



Supporting Information

for

Functionalization of the imidazo[1,2-*a*]pyridine ring in α -phosphonoacrylates and α -phosphonopropionates via microwave-assisted Mizoroki–Heck reaction

Damian Kusy, Agata Wojciechowska, Joanna Małolepsza and Katarzyna M. Błażewska

Beilstein J. Org. Chem. **2020**, *16*, 15–21. doi:10.3762/bjoc.16.3

Full experimental details, including copies of spectra (^1H NMR, ^{13}C NMR, ^{31}P NMR) of all new compounds. The experimental details and NMR description of the starting compounds synthesized according to our previously published procedure

Table of Contents

1. General information	S3
General procedure for the synthesis of compounds 3 , 6–22	S4
2. Characterization data, copies of ¹ H NMR, ¹³ C NMR and ³¹ P NMR spectra	S5
Figure S1. ¹ H NMR of compound 3 (700 MHz, CDCl ₃).....	S5
Figure S2. ³¹ P NMR of compound 3 (ratio <i>E/Z</i> 100:3) (283 MHz, CDCl ₃).	S6
Figure S3. ¹³ C NMR of compound 3 (176 MHz, CDCl ₃)	S6
Figure S4. ¹ H NMR of compound 6 (700 MHz, CDCl ₃).....	S7
Figure S5. ³¹ P NMR of compound 6 (ratio <i>E/Z</i> 100:3) (283 MHz, CDCl ₃)	S8
Figure S6. ¹³ C NMR of compound 6 (176 MHz, CDCl ₃)	S8
Figure S7. ¹ H NMR of compound 7 (700 MHz, CDCl ₃).....	S9
Figure S8. ³¹ P NMR of compound 7 (ratio <i>E/Z</i> 100:6) (283 MHz, CDCl ₃)	S10
Figure S9. ¹³ C NMR of compound 7 (176 MHz, CDCl ₃)	S10
Figure S10. ¹ H NMR of compound 8 (700 MHz, CDCl ₃).....	S11
Figure S11. ³¹ P NMR of compound 8 (ratio <i>E/Z</i> 100:11) (283 MHz, CDCl ₃)	S12
Figure S12. ¹³ C NMR of compound 8 (176 MHz, CDCl ₃)	S12
Figure S13. ¹ H NMR of compound 9 (700 MHz, CDCl ₃).....	S13
Figure S14. ³¹ P NMR of compound 9 (ratio <i>E/Z</i> 100:15) (283 MHz, CDCl ₃)	S14
Figure S15. ¹³ C NMR of compound 9 (176 MHz, CDCl ₃)	S14
Figure S16. ¹ H NMR of compound 10 (700 MHz, CDCl ₃).....	S16
Figure S17. ³¹ P NMR of compound 10 (ratio <i>E/Z</i> 100:4) (283 MHz, CDCl ₃)	S16
Figure S18. ¹³ C NMR of compound 10 (176 MHz, CDCl ₃)	S17
Figure S19. Composition of the reaction mixture (compound 11).....	S18
Figure S20. ¹ H NMR of compound 11 (700 MHz, CDCl ₃).....	S19
Figure S21. ³¹ P NMR of compound 11 (283 MHz, CDCl ₃).....	S19
Figure S22. ¹³ C NMR of compound 11 (176 MHz, CDCl ₃)	S20
Figure S23. ¹ H NMR of compound 12 (residual DIPEA·HBr at 1.5, 3.1, 3.6 ppm) (700 MHz, CDCl ₃).....	S21
Figure S24. ³¹ P NMR of compound 12 (ratio <i>E/Z</i> 100:16) (283 MHz, CDCl ₃)	S21
Figure S25. ¹³ C NMR of compound 12 (176 MHz, CDCl ₃)	S22
Figure S26. ¹ H NMR of compound 13 (700 MHz, CDCl ₃).....	S23

Figure S27. ^{31}P NMR of compound 13 (283 MHz, CDCl_3)	S23
Figure S28. ^{13}C NMR of compound 13 (176 MHz, CDCl_3)	S24
Figure S29. ^1H NMR of compound 15 (700 MHz, CDCl_3).....	S25
Figure S30. ^{31}P NMR of compound 15 (283 MHz, CDCl_3).....	S25
Figure S31. ^{13}C NMR of compound 15 (176 MHz, CDCl_3)	S26
Figure S32. ^1H NMR of compound 14 (700 MHz, CDCl_3).....	S27
Figure S33. ^{31}P NMR of compound 14 (mixture of Heck products) (283 MHz, CDCl_3)	27
Figure S34. ^{13}C NMR of compound 14 (176 MHz, CDCl_3)	S28
Figure S35. ^1H NMR of compound 16 (700 MHz, CDCl_3).....	S29
Figure S36. ^{31}P NMR of compound 16 (mixture of Heck products) (283 MHz, CDCl_3)	S29
Figure S37. ^{13}C NMR of compound 16 (176 MHz, CDCl_3)	S30
Figure S38. ^1H NMR of compound 17 (700 MHz, CDCl_3).....	S31
Figure S39. ^{31}P NMR of compound 17 (283 MHz, CDCl_3).....	S31
Figure S40. ^{13}C NMR of compound 17 (176 MHz, CDCl_3)	S32
Figure S41. ^1H NMR of compound 18 (700 MHz, CDCl_3).....	S33
Figure S42. ^{31}P NMR of compound 18 (286 MHz, CDCl_3).....	S33
Figure S43. ^{13}C NMR of compound 18 (176 MHz, CDCl_3)	S34
Figure S44. ^1H NMR of compound 19 (700 MHz, CDCl_3).....	S35
Figure S45. ^{31}P NMR of compound 19 (284 MHz, CDCl_3).....	S35
Figure S46. ^{13}C NMR of compound 19 (176 MHz, CDCl_3)	S36
Figure S47. ^1H NMR of compound 20 (700 MHz, CDCl_3).....	S37
Figure S48. ^{31}P NMR of compound 20 (283 MHz, CDCl_3).....	S37
Figure S49. ^{13}C NMR of compound 20 (176 MHz, CDCl_3)	S38
Figure S50. ^1H NMR of compound 21 (residual DIPEA·HBr at 1.5, 3.1, 3.6 ppm) (700 MHz, CDCl_3).....	S39
Figure S51. ^{31}P NMR of compound 21 (283 MHz, CDCl_3).....	S39
Figure S52. ^1H NMR of compound 22 (700 MHz, CDCl_3).....	S41
Figure S53. ^{31}P NMR of compound 22 (283 MHz, CDCl_3).....	S41
Figure S54. ^{13}C NMR of compound 22 (176 MHz, CDCl_3)	S42
Figure S55. ^1H NMR of compound 4 (700 MHz, CDCl_3).....	S43
Figure S56. ^{31}P NMR of compound 4 (283 MHz, CDCl_3).....	S43

Figure S57. ^1H NMR of compound 5 (700 MHz, CDCl_3).....	S44
Figure S58. ^{31}P NMR of compound 5 (283 MHz, CDCl_3).....	S45
Figure S59. ^{13}C NMR of compound 5 (176 MHz, CDCl_3)\.....	S45
Figure S60. Infrared spectroscopy of 5	S46
Side product 5 obtained via different synthetic route [1]	S46
Figure S61. ^1H NMR of compound 5' (700 MHz, CDCl_3)	S47
Figure S62. ^{31}P NMR of compound 5' (283 MHz, CDCl_3).....	S48
Figure S63. ^{13}C NMR of compound 5' (176 MHz, CDCl_3)	S48
Figure S64. Comparing the ^{13}C NMR spectra of compounds 5 (blue) and 5' (red).....	S49
Figure S65. Comparing the ^1H NMR spectra of compounds 5 (blue) and 5' (red)	S49
Figure S66. ^1H NMR spectra of mixture of side product 5 and synthesized compound 5'	S50
Figure S67. ^1H NMR of compound 23 (700 MHz, CDCl_3).....	S53
Figure S68. ^{31}P NMR of compound 23 (283 MHz, CDCl_3	S53
Figure S69. Comparing ^{31}P NMR spectra of reaction mixture after Heck reaction performed on compound 23	S54
Figure S70. Comparing ^1H NMR spectra of reaction mixture after Heck reaction performed on compound 23	S55
Figure S71. Comparing ^1H NMR spectra of reaction mixture after Heck reaction performed on compound 23 (range 0–4.7).....	S55
General procedure for the synthesis of starting materials (1,2 , and 23) [1]	S56
<i>General procedure for the synthesis of compounds (1)</i>	S56
<i>General procedure for the synthesis of compounds (2)</i>	S57
<i>General procedure for the synthesis of compounds (23)</i>	S58
Figure S72. ^1H NMR of compound 23 (250 MHz, CDCl_3).....	S59
Figure S73. ^{31}P NMR of compound 23 (101 MHz, CDCl_3).....	S60
References	S60

1. General information

NMR spectra were measured at 250.13 or 700 MHz for ^1H NMR, 62.90 or 170 MHz for ^{13}C NMR, 283 or 101.30 MHz for ^{31}P NMR on Bruker Avance DPX 250 and Bruker Avance II Plus 700 spectrometers, respectively. Chemical shifts (δ) are reported in parts per million (ppm) relative to internal residual CHCl_3 in CDCl_3 (δ 7.26 ^1H NMR), CDCl_3 signal in ^{13}C NMR (δ 77.16) or external 85% H_3PO_4 (δ 0 ppm ^{31}P NMR). ^{31}P NMR and ^{13}C NMR spectra were proton-decoupled. Coupling constants (J) are quoted in Hz. The assignment of the signals in ^1H NMR and ^{13}C NMR spectra was supported by two-dimensional experiments

(COSY, HMQC, HMBC, DEPT-135). In the case of compounds obtained as diastereomeric mixtures, the ratio of diastereomers was determined based on ^{31}P NMR and (if possible) sufficiently separated signals in ^1H NMR. IR spectra were measured on an FT-IR Alpha Bruker (ATR) instrument and were reported in cm^{-1} .

A monomode microwave reactor (CEM Discover SP) equipped with an IntelliVent pressure control system was used. The standard method was applied and maximum pressure was set to 250 psi. Temperatures of the reaction mixtures were measured with an external infrared sensor.

Samples were analyzed in positive ion mode with an Agilent 6220 mass spectrometer coupled with an Agilent 1200 series HPLC. Three μL of the sample were injected at a flow rate of 200 $\mu\text{L}/\text{min}$, methanol + 0.1% formic acid. Mass spectrometry parameters were as follows: m/z range 100–3000, fragmentor 350 V, skimmer 65 V, gas temp 325 $^{\circ}\text{C}$, drying gas 8 L/min, nebulizer 45 psig, capillary 4000 V.

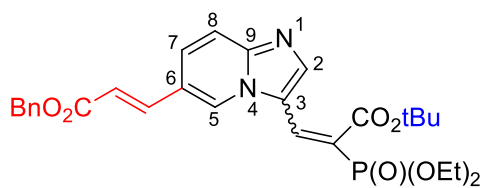
The spectra of the main fractions after flash chromatography purification were given. The impurities are indicated and defined in the spectra.

The reactions were carried out using substrate **1**, which was in most cases used as the mixture of (*E*) and (*Z*)-stereoisomers (typically up to 85:15 ratio). Therefore, in the ^{31}P NMR spectra of products derived from **1**, a mixture of (*E*) and (*Z*) products is present, as indicated for the example of compound **3**. The ratio is also included in the description of each compound. However, the presence of *E/Z*-stereoisomers is due to the stereochemistry of the double bond already present in the substrate **1** and has nothing to do with the stereochemistry of the newly formed double bond. In most examples, the double bond formed in the reaction is *E*-configured (*E*) >98%). The isomers were identified and their ratio determined based on the ^{31}P NMR spectra and the values of vicinal coupling constants in the ^1H NMR spectra: $^3J_{\text{HP}}$ (for substrates **1**) and $^3J_{\text{HP}}/^3J_{\text{HH}}$ (for products). It has been presented on the example of compound **11** (see Figure S19 and pages S19,S20). The chemical shifts in ^{13}C and ^1H NMR are reported only for the major isomers. The chemical shifts in ^{31}P NMR are given for both isomers.

General procedure for the synthesis of compounds 3, 6–22

$\text{Pd}(\text{OAc})_2$ (2.45 mg, 0.0108 mmol, 0.05 equiv) and tri(*o*-tolyl)phosphine (2.98 mg, 0.0098 mmol, 0.045 equiv) were added to a solution of **1a** (0.2177 mmol, 1.0 equiv), DIPEA (0.057 mL, 0.327 mmol, 1.5 equiv), benzyl acrylate (0.036 mL, 0.24 mmol, 1.1 equiv) in PCN (2 mL), and the mixture placed in pressure vial equipped with a magnetic stirring bar. The mixture was stirred for 1 min and purged with argon via a syringe. Then, MW irradiation (with initial 150 W power) was applied. The following conditions were used: 30 min, 110 $^{\circ}\text{C}$. Afterwards, the reaction mixture was diluted with DCM (10 mL), and adsorbed on silica gel (≈ 3 g). The solvent was evaporated, and the residue was subjected to column chromatography using gradient DCM/acetone as eluent to give the product as orange oil. Depending on the products different gradients were used: for compounds **3**, **6–8**, **10–15** (100:0 $\Rightarrow$ 70:30, for compounds **16–19**, **21–22** gradient 100:0 $\Rightarrow$ 40:60, for compounds **9** and **20** gradient 100:0 $\Rightarrow$ 10:90).

2. Characterization data, copies of ^1H NMR, ^{13}C NMR and ^{31}P NMR spectra



3

tert-Butyl 3-(6-((*E*)-3-(benzyloxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (3). Yield 91%

HRMS m/z : calculated 541.2098 ($\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), found 541.2104 ($\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), ^1H NMR (700 MHz, CDCl_3) δ : 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 1.56 (s, $\text{C}(\text{CH}_3)_3$, 9H), 4.06 – 4.24 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 4H), 5.26 (s, PhCH_2O , 2H), 6.52 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.36 – 7.44 (m, PhCH_2O , 5H), 7.55 (dd, $^3J_{\text{HH}} = 9.4$ Hz, $^4J_{\text{HH}} = 1.4$ Hz, $\text{CH}_{(7)}$, 1H), 7.68 (d, $^3J_{\text{HH}} = 9.4$ Hz, $\text{CH}_{(8)}$, 1H), 7.70 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.81 (d, $^3J_{\text{HH}} = 23.9$ Hz, (*E*) $\text{CH}=\text{CP}$, 1H), 8.42 (s, $\text{CH}_{(5)}$, 1H), 8.44 (s, $\text{CH}_{(2)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 16.09 – (*E*) $\text{CH}=\text{CP}$, 12.85 – (*Z*) $\text{CH}=\text{CP}$ (*E*:*Z*)=(1:0.03), ^{13}C NMR (176 MHz, CDCl_3) δ : 16.42 (d, $^4J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 28.15 (s, $\text{C}(\text{CH}_3)_3$, 3C), 62.63 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 66.78 (s, PhCH_2O , 1C), 82.96 (s, $\text{C}(\text{CH}_3)_3$, 1C), 118.81 (s, $\text{CH}_{(8)}$, 1C), 119.87 (d, $^1J_{\text{PC}} = 181.8$ Hz, CP , 1C), 119.94 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C), 121.14 (d, $^3J_{\text{PC}} = 24.8$ Hz, $\text{C}_{(3)}$, 1C), 122.46 (s, $\text{C}_{(6)}$, 1C), 124.31 (s, $\text{CH}_{(7)}$, 1C), 125.18 (s, $\text{CH}_{(5)}$, 1C), 128.76 – 128.46, (Ph, 5C), 131.64 (d, $^2J_{\text{PC}} = 10.1$ Hz, $\text{CH}=\text{CP}$, 1C), 135.86 (s, Ph – C_{IV} , 1C), 140.17 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C), 141.09 (s, $\text{CH}_{(2)}$, 1C), 147.35 (s, C_9 , 1C), 164.95 (d, $^2J_{\text{PC}} = 10.8$ Hz, CO_2tBu , 1C), 165.96 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C).

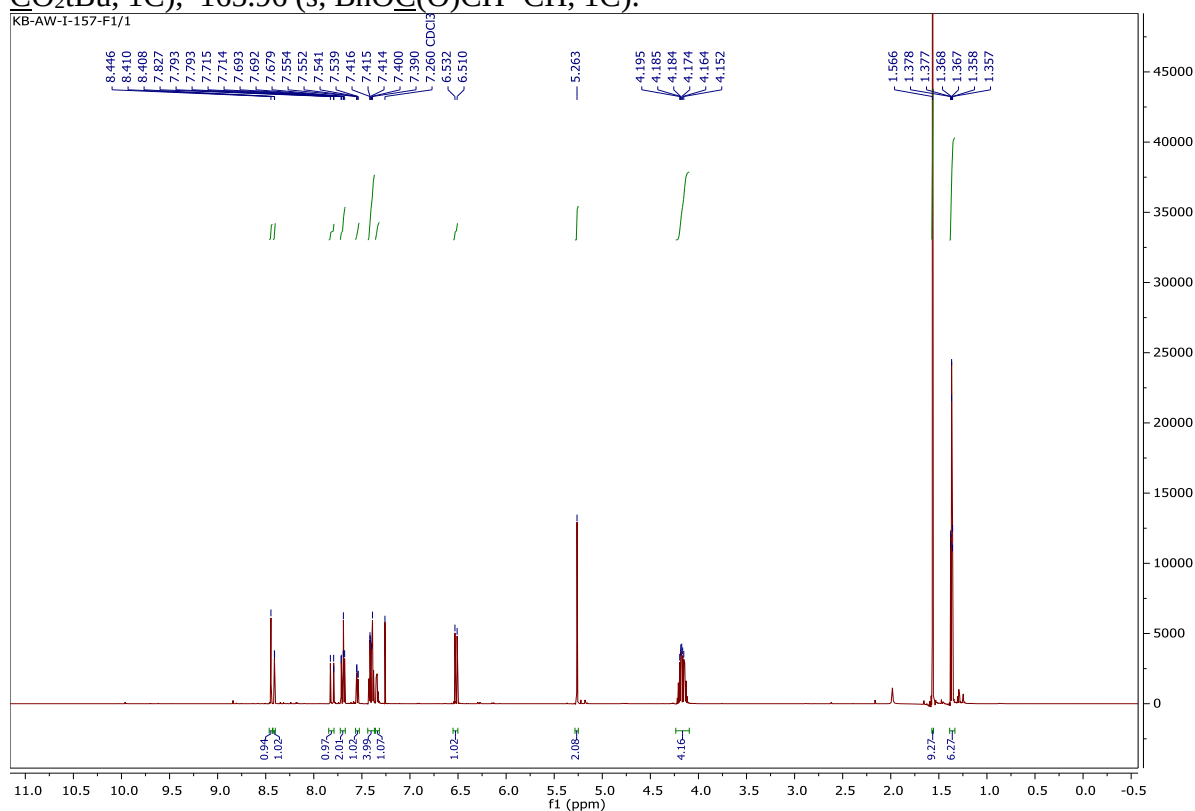


Figure S1. ^1H NMR of compound 3 (700 MHz, CDCl_3).

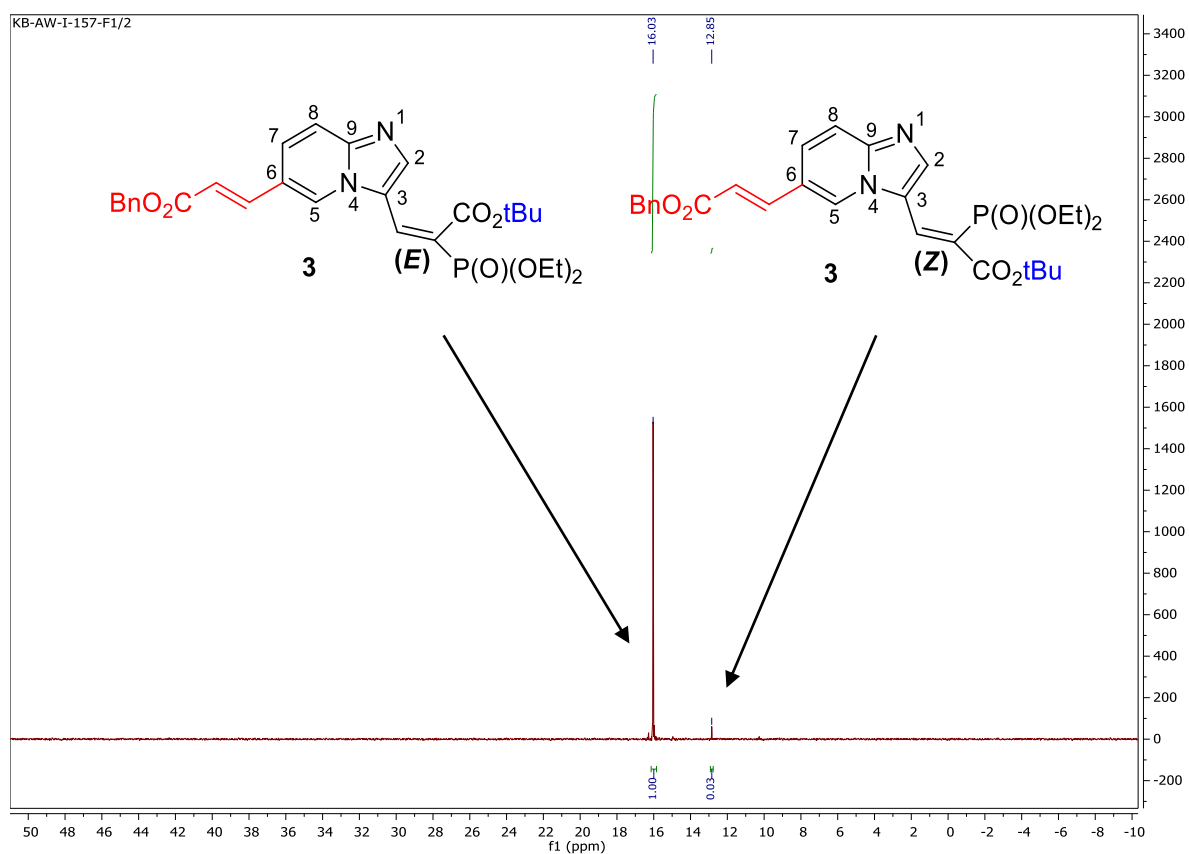


Figure S2. ^{31}P NMR of compound **3** (ratio E/Z 100/3) (283 MHz, CDCl_3).

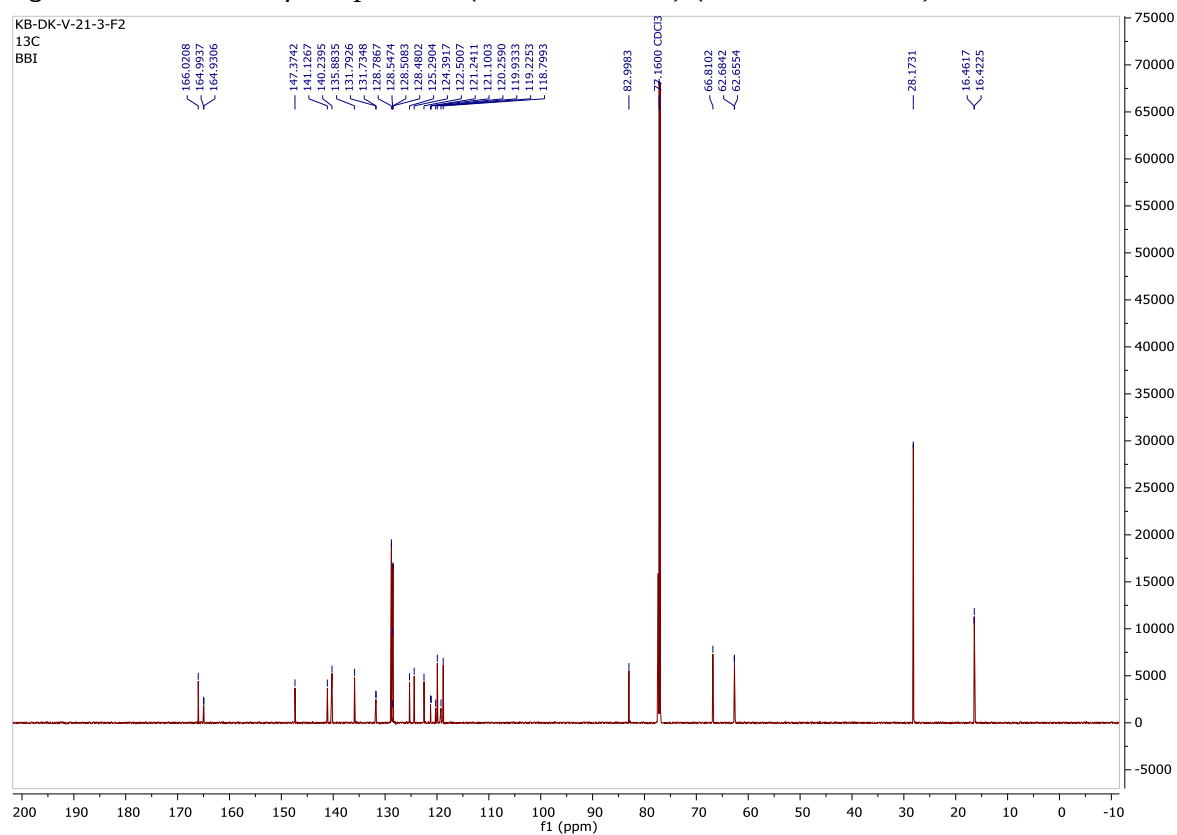
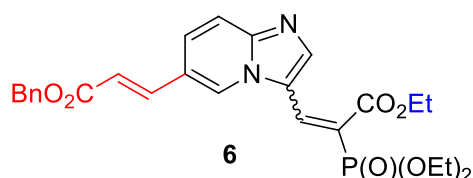


Figure S3. ^{13}C NMR of compound **3** (176 MHz, CDCl_3)



Ethyl 3-(6-((*E*)-3-(benzyloxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (6**). Yield 55%**

HRMS m/z : calculated 513.1785 ($C_{26}H_{29}N_2O_7P + H$)⁺, found 513.1797 ($C_{26}H_{29}N_2O_7P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.31-1.43 (m, (CH₃CH₂O)₂P, CH₃CH₂OC, 9H), 4.07 – 4.30 (m, (CH₃CH₂O)₂P, 4H), 4.37 (q, ³J_{HH} = 7.1 Hz, CH₃CH₂OC, 2H), 5.27 (s, PhCH₂O, 2H), 6.54 (d, ³J_{HH} = 15.9 Hz, BnOC(O)CH=CH, 1H), 7.30 – 7.47 (m, PhCH₂O, 5H), 7.58 (dd, ³J_{HH} = 9.4 Hz, ⁴J_{HH} = 1.6 Hz, CH₍₇₎, 1H), 7.65-7.78 (m, CH₍₈₎, BnOC(O)CH=CH, 2H), 7.97 (d, ³J_{HH} = 23.8 Hz, (*E*) CH=CP, 1H), 8.47 (s, CH₍₅₎, 1H), 8.50 (s, CH₍₂₎, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 16.19 – (*E*) CH=CP, 12.83 – (*E*) CH=CP, (*E*:*Z*)=(1:0.03), ¹³C NMR (176 MHz, CDCl₃) δ : 14.15 (s, CH₃CH₂OC, 1C), 16.36 (d, ⁴J_{PC} = 6.5 Hz, CH₃CH₂OP, 2C), 61.71 (s, CH₃CH₂OC, 1C), 62.81 (d, ³J_{PC} = 5.2 Hz, (CH₃CH₂O)₂P, 2C), 66.71 (s, PhCH₂O, 1C), 117.28 (d, ¹J_{PC} = 183.7 Hz, CP, 1C), 118.72 (s, CH₍₈₎, 1C), 119.97 (s, BnOC(O)CH=CH, 1C), 121.14 (d, ³J_{PC} = 24.3 Hz, C₍₃₎, 1C), 122.58 (s, C₍₆₎, 1C), 124.68 (s, CH₍₇₎, 1C), 125.23 (s, CH₍₅₎, 1C), 128.37, 128.40, 128.68, (Ph, 5C), 133.30 (d, ²J_{PC} = 10.0 Hz, CH=CP, 1C), 135.78 (s, Ph – C_{IV}, 1C), 140.06 (s, BnOC(O)CH=CH, 1C), 141.80 (s, CH₍₂₎, 1C), 147.51 (s, C₉, 1C), 165.56 (d, ²J_{PC} = 11.5 Hz, CO₂tBu, 1C), 165.88 (s, BnOC(O)CH=CH, 1C).

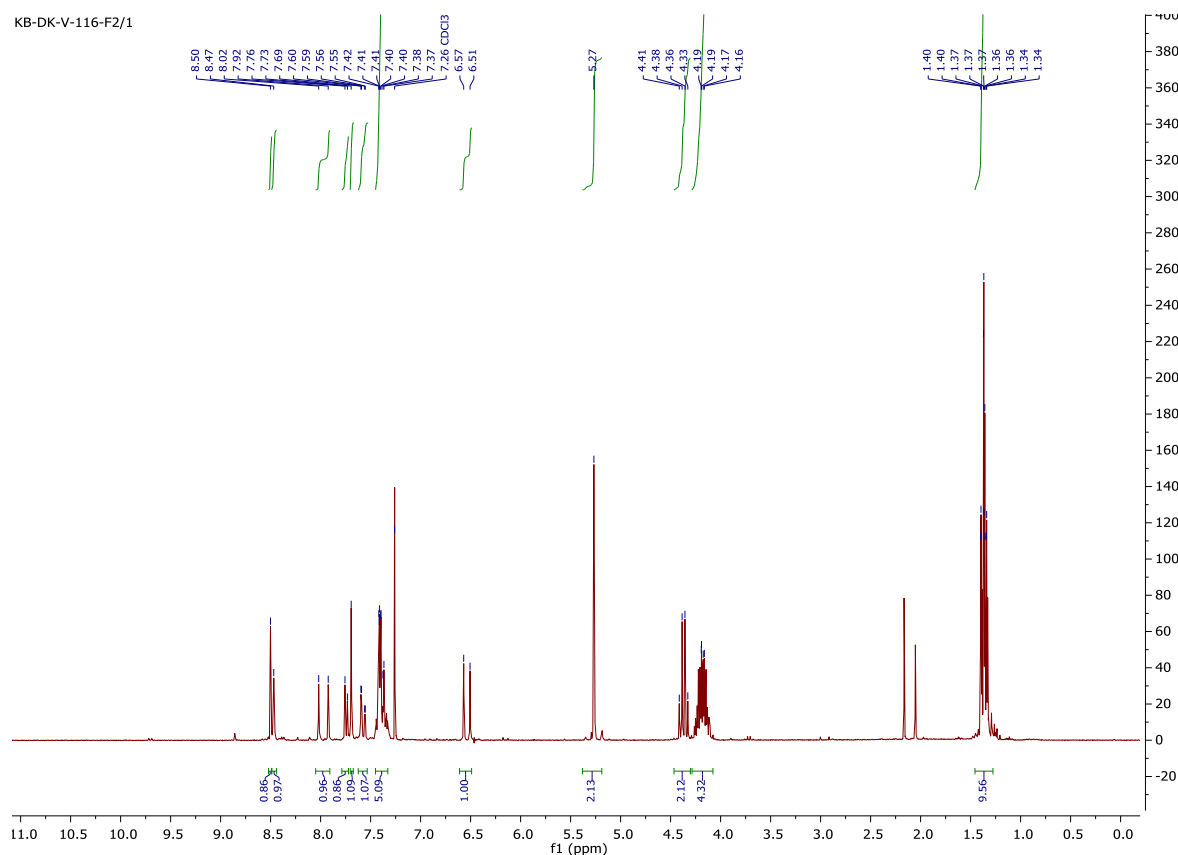


Figure S4. ¹H NMR of compound **6** (700 MHz, CDCl₃)

KB-DK-V-116-3-F2/3

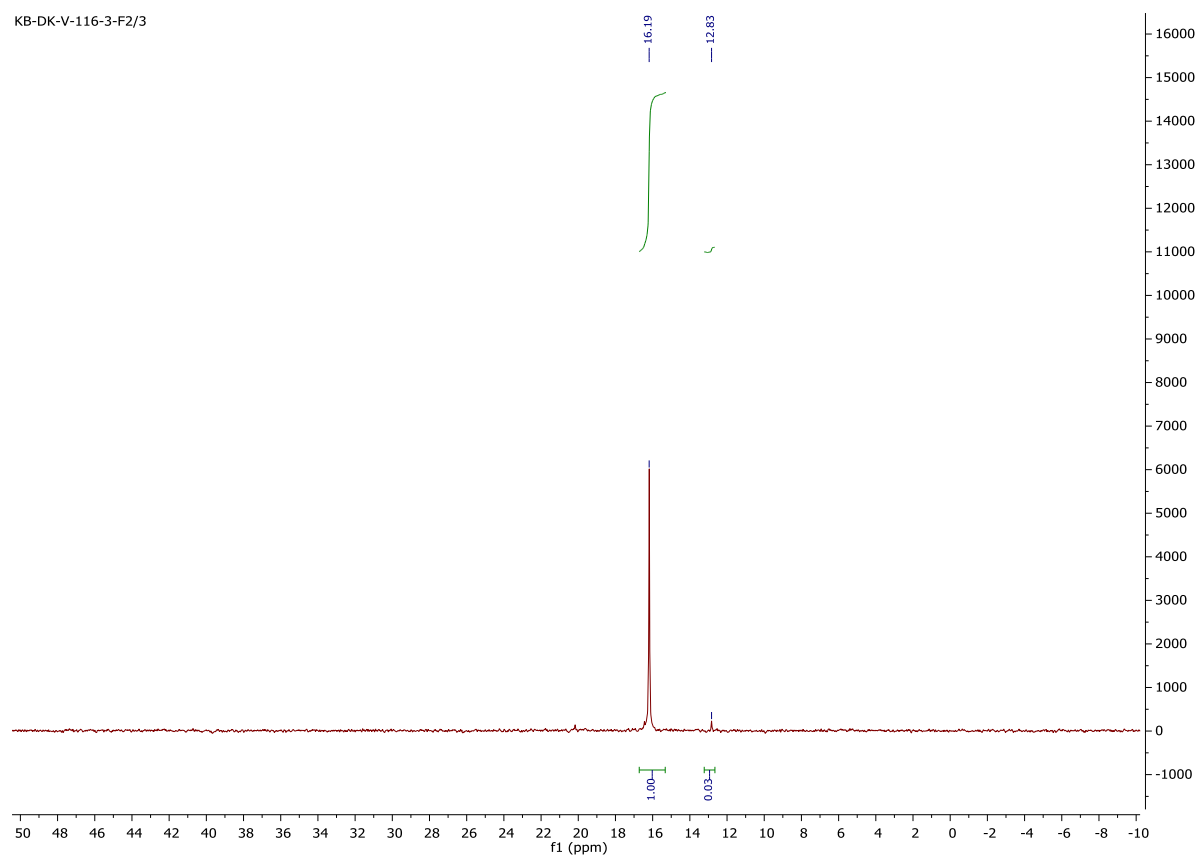


Figure S5. ^{31}P NMR of compound **6** (ratio E/Z 100/3) (283 MHz, CDCl_3)

KB-AW-I-125-F1-2/3
13C

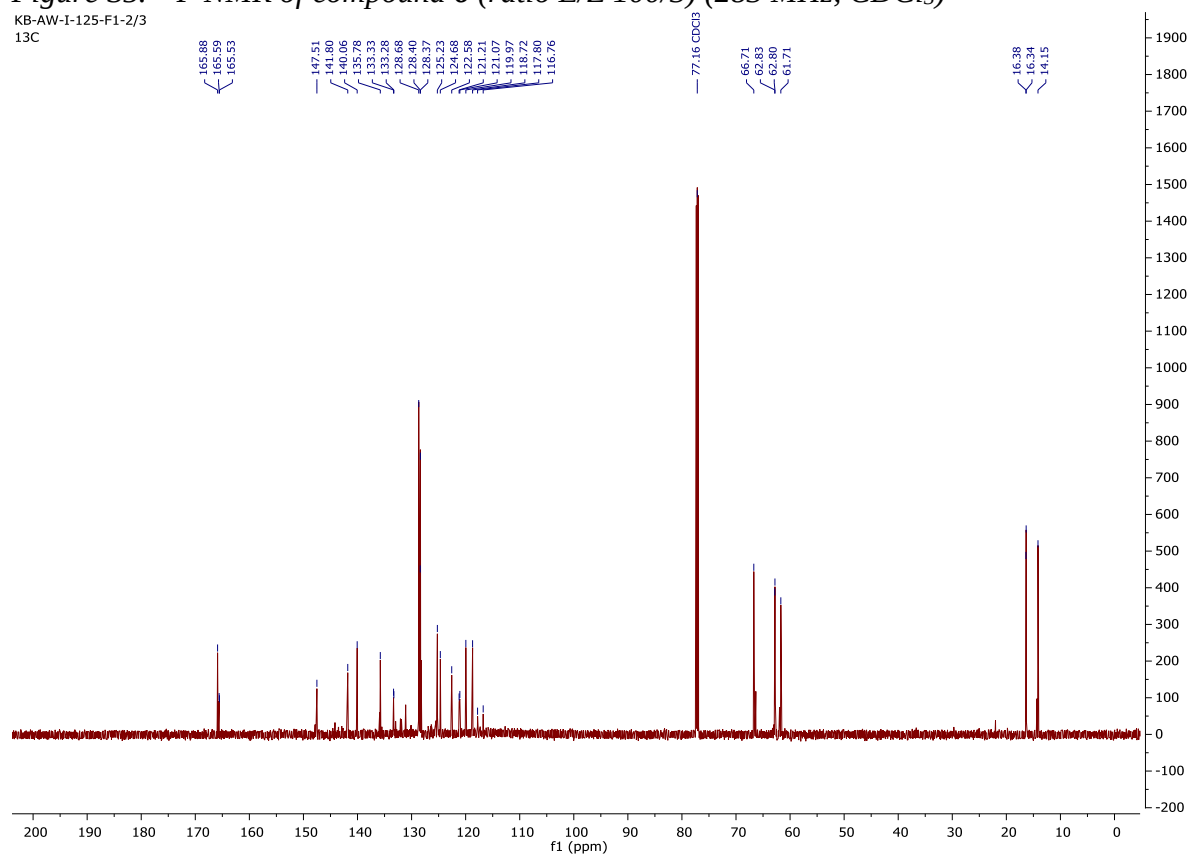
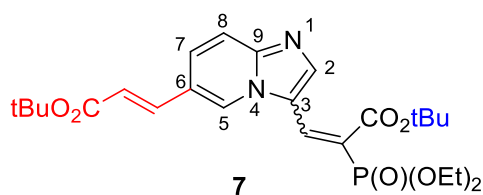


Figure S6. ^{13}C NMR of compound **6** (176 MHz, CDCl_3)



tert-Butyl 3-(6-((*E*)-3-(*tert*-butoxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (7). Yield 68%.

HRMS m/z : calculated 507.2255 ($C_{25}H_{35}N_2O_7P + H$)⁺, found 507.2267 ($C_{25}H_{35}N_2O_7P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.35 (t, ³ J_{HH} = 7.1 Hz, CH₃CH₂OP, 6H), 1.52 (s, C(CH₃)₃, 9H), 1.55 (s, C(CH₃)₃, 9H), 3.91 – 4.37 (m, CH₃CH₂OP, 4H), 6.39 (d, ³ J_{HH} = 15.9 Hz, *t*-BuOC(O)CH=CH, 1H), 7.53 (dd, ³ J_{HH} = 9.3 Hz, ⁴ J_{HH} = 1.6 Hz, CH₍₇₎, 1H), 7.54 (d, ³ J_{HH} = 15.9 Hz *t*-BuOC(O)CH=CH, 1H), 7.66 (d, ³ J_{HH} = 9.3 Hz, ⁵ J_{HH} = 0.7 Hz, CH₍₈₎, 1H), 7.82 (d, ³ J_{HH} = 24.0 Hz, CH=CP, 1H), 8.42 (bs, CH₍₅₎, 1H), 8.43 (s, CH₍₂₎, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 16.16 – (*E*) CH=CP, 12.95 – (*Z*) CH=CP (*E*:*Z*)=(1:0.06), ¹³C NMR (176 MHz, CDCl₃) δ : 16.42 (d, ³ J_{PC} = 6.9 Hz, CH₃CH₂OP, 2C), 28.15 (s, C(CH₃)₃, 3C), 28.28 (s, C(CH₃)₃, 3C), 62.61 (d, ² J_{PC} = 5.1 Hz, CH₃CH₂OP, 2C), 81.15 (s, C(CH₃)₃, 1C), 82.91 (s, C(CH₃)₃, 1C), 118.65 (s, CH₍₈₎, 1C), 119.43 (d, ¹ J_{PC} = 182.1 Hz, CP, 1C), 121.05 (d, ³ J_{PC} = 24.8 Hz, C₍₃₎, 1C), 122.35 (s, *t*-BuOC(O)CH=CH, 1C), 122.79 (s, C₍₆₎, 1C), 124.61 (s, CH₍₇₎, 1C), 124.68 (s, CH₍₅₎, 1C), 131.80 (d, ² J_{PC} = 10.1 Hz, CH=CP, 1C), 138.51 (s, *t*-BuOC(O)CH=CH, 1C), 141.04 (s, CH₍₂₎, 1C), 147.33 (s, C₍₉₎, 1C), 164.96 (d, ² J_{PC} = 11.2 Hz, CO₂*t*-Bu, 1C), 165.40 (s, *t*-BuOC(O)CH=CH, 1C).

