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# A simple and one-pot synthesis and investigation of biological activity of phosphonate derivatives

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**Abstract:** A simple, rapid, efficient and environmental method for the preparation of phosphonate derivatives has been realized using the reaction of aminohydroxy acethophenone, acetylenic compound, malononitrile or ethyl cyanoacetate and trialkyl phosphites or triaryl phosphites in water as the solvent at room temperature. The ability of some synthesized compounds to scavenge the DPPH radical was measured and the results proved this observation. Moreover, the antimicrobial activity of some synthesized compounds proved by employing the disk diffusion test on Gram-positive and Gram-negative bacteria. The obtained results of disk diffusion test showed that compound **5** prevented the bacterial growth.

**Keywords:** Aminohydroxy acethophenone, Malononitrile, Ethyl cyanoacetate, Phosphonate derivatives, Multi component reaction.

## Introduction

The use of water as a green media for organic synthesis has become a chief study area. In addition to the economical and environmental advantages, water also shows single physical and chemical properties which lead to exclusive reactivity and selectivity in assessment with organic solvents. Thus, the expansion of organic reaction in water medium is necessitating in the present days [1-7]. Performing organic reactions in water have become highly attractive in recent years to assemble environmental considerations [8-10]. Phosphorus compounds including the P–C bond are not mainly plentiful in nature but they have diverse biological activity and have attracted significant synthetic and pharmacological importance [11, 12].

Phosphonates have important applications in flame retardancy [13, 14], organic synthesis [15], and biological applications [16, 17]. Phosphonates have been utilized as substitutes of the corresponding esters and acids of high biological activity [18, 19] and as suitable probes for designing antibodies on the basis of transition state models.

Hence, a large number of methods have described novel synthesis of phosphonate systems [20-23]. Benzofuran derivatives exist in some natural products. [24]. It is noteworthy to mention that this class of compounds have potent biological and medicinal properties and are employed in the treatment of severe migraine and MS diseases. Many diseases such as cardiovascular, inflammatory bowel syndrome, cancer, ageing, atherosclerosis, and Alzheimer's disease could be prevented or decreased by employing these compounds. At present, bacteria that are resistant to drugs have generated considerable problems in the

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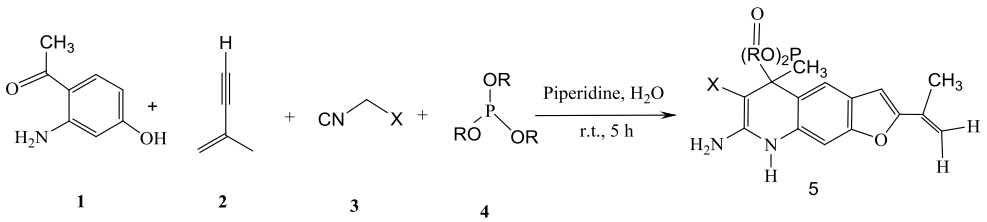
performance of many communicable diseases. Therefore, discovering new ways to extirpate these pathogens are important. For this reason, recent studies have focused on the study of the antibacterial effects of new synthesized compounds.

Herein, we display an efficient synthesis of phosphonate derivatives **5** *via* the reaction of aminohydroxy acethophenone, **1**, acetylenic compound **2** malononitrile or ethyl cyanoacetate **3** in the presence of trialkyl phosphite or triaryl phosphite **4** in water at room temperature (Scheme **1**).




1 2 3 4 5

| 5 | R | X | Yield/ % of **5** |
|---|---|---|---|
| **a** | Me | CN | 90 |
| **b** | Et | CN | 87 |
| **c** | Ph | CN | 85 |
| **d** | Me | $CO_2Et$ | 85 |
| **e** | Et | $CO_2Et$ | 87 |
| **f** | Ph | $CO_2Et$ | 80 |

