

Supplementary Information

Synthesis of New Conjugates 1*H*-Pyrazolo[3,4-*b*]pyridine-phosphoramidate and Evaluation against *Leishmania amazonensis*

Antonia C. R. F. Medeiros,^a Julio C. Borges,^{a,b} Klaus M. Becker,^c Raquel F. Rodrigues,^c Leonor L. Leon,^c Marilene Canto-Cavalheiro,^c Alice M. R. Bernardino,^a Marcos C. de Souza^a and Leandro F. Pedrosa^{*a,d}

^aDepartamento de Química Orgânica, Universidade Federal Fluminense, 24020-141 Niterói-RJ, Brazil

^bInstituto Federal de Educação Ciência e Tecnologia do Rio de Janeiro, Campus Nilópolis, 26530-060 Nilópolis-RJ, Brazil

^cLaboratório de Bioquímica de Tripanosomatídeos, Fundação Oswaldo Cruz, 21040-900 Rio de Janeiro-RJ, Brazil

^dDepartamento de Química, Instituto de Ciências Exatas, Universidade Federal Fluminense, 27213-145 Volta Redonda-RJ, Brazil

Diisopropyl 2-(5-(ethoxycarbonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)ethyl phosphoramidate (**14a**)

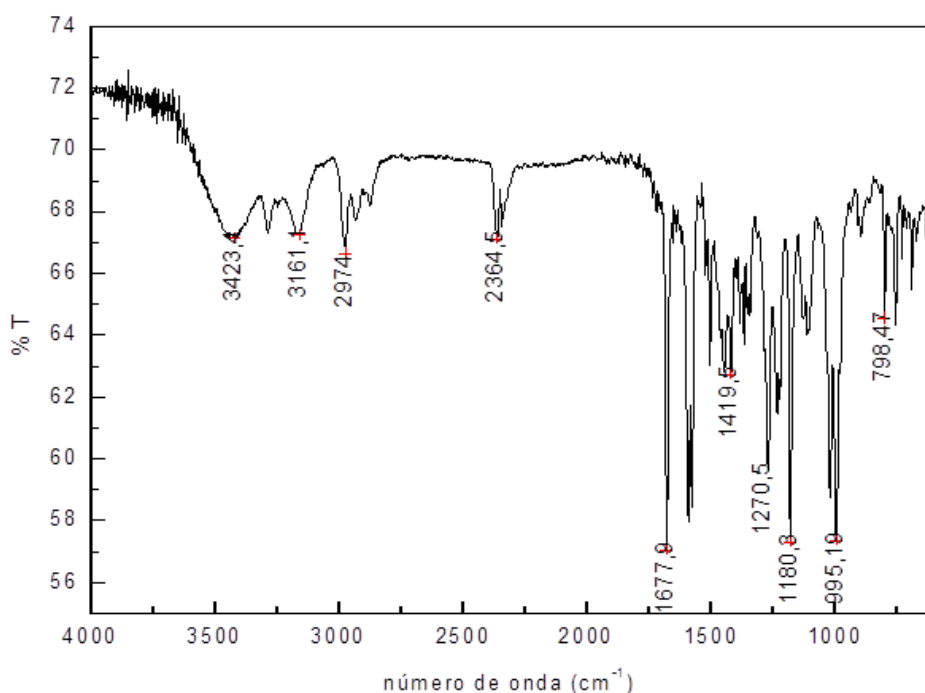
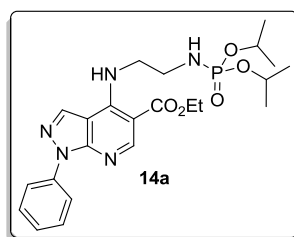


Figure S1. FTIR (KBr) spectrum of **14a**.

*e-mail: leandropedrosa@id.uff.br

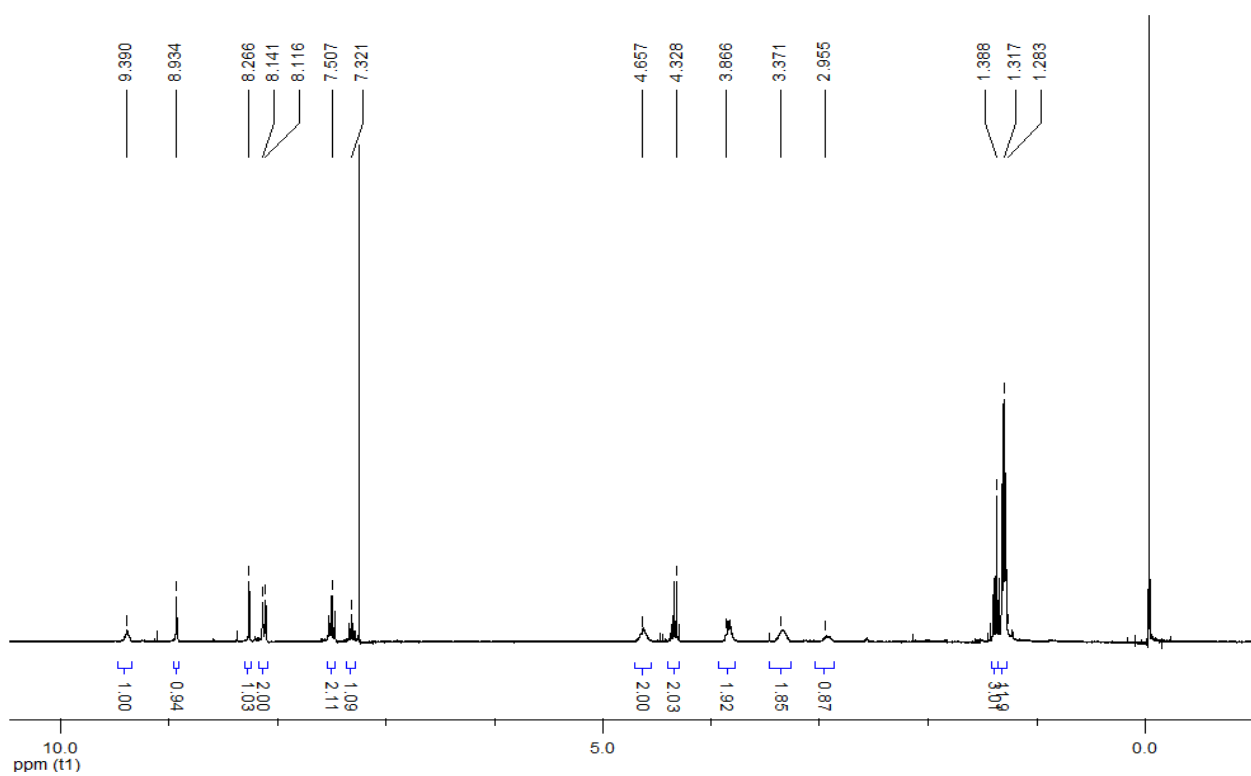


Figure S2. ¹H NMR spectrum (300 MHz, CDCl₃) of **14a**.

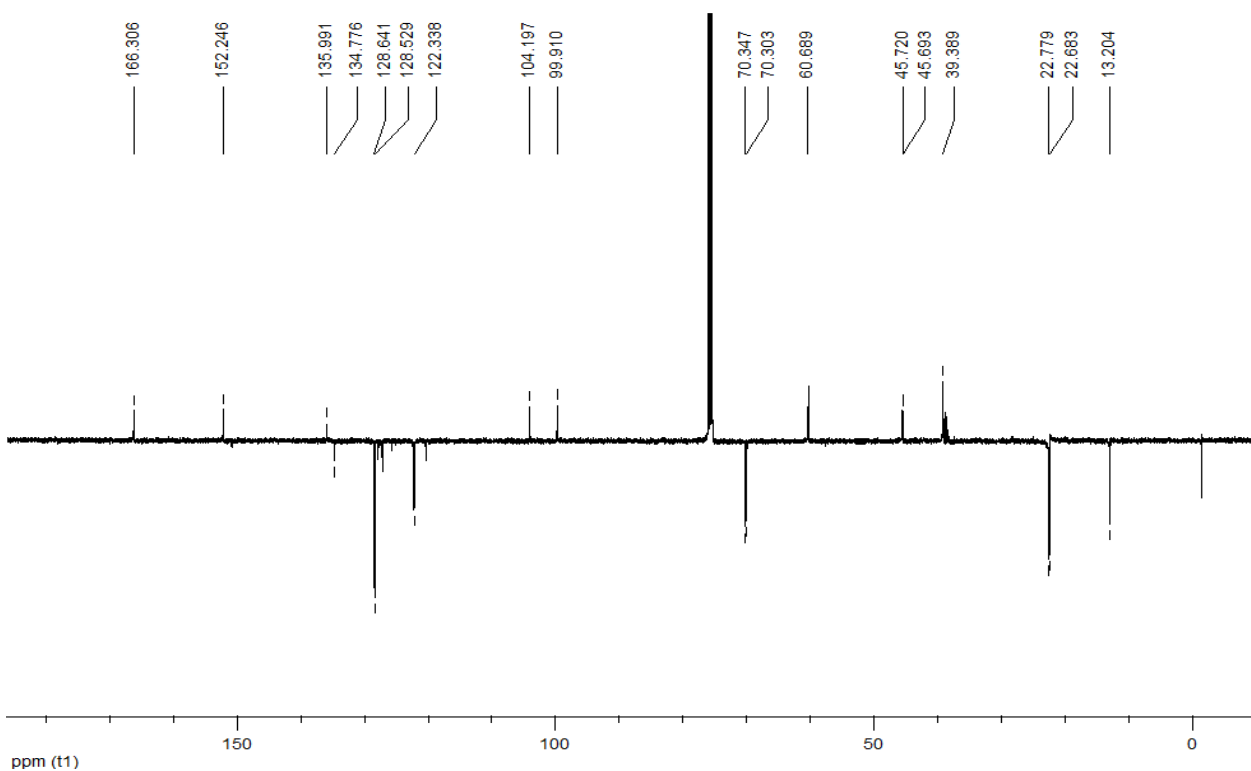


Figure S3. ¹³C NMR spectrum (125 MHz, CDCl₃) of **14a**.

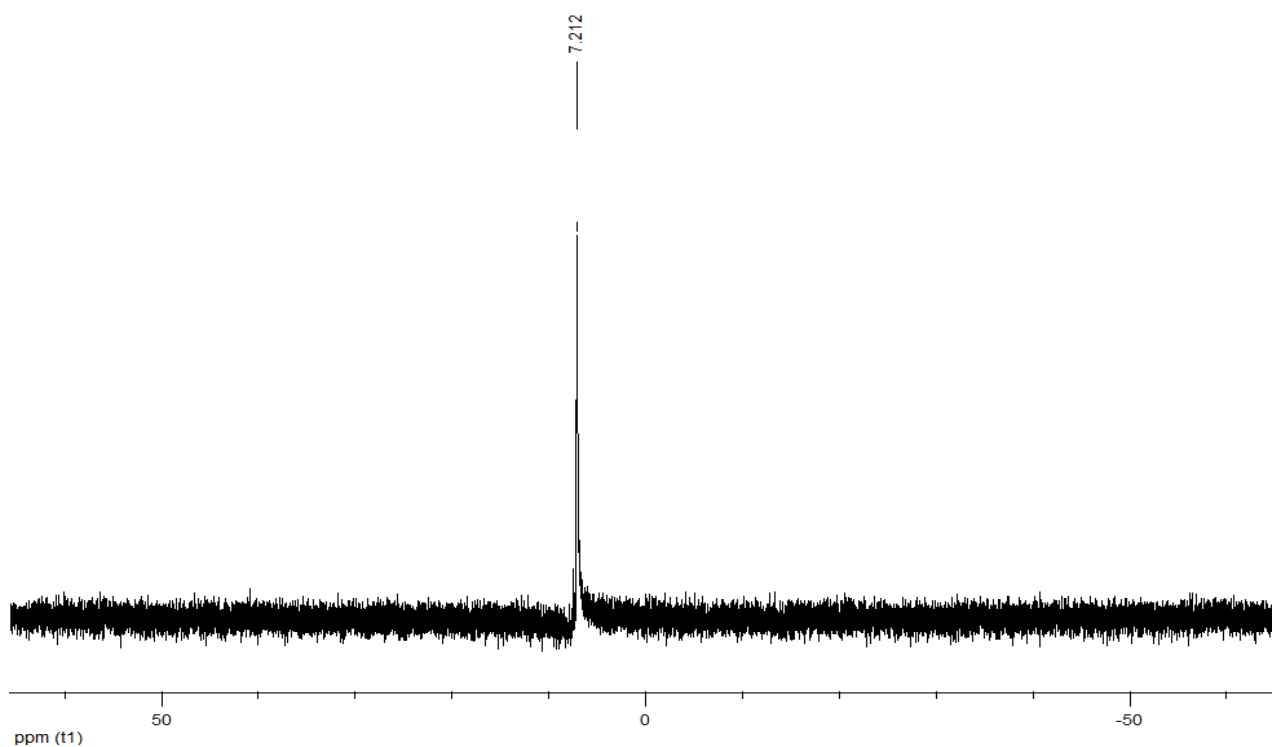


Figure S4. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **14a**.

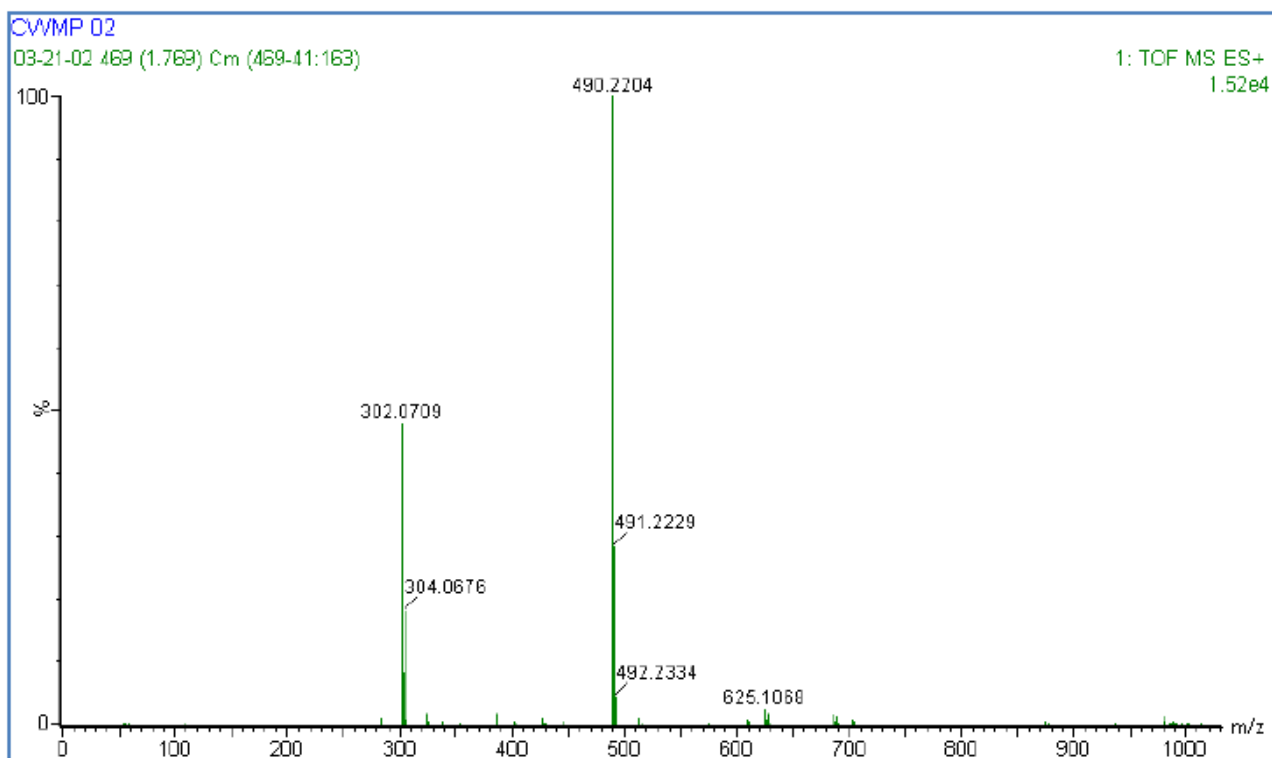


Figure S5. HRMS spectrum of **14a**.

Diisopropyl 3-(5-(ethoxycarbonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)propyl phosphoramidate (**14b**)

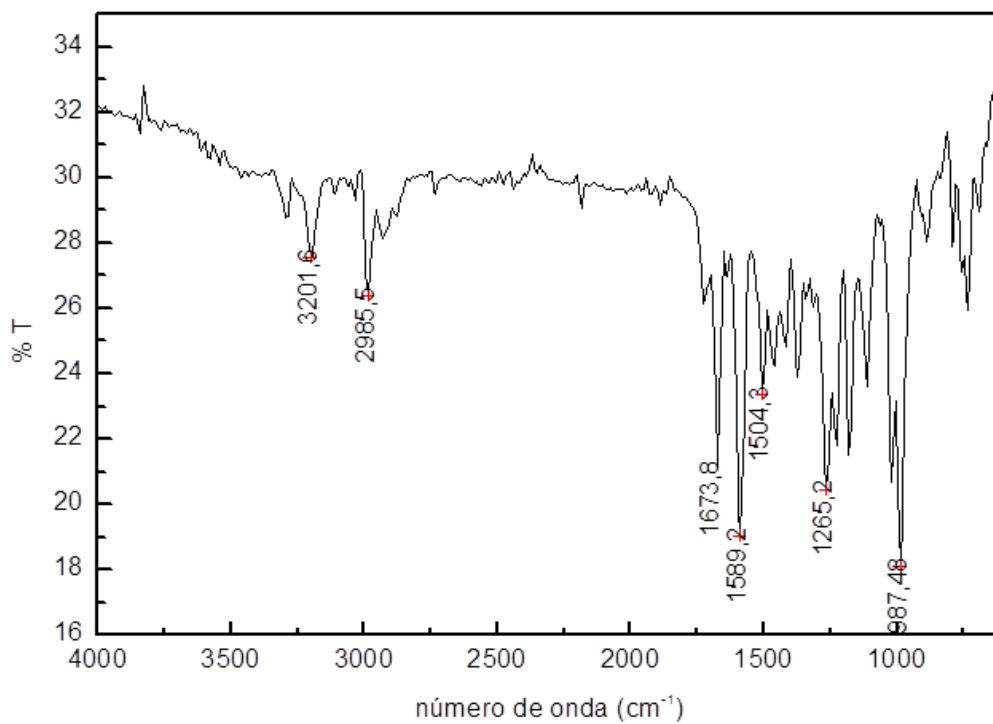
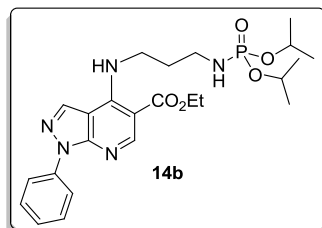


Figure S6. FTIR (KBr) spectrum of **14b**.

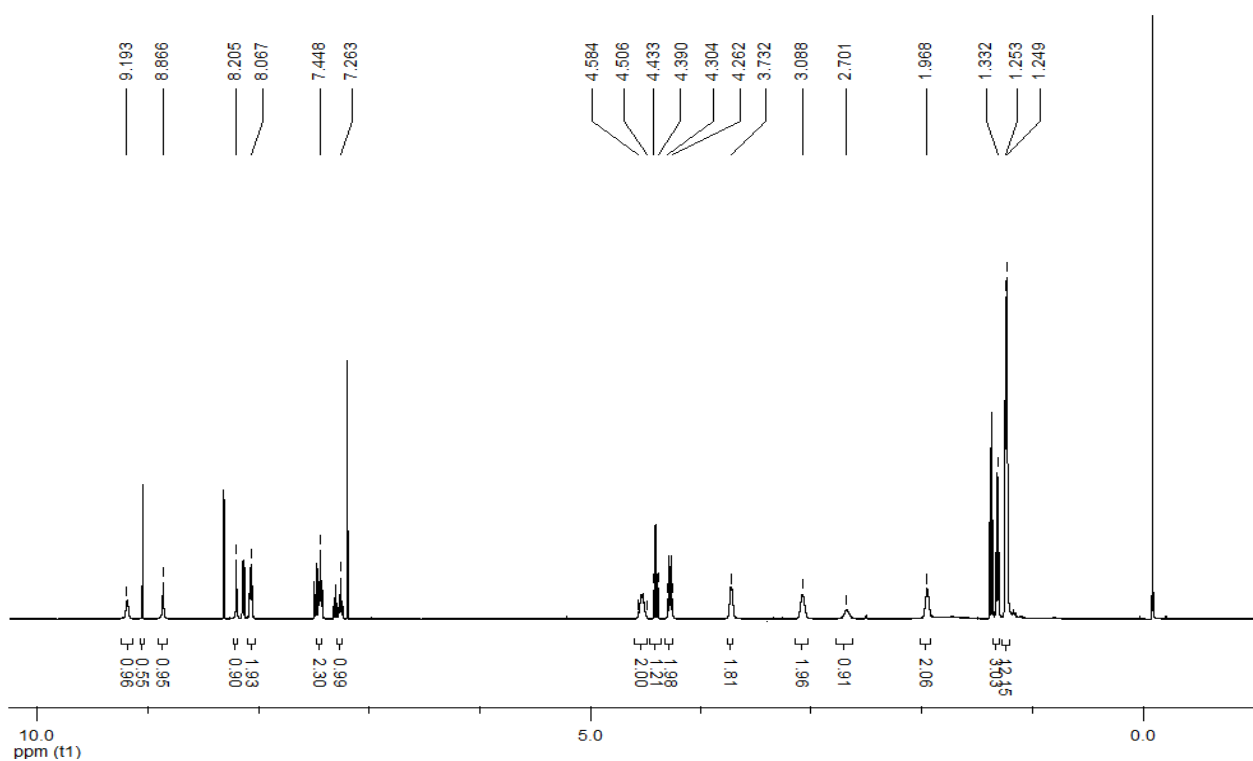


Figure S7. ¹H NMR spectrum (500 MHz, CDCl₃) of **14b**.

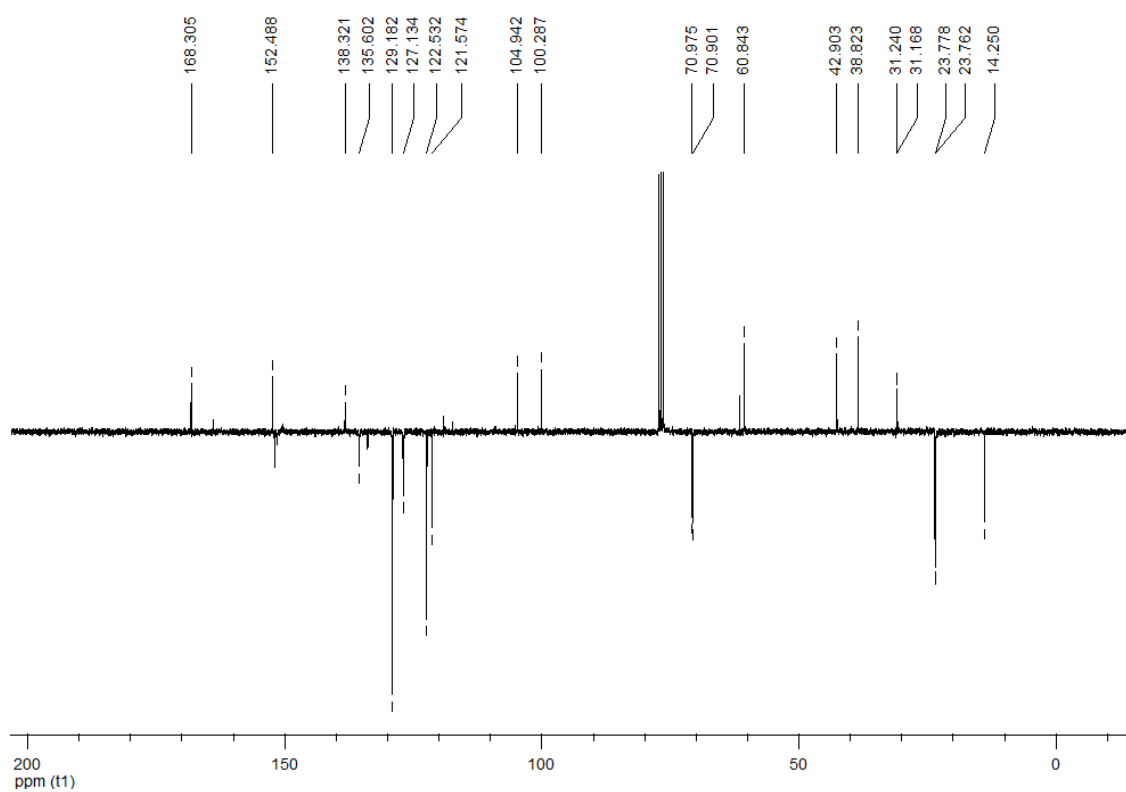


Figure S8. ^{13}C NMR spectrum (75 MHz, CDCl_3) of **14b**.

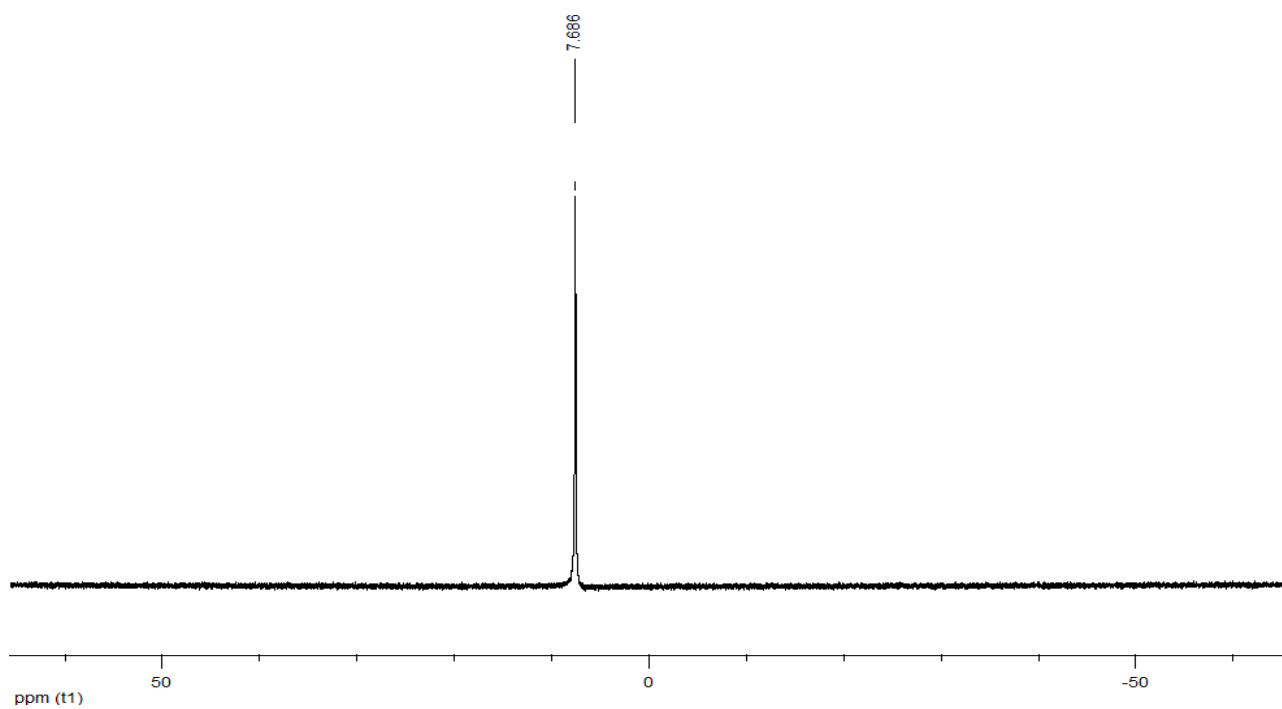


Figure S9. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **14b**.

