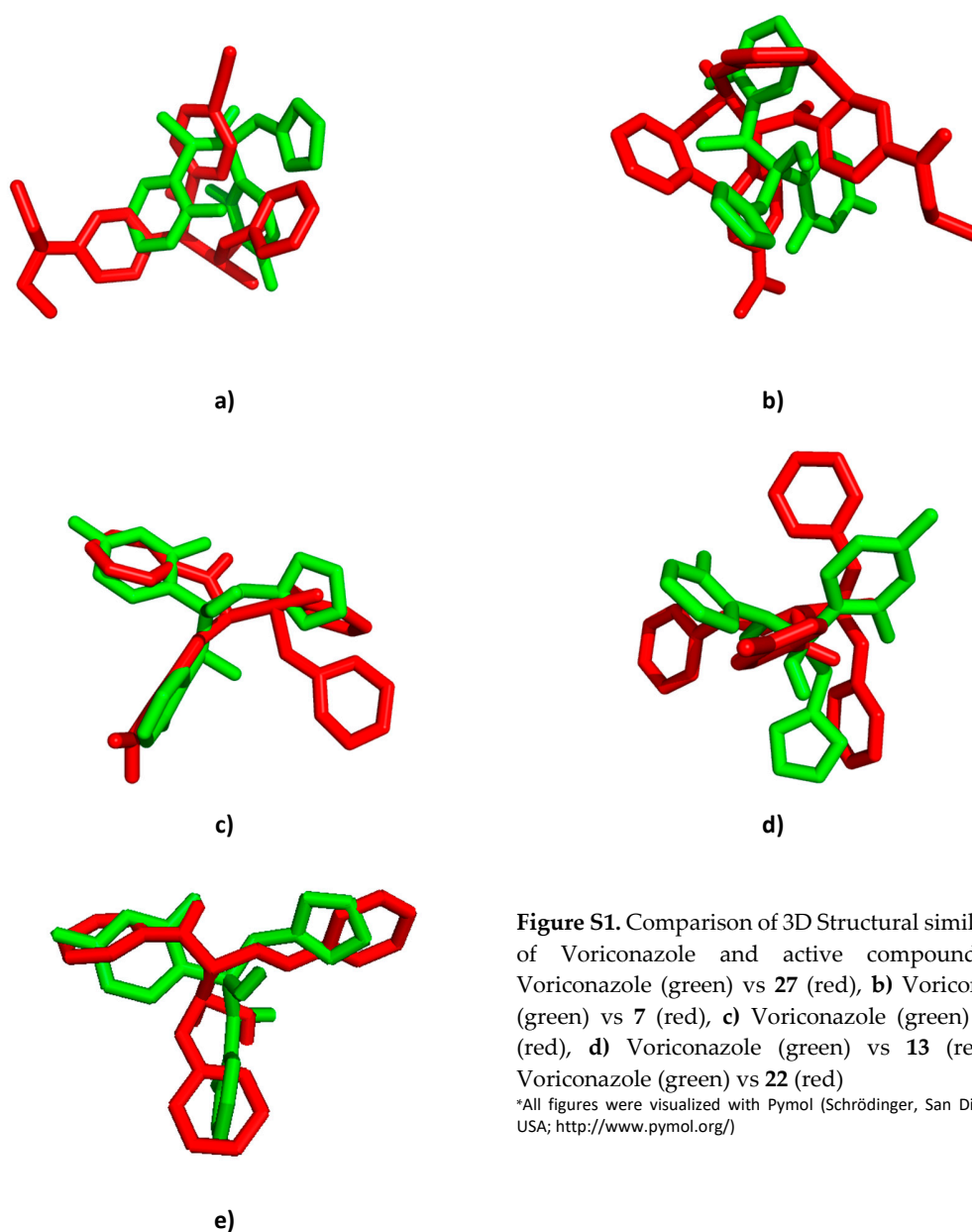


Supporting Information

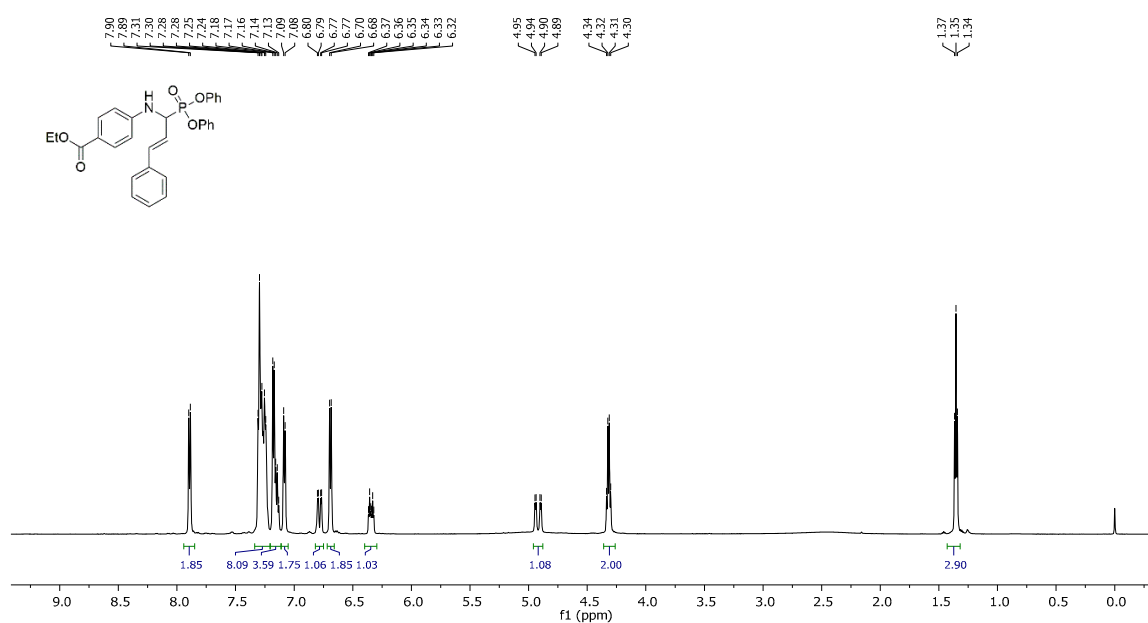
**Microwave-Assisted Synthesis of Aminophosphonic Derivatives and Their Antifungal Evaluation against *Lomentospora prolificans*.**

Zuleyma Martínez-Campos<sup>1</sup>, Mariana-Elizondo-Zertuche<sup>2</sup>, Emanuel Hernández-Núñez<sup>3</sup>, Eugenio Hernández-Fernández<sup>1\*</sup>, Efrén Robledo-Leal<sup>4\*</sup>, and Susana T. López-Cortina<sup>1\*</sup>

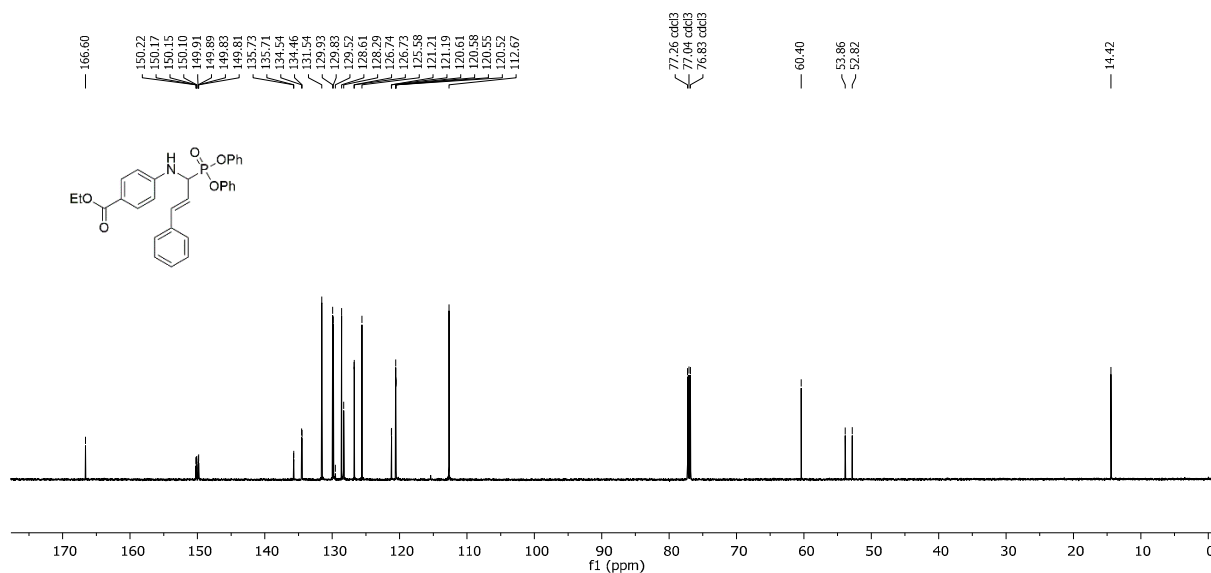


**Figure S1.** Comparison of 3D Structural similarities of Voriconazole and active compounds, **a)** Voriconazole (green) vs **27** (red), **b)** Voriconazole (green) vs **7** (red), **c)** Voriconazole (green) vs **11** (red), **d)** Voriconazole (green) vs **13** (red), **e)** Voriconazole (green) vs **22** (red)

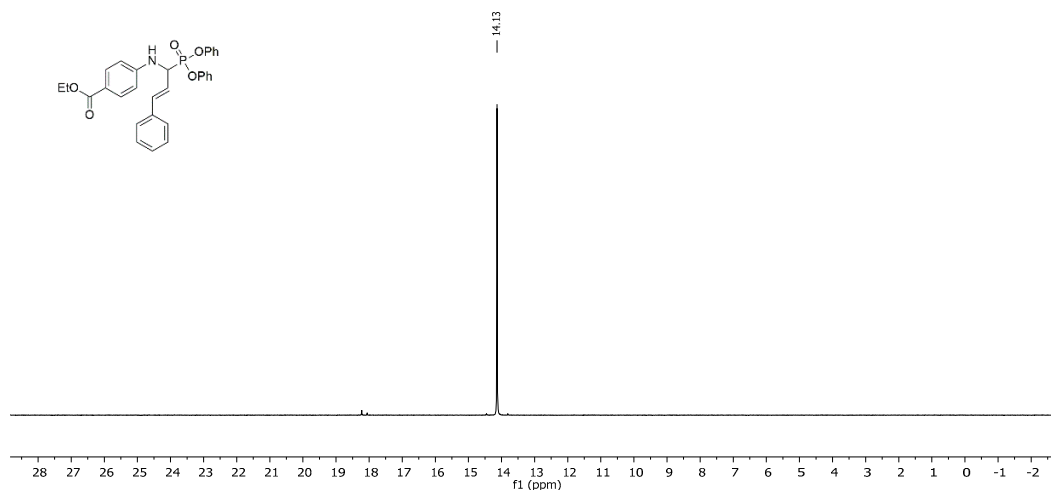
\*All figures were visualized with Pymol (Schrödinger, San Diego, CA, USA; <http://www.pymol.org/>)



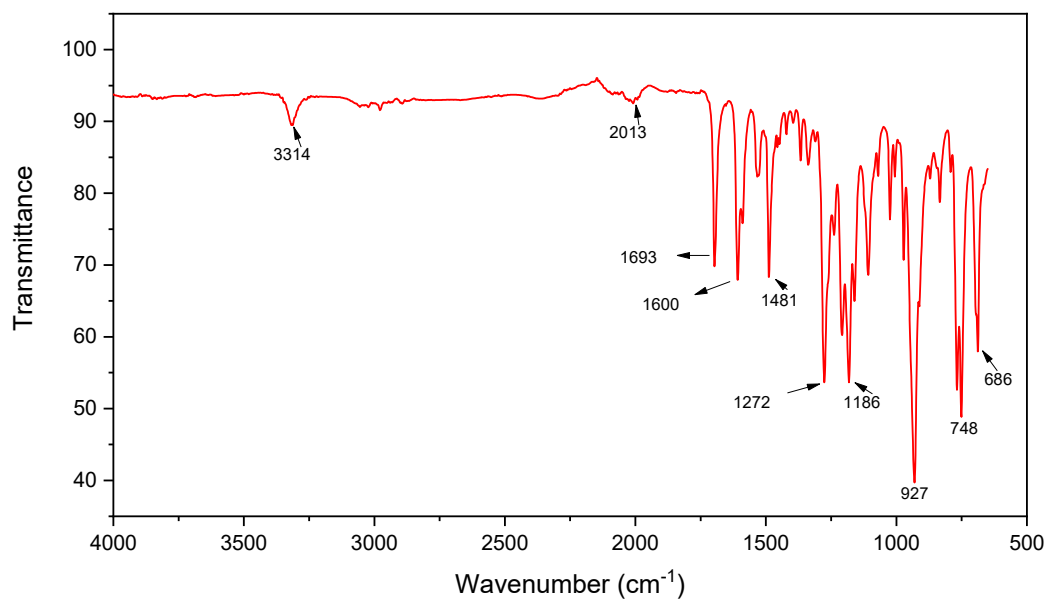
**Figure S2.** <sup>1</sup>H NMR (700 MHz, CDCl<sub>3</sub>) of (*E*)-ethyl 4-((1-(diphenoxyphosphoryl)-3-phenylallyl)amino)benzoate (5)



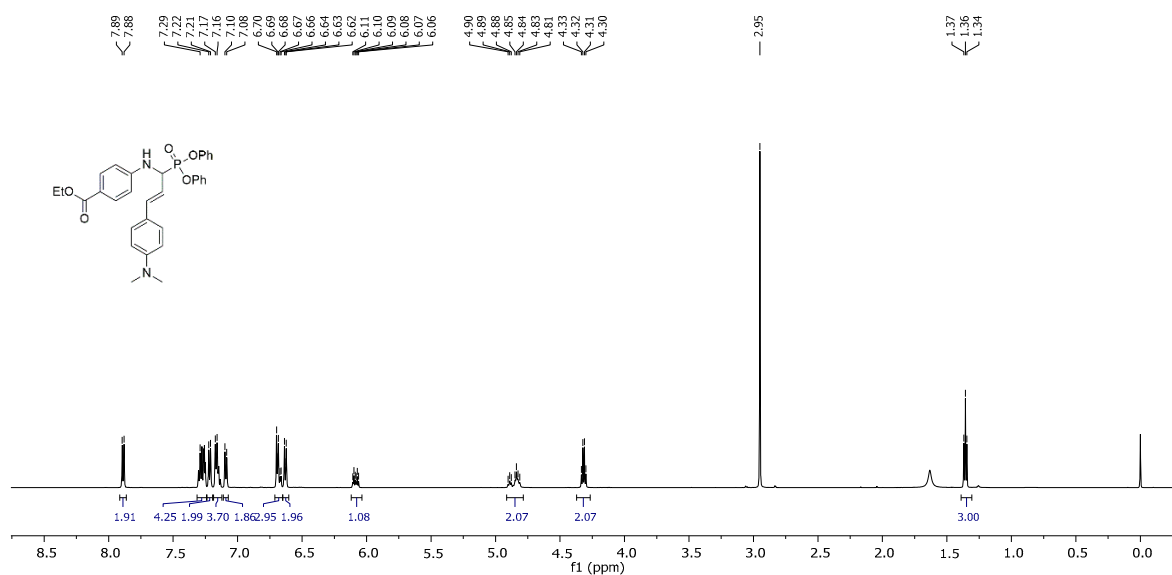
**Figure S3.** <sup>13</sup>C NMR (176 MHz, CDCl<sub>3</sub>) of (*E*)-ethyl 4-((1-(diphenoxyphosphoryl)-3-phenylallyl)amino)benzoate (5)



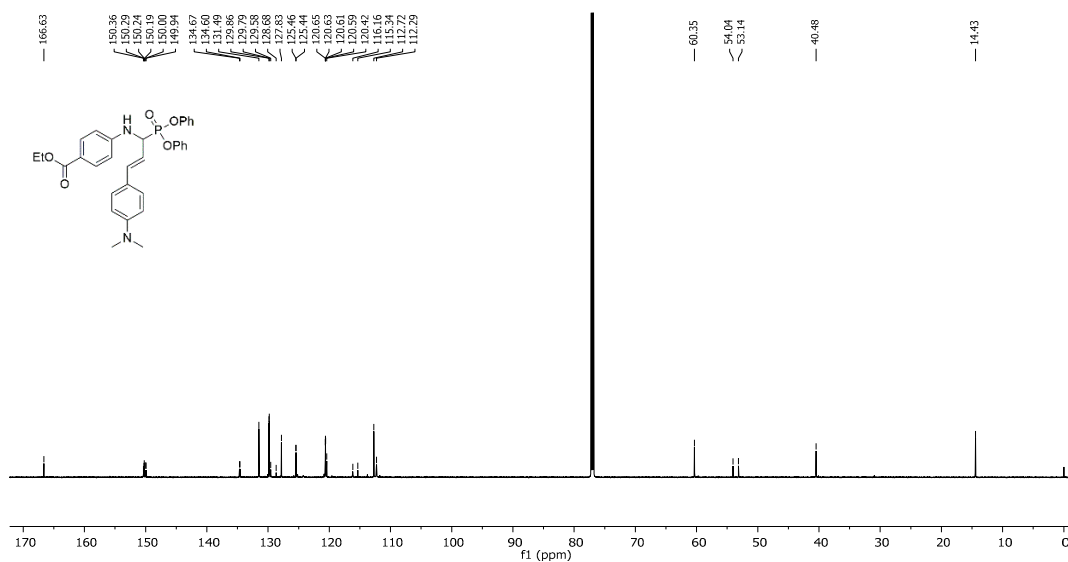
**Figure S4.** <sup>31</sup>P NMR (243 MHz CDCl<sub>3</sub>) of (*E*)-ethyl 4-((1-(diphenoxyphosphoryl)-3-phenylallyl)amino)benzoate (5)



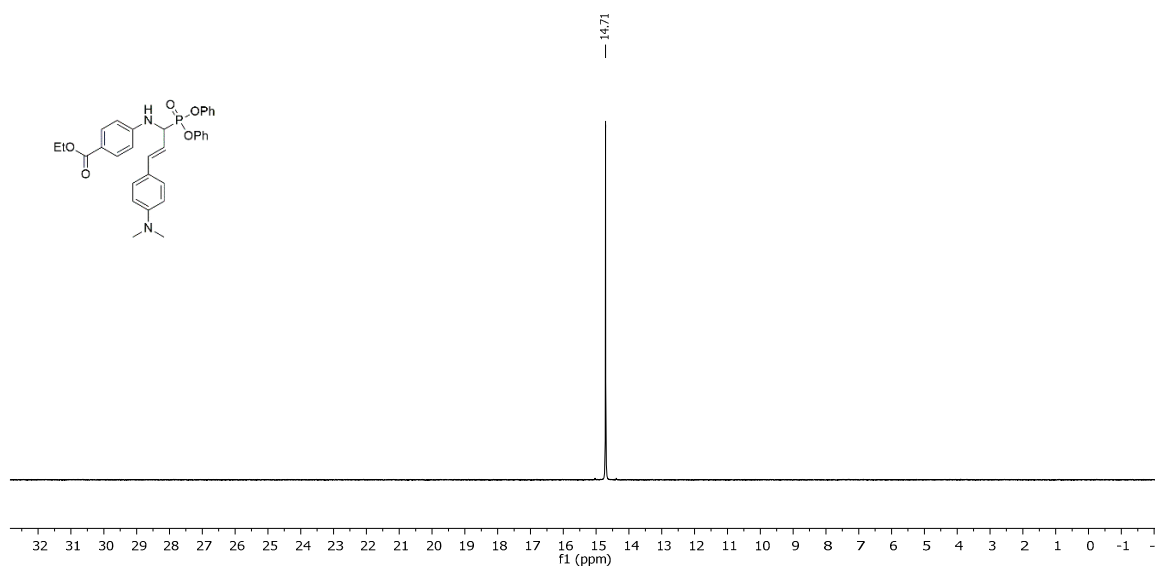
**Figure S5.** IR spectrum of (*E*)-ethyl 4-((1-(diphenoxyphosphoryl)-3-phenylallyl)amino)benzoate (5)



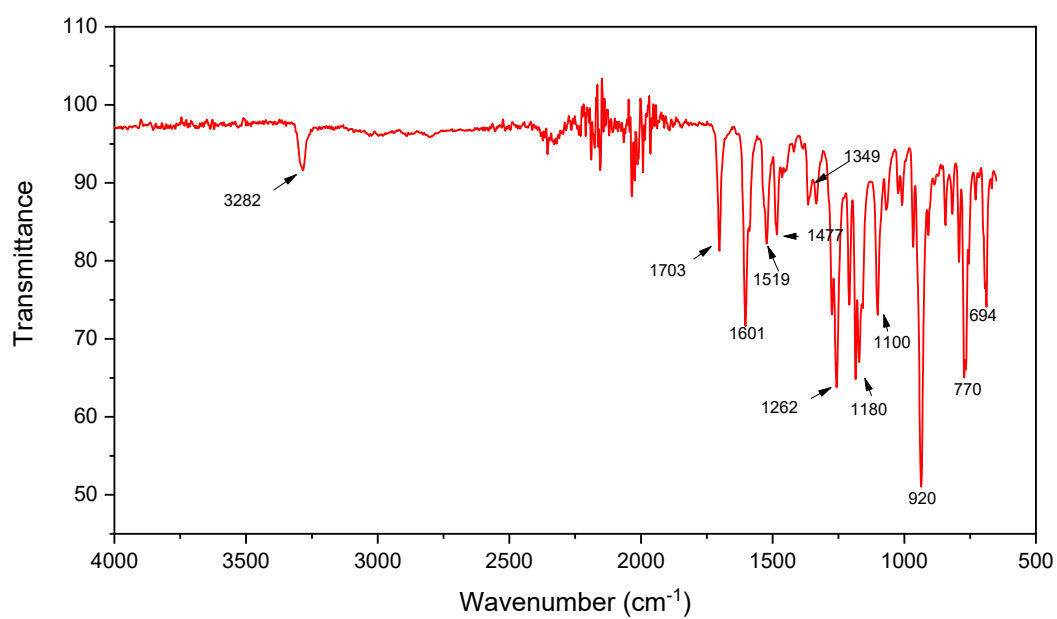
**Figure S6.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(diphenoxyphosphoryl)allyl)amino)benzoate (**6**)



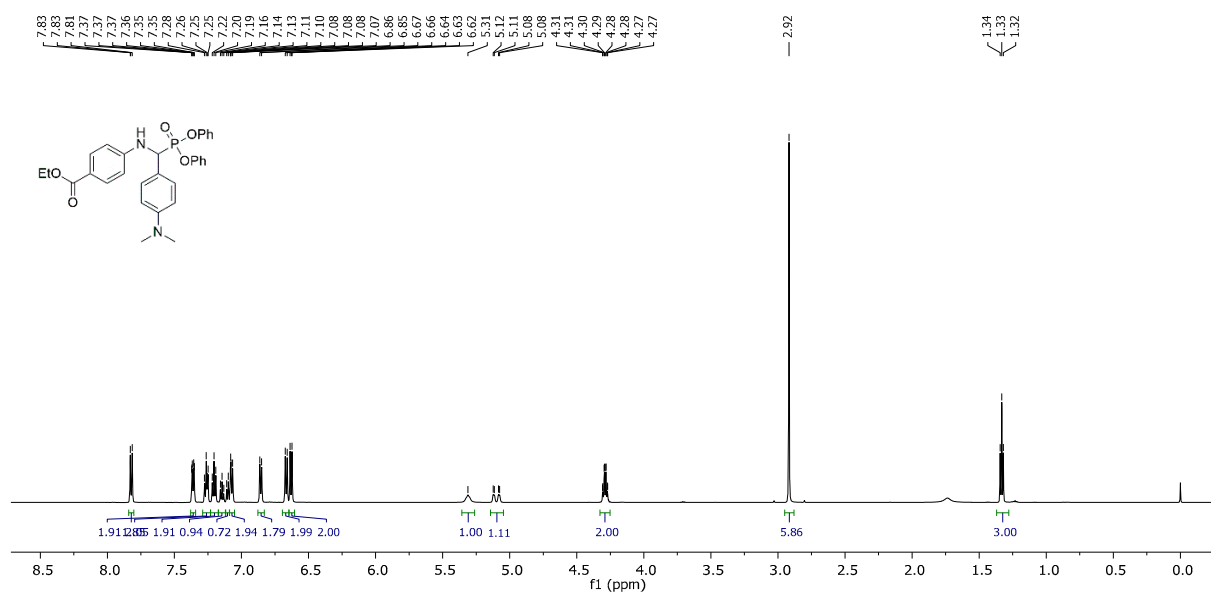
**Figure S7.** <sup>13</sup>C NMR (176 MHz, CDCl<sub>3</sub>) of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(diphenoxyphosphoryl)allyl)amino)benzoate (**6**)



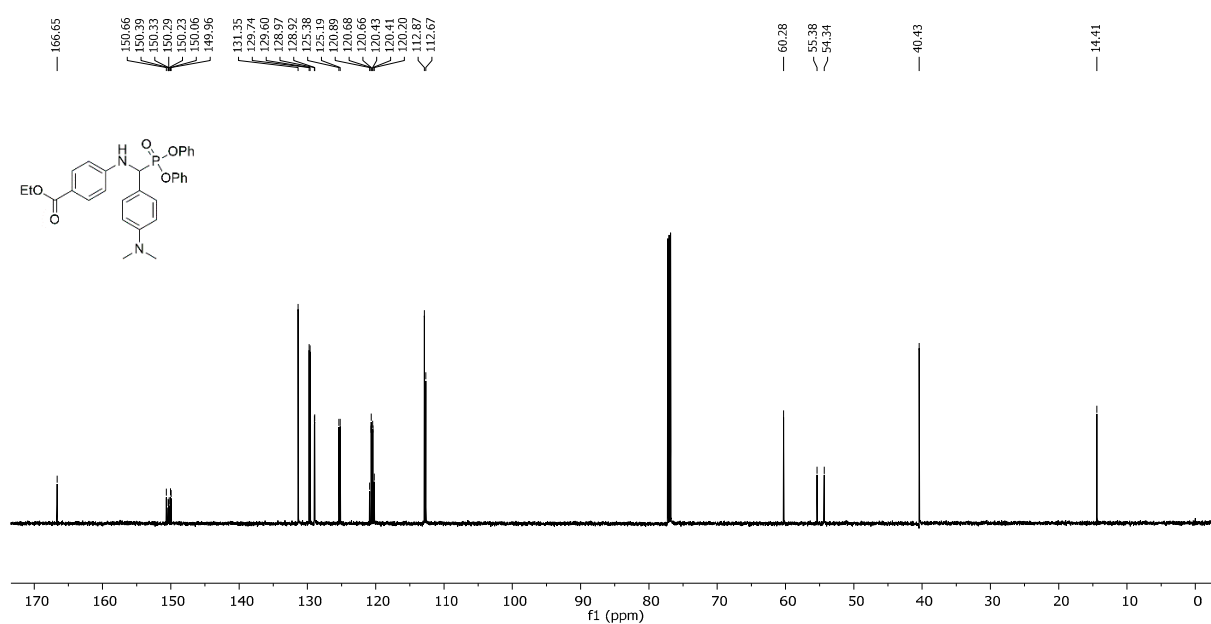
**Figure S8.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(diphenoxyphosphoryl)allyl)amino)benzoate (**6**)