**Scheme 1.** Synthesis of phosphonate derivatives **5**.

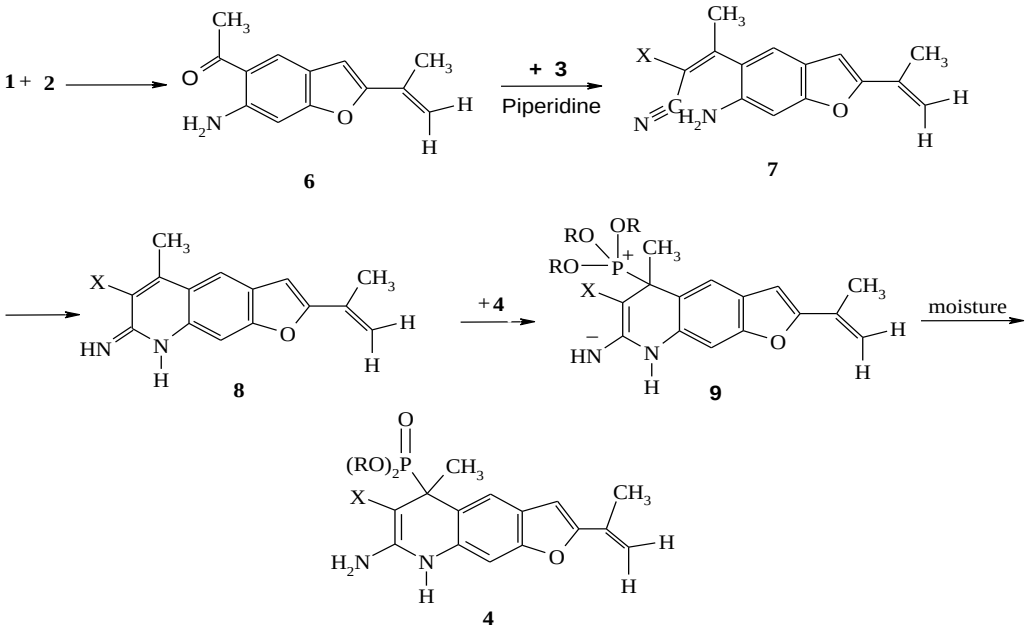
## Results and discussion

Four component reactions between aminohydroxy acethophenone, **1**, acetylenic compound **2** malononitrile or ethyl cyanoacetate **3** in the presence of trialkyl phosphite or triaryl phosphite **4** was produced phosphonate derivatives **5** in excellent yields (Scheme **1**). Structures of compounds **5a–5f** were assumed from their IR, mass, $^1$H NMR and $^{13}$C NMR spectra. The $^1$H NMR spectrum of **5a** exhibited one doublet at 1.75 ppm (d, $^3J_{PH}$ = 10.2 Hz) for methyl protons and one singlet for another methyl protons at $\delta$ 2.15 ppm. The methoxy groups of the phosphoranyl moiety are diastereotopic and display two separate doublets at 3.68 (d, $^3J_{PH}$ = 9.8 Hz) and 3.78 (d, $^3J_{PH}$ = 9.8 Hz) ppm. The $^{13}$C NMR spectrum of **5a** showed one doublet for methyl at 16.8 (d, $^2J_{PC}$ = 8.5 Hz) and two doublets for methoxy groups of the phosphoranyl moiety at 51.2 (d, $^2J_{PC}$ = 8.7 Hz) and 52.4 (d, $^2J_{PC}$ = 8.7 Hz) in agreement with the proposed structure. $^{31}$P NMR signal was found at $\delta$ = 19.4 ppm. A proposed mechanism for the formation of compound **5** is shown in Scheme 2. It is plausible that the initial event is the formation of intermediate **6** from the addition reaction of **1** and 2. Intermediate 5 react with malononitrile or ethyl cyanoacetate **3** and produced intermediate **6**. Cyclization of intermediate **6** produces intermediate **7**. Intermediate **7** converted to **8** by phospha-michael addition of phosphite **4**. Finally, in the presence of moisture, intermediate **8** generates compound **5**.

### *Study of antioxidant activity employing Diphenyl-2-picrylhydrazyl (DPPH):*

For determination of antioxidant activity of some synthesized compounds and their antioxidant property in foods and biological systems as well as power of compounds to take free radicals, diphenyl-2-picrylhydrazyl (DPPH) radical trapping experiment is widely used. In this experiment, the DPPH radical takes the hydrogen atom (or one electron) of synthesized compounds 5a-5d and gives an evaluation of antioxidant activity basis of free radical trapping. The absorption of DPPH radical was observed area 517 nm but when DPPH radical is reduced by an antioxidant or a radical species its absorption decreases. As shown from the results, free radical trapping activity of compounds 5a-5d is weaker than to BHT and TBHQ. Therefore, concentration and structure were key factor on the DPPH trapping activity ($P<0.05$) (Figure 1). Normally, the DPPH scavenging ability of these compounds was attained TBHQ>BHT>5b>5d>5c>5a respectively. The free radical trapping power had been enhanced from 200 to 1000 ppm. So, by rising concentration in all samples, the free radical activity was raised. For instance,

compound 5b with a concentration of 1000 ppm had 91.76% inhibition while a concentration of 200 ppm of compound 5b was exhibited 47.93% free radical inhibition.




