Tetrahedron 69 (2013) 10544–10551

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# Synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates and 2-amino-4*H*-chromenes catalyzed by tetramethylguanidine

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ARTICLE INFO

*Article history:*
Received 3 September 2013
Received in revised form 14 October 2013
Accepted 16 October 2013
Available online 23 October 2013

*Keywords:*
Solvent-free reaction
One-pot synthesis
Multi-component reactions
Phosphorus-containing chromenes
Tetramethylguanidine

ABSTRACT

Synthesis of 2-amino-4*H*-chromen-4-ylphosphonates and 2-amino-4*H*-chromenes has been accomplished by the reaction of salicylaldehyde, malononitrile, dialkyl/diphenylphosphites catalyzed by 1,1,3,3-tetramethylguanidine (TMG) under neat conditions at room temperature. The applicability of catalytic TMG for the synthesis of 2-amino-4*H*-chromenes also has been described. The mild reaction conditions, simple work-up procedure, and use of TMG as an inexpensive catalyst provides an economical protocol for the preparation of important phosphorus-containing compounds.



## 1. Introduction

The development of operationally simple and eco-friendly routes for the synthesis of organic and medicinal compounds with important biological properties are the most significant objectives in synthetic chemistry. Conducting reactions in the absence of a solvent (i.e., neat conditions) is an important research field in green (or sustainable) chemistry,[1–3] in addition, the accomplishment of various transformations in a single operation is highly compatible with the goals of green chemistry. One-pot reaction in which three or more reactants are combined to forma new preferred compound without isolation of any intermediate is, known as multi-component reactions (MCRs),[4] are highly attractive in terms of their ability to fabricate two or more C–C, C–P, C–N, or C–S bonds in a single step.

Phosphorus compounds play an important role in medicinal chemistry because of their wide range of biological activities;[5] P-containing natural products exhibit significant biological activities.[6] Among these, phosphonates are an important intermediates in organic synthesis and are used widely as enzyme inhibitors and metabolic probes,[7] peptide mimetics,[8] antibiotics, and pharmacological agents,[9] due to wide range of applications the continued development of efficient protocols for the synthesis of phosphonates and related compounds through C–P bond-forming reactions, are an important tools for the synthetic chemist.[10] Important C–P bond-forming protocols include the Kabachnik-Field,[11] Michaelis-Arbuzov,[11] Michaelis-Becker,[12] and phospha-Michael reactions.[13] A number of methods have been reported for the synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates, some of which involve phospha-Michael addition catalyzed by diethylamine,[14] ethylenediaminediacetate,[15] $K_3PO_4$,[16] $I_2$,[17] PEG,[18] β-cyclodextrin,[19] $InCl_3$,[20] and silica-bonded 2-hydroxyethylammonium acetate (HEAA)[21] (Scheme 1). These methods show varying degrees of success as well as limitations, such as prolonged reaction times, low yields, requirement of excess reagent or catalyst, use of toxic solvent, and laborious work-up procedures; based on this still they need alternate milder and environmentally sustainable procedures for the synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates.

Guanidine compounds, which have been known to chemists for over 150 years, organic super bases possessing great utility in organic synthesis; in particular, guanidine are recently drawn much attention because of their outstanding roles in organocatalysis.[22] From a structural point of view, guanidine organo-catalysts can be classified based upon the inclusion of a guanidine group either as open-chain or ring structures (mono or bicyclic). General structures of guanidine organocatalysts are illustrated in Fig. 1; typical open-chain guanidine is 1,1,3,3-tetramethylguanidine (TMG), whereas monocyclic guanidine isimidazolidin-2-imine (IMI) and bicyclic guanidine general structure is 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD).

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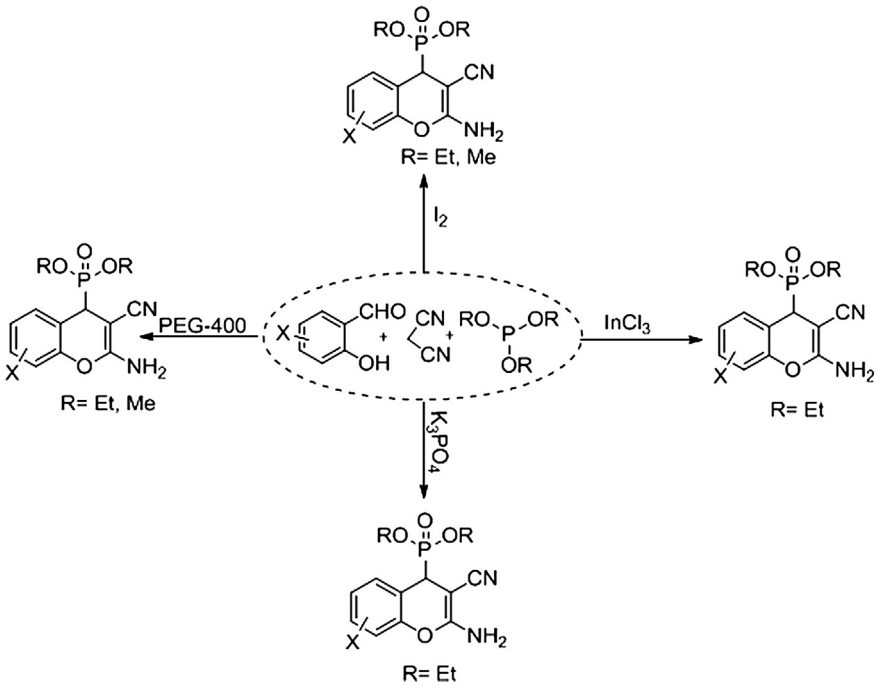
http://dx.doi.org/10.1016/j.tet.2013.10.052




**Scheme 1.** Earlier reported methods for the synthesis of 2-amino-3-cyano-4*H*-choromenyl-4-ylphosphonates.

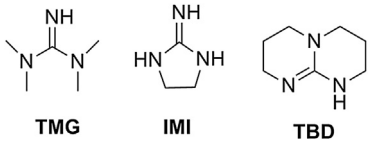
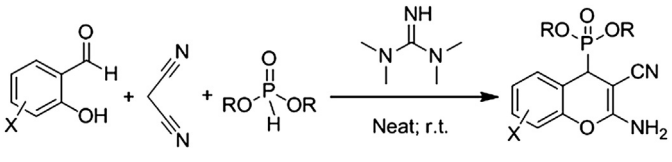



**Fig. 1.** Structures of open-chain (TMG), monocyclic (IMI) and bicyclic (TBD) guanidines.

An extensive survey of the literature has revealed that there are (to the best of our knowledge) no reports on the synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates are promoted by TMG. As part of our research program focusing on the discovery and applications of green synthetic protocols,[23,24] our aim was to develop and expand upon an environment-friendly reaction methodology toward this end. Herein, we report an eco-friendly one-pot synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates through a three-component condensation of salicylaldehyde (SA), malononitrile (MN), dialkylphosphite (DAP), and diphenylphosphite (DPP) in the presence of TMG under neat conditions at room temperature Scheme 2.




| Compound | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| X | H | H | H | H | Br | Br | Br | Br | Cl | Cl | Cl | Cl |
| R | Me | Et | Bu | Ph | Me | Et | Bu | Ph | Me | Et | Bu | Ph |

| Compound | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| X | $NO_2$ | $NO_2$ | $NO_2$ | $NO_2$ | Me | Me | Me | Me | $^t$Bu | $^t$Bu | $^t$Bu | $^t$Bu |
| R | Me | Et | Bu | Ph | Me | Et | Bu | Ph | Me | Et | Bu | Ph |