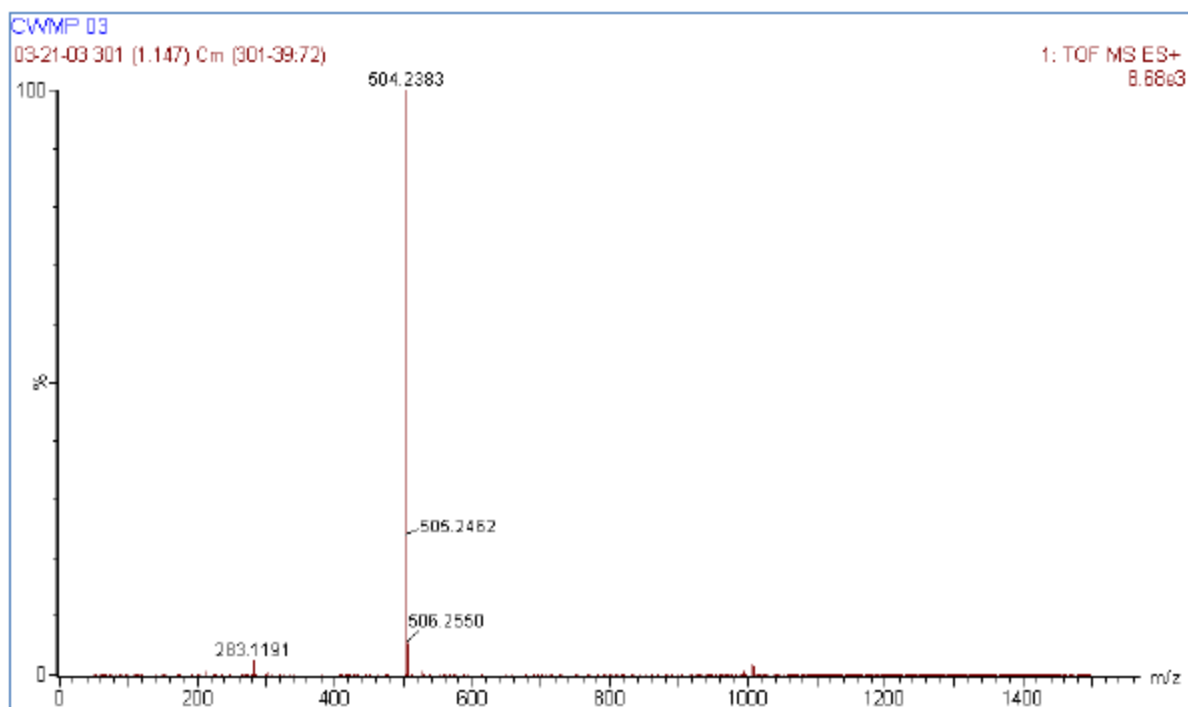


Figure S10. HRMS spectrum of **14b**.

Diisopropyl 4-(5-(ethoxycarbonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)butyl phosphoramidate (**14c**)

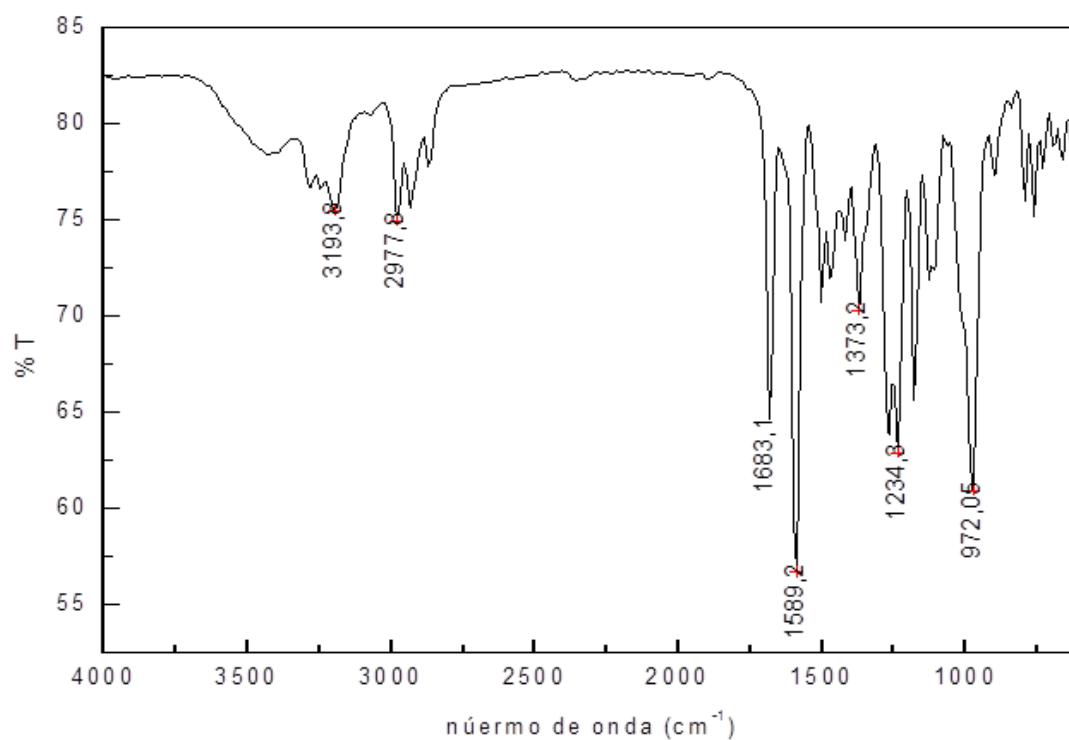
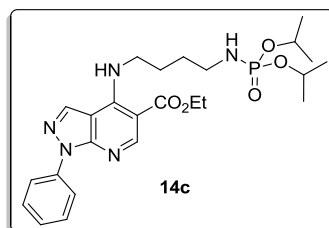


Figure S11. FTIR (KBr) spectrum of **14c**.

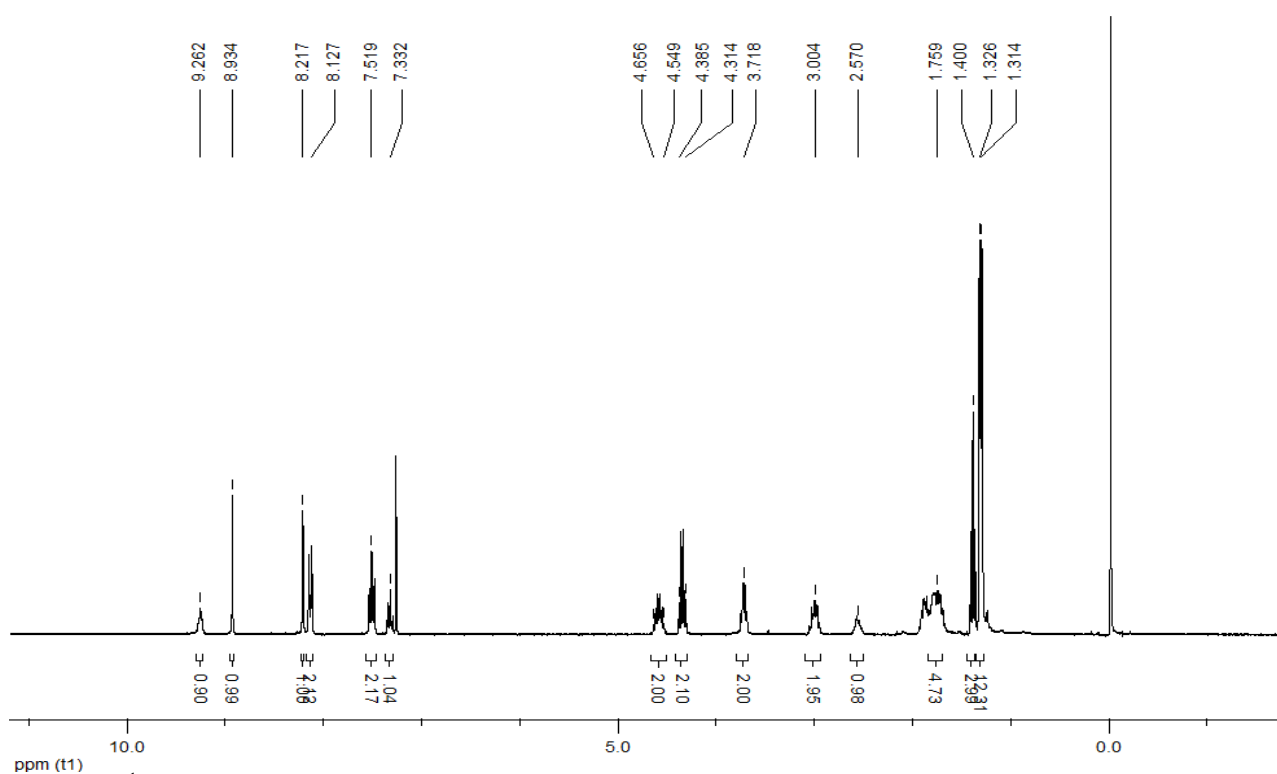


Figure S12. ¹H NMR spectrum (300 MHz, CDCl₃) of **14c**.

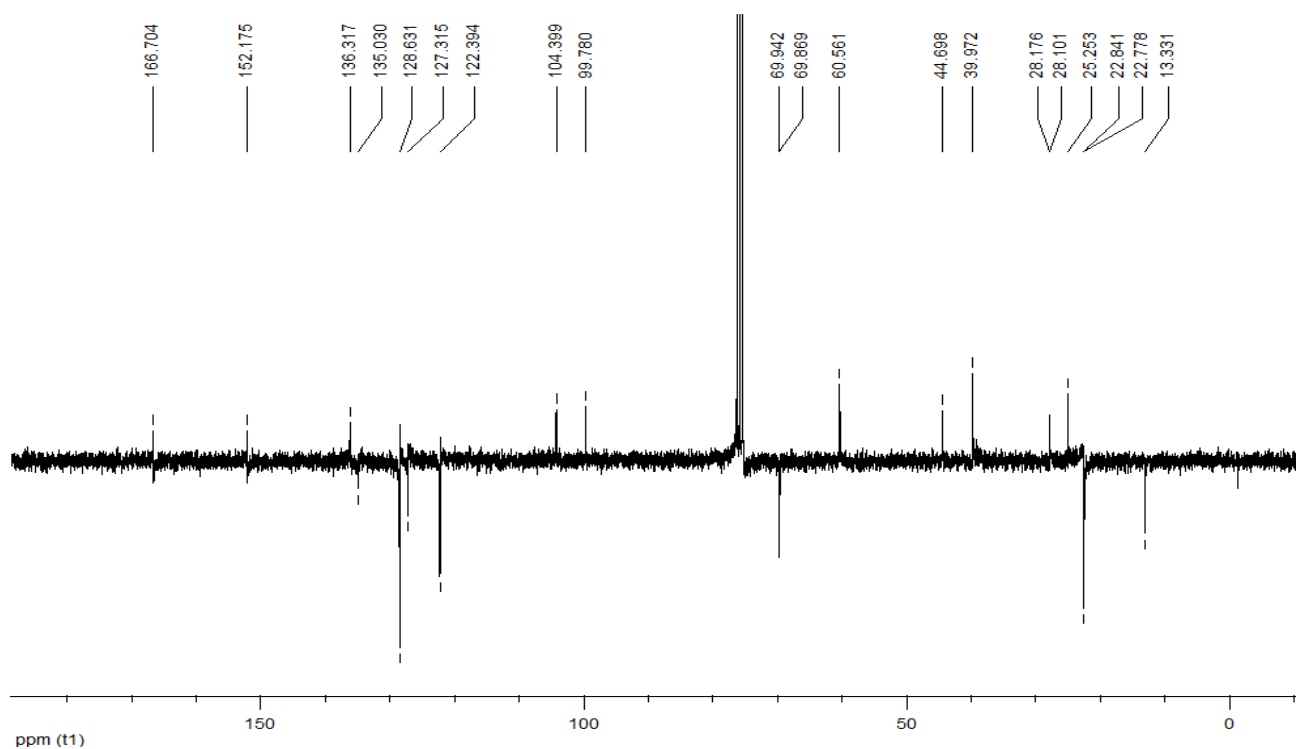


Figure S13. ¹³C NMR spectrum (75 MHz, CDCl₃) of **14c**.

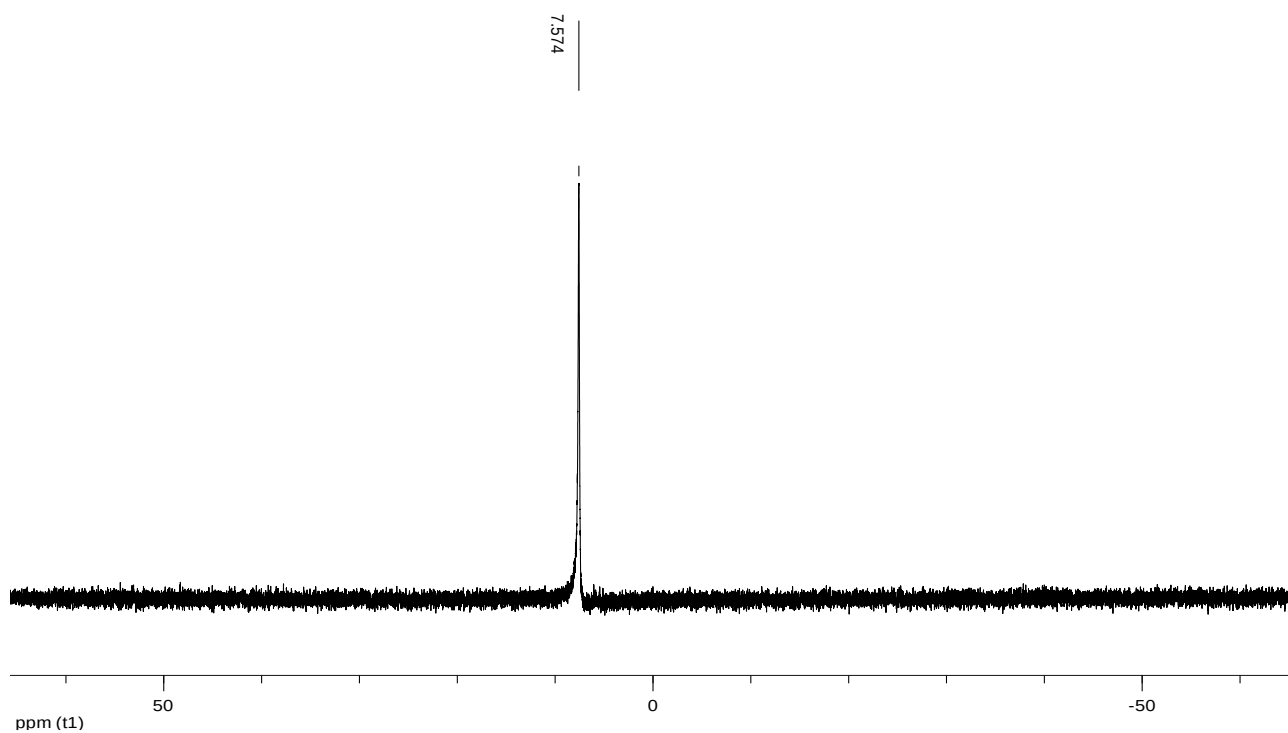


Figure S14. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (121 MHz, CDCl_3) of **14c**.

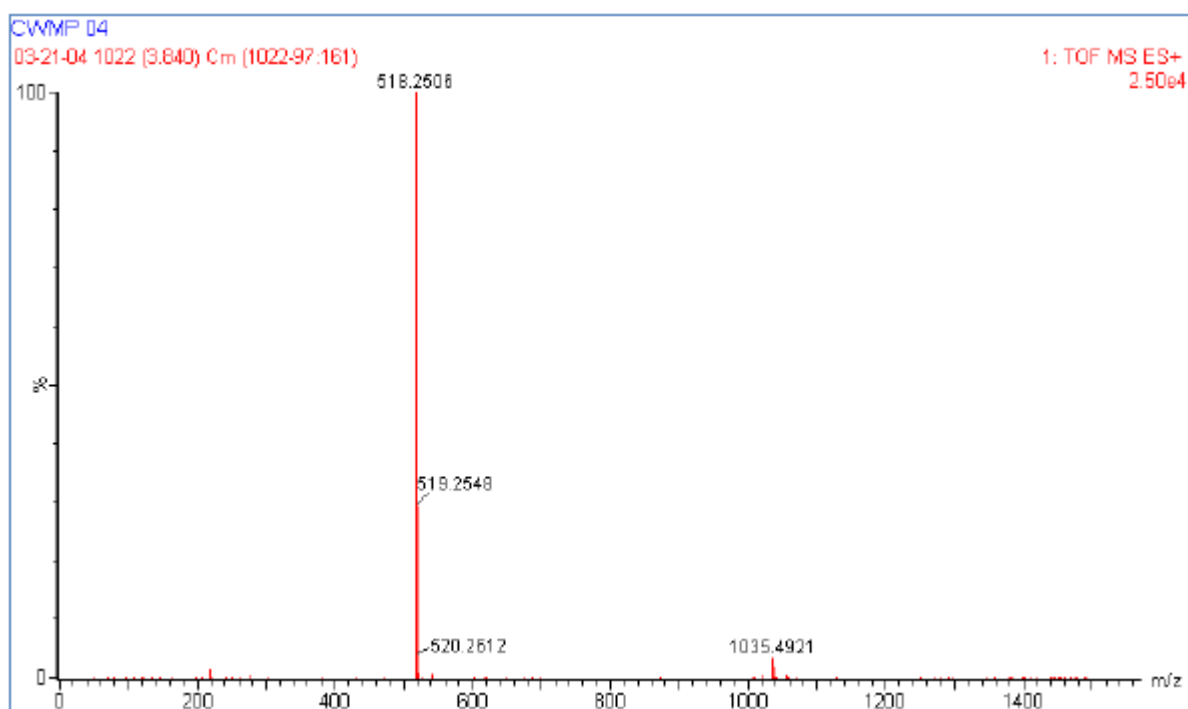


Figure S15. HRMS spectrum of **14c**.

Diisopropyl 5-(5-(ethoxycarbonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)pentyl phosphoramidate (**14d**)

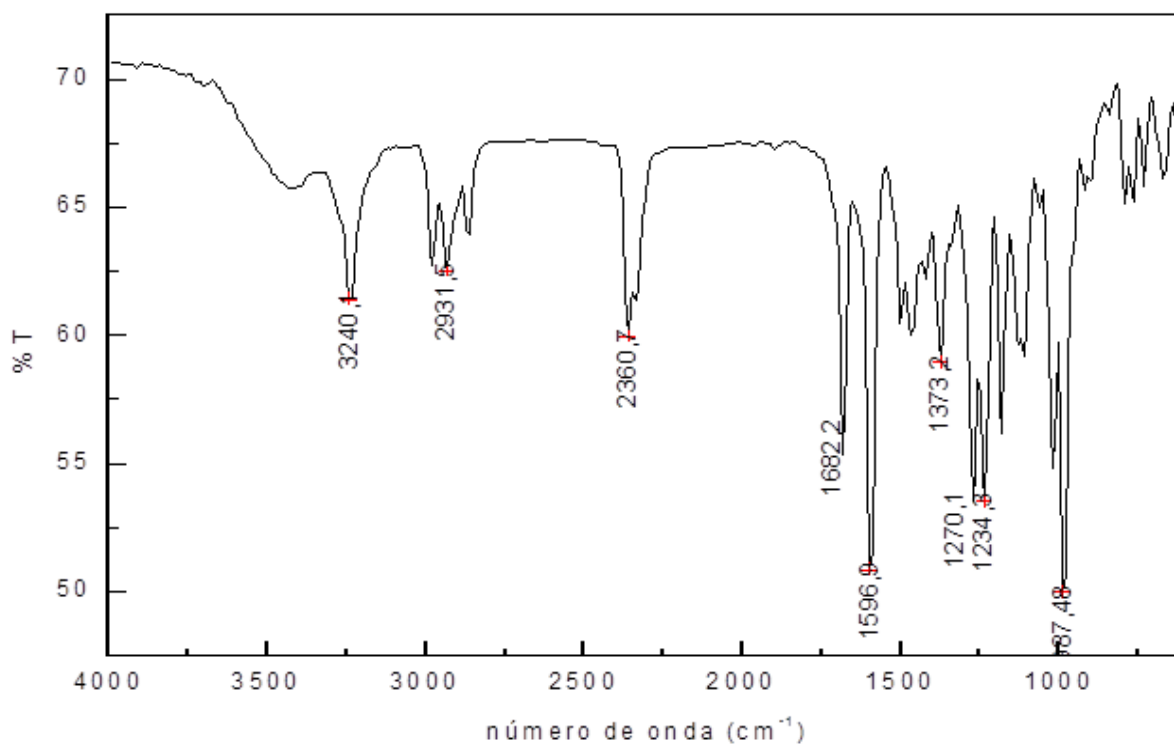
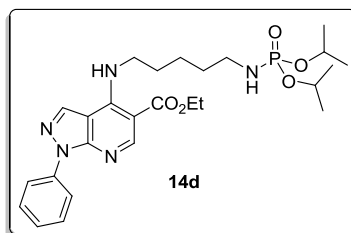


Figure S16. FTIR (KBr) spectrum of **14d**.

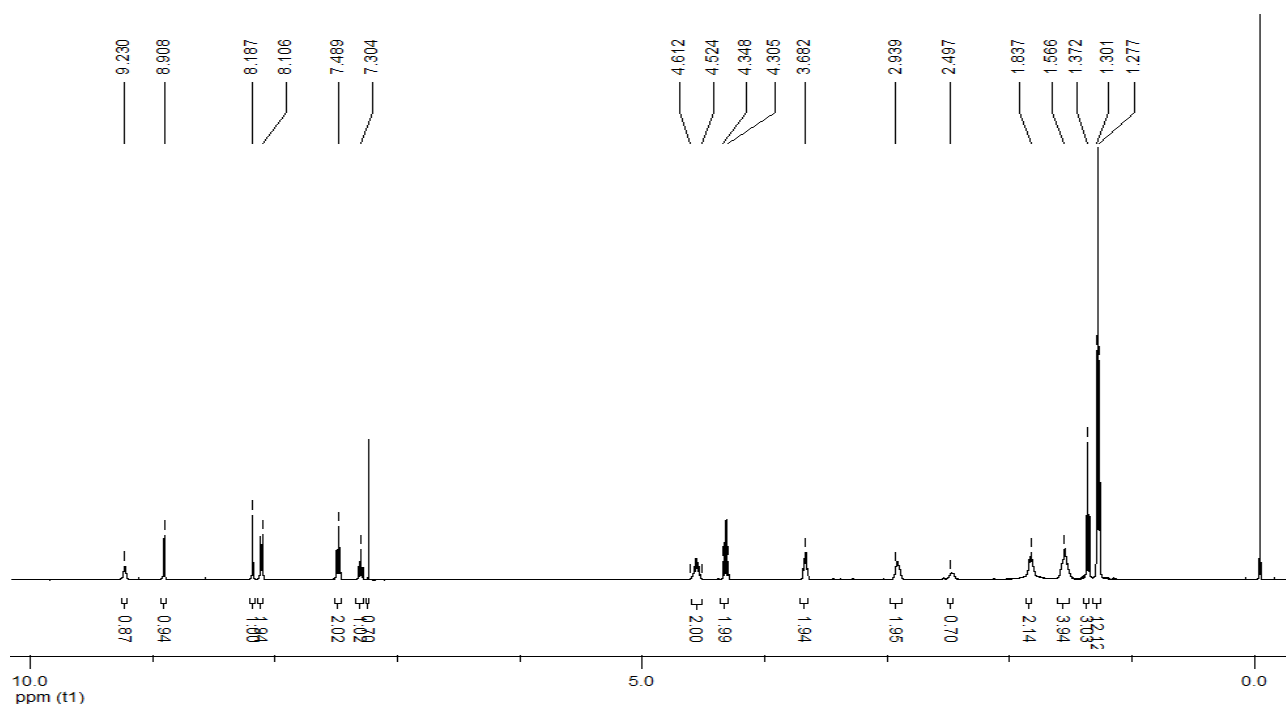


Figure S17. ^1H NMR spectrum (500 MHz, CDCl_3) of **14d**.

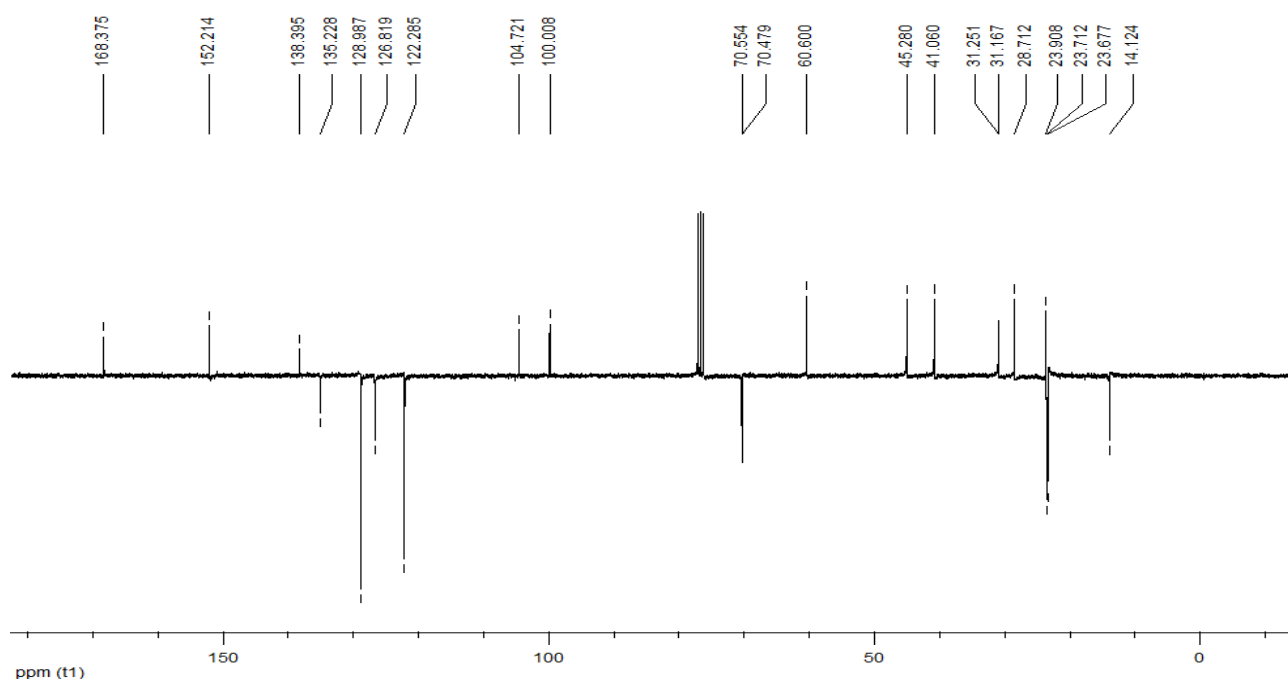


Figure S18. ^{13}C NMR spectrum (75 MHz, CDCl_3) of **14d**.

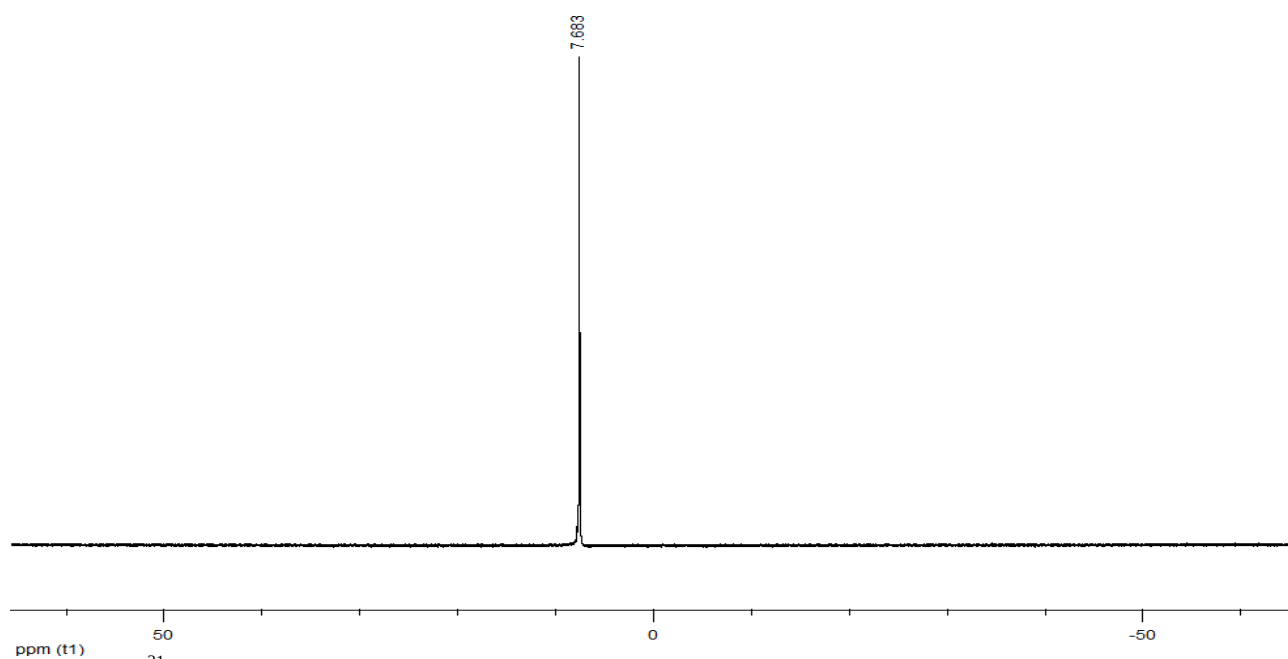


Figure S19. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **14d**.

