Electronic Supplementary Information for

Synthesis of novel pyrazolo[3,4-*b*]quinolinebisphosphonic acids and an unexpected intramolecular cyclization and phosphonylation reaction

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1. ^{1}H, ^{31}P and ^{13}C NMR spectra for synthesized compounds

NMR spectrum of 1*H*-pyrazolo[3,4-*b*]quinoline (2)

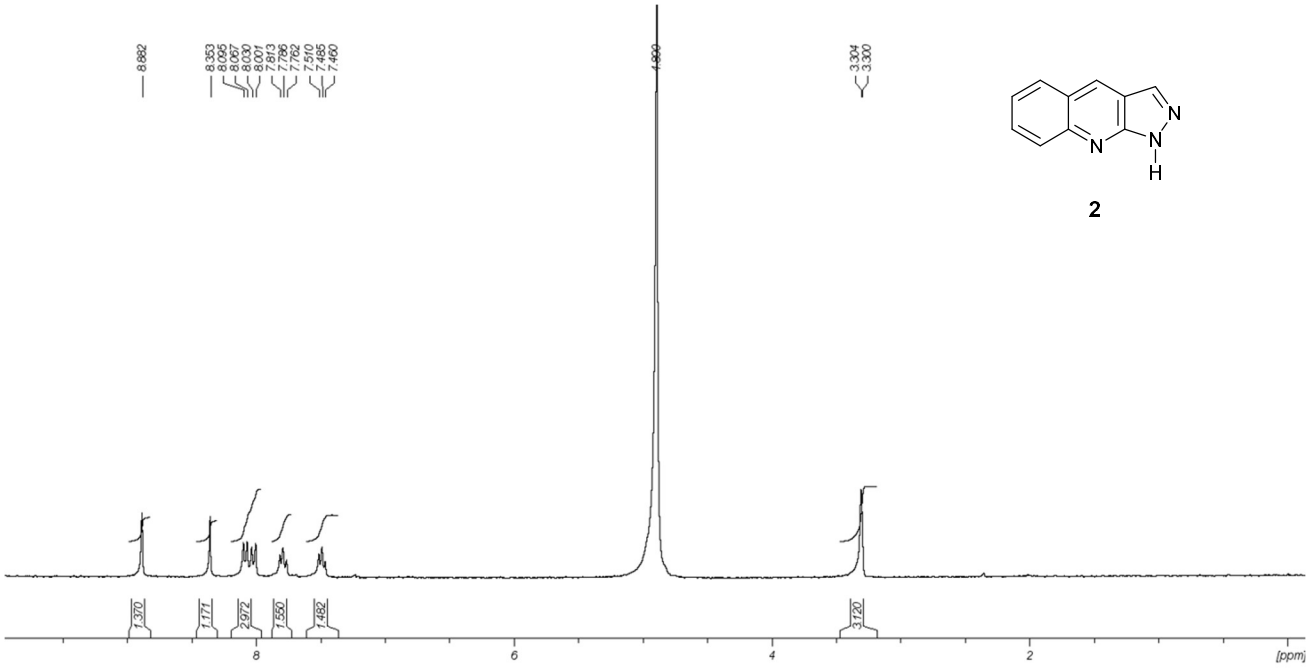

Figure S1. ^{1}H NMR spectrum (300 MHz, MeOD) of compound **2**.

NMR spectra of ethyl 1*H*-pyrazolo[3,4-*b*]quinolin-1-ylacetate (3a)

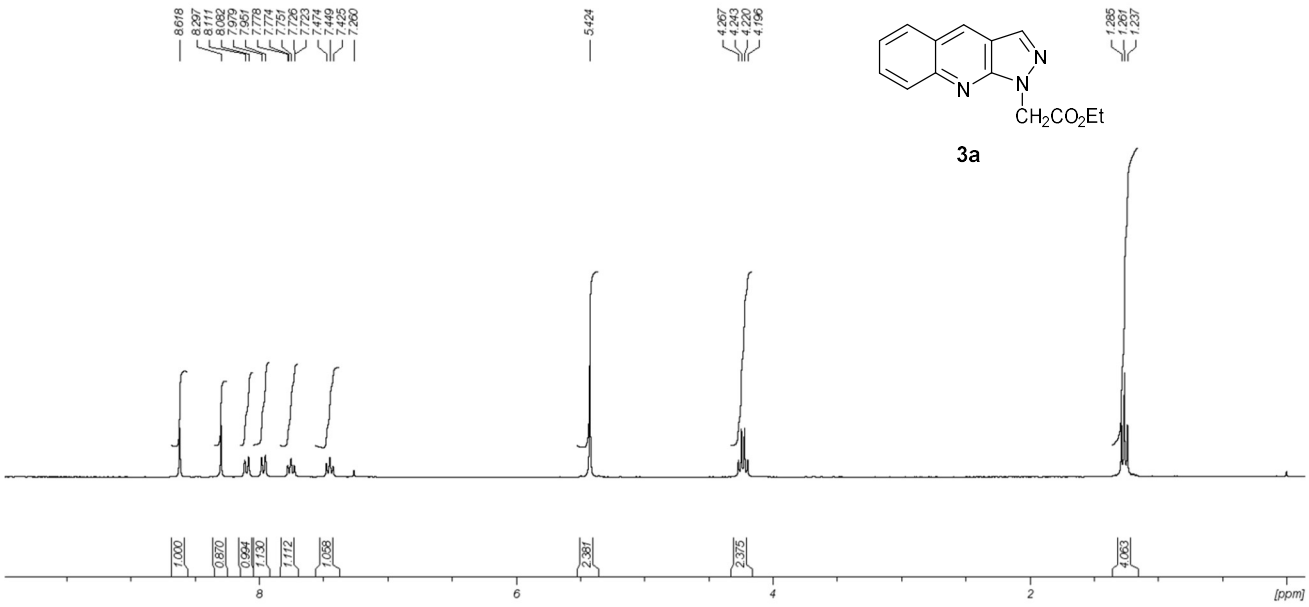

Figure S2. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3a**.

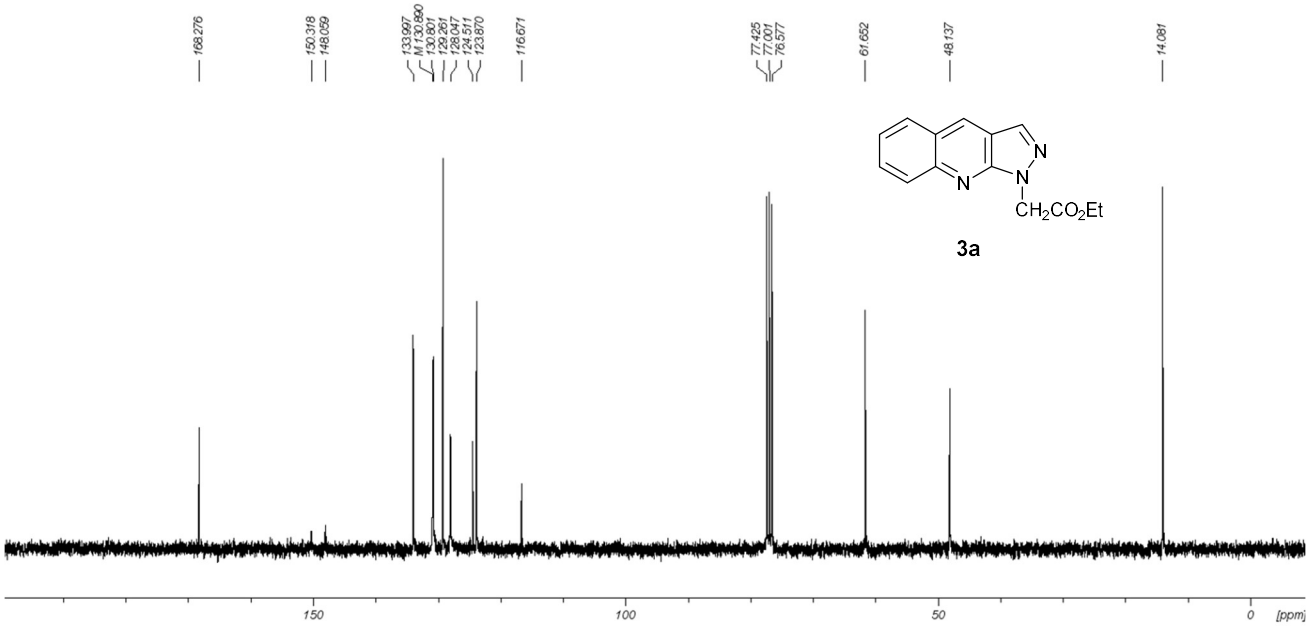

Figure S3. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **3a**.

NMR spectra of ethyl 3-(1*H*-pyrazolo[3,4-*b*]quinolin-1-yl)propanoate (3b)

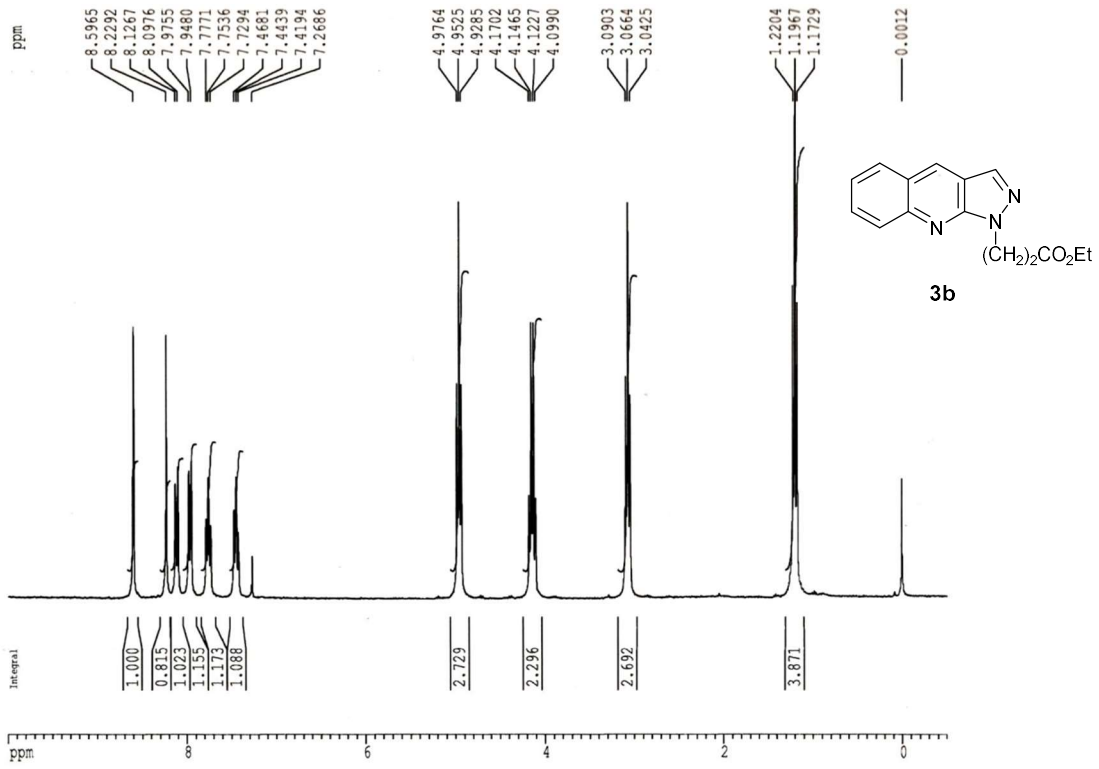

Figure S4. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3b**.

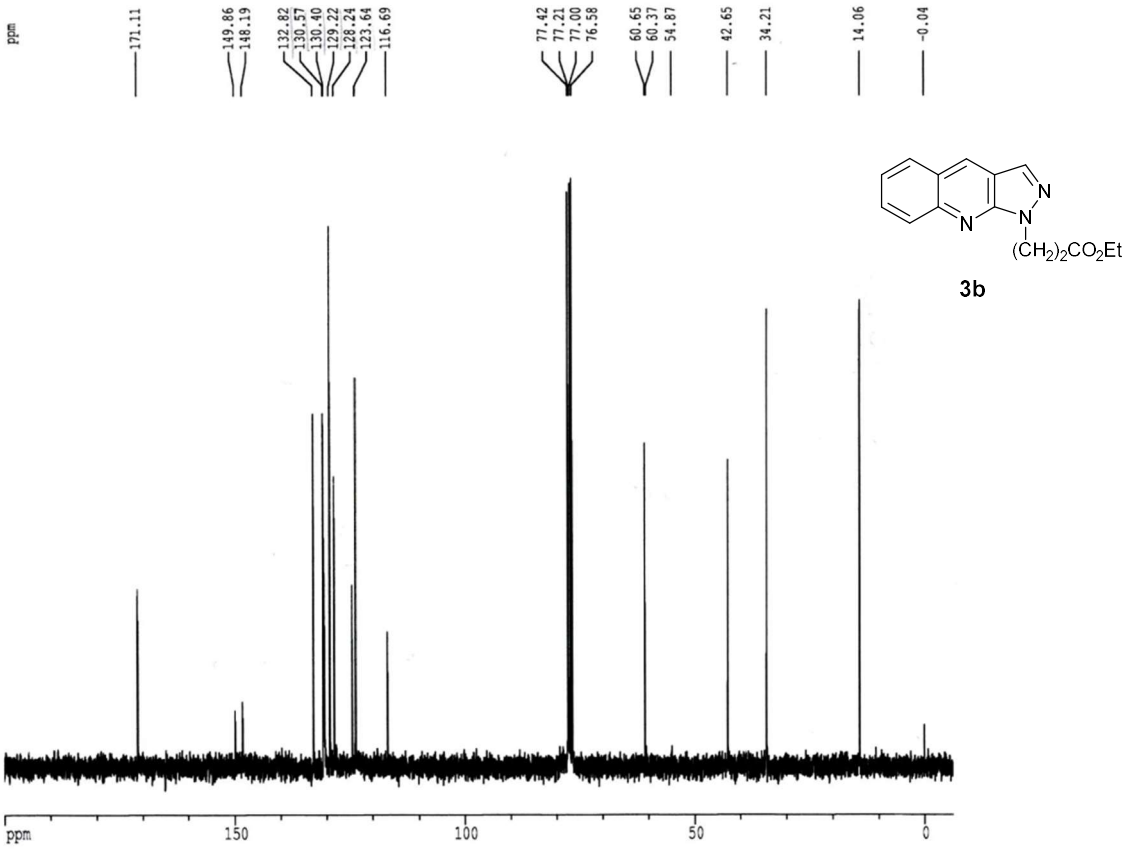

Figure S5. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **3b**.