**Scheme 2**: Proposed mechanism for the one-pot synthesis of compound **5**

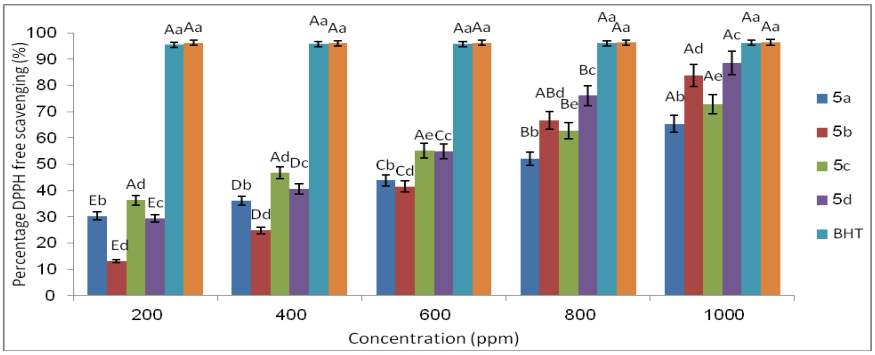



**Figure 1.** Radical trapping activity (RSA) of compounds **5a-5d:**

**Analysis of the antibacterial activity of synthesized compounds:**

Also, a comparison between the activity of our synthesized compounds with Streptomycin and Gentamicin as standard drug was discussed. The results of the antimicrobial activity of some synthezized compounds on bacterial species are shown in Table 4. The present study indicated that the type of bacteria and concentration of compounds are effective on the diameter of the inhibition zone. It is apparent from the data listed in Table 3, the synthesized compounds **5a-5f** are active against Gram positive and Gram negative bacteria So that the inhibition zone diameter of compounds has the maximum effect on *Escherichia coli*.

**Table 4.** The antibacterial activity of the tested compounds:

| *Compounds* | *Staphylococcus aureus* (+) | *Bacillus subtilis* (+) | *Bacillus cereus* (+) | *Pseudomonas aurignosa* (-) | *Escherichia coli*(-) | *Klebsiella pneumoniae* (-) |
|---|---|---|---|---|---|---|
| **5a** | 8 | 6 | 10 | 8 | 12 | --- |
| **5b** | **15** | **19** | **19** | **17** | **24** | **20** |
| **5c** | **18** | **19** | **21** | **18** | **25** | **17** |
| **5d** | 8 | --- | 9 | 8 | 10 | 8 |
| **5e** | **16** | **18** | **20** | **16** | **23** | **21** |
| **5f** | 8 | 10 | 9 | 9 | 12 | --- |
| **Streptomycin** | 16 | 24 | 24 | 19 | 25 | 23 |
| **Gentamicin** | 19 | 22 | 23 | 18 | 24 | 21 |

## Conclusion

In conclusion, we described a new and successful strategy for the convenient synthesis of phosphonate derivatives **5** in excellent yields *via* a four component reactions between aminohydroxy acethophenone, **1**, acetylenic compound **2** malononitrile or ethyl cyanoacetate **3** in the presence of trialkyl phosphite or triaryl phosphite **4**. The method offers several advantages including high yields of products and an easy experimental work-up procedure.

## Experimental

Other chemicals were obtained from commercial sources. Melting points were measured on a Kofler hot stage apparatus and were uncorrected. $^{1}$H NMR and $^{13}$C NMR spectra were obtained with a Bruker FT-500 spectrometer in chloroform-d1, and tetramethylsilane (TMS) was used as an internal standard. Mass spectra were recorded with a Finnigan Mat TSQ-70 spectrometer. Infrared (IR) spectra were acquired on a Nicollet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, N) were within ±0.4% of the calculated values.