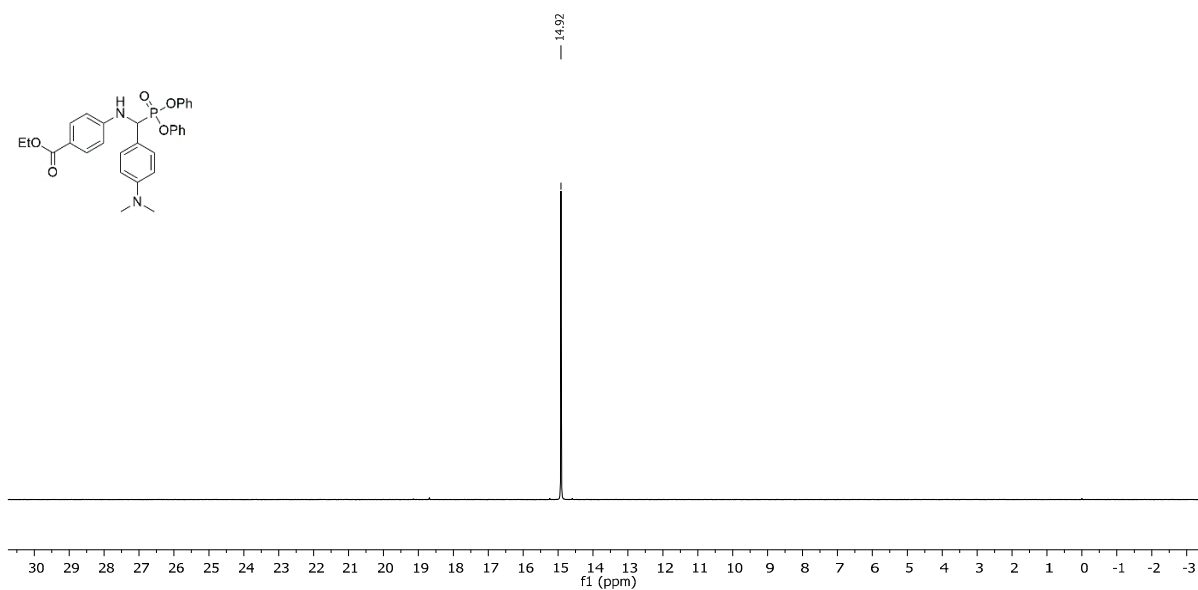
**Figure S9.** IR spectrum of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(diphenoxyphosphoryl)allyl)amino)benzoate (**6**)



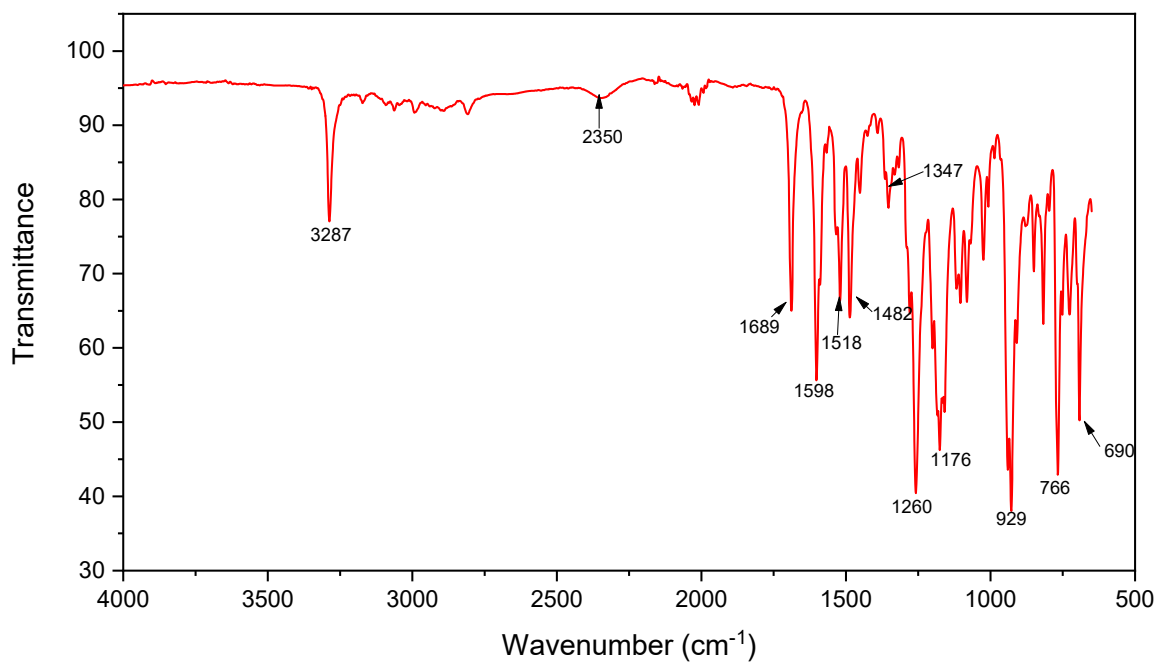
**Figure S10.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (7)



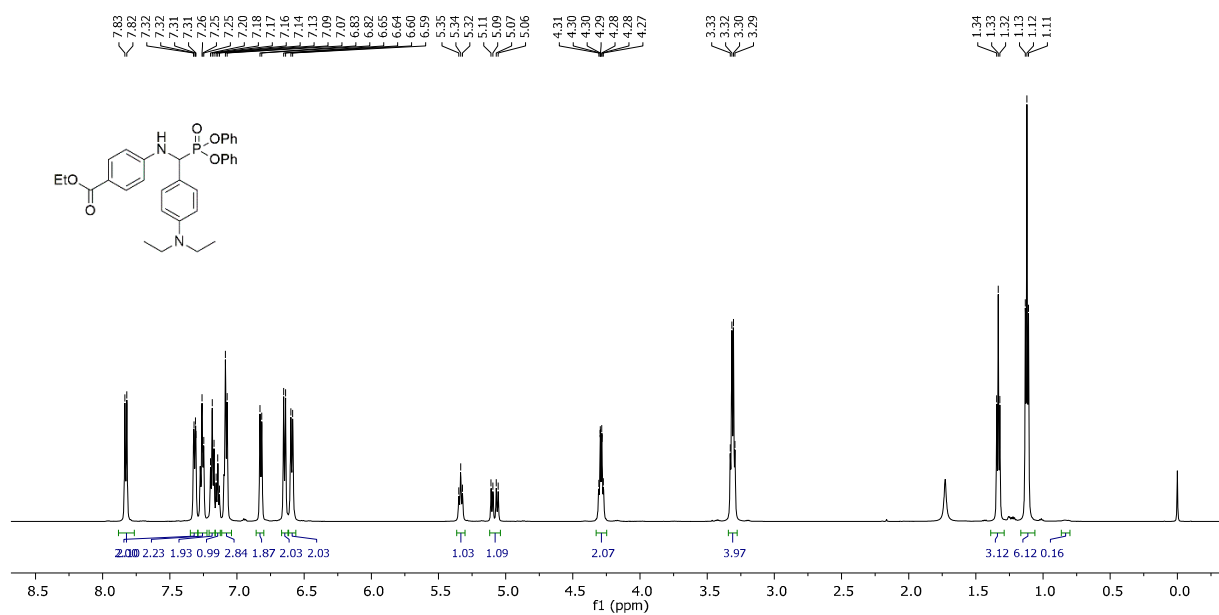
**Figure S11.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (7)



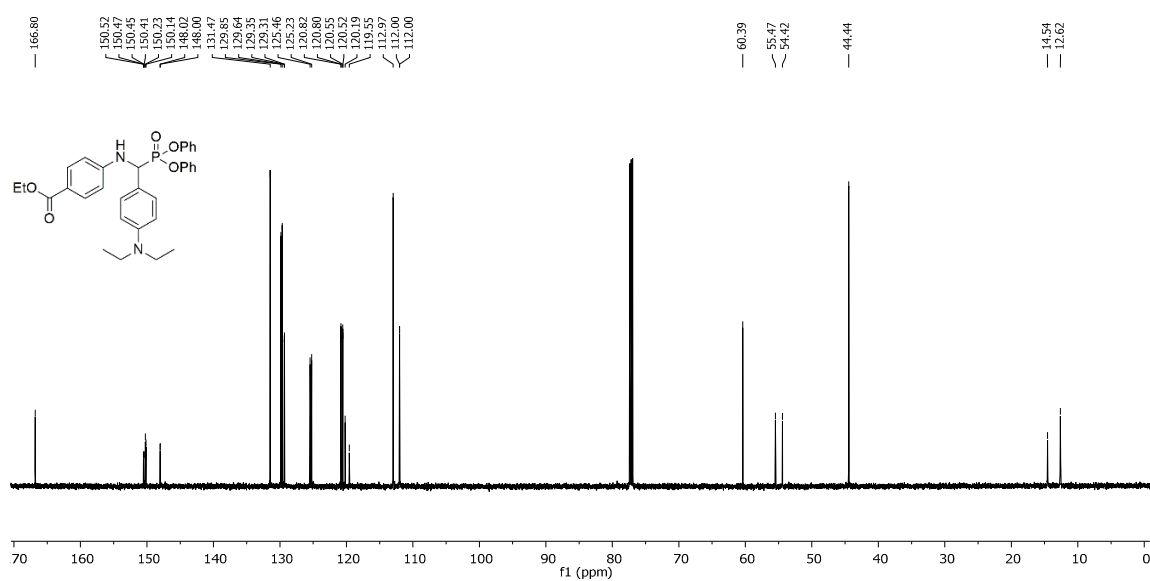
**Figure S12.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (**7**)



**Figure S13.** IR spectrum of ethyl 4-(((4-(dimethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (**7**)

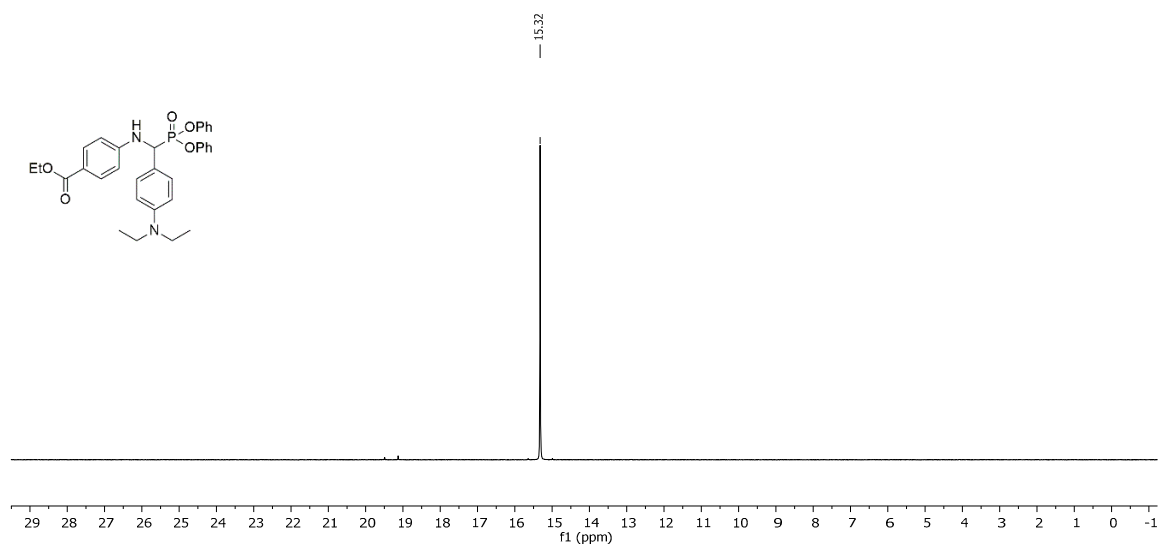


**Figure S14.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(diethylamino)phenyl)(diphenoxyposphoryl)methyl)amino)benzoate (**8**)

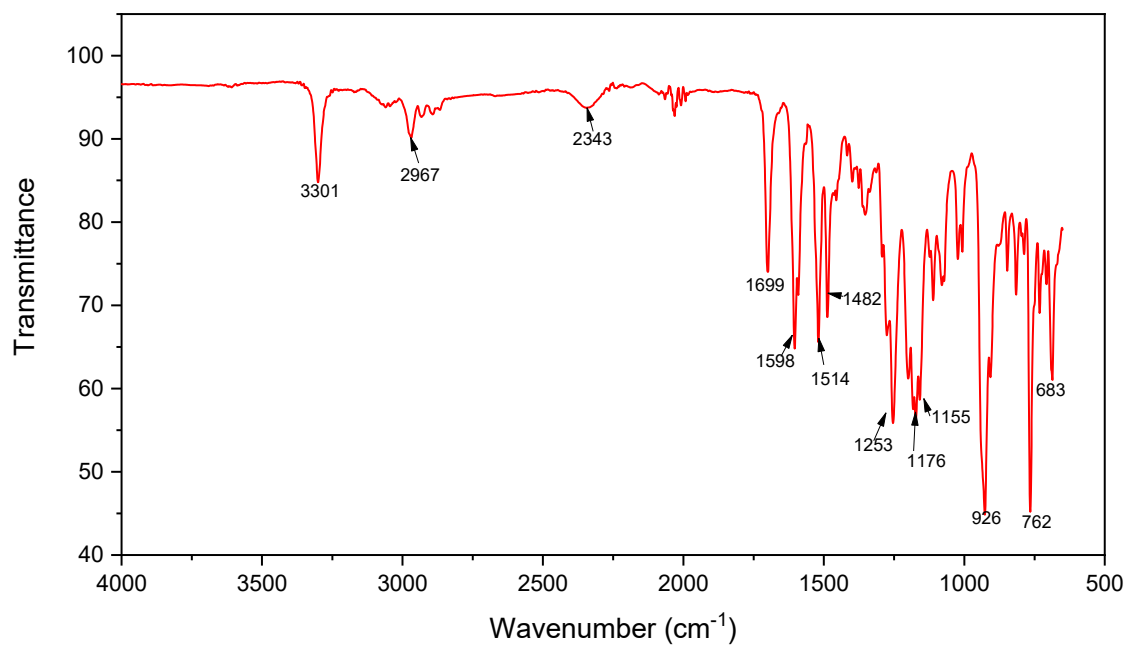


**Figure S15.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(diethylamino)phenyl)(diphenoxyposphoryl)methyl)amino)benzoate (**8**)

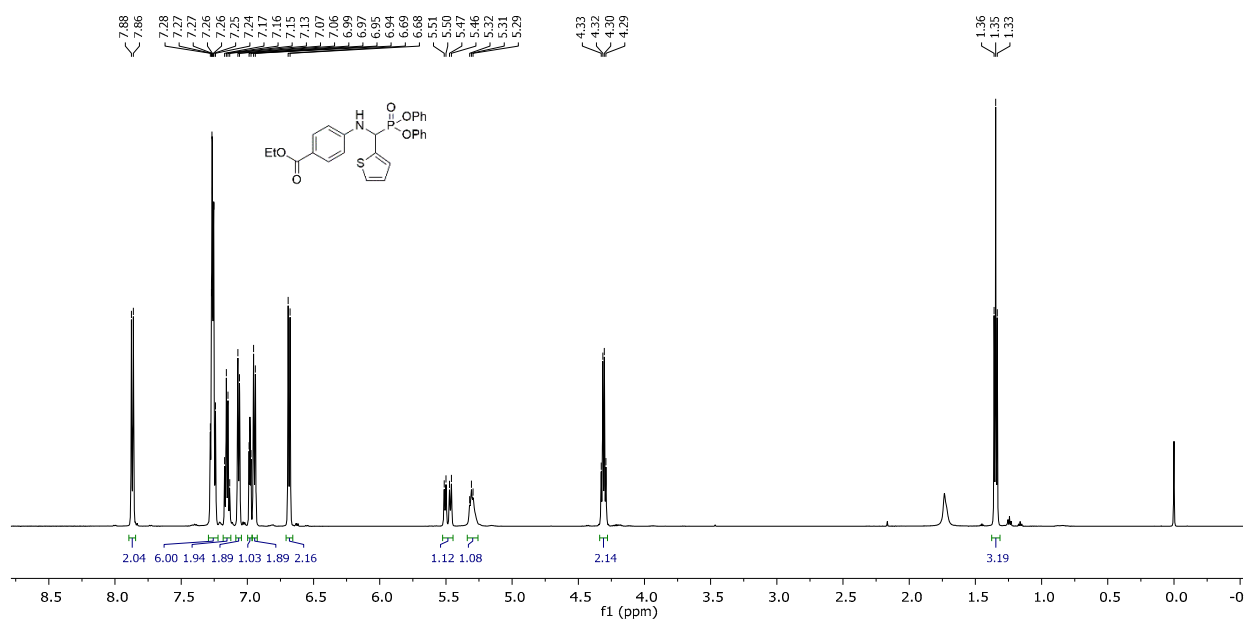




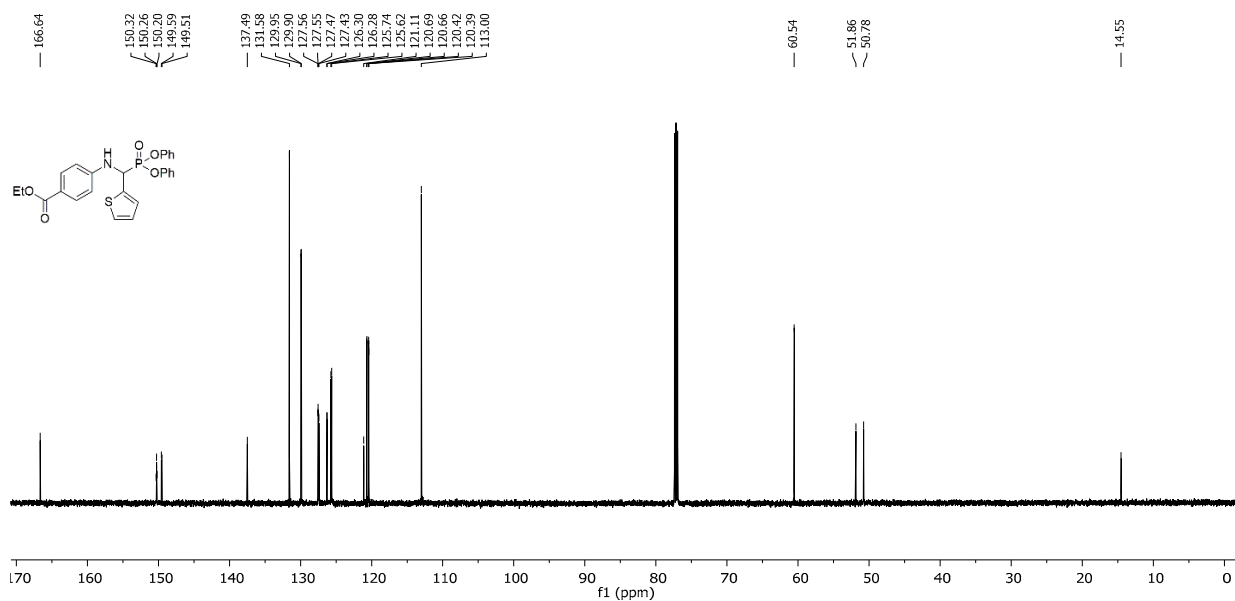
**Figure S16.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of ethyl 4-(((4-(diethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (**8**)



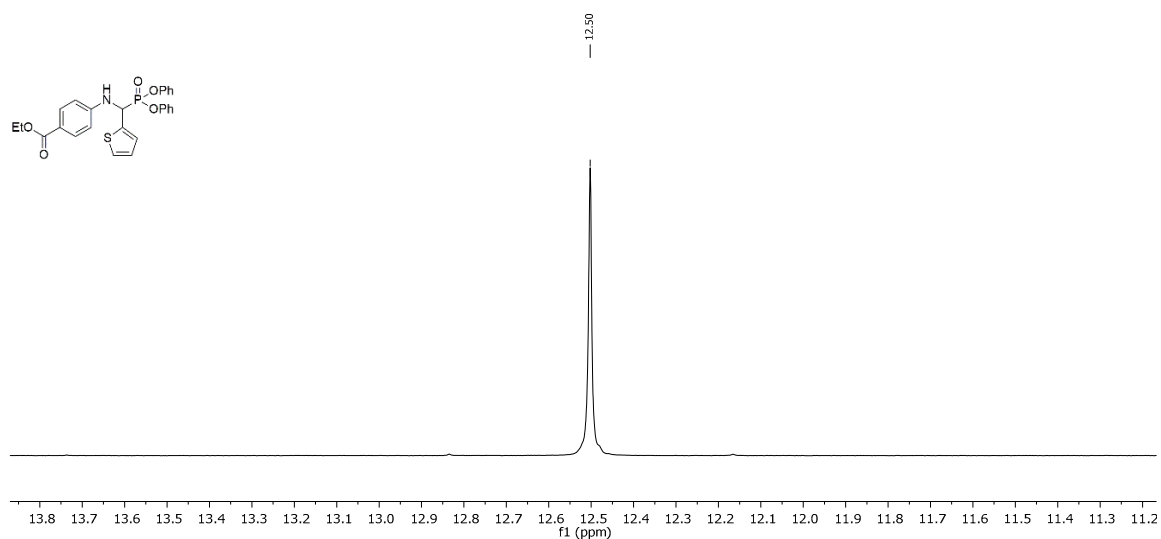
**Figure S17.** IR spectrum of ethyl 4-(((4-(diethylamino)phenyl)(diphenoxyphosphoryl)methyl)amino)benzoate (**8**)



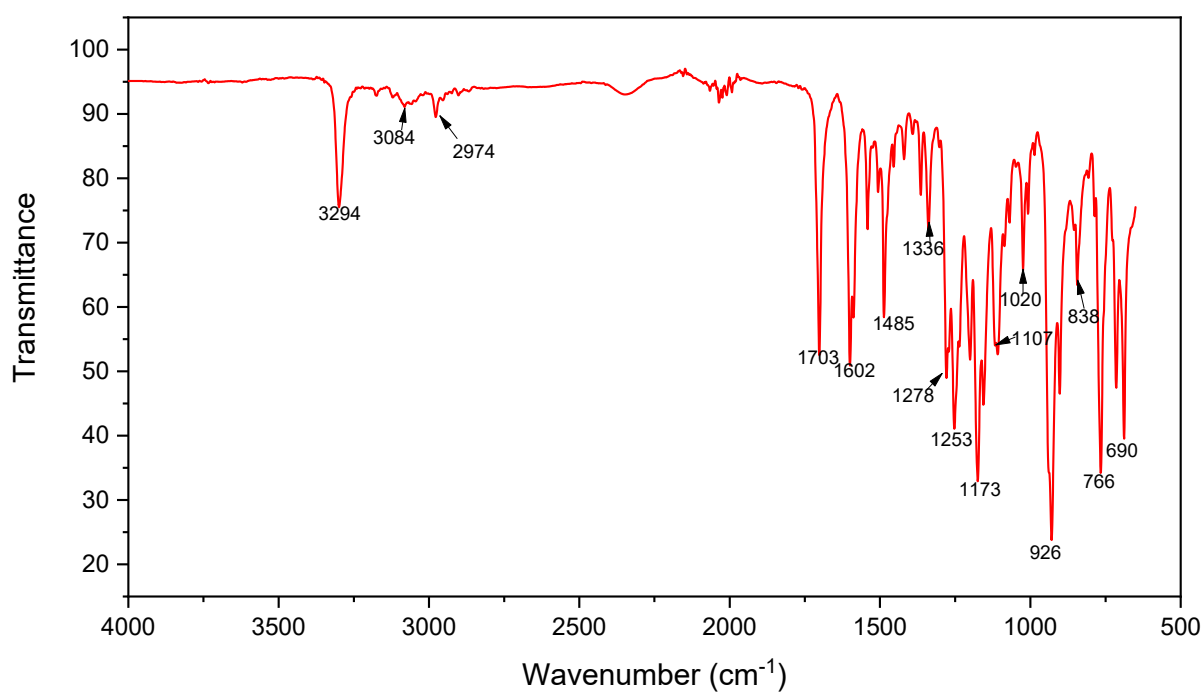
**Figure S18.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of ethyl 4-(((diphenoxyphosphoryl)(thiophen-2-yl)methyl)amino)benzoate (9)



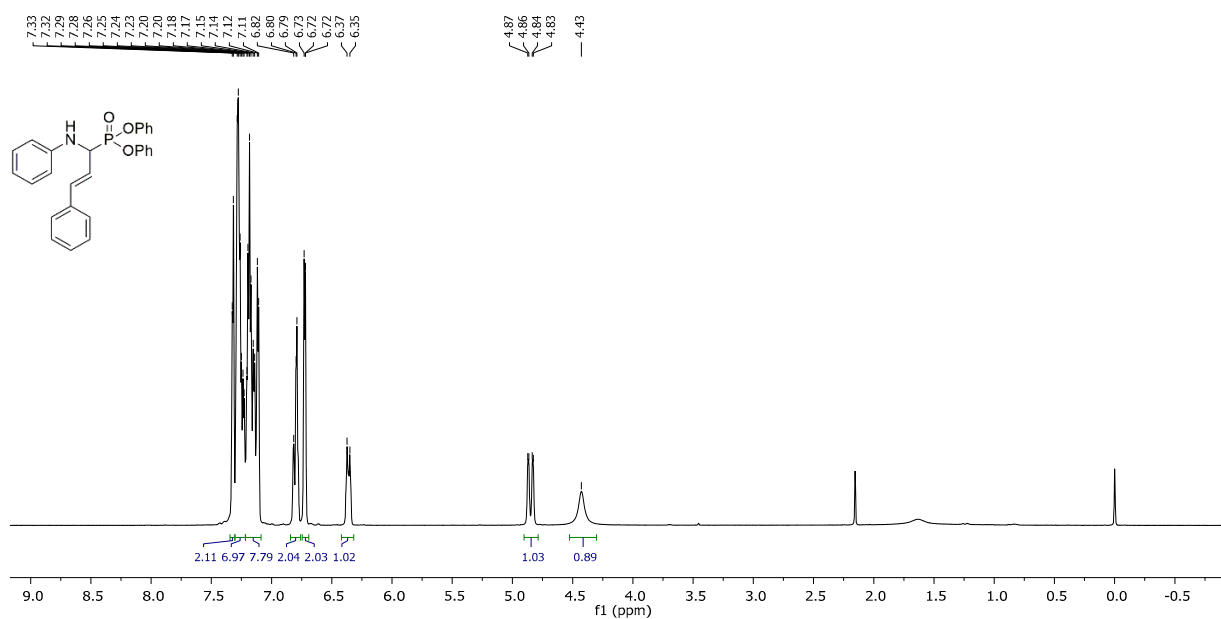
**Figure S19.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of ethyl 4-(((diphenoxyphosphoryl)(thiophen-2-yl)methyl)amino)benzoate (9)



