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Phosphorus-containing Lewis base catalyzed highly regioselective cyclization of isatin derived electron-deficient alkenes with but-3-yn-2-one

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ABSTRACT

In this paper, we reported that phosphorus-containing Lewis bases catalyzed [4+2] cyclization of *N*-protected isatin derived electron-deficient alkenes with but-3-yn-2-one could proceed smoothly to give the corresponding dihydropyrano[2,3-*b*]indoles in good to excellent yields under mild conditions. The substrate scope has been carefully examined and the plausible reaction mechanism has been also proposed.

1. Introduction

Heterocyclic compounds hold a special place in organic chemistry because of their abundance in natural products and the diverse biological properties associated with them. Many heterocycles have received an enormous amount of attention from synthetic chemists, and among them indole and pyran ring systems are of particular importance.[1] The benzopyran or chromene core containing chemicals are prevalent in compounds with proven pharmacological properties.[2] Fused chromenes (polycyclic pyrans) are also of great interest because of their well-documented antibacterial and novobiocin activities.[3] Thus, the need for the development of efficient and practical syntheses of novel heterocycles with these ring systems is of great significance. The hetero-Diels–Alder reaction is one of the most important reactions for the construction of heterocyclic six-membered rings.[4–8] Over the past few years, syntheses of several complex annulated dihydropyrans have been achieved using the hetero-Diels–Alder reaction.[9,10] Recently, our group reported a novel phosphorus-containing Lewis base catalyzed highly geometric selective [3+2] annulation of isatin derived α,β-unsaturated diesters with α-allenic ester, affording the functionalized spirocyclic products in good to excellent yields (Scheme 1).[11] Subsequently, we also reported novel nitrogen and phosphorus-containing Lewis bases catalyzed [4+2] and [3+2] annulations of isatin with but-3-yn-2-one, giving the corresponding spiro[indoline-3,2′-pyran]-2,4′(3′*H*)-dione and spiro[furan-2,3′-indoline]-2′,4(5*H*)-dione in good to excellent yields under mild conditions (Scheme 1).[12] Herein, we wish to present an interesting phosphorus-containing Lewis base PPh_3-catalyzed highly regioselective [4+2] cyclization of isatin derived electron-deficient alkenes with but-3-yn-2-one, providing dihydropyrano [2,3-b]indoles in good to excellent yields under mild conditions (Scheme 2).

2. Results and discussion

Initially, we utilized diethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)malonate **1a** and but-3-yn-2-one **2** as the substrates to investigate their cyclization behaviors in the presence of various Lewis bases, such as nitrogen and phosphorus-containing Lewis bases (for example, PPh_3, PPh_2Me, DABCO, DBU, and so on) at room temperature. To our disappointment, no reactions occurred under various reaction conditions (Scheme 3). Using isatin derived electron-deficient alkene **3a** as the substrate in which the alkenyl moiety should be more electron-deficient than that of **1a**, we found that the [4+2] cyclization took place smoothly to give the corresponding cyclic product **4a** in good yield in the presence of PPh_3 (Scheme 3). Moreover, using more electron-deficient alkene, such as isatylidene malononitrile **5a** as the substrate did not give an ideal reaction outcome, affording complex product mixtures (Scheme 3). The general procedure for the preparation of isatin derived electron-deficient alkene **3a** is shown in the Supplementary data.

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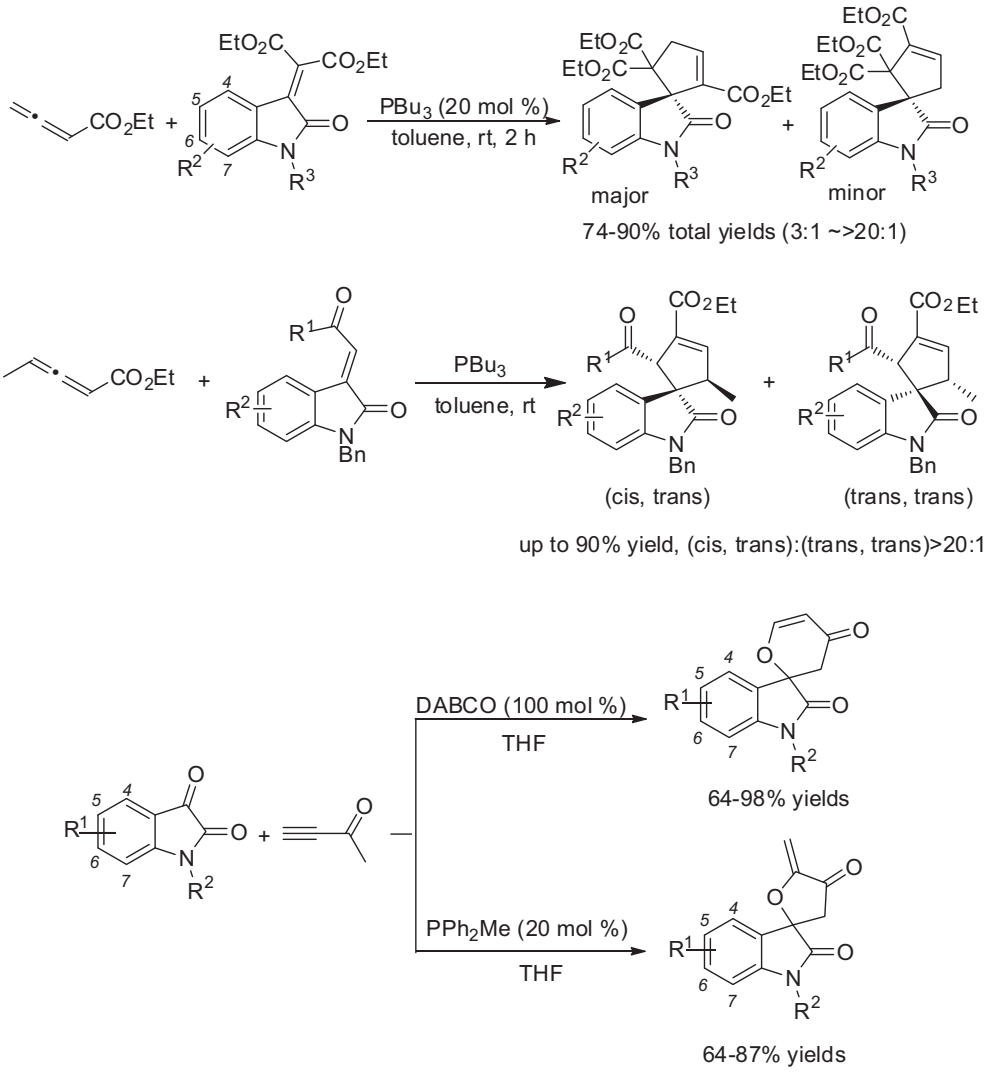
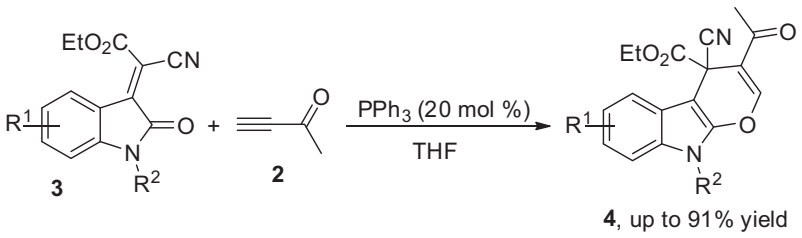
Previous work:



Scheme 1. Nitrogen and phosphorus-containing Lewis bases mediated/catalyzed [4+2] and [3+2] annulations in our previous work.