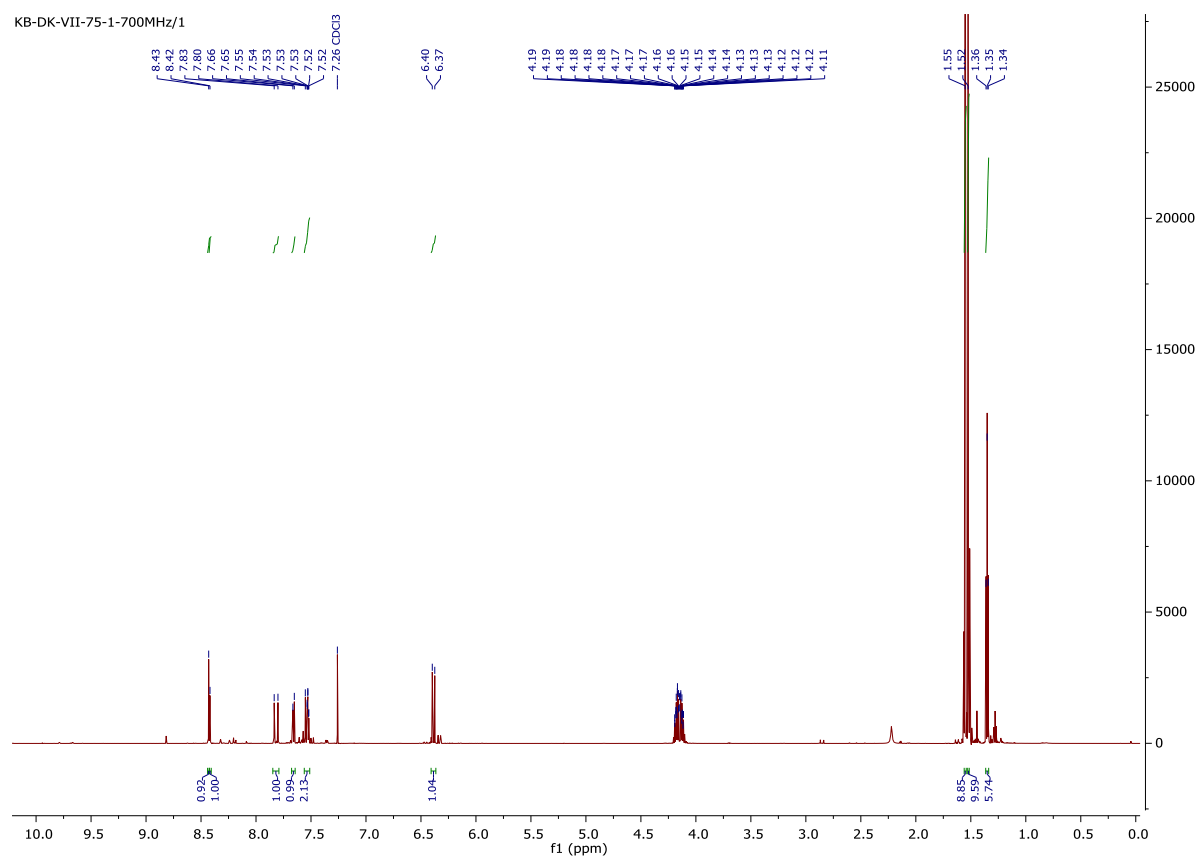


Figure S7. ¹H NMR of compound **7** (700 MHz, CDCl₃).

KB-DK-VII-75-F1/2

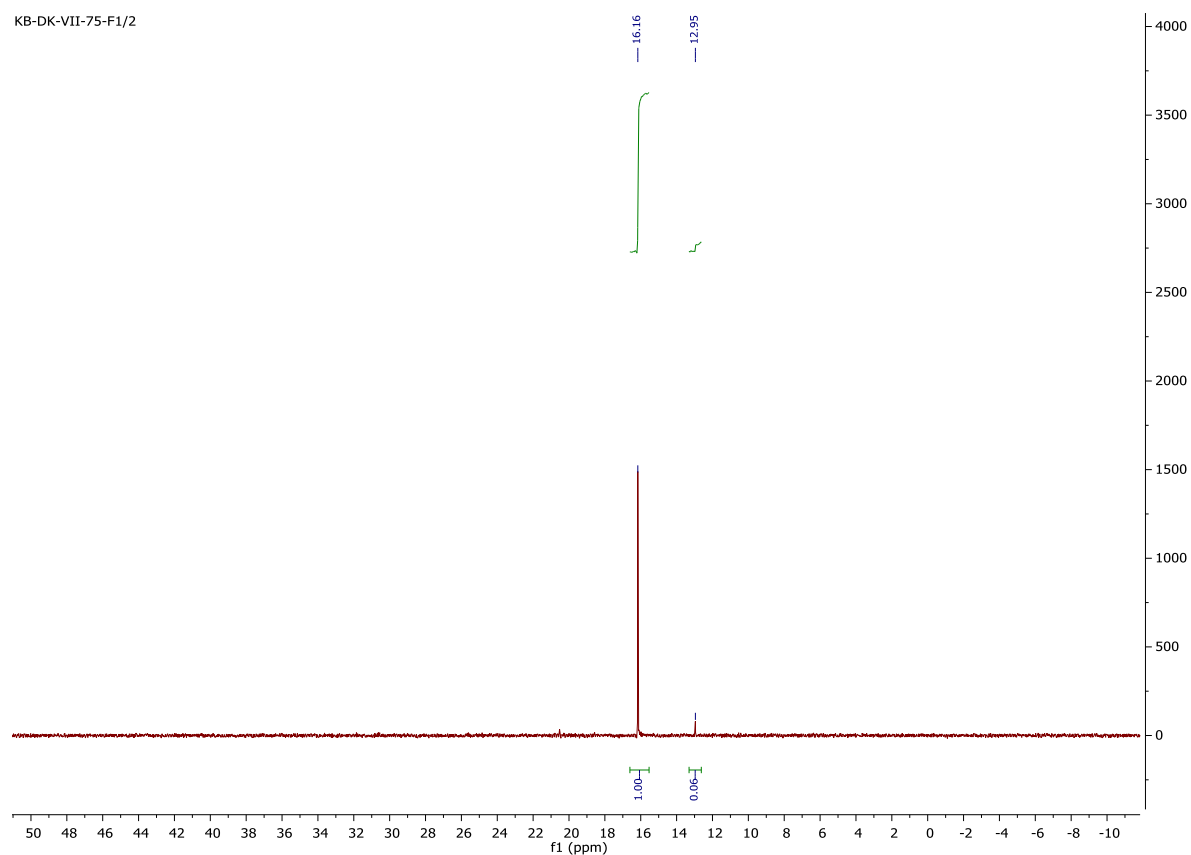


Figure S8. ^{31}P NMR of compound 7 (ratio E/Z 100/6) (283 MHz, CDCl_3)

KB-DK-VII-75-1-700MHz/3

^{13}C

ns=512

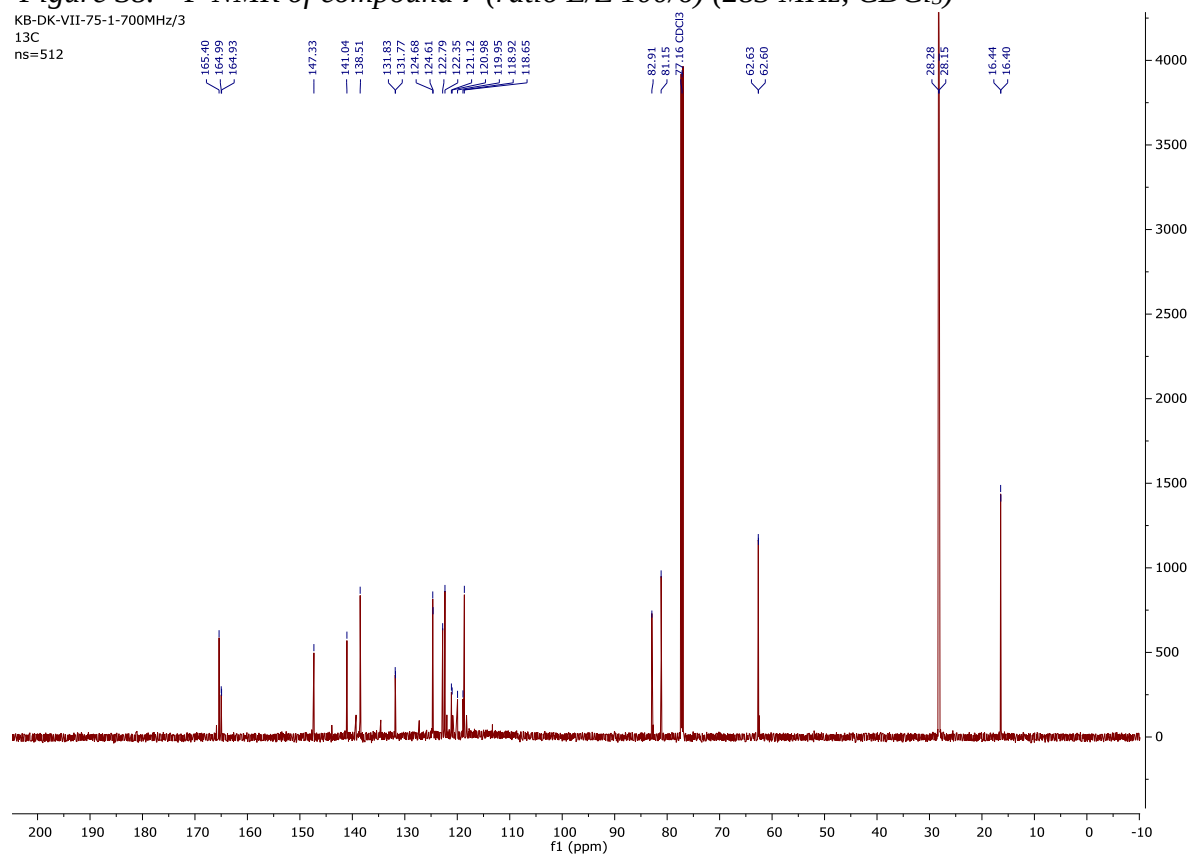
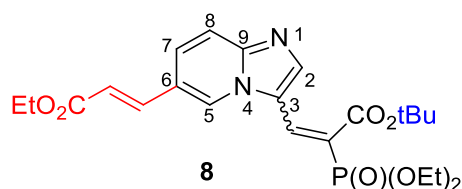


Figure S9. ^{13}C NMR of compound 7 (176 MHz, CDCl_3)



tert-Butyl 2-(diethoxyphosphoryl)-3-(6-((E)-3-ethoxy-3-oxoprop-1-en-1-yl)imidazo[1,2-a]pyridin-3-yl)acrylate (8). Yield 74%.

HRMS m/z : calculated 479.1942 ($C_{23}H_{31}N_2O_7P + H$)⁺, found 479.1953 ($C_{23}H_{31}N_2O_7P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.31 (t, ³ J_{HH} = 7.1 Hz, CH₃CH₂OC=O, 3H), 1.34 (t, ³ J_{HH} = 7.1 Hz, CH₃CH₂OP, 6H), 1.54 (s, C(CH₃)₃, 9H), 4.03 – 4.21 (m, CH₃CH₂OP, 4H), 4.23 – 4.26 (q, ³ J_{HH} = 7.1 Hz, CH₃CH₂OC=O, 2H), 6.45 (d, ³ J_{HH} = 16.1 Hz, EtOC(O)CH=CH, 1H), 7.52 (dd, ³ J_{HH} = 9.4 Hz, ⁴ J_{HH} = 1.6 Hz, CH₇, 1H), 7.64 (d, ³ J_{HH} = 15.9 Hz, EtOC(O)CH=CH, 1H), 7.66 (d, ³ J_{HH} = 9.4 Hz, CH₈, 1H), 7.82 (d, ³ J_{HH} = 24.0 Hz, (E) CH=CP, 1H), 8.42 (s, CH₂, 1H), 8.48 (bs, CH₅, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 16.26 – (E) CH=CP, 12.86 – (Z) CH=CP (E:Z)=(1:0.11), ¹³C NMR (176 MHz, CDCl₃) δ : 14.28 (s, CH₃CH₂OC=O, 1C), 16.33 (d, ⁴ J_{PC} = 6.9 Hz, CH₃CH₂OP, 2C), 28.06 (s, C(CH₃)₃, 3C), 60.81 (s, CH₃CH₂OC=O, 1C), 62.53 (d, ³ J_{CP} = 5.2 Hz, CH₃CH₂OP, 2C), 82.83 (s, C(CH₃)₃, 1C), 118.64 (s, CH₈, 1C), 119.54 (d, ¹ J_{PC} = 181.5 Hz, CP, 1C), 120.18 (s, EtOC(O)CH=CH, 1C), 121.03 (d, ³ J_{PC} = 24.8 Hz, C₃, 1C), 122.48 (s, C₆, 1C), 124.36 (s, CH₇, 1C), 125.04 (s, CH₅, 1C), 131.72 (d, ² J_{PC} = 10.1 Hz, CH=CP, 1C), 139.59 (s, EtOC(O)CH=CH, 1C), 141.00 (s, CH₂, 1C), 147.26 (s, C₉, 1C), 164.85 (d, ² J_{PC} = 10.9 Hz, CO₂t-Bu, 1C), 166.10 (s, EtOC(O)CH=CH, 1C).

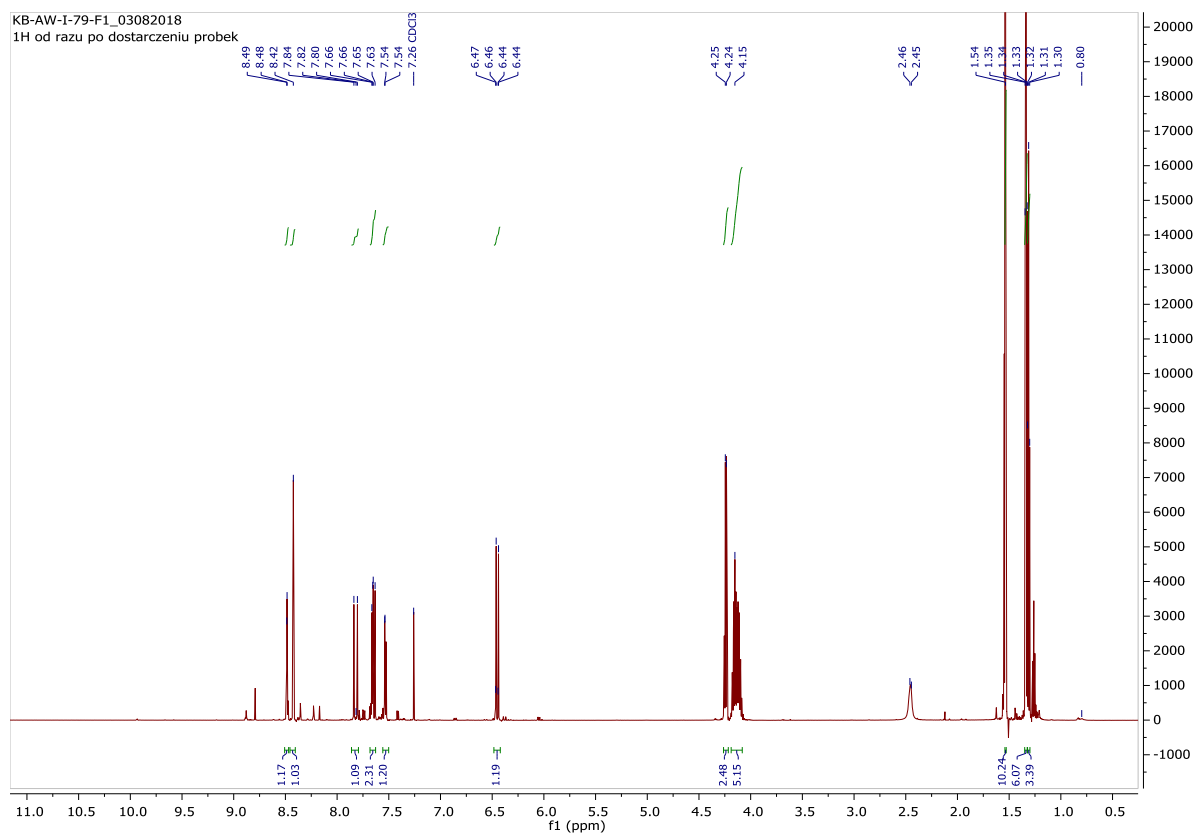


Figure S10. ¹H NMR of compound **8** (700 MHz, CDCl₃)

KB-AW-I-79-F1_03082018
³¹P od razu po dostarczeniu probek

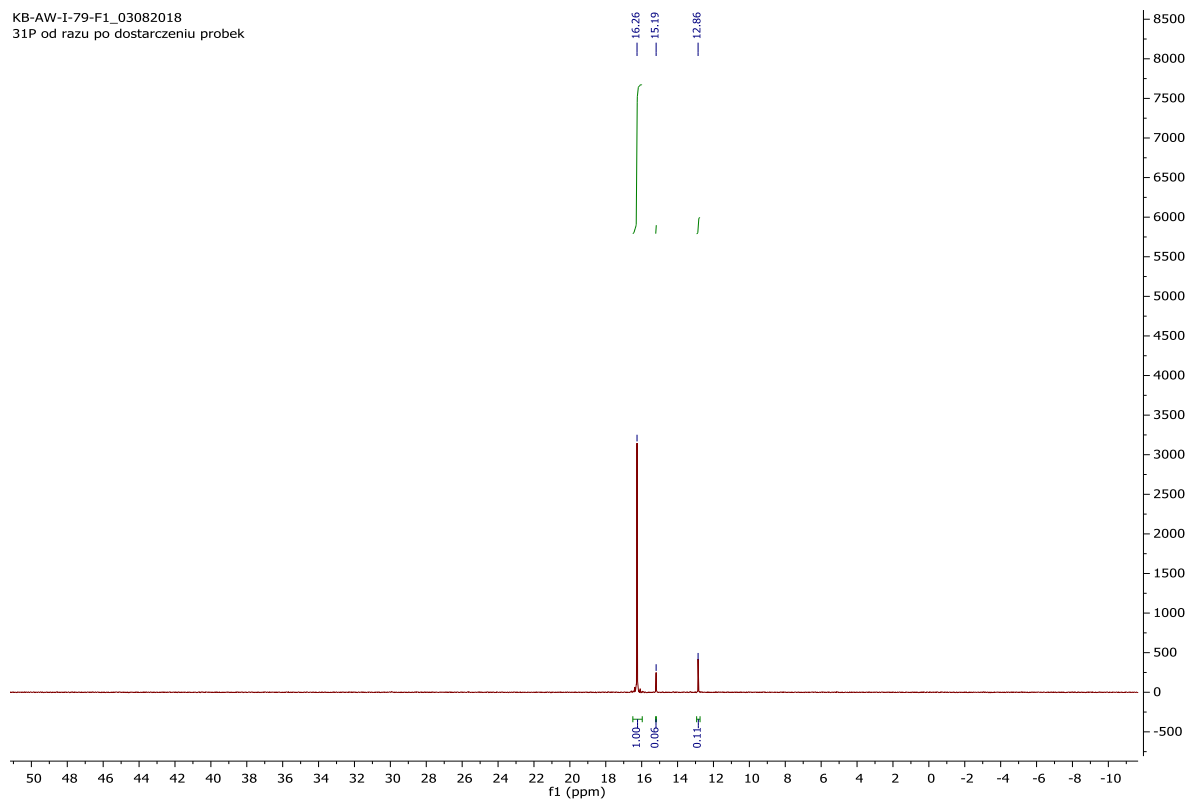


Figure S11. ³¹P NMR of compound **8** (ratio E/Z 100/11) (283 MHz, CDCl₃)

KB-AW-I-79-F1_03082018
¹³C

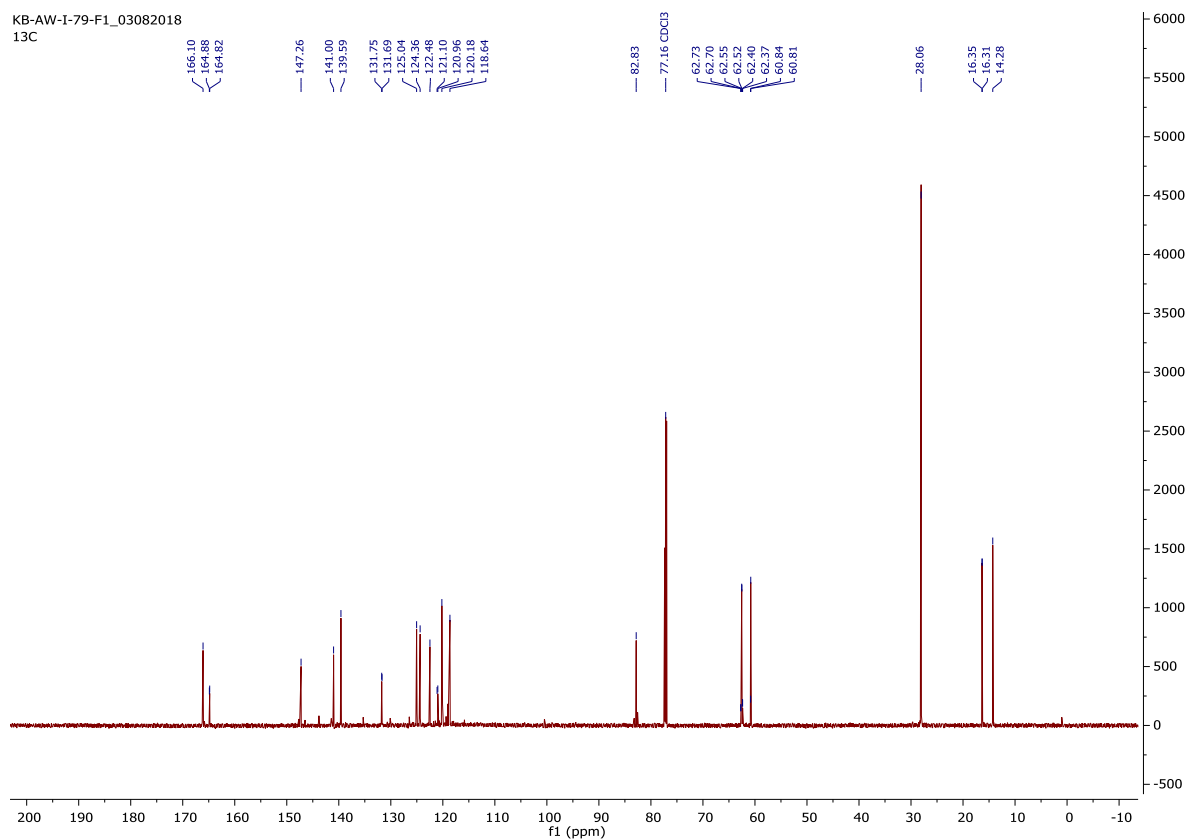
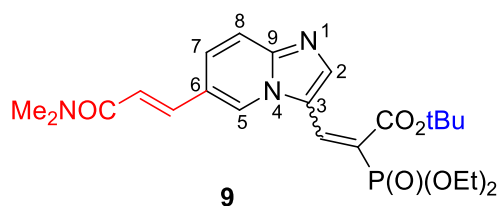


Figure S12. ¹³C NMR of compound **8** (176 MHz, CDCl₃)



***tert*-Butyl 2-(diethoxyphosphoryl)-3-(6-((*E*)-3-(dimethylamino)-3-oxoprop-1-en-1-yl)imidazo[1,2-*a*]pyridin-3-yl)acrylate (9).** Yield 79%.

HRMS m/z : calculated 478.2101 ($C_{23}H_{32}N_3O_6P + H$)⁺, found 478.2107 ($C_{23}H_{32}N_3O_6P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.34 (t, ³ J_{HH} = 7.1 Hz, CH₃CH₂OP, 6H), 1.54 (s, C(CH₃)₃, 9H), 3.05 (s, NCH₃, 3H), 3.17 (s, NCH₃, 3H), 4.08 – 4.20 (m, CH₃CH₂OP, 4H), 6.94 (d, ³ J_{HH} = 15.4 Hz, (CH₃)₂NC(O)CH=CH, 1H), 7.54 (dd, ³ J_{HH} = 9.3 Hz, ⁴ J_{HH} = 1.6 Hz, CH₇, 1H), 7.62 (d, ³ J_{HH} = 15.4 Hz, (CH₃)₂NC(O)CH=CH, 1H), 7.65 (d, ³ J_{HH} = 9.3 Hz, CH₈, 1H), 7.81 (d, ³ J_{HH} = 23.9 Hz, (*E*) CH=CP, 1H), 8.41 (s, CH₂, 1H), 8.48 (bs, CH₅, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 16.58 – (*E*) CH=CP, 13.35 – (*Z*) CH=CP, (E:Z)=(1:0.15), ¹³C NMR (176 MHz, CDCl₃) δ : 16.39 (d, ⁴ J_{PC} = 6.8 Hz, CH₃CH₂OP, 2C), 28.12 (s, C(CH₃)₃, 3C), 36.08 (s, NCH₃, 1C), 37.58 (s, NCH₃, 1C), 62.61 (d, ³ J_{CP} = 5.2 Hz, CH₃CH₂OP, 2C), 82.89 (s, C(CH₃)₃, 1C), 118.43 (s, CH₈, 1C), 119.37 (s, (CH₃)₂NC(O)CH=CH, 1C), 119.41 (d, ¹ J_{PC} = 182.6 Hz, CP, 1C), 121.04 (d, ³ J_{PC} = 24.9 Hz, C₃, 1C), 123.36 (s, C₆, 1C), 124.27 (s, CH₅, 1C), 125.14 (s, CH₇, 1C), 131.76 (d, ² J_{PC} = 10.1 Hz, CH=CP, 1C), 137.62 (s, (CH₃)₂NC(O)CH=CH, 1C), 140.91 (s, CH₂, 1C), 147.25 (s, C₉, 1C), 165.00 (d, ² J_{PC} = 11.1 Hz, CO₂*t*-Bu, 1C), 165.90 (s, CCH=CH, 1C).

KB-AW-II-3-F1-E/1

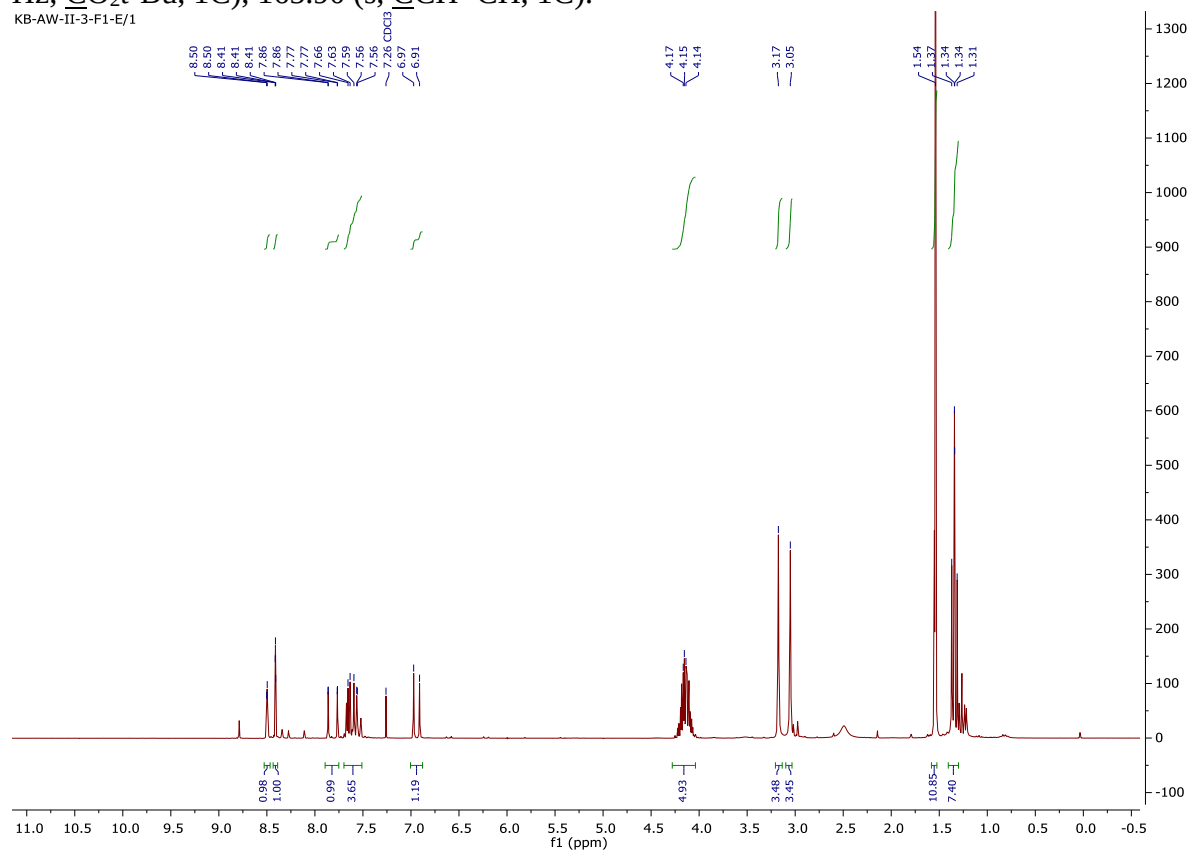


Figure S13. ¹H NMR of compound **9** (700 MHz, CDCl₃)

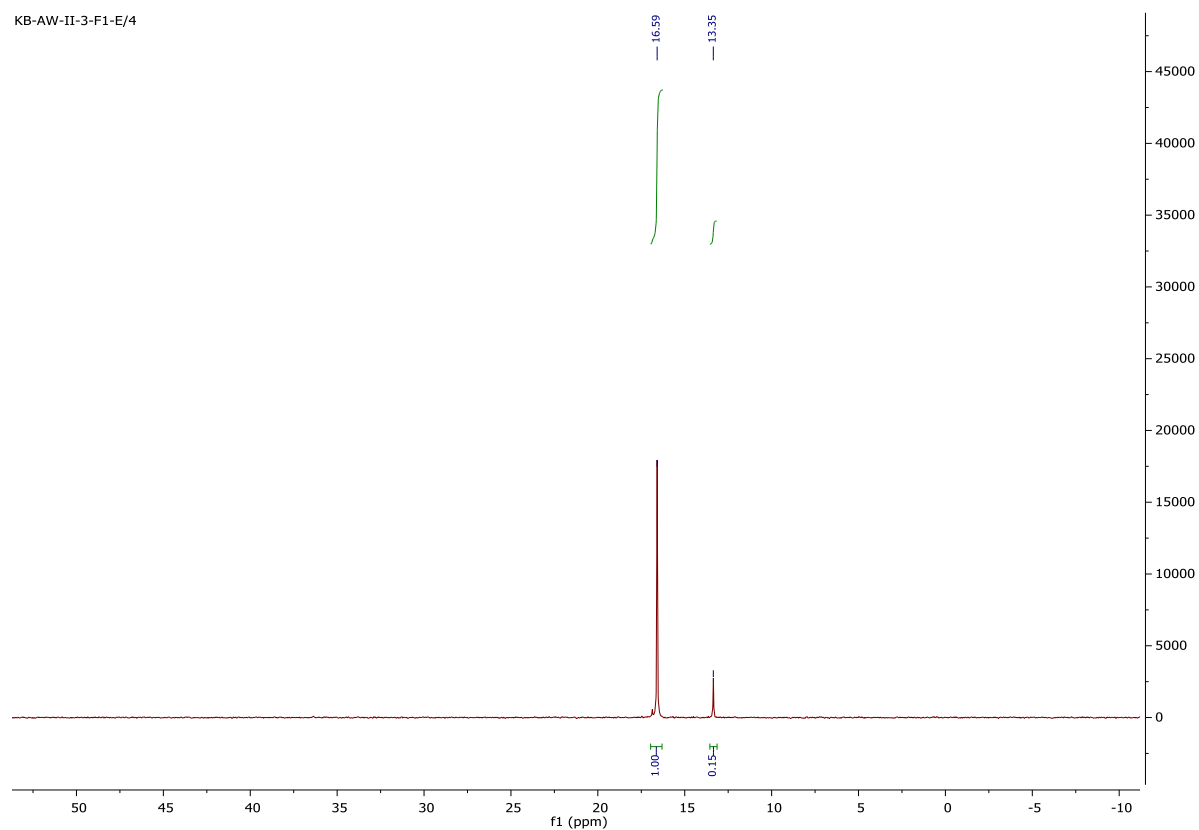


Figure S14. ^{31}P NMR of compound **9** (ratio E/Z 100/15) (283 MHz, CDCl_3)

KB-AW-II-3-F1-E2
 ^{13}C

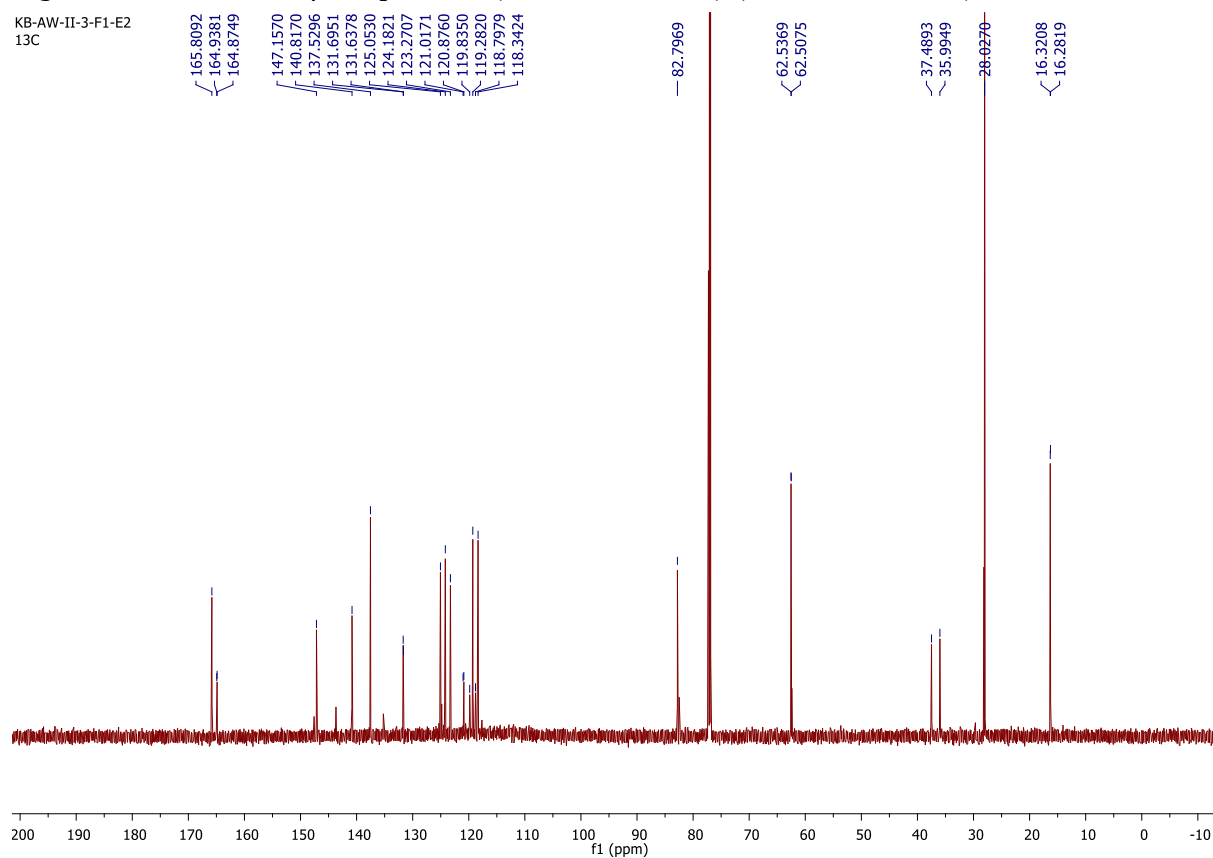
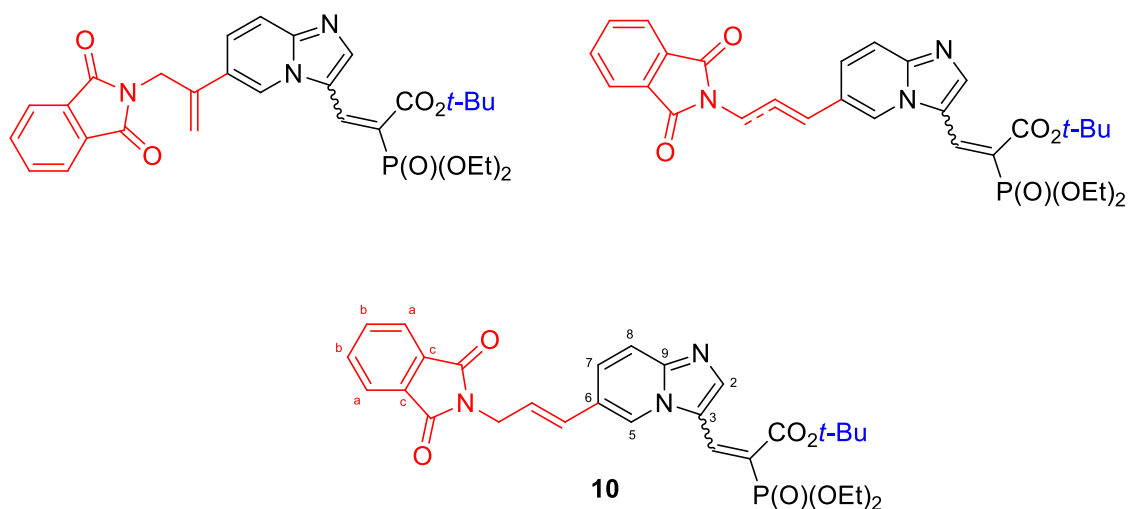


Figure S15. ^{13}C NMR of compound **9** (176 MHz, CDCl_3)

Other possible Heck products



Main product

***tert*-Butyl 2-(diethoxyphosphoryl)-3-(6-((*E*)-3-(1,3-dioxoisindolin-2-yl)prop-1-en-1-yl)imidazo[1,2-*a*]pyridin-3-yl)acrylate (**10**). Yield 65%.**

HRMS *m/z*: calculated 566.2051 ($C_{29}H_{32}N_3O_7P + H^+$), found 566.2061 ($C_{29}H_{32}N_3O_7P + H^+$), 1H NMR (700 MHz, $CDCl_3$) δ : 1.30 (t, $^3J_{HH} = 7.1$ Hz, CH_3CH_2OP , 6H), 1.51 (s, $C(CH_3)_3$, 9H), 4.00 – 4.19 (m, CH_3CH_2OP , 4H), 4.43 (bd, $^3J_{HH} = 5.6$ Hz, $PhtCH_2CH=CH$, 2H), 6.28 (dt, $^3J_{HH} = 15.8$ Hz, $^3J_{HH} = 5.9$ Hz, $PhtCH_2CH=CH$, 1H), 6.52 (d, $^3J_{HH} = 15.8$ Hz, $PhtCH_2CH=CH$, 1H), 7.43 (bd, $^3J_{HH} = 9.2$ Hz, $CH_{(7)}$, 1H), 7.55 (bd, $^3J_{HH} = 9.2$ Hz, $CH_{(8)}$, 1H), 7.68 (m, $CH_{(b)}$, 2H), 7.73 (d, $^3J_{HH} = 24.1$ Hz, $CH=CP$, 1H), 7.81 (m, $CH_{(a)}$, 2H), 8.16 (bs, $CH_{(5)}$, 1H), 8.36 (s, $CH_{(2)}$, 1H), ^{31}P NMR (283 MHz, $CDCl_3$) δ : 16.69 – (*E*) $CH=CP$, 13.31 – (*Z*) $CH=CP$, (*E*:*Z*)=(1:0.04), ^{13}C NMR (176 MHz, $CDCl_3$) δ : 16.30 (d, $^4J_{PC} = 6.5$ Hz, CH_3CH_2OP , 2C), 28.04 (s, $C(CH_3)_3$, 3C), 39.25 ($PhtCH_2$, 1C), 62.40 (d, $^3J_{PC} = 5.0$ Hz, CH_3CH_2OP , 2C), 82.61 (s, $C(CH_3)_3$, 1C), 118.08 (s, $CH_{(8)}$, 1C), 118.21 (d, $^1J_{PC} = 182.7$ Hz, CP , 1C), 120.66 (d, $^3J_{PC} = 25.1$ Hz, $C_{(3)}$, 1C), 122.11 (s, $CH_{(5)}$, 1C), 123.49 (s, $CH_{(a)}$, 2C), 124.11 (s, $C_{(6)}$, 1C), 124.83 (s, $CH_{(7)}$, 1C), 125.26 (s, $PhtCH_2CH=CH$, 1C), 128.05 (s, $PhtCH_2CH=CH$, 1C), 132.01 (s, $CH_{(c)}$, 2C), 132.07 (d, $HC=CP$, $^2J_{PC} = 9.8$ Hz), 134.15 (s, $CH_{(b)}$, 2C), 140.72 (s, $CH_{(2)}$, 1C), 146.96 (s, $C_{(9)}$, 1C), 164.98 (d, $^2J_{PC} = 11.4$ Hz, CO_2t-Bu , 1C), 167.84 (s, $O=CN$, 2C).

^{31}P NMR of fraction after chromatographical purification showing the presence of 4 Heck products; differentiated by the geometry of pre-existing double bond in substrate.