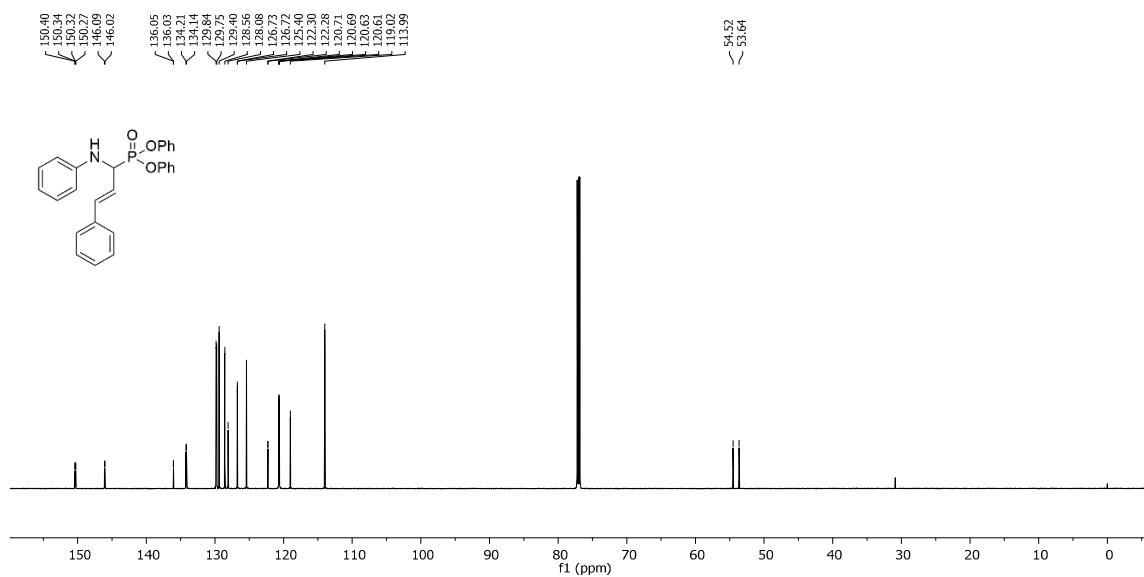
**Figure S20.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of ethyl 4-(((diphenoxyphosphoryl)(thiophen-2-yl)methyl)amino)benzoate (**9**)



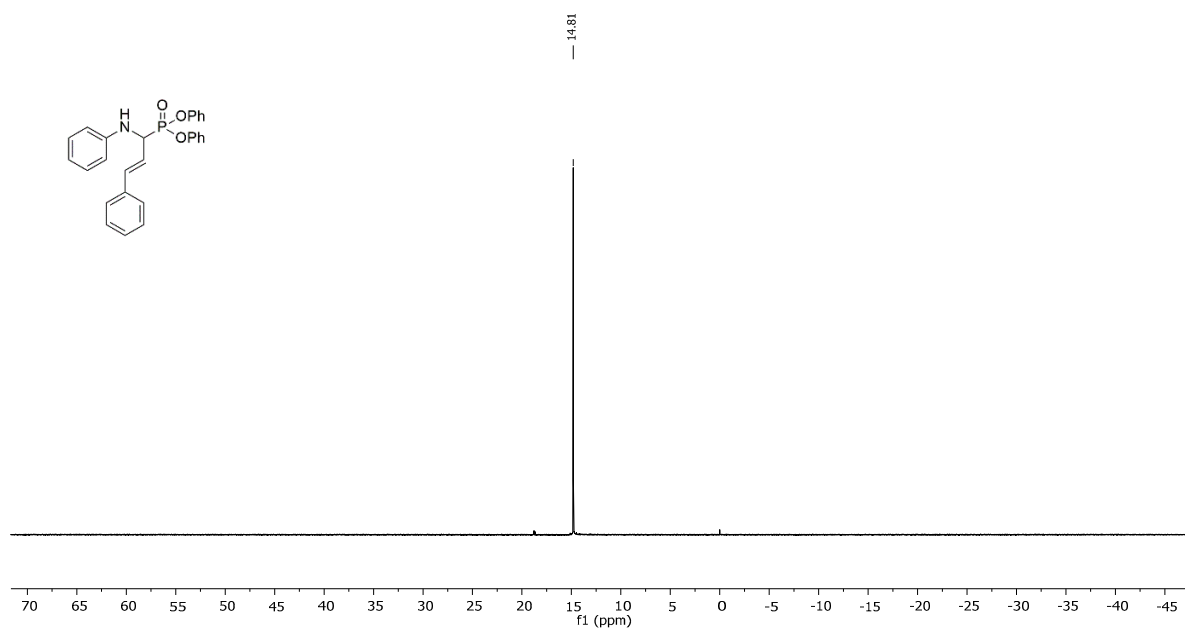
**Figure S21.** IR spectrum of ethyl 4-(((diphenoxyphosphoryl)(thiophen-2-yl)methyl)amino)benzoate (**9**)



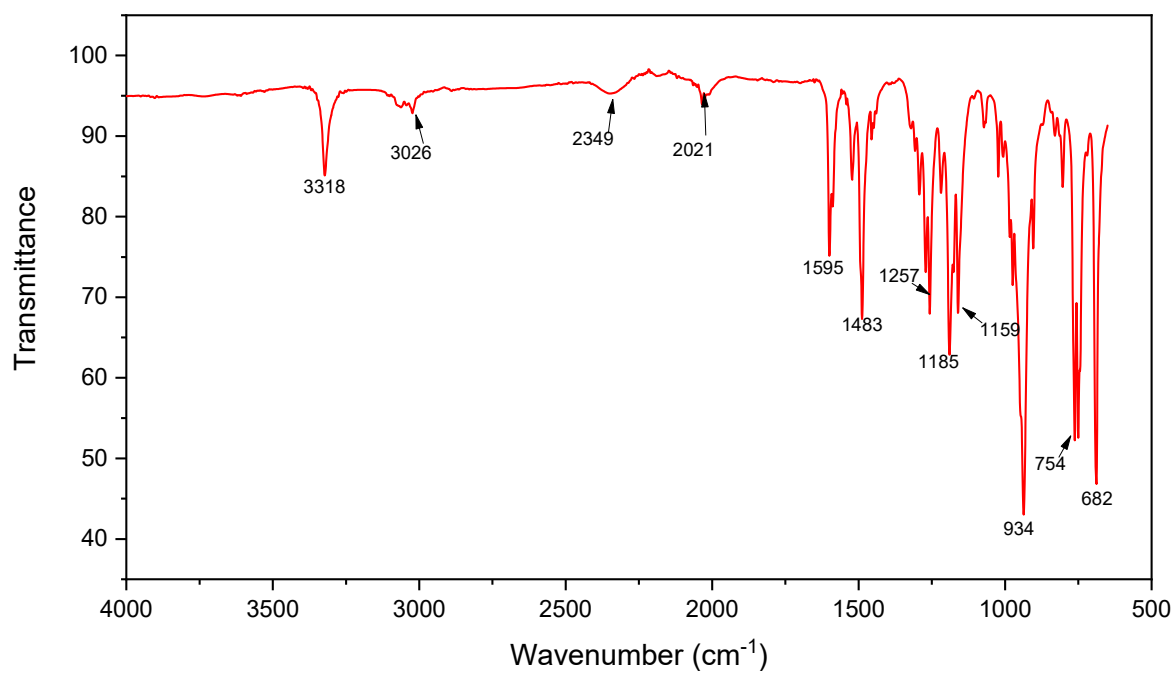
**Figure S22.** <sup>1</sup>H NMR (700 MHz, CDCl<sub>3</sub>) of (E)-diphenyl (3-phenyl-1-(phenylamino)allyl)phosphonate (**10**)



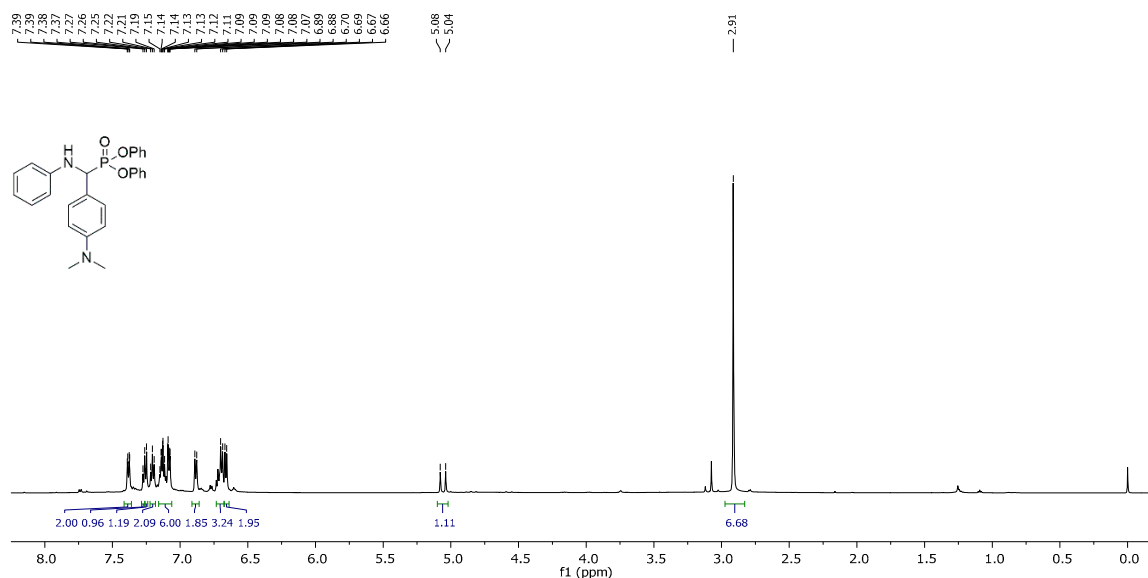
**Figure S23.** <sup>13</sup>C NMR (176 MHz, CDCl<sub>3</sub>) of (E)-diphenyl (3-phenyl-1-(phenylamino)allyl)phosphonate (**10**)



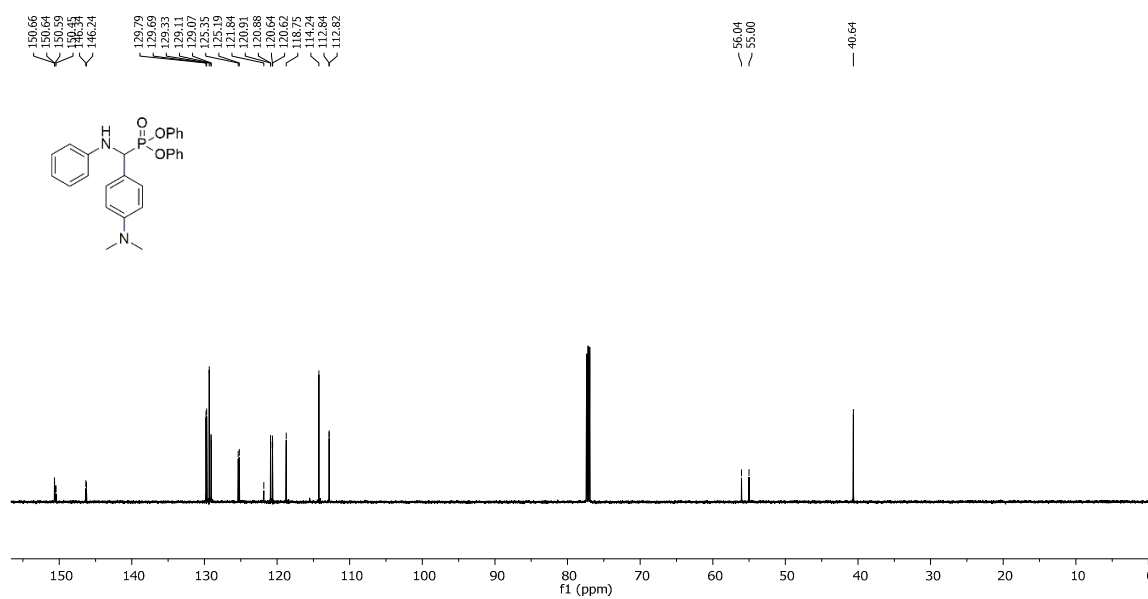
**Figure S24.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of (*E*)-diphenyl (3-phenyl-1-(phenylamino)allyl)phosphonate (10)



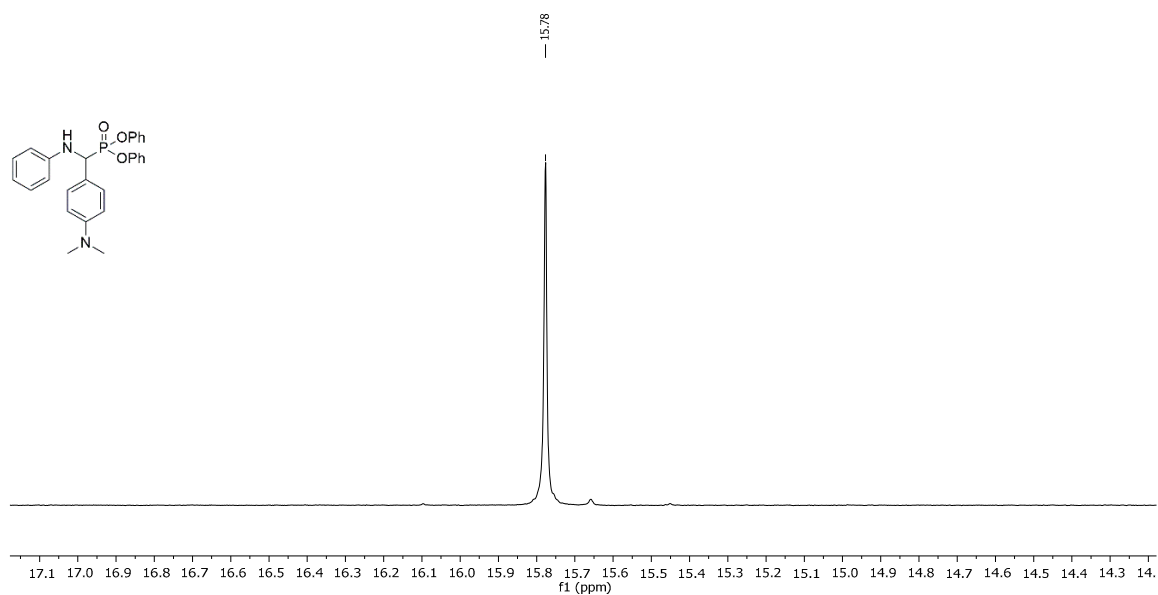
**Figure S25.** IR spectrum of (*E*)-diphenyl (3-phenyl-1-(phenylamino)allyl)phosphonate (10)



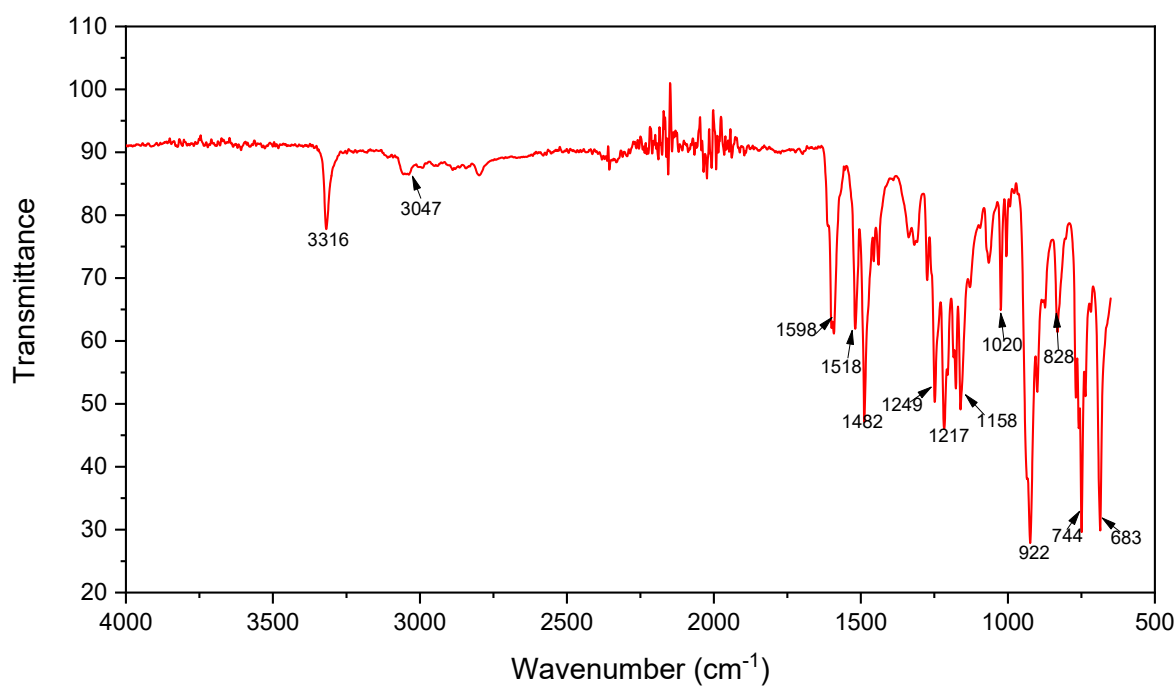
**Figure S26.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of diphenyl ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**11**)



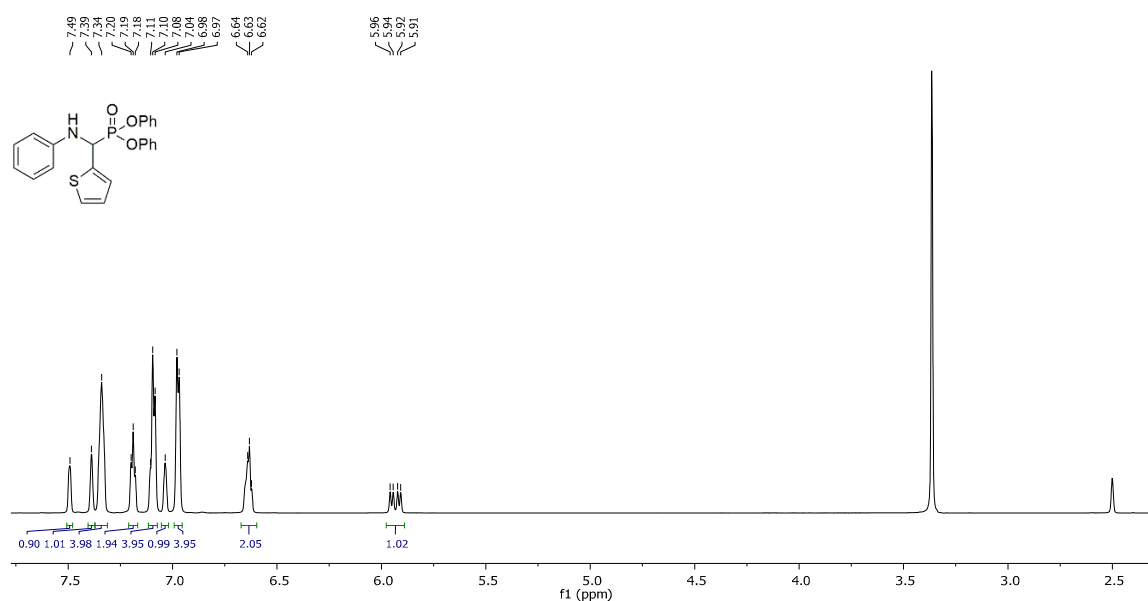
**Figure S27.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of diphenyl ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**11**)



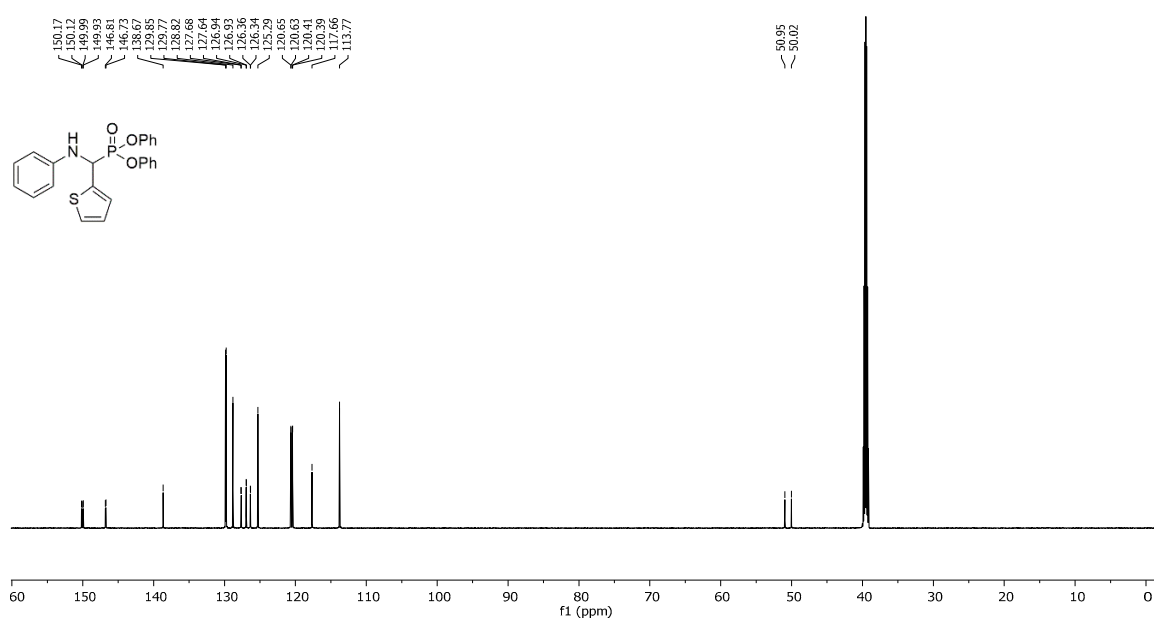
**Figure S28.**  $^{31}\text{P}$  NMR (243 MHz,  $\text{CDCl}_3$ ) of diphenyl ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**11**)



**Figure S29.** IR spectrum of diphenyl ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**11**)

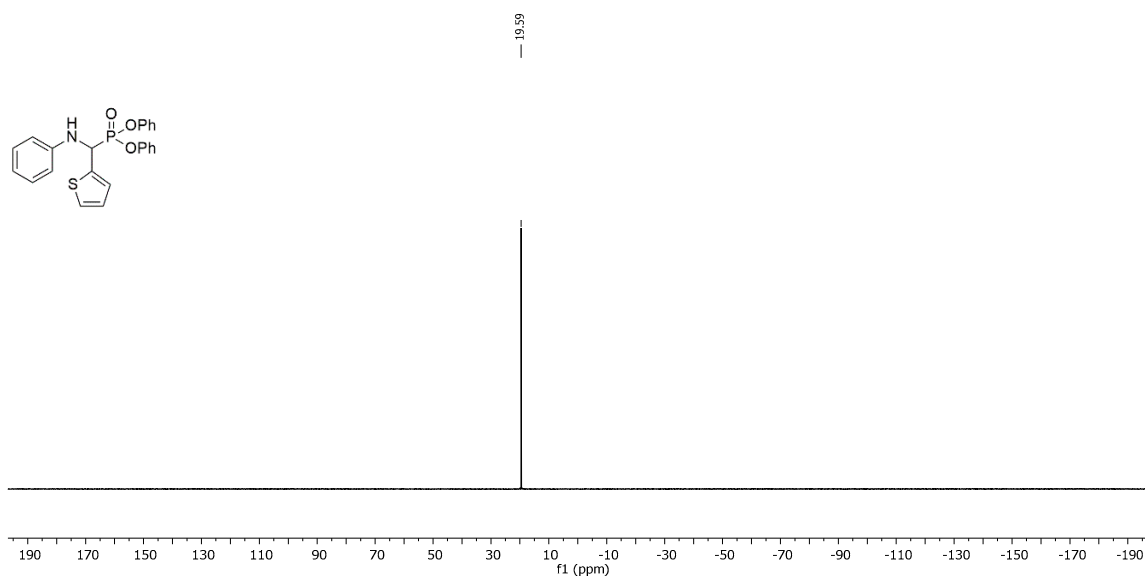


**Figure S30.** <sup>1</sup>H NMR (700 MHz, DMSO-*d*<sub>6</sub>) of diphenyl ((phenylamino)(thiophen-2-yl)methyl)phosphonate (12)

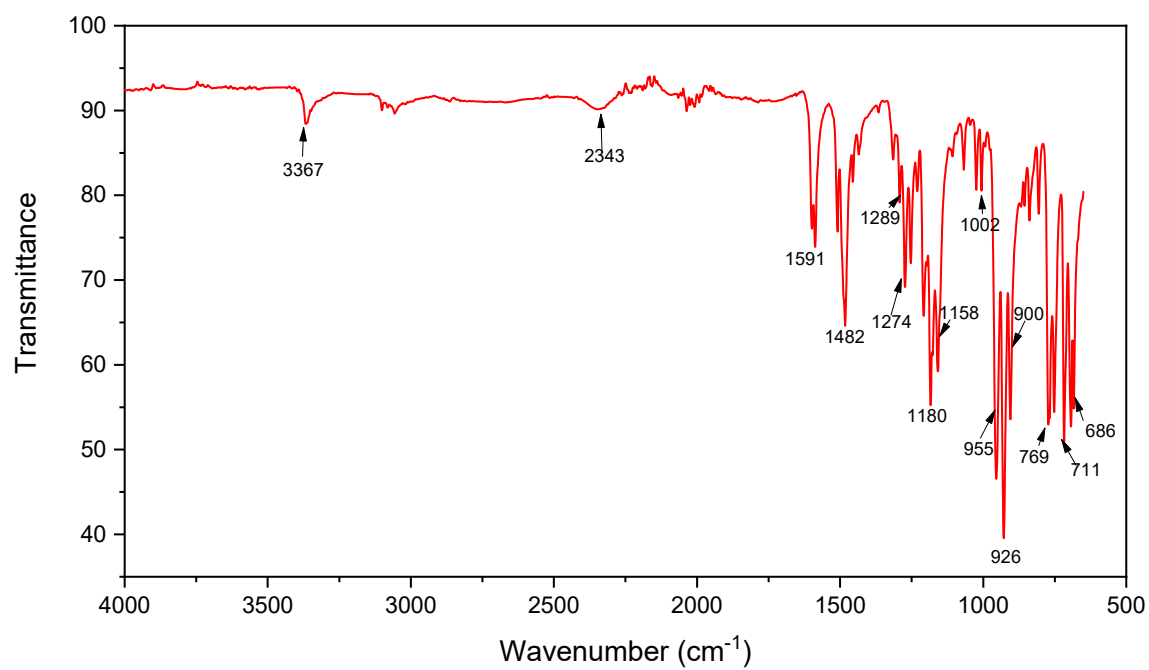


**Figure S31.** <sup>13</sup>C NMR (176 MHz, DMSO-*d*<sub>6</sub>) of diphenyl ((phenylamino)(thiophen-2-yl)methyl)phosphonate (12)