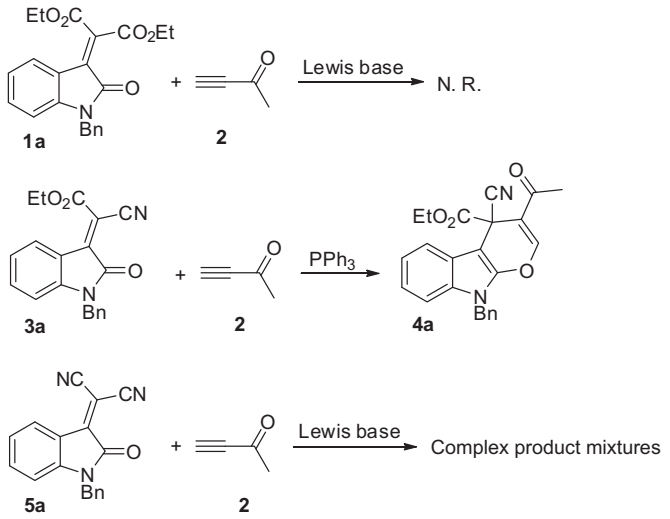
This work



Scheme 2. PPh_3-catalyzed cycloaddition of isatin derived electron-deficient alkenes with but-3-yn-2-one.

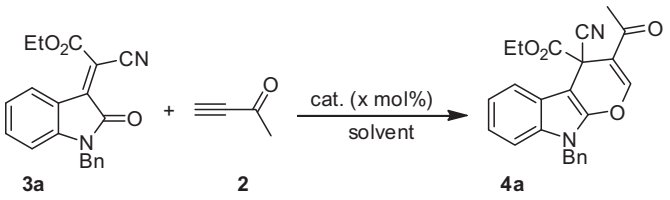
Moreover, the *E*-configuration of **3a** has been determined by X-ray diffraction (see Supplementary data for the details).[13]

Subsequently, we attempted to optimize the reaction conditions in cyclization of isatin derived electron-deficient alkene **3a** with but-3-yn-2-one **2** in the presence of various Lewis bases. The initial investigation aroused from the reaction of (*E*)-ethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)-2-cyanoacetate **3a** (1.0 equiv) and but-3-yn-2-one **2** (1.5 equiv) in the presence of triphenylphosphine (PPh_3) (20 mol %) in tetrahydrofuran (THF) at room temperature (20 °C). We found that oxygen atom-containing six-membered cyclic product ethyl 3-acetyl-9-benzyl-4-cyano-4,9-dihydropyrano[2,3-*b*]indole-4-carboxylate **4a** was obtained in 50% yield (Table 1, entry 1). The structure of product **4a** was assigned on the basis of spectroscopic analyses. Its structure has been further unambiguously determined by X-ray diffraction of single crystals of its analogue **4j** (see Table 2, entry 9). Its ORTEP drawing is shown in Fig. 1 and the CIF data are presented in the Supplementary data.[14] The examination of various phosphorus containing catalysts, such as PPh_2Me, $PPhMe_2$, and PBu_3 for this reaction indicated that PPh_3 was the best catalyst for this reaction (Table 1, entries 2–4). Using



Scheme 3. Cycloaddition of isatin derived electron-deficient alkenes with but-3-yn-2-one 2 catalyzed by Lewis base.

Table 1
Optimization of the reaction conditions[a]



Entry	**3a**/**2**	Cat.	× (mol %)	Solvent	Yield[b] (%)
					4a
1	1:1.5	PPh_3	20	THF	50
2	1:1.5	PPh_2Me	20	THF	44
3	1:1.5	$PPhMe_2$	20	THF	31
4	1:1.5	PBu_3	20	THF	22
5	1:1.5	DM AP	20	THF	Trace
6	1:1.5	DABCO	20	THF	Trace
7	1:1.5	DBU	20	THF	Trace
8	1:1.5	Et_3N	20	THF	Trace
9	1:2	PPh_3	20	THF	58
10	*1:3*	*PPh_3*	*20*	*THF*	*93*
11	1:3	PPh_3	10	THF	45
12	1:3	PPh_3	5	THF	28
13	1:3	PPh_3	20	CH_3CN	25
14	1:3	PPh_3	20	Et_2O	79
15	1:3	PPh_3	20	DCM	31
16	1:3	PPh_3	20	Toluene	55
17	1:3	PPh_3	20	DMF	48

Italic values represents the best reaction conditions.
[a] Compound **3a** (0.1 mmol) and catalyst were dissolved in solvent (1 mL), then compound **2** was added and the reaction mixture was stirred for about 5 h.
[b] Isolated yields.

nitrogen-containing Lewis bases as the catalysts, we found that only trace product **4a** was formed in the presence of 4-*N*,*N*-dimethylpyridine (DMAP), 1,4-diazabicyclo[2,2,2]octane (DABCO), 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) or triethylamine (TEA) in THF (Table 1, entries 5–8). Delightfully, increasing the employed amount of but-3-yn-2-one **2** to 2.0 equiv and 3.0 equiv afforded product **4a** in 58% and 93% yields, respectively (Table 1, entries 9 and 10). However, we found that decreasing the employed amounts of PPh_3 to 0.1 or 0.05 equiv led to a dramatic drop in the yield of product **4a** (Table 1, entries 11 and 12). The examination of solvent effects revealed that THF is the solvent of choice for this novel cyclization (Table 1, entries 13–17).

Having identified the optimal reaction conditions, we next set out to examine the substrate scope of this [4+2] cyclization catalyzed by PPh_3 using various isatin derived electron-deficient alkene derivatives **3** with different substituents on their benzene rings and the results are summarized in Table 2. As can be seen from Table 2, the reactions proceeded smoothly to give the corresponding products **4b**–**h** in moderate to good yields whether electron-withdrawing or electron-donating groups were introduced at the 5-, 6-, or 7-position of their benzene rings of *N*-Bn protected isatins **3**, suggesting that the electronic property of the substituents on the benzene rings did not have significant impact on the reaction outcomes (Table 2, entries 1–7). It should be also noted that, in the case of other isatin derivatives **3i**–**m** bearing different *N*-protecting groups, the reactions also proceeded efficiently to produce the corresponding oxa-cycloadducts **4i**–**m** in moderate to good yields (Table 2, entries 8–12). We also found that these products **4a**–**m** are quite stable during the isolation by silica gel column chromatography.

A plausible reaction mechanism for the formation of **4a** shown in Scheme 4 may be invoked to rationalize the reaction outcome. Initially, the reaction of PPh_3 with but-3-yn-2-one **2** generates the zwitterionic intermediate **A**.[15] Then nucleophilic addition of intermediate **A** to the alkenyl group of **3a** produces intermediate **B**. The intramolecular Michael addition of O^- anion to the olefin moiety in intermediate **B** gives ylide-type intermediate **C**, which subsequently undergoes the elimination of phosphine to give the final product **4a** and regenerates PPh_3 to complete the catalytic cycle.[16]

An unexpected finding is that during our preparation of *N*-Bn protected isatin derived electron-deficient alkene derivative **3** using 5-Cl substituted isatin as the substrate under the standard procedure, we found that compound **6** was formed rather than the desired isatylidene derivative **3**, presumably due to the electronic effect.[17] Using compound **6** (1.0 M) in THF as the substrate in the reaction with but-3-yn-2-one **2** (3 equiv) in the presence of PPh_3 (0.2 equiv) under the standard conditions, it was found that the corresponding product **7** was formed in the yield of 91% as a single diastereoisomer via a similar mechanism shown in Scheme 4 (Scheme 5). The structure of product **7** has been assigned on the basis of spectroscopic analyses. Its structure has been also further unambiguously determined by X-ray diffraction of its single crystals. The ORTEP drawing is shown in Fig. 2 and the CIF data are presented in the Supplementary data.[18]