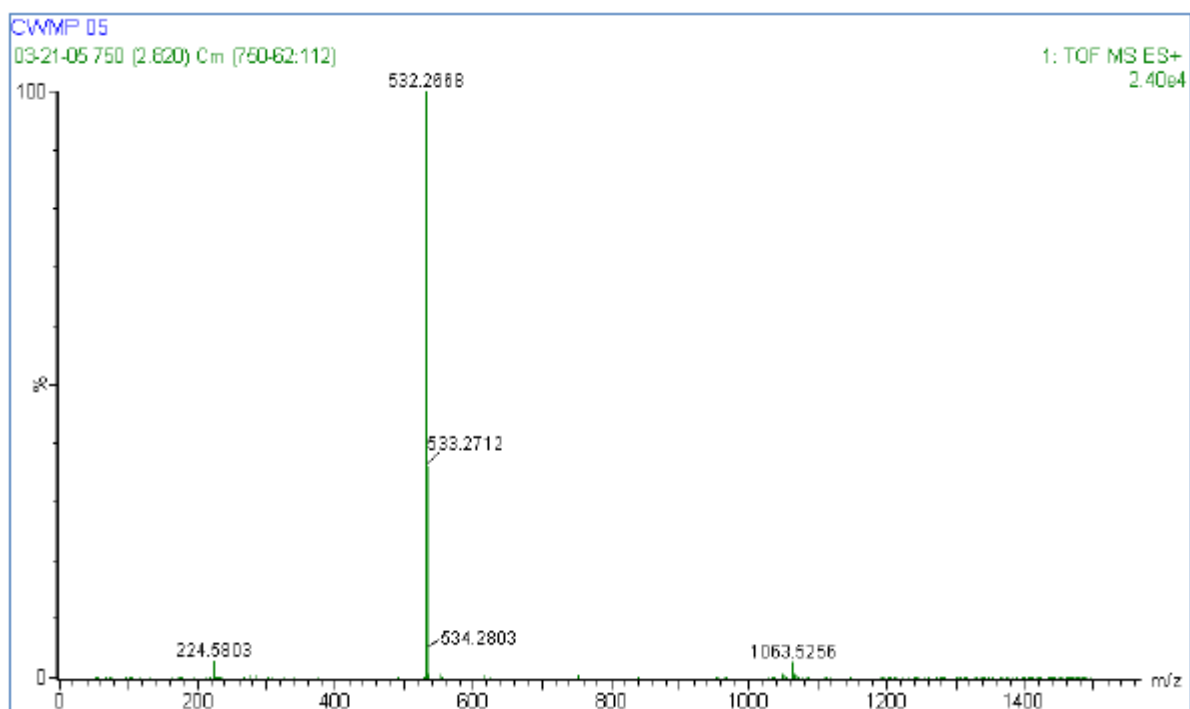


Figure S20. HRMS spectrum of **14d**.

Diisopropyl 6-(5-(ethoxycarbonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)hexyl phosphoramidate (**14e**)

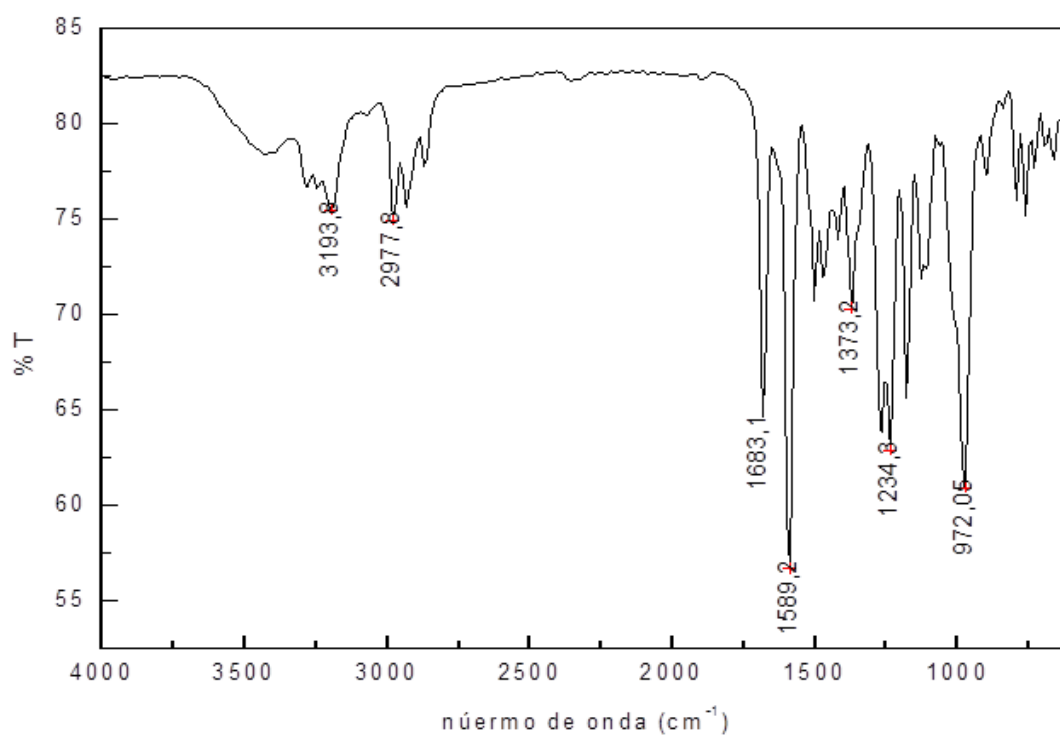
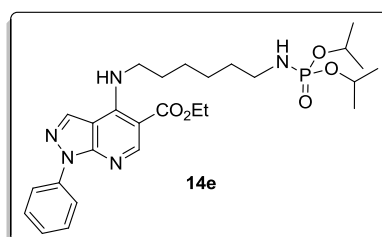


Figure S21. FTIR (KBr) spectrum of **14e**.

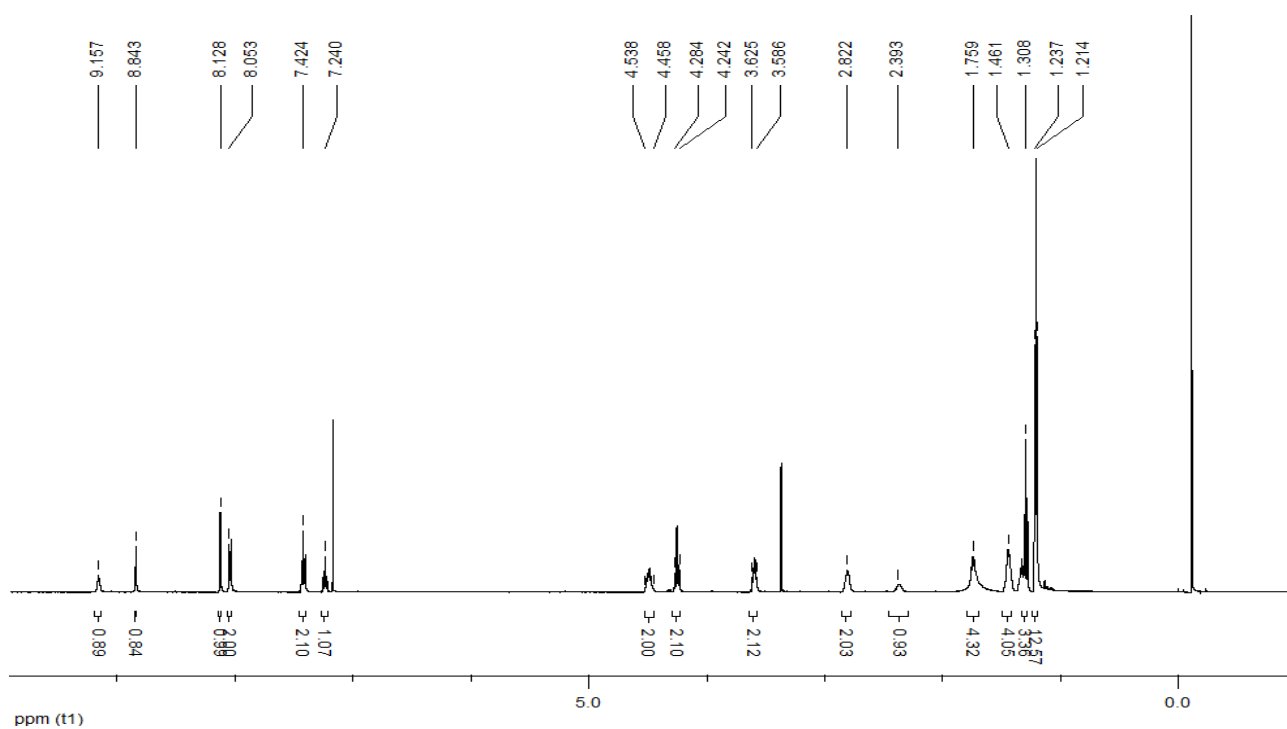


Figure S22. ¹H NMR spectrum (500 MHz, CDCl₃) of **14e**.

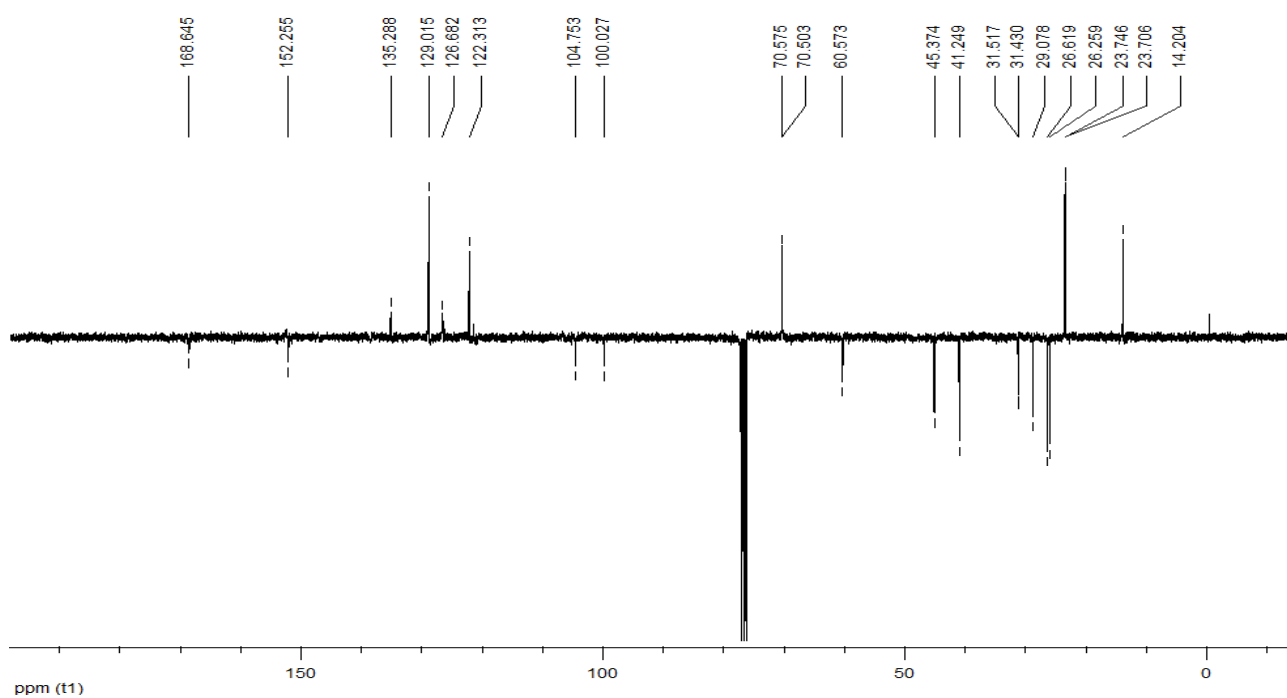


Figure S23. ¹³C NMR spectrum (75 MHz, CDCl₃) of **14e**.

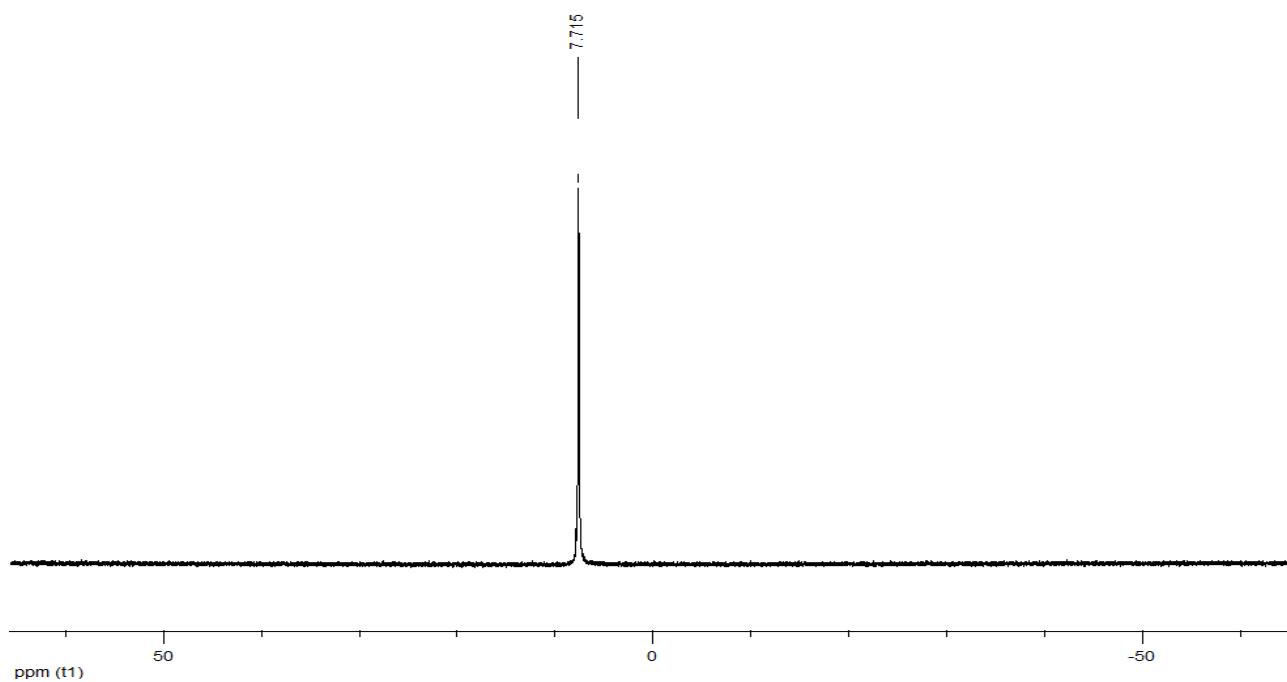


Figure S24. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **14e**.

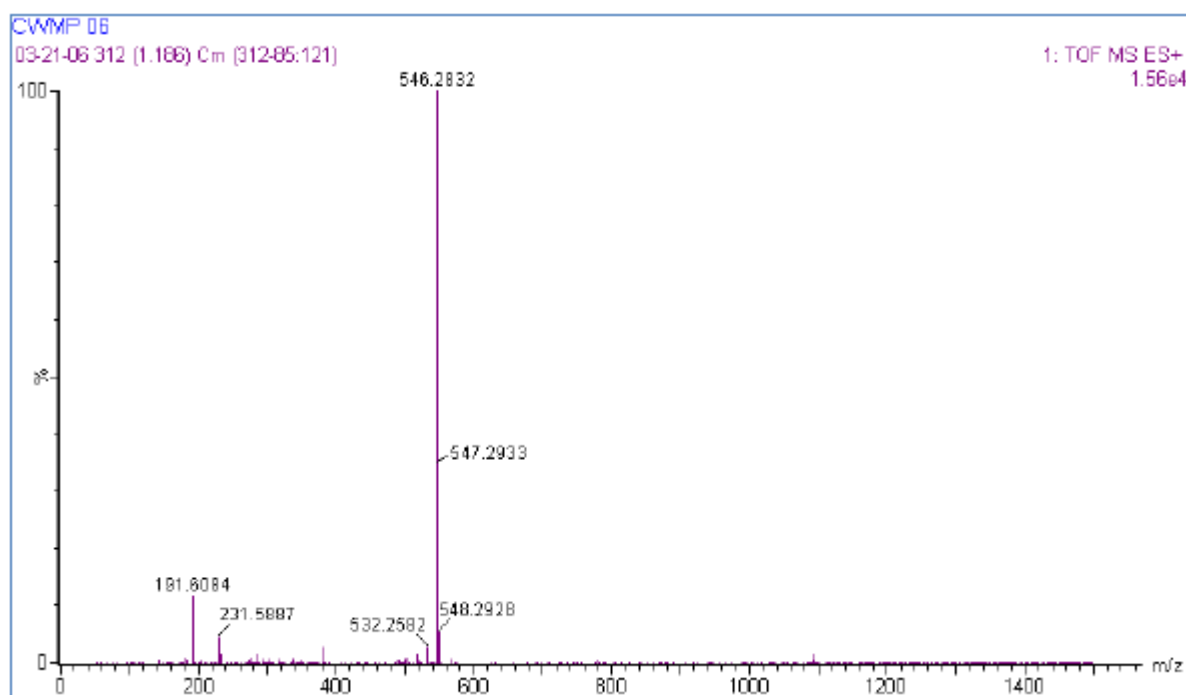
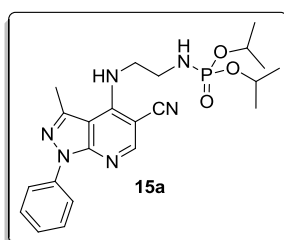


Figure S25. HRMS spectrum of **14e**.

Diisopropyl 2-(5-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)ethyl phosphoramidate (**15a**)



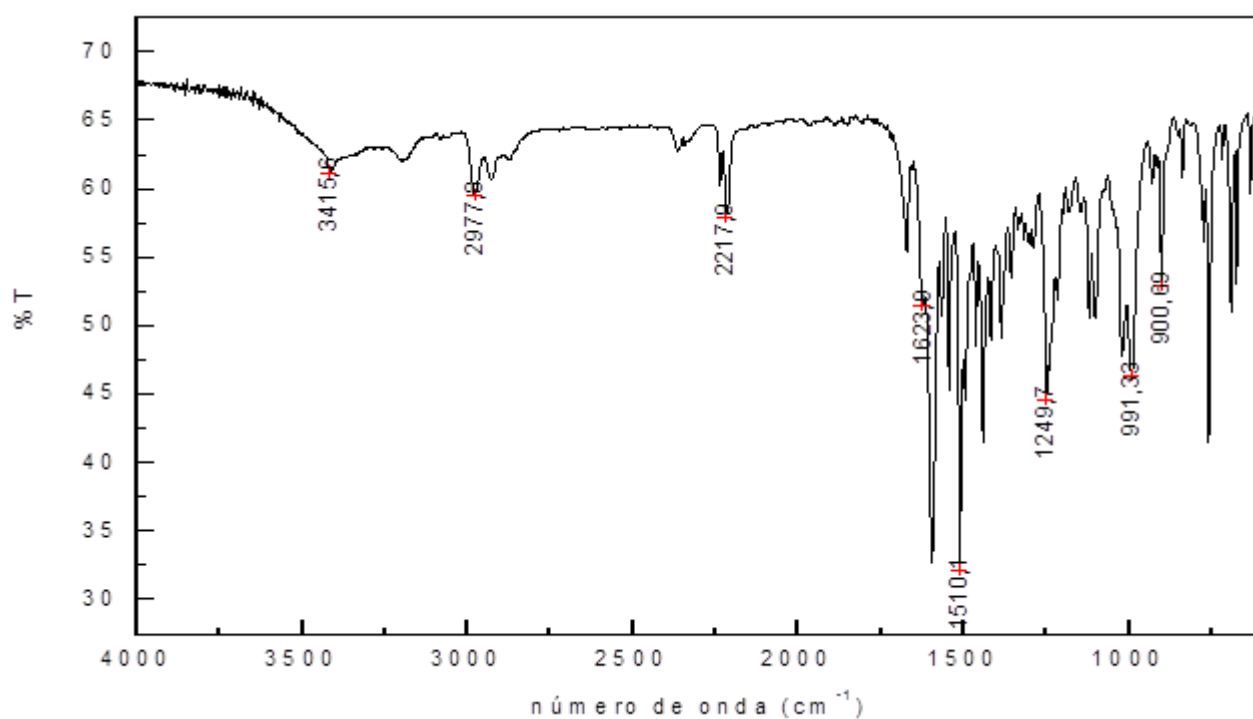


Figure S26. FTIR (KBr) spectrum of **15a**.

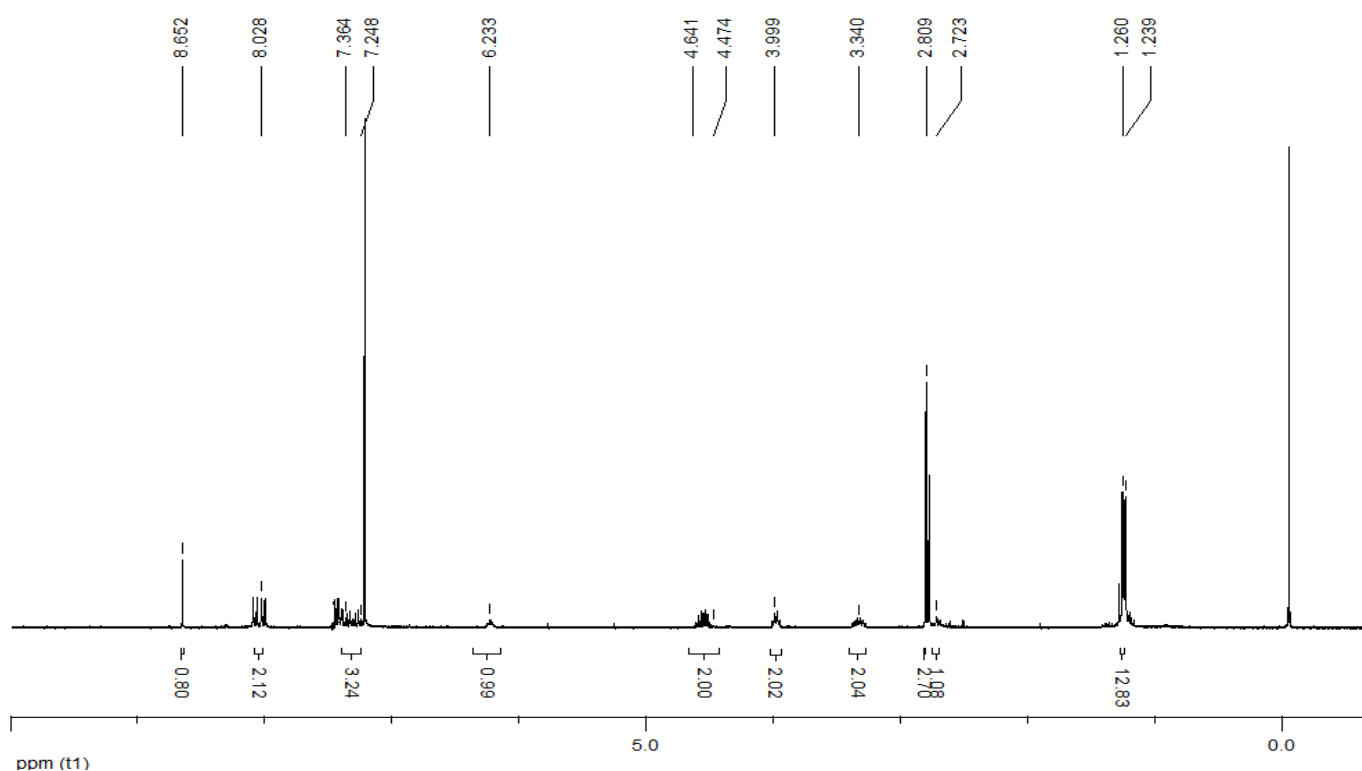


Figure S27. ^1H NMR spectrum (300 MHz, CDCl_3) of **15a**.

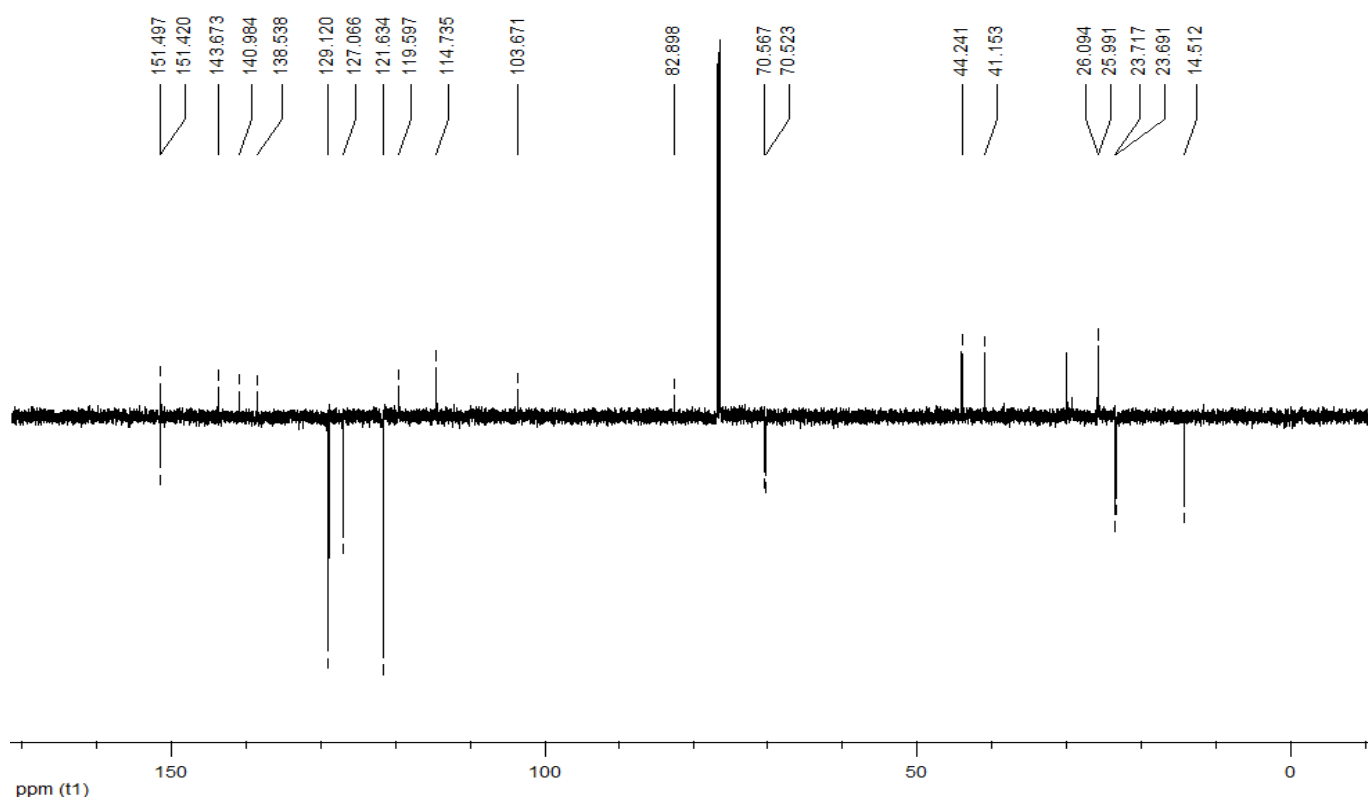


Figure S28. ¹³C NMR spectrum (125 MHz, CDCl₃) of **15a**.

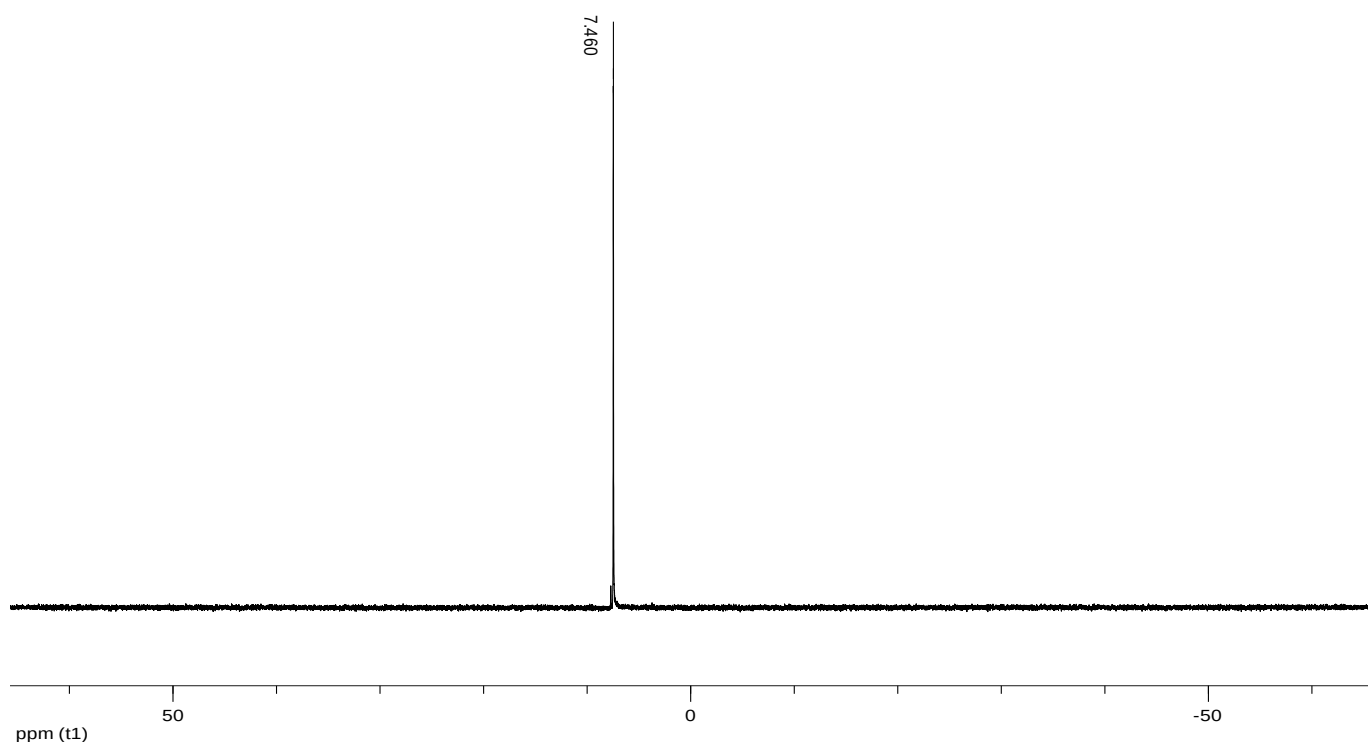


Figure S29. ³¹P{¹H} NMR spectrum (202 MHz, CDCl₃) of **15a**.

