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A Simple and Green Tandem Knoevenagel–Phospha-Michael Reaction for One-Pot Synthesis of 2-Oxindol-3-ylphosphonates Catalyzed by a DABCO-Based Ionic Liquid

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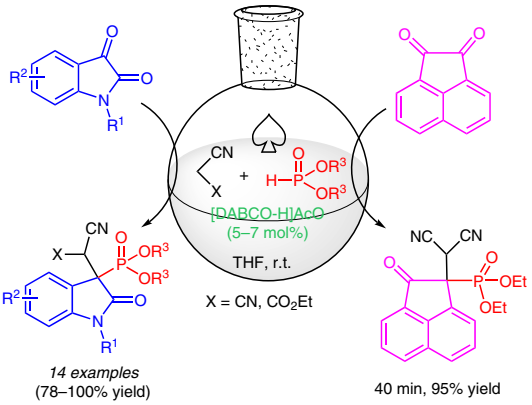

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Abstract A simple, clean, and efficient approach for the one-pot synthesis of 2-oxindol-3-ylphosphonates has been successfully developed. With 7 mol% loading of the 1,4-diazabicyclo[2.2.2]octane-based ionic liquid catalyst, 2-oxindol-3-ylphosphonates form in good to excellent yields within short times. This tandem reaction involves a phospha-Michael addition to the activated alkenes, which form *in situ* by Knoevenagel condensation. The corresponding products are easily separated and purified by simple crystallization. The catalyst can be recycled five times without significant activity loss. This approach is readily amenable to large-scale synthesis.

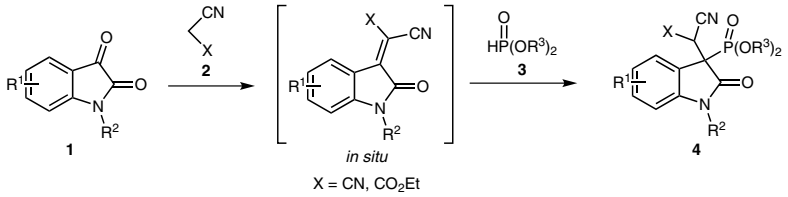
Keywords phosphonates, oxindoles, ionic liquid, Knoevenagel condensation, phospha-Michael addition, tandem reaction

Multicomponent reactions (MCRs) are some of the most important reactions, and are widely used in organic synthesis for the construction of bioactive heterocyclic compounds.[1] MCRs offer an efficient way for the construction of highly complex molecules from simple starting materials *via* one-pot procedures without complicated purification steps. These reactions also comply with the principles of green chemistry, such as saving solvents, time, and reagents.

Indoles and their derivatives are widespread in natural compounds. They have been identified as one of the most intriguing heterocyclic compounds.[2] Compounds containing the indole framework often display a wide variety of pharmacological and biological activities.[3] Oxindoles are key compounds among the indole derivatives. In particular, C3-functionalized oxindoles often appear as the heterocyclic nucleus in natural products and medicinally relevant compounds.[4] Organophosphorus compounds are major components of the living body of both people and animals. Natural products containing phosphorus often show interesting biological activities.[5] Of the various organophosphorus compounds, much attention has been paid to phosphonates and their derivatives due to their usefulness in industrial, agricultural, and medicinal chemistry.[6–11]

2-Oxindol-3-ylphosphonate compounds contain two major components, 3,3-disubstituted oxindoles and β-phosphonomalonates. Many synthetic protocols have been developed for the synthesis of β-phosphonomalonates.[12] However, reports for the synthesis of 2-oxindol-3-ylphosphonates are rare.[13] In addition, these methods are often associated with limitations such as moderate yields, limited substrates, and elevated temperatures. In particular, two-pot procedures are often needed, in which the α,β-unsaturated malonate intermediates are prepared in a separate step, followed by the phosphorus–carbon bond formation in the next separate step.[13a] As a result, the development of a simple, clean, and efficient method for the one-pot synthesis of 2-oxindol-3-ylphosphonates in excellent yields tolerating a broad range of substrates is still considered a significant challenge.

