, 1H), 6.40-6.62 (m, 1H), 5.50 (s, 1H), 4.01-4.17 (m, 2H), 3.81-4.00 (m, 2H), 3.57 (s, 3H), 2.59 (s, 3H), 2.35 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.71, 146.23 (d, *J* = 12.6 Hz), 139.77 (d, *J* = 190.7 Hz), 139.32, 135.61, 133.40, 132.68, 130.20, 129.66, 128.48, 125.52, 123.80, 120.46, 112.94, 111.79, 65.26 (d, *J* = 19.2 Hz), 62.79 (d, *J* = 5.9 Hz), 62.67 (d, *J* = 6.3 Hz), 60.84 (d, *J* = 15.0 Hz), 53.31 (d, *J* = 13.0 Hz), 30.52, 20.79, 18.86, 16.22 (d, *J* = 6.4 Hz), 16.02 (d, *J* = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.57. HRMS calculated $[M+Na]^+$ for $C_{27}H_{28}N_3O_4P$: 512.1715, found: 512.1707.

Diethyl(5,5-dicyano-1'-methyl-2'-oxo-4-propylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3j). White solid; mp 150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.41 (d, *J* = 11.1 Hz, 1H), 4.30 (d, *J* = 10.1 Hz, 1H), 4.20 (dd, *J* = 7.0, 4.1 Hz, 4H), 3.29 (s, 3H), 2.29 (ddd, *J* = 20.2, 10.6, 5.1 Hz, 1H), 1.87-2.03 (m, 1H), 1.69-1.80 (m, 1H), 1.57-1.69 (m, 1H), 1.41 (t, *J* = 7.0 Hz, 6H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.88, 144.44, 144.26 (d, *J* = 11.1 Hz), 141.08 (d, *J* = 186.4 Hz), 131.41, 126.56, 123.81, 123.16, 113.41, 111.71, 109.16, 65.47 (d, *J* = 19.2 Hz), 62.83 (d, *J* = 4.3 Hz), 62.78 (d, *J* = 4.8 Hz), 53.99 (d, *J* = 15.2 Hz), 49.52 (d, *J* = 13.3 Hz), 32.93, 27.03, 20.52, 16.38 (d, *J* = 6.2 Hz), 13.90; ^{31}P NMR (162 MHz, $CDCl_3$): δ 10.66. HRMS calculated $[M+Na]^+$ for $C_{22}H_{26}N_3O_4P$: 450.1559, found: 450.1554.

Diethyl(5,5-dicyano-1',5'-dimethyl-2'-oxo-4-propylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3k). White solid; mp 153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (s, 1H), 7.29 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.40 (d, *J* = 11.1 Hz, 1H), 4.30 (d, *J* = 9.6 Hz, 1H), 4.21 (dd, *J* = 12.5, 6.8 Hz, 4H), 3.27 (s, 3H), 2.42 (s, 3H), 2.29 (ddd, *J* = 15.4, 10.9, 5.3 Hz, 1H), 1.88-2.01 (m, 1H), 1.68-1.79 (m, 1H), 1.56-1.66 (m, 1H), 1.41 (t, *J* = 7.0 Hz, 6H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.78, 144.64 (d, *J* = 12.7 Hz), 141.79, 139.96, 133.59, 131.63, 127.27, 123.17, 113.45, 111.72, 108.86, 65.49 (d, *J* = 19.2 Hz), 62.77 (t, *J* = 4.8 Hz), 53.95 (d, *J* = 15.5 Hz), 49.57 (d, *J* = 13.0 Hz), 32.91, 27.02, 21.16, 20.51, 16.37 (d, *J* = 6.3 Hz), 13.89; ^{31}P NMR (162 MHz, $CDCl_3$): δ 10.76. HRMS calculated $[M+Na]^+$ for $C_{23}H_{28}N_3O_4P$: 464.1715, found: 464.1710.

Diethyl(5,5-dicyano-1',7'-dimethyl-2'-oxo-4-propylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3l). White solid; mp 151 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.38 (d, *J* = 11.1 Hz, 1H), 4.29 (d, *J* = 9.6 Hz, 1H), 4.15-4.26 (m, 4H), 3.56 (s, 3H), 2.63 (s, 3H), 2.22-2.35 (m, 1H), 1.94 (td, *J* = 14.8, 4.3 Hz, 1H), 1.73 (dd, *J* = 11.8, 6.3 Hz, 1H), 1.59 (dd, *J* = 22.9, 6.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.66, 144.60 (d, *J* = 12.6 Hz), 141.92, 140.87 (d, *J* = 186.6 Hz), 135.16, 124.45, 123.76, 123.59, 120.81, 113.54, 111.62, 65.02 (d, *J* = 19.5 Hz), 62.80 (d, *J* = 2.4 Hz), 62.75 (d, *J* = 3.7 Hz), 53.95 (d, *J* = 15.7 Hz), 49.96 (d, *J* = 12.7 Hz), 32.92, 30.49, 20.51, 19.07, 16.37 (d, *J* = 6.2 Hz), 13.90; ^{31}P NMR (162 MHz,

