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Efficient one-pot synthesis of β-phosphono malonates and 2-amino-4*H*-chromen-4-ylphosphonate derivatives by ethylenediamine diacetate-catalyzed three-component reactions

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ABSTRACT

One-pot three-component reactions of arylaldehyde or salicylaldehyde with malononitrile (or ethylcyanoacetate) and triethyl phosphite are carried out in the presence of ethylenediamine diacetate (EDDA) as a catalyst for the synthesis of biologically interesting β-phosphono malonates and 2-amino-4*H*-chromen-4-ylphosphonate derivatives. The value of this method lies in its mild reaction catalyst and conditions, good yields, and ease of handling.

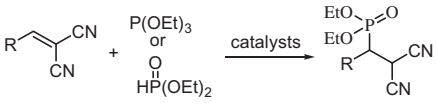
1. Introduction

Organophosphorus compounds are important substrates in the study of biochemical processes and are widely used as biologically active compounds.[1] Among these, phosphonates and their derivatives have attracted considerable attention due to their biological activities and application as enzyme inhibitors, antimetabolites, peptide mimetics, and antibiotics.[2–5] For the synthesis of phosphonate derivatives, phosphorus–carbon (P–C) bond formations are one of the most versatile and powerful tools.[6] The reactions for P–C bond formation are commonly promoted by bases,[7] Lewis acids,[8] microwaves,[9] transition metals,[10] and radical inhibitors.[11]

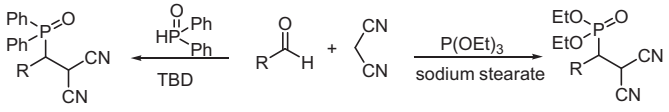
Among the several synthetic approaches for β-phosphono malonates that have been reported, one method consists of the conjugate addition of phosphorous nucleophiles to α,β-unsaturated malonates catalyzed by AP-SiO_2,[12] $HClO_4$–SiO_2,[13] or NF–ZnO[7c] (Scheme 1). Another reported method is three-component condensation of aldehydes with malononitrile and diphenylphosphine oxide or triethyl phosphite catalyzed by 1,5,7-triazabicylo[4.4.0]dec-5ene[14] (TBD) or sodium stearate[15] (Scheme 2).

2-Amino-4*H*-chromenes are widely employed as cosmetics, pigments[16] and potential biodegradable agrochemicals.[17] They also show a variety of biological activities, including anticancer,[18] anti-inflammatory,[19] antimalarial,[20] and pesticidal activities.[21] This wide range of biological activities and pharmacological properties has stimulated interest in new approaches for the synthesis of a variety of phosphonate derivatives with 2-aminochromenyl rings utilizing multicomponent reactions as a key step.

Recently, two multicomponent reactions for the synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates have been developed. The methods involve $InCl_3$[22] and β-cyclodextrin[23] catalyzed condensation of salicylaldehyde with malononitrile and triethyl phosphite (Scheme 3).



Scheme 1.



Scheme 2.

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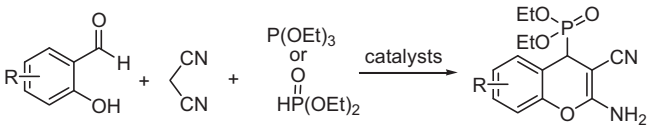


Scheme 3.

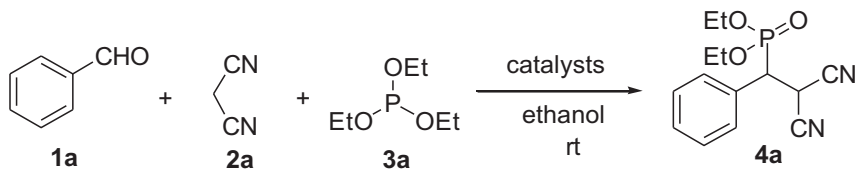
Although several methods for the synthesis of β-phosphono malonates and 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate derivatives have been reported, the need remains for simpler, cost effective, and environmentally benign methods.

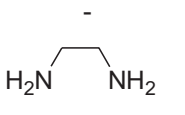
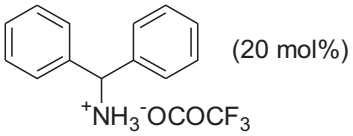
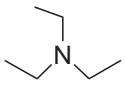
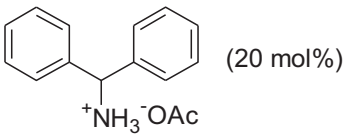
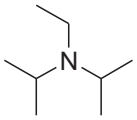
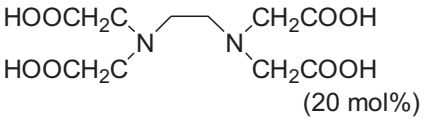
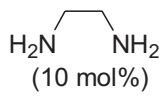
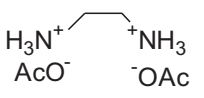
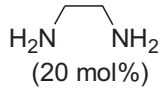
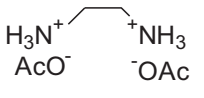
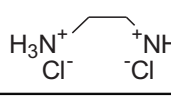
The Brønsted acids[24] and bases[25,26] have demonstrated their potential to serve as active catalysts for a variety of synthetically useful reactions in organic synthesis. Recently, we developed a new methodology for the synthesis of biologically interesting spirooxindoles[27] or 3,4-dihydroquinoxalin-2-amines[28] by using Brønsted acid-catalyzed multicomponent reaction. As a part of an ongoing study into the synthetic efficacy of Brønsted acid as a catalyst for the development of organic reactions, we examine ethylenediamine diacetate-catalyzed three-component reactions of arylaldehyde or salicylaldehyde with malononitrile and triethyl phosphite to afford a variety of β-phosphono malonates and 2-amino-4*H*-chromen-4-ylphosphonates. We report herein an efficient one-pot synthesis of β-phosphono malonates and 2-amino-4*H*-chromen-4-ylphosphonate derivatives.

2. Results and discussion

Three-component reaction of benzaldehyde (**1a**) with malononitrile (**2a**) and triethyl phosphite (**3a**) under 20 mol % of several Brønsted acid and base catalysts at room temperature in ethanol was first attempted (Table 1). When no catalyst was used at room temperature for 12 h in ethanol, no products were produced (entry 1). The use of 20 mol % of ethylenediamine, triethylamine, and *N*,*N*-diisopropylethylamine as Brønsted base catalysts at room temperature for 12 h provided **4a** in 22, 61, and 40% yields, respectively

Table 1
Reaction of benzaldehyde (**1a**), malononitrile (**2a**), and triethyl phosphite (**3a**) under several catalysts



Entry	Catalyst	Time (h)	Yield (%)	Entry	Catalyst	Time (h)	Yield (%)
1		12	0				
2	 (20 mol%)	12	22	9	 (20 mol%)	6	40
3	 (20 mol%)	12	61	10	 (20 mol%)	6	45
4	 (20 mol%)	12	40	11	 (20 mol%)	6	70
5	AcOH (20 mol%)	6	68	12	 (20 mol%)	5	72
6	 (10 mol%) + AcOH (20 mol%)	10	65	13	 (20 mol%)	4	88
7	 (20 mol%) + AcOH (10 mol%)	10	32	14	 (10 mol%)	12	86
8	 (20 mol%)	12	65				

(entries 2–4). With acetic acid as a Brønsted acid, **4a** was obtained in 68% yield (entry 5). With 20 mol % of ethylenediamine and 10 mol % of acetic acid as co-catalysts, **4a** was produced in 65% yield (entry 6). When the ratio of co-catalysts was changed, no improvement of yield (32%) was observed (entry 7). With Brønsted acids and bases as a bifunctional catalyst, the desired product was produced. For examples, reactions under several salts such as ethylenediamine dihydrochloride, *o*,*o*-diphenylmethylammonium trifluoroacetic acid, and *o*,*o*-diphenylmethylammonium acetic acid gave **4a** in 65, 40, and 45% yields, respectively (entries 8–10). Similarly, reactions in the presence of ethylenediaminetetraacetic acid and ammonium acetate provided **4a** in 70 and 72% yields, respectively (entries 11–12). Importantly, when we used 20 mol % of ethylenediamine diacetate as a catalyst, **4a** was produced in high yield (88%). However, with 10 mol % of ethylenediamine diacetate as a catalyst, longer reaction time (12 h) was required. Interestingly, we found that Brønsted acids are better catalysts than Brønsted bases for the completion of this reaction. Importantly, the use of salts of ammonium acetate and ethylenediamine diacetate as a bifunctional catalyst improved the yields. The structure of compound **4a** was determined by ^{1}H NMR analysis and by comparison directly with the reported data.[13] ^{1}H NMR spectrum of **4a** showed the characteristic methine peak of the C–P bond at 3.56 as a double doublet (J_{HH}=8.1 Hz and J_{HP}=21.0 Hz) and another methine peak appeared at δ 4.48 as a triplet (J_{HH}=8.4 Hz). In the ^{13}C NMR spectrum, the characteristic carbon peak of the C–P bond appeared at δ 44.4 as a doublet with a coupling constant of 143.4 Hz.