3. Conclusion

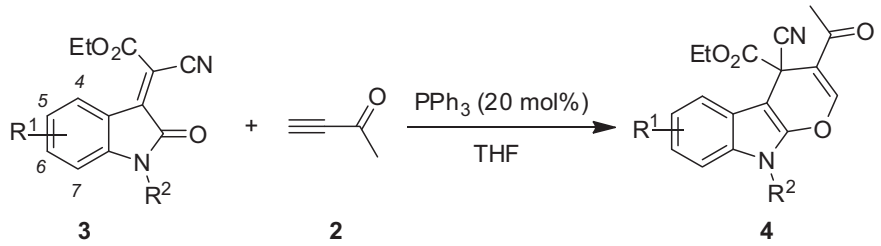
In summary, we have disclosed a facile synthetic protocol for the preparation of functionalized dihydropyrano[2,3-*b*]indole derivatives in good to excellent yields by phosphorus-containing Lewis bases catalyzed cyclization of *N*-protected isatin derived electron-deficient alkene **3** with but-3-yn-2-one **2** under mild conditions. These cyclizations are suitable to a variety of isatin derived electron-deficient alkenes. Efforts are underway to elucidate the mechanistic details of this cyclization and to explore some other interesting annulation reactions using *N*- and *P*-containing Lewis bases.

4. Experimental section

4.1. General remarks

Mps were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded for a solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. *J*-values are in 300 M or 400 MHz. Mass spectra were recorded with an HP-5989 instrument and HRMS was

Table 2
Substrate scope of PPh_3-catalyzed [4+2] cycloaddition reaction[a]

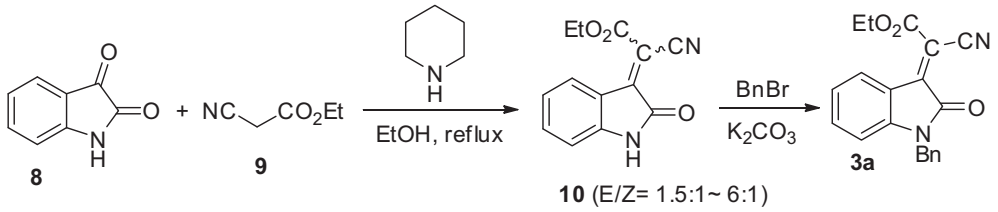


Entry	R^1	R^2	Yield[b] (%)
			4
1	5-F	Bn, **3b**	**4b**, 91
2	5-Me	Bn, **3c**	**4c**, 89
3	5-Br	Bn, **3d**	**4d**, 81
4	6-Br	Bn, **3e**	**4e**, 75
5	6-CH_3	Bn, **3f**	**4f**, 73
6	5,7-Me_2	Bn, **3g**	**4g**, 81
7	5-MeO	Bn, **3h**	**4h**, 88
8	H	Me, **3i**	**4i**, 71
9	H	Allyl, **3j**	**4j**, 77
10	H	Anthracen-10-ylmethyl, **3k**	**4k**, 90
11	H	Boc, **3l**	**41**, 76
12	H	Mom, **3m**	**4m**, 79

[a] Compound **3** (0.1 mmol) and PPh_3 (0.02 mmol) were dissolved in solvent (1 mL), then compound **2** (0.3 mmol) was added and the reaction mixture was stirred for about 5 h.
[b] Isolated yields.

measured by a Finnigan MA^+ mass spectrometer. The solid compounds reported in this paper gave satisfactory CHN microanalyses with a Carlo-Erba 1106 analyzer. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure. Reaction experiments were performed under argon condition.

*4.1.1. Typical reaction procedure for the preparation of **3**.*



To a solution of the appropriate isatins **8** (10 mol) in dry ethanol (20.0 mL), ethyl 2-cyanoacetate **9** (10 mol) was added, as well as two drops of piperidine as catalyst. Then the reaction mixture was refluxed for nearly 2 h, and after allowing the mixture to cool to room temperature, crystalline products of **10** precipitated. The precipitated solids of compound **10** were filtered off and washed several times with cold ethanol (10 mL) to afford analytically pure compounds.

K_2CO_3 (1.2 mmol) was added to a solution of ethyl 2-cyano-2-(2-oxoindolin-3-ylidene)acetate **10** (1.0 mmol) and benzyl bromide (1.2 mmol) in DMF (15 mL) at room temperature and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2 and washed with water. The organic layer was dried over anhydrous $MgSO_4$, filtered, the solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/petroleum ether (1:5, v/v) to afford the products **3** mainly as *E*-configuration.

*4.1.1.1. (E)-Ethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3a**).* Mp 147–149 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.42 (t, 3H, J=7.2 Hz, CH_3), 4.45 (q, 2H, J=7.2 Hz, CH_2), 4.90 (s, 2H, CH_2), 6.70 (d, 1H, J=8.0 Hz, ArH), 7.05 (t, 1H, J=8.0 Hz, ArH), 7.24–7.35 (m, 6H, ArH), 8.28 (d, 1H, J=8.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 43.9, 63.4, 106.5, 109.7, 114.0, 118.7, 123.1, 125.2, 127.4, 128.9, 129.9, 134.5, 135.6, 139.8, 145.6, 161.5, 164.4; IR (CH_2Cl_2): ν 3032, 2982, 2213, 1720, 1583, 1380, 1059, 821, 599 cm^{-1}; MS (%) (EI) m/z 332 (M^+, 20.6), 303 (9.7), 258 (17.5), 230 (5.6), 92 (10.4), 91 (100), 65 (12.4). HRMS (EI) calcd for $C_{20}H_{16}N_2O_3$ requires 332.1161, found: 332.1164.

*4.1.1.2. (E)-Ethyl 2-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3b**).* ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.45 (t, 3H, J=7.2 Hz, CH_3), 4.47 (q, 2H, J=6.8 Hz, CH_2), 4.93 (s, 2H, CH_2), 6.65 (dd, 1H, J_1=4.0 Hz, J_2=8.4 Hz, ArH), 7.06–7.11 (m, 1H, ArH), 7.26–7.36 (m, 5H, ArH), 8.16 (dd, 1H, J_1=2.4 Hz, J_2=9.2 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 44.1, 63.7, 108.0, 110.3 (d, J=8.2 Hz), 113.7, 117.4 (d, J=27.2 Hz), 119.5 (d, J=8.8 Hz), 122.0 (d, J=24.3 Hz), 127.4, 128.1, 129.0, 134.4, 141.9, 144.2, 158.5 (d, J=239.6 Hz), 161.2, 164.2; ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$)