NMR spectra of ethyl 3-(2*H*-pyrazolo[3,4-*b*]quinolin-2-yl)propanoate (4b)

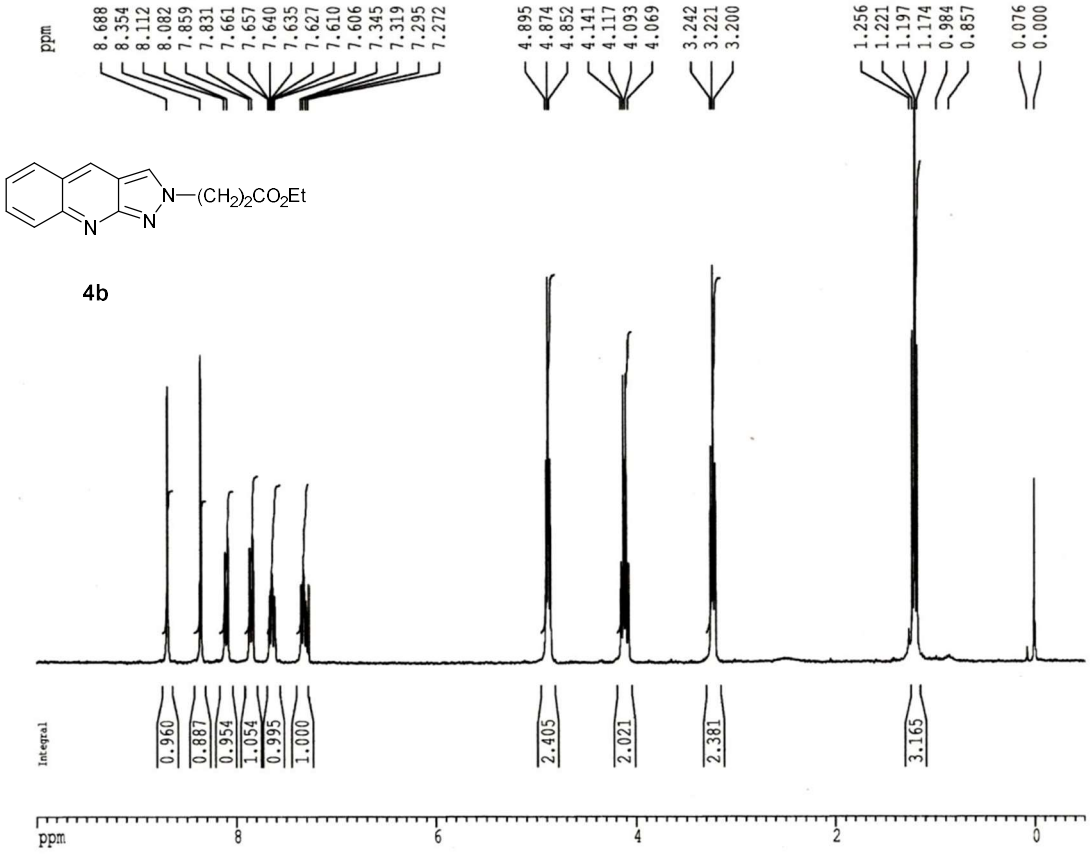

Figure S6. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **4b**.

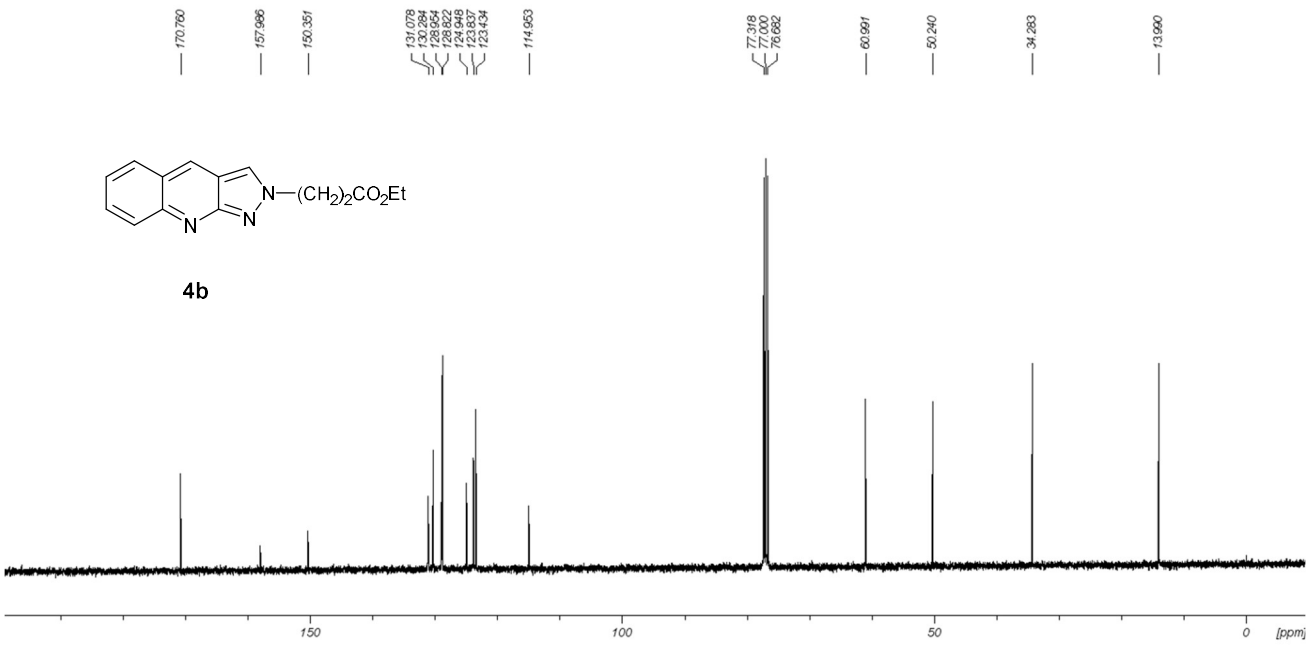

Figure S7. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **4b**.

NMR spectra of ethyl 4-(1*H*-pyrazolo[3,4-*b*]quinolin-1-yl)butanoate (3c)

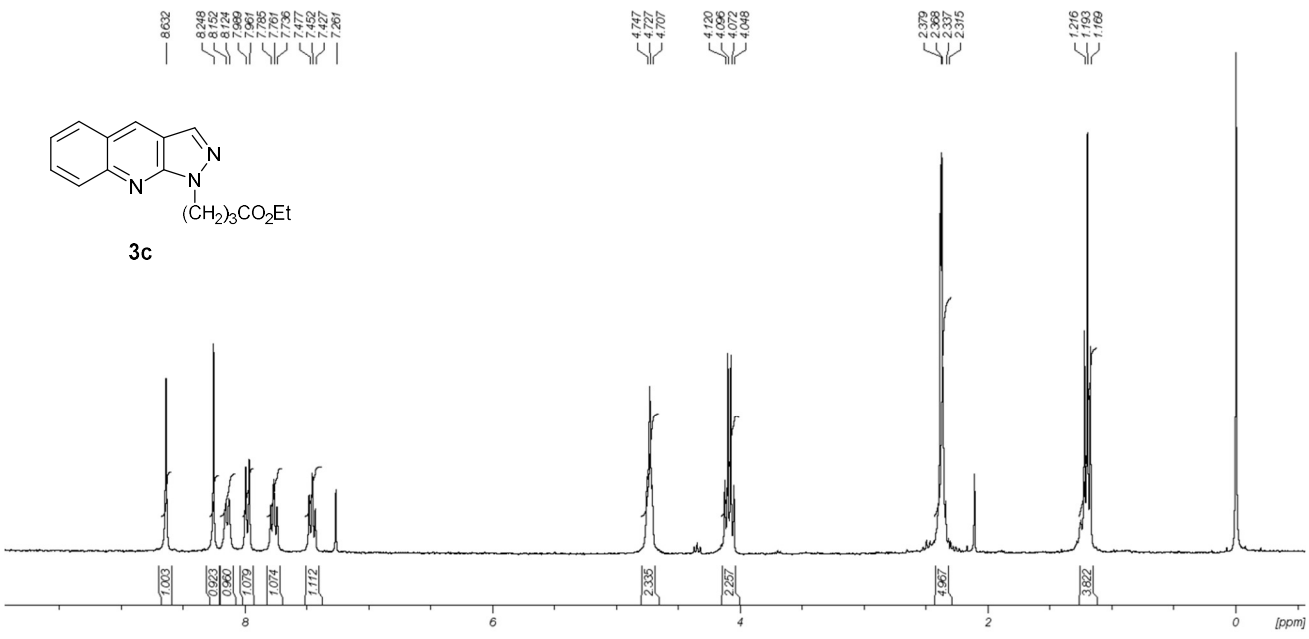

Figure S8. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3c**.

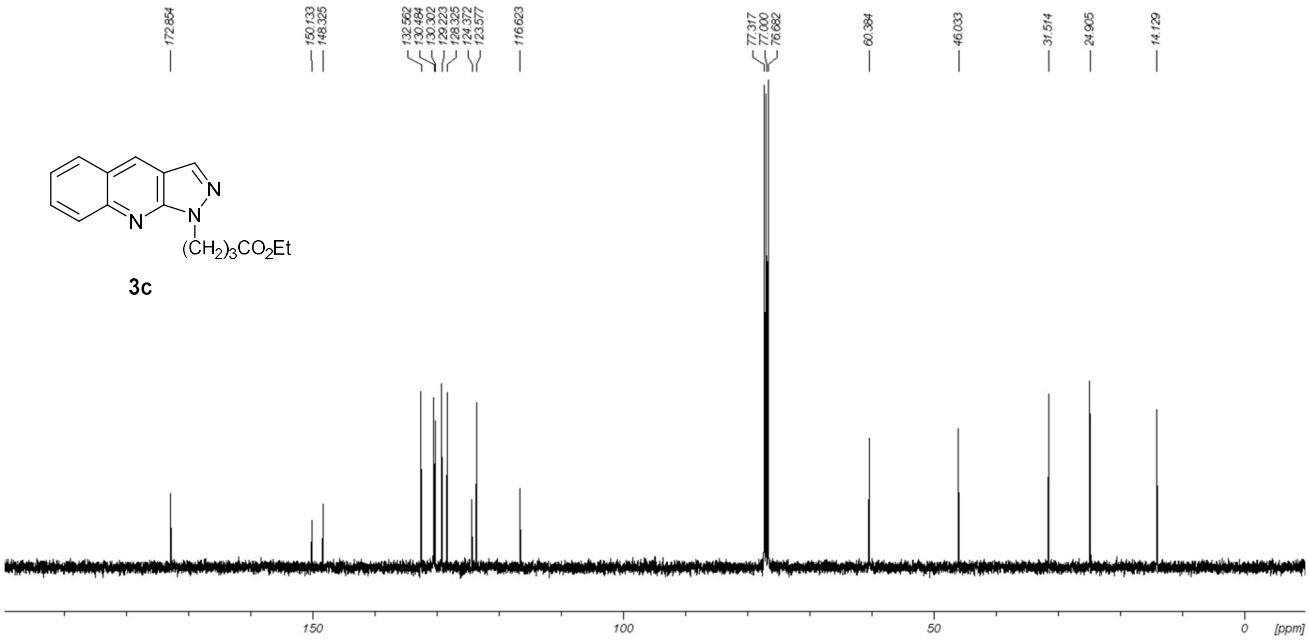

Figure S9. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3c**.

NMR spectra of 1*H*-pyrazolo[3,4-*b*]quinolin-1-ylacetic acid (5a)

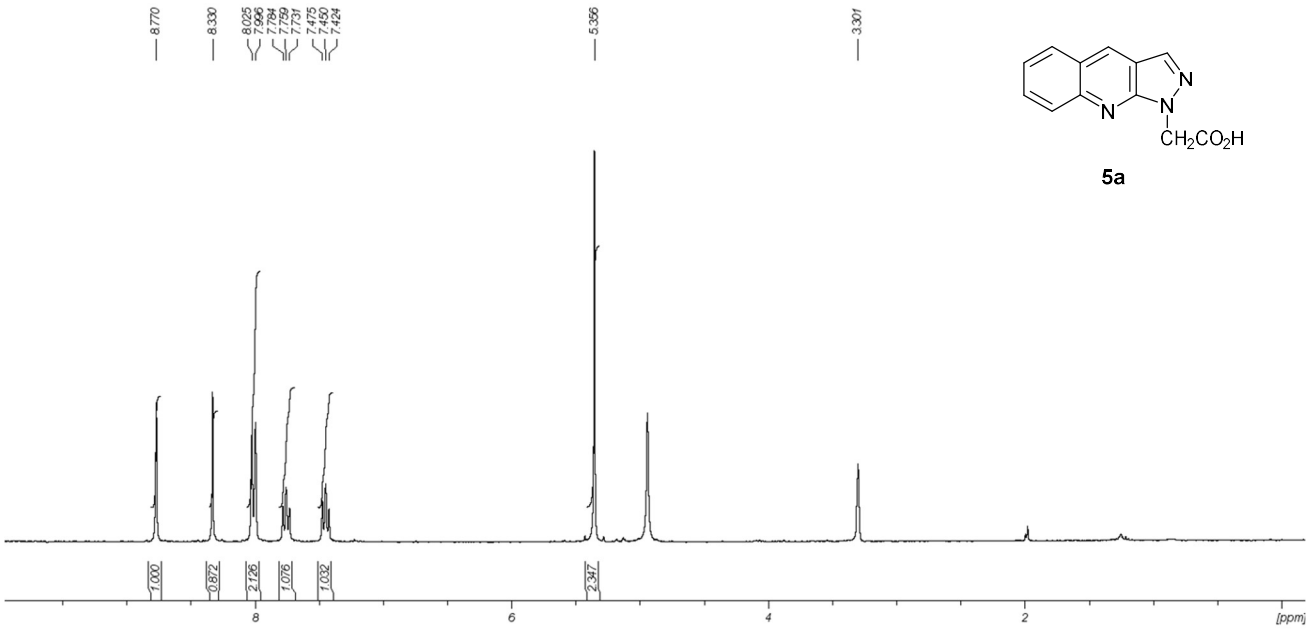

Figure S10. ^{1}H NMR spectrum (300 MHz, MeOD) of compound **5a**.