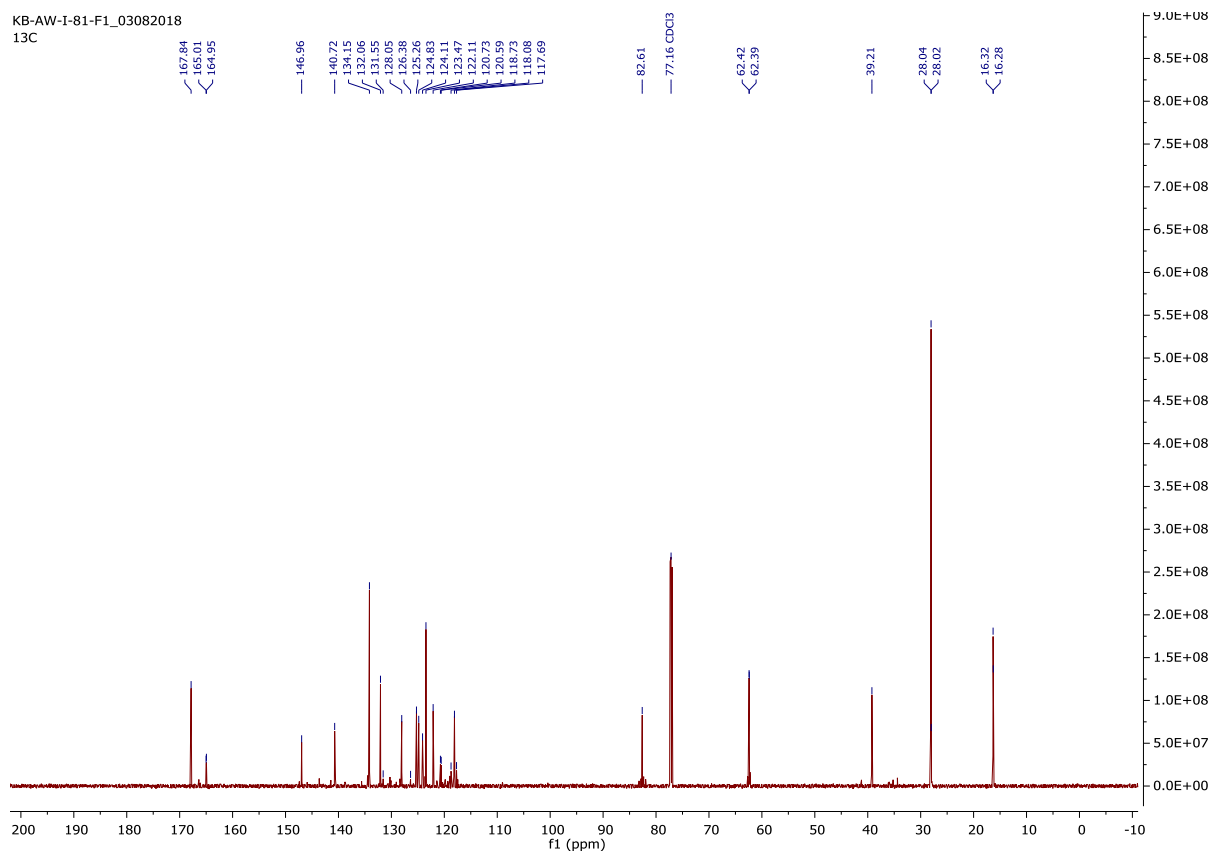
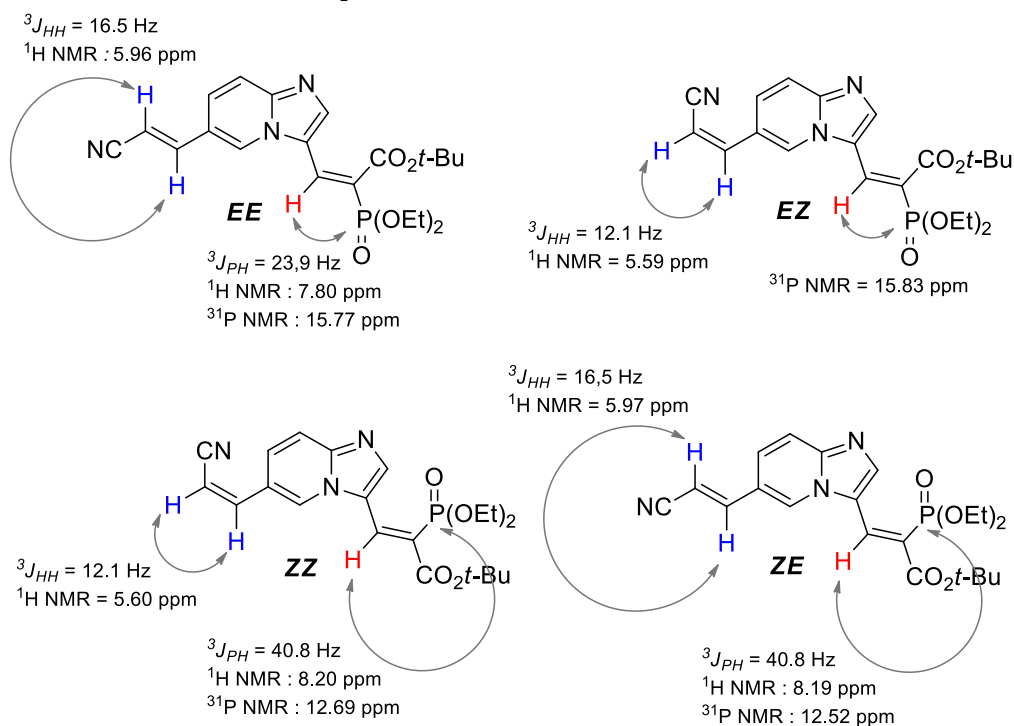


Figure S18. ^{13}C NMR of compound **10** (176 MHz, CDCl_3)

Composition of the reaction mixture



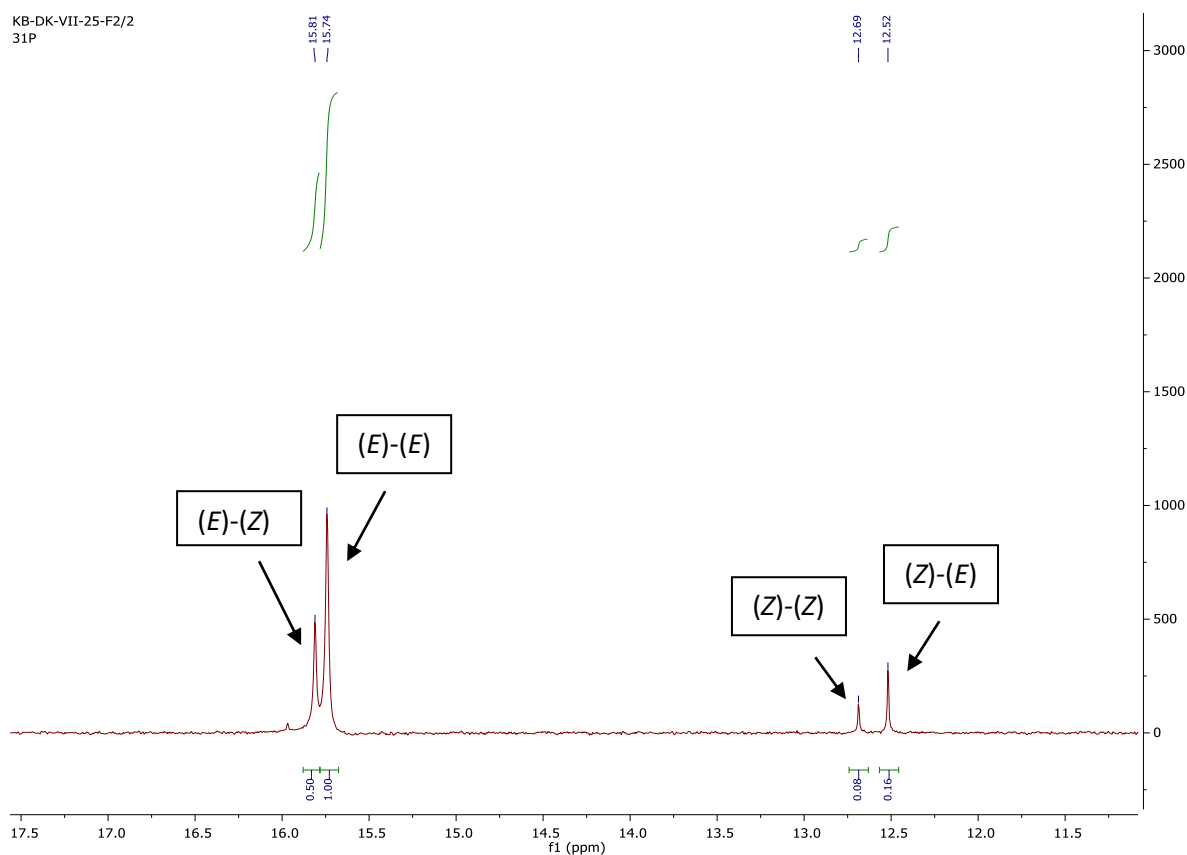
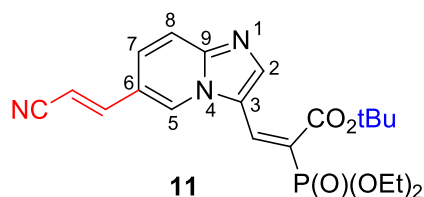


Figure S19. Composition of the reaction mixture (compound **11**)



Main isomer

(E)-tert-Butyl 3-(6-((E)-2-cyanovinyl)imidazo[1,2-a]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (11**).** Yield 50%.

HRMS m/z : calculated 432.1683 ($C_{21}H_{26}N_3O_5P + H$)⁺, found 432.1697 ($C_{21}H_{26}N_3O_5P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.34 – 1.40 (m, CH₃CH₂OP, 6H), 1.56 (s, C(CH₃)₃, 9H), 4.08 – 4.23 (m, CH₃CH₂OP, 4H), 5.96 (d, ³J_{HH} = 16.5 Hz, NCCH=CH, 1H), 7.39 (d, ³J_{HH} = 16.5 Hz, NCCH=CH, 1H), 7.46 (dd, ³J_{HH} = 9.3 Hz, ⁴J_{HH} = 1.7 Hz, CH₇, 1H), 7.71 (d, ³J_{HH} = 9.3 Hz, CH₈, 1H), 7.80 (d, ³J_{HH} = 23.9 Hz, (E) CH=CP, 1H), 8.45 (bs, CH₅, 1H), 8.45 (s, CH₂, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 16.09 – (E) CH=CP, 12.87 – (Z) CH=CP, (E:Z)=(1:0.12), ¹³C NMR (176 MHz, CDCl₃) δ : 16.43 (d, ³J_{PC} = 6.9 Hz, CH₃CH₂OP, 2C), 28.16 (s, C(CH₃)₃, 3C), 62.73 (d, ²J_{PC} = 5.1 Hz, CH₃CH₂OP, 2C), 83.14 (s, C(CH₃)₃, 1C), 98.36 (s, NCCH=CH, 1C), 117.41 (s, NCCH=CH, 1C), 119.19 (s, CH₈, 1C), 120.68 (d, ¹J_{PC} = 181.4 Hz, CP, 1C), 121.41 (d, ³J_{PC} = 25.0 Hz, C₃, 1C), 121.71 (s, C₆, 1C), 122.89 (s, CH₇, 1C), 125.22 (s, CH₅, 1C), 131.35 (d, ²J_{PC} = 10.1 Hz, CH=CP, 1C), 141.21 (s, CH₂, 1C), 145.70 (s, NCCH=CH, 1C), 147.25 (s, C₉, 1C), 164.86 (d, ²J_{PC} = 10.8 Hz, CO₂t-Bu, 1C).

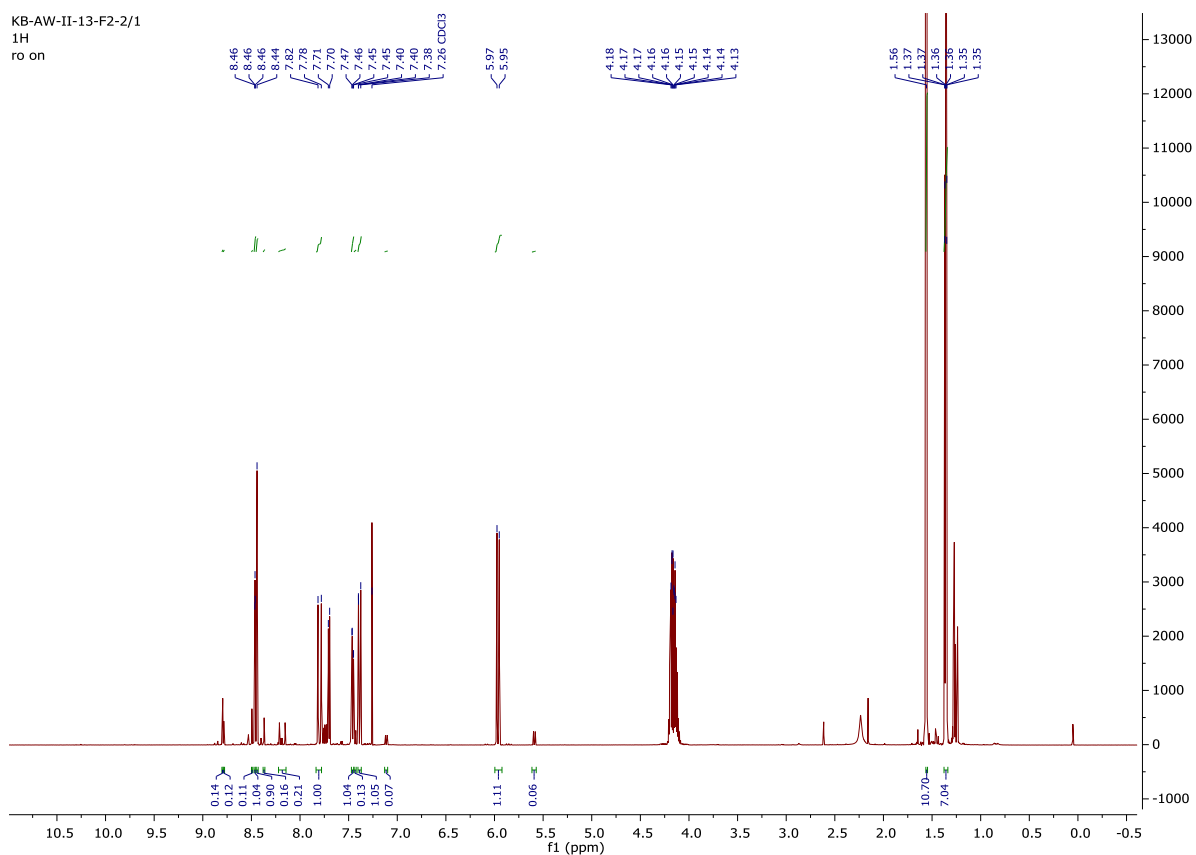


Figure S20. ^1H NMR of compound **11** (700 MHz, CDCl_3)

KB-AW-II-13-F2/4

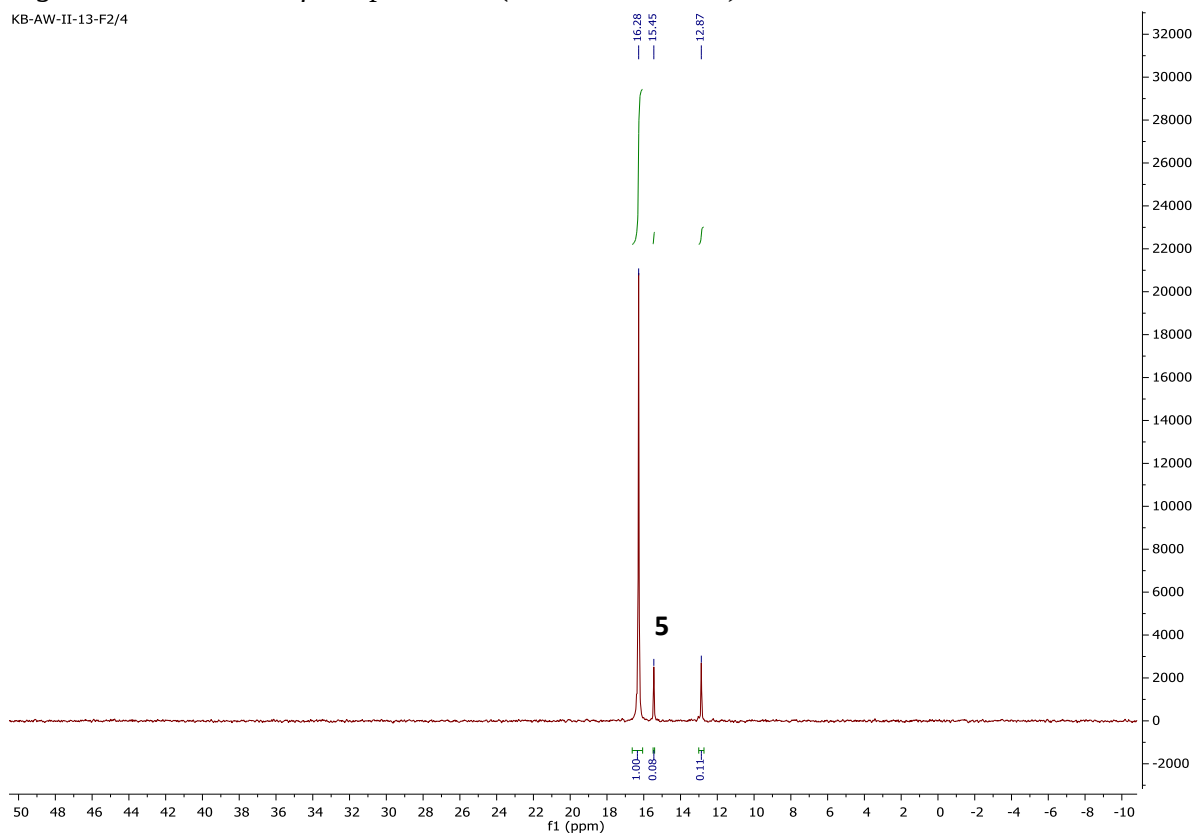


Figure S21. ^{31}P NMR of compound **11** (283 MHz, CDCl_3)

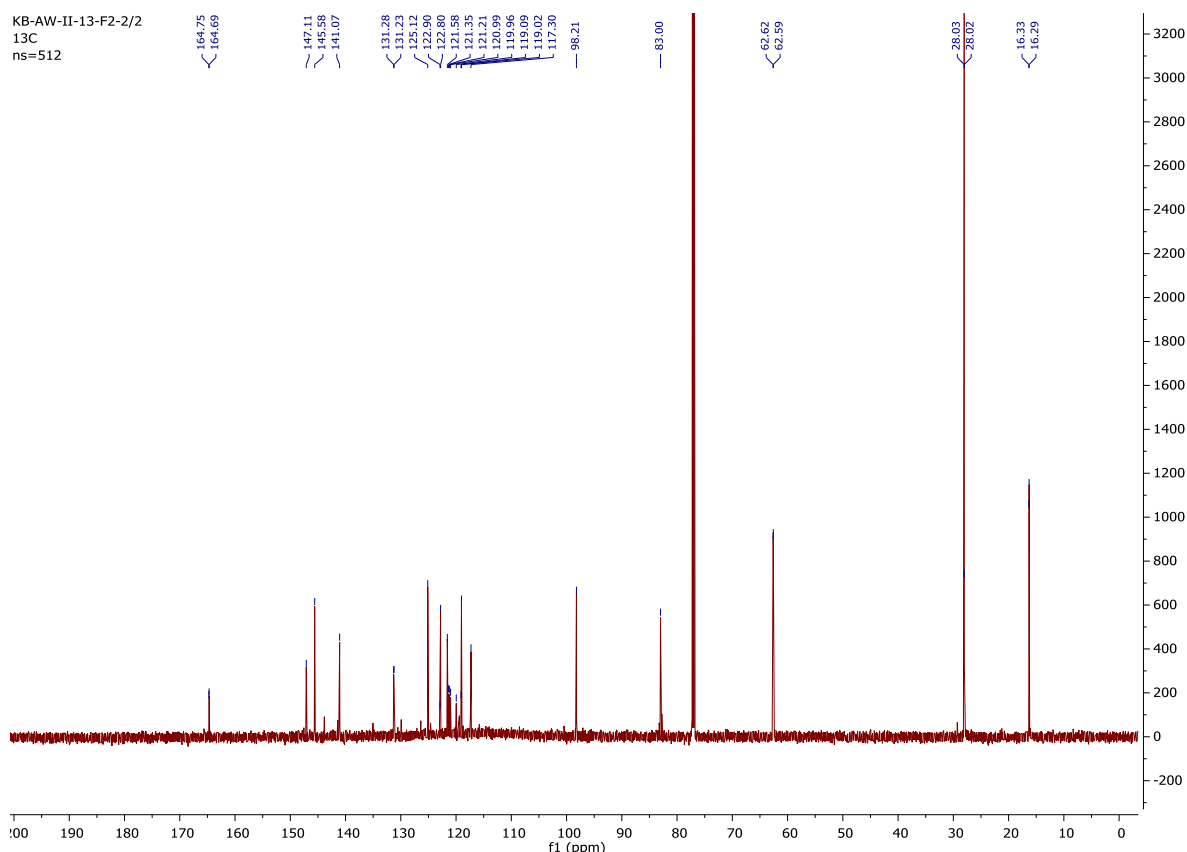
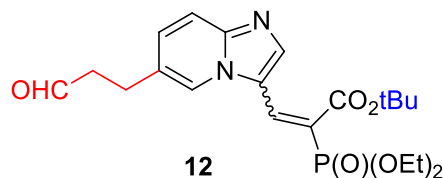
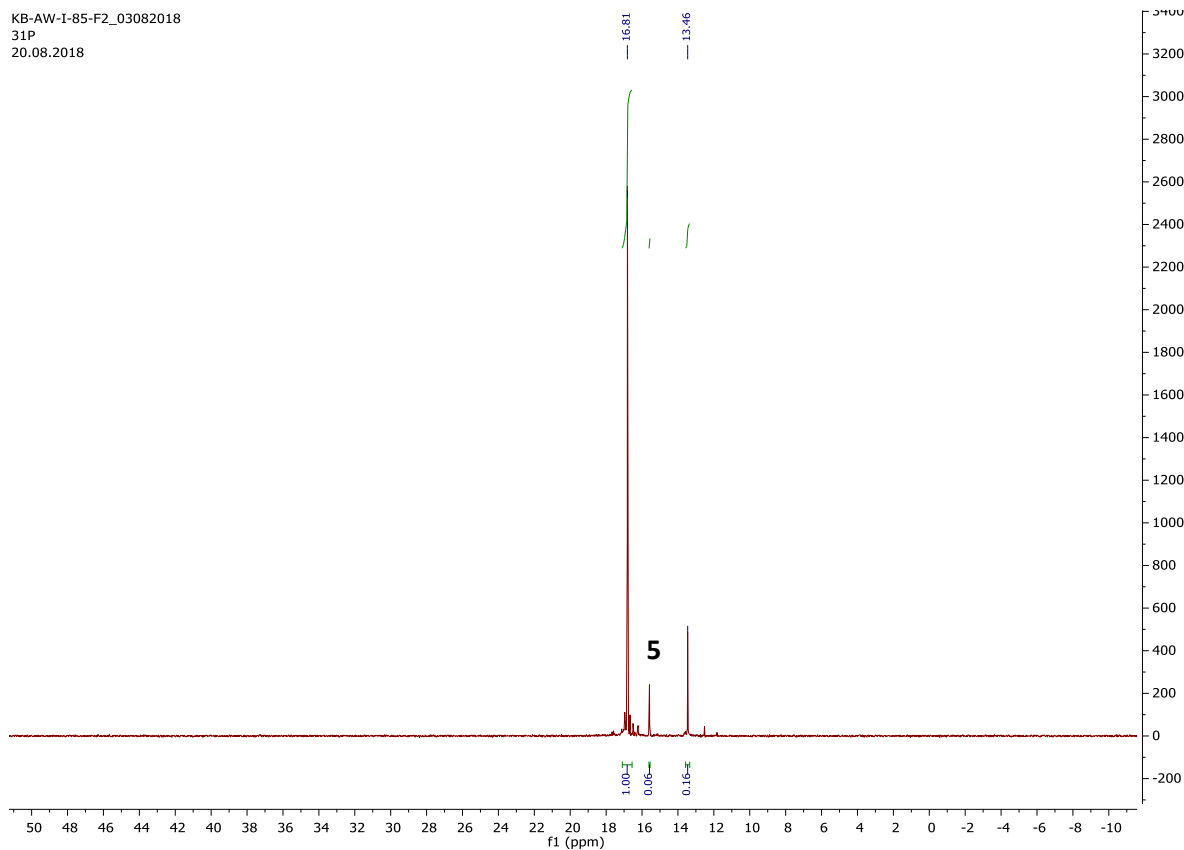
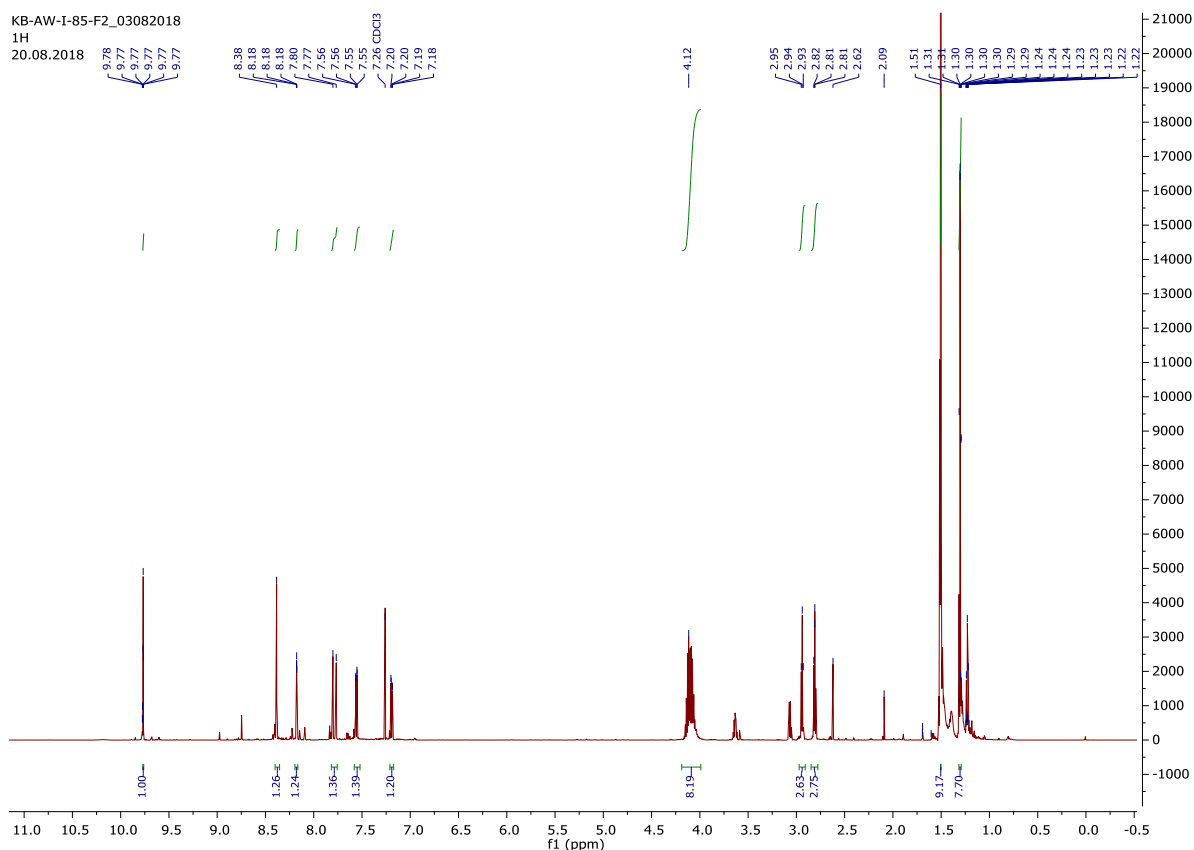


Figure S22. ^{13}C NMR of compound **11** (176 MHz, CDCl_3)



***tert*-Butyl 2-(diethoxyphosphoryl)-3-(6-(3-oxopropyl)imidazo[1,2-*a*]pyridin-3-yl)acrylate (**12**).** Yield 67%.

HRMS m/z : calculated 437.1836 ($\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_6\text{P} + \text{H}^+$), found 437.1840 ($\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_6\text{P} + \text{H}^+$), ^1H NMR (700 MHz, CDCl_3) δ : 1.30 (t, $^3J_{\text{HH}} = 7.0$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 1.51 (s, $\text{C}(\text{CH}_3)_3$, 9H), 2.81 (t, $\text{CHOCH}_2\text{CH}_2$, $^3J_{\text{HH}} = 7.2$ Hz, 2H), 2.94 (t, $\text{CHOCH}_2\text{CH}_2$, $^3J_{\text{HH}} = 7.2$ Hz, 2H), 3.94–4.23 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 4H), 7.19 (dd, $^3J_{\text{HH}} = 9.1$ Hz, $^4J_{\text{HH}} = 1.6$ Hz, $\text{CH}_{(7)}$, 1H), 7.56 (dd, $^3J_{\text{HH}} = 9.1$ Hz, $^4J_{\text{HH}} = 0.5$ Hz, $\text{CH}_{(8)}$, 1H), 7.78 (d, $^3J_{\text{PH}} = 24.0$ Hz, $\text{CH}=\text{CP}$, 1H), 8.18 (bs, $\text{CH}_{(5)}$, 1H), 8.38 (s, $\text{CH}_{(2)}$, 1H), 9.77 (t, $^3J_{\text{HH}} = 0.9$ Hz, CHO , 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 16.81 – (*E*) $\text{CH}=\text{CP}$, 13.46 – (*Z*) $\text{CH}=\text{CP}$, (*E*:*Z*)=(1:0.16), ^{13}C NMR (176 MHz, CDCl_3) δ : 16.29 (d, $^4J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 24.97 (s, $\text{CHOCH}_2\text{CH}_2$, 1C), 28.03 (s, $\text{C}(\text{CH}_3)_3$, 3C), 44.59 (s, $\text{CHOCH}_2\text{CH}_2$, 1C), 62.43 (d, $^3J_{\text{PC}} = 5.2$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 82.59 (s, $\text{C}(\text{CH}_3)_3$, 1C), 117.60 (d, $^1J_{\text{PC}} = 182.7$ Hz, CP , 1C), 118.05 (s, $\text{CH}_{(8)}$, 1C), 120.27 (d, $^3J_{\text{PC}} = 24.8$ Hz, $\text{C}_{(3)}$, 1C), 122.05 (s, $\text{CH}_{(5)}$, 1C), 127.07 (s, $\text{C}_{(6)}$, 1C), 128.95 (s, $\text{CH}_{(7)}$, 1C), 132.39 (d, $^2J_{\text{PC}} = 10.2$ Hz, $\text{CH}=\text{CP}$, 1C), 140.61 (s, $\text{CH}_{(2)}$, 1C), 146.69 (s, $\text{C}_{(9)}$, 1C), 165.00 (d, $^2J_{\text{PC}} = 11.3$ Hz, $\text{CO}_2t\text{-Bu}$, 1C), 200.19 (s, CHO , 1C).



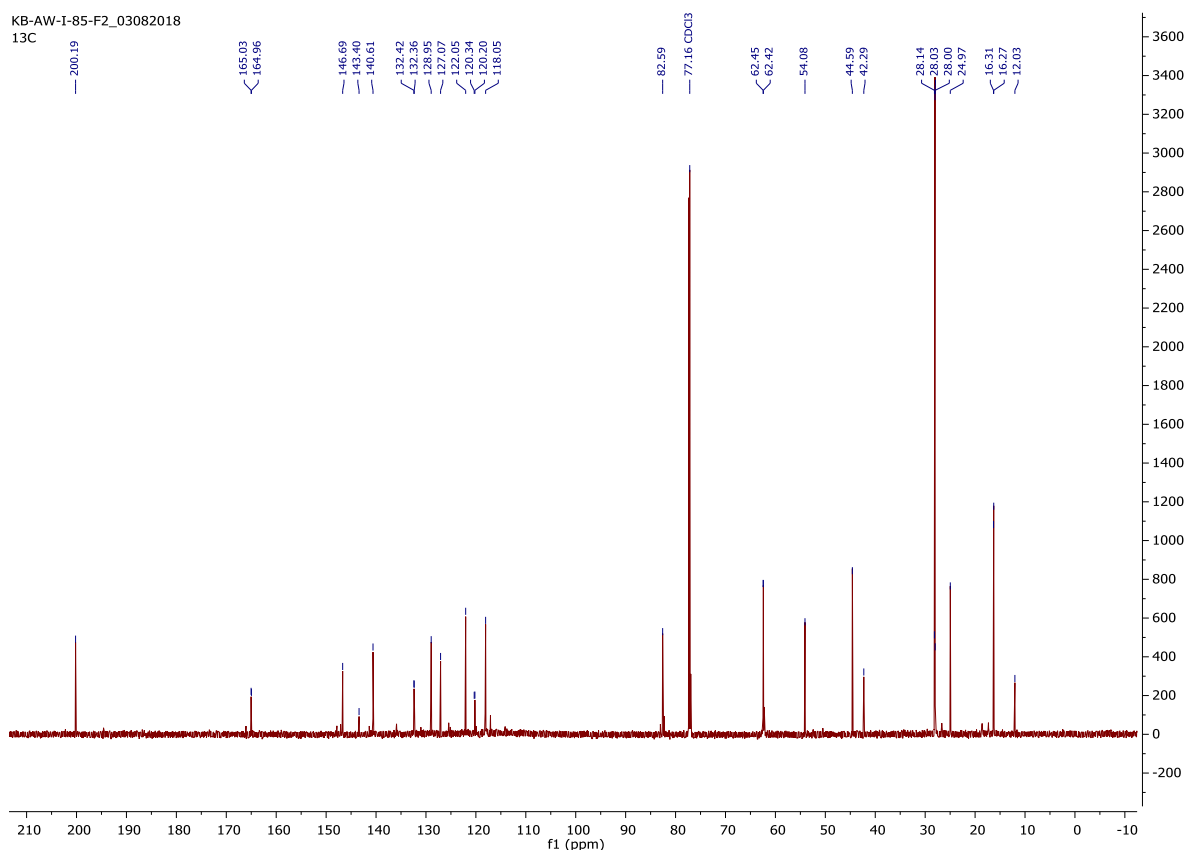
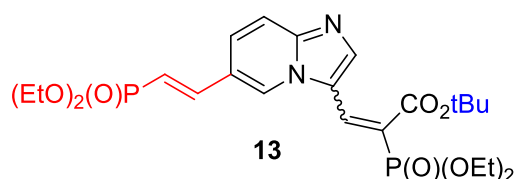
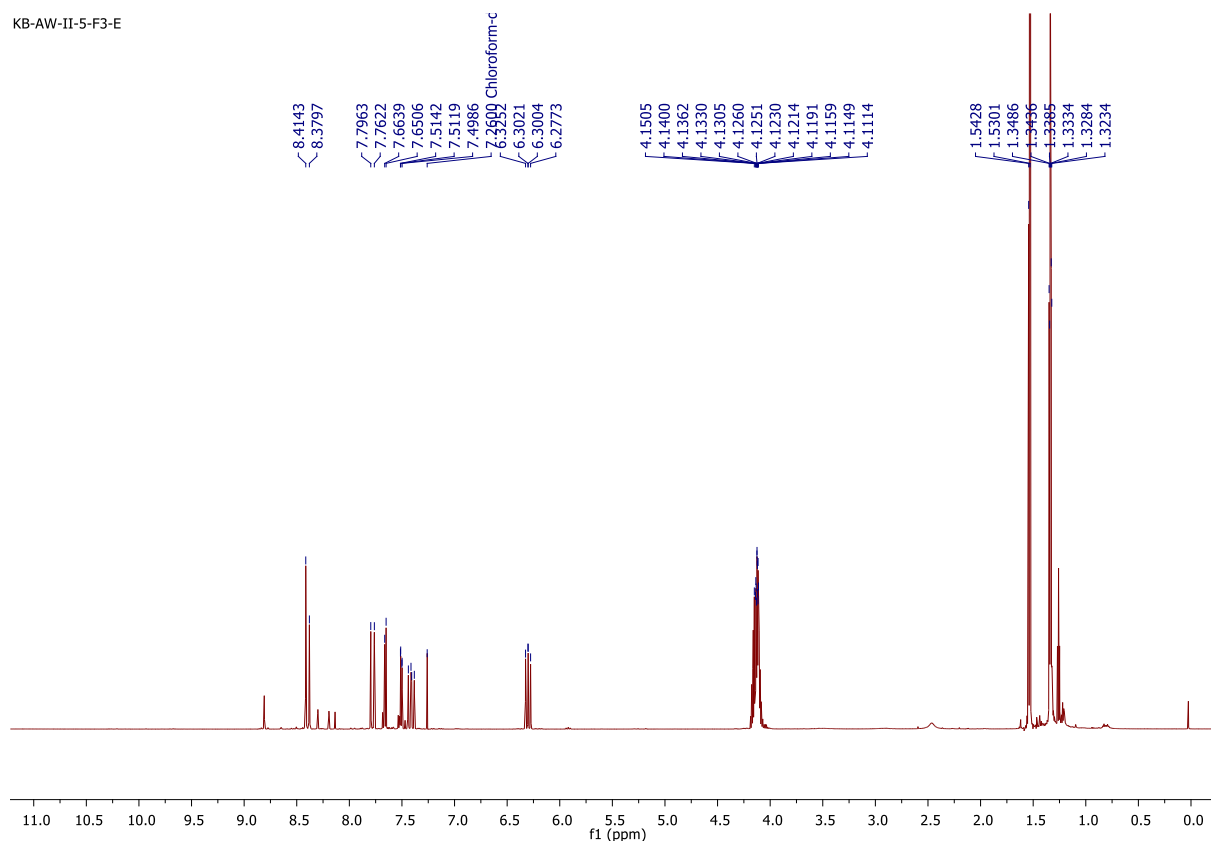
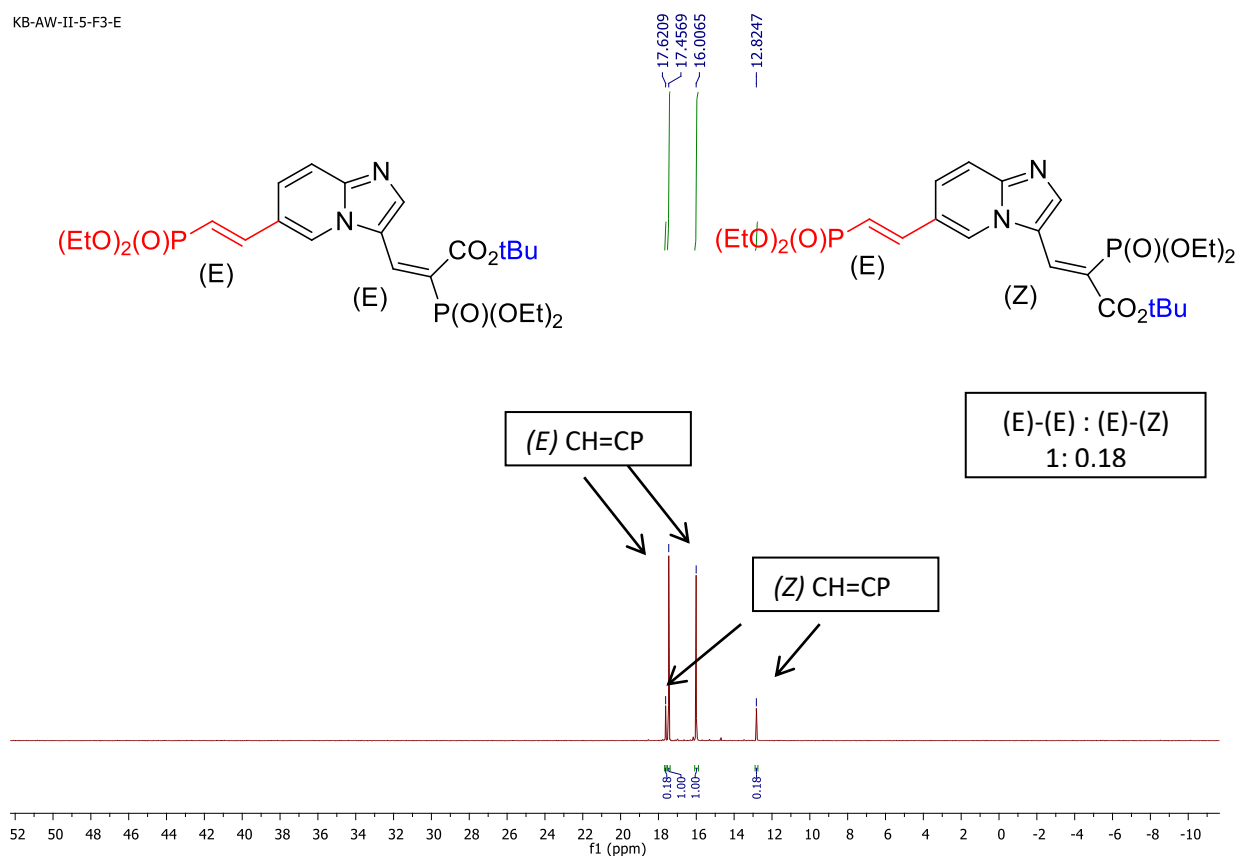


Figure S25. ^{13}C NMR of compound **12** (176 MHz, CDCl_3)



tert-Butyl 2-((diethoxyphosphoryl)-3-(6-((E)-2-(diethoxyphosphoryl)vinyl)imidazo[1,2-a]pyridin-3-yl)acrylate (13). Yield 65%.

HRMS m/z : calculated 543.2020 ($\text{C}_{24}\text{H}_{36}\text{N}_2\text{O}_8\text{P}_2 + \text{H}^+$), found 543.2030 ($\text{C}_{24}\text{H}_{36}\text{N}_2\text{O}_8\text{P}_2 + \text{H}^+$), ^1H NMR (700 MHz, CDCl_3) δ : 1.33 (t, $^3J_{\text{HH}} = 7.1$ Hz, $(\text{CH}_3\text{CH}_2)_2\text{OP}$, 6H), 1.34 (t, $^3J_{\text{HH}} = 7.1$ Hz, $(\text{CH}_3\text{CH}_2)_2\text{OP}$, 6H), 1.53 (s, $\text{C}(\text{CH}_3)_3$, 9H), 4.07–4.18 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 8H), 6.30 (dd, $^3J_{\text{HH}} = 17.4$ Hz, $^2J_{\text{PH}} = 16.5$ Hz, $\text{PCH}=\text{CH}$, 1H), 7.41 (dd, $^3J_{\text{PH}} = 22.2$ Hz, $^3J_{\text{HH}} = 17.4$ Hz, $\text{PCH}=\text{CH}$, 1H), 7.51 (dd, $^3J_{\text{HH}} = 9.3$ Hz, $^4J_{\text{HH}} = 1.6$ Hz, $\text{CH}_{(7)}$, 1H), 7.71 (d, $^3J_{\text{HH}} = 9.3$ Hz, $\text{CH}_{(8)}$, 1H), 7.78 (d, $^3J_{\text{HH}} = 23.9$ Hz, (E) $\text{CH}=\text{CP}$, 1H), 8.38 (bs, $\text{CH}_{(5)}$, 1H), 8.41 (s, $\text{CH}_{(2)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 16.01 – (E) $\text{CH}=\text{CP}$, 17.46 – (E) $\text{CH}=\text{CHP}$, 12.89 – (Z) $\text{CH}=\text{CP}$, 17.62 – (Z) $\text{CH}=\text{CHP}$, $(E:Z)$ $\text{CH}=\text{CP} = (1:0.18)$, ^{13}C NMR (176 MHz, CDCl_3) δ : 16.37 (d, $^3J_{\text{PC}} = 7.0$ Hz, $(\text{CH}_3\text{CH}_2)_2\text{OP}$, 2C), 16.48 (d, $^3J_{\text{PC}} = 6.3$ Hz, $(\text{CH}_3\text{CH}_2)_2\text{OP}$, 2C), 28.09 (s, $\text{C}(\text{CH}_3)_3$, 3C), 62.19 (d, $^2J_{\text{PC}} = 5.6$ Hz, $(\text{CH}_3\text{CH}_2)_2\text{OP}$, 2C), 62.57 (d, $^2J_{\text{PC}} = 5.3$ Hz, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 2C), 82.88 (s, $\text{C}(\text{CH}_3)_3$, 1C), 116.67 (d, $^1J_{\text{PC}} = 192.4$ Hz, $\text{PCH}=\text{CH}$, 1C), 118.65 (s, $\text{CH}_{(8)}$, 1C), 119.76 (d, $^1J_{\text{PC}} = 181.7$ Hz, CP , 1C), 121.06 (d, $^3J_{\text{PC}} = 25.0$ Hz, $\text{C}_{(3)}$, 1C), 122.95 (d, $^3J_{\text{PC}} = 24.4$ Hz, $\text{C}_{(6)}$, 1C), 124.24 (s, $\text{CH}_{(7)}$, 1C), 124.62 (s, $\text{CH}_{(5)}$, 1C), 131.58 (d, $^2J_{\text{PC}} = 10.0$ Hz, $\text{CH}=\text{CP}$, 1C), 141.07 (s, $\text{CH}_{(2)}$, 1C), 143.18 (d, $^2J_{\text{PC}} = 7.0$ Hz, $\text{CH}=\text{CH}$, 1C), 147.28 (s, $\text{C}_{(9)}$, 1C), 164.87 (d, $^2J_{\text{PC}} = 10.9$ Hz, $\text{CO}_2\text{t-Bu}$, 1C).