### *General procedure for preparation of compounds 5a-f :*

To a magnetically stirred mixture of **1** (2 mmol) and **2** was added malononitrile or ethyl cyanoacetate **3** (2 mmol) and piperidine (2 mmol) in water (5 mL) as the solvent, phosphites **4** (2 mmol) were added after 45 min. The reaction mixture was stirred for 5h. After completion of reaction (monitored by TLC), the reaction mixture was filtered and the solid residue was purified by cold diethylether to afford **5**.

### *Dimethyl(7-amino-6-cyano-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-5-yl)phosphonate (5a):*

Yellow powder; m.p.: 162-164 °C; yield: 0.67 g (90%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3342, 3158, 2985, 2167, 1647, 1485, 1295 cm$^{-1}$. $^{1}$H NMR (500.1 MHz, $CDCl_3$): $\delta$ = 1.75 (3 H, d, $^{3}J_{PH}$ = 10.2 Hz, $CH_3$), 2.15 (3 H, s, $CH_3$), 3.68 (3 H, d, $^{3}J_{PH}$ = 9.8 Hz, $CH_3O$), 3.78 (3 H, d, $^{3}J_{PH}$ = 9.8 Hz, $CH_3O$), 4.75 (1 H, d, $^{2}J$ = 4.2 Hz, CH), 5.42 (1 H, s, CH), 5.76 (1 H, d, $^{2}J$ = 4.2 Hz, CH), 7.34 (1 H, s, CH), 7.87 (1 H, s, CH), 8.04 (2 H, s, $NH_2$). $^{13}$C NMR (125.7 MHz, $CDCl_3$): $\delta$ = 16.8 (d, $^{2}J_{PC}$ = 8.5 Hz, $CH_3$), 18.6 ($CH_3$), 41.2 (d, $^{1}J_{PC}$ = 140.2 Hz, C), 51.2 (d, $^{2}J_{PC}$ = 8.7 Hz, MeO), 52.4 (d, $^{2}J_{PC}$ = 8.7 Hz, MeO), 71.4 (CH), 73.4 (d, $^{2}J_{PC}$ = 9.2 Hz, C), 96.3 (CH), 111.4 (d, $^{2}J_{PC}$ = 7.6 Hz, C), 113.5 (d, $^{3}J_{PC}$ = 18.6 Hz, CN),114.3 ($CH_2$), 125.3 (C), 126.2 (d, $^{3}J_{PC}$ = 22.4 Hz, CH), 136.2 (C), 142.3 (d, $^{3}J_{PC}$ = 21.7 Hz, C), 155.2 (C), 157.3 (d, $^{3}J_{PC}$ = 22.4 Hz, C), 158.3 (C). $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 19.4. MS: *m/z* (%) = 374 ($M^+$, 15), 343 (68), 31 (100). Anal. Calc. for $C_{18}H_{19}N_2O_5P$ (374.33): C, 57.75; H, 5.12; N, 7.48 found: C, 57.83; H, 5.23; N, 7.56%.

### *Diethyl(7-amino-6-cyano-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-5-yl)phosphonate (5b):*

Yellow powder; m.p.: 175-178 °C; yield: 0.69 g (87%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3338, 3167, 2994, 2174, 1658, 1482, 1283 cm$^{-1}$. $^{1}$H NMR (500.1 MHz, $CDCl_3$):