$CDCl_3$): δ 10.75; HRMS calculated $[M+Na]^+$ for $C_{23}H_{28}N_3O_4P$: 464.1715, found: 464.1715.

Diethyl(5,5-dicyano-1',5',7'-trimethyl-2'-oxo-4-propylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3m). White solid; mp 151 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.24 (s, 1H), 7.03 (s, 1H), 6.38 (d, *J* = 11.2 Hz, 1H), 4.30 (d, *J* = 9.7 Hz, 1H), 4.13-4.26 (m, 4H), 3.53 (s, 3H), 2.58 (s, 3H), 2.35 (s, 3H), 2.28 (ddd, *J* = 15.3, 10.8, 5.1 Hz, 1H), 1.94 (td, *J* = 14.9, 4.6 Hz, 1H), 1.69-1.80 (m, 1H), 1.60 (td, *J* = 13.9, 7.0 Hz, 1H), 1.41 (t, *J* = 7.0 Hz, 6H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.56 (d, *J* = 2.2 Hz), 144.89 (d, *J* = 12.9 Hz), 140.67 (d, *J* = 186.6 Hz), 139.44, 135.58, 133.29, 125.09, 123.84, 120.43, 113.59, 111.62, 65.07 (d, *J* = 19.1 Hz), 62.75 (t, *J* = 4.8 Hz), 53.91 (d, *J* = 15.4 Hz), 50.01 (d, *J* = 13.3 Hz), 32.91, 30.42, 20.82, 20.52, 18.89, 16.37 (d, *J* = 6.3 Hz), 13.90; ^{31}P NMR (162 MHz, $CDCl_3$): δ 10.86. HRMS calculated $[M+Na]^+$ for $C_{24}H_{30}N_3O_4P$: 478.1872, found: 478.1869.

Diethyl(5,5-dicyano-4-(furan-2-yl)-1'-methyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3n). White solid; mp 188 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.58 (s, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.77 (s, 1H), 6.54 (d, *J* = 10.8 Hz, 1H), 6.50 (s, 1H), 5.64 (s, 1H), 4.01-4.20 (m, 4H), 3.33 (s, 3H), 1.35 (t, *J* = 6.9 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.78, 145.92, 145.45 (d, *J* = 12.7 Hz), 144.14, 144.05, 138.17 (d, *J* = 191.6 Hz), 131.55, 126.86, 123.98, 122.86, 112.56, 112.41, 111.78, 111.13, 109.26, 65.34 (d, *J* = 18.7 Hz), 62.87 (t, *J* = 6.3 Hz), 54.42 (d, *J* = 14.1 Hz), 50.66 (d, *J* = 12.2 Hz), 27.14, 16.28 (d, *J* = 6.2 Hz), 16.19 (d, *J* = 7.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.81; HRMS calculated $[M+Na]^+$ for $C_{23}H_{22}N_3O_5P$: 474.1195, found: 474.1192.

Diethyl(1'-benzyl-5,5-dicyano-4-(furan-2-yl)-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3o). White solid; mp 155 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.4 Hz, 1H), 7.59 (s, 1H), 7.38 (d, *J* = 12.0 Hz, 5H), 7.34 (d, *J* = 5.9 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.79 (s, 1H), 6.59 (d, *J* = 10.9 Hz, 1H), 6.51 (s, 1H), 5.70 (s, 1H), 5.17 (d, *J* = 15.6 Hz, 1H), 4.80 (d, *J* = 15.5 Hz, 1H), 4.13 (d, *J* = 6.9 Hz, 4H), 1.35 (t, *J* = 6.9 Hz, 3H), 1.29 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.01, 145.86, 145.67 (d, *J* = 12.4 Hz), 144.19, 143.27, 138.30 (d, *J* = 191.5 Hz), 134.29, 131.43, 129.07, 128.20, 127.56, 126.95, 123.98, 122.92, 112.72, 112.48, 111.79, 111.15, 110.35, 65.19 (d, *J* = 19.0 Hz), 62.93 (d, *J* = 6.6 Hz), 62.87 (d, *J* = 6.4 Hz), 54.53 (d, *J* = 13.9 Hz), 50.68 (d, *J* = 12.1 Hz), 44.89, 16.31 (d, *J* = 6.6 Hz), 16.21 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.80; HRMS calculated $[M+Na]^+$ for $C_{29}H_{26}N_3O_5P$: 550.1508, found: 550.1505.