Ionic liquids (ILs) as environmentally friendly solvents have been employed in many important transformations.[14] In recent years, many IL catalysts have been prepared and have shown notable performances in various reactions.[15–19] Recently, we synthesized several kinds of highly efficient IL catalysts and applied them in many important carbon–

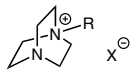


Scheme 1 Tandem reaction for the one-pot synthesis of 2-oxindol-3-ylphosphonates **4**

carbon and phosphorus–carbon bond-formation reactions.[20–24] As part of our ongoing investigations on IL-catalyzed organic reactions, we report here the results of using ILs based on 1,4-diazabicyclo[2.2.2]octane (DABCO) as catalysts for the preparation of 2-oxindol-3-ylphosphonates *via* a one-pot tandem Knoevenagel–phospha-Michael reaction. In this procedure, firstly, activated alkenes are formed *in situ* from isatins and active methylenes *via* Knoevenagel condensation. Then a phospha-Michael addition takes place, affording the desired products in excellent yields (Scheme 1).

Eight kinds of DABCO-based IL catalysts were synthesized, and they are shown in Figure **1**.[21] We initiated our investigations by screening for the best DABCO-based IL catalyst for the model reaction between isatin (**1a**), malononitrile (**2a**), and diethyl phosphite (**3a**) in MeCN at room temperature. The results are summarized in Table 1. All tested DABCO-based IL catalysts could promote the reaction, and afforded the corresponding product **4a** in moderate to good yields. When the reactions were carried out in the presence of IL catalysts containing strong acids or alkyl substituents, the reactions required longer reaction times and afforded **4a** in moderate yields. The IL catalysts with longer carbon chain substituents gave the product **4a** in higher yield than that obtained with short carbon chain substituents (entries 5 vs 6, 7 vs 8). Among the different DABCO-based catalysts, [DABCO-H][AcO] gave **4a** in an excellent yield of 95% within only one hour at room temperature (entry 1).

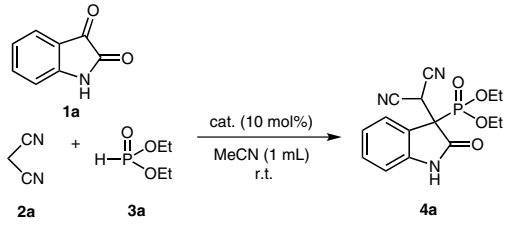
Next, different solvents were screened in the presence of the catalyst [DABCO-H][AcO]. As shown in Table 2, the yield of **4a** differed significantly for different solvents.



[DABCO-H][AcO], X = AcO, R = H
[DABCO-H][HSO_4], X = HSO_4, R = H
[DABCO-H]Cl, X = Cl, R = H
[DABCO-H][BF_4], X = BF_4, R = H
[DABCO-C_4]Cl, X = Cl, R = *n*-butyl
[DABCO-C_8]Cl, X = Cl, R = *n*-octyl
[DABCO-C_2OH]Cl, X = Cl, R = 2-hydroxyethyl
[DABCO-C_3OH]Cl, X = Cl, R = 3-hydroxypropyl

Figure 1 Structures of the DABCO-based ionic liquid catalysts

Table 1 The Effect of the DABCO-Based Ionic Liquid Catalysts on the Tandem Reaction for the Synthesis of 2-Oxindol-3-ylphosphonate **4a**[a]

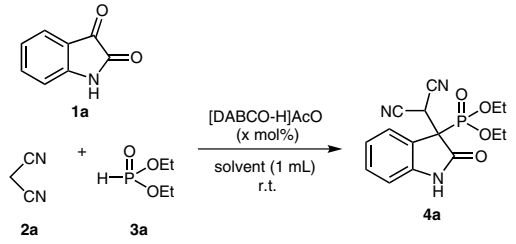


Entry	Cat. (10 mol%)	Time (h)	Yield (%)[b]
1	[DABCO-H][AcO]	1	95
2	[DABCO-H][HSO_4]	24	74
3	[DABCO-H]Cl	24	87
4	[DABCO-H][BF_4]	24	90
5	[DABCO-C_4]Cl	24	32
6	[DABCO-C_8]Cl	24	54
7	[DABCO-C_2OH]Cl	24	26
8	[DABCO-C_3OH]Cl	24	67

[a] Reaction conditions: isatin (**1a**, 1 mmol), malononitrile (**2a**, 1 mmol), diethyl phosphite (**3a**, 1 mmol), DABCO-based IL catalyst (0.1 mmol), MeCN (1 mL).
[b] Isolated yield.