In order to establish the generality of this methodology, additional reactions of various substituted arylaldehydes **1b**–**1l** with malononitrile (**2a**) and triethyl phosphite (**3a**) were carried out in the presence of 20 mol % of EDDA in ethanol. The results are summarized in Table 2. Reactions of arylaldehydes **1b**–**1g** with electron-donating groups on the benzene ring at room temperature for 2–5 h produced **4b**–**4e** in 72–90% yields (entries 1–6). With arylaldehydes **1h**–**1j** with electron-withdrawing groups on the benzene ring, the products **4h**–**4j** were produced in 82–90% yields (entries 7–9). With 1 and 2-naphthaldehyde, products **4k** and **4l** were also produced in 50 and 73% yields, respectively (entries 10 and 11). These reactions provided a rapid route to the synthesis of a variety of β-phosphono malonates in good yield.

Next, to expand the utility of this methodology, other three-component reactions of salicylaldehyde (**5a**) with malononitrile (**2a**), and triethyl phosphite (**3a**) under 20 mol % of several Brønsted acid and base catalysts in ethanol at room temperature were carried out (Table 3). In this reaction, we found that Brønsted bases are better catalysts than Brønsted acids. Importantly, when we used 20 mol % of ethylenediamine diacetate as a salt, the desired product **6a** was produced in high yield (90%). The structure of **6a** was identified by ^{1}H NMR analysis and by comparison with the reported data.[23] ^{1}H NMR spectrum of **6a** showed the characteristic peak of a methine at δ 4.09–3.90 as multiplets because the methine peak of the C–P bond merged in the two ethoxy protons. In the ^{13}C NMR spectrum, the characteristic carbon peak of the C–P bond appeared at δ 34.5 as a doublet with a coupling constant of 144.9 Hz.

Additional reactions of various substituted salicylaldehydes **5a**–**5i** with malononitrile (**2a**) or ethylcyanoacetate (**2b**), and triethyl phosphite (**3a**) were carried out in the presence of 20 mol % of EDDA in ethanol. The results are summarized in Table 4. The reactions worked well with substituted salicylaldehydes bearing both electron-donating and electron-withdrawing groups on the benzene ring. For example, reactions of 3-methylsalicylaldehyde (**5b**), 5-methylsalicylaldehyde (**5c**), 4-methoxysalicylaldehyde (**5d**), and 5-methoxysalicylaldehyde (**5e**) with electron-donating groups provided products **6b**–**6e** in 83, 90, 72, and 70% yields, respectively (entries 1–4), whereas those of 5-bromosalicylaldehyde (**5f**), 3,5-dibromosalicylaldehyde (**5g**), and 5-nitrosalicylaldehyde (**5h**) with electron-withdrawing groups afforded products **6f**–**6h** in 82, 80, and 75% yields, respectively (entries 5–7). With 2-hydroxy-1-naphthaldehyde (**5i**), the desired product **6i** was produced in 62% yield (entry 8). When the reaction was carried out by replacing malononitrile (**2a**) with ethylcyanoacetate (**2b**), the desired products **6j** and **6k** were produced in 75 and 65% yields (entries 9 and 10). These reactions provided rapid access to various 2-amino-4*H*-chromen-4-ylphosphonate derivatives **6b**–**6k** in good yields.

The formation of **4a** can be explained by the proposed mechanism as shown in Scheme 4. Reaction of benzaldehyde (**1a**) and malononitrile (**2a**) in the presence of EDDA first gives **7** through the Knoevenagel condensation. Nucleophilic addition of triethyl phosphite to **7** gives intermediate **8**, which is further reacted to furnish **4a**.

The formation of **6a** can be also explained by the plausible mechanism as shown in Scheme 5. Reaction of salicylaldehyde (**5a**) and malononitrile (**2a**) in the presence of EDDA first gives **9** through the Knoevenagel condensation. Intramolecular cyclization of hydroxyl group of **9** on the cyano group leads to imino coumarin **10** through the intramolecular Pinner reaction. Nucleophilic addition of triethyl phosphite to **10** gives intermediate **11**, which is further reacted to produce **6a**.

As further application of this methodology, we extended the protocol to afford several 2-amino-4*H*-chromen-4-ylphosphonate derivatives through transesterification reactions utilizing triphenyl phosphite or triethyl phosphite in alcohols as shown in Table 5. Reactions of salicylaldehyde (**5a**) with malononitrile (**2a**) and triphenyl phosphite (**3b**) in the presence of 20 mol % of EDDA in ethanol at room temperature for 12 h gave product **6a** (41%) through transesterification (entry 1), whereas treatment in methanol or 1-propanol afforded products **6l** and **6m** in 55 and 40% yields, respectively (entries 2 and 3). The structures of **6a**, **6l**, and **6m** were identified by analysis of the spectroscopic data. Similarly, treatment of **5a** with malononitrile (**2a**) and triethyl phosphite (**3b**) in the presence of 20 mol % of EDDA in methanol or 1-propanol at room temperature for 12 h afforded products **6l** and **6m** in 65 and 62% yields, respectively (entries 4 and 5).

3. Experimental

3.1. General

All experiments were carried out in an aqueous layer. Merck, pre-coated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Model ARX (at 300 and 75 MHz, respectively) spectrometer in acetone, DMSO, and $CDCl_3$ as the solvent chemical shift. All IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. HRMS and MS data were carried out at the Korea Basic Science Institute.

3.2. General procedure for the preparation of β-phosphono malonates and 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate

EDDA (0.2 mmol) was added to a solution of arylaldehyde (1.0 mmol) or salicylaldehyde (1.0 mmol) with malononitrile (1.0 mmol) and triethyl phosphite (1.0 mmol) in 5 mL of ethanol. The resulting mixture was stirred at room temperature until completion of the reaction, as indicated by TLC (ethyl acetate/*n*-hexane). The reaction mixture was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using EtOAc/*n*-hexane as the eluent to give the desired products.

Table 2
Additional reactions of arylaldehydes, malononitrile, and triethyl phosphite in 20 mol % of EDDA