**Scheme 2.** Synthesis of 2-amino-3-cyano-4*H*-choromenyl-4-ylphosphonates.

## 2. Results and discussion

In general, MCRs often times require high reaction temperatures, long reaction times, and high catalyst loadings to promote the formation of the desired product. Attempts at a one-pot three-component reaction of SA, MN, and DAP (1 mmol each) were first performed using various types of catalysts at rt in an ethanol solvent Table 1. First, acidic species, such as $BF_3{\cdot}OEt_2$, $BF_3{\cdot}SiO_2$, silica-supported $H_2SO_4$, and trifluoroacetic acid (10 mol %) were examined at rt over 3–4 h of reaction. Compound **1** was obtained in 40%, 20%, 30% and 10% yields, respectively (entries 1–4), whereas in the presence of base catalysts, such as $NEt_3$, $NH_4OH$, KOH, and DMAP at rt, a mixture of products chromenylphosphonate and iminocoumarin (IC) was observed in all cases based on the TLC analysis of the reaction mixture after 5 h. After stirring continuously for an additional 5 h, this mixture of products remained, and very low yields of products were obtained (entries 5–8). Next, we attempted to carry out the reaction in the presence of metal salts $Mg(ClO_4)_2$ and $Y(CF_3OOC)_3{\cdot}nH_2O$ no product was observed under these conditions; however, intermediate IC was isolated in almost quantitative yield 90% (entries 9 and 10). We then examined the polymer-based catalysts Amberlyst-15 and PEG–$SO_3H$ for their potential reactivity; again, intermediate IC was obtained in acceptable yields with these catalysts 75% and 65% (entries 11 and 12). Finally, we attempted the three-component reaction in the presence of 3.5 mmol (TMG), an efficient Lewis base as well as a hydrogen-bond donor and acceptor. Initially, the reaction was carried out in ethanol; we were pleased to see that the TMG catalyst facilitated the formation of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonate in good yields 85% but required long reaction times 3–4 h (entry 13). It was decided to carry out the reaction under neat conditions in the presence of the TMG catalyst, and the reaction was found to be completed within 30 min in quantitative yield 96% (entry 14). Interestingly, the super base TMG was found to be superior to common catalytic species, including Lewis acids, heterogeneous acids, Brønsted bases, and metal salts.

To determine the appropriate concentration of TMG, we investigated the model reaction at different catalyst loadings: 1.0, 1.5,

**Table 1**
Influence of various catalyst systems for the production of compound **1** in ethanol solvent at room temperature[a]

| Entry | Catalyst used | Time (h) | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $BF_3O(Et)_2$ | 4 | **1** | 40 |
| 2 | $BF_3$–$SiO_2$ | 4 | **1** | 20 |
| 3 | $SiO_2$–$SO_3H$ | 6 | **1** | 30 |
| 4 | $H_3BO_3$ | 5 | **1** | 10 |
| 5 | $Et_3N$ | 6 | **1**+IC[c] | 10+50 |
| 6 | $NH_4OH$ | 5 | **1**+IC | 20+60 |
| 7 | KOH | 7 | **1**+IC | 15+55 |
| 8 | DMAP | 5 | **1**+IC | 30+60 |
| 9 | $Mg(ClO_4)_2$ | 2 | IC | 85 |
| 10 | $Y(CF_3OOC)_3 \cdot nH_2O$ | 1 | IC | 90 |
| 11 | Amberlyst-15 | 2 | IC | 75 |
| 12 | PEG–$SO_3H$ | 3 | IC | 65 |
| 13 | TMG | 4 | **1** | 85 |
| 14 | TMG, neat[d] | 0.25 | **1** | 95 |

[a] Reaction conditions: ethanol=5 mL, catalyst=10 mol %, SA=1 mmol, MN=1 mmol, and DAP=1 mmol.
[b] Yields based upon TLC comparison with authentic samples.
[c] Iminocoumarin.
[d] Reaction at neat condition with 3.5 mmol of TMG.

2.0, 2.5, 3.0, 3.5, and 4.0 mmol, which gave product yields of 65%, 72%, 78%, 83%, 90%, 96, and 96%, respectively. The product yield remained constant at 96% when the catalyst was increased from 3.5 to 4.0 mmol, indicating that a 3.5 mmol loading was sufficient for optimal results considering the reaction time and product yield. The results are summarized in Fig. 2.

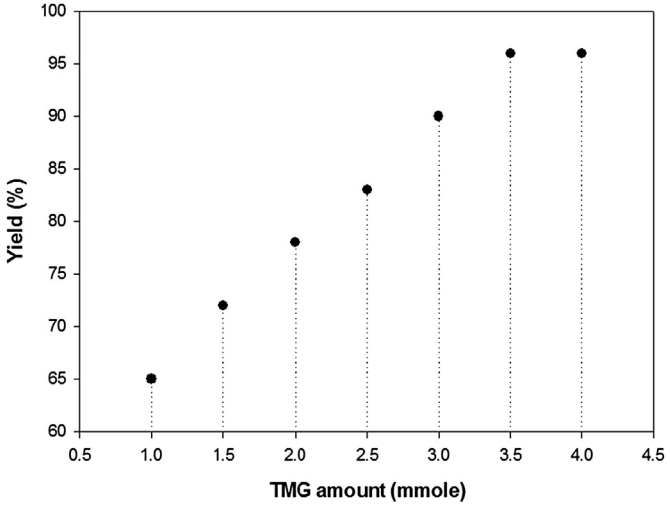



**Fig. 2.** Effect of the amount of TMG catalyst on the yield of compound **1**. Conditions: salicylaldehyde (1 mmol), malononitrile (1 mmol), dialkylphosphite (1 mmol), TMG (3.5 mmol), neat, rt.

In order to establish the generality of this methodology, additional reactions employing various substituted SAs with MN and various DAPs were carried out in the presence of 3.5 mmol TMG under neat conditions. The results are summarized in Experimental section. Reaction with 3-methyl SA (compounds **17**–**20**) produced the corresponding phosphonates in good yields (80–86%) because of the electron-donating methyl group at the 3-position of SA; similarly, in the case of reactions using 3-*tert*-butyl SA with DAPs, excellent yields were obtained (91%, 95%, 93%) within 10 min (compounds **21**, **22**, and **23**) because of the highly reactivity of DAPs. Reaction with DPP did not yield product because of its reduced reactivity, in addition to the highly hindered SA. Conversely, substituted SAs with electron-withdrawing groups (bromo, chloro, nitro) produced good yields, with reactions typically completed within 30 min (compounds **5**–**16**). In all cases, the 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates were obtained in a short time in high yields. Next, we investigated the replacement of DMP with DEP, DBP, and DPP. The reaction was observed to proceed smoothly for all DAPs in good yield; while the reaction with DPP also proceeded smoothly but in a comparatively lower yield than that of DAPs. The structures of compound **2** were elucidated by the NMR analysis and direct comparison with the reported data.[15] The $^1$H NMR spectrum of compound **2** showed the characteristic methine peak of the C–P proton at $\delta$ 4.31–3.99 as multiplet because of the overlapping of this signal with the two ethoxymethylene protons, whereas in the $^{13}$C NMR spectrum, the characteristic carbon peak of the C–P bond appeared at $\delta$ 35.3 as a doublet with a coupling constant of 147.4 Hz.

Subsequent to this initial success in the improvement of a one-pot synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates, we attempted to expand the applicability of this protocol towards the preparation of a few biologically active compounds. In this context, we directed our interest to the synthesis of 2-amino-4*H*-chromenes Fig 3.