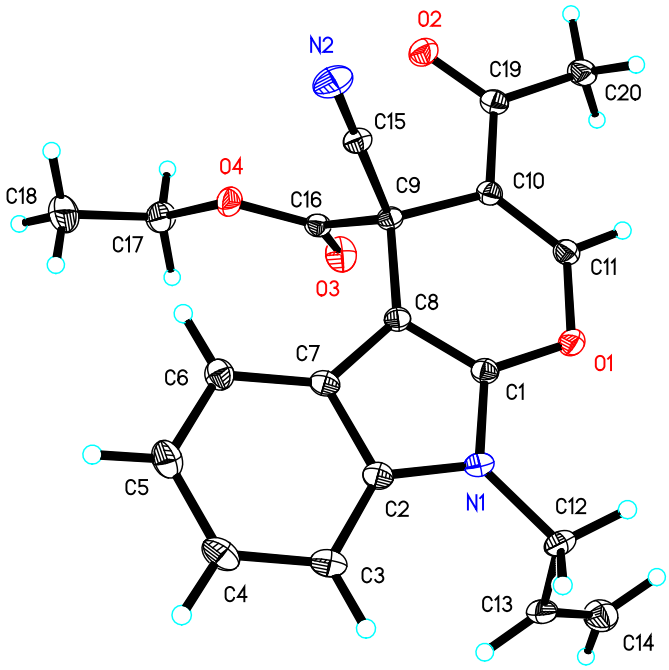
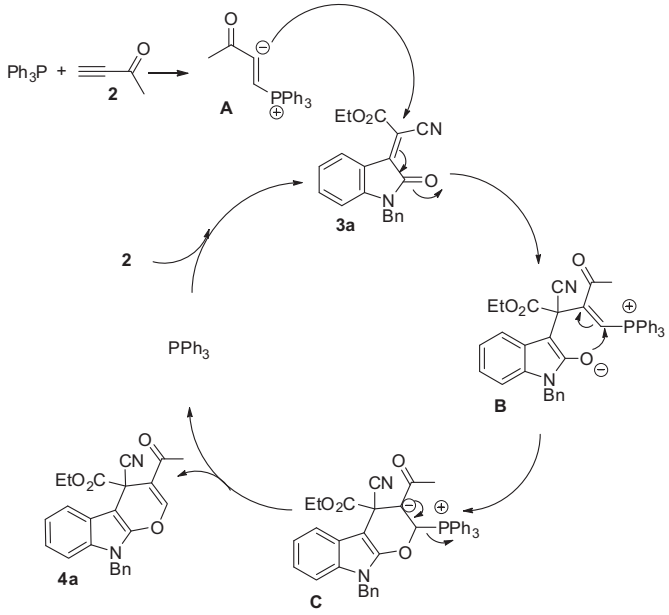
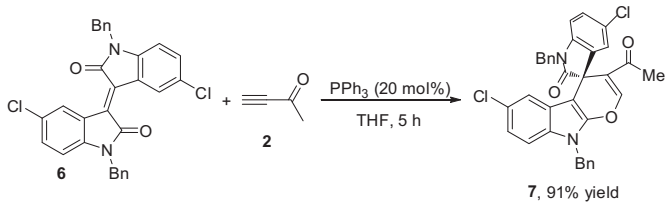


Fig. 1. ORTEP drawing of **4j**.



Scheme 4. A plausible mechanism of the formation of **4a**.



Scheme 5. A control experiment.

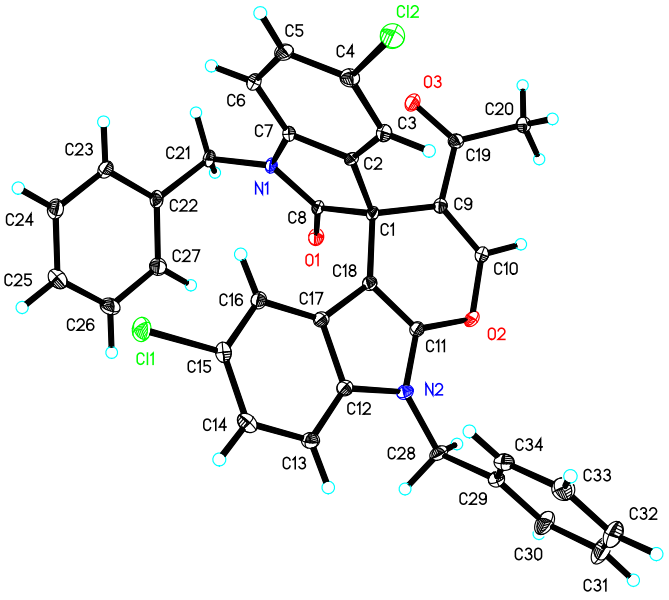


Fig. 2. ORTEP drawing of **7**.

δ −118.8; IR (CH_2Cl_2): ν 2952, 2851, 1733, 1716, 1608, 1574, 1464, 1347, 1285, 1190, 1105, 775, 759, 734 cm^{-1}; MS (%) (EI) m/z 350 (M^+, 14.3), 321 (3.6), 276 (8.5), 248 (3.3), 92 (8.6), 91 (100), 65 (8.0). HRMS (EI) calcd for $C_{20}H_{15}N_2O_3F$ requires 350.1067, found: 350.1064.

*4.1.1.3. (E)-Ethyl 2-(1-benzyl-5-methyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3c**).* Mp 140–143 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.42 (t, 3H, J=7.2 Hz, CH_3), 2.32 (s, 3H, CH_3), 4.47 (q, 2H, J=7.2 Hz, CH_2), 4.85 (s, 2H, CH_2), 6.59 (d, 1H, J=8.4 Hz, ArH), 7.13–7.15 (m, 1H, ArH), 7.27–7.33 (m, 5H, ArH), 7.89 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 20.9, 43.7, 63.2, 106.0, 109.4, 114.0, 118.6, 125.4, 127.3, 128.7, 130.1, 132.5, 134.7, 136.1, 143.4, 144.6, 161.4, 164.3; IR (CH_2Cl_2): ν 2957, 2925, 2856, 1718, 1560, 1340, 1124, 1011, 820, 698 cm^{-1}; MS (%) (EI) m/z 346 (M^+, 17.4), 272 (10.5), 91 (100), 65 (8.7). HRMS (EI) calcd for $C_{21}H_{18}N_2O_3$ requires 346.1317, found: 346.1320.

*4.1.1.4. (E)-Ethyl 2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3d**).* Mp 173–174 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.46 (t, 3H, J=7.2 Hz, CH_3), 4.48 (q, 2H, J=7.2 Hz, CH_2), 4.92 (s, 2H, CH_2), 6.61 (d, 1H, J=8.0 Hz, ArH), 7.24–7.35 (m, 5H, ArH), 7.44–7.48 (m, 1H, ArH), 8.51 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 44.1, 63.8, 108.1, 111.1, 115.8, 120.2, 127.4, 128.2, 129.0, 132.7, 134.2, 138.0, 143.4, 144.5, 161.1, 163.9; IR (CH_2Cl_2): ν 3026, 2926, 2872, 2218, 1716, 1621, 1455, 1380, 1253, 1125, 1011, 937, 821, 699, 599 cm^{-1}; MS (%) (EI) m/z 410 (M^+, 6.4), 336 (3.4), 91 (100), 65 (8.2). HRMS (EI) calcd for $C_{20}H_{15}N_2O_3Br$ requires 410.0266, found: 410.0271.

*4.1.1.5. (E)-Ethyl 2-(1-benzyl-6-bromo-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3e**).* Mp 167–170 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.44 (t, 3H, J=7.2 Hz, CH_3), 4.45 (q, 2H, J=7.2 Hz, CH_2), 4.91 (s, 2H, CH_2), 6.89 (d, 1H, J=2.0 Hz, ArH), 7.16 (dd, 1H, J_1=2.0 Hz, J_2=8.8 Hz, ArH), 7.30–7.35 (m, 5H, ArH), 8.26 (d, 1H, J=8.8 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 44.1, 63.6, 113.1, 114.0, 117.7, 126.3, 127.4, 128.3, 129.0, 129.1, 130.6, 131.2, 134.2, 143.6, 146.6, 161.5, 164.4; IR (CH_2Cl_2): ν 2989, 2981, 2925, 2207, 1791, 1760, 1734, 1683, 1621, 1600, 1506, 1464, 1350, 1253, 1150, 1011, 774, 734, 699 cm^{-1}; MS (%) (EI) m/z 410 (M^+, 6.7), 338 (5.7), 336 (5.3), 139 (4.7), 92 (8.2), 91 (100), 65 (10.3). HRMS (EI) calcd for $C_{20}H_{15}N_2O_3Br$ requires 410.0266, found: 410.0264.