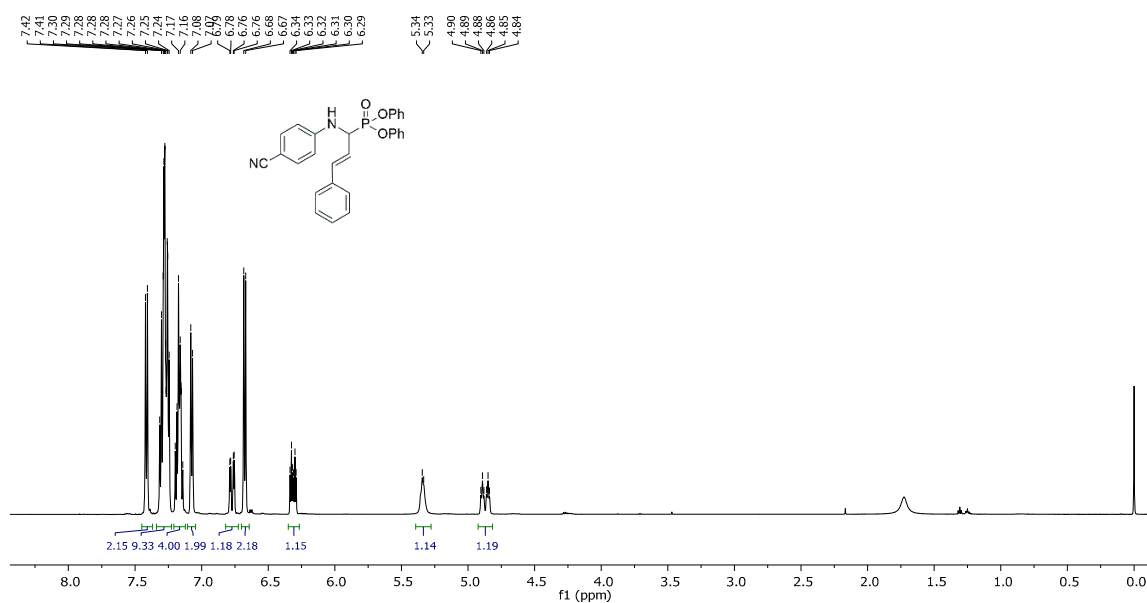




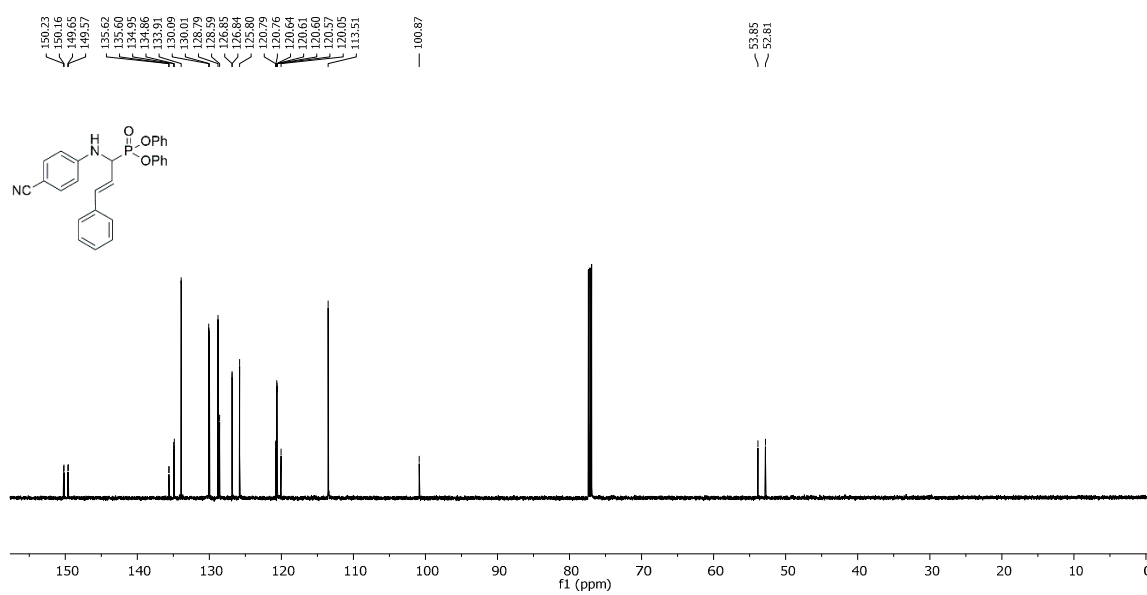
**Figure S32.**  $^{31}\text{P}$  NMR (243 MHz,  $\text{DMSO}-d_6$ ) of diphenyl ((phenylamino)(thiophen-2-yl)methyl)phosphonate (**12**)



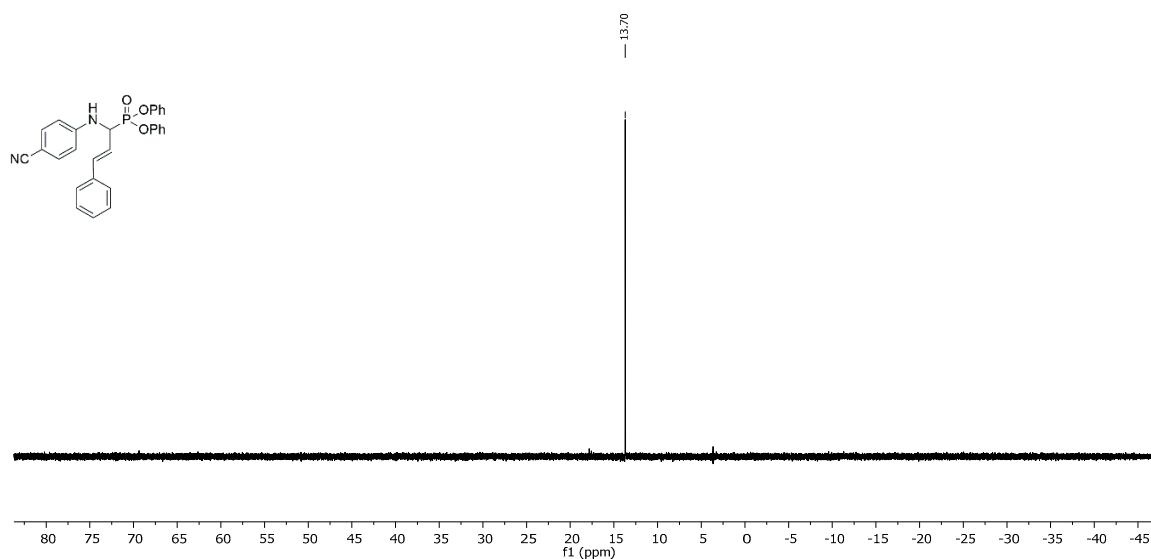
**Figure S33.** IR spectrum of diphenyl ((phenylamino)(thiophen-2-yl)methyl)phosphonate (**12**)



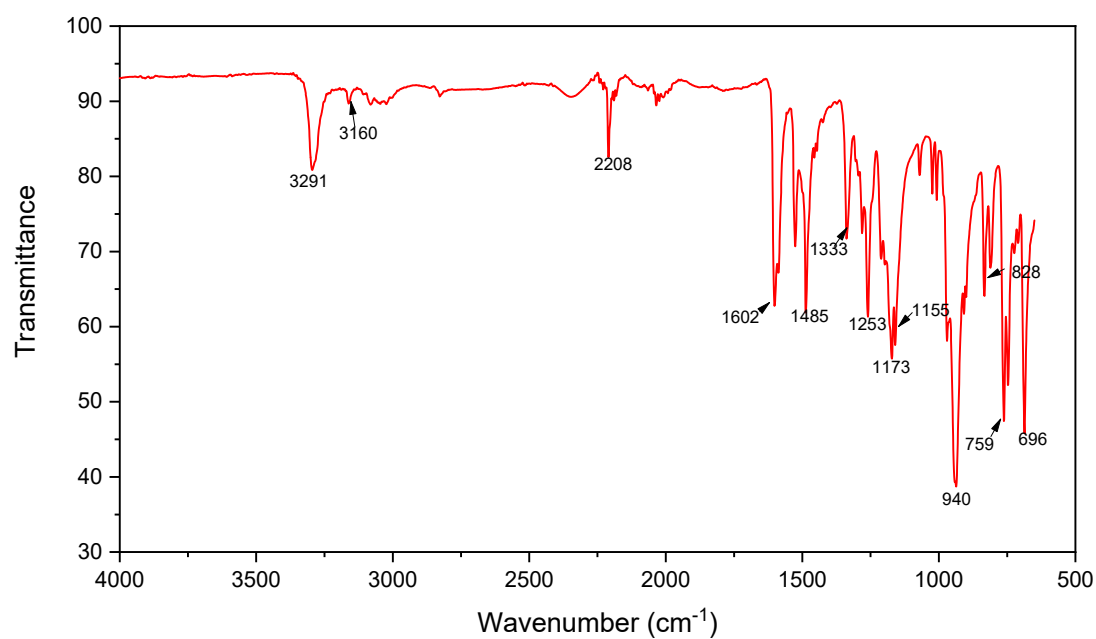
**Figure S34.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of (E)-diphenyl 1-((4-cyanophenyl)amino)-3-phenylallylphosphonate (13)



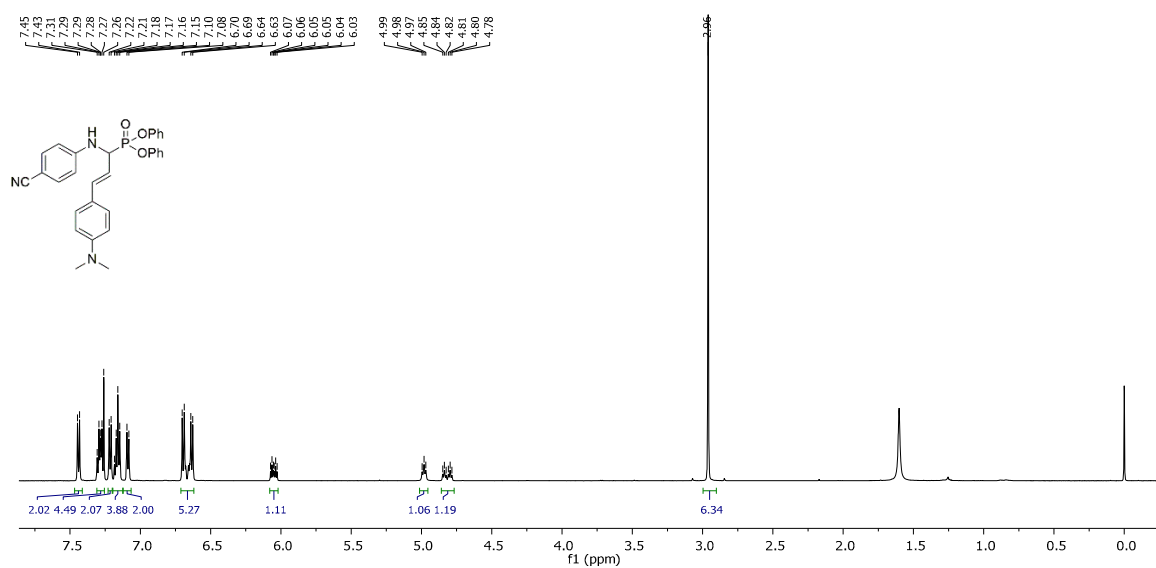
**Figure S35.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of (E)-diphenyl 1-((4-cyanophenyl)amino)-3-phenylallylphosphonate (13)



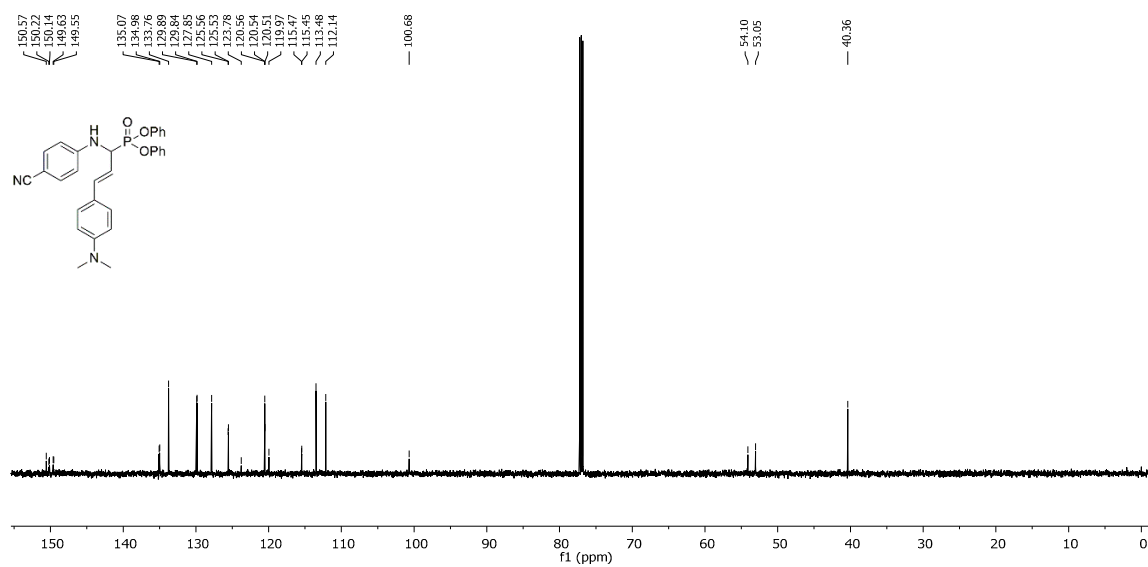
**Figure S36.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of (*E*)-diphenyl 1-((4-cyanophenyl)amino)-3-phenylallylphosphonate (13)



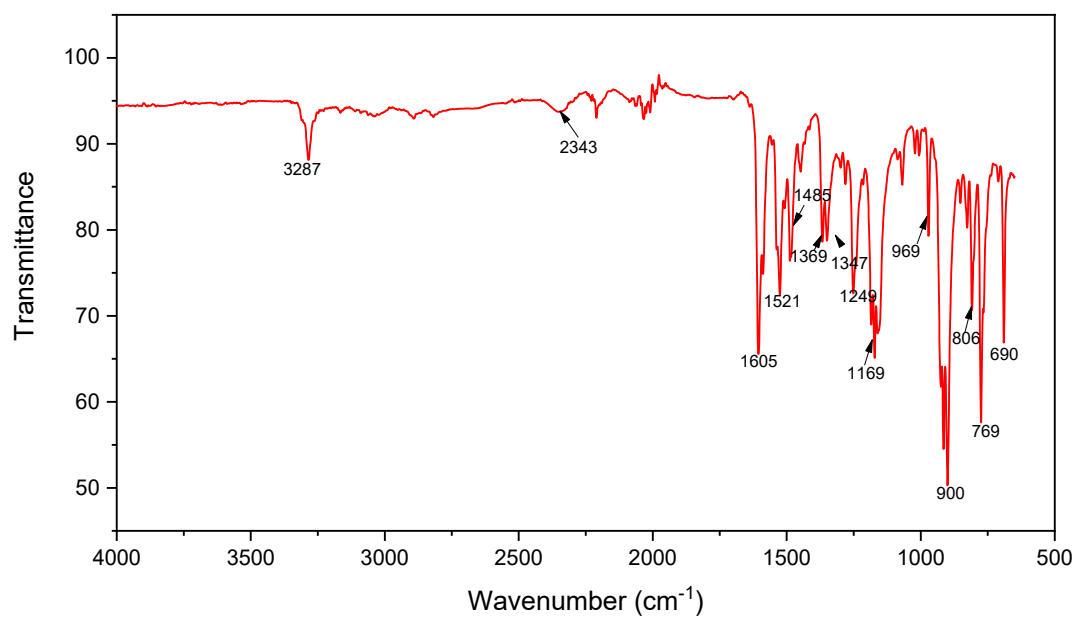
**Figure S37.** IR spectrum of (*E*)-diphenyl 1-((4-cyanophenyl)amino)-3-phenylallylphosphonate (13)



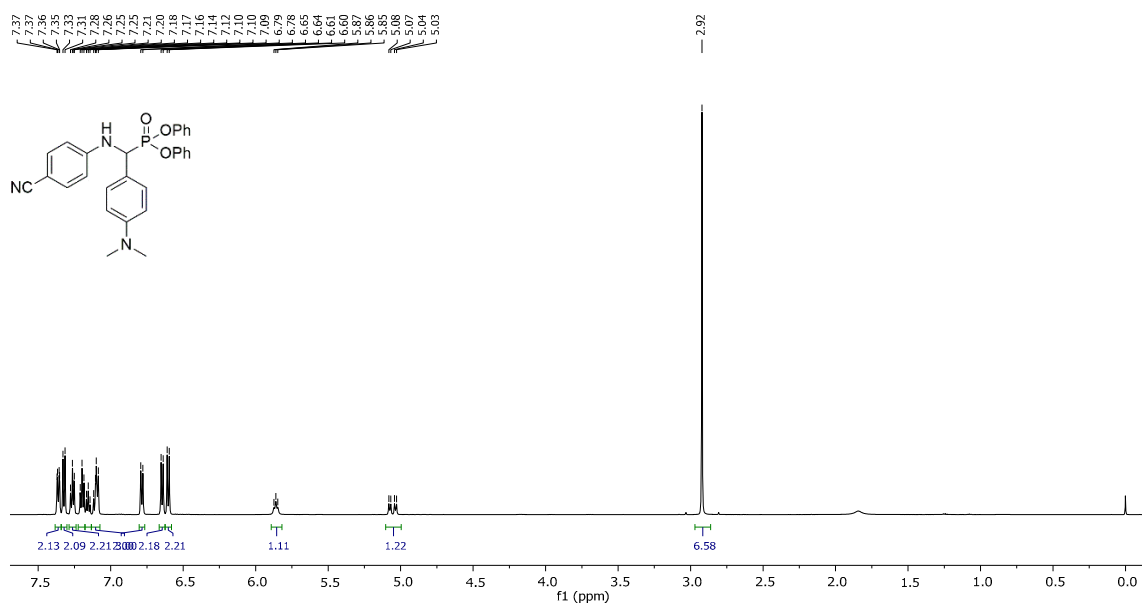
**Figure S38.** <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of (*E*)-diphenyl 1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (**14**)



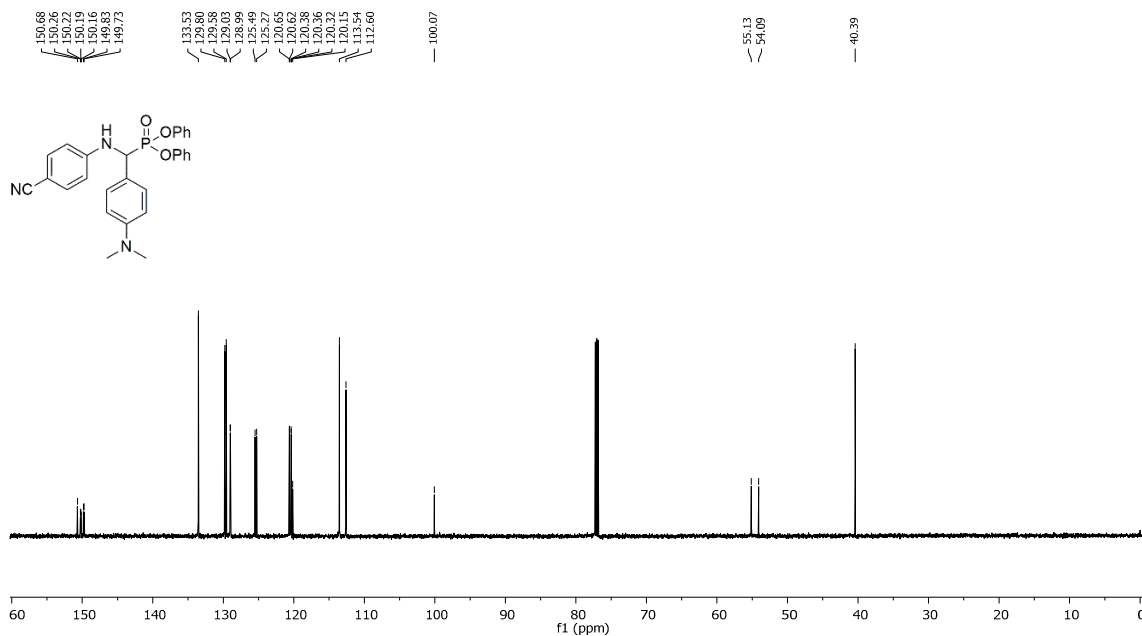
**Figure S39.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of (*E*)-diphenyl 1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (**14**)



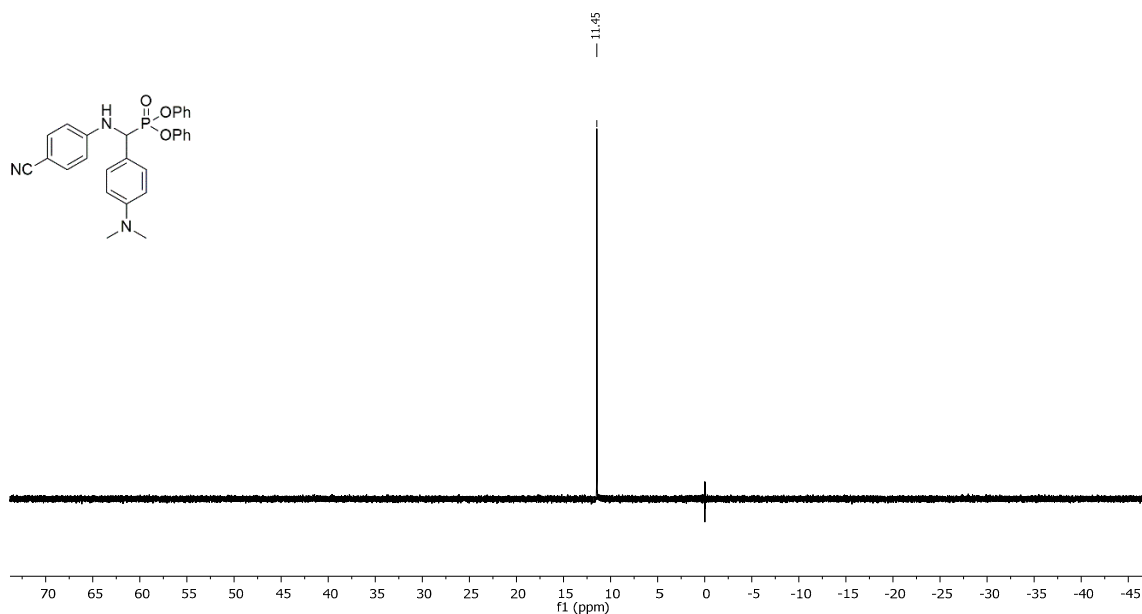
**Figure S40.** IR spectrum of (*E*)-diphenyl 1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allylphosphonate (**14**)



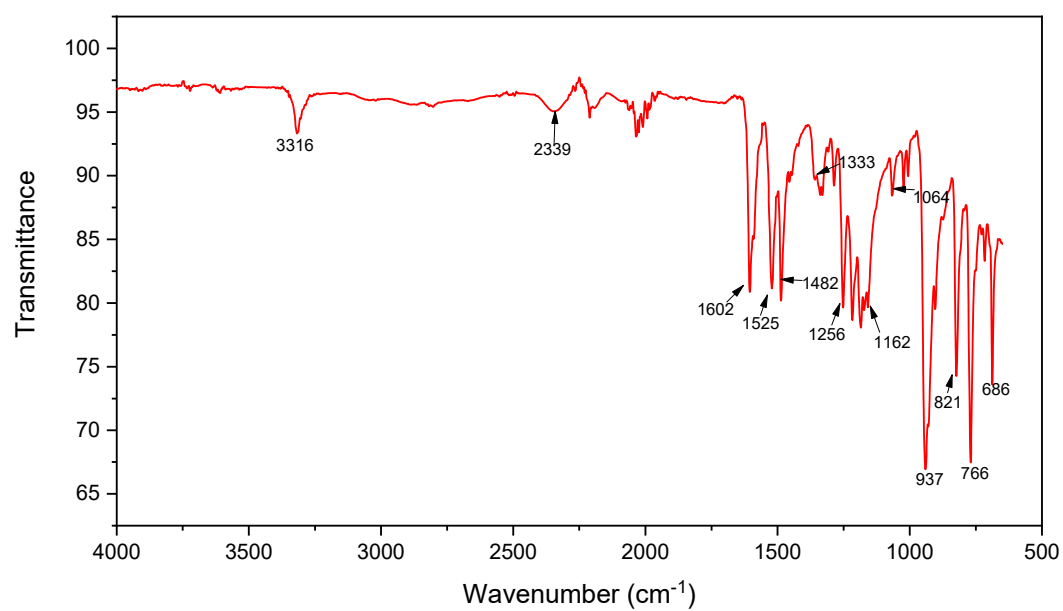
**Figure S41.**  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) of diphenyl (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**15**)



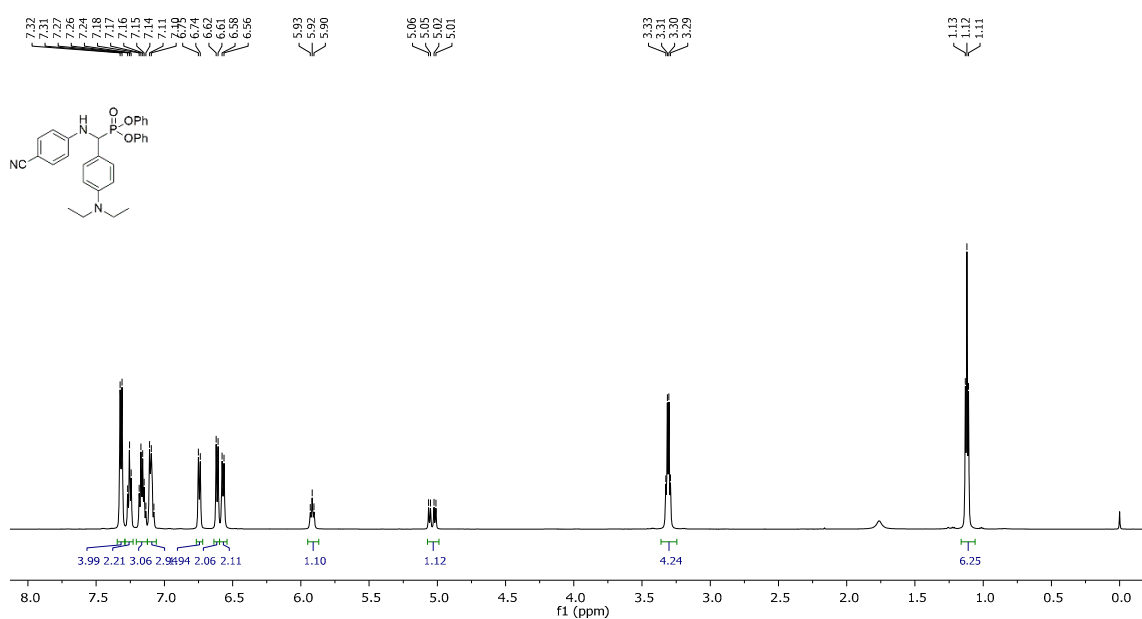
**Figure S42.**  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ ) of diphenyl (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**15**)