When the reaction was performed in the classic organic solvents MeCN, EtOH, 1,2-dichloroethane (DCE), and THF, the target product was formed in good to excellent yield (entries 1–4). Especially in THF, all the substrates dissolve very well, and a near quantitative yield is obtained in only 20 minutes at room temperature (entry 4). When water was used as the solvent, product **4a** was obtained in a very low yield (entry 5), because of poor dissolution. We next tried to decrease the catalyst loading and the amount of solvent. When the reaction was performed in 0.3 mL THF, catalyst loadings of 10 mol%, 7 mol%, and 5 mol% could all result in quantitative yield, but the reaction time had to be increased when reducing the catalyst loading (entries 6–8). When the loading of the catalyst [DABCO-H][AcO] was reduced to 3 mol%, product **4a** was obtained in only 15% yield (entry 9). Importantly, in the absence of the [DABCO-H][AcO] IL, no **4a** was produced, even after one day (entry 10).

Table 2 Optimization of the Reaction Conditions[a]



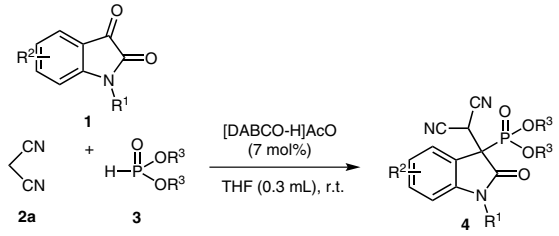
Entry	x (mol%)	Solvent	Time (min)	Yield (%)[b]
1	10	MeCN	60	95
2	10	EtOH	120	82
3	10	DCE	180	95
4	10	THF	20	98
5	10	H_2O	120	<5
6[c]	10	THF	12	100
7[c]	7	THF	17	100
8[c]	5	THF	40	100
9[c]	3	THF	120	15
10[c]	0	THF	24 h	–

[a] Reaction conditions: isatin (**1a**, 1 mmol), malononitrile (**2a**, 1 mmol), diethyl phosphite (**3a**, 1 mmol), [DABCO-H][AcO] (0.1 mmol), solvent (1 mL).
[b] Isolated yield.
[c] THF (0.3 mL) used.

With the established optimal reaction conditions in hand, a variety of isatins **1** with malononitrile (**2a**), and dialkyl or diphenyl phosphites **3** were next examined in the reaction catalyzed by [DABCO-H][AcO] (7 mol%) in THF at room temperature. As shown in Table 3, all isatins containing electron-withdrawing or -donating groups could react well with malononitrile and diethyl phosphite, and converted into the corresponding 2-oxindol-3-ylphosphonates in good to excellent yields (87–100%) within 5–300 minutes (entries 1–9). To show the generality and scope of this new protocol, dimethyl phosphite (**3b**) and diphenyl phosphite (**3c**) were also studied in this one-pot, three-component tandem Knoevenagel–phospha-Michael reaction (entries 10 and 11). They also worked well under the optimal reaction conditions. Notably, even diphenyl phosphite, which contains sterically hindered phenyl groups, could also be converted into the desired product **4k** in a good yield of 90%.

Compared to malononitrile (**2a**), ethyl cyanoacetate (**2b**) is a less reactive substrate, because the electron-withdrawing ability of the carboxylate group is weaker than that of the CN group. Therefore, the reaction of ethyl cyanoacetate (**2b**) with isatin (**1a**) and diethyl phosphite (**3a**) was carried out under heating, and afforded the corresponding product **4l** in a yield of 78% after a longer reaction time (Scheme 2).

Table 3 Synthesis of 2-Oxindol-3-ylphosphonates **4** by Using [DABCO-H][AcO] at Room Temperature[a]