*4.1.1.6. (E)-Ethyl 2-(1-benzyl-6-methyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3f**).* Mp 141–143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.35 (t, 3H, J=6.8 Hz, CH_3), 2.24 (s, 3H, CH_3), 4.36 (q, 2H, J=6.8 Hz, CH_2), 4.82 (s, 2H, CH_2), 6.45 (s, 1H, ArH), 6.78 (d, 1H, J=8.4 Hz, ArH), 7.18–7.29 (m, 5H, ArH), 8.15 (d, 1H, J=8.4 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 22.6, 43.8, 63.2, 104.9, 110.4, 114.3, 116.4, 124.0, 127.3, 127.9, 128.8, 130.0, 134.9, 144.5, 146.1, 147.8, 161.7, 164.9; IR (CH_2Cl_2): ν 2962, 2920, 2840, 2218, 1717, 1608, 1584, 1558, 1540, 1472, 1372, 1338, 1269, 1186, 1160, 1096, 1013, 735, 542 cm^{-1}; MS (%) (EI) m/z 346 (M^+, 24.8), 317 (8.7), 272 (17.0), 244 (7.3), 92 (7.7), 91 (100), 71 (6.5), 65 (9.8). HRMS (EI) calcd for $C_{21}H_{18}N_2O_3$ requires 346.1317, found: 346.1321.

*4.1.1.7. (E)-Ethyl 2-(1-benzyl-5,7-dimethyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3g**).* Mp 145–148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.45 (t, 3H, J=7.2 Hz, CH_3), 2.21 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 4.46 (q, 2H, J=7.2 Hz, CH_2), 5.19 (s, 2H, CH_2), 6.94 (s, 1H, ArH), 7.14 (d, 2H, J=8.0 Hz, ArH), 7.25–7.33 (m, 3H, ArH), 7.92 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 18.7, 20.7, 45.3, 63.4, 105.8, 114.3, 119.6, 120.2, 123.7, 125.6, 127.4, 128.9, 132.6, 136.7, 140.5, 141.5, 143.8, 161.7, 165.6; IR (CH_2Cl_2): ν 2957, 2925, 2212, 1718, 1618, 1560, 1379, 1253, 1195, 1124, 1011, 820, 734, 698 cm^{-1}; MS (%) (EI) m/z 360 (M^+, 18.6), 331 (4.4), 272 (17.0), 286 (69), 92 (7.6), 91 (100), 65 (7.3). HRMS (EI) calcd for $C_{22}H_{20}N_2O_3$ requires 360.1474, found: 360.1473.

*4.1.1.8. (E)-Ethyl 2-(1-benzyl-5-methoxy-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3h**).* Mp 150–152 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.44 (t, 3H, J=7.2 Hz, CH_3), 3.77 (s, 3H, CH_3), 4.45 (q, 2H, J=7.2 Hz, CH_2), 4.89 (s, 2H, CH_2), 6.60 (d, 1H, J=8.1 Hz, ArH), 6.90 (t, 1H, J=8.1 Hz, ArH), 7.27–7.31 (m, 5H, ArH), 7.98 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 43.9, 55.8, 63.4, 106.7, 110.2, 114.1, 115.3, 119.3, 120.4, 121.6, 127.4, 128.9, 134.8, 139.6, 145.1, 155.6, 161.4, 164.3; IR (CH_2Cl_2): ν 3032, 2927, 2861, 2213, 1716, 1584, 1455, 1124, 937, 699 cm^{-1}; MS (%) (EI) m/z 362 (M^+, 27.5), 288 (4.4), 260 (3.4), 199 (2.9), 91 (100), 65 (7.7). HRMS (EI) calcd for $C_{21}H_{18}N_2O_4$ requires 362.1267, found: 362.1266.

*4.1.1.9. (E)-Ethyl 2-cyano-2-(1-methyl-2-oxoindolin-3-ylidene) acetate (**3i**).* Mp 121–125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.44 (t, 3H, J=6.8 Hz, CH_3), 3.25 (s, 3H, CH_3), 4.45 (q, 2H, J=6.8 Hz, CH_2), 6.81 (d, 1H, J=8.0 Hz, ArH), 7.02–7.07 (m, 1H, ArH), 7.45–7.49 (m, 1H, ArH), 8.30 (d, 1H, J=8.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 26.3, 63.3, 106.3, 108.8, 114.0, 118.6, 123.1, 129.9, 135.7, 144.7, 146.5, 161.4, 164.2; IR (CH_2Cl_2): ν 3031, 2981, 2920, 2207, 1719, 1654, 1585, 1496, 1355, 1184, 1004, 749, 699 cm^{-1}; MS (%) (EI) m/z 256 (M^+, 100), 211 (30.0), 184 (68.0), 155 (60.3), 128 (25.8). HRMS (EI) calcd for $C_{14}H_{12}N_2O_3$ requires 256.0848, found: 256.0845.

*4.1.1.10. (E)-Ethyl 2-(1-allyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3j**).* Mp 132–133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.44 (t, 3H, J=6.8 Hz, CH_3), 4.37 (d, 2H, J=5.6 Hz, =CH_2), 4.46 (q, 2H, J=6.8 Hz, CH_2), 5.28 (d, 2H, J=7.6 Hz, CH_2), 5.79–5.86 (m, 1H, =CH), 6.81 (d, 1H, J=8.0 Hz, ArH), 7.04 (t, 1H, J=8.0 Hz, ArH), 7.43 (t, 1H, J=8.0 Hz, ArH), 8.31 (d, 1H, J=8.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 42.5, 63.4, 106.4, 109.6, 114.0, 118.4, 118.7, 123.1, 129.9, 130.4, 135.6, 144.5, 145.8, 161.5, 164.0; IR (CH_2Cl_2): ν 2984, 2925, 2207, 1718, 1610, 1380, 1299, 1194, 1124, 1003, 855, 699 cm^{-1}; MS (%) (EI) m/z 282 (M^+, 100), 303 (9.7), 208 (66.8), 180 (38.1), 154 (20.4), 41 (47.4). HRMS (EI) calcd for $C_{16}H_{14}N_2O_3$ requires 282.1004, found: 282.0999.

*4.1.1.11. (E)-Ethyl 2-(1-(anthracen-10-ylmethyl)-2-oxoindolin-3-ylidene)-2-cyanoacetate (**3k**).* Mp 142–145 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.43 (t, 3H, J=7.2 Hz, CH_3), 4.44 (q, 2H, J=7.2 Hz, CH_2), 5.95 (s, 2H, CH_2), 6.23 (d, 1H, J=8.0 Hz, ArH), 6.77 (t, 1H, J=8.0 Hz, ArH), 6.89 (t, 1H, J=8.0 Hz, ArH), 7.51 (t, 2H, J=8.0 Hz, ArH), 7.62 (t, 2H, J=8.0 Hz, ArH), 8.04 (d, 2H, J=8.0 Hz, ArH), 8.14 (d, 1H, J=8.0 Hz, ArH), 8.38 (d, 2H, J=8.0 Hz, ArH), 8.50 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 37.9, 63.4, 106.6, 110.8, 114.4, 118.8, 122.8, 123.4, 124.5, 125.2, 127.3, 129.3, 129.5, 129.7, 130.8, 131.3, 135.5, 144.4, 145.9, 161.5, 164.5; IR (CH_2Cl_2): ν 2978, 2845, 1716, 1609, 1583, 1468, 1380, 1275, 1108, 855, 764, 600, 515 cm^{-1}; MS (MALDI/DHB) m/z (%): 455.1 $[M+Na]^+$ (100); MS (MALDI/DHB) calcd for $C_{28}H_{20}N_2NaO_3$ $[M+Na]^+$ requires 455.1366, found: 455.1361.