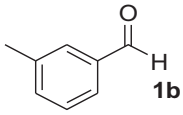
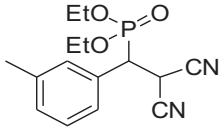
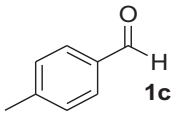
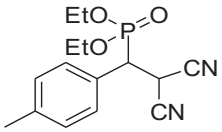
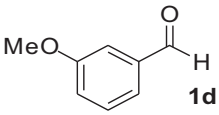
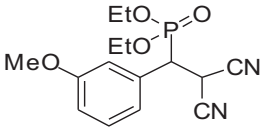
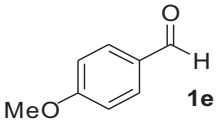
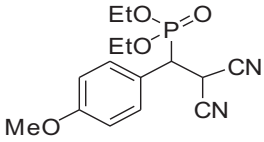
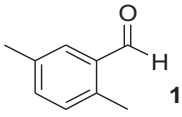
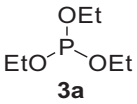
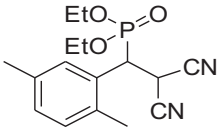
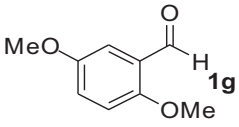
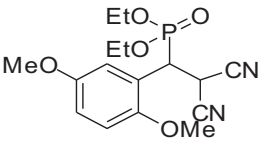
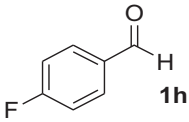
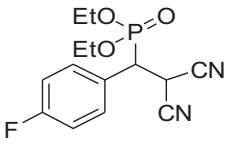
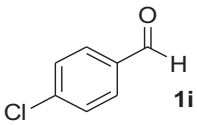
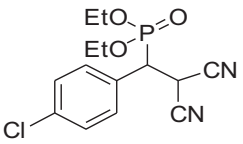
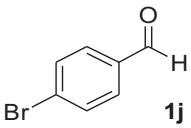
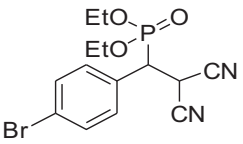
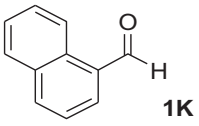
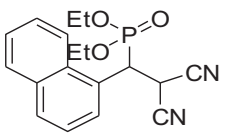
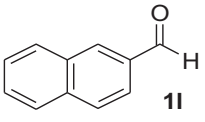
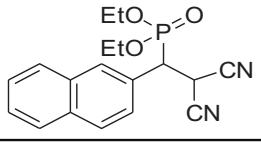
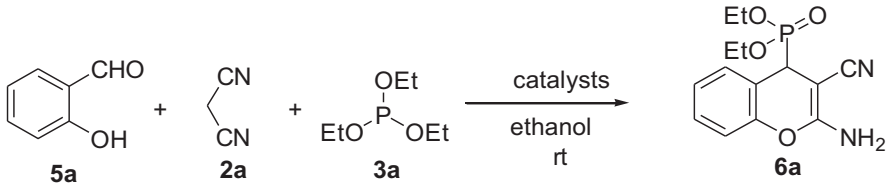
Entry	Arylaldehyde	Malononitrile	Triethyl phosphite	Time (h)	Product	Yield (%)
1	 **1b**			4	 **4b**	85
2	 **1c**			5	 **4c**	75
3	 **1d**			4	 **4d**	90
4	 **1e**			3	 **4e**	72
5	 **1f**	 **2a**	 **3a**	2	 **4f**	88
6	 **1g**			3	 **4g**	75
7	 **1h**			2	 **4h**	82
8	 **1i**			3	 **4i**	86
9	 **1j**			2	 **4j**	90
10	 **1K**			3	 **4k**	50
11	 **1l**			3	 **4l**	73

Table 3
Reaction of salicylaldehyde (**5a**), malononitrile (**2a**), and triethyl phosphite (**3a**) under several catalysts



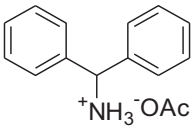
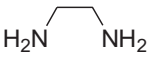
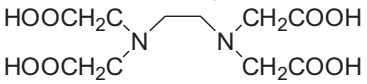
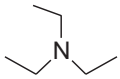
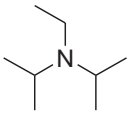
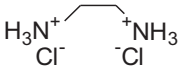
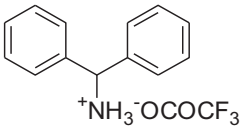
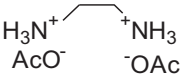
Entry	Catalyt (20 mol %)	Time	Yield (%)	Entry	Catalyt (20 mol %)	Time	Yield (%)
1	—	12	0				
2	AcOH	12	16	7		12	50
3		8	60	8		12	55
4		8	75	9	$^{+}NH_4^{-}OAc$	4	71
5		8	70	10		3	75
6		12	17	11		2	90

Table 4
Additional reactions of salicylaldehydes, malononitrile or ethylcyanoacetate, and triethyl phosphite in 20 mol % EDDA

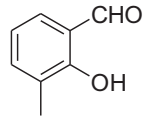
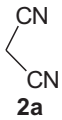
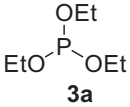
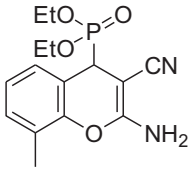
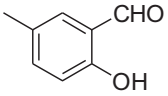
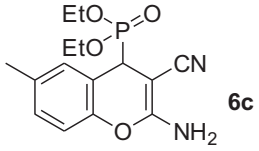
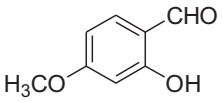
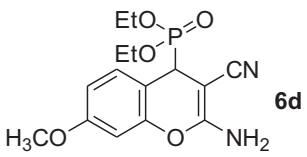
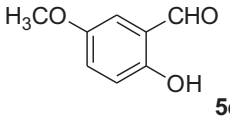
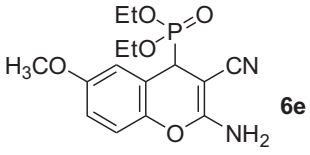
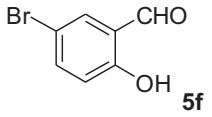
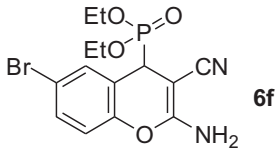
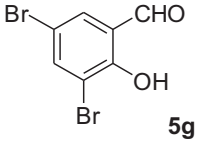
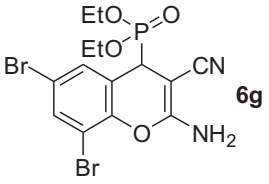
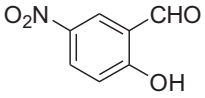
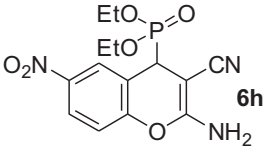
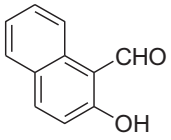
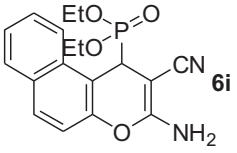
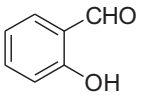
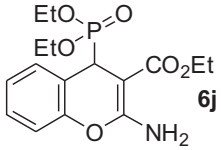
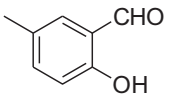
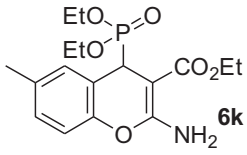
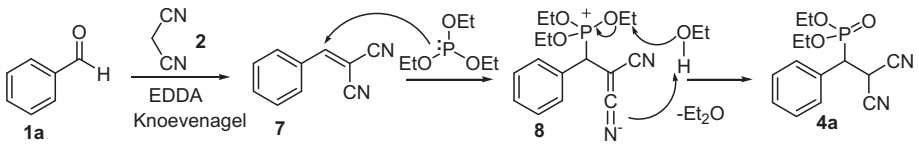
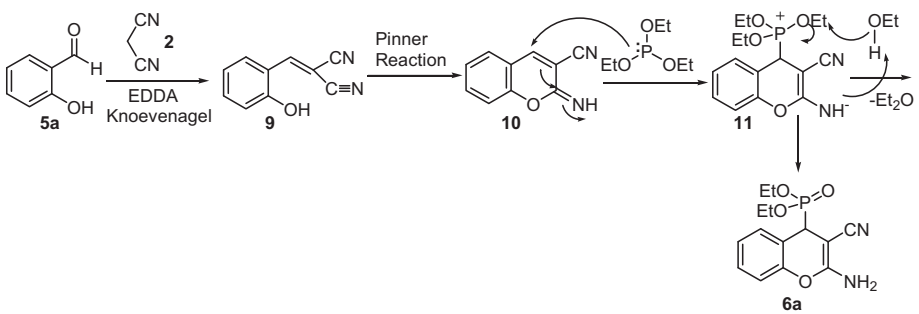
Entry	Salicyladehyde	Malononitrile or ethylcyanoacetate	Triethyl phosphite	Time (h)	Product	Yield (%)
1	 **5b**	 **2a**	 **3a**	2	 **6b**	83
2	 **5c**			3	 **6c**	90
3	 **5d**			3	 **6d**	72
4	 **5e**			3	 **6e**	70

Table 4 (*continued*)