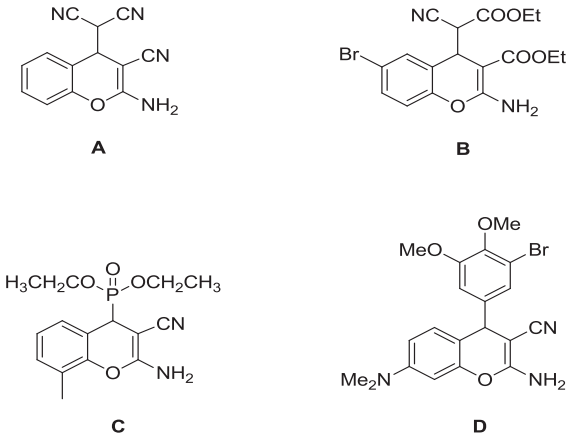
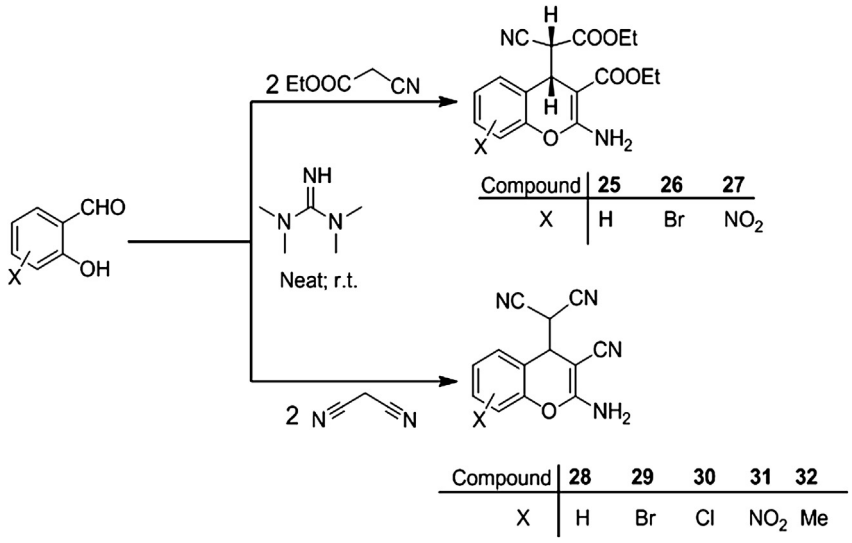



**Fig. 3.** Structures of a few biologically active 2-amino-4*H*-chromenes.

2-Amino-4*H*-chromenes are widely employed as pigments, cosmetics,[25] and potential biodegradable agrochemicals.[26] Fused-chromenes are also used as anticancer,[27] antiviral,[28] anti-inflammatory,[29] and pesticidal compounds.[30] In spite of such important biological properties of 2-amino-4*H*-chromenes, it remains a challenging task to develop an easy and efficient method for their synthesis. Synthesis of various 2-amino-4*H*-chromene derivatives have been previously reported using diethylamine,[31] KF,[32] and Amberlyst-21[33] as catalysts. We envisaged that the TMG catalysis of the MCR of SA and 2 equiv of ethyl-cyanoacetate (ECA) would easily afford **25**. The reaction is depicted in Scheme 3.

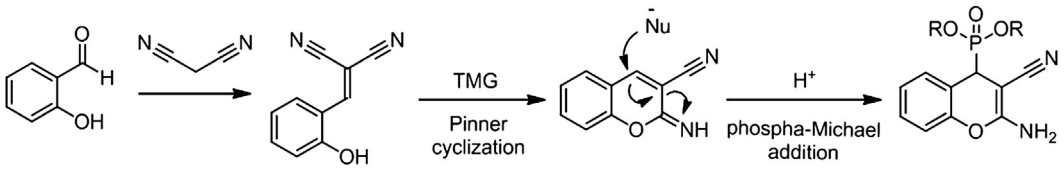
The synthesis of **25** was achieved by the reaction of SA and ECA (1:2 equiv) in the presence of TMG as a catalyst at rt. An exothermic reaction took place upon the addition of the catalyst. After completion of the reaction (TLC), water was added and the solution was stirring continuously until a solid was obtained; the solid was filtered, washed with water (15 mL) four times, and dried in air. The comparison with the previously reported $^1$H NMR data showed that the resultant product was obtained as a single diastereoisomer having an *erythro* configuration ($^1$H NMR). In order to extend the above reaction Scheme 3 to compile a compound library, SAs (1 equiv) were allowed to react with ECA (2 equiv). In all cases, the products were obtained in good yield and as a single diastereoisomer.




**Scheme 3.** TMG catalyzed synthesis of 2-amino-4*H*-chromenes.

Treatment of SA with MN under similar conditions gave the corresponding 2-amino-4*H*-chromene derivative **28** in good yield with high diastereoselectivity. The reactions proceeded efficiently with different SAs in high yields at rt in all cases. The extent of electron density and nature of the substituent on the aromatic ring exhibited some effects on this conversion. SAs carrying electron-withdrawing substituent, such as halide or nitro groups gave the products in high yields in a short reaction time. In contrast, unsubstituted and electron-rich SAs required longer reaction times and gave lower yields compared to those of their electron-deficient counterparts.

The formation of **1** can be explained by the plausible mechanism shown in Scheme 4. Reaction of SA and MN in the presence of TMG first 2-(2-hydroxybenzylidene)malononitrile through a Knoevenagel-condensation; the newly-formed hydroxy cyano olefin undergoes an intramolecular Pinner reaction to form iminocoumarin. Subsequent *phospha*-Michael addition of DAP provides the target compound **1**.




**Scheme 4.** Plausible mechanism for the formation of 2-amino-3-cynao-4*H*-chromen-4-ylphosphonates.

## 3. Conclusions

In conclusion, the development of a simple, procedure for the synthesis of 2-amino-3-cyano-4*H*-chromen-4-ylphosphonates and 2-amino-4*H*-chromenes under TMG catalysis and solvent-free conditions has been described. This low-cost protocol has several advantages, including a cleaner reaction medium (solvent-free), use of easily available chemicals, high yields, and easy work-up procedures. This protocol provides the synthetic chemist with a rapid method for preparing both phosphorus-containing heterocycles and biologically important 2-amino-4*H*-chromenes.

## 4. Experimental

### 4.1. General

Various substituted SAs, phosphites (dimethyl, diethyl, and diphenyl), ethyl-cyanoacetate (Sigma–Aldrich Co), dibutylphosphite, MN (Thermo Fisher Scientific Inc.), and TMG (Alfa-Aesar) were used as received. All experiments were carried out under neat conditions; pre-coated silica gel plates (Merck Chemicals) developed with iodine was used for the analytical TLC. Melting points were uncorrected and determined on a digital Stuart SMP3 apparatus (Bibby Scientific Limited, Staffordshire, UK). The $^{1}$H NMR (400 MHz), $^{13}$C NMR (100 MHz), and $^{31}$P NMR (161.9 MHz) spectra were recorded on a Varian INOVA 400 NMR spectrometer at rt. Chemical shift values were relative to $Me_4Si$. Data are presented as follows: chemical shift (parts per million), multiplicity (s=singlet, d=doublet, dd=doublet of doublet, t=triplet, m=multiplet, br s=broad singlet, coupling constant *J* (Hertz)). FTIR spectra were recorded on a Shimadzu IR Prestige 21 spectrometer at rt. The spectra were taken in KBr discs in the range 3500–500 cm$^{-1}$. Elemental analyses were performed on a Vario EL III Element Analyzer (Elementar Analysensysteme GmbH, Germany).

### 4.2. General procedure for synthesis of (2-amino-3-cyano-4*H*-chromene-4-yl)phosphonates (1–24) and 2-amino-4*H*-chromenes (25–32)

TMG (3.5 mmol) was added to a mixture of SA (1 mmol), MN (1 mmol) and DAP (1 mmol) in neat condition. The resulting mixture was stirred at room temperature. After completion of the

reaction (monitored by TLC), distilled water (15 mL) was added to the reaction mixture and stirring continued till a free flowing solid was obtained. It was filtered and then washed successively with water, *n*-hexane. The crude product was purified by re-crystallization from ethanol solution. For this, the crude product was saturated in boiling ethanol and then the solution mixture was filtered when it was hot to remove the undissolved solid. The hot filtrate cooled down to room temperature to afford elemental analytically pure crystalline product. The similar experimental procedures were adopted for the synthesis of all the 2-amino-4*H*-chrormens.