Figure S26. ^1H NMR of compound **13** (700 MHz, CDCl_3)Figure S27. ^{31}P NMR of compound **13** (283 MHz, CDCl_3)

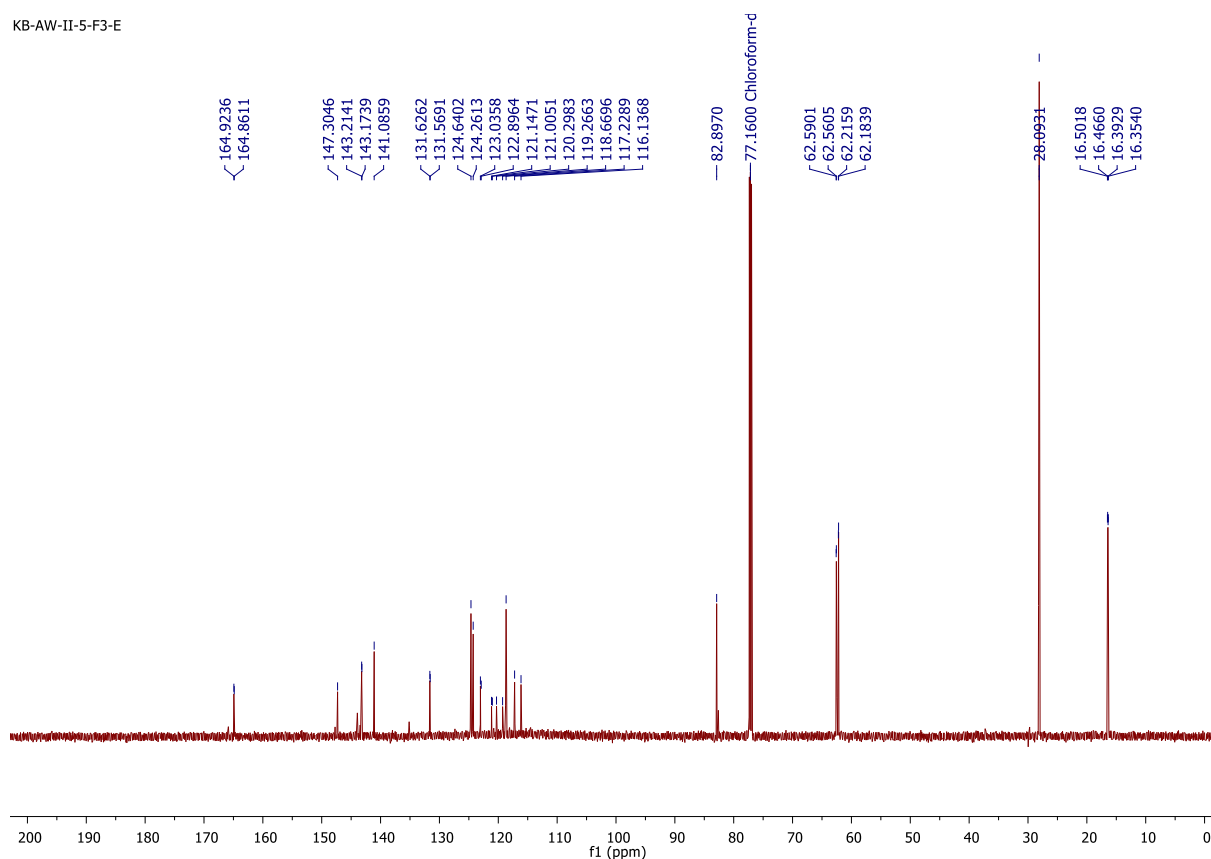
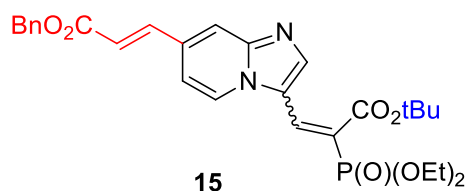


Figure S28. ^{13}C NMR of compound **13** (176 MHz, CDCl_3)



tert-Butyl 3-(7-((E)-3-(benzyloxy)-3-oxoprop-1-en-1-yl)imidazo[1,2-a]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (15). Yield 65%

HRMS m/z : calculated 541.2098 ($\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}$)⁺, found 541.2115 ($\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}$)⁺, ^1H NMR (700 MHz, CDCl_3) δ : 1.35 (t, $^3J_{\text{HH}} = 7.0$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 1.55 (s, $\text{C}(\text{CH}_3)_3$, 9H), 4.06 – 4.22 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 4H), 5.25 (s, PhCH_2O , 2H), 6.55 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.14 (d, $^3J_{\text{HH}} = 7.2$ Hz, $\text{CH}_{(6)}$, 1H), 7.31 – 7.41 (m, PhCH_2O , 5H), 7.69 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.74 (bs, $\text{CH}_{(8)}$, 1H), 7.81 (d, $^3J_{\text{HH}} = 24.0$ Hz, (E) $\text{CH}=\text{CP}$, 1H), 8.33 (d, $^3J_{\text{HH}} = 7.2$ Hz, $\text{CH}_{(5)}$, 1H), 8.47 (s, $\text{CH}_{(2)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 16.58 – (E) $\text{CH}=\text{CP}$, 13.28 – (Z) $\text{CH}=\text{CP}$ (E:Z)=(1:0.12), ^{13}C NMR (176 MHz, CDCl_3) δ : 16.38 (d, $^4J_{\text{PC}} = 6.8$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 28.12 (s, $\text{C}(\text{CH}_3)_3$, 3C), 62.61 (d, $^3J_{\text{PC}} = 5.2$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 66.80 (s, PhCH_2O , 1C), 82.95 (s, $\text{C}(\text{CH}_3)_3$, 1C), 111.61 (s, $\text{CH}_{(6)}$, 1C), 119.20 (s, $\text{CH}_{(8)}$, 1C), 119.65 (d, $^1J_{\text{PC}} = 182.0$ Hz, CP , 1C), 120.92 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C), 121.34 (d, $^3J_{\text{PC}} = 24.9$ Hz, $\text{C}_{(3)}$, 1C), 123.91 (s, $\text{CH}_{(5)}$, 1C), 128.44, 128.48, 128.72 (s, Ph, 5C), 131.77 (d, $^2J_{\text{PC}} = 10.2$ Hz, $\text{CH}=\text{CP}$, 1C), 133.26 (s, $\text{C}_{(7)}$, 1C), 135.81 (s, Ph – C_{IV} , 1C), 141.55 (s, $\text{CH}_{(2)}$, 1C), 142.02 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C), 147.24 (s, C_9 , 1C), 164.92 (d, $^2J_{\text{PC}} = 11.1$ Hz, CO_2tBu , 1C), 166.05 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C).

KB-AW-I-107-F2-2
¹H
 ro off

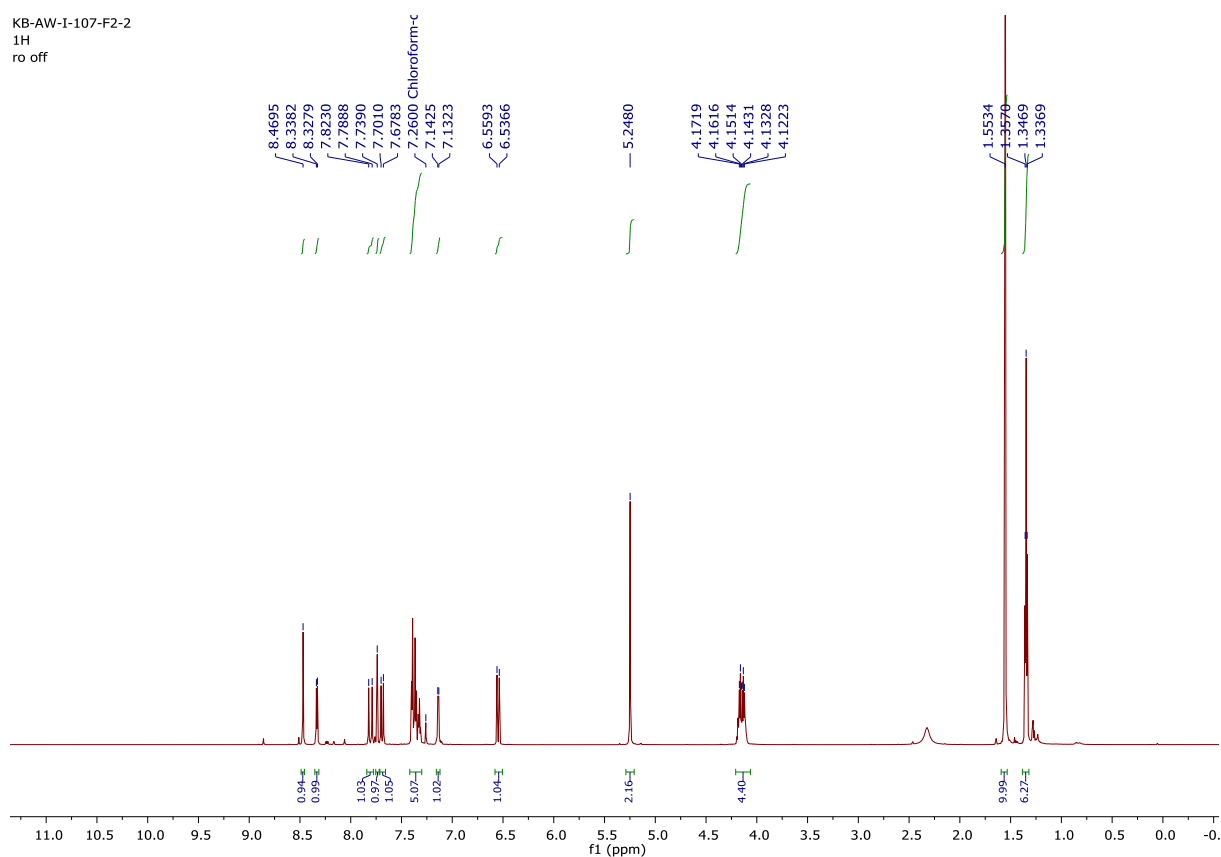


Figure S29. ¹H NMR of compound **15** (700 MHz, CDCl₃)

KB-AW-I-107-F2

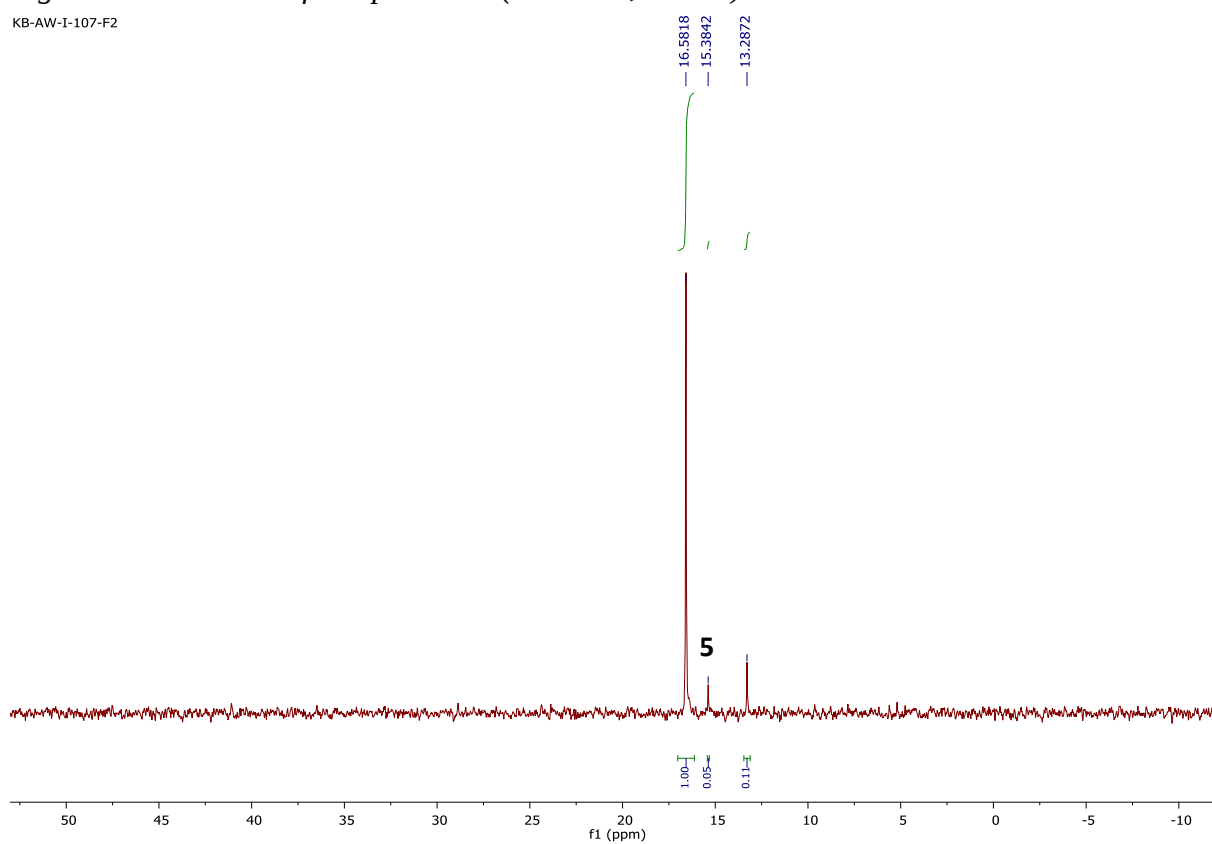


Figure S30. ³¹P NMR of compound **15** (283 MHz, CDCl₃)

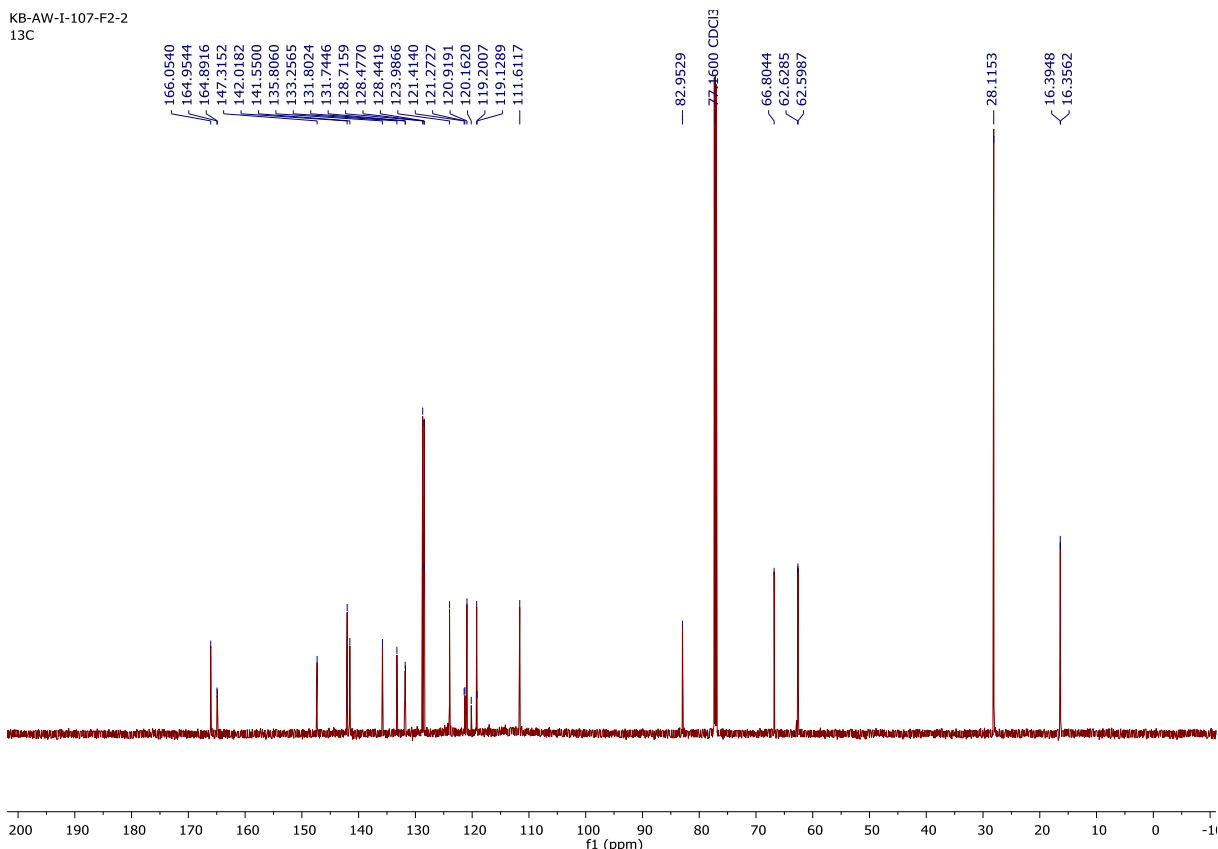
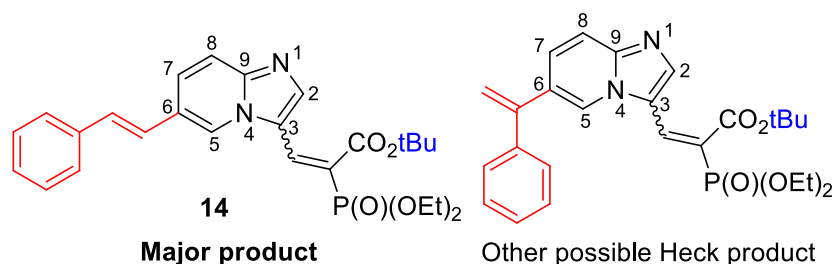


Figure S31. ^{13}C NMR of compound **15** (176 MHz, CDCl_3)



tert-Butyl 2-(diethoxyphosphoryl)-3-(6-((*E*)-styryl)imidazo[1,2-*a*]pyridin-3-yl)acrylate (14**), Yield 60%.**

^1H NMR (700 MHz, CDCl_3) δ : 1.38 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 1.58 (s, $\text{C}(\text{CH}_3)_3$, 9H), 4.09 – 4.29 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 4H), 7.09 (d, $^3J_{\text{HH}} = 16.3$ Hz, $\text{PhCH}=\text{CH}$, 1H), 7.15 (d, $^3J_{\text{HH}} = 16.3$ Hz, $\text{PhCH}=\text{CH}$, 1H), 7.28–7.34 (m, Ph, 1H), 7.37–7.42 (m, Ph, 2H), 7.50–7.54 (m, Ph, 2H), 7.67 (dd, $^3J_{\text{HH}} = 9.4$ Hz, $^4J_{\text{HH}} = 1.5$ Hz, $\text{CH}_{(7)}$, 1H), 7.68 (dd, $^3J_{\text{HH}} = 9.3$ Hz, $^5J_{\text{HH}} = 0.7$ Hz, $\text{CH}_{(8)}$, 1H), 7.89 (d, $^3J_{\text{HH}} = 24.0$ Hz, (*E*) $\text{CH}=\text{CP}$, 1H), 8.35 (bs, $\text{CH}_{(5)}$, 1H), 8.46 (s, $\text{CH}_{(2)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 16.75 – (*E*) $\text{CH}=\text{CP}$, 13.45 – (*Z*) $\text{CH}=\text{CP}$, (*E*:*Z*)=(1:0.3), ^{13}C NMR (176 MHz, CDCl_3) δ : 16.48 (d, $^4J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 28.22 (s, $\text{C}(\text{CH}_3)_3$, 3C), 62.57 (d, $^3J_{\text{CP}} = 5.1$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 82.79 (s, $\text{C}(\text{CH}_3)_3$, 1C), 118.31 (d, $^1J_{\text{PC}} = 182.3$ Hz, CP , 1C), 118.36 (s, $\text{CH}_{(8)}$, 1C), 120.83 (d, $^3J_{\text{PC}} = 24.7$ Hz, $\text{C}_{(3)}$, 1C), 122.03 (s, $\text{CH}_{(5)}$, 1C), 123.66 (s, $\text{PhCH}=\text{CH}$, 1C), 124.94 (s, $\text{CH}_{(7)}$, 1C), 125.43 (s, $\text{C}_{(6)}$, 1C), 126.74 (s, Ph, 2C), 128.44 (s, Ph, 1C), 129.01 (s, Ph, 2C), 130.81 (s, $\text{PhCH}=\text{CH}$, 1C), 132.33 (d, $^2J_{\text{PC}} = 10.2$ Hz, $\text{CH}=\text{CP}$, 1C), 136.54 (s, Ph- C_{IV} , 1C), 140.94 (s, $\text{CH}_{(2)}$, 1C), 147.12 (s, $\text{C}_{(9)}$, 1C), 165.18 (d, $^2J_{\text{PC}} = 11.3$ Hz, $\text{CO}_2t\text{-Bu}$, 1C),

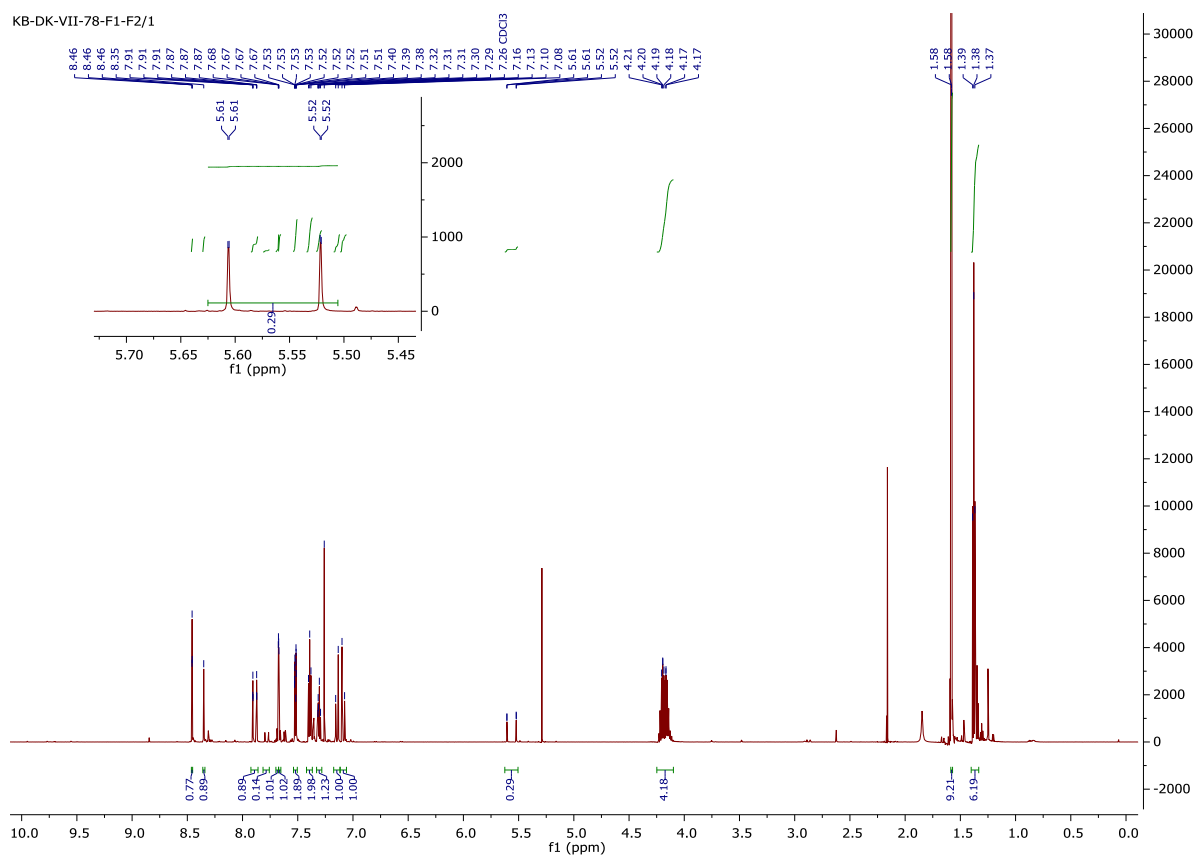


Figure S32. ^1H NMR of compound **14** (700 MHz, CDCl_3)

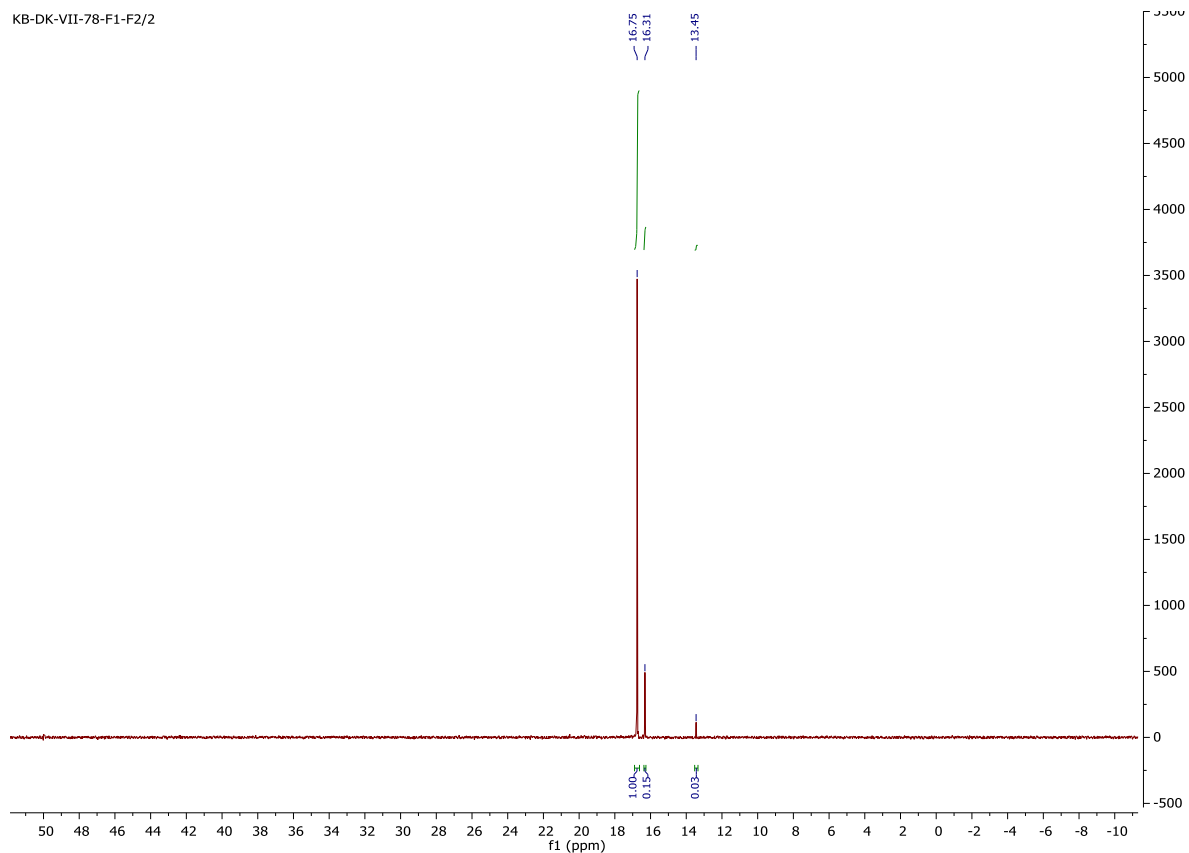


Figure S33. ^{31}P NMR of compound **14** (mixture of Heck products) (283 MHz, CDCl_3)

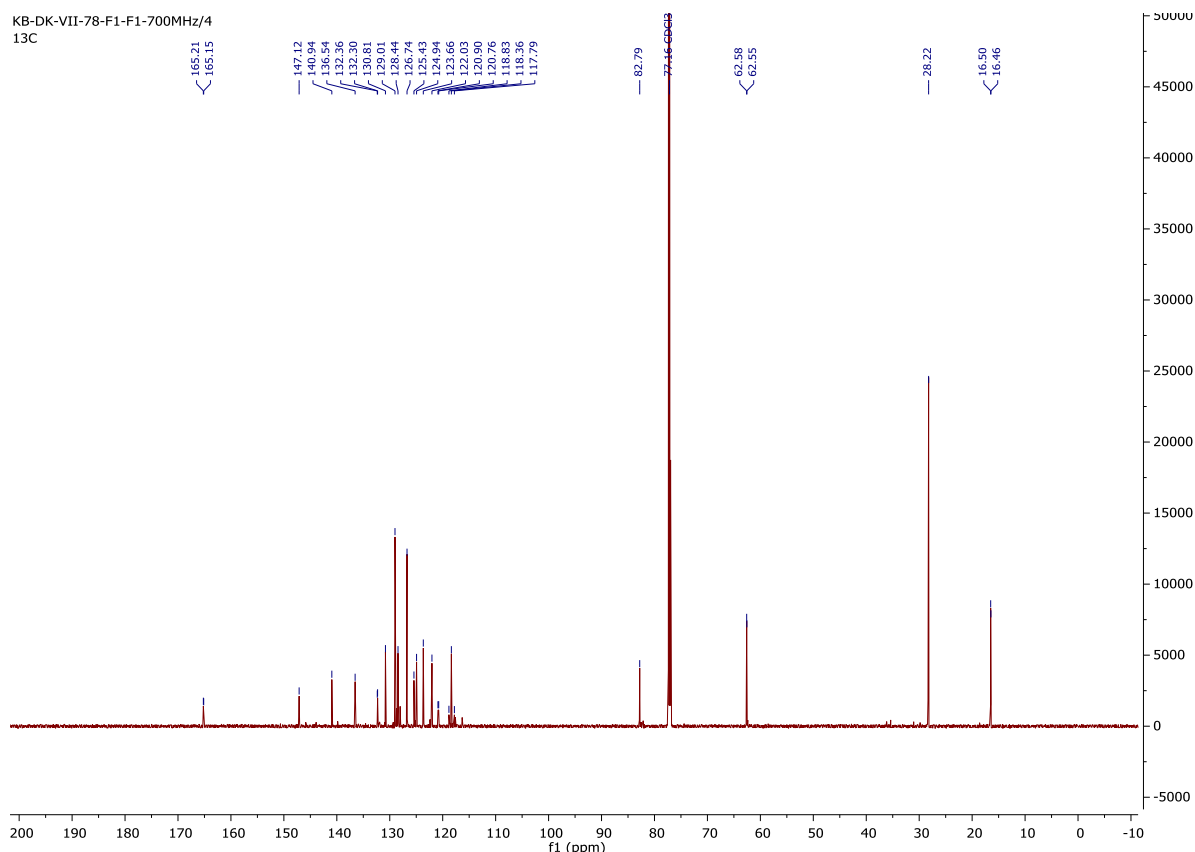
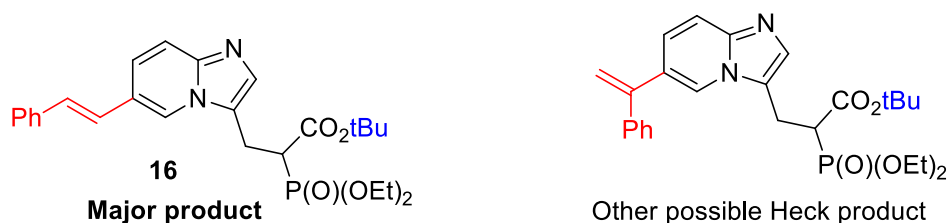


Figure S34. ^{13}C NMR of compound **14** (176 MHz, CDCl_3)



(E)-tert-Butyl 2-(diethoxyphosphoryl)-3-(6-styrylimidazo[1,2-a]pyridin-3-yl)propanoate (16), Yield 84%

^1H NMR (700 MHz, CDCl_3) δ : 1.33-1.39 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, $\text{C}(\text{CH}_3)_3$, 15H), 3.26 (ddd, $^2J_{\text{PH}} = 22.7$, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HH}} = 2.9$, CH_2CHP , 1H), 3.34 (ddd, $^2J_{\text{HH}} = 15.7$, $^3J_{\text{PH}} = 10.1$, $^3J_{\text{HH}} = 2.9$, CH_2CHP , 1H), 3.57 (ddd, $^2J_{\text{HH}} = 15.7$, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{PH}} = 6.7$, CH_2CHP , 1H), 4.16-4.23 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 4H), 7.04 (d, $^3J_{\text{AB}} = 16.2$, $\text{PhCH}=\text{CH}$, 1H), 7.07 (d, $^3J_{\text{AB}} = 16.2$, $\text{PhCH}=\text{CH}$, 1H), 7.23-7.28 (m, Ph , 1H), 7.32-7.37 (m, Ph , 2H), 7.40 (s, $\text{CH}_{(2)}$, 1H), 7.47 (dd, $^3J_{\text{HH}} = 9.4$, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{(7)}$, 1H), 7.48-7.50 (m, Ph , 2H), 7.56 (dd, $^3J_{\text{HH}} = 9.4$, $^5J_{\text{HH}} = 0.8$, $\text{CH}_{(8)}$, 1H), 8.02 (bs, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 21.61, ^{13}C NMR (176 MHz, CDCl_3) δ : 16.44-16.57 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 21.67 (d, $^2J_{\text{PC}} = 3.4$ Hz, CH_2CHP , 1C), 27.88 (s, $\text{C}(\text{CH}_3)_3$, 3C), 45.32 (d, $^1J_{\text{PC}} = 128.8$ Hz, CH_2CHP , 1C), 63.04 (d, $^2J_{\text{PC}} = 7.0$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 63.11 (d, $^2J_{\text{PC}} = 6.4$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 82.68 (s, $\text{C}(\text{CH}_3)_3$, 1C), 117.89 (s, $\text{CH}_{(8)}$, 1C), 121.65 (s, $\text{CH}_{(7)}$, 1C), 121.70 (s, $\text{CH}_{(5)}$, 1C), 121.89 (d, $^3J_{\text{PC}} = 19.1$ Hz, $\text{C}_{(3)}$, 1C), 123.45 (s, $\text{C}_{(6)}$, 1C), 124.49 (s, $\text{PhCH}=\text{CH}$, 1C), 126.52 (s, Ph , 2C), 127.99 (s, Ph , 1C), 128.83 (s, Ph , 2C), 129.39 (s, $\text{PhCH}=\text{CH}$, 1C), 132.05 (s, $\text{CH}_{(2)}$, 1C), 136.83 (s, Ph-C_{IV} , 1C), 145.10 (s, $\text{C}_{(9)}$, 1C), 167.34 (d, $^2J_{\text{PC}} = 5.2$ Hz, $\text{CO}_2t\text{-Bu}$, 1C).

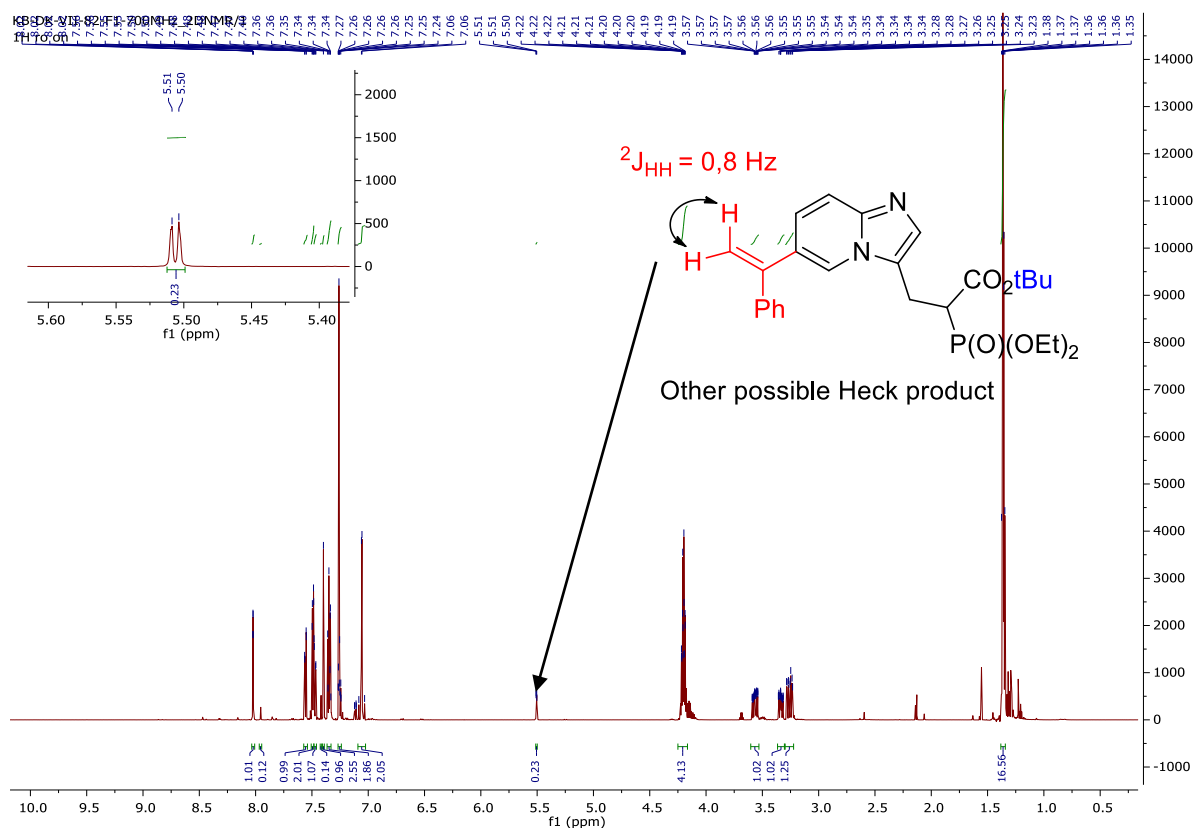


Figure S35. ^1H NMR of compound 16 (700 MHz, CDCl_3)

KB-DK-VII-82-F1-700MHz_2DNMR/2
31P

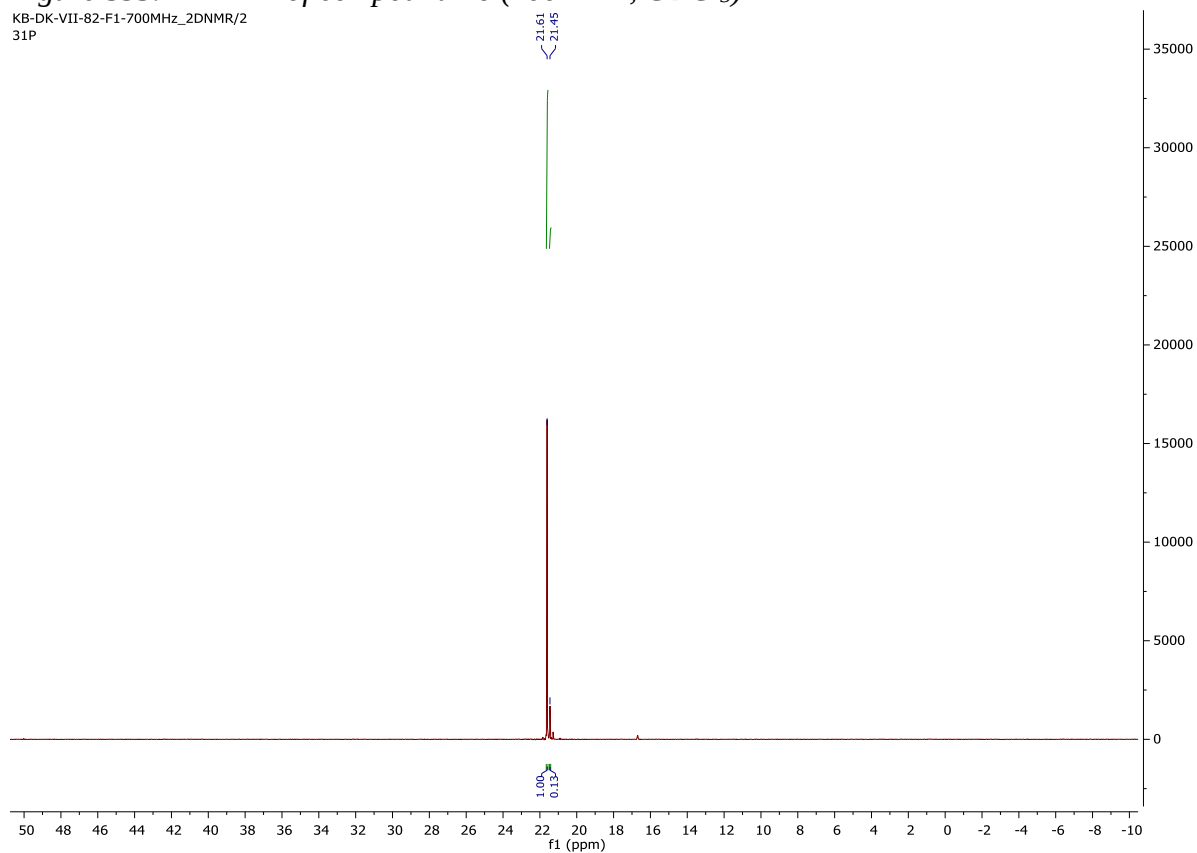


Figure S36. ^{31}P NMR of compound 16 (mixture of Heck products) (283 MHz, CDCl_3)

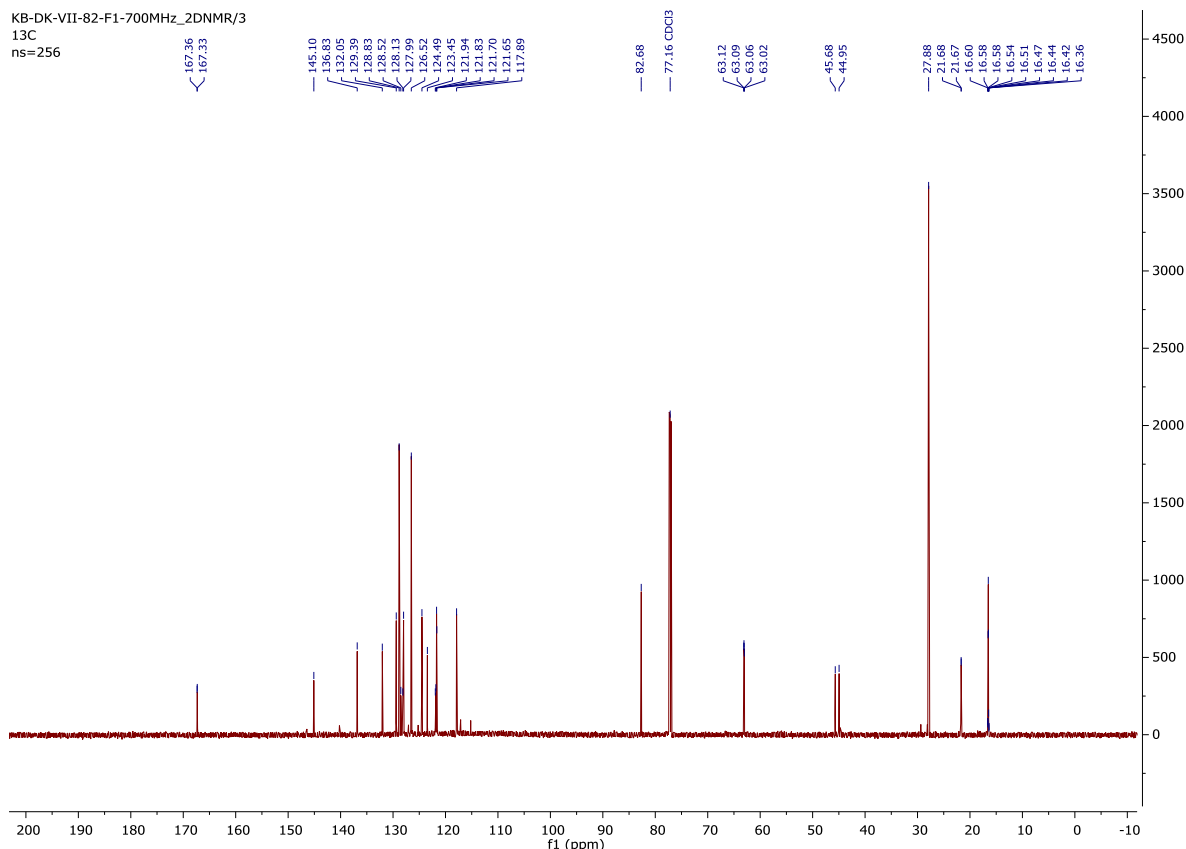
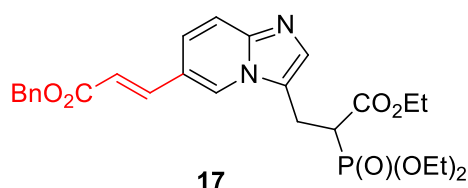


Figure S37. ^{13}C NMR of compound **16** (176 MHz, CDCl_3)



(E)-Benzyl 3-(3-(2-(diethoxyphosphoryl)-3-ethoxy-3-oxopropyl)imidazo[1,2-a]pyridin-6-yl)acrylate (17**). Yield 58%**

^1H NMR (700 MHz, CDCl_3) δ : 1.20 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OC}$, 3H), 1.37 (t, $^3J_{\text{HH}} = 7.1$ Hz, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 6H), 3.35 (ddd, $^2J_{\text{PH}} = 23.0$, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{PH}} = 3.3$, CH_2CHP , 1H), 3.36–3.41 (m, CH_2CHP , 1H), 3.61 (ddd, $^2J_{\text{HH}} = 16.5$, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{PH}} = 7.2$, CH_2CHP , 1H), 4.06 – 4.25 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, $\text{CH}_3\text{CH}_2\text{OC}$, 6H), 5.27 (s, PhCH_2 , 2H), 6.49 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.34–7.38 (m, $\text{CH}_2\text{C}_6\text{H}_5$, 1H), 7.37–7.42 (m, $\text{CH}_2\text{C}_6\text{H}_5$, $\text{CH}_{(7)}$, 3H), 7.42–7.46 (m, $\text{CH}_2\text{C}_6\text{H}_5$, $\text{CH}_{(2)}$, 3H), 7.59 (d, $^3J_{\text{HH}} = 9.5$ Hz, $\text{CH}_{(8)}$, 1H), 7.72 (d, $^3J_{\text{HH}} = 15.9$ Hz, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1H), 8.15 (bs, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 20.95, ^{13}C NMR (176 MHz, CDCl_3) δ : 13.96 (s, $\text{CH}_3\text{CH}_2\text{OC}$, 1C), 16.34 (d, $^3J_{\text{PC}} = 6.2$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 16.38 (d, $^3J_{\text{PC}} = 6.1$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 21.44 (d, $^2J_{\text{PC}} = 3.7$ Hz, CH_2CHP , 1C), 44.40 (d, $^1J_{\text{PC}} = 129.6$ Hz, CH_2CHP , 1C), 61.93 (s, $\text{CH}_3\text{CH}_2\text{OC}$, 1C), 63.12 (d, $^2J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 63.24 (d, $^2J_{\text{PC}} = 6.2$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 66.47 (s, CH_2Ph , 1C), 118.26 (s, $\text{CH}_{(8)}$, 1C), 118.43 (s, $\text{BnOC}(\text{O})\text{CH}=\text{CH}$, 1C), 120.66 (s, $\text{C}_{(6)}$, 1C), 121.12 (s, $\text{CH}_{(7)}$, 1C), 122.25 (d, $^3J_{\text{PC}} = 18.2$ Hz, $\text{C}_{(3)}$, 1C), 125.08 (s, $\text{CH}_{(5)}$, 1C), 128.28 (s, $\text{CH}_2\text{C}_6\text{H}_5$, 3C), 128.58 (s, $\text{CH}_2\text{C}_6\text{H}_5$, 2C), 132.68 (s, $\text{CH}_{(2)}$, 1C), 135.87 (s, $\text{CH}_2\text{C}_6\text{H}_5$ - C_{IV} , 1C), 141.03 (s,

$BnOC(O)CH=CH$, 1C), 145.33 (s, $C_{(9)}$, 1C), 166.20 (s, $BnO\ C(O)CH=CH$, 1C), 168.12 (d, $^2J_{PC} = 5,2\text{ Hz}$, C_{O_2Et} , 1C).