*4.1.1.12. (E)-tert-Butyl 3-(1-cyano-2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**3l**).* Mp 130–131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.41 (t, 3H, J=7.2 Hz, CH_3), 1.63 (s, 9H, CH_3), 4.46 (q, 2H, J=7.2 Hz, CH_2), 7.27 (d, 1H, J=5.6 Hz, ArH), 7.54 (t, 1H, J=7.2 Hz, ArH), 7.91 (d, 1H, J=8.0 Hz, ArH), 8.20 (d, 1H, J=8.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 27.9, 63.7, 85.5, 106.8, 113.9, 115.7, 118.6, 124.7, 125.1, 134.9, 138.2, 142.1, 148.1, 160.4, 162.0; IR (CH_2Cl_2): ν 2962, 2925, 1717, 1577, 1368, 1091, 1010, 855, 746, 678 cm^{-1}; MS (%) (EI) m/z 342 (M^+, 3.6), 242 (72.4), 196 (29.1), 168 (28.2), 57 (100), 41 (18.3). HRMS (EI) calcd for $C_{18}H_{18}N_2O_5$ requires 342.1216, found: 342.1217.

*4.1.1.13. (E)-Ethyl 2-cyano-2-(1-(methoxymethyl)-2-oxoindolin-3-ylidene)acetate (**3m**).* Mp 137–140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.45 (t, 3H, J=7.2 Hz, CH_3), 3.37 (s, 3H, CH_3), 4.46 (q, 2H, J=7.2 Hz, CH_2), 5.17 (s, 2H, CH_2), 7.03–7.14 (m, 1H, ArH), 7.47–7.49 (m, 1H, ArH), 7.63–7.67 (m, 1H, ArH), 8.34 (d, 1H, J=8.1 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 56.7, 63.5, 71.5, 110.3, 111.6, 123.7, 125.4, 129.9, 135.9, 138.6, 144.2, 144.9, 161.4, 164.8; IR (CH_2Cl_2): ν 2973, 2941, 2212, 1720, 1620, 1380, 1171, 1124, 820, 735 cm^{-1}; MS (%) (EI) m/z 286 (M^+, 1.33), 191 (24.0), 146 (100), 132 (24.6), 90 (21.9), 77 (16.6), 45 (22.1). HRMS (EI) calcd for $C_{15}H_{14}N_2O_4$ requires 286.0954, found: 286.0950.

*4.1.2. Typical reaction procedure for the preparation of **4**.* Under an argon atmosphere, *N*-protected isatin derived electron-deficient alkene **3a** (0.1 mmol), but-3-yn-2-one **2** (0.3 mmol), PPh_3 (0.02 mmol), and THF (1.0 mL) were added into a Schlenk tube. The reaction mixture was stirred at room temperature for 5 h and the reaction proceeding was monitored by TLC. Then, the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel PE/EtOAc=2:1) to afford compound **4a** as a white solid in 93% yield.

*4.1.2.1. Ethyl 3-acetyl-9-benzyl-4-cyano-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4a**).* Yield 37 mg, 93%. Mp 219–221 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.36 (t, 3H, J=6.9 Hz, CH_3), 2.44 (s, 3H, CH_3), 4.21–4.34 (m, 2H, CH_2), 4.29 (s, 2H, CH_2), 7.14 (d, 2H, J=6.9 Hz, ArH), 7.23–7.32 (m, 6H, ArH), 7.83–7.85 (m, 1H, ArH), 7.89 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 25.3, 42.1, 45.8, 63.6, 83.7, 109.8, 116.5, 119.3, 121.7, 122.3, 122.4, 122.7, 126.6, 128.0, 129.0, 132.3, 135.8, 142.5, 152.2, 166.5, 193.3. IR (CH_2Cl_2): ν 3031, 2957, 2930, 2101, 1747, 1651, 1282, 1249, 1153, 1030, 772 cm^{-1}; MS (MALDI/DHB) m/z (%): 423.2 $[M+Na]^+$ (100); MS (MALDI/DHB) calcd for $C_{24}H_{21}N_2O_4$ $[M+H]^+$ requires 401.1496, found: 401.1494.

*4.1.2.2. Ethyl 3-acetyl-9-benzyl-4-cyano-6-fluoro-4,9-dihydro pyrano[2,3-b]indole-4-carboxylate (**4b**).* Yield 38 mg, 91%. Mp 227–230 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.37 (t, 3H, J=7.2 Hz, CH_3), 2.44 (s, 3H, CH_3), 4.28–4.39 (m, 2H, CH_2), 5.29 (s, 2H, CH_2), 6.93 (dt, 1H, J_1=2.4 Hz, J_2=9.0 Hz, ArH), 7.12–7.17 (m, 3H, ArH), 7.31–7.36 (m, 3H, ArH), 7.50 (dd, 1H, J_1=2.4 Hz, J_2=9.0 Hz, ArH), 7.90 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.2, 41.9, 46.0, 63.7, 84.0, 105.1 (d, J=25.9 Hz), 110.8 (d, J=14.2 Hz), 111.0 (d, J=12.1 Hz), 116.3 (d, J=3.6 Hz), 122.9 (d, J=10.4 Hz), 126.6, 127.5,

128.1, 128.6, 128.9 (d, J=8.7 Hz), 135.4, 143.3, 152.1, 158.0 (d, J=236.4 Hz), 166.2, 193.2. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$) δ −118.3; IR (CH_2Cl_2): ν 2952, 2924, 2856, 1746, 1671, 1491, 1238, 1089, 772 cm^{-1}; MS (MALDI/DHB) m/z (%): 419.1 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{24}H_{20}N_2O_4F$ $[M+H]^+$ requires 419.1402, found: 419.1409.

*4.1.2.3. Ethyl 3-acetyl-9-benzyl-4-cyano-6-methyl-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4c**).* Yield 37 mg, 89%. Mp 220–223 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.37 (t, 3H, J=7.2 Hz, CH_3), 2.43 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 4.28–4.38 (m, 2H, CH_2), 5.30 (s, 2H, CH_2), 7.03 (d, 1H, J=8.4 Hz, ArH), 7.11–7.15 (m, 3H, ArH), 7.26–7.33 (m, 3H, ArH), 7.63 (s, 1H, ArH), 7.88 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 18.9, 25.1, 42.2, 46.8, 63.4, 83.3, 116.4, 116.6, 116.9, 120.9, 123.4, 125.0, 127.4, 127.5, 129.0, 129.2, 131.2, 137.7, 142.7, 152.2, 166.4, 193.4. IR (CH_2Cl_2): ν 2968, 2924, 2861, 1746, 1650, 1582, 1495, 1378, 1291, 1090, 1039, 734, 701 cm^{-1}; MS (MALDI/DHB) m/z (%): 415.2 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$ requires 415.1652, found: 415.1653.

*4.1.2.4. Ethyl 3-acetyl-9-benzyl-6-bromo-4-cyano-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4d**).* Yield 38 mg, 81%. Mp 235–238 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.31 (t, 3H, J=7.2 Hz, CH_3), 2.36 (s, 3H, CH_3), 4.21–4.33 (m, 2H, CH_2), 5.20 (s, 2H, CH_2), 7.01–7.05 (m, 3H, ArH), 7.18–7.27 (m, 4H, ArH), 7.82 (s, 1H, ArH), 7.89 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.3, 41.9, 45.9, 63.8, 83.4, 111.4, 114.9, 116.3, 116.4, 121.8, 123.9, 125.7, 126.5, 128.2, 129.0, 135.2, 130.9, 143.0, 152.0, 166.0, 193.1; IR (CH_2Cl_2): ν 2952, 2924, 2851, 1745, 1649, 1488, 1352, 1290, 1234, 1091, 1038, 799 cm^{-1}; MS (MALDI/DHB) m/z (%): 479.1 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{24}H_{20}N_2O_4Br$ $[M+H]^+$ requires 479.0601, found: 479.0619.