*4.2.1. Dimethyl 2-amino-3-cyano-4H-chromen-4-ylphosphonate (**1**).* 90% yield in 15 min of reaction; Solid, mp 156–158 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.33 (d, 1H, $J$=7.6 Hz, Ar–H), 7.27 (d, 1H, $J$=8.0 Hz, Ar–H), 7.14 (t, 1H, $J$=7.2 Hz, Ar–H), 6.98 (d, 1H, $J$=8.4 Hz, Ar–H), 4.84 (br s, 2H, $-NH_2$), 3.92 (d, 1H, $J$=17.6 Hz, –P–CH), 3.76 (d, 3H, $J$=10.4 Hz, $-OCH_3$), 3.64 (d, 3H, $J$=10.4 Hz, $-OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.6, 149.7, 129.5, 129.1, 125.1, 119.1, 116.5, 109.5, 53.8, 51.8, 35.0 (d, $^1J_{CP}$=146.1 Hz); $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 24.2; FTIR (KBr): $\nu$=3340, 3162, 2971, 2192, 1651, 1492, 1241, 1030, 981 cm$^{-1}$. Anal. Calcd for $C_{12}H_{13}N_2O_4P$: C, 51.43; H, 4.68; N, 10.00. Found: C, 51.39; H, 4.52; N, 9.95.

*4.2.2. Diethyl 2-amino-3-cyano-4H-chromen-4-ylphosphonate (**2**).* 93% yield in 10 min of reaction; Solid, mp 152–153 °C (140–142 °C);[14] $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.43–6.97 (m, 4H, Ar–H), 4.81 (br s, 2H, $-NH_2$), 4.31–3.99 (m, 5H, $-OCH_2$, and P–CH), 1.33 (t, 3H, $J$=7.2 Hz, $-CH_3$), 1.16 (t, 3H, $J$=7.2 Hz, $-CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.6, 149.7, 129.6, 129.5, 128.9, 125.0, 119.2, 116.4, 63.2, 52.2, 35.3 (d, $^1J_{CP}$=147.4 Hz), 16.3; $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.6; FTIR (KBr): $\nu$=3341, 3165, 2898, 2184, 1640, 1495, 1248, 1034, 961 cm$^{-1}$. Anal. Calcd for $C_{14}H_{17}N_2O_4P$: C, 54.55; H, 5.56; N, 9.09. Found: C, 54.50; H, 5.49; N, 8.97.

*4.2.3. Dibutyl 2-amino-3-cyano-4H-chromen-4-ylphosphonate (**3**).* 94% yield in 10 min of reaction; Solid, mp 146–148 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.31–6.93 (m, 4H, Ar–H), 5.02 (br s, 2H, $-NH_2$), 4.11–3.81 (m, 5H, $-OCH_2$, and P–CH), 1.65–1.16 (m, 8H, $-(CH_2)_4$), 0.89 (t, 3H, $J$=7.2 Hz, $-CH_3$), 0.82(t, 3H, $J$=7.2 Hz, $-CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.8, 149.8, 129.5, 128.9, 124.9, 119.4, 116.4, 116.3, 66.7, 51.6, 36.1 (d, $^1J_{CP}$=140.2 Hz), 32.4, 18.6, 13.5; $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.8; FTIR (KBr): $\nu$=3339, 3172, 2964, 2174, 1644, 1492, 1320, 1020, 970 cm$^{-1}$. Anal. Calcd for $C_{18}H_{25}N_2O_4P$: C, 59.33; H, 6.92; N, 7.69. Found: C, 59.59; H, 7.02; N, 7.70.

*4.2.4. Diphenyl 2-amino-3-cyano-4H-chromen-4-ylphosphonate (**4**).* 86% yield in 25 min of reaction; Solid, mp 158–160 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.37 (br s, 2H, $-NH_2$), 7.74–7.02 (m, 14H, Ar–H), 5.82 (d, 1H, $J$=16.5 Hz, –P–CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 163.8, 151.3, 139.3, 131.6, 130.2, 128.9, 125.8, 124.9, 121.0, 120.1, 118.2, 117.2, 49.9, 33.4 (d, $^1J_{CP}$=140.2 Hz); $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 16.0; FTIR (KBr): $\nu$=3320, 3182, 2983, 2179, 1654, 1440, 1224, 1039, 965 cm$^{-1}$. Anal. Calcd for $C_{22}H_{17}N_2O_4P$: C, 65.35; H, 4.24; N, 6.93. Found: C, 65.30; H, 4.21; N, 6.95.

*4.2.5. Dimethyl 2-amino-6-bromo-3-cyano-4H-chromen-4-ylphosphonate (**5**).* 94% yield in 10 min of reaction; Solid, mp 160–161 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.44 (s, 1H, Ar–H), 7.37 (d, 1H, $J$=8.8 Hz, Ar–H), 6.87 (d, 1H, $J$=8.8 Hz, Ar–H), 4.94 (br s, 2H, $-NH_2$), 3.85 (d, 1H, $J$=18.0 Hz, –P–CH), 3.77 (d, 3H, $J$=10.8 Hz, $-OCH_3$), 3.71 (d, 3H, $J$=10.8 Hz, $-OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.5, 148.8, 132.1, 132.0, 131.9, 118.7, 118.2, 117.5, 53.8, 53.5, 34.8 (d, $^1J_{CP}$=148.4 Hz); $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 23.3; FTIR (KBr): $\nu$=3329, 3175, 2980, 2184, 1646, 1452, 1241, 1032, 895 cm$^{-1}$. Anal. Calcd for $C_{12}H_{12}BrN_2O_4P$: C, 40.13; H, 3.37; N, 7.80. Found: C, 39.79; H, 3.63; N, 8.06.

*4.2.6. Diethyl 2-amino-6-bromo-3-cyano-4H-chromen-4-ylphosphonate (**6**).* 95% yield in 9 min of reaction; Solid, mp 177–178 °C (180–182 °C);[14] $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 8.25 (t, 1H, $J$=2.6 Hz, Ar–H), 8.17 (t, 1H, $J$=2.4 Hz, Ar–H), 7.12 (d, 1H, $J$=8.8 Hz, Ar–H), 4.86 (br s, 2H, $-NH_2$), 4.13–4.09 (m, 4H, $-OCH_2$), 3.93 (d, 1H, $J$=18.8 Hz, –P–CH), 1.33 (t, 3H, $J$=7.0 Hz, $-CH_3$), 1.27 (t, 3H, $J$=7.0 Hz, $-CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.3, 148.9, 132.2, 131.9, 118.8, 118.7, 117.5, 117.4, 63.3, 51.9, 35.2 (d, $^1J_{CP}$=149.0 Hz), 16.3; $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 20.8; FTIR (KBr): $\nu$=3335, 3150, 2975, 2167, 1656, 1474, 1248, 1034, 876 cm$^{-1}$. Anal. Calcd for $C_{14}H_{16}BrN_2O_4P$: C, 43.43; H, 4.17; N, 7.24. Found: C, 46.25; H, 2.28; N, 9.21.