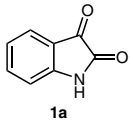
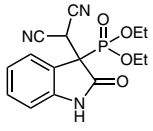
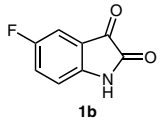
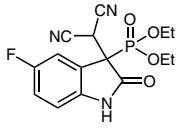
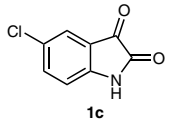
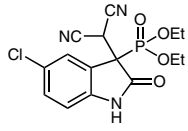
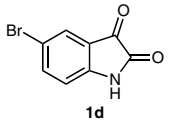
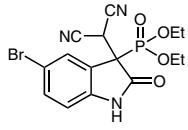
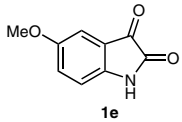
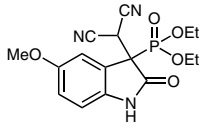
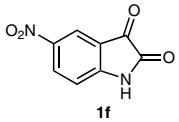
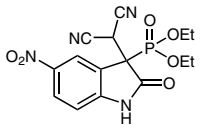
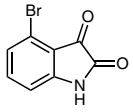
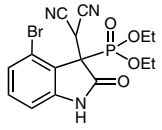
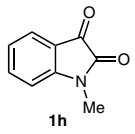
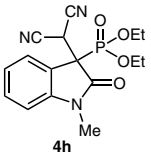
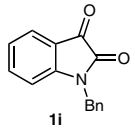
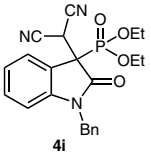
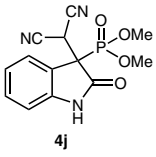
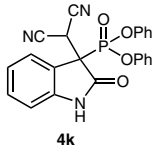
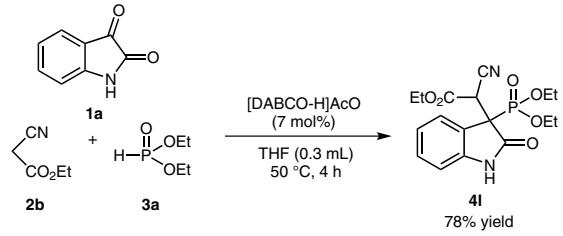
Entry	Isatin **1**	R^3	Product **4**	Time (min)	Yield (%)[b]
1	 **1a**	Et	 **4a**	17	100
2	 **1b**	Et	 **4b**	60	97
3	 **1c**	Et	 **4c**	40	97
4	 **1d**	Et	 **4d**	20	100
5	 **1e**	Et	 **4e**	5	100
6	 **1f**	Et	 **4f**	120	91
7	 **1g**	Et	 **4g**	300	87

Table 3 (continued)

Entry	Isatin **1**	R^3	Product **4**	Time (min)	Yield (%)[b]
8	 **1h**	Et	 **4h**	15	98
9	 **1i**	Et	 **4i**	15	100
10	**1a**	Me	 **4j**	20	94
11	**1a**	Ph	 **4k**	100	90

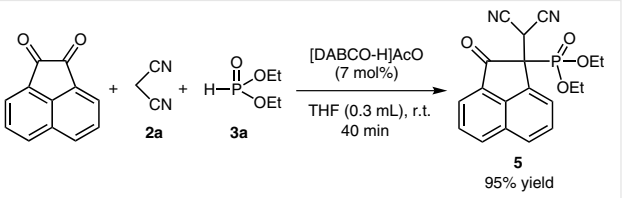
[a] Reaction conditions: isatin **1** (1 mmol), malononitrile (**2a**, 1 mmol), phosphite **3** (1 mmol), [DABCO-H][AcO] (0.07 mmol), THF (0.3 mL), r.t.
[b] Isolated yield.



Scheme 2 Reaction of isatin with ethyl cyanoacetate and diethyl phosphite

Isatins were replaced by acenaphthenequinone in the reaction with malononitrile (**2a**) and diethyl phosphite (**3a**) under the optimized conditions. As expected, the reaction proceeded very cleanly and afforded the corresponding product **5** in an excellent yield of 95% (Scheme 3). No undesirable side reactions were observed under the mild conditions.

The recyclability and reusability of the catalyst was examined for the synthesis of **4a**. When the reaction was complete, the crude products were filtered and washed with cold water. The 2-oxindol-3-ylphosphonates could be purified simply by crystallization, and no chromatographic



Scheme 3 Reaction of acenaphthenequinone with malononitrile and diethyl phosphite

technique was needed. In this procedure, the ionic liquid catalysts dissolved in water, which could be easily recovered and directly reused in the same reaction. It was observed that the DABCO-based catalyst can be recovered and reused for five times at least. The results are presented in Figure 2.

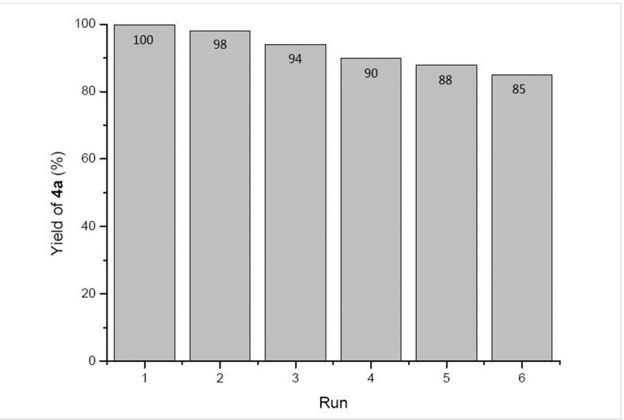
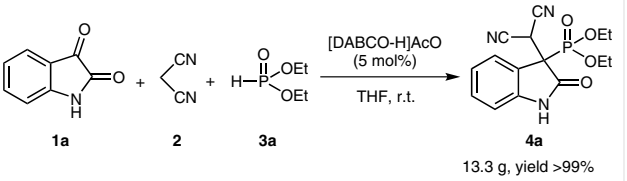