Entry	Salicyladehyde	Malononitrile or ethylcyanoacetate	Triethyl phosphite	Time (h)	Product	Yield (%)
5	 **5f**			3	 **6f**	82
6	 **5g**			3	 **6g**	80
7	 **5h**			3	 **6h**	75
8	 **5i**			4	 **6i**	62
9	 **5a**	 **2b**		3	 **6j**	75
10	 **5c**			2	 **6k**	65

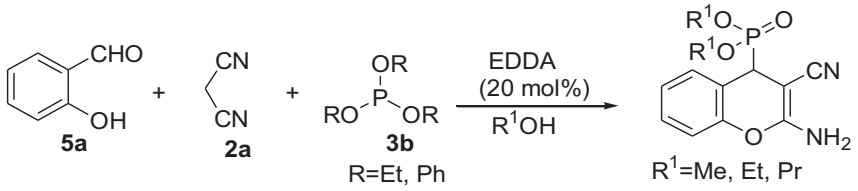


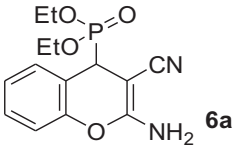
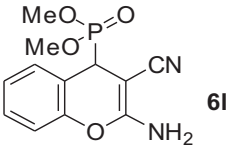
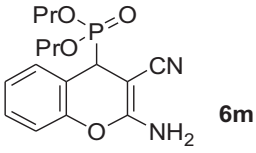
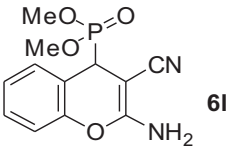
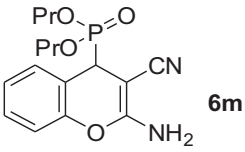
Scheme 4.



Scheme 5.

Table 5
EDDA catalyzed additional reactions of salicylaldehyde (**5a**), malononitrile (**2a**), and triphenyl phosphite (**3b**) in several alcohols



Entry	$P(OR)_3$	Solvent	Time (h)	Product	Yield (%)
1	R=Ph	EtOH	12	 **6a**	41
2	R=Ph	MeOH	12	 **6l**	55
3	R=Ph	1-PrOH	12	 **6m**	40
4	R=Et	MeOH	12	 **6l**	65
5	R=Et	1-PrOH	12	 **6m**	62

3.3. General procedure for the preparation of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate by transesterification

EDDA (0.2 mmol) was added to a solution of (1 mmol) with malononitrile (1 mmol) and triphenyl phosphite (1 mmol) in 5 mL of alcohol. The resulting mixture was stirred at room temperature until completion of the reaction, as indicated by TLC (ethyl acetate/*n*-hexane). The reaction mixture was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using EtOAc/*n*-hexane as the eluent to give the desired products.

3.4. Diethyl 2,2-dicyano-1-phenylethylphosphonate (4a)[13]

A mixture of benzaldehyde (**1a**) (106 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 4 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4a** (258 mg, 88%) as a solid: mp 56–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (br s, 5H), 4.48 (t, 1H, $^3J_{HH}$=8.4 Hz), 4.18–4.12 (m, 2H), 4.02–3.92 (m, 1H), 3.78–3.67 (m, 1H), 3.56 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^2J_{HP}$=21.0 Hz), 1.33 (t, 3H, $^3J_{HH}$=7.2 Hz), 1.10 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 130.4, 129.5, 129.4, 129.3, 111.5 (d, $^3J_{CP}$=9.9 Hz), 111.4 (d, $^3J_{CP}$=12.6 Hz), 64.3 (d, $^2J_{CP}$=6.6 Hz), 63.3 (d, $^2J_{CP}$=7.1 Hz), 44.4 (d, $^1J_{CP}$=143.4 Hz), 25.5, 16.2 (d, $^3J_{CP}$=5.5 Hz), 16.0 (d, $^3J_{CP}$=5.5 Hz); IR (KBr) 2988, 2870, 2614, 2487, 2378, 2257, 1456, 1388, 1237, 1036 cm^{-1}; MS (*m*/*z*, EI) 292 (M^+, 12), 155 (17), 154 (22), 138 (27), 129 (100), 111 (15), 109 (18), 91 (10).

3.5. Diethyl 2,2-dicyano-1-*m*-tolylethylphosphonate (4b)[7c]

A mixture of *m*-tolualdehyde (**1b**) (120 mg, 1.0 mmol), malononitrile **2a** (66 mg, 1.0 mmol) and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 4 h. After completion

of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4b** (261 mg, 85%) as a solid: mp 56–57 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13–6.99 (m, 4H), 4.27 (t, 1H, $^3J_{HH}$=8.7 Hz), 3.99–3.87 (m, 2H), 3.85–3.72 (m, 1H), 3.60–3.46 (m, 1H), 3.32 (dd, 1H, $^3J_{HH}$=8.4 Hz and $^2J_{HP}$=21.0 Hz), 2.17 (s, 3H), 1.14 (t, 3H, $^3J_{HH}$=7.2 Hz), 0.90 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 139.2, 130.3, 130.0, 129.9, 129.2, 126.2, 111.6 (d, $^3J_{CP}$=7.7 Hz), 111.5 (d, $^3J_{CP}$=13.1 Hz), 64.3 (d, $^2J_{CP}$=7.1 Hz), 63.4 (d, $^2J_{CP}$=7.1 Hz), 44.5 (d, $^1J_{CP}$=142.8 Hz), 25.5, 21.4, 16.2 (d, $^3J_{CP}$=5.5 Hz), 16.1 (d, $^3J_{CP}$=5.5 Hz); IR (KBr) 2979, 2906, 2609, 2480, 2257, 1605, 1466, 1387, 1241, 1026 cm^{-1}; MS (*m*/*z*, EI) 306 (M$^+$, 35), 169 (22), 168 (34), 143 (100), 140 (17), 138 (64), 115 (16), 111 (37), 109 (21), 105 (23), 81 (12).

3.6. Diethyl 2,2-dicyano-1-*p*-tolylethylphosphonate (4c)[7c,12]

A mixture of *p*-tolualdehyde (**1c**) (120 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol) and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 5 h. After completion of the reaction the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (7:3) gave product **4c** (230 mg, 75%) as a solid: mp 88–90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J*=6.6 Hz), 7.15 (d, 2H, *J*=6.6 Hz), 4.40 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^3J_{HP}$=9.0 Hz), 4.16–4.06 (m, 2H), 3.97–3.90 (m, 1H), 3.73–3.68 (m, 1H), 3.46 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^2J_{HP}$=21.3 Hz), 2.29 (s, 3H), 1.27 (t, 3H, $^3J_{HH}$=6.9 Hz), 1.06 (t, 3H, $^3J_{HH}$=7.2 Hz); ^{13}C NMR (75 MHz) δ 139.2, 130.1, 129.2 (d, $^3J_{CP}$=6.0 Hz), 127.2 (d, $^3J_{CP}$=6.0 Hz), 111.6 (d, $^3J_{CP}$=11.0 Hz), 111.4 (d, $^3J_{CP}$=12.6 Hz), 64.3 (d, $^2J_{CP}$=7.1 Hz), 63.3 (d, $^2J_{CP}$=7.2 Hz), 44.2 (d, $^1J_{CP}$=143.4 Hz), 25.6, 21.2, 16.2 (d, $^3J_{CP}$=6.0 Hz), 16.1 (d, $^3J_{CP}$=6.1 Hz); IR (KBr) 2989, 2858, 2608, 2507, 2375, 2255, 1515, 1450, 1387, 1238, 1024 cm^{-1}; MS (*m*/*z*, EI) 306 (M$^+$, 31), 241 (21), 169 (18), 143 (100), 138 (37), 115 (13), 111 (17), 109 (15), 105 (44), 81 (10).