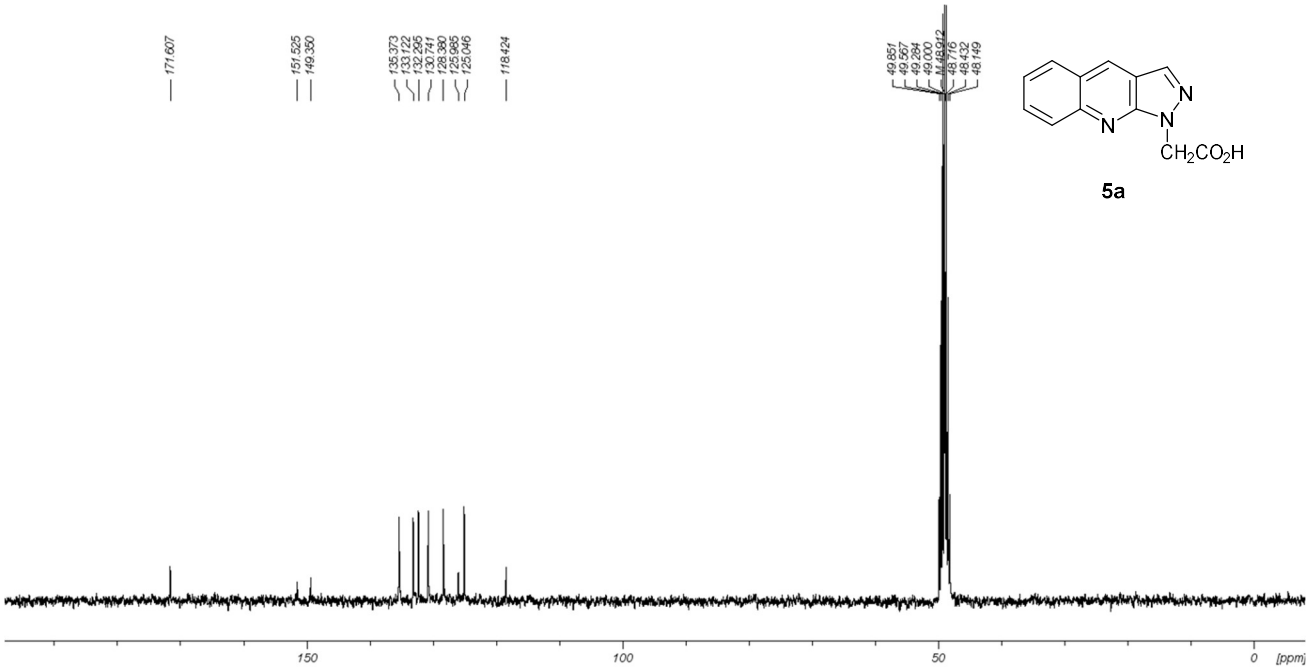

Figure S11. ^{13}C NMR spectrum (75 MHz, MeOD) of compound **5a**.

NMR spectra of 3-1*H*-pyrazolo[3,4-*b*]quinolin-1-ylpropionic acid (5b)

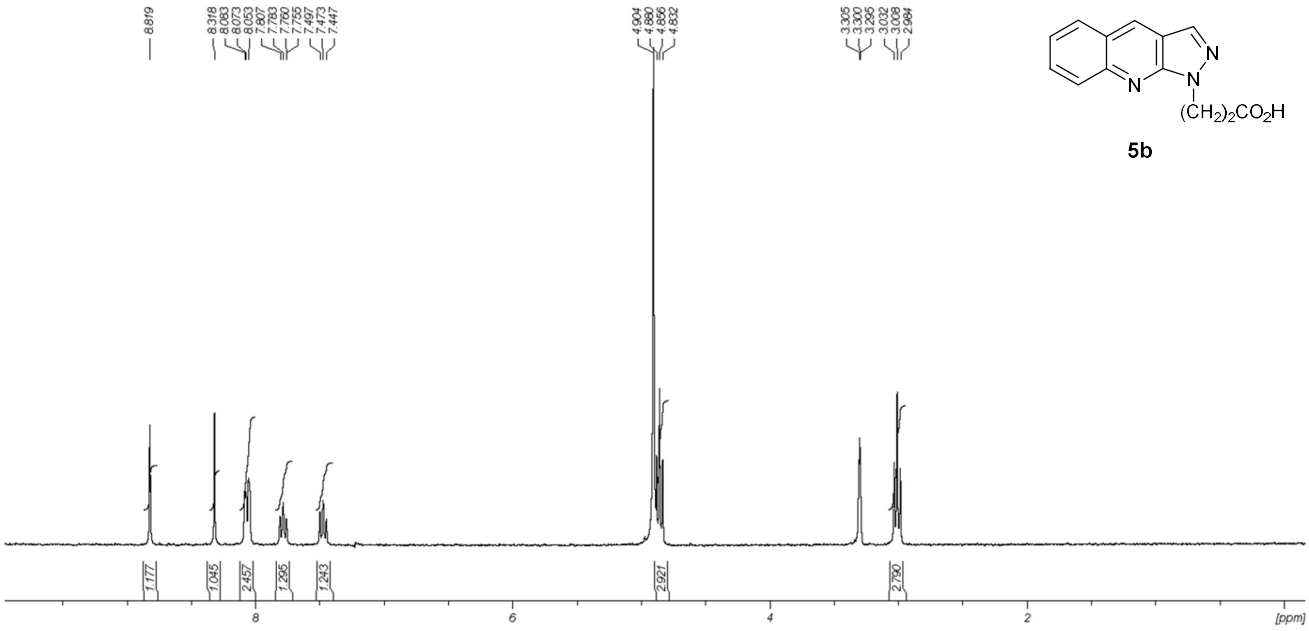

Figure S12. ^{1}H NMR spectrum (300 MHz, MeOD) of compound **5b**.

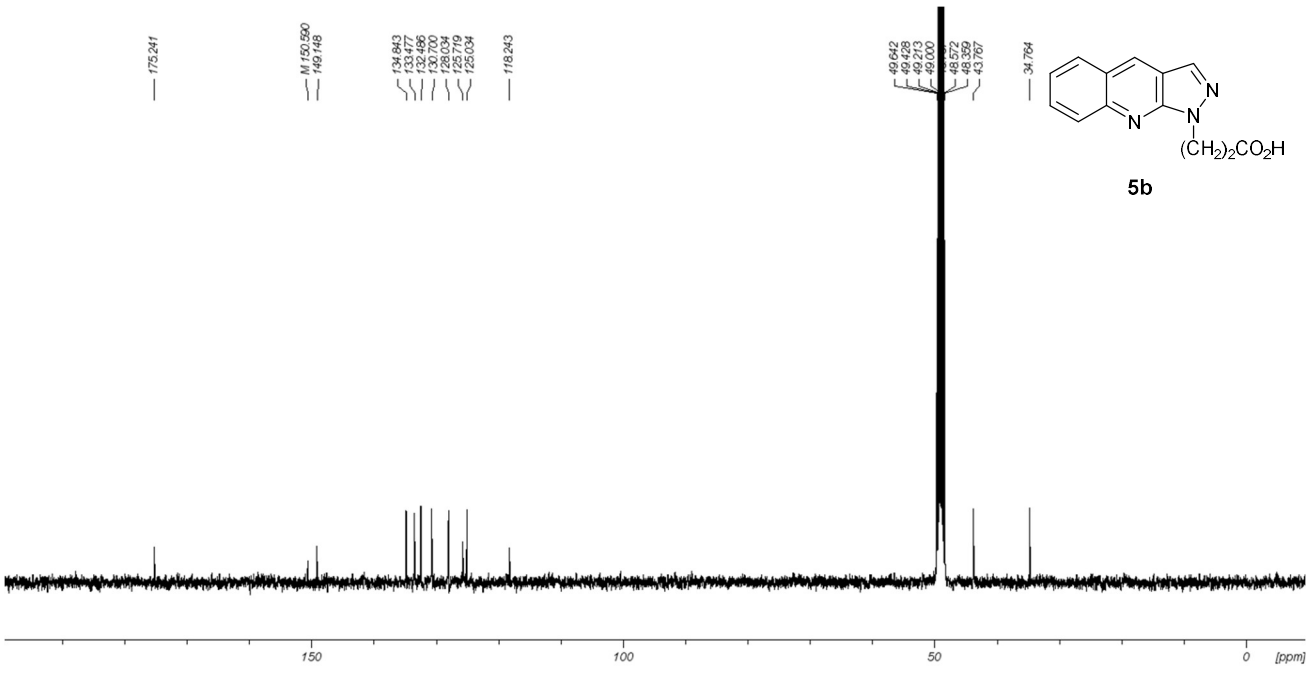

Figure S13. ^{13}C NMR spectrum (100 MHz, MeOD) of compound **5b**.

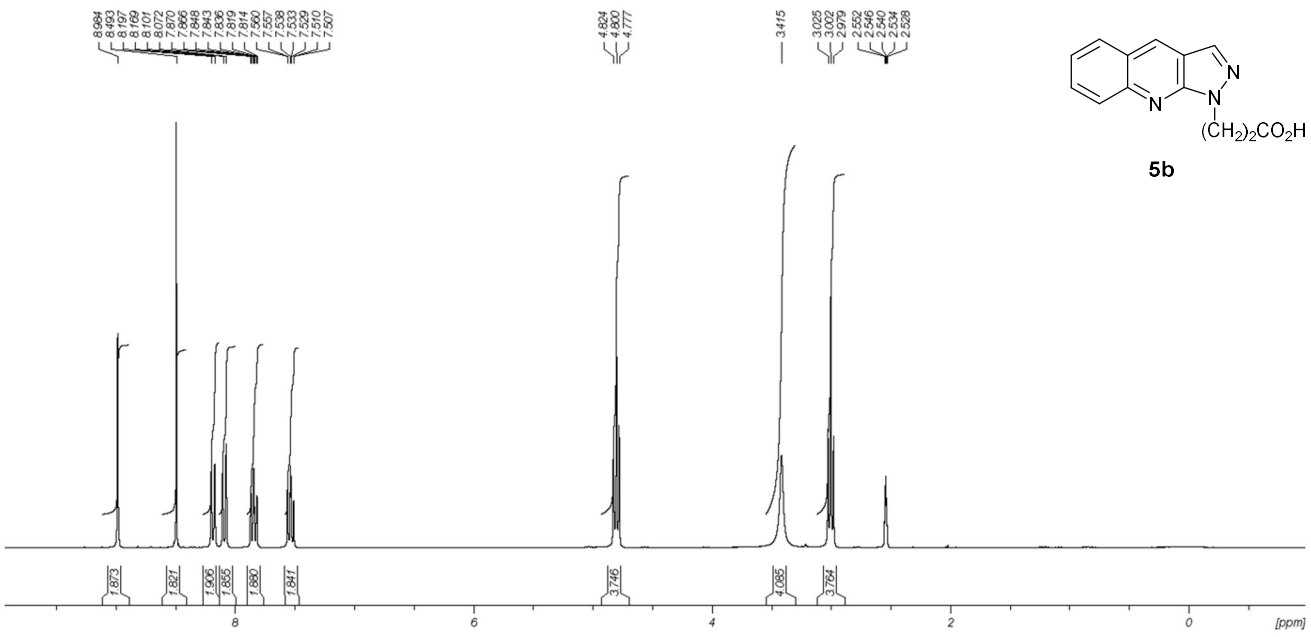

Figure S14. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound **5b**.

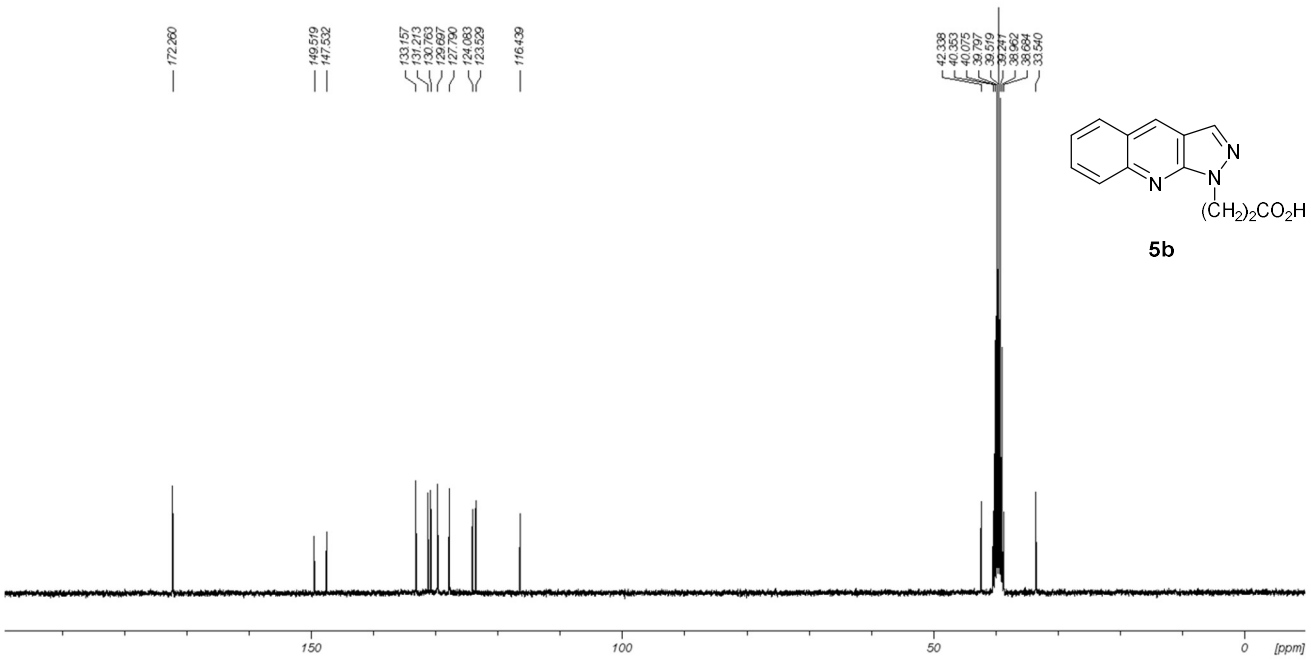

Figure S15. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of compound **5b**.