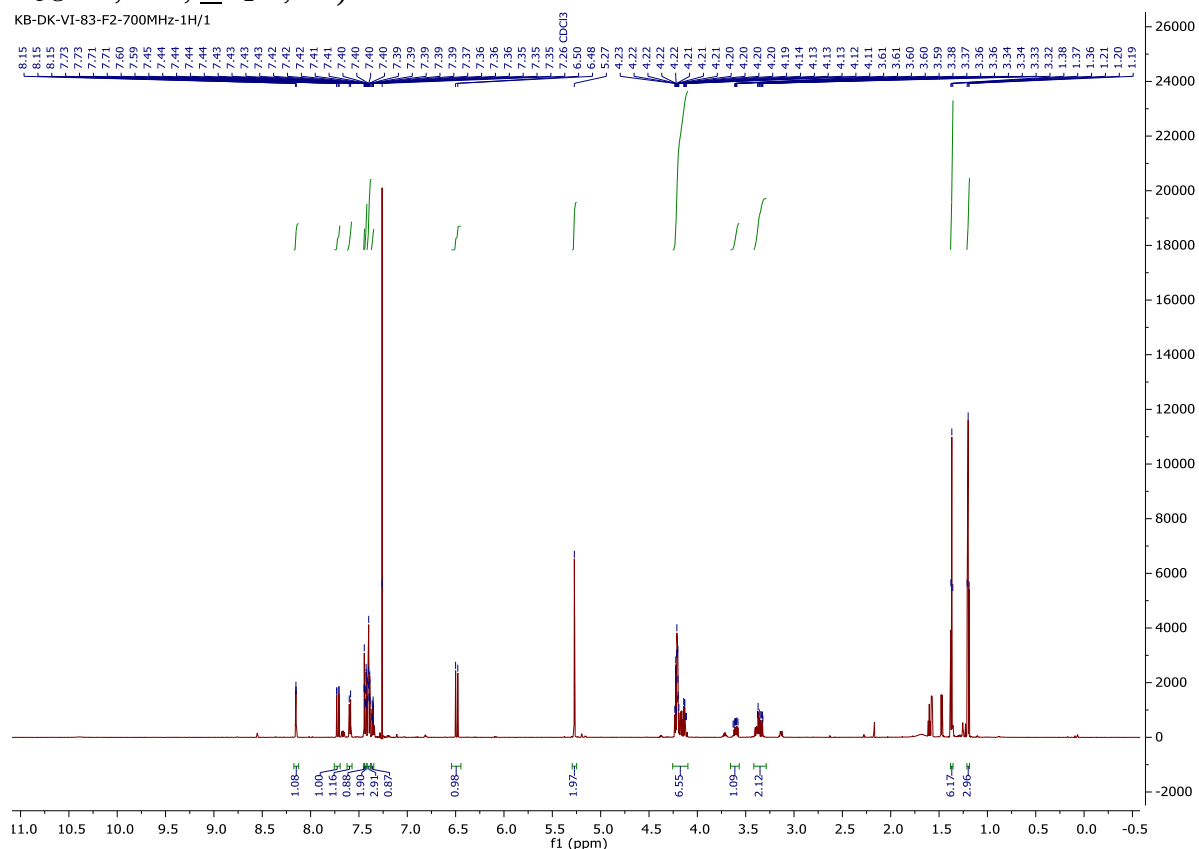


Figure S38. 1H NMR of compound **17** (700 MHz, $CDCl_3$)

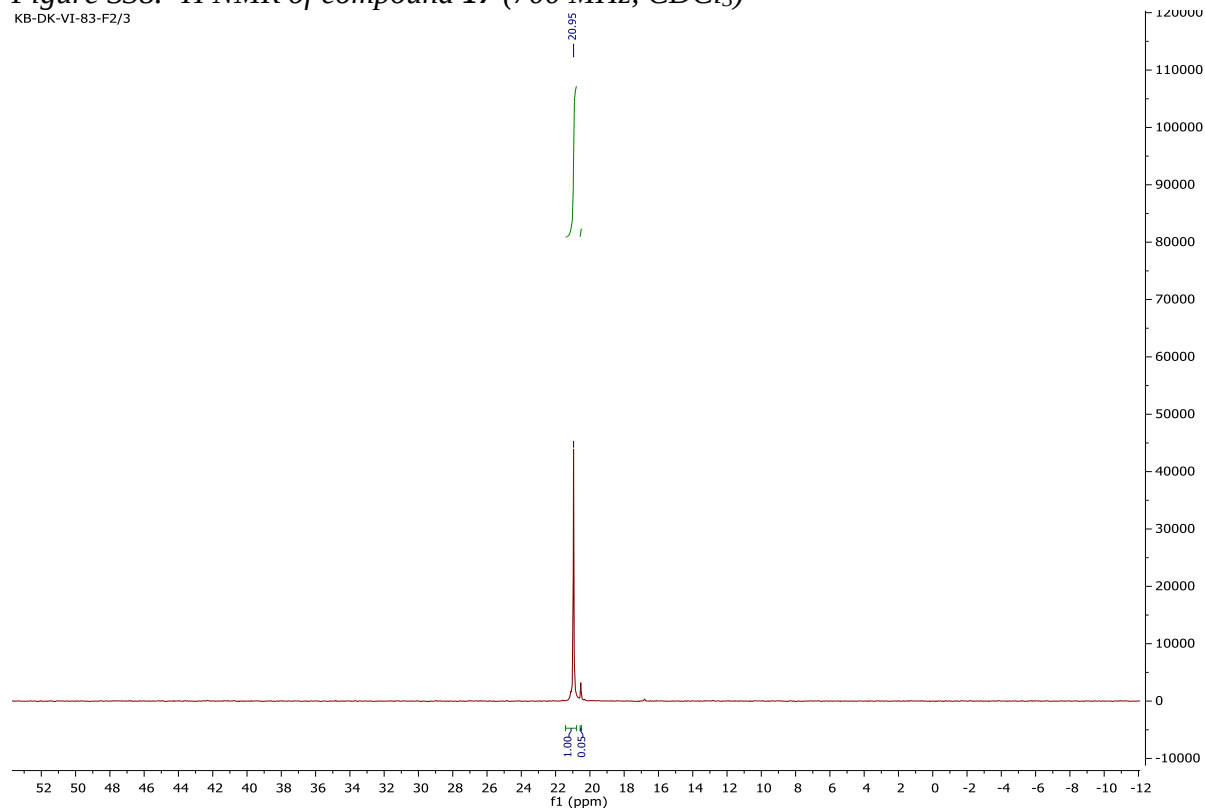


Figure S39. ^{31}P NMR of compound **17** (283 MHz, $CDCl_3$)

KB-DK-VI-83-F2-700MHz
13C

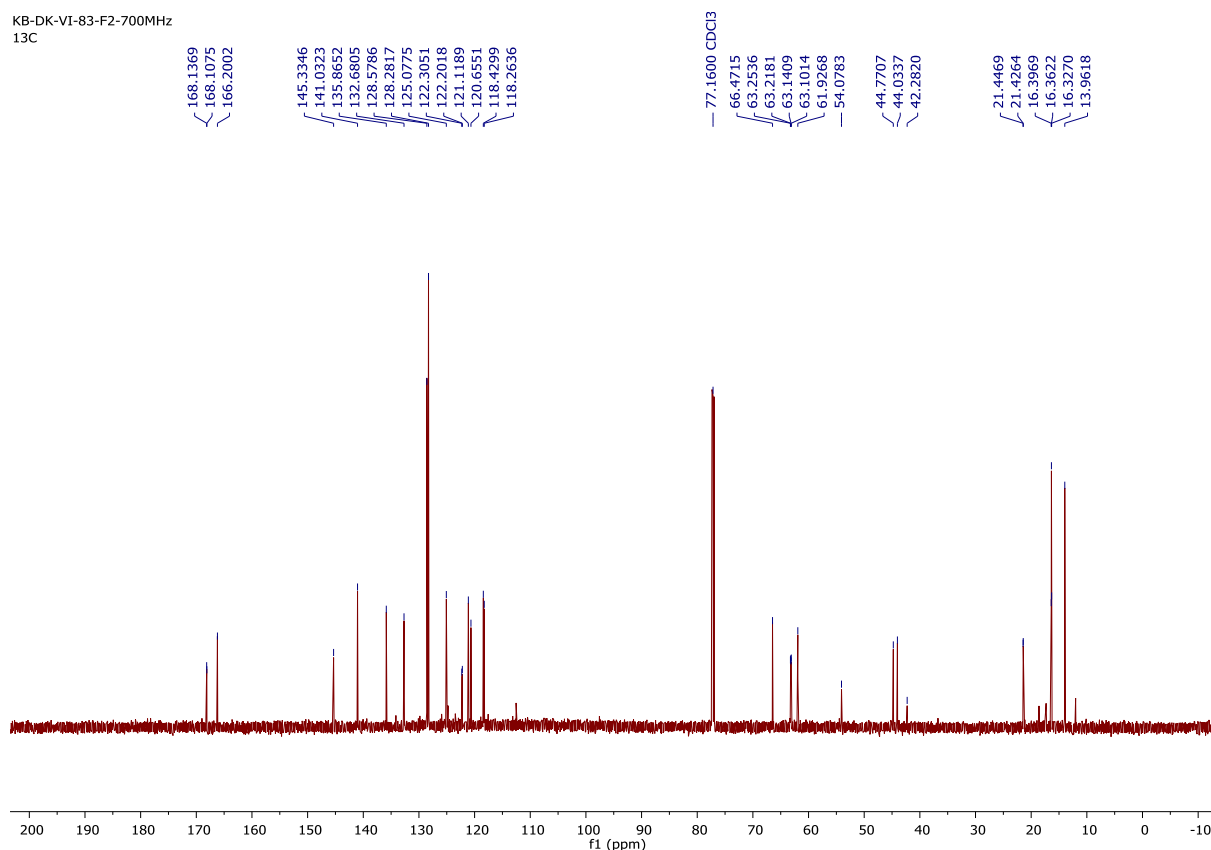
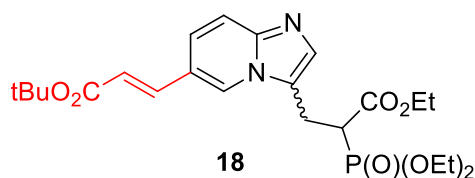


Figure S40. ^{13}C NMR of compound **17** (176 MHz, CDCl_3)



(E)-tert-Butyl 3-(3-(2-(diethoxyphosphoryl)-3-ethoxy-3-oxopropyl)imidazo[1,2-a]pyridin-6-yl)acrylate (18). Yield 66%

HRMS m/z : calculated 481.2098 ($\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), found 481.2106 ($\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), ^1H NMR (700 MHz, CDCl_3) δ : 1.20 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OC}$, 3H), 1.37 (t, $^3J_{\text{HH}} = 7.1$ Hz, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 6H), 1.55 (s, $\text{C}(\text{CH}_3)_3$, 9H), 3.31-3.42 (m, CH_2CHP , 2H) 3.61 (ddd, $^2J_{\text{HH}} = 16.3$, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{PH}} = 7.2$, CH_2CHP , 1H), 4.09 – 4.25 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, $\text{CH}_3\text{CH}_2\text{OC}$, 6H), 6.37 (d, $^3J_{\text{HH}} = 15.8$ Hz, $t\text{-BuOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.40 (dd, $^3J_{\text{HH}} = 9.4$ Hz, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{(7)}$, 1H), 7.44 (s, $\text{CH}_{(2)}$, 1H), 7.57 (d, $^3J_{\text{HH}} = 15.8$ Hz, $t\text{-BuOC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.60 (d, $^3J_{\text{HH}} = 9.4$ Hz, $\text{CH}_{(8)}$, 1H), 8.12 (bs, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 20.63, ^{13}C NMR (176 MHz, CDCl_3) δ : 14.15 (s, $\text{CH}_3\text{CH}_2\text{OC}$, 1C), 16.54 (d, $^3J_{\text{PC}} = 6.0$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 16.58 (d, $^3J_{\text{PC}} = 6.0$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 28.35 (s, $\text{C}(\text{CH}_3)_3$, 3C), 21.66 (d, $^2J_{\text{PC}} = 3.5$ Hz, CH_2CHP , 1C), 44.60 (d, $^1J_{\text{PC}} = 129.6$ Hz, CH_2CHP , 1C), 62.14 (s, $\text{CH}_3\text{CH}_2\text{OC}$, 1C), 63.31 (d, $^2J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 63.43 (d, $^2J_{\text{PC}} = 6.6$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 81.02 (s, $\text{C}(\text{CH}_3)_3$, 1C), 118.33 (s, $\text{CH}_{(8)}$, 1C), 121.16 (s, $t\text{-BuOC}(\text{O})\text{CH}=\text{CH}$, 1C), 121.25 (s, $\text{C}_{(6)}$, 1C), 121.68 (s, $\text{CH}_{(7)}$, 1C), 122.32 (d, $^3J_{\text{PC}} = 18.4$ Hz, $\text{C}_{(3)}$, 1C), 124.62 (s, $\text{CH}_{(5)}$, 1C), 132.56 (s, $\text{CH}_{(2)}$, 1C), 139.44 (s, $t\text{-BuOC}(\text{O})\text{CH}=\text{CH}$, 1C), 145.43 (s, $\text{C}_{(9)}$, 1C), 165.86 (s, $t\text{-BuOC}(\text{O})\text{CH}=\text{CH}$, 1C), 168.29 (d, $^2J_{\text{PC}} = 5.2$ Hz, CO_2Et , 1C).

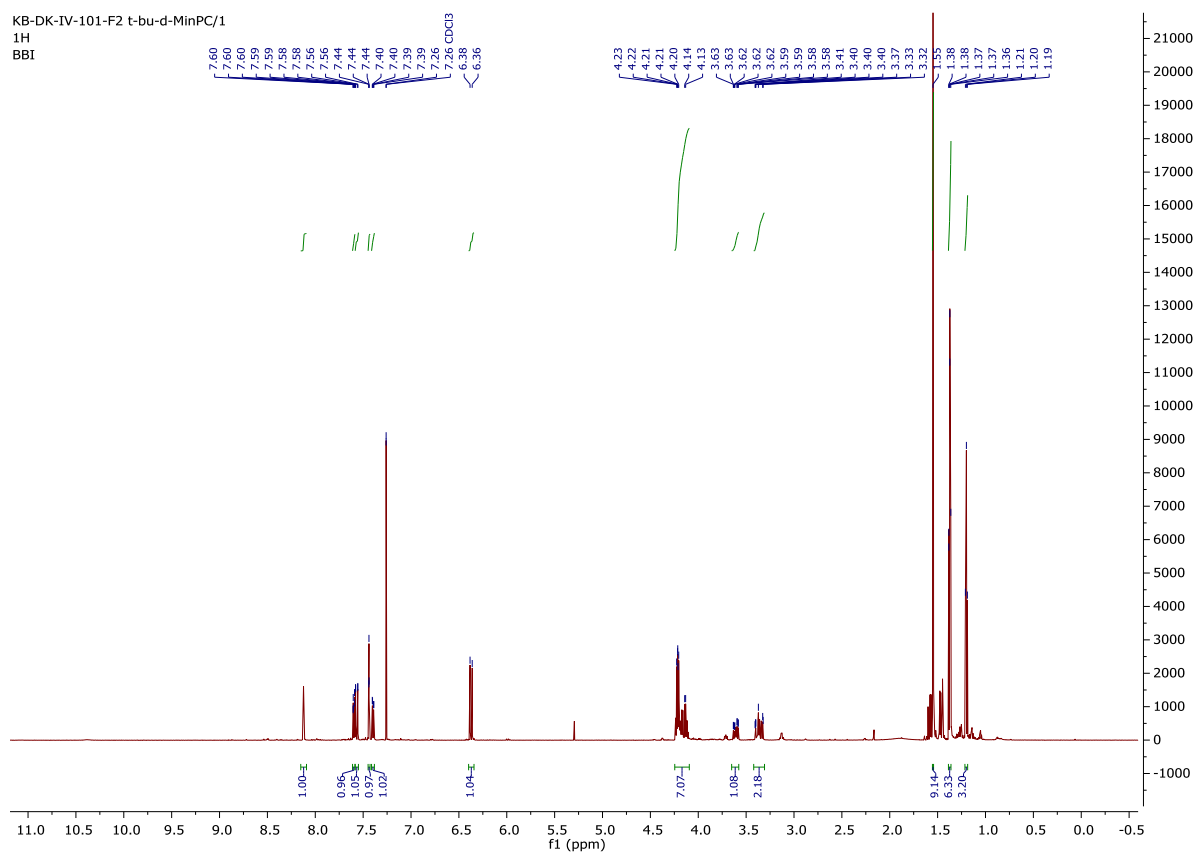


Figure S41. ^1H NMR of compound **18** (700 MHz, CDCl_3)

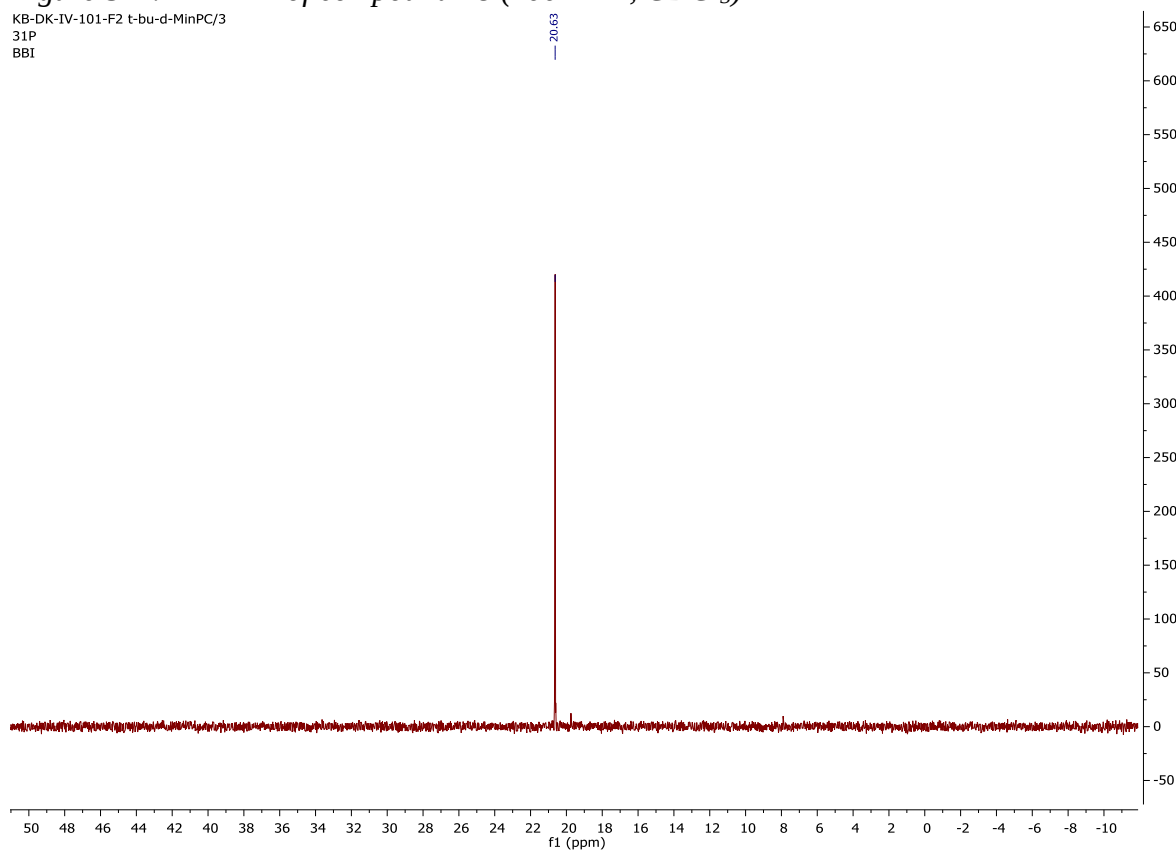


Figure S42. ^{31}P NMR of compound **18** (286 MHz, CDCl_3)

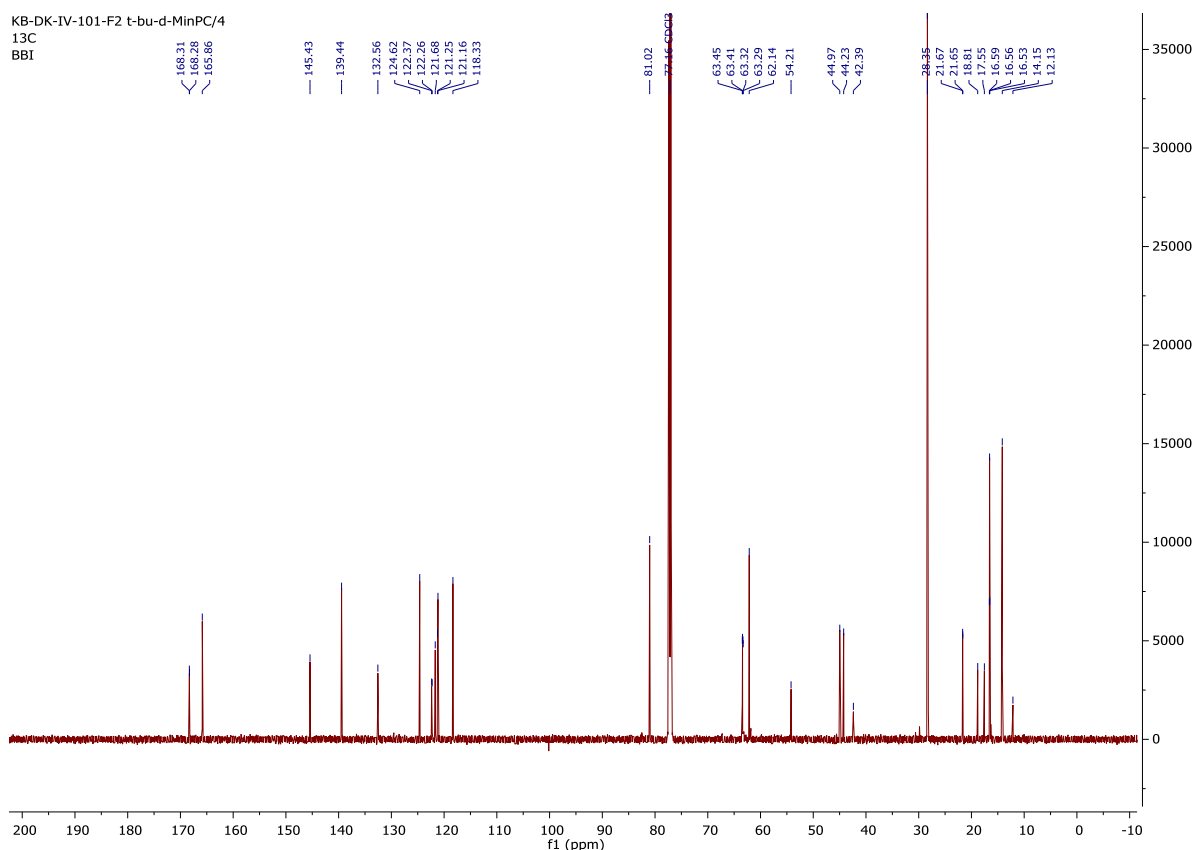
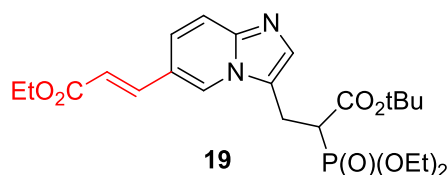


Figure S43. ^{13}C NMR of compound **18** (176 MHz, CDCl_3)



(E)-Ethyl 3-(3-(3-(tert-butoxy)-2-(diethoxyphosphoryl)-3-oxopropyl)imidazo[1,2-a]pyridin-6-yl)acrylate (19). Yield 67%.

HRMS m/z : calculated 481.2098 ($\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), found 481.2097 ($\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_7\text{P} + \text{H}^+$), ^1H NMR (700 MHz, CDCl_3) δ : 1.33 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 3H), 1.35-1.37 (m, $(\text{CH}_3\text{CH}_2\text{O})_2(\text{O})\text{P}$, $\text{C}(\text{CH}_3)_3$, 15H), 3.23 (ddd, $^2J_{\text{PH}} = 22.8$, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HH}} = 3.2$, CH_2CHP , 1H), 3.33 (ddd, $^2J_{\text{HH}} = 15.7$, $^3J_{\text{PH}} = 10.0$, $^3J_{\text{HH}} = 3.2$, CH_2CHP , 1H), 3.55 (ddd, $^2J_{\text{HH}} = 15.7$, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{PH}} = 6.9$, CH_2CHP , 1H), 4.15-4.22 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 4H), 4.26 (q, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 2H), 6.41 (d, $^3J_{\text{HH}} = 15.9$ Hz, $(\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.38 (dd, $^3J_{\text{HH}} = 9.5$ Hz, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{(7)}$, 1H), 7.43 (s, $\text{CH}_{(2)}$, 1H), 7.57 (bd, $^3J_{\text{HH}} = 9.5$ Hz, $\text{CH}_{(8)}$, 1H), 7.66 (d, $^3J_{\text{HH}} = 15.9$ Hz, $(\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1H), 8.15 (bs, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (284 MHz, CDCl_3) δ : 21.33, ^{13}C NMR (176 MHz, CDCl_3) δ : 14.42 (s, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1C), 16.47-16.62 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 21.60 (d, $^2J_{\text{PC}} = 3.4$ Hz, CH_2CHP , 1C), 27.90 (s, $\text{C}(\text{CH}_3)_3$, 3C), 45.41 (d, $^1J_{\text{PC}} = 129.2$ Hz, CH_2CHP , 1C), 60.78 (s, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1C), 63.11 (d, $^2J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 63.22 (d, $^2J_{\text{PC}} = 6.4$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 82.83 (s, $\text{C}(\text{CH}_3)_3$, 1C), 118.37 (s, $\text{CH}_{(8)}$, 1C), 118.92 (s, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1C), 120.84 (s, $\text{C}_{(6)}$, 1C), 121.22 (s, $\text{CH}_{(7)}$, 1C), 122.58 (d, $^3J_{\text{PC}} = 19.1$ Hz, $\text{C}_{(3)}$, 1C), 125.13 (s, $\text{CH}_{(5)}$, 1C), 132.78 (s, $\text{CH}_{(2)}$, 1C), 140.64 (s, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1C), 145.45 (s, $\text{C}_{(9)}$, 1C), 166.59 (s, $\text{CH}_3\text{CH}_2\text{OC}(\text{O})\text{CH}=\text{CH}$, 1C), 167.32 (d, $^2J_{\text{PC}} = 5.1$ Hz, $\text{CO}_2t\text{-Bu}$, 1C).

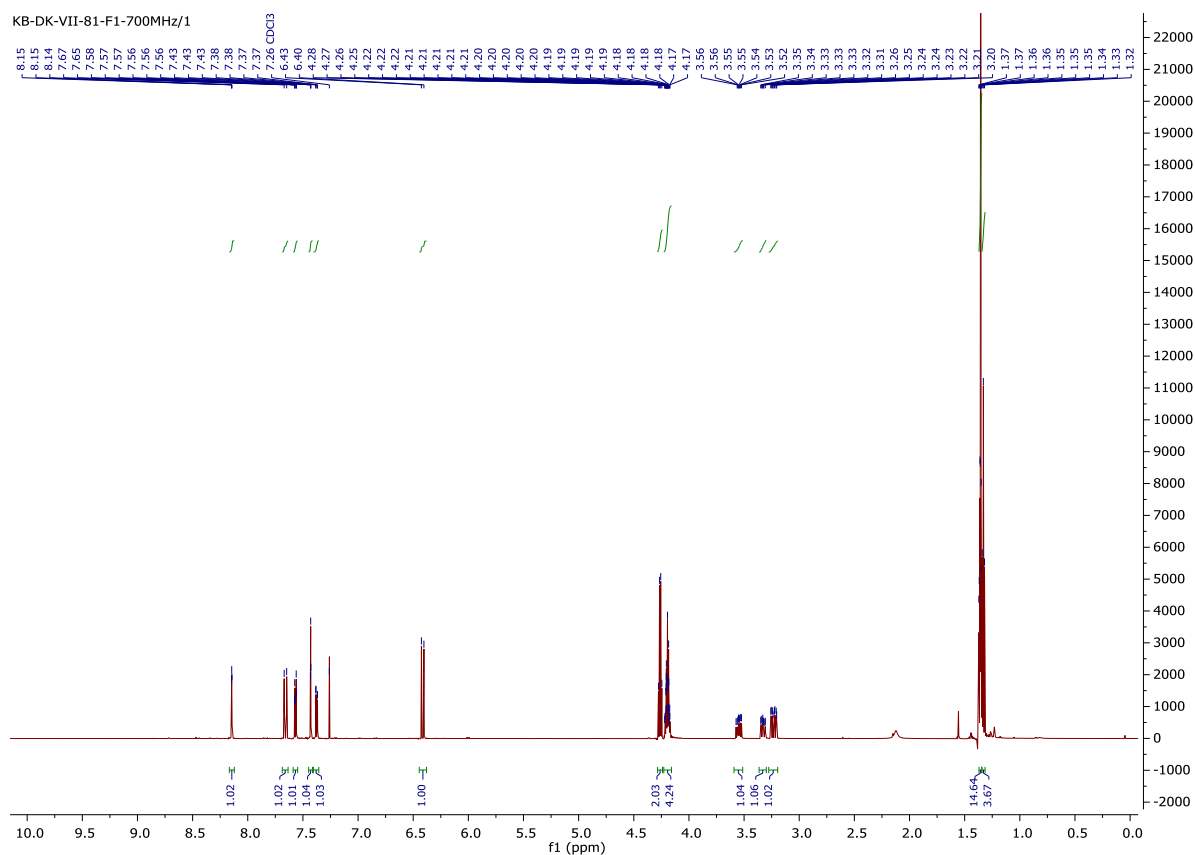


Figure S44. ^1H NMR of compound **19** (700 MHz, CDCl_3)

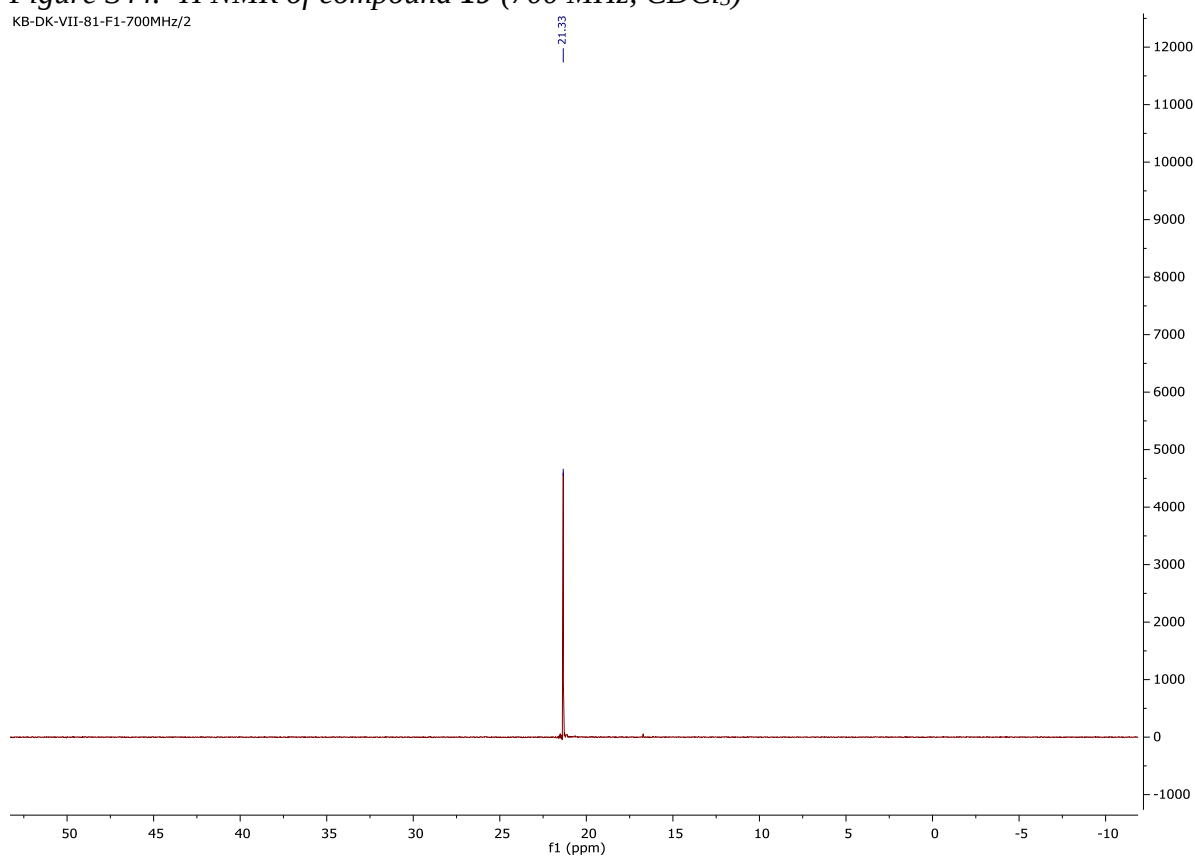


Figure S45. ^{31}P NMR of compound **19** (284 MHz, CDCl_3)

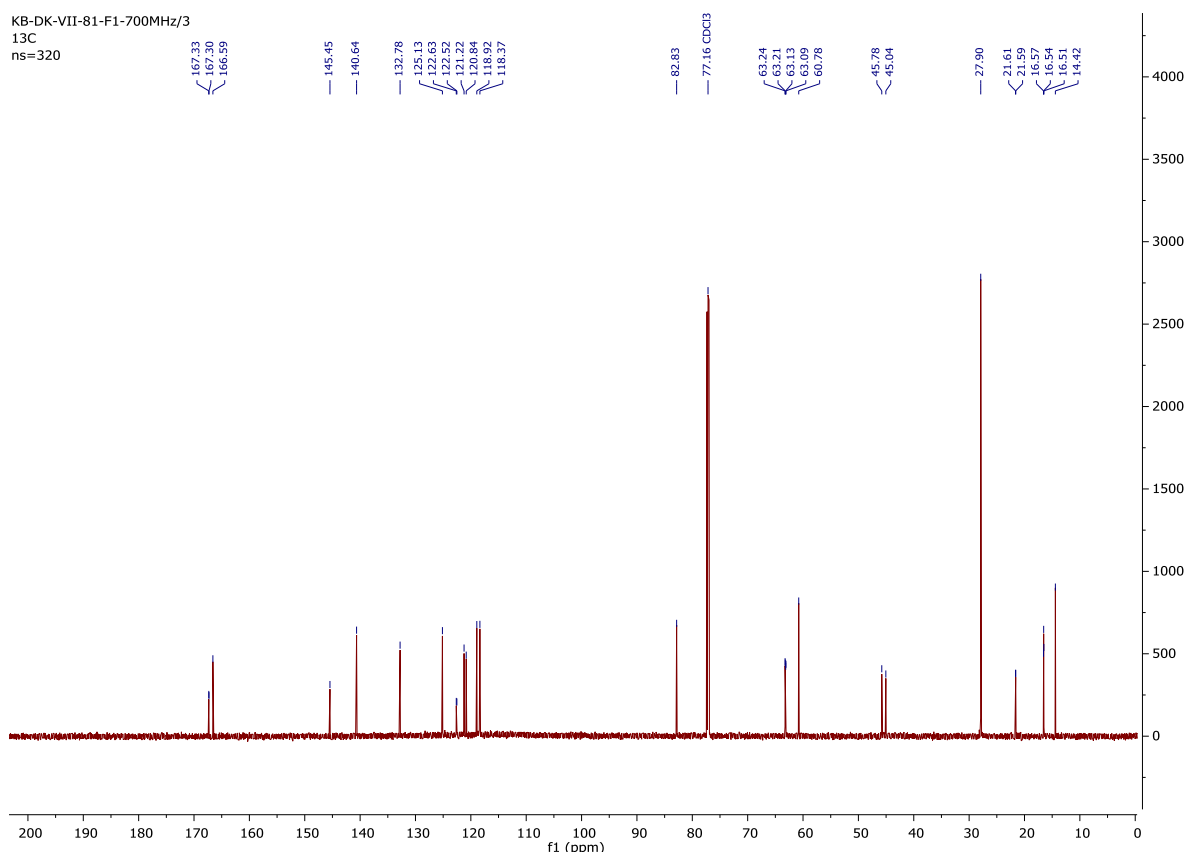
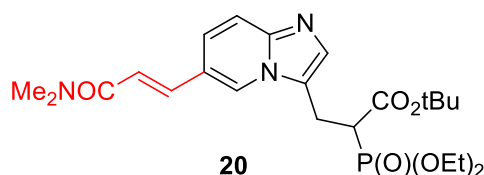


Figure S46. ^{13}C NMR of compound **19** (176 MHz, CDCl_3)



(E)-tert-Butyl 2-(diethoxyphosphoryl)-3-(6-(3-(dimethylamino)-3-oxoprop-1-en-1-yl)imidazo[1,2-a]pyridin-3-yl)propanoate (20). Yield 69%

HRMS m/z : calculated 480.2258 ($\text{C}_{23}\text{H}_{34}\text{N}_3\text{O}_6\text{P} + \text{H}$)⁺, found 480.2261 ($\text{C}_{23}\text{H}_{34}\text{N}_3\text{O}_6\text{P} + \text{H}$)⁺,

^1H NMR (700 MHz, CDCl_3) δ : 1.30-1.38 (m, $(\text{CH}_3\text{CH}_2\text{O})_2(\text{O})\text{P}$, $\text{C}(\text{CH}_3)_3$, 15H), 3.09 (s, NCH_3 , 3H), 3.20 (s, NCH_3 , 3H), 3.26 (ddd, $^2J_{\text{PH}} = 22.8$, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{HH}} = 3.1$, CH_2CHP , 1H), 3.34 (ddd, $^2J_{\text{HH}} = 16.8$, $^3J_{\text{PH}} = 9.8$, $^3J_{\text{HH}} = 3.1$, CH_2CHP , 1H), 3.57 (ddd, $^2J_{\text{HH}} = 16.8$, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{PH}} = 6.9$, CH_2CHP , 1H), 4.16 – 4.26 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 4H), 6.91 (d, $^3J_{\text{HH}} = 15.3$ Hz, $(\text{CH}_3)_2\text{NC}(\text{O})\text{CH}=\text{CH}$, 1H), 7.41 (dd, $^3J_{\text{HH}} = 9.4$ Hz, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{(7)}$, 1H), 7.44 (s, $\text{CH}_{(2)}$, 1H), 7.58 (d, $^3J_{\text{HH}} = 9.4$ Hz, $\text{CH}_{(8)}$, 1H), 7.67 (d, $^3J_{\text{HH}} = 15.3$ Hz, $(\text{CH}_3)_2\text{NC}(\text{O})\text{CH}=\text{CH}$, 1H), 8.16 (bs, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 21.40, ^{13}C NMR (176 MHz, CDCl_3) δ : 16.40-16.57 (m, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 21.61 (d, $^2J_{\text{PC}} = 3.6$ Hz, CH_2CHP , 1C), 27.85 (s, $\text{C}(\text{CH}_3)_3$, 3C), 36.03 (s, NCH_3 , 1C), 37.49 (s, NCH_3 , 1C), 45.27 (d, $^1J_{\text{PC}} = 129.1$ Hz, CH_2CHP , 1C), 63.02 (d, $^2J_{\text{PC}} = 6.9$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 63.15 (d, $^2J_{\text{PC}} = 6.4$ Hz, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 82.70 (s, $\text{C}(\text{CH}_3)_3$, 1C), 117.91 (s, $(\text{CH}_3)_2\text{NC}(\text{O})\text{CH}=\text{CH}$, 1C), 118.07 (s, $\text{CH}_{(8)}$, 1C), 121.48 (s, $\text{C}_{(6)}$, 1C), 121.54 (s, $\text{CH}_{(7)}$, 1C), 122.40 (d, $^3J_{\text{PC}} = 19.0$ Hz, $\text{C}_{(3)}$, 1C), 124.39 (s, $\text{CH}_{(5)}$, 1C), 132.51 (s, $\text{CH}_{(2)}$, 1C), 138.43 (s, $(\text{CH}_3)_2\text{NC}(\text{O})\text{CH}=\text{CH}$, 1C), 145.32 (s, $\text{C}_{(9)}$, 1C), 166.19 (s, $\text{N}(\text{O})\text{CH}=\text{CH}$, 1C), 167.25 (d, $^2J_{\text{PC}} = 5.1$ Hz, $\text{CO}_2t\text{-Bu}$, 1C).