Figure 2 Recycling of the catalyst [DABCO-H][AcO] for the synthesis of **4a**. *Reagents and conditions*: isatin (**1a**, 5 mmol), malononitrile (**2a**, 5 mmol), diethyl phosphite (**3a**, 5 mmol), catalyst (7 mol%) THF (2 mL), r.t.

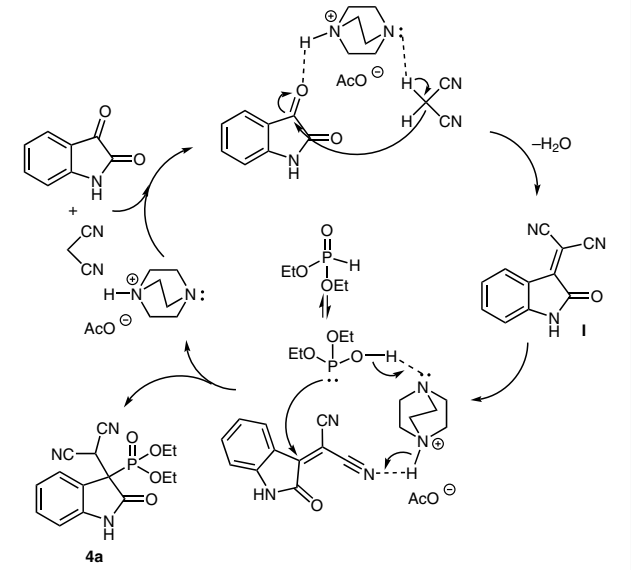
To display the potential applicability of this methodology, we tried out this one-pot three-component tandem reaction on a 40-mmol scale in the presence of only 5 mol% of the catalyst, and obtained 13.3 grams of **4a** in >99% yield (Scheme 4).



Scheme 4 Synthesis of 2-oxindol-3-ylphosphonate **4a** on 40-mmol scale

A plausible mechanism is proposed and shown in Scheme 5. The tandem reaction involves a double activation. First, both of the carbonyl groups of the isatin, as well as the malononitrile, are activated by the catalyst [DABCO-H][AcO], to afford the key intermediate alkene **I**. Then, an-

other double activation of the cyano group and diethyl phosphite occurred. The catalyst removes a proton from diethyl phosphite and transfers a proton, attaching to itself to the cyano group. Finally, tautomerization *via* a [1,3] hydrogen shift takes place to produce the desired product **4a**.



Scheme 5 Proposed mechanism

In conclusion, we have introduced a clean, efficient, and atom-economical method for the preparation of 2-oxindol-3-ylphosphonates from readily available starting materials *via* a one-pot three-component tandem reaction. The reaction involves a phospha-Michael addition of a phosphite to an activated alkene, which formed *in situ* from an isatin and an active methylene by Knoevenagel condensation. This unique tandem Knoevenagel–phospha-Michael reaction allows the preparation of 2-oxindol-3-ylphosphonates in just one step. The DABCO-based ionic liquid catalyst, which is inexpensive and recyclable, drives the reaction to afford the desired products in high yields within short times. This procedure also offers other significant advantages including a green workup, ease of separation and recyclability of the catalyst, scaling up to multigram quantities, and no byproduct formation. A plausible reaction mechanism was proposed. We believe that this method will find useful applications in organic synthesis.

All chemicals were purchased from commercial suppliers and were used without further purification. Melting points were determined with an X-4 apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer with DMSO-d_6 or $CDCl_3$ as the solvent. Chemical shifts are reported relative to TMS as internal standard.

2-Oxindol-3-ylphosphonates 4; General Procedure

Isatin **1** (1 mmol), active methylene **2** (1 mmol), phosphite **3** (1 mmol), and [DABCO-H][AcO] (17.2 mg, 0.1 mmol) were added to THF (0.3 mL). Then the reaction mixture was vigorously stirred at r.t. The progress of the reaction was monitored by TLC (*n*-hexane–EtOAc, 4:1). After completion of the reaction, cold H_2O (2 mL) was added. The IL catalyst dissolved in the H_2O and the insoluble crude products were isolated by simple filtration. The crude products were recrystallized from EtOH to afford pure final products. After removal of the H_2O under reduced pressure, the catalyst [DABCO-H][AcO] could be directly reused for the next run under similar reaction conditions.