*4.1.2.5. Ethyl 3-acetyl-9-benzyl-7-bromo-4-cyano-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4e**).* Yield 36 mg, 75%. Mp 231–235 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.32 (t, 3H, J=7.2 Hz, CH_3), 2.42 (s, 3H, CH_3), 4.27–4.34 (m, 2H, CH_2), 5.23 (s, 2H, CH_2), 7.11–7.13 (m, 2H, ArH), 7.25–7.40 (m, 5H, ArH), 7.70 (d, 1H, J=8.4 Hz, ArH), 7.89 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.2, 41.9, 45.8, 63.6, 83.9, 112.8, 116.0, 116.3, 120.5, 121.2, 124.9, 126.5, 128.0, 128.1, 129.0, 132.9, 135.2, 142.6, 152.1, 166.1, 193.2. IR (CH_2Cl_2): ν 2952, 2924, 1747, 1652, 1575, 1290, 1091, 770 cm^{-1}; MS (MALDI/DHB) m/z (%): 478.1 $[M]^+$ (100); MS (MALDI/DHB) calcd for $C_{24}H_{20}N_2O_4Br$ $[M+H]^+$ requires 479.0601, found: 479.0596.

*4.1.2.6. Ethyl 3-acetyl-9-benzyl-4-cyano-7-methyl-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4f**).* Yield 31 mg, 73%. Mp 227–230 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.37 (t, 3H, J=7.2 Hz, CH_3), 2.43 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 4.27–4.39 (m, 2H, CH_2), 5.28 (s, 2H, CH_2), 7.03 (d, 1H, J=8.4 Hz, ArH), 7.11–7.14 (m, 3H, ArH), 7.26–7.33 (m, 3H, ArH), 7.63 (s, 1H, ArH), 7.88 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 21.2, 25.2, 42.2, 46.8, 63.4, 83.3, 116.4, 116.6, 116.9, 120.9, 123.4, 125.1, 127.4, 127.6, 129.0, 129.2, 131.2, 137.7, 142.7, 152.2, 166.4, 193.4. IR (CH_2Cl_2): ν 2968, 2924, 2861, 1746, 1650, 1582, 1495, 1378, 1291, 1090, 1039, 734, 701 cm^{-1}; MS (MALDI/DHB) m/z (%): 415.2 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$ requires 415.1652, found: 415.1653.

*4.1.2.7. Ethyl 3-acetyl-9-benzyl-4-cyano-6,8-dimethyl-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4g**).* Yield 35 mg, 81%. Mp 220–222 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.28 (t, 3H, J=7.2 Hz, CH_3), 2.32 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.18–4.30 (m, 2H, CH_2), 5.44 (s, 2H, CH_2), 6.70 (s, 1H, ArH), 6.84 (d, 2H, J=7.6 Hz, ArH), 7.17–7.23 (m, 3H, ArH), 7.24 (s, 1H, ArH), 7.75 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 18.9, 21.2, 25.2, 42.2, 46.8, 63.4, 83.3, 116.4, 116.6, 116.9, 120.9, 123.4, 125.1, 127.4, 127.6, 129.0, 129.2, 131.2, 137.7, 142.7, 152.2, 166.4, 193.4. IR (CH_2Cl_2): ν 2961, 2925, 1746, 1672, 1581, 1355, 1237, 1039, 799, 736 cm^{-1}; MS (MALDI/DHB) m/z (%): 451.2 $[M+Na]^+$ (100); MS (MALDI/DHB) calcd for $C_{26}H_{25}N_2O_4$ $[M+H]^+$ requires 429.1809, found: 429.1818.

*4.1.2.8. Ethyl 3-acetyl-9-benzyl-4-cyano-6-methoxy-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4h**).* Yield 38 mg, 88%. Mp 224–225 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.35 (t, 3H, J=7.2 Hz, CH_3), 2.41 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 4.25–4.37 (m, 2H, CH_2), 5.25 (s, 2H, CH_2), 6.82 (dd, 1H, J_1=2.8 Hz, J_2=8.8 Hz, ArH), 7.10–7.13 (m, 3H, ArH), 7.27–7.30 (m, 4H, ArH), 7.87 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.1, 25.2, 42.1, 45.8, 55.7, 63.4, 83.5, 101.5, 110.7, 112.3, 116.3, 116.4, 123.0, 126.5, 126.9, 127.9, 128.9, 135.8, 142.5, 152.2, 155.4, 166.3, 193.3. IR (CH_2Cl_2): ν 2961, 2851, 1747, 1673, 1582, 1353, 1241, 1089, 1030, 799 cm^{-1}; MS (MALDI/DHB) m/z (%): 431.2 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{25}H_{23}N_2O_5$ $[M+H]^+$ requires 431.1602, found: 431.1603.

*4.1.2.9. Ethyl 3-acetyl-4-cyano-9-methyl-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4i**).* Yield 23 mg, 71%. Mp 190–192 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.34 (t, 3H, J=6.8 Hz, CH_3), 2.44 (s, 3H, CH_3), 3.68 (s, 3H, CH_3), 4.25–4.35 (m, 2H, CH_2), 7.23–7.28 (m, 3H, ArH), 7.79–7.81 (m, 1H, ArH), 7.92 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.2, 28.1, 42.1, 63.5, 83.2, 109.2, 116.4, 116.6, 119.1, 121.4, 122.2, 122.4, 132.6, 142.5, 152.2, 166.5, 193.4; IR (CH_2Cl_2): ν 3061, 2960, 2925, 1746, 1673, 1582, 1354, 1291, 1235, 1185, 1090, 1039, 964, 799, 701 cm^{-1}; MS (MALDI/DHB) m/z (%): 325.1 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{18}H_{17}N_2O_4$ $[M+H]^+$ requires 325.1183, found: 325.1180.

*4.1.2.10. Ethyl 3-acetyl-9-allyl-4-cyano-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4j**).* Yield 27 mg, 77%. Mp 198–203 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.30 (t, 3H, J=7.2 Hz, CH_3), 2.39 (s, 3H, CH_3), 4.22–4.31 (m, 2H, CH_2), 4.66–4.68 (m, 1H, CH_2), 4.66–4.68 (m, 1H, =CH), 5.03 (dd, 1H, J_1=0.8 Hz, J_2=16.8 Hz, =CH), 5.17 (dd, 1H, J_1=0.8 Hz, J_2=10.4 Hz, =CH), 5.85 (m, 1H, CH_2), 7.17–7.24 (m, 3H, ArH), 7.76–7.79 (m, 1H, ArH), 7.87 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.2, 42.1, 44.4, 63.4, 83.4, 109.7, 116.3, 116.5, 117.7, 119.2, 121.5, 122.3, 122.5, 131.6, 132.0, 142.2, 152.2, 166.4, 193.4. IR (CH_2Cl_2): ν 3031, 2961, 2854, 1746, 1673, 1489, 1455, 1291, 1234, 1090, 1039, 800, 701 cm^{-1}; MS (MALDI/DHB) m/z (%): 351.2 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{20}H_{19}N_2O_4$ $[M+H]^+$ requires 351.1339, found: 351.1344.