NMR spectra of 4-1*H*-pyrazolo[3,4-*b*]quinolin-1-ylbutyric acid (5c)

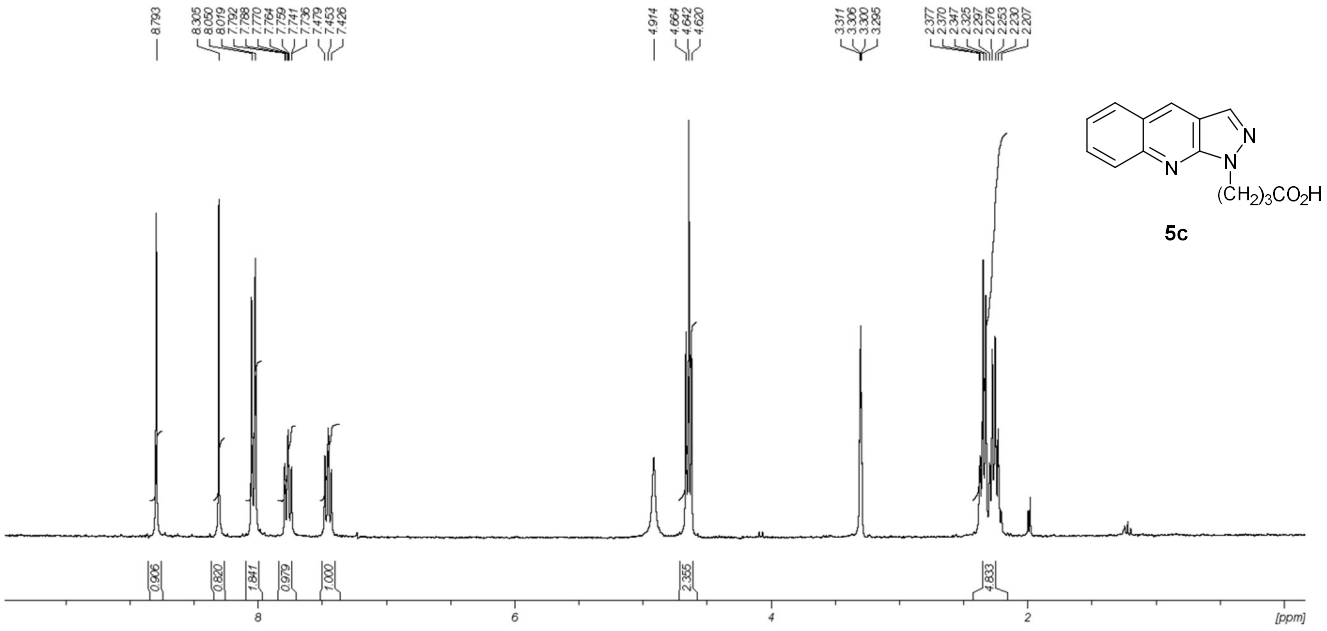

Figure S16. ^{1}H NMR spectrum (300 MHz, MeOD) of compound **5c**.

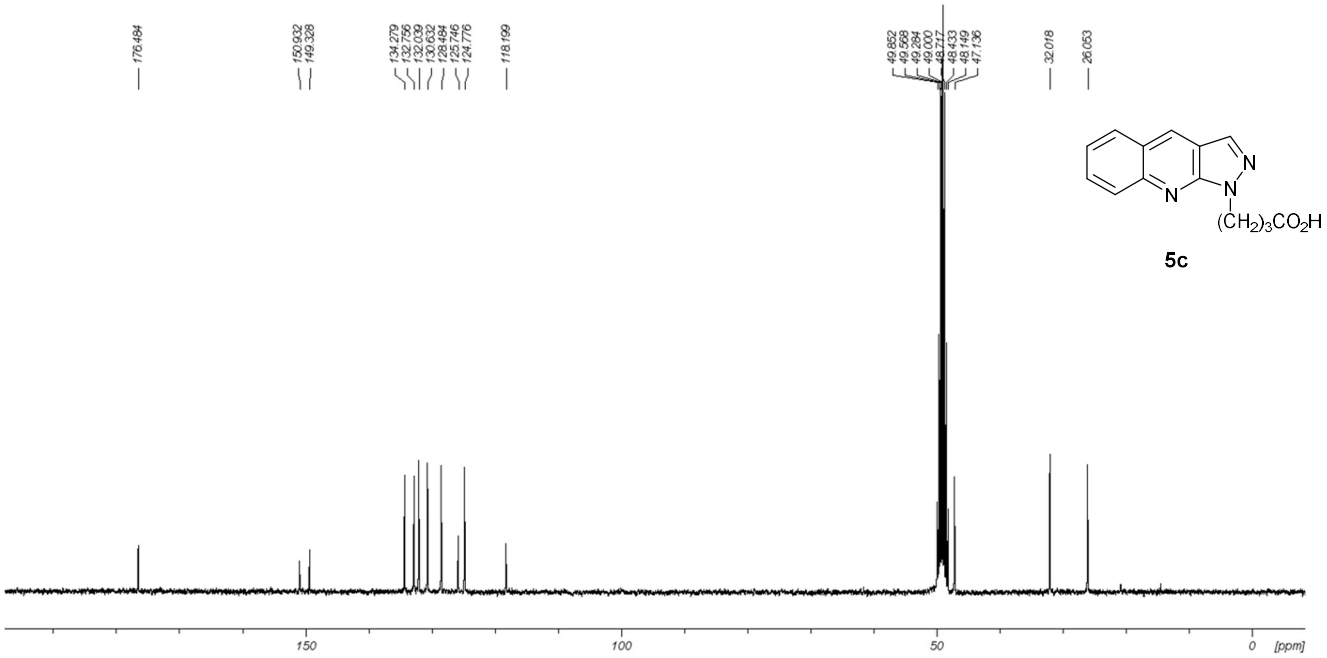

Figure S17. ^{13}C NMR spectrum (75 MHz, MeOD) of compound **5c**.

NMR spectra of 1*H*-pyrazolo[3,4-*b*]quinolin-1-yl)acetylphosphonic acid (9)

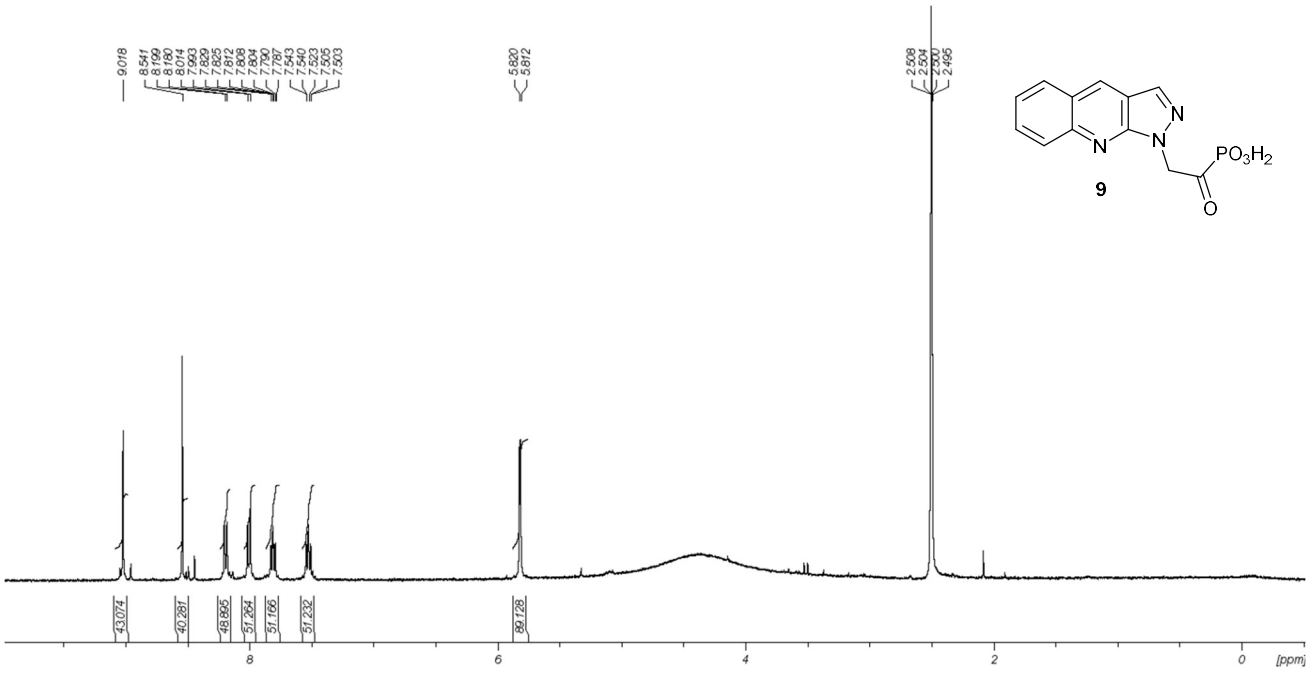

Figure S18. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **9**.

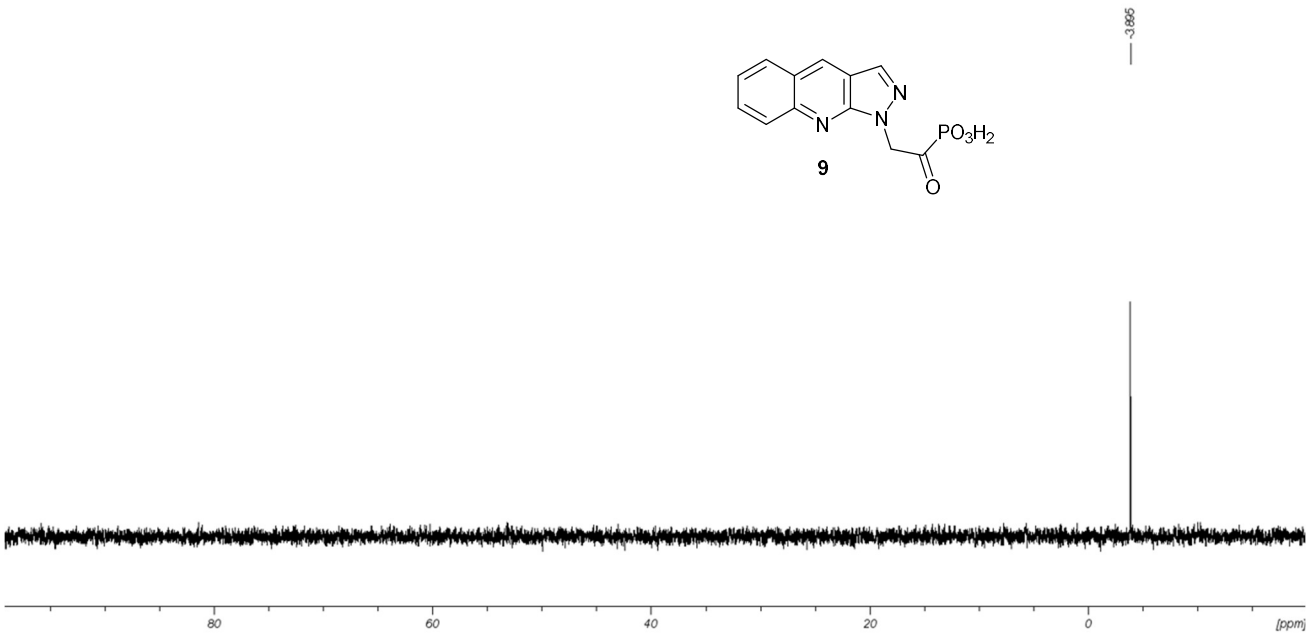

Figure S19. ^{31}P NMR spectrum (162 MHz, DMSO-d_6) of compound **9**.