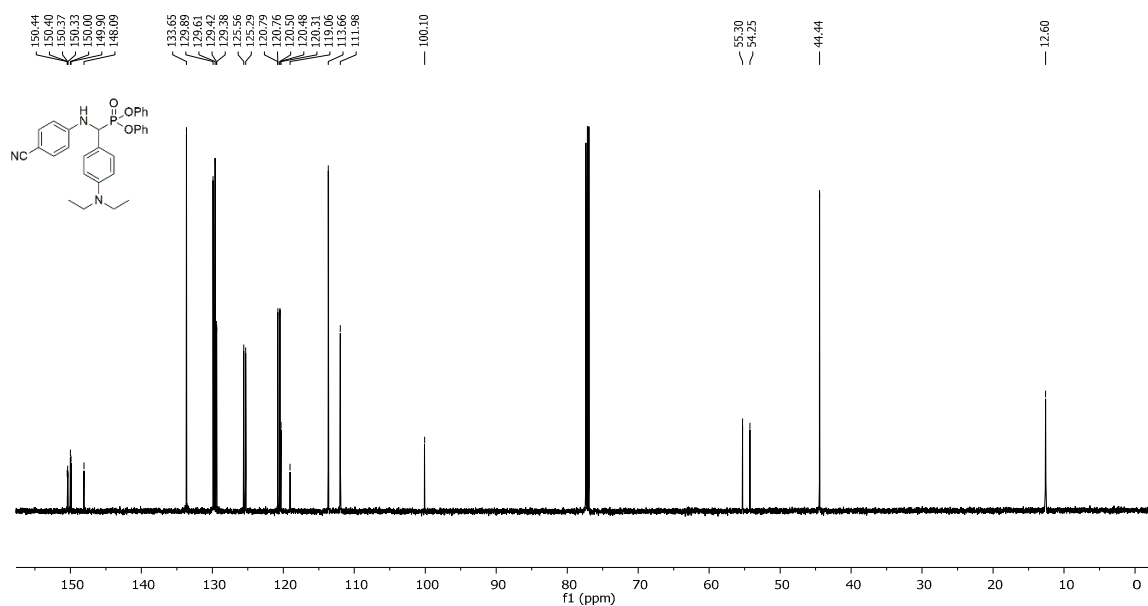
**Figure S43.**  $^{31}\text{P}$  NMR (243 MHz,  $\text{CDCl}_3$ ) of diphenyl (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**15**)



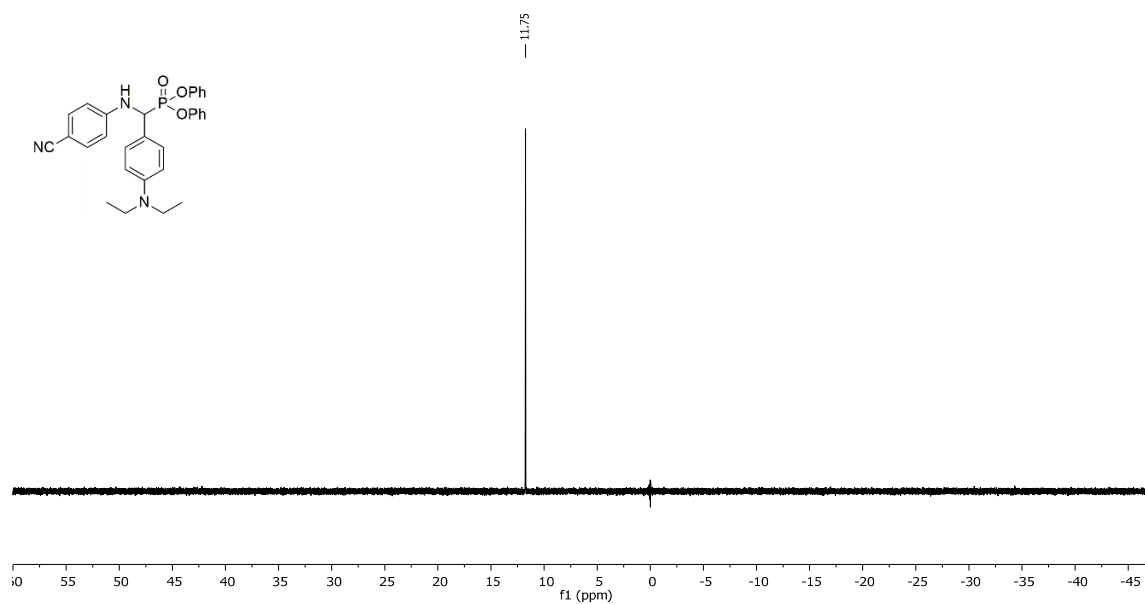
**Figure S44.** IR spectrum of diphenyl (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (15)



**Figure S45.**  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) of diphenyl (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (16)

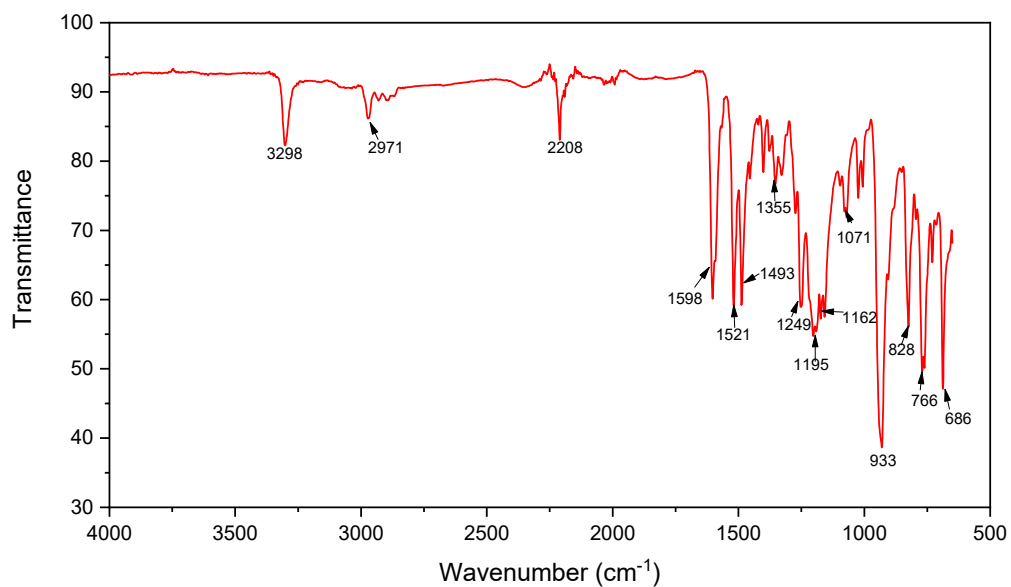


**Figure S46.** <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of diphenyl (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**16**)

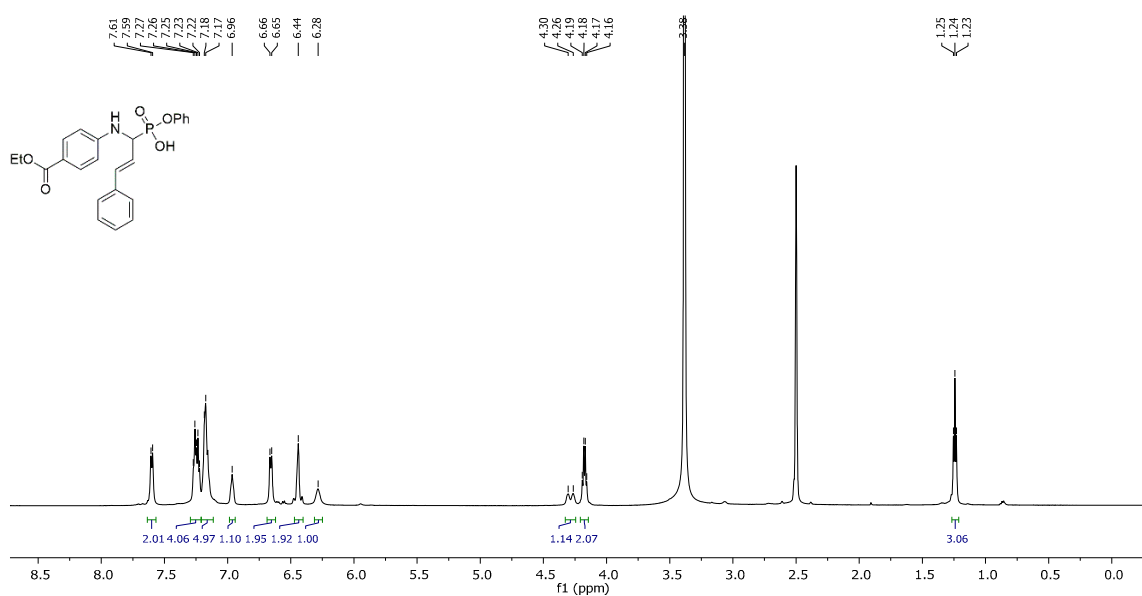


**Figure S47.** <sup>31</sup>P NMR (243 MHz, CDCl<sub>3</sub>) of diphenyl (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**16**)

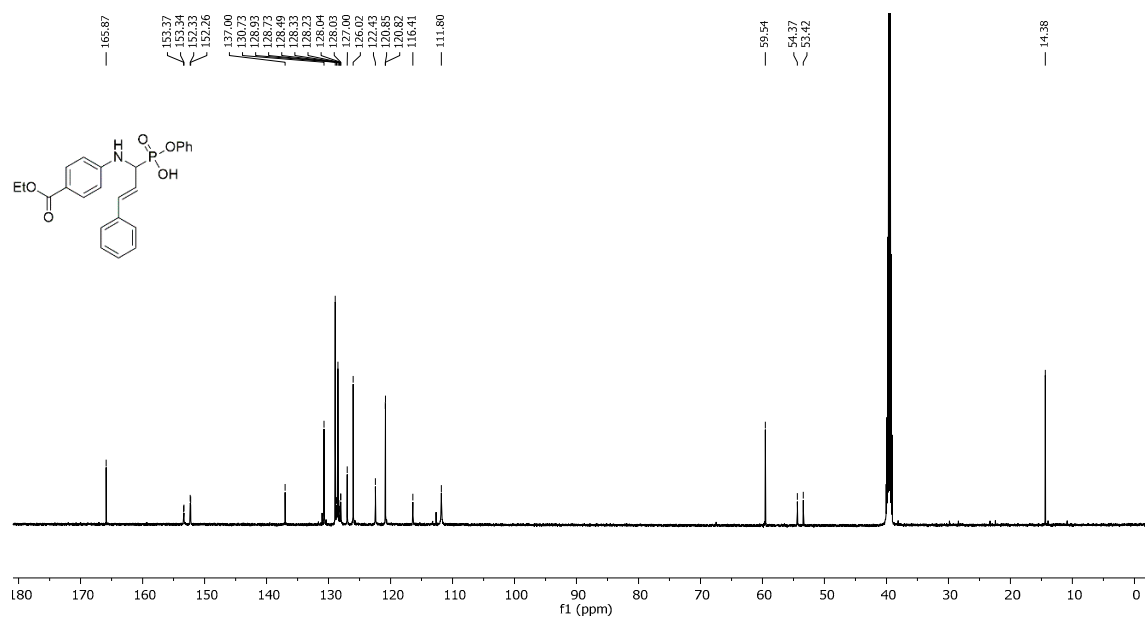




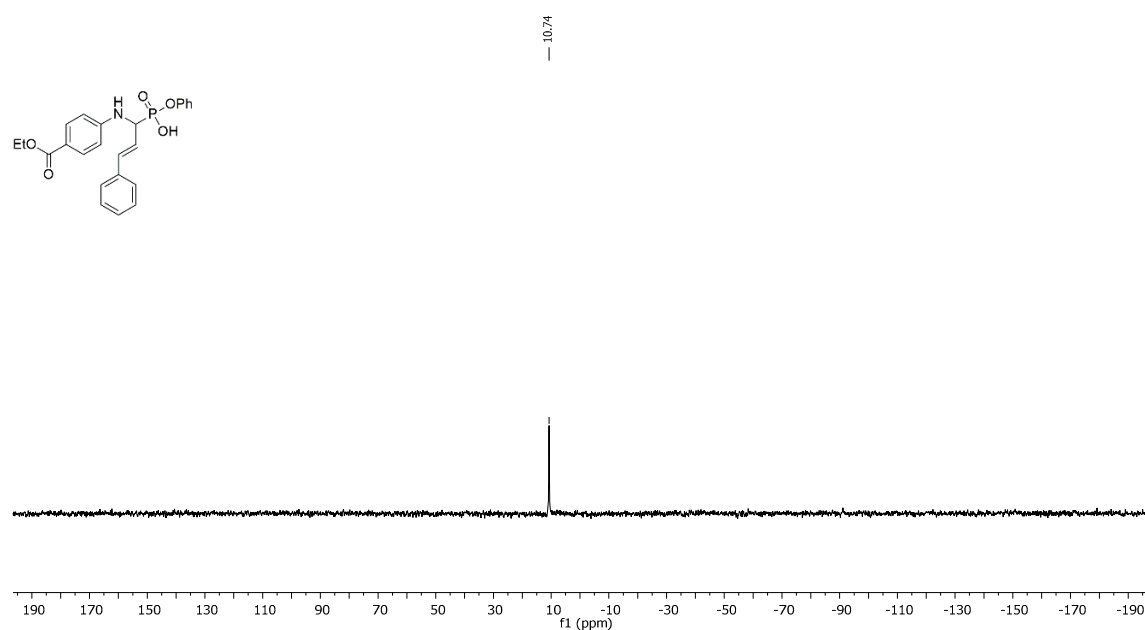
**Figure S48.** IR spectrum of diphenyl (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**16**)



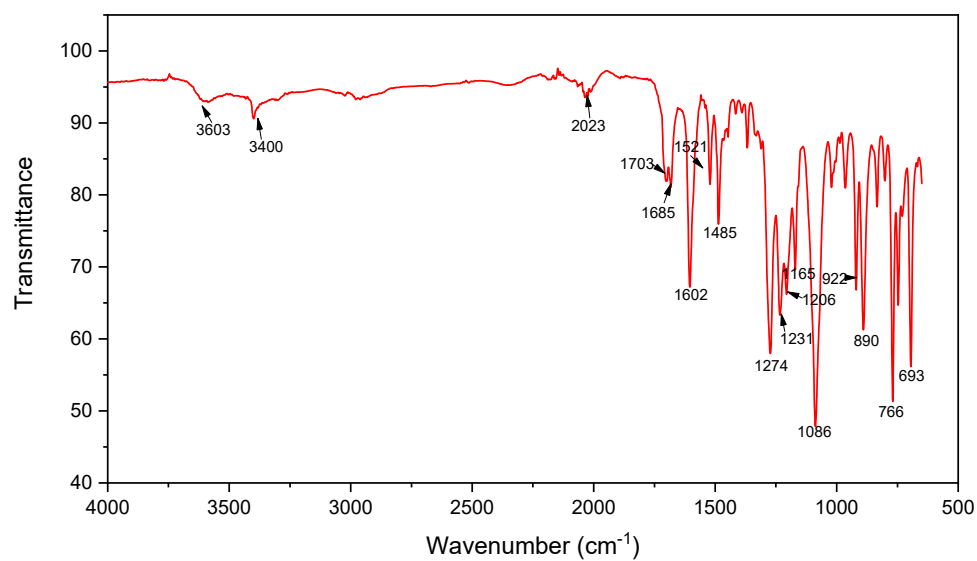
**Figure S49.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of (*E*)-ethyl 4-((1-(hydroxy(phenoxy)phosphoryl)-3-phenylallyl)amino)benzoate (**17**)



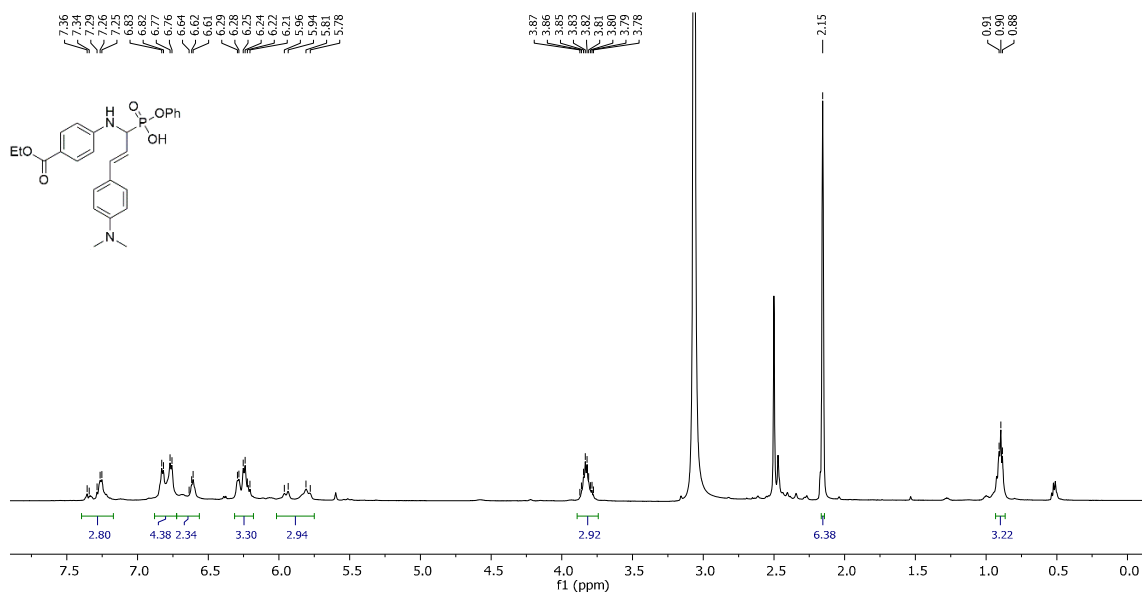
**Figure S50.** <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-ethyl 4-((1-(hydroxy(phenoxy)phosphoryl)-3-phenylallyl)amino)benzoate (17)



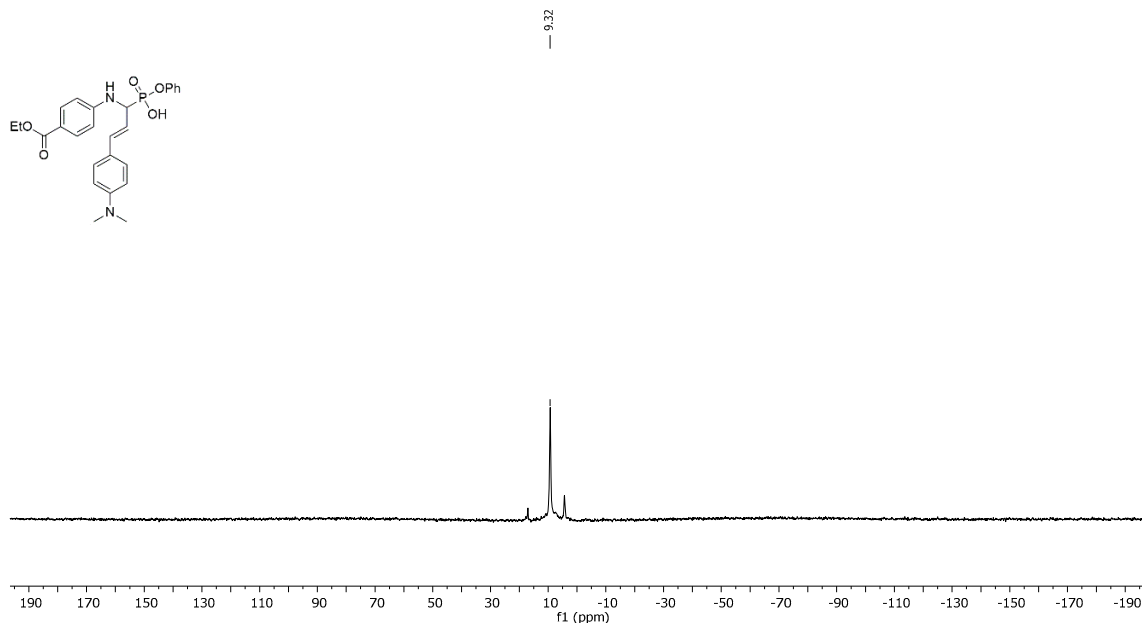
**Figure S51.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-ethyl 4-((1-(hydroxy(phenoxy)phosphoryl)-3-phenylallyl)amino)benzoate (17)



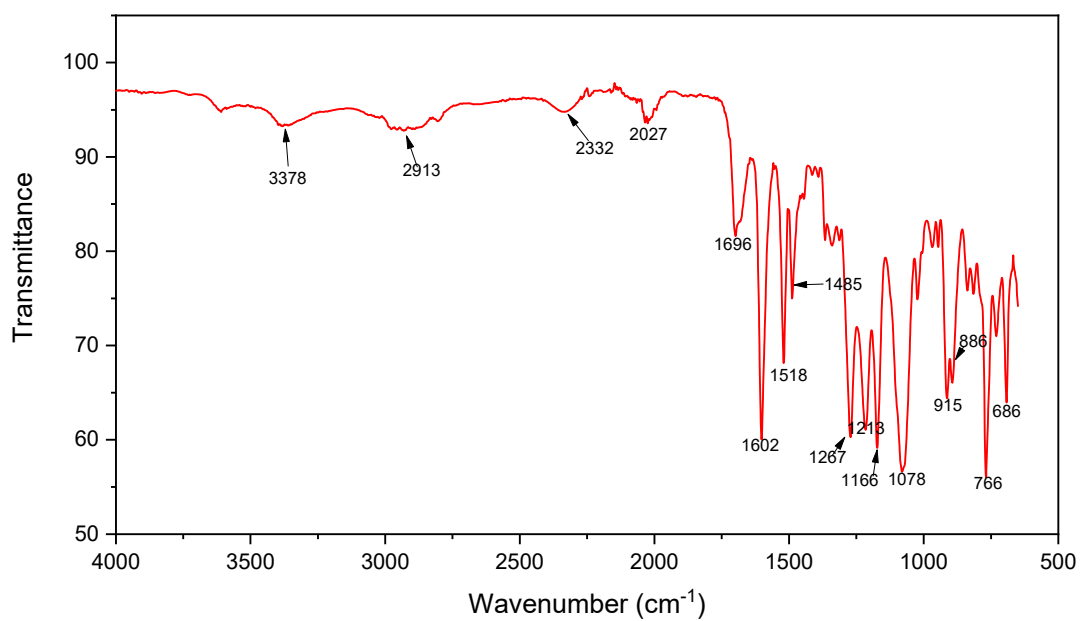
**Figure S52.** IR spectrum of (*E*)-ethyl 4-((1-(hydroxy(phenoxy)phosphoryl)-3-phenylallyl)amino)benzoate (**17**)



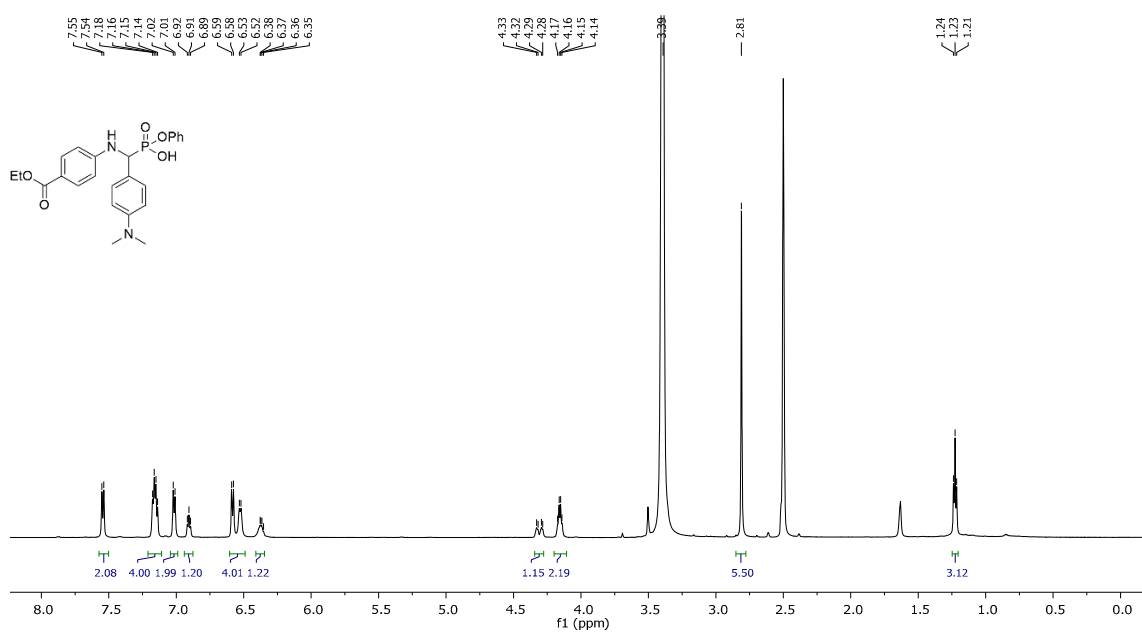
**Figure S53.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(hydroxy(phenoxy)phosphoryl)allyl)amino)benzoate (**18**)



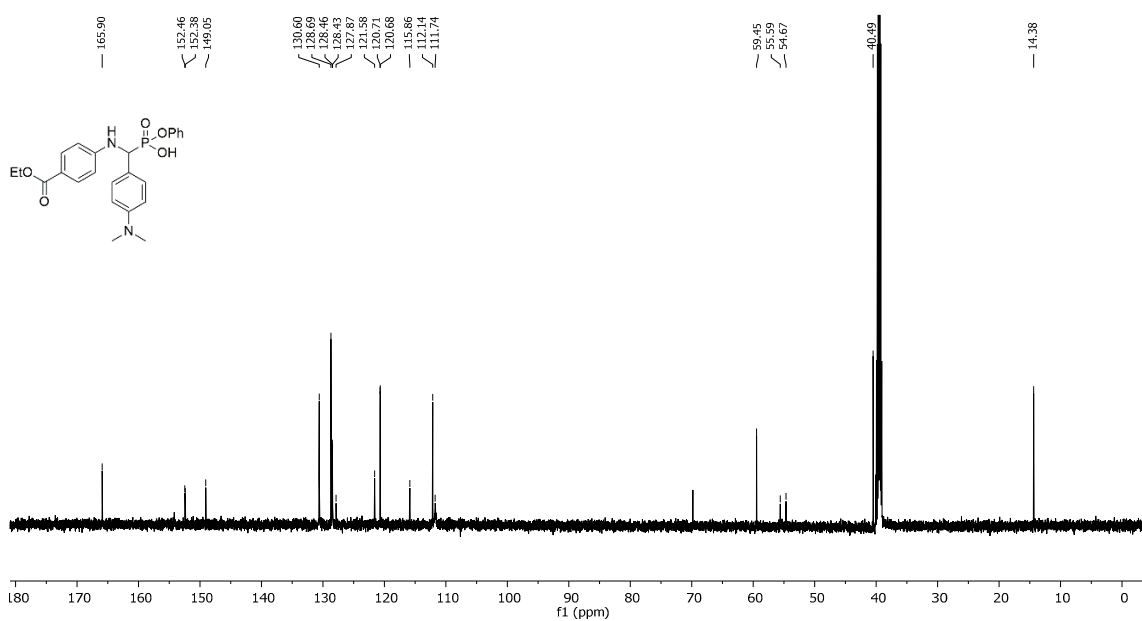
**Figure S54.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(hydroxy(phenoxy)phosphoryl)allyl)amino)benzoate (**18**)