$\delta$ = 1.23 (3 H, t, $^3J_{HH}$ = 7.5 Hz, $CH_3$), 1.34 (3 H, t, $^3J_{HH}$ = 7.4 Hz, $CH_3$), 1.82 (3 H, d, $^3J_{PH}$ = 10.5 Hz, $CH_3$), 2.17 (3 H, s, $CH_3$), 3.85 (2 H, m, $CH_2O$), 4.12 (2 H, m, $CH_2O$), 4.82 (1 H, d, $^2J$ = 3.6 Hz, CH), 5.53 (1 H, s, CH), 5.82 (1 H, d, $^2J$ = 3.6 Hz, CH), 7.36 (1 H, s, CH), 7.85 (1 H, s, CH), 8.06 (2 H, s, $NH_2$). $^{13}$C NMR (125.7 MHz, $CDCl_3$): $\delta$ = 14.3 (d, $^3J_{PC}$ = 13.8 Hz, $CH_3$), 14.6 (d, $^3J_{PC}$ = 13.8 Hz, $CH_3$), 17.2 (d, $^2J_{PC}$ = 9.4 Hz, $CH_3$), 18.7 ($CH_3$), 41.5 (d, $^1J_{PC}$ = 139.7 Hz, C), 61.2 (d, $^2J_{PC}$ = 9.3 Hz, $CH_2O$), 62.4 (d, $^2J_{PC}$ = 9.3 Hz, $CH_2O$), 72.4 (CH), 74.6 (d, $^2J_{PC}$ = 9.5 Hz, C), 97.6 (CH), 110.8 (d, $^2J_{PC}$ = 8.3 Hz, C), 113.7 (d, $^3J_{PC}$ = 21.4 Hz, CN),114.8 ($CH_2$), 126.2 (C), 126.8 (d, $^3J_{PC}$ = 23.2 Hz, CH), 136.6 (C), 143.4 (d, $^3J_{PC}$ = 22.3 Hz, C), 156.7 (C), 157.5 (d, $^3J_{PC}$ = 22.4 Hz, C), 159.4 (C). $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 20.4. MS: *m*/*z* (%) = 402 ($M^+$, 10), 357 (88), 45 (100). Anal. Calc. for $C_{20}H_{23}N_2O_5P$ (402.38): C, 59.70; H, 5.76; N, 6.96. found: C, 59.83; H, 5.85; N, 7.07%.

***Diphenyl(7-amino-6-cyano-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-5-yl)phosphonate (5c):***

Yellow powder; m.p.: 183-185 °C; yield: 0.85 g (85%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3343, 3214, 2857, 1695, 1547, 1354 cm$^{-1}$. $^1$H NMR (500.1 MHz, $CDCl_3$): $\delta$ = 1.94 (3 H, d, $^3J_{PH}$ = 11.2 Hz, $CH_3$), 2.15 (3 H, s, $CH_3$), 4.78 (1 H, d, $^2J$ = 3.8 Hz, CH), 5.68 (1 H, s, CH), 5.87 (1 H, d, $^2J$ = 3.8 Hz, CH), 6.87 (2 H, d, $^3J_{HH}$ = 7.4 Hz, 2 CH), 7.12 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.24 (2 H, t, $^3J_{HH}$ = 7.3 Hz, 2 CH), 7.32 (2 H, t, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.38 (1 H, t, $^3J_{HH}$ = 7.3 Hz, CH), 7.42 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.54 (1 H, s, CH), 7.92 (1 H, s, CH), 8.24 (2 H, s, $NH_2$). $^{13}$C NMR (125.7 MHz, $CDCl_3$): $\delta$ = 17.5 (d, $^2J_{PC}$ = 9.8 Hz, $CH_3$), 19.2 ($CH_3$), 42.3 (d, $^1J_{PC}$ = 141.4 Hz, C), 73.8 (CH), 82.4 (d, $^2J_{PC}$ = 10.2 Hz, C), 98.3 (CH), 113.7 ($CH_2$), 114.2 (d, $^2J_{PC}$ = 9.5 Hz, C), 115.4 (d, $^3J_{PC}$ = 20.8 Hz, CN), 119.4 (d, $^3J_{PC}$ = 22.5 Hz, 2 CH), 121.3 (d, $^3J_{PC}$ = 22.6 Hz, 2 CH), 122.4 (CH), 123.5 (CH), 126.5 (C), 127.2 (d, $^3J_{PC}$ = 22.6 Hz, CH), 128.0 (2 CH), 128.6 (2 CH), 134.6 (C), 138.4 (d, $^3J_{PC}$ = 23.2 Hz, C), 148.5 (d, $^2J_{PC}$ = 11.8 Hz, C), 149.6 (d, $^2J_{PC}$ = 11.8 Hz, C), 155.4 (C), 158.6 (d, $^3J_{PC}$ = 22.8 Hz, C), 159.6 (C). $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 21.2. MS: *m*/*z* (%) = 498 ($M^+$, 20), 405 (68), 93 (86), 77 (100). Anal. Calc. for $C_{28}H_{23}N_2O_5P$ (498.47): C, 67.47; H, 4.65; N, 5.62. found: C, 67.56; H, 4.73; N, 5.72%.