Diethyl(5,5-dicyano-4-(furan-2-yl)-5'-methoxy-1'-methyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3p). White solid; mp 175 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.31 (s, 1H), 7.04 (d, *J* = 8.6 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 6.77 (s, 1H), 6.54 (d, *J* = 10.9 Hz, 1H), 6.50 (s, 1H), 5.63 (s, 1H), 4.02-4.16 (m, 4H), 3.85 (s, 3H), 3.30 (s, 3H), 1.35 (t, *J* = 6.9 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.50, 156.71, 145.95, 145.44 (d, *J* = 12.6 Hz), 144.13, 139.10, 137.19, 123.83, 116.77, 113.33, 112.53, 112.41, 111.81, 111.13, 109.81, 65.68 (d, *J* = 18.6 Hz), 62.91 (d, *J* = 5.4 Hz), 62.83 (d, *J* = 5.7 Hz), 55.97, 54.44 (d, *J* = 14.0 Hz), 50.70 (d, *J* = 11.9 Hz), 27.19, 16.28 (d, *J* = 6.3 Hz), 16.18 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.86; HRMS calculated $[M+Na]^+$ for $C_{24}H_{24}N_3O_6P$: 504.1300, found: 504.1299.

Diethyl(5,5-dicyano-4-(furan-2-yl)-6'-methoxy-1'-methyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3q). White solid; mp 153 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49-7.65 (m, 2H), 6.67-6.80 (m, 2H), 6.52 (d, *J* = 15.5 Hz, 3H), 5.58 (s, 1H), 4.03-4.16 (m, 4H), 3.90 (s, 3H), 3.29 (s, 3H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.38, 162.63, 146.07, 145.93 (d, *J* = 12.3 Hz), 145.48, 144.06, 137.78 (d, *J* = 191.4 Hz), 127.83, 114.51, 112.66, 112.29, 111.95, 111.10, 107.55, 97.34, 65.29 (d, *J* = 18.8 Hz), 62.86 (d, *J* = 6.8 Hz), 62.79 (d, *J* = 7.1 Hz), 55.74, 54.22 (d, *J* = 14.1 Hz), 50.85 (d, *J* = 11.9 Hz), 27.13, 16.28 (d, *J* = 6.6 Hz), 16.18 (d, *J* = 6.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.96; HRMS calculated $[M+Na]^+$ for $C_{24}H_{24}N_3O_6P$: 504.1300, found: 504.1299.

Diethyl(5,5-dicyano-4-(furan-2-yl)-1',7'-dimethyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3r). White solid; mp 163 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.76 (s, 1H), 6.51 (d, *J* = 11.3 Hz, 2H), 5.62 (s, 1H), 4.03-4.16 (m, 4H), 3.59 (s, 3H), 2.64 (s, 3H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.55, 146.00, 145.65 (d, *J* = 12.5 Hz), 144.10, 141.76, 137.95 (d, *J* = 191.3 Hz), 135.28, 124.77, 123.76, 123.47, 120.91, 112.70, 112.37, 111.69, 111.11, 64.94 (d, *J* = 18.7 Hz), 62.84 (t, *J* = 6.2 Hz), 54.42 (d, *J* = 13.9 Hz), 51.07 (d, *J* = 12.4 Hz), 30.60, 19.06, 16.28 (d, *J* = 6.8 Hz), 16.19 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.89; HRMS calculated $[M+Na]^+$ for $C_{24}H_{24}N_3O_5P$: 488.1351, found:488.1353.

Diethyl(5'-bromo-5,5-dicyano-4-(furan-2-yl)-1'-methyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3s). White solid; mp 193 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.58 (s, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.77 (s, 1H), 6.51 (s, 2H), 5.61 (s, 1H), 4.10 (dt, *J* = 14.8, 7.4 Hz, 4H), 3.31 (s, 3H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.28, 145.62, 144.46 (d, *J* = 12.7 Hz), 144.24, 143.09, 138.81 (d, *J* = 191.6 Hz), 134.48, 130.03, 128.64 (d, *J* = 81.4 Hz), 124.75, 116.57, 112.55, 111.92 (d, *J* = 78.6 Hz), 111.19, 110.67, 65.07 (d, *J* = 18.9 Hz), 62.96 (d, *J* = 4.0 Hz), 62.91 (d, *J* = 4.4 Hz), 54.56 (d, *J* = 13.9 Hz), 50.46 (d, *J* = 12.4 Hz), 27.26, 16.28 (d, *J* = 7.7 Hz), 16.21 (d, *J* = 7.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.43; HRMS calculated $[M+Na]^+$ for $C_{23}H_{21}BrN_3O_5P$: 552.0300, found:552.0293.