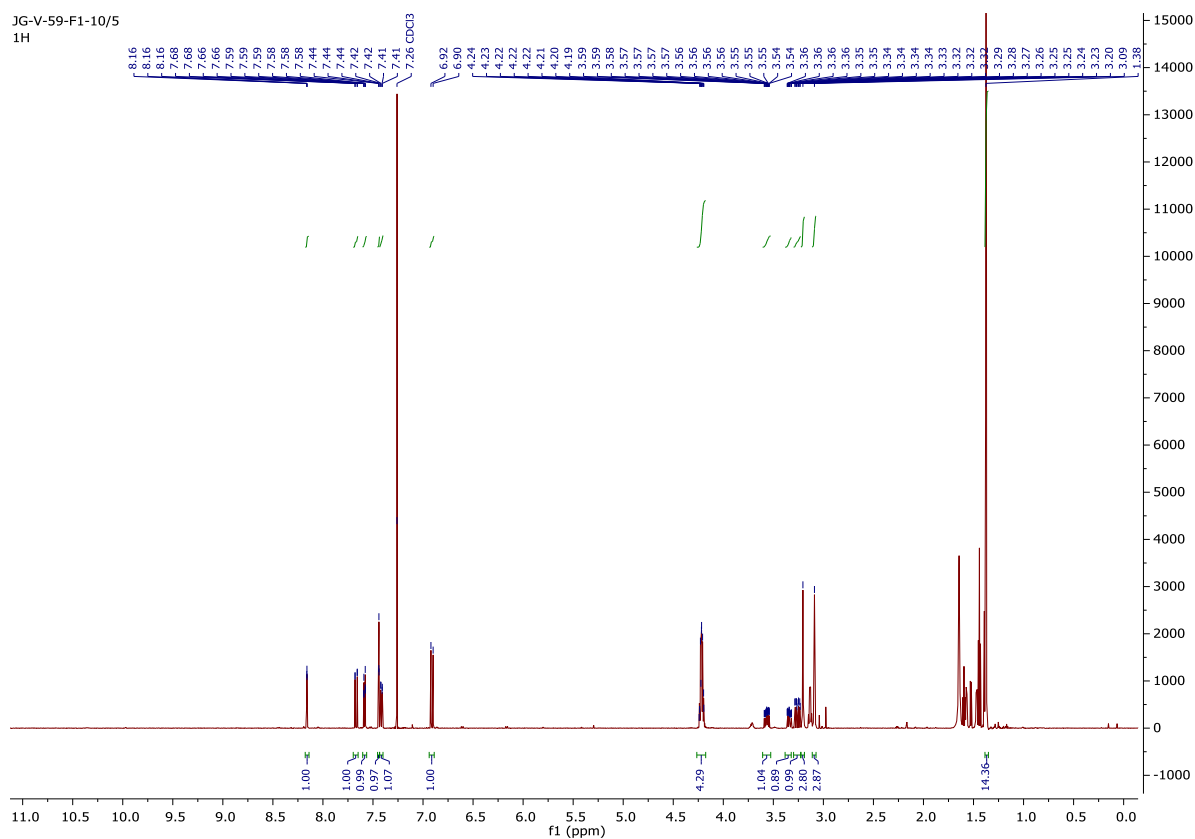


Figure S47. ¹H NMR of compound **20** (700 MHz, CDCl₃)

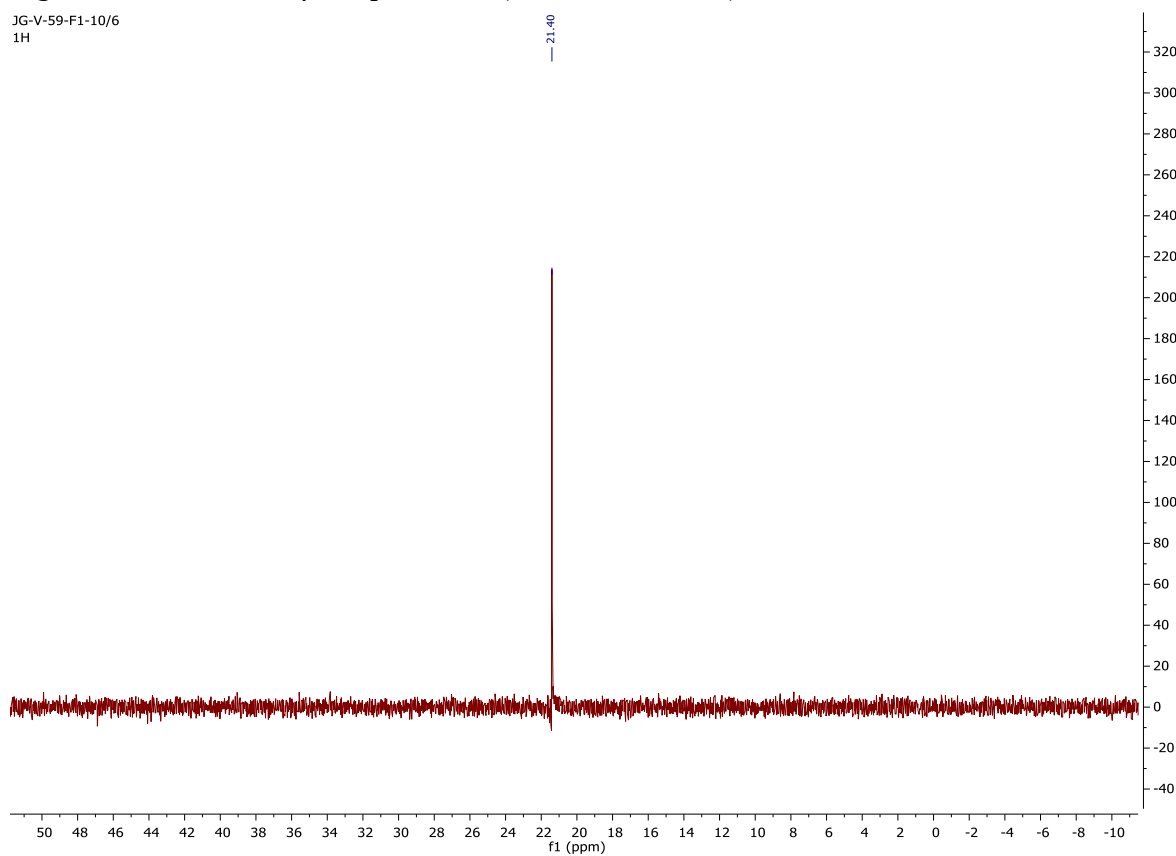


Figure S48. ³¹P NMR of compound **20** (283 MHz, CDCl₃)

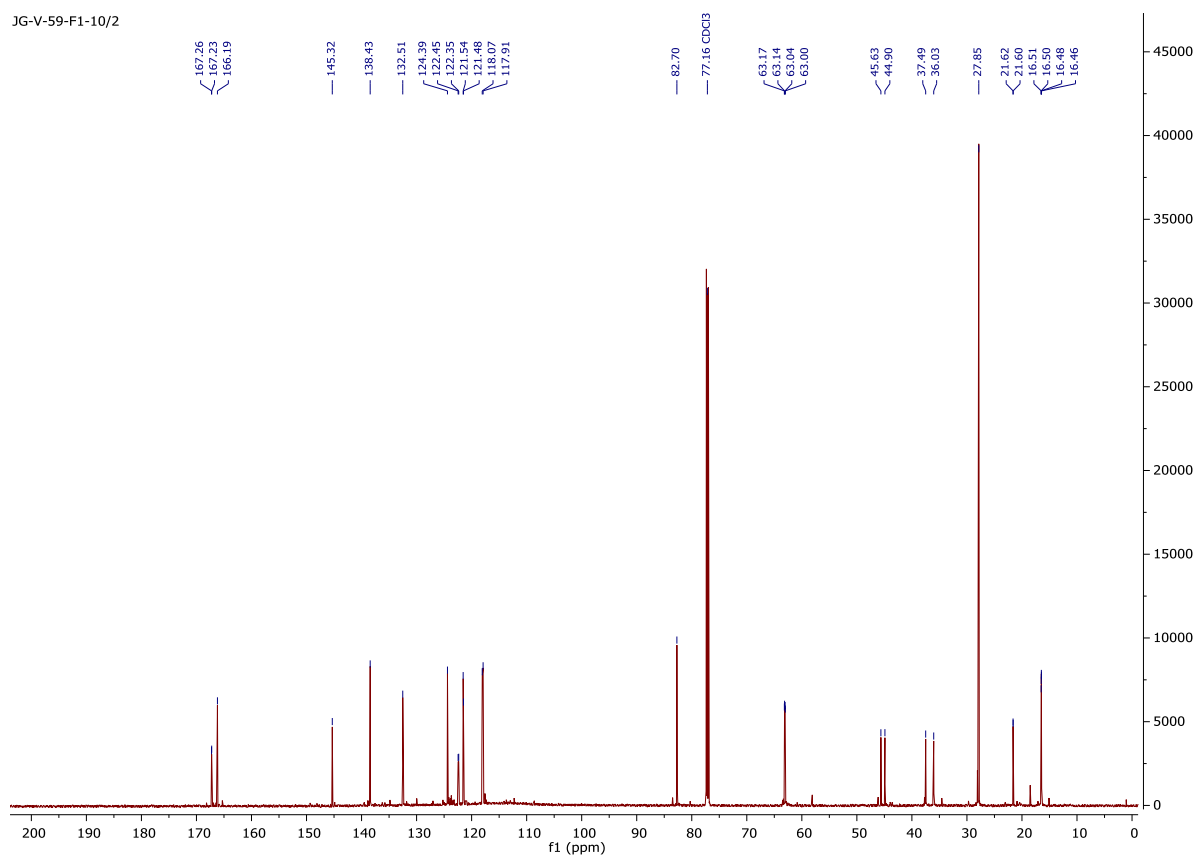
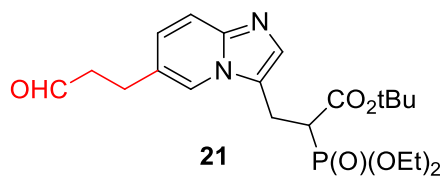


Figure S49. ¹³C NMR of compound **20** (176 MHz, CDCl₃)



tert-Butyl 2-(diethoxyphosphoryl)-3-(6-(3-oxopropyl)imidazo[1,2-a]pyridin-3-yl)propanoate (21). Yield 60%.

HRMS *m/z*: calculated 439.1992 (C₂₁H₃₁N₂O₆P + H)⁺, found 439.2006 (C₂₁H₃₁N₂O₆P + H)⁺, ¹H NMR (700 MHz, CDCl₃) δ: 1.25-1.42 (m, C(CH₃)₃, (CH₃CH₂O)₂P, 15H), 2.76-2.90 (m, CHOCH₂CH₂, 2H), 2.94-3.04 (m, CHOCH₂CH₂, 2H), 3.12-3.41 (m, CH₂CHP, CH₂CHP, 2H), 3.44-3.65 (m, CH₂CHP, 1H), 4.08 – 4.29 (m, (CH₃CH₂O)₂P, 4H), 7.19 (dd, ³J_{HH} = 9.3 Hz, ⁴J_{HH} = 1.7 Hz, CH₍₇₎, 1H), 7.43 (s, CH₍₂₎, 1H), 7.71 (d, ³J_{HH} = 9.3 Hz, ⁵J_{HH} = 0.9 Hz CH₍₈₎, 1H), 7.97 (bs, CH₍₅₎, 1H), 9.82 (t, ³J_{HH} = 0.9 Hz, CHO, 1H), ³¹P NMR (283 MHz, CDCl₃) δ: 21.87

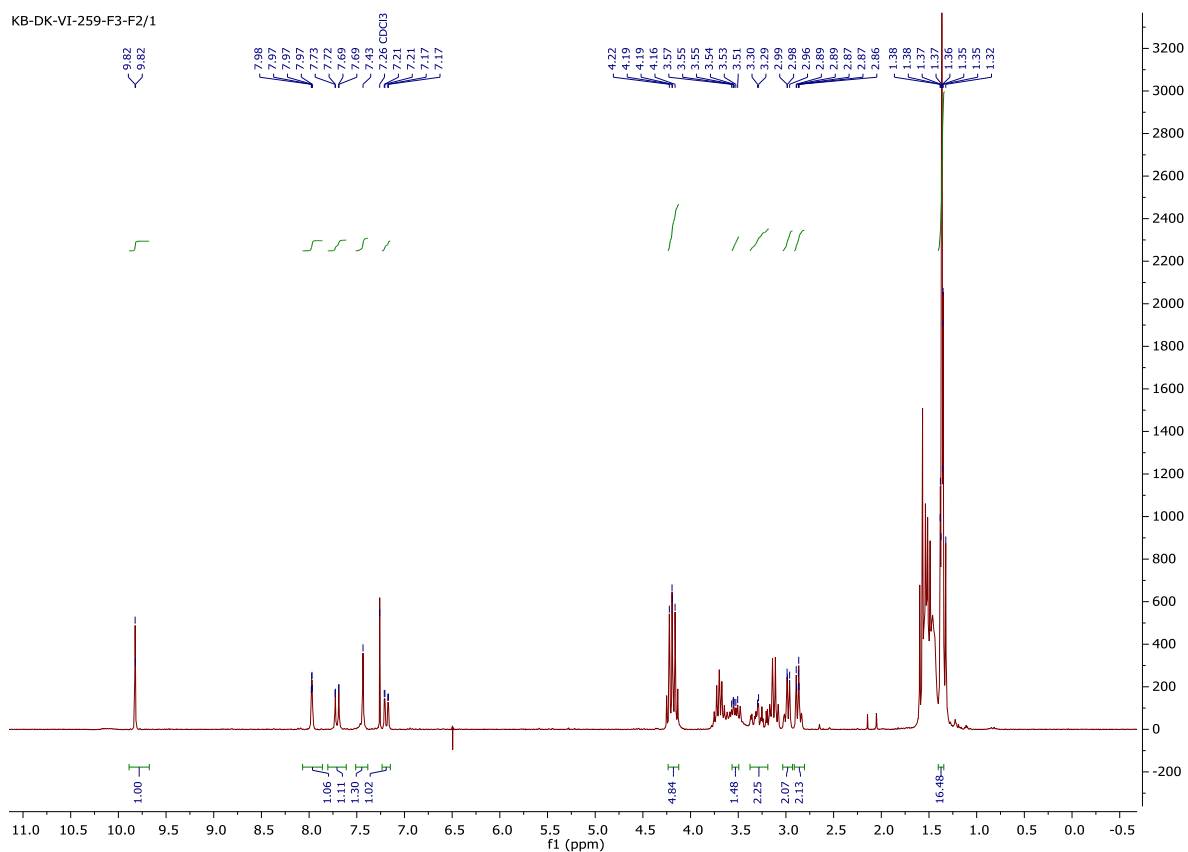


Figure S50. ^1H NMR of compound **21** (residual DIPEA $\times$ HBr at 1.5, 3.1, 3.6 ppm) (700 MHz, CDCl_3)

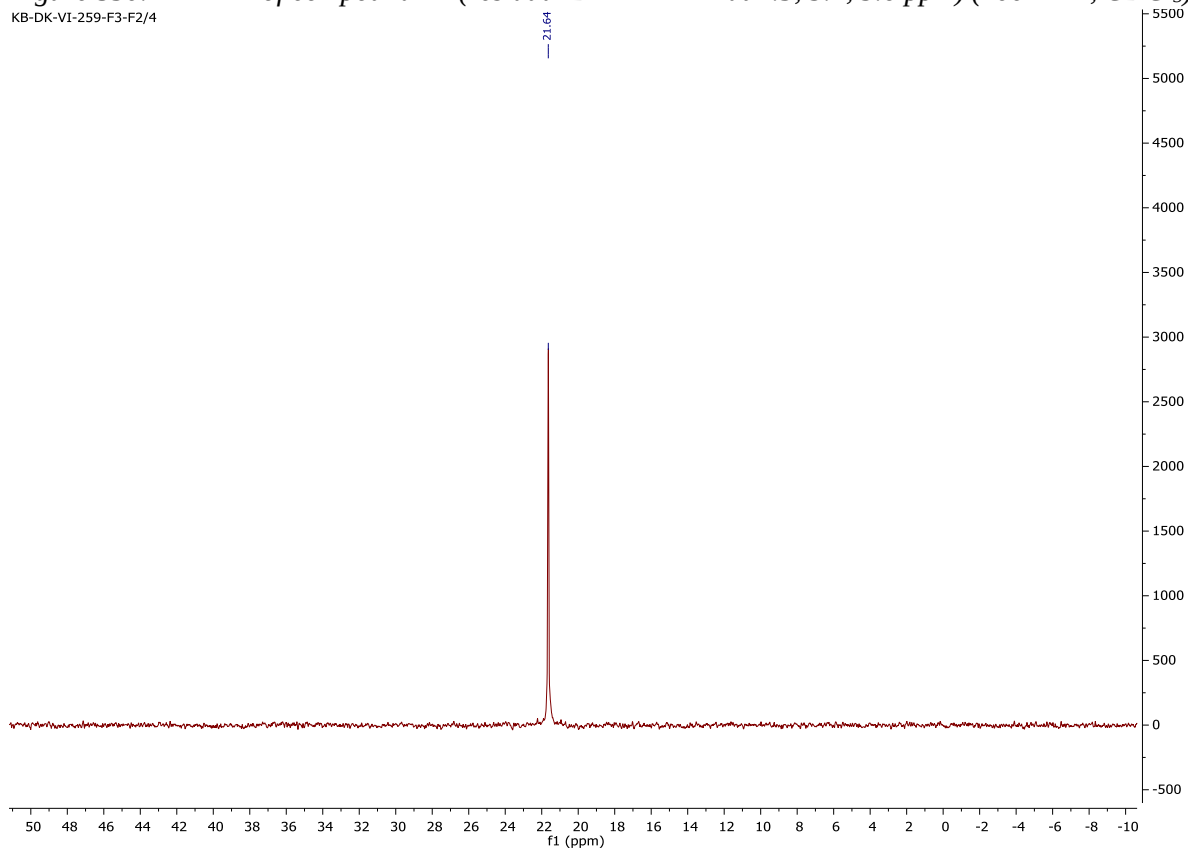
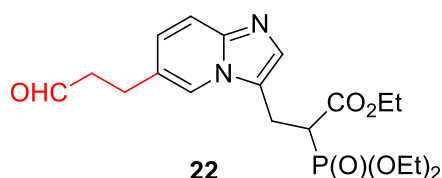


Figure S51. ^{31}P NMR of compound **21** (283 MHz, CDCl_3)



Ethyl 2-(diethoxyphosphoryl)-3-(6-(3-oxopropyl)imidazo[1,2-a]pyridin-3-yl)propanoate (22). Yield 41%.

¹H NMR (700 MHz, CDCl₃) δ : 1.17 (t, $^3J_{HH} = 7.1$ Hz, CH₃CH₂OC, 3H), 1.33 (t, $^3J_{HH} = 7.1$ Hz, (CH₃CH₂O)₂P, 3H), 1.34 (t, $^3J_{HH} = 7.1$ Hz, (CH₃CH₂O)₂P, 6H), 2.84 (t, CHOCH₂CH₂, $^3J_{HH} = 7.2$ Hz, 2H), 2.96 (t, CHOCH₂CH₂, $^3J_{HH} = 7.2$ Hz, 2H), 3.27-3.36 (m, CH₂CHP, CH₂CHP, 2H), 3.56 (ddd, $^2J_{HH} = 16.5$, $^3J_{HH} = 11.6$, $^3J_{PH} = 7.2$, CH₂CHP, 1H), 4.00 – 4.20 (m, (CH₃CH₂O)₂P, CH₃CH₂OC, 6H), 7.11 (dd, $^3J_{HH} = 9.1$ Hz, $^4J_{HH} = 1.6$ Hz, CH₍₇₎, 1H), 7.39 (s, CH₍₂₎, 1H), 7.60 (d, $^3J_{HH} = 9.1$ Hz, CH₍₈₎, 1H), 7.91 (bs, CH₍₅₎, 1H), 9.81 (bs, CHO, 1H), **³¹P NMR** (283 MHz, CDCl₃) δ : 20.72, **¹³C NMR** (176 MHz, CDCl₃) δ : 14.05 (s, CH₃CH₂OC, 1C), 16.41 (d, $^3J_{PC} = 6.1$ Hz, CH₃CH₂OP, 1C), 16.45 (d, $^3J_{PC} = 5.7$ Hz, CH₃CH₂OP, 1C), 21.53 (d, $^2J_{PC} = 3.7$ Hz, CH₂CHP, 1C), 25.06 (s, CHOCH₂CH₂, 1C), 44.22 (d, $^1J_{PC} = 129.5$ Hz, CH₂CHP, 1C), 44.48 (s, CHOCH₂CH₂, 1C), 62.02 (s, CH₃CH₂OC, 1C), 63.27 (d, $^2J_{PC} = 7.0$ Hz, CH₃CH₂OP, 1C), 63.35 (d, $^2J_{PC} = 6.3$ Hz, CH₃CH₂OP, 1C), 117.21 (s, CH₍₈₎, 1C), 121.45 (d, $^3J_{PC} = 18.2$ Hz, C₍₃₎, 1C), 121.47 (s, CH₍₅₎, 1C), 125.77 (s, C₍₆₎, 1C), 126.94 (s, CH₍₇₎, 1C), 130.03 (s, CH₍₂₎, 1C), 143.93 (s, C₍₉₎, 1C), 168.17 (d, $^2J_{PC} = 5.1$ Hz, CO₂Et, 1C), 200.45 (s, CHO, 1C).

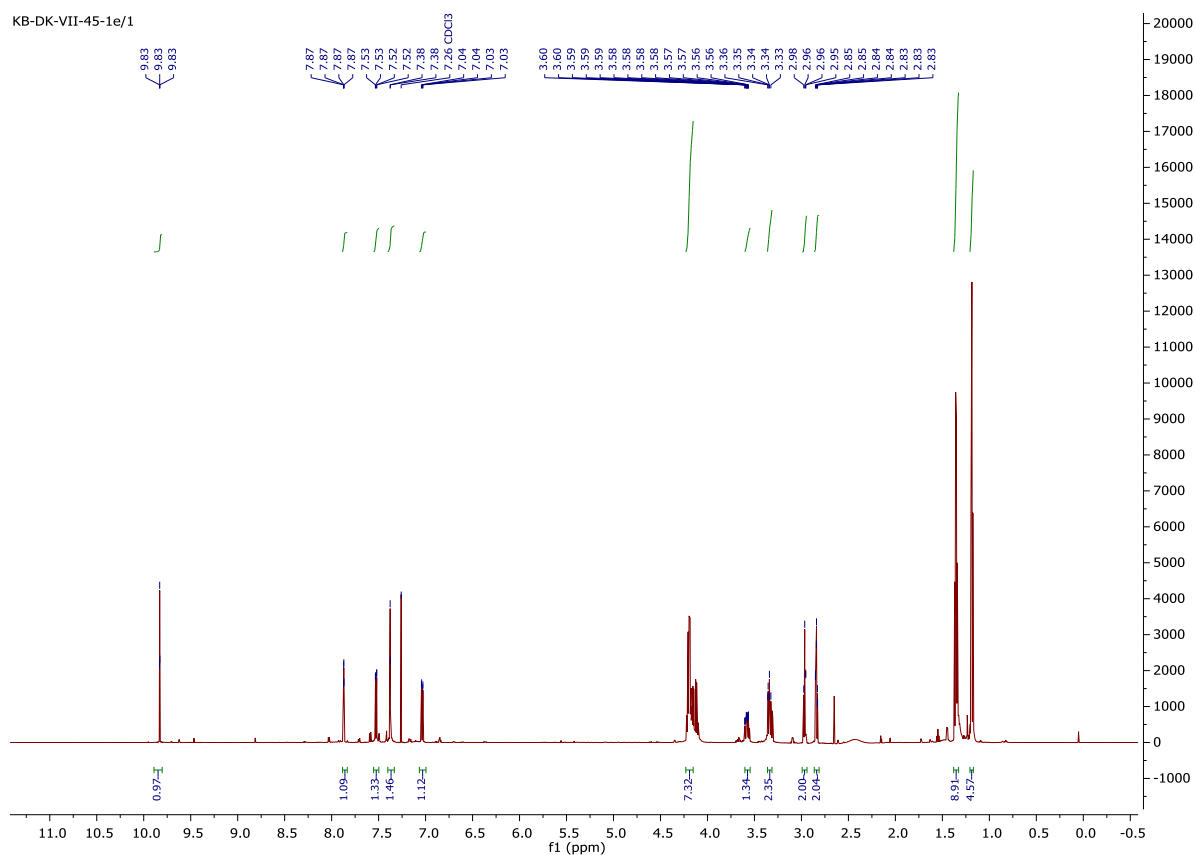


Figure S52. ^1H NMR of compound **22** (700 MHz, CDCl_3)

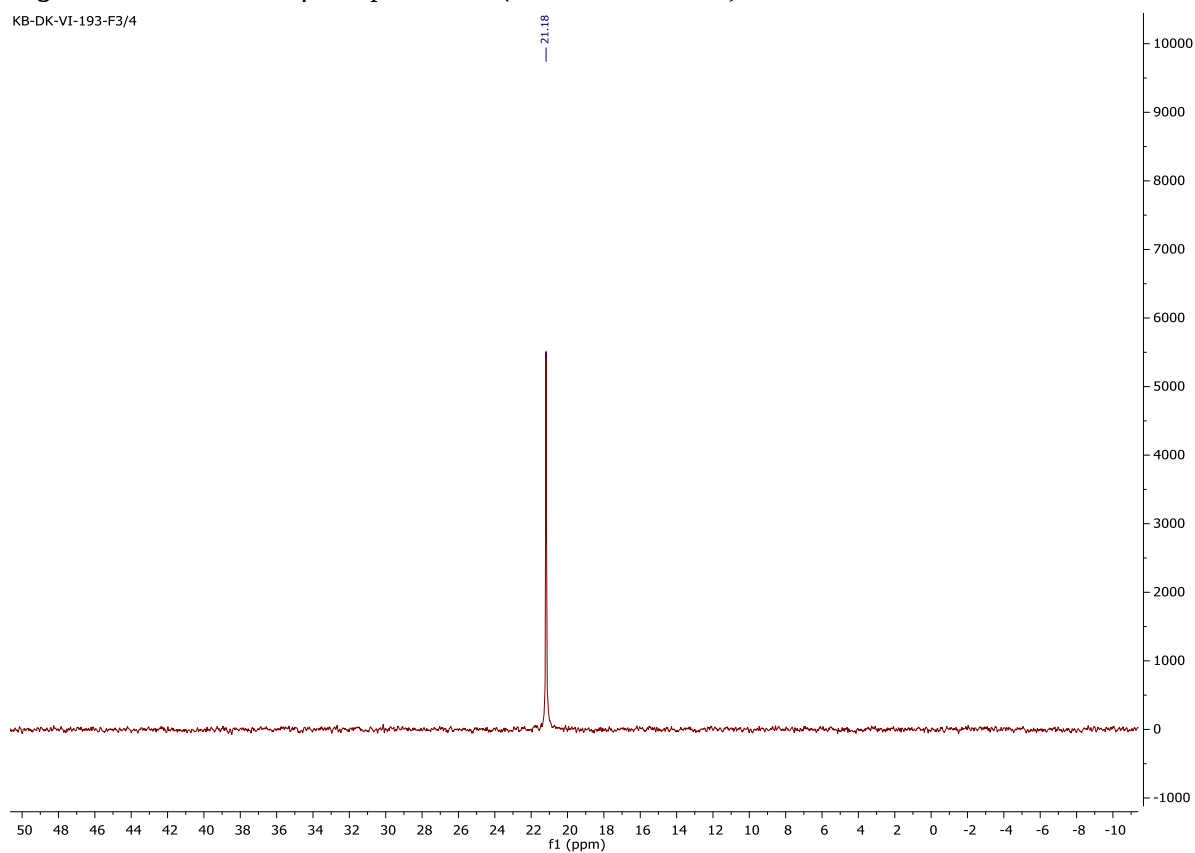


Figure S53. ^{31}P NMR of compound **22** (283 MHz, CDCl_3)

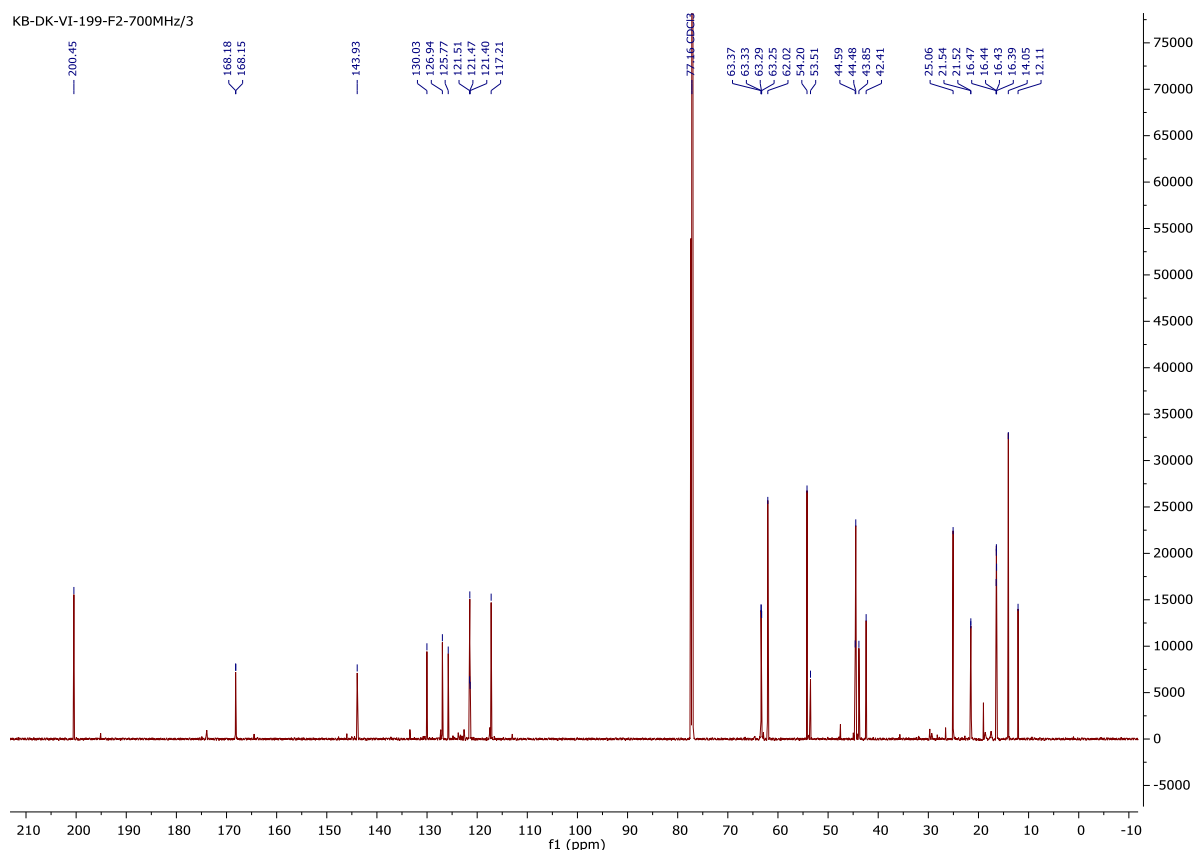
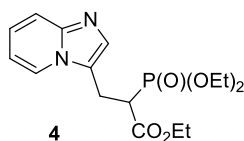


Figure S54. ^{13}C NMR of compound **22** (176 MHz, CDCl_3)



Ethyl 2-(diethoxyphosphoryl)-3-(imidazo[1,2-*a*]pyridin-3-yl)propanoate (**4**).

HRMS m/z : calculated 355.1417 ($\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_5\text{P} + \text{H}$)⁺, found 355.1428 ($\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_5\text{P} + \text{H}$)⁺, ^1H NMR (700 MHz, CDCl_3) δ : 1.17 (t, $^3J_{\text{HH}} = 7.1$ Hz, $\text{CH}_3\text{CH}_2\text{OC}$, 3H), 1.36 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, 6H), 3.22-3.47 (m, CH_2CHP , CH_2CHP , 2H), 3.53-3.73 (m, CH_2CHP , 1H), 4.04 – 4.30 (m, $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$, $\text{CH}_3\text{CH}_2\text{OC}$, 6H), 6.86 (td, $^3J_{\text{HH}} = 6.8$ Hz, $^4J_{\text{HH}} = 1.2$ Hz, $\text{CH}_{(6)}$, 1H), 7.18 (ddd, $^3J_{\text{HH}} = 9.1$ Hz, $^3J_{\text{HH}} = 6.8$ Hz, $^4J_{\text{HH}} = 1.2$ Hz, $\text{CH}_{(7)}$, 1H), 7.43 (s, $\text{CH}_{(2)}$, 1H), 7.60 (dt, $^3J_{\text{HH}} = 9.1$ Hz, $^4J_{\text{HH}} = 1.2$ Hz, $\text{CH}_{(8)}$, 1H), 8.04 (dt, $^3J_{\text{HH}} = 6.8$ Hz, $^4J_{\text{HH}} = 1.2$ Hz, $\text{CH}_{(5)}$, 1H), ^{31}P NMR (283 MHz, CDCl_3) δ : 21.29.

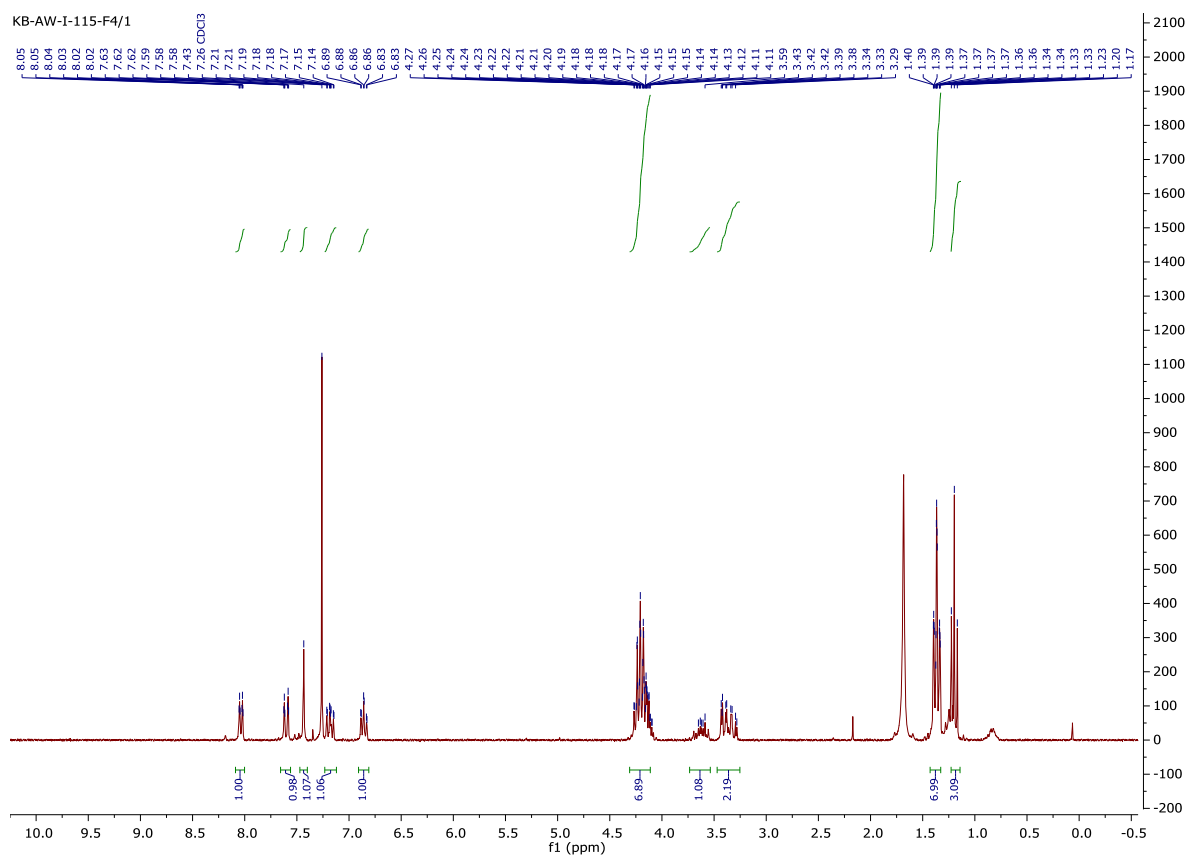


Figure S55. ^1H NMR of compound **4** (700 MHz, CDCl_3)

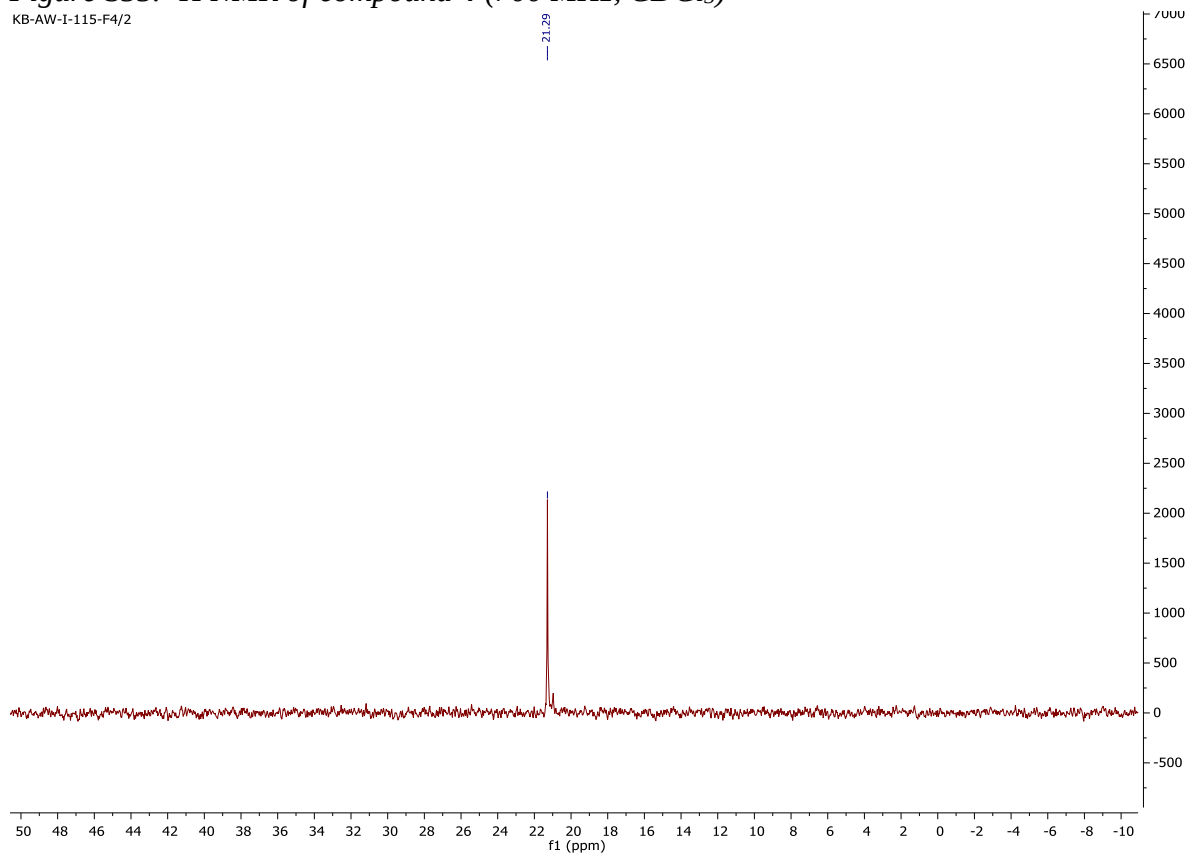
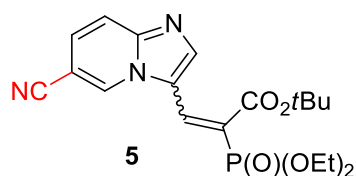


Figure S56. ^{31}P NMR of compound **4** (283 MHz, CDCl_3)



(E)-tert-Butyl 3-(6-cyanoimidazo[1,2-a]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (5).

HRMS m/z : calculated 406.1526 ($C_{19}H_{24}N_3O_5P + H$)⁺, found 406.1528 ($C_{19}H_{24}N_3O_5P + H$)⁺, ¹H NMR (700 MHz, CDCl₃) δ : 1.38 (t, ³J_{HH} = 7.1 Hz, CH₃CH₂OP, 6H), 1.57 (s, C(CH₃)₃, 9H), 4.12 – 4.24 (m, CH₃CH₂OP, 4H), 7.45 (dd, ³J_{HH} = 9.3 Hz, ⁴J_{HH} = 1.6 Hz, CH₍₇₎, 1H), 7.76 (d, ³J_{HH} = 23.7 Hz, CH=CP, 1H), 7.78 (dd, ³J_{HH} = 9.2 Hz, ⁴J_{HH} = 1.0 Hz, CH₍₈₎, 1H), 8.51 (s, CH₍₂₎, 1H), 8.74 (bs, CH₍₅₎, 1H), ³¹P NMR (283 MHz, CDCl₃) δ : 14.93 – (E) CH=CP, ¹³C NMR (176 MHz, CDCl₃) δ : 16.48 (d, ⁴J_{PC} = 6.8 Hz, CH₃CH₂OP, 2C), 28.18 (s, C(CH₃)₃, 3C), 62.86 (d, ³J_{CP} = 5.2 Hz, CH₃CH₂OP, 2C), 83.41 (s, C(CH₃)₃, 1C), 100.64 (s, C₍₆₎, 1C), 115.92 (s, CN, 1C), 119.62 (s, CH₍₈₎, 1C), 121.47 (d, ³J_{PC} = 25.0 Hz, C₍₃₎, 1C), 122.72 (d, ¹J_{PC} = 180.2 Hz, CP, 1C), 126.49 (s, CH₍₇₎, 1C), 129.92 (s, CH₍₅₎, 1C), 130.62 (d, ²J_{PC} = 10.0 Hz, CH=CP, 1C), 141.62 (s, CH₍₂₎, 1C), 146.61 (s, C₍₉₎, 1C), 164.67 (d, ²J_{PC} = 10.4 Hz, CO₂t-Bu, 1C).