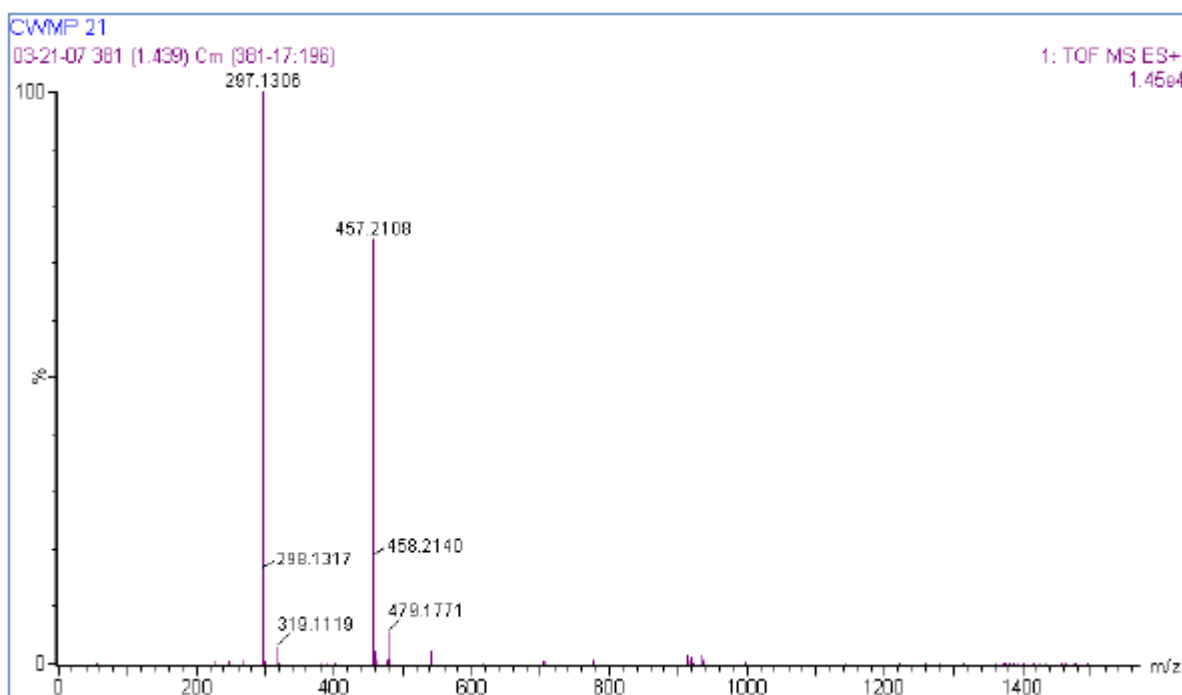


Figure S30. HRMS spectrum of **15a**.

Diisopropyl 3-(5-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)propyl phosphoramidate (**15b**)

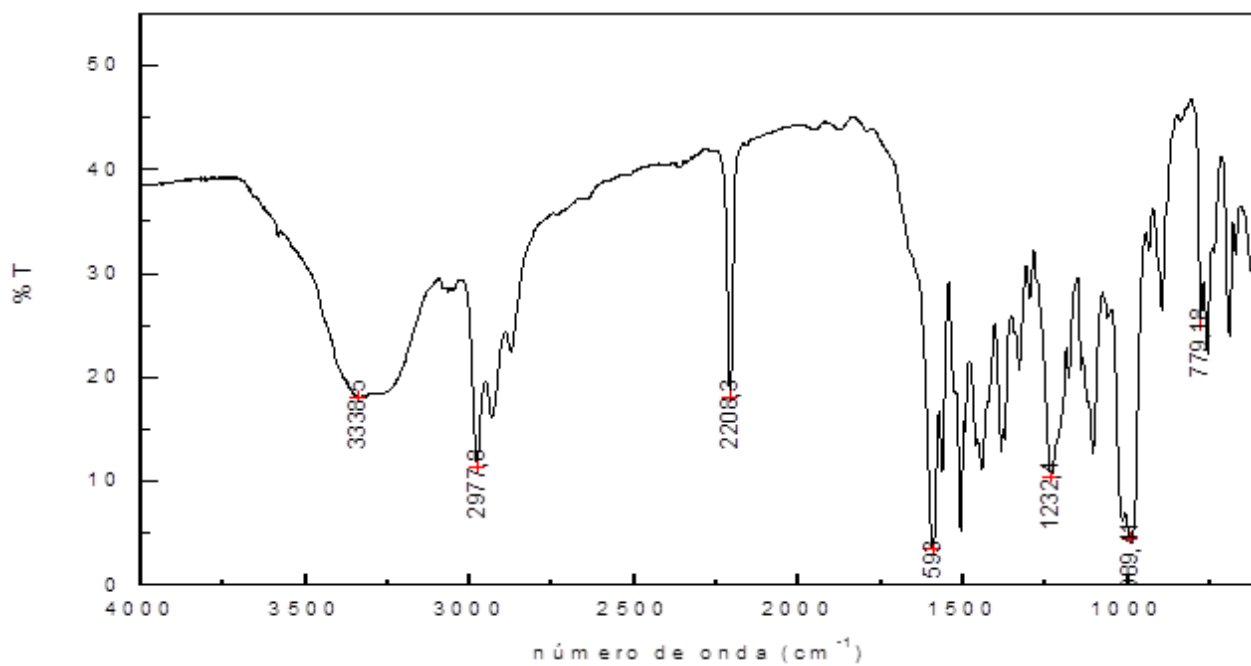
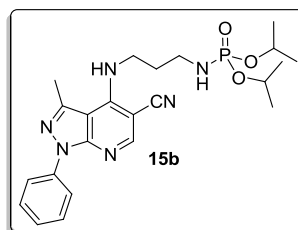


Figure S31. FTIR (KBr) spectrum of **15b**.

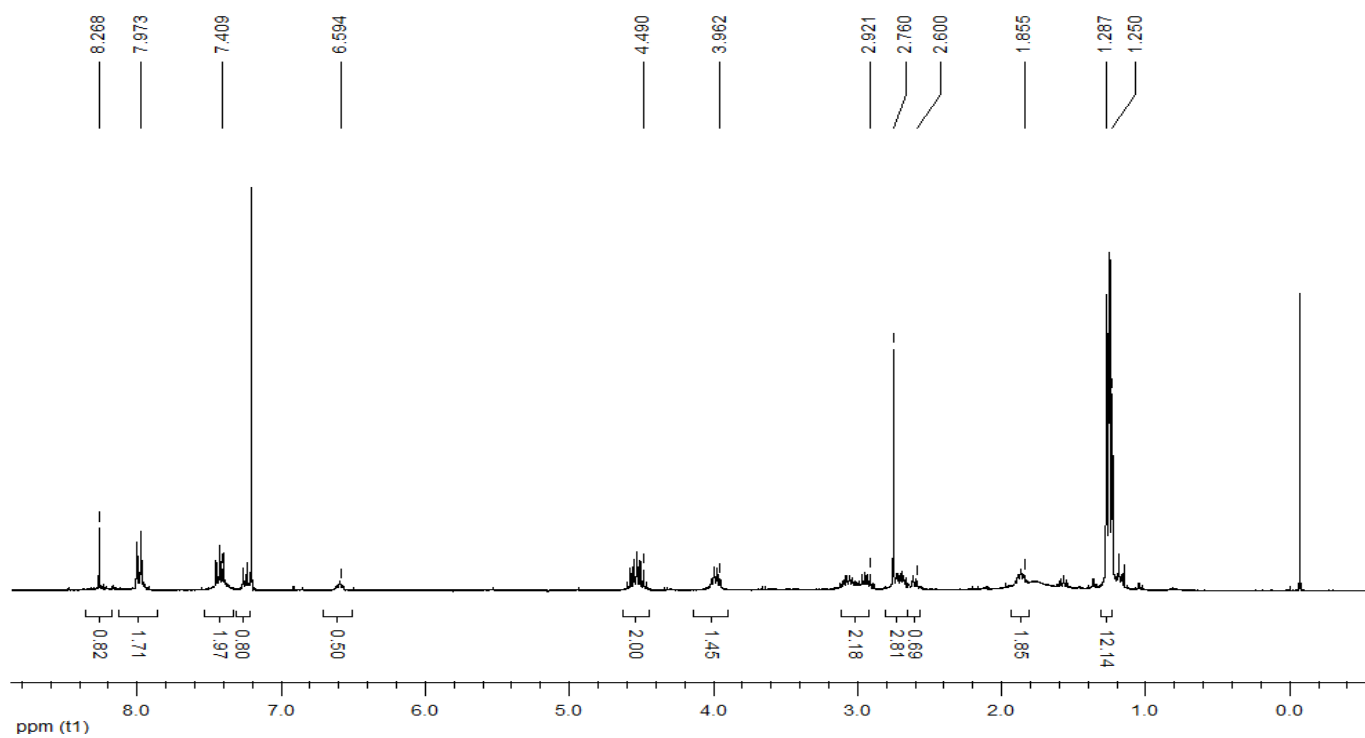


Figure S32. ¹H NMR spectrum (300 MHz, CDCl₃) of **15b**.

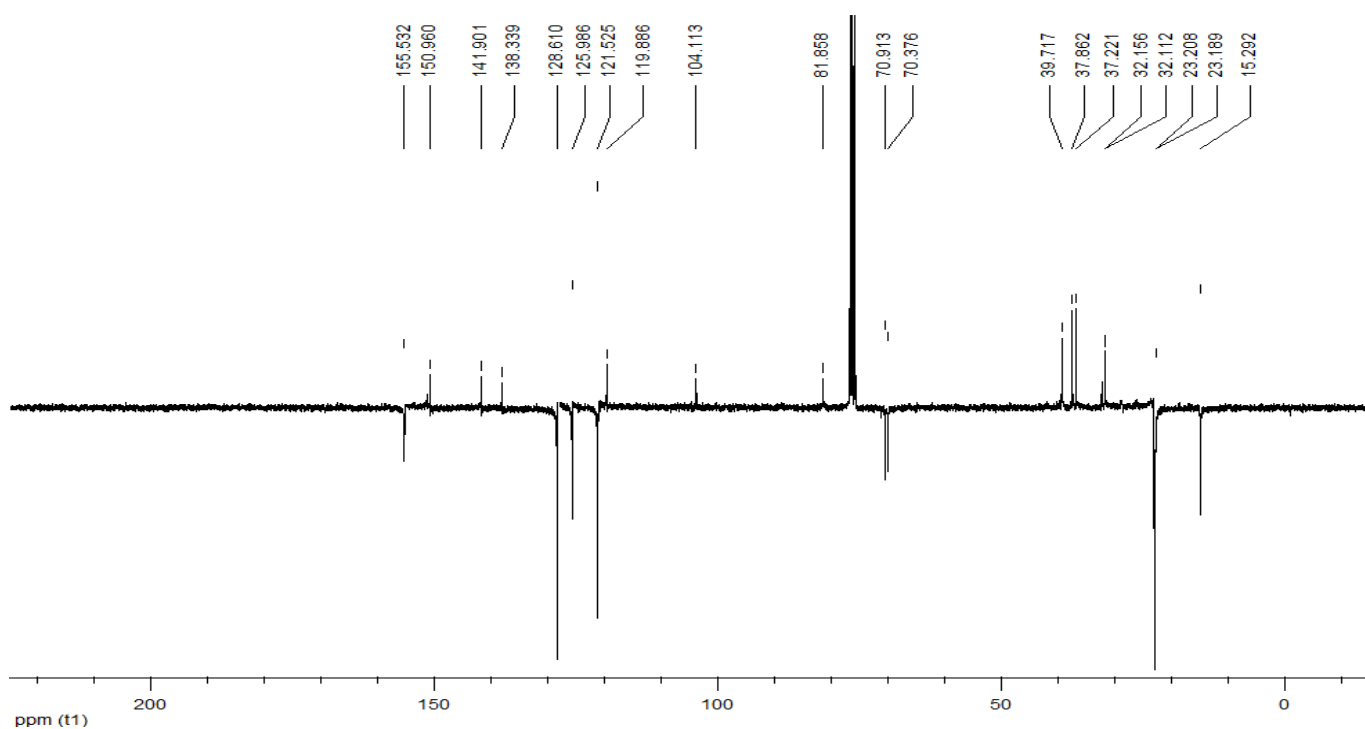


Figure S33. ¹³C NMR spectrum (75 MHz, CDCl₃) of **15b**.

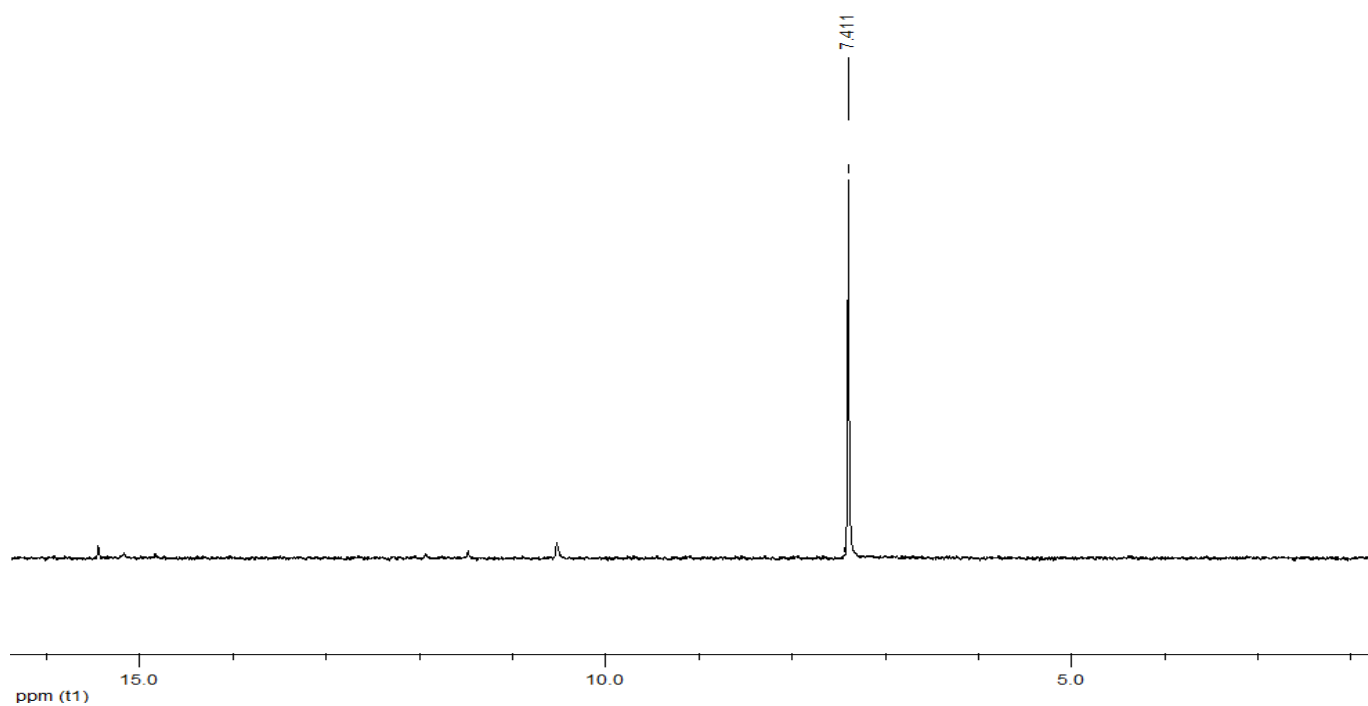


Figure S34. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **15b**.

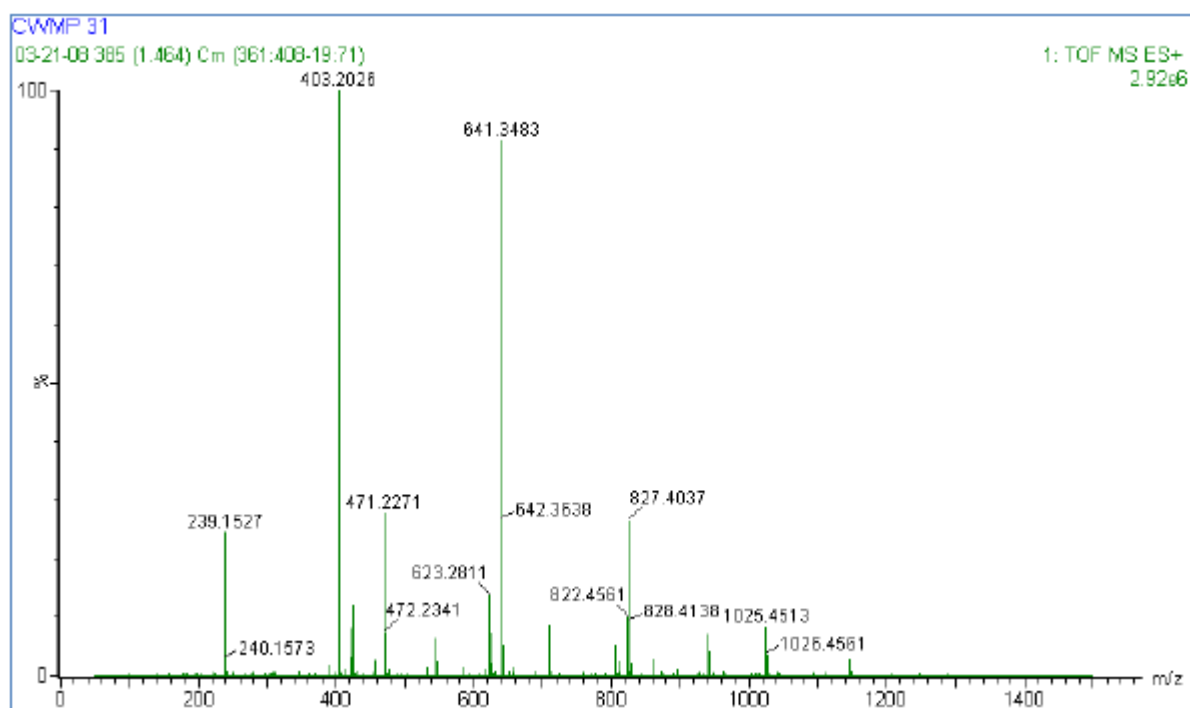


Figure S35. HRMS spectrum of **15b**.

Diisopropyl 4-(5-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)butyl phosphoramidate (**15c**)

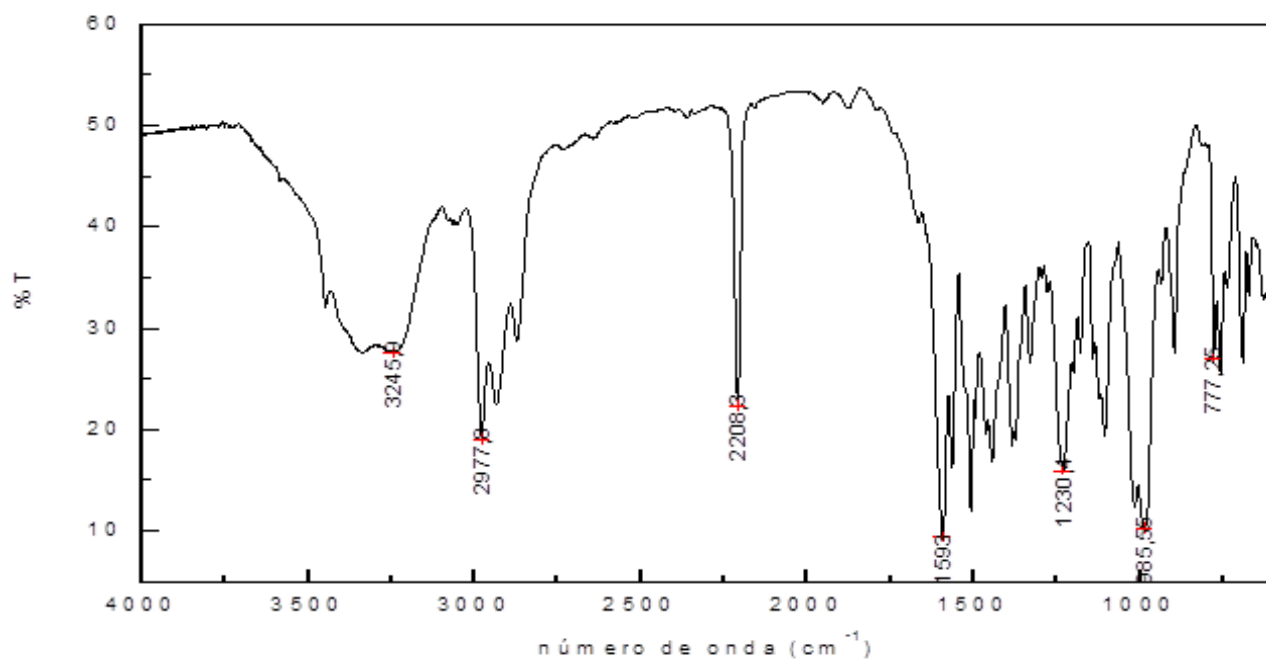
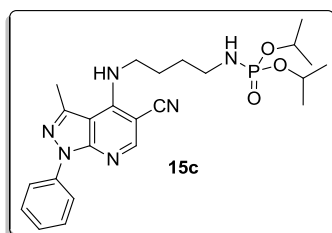


Figure S36. FTIR (KBr) spectrum of **15c**.

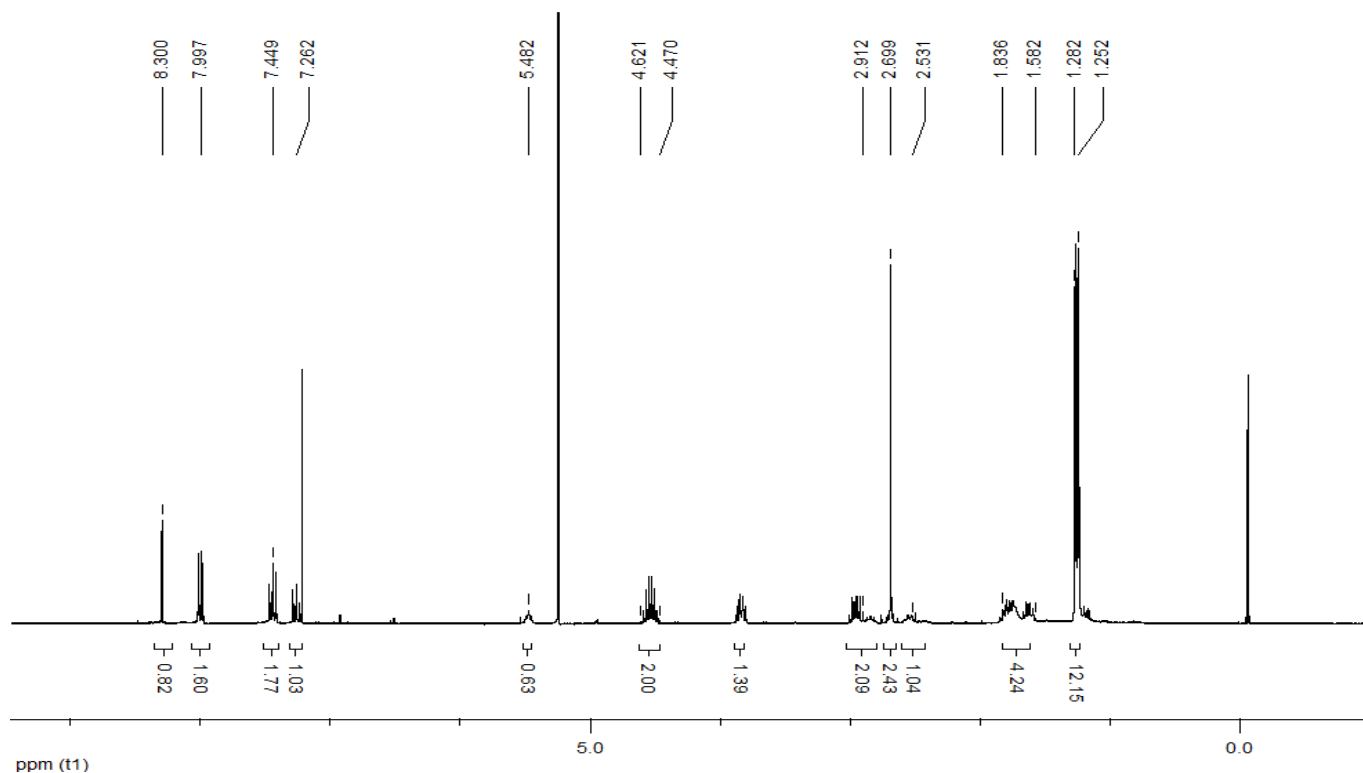


Figure S37. ^1H NMR spectrum (300 MHz, CDCl_3) of **15c**.

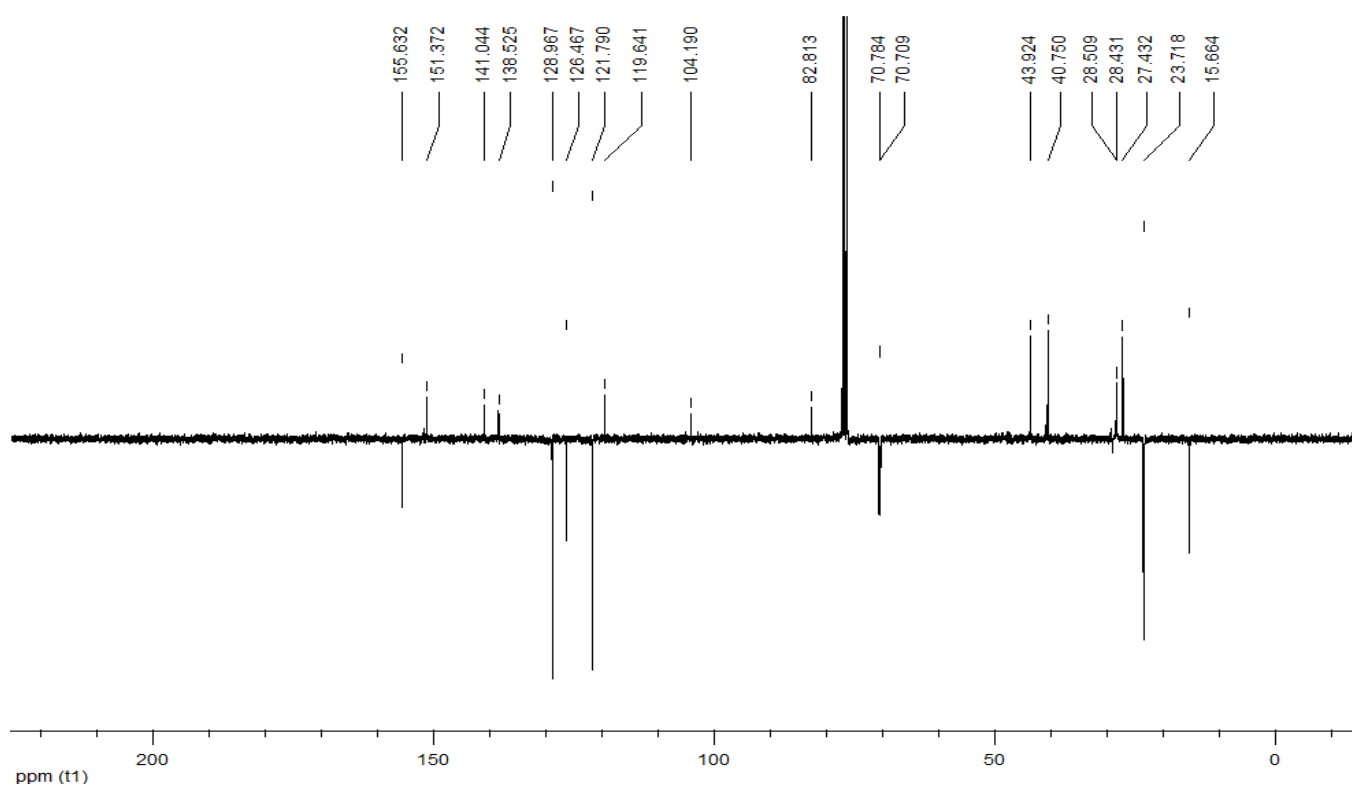


Figure S38. ^{13}C NMR spectrum (75 MHz, CDCl_3) of **15c**.