Diethyl(5,5-dicyano-4-(furan-2-yl)-1',6'-dimethyl-2'-oxospiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3t). White solid; mp 181 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 7.12 (t,

J = 7.7 Hz, 1H), 6.76 (d, J = 3.0 Hz, 1H), 6.51 (d, J = 10.9 Hz, 2H), 5.63 (s, 1H), 4.02-4.15 (m, 4H), 3.59 (s, 3H), 2.64 (s, 3H), 1.34 (t, J = 7.0 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.59, 145.99, 145.67 (d, J = 12.4 Hz), 144.10, 141.77, 137.96 (d, J = 191.5 Hz), 135.28, 124.79, 123.77, 123.48, 120.90, 112.70, 112.37, 111.69, 111.11, 64.95 (d, J = 18.6 Hz), 62.84 (t, J = 6.3 Hz), 54.43 (d, J = 13.9 Hz), 51.07 (d, J = 11.7 Hz), 30.61, 19.07, 16.28 (d, J = 6.6 Hz), 16.19 (d, J = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.90; HRMS calculated $[M+Na]^+$ for $C_{24}H_{24}N_3O_5P$: 488.1351, found: 488.1353.

Diethyl(5,5-dicyano-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3u). White solid; mp 253 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 3.8 Hz, 2H), 7.49 (d, J = 3.2 Hz, 3H), 7.43 (t, J = 7.8 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 6.70 (d, J = 11.2 Hz, 1H), 5.46 (s, 1H), 3.97-4.08 (m, 4H), 1.22 (q, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, DMSO): δ 172.14, 146.54 (d, J = 12.8 Hz), 142.84, 138.75, 136.88, 133.04, 131.27, 129.46, 129.07 (d, J = 140.7 Hz), 126.64, 123.74, 122.57, 113.19, 112.13, 110.71, 65.75 (d, J = 19.1 Hz), 62.42 (d, J = 6.0 Hz), 62.19 (d, J = 5.9 Hz), 59.99 (d, J = 16.0 Hz), 52.35 (d, J = 12.8 Hz), 15.93 (d, J = 6.3 Hz), 15.75 (d, J = 6.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.99; HRMS calculated $[M+Na]^+$ for $C_{24}H_{22}N_3O_4P$: 470.1246, found: 470.1237.

Diethyl(1'-benzyl-5,5-dicyano-2'-oxo-4-phenylspiro[cyclopent[2]ene-1,3'-indolin]-3-yl)phosphonate (3v). White solid; mp168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 7.6 Hz, 1H), 7.60-7.65 (m, 2H), 7.46-7.52 (m, 3H), 7.40 (dt, J = 15.3, 7.5 Hz, 5H), 7.31-7.35 (m, 1H), 7.21 (t, J = 7.7 Hz, 1H), 6.86 (d, J = 7.9 Hz, 1H), 6.62 (dd, J = 11.0, 2.6 Hz, 1H), 5.58 (s, 1H), 5.20 (d, J = 15.6 Hz, 1H), 4.80 (d, J = 15.6 Hz, 1H), 4.20 – 4.02 (m, 2H), 4.01 – 3.85 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.24, 146.02 (d, J = 12.6 Hz), 143.31, 140.26 (d, J = 190.6 Hz), 134.35, 132.47, 131.34, 130.24, 129.77, 129.06, 128.56, 128.18, 127.58, 127.01, 123.94, 123.16, 112.91, 111.85, 110.28, 65.43 (d, J = 18.8 Hz), 62.88 (d, J = 5.9 Hz), 62.76 (d, J = 6.3 Hz), 60.99 (d, J = 14.8 Hz), 52.84 (d, J = 13.2 Hz), 44.92, 16.24 (d, J = 6.3 Hz), 16.04 (d, J = 6.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.40; HRMS calculated $[M+Na]^+$ for $C_{31}H_{28}N_3O_4P$: 560.1715, found: 560.1714.

Notes and references

[a] State Key Laboratory and Institute of Elemento-Organic Chemistry, Nankai University, Weijin Road 94, Tianjin 300071, People's Republic of China.

[b] Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300071, People's Republi c of China.

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