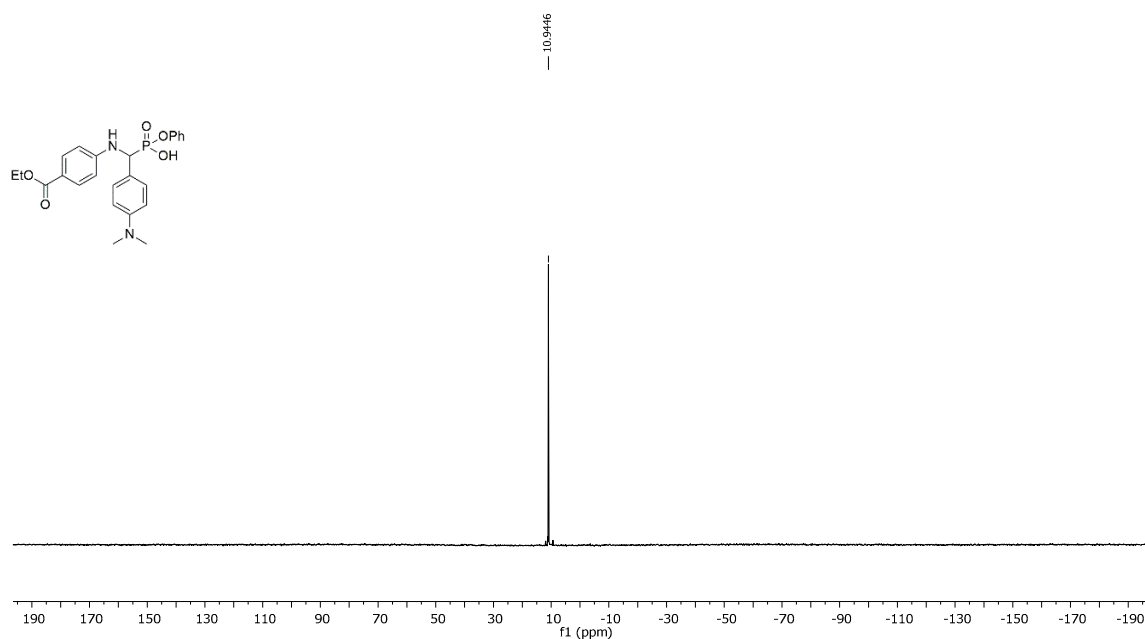
**Figure S55.** IR spectrum of (*E*)-ethyl 4-((3-(4-(dimethylamino)phenyl)-1-(hydroxy(phenoxy)phosphoryl)allyl)amino)benzoate (**18**)



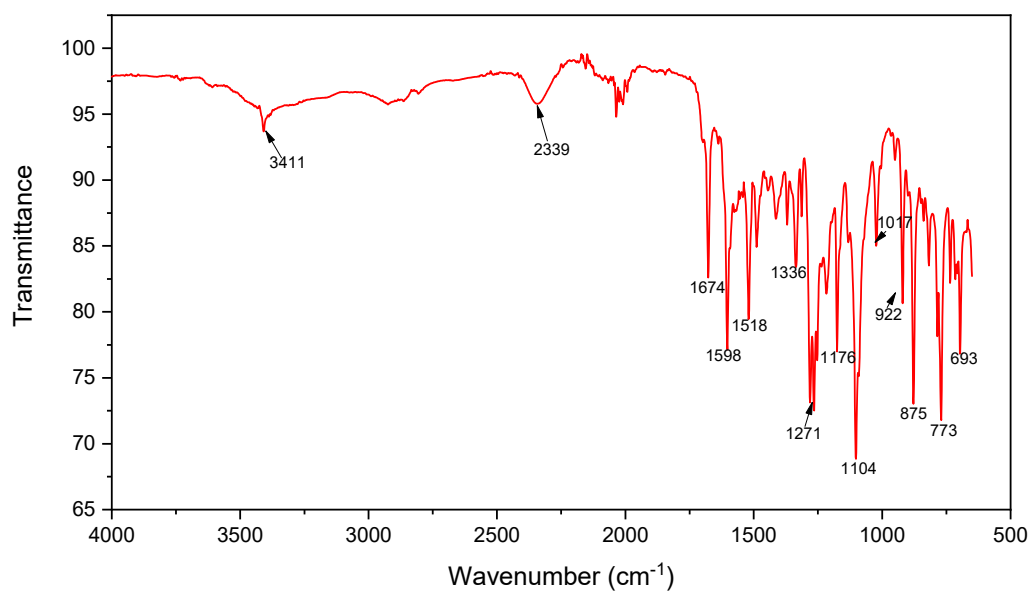
**Figure S56.** <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**19**)



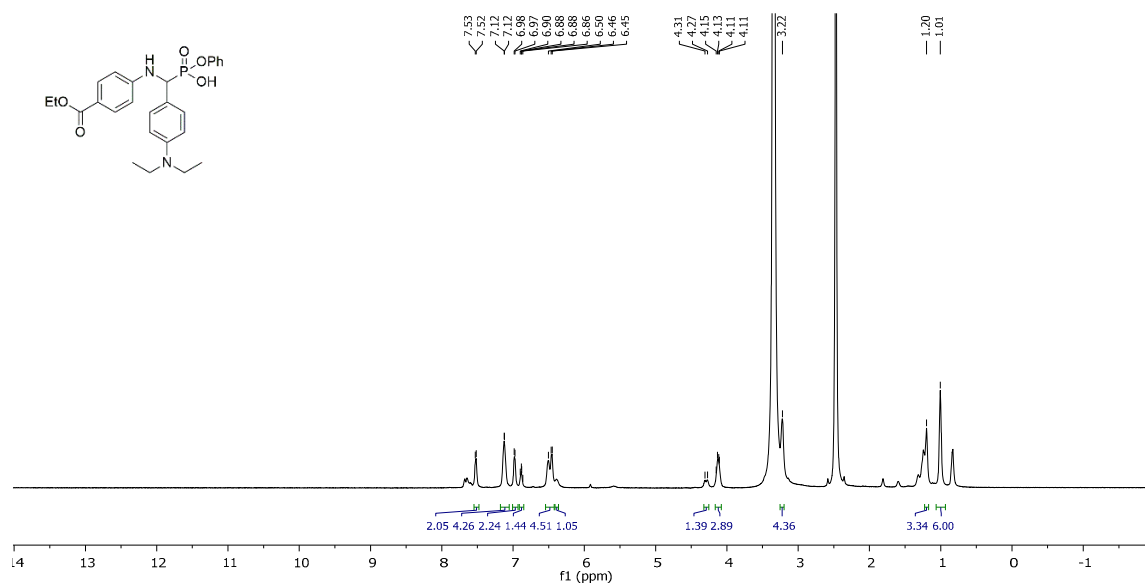
**Figure S57.** <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**19**)



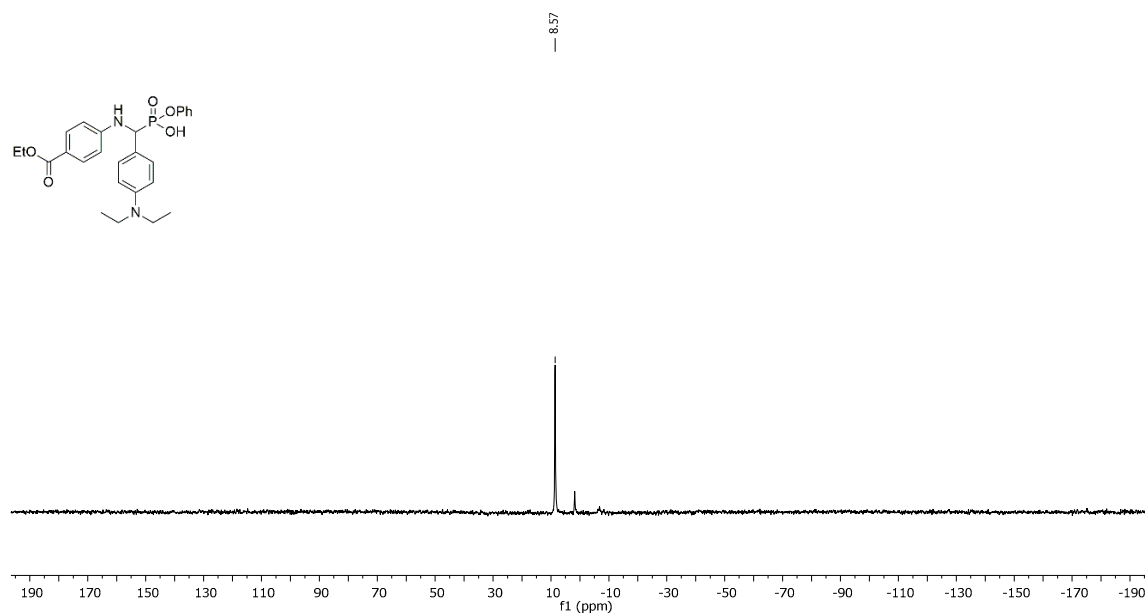
**Figure S58.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of ethyl 4-(((4-(dimethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**19**)



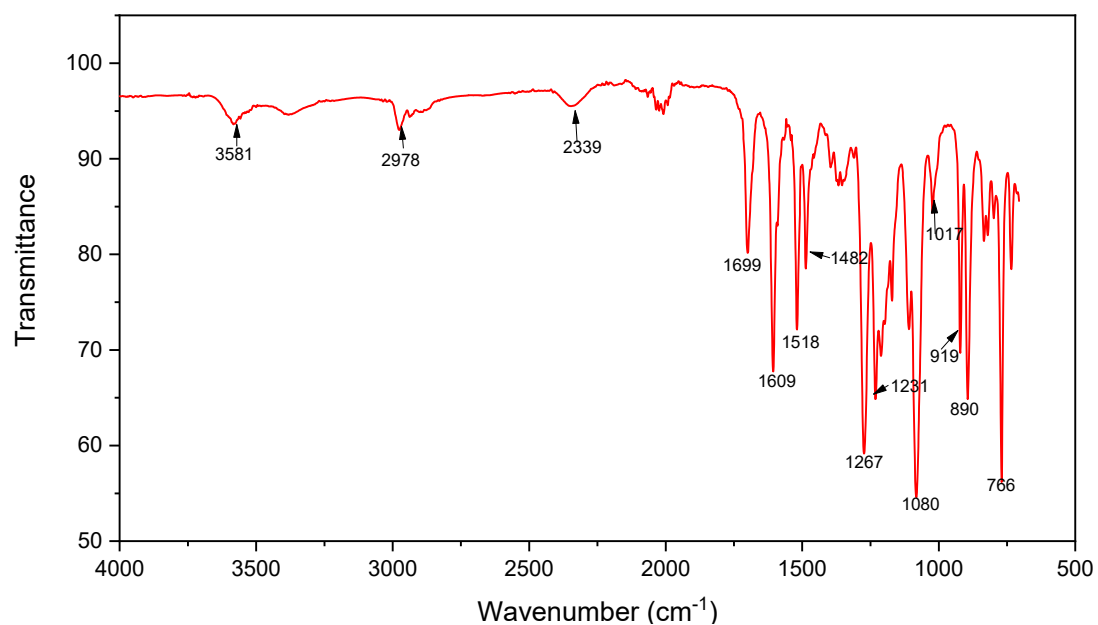
**Figure S59.** IR spectrum of ethyl 4-(((4-(dimethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**19**)



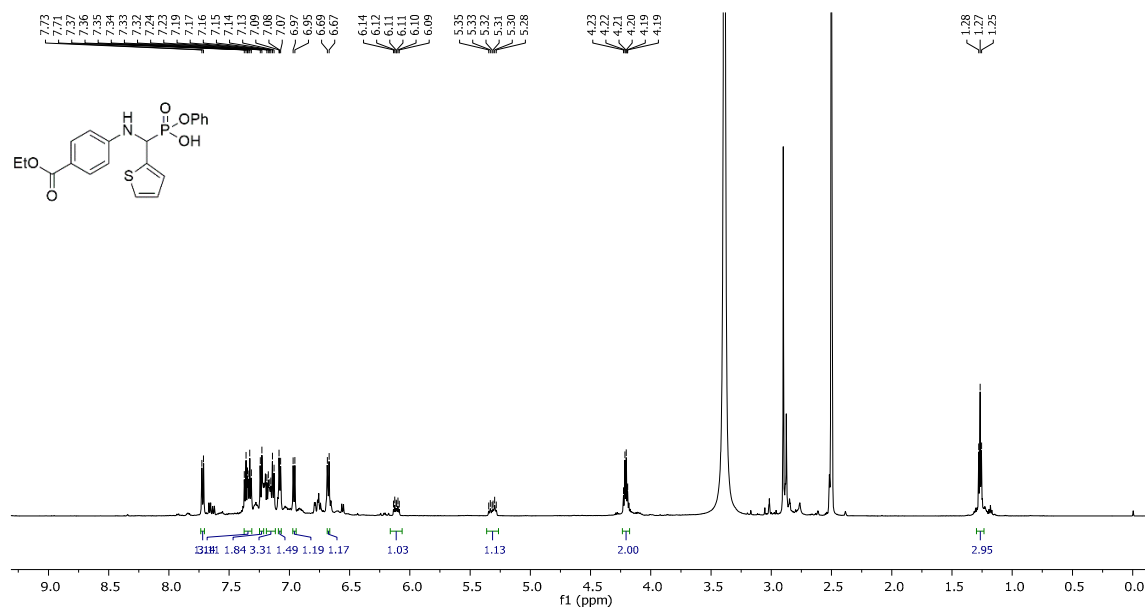
**Figure S60.** <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) of ethyl 4-(((4-(diethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**20**)



**Figure S61.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of ethyl 4-(((4-(diethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**20**)

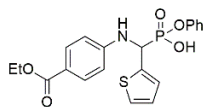


**Figure S62.** IR spectrum of ethyl 4-(((4-(diethylamino)phenyl)(hydroxy(phenoxy)phosphoryl)methyl)amino)benzoate (**20**)

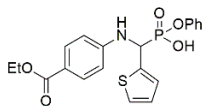


**Figure S63.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of ethyl 4-(((hydroxy(phenoxy)phosphoryl)(thiophen-2-yl)methyl)amino)benzoate (**21**)

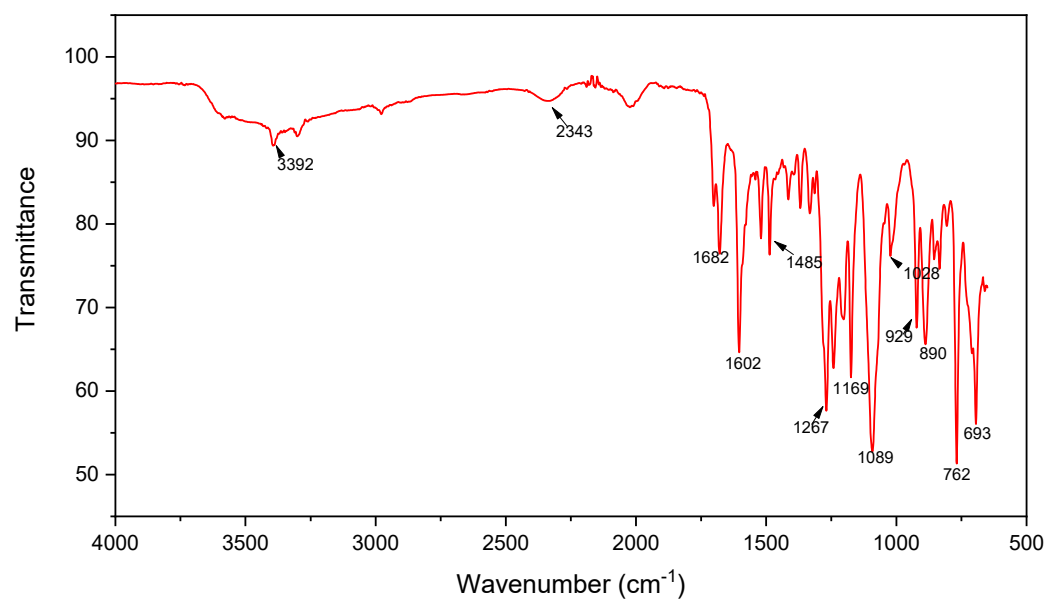




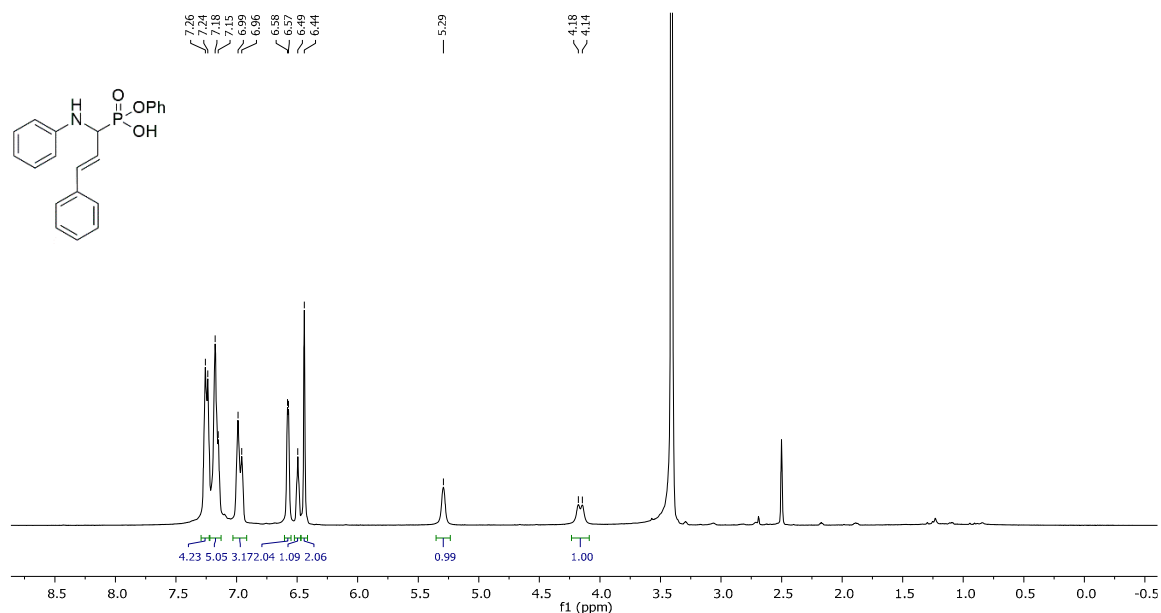
**Figure S64.**  $^{13}\text{C}$  NMR (176 MHz, DMSO- $d_6$ ) of ethyl 4-(((hydroxy(phenoxy)phosphoryl)(thiophen-2-yl)methyl)amino)benzoate (**21**)



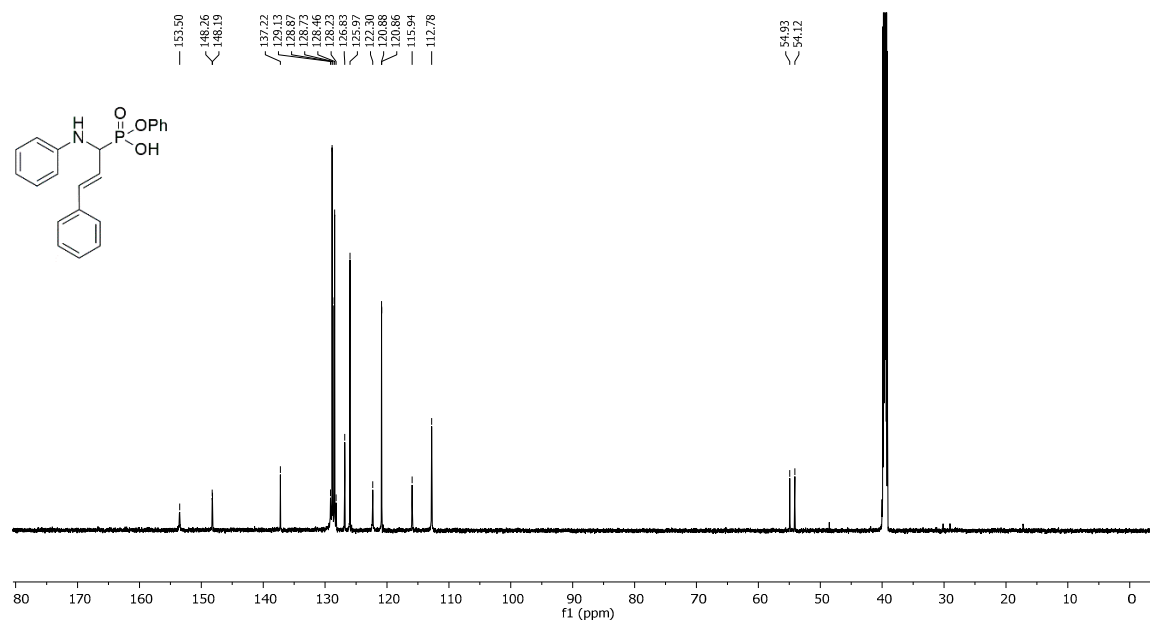
**Figure S65.**  $^{31}\text{P}$  NMR (243 MHz, DMSO- $d_6$ ) of ethyl 4-(((hydroxy(phenoxy)phosphoryl)(thiophen-2-yl)methyl)amino)benzoate (**21**)



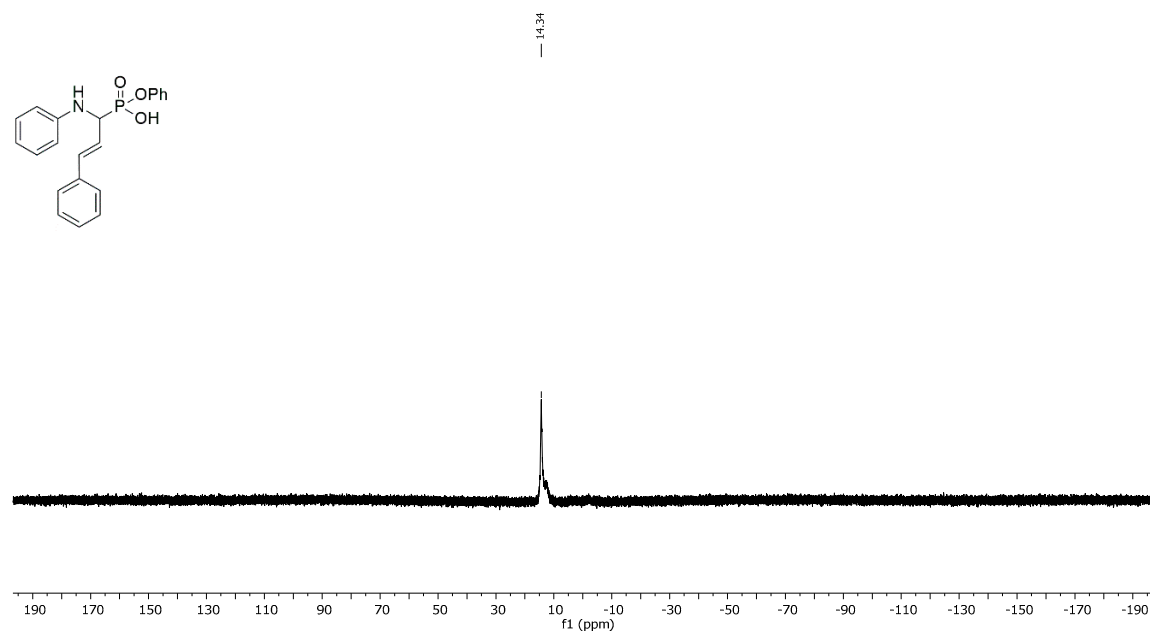
**Figure S66.** IR spectrum of ethyl 4-(((hydroxy(phenoxy)phosphoryl)(thiophen-2-yl)methyl)amino)benzoate (21)



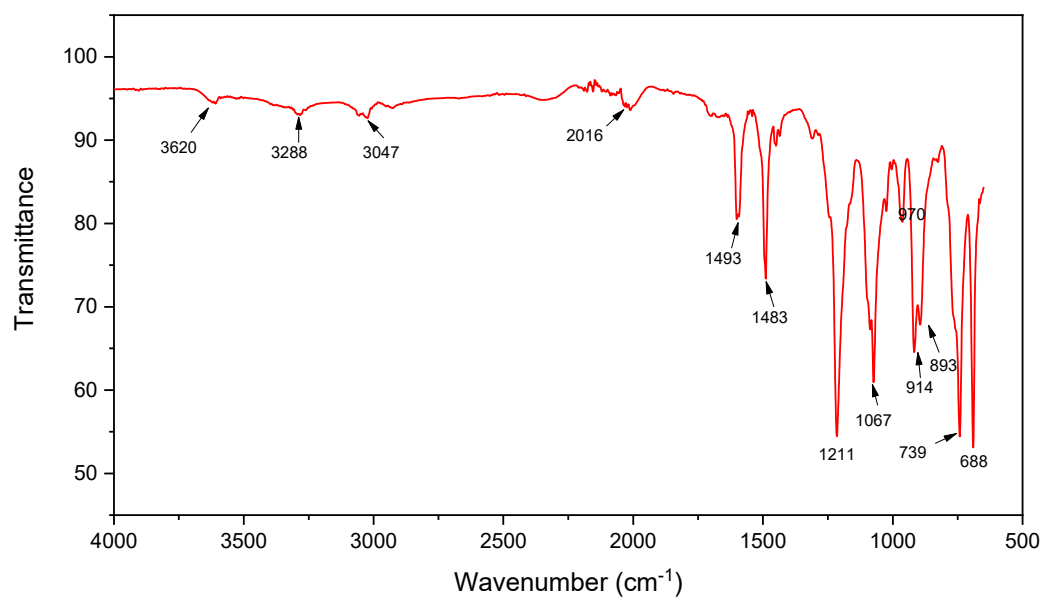
**Figure S67.**  $^1\text{H}$  NMR (700 MHz,  $\text{DMSO}-d_6$ ) of (*E*)-phenyl hydrogen (3-phenyl-1-(phenylamino)allyl)phosphonate (22)