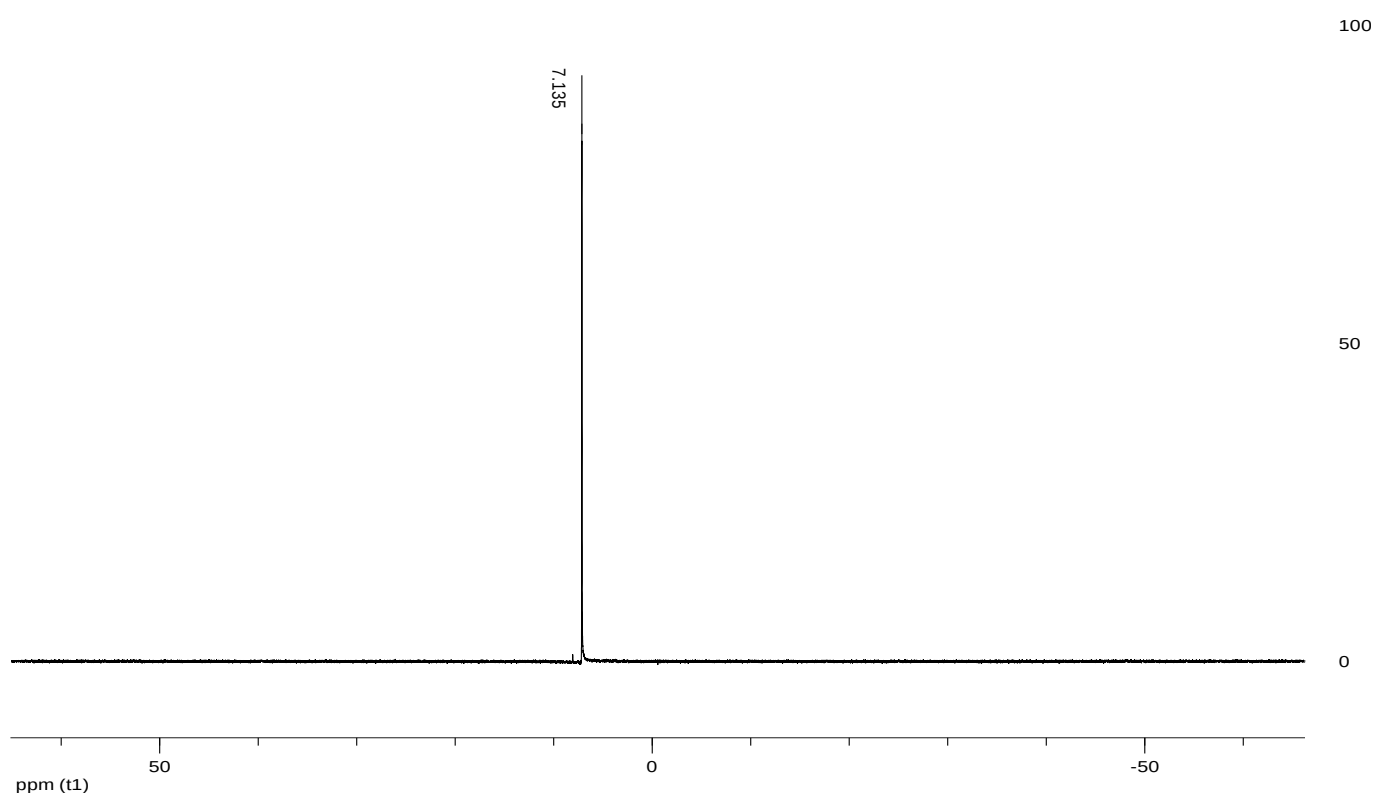


Figure S39. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **15c**.

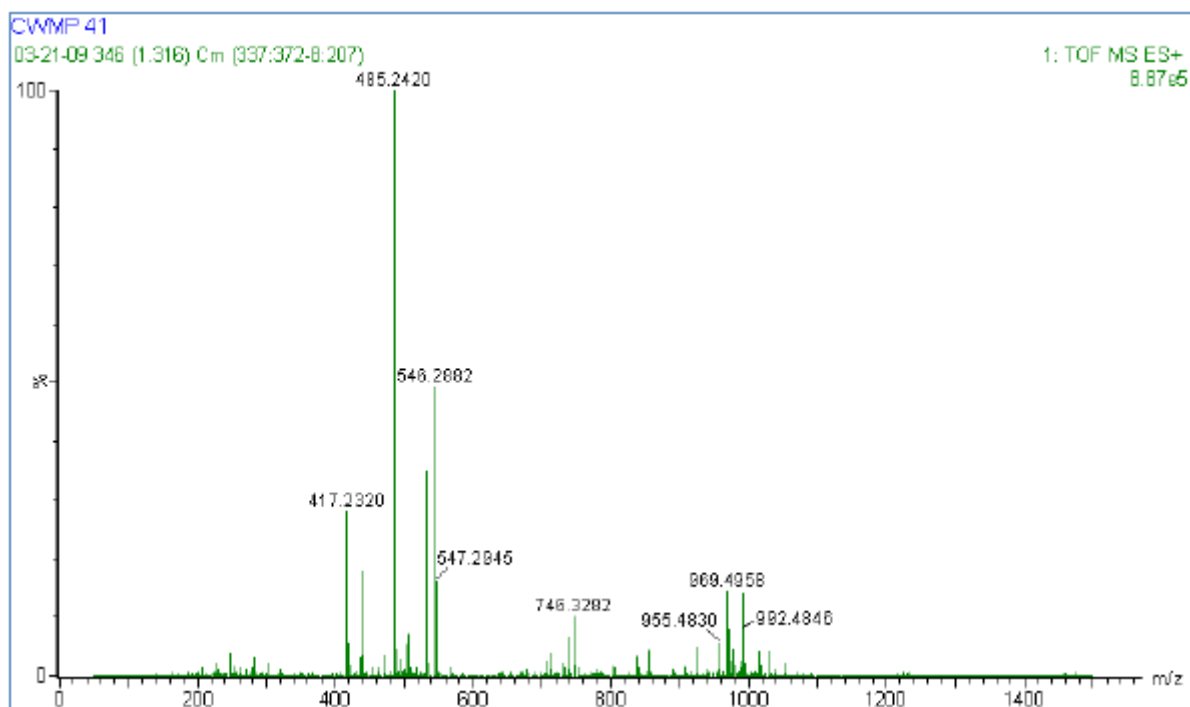


Figure S40. HRMS spectrum of **15c**.

Diisopropyl 5-(5-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)pentyl phosphoramidate (**15d**)

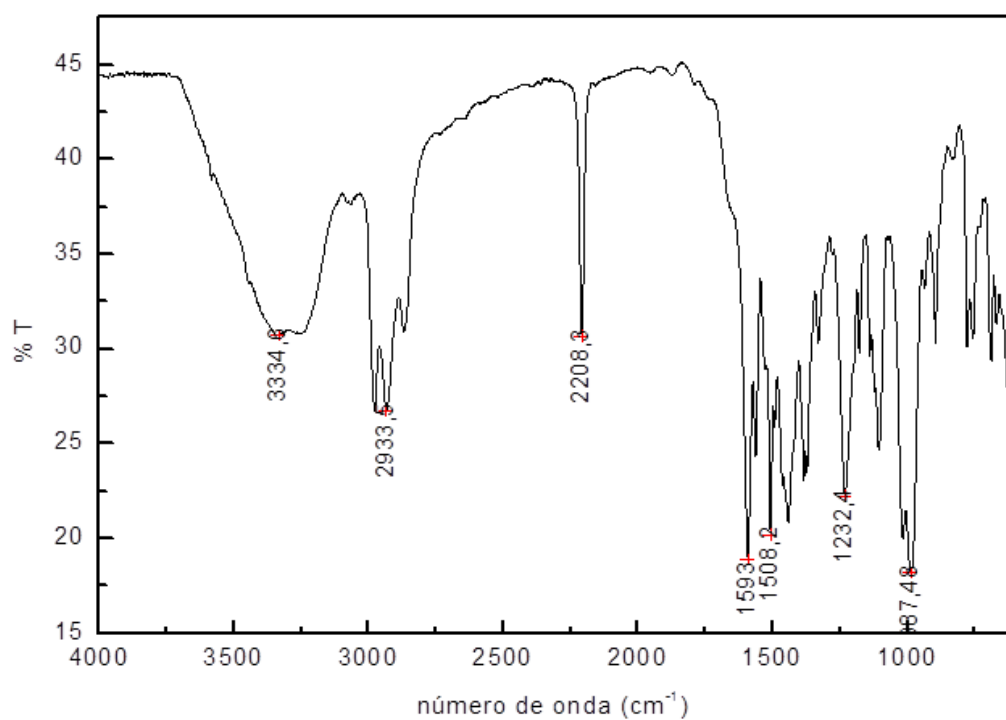
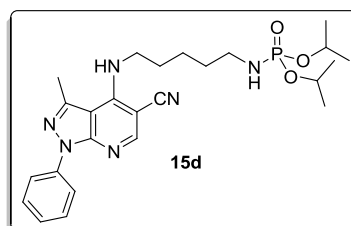


Figure S41. FTIR (KBr) spectrum of **15d**.

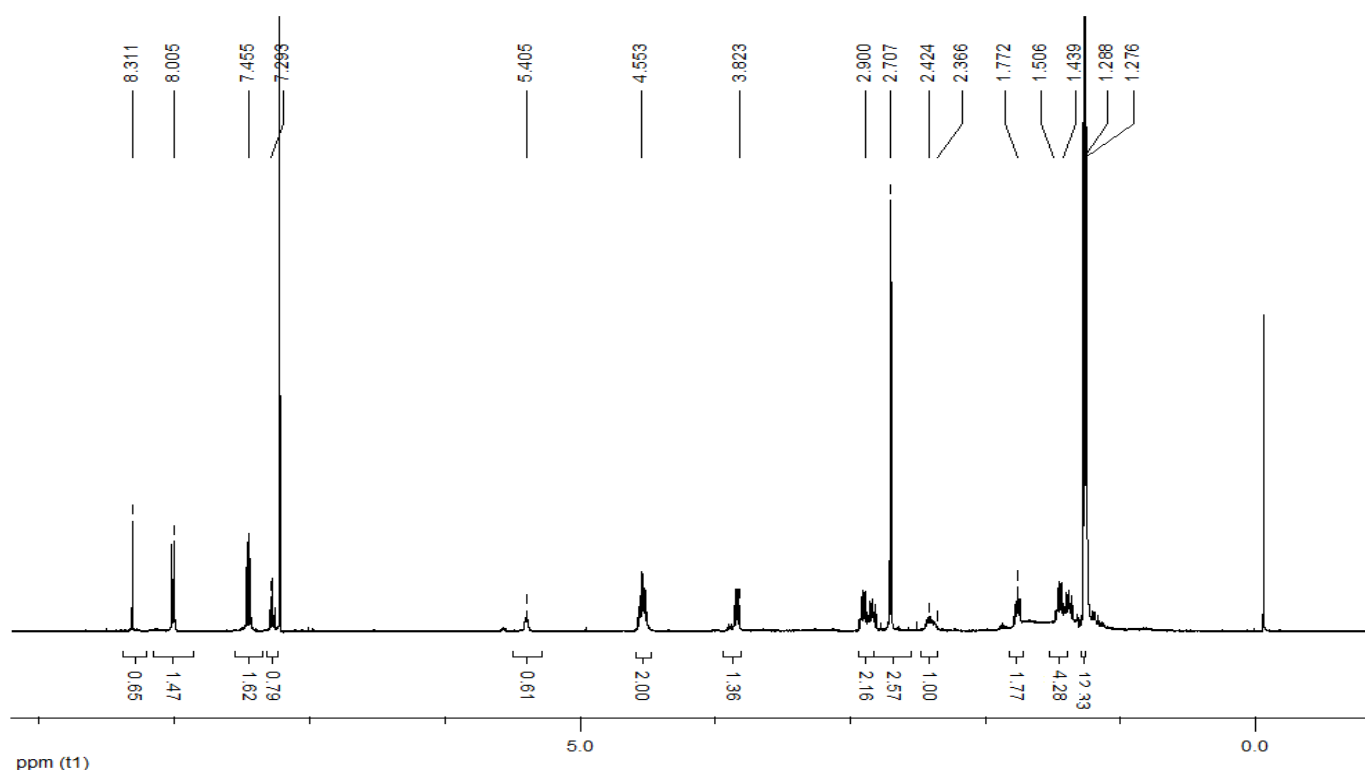


Figure S42. ¹H NMR spectrum (500 MHz, CDCl₃) of **15d**.

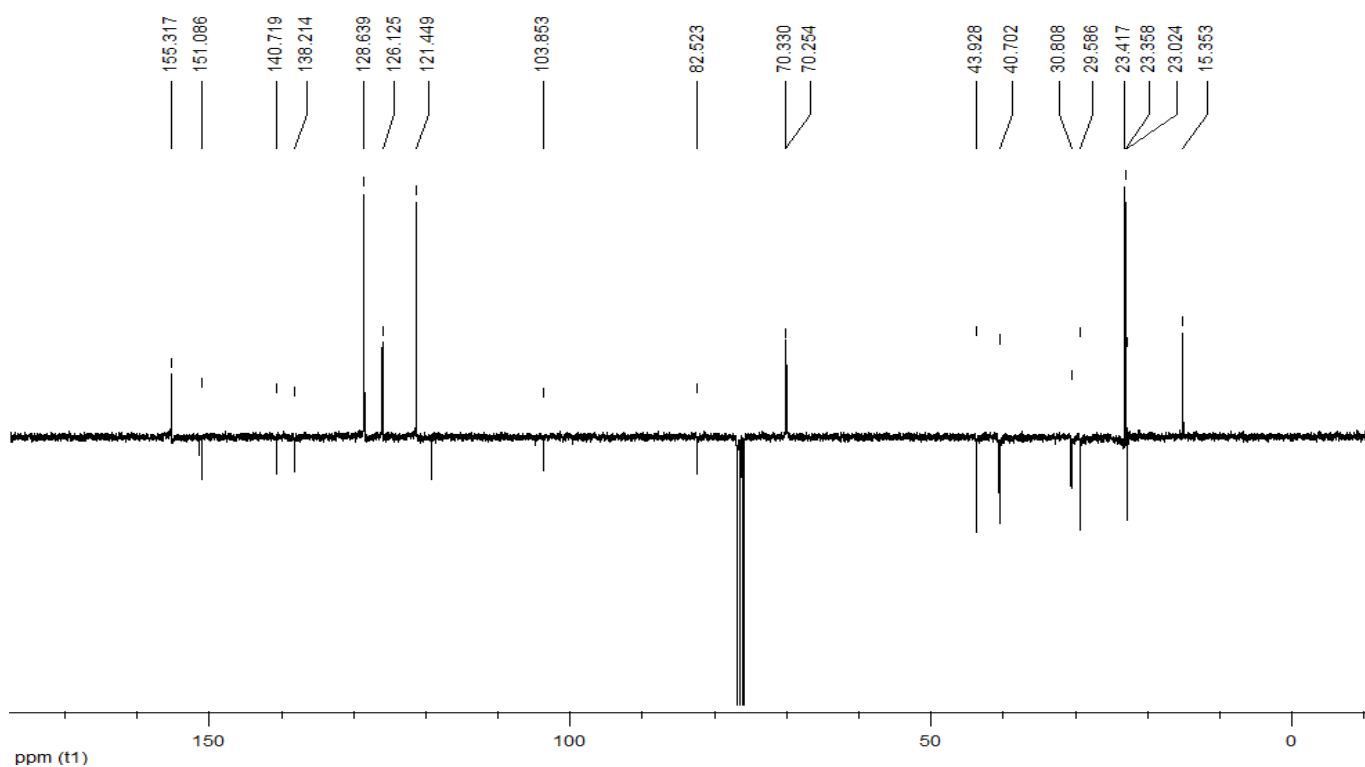


Figure S43. ¹³C NMR spectrum (75 MHz, CDCl₃) of **15d**.

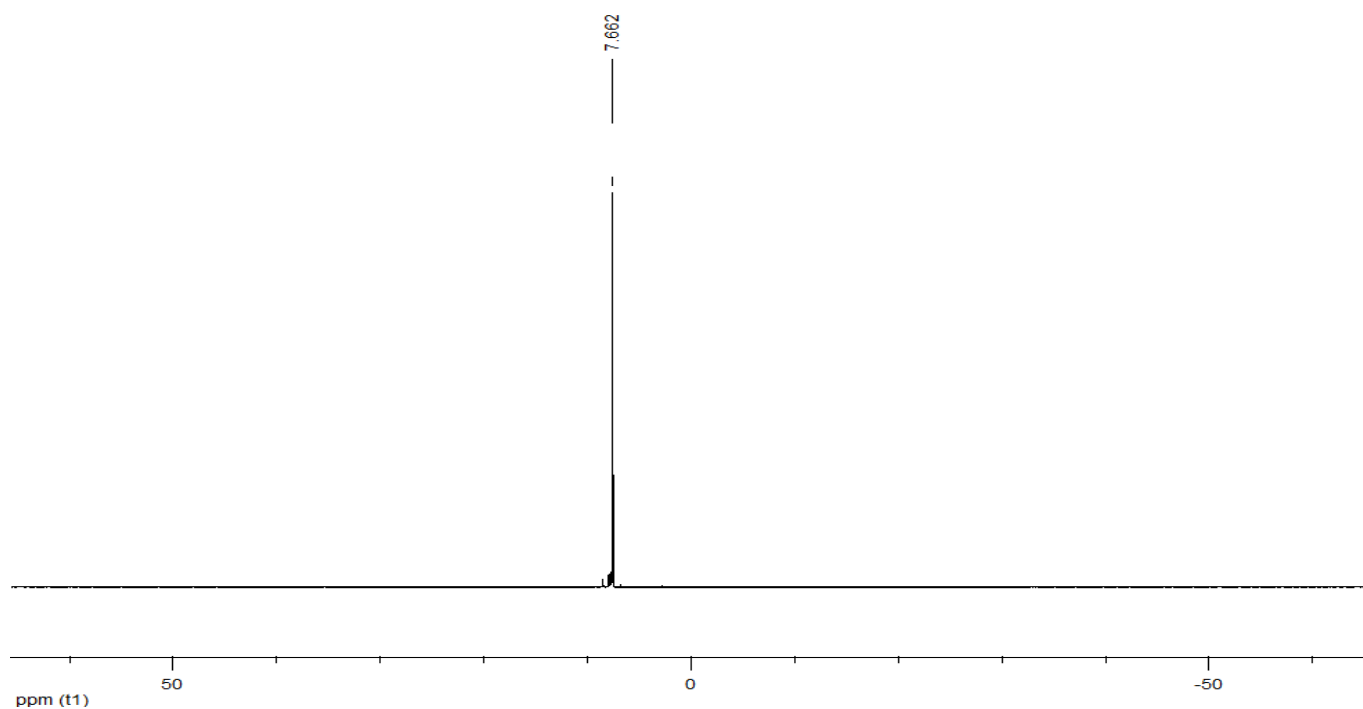


Figure S44. ³¹P{H} NMR spectrum (202 MHz, CDCl₃) of **15d**.

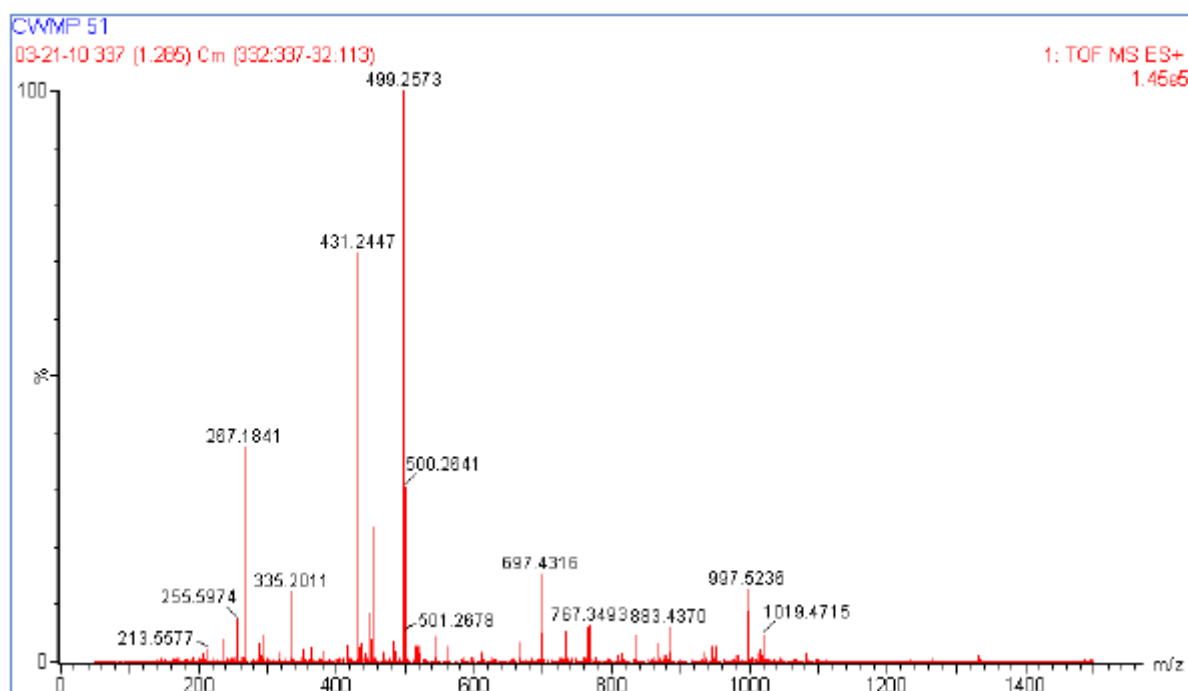


Figure S45. HRMS spectrum of **15d**.

Diisopropyl 6-(5-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)hexyl phosphoramidate (**15e**)

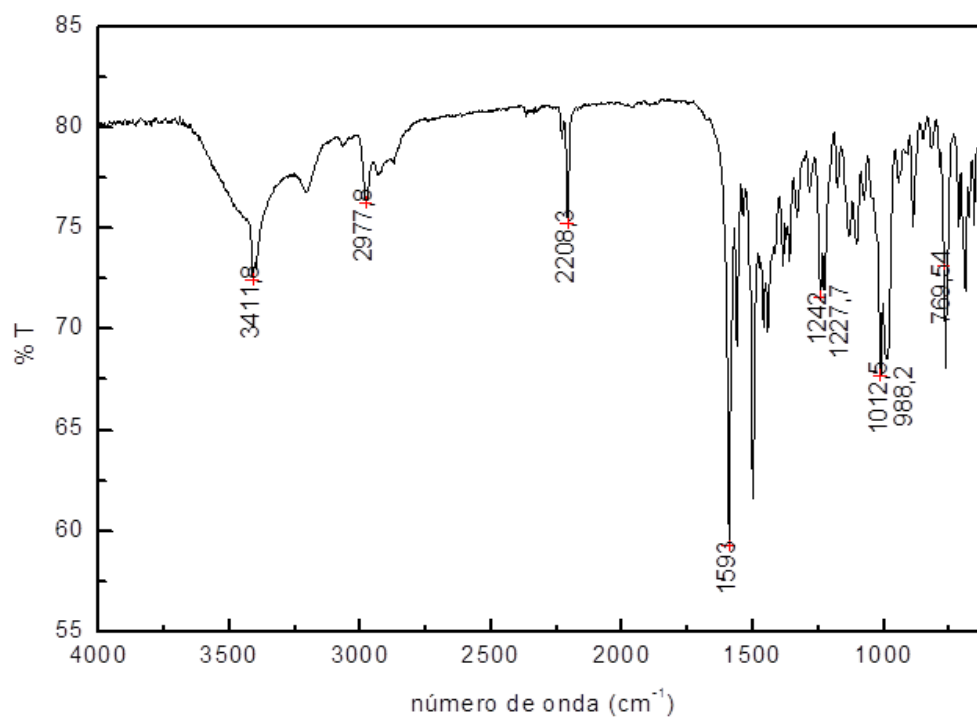
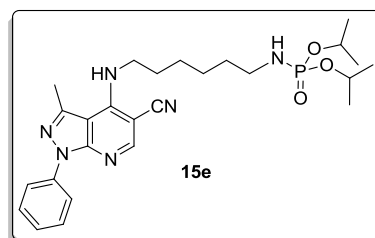


Figure S46. FTIR (KBr) spectrum of **15e**.

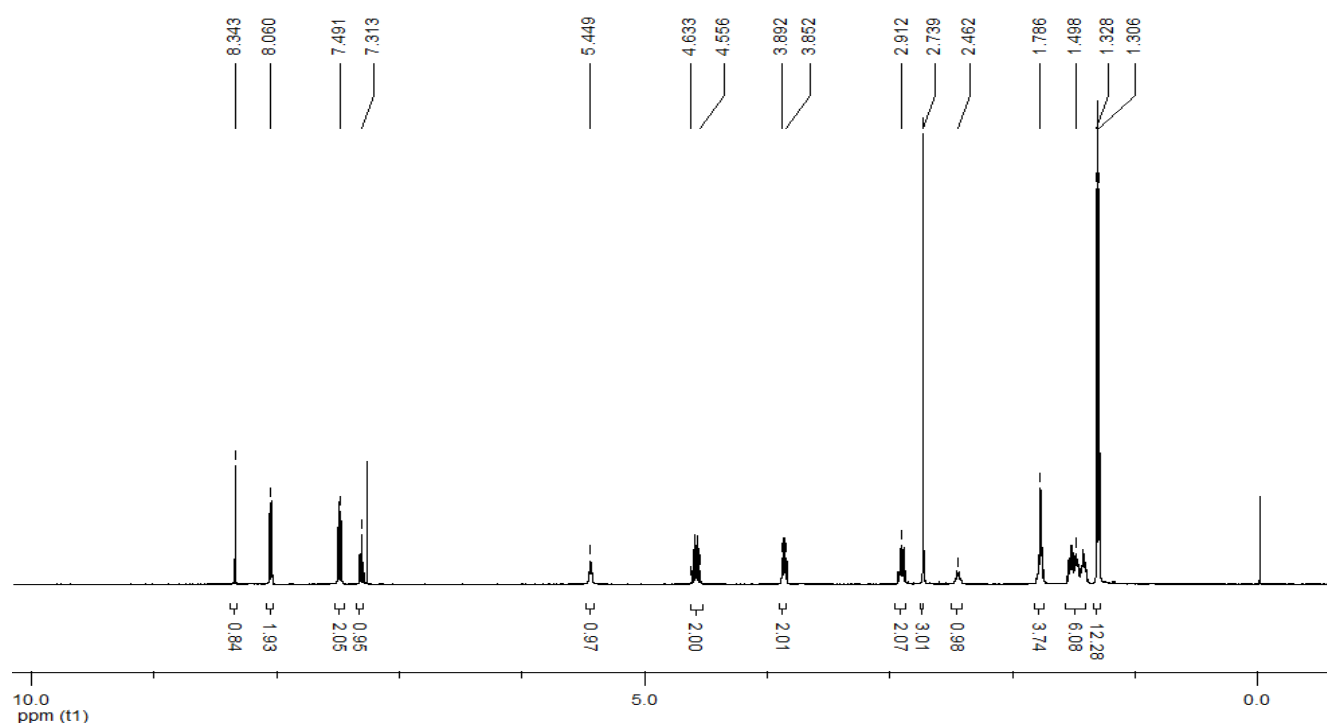


Figure S47. ¹H NMR spectrum (500 MHz, CDCl₃) of **15e**.