*4.1.2.11. Ethyl 3-acetyl-9-(anthracen-10-ylmethyl)-4-cyano-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4k**).* Yield 47 mg, 90%. Mp 215–220 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.30 (t, 3H, J=7.2 Hz, CH_3), 2.31 (s, 3H, CH_3), 4.22–4.30 (m, 2H, CH_2), 6.08 (s, 2H, CH_2), 6.98–7.00 (m, 2H, ArH), 7.12–7.15 (m, 1H, ArH), 7.45–7.52 (m, 4H, ArH), 7.58 (s, 1H, ArH), 7.78 (d, 1H, J=8.0 Hz, ArH), 8.04 (d, 2H, J=8.0 Hz, ArH), 8.19 (d, 2H, J=8.0 Hz, ArH), 8.53 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.1, 40.4, 63.4, 83.8, 110.3, 116.0, 116.4, 119.2, 121.4, 122.5, 122.6, 122.7, 123.2, 124.7, 125.1, 127.1, 129.3, 129.5, 130.9, 131.2, 132.5, 143.0, 152.1, 166.3, 193.3. IR (CH_2Cl_2): ν 2962, 2923, 2851, 1970, 1718, 1290, 1245, 1024, 799 cm^{-1}; MS (MALDI/DHB) m/z (%): 523.2 $[M+Na]^+$ (100); MS (MALDI/DHB) calcd for $C_{32}H_{24}N_2O_4Na$ $[M+Na]^+$ requires 523.1628, found: 523.1617.

*4.1.2.12. 9-tert-Butyl 4-ethyl 3-acetyl-4-cyanopyrano[2,3-b]indole-4,9(4H)-dicarboxylate (**4l**).* Yield 33 mg, 76%. Mp 187–191 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.33 (t, 3H, J=7.2 Hz, CH_3), 1.70 (s, 9H, CH_3), 2.45 (s, 3H, CH_3), 4.25–4.28 (m, 2H, CH_2), 7.33–7.36 (m, 2H, ArH), 7.80–7.83 (m, 1H, ArH), 7.92 (s, 1H, ArH), 8.09–8.12 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.2, 28.1, 41.7, 63.8, 85.7, 89.8, 115.2, 115.7, 115.8, 119.1, 122.9, 124.2, 125.0, 131.6, 142.1, 147.9, 152.1, 166.0, 193.2. IR (CH_2Cl_2): ν 2968, 2898, 1748, 1652, 1558, 1275, 1260, 750 cm^{-1}; MS (MALDI/DHB) m/z (%): 449.1

$[M+K]^+$ (100); MS (MALDI/DHB) calcd for $C_{22}H_{22}N_2O_6Na$ $[M+Na]^+$ requires 433.1370, found: 433.1371.

*4.1.2.13. Ethyl 3-acetyl-4-cyano-9-(methoxymethyl)-4,9-dihydropyrano[2,3-b]indole-4-carboxylate (**4m**).* Yield 30 mg, 79%. Mp 195–200 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.28 (t, 3H, J=7.2 Hz, CH_3), 2.38 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 4.18–4.30 (m, 2H, CH_2), 5.39 (s, 2H, CH_2), 7.19–7.23 (m, 2H, ArH), 7.37–7.39 (m, 1H, ArH), 7.74–7.76 (m, 1H, ArH), 7.85 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 25.3, 42.0, 56.5, 63.6, 73.0, 84.6, 110.0, 116.3, 116.5, 119.3, 122.3, 122.5, 123.2, 132.4, 142.4, 152.0, 166.3, 193.3. IR (CH_2Cl_2): ν 2961, 2925, 1746, 1672, 1581, 1355, 1237, 1039, 799, 736 cm^{-1}; MS (MALDI/DHB) m/z (%): 377.3 $[M+Na]^+$ (100); MS (MALDI/DHB) calcd for $C_{19}H_{18}N_2O_5Na$ $[M+Na]^+$ requires 377.1108, found: 377.1103.

Compound **7**. Yield 47 mg, 91%. Mp 262–265 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.29 (s, 3H, CH_3), 4.95 (d, 1H, J=15.6 Hz, CH_2), 5.21 (d, 1H, J=15.6 Hz, CH_2), 5.29 (s, 2H, CH_2), 6.53 (s, 1H, ArH), 6.77 (d, 1H, J=7.6 Hz, ArH), 6.92 (s, 1H, ArH), 6.98–7.07 (m, 1H, ArH), 7.12–7.17 (m, 1H, ArH), 7.24–7.29 (m, 3H, ArH), 7.30–7.35 (m, 4H, ArH), 7.41 (t, 2H, J=7.2 Hz, ArH), 7.54 (d, 2H, J=7.2 Hz, ArH), 7.98 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ25.7, 45.1, 45.8, 48.6, 88.3, 110.0, 110.7, 117.8, 120.0, 122.2, 123.6, 123.9, 126.5, 126.6, 127.7, 127.8, 128.0, 128.2, 128.5, 129.0, 129.1, 130.7, 134.9, 135.5, 135.9, 141.5, 144.2, 153.2, 176.9, 194.1. IR (CH_2Cl_2): ν 2968, 2924, 2861, 1746, 1650, 1582, 1495, 1378, 1291, 1090, 1039, 734, 701 cm^{-1}; MS (MALDI/DHB) m/z (%): 579.1 $[M+H]^+$ (100); MS (MALDI/DHB) calcd for $C_{34}H_{25}N_2O_3Cl_2$ $[M+H]^+$ requires 519.1237, found: 519.1218.

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Supplementary data

The ^{1}H and ^{13}C NMR spectroscopic data and charts of the compounds shown in Tables 1 and 2 and X-ray crystal data of products **3a**, **4j**, and **7** are included in the Supplementary data. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2012.01.036.

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13. The crystal data of **3a** have been deposited in CCDC with number 805743. Empirical formula: $C_{20}H_{16}N_2O_3$; Formula weight: 332.35; crystal color, habit: colorless; crystal dimensions: 0.405×0.285×0.067 mm; crystal system: orthorhombic; lattice parameters: a=15.187(3) Å, b=24.995(5) Å, c=4.4581(9) Å, α=90°, β=90°, γ=90°, V=1692.3(6) Å^3; space group: *Pna*2(1); Z=4; D_{calcd}=1.304 g/cm^3; F_{000}=696; diffractometer: Rigaku AFC7R; residuals: R; R_w: 0.0500, 0.1219.
14. The crystal data of **4j** have been deposited in CCDC with number 824482. Empirical formula: $C_{20}H_{18}N_2O_4$; formula weight: 350.36; Crystal color, habit: colorless; crystal dimensions: 0.35×0.28×0.18 mm; crystal system: triclinic; lattice parameters: a=12.220(2) Å, b=12.549(2) Å, c=19.013(3) Å, α=78.526(3)°, β=82.058(3)°, γ=66.143(3)°, V=1784.8(6)° Å^3; Space group: P–1; Z=4;D_{calcd}=1.304 g/cm^3; F_{000}=736; final R indices [$I>2\sigma(I)$] $R1$=0.0559, $wR2$=0.1575.
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18. The crystal data of **7** have been deposited in CCDC with number 821911. Empirical formula: $C_{35}H_{25}Cl_5N_2O_3$; formula weight: 698.82; crystal color, habit: colorless; crystal dimensions: 0.38×0.30×0.10 mm; crystal system: triclinic; lattice type: primitive; lattice parameters: a=9.5528(19) Å, b=10.166(2) Å, c=17.258(3) Å, α=85.184(3)°, β=84.545(3)°, γ=70.455(3)°, V=1569.9(5) Å^3; Space group: P–1; Z=2; D_{calcd}=1.478 g/cm^3; F_{000}=716; final R indices [$I>2\sigma(I)$] $R1$=0.0485, $wR2$=0.1352.