Diethyl [3-(Dicyanomethyl)-2-oxindol-3-yl]phosphonate (4a)[13c]

Yield: 333 mg (100%); white solid; mp 174–176 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.35 (t, 3 H, *J* = 6.8 Hz, CH_3), 4.14–4.19 (m, 4 H, OCH_2), 4.87 (d, *J* = 6.8 Hz, 1 H, CH), 7.00 (d, *J* = 7.2 Hz, 1 H, ArH), 7.14 (t, *J* = 7.6 Hz, 1 H, ArH), 7.37 (t, *J* = 6.8 Hz, 1 H, ArH), 7.69 (d, *J* = 6.8 Hz, 1 H, ArH), 10.83 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.76, 26.94, 53.06 (d, $^1J_{CP}$ = 139 Hz, C-P), 64.36, 65.02, 109.74, 110.25, 110.70, 120.58, 122.50, 125.67, 130.61, 142.77, 170.42.

^{31}P NMR (161 MHz, $CDCl_3$): δ = 17.05.

Diethyl [3-(Dicyanomethyl)-5-fluoro-2-oxindol-3-yl]phosphonate (4b)[25]

Yield: 340 mg (97%); pale solid; mp 195–197 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.36 (t, *J* = 6.8 Hz, 3 H, CH_3), 4.17–4.24 (m, 4 H, OCH_2), 5.11 (d, *J* = 6.8 Hz, 1 H, CH), 6.97 (dd, *J* = 4.4, 4.4 Hz, 1 H, ArH), 7.11 (t, *J* = 8.8 Hz, 1 H, ArH), 7.42 (d, *J* = 8.0 Hz, 1 H, ArH), 11.09 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$–DMSO-d_6): δ = 16.11, 27.21, 53.73 (d, $^1J_{CP}$ = 138.6 Hz, C-P), 64.85, 65.57, 109.82, 110.43, 111.85, 113.95, 117.65, 122.40, 139.27, 158.74, 170.68.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 16.54.

Diethyl [5-Chloro-3-(dicyanomethyl)-2-oxindol-3-yl]phosphonate (4c)[13c]

Yield: 356 mg (97%); white solid; mp 193–195 °C.

^{1}H NMR (400 MHz, $CDCl_3$–DMSO-d_6): δ = 1.31 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.36 (t, *J* = 6.8 Hz, 3 H, CH_3), 4.10–4.29 (m, 4 H, OCH_2), 5.09 (d, *J* = 6.8 Hz, 1 H, CH), 6.96 (d, *J* = 8.4 Hz, 1 H, ArH), 7.36 (d, *J* = 8.0 Hz, 1 H, ArH), 7.63 (s, 1 H, ArH), 11.14 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$–DMSO-d_6): δ = 16.07, 27.09, 53.46 (d, $^1J_{CP}$ = 138.5 Hz), 64.84, 65.57, 109.78, 110.29, 112.11, 122.59, 126.16, 127.88, 130.94, 141.72, 170.38.

^{31}P NMR (162 MHz, $CDCl_3$–DMSO-d_6): δ = 11.56.

Diethyl [5-Bromo-3-(dicyanomethyl)-2-oxindol-3-yl]phosphonate (4d)[13c]

Yield: 411 mg (100%); white solid; mp 186–188 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28–1.35 (m, 6 H, CH_3), 4.20 (t, *J* = 6.4 Hz, 4 H, OCH_2), 4.81 (d, *J* = 4.4 Hz, 1 H, CH), 6.86 (d, *J* = 8.0 Hz, 1 H, ArH), 7.48 (s, 1 H, ArH), 7.75 (d, *J* = 5.2 Hz, 1 H, ArH), 10.93 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$–DMSO-d_6): δ = 15.78, 26.80, 53.07 (d, $^1J_{CP}$ = 137.7 Hz, C-P), 64.54, 65.28, 110.09, 112.26, 114.72, 122.77, 128.59, 133.49, 142.01, 169.98.

^{31}P NMR (162 MHz, $CDCl_3$–DMSO-d_6): δ = 11.60.

Diethyl [3-(Dicyanomethyl)-5-methoxy-2-oxindol-3-yl]phosphonate (4e)[25]

Yield: 363 mg (100%); pale solid; mp 179–181 °C.