3.7. Diethyl 2,2-dicyano-1-(3-methoxyphenyl) ethylphosphonate (4d)[12]

A mixture of *m*-anisaldehyde (**1d**) (136 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 4 h. After completion of the reaction the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4d** (290 mg, 90%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (t, 1H, $^3J_{HH}$=7.8 Hz), 6.98 (s, 2H), 6.85 (d, 1H, $^3J_{HH}$=8.1 Hz), 4.67 (t, 1H, $^3J_{HH}$=8.7 Hz), 4.10–4.05 (m, 2H), 3.99–3.90 (m, 1H), 3.77–3.71 (m, 4H), 3.58 (dd, 1H, $^3J_{HH}$=7.8 Hz and $^2J_{HP}$=21.3 Hz), 1.25 (t, 3H, $^3J_{HH}$=6.6 Hz), 1.05 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 159.9, 131.7 (d, $^3J_{CP}$=6.0 Hz), 130.2, 121.4 (d, $^3J_{CP}$=6.0 Hz), 114.9, 114.8, 111.6 (d, $^3J_{CP}$=4.9 Hz), 111.5 (d, $^3J_{CP}$=7.2 Hz), 64.2 (d, $^2J_{CP}$=6.6 Hz), 63.2 (d, $^2J_{CP}$=7.1 Hz), 55.2, 44.0 (d, $^1J_{CP}$=142.8 Hz), 25.3, 16.0 (d, $^3J_{CP}$=6.0 Hz), 15.9 (d, $^3J_{CP}$=6.0 Hz); IR (neat) 2980, 2920, 2597, 2257, 1597, 1471, 1249, 1164, 1031 cm^{-1}; MS (*m*/*z*, EI) 322 (M$^+$, 80), 229 (25), 185 (36), 159 (96), 138 (100), 121 (45), 111 (61), 110 (21), 109 (28), 81 (21).

3.8. Diethyl 2,2-dicyano-1-(4-methoxyphenyl) ethylphosphonate (4e)[7c,12]

A mixture of *p*-anisaldehyde (**1e**) (136 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (1:1) gave product **4e** (232 mg, 72%) as a solid: mp 57–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.37 (m, 2H), 6.93 (d, 2H, $^3J_{HH}$=8.7 Hz), 4.43 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^3J_{HP}$=8.7 Hz), 4.20–4.09 (m, 2H), 4.03–3.93 (m, 1H), 3.80 (s, 3H), 3.75–3.70 (m, 1H), 3.51 (dd, 1H, $^3J_{HH}$=7.8 Hz and $^2J_{HP}$=21.3 Hz), 1.33 (t, 3H, $^3J_{HH}$=7.2 Hz), 1.13 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 160.2, 130.5 (d, $^3J_{CP}$=6.0 Hz), 122.0 (d, $^3J_{CP}$=5.4 Hz), 114.6, 111.6 (d, $^3J_{CP}$=11.0 Hz), 111.5 (d, $^3J_{CP}$=12.6 Hz), 64.1 (d, $^2J_{CP}$=7.1 Hz), 63.1 (d, $^2J_{CP}$=7.7 Hz), 55.1, 43.4 (d, $^1J_{CP}$=143.9 Hz), 25.6, 16.0 (t, $^3J_{CP}$=6.0 Hz); IR (KBr) 2987, 2857, 2607, 2507, 2374, 2256, 1611, 1512, 1248, 1026 cm^{-1}; MS (*m*/*z*, EI) 322 (M$^+$, 28), 258 (13), 257 (100), 185 (27), 159 (20), 121 (97), 111 (8).

3.9. Diethyl 2,2-dicyano-1-(2,5-dimethylphenyl) ethylphosphonate (4f)

A mixture of 2,5-dimethlybenzaldehyde (**1f**) (134 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After completion of the reaction the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4f** (282 mg, 88%) as a solid: mp: 73–75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.11 (d, 1H, $^3J_{HH}$=7.8 Hz), 7.04 (d, 1H, $^3J_{HH}$=7.8 Hz), 4.48 (t, 1H, $^3J_{HH}$=9.3 Hz), 4.21–4.02 (m, 2H), 3.95–3.81 (m, 2H), 3.61–3.48 (m, 1H), 2.33 (s, 3H), 2.30 (s, 3H), 1.34 (t, 3H, $^3J_{HH}$=7.2 Hz), 1.00 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8, 134.4 (d, $^3J_{CP}$=7.7 Hz), 131.4, 130.2, 128.8 (d, $^3J_{CP}$=6.0 Hz), 128.1, 111.6 (d, $^3J_{CP}$=6.6 Hz), 111.4, 64.5 (d, $^2J_{CP}$=7.2 Hz), 63.3 (d, $^2J_{CP}$=7.1 Hz), 39.7 (d, $^1J_{CP}$=143.9 Hz), 25.3, 21.2, 19.6, 16.3 (d, $^3J_{CP}$=6.0 Hz), 16.1 (d, $^3J_{CP}$=5.4 Hz); IR (KBr) 2981, 2871, 2609, 2359, 2258, 1690, 1455, 1242, 1041 cm^{-1}; HRMS *m*/*z* (M$^+$) calcd for $C_{16}H_{21}N_2O_3P$: 320.1290; found: 320.1288.

3.10. Diethyl 2,2-dicyano-1-(2,5-dimethoxyphenyl) ethylphosphonate (4g)

A mixture of 2,5-dimethoxybenzaldehyde (**1g**) (166 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4g** (265 mg, 75%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 1H), 6.82 (br s, 2H), 4.55 (t, 1H, $^3J_{HH}$=9.0 Hz), 4.26 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^2J_{HP}$=21.0 Hz), 4.16–3.92 (m, 4H), 3.76 (s, 3H), 3.70 (s, 3H), 1.27 (t, 3H, $^3J_{HH}$=6.9 Hz), 1.09 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 153.7, 151.5 (d, $^3J_{CP}$=7.1 Hz), 119.6 (d, $^3J_{CP}$=5.4 Hz), 115.6, 115.2 (d, $^3J_{CP}$=4.4 Hz), 112.6, 111.7 (d, $^3J_{CP}$=6.6 Hz), 111.5 (d, $^3J_{CP}$=11.0 Hz), 64.0 (d, $^2J_{CP}$=6.6 Hz), 63.2 (d, $^2J_{CP}$=7.1 Hz), 56.4, 55.7, 36.6 (d, $^1J_{CP}$=145.5 Hz), 24.9, 16.2 (d, $^3J_{CP}$=6.0 Hz), 16.1 (d, $^3J_{CP}$=6.0 Hz); IR (neat) 2977, 2257, 1616, 1496, 1240, 1034 cm^{-1}; HRMS *m*/*z* (M$^+$) calcd for $C_{16}H_{21}N_2O_5P$: 352.1188; found: 352.1188.

3.11. Diethyl 2,2-dicyano-1-(4-fluorophenyl) ethylphosphonate (4h)

A mixture of 4-fluorobenzaldehyde (**1h**) (124 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After

completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4h** (255 mg, 82%) as a solid: mp 80–82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 7.07 (t, 2H, $^3J_{HH}$=8.4 Hz), 4.57 (dd, 1H, $^3J_{HH}$=7.8 Hz and $^3J_{HP}$=8.7 Hz), 4.17–4.04 (m, 2H), 4.02–3.91 (m, 1H), 3.85–3.72 (m, 1H), 3.58 (dd, 1H, $^3J_{HH}$=7.2 Hz and $^2J_{HP}$=21.3 Hz), 1.28 (t, 3H, $^3J_{HH}$=7.2 Hz), 1.10 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.4, 131.3, 126.4, 126.3, 116.7, 116.4, 111.5 (d, $^3J_{CP}$=10.9 Hz), 111.3 (d, $^3J_{CP}$=11.5 Hz), 64.4 (d, $^2J_{CP}$=7.1 Hz), 63.5 (d, $^2J_{CP}$=7.7 Hz), 43.7 (d, $^1J_{CP}$=144.0 Hz), 25.7, 16.3 (d, $^3J_{CP}$=6.6 Hz), 16.2 (d, $^3J_{CP}$=6.0 Hz); IR (KBr) 2993, 2922, 2261, 1606, 1512, 1387, 1244, 1029 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{14}H_{16}FN_2O_3P$: 310.0883; found: 310.0884.