*4.2.7. Dibutyl 2-amino-6-bromo-3-cyano-4H-chromen-4-ylphosphonate (**7**).* 96% yield in 10 min of reaction; Solid, mp 148–150 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.45 (t, 1H, $J$=2.2 Hz, Ar–H), 7.36 (t, 1H, $J$=1.8 Hz, Ar–H), 6.85 (d, 1H, $J$=8.8 Hz, Ar–H), 4.82 (br s, 2H, $-NH_2$), 4.11–3.90 (m, 4H, $-OCH_2$), 3.82 (d, 1H, $J$=18.4 Hz, –P–CH), 1.67–1.23 (m, 8H, $-(CH_2)_4$), 0.92 (t, 3H, $J$=7.4 Hz, $-CH_3$), 0.87 (t, 3H, $J$=7.4 Hz, $-CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.3, 148.8, 132.1, 131.8, 118.8, 118.7, 118.0, 117.4, 66.9, 51.9, 34.5 (d, $^1J_{CP}$=140.2 Hz), 32.6, 18.5, 13.5; $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.3; FTIR (KBr): $\nu$=3352, 3158, 2969, 2159, 1654, 1462, 1249, 1050, 975 cm$^{-1}$. Anal. Calcd for $C_{18}H_{24}BrN_2O_4P$: C, 48.77; H, 5.46; N, 6.32. Found: C, 48.63; H, 5.24; N, 6.58.

*4.2.8. Diphenyl 2-amino-6-bromo-3-cyano-4H-chromen-4-ylphosphonate (**8**).* 86% yield in 25 min of reaction; Solid, mp 165–166 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 8.18 (br s, 2H, $-NH_2$), 7.29–7.02 (m, 13H, Ar–H), 3.46 (d, 1H, $J$=16.5 Hz, –P–CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 160.8, 157.6, 155.6, 153.3, 150.2, 138.1, 131.2, 118.4, 117.6, 112.9, 108.7, 104.4, 61.0, 30.6 (d, $^1J_{CP}$=143.4 Hz); $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 30.9; FTIR (KBr): $\nu$=3326, 3155, 2985, 2186, 1646, 1485, 1246, 1042, 892 cm$^{-1}$. Anal. Calcd for $C_{22}H_{16}BrN_2O_4P$: C, 54.68; H, 3.34; N, 5.80. Found: C, 54.60; H, 3.32; N, 5.77.

*4.2.9. Dimethyl 2-amino-6-chloro-3-cyano-4H-chromen-4-ylphosphonate (**9**).* 92% yield in 10 min of reaction; Solid, mp 166–168 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.30 (t, 1H, $J$=2.4 Hz, Ar–H), 7.21 (t, 1H, $J$=2.2 Hz, Ar–H), 6.93 (d, 1H, $J$=8.8 Hz, Ar–H), 4.84 (br s, 2H, $-NH_2$), 3.86 (d, 1H, $J$=18.8 Hz, –P–CH), 3.77 (d, 3H, $J$=10.8 Hz, $-OCH_3$), 3.70 (d, 3H, $J$=10.8 Hz, $-OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.7, 148.3, 130.2, 129.2, 129.0, 118.9, 118.0, 117.9, 53.9, 50.9, 34.9 (d, $^1J_{CP}$=148.4 Hz); $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 23.3; FTIR (KBr): $\nu$=3360, 3184, 2972, 2188, 1596, 1460, 1310, 1051, 956 cm$^{-1}$. Anal. Calcd for $C_{12}H_{12}ClN_2O_4P$: C, 45.80; H, 3.84; N, 8.90. Found: C, 42.30; H, 4.31; N, 8.03.

*4.2.10. Diethyl 2-amino-6-chloro-3-cyano-4H-chromen-4-ylphosphonate (**10**).* 94% yield in 12 min of reaction; Solid, mp 148–150 °C (150–152 °C);[14] $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.30 (t, 1H, $J$=3.4 Hz, Ar–H), 7.19 (t, 1H, $J$=2.2 Hz, Ar–H), 6.90 (d, 1H, $J$=8.8 Hz, Ar–H), 4.94 (br s, 2H, $-NH_2$), 4.14–4.01 (m, 4H, $-OCH_2$), 3.81 (d, 1H, $J$=18.4 Hz, –P–CH), 1.32 (t, 3H, $J$=7.0 Hz, $-CH_3$), 1.22 (t, 3H, $J$=7.0 Hz, $-CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.5, 148.3, 130.0, 129.9, 129.1, 118.9, 118.3, 117.7, 63.3, 51.4, 35.3 (d, $^1J_{CP}$=146.7 Hz), 16.4; $^{31}$P NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 20.8; FTIR (KBr): $\nu$=3325, 3164, 2965, 2172, 1670, 1491, 1309, 1062,

920 $cm^{-1}$. Anal. Calcd for $C_{14}H_{16}ClN_2O_4P$: C, 49.06; H, 4.71; N, 8.17. Found: C, 49.22; H, 4.65; N, 7.93.

*4.2.11. Dibutyl 2-amino-6-chloro-3-cyano-4H-chromen-4-ylphosphonate (**11**).* 96% yield in 10 min of reaction; Solid, mp 138–140 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.31 (t, 1H, $J$=2.4 Hz, Ar–H), 7.20 (t, 1H, $J$=2.4 Hz, Ar–H), 6.91 (d, 1H, $J$=8.8 Hz, Ar–H), 4.80 (br s, 2H, $-NH_2$), 4.07–3.91 (m, 4H, $-OCH_2$), 3.82 (d, 1H, $J$=18.4 Hz, –P–CH), 1.71–1.29 (m, 8H, $-(CH_2)_4$), 0.92 (t, 3H, $J$=7.4 Hz, $-CH_3$), 0.87(t, 3H, $J$=7.4 Hz, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.3, 148.2, 130.0, 129.3, 128.8, 118.8, 118.4, 117.6, 66.9, 52.0, 36.0 (d, $^1J_{CP}$=148.4 Hz), 32.5, 18.6, 13.6; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 20.9; FTIR (KBr): $\nu$=3362, 3156, 2956, 2173, 1682, 1425, 1325, 1065, 932 $cm^{-1}$. Anal. Calcd for $C_{18}H_{24}ClN_2O_4P$: C, 54.21; H, 6.07; N, 7.02. Found: C, 53.79; H, 5.93; N, 7.04.

*4.2.12. Diphenyl 2-amino-6-chloro-3-cyano-4H-chromen-4-ylphosphonate (**12**).* 80% yield in 25 min of reaction; Solid, mp 158–160 °C; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.33 (br s, 2H, $-NH_2$), 7.75–6.71 (m, 13H, Ar–H), 4.35 (dd, 1H, $J$=16.5, 10.0 Hz, –P–CH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 164.8, 151.3, 149.4, 146.5, 132.6, 130.2, 128.2, 125.8, 120.1, 119.6, 118.6, 115.3,49.4, 32.6 (d, $^1J_{CP}$=141.2 Hz); $^{31}P$ NMR (161.9 MHz, DMSO-$d_6$): $\delta$ (ppm) 23.2; FTIR (KBr): $\nu$=3346, 3176, 2968, 2185, 1659, 1452, 1310, 1062, 936 $cm^{-1}$. Anal. Calcd for $C_{22}H_{16}ClN_2O_4P$: C, 60.22; H, 3.68; N, 6.38. Found: C, 60.24; H, 3.63; N, 6.40.