^{1}H NMR (400 MHz, $CDCl_3$–DMSO-d_6): δ = 1.25–1.37 (m, 6 H, CH_3), 3.76–3.81 (m, 3 H, OCH_3), 4.18–4.2 (m, 4 H, OCH_2), 4.96 (d, *J* = 6 Hz, 1 H, CH), 6.87–6.92 (m, 2 H, ArH), 7.28 (s, 1 H, ArH), 10.77 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$–DMSO-d_6): δ = 16.55, 27.78, 54.19 (d, $^1J_{CP}$ = 141 Hz, C-P), 56.11, 65.12, 65.86, 110.17, 110.93, 112.01, 113.10, 116.42, 122.33, 136.69, 156.18, 171.01.

^{31}P NMR (162 MHz, $CDCl_3$–DMSO-d_6): δ = 12.42.

Diethyl [3-(Dicyanomethyl)-5-nitro-2-oxindol-3-yl]phosphonate (4f)[13c]

Yield: 344 mg (91%); brown solid; mp 186–188 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.18 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.28 (t, *J* = 6.8 Hz, 3 H, CH_3), 4.06–4.20 (m, 4 H, OCH_2), 6.2 (s, 1 H, CH), 7.26 (d, *J* = 8.4 Hz, 1 H, ArH), 8.40 (d, *J* = 7.6 Hz, 2 H, ArH), 12.13 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.06, 26.53, 52.56 (d, $^1J_{CP}$ = 136.4 Hz, C-P), 65.05, 65.70, 111.31, 121.59, 122.78, 128.18, 142.73, 149.27, 171.14.

^{31}P NMR (162 MHz, DMSO-d_6): δ = 11.16.

Diethyl [4-Bromo-3-(dicyanomethyl)-2-oxindol-3-yl]phosphonate (4g)[25]

Yield: 358 mg (87%); white solid; mp 193–195 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.10 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.25 (t, *J* = 6.8 Hz, 3 H, CH_3), 3.92–4.06 (m, 2 H, OCH_2), 4.10–4.18 (m, 2 H, OCH_2), 6.08 (s, 1 H, CH), 6.99–7.02 (m, 1 H, ArH), 7.31–7.33 (m, 2 H, ArH), 11.58 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.37, 16.51, 25.63, 56.26 (d, $^1J_{CP}$ = 131.8 Hz, C-P), 65.02, 65.55, 110.51, 119.84, 121.76, 127.59, 132.98, 145.46, 170.58.

^{31}P NMR (162 MHz, DMSO-d_6): δ = 11.26.

Diethyl [3-(Dicyanomethyl)-1-methyl-2-oxindol-3-yl]phosphonate (4h)[25]

Yield: 340 mg (98%); white solid; mp 114–116 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.36 (t, *J* = 7.2 Hz, 3 H, CH_3), 3.30 (s, 3 H, CH_3), 4.17–4.23 (m, 4 H, OCH_2), 4.79 (d, *J* = 6.4 Hz, 1 H, CH), 6.98 (d, *J* = 8 Hz, 1 H, ArH), 7.23 (t, *J* = 7.6 Hz, 1 H, ArH), 7.49 (t, *J* = 7.6 Hz, 1 H, ArH), 7.76 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$–DMSO-d_6): δ = 11.24, 22.53, 48.32 (d, $^1J_{CP}$ = 139.3 Hz, C-P), 59.83, 60.77, 104.46, 105.27, 115.25, 118.94, 121.17, 126.37, 139.58, 164.23.

^{31}P NMR (162 MHz, $CDCl_3$–DMSO-d_6): δ = 7.42.

Diethyl [1-Benzyl-3-(dicyanomethyl)-2-oxindol-3-yl]phosphonate (4i)[13b]

Yield: 423 mg (100%); white solid; mp 178–180 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.35 (t, *J* = 6.8 Hz, 3 H, CH_3), 4.11–4.26 (m, 4 H, OCH_2), 4.85 (d, *J* = 6 Hz, 1 H, CH), 4.89 (d, *J* = 16 Hz, 1 H, NCH_2), 5.09 (d, *J* = 16 Hz, 1 H, NCH_2), 6.81 (d, *J* = 7.6 Hz, 1 H, ArH), 7.18 (t, *J* = 7.6 Hz, 1 H, ArH), 7.25–7.36 (m, 6 H, ArH), 7.77 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.25, 27.44, 44.71, 53.34 (d, $^1J_{CP}$ = 138.9 Hz), 64.98, 65.95, 109.61, 110.50, 120.22, 123.91, 126.23, 127.22, 128.02, 128.93, 131.23, 134.34, 143.72, 169.45.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 7.57.