3.12. Diethyl 1-(4-chlorophenyl)-2,2-dicyanoethylphosphonate (4i)[12,13]

A mixture of 4-chlorobenzaldehyde (**1i**) (140 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4i** (281 mg, 86%) as a solid: mp 94–96 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (br s, 4H), 4.45 (t, 1H, $^3J_{HH}$=8.4 Hz), 4.19–4.11 (m, 2H), 4.07–3.97 (m, 1H), 3.90–3.77 (m, 1H), 3.53 (dd, 1H, $^3J_{HH}$=7.5 Hz and $^2J_{HP}$=21.3 Hz), 1.33 (t, 3H, $^3J_{HH}$=6.9 Hz), 1.16 (t, 3H, $^3J_{HH}$=7.2 Hz); ^{13}C NMR (75 MHz) δ 135.7, 130.8, 129.6, 129.0, 111.4 (d, $^3J_{CP}$=10.9 Hz), 111.2 (d, $^3J_{CP}$=13.2 Hz), 64.4 (d, $^2J_{CP}$=7.1 Hz), 63.6 (d, $^2J_{CP}$=7.1 Hz), 43.8 (d, $^1J_{CP}$=143.4 Hz), 25.5, 16.3 (d, $^3J_{CP}$=6.6 Hz), 16.2 (d, $^3J_{CP}$=5.5 Hz); IR (KBr) 2993, 2854, 2612, 2257, 1931, 1587, 1493, 1239, 1021 cm^{-1}; MS (*m*/*z*, EI) 326 (M^+, 16), 189 (14), 165 (31), 163 (100), 138 (19), 125 (18), 109 (27), 81 (12).

3.13. Diethyl 1-(4-bromophenyl)-2,2-dicyanoethylphosphonate (4j)[12]

A mixture of 4-bromobenzaldehyde (**1j**) (185 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4j** (334 mg, 90%) as a solid: mp 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 2H, $^3J_{HH}$=8.4 Hz), 7.35 (d, 2H, $^3J_{HH}$=8.4 Hz), 4.45 (dd, 1H, $^3J_{HH}$=7.8 Hz and $^3J_{HP}$=8.7 Hz), 4.19–4.11 (m, 2H), 4.07–3.97 (m, 1H), 3.88–3.77 (m, 1H), 3.52 (dd, 1H, $^3J_{HH}$=7.5 Hz and $^2J_{HP}$=21.3 Hz), 1.33 (t, 3H, $^3J_{HH}$=6.9 Hz), 1.16 (t, 3H, $^3J_{HH}$=7.2 Hz); ^{13}C NMR (75 MHz) δ 132.6, 131.0 (d, $^3J_{CP}$=6.0 Hz), 129.5 (d, $^3J_{CP}$=6.0 Hz), 124.0, 111.4 (d, $^3J_{CP}$=10.5 Hz), 111.2 (d, $^3J_{CP}$=11.5 Hz), 64.5 (d, $^2J_{CP}$=7.1 Hz), 63.6 (d, $^2J_{CP}$=6.6 Hz), 44.0 (d, $^1J_{CP}$=143.4 Hz), 25.4, 16.3 (d, $^3J_{CP}$=6.1 Hz), 16.2 (d, $^3J_{CP}$=5.5 Hz); IR (KBr) 2991, 2853, 2613, 2377, 2256, 1492, 1238, 1020 cm^{-1}; MS (*m*/*z*, EI) 371 (M^+, 5), 305 (15), 209 (96), 207 (100), 169 (20), 154 (22), 138 (42), 109 (43), 81 (18).

3.14. Diethyl 2,2-dicyano-1-(naphthalen-1-yl) ethylphosphonate (4k)

A mixture of 1-napthaldehyde (**1k**) (156 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (7:3) gave product **4k** (172 mg, 50%) as a solid: mp 104–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, 1H, $^3J_{HH}$=7.8 Hz), 7.90 (d, 2H, $^3J_{HH}$=7.8 Hz), 7.82–7.80 (m, 1H), 7.65–7.50 (m, 3H), 4.69–4.55 (m, 2H), 4.23–4.16 (m, 2H), 3.85–3.74 (m, 1H), 3.45–3.34 (m, 1H), 1.35 (t, 3H, $^3J_{HH}$=7.2 Hz), 0.81 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 134.2, 131.7, 130.2, 129.5, 127.6, 127.5, 126.6, 126.5, 125.3, 122.1, 111.7 (d, $^3J_{CP}$=7.2 Hz), 111.6 (d, $^3J_{CP}$=15.3 Hz), 64.5 (d, $^2J_{CP}$=7.1 Hz), 63.5 (d, $^2J_{CP}$=7.6 Hz), 38.2 (d, $^1J_{CP}$=142.8 Hz), 25.6, 16.3 (d, $^3J_{CP}$=6.6 Hz), 15.9 (d, $^3J_{CP}$=5.4 Hz); IR (KBr) 2985, 2857, 2612, 2366, 2260, 1390, 1243, 1025 m^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{18}H_{19}N_2O_3P$: 342.1133; found: 342.1134.

3.15. Diethyl 2,2-dicyano-1-(naphthalen-2-yl) ethylphosphonate (4l)[12,13]

A mixture of 2-napthaldehyde (**1l**) (156 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **4l** (250 mg, 73%) as a solid: mp 88–90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.80–7.74 (m, 3H), 7.49–7.40 (m, 3H), 4.68 (t, 1H, $^3J_{HH}$=8.4 Hz), 4.07–4.05 (m, 2H), 3.95–3.82 (m, 1H), 3.79–3.76 (m, 1H), 3.67 (dd, 1H, $^3J_{HH}$=8.1 Hz and $^2J_{HP}$=19.2 Hz), 1.23 (t, 3H, $^3J_{HH}$=6.6 Hz), 0.96 (t, 3H, $^3J_{HH}$=6.9 Hz); ^{13}C NMR (75 MHz) δ 133.3, 133.2, 129.3, 129.1, 128.1, 127.8, 127.7, 127.1, 126.8, 126.0 (d, $^3J_{CP}$=4.9 Hz), 111.6 (d, $^3J_{CP}$=7.6 Hz), 111.5 (d, $^3J_{CP}$=12.0 Hz), 64.3 (d, $^2J_{CP}$=6.6 Hz), 63.4 (d, $^2J_{CP}$=7.2 Hz), 44.5 (d, $^1J_{CP}$=142.8 Hz), 25.6, 16.2 (d, $^3J_{CP}$=5.4 Hz), 16.0 (d, $^3J_{CP}$=5.4 Hz); IR (KBr) 3056, 2984, 2864, 2612, 2494, 2255, 1711, 1605, 1386, 1237, 1015 cm^{-1}; MS (*m*/*z*, EI) 342 (M^+, 89), 291 (65), 277 (60), 205 (45), 204 (44), 179 (78), 172 (21), 141 (100), 138 (52), 127 (36), 111 (27), 109 (14), 81 (13).

3.16. Diethyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate (6a)[22,23]

A mixture of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6a** (277 mg, 90%) as a solid: mp 143–145 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.39–7.35 (1H, m), 7.33–7.27 (1H, m), 7.19–7.13 (1H, m), 7.00 (1H, d, *J*=8.1 Hz), 6.36 (2H, br s), 4.09–3.90 (5H, m), 1.27 (3H, t, *J*=6.9 Hz), 1.17 (3H, t, *J*=6.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.6, 149.9, 129.5, 128.7, 124.2, 120.1, 117.7, 115.9, 62.3 (d, $^2J_{CP}$=7.2 Hz), 62.1 (d, $^2J_{CP}$=7.1 Hz), 47.4 (d, $^2J_{CP}$=7.6 Hz), 34.5 (d, $^1J_{CP}$=144.9), 16.2, 16.1; IR (KBr) 3343, 3167, 2985, 2190, 1656, 1418, 1236, 1034, 967, 766 cm^{-1}; MS (*m*/*z*, EI) 308 (M^+, 4), 172 (12), 171 (100), 143 (3), 116 (3), 89 (2).

3.17. Diethyl 2-amino-3-cyano-8-methyl-4*H*-chromen-4-ylphosphonate (6b)

A mixture of 3-methylsalicylaldehyde (**5b**) (136 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After completion of the reaction, the mixture was evaporated under

reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (1:1) gave product **6b** (267 mg, 83%) as a solid: mp 160–162 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.18–7.13 (2H, m), 7.06–7.01 (1H, m), 6.40 (2H, br s), 4.05–3.94 (4H, m), 3.90 (1H, d, $^2J_{PH}$=15.3 Hz), 2.25 (3H, s), 1.26 (3H, t, J=6.9 Hz), 1.17 (3H, t, J=6.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.8, 148.3, 129.9, 126.9, 124.9, 123.6, 120.1, 117.5, 62.3 (d, $^2J_{CP}$=7.1 Hz), 62.1 (d, $^2J_{CP}$=7.1 Hz), 47.5 (d, $^2J_{CP}$=7.1 Hz), 34.8 (d, $^1J_{CP}$=144.5 Hz), 16.2, 16.1, 15.0; IR (KBr) 3348, 3183, 2985, 2189, 1651, 1597, 1412, 1223, 1038, 968 cm^{-1}; HRMS m/z (M^+) calcd for $C_{15}H_{19}N_2O_4P$: 322.1082; found: 322.1085.