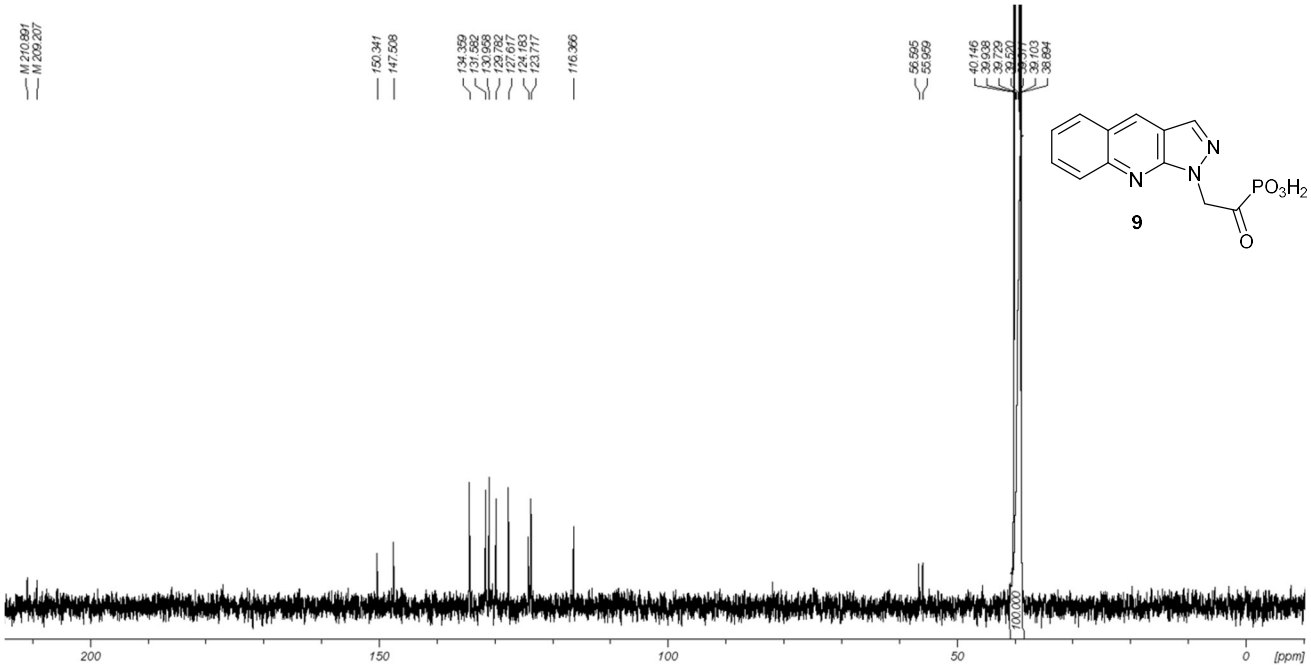

Figure S20. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **9**.

NMR spectra of [1-hydroxy-2-(1*H*-pyrazolo[3,4-*b*]quinolin-1-yl)ethane-1,1-diyl]bis(phosphonic acid) (6)

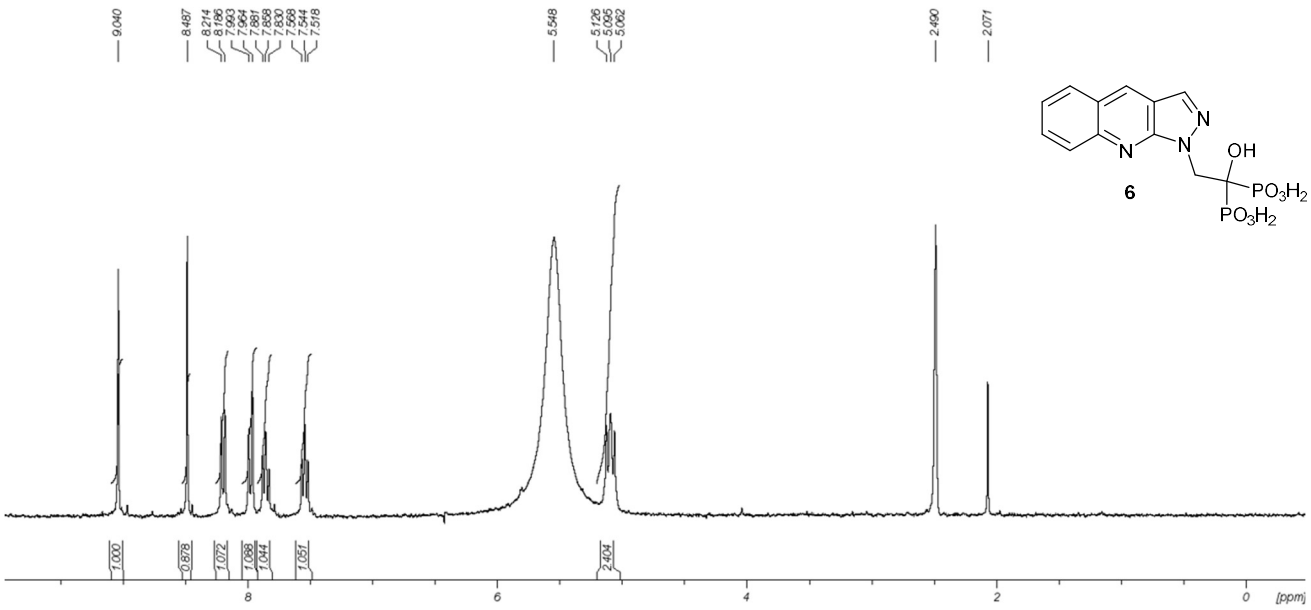

Figure S21. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound **6**.

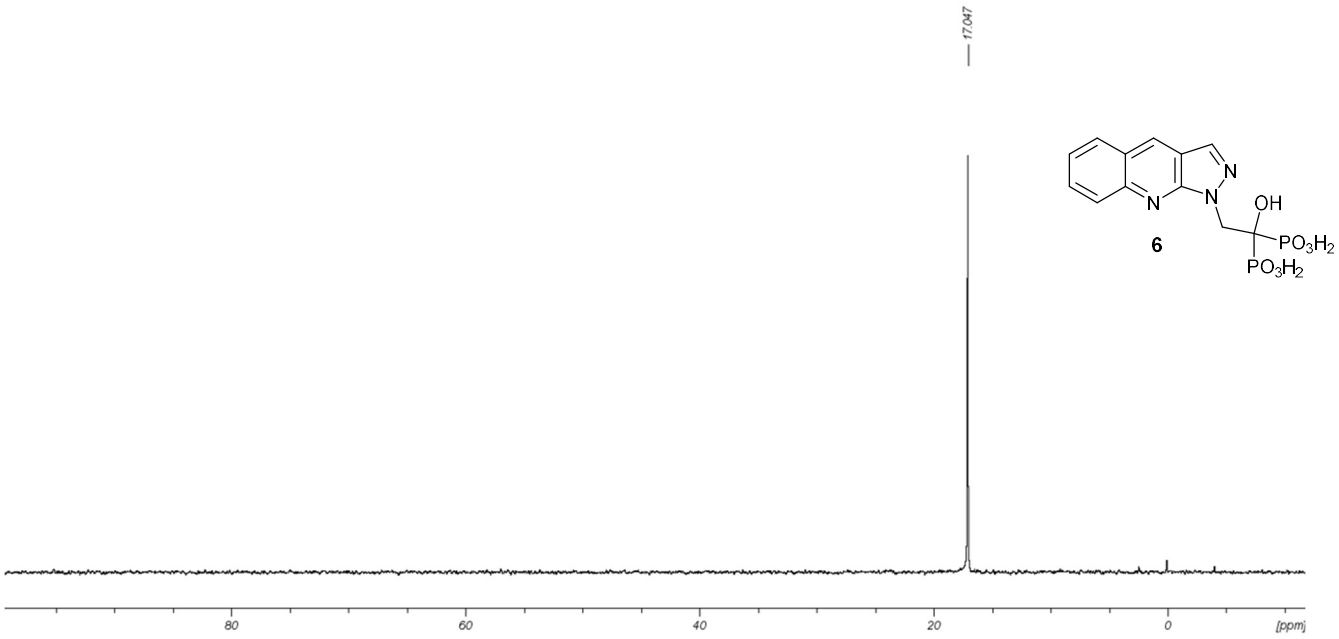

Figure S22. ^{31}P NMR spectrum (121 MHz, DMSO-d_6) of compound **6**.

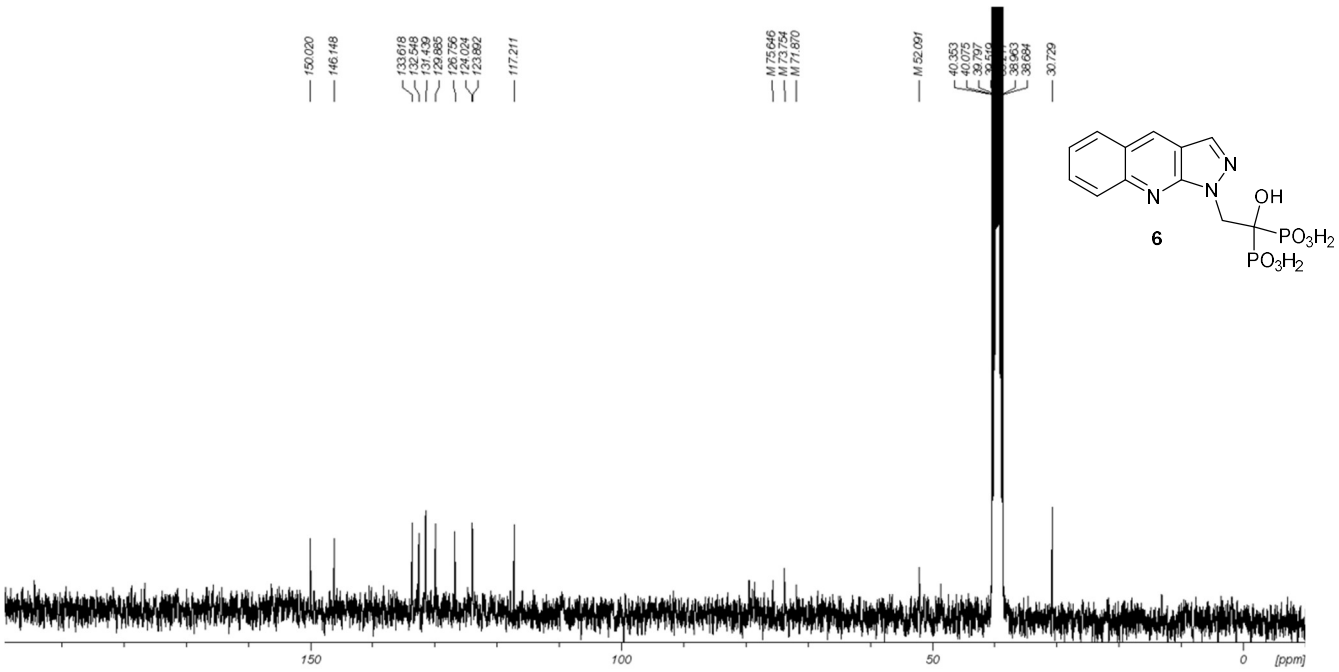

Figure S23. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of [compound **6**.

NMR spectra of [1-hydroxy-4-(1*H*-pyrazolo[3,4-*b*]quinolin-1-yl)butane-1,1-diyl]bis(phosphonic acid) (8)

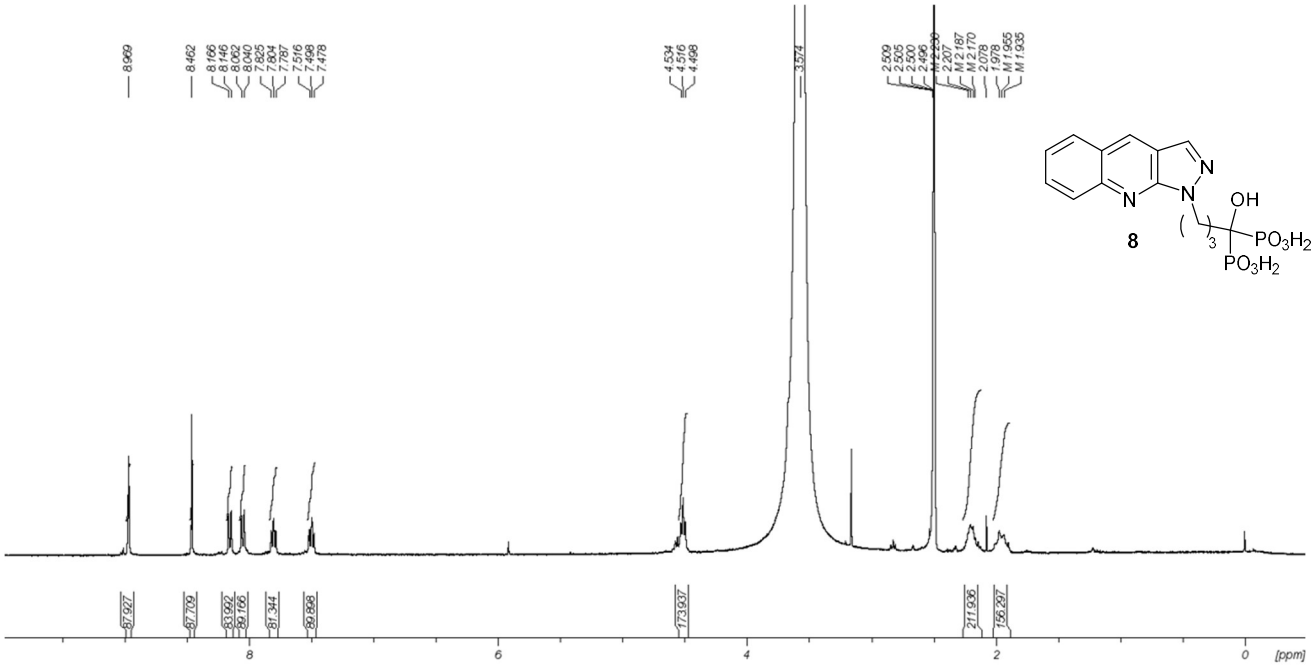

Figure S24. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **8**.