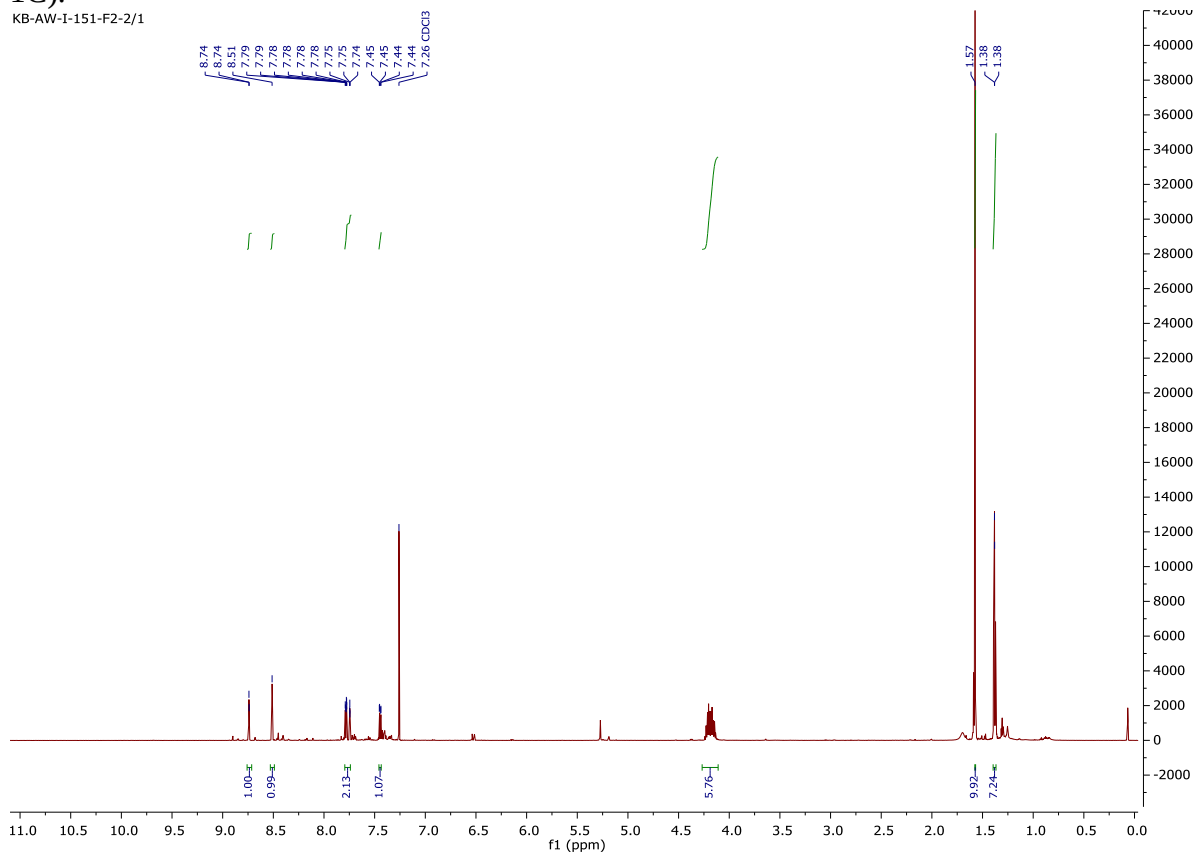


Figure S57. ¹H NMR of compound 5 (700 MHz, CDCl₃)

KB-AW-I-151-F2-2/2

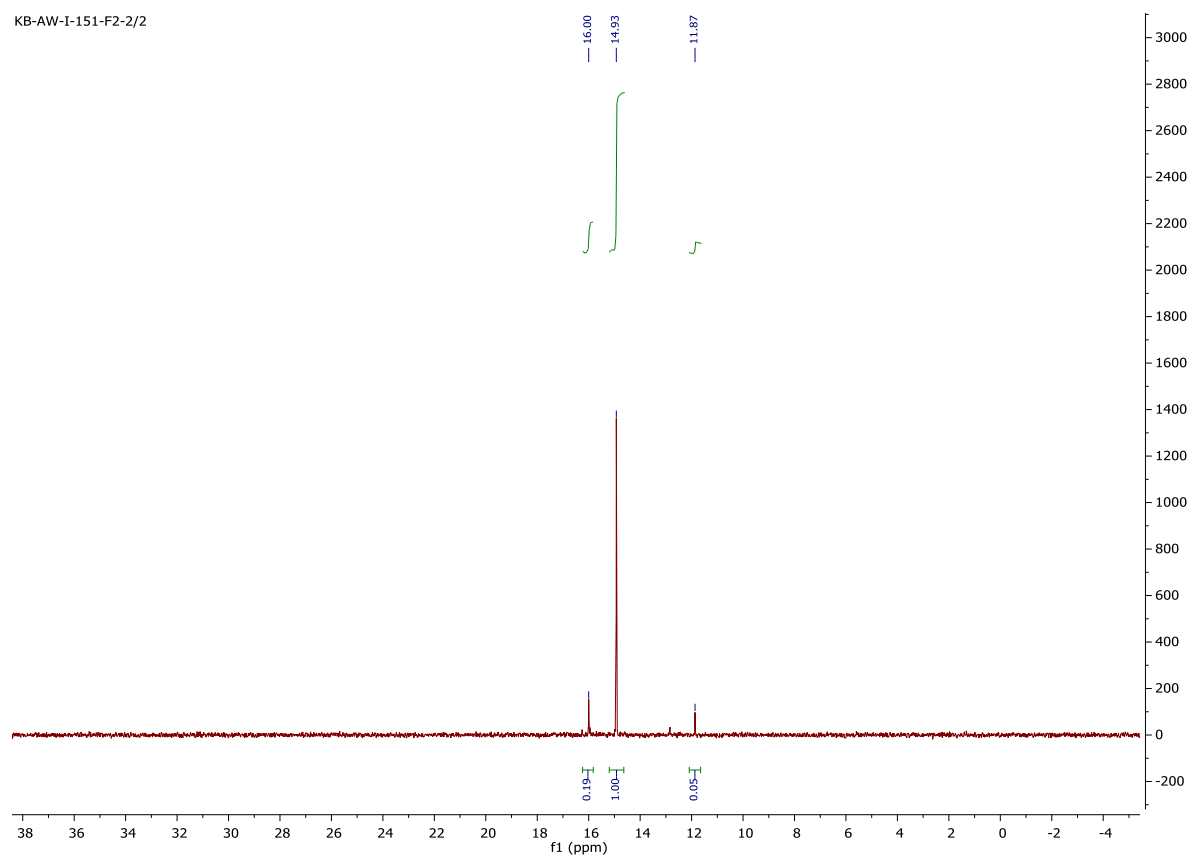


Figure S58. ^{31}P NMR of compound 5 (283 MHz, CDCl_3)

KB-AW-I-151-F2-2/3

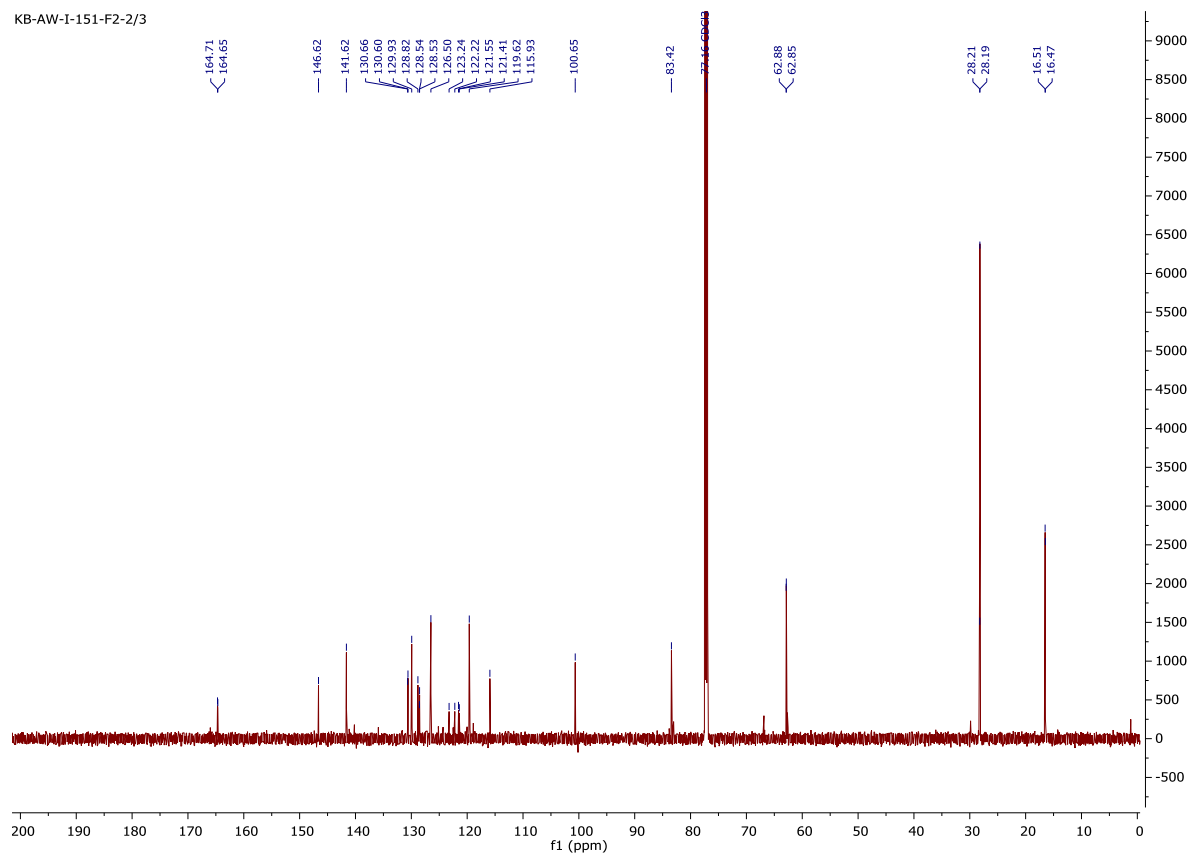


Figure S59. ^{13}C NMR of compound 5 (176 MHz, CDCl_3)

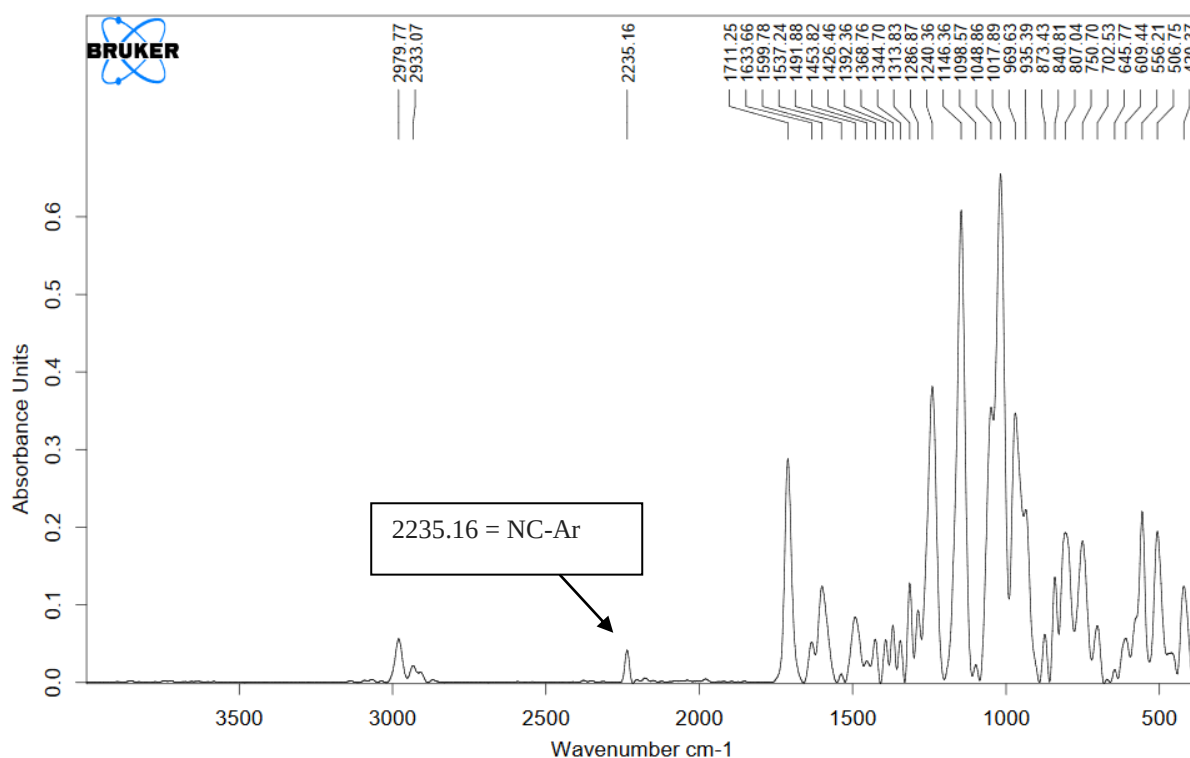
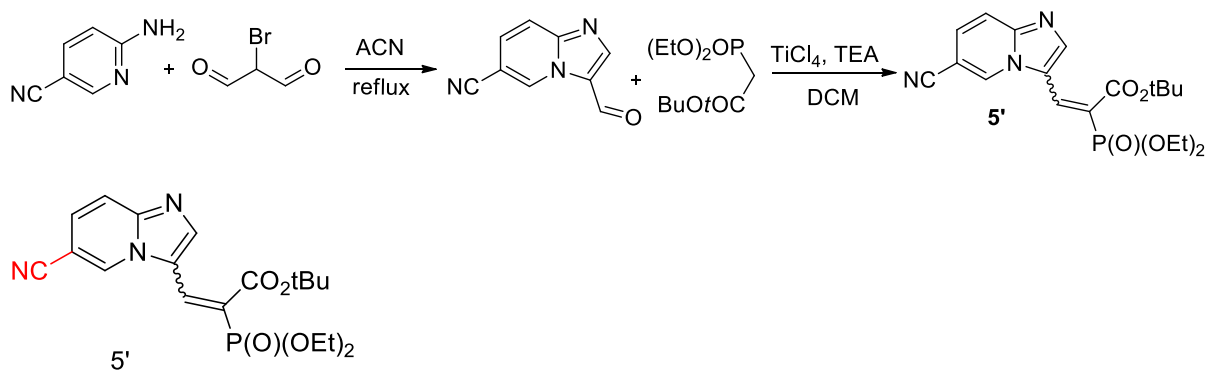


Figure S60. Infrared spectroscopy of **5**

Side product **5** obtained via different synthetic route [1]



(E)-tert-Butyl 3-(6-cyanoimidazo[1,2-a]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (5'**)**

¹H NMR (700 MHz, CDCl₃) δ: 1.30 (t, ³J_{HH} = 7.1 Hz, CH₃CH₂OP, 6H), 1.50 (s, C(CH₃)₃, 9H), 4.03 – 4.16 (m, CH₃CH₂OP, 4H), 7.39 (dd, ³J_{HH} = 9.2 Hz, ⁴J_{HH} = 1.6 Hz, CH₍₇₎, 1H), 7.69-7.75 (m, CH=CP, CH₍₈₎, 2H), 8.42 (s, CH₍₂₎, 1H), 8.76 (bs, CH₍₅₎, 1H), ³¹P NMR (283 MHz, CDCl₃) δ: 14.82 – (E) CH=CP, ¹³C NMR (176 MHz, CDCl₃) δ: 16.26 (d, ⁴J_{PC} = 6.8 Hz, CH₃CH₂OP, 2C), 27.96 (s, C(CH₃)₃, 3C), 62.62 (d, ³J_{CP} = 5.2 Hz, CH₃CH₂OP, 2C), 83.13 (s, C(CH₃)₃, 1C), 100.33 (s, C₍₆₎, 1C), 115.79 (s, CN, 1C), 119.31 (s, CH₍₈₎, 1C), 121.31 (d, ³J_{PC} = 25.0 Hz, C₍₃₎, 1C), 122.41 (d, ¹J_{PC} = 180.6 Hz, CP, 1C), 126.35 (s, CH₍₇₎, 1C), 130.02

(s, $\underline{\text{CH}}_{(5)}$, 1C), 130.47 (d, $^2J_{PC} = 10.0$ Hz, $\underline{\text{CH}}=\text{CP}$, 1C), 141.28 (s, $\underline{\text{CH}}_{(2)}$, 1C), 146.40 (s, $\text{C}_{(9)}$, 1C), 164.51 (d, $^2J_{PC} = 10.4$ Hz, $\underline{\text{CO}}_2t\text{-Bu}$, 1C).

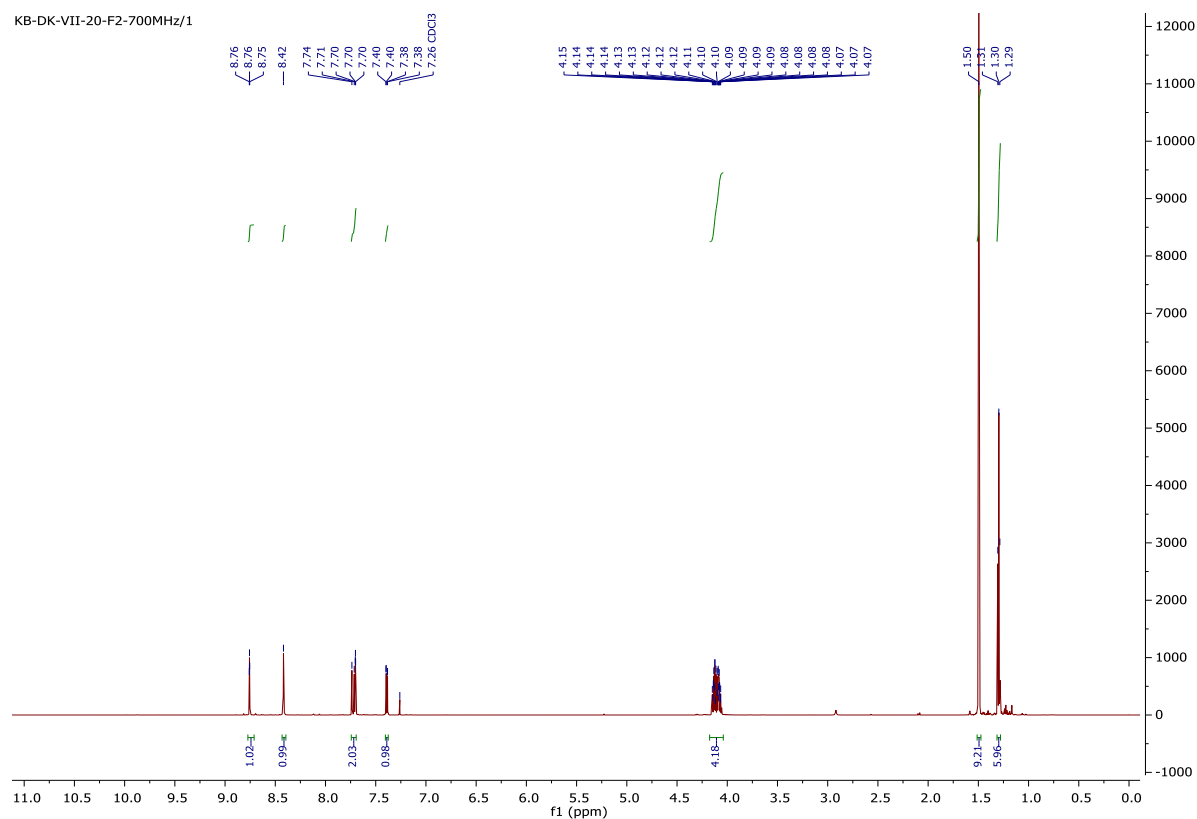


Figure S61. ^1H NMR of compound **5'** (700 MHz, CDCl_3)

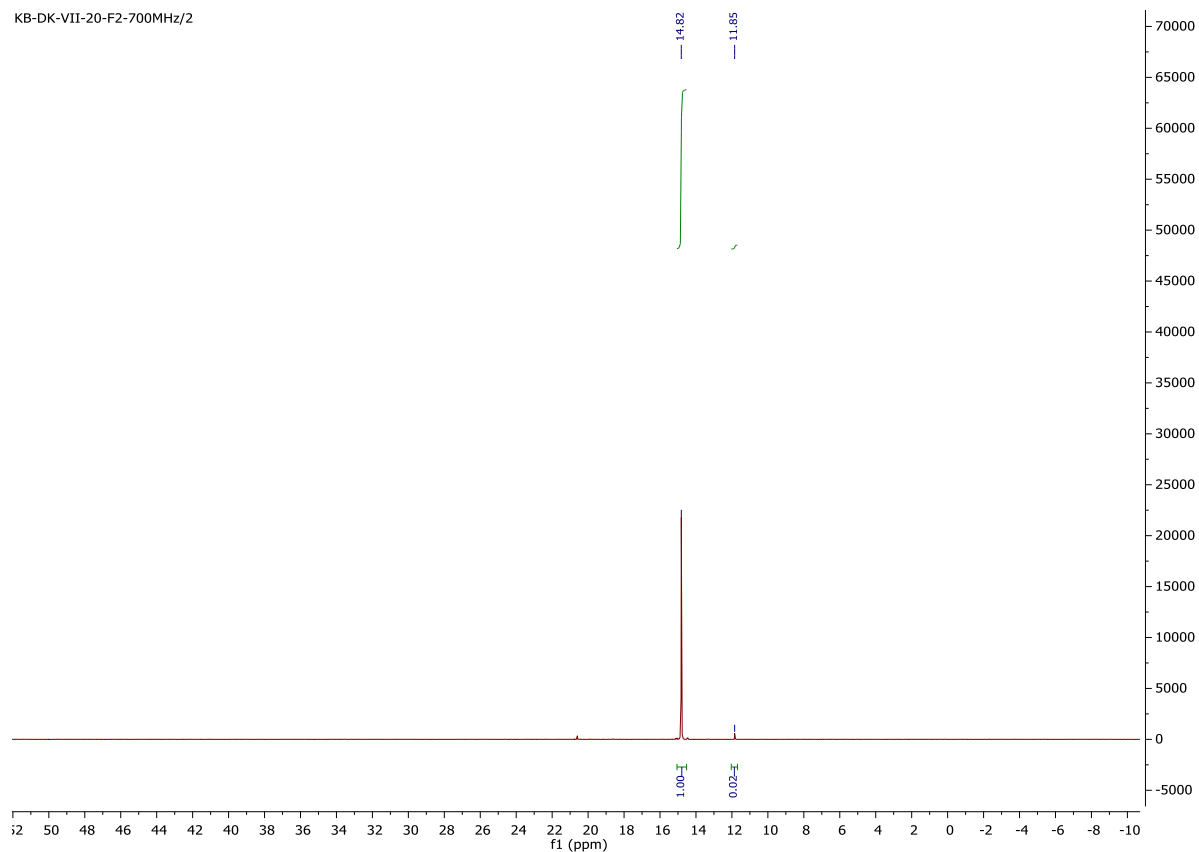


Figure S62. ^{31}P NMR of compound **5'** (283 MHz, CDCl_3)

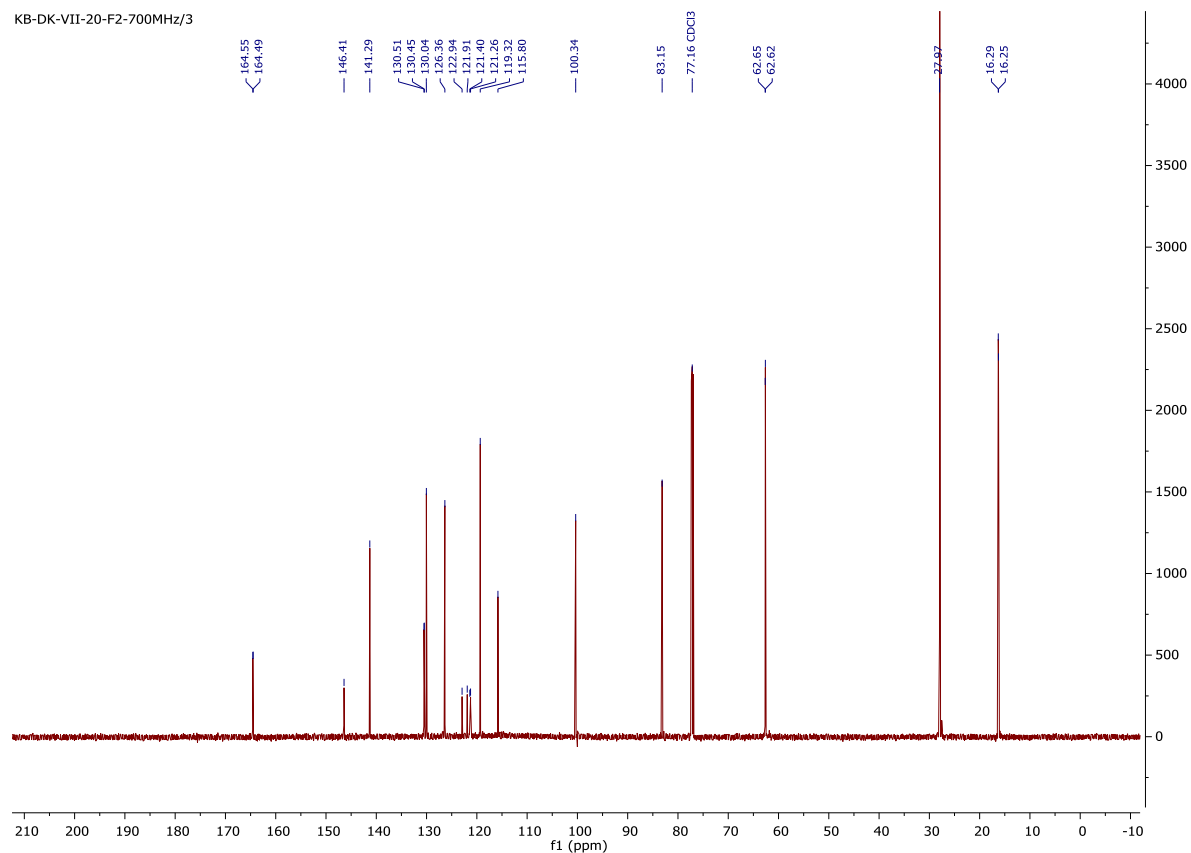


Figure S63. ^{13}C NMR of compound **5'** (176 MHz, CDCl_3)

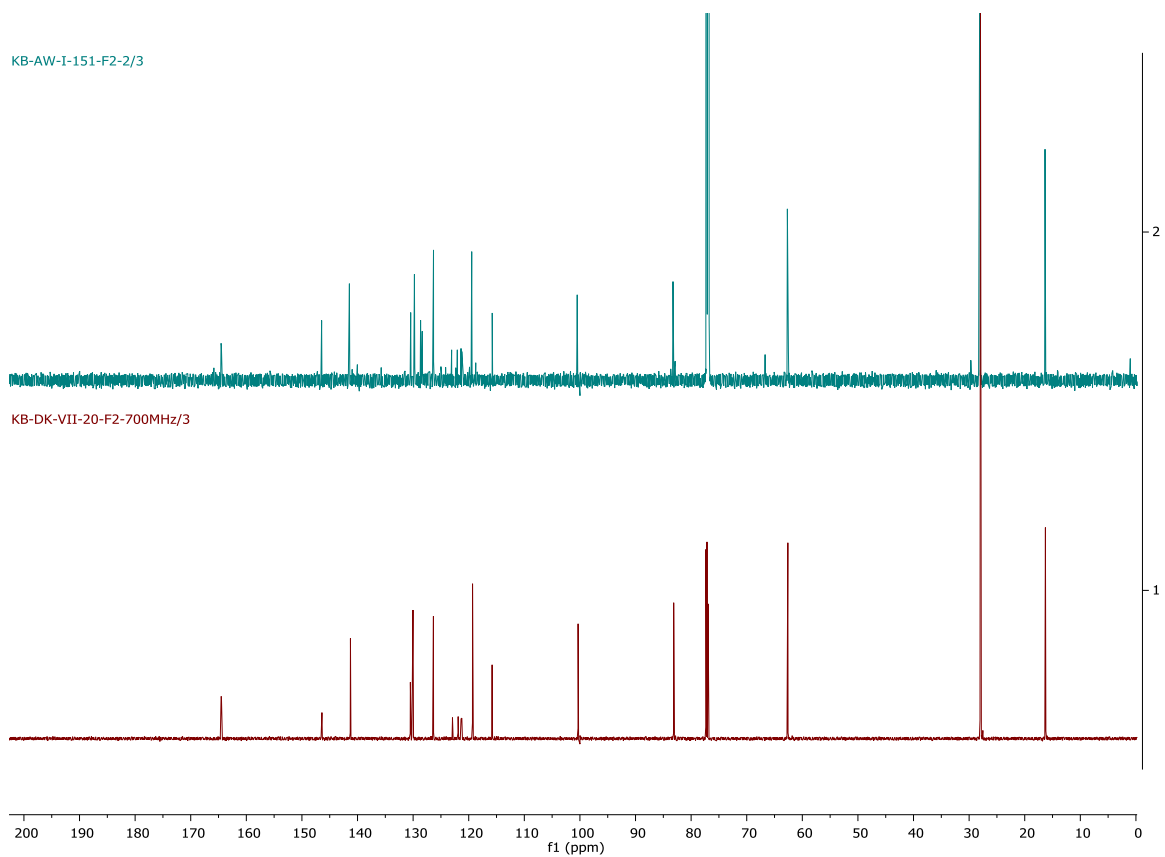


Figure S64. Comparing the ^{13}C NMR spectra of compounds 5 (blue) and 5' (red)

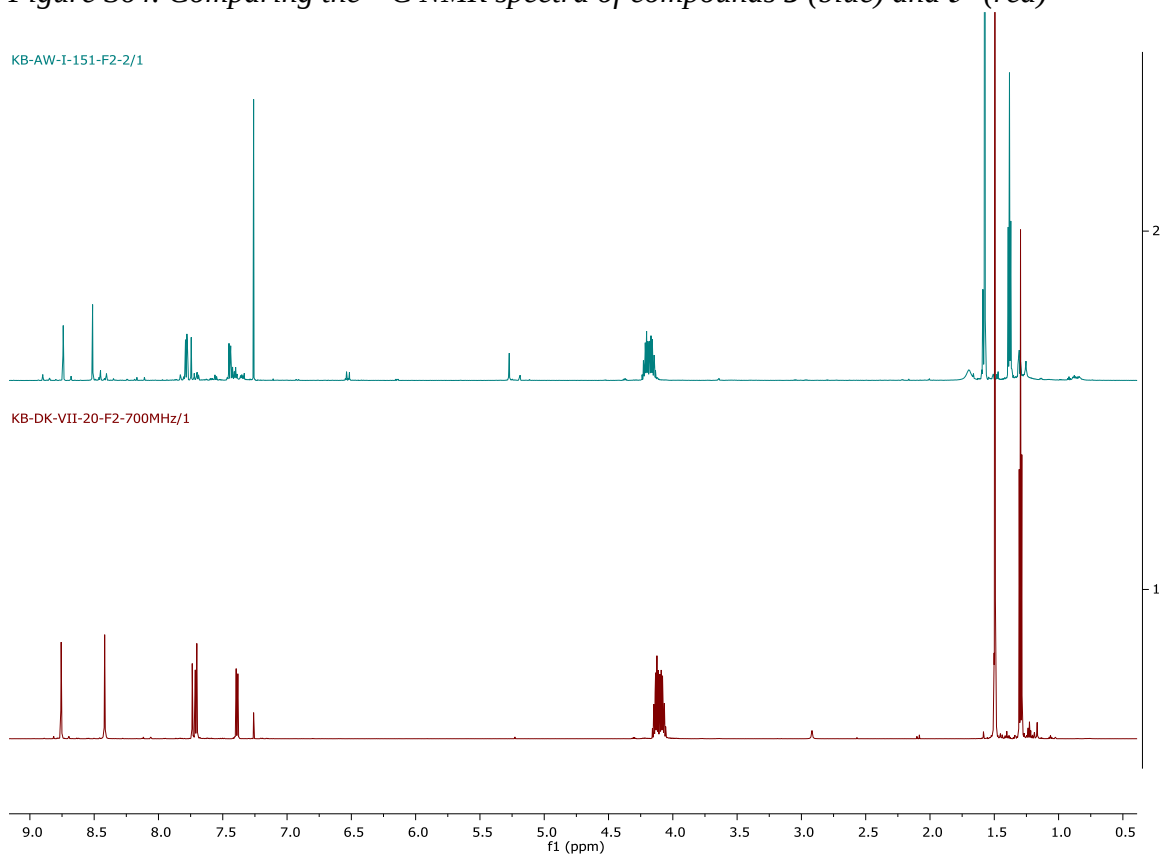


Figure S65. Comparing the ^1H NMR spectra of compounds 5 (blue) and 5' (red)

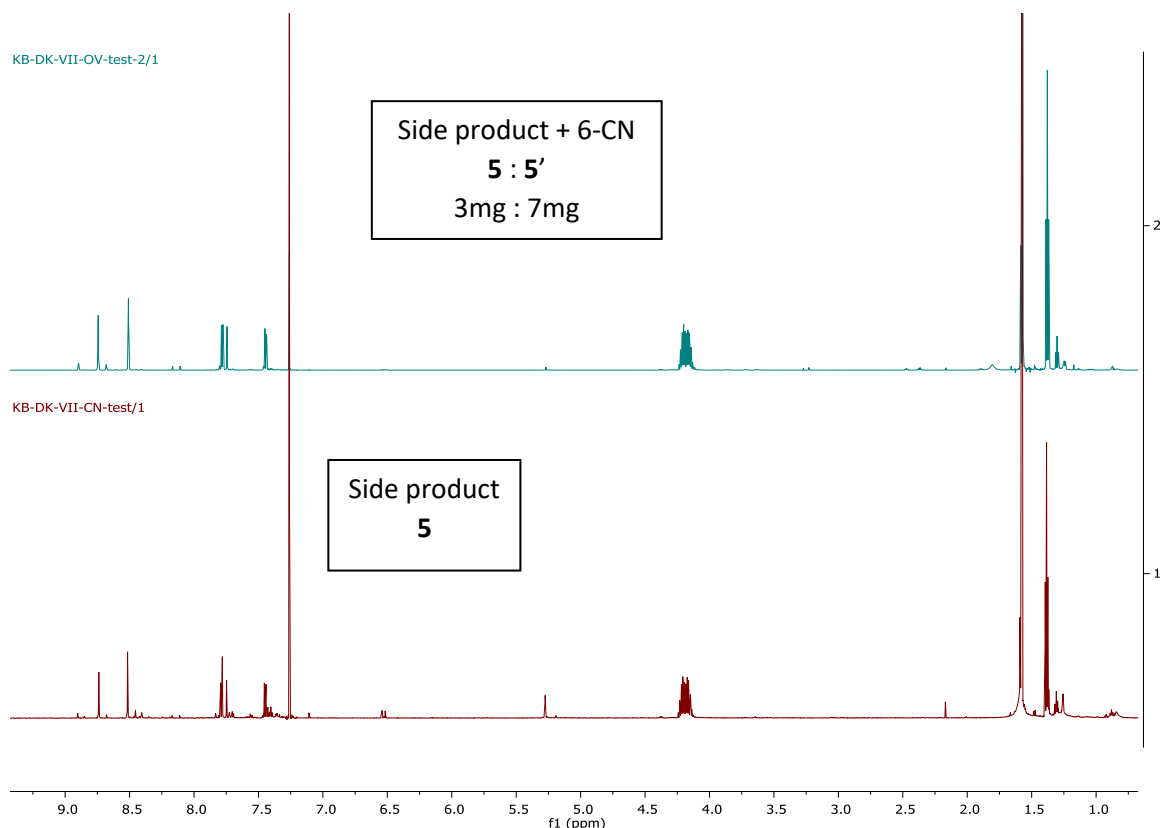
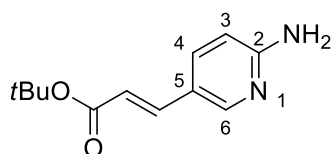
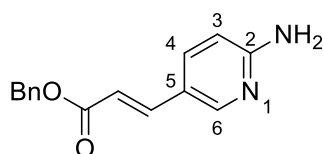


Figure S66. ^1H NMR spectra of mixture of side product **5** and synthesized compound **5'**



(E)-tert-Butyl 3-(6-aminopyridin-3-yl)acrylate

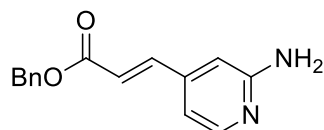
Yield (86%) ^1H NMR (250 MHz, CDCl_3) δ : 1.54 (s, $\text{C}(\text{CH}_3)_3$, 9H), 6.20 (d, $^3J_{\text{HH}} = 16.0$, $\text{CO}-\text{CH}=\text{CH}$ 1H), 6.51 (d, $^3J_{\text{HH}} = 8.7$, $\text{CH}_{(3)}$, 1H), 7.49 (d, $^3J_{\text{HH}} = 16.0$, $\text{CO}-\text{CH}=\text{CH}$, 1H), 7.64 (dd, $^3J_{\text{HH}} = 8.7$, $^4J_{\text{HH}} = 2.2$, $\text{CH}_{(4)}$, 1H), 8.19 (d, $^4J_{\text{HH}} = 2.2$, $\text{CH}_{(6)}$, 1H).



(E)-Benzyl 3-(6-aminopyridin-3-yl)acrylate

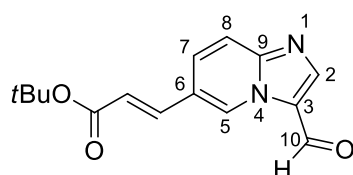
Yield (92%), ^1H NMR (250 MHz, CDCl_3) δ : 5.25 (s, CH_2Ph , 2H), 6.32 (d, $^3J_{\text{HH}} = 15.9$, $\text{CO}-\text{CH}=\text{CH}$ 1H), 6.51 (d, $^3J_{\text{HH}} = 8.8$, $\text{CH}_{(3)}$, 1H), 7.34 – 7.44 (m, Ph, 5H), 7.63 (d, $^3J_{\text{HH}} = 15.8$, $\text{CO}-\text{CH}=\text{CH}$, 1H), 7.65 (dd, $^3J_{\text{HH}} = 8.8$, $^4J_{\text{HH}} = 2.1$, $\text{CH}_{(4)}$, 1H), 8.20 (d, $^4J_{\text{HH}} = 2.1$, $\text{CH}_{(6)}$, 1H). ^{13}C NMR (250 MHz, CDCl_3) δ : 66.23 (s, $\text{Ph}-\text{CH}_2$, 1C), 108.69 (s, $\text{C}_{(3)}$, 1C), 114.47 (s, $\text{CO}-\text{CH}=\text{CH}$, 1C), 120.78 (s, $\text{C}_{(5)}$, 1C), 120.23 (s, $\text{C}_{(\text{Ar})}$ 2C), 120.26 (s, $\text{C}_{(\text{Ar})}$, 1C), 128.60 (s, $\text{C}_{(\text{Ar})}$,

2C), 135.79 (s, C₍₃₎, 1C), 136.20 (s, C_(Ar)-CH₂, 1C), 142.25 (s, CO-CH=CH, 1C), 159.68 (s, C₍₃₎, 1C), 167.01 (s, CO₂Bn, 1C).



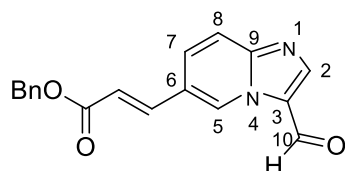
(E)-Benzyl 3-(2-aminopyridin-4-yl)acrylate

¹H NMR (250 MHz, CDCl₃) δ: 5.25 (s, COCH₂Bn, 2H), 6.54 (bs, CH(3), 1H), 6.55 (d, ³J_{HH} = 16.0 Hz, CH=CH, 1H), 6.75 (dd, ³J_{HH} = 5.5, ⁴J_{HH} = 1.3 Hz, CH(5), 1H), 7.46 – 7.33 (m, C₆H₅CH₂CO, 5H), 7.53 (d, ³J_{HH} = 16.0 Hz, CH=CH, 1H), 8.06 (d, ³J_{HH} = 5.5 Hz, CH(6), 1H).



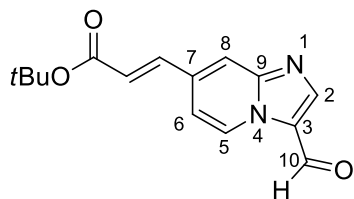
(E)-tert-Butyl 3-(3-formylimidazo[1,2-a]pyridin-6-yl)acrylate

Yield (86%) ¹H NMR (250 MHz, CDCl₃) δ: 1.53 (s, CCH₃, 9H), 6.43 (d, ³J_{HH} = 16.0, tBuO₂C-CH=CH, 1H), 7.58 (d, ³J_{HH} = 16.0, tBuO₂C-CH=CH, 1H), 7.72 (d, ³J_{HH} = 9.3, CH₍₇₎, 1H), 7.78 (d, ³J_{HH} = 9.3, CH₍₈₎, 1H), 8.31 (s, CH₍₂₎, 1H), 9.59 (bs, CH₍₅₎, 1H), 9.95 (s, C(O)H₍₁₀₎, 1H).



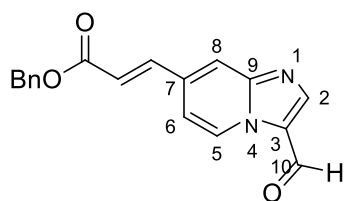
(E)-Benzyl 3-(3-formylimidazo[1,2-a]pyridin-6-yl)acrylate

Yield (88%) ¹H NMR (250 MHz, CDCl₃) δ: 5.23 (s, CH₂-Ph, 2H), 6.52 (d, ³J_{HH} = 16.0, BnO₂C-CH=CH, 1H), 7.34-7.49 (m, PhCH₂, 5H), 7.67 (d, ³J_{HH} = 9.3, CH₍₇₎, 1H), 7.70 (d, ³J_{HH} = 16.0, BnO₂C-CH=CH, 1H), 7.73 (d, ³J_{HH} = 9.3, CH₍₈₎, 1H), 8.26 (s, CH₍₂₎, 1H), 8.56 (bs, CH₍₅₎, 1H), 9.90 (s, C(O)H₍₁₀₎, 1H). ¹³C NMR (700 MHz, CDCl₃) δ: 66.89 (s, Ph-CH₂, 1C), 118.27 (s, C₍₈₎, 1C), 120.40 (s, BnO₂C-CH=CH, 1C), 123.79 (s, C₍₆₎, 1C), 125.52 (s, C₍₃₎, 1C), 127.74 (s, C₍₇₎, 1C), 128.52 (s, C_(Ar), 2C), 128.57 (s, C_(Ar), 1C), 128.83 (s, C_(Ar), 2C), 129.67 (s, C₍₅₎, 1C), 135 (s, C_(Ar)-CH₂, 1C), 140.14 (BnO₂C-CH=CH, 1C), 147.38 (s, C₍₂₎, 1C), 149.13 (s, C₍₉₎, 1C), 165.93 (s, CO₂Bn, 1C), 178.37 (s, CHO, 1C).