*4.2.13. Dimethyl 2-amino-6-nitro-3-cyano-4H-chromen-4-ylphosphonate (**13**).* 95% yield in 10 min of reaction; Solid, mp 216–218 °C; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.21 (br s, 2H, $-NH_2$), 8.14 (t, 1H, $J$=4.0 Hz, Ar–H),7.40 (d, 1H, $J$=7.2 Hz, Ar–H), 7.24 (t, 1H, $J$=4.4 Hz, Ar–H), 4.48 (d, 1H, $J$=18.8 Hz, –P–CH), 3.61 (d, 3H, $J$=1.2 Hz, $-OCH_3$), 3.59 (d, 3H, $J$=1.2 Hz, $-OCH_3$); $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 162.2, 154.7, 1v43.9, 125.5, 125.2, 119.8, 117.9, 117.8, 53.6, 47.3, 33.9 (d, $^1J_{CP}$=149.8 Hz); $^{31}P$ NMR (161.9 MHz, DMSO-$d_6$): $\delta$ (ppm) 13.9; FTIR (KBr): $\nu$=3319, 3124, 2958, 2167, 1656, 1467, 1298, 1030, 925 $cm^{-1}$. Anal. Calcd for $C_{12}H_{12}N_3O_6P$: C, 44.32; H, 3.72; N, 12.92. Found: C, 44.28; H, 3.75; N, 12.85.

*4.2.14. Diethyl 2-amivno-6-nitro-3-cyano-4H-chromen-4-ylphosphonate (**14**).* 96% yield in 10vmin of reaction; Solid, mp 222–224 °C (216–218 °C);[14] $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.46 (t, 1H, $J$=2.4 Hz, Ar–H), 7.36 (t, 1H, $J$=4.0 Hz, Ar–H), 6.85 (d, 1H, $J$=12.0 Hz, Ar–H), 4.81 (br s, 2H, $-NH_2$), 4.14–3.98 (m, 4H, $-OCH_2$), 3.81 (d, 1H, $J$=16.0 Hz, –P–CH), 1.33 (t, 3H, $J$=8.0 Hz, $-CH_3$), 1.22 (t, 3H, $J$=8.0 Hz, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 160.7, 153.8, 144.4, 125.5, 124.7, 118.3, 118.1, 117.9, 63.6, 52.0, 36.1 (d, $^1J_{CP}$=146.2 Hz), 16.4; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.5; FTIR (KBr): $\nu$=3346, 3145, 2965, 2178, 1648, 1485, 1286, 1086, 886 $cm^{-1}$. Anal. Calcd for $C_{14}H_{16}N_3O_6P$: C, 47.60; H, 4.57; N, 11.89. Found: C, 47.62; H, 4.53; N, 11.80.

*4.2.15. Dibutyl 2-amino-6-nitro-3-cyano-4H-chromen-4-ylphosphonate (**15**).* 91% yield in 15 min of reaction %; Solid, mp 148–150 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 8.24 (d, 1H, $J$=3.2 Hz, Ar–H), 8.16 (d, 1H, $J$=4.8 Hz, Ar–H), 7.12 (d, 1H, $J$=9.6 Hz, Ar–H), 4.97 (br s, 2H, $-NH_2$), 4.08–3.92 (m, 4H, $-OCH_2$), 3.79 (d, 1H, $J$=18.2 Hz, –P–CH), 1.71–1.28 (m, 8H, $-(CH_2)_4$), 0.80 (t, 6H, $J$=7.2 Hz, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 160.7, 155.6, 153.8, 144.5, 125.3, 124.7, 118.1, 117.3,67.1, 51.9, 35.2 (d, $^1J_{CP}$=148.4 Hz), 32.4, 18.6, 13.5; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.4; IR (KBr): $\nu$=3385, 3168, 2974, 2154, 1632, 1492, 1265, 1044, 892 $cm^{-1}$. Anal. Calcd for $C_{18}H_{24}N_3O_6P$: C, 52.81; H, 5.91; N, 10.26. Found: C, 51.22; H, 5.85; N, 9.93.

*4.2.16. Diphenyl 2-amino-6-nitro-3-cyano-4H-chromen-4-ylphosphonate (**16**).* 88% yield in 20 min of reaction; Solid, mp 150–151 °C; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 9.27 (br s, 2H, $-NH_2$), 8.62–6.68 (m, 13H, Ar–H), 5.82 (dd, 1H, $J$=16.5, 12.3 Hz, –P–CH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 163.9, 157.6, 154.2, 144.2, 130.2, 129.7, 126.8, 125.9, 120.1, 118.6, 117.7, 115.3, 49.0, 33.5 (d, $^1J_{CP}$=142.4 Hz); $^{31}P$ NMR (161.9 MHz, DMSO-$d_6$): $\delta$ (ppm) 24.2; FTIR (KBr): $\nu$=3376, 3184, 2976, 2169, 1648, 1462, 1254, 1048, 912 $cm^{-1}$. Anal. Calcd for $C_{22}H_{16}N_3O_6P$: C, 58.80; H, 3.59; N, 9.35. Found: C, 58.79; H, 3.21; N, 9.04.

*4.2.17. Dimethyl 2-amino-8-methyl-3-cyano-4H-chromen-4-ylphosphonate (**17**).* 84% yield in 10 min of reaction; Solid, mp 148–150 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.14 (d, 1H, $J$=6.8 Hz, Ar–H), 7.10 (d, 1H, $J$=7.6 Hz, Ar–H), 7.02 (t, 1H, $J$=7.4 Hz, Ar–H), 4.79 (br s, 2H, $-NH_2$), 3.90 (d, 1H, $J$=18.0 Hz, –P–CH), 3.74 (d, 3H, $J$=10.8 Hz, $-OCH_3$), 3.65 (d, 3H, $J$=10.8 Hz, $-OCH_3$), 2.25 (s, 3H, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.7, 131.2, 125.8, 124.6, 119.1, 118.4, 117.4, 115.6, 56.5, 45.7, 35.8 (d, $^1J_{CP}$=148.0 Hz), 15.7; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 24.2; FTIR (KBr): $\nu$=3358, 3168, 2986, 2176, 1674, 1486, 1256, 1064, 936 $cm^{-1}$. Anal. Calcd for $C_{13}H_{15}N_2O_4P$: C, 53.06; H, 5.14; N, 9.52. Found: C, 53.71; H, 5.38; N, 9.17.

*4.2.18. Diethyl 2-amino-8-methyl-3-cyano-4H-chromen-4-ylphosphonate (**18**).* 85% yield in 12 min of reaction; Solid, mp 158–160 °C (161–164 °C);[14] $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.13 (d, 1H, $J$=7.6 Hz, Ar–H), 7.08 (d, 1H, $J$=7.6 Hz, Ar–H), 7.04 (t, 1H, $J$=7.4 Hz, Ar–H), 4.90 (br s, 2H, $-NH_2$), 4.11–3.90 (m, 4H, $-OCH_2$), 3.85 (d, 1H, $J$=18.0 Hz, –P–CH), 2.24 (s, 3H, $-CH_3$) 1.31 (t, 3H, $J$=7.2 Hz, $-CH_3$), 1.18 (t, 3H, $J$=7.2 Hz, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.8, 148.2, 130.5, 127.1, 125.6, 124.4, 119.3, 116.1, 63.2, 52.0, 36.4 (d, $^1J_{CP}$=148.9 Hz), 16.4, 15.5; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 21.8; FTIR (KBr): $\nu$=3346, 3179, 2948, 2153, 1692, 1458, 1276, 1068, 940 $cm^{-1}$. Anal. Calcd for $C_{15}H_{19}N_2O_4P$: C, 55.90; H, 5.94; N, 8.69. Found: C, 57.38; H, 6.04; N, 8.68.