***Ethyl 7-amino-5-(dimethoxyphosphoryl)-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-6-carboxylate (5d):***

Yellow powder; m.p.: 148-150 °C; yield: 0.71g (85%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3340, 3164, 2992, 2175, 1668, 1492, 1285 cm$^{-1}$. $^1$H NMR (500.1 MHz, $CDCl_3$): $\delta$ = 1.24 (3 H, t, $^3J_{HH}$ = 7.3 Hz, $CH_3$), 1.84 (3 H, d, $^3J_{PH}$ = 10.5 Hz, $CH_3$), 2.17 (3 H, s, $CH_3$), 3.65 (3 H, d, $^3J_{PH}$ = 9.2 Hz, $CH_3O$), 3.75 (3 H, d, $^3J_{PH}$ = 9.2 Hz, $CH_3O$), 4.22 (2 H, q, $^3J_{HH}$ = 7.3 Hz, $CH_2O$), 4.78 (1 H, d, $^2J$ = 3.5 Hz, CH), 5.57 (1 H, s, CH), 5.82 (1 H, d, $^2J$ = 3.5 Hz, CH), 7.42 (1 H, s, CH), 7.93 (1 H, s, CH), 8.12 (2 H, s, $NH_2$). $^{13}$C NMR (125.7 MHz, $CDCl_3$): $\delta$ = 14.0 ($CH_3$), 17.3 (d, $^2J_{PC}$ = 9.4 Hz, $CH_3$), 18.7 ($CH_3$), 42.4 (d, $^1J_{PC}$ = 138.4 Hz, C), 51.5 (d, $^2J_{PC}$ = 9.0 Hz, MeO), 52.6 (d, $^2J_{PC}$ = 9.0 Hz, MeO), 61.4 ($CH_2O$), 82.7 (CH), 85.6 (d, $^2J_{PC}$ = 9.7 Hz, C), 97.5 (CH), 112.3 (d, $^2J_{PC}$ = 8.9 Hz, C), 113.8 ($CH_2$), 123.4 (C), 125.5 (CH), 136.2 (C), 140.2 (d, $^3J_{PC}$ = 22.3 Hz, C), 156.2 (C), 157.8 (C), 158.2 (d, $^3J_{PC}$ = 22.5 Hz, C), 164.2 (d, $^3J_{PC}$ = 21.3 Hz, C=O). $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 18.6. MS: *m*/*z* (%) = 421 ($M^+$, 10), 390 (88), 31 (100). Anal. Calc. for $C_{20}H_{24}NO_7P$ (421.38): C, 57.01; H, 5.12; N, 3.32. found: C, 57.14; H, 5.23; N, 3.42%.

***Ethyl 7-amino-5-(diethoxyphosphoryl)-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-6-carboxylate (5e):***

Yellow powder; m.p.: 153-155 °C; yield: 0.78 g (87%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3340, 3165, 2986, 2147, 1696, 1452, 1297 cm$^{-1}$. $^1$H NMR (500.1 MHz, $CDCl_3$): $\delta$ = 1.19 (3 H, t, $^3J_{HH}$ = 7.4 Hz, $CH_3$), 1.25 (3 H, t, $^3J_{HH}$ = 7.3 Hz, $CH_3$), 1.32 (3 H, t, $^3J_{HH}$ = 7.3 Hz, $CH_3$), 1.79 (3 H, d, $^3J_{PH}$ = 10.2 Hz, $CH_3$), 2.12 (3 H, s, $CH_3$), 4.03 (2 H, m, $CH_2O$), 4.15 (2 H, m, $CH_2O$), 4.24 (2 H, q, $^3J_{HH}$ = 7.3 Hz, $CH_2O$), 5.02 (1 H, d, $^2J$ = 3.5 Hz, CH), 5.85 (1 H, s, CH), 5.93 (1 H, d, $^2J$ = 3.5 Hz, CH), 7.42 (1 H, s, CH), 7.87 (1 H, s, CH), 8.15 (2 H, s, $NH_2$). $^{13}$C NMR (125.7 MHz, $CDCl_3$): $\delta$ = 14.2 ($CH_3$), 15.8 (d, $^3J_{PC}$ = 14.5 Hz, $CH_3$), 16.2 (d, $^3J_{PC}$ = 14.5 Hz, $CH_3$), 17.5 (d, $^2J_{PC}$ = 9.3 Hz, $CH_3$), 19.3 ($CH_3$), 42.3 (d, $^1J_{PC}$ = 141.2 Hz, C), 61.2 ($CH_2O$), 62.3 (d, $^2J_{PC}$ = 10.2 Hz, $CH_2O$), 62.7 (d, $^2J_{PC}$ = 10.2 Hz, $CH_2O$), 82.4 (CH), 84.6 (d, $^2J_{PC}$ = 10.8 Hz, C), 98.3 (CH), 111.3 (d, $^2J_{PC}$ = 9.5 Hz, C), 113.4 ($CH_2$), 123.4 (C), 124.8 (CH), 134.6 (C), 140.3 (d, $^3J_{PC}$ = 21.4 Hz, C), 155.3 (C), 156.5 (C), 158.2 (d, $^3J_{PC}$ = 22.6 Hz, C), 167.4 (d, $^3J_{PC}$ = 23.4 Hz, C=O). $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 21.7. MS: *m*/*z* (%) = 449 ($M^+$, 15), 404 (78), 45 (100). Anal. Calc. for $C_{22}H_{28}NO_7P$ (449.43): C, 58.79; H, 6.28; N, 3.12. found: C, 58.87; H, 6.36; N, 3.24%.