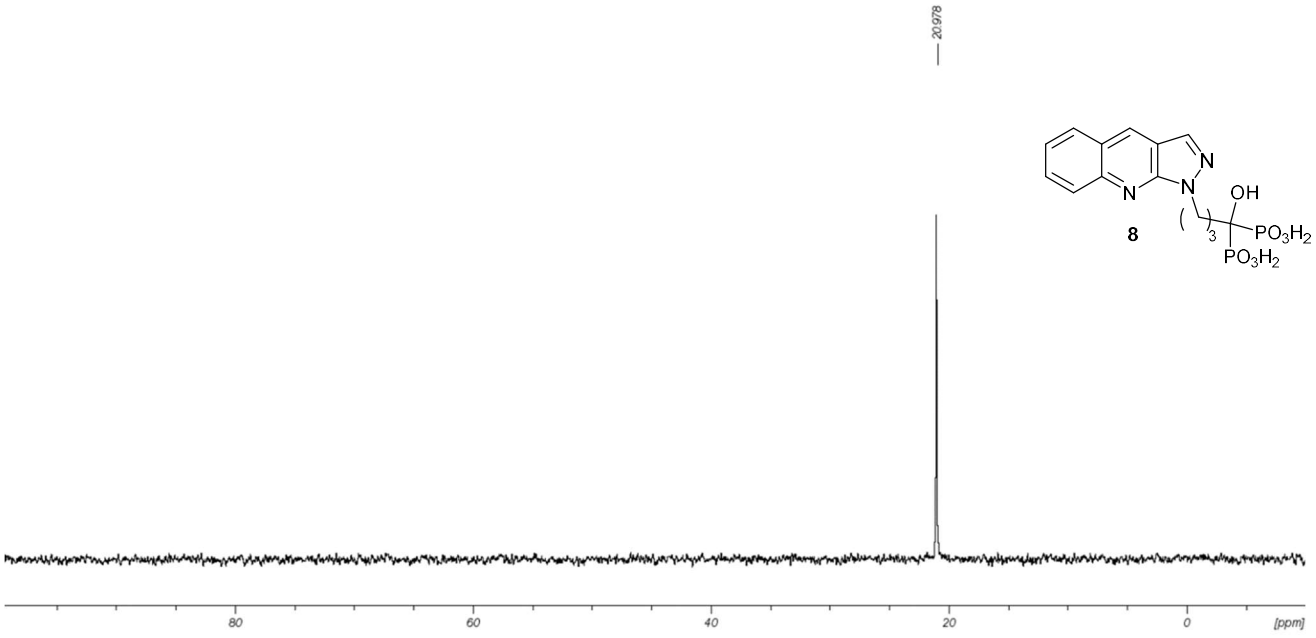

Figure S25. ^{31}P NMR spectrum (121 MHz, DMSO-d_6) of compound **8**.

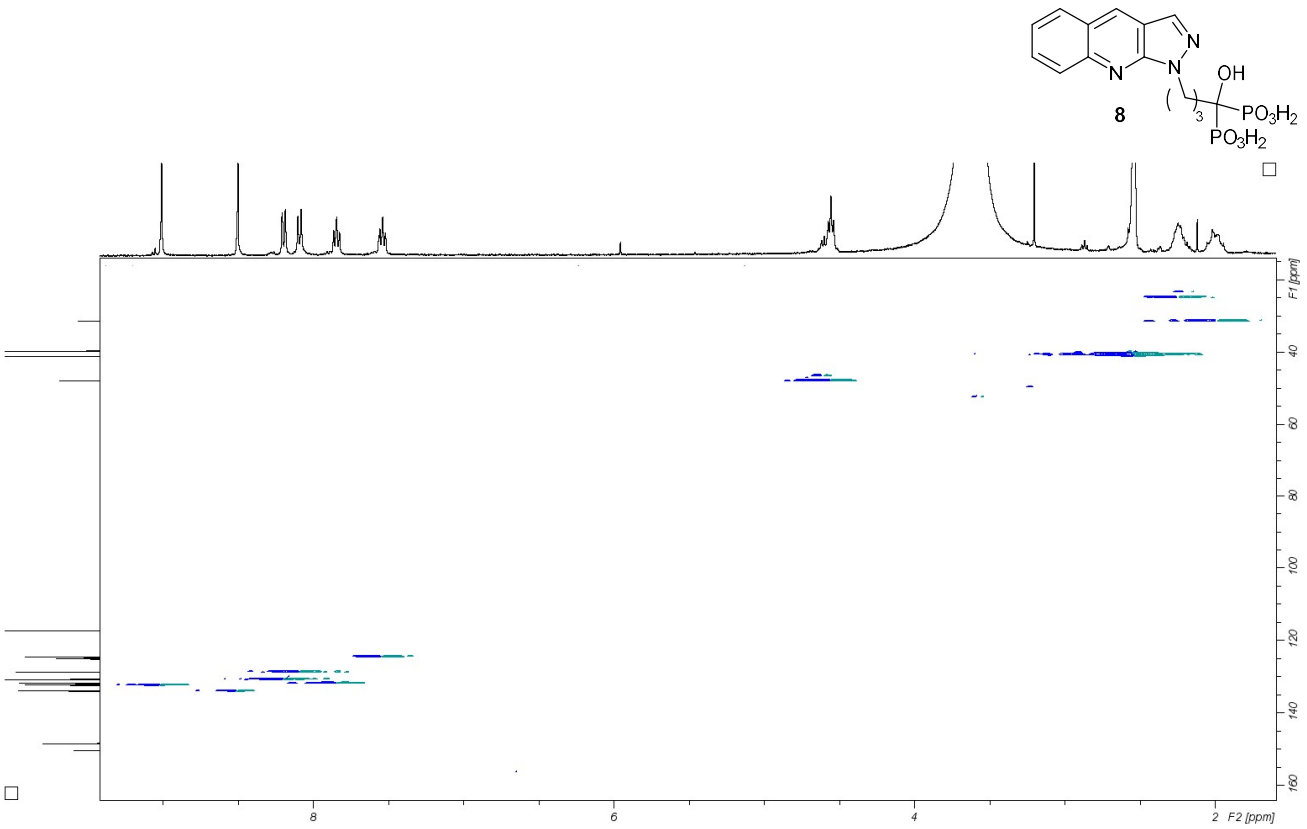

Figure S26. HSQC NMR spectrum of compound **8**.

NMR spectra of (1-oxo-2,3-dihydro-1*H*,6*H*-3*a*,4,10*b*-triazaacephenanthrylen-6-yl)phosphonic acid (10)

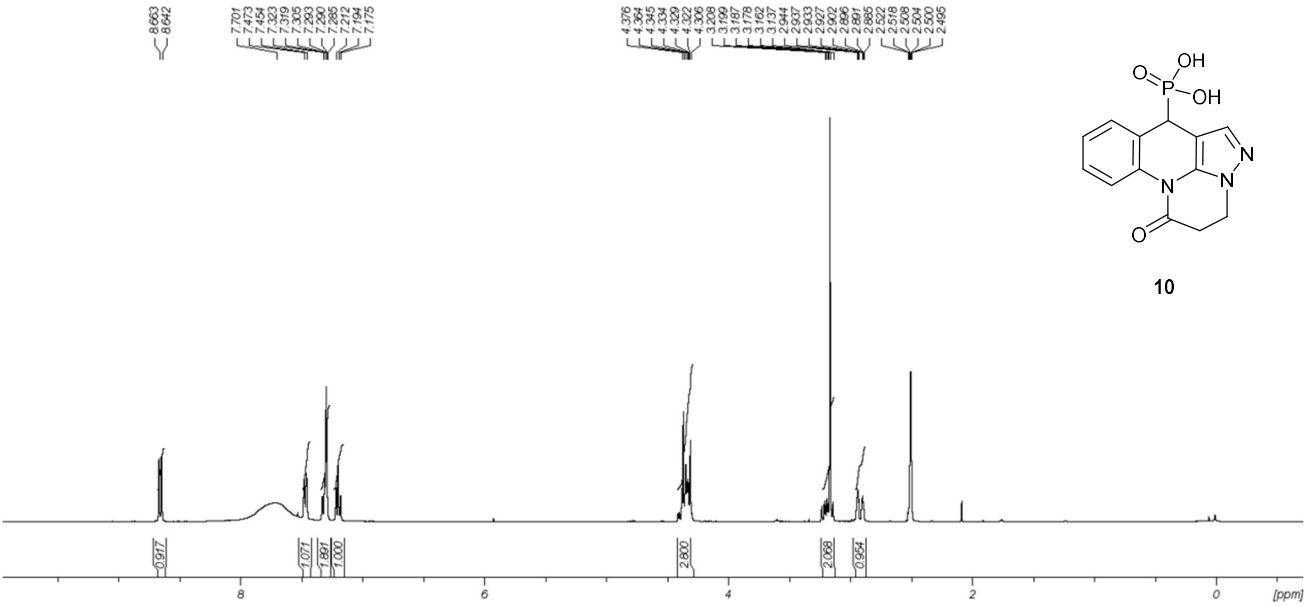

Figure S27. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **10**.

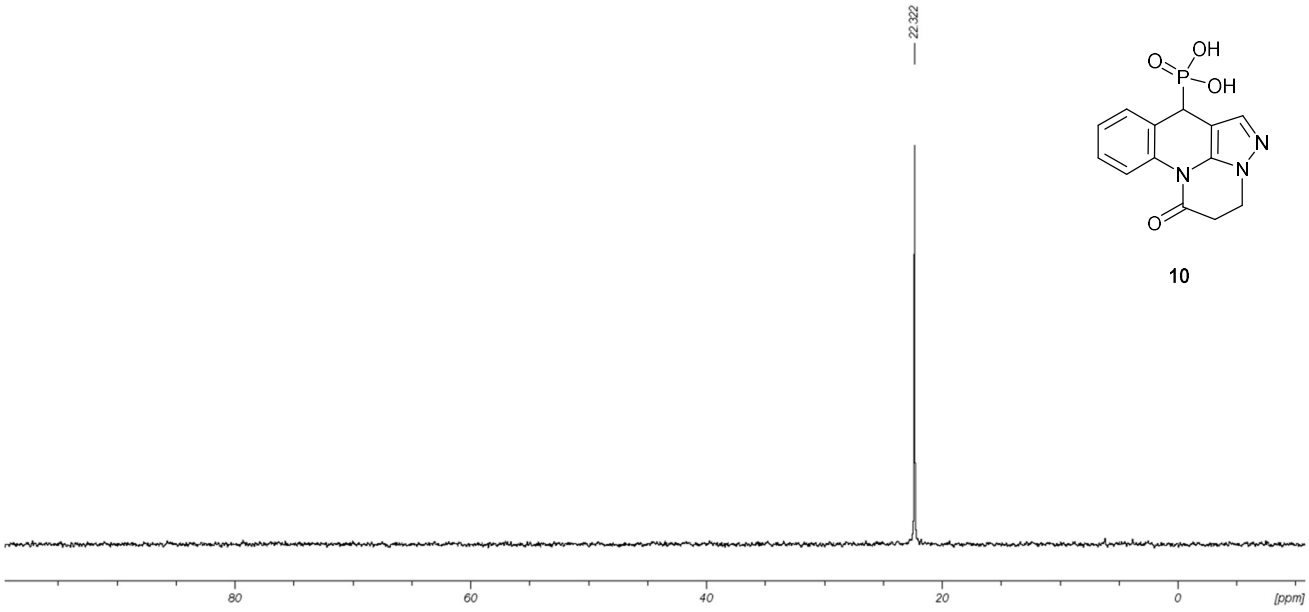

Figure S28. ^{31}P NMR spectrum (121 MHz, DMSO-d_6) of compound **10**.

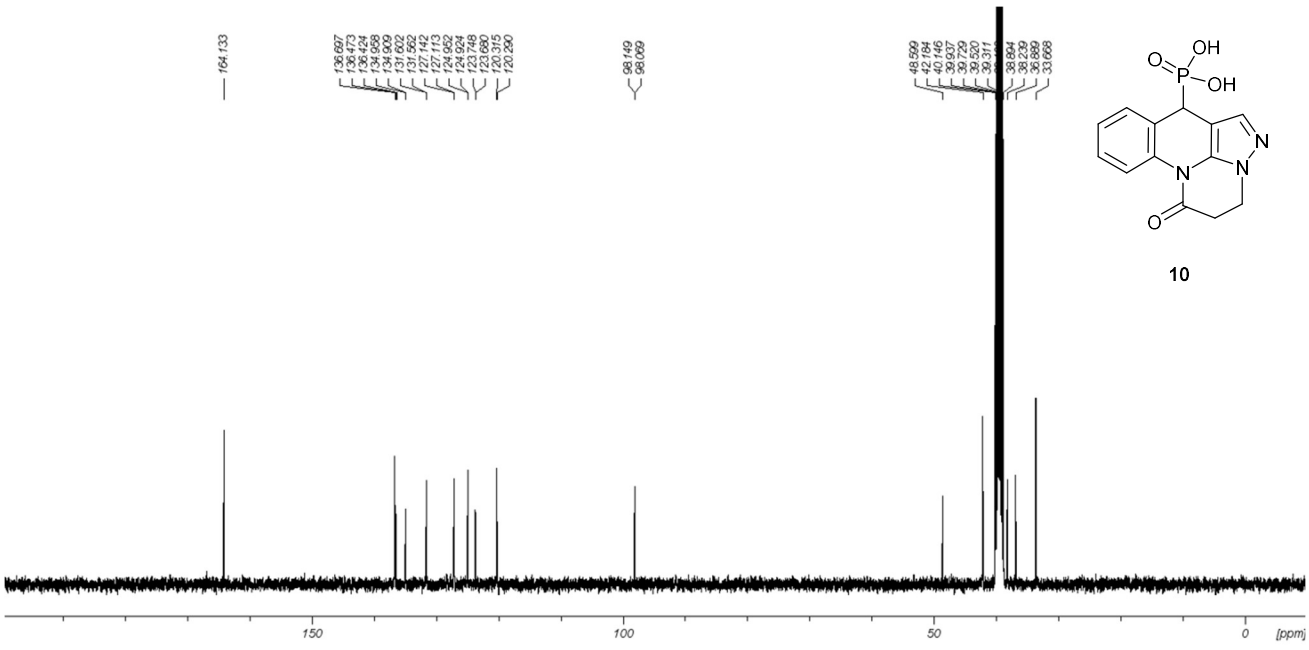

Figure S29. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **10**.