3.18. Diethyl 2-amino-3-cyano-6-methyl-4*H*-chromen-4-ylphosphonate (6c)[22]

A mixture of 5-methylsalicylaldehyde (**5c**) (136 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6c** (290 mg, 90%) as a solid: mp 180–182 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.16 (1H, s), 7.10 (1H, d, J=8.4 Hz), 6.90 (1H, d, J=8.4 Hz), 6.48 (2H, br s), 4.08–3.92 (4H, m), 3.88 (1H, d, $^2J_{PH}$=17.7 Hz), 2.30 (3H, s), 1.26 (3H, t, J=7.2 Hz), 1.18 (3H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.8, 148.0, 133.3, 129.7, 129.2, 120.2, 117.4, 115.7, 62.3 (d, $^2J_{CP}$=7.2 Hz), 62.2 (d, $^2J_{CP}$=7.1 Hz), 47.3 (d, $^2J_{CP}$=7.6 Hz), 34.5 (d, $^1J_{CP}$=144.4 Hz), 20.3, 16.3, 16.2; IR (KBr) 3355, 3166, 2985, 2188, 1646, 1496, 1420, 1231, 1030, 811 cm^{-1}; MS (m/z, EI) 322 (M^+, 3), 186 (12), 185 (100), 149 (3), 140 (2), 130 (1), 103 (1), 81 (1).

3.19. Diethyl 2-amino-3-cyano-7-methoxy-4*H*-chromen-4-ylphosphonate (6d)

A mixture of 4-methoxysalicylaldehyde (**5d**) (152 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:7) gave product **6d** (244 mg, 72%) as a solid: mp 218–220 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.22 (1H, dd, J=8.4 and 1.8 Hz), 7.01 (2H, br s), 6.75 (1H, dd, J=8.4 and 2.1 Hz), 6.57 (1H, d, J=2.1 Hz), 4.05–3.90 (5H, m), 3.78 (3H, s), 1.23 (3H, t, J=7.2 Hz), 1.16 (3H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.6, 159.6, 150.7, 130.2, 120.2, 110.6, 109.3, 101.3, 62.3 (d, $^2J_{CP}$=7.2 Hz), 62.2 (d, $^2J_{CP}$=6.5 Hz), 55.5, 47.7 (d, $^2J_{CP}$=7.1 Hz), 33.8 (d, $^1J_{CP}$=145.5 Hz), 16.4, 16.3; IR (KBr) 3420, 3151, 2983, 2187, 1647, 1509, 1408, 1221, 1158, 1036 cm^{-1}; HRMS m/z (M^+) calcd for $C_{15}H_{19}N_2O_5P$: 338.1032; found: 338.1029.

3.20. Diethyl 2-amino-3-cyano-6-methoxy-4*H*-chromen-4-ylphosphonate (6e)

A mixture of 5-methoxysalicylaldehyde (**5e**) (152 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:7) gave product **6e** (237 mg, 70%) as a solid: mp 180–182 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 6.96 (1H, s), 6.93–6.91 (1H, m), 6.87–6.84 (1H, m), 6.30 (2H, br s), 4.08–3.89 (4H, m), 3.92 (1H, d, $^2J_{PH}$=18.0 Hz), 3.78 (3H, s), 1.28 (3H, t, J=6.9 Hz), 1.19 (3H, t, J=6.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.0, 155.5, 144.0, 120.4, 118.7, 118.6, 116.8, 114.2, 62.5 (d, $^2J_{CP}$=7.1 Hz), 62.3 (d, $^2J_{CP}$=7.1 Hz), 55.5, 47.0 (d, $^2J_{CP}$=7.6 Hz), 34.9 (d, $^1J_{CP}$=144.5 Hz), 16.3, 16.2; IR (KBr) 3420, 3151, 2983, 2187, 1647, 1509, 1408, 1221, 1036, 963 cm^{-1}; HRMS m/z (M^+) calcd for $C_{15}H_{19}N_2O_5P$: 338.1032; found: 338.1035.

3.21. Diethyl 2-amino-6-bromo-3-cyano-4*H*-chromen-4-ylphosphonate (6f)[22]

A mixture of 5-bromo salicylaldehyde (**5f**) (201 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite **3a** (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6f** (318 mg, 82%) as a solid: mp 178–180 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.53 (1H, s), 7.46 (1H, d, J=8.7 Hz), 6.99 (1H, d, J=8.7 Hz), 6.46 (2H, br s), 4.12–3.98 (5H, m), 1.28 (3H, t, J=6.9 Hz), 1.20 (3H, t, J=6.9 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 163.2, 150.6, 133.2, 132.5, 121.5, 119.7, 119.1, 117.0, 63.5 (d, $^2J_{CP}$=7.1 Hz), 63.3 (d, $^2J_{CP}$=7.2 Hz), 50.6 (d, $^2J_{CP}$=8.2 Hz), 36.1 (d, $^1J_{CP}$=146.1 Hz), 16.8, 16.7; IR (KBr) 3342, 3158, 2981, 2919, 2188, 1653, 1420, 1242, 1036, 963 cm^{-1}; MS (m/z, EI) 386 (M^+, 5), 252 (11), 249 (100), 170 (15), 143 (9), 115 (3), 81 (2).

3.22. Diethyl 2-amino-6,8-dibromo-3-cyano-4*H*-chromen-4-ylphosphonate (6g)[22,23]

A mixture of 3,5-dibromosalicylaldehyde (**5g**) (280 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (1:1) gave product **6g** (373 mg, 80%) as a solid: mp 198–200 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.76 (1H, t, J=2.1 Hz), 7.54–7.53 (1H, m), 6.73 (2H, br s), 4.12–3.98 (5H, m), 1.28 (3H, t, J=7.2 Hz), 1.20 (3H, t, J=6.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.1, 146.5, 134.1, 131.5, 122.1, 119.4, 116.0, 110.6, 62.7 (d, $^2J_{CP}$=7.1 Hz), 62.6 (d, $^2J_{CP}$=7.1 Hz), 47.5 (d, $^2J_{CP}$=7.7 Hz), 34.6 (d, $^1J_{CP}$=144.5 Hz), 16.3, 16.2; IR (KBr) 3341, 3159, 2984, 2198, 1662, 1412, 1235, 1165, 1040, 861 cm^{-1}; MS (m/z, EI) 466 (M^+, 6), 331 (48), 330 (12), 329 (100), 327 (51), 293 (14), 169 (9), 149 (37), 85 (4), 71 (7).

3.23. Diethyl 2-amino-3-cyano-6-nitro-4*H*-chromen-4-ylphosphonate (6h)

A mixture of 5-nitrosalicylaldehyde (**5h**) (167 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:7) gave product **6h** (265 mg, 75%) as a solid: mp 213–215 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.30 (1H, s), 8.21 (1H, d, J=9.0 Hz), 7.28 (1H, d, J=9.0 Hz), 6.65 (2H, br s), 4.23 (1H, d, $^2J_{PH}$=18.6 Hz), 4.14–4.00 (4H, m), 1.27 (3H, t, J=7.2 Hz), 1.21 (3H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.7, 154.4, 143.4, 125.3, 124.7, 119.6, 119.4, 117.4, 62.6 (d, $^2J_{CP}$=7.1 Hz), 62.5 (d, $^2J_{CP}$=7.1 Hz), 47.1 (d, $^2J_{CP}$=7.7 Hz), 34.1 (d, $^1J_{CP}$=143.9 Hz), 16.2, 16.1; IR (KBr) 3335, 3154,

2986, 2192, 1654, 1528, 1413, 1345, 1248, 1037 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{14}H_{16}N_3O_6P$: 353.0777; found: 353.0778.