***Ethyl 7-amino-5-(diphenoxyphosphoryl)-2-isopropenyl-5-methyl-5H-furo[3,2-g]chromene-6-carboxylate (5f):***

Yellow powder; m.p.: 193-195 °C; yield: 0.87 g (80%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3342, 3225, 2864, 1692,

1567, 1326, 1274 $cm^{-1}$. $^1H$ NMR (500.1 MHz, $CDCl_3$): $\delta$ = 1.25 (3 H, t, $^3J_{HH}$ = 7.3 Hz, $CH_3$), 1.95 (3 H, d, $^3J_{PH}$ = 10.8 Hz, $CH_3$), 2.18 (3 H, s, $CH_3$), 4.25 (2 H, q, $^3J_{HH}$ = 7.3 Hz, $CH_2O$), 4.83 (1 H, d, $^2J$ = 4.5 Hz, CH), 5.74 (1 H, d, $^2J$ = 4.5 Hz, CH), 6.02 (1 H, s, CH), 6.92 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.17 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.28 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.35 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.43 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.62 (1 H, s, CH), 8.12 (1 H, s, CH), 10.2 (2 H, s, $NH_2$). $^{13}C$ NMR (125.7 MHz, $CDCl_3$): $\delta$ = 14.2 ($CH_3$), 18.2 (d, $^2J_{PC}$ = 10.5 Hz, $CH_3$), 19.5 ($CH_3$), 43.7 (d, $^1J_{PC}$ = 142.4 Hz, C), 61.4 ($CH_2O$), 79.5 (CH), 98.3 (CH), 102.4 (d, $^2J_{PC}$ = 10.8 Hz, C), 114.2 ($CH_2$), 114.6 (d, $^2J_{PC}$ = 9.6 Hz, C), 115.4 (d, $^3J_{PC}$ = 20.8 Hz, CN), 119.6 (d, $^3J_{PC}$ = 22.6 Hz, 2 CH), 122.4 (d, $^3J_{PC}$ = 22.6 Hz, 2 CH), 123.2 (CH), 123.8 (CH), 125.8 (C), 126.5 (d, $^3J_{PC}$ = 22.4 Hz, CH), 128.2 (2 CH), 128.7 (2 CH), 135.2 (C), 136.2 (d, $^3J_{PC}$ = 23.5 Hz, C), 149.2 (d, $^2J_{PC}$ = 12.0 Hz, C), 150.1 (d, $^2J_{PC}$ = 12.0 Hz, C), 156.2 (C), 157.2 (C), 159.6 (d, $^3J_{PC}$ = 23.2 Hz, C), 164.3 (d, $^3J_{PC}$ = 21.4 Hz, C=O) ppm. $^{31}P$ NMR (202 MHz, $CDCl_3$): $\delta$ 20.7. MS: *m/z* (%) = 545 ($M^+$, 15), 452 (48), 93 (62), 77 (100). Anal. Calc. for $C_{30}H_{28}NO_7P$ (545.52): C, 66.05; H, 5.17; N, 2.57. found: C, 66.18; H, 5.32; N, 2.68%.

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