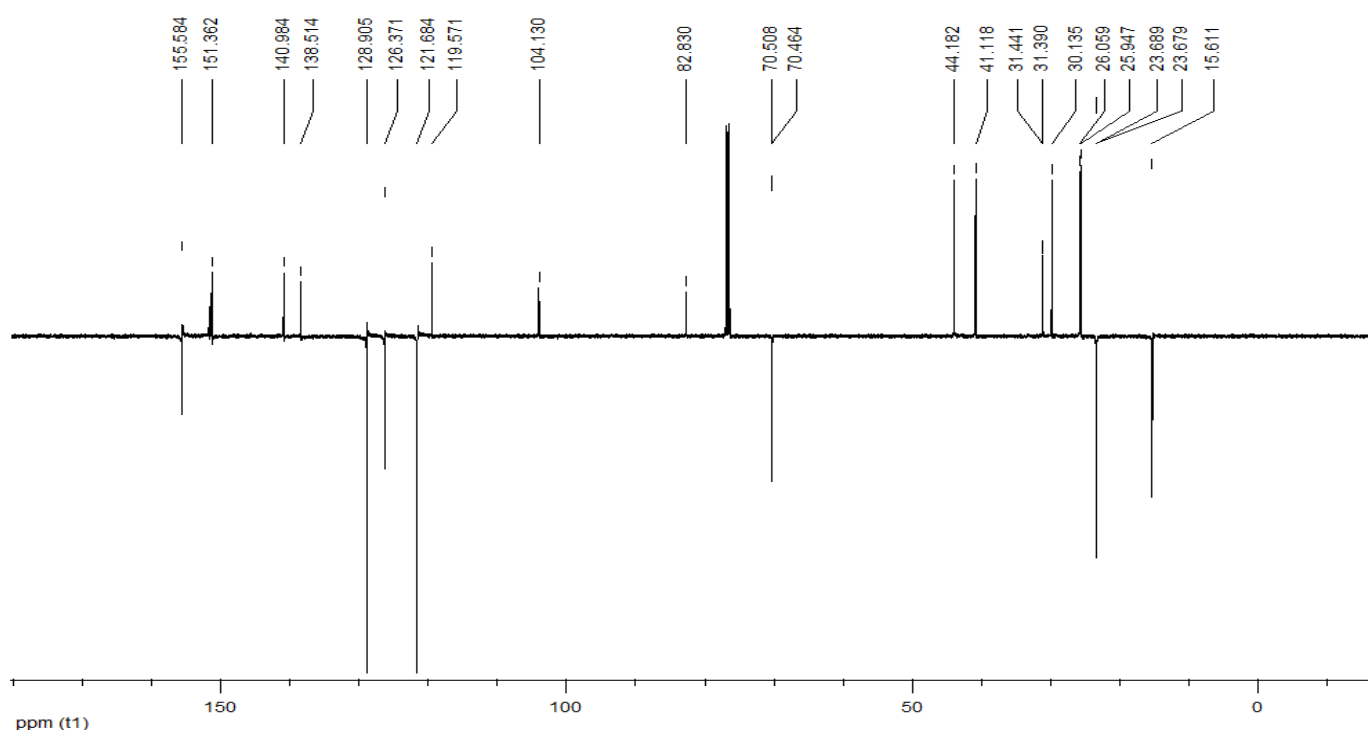


Figure S48. ^{13}C NMR spectrum (125 MHz, CDCl_3) of **15e**.

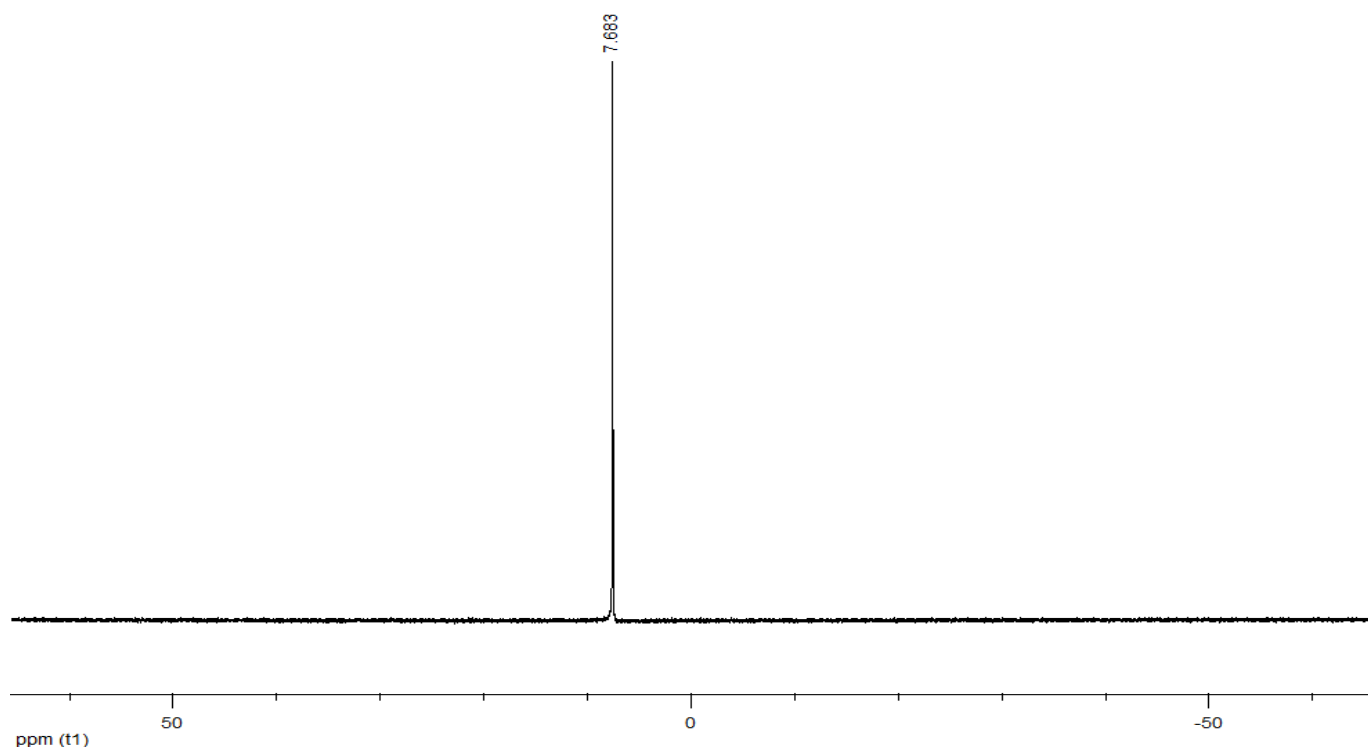


Figure S49. $^{31}\text{P}\{\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) of **15e**.

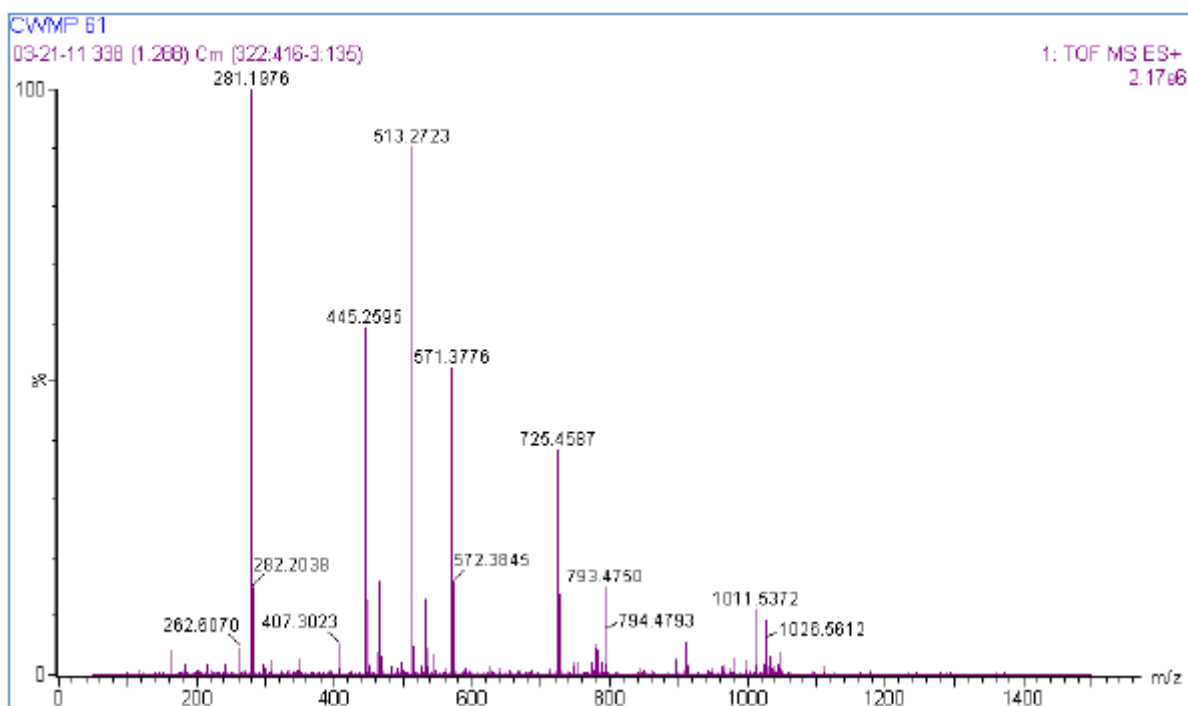


Figure S50. HRMS spectrum of **15e**.

Diisopropyl 2-(5-cyano-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)ethyl phosphoramidate (**16a**)

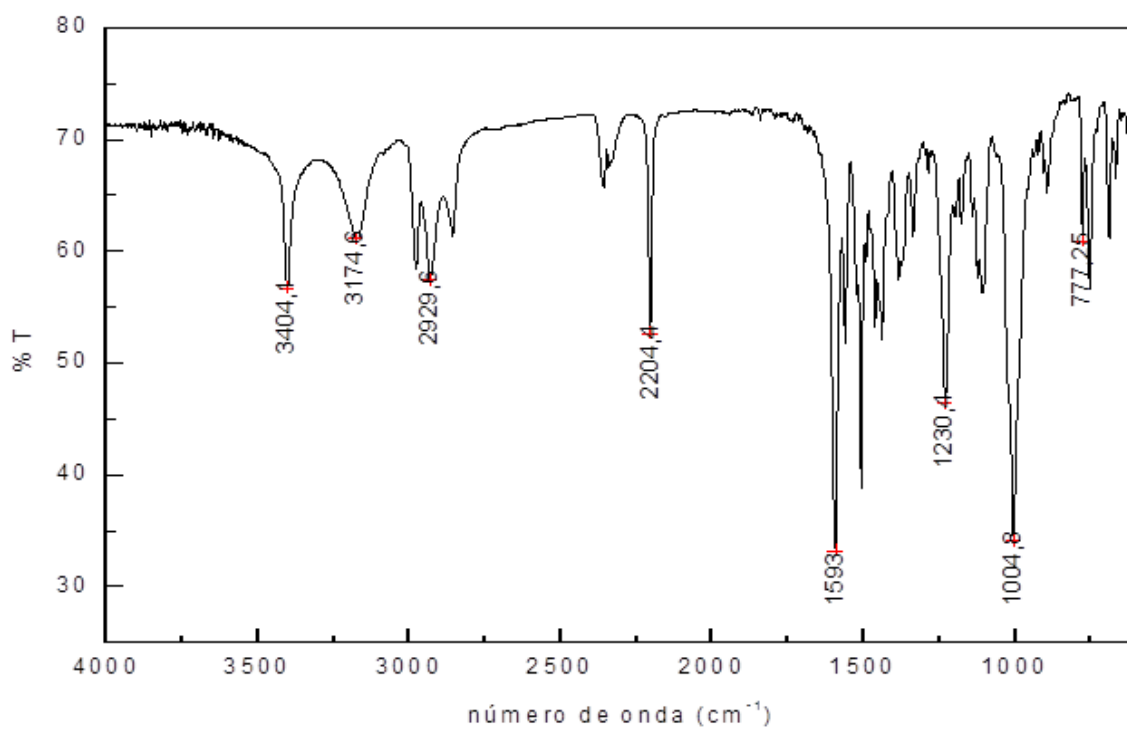
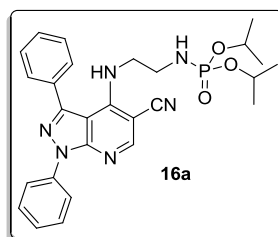


Figure S51. FTIR (KBr) spectrum of **16a**.

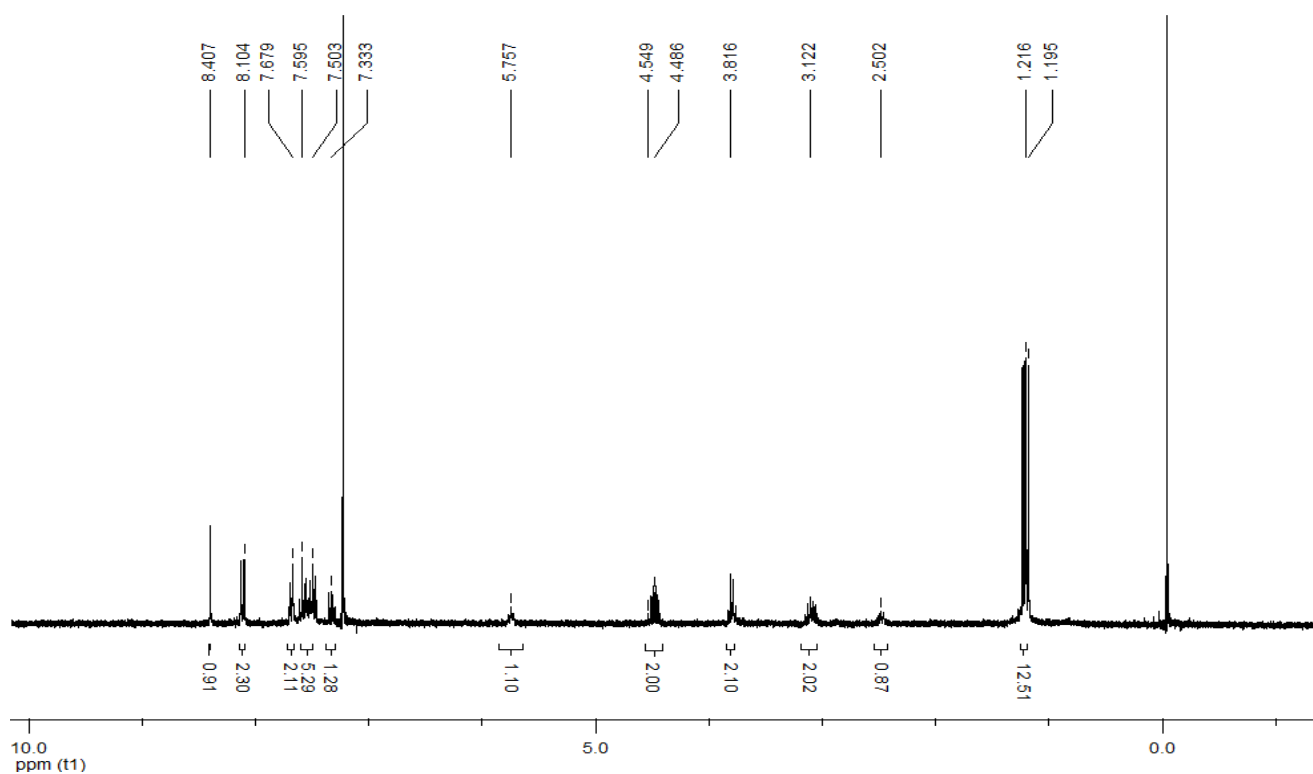


Figure S52. ¹H NMR spectrum (300 MHz, CDCl₃) of **16a**.

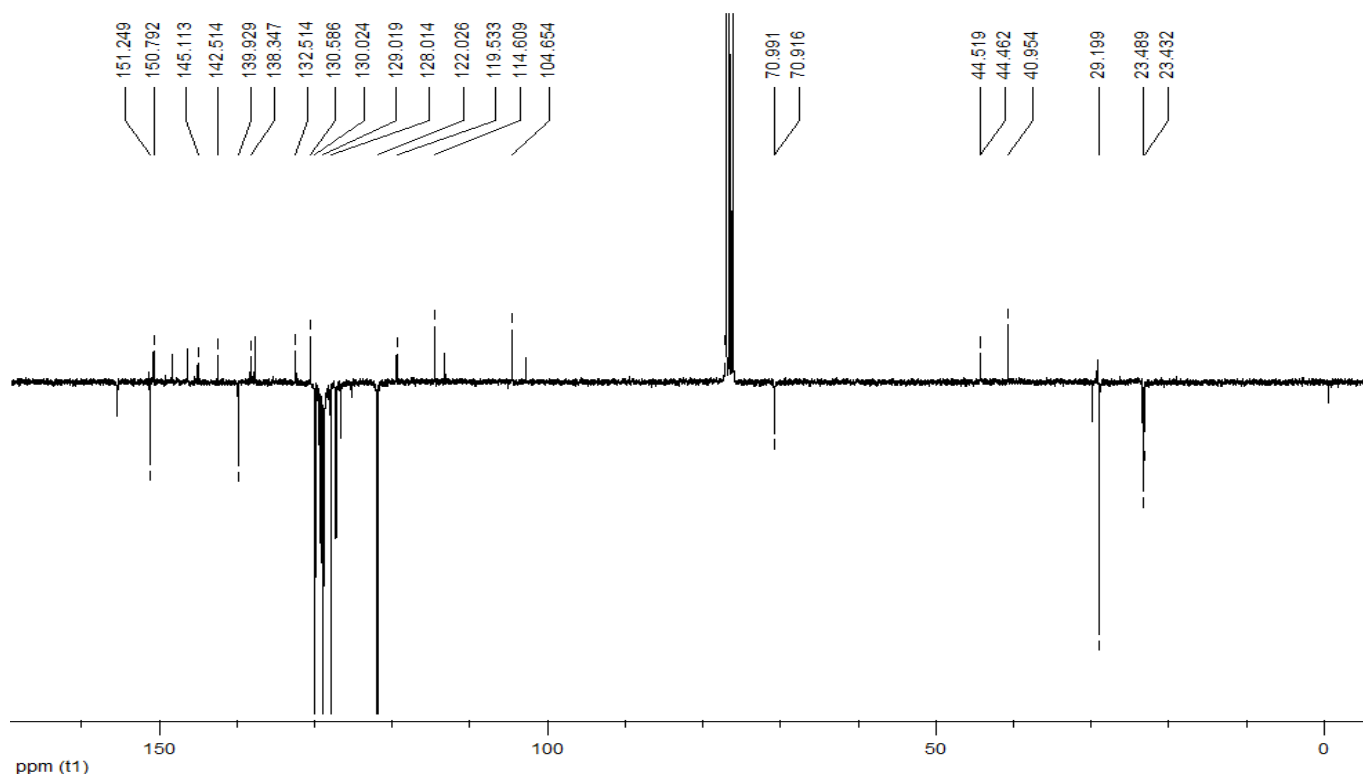


Figure S53. ¹³C NMR spectrum (75 MHz, CDCl₃) of **16a**.

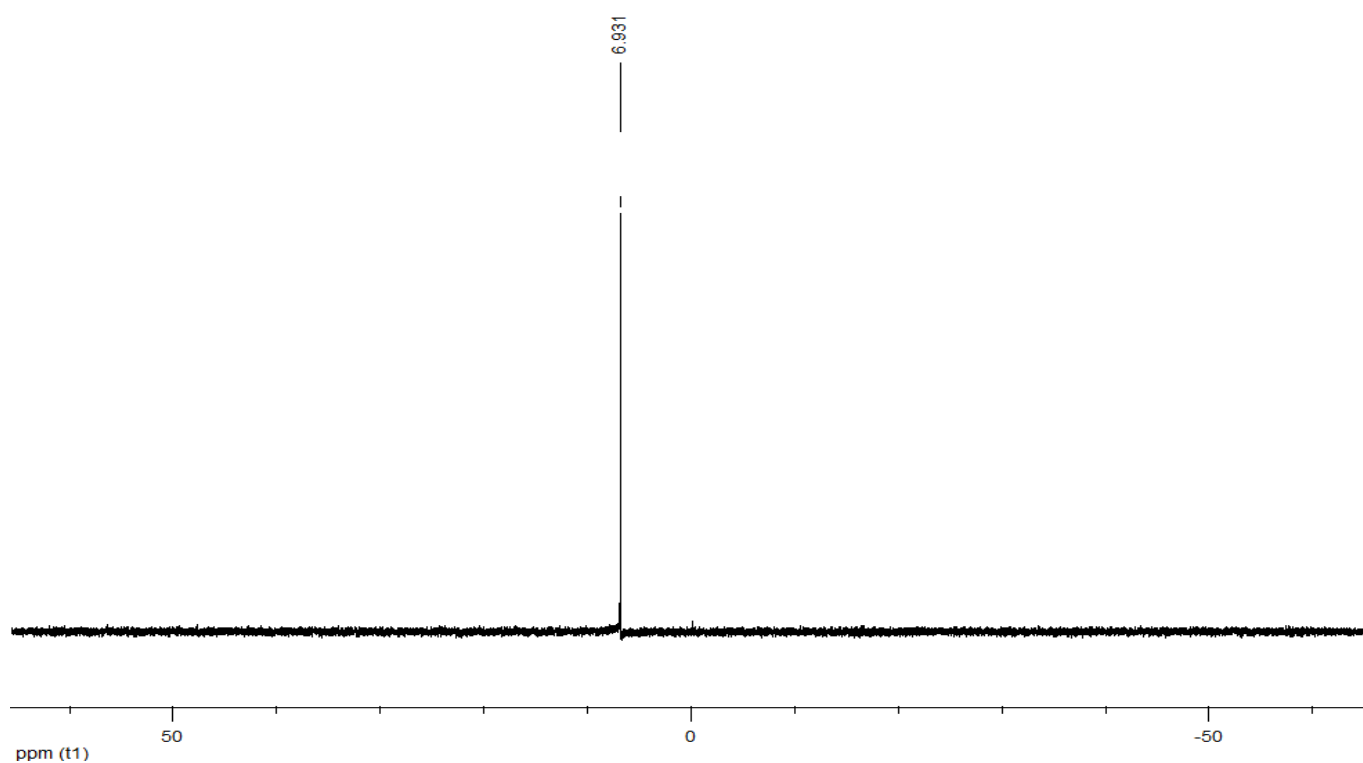


Figure S54. ³¹P{H} NMR spectrum (202 MHz, CDCl₃) of **16a**.

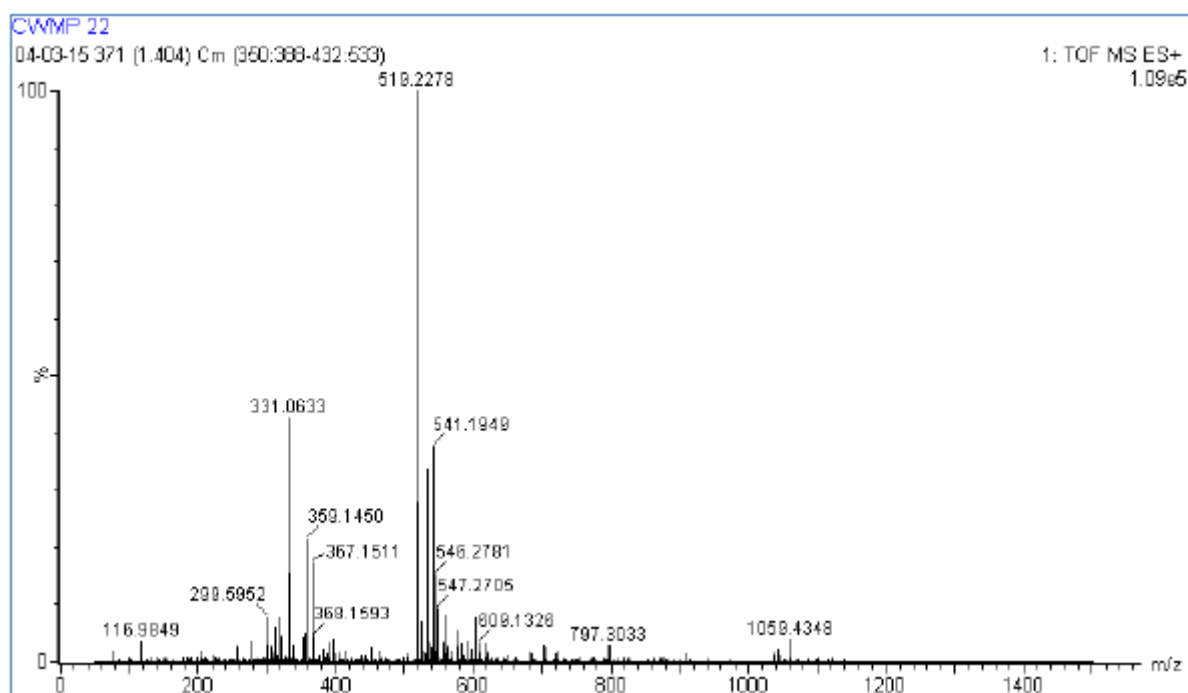


Figure S55. HRMS spectrum of **16a**.

Diisopropyl 3-(5-cyano-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)propyl phosphoramidate (**16b**)

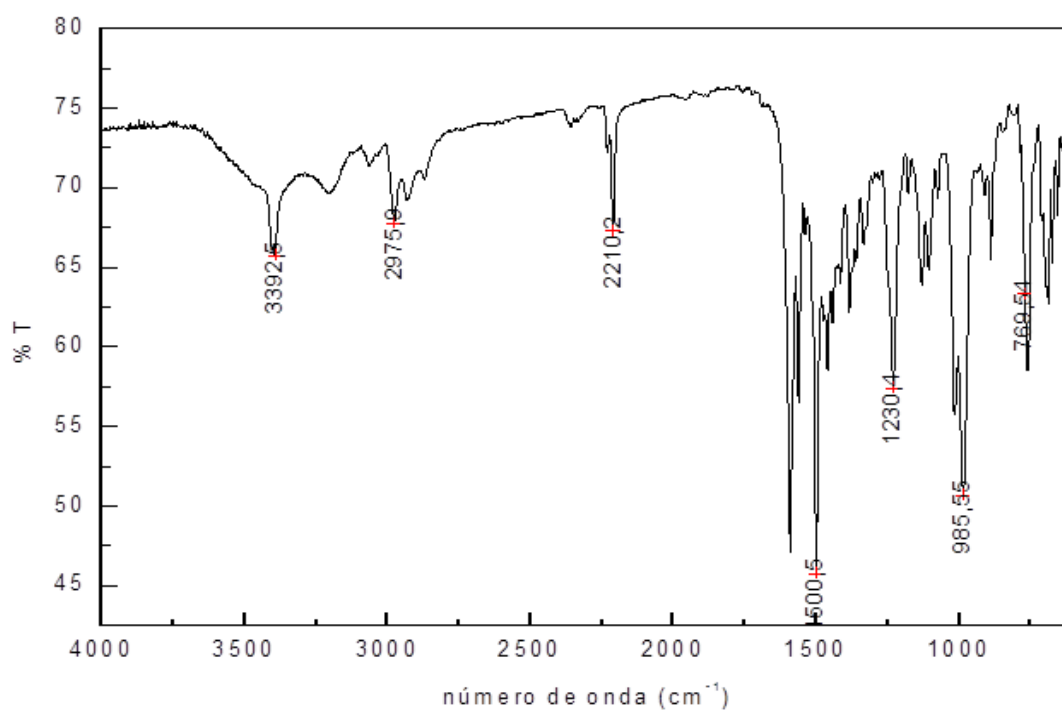
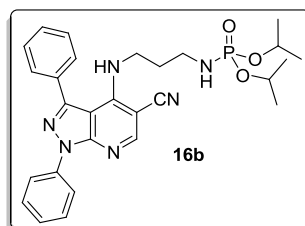


Figure S56. FTIR (KBr) spectrum of **16b**.

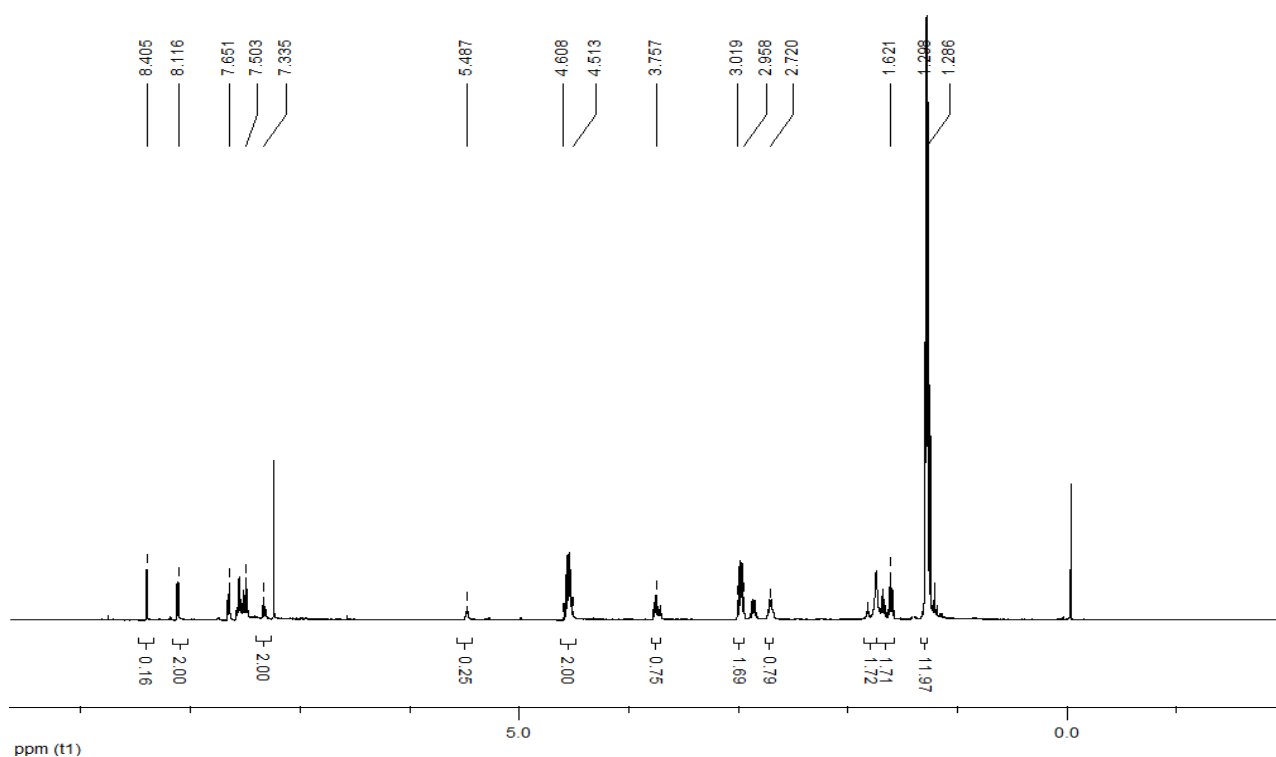


Figure S57. ^1H NMR spectrum (500 MHz, CDCl_3) of **16b**.