3.24. Diethyl 3-amino-2-cyano-1*H*-benzo[*f*]chromen-1-ylphosphonate (6i)

A mixture of 2-hydroxy-1-naphthaldehyde (**5i**) (172 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 4 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (1:4) gave product **6i** (222 mg, 62%) as a solid: mp 220–222 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.23 (1H, d, *J*=8.7 Hz), 7.92 (2H, d, *J*=8.4 Hz), 7.63–7.58 (1H, m), 7.52–7.47 (1H, m), 7.26 (1H, d, *J*=8.7 Hz), 6.81 (2H, br s), 4.65 (1H, d, $^2J_{PH}$=16.5 Hz), 4.00–3.83 (4H, m), 1.16–1.09 (6H, m); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.3, 148.5, 130.7, 130.3, 129.6, 128.0, 126.6, 125.2, 124.9, 120.3, 116.7, 112.0, 62.4 (d, $^2J_{CP}$=7.1 Hz), 62.1 (d, $^2J_{CP}$=6.6 Hz), 48.2 (d, $^2J_{CP}$=7.1 Hz), 31.9 (d, $^1J_{CP}$=145.5 Hz), 16.3 (d, $^3J_{CP}$=5.5 Hz), 16.2 (d, $^3J_{CP}$=5.5 Hz); IR (KBr) 3361, 3169, 2981, 2191, 1660, 1418, 1237, 1035, 812 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{18}H_{19}N_2O_4P$: 358.1082; found: 358.1080.

3.25. Ethyl 2-amino-4-(diethoxyphosphoryl)-4*H*-chromene-3-carboxylate (6j)[23]

A mixture of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), ethylcyanoacetate (**2b**) (113 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 3 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:2) gave product **6j** (267 mg, 75%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (1H, d, *J*=7.5 Hz), 7.20–7.13 (1H, m), 7.05 (1H, t, *J*=7.5 Hz), 6.91 (1H, d, *J*=8.1 Hz), 6.49 (2H, br s), 4.35 (1H, d, $^2J_{PH}$=19.5 Hz), 4.23–4.08 (2H, m), 4.02–3.92 (2H, m), 3.88–3.67 (2H, m), 1.26 (3H, t, *J*=7.2 Hz), 1.19 (3H, t, *J*=7.2 Hz), 1.06 (3H, t, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 161.9, 150.8, 129.6, 128.4, 124.5, 120.0, 116.0, 70.7, 62.8 (d, $^2J_{CP}$=7.6 Hz), 62.5 (d, $^2J_{CP}$=7.1 Hz), 59.8, 35.1 (d, $^1J_{CP}$=144.5 Hz), 16.5 (d, $^3J_{CP}$=6.0 Hz), 16.4 (d, $^3J_{CP}$=5.5 Hz), 14.7; IR (neat) 3380, 3278, 2982, 1678, 1627, 1528, 1482, 1305, 1238, 1046 cm^{-1}; MS (*m*/*z*, EI) 355 (M^+, 1), 219 (17), 218 (100), 173 (10), 172 (38), 145 (5), 118 (6), 116 (4), 89 (4), 81 (2).

3.26. Ethyl 2-amino-4-(diethoxyphosphoryl)-6-methyl-4*H*-chromene-3-carboxylate (6k)

A mixture of 5-methylsalicylaldehyde (**5c**) (136 mg, 1.0 mmol), ethylcyanoacetate (**2b**) (113 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in ethanol (5 mL) in the presence of 20 mol % of EDDA (36 mg) was stirred at room temperature for 2 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (1:1) gave product **6k** (240 mg, 65%) as an oil: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.14 (1H, s), 7.06 (1H, d, *J*=8.1 Hz), 6.88 (1H, d, *J*=8.1 Hz), 4.27 (1H, d, $^2J_{PH}$=19.5 Hz), 4.23–3.77 (6H, m), 2.30 (3H, s), 1.28 (3H, t, *J*=6.9 Hz), 1.19 (3H, t, *J*=6.9 Hz), 1.11 (3H, t, *J*=7.2 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 163.5, 149.9, 134.3, 130.8, 130.7, 129.6, 129.5, 121.1, 116.3, 62.8 (d, $^2J_{CP}$=7.6 Hz), 62.7 (d, $^2J_{CP}$=7.1 Hz), 59.9, 35.9 (d, $^1J_{CP}$=143.9 Hz), 20.7, 16.9, 16.8, 15.0; IR (neat): 3388, 3288, 2982, 2931, 1676, 1627, 1532, 1492, 1412, 1308, 1204, 1046 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{17}H_{24}NO_6P$: 369.1341; found: 369.1340.

3.27. Diethyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate 6a from 3b (through transesterification)

To a solution of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triphenyl phosphite (**3b**) (310 mg, 1.0 mmol) in 5 mL of ethanol was added 20 mol % of EDDA (36 mg). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6a** (126 mg, 41%). The physical and spectral data are the same as described above.

3.28. Dimethyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate 6l from 3b (through transesterification)

To a solution of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triphenyl phosphite (**3b**) (310 mg, 1.0 mmol) in 5 mL of methanol was added 20 mol % of EDDA (36 mg). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:7) gave product **6l** (154 mg, 55%) as a solid: mp: 160–162 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.44–7.36 (m, 2H), 7.26–7.21 (m, 1H), 7.10 (d, 1H, *J*=7.8 Hz), 6.81 (s, 2H), 4.14 (d, 1H, $^2J_{PH}$=17.7 Hz), 3.77 (d, 3H, $^2J_{PH}$=11.1 Hz), 3.72 (d, 3H, $^2J_{PH}$=10.5 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 163.6, 151.1, 130.4, 129.6, 125.2, 120.2, 118.4, 117.0, 53.7 (d, $^2J_{CP}$=7.2 Hz), 53.5 (d, $^2J_{CP}$=7.1 Hz), 49.5, 35.6 (d, $^1J_{CP}$=146.1 Hz); IR (KBr) 3401, 3293, 3138, 2955, 2856, 2181, 1653, 1417, 1235, 1040 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{12}H_{13}N_2O_4P$: 280.0613; found: 280.0613.

3.29. Dipropyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate 6m from 3b (through transesterification)

To a solution of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triphenyl phosphite (**3b**) (310 mg, 1.0 mmol) in 5 mL of 1-propanol was added 20 mol % of EDDA (36 mg). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6m** (134 mg, 40%) as a solid: mp: 113–115 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.25 (d, 1H, *J*=7.5 Hz), 7.16 (t, 1H, *J*=7.8 Hz), 7.02 (t, 1H, *J*=7.5 Hz), 6.87 (d, 1H, *J*=7.8 Hz), 6.30 (s, 2H), 3.93–3.65 (m, 5H), 1.56–1.49 (2H, m), 1.45–1.39 (2H, m), 0.79 (t, 3H, *J*=7.2 Hz), 0.72 (t, 3H, *J*=7.5 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 163.4, 151.2, 130.7, 129.6, 125.2, 120.1, 118.7, 116.9, 68.7 (d, $^2J_{CP}$=7.7 Hz), 68.6 (d, $^2J_{CP}$=7.1 Hz), 50.8, 36.3 (d, $^1J_{CP}$=146.1 Hz), 24.7, 24.6, 10.4, 10.3; IR (KBr) 3315, 3180, 2966, 2190, 1655, 1412, 1235, 1009 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{16}H_{21}N_2O_4P$: 336.1239; found: 336.1237.

3.30. Dimethyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate 6l from 3a (through transesterification)

To a solution of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in 5 mL of methanol was added 20 mol % of EDDA (36 mg). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (3:7) gave product **6l** (182 mg, 65%) as a solid. All spectral data of **6l** are the same as described above.

3.31. Dipropyl 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate 6m from 3a (through transesterification)

To a solution of salicylaldehyde (**5a**) (122 mg, 1.0 mmol), malononitrile (**2a**) (66 mg, 1.0 mmol), and triethyl phosphite (**3a**) (166 mg, 1.0 mmol) in 5 mL of 1-propanol was added 20 mol % of EDDA (36 mg). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure and crude product was purified by column chromatography on silica gel using hexane/ethylacetate (2:3) gave product **6m** (208 mg, 62%) as a solid. All spectral data of **6m** are the same as described above.

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