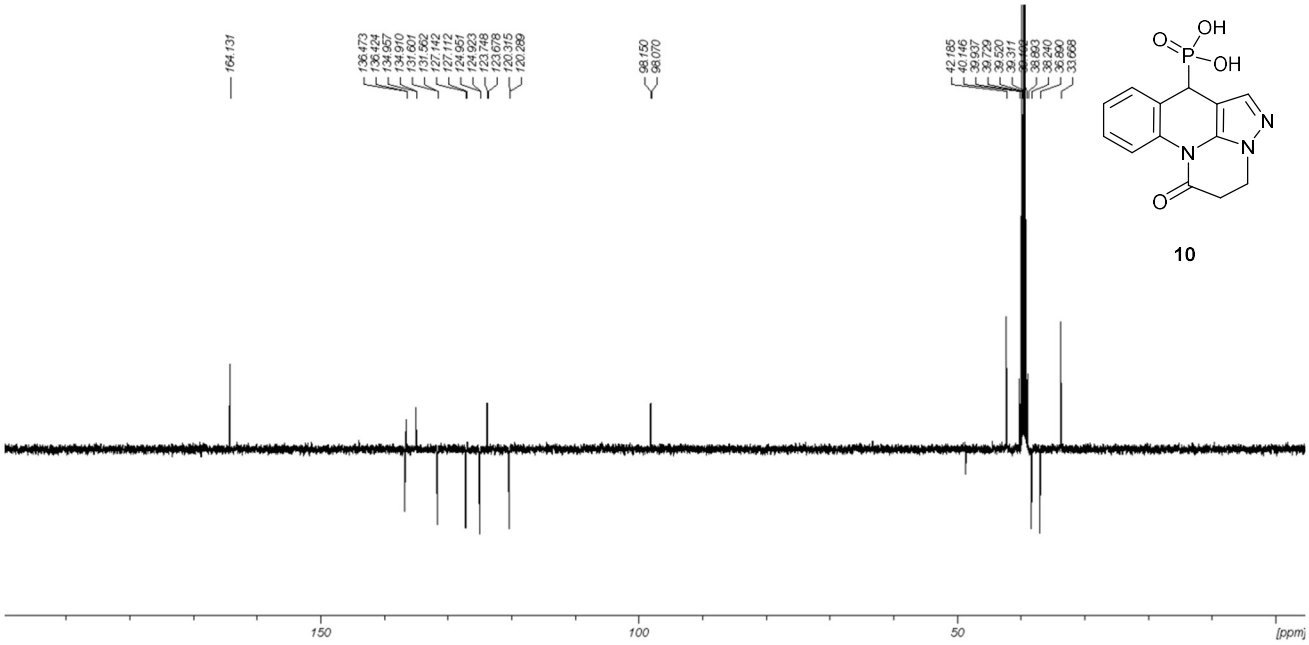

Figure S30. APT NMR spectrum (100 MHz, DMSO-d_6) of compound **10**.

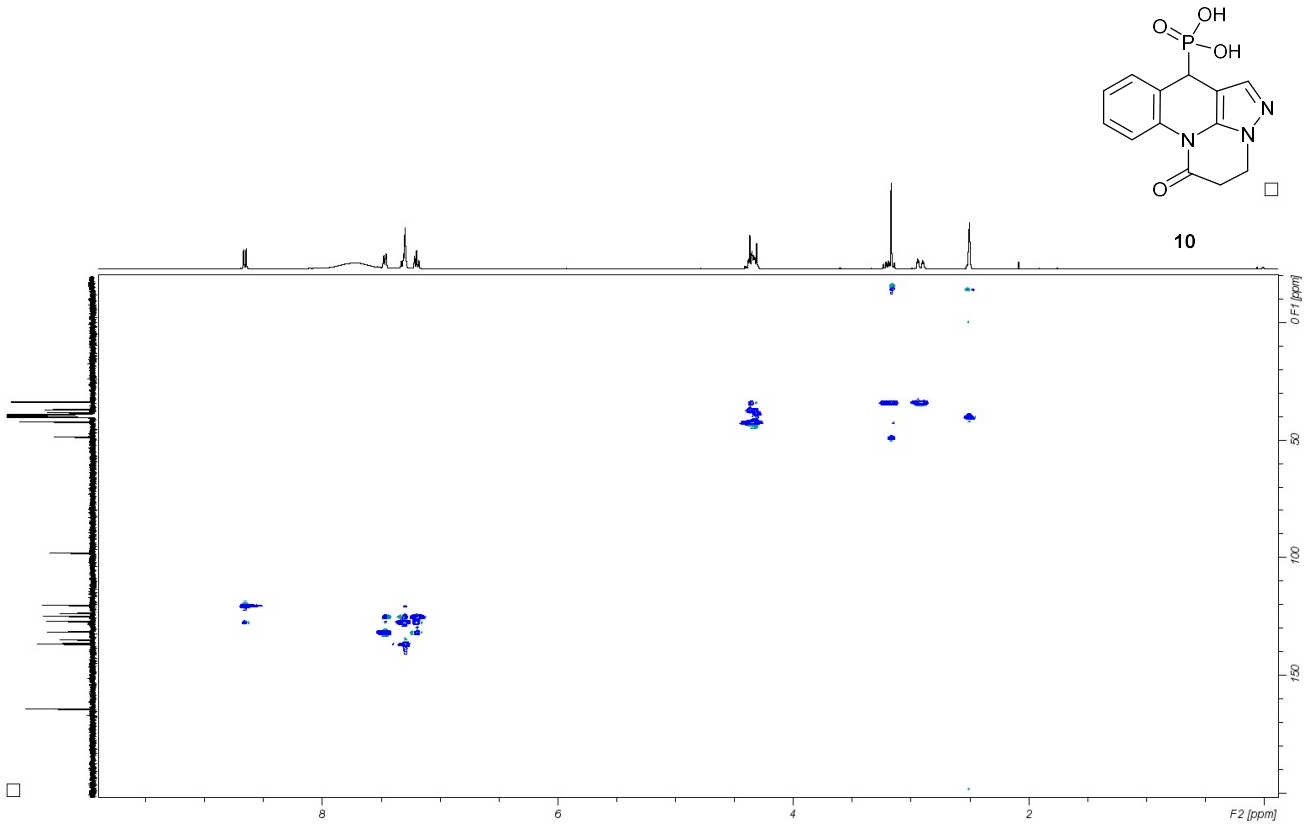

Figure S31. HSQC NMR spectrum of compound **10**.

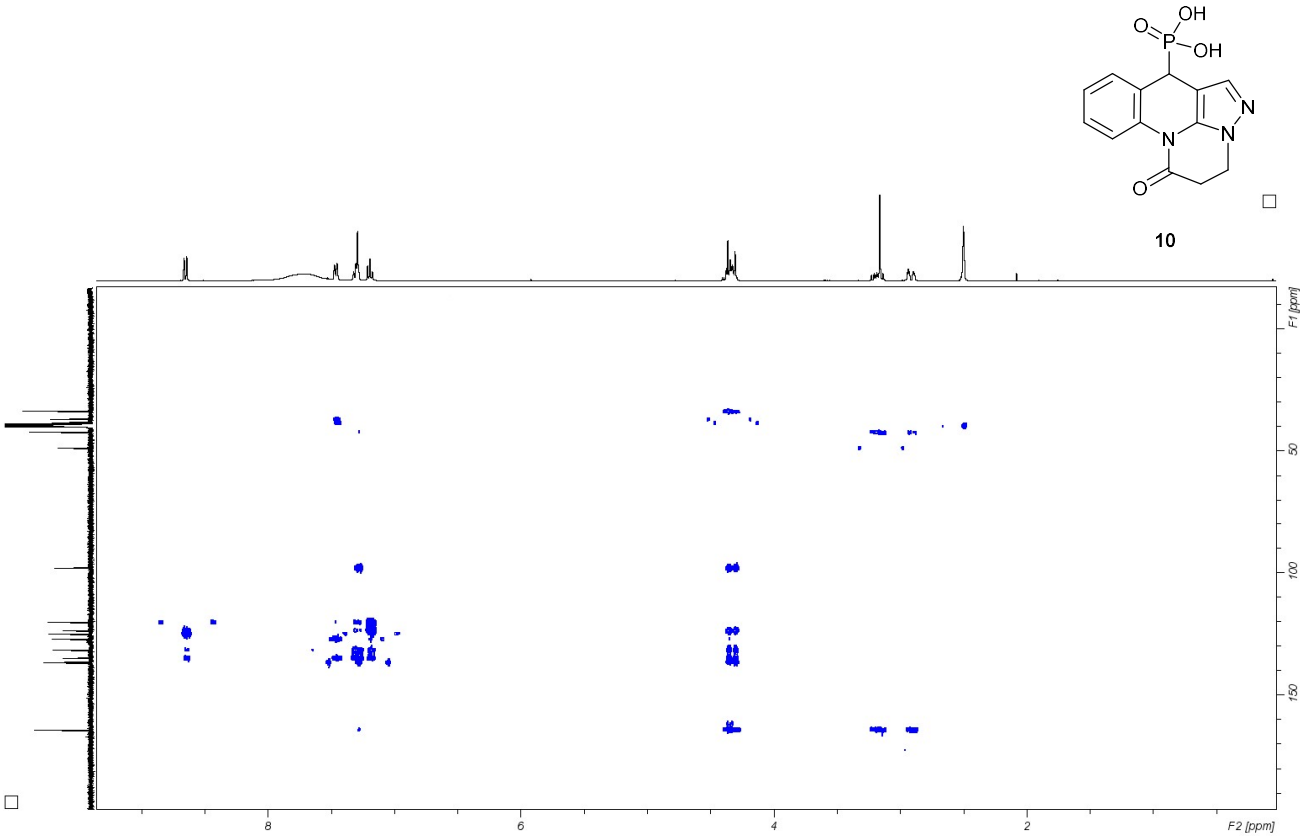

Figure S32. HMBC NMR spectrum of compound **10**.

NMR spectra of diethyl (1-oxo-2,3-dihydro-1H,6H-3*a*,4,10*b*-triazaacephenanthrylen-6-yl)phosphonate (11)

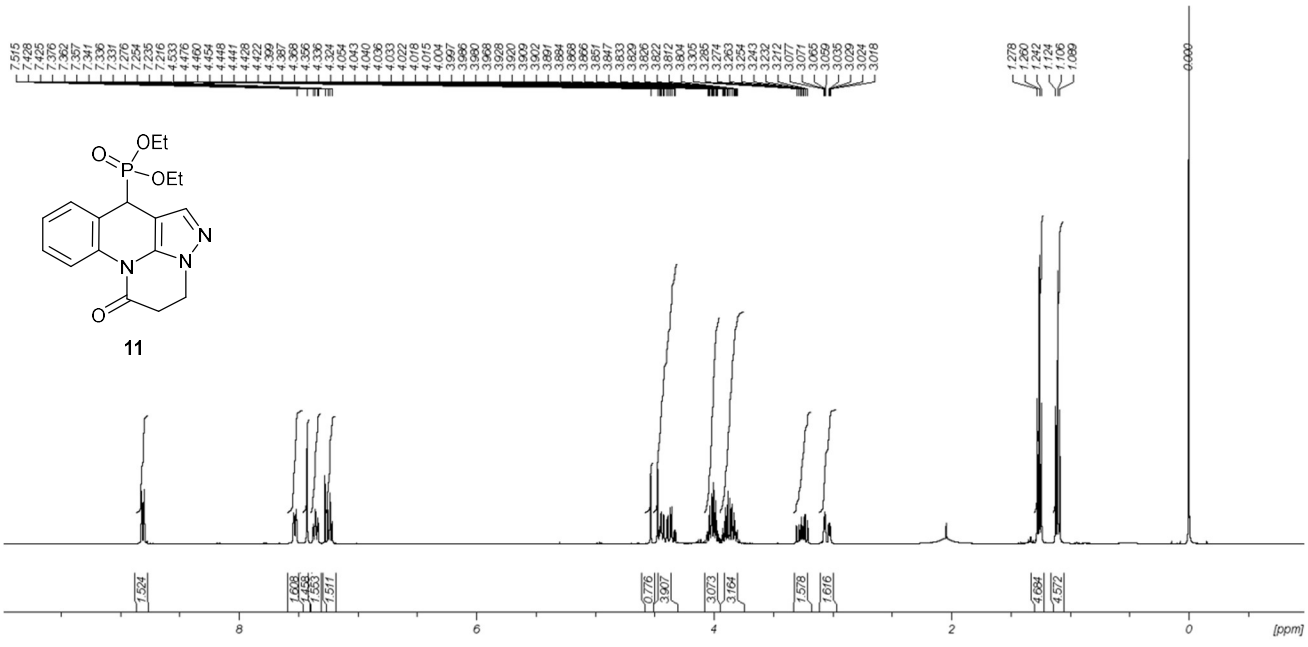

Figure S33. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **11**.

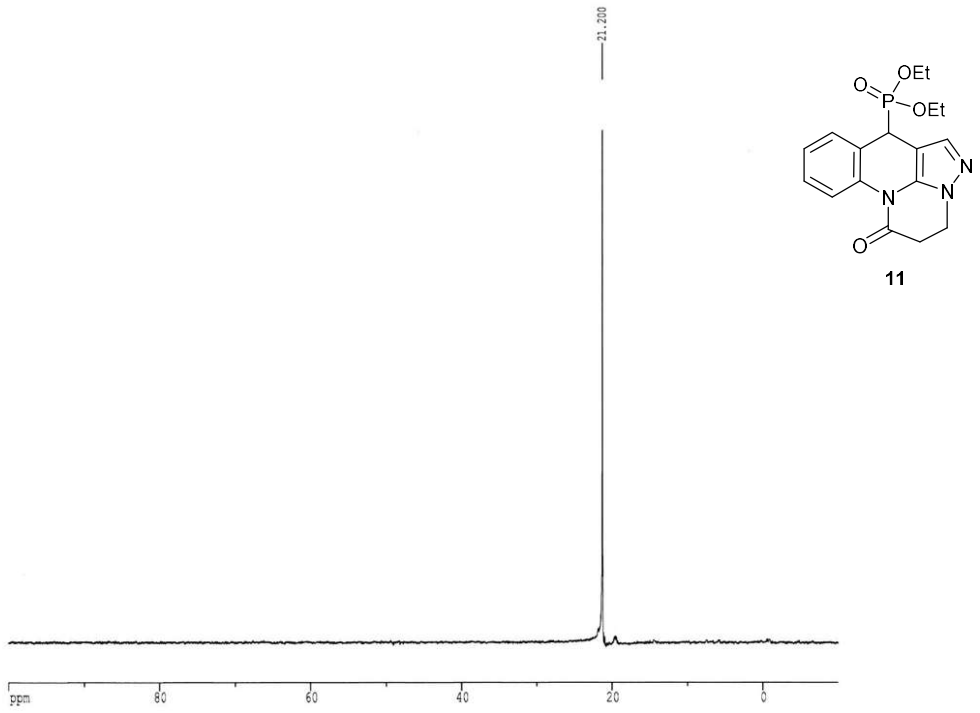

Figure S34. ^{31}P NMR spectrum (121 MHz, $CDCl_3$) of compound **11**.