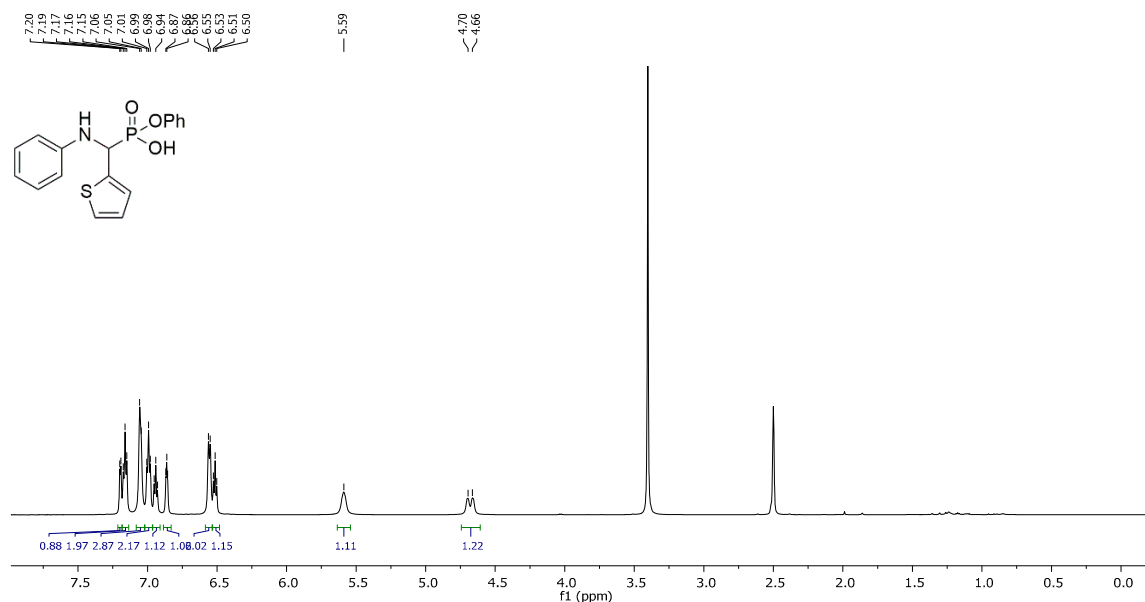
**Figure S68.** <sup>13</sup>C NMR (176 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-phenyl hydrogen (3-phenyl-1-(phenylamino)allyl)phosphonate (**22**)



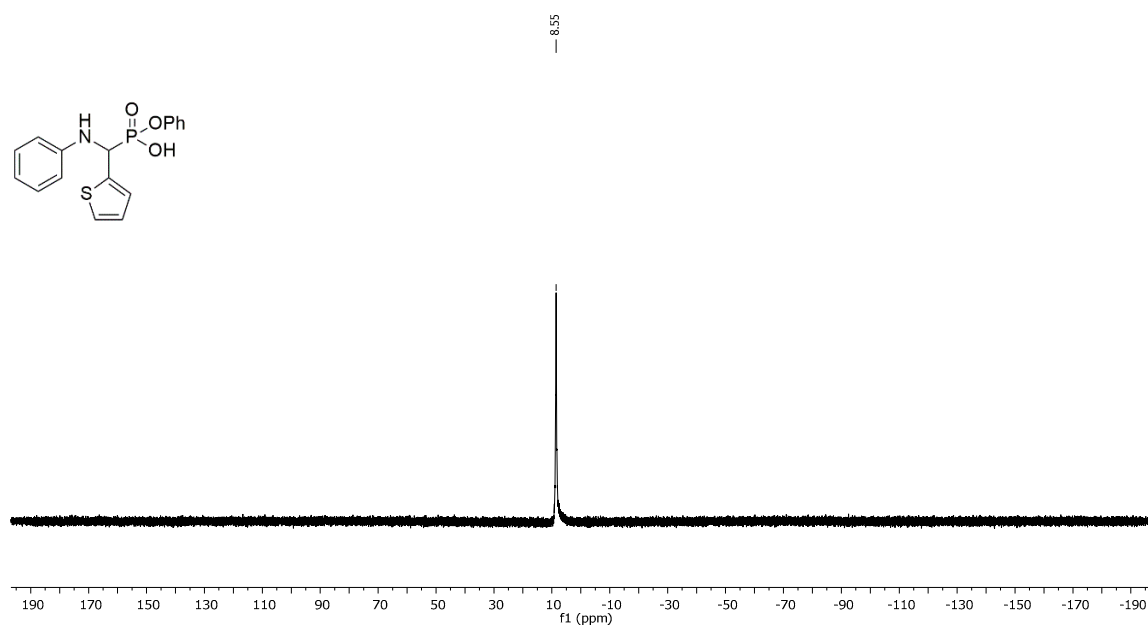
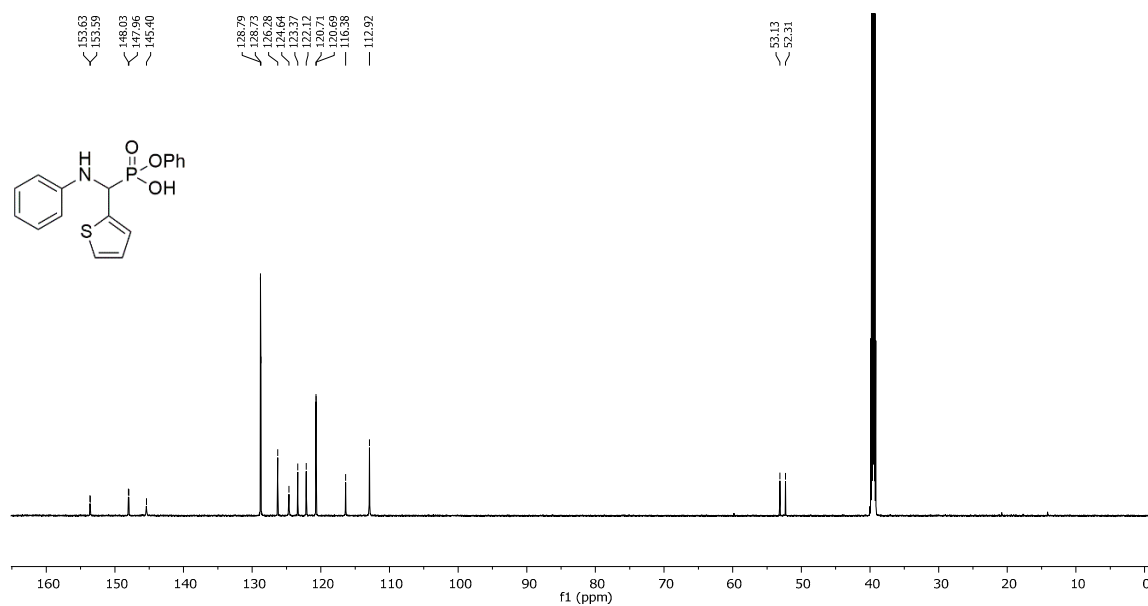
**Figure S69.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-phenyl hydrogen (3-phenyl-1-(phenylamino)allyl)phosphonate (**22**)

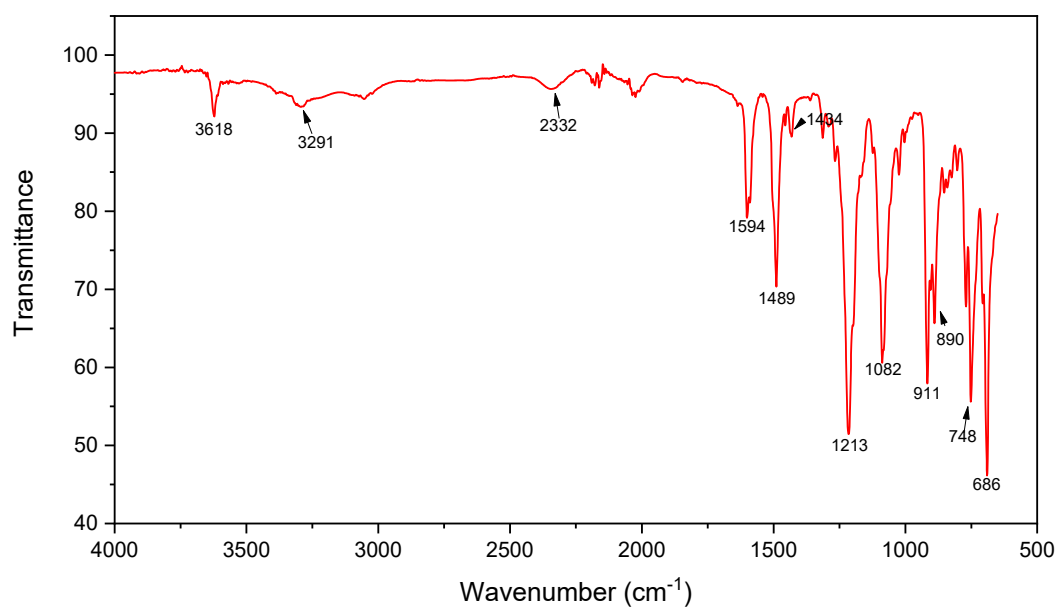


**Figure S70.** IR spectrum of (*E*)-phenyl hydrogen (3-phenyl-1-(phenylamino)allyl)phosphonate (**22**)

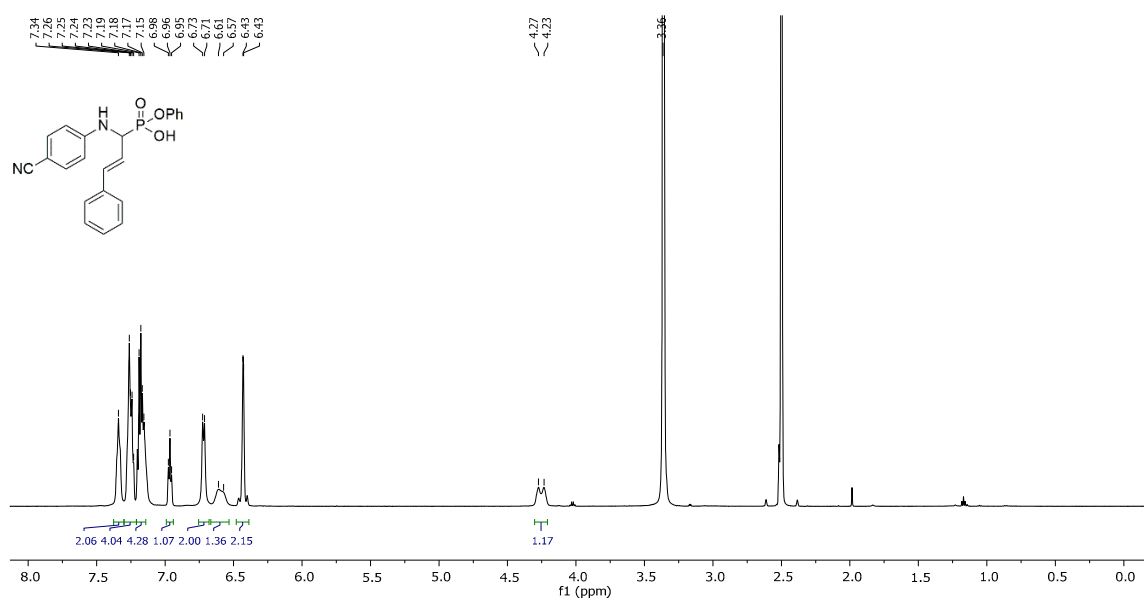


**Figure S71.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of phenyl hydrogen ((phenylamino)(thiophen-2-yl)methyl)phosphonate (**23**)

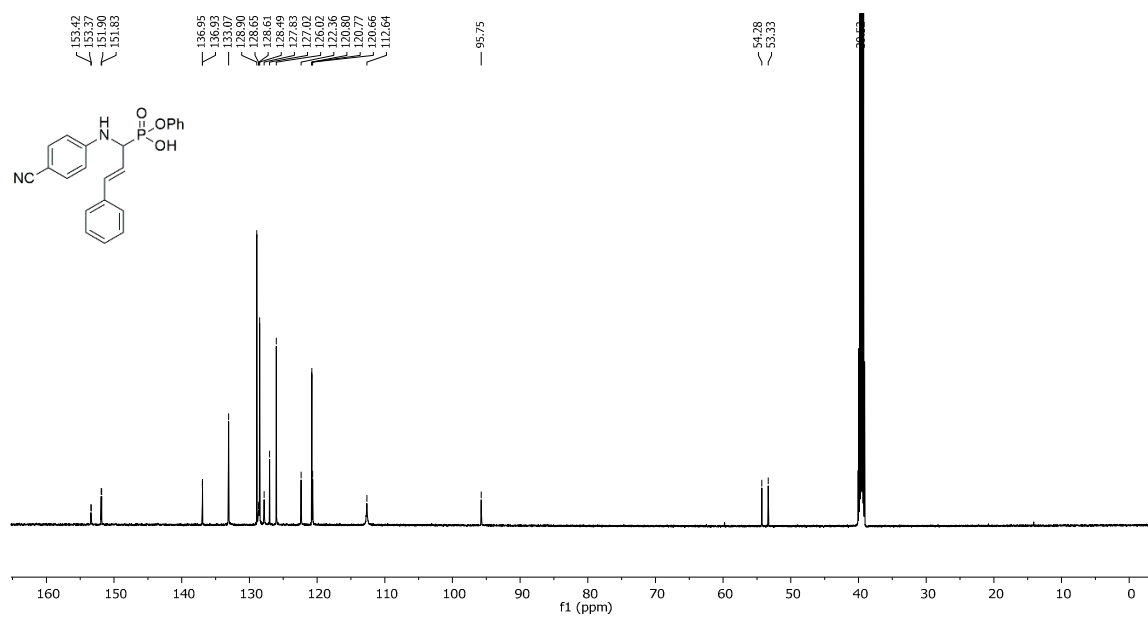




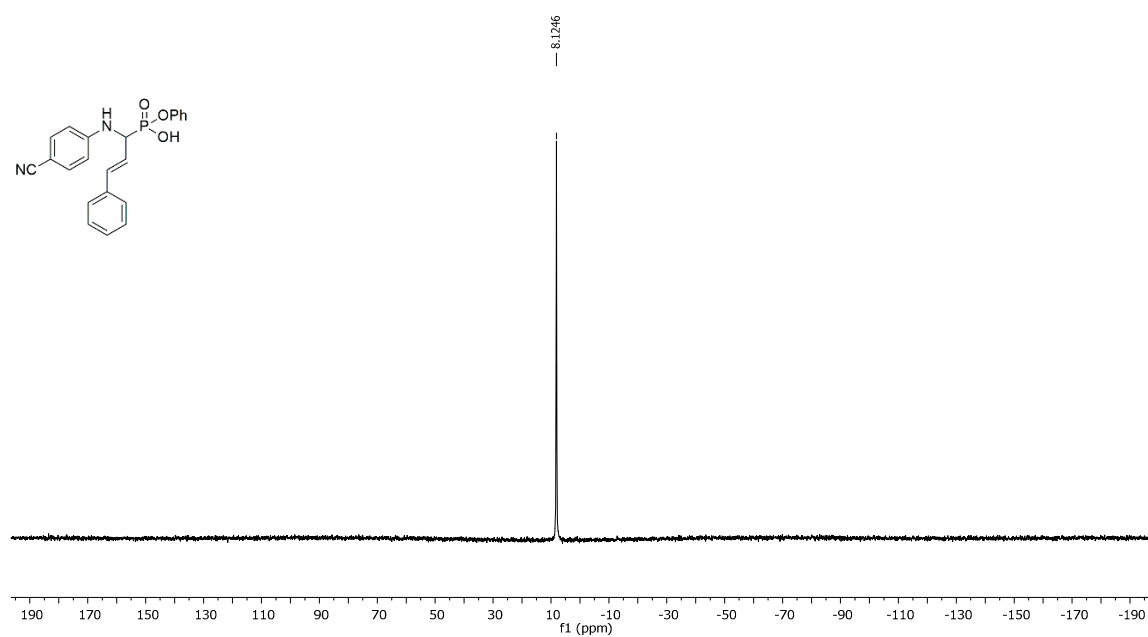
**Figure S74.** IR spectrum of phenyl hydrogen ((phenylamino)(thiophen-2-yl)methyl)phosphonate (**23**)



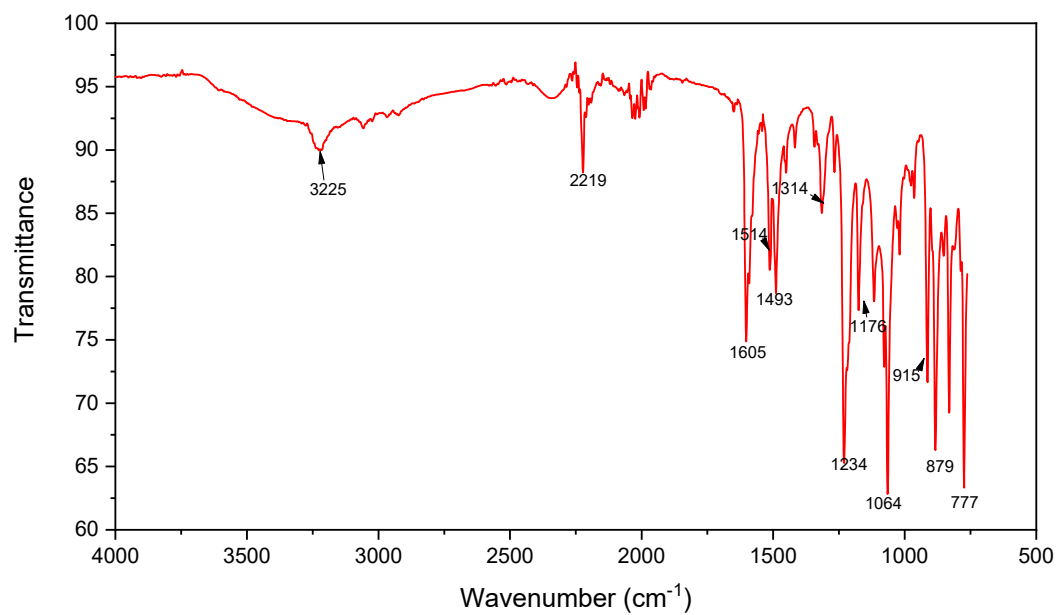
**Figure S75.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-phenylallyl)phosphonate (**24**)



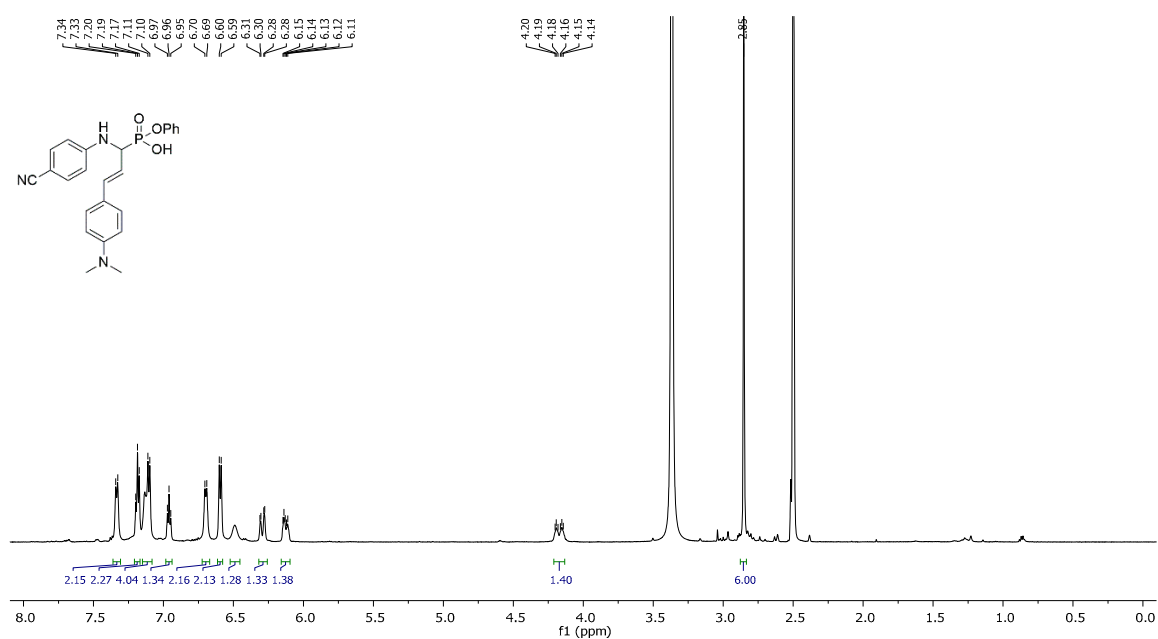
**Figure S76.** <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) of (E)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-phenylallyl)phosphonate (**24**)



**Figure S77.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of (E)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-phenylallyl)phosphonate (**24**)

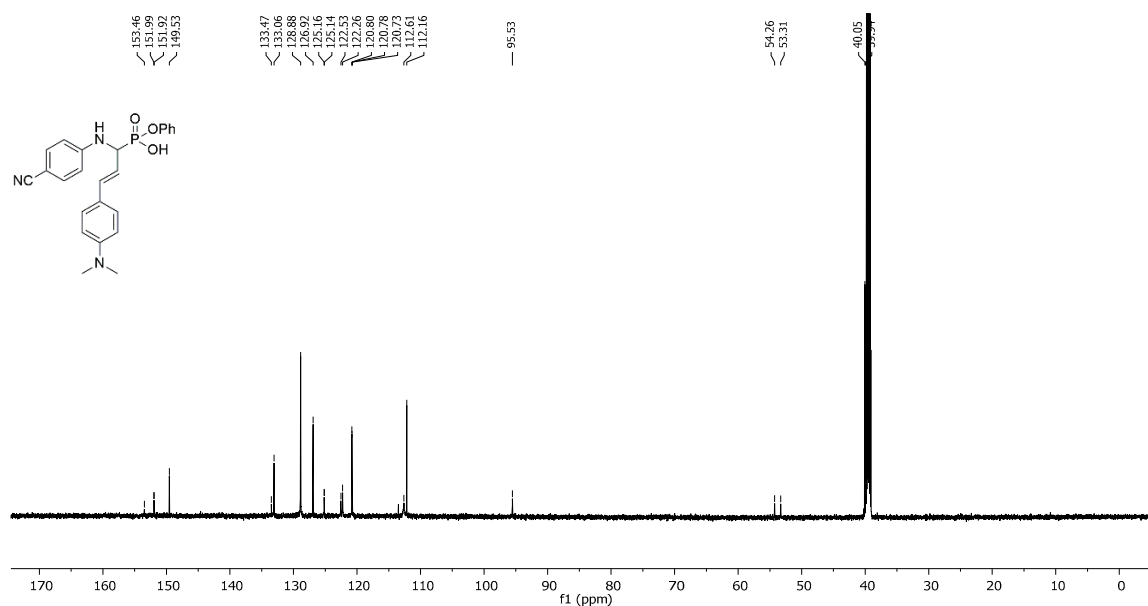


**Figure S78.** IR spectrum of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-phenylallyl)phosphonate (**24**)

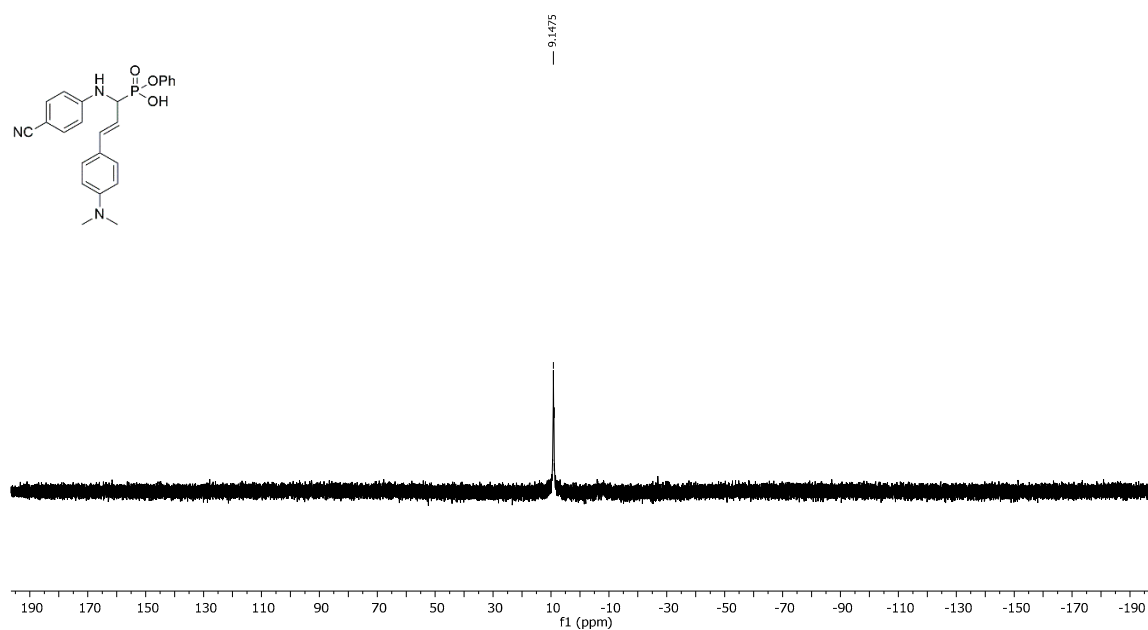


**Figure S79.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (**25**)

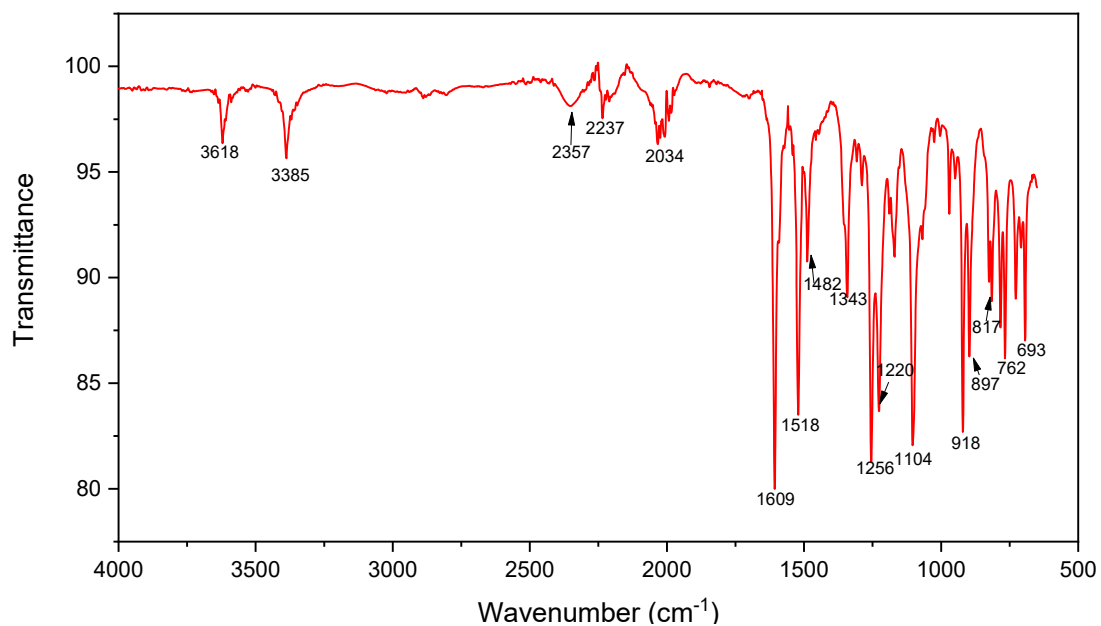




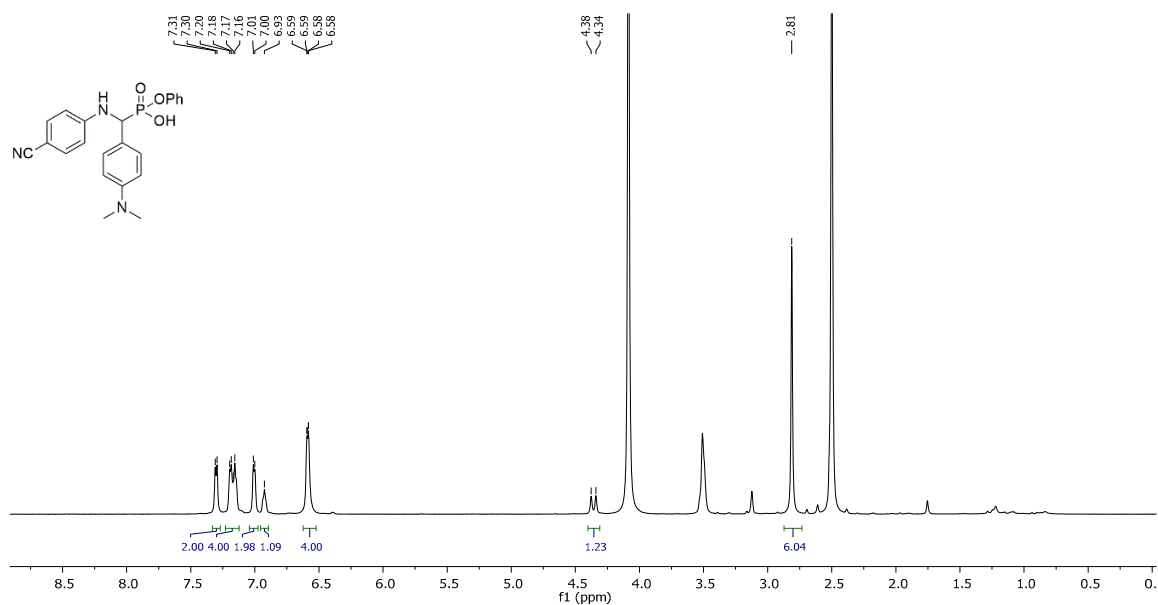
**Figure S80.** <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (25)