*4.2.19. Dibutyl 2-amino-8-methyl-3-cyano-4H-chromen-4-ylphosphonate (**19**).* 86% yield in 14 min of reaction; Solid, mp 134–136 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.14 (d, 1H, $J$=7.6 Hz, Ar–H), 7.08 (d, 1H, $J$=7.2 Hz, Ar–H), 7.01 (t, 1H, $J$=7.6 Hz, Ar–H), 4.78 (br s, 2H, $-NH_2$), 4.04–3.80 (m, 4H, $-OCH_2$), 3.73 (d, 1H, $J$=16.4 Hz, –P–CH), 2.24 (s, 3H, $-CH_3$), 1.67–1.22 (m, 8H, $-(CH_2)_4$), 0.91 (t, 3H, $J$=7.4 Hz, $-CH_3$), 0.84 (t, 3H, $J$=7.4 Hz, $-CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 161.5, 148.1, 130.4, 125.6, 124.5, 119.2, 116.4, 116.2, 66.7, 52.5, 34.6 (d, $^1J_{CP}$=140.2 Hz), 32.5, 18.6, 15.5, 13.5; $^{31}P$ NMR (161.9 MHz, $CDCl_3$): $\delta$ (ppm) 22.0; FTIR (KBr): $\nu$=3380, 3192, 2965, 2092, 1645, 1476, 1193, 1045, 890 $cm^{-1}$. Anal. Calcd for $C_{19}H_{27}N_2O_4P$: C, 60.31; H, 7.19; N, 7.40. Found: C, 60.79; H, 7.29; N, 7.35.

*4.2.20. Diphenyl 2-amino-8-methyl-3-cyano-4H-chromen-4-ylphosphonate (**20**).* 80% yield in 30 min of reaction; Solid, mp 214–216 °C; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 7.29–7.02 (m, 13H, Ar–H), 6.69 (br s, 2H, $-NH_2$), 4.84 (d, 1H, $J$=16.5 Hz, –P–CH), 2.26 (s, 3H, $-CH_3$); $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 160.9, 157.3, 150.0, 140.8, 138.6, 126.1, 124.3, 123.3, 120.2, 118.8, 116.2, 114.0, 71.0, 31.6 (d, $^1J_{CP}$=142.4 Hz), 15.7; $^{31}P$ NMR (161.9 MHz, DMSO-$d_6$): $\delta$ (ppm) 16.3; FTIR (KBr): $\nu$=3346, 3194, 2960, 2094, 1686, 1489, 1143, 1086, 976 $cm^{-1}$. Anal. Calcd for $C_{23}H_{19}N_2O_4P$: C, 66.03; H, 4.58; N, 6.70. Found: C, 63.81; H, 4.39; N, 6.68.

*4.2.21. Dimethyl 2-amino-8-tert-butyl-3-cyano-4H-chromen-4-ylphosphonate (**21**).* 91% yield in 10 min of reaction; Solid, mp 205–207 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.27–7.25 (m, 1H, Ar–H), 7.18–7.16 (m, 1H, Ar–H), 7.07 (t, 1H, $J$=7.8 Hz, Ar–H), 4.85 (br s, 2H, $-NH_2$), 3.89 (d, 1H, $J$=17.6 Hz, –P–CH), 3.75 (d, 3H, $J$=10.4 Hz, $-OCH_3$), 3.58 (d, 3H, $J$=10.4 Hz, $-OCH_3$), 1.38 (s, 9H,

–$(CH_3)_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.3, 148.8, 137.5, 127.7, 126.7, 124.6, 119.0, 116.8, 53.2, 52.3, 36.3, 34.8 (d, $^1J_{CP}$=142.1 Hz), 30.1; $^{31}$P NMR (161.9 MHz, $CDCl_3$): δ (ppm) 24.2; FTIR (KBr): ν=3325, 3165, 2956, 2085, 1689, 1456, 1265, 1070, 985 cm$^{-1}$. Anal. Calcd for $C_{16}H_{21}N_2O_4P$: C, 57.14; H, 6.29; N, 8.33. Found: C, 56.77; H, 6.34; N, 8.13.

*4.2.22. Diethyl 2-amino-8-tert-butyl-3-cyano-4H-chromen-4-ylphosphonate (**22**).* 95% yield in 10 min of reaction; Solid, mp 235–237 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.25 (s, 1H, Ar–H), 7.18 (d, 1H, *J*=7.6 Hz, Ar–H), 7.06 (t, 1H, *J*=7.8 Hz, Ar–H), 4.78 (br s, 2H, –$NH_2$), 4.15–3.82 (m, 4H, –$OCH_2$), 3.03 (s, 1H, –P–CH), 1.37 (s, 9H, –$(CH_3)_3$), 1.33 (t, 3H, *J*=7.2 Hz, –$CH_3$), 1.13 (t, 3H, *J*=7.2 Hz, –$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.2, 148.7, 137.3, 127.8, 126.5, 124.5, 119.1, 117.1, 63.1, 52.8, 36.6, 34.9 (d, $^1J_{CP}$=148.9 Hz), 30.1, 16.4; $^{31}$P NMR (161.9 MHz, $CDCl_3$): δ (ppm) 21.8; FTIR (KBr): ν=3342, 3162, 2985, 2068, 1692, 1458, 1285, 1040, 939 cm$^{-1}$. Anal. Calcd for $C_{18}H_{25}N_2O_4P$: C, 59.33; H, 6.92; N, 7.69. Found: C, 59.65; H, 7.14; N, 7.87.

*4.2.23. Dibutyl 2-amino-8-tert-butyl-3-cyano-4H-chromen-4-ylphosphonate (**23**).* 93% yield in 9 min of reaction; Solid, mp 180–182 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.25 (t, 1H, *J*=1.8 Hz, Ar–H), 7.20–7.17 (m, 1H, Ar–H), 7.06 (t, 1H, *J*=7.8 Hz, Ar–H), 4.73 (br s, 2H, –$NH_2$), 4.07–3.73 (m, 5H, –$OCH_2$ &–P–CH), 1.70–1.40 (m, 8H, –$(CH_2)_4$), 1.37 (s, 9H, –$(CH_3)_3$), 0.91 (t, 3H, *J*=7.2 Hz, –$CH_3$), 0.83 (t, 3H, *J*=7.2 Hz, –$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.3, 148.7, 137.3, 127.8, 126.5, 124.4, 119.2, 117.3, 66.7, 52.4, 36.6, 34.9 (d, $^1J_{CP}$=142.8 Hz), 33.2, 32.4, 18.6, 13.5; $^{31}$P NMR (161.9 MHz, $CDCl_3$): δ (ppm) 21.7; FTIR (KBr): ν=3362, 3129, 2896, 2085, 1694, 1492, 1286, 1040, 958 cm$^{-1}$. Anal. Calcd for $C_{22}H_{33}N_2O_4P$: C, 62.84; H, 7.91; N, 6.66. Found: C, 63.57; H, 8.21; N, 6.76.

*4.2.24. Diphenyl 2-amino-8-tert-butyl-3-cyano-4H-chromen-4-ylphosphonate (**24**)*[a]. [a]Not formed.

*4.2.25. Ethyl 2-amino-4-(1-cyano-2-ethoxy-2-oxoethyl)-4H-chromene-3-carboxylate (**25**).* 95% yield in 40 min of reaction; Solid, mp 144–146 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30–7.28 (m, 1H, Ar–H), 7.27 (br s, 2H, –$NH_2$), 7.09–7.05 (m, 3H, Ar–H), 4.70 (d, 1H, *J*=3.6 Hz, –CH), 4.27–4.20 (m, 4H, –$OCH_2$), 3.95 (d, 1H, *J*=3.6 Hz, –CH), 1.32 (t, 3H, *J*=7.0 Hz), 1.26 (t, 3H, *J*=7.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 168.0, 165.0, 162.4, 150.4, 129.2, 128.1, 124.6, 120.1, 116.5, 115.4, 73.4, 62.6, 59.9, 46.7, 36.8, 14.5, 13.9; FTIR (KBr): ν=3348, 2874, 2365, 2209, 1720, 1643, 827 cm$^{-1}$. Anal. Calcd for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.75; H, 5.69; N, 8.40.