Dimethyl [3-(Dicyanomethyl)-2-oxindol-3-yl]phosphonate (4j)[13c]

Yield: 287 mg (94%); white solid; mp 175–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (d, *J* = 10.8 Hz, 3 H, CH_3), 3.75 (d, *J* = 10.8 Hz, 3 H, CH_3), 5.98 (br s, 1 H, CH), 7.00 (d, *J* = 8.0 Hz, 1 H, ArH), 7.16 (t, *J* = 7.6 Hz, 1 H, ArH), 7.41 (t, *J* = 7.2 Hz, 1 H, ArH), 7.52 (d, *J* = 7.2 Hz, 1 H, ArH), 11.37 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.92, 52.75 (d, $^1J_{CP}$ = 139 Hz, C-P), 55.03 (d, $^2J_{CP}$ = 78 Hz, C-P), 110.76, 121.32, 122.71, 125.69, 131.06, 142.94, 170.41.

^{31}P NMR (161 MHz, $CDCl_3$): δ = 14.99.

Diphenyl [3-(Dicyanomethyl)-2-oxindol-3-yl]phosphonate (4k)[13c]

Yield: 386 mg (90%); white solid; mp 170–172 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.44 (br s, 1 H, CH), 6.83 (d, *J* = 8.0 Hz, 2 H, ArH), 7.10 (d, *J* = 8.0 Hz, 1 H, ArH), 7.15–7.24 (m, 4 H, ArH), 7.27–7.32 (m, 3 H, ArH), 7.42–7.54 (m, 3 H, ArH), 7.69 (d, *J* = 7.6 Hz, 1 H, ArH), 11.64 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 26.99, 52.40 (d, $^1J_{CP}$ = 145.3 Hz, C-P), 111.12, 119.97, 120.21, 123.08, 125.86, 126.18, 129.88, 130.29, 131.66, 143.09, 149.11, 169.48.

^{31}P NMR (162 MHz, DMSO-d_6): δ = 5.56.

Ethyl 2-Cyano-2-[3-(diethoxyphosphoryl)-2-oxindol-3-yl]acetate (4l)[13c]

Yield: 297 mg (78%); white solid; mp 187–189 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.86 (t, *J* = 6.8 Hz, 3 H, $CO_2CH_2CH_3$), 1.16–1.26 (m, 6 H, CH_3), 3.85–3.91 (m, 2 H, CO_2CH_2), 4.01–4.10 (m, 4 H, OCH_2), 4.90 (t, *J* = 7.2 Hz, 1 H, CH), 6.90 (d, *J* = 7.2 Hz, 1 H, ArH), 7.00–7.06 (m, 1 H, ArH), 7.30 (t, *J* = 6.8 Hz, 1 H, ArH), 7.44 (d, *J* = 7.2 Hz, 1 H, ArH), 11.04 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.11, 15.90, 53.61 (d, $^1J_{CP}$ = 134.4 Hz, C-P), 62.60, 63.85, 64.16, 109.87, 114.84, 121.52, 122.67, 125.45, 129.85, 143.56, 162.84, 172.09.

^{31}P NMR (162 MHz, DMSO-d_6): δ = 14.38.

Diethyl [1-(Dicyanomethyl)-2-oxo-1,2-dihydroacenaphthylen-1-yl)phosphonate (5)[13b]

Yield: 350 mg (95%); purple solid; mp 153–155 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.20 (t, *J* = 6.8 Hz, 3 H, CH_3), 3.82–3.91 (m, 1 H, OCH_2), 3.96–4.02 (m, 1 H, OCH_2), 4.04–4.12 (m, 2 H, OCH_2), 6.18 (d, *J* = 8.0 Hz, 1 H, CH), 7.89–7.98 (m, 3 H, ArH), 8.21 (t, *J* = 7.6 Hz, 2 H, ArH), 8.47 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 15.63, 15.94, 26.49, 56.88 (d, $^1J_{CP}$ = 135.9 Hz, C-P), 64.27, 64.75, 124.07, 127.17, 128.98, 129.32, 130.35, 133.69, 141.74, 194.63.

^{31}P NMR (162 MHz, DMSO-d_6): δ = 12.96.

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Supporting Information

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