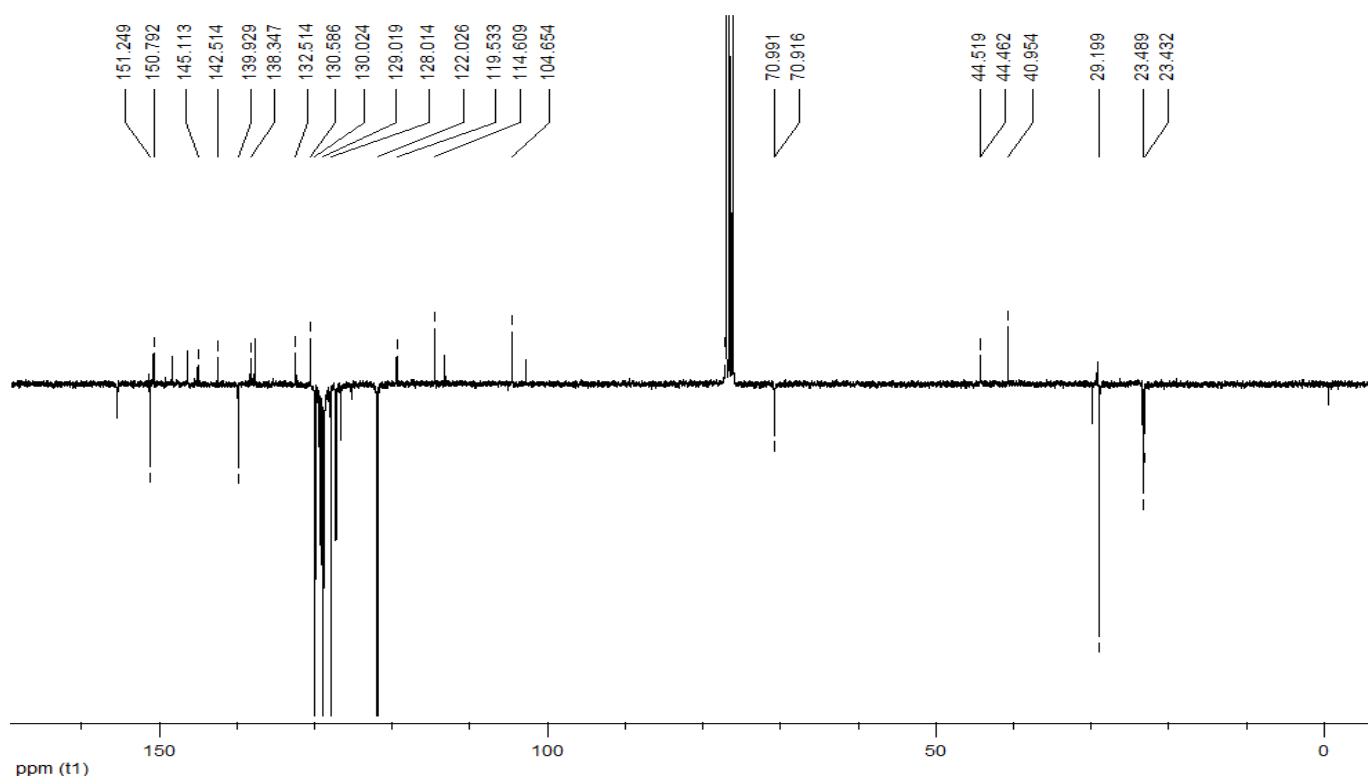


Figure S58. ¹³C NMR spectrum (75 MHz, CDCl₃) of **16b**.

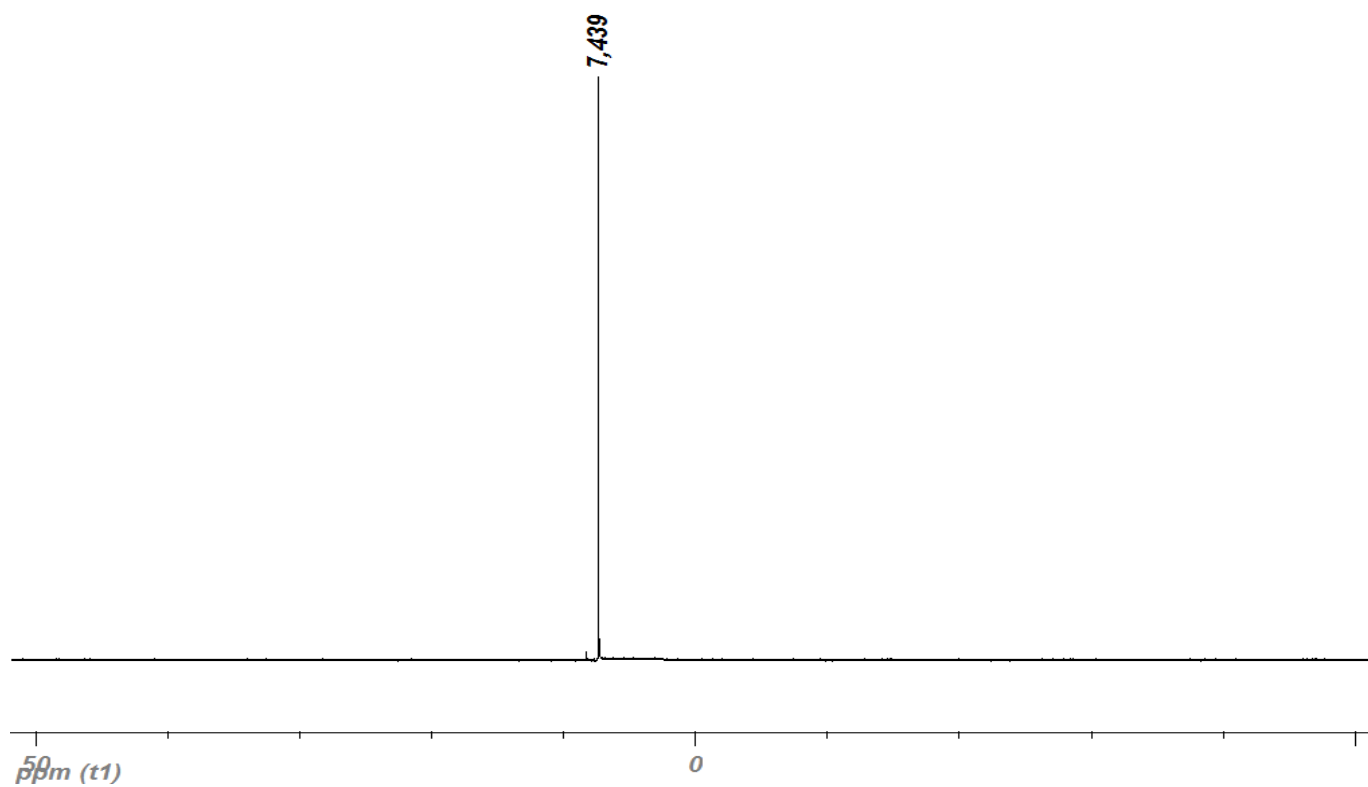


Figure S59. ³¹P{¹H} NMR spectrum (202 MHz, CDCl₃) of **16b**.

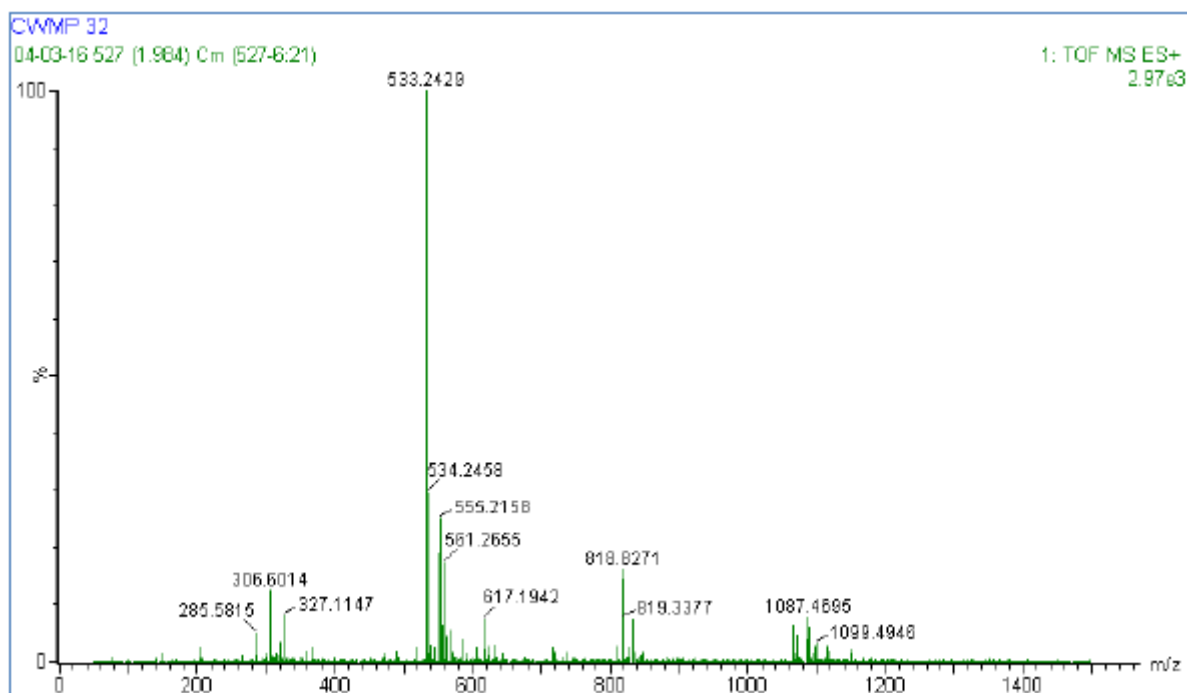


Figure S60. HRMS spectrum of **16b**.

Diisopropyl 4-(5-cyano-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)butyl phosphoramidate (**16c**)

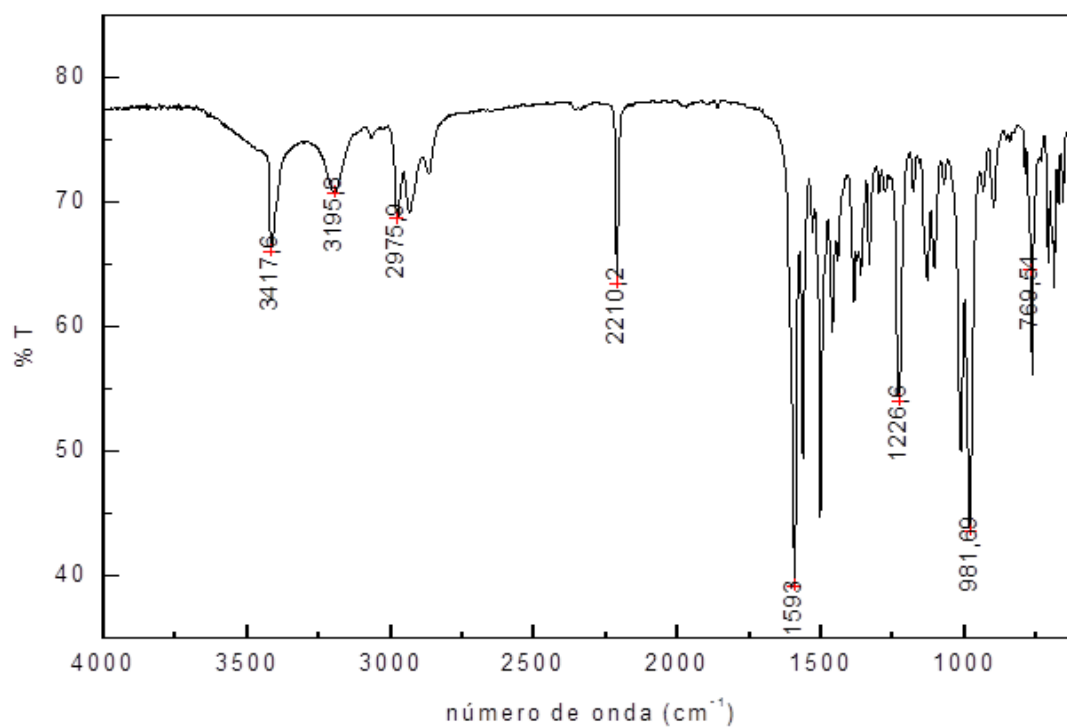
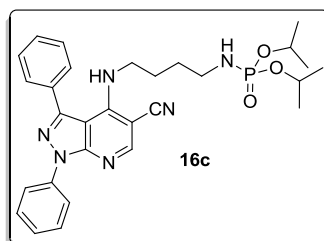


Figure S61. FTIR (KBr) spectrum of **16c**.

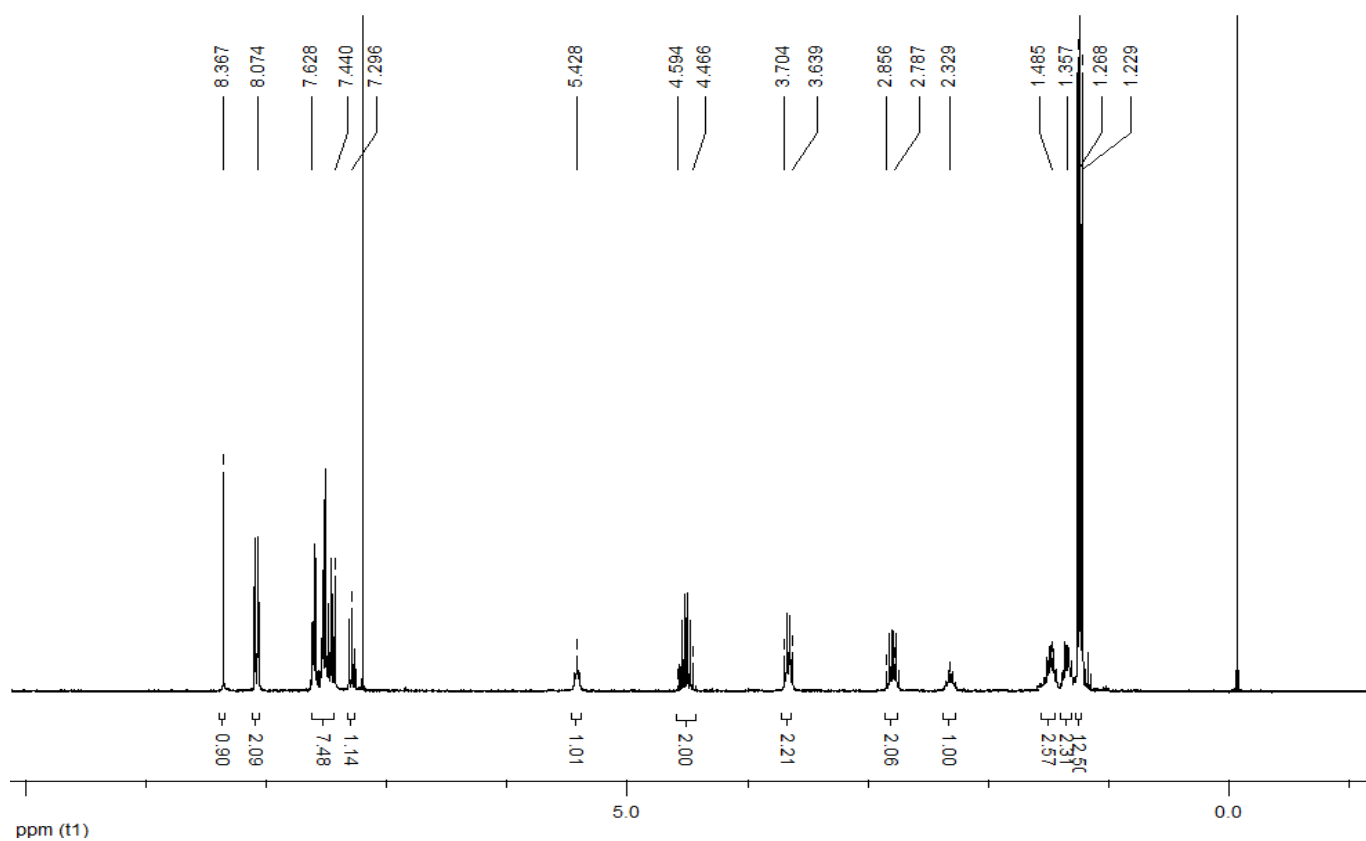


Figure S62. ¹H NMR spectrum (300 MHz, CDCl₃) of **16c**.

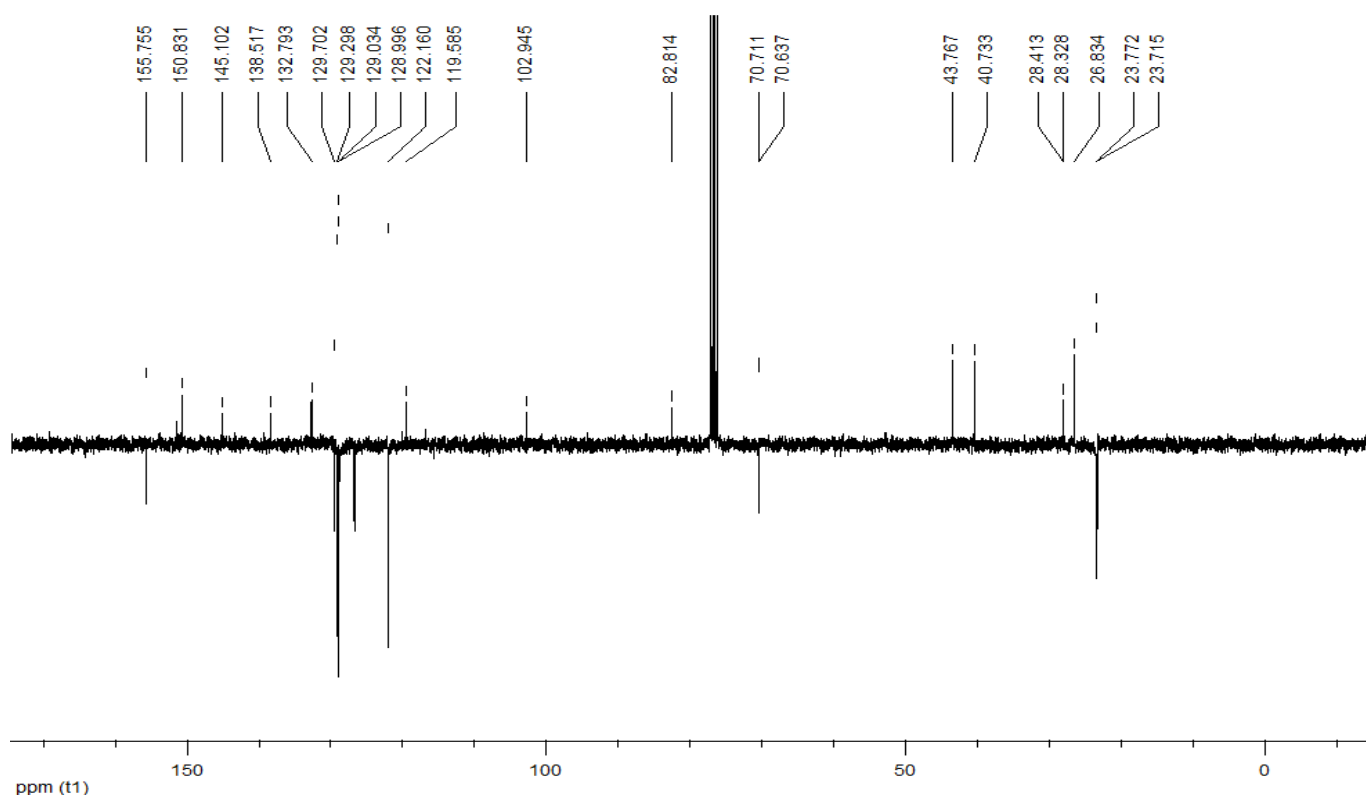


Figure S63. ¹³C NMR spectrum (75 MHz, CDCl₃) of **16c**.

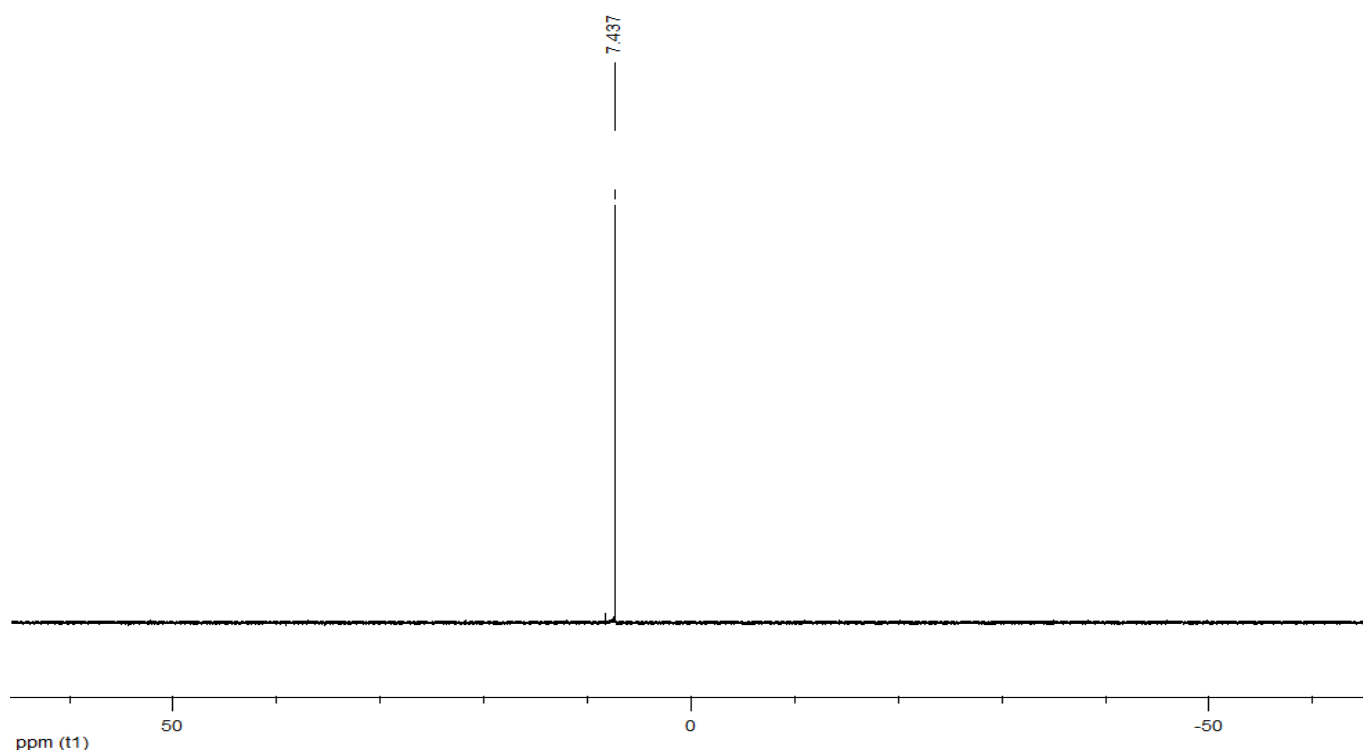


Figure S64. ³¹P{H} NMR spectrum (202 MHz, CDCl₃) of **16c**.

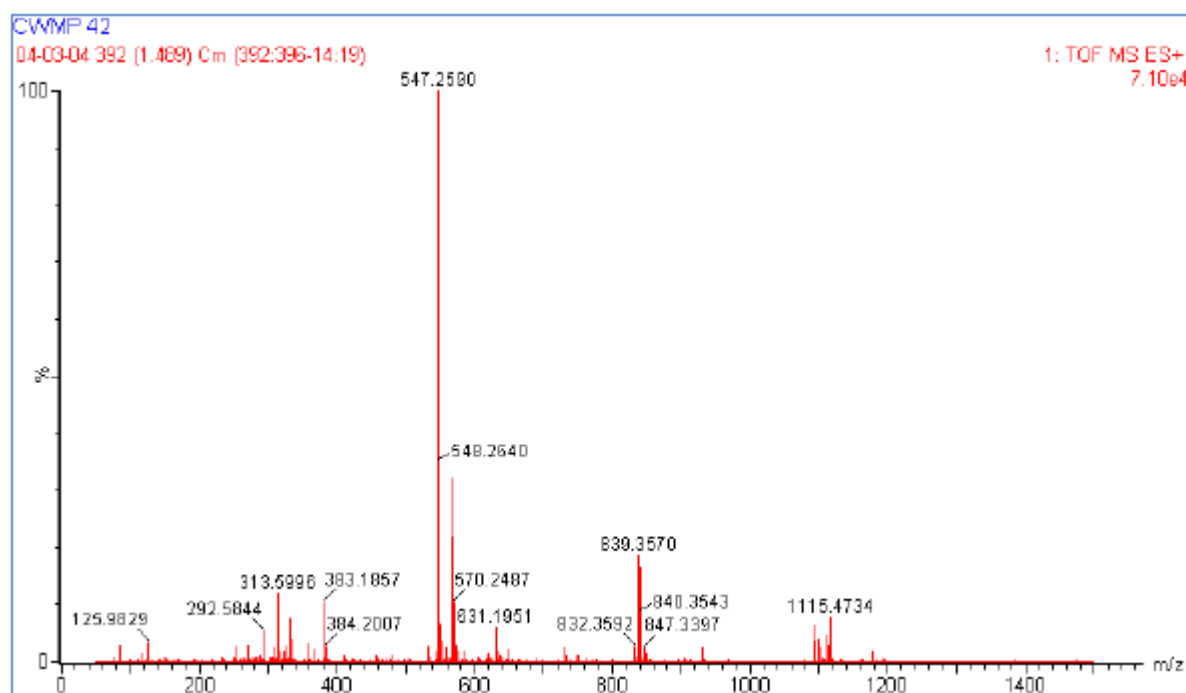


Figure S65. HRMS spectrum of **16c**.

Diisopropyl 5-(5-cyano-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)pentyl phosphoramidate (**16d**)

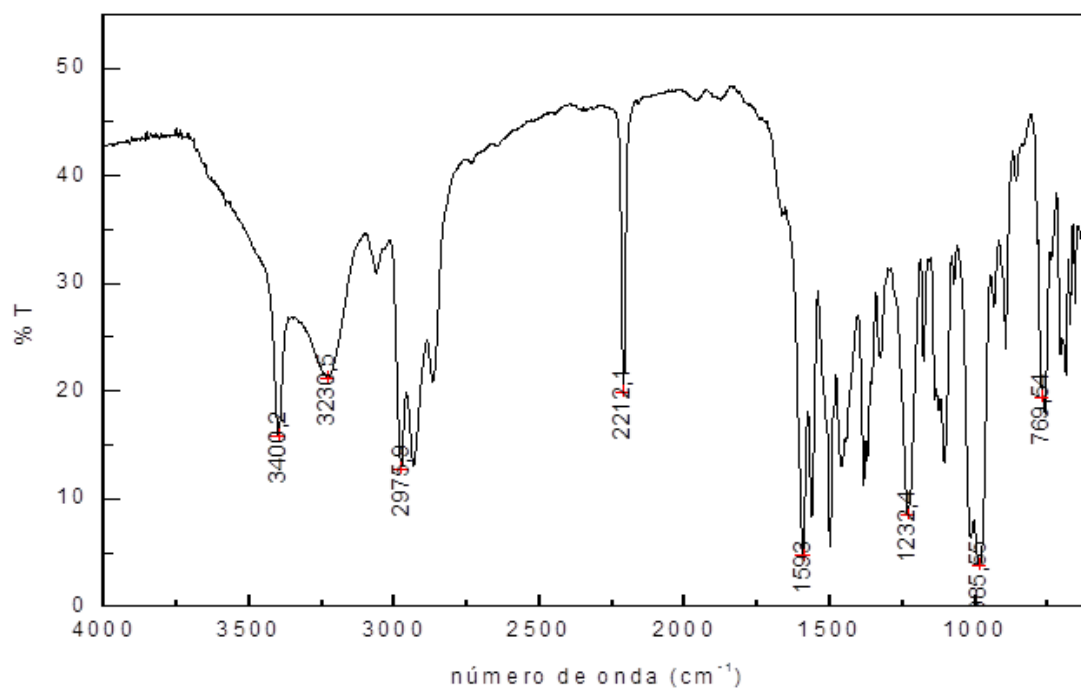
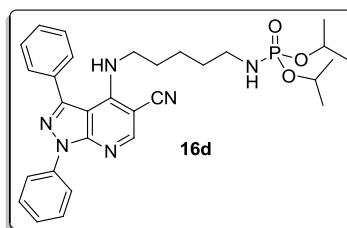


Figure S66. FTIR (KBr) spectrum of **16d**.