*4.2.26. Ethyl 2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)-4H-chromene-3-carboxylate (**26**).* 94% yield in 35 min of reaction; Solid, mp 135–136 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40 (d, 1H, *J*=2.8 Hz, Ar–H), 7.38 (d, 1H, *J*=2.0 Hz, Ar–H), 7.25 (br s, 2H, –$NH_2$), 6.96 (d, 1H, *J*=8.8 Hz, Ar–H), 4.66 (d, 1H, *J*=3.6 Hz, –CH), 4.32–4.22 (m, 4H, –$OCH_2$), 3.96 (d, 1H, *J*=3.6 Hz), 1.34–1.28 (m, 6H, –$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.7, 164.8, 162.1, 149.5, 132.2, 130.9, 122.1, 118.3, 116.9, 115.1, 73.0, 63.0, 60.0, 46.5, 36.7, 14.5, 14.0; FTIR (KBr): ν=3336, 2854, 2375, 2219, 1735, 1649, 828 cm$^{-1}$. Anal. Calcd for $C_{17}H_{17}BrN_2O_5$: C, 49.89; H, 4.19; N, 6.85. Found: C, 49.76; H, 4.08; N, 6.71.

*4.2.27. Ethyl 2-amino-6-nitro-4-(1-cyano-2-ethoxy-2-oxoethyl)-4H-chromene-3-carboxylate (**27**).* 95% yield in 35 min of reaction; Solid, mp 141–142 °C; $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.20 (dd, 1H, *J*=2.8, 2.8 Hz, Ar–H), 8.07 (d, 1H, *J*=2.8 Hz, Ar–H), 7.21 (d, 1H, *J*=8.8 Hz, Ar–H), 5.28 (br s, 2H, –$NH_2$), 4.79 (d, 1H, *J*=3.2 Hz, –CH), 4.33–4.24 (m, 4H, –$OCH_2$), 4.02 (d, 1H, *J*=3.6 Hz), 1.34 (t, 3H, *J*=7.0 Hz, –$CH_3$), 1.29 (t, 3H, *J*=7.0 Hz, –$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.4, 164.5, 161.3, 154.6, 144.2, 125.1, 124.4, 121.2, 117.6, 114.8, 72.9, 63.3, 60.7, 46.6, 36.6, 14.4, 13.9; FTIR (KBr): ν=3345, 2845, 2357, 2240, 1725, 1664, 720 cm$^{-1}$. Anal. Calcd for $C_{17}H_{17}N_3O_7$: C, 54.40; H, 4.57; N, 11.20. Found: C, 54.34; H, 4.65; N, 11.10.

*4.2.28. 2(-2-Amino-3-cyano-4H-chromen-4-yl)malononitrile (**28**).* 95% yield in 25 min of reaction; Solid, mp 156–158 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): δ (ppm) 7.56–7.05 (m, 4H, Ar–H), 5.82 (br s, 2H, –$NH_2$), 5.02 (d, 1H, *J*=4.0 Hz, –P–CH), 4.55 (d, 1H, *J*=4.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 163.8, 150.1, 147.3, 130.5, 129.2, 125.4, 119.7, 118.3, 116.7, 37.5, 32.8; FTIR (KBr): ν=3359, 2876, 2363, 2209, 1643, 827 cm$^{-1}$. Anal. Calcd for $C_{13}H_8N_4O$: C, 66.10; H, 3.41; N, 23.72. Found: C, 65.85; H, 3.30; N, 23.60.

*4.2.29. 2(-2-Amino-6-bromo-3-cyano-4H-chromen-4-yl)malononitrile (**29**).* 98% yield in 34 min of reaction; Solid, mp 160–162 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): δ (ppm) 7.67 (d, 1H, *J*=4.0 Hz, Ar–H), 7.58 (t, 1H, *J*=2.4 Hz, Ar–H), 7.55 (br s, 2H, –$NH_2$), 7.08 (d, 1H, *J*=8.8 Hz, Ar–H), 5.10 (d, 1H, *J*=4.0 Hz), 4.58 (d, 1H, *J*=4.0 Hz); $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ (ppm) 163.6, 149.4, 132.0, 131.2120.7, 119.5, 119.2, 116.8, 113.4,48.8, 37.0, 32.4; FTIR (KBr): ν=3351, 2879, 2366, 2206, 1642, 826 cm$^{-1}$. Anal. Calcd for $C_{13}H_7BrN_4O$: C, 49.55; H, 2.24; N, 17.78. Found: C, 49.42; H, 2.18; N, 17.62.

*4.2.30. 2(-2-Amino-6-chloro-3-cyano-4H-chromen-4-yl)malononitrile (**30**).* 99% yield in 40 min of reaction; Solid, mp 158–160 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): δ (ppm) 7.55 (br s, 2H, –$NH_2$), 7.45 (d, 1H, *J*=1.6 Hz, Ar–H), 7.43 (d, 1H, *J*=2.4 Hz, Ar–H), 7.14 (d, 1H, *J*=8.8 Hz, Ar–H), 5.10 (d, 1H, *J*=4.0 Hz), 4.58 (d, 1H, *J*=3.6 Hz); $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ (ppm) 163.6, 148.9, 130.1, 129.0, 128.8, 128.6, 120.3, 119.5, 113.7 48.8, 37.3, 32.5; FTIR (KBr): ν=3351, 2888, 2189, 1650, 817 cm$^{-1}$. Anal. Calcd for $C_{13}H_7ClN_4O$: C, 57.69; H, 2.61; N, 20.70. Found: C, 56.95; H, 2.49; N, 20.52.

*4.2.31. 2(-2-Amino-6-nitro-3-cyano-4H-chromen-4-yl)malononitrile (**31**).* 97% yield in 40 min of reaction; Solid, mp 166–168 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): δ (ppm) 8.47 (d, 1H, *J*=2.8 Hz, Ar–H), 8.26 (d, 1H, *J*=2.4 Hz, Ar–H), 7.74 (br s, 2H, –$NH_2$), 7.36 (d, 1H, *J*=9.2 Hz, Ar–H), 5.18 (d, 1H, *J*=4.0 Hz), 4.76 (d, 1H, *J*=3.6 Hz); $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ (ppm) 163.1, 154.5, 144.2, 126.2, 125.7, 119.6, 118.5, 113.2, 113.0, 48.9, 37.2, 32.7; FTIR (KBr): ν=3317, 2896, 2206, 1659, 767 cm$^{-1}$. Anal. Calcd for $C_{13}H_7N_5O_3$: C, 55.52; H, 2.51; N, 24.90. Found: C, 55.50; H, 2.49; N, 24.89.

*4.2.32. 2(-2-Amino-8-methyl-3-cyano-4H-chromen-4-yl)malononitrile (**32**).* 95% yield in 36 min of reaction; Solid, mp 178–180 °C; $^1$H NMR (400 MHz, acetone-$d_6$): δ (ppm) 7.38 (d, 1H, *J*=7.6 Hz, Ar–H), 7.29 (d, 1H, *J*=7.2 Hz, Ar–H), 7.16 (t, 1H, *J*=7.4 Hz, Ar–H), 6.81 (br s, 2H, –$NH_2$), 4.73 (d, 1H, *J*=3.6 Hz), 4.53(d, 1H, *J*=3.2 Hz), 2.0 (s, 3H, –$CH_3$); $^{13}$C NMR (100 MHz, acetone-$d_6$): δ (ppm) 163.6, 148.5, 146.5, 131.4, 126.4, 126.0, 124.6, 118.0, 112.2, 51.0, 38.5, 32.2, 14.6; FTIR (KBr): ν=3315, 2898, 2203, 1649, 763 cm$^{-1}$. Anal. Calcd for $C_{14}H_{10}N_4O$: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.22; H, 4.05; N, 22.36.

## Acknowledgements

This work was supported by a two-year research grant from Pusan National University. The authors also thank to $BK_{21}$ PLUS Program for the financial support.

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