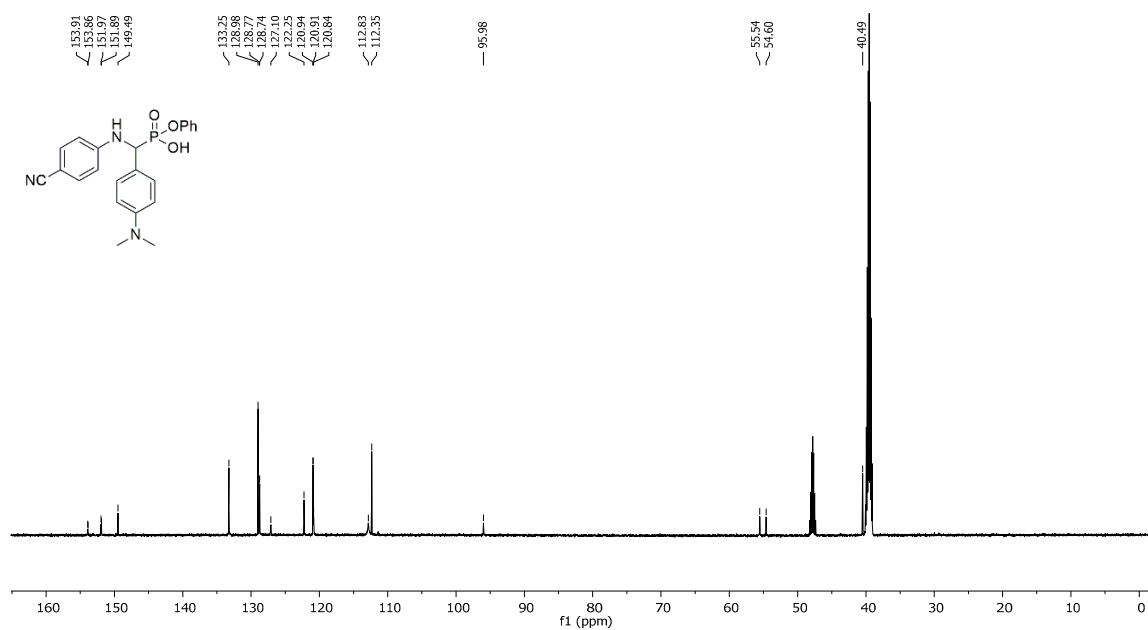
**Figure S81.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (25)



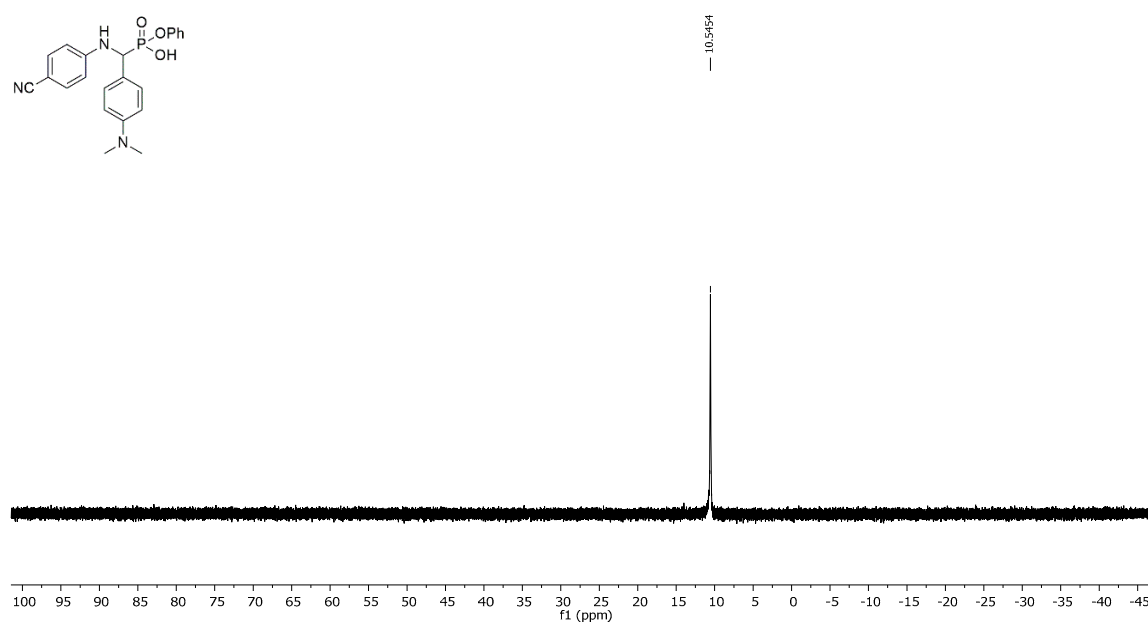
**Figure S82.** IR spectrum of (*E*)-phenyl hydrogen (1-((4-cyanophenyl)amino)-3-(4-(dimethylamino)phenyl)allyl)phosphonate (**25**)



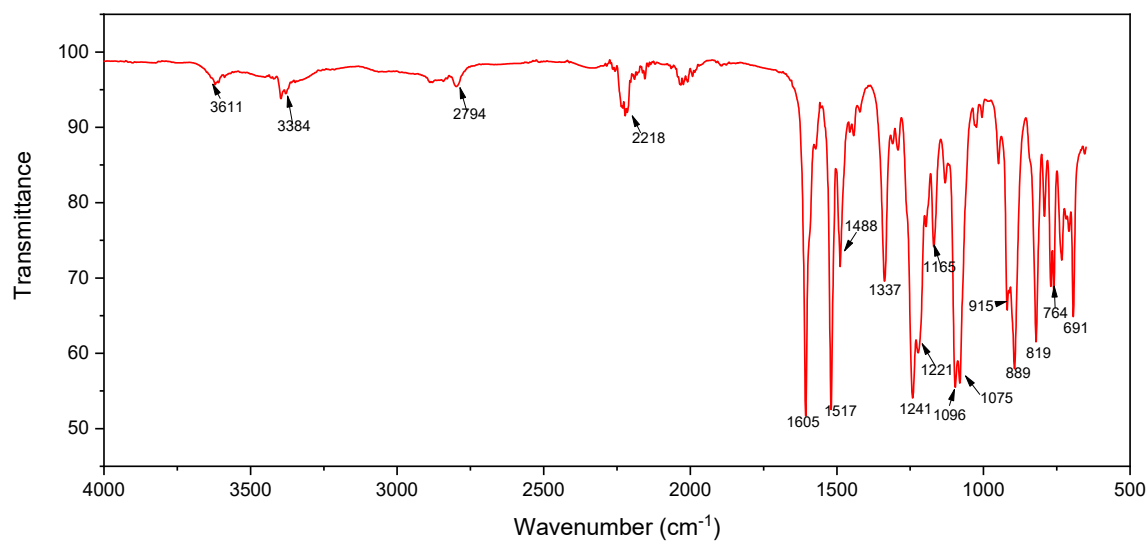
**Figure S83.**  $^1\text{H}$  NMR (600 MHz,  $\text{CD}_3\text{OD}/\text{DMSO}-d_6$ ) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**26**)



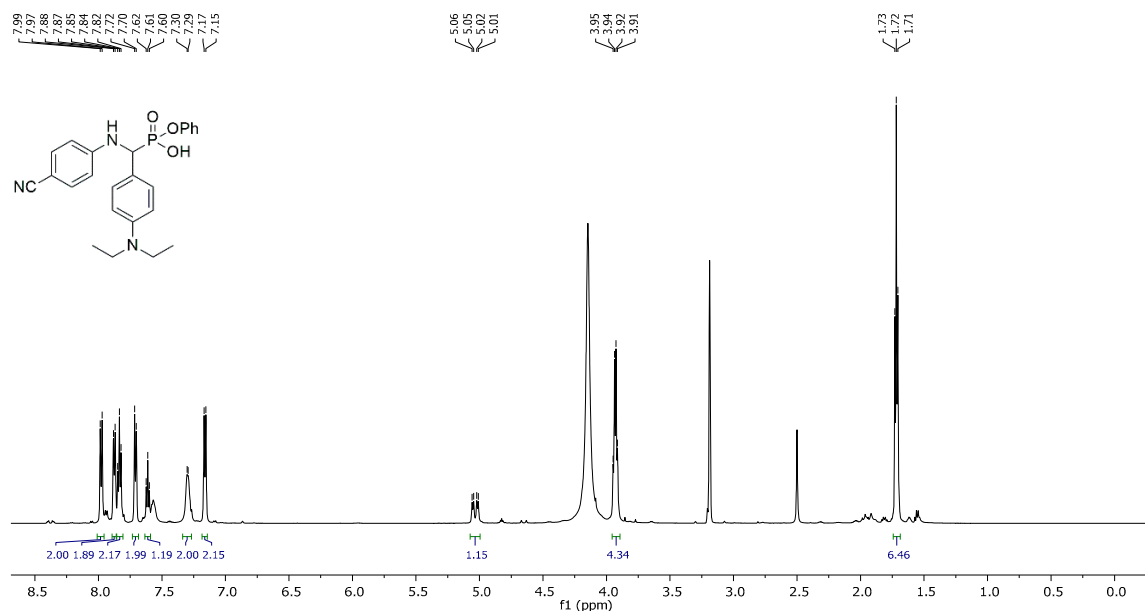
**Figure S84.** <sup>13</sup>C NMR (151 MHz, CD<sub>3</sub>OD/DMSO-*d*<sub>6</sub>) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**26**)



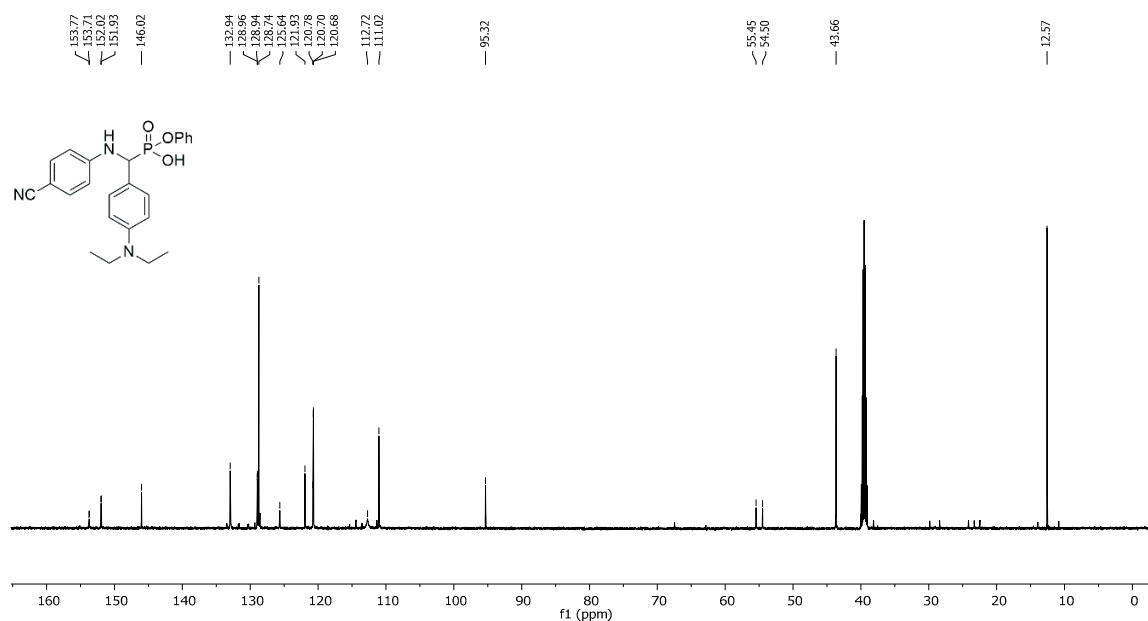
**Figure S85.** <sup>31</sup>P NMR (243 MHz, CD<sub>3</sub>OD/DMSO-*d*<sub>6</sub>) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**26**)



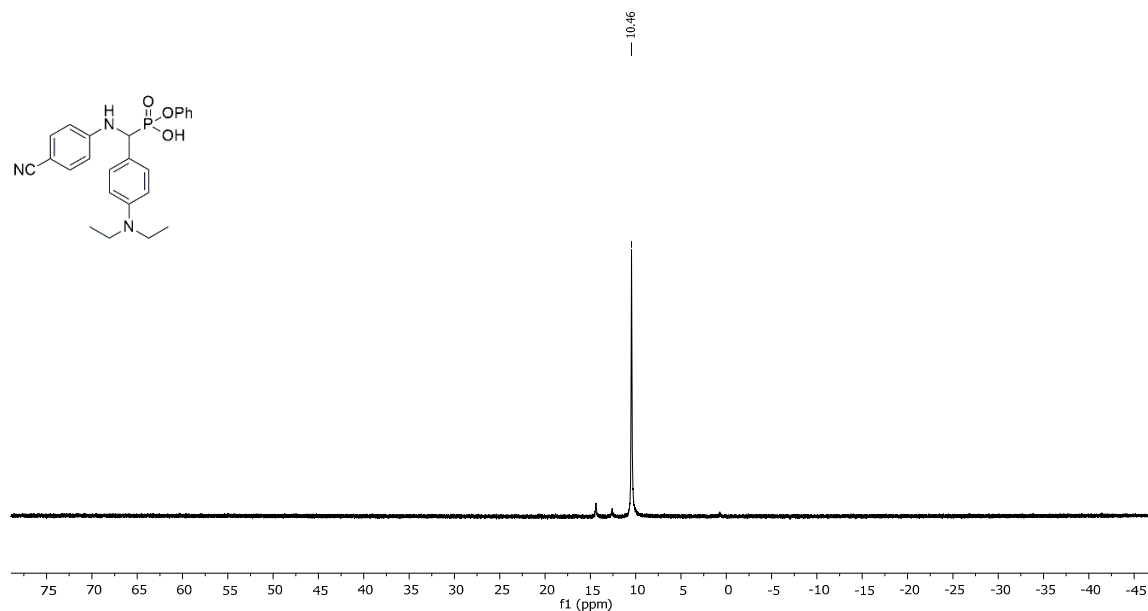
**Figure S86.** IR spectrum of phenyl hydrogen (((4-cyanophenyl)amino)(4-(dimethylamino)phenyl)methyl)phosphonate (**26**)



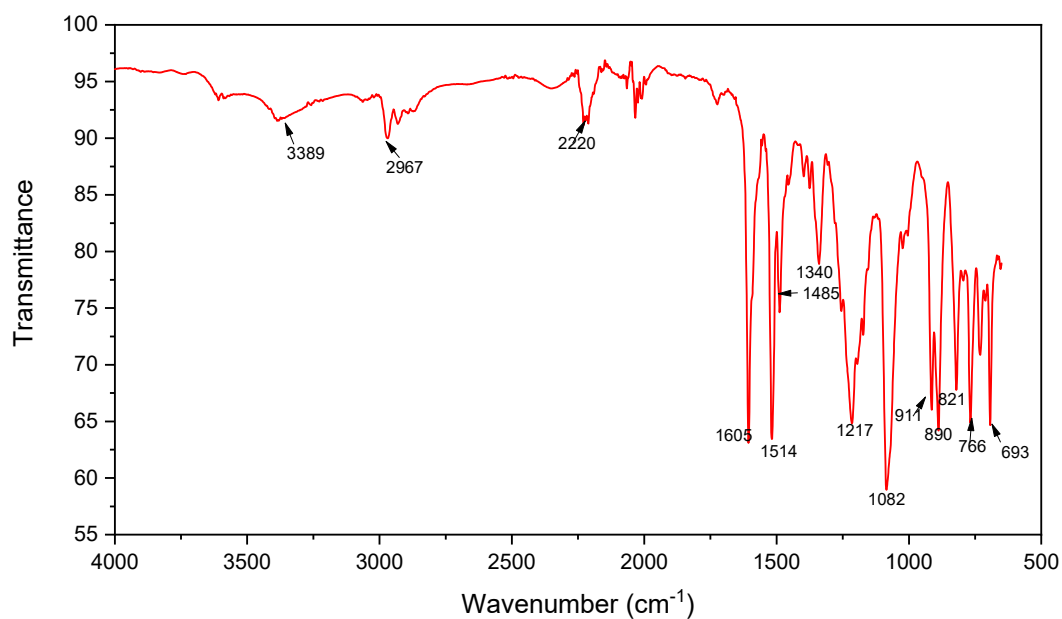
**Figure S87.** <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**27**)



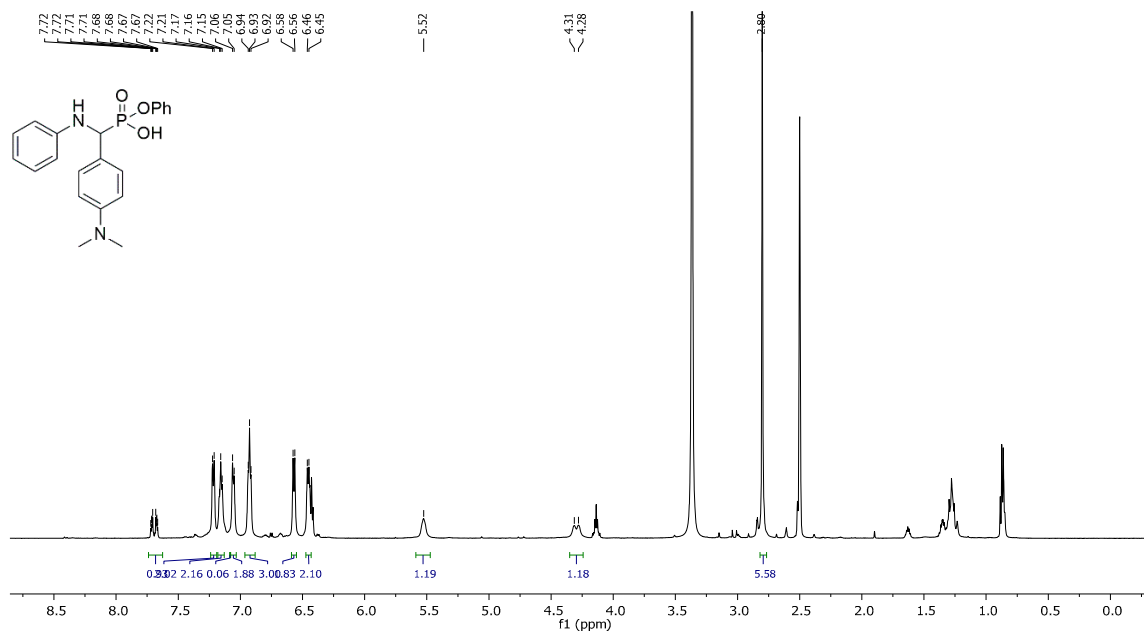
**Figure S88.** <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**27**)



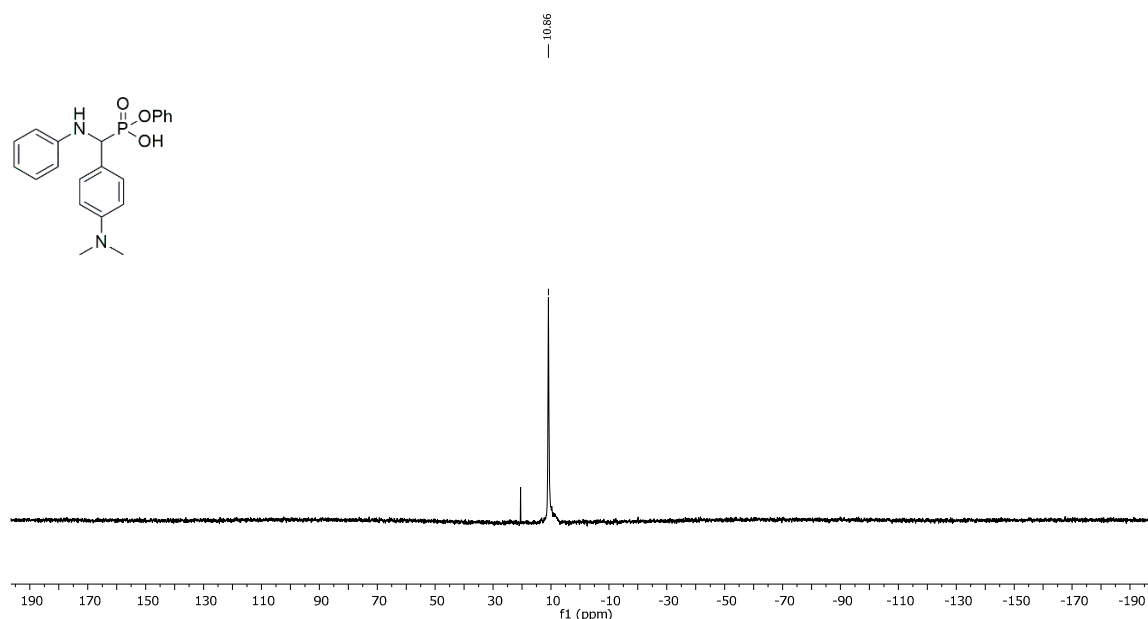
**Figure S89.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of phenyl hydrogen (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**27**)



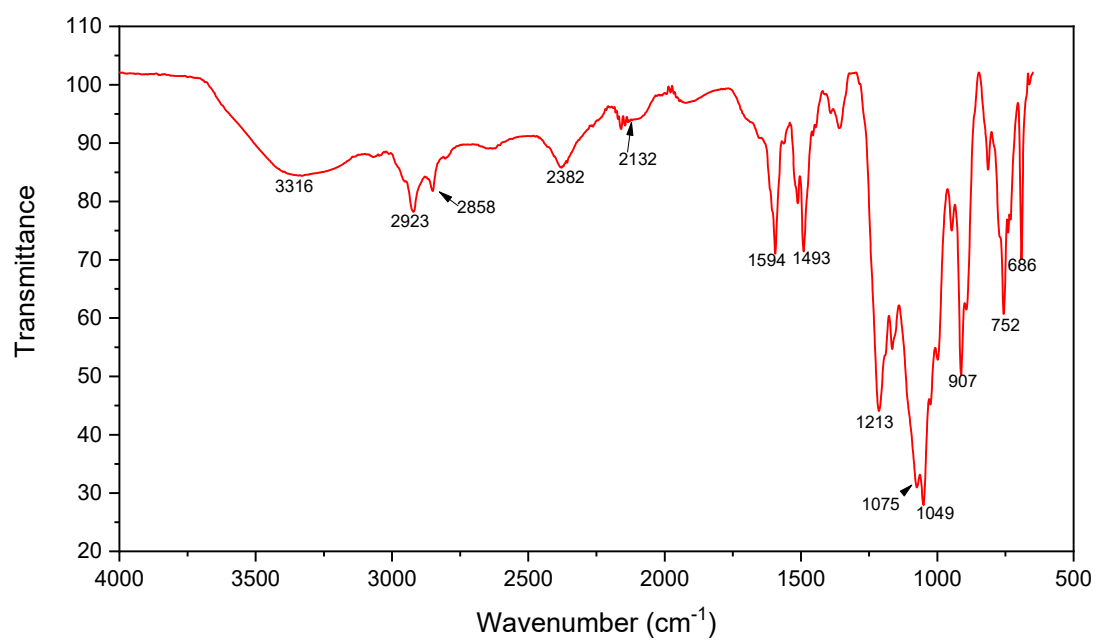
**Figure S90.** IR spectrum of phenyl hydrogen (((4-cyanophenyl)amino)(4-(diethylamino)phenyl)methyl)phosphonate (**27**)



**Figure S91.**  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ ) of phenyl hydrogen ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**28**)



**Figure S92.** <sup>31</sup>P NMR (243 MHz, DMSO-*d*<sub>6</sub>) of phenyl hydrogen ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**28**)



**Figure S93.** IR spectrum of phenyl hydrogen ((4-(dimethylamino)phenyl)(phenylamino)methyl)phosphonate (**28**)