(E)-tert-Butyl 3-(3-formylimidazo[1,2-a]pyridin-7-yl)acrylate

Yield (30%), ^1H NMR (250 MHz, CDCl_3) δ : 1.54 (s, CCH_3 , 9H), 6.53 (d, $^3J_{\text{HH}} = 16.0$, $t\text{BuO}_2\text{C}-\text{CH}=\text{CH}$, 1H), 7.06 (dd, $^3J_{\text{HH}} = 7.3$, $^4J_{\text{HH}} = 1.4$, $\text{CH}_{(6)}$, 1H), 7.59 (d, $^3J_{\text{HH}} = 16.0$, $t\text{BuO}_2\text{C}-\text{CH}=\text{CH}$, 1H), 7.83 (bs, $\text{CH}_{(8)}$, 1H), 8.34 (s, $\text{CH}_{(2)}$, 1H), 9.42 (d, $^3J_{\text{HH}} = 7.3$, $\text{CH}_{(5)}$, 1H), 9.95 (s, $\text{C(O)H}_{(10)}$, 1H).



(E)-Benzyl 3-(3-formylimidazo[1,2-a]pyridin-7-yl)acrylate

Yield (70%), ^1H NMR (250 MHz, CDCl_3) δ : 5.29 (s, $\text{CH}_2\text{-Ph}$, 2H), 6.64 (d, $^3J_{\text{HH}} = 16.0$, $\text{BnO}_2\text{C}-\text{CH}=\text{CH}$, 1H), 7.06 (dd, $^3J_{\text{HH}} = 7.3$, $^4J_{\text{HH}} = 1.5$, $\text{CH}_{(6)}$, 1H), 7.35-7.46 (m, PhCH_2 , 5H), 7.74 (d, $^3J_{\text{HH}} = 16.0$, $\text{BnO}_2\text{C}-\text{CH}=\text{CH}$, 1H), 7.86 (bs, $\text{CH}_{(8)}$, 1H), 8.35 (s, $\text{CH}_{(2)}$, 1H), 9.44 (d, $^3J_{\text{HH}} = 7.3$, $\text{CH}_{(5)}$, 1H), 9.97 (s, $\text{C(O)H}_{(10)}$, 1H).

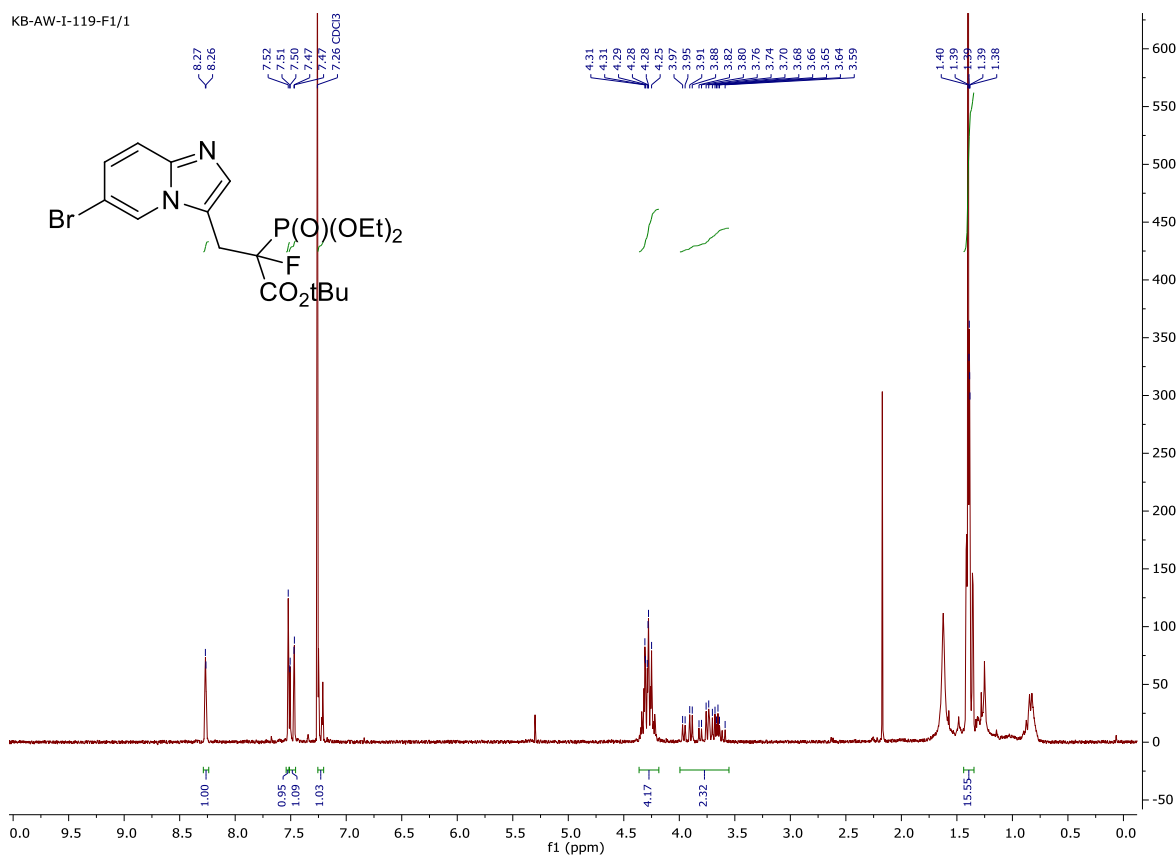


Figure S67. ¹H NMR of compound **23** (700 MHz, CDCl₃)

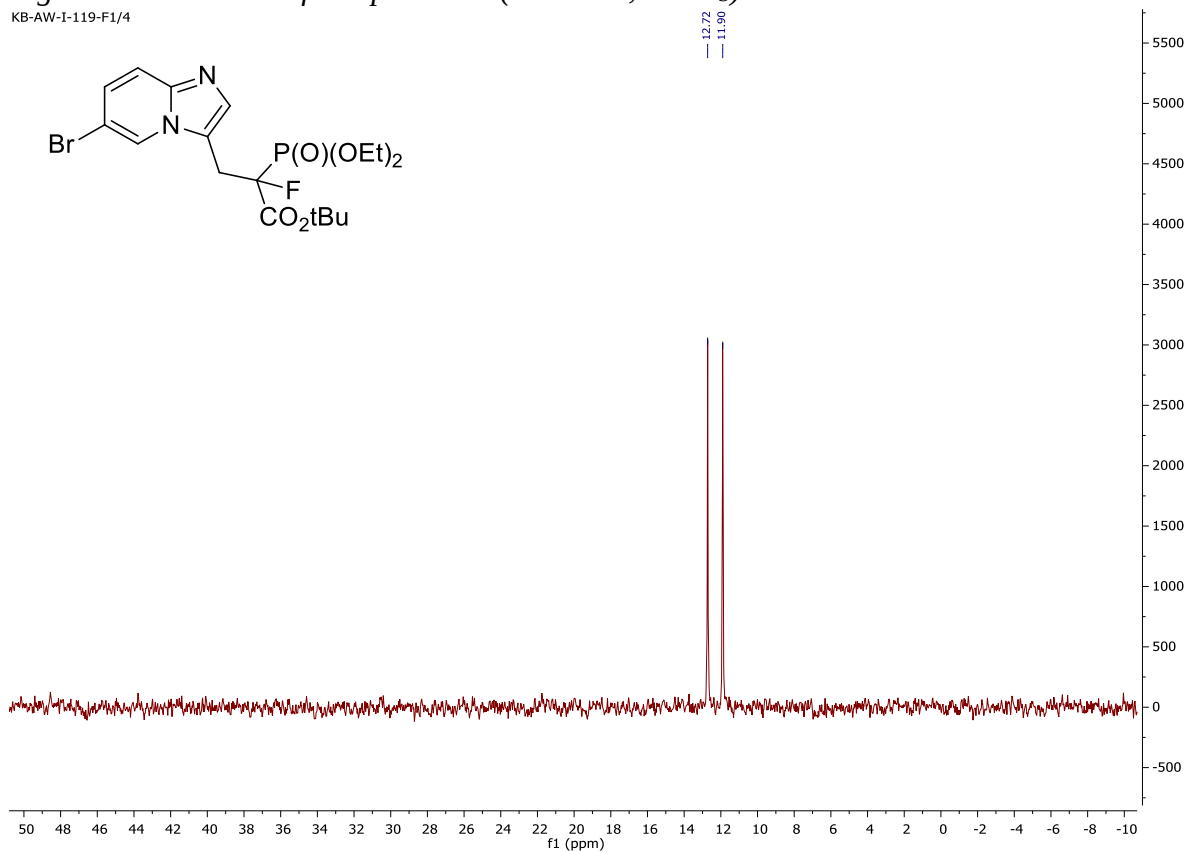


Figure S68. ³¹P NMR of compound **23** (283 MHz, CDCl₃)

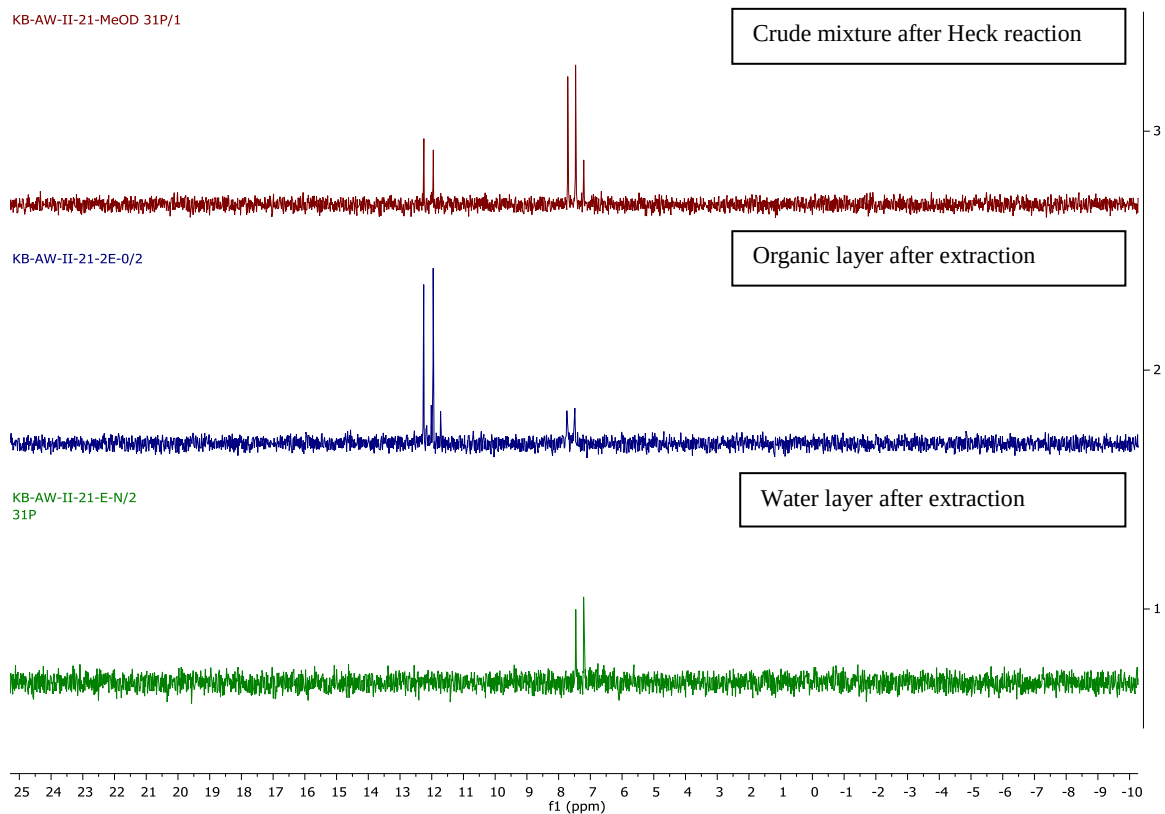
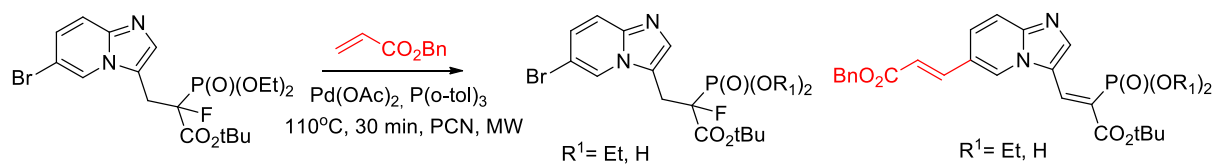


Figure 69. Comparing ³¹P NMR spectra of reaction mixture after Heck reaction performed on compound **23**.

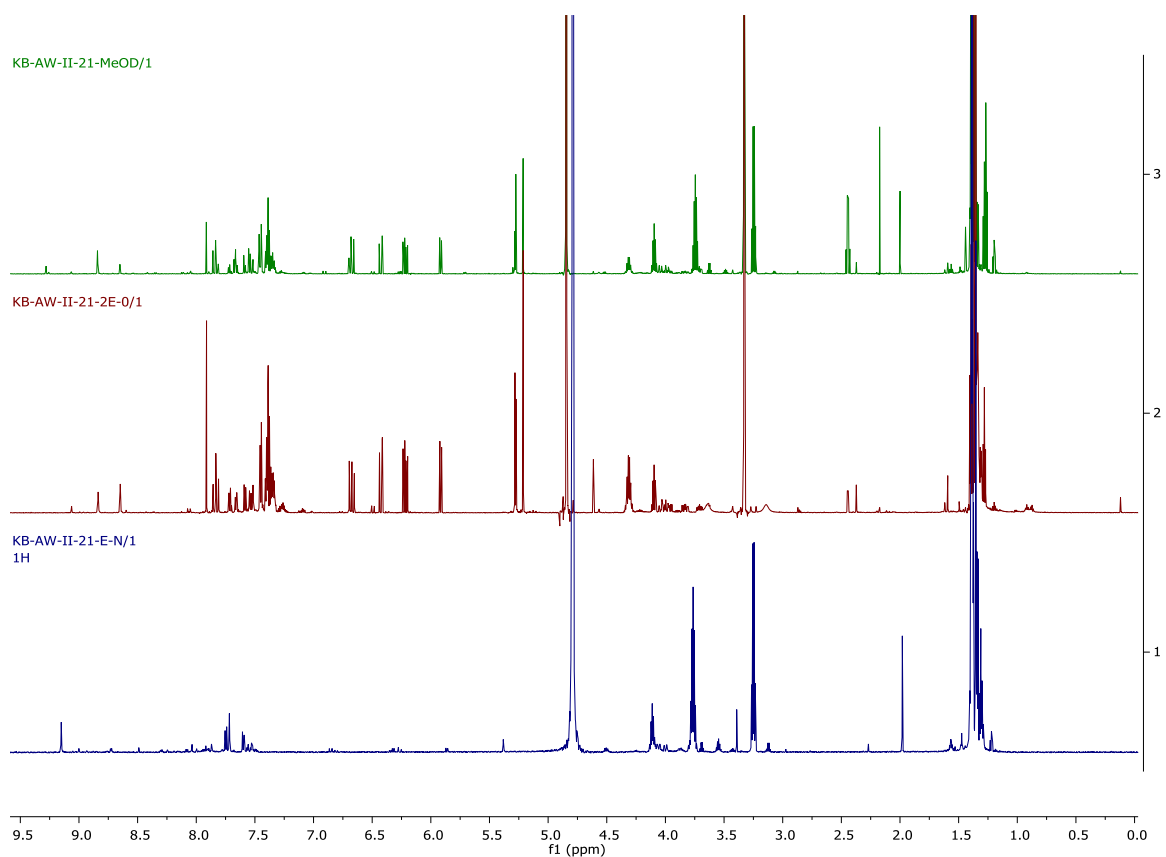


Figure 70. Comparing ^1H NMR spectra of reaction mixture after Heck reaction performed on compound **23**

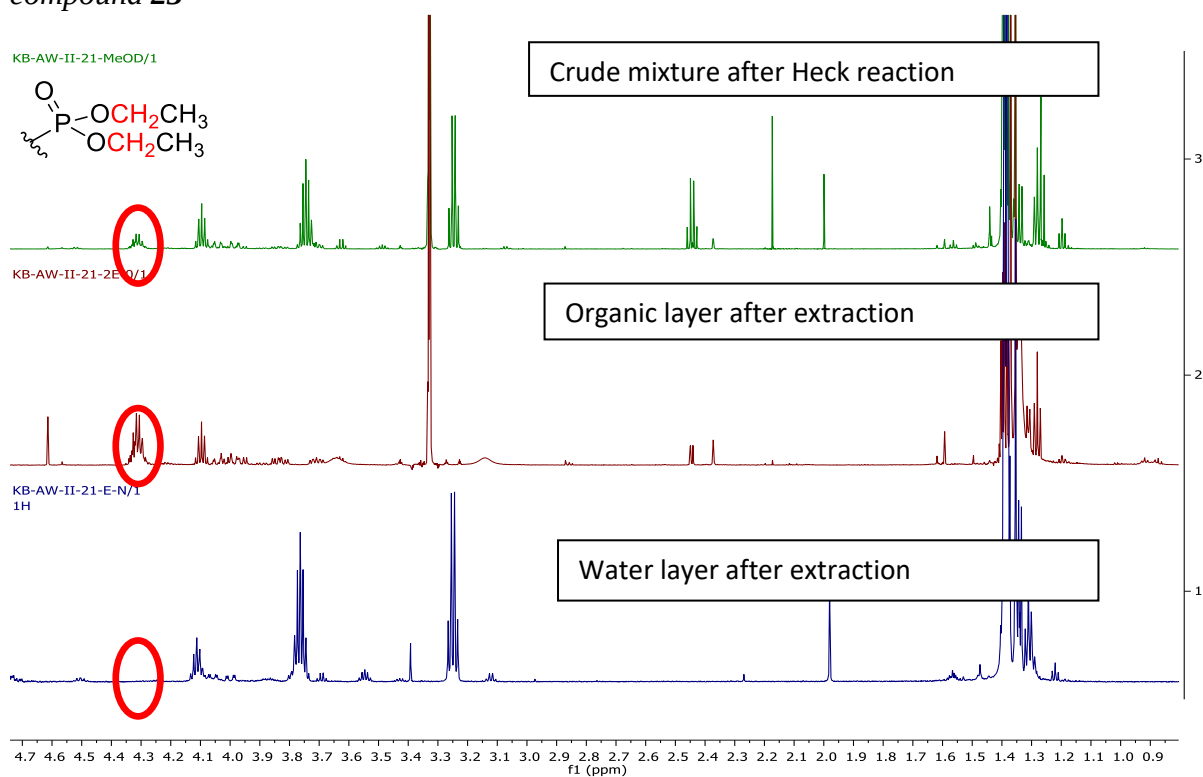


Figure 71. Comparing ^1H NMR spectra of reaction mixture after Heck reaction performed on compound **23** (range 0-4.7)

General procedure for the synthesis of starting materials (**1**, **2**, and **23**) [1]

General procedure for the synthesis of compounds (1).

The reaction was carried out under argon atmosphere using oven-dried glassware. A 100 mL two-necked round-bottomed flask was charged with triethyl phosphonoacetate (1.79 g, 8.0 mmol, 1.2 equiv) dissolved in DCM (20 mL). The solution was cooled below $-30\text{ }^{\circ}\text{C}$ (internal temperature control), and TiCl_4 (0.877 mL, 8 mmol, 1.2 equiv) was slowly added via a syringe, followed by Et_3N (2.63 mL, 0.0187 mol, 2.8 equiv). The reaction mixture was stirred for 15 min at $-30\text{ }^{\circ}\text{C}$. Then, a solution of 6-bromoimidazo[1,2-*a*]pyridine-3-carbaldehyde (6.67 mmol, 1 equiv) in DCM (20 mL) was dropwisely added over 15 min at a the temperature kept below $-30\text{ }^{\circ}\text{C}$. The resulting mixture was stirred at room temperature for 16 h, then quenched with 25 mL of water and was made basic with saturated Na_2CO_3 aqueous solution to $\text{pH} > 9$. The aqueous layer was extracted with diethyl ether ($5 \times 25\text{ mL}$). The organic layer was dried over anhydrous Mg_2SO_4 , the solvent evaporated and the residue subjected to column chromatography using DCM/acetone 85:15 as eluent to give the product as (*Z/E*) mixture in the form of an orange oil.

***tert*-Butyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (**1a**).**

^1H NMR (700 MHz, CDCl_3) δ 1.31 (t, $^3J_{\text{HH}} = 7.5$, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 1.51 (s, $\text{C}(\text{CH}_3)_3$, 9H), 4.06 – 4.17 (m, CH_2OP , 4H), 7.35 (dd, $^3J_{\text{HH}} = 9.4$, $^4J_{\text{HH}} = 1.5$, $\text{CH}_{\text{Ar}(7)}$, 1H), 7.52 (d, $^3J_{\text{HH}} = 9.4$, $\text{CH}_{\text{Ar}(8)}$, 1H), 7.71 (d, $^3J_{\text{PH}} = 23.9$, $\text{C}=\text{CH}$, 1H), 8.36 (s, $\text{CH}_{\text{Ar}(2)}$, 1H), 8.42 (bs, $\text{CH}_{\text{Ar}(5)}$, 1H). **^{13}C NMR** (176 MHz, CDCl_3) δ 16.32 (d, $^3J_{\text{PC}} = 6.5$, $\text{CH}_3\text{CH}_2\text{OP}$, 2C), 28.04 (s, $\text{C}(\text{CH}_3)_3$, 3C), 62.50 (d, $^2J_{\text{PC}} = 5.1$, CH_2OP , 2C), 82.83 (s, $\text{C}(\text{CH}_3)_3$, 1C), 109.03 (s, $\text{C}_{\text{Ar}(6)}$, 1C), 118.96 (s, $\text{CH}_{\text{Ar}(8)}$, 1C), 119.78 (d, $^1J_{\text{PC}} = 181.4$, PC , 1C), 120.58 (d, $^3J_{\text{PC}} = 25.2$, $\text{C}_{\text{Ar}(3)}$, 1C), 124.09 (s, $\text{CH}_{\text{Ar}(5)}$, 1C), 130.25 (s, $\text{CH}_{\text{Ar}(7)}$, 1C), 131.54 (d, $^2J_{\text{PC}} = 10.1$, $\text{PC}=\text{CH}$, 1C), 140.59 (s, $\text{CH}_{\text{Ar}(2)}$, 1C), 145.93 (s, $\text{C}_{\text{Ar}(9)}$, 1C), 164.85 (d, $^2J_{\text{PC}} = 10.3$, CO_2 , 1C). **^{31}P NMR** (238 MHz, CDCl_3) δ 15.93.

Ethyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (1b**).** Yield:

52%, scale: 0.34 g, (*E*)/(*Z*) 50/1, $R_{\text{f}(\text{E})}$ 0.36, (CH_2Cl_2 :acetone 85:15), (***E***)-**1b**: **^{31}P NMR** (101 MHz, CDCl_3) δ : 16.52 (*E*) and 13.27 (*Z*), **^1H NMR** (700 MHz, CDCl_3) δ : 1.35 (t, $^3J_{\text{HH}} = 7.10$, $\text{CH}_3\text{CH}_2\text{OC}$, 3H), 1.36 (t, $^3J_{\text{HH}} = 7.1$, $\text{CH}_3\text{CH}_2\text{OP}$, 6H), 4.12 - 4.25 (m, CH_2OP , 4H), 4.36 (q, $^3J_{\text{HH}} = 7.1$, CH_2OC , 2H), 7.43 (dd, $^3J_{\text{HH}} = 9.4$, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{\text{Ar}(7)}$, 1H), 7.59 (d, $^3J_{\text{HH}} = 9.4$, $\text{CH}_{\text{Ar}(8)}$, 1H), 7.90 (d, $^3J_{\text{PH}}(\text{Z}) = 23.8$, $\text{C}=\text{CH}$, 1H), 8.45 (s, $\text{CH}_{\text{Ar}(2)}$, 1H), 8.52 (d, $^4J_{\text{HH}} = 1.7$, $\text{CH}_{\text{Ar}(5)}$, 1H), **^{13}C NMR** (176 MHz, CDCl_3) δ : 14.2 (s, $\text{CH}_3\text{CH}_2\text{OC}$), 16.42 (s, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 16.44 (s, $\text{CH}_3\text{CH}_2\text{OP}$, 1C), 61.8 (s, CH_2OC , 1C), 62.87 (s, CH_2OP , 1C), 62.90 (s, CH_2OP , 1C), 109.4 (s, $\text{CH}_{\text{Ar}(6)}$, 1C), 117.5 (d, $^1J_{\text{PC}} = 184.3$, $\text{C}=\text{CH}$, 1C), 119.1 (s, $\text{CH}_{\text{Ar}(8)}$, 1H), 120.8 (d, $^3J_{\text{PC}} = 24.2$, $\text{C}_{\text{Ar}(3)}$, 1C), 124.3 (s, $\text{CH}_{\text{Ar}(5)}$, 1C), 130.8 (s, $\text{CH}_{\text{Ar}(7)}$, 1C), 133.3 (d,

$^2J_{PC} = 10.1$, $C=\underline{C}H$, 1C), 141.5 (s, $CH_{Ar(2)}$, 1C), 146.3 (s, $C_{Ar(9)}$, 1C), 165.7 (d, $^2J_{PC} = 11.7$, $\underline{C}O_2$, 1C).

***tert*-Butyl 3-(7-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (1c),**

1H NMR (700 Hz, $CDCl_3$) δ : 1.35 (t, $^3J_{HH} = 7.0$ Hz, CH_3CH_2OP , 6H), 1.56 (s, $C(CH_3)_3$, 9H), 4.04 – 4.25 (m, CH_3CH_2OP , 4H), 7.09 (dd, $^3J_{HH} = 7.2$ Hz, $^4J_{HH} = 1.9$ Hz, $CH_{(6)}$, 1H), 7.77 (d, $^3J_{HH} = 23.9$ Hz, (*E*) $CH=CP$, 1H), 7.87 (dd, $^4J_{HH} = 1.9$ Hz, $^5J_{HH} = 0.8$ Hz, $CH_{(8)}$, 1H), 8.21 (d, $^3J_{HH} = 7.1$ Hz, $CH_{(5)}$, 1H), 8.42 (s, $CH_{(2)}$, 1H), ^{31}P NMR (700 Hz, $CDCl_3$) δ : 16.60 – (*E*) $CH=CP$.

***tert*-Butyl 3-(8-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (1d),**

1H NMR (700 Hz, $CDCl_3$) δ : 1.37 (t, $^3J_{HH} = 7.1$ Hz, CH_3CH_2OP , 6H), 1.57 (s, $C(CH_3)_3$, 9H), 4.06 – 4.28 (m, CH_3CH_2OP , 4H), 6.89 (t, $^3J_{HH} = 7.2$ Hz, $CH_{Ar(6)}$, 1H), 7.62 (dd, $^3J_{HH} = 7.2$ Hz, $^4J_{HH} = 1.0$ Hz, $CH_{(7)}$, 1H), 7.74 (d, $^3J_{HH} = 23.8$ Hz, (*E*) $CH=CP$, 1H), 8.32 (m, $CH_{(5)}$, 1H), 8.42 (s, $CH_{(2)}$, 1H), ^{31}P NMR (700 Hz, $CDCl_3$) δ : 15.90 – (*E*) $CH=CP$.

***tert*-Butyl 3-(6-chloroimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)acrylate (1e),**

1H NMR (700 Hz, $CDCl_3$) δ : 1.37 (t, $^3J_{HH} = 7.1$ Hz, CH_3CH_2OP , 6H), 1.57 (s, $C(CH_3)_3$, 9H), 4.06 – 4.28 (m, CH_3CH_2OP , 4H), 7.32 (dd, $^3J_{HH} = 9.5$ Hz, $^4J_{HH} = 1.8$ Hz, $CH_{(7)}$, 1H), 7.64 (dd, $^3J_{HH} = 9.5$ Hz, $^4J_{HH} = 0.8$ Hz, $CH_{(8)}$, 1H), 7.76 (d, $^3J_{HH} = 23.9$ Hz, (*E*) $CH=CP$, 1H), 8.37 (d, $^4J_{HH} = 1.8$ Hz, $CH_{(5)}$, 1H), 8.52 (s, $CH_{(2)}$, 1H), ^{31}P NMR (700 Hz, $CDCl_3$) δ : 16.34 – (*E*) $CH=CP$.

General procedure for the synthesis of compounds (2).

Ethyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)propanoate (2b). A 50 mL two-necked round-bottomed flask was charged with **1b** (1.83 mmol, 1 equiv), $NiCl_2 \cdot 6H_2O$ (0.52 g, 2.2 mmol, 1.2 equiv) which were dissolved in methanol (10 mL). The flask was submerged in a dry ice/acetone cooling bath (-40 °C) and then $NaBH_4$ (0.083 g, 2.2 mmol, 1.2 equiv) was added. The mixture was stirred at (-40 °C, internal control) for 8 min then quenched by the addition of 4 mL NH_4Cl . The solution was made basic with saturated Na_2CO_3 solution to pH > 9. The aqueous layer was extracted with dichloromethane (4×10 mL). The organic layer was dried over anhydrous $MgSO_4$, the solvent evaporated and the residue subjected to column chromatography using DCM/acetone 100:20 as eluent to give the product as orange oil.

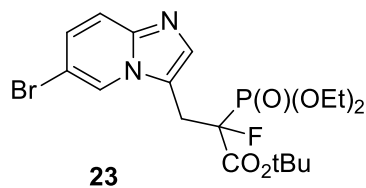
tert-Butyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)propanoate (2a). ¹H NMR (700 MHz, CDCl₃) δ 8.18 (dd, ⁴J_{HH} = 1.8, ⁵J_{HH} = 0.8, CH_{Ar(5)}, 1H), 7.49 (dd, ³J_{HH} = 9.5, ⁵J_{HH} = 0.8, CH_{Ar(8)}, 1H), 7.45 (s, CH_{Ar(2)}, 1H), 7.22 (dd, ³J_{HH} = 9.5, ⁴J_{HH} = 1.8, CH_{Ar(7)}, 1H), 4.18-4.25 (m, CH₂OP, 4H), 3.53 (ddd, ²J_{HH} = 15.8, ³J_{HH} = 11.5, ³J_{PH} = 6.8 CH₂CHP, 1H), 3.30 (ddd, ²J_{HH} = 15.8, ³J_{PH} = 10.0, ³J_{HH} = 3.1 CH₂CHP, 1H), 3.23 (ddd, ²J_{PH} = 22.8, ³J_{HH} = 11.5, ³J_{HH} = 3.1 CH₂CHP, 1H), 1.39 (s, C(CH₃)₃, 9H), 1.35-1.38 (m, CH₃CH₂OP, 6H). ¹³C NMR (176 MHz, CDCl₃) δ 167.34 (d, ²J_{PC} = 5.1, CO₂, 1C), 144.12 (s, C_{Ar(9)}, 1C), 132.60 (d, ⁴J_{PC} = 9.3, CH_{Ar(2)}, 1C), 127.32 (s, CH_{Ar(7)}, 1C), 123.57 (s, CH_{Ar(5)}, 1C), 122.12 (d, ³J_{PC} = 19.1, C_{Ar(3)}, 1C), 118.72 (s, CH_{Ar(8)}, 1C), 107.36 (s, C_{Ar(6)}, 1C), 82.90 (s, C(CH₃)₃, 1C), 63.24 (d, ²J_{PC} = 6.8, CH₂OP, 1C), 63.10 (d, ²J_{PC} = 6.8, CH₂OP, 1C), 45.35 (d, ¹J_{PC} = 128.5, CHP, 1C), 27.94 (d, ⁵J_{PC} = 3.5, C(CH₃)₃, 3C), 16.53 (d, ³J_{PC} = 3.1, CH₃CH₂OP, 1C), 21.70 (s, CH₂CHP, 1C), 16.56 (d, ²J_{PC} = 3.1, CH₃CH₂OP, 1C). ³¹P NMR (283 MHz, CDCl₃) δ 21.32.

Ethyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)propanoate (2b). Yield: 75 %, scale (0.32 g), R_f 0.08, (CH₂Cl₂:acetone 85:15), ¹H NMR (700 MHz, CDCl₃) δ: 1.18 (t, ³J_{HH} = 7.10, CH₃CH₂OC, 3H), 1.34 (t, ³J_{HH} = 7.10, CH₃CH₂OP, 6H), 3.21 - 3.41 (m, CH₂CHP, 2H), 3.45-3.64 (m, CH₂CHP, 1H), 4.03-4.28 (m, CH₂OP, CH₂OC, 6H), 7.20 (dd, ³J_{HH} = 9.5, ⁴J_{HH} = 1.8, CH_{Ar(7)}, 1H), 7.40 (s, CH_{Ar(2)}, 1H), 7.46 (d, ³J_{HH} = 9.5, ⁵J_{HH} = 0.8, CH_{Ar(8)}, 1H), 8.16 (d, ⁴J_{HH} = 1.8, ⁵J_{HH} = 0.8, CH_{Ar(5)}, 1H), ³¹P NMR (283 MHz, CDCl₃): 21.40.

General procedure for the synthesis of compounds (23).

Ethyl 3-(6-bromoimidazo[1,2-*a*]pyridin-3-yl)-2-(diethoxyphosphoryl)-2-fluoropropanoate (23). The reaction was carried out under an argon atmosphere using oven-dried glassware. A solution of phosphonocarboxylate triester **2b** (1 equiv, 1.01 mmol) in anhydrous THF (8 mL) was cooled to −78 °C, and *n*-BuLi (1.6 M in hexanes, 1.5 equiv) was added via a syringe. The solution was stirred for 10 min at −78 °C, allowed to warm to 0 °C, and stirred at this temperature for 1 h. Then it was cooled back to −78 °C and a solution of *N*-fluoro-*N*-(phenylsulfonyl)benzenesulfonamide (1.2 equiv) in anhydrous THF (8 mL) was added dropwise via syringe. The reaction mixture was stirred at −78 °C for 10 min, warmed to rt and stirred for additional 4.5 h. The reaction mixture was quenched with saturated aqueous NH₄Cl, and concentrated under vacuum. It was made basic with Na₂CO₃ solution (to pH 9)

and extracted with CHCl_3 (3 $\times$). The organic layer was dried over anhydrous MgSO_4 , concentrated to dryness under vacuum, and purified by column chromatography.



tert-Butyl 3-(6-bromoimidazo[1,2-a]pyridin-3-yl)-2-(diethoxyphosphoryl)-2-fluoropropanoate (23). Yield: 86%, scale: 0.37 g, (CH_2Cl_2 /acetone 75:25), ^1H NMR (250 MHz, CDCl_3) δ : 1.30 - 1.48 (m, $\text{C}(\text{CH}_3)_3$, $\text{CH}_3\text{CH}_2\text{O}(\text{O})\text{P}$, 15H), 3.48 - 4.07 (m, CH_2CFP , 2H), 4.11 - 4.40 (m, $\text{CH}_3\text{CH}_2\text{O}(\text{O})\text{P}$, 4H), 7.24 (dd, $^3J_{\text{HH}} = 9.5$, $^4J_{\text{HH}} = 1.8$ $\text{CH}_{\text{Ar}(7)}$, 1H), 7.49 (dd, $^3J_{\text{HH}} = 9.5$, $^5J_{\text{HH}} = 0.8$ $\text{CH}_{\text{Ar}(8)}$, 1H), 7.52 (s, $\text{CH}_{\text{Ar}(2)}$, 1H), 8.27 (bs, $\text{CH}_{\text{Ar}(5)}$, 1H), ^{31}P NMR (101 MHz, CDCl_3) δ : 12.31 (d, $^2J_{\text{PF}} = 83.3$).

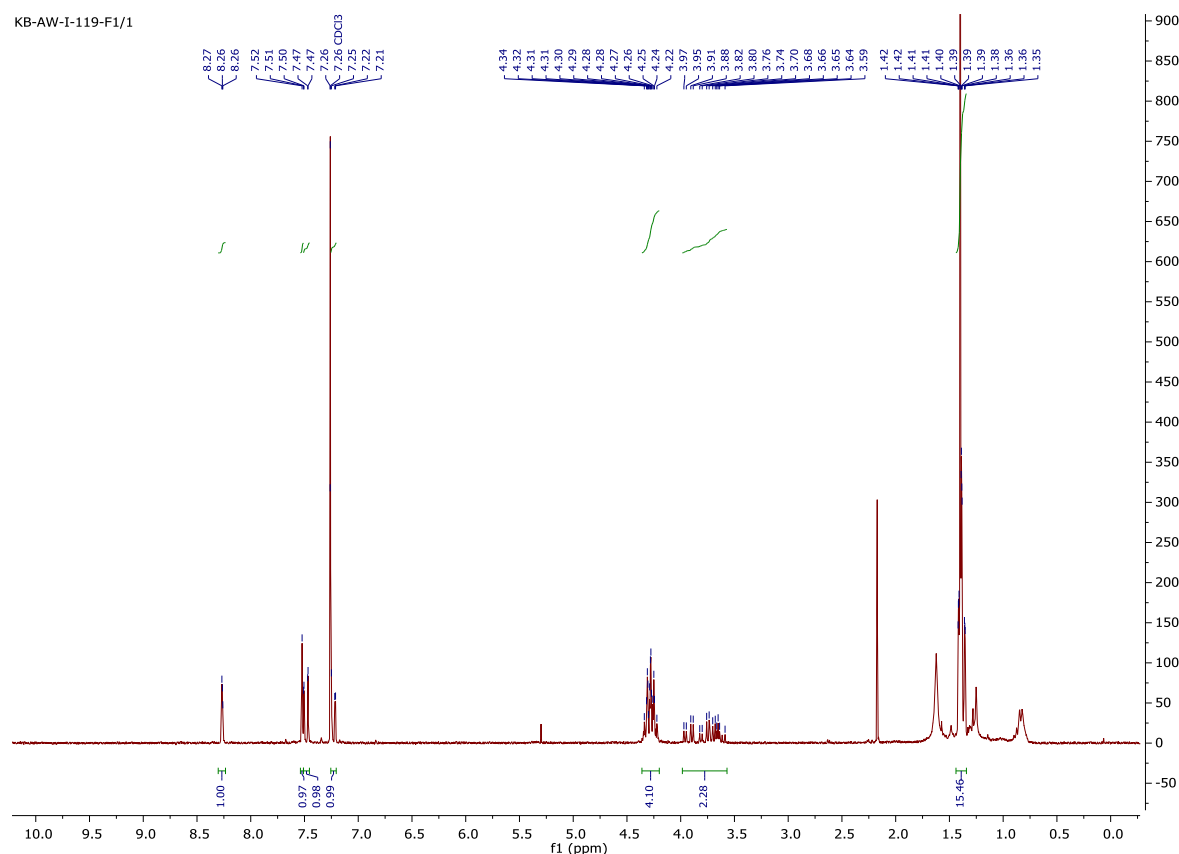


Figure S72. ^1H NMR of compound **23** (250 MHz, CDCl_3)

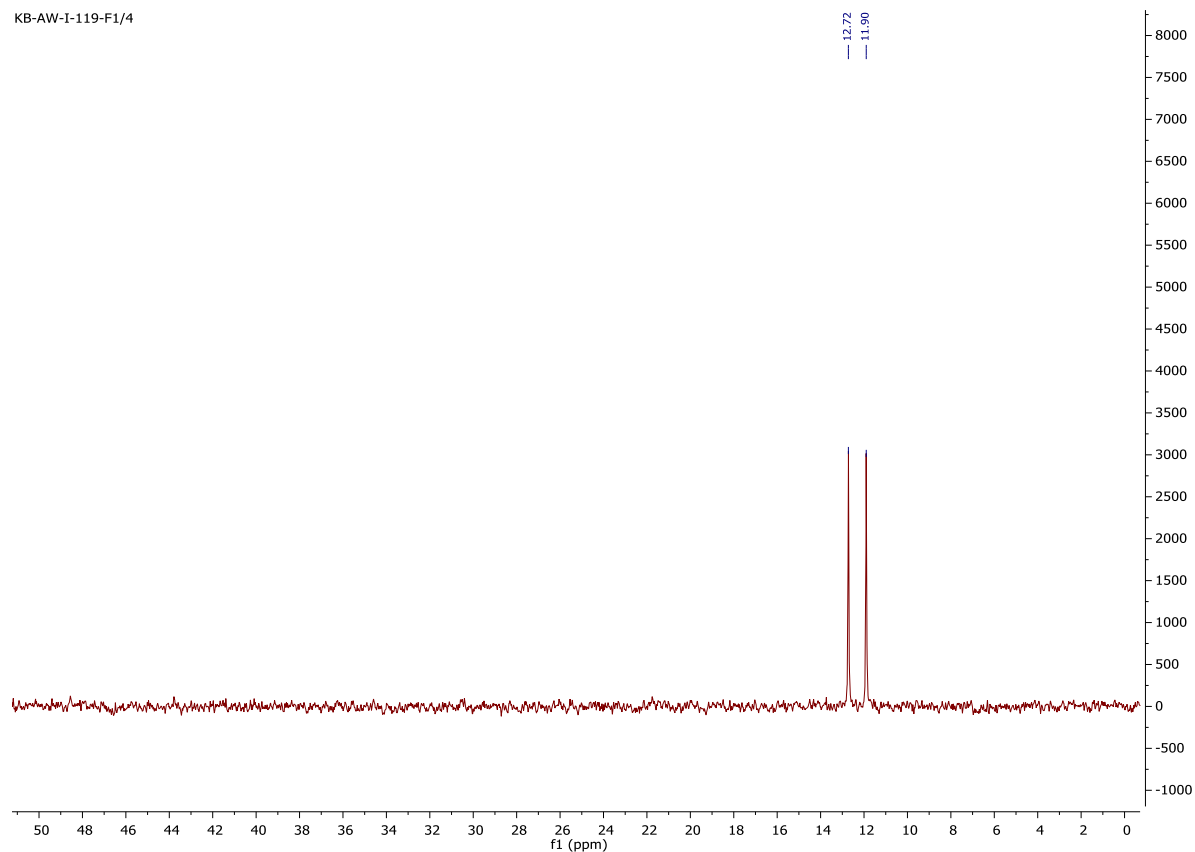


Figure S73. ^{31}P NMR of compound **23** (101 MHz, CDCl_3)

References

- [1] Kaźmierczak, A.; Kusy, D.; Niinivehmas, S. P.; Gmach, J.; Joachimiak, Ł.; Pentikäinen, O. T.; Gendaszewska-Darmach, E.; Błażewska, K. M. Identification of the Privileged Position in the Imidazo[1,2-a]pyridine Ring of Phosphonocarboxylates for Development of Rab Geranylgeranyl Transferase (RGGT) Inhibitors. *J. Med. Chem.* **2017**, *60*, 8781-8800.