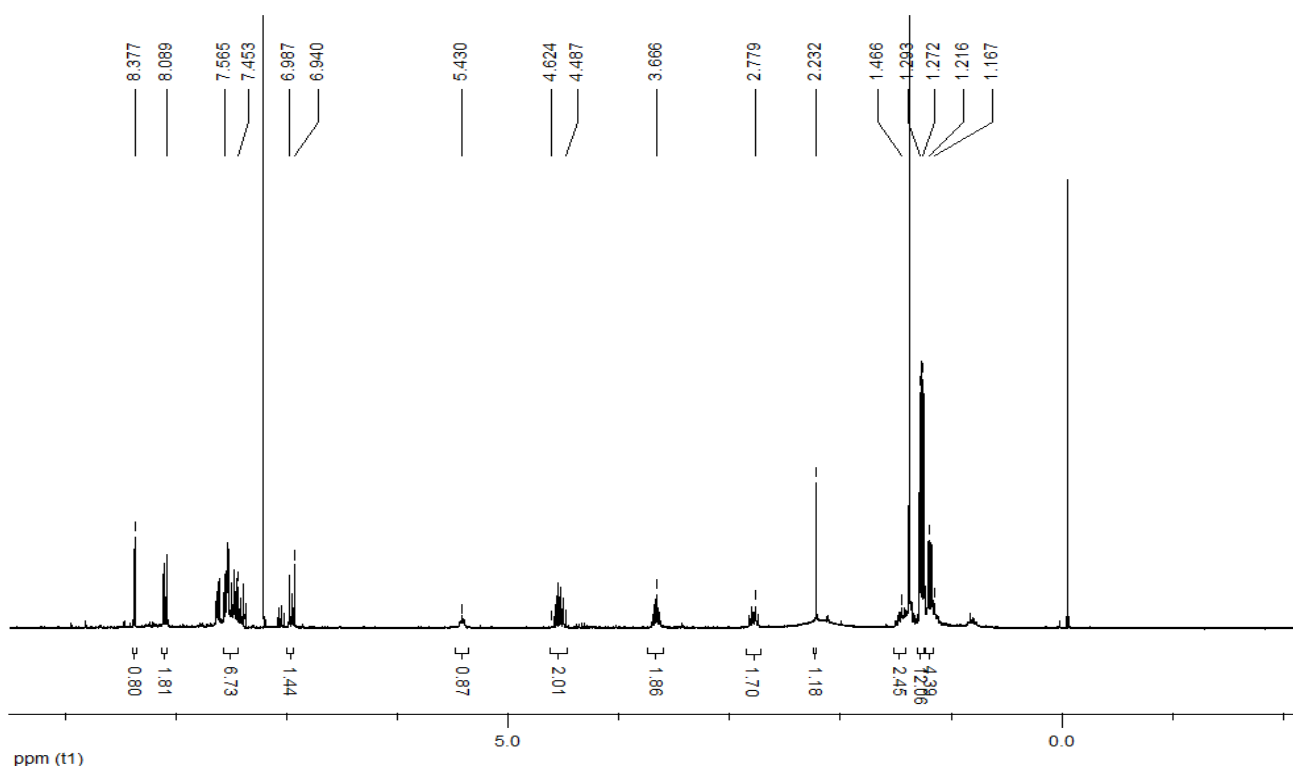


Figure S67. ^1H NMR spectrum (300 MHz, CDCl_3) of **16d**.

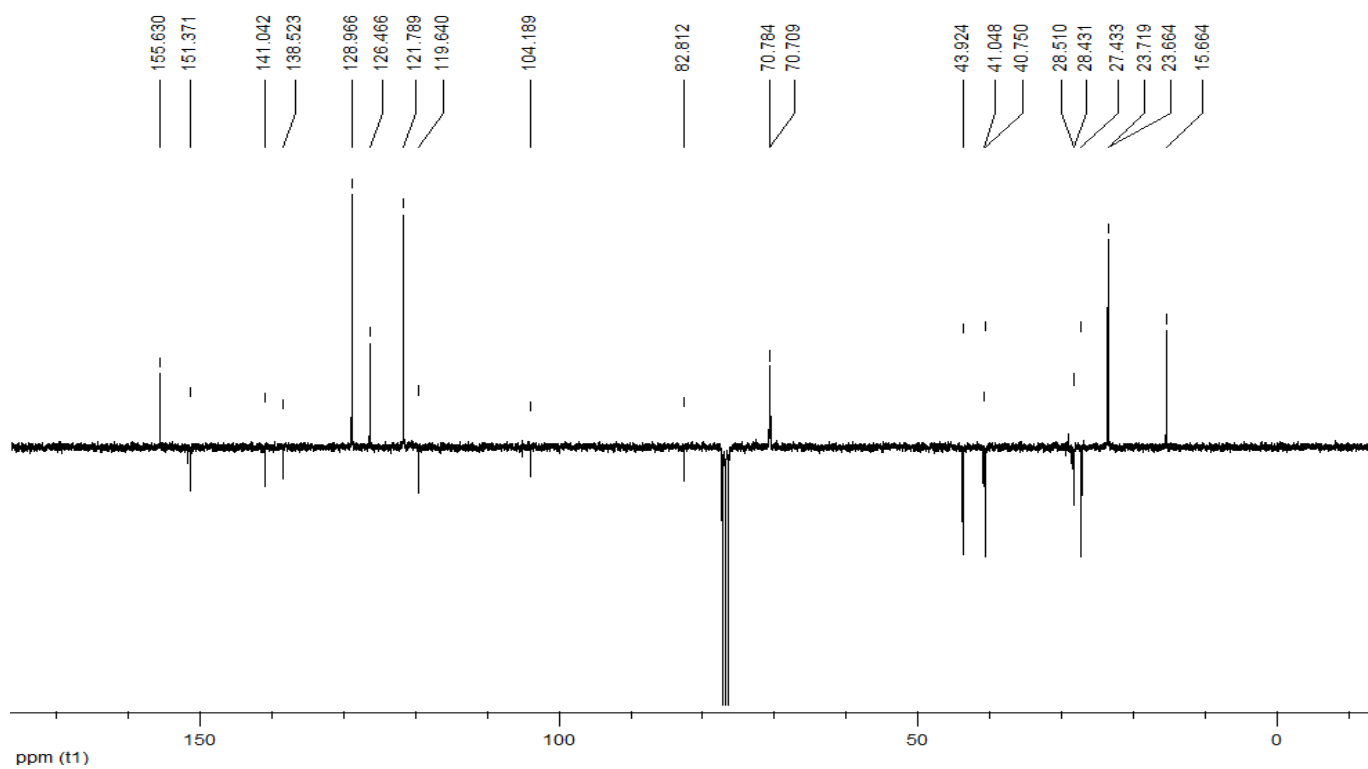


Figure S68. ¹³C NMR spectrum (75 MHz, CDCl₃) of **16d**.

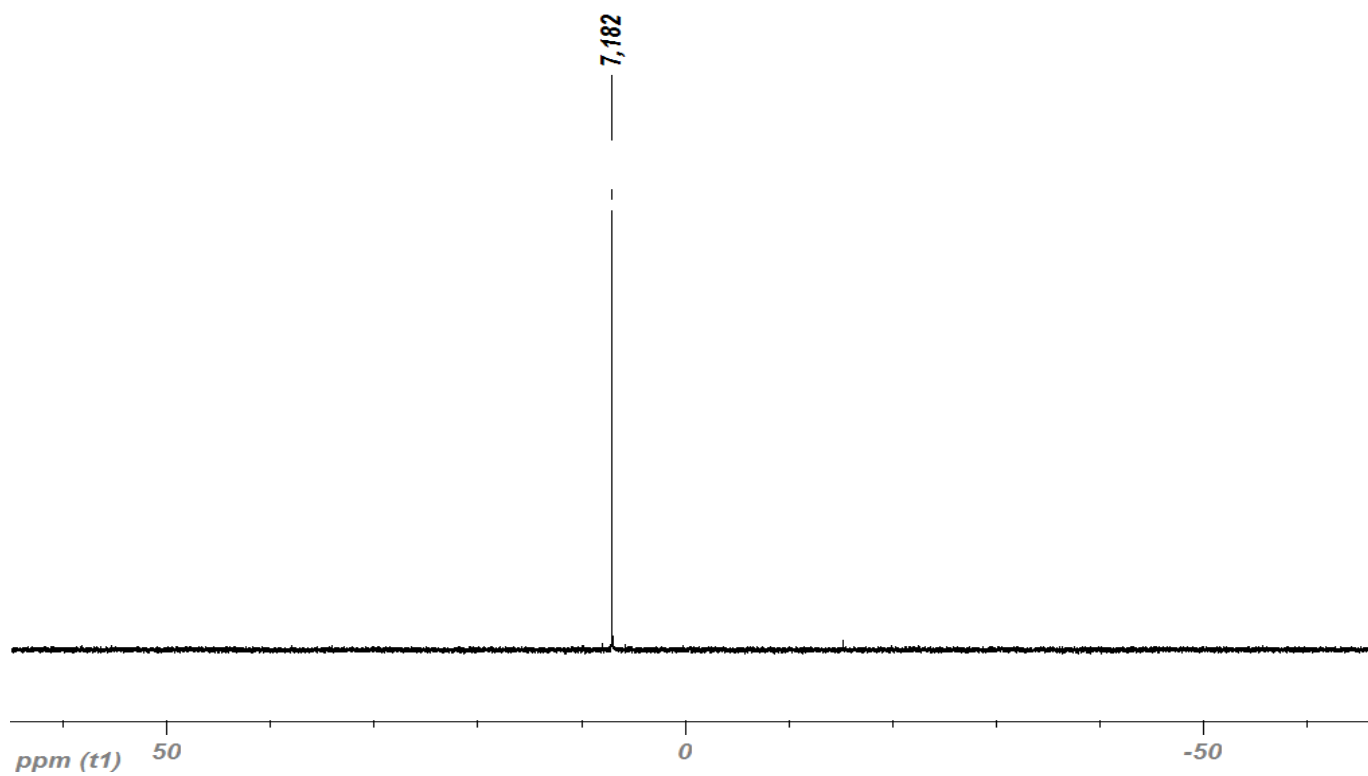


Figure S69. ³¹P{¹H} NMR spectrum (121 MHz, CDCl₃) of **16d**.

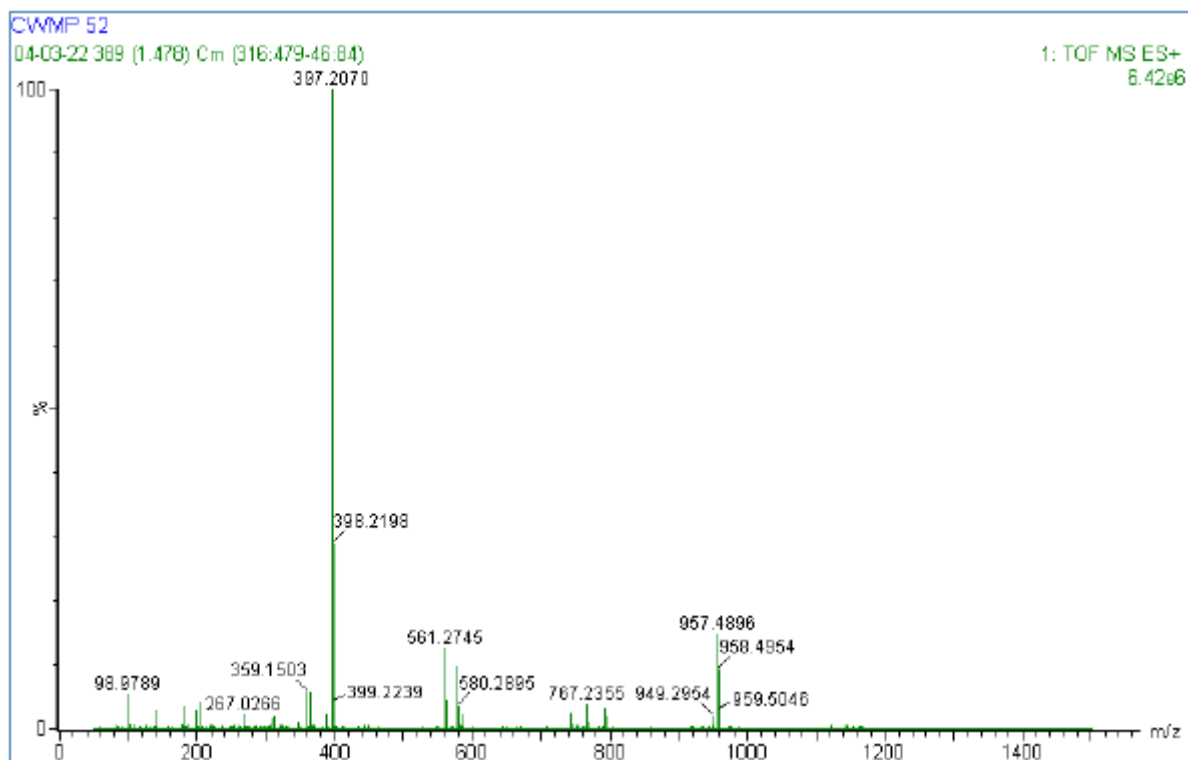


Figure S70. HRMS spectrum of **16d**.

Diisopropyl 6-(5-cyano-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ylamino)hexyl phosphoramidate (**16e**)

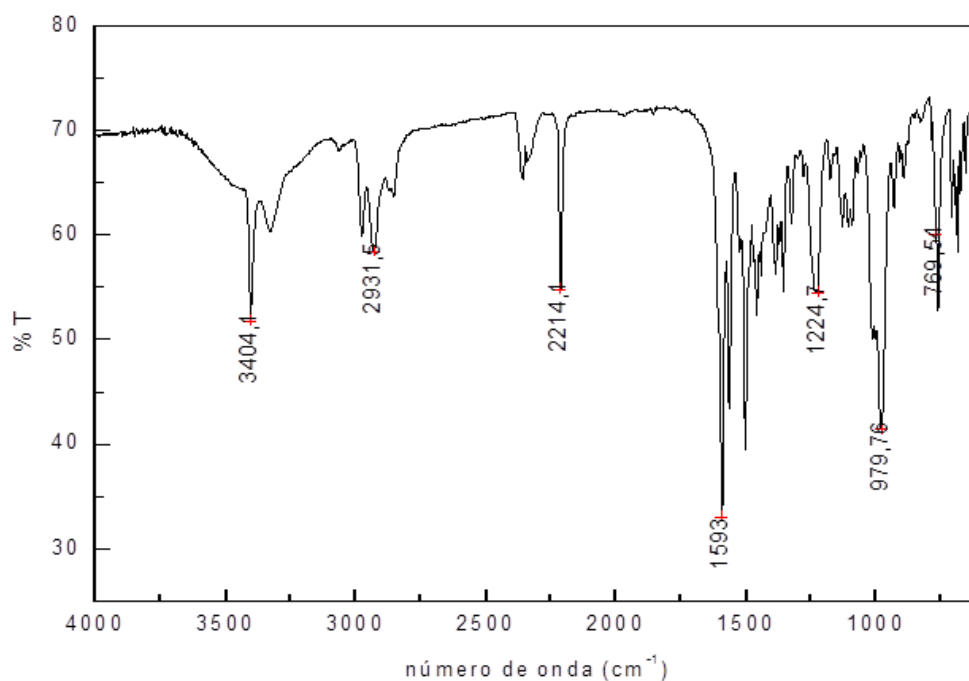
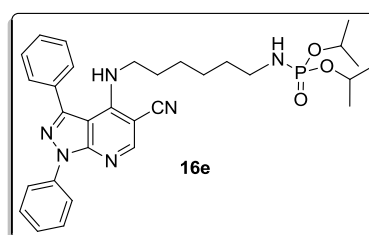


Figure S71. FTIR (KBr) spectrum of **16e**.

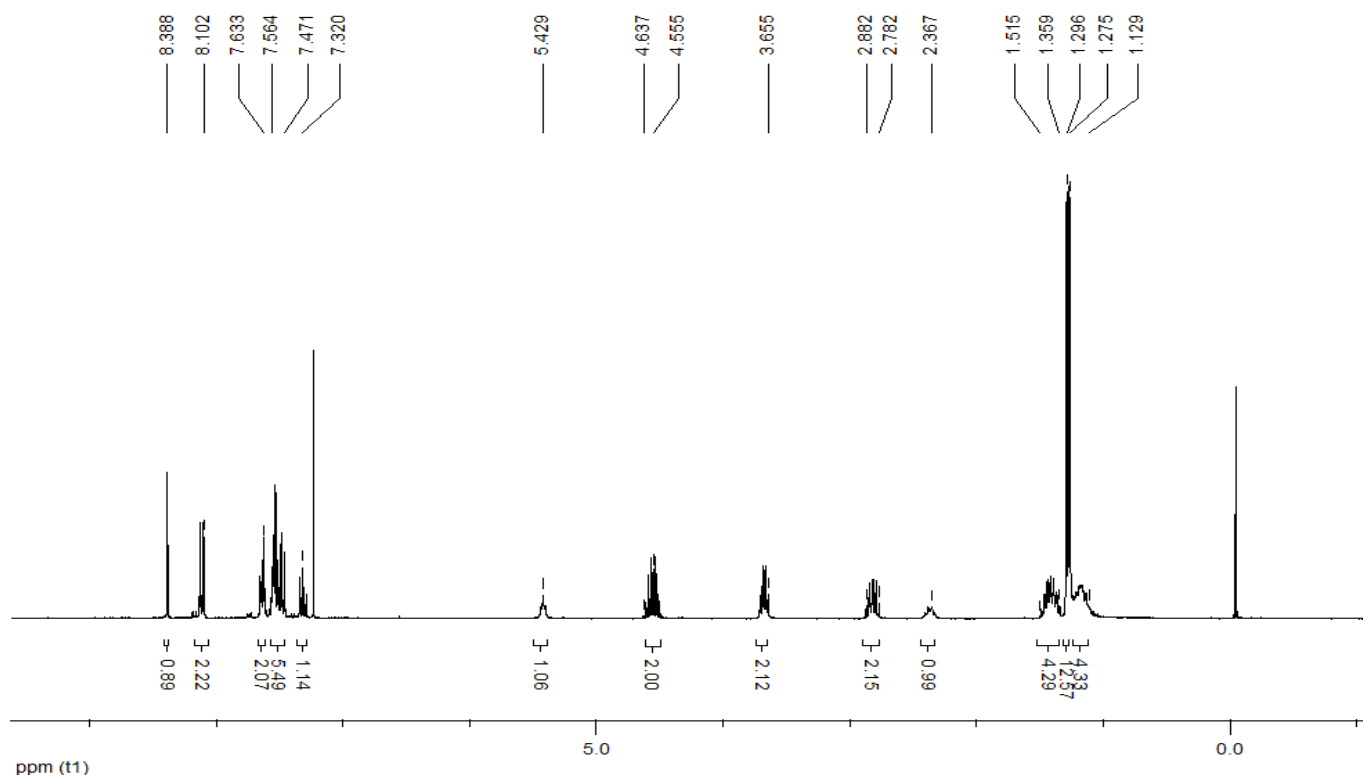


Figure S72. ¹H NMR spectrum (300 MHz, CDCl₃) of **16e**.

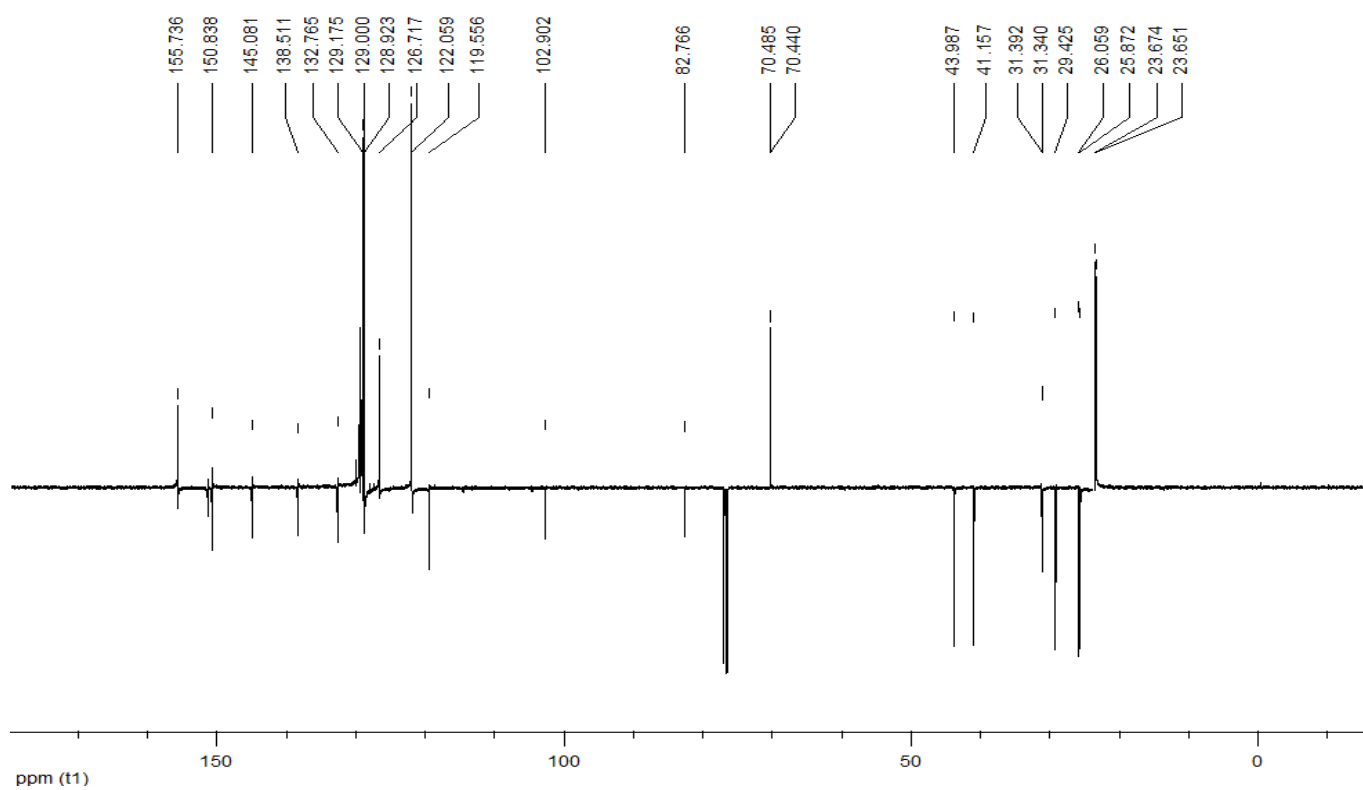


Figure S73. ¹³C NMR spectrum (125 MHz, CDCl₃) of **16e**.

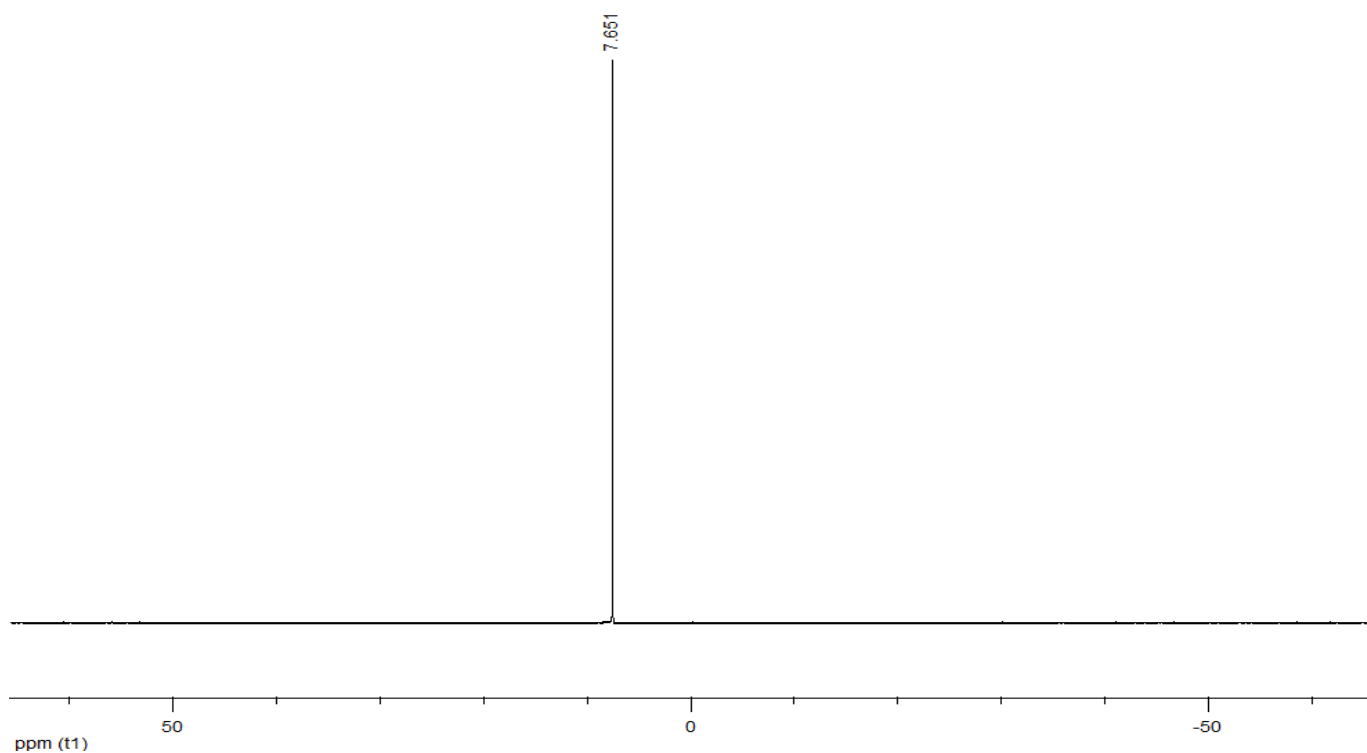


Figure S74. ³¹P{H} NMR spectrum (121 MHz, CDCl₃) of **16e**.

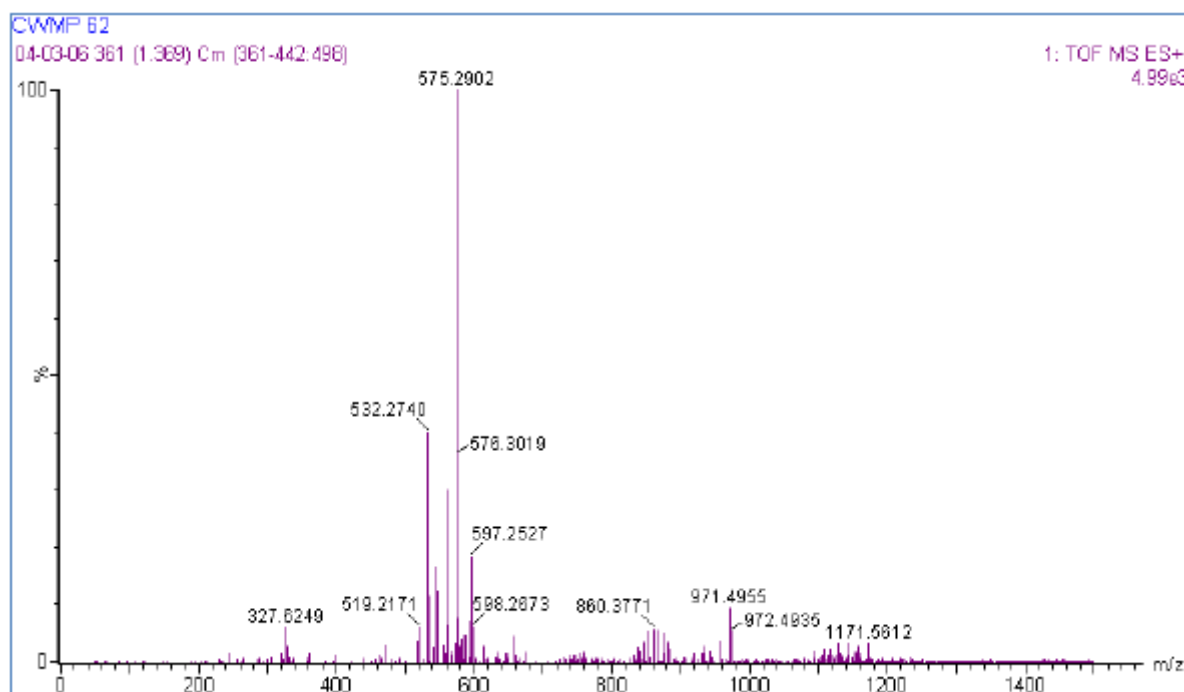


Figure S75. HRMS spectrum of **16e**.