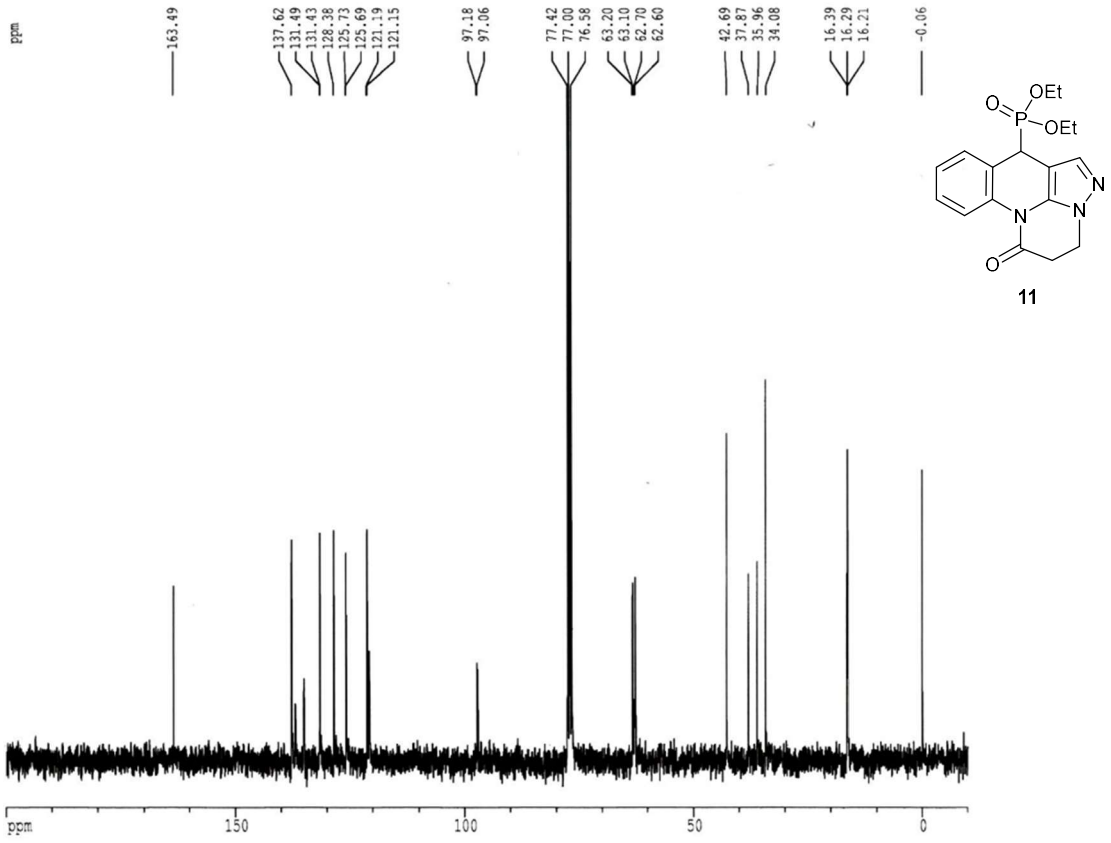

Figure S35. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **11**.

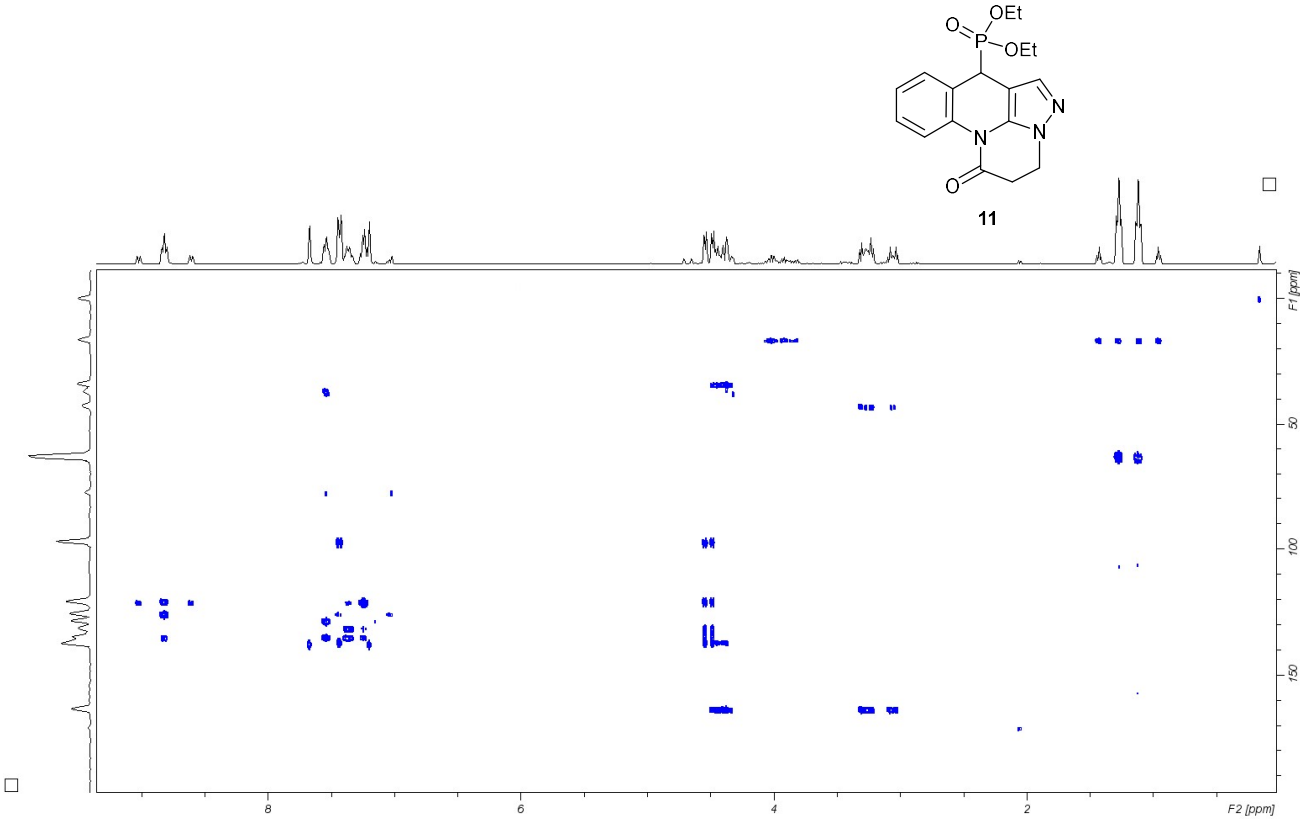

Figure S36. HMBC NMR spectrum of compound **11**.

2. CheckCIF/PLATON report for compound 11-I

Structure factors have been supplied for datablock(s) 1

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1

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Temperature:     296 K

                Calculated                Reported
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Hall group      -P 2yn                    -P 2yn
Moiety formula  C17 H20 N3 O4 P           ?
Sum formula     C17 H20 N3 O4 P           C17 H20 N3 O4 P
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Dx,g cm-3       1.390                     1.390
Z               4                         4
Mu (mm-1)       0.187                     0.187
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F000'           760.74
h,k,lmax        10,14,30                  10,14,30
Nref            4856                      4838
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Tmin'           0.976

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S = 1.040                 Npar= 226
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

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PLAT220_ALERT_2_C NonSolvent   Resd 1  C   Ueq(max)/Ueq(min) Range        3.1 Ratio
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00436 Ang.
PLAT360_ALERT_2_C Short  C(sp3)-C(sp3) Bond  C15      - C16      .       1.43 Ang.
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          2 Report
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Alert level G

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PLAT793_ALERT_4_G Model has Chirality at C4         (Centro SPGR)          R Verify
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          3 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         14 Note
PLAT933_ALERT_2_G Number of OMIT Records in Embedded .res File ...          4 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          1 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by          3 Check
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   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   4 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   7 ALERT level G = General information/check it is not something unexpected

   1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   4 ALERT type 2 Indicator that the structure model may be wrong or deficient
   3 ALERT type 3 Indicator that the structure quality may be low
   2 ALERT type 4 Improvement, methodology, query or suggestion
   1 ALERT type 5 Informative message, check
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It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

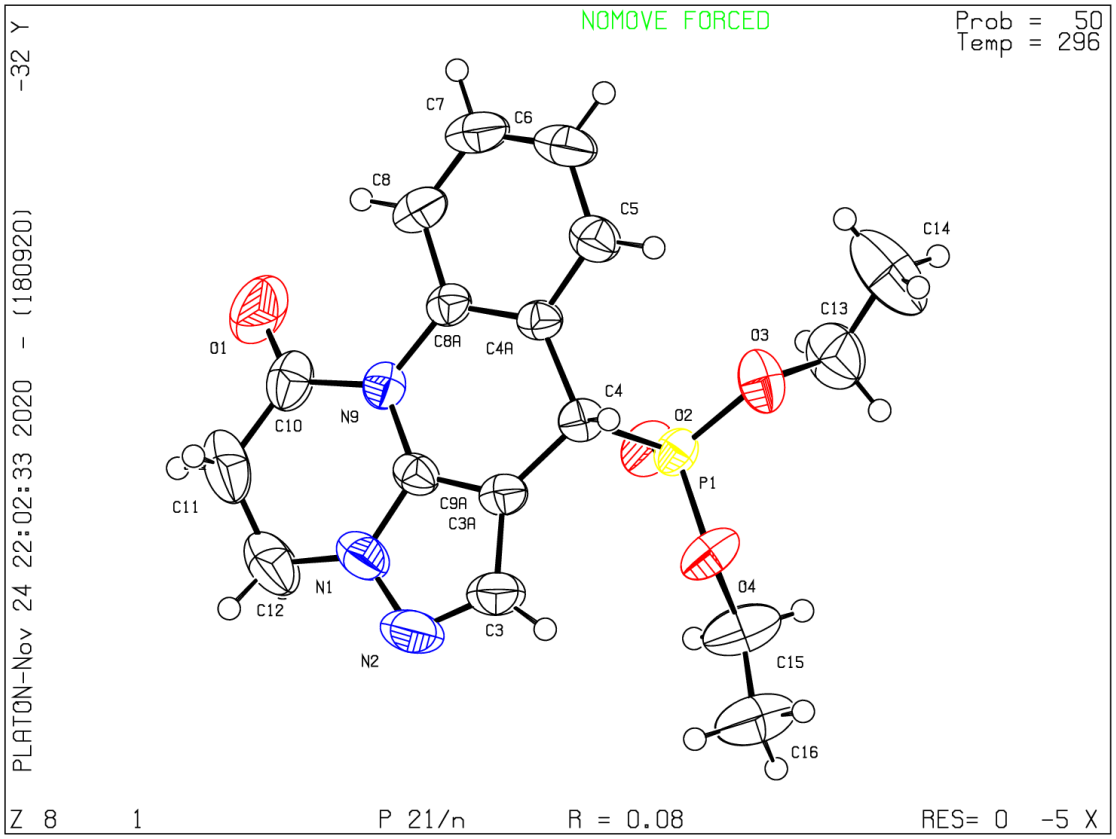
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 18/09/2020; check.def file version of 20/08/2020

Datablock 1 - ellipsoid plot



3. CheckCIF/PLATON report for compound 11-II

Structure factors have been supplied for datablock(s) 2

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 2

```
Bond precision:  C-C = 0.0067 A          Wavelength=0.71073

Cell:            a=11.592(3)    b=7.7150(15)         c=19.848(5)
                 alpha=90       beta=105.237(7)      gamma=90
Temperature:     296 K
```

	Calculated	Reported
Volume	1712.7(7)	1712.7(7)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C17 H20 N3 O4 P	?
Sum formula	C17 H20 N3 O4 P	C17 H20 N3 O4 P
Mr	361.33	361.33
Dx,g cm-3	1.401	1.401
Z	4	4
Mu (mm-1)	0.188	0.188
F000	760.0	760.0
F000’	760.74	
h,k,lmax	13,9,23	13,9,23
Nref	3142	3108
Tmin,Tmax	0.989,0.993	0.989,0.993
Tmin’	0.972	

```
Correction method= # Reported T Limits: Tmin=0.989 Tmax=0.993
AbsCorr = MULTI-SCAN

Data completeness= 0.989          Theta(max)= 25.361

R(reflections)= 0.0817( 1786)     wR2(reflections)= 0.2347( 3108)

S = 0.960                 Npar= 227
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00671 Ang.
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600         15 Report
```

Alert level G

```
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical          ? Check
PLAT793_ALERT_4_G Model has Chirality at C4          (Centro SPGR)          R Verify
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          3 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         17 Note
PLAT933_ALERT_2_G Number of OMIT Records in Embedded .res File ...         12 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ...........        2.7 Low
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          0 Info
```

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   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   8 ALERT level G = General information/check it is not something unexpected

   2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   2 ALERT type 2 Indicator that the structure model may be wrong or deficient
   4 ALERT type 3 Indicator that the structure quality may be low
   2 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 18/09/2020; check.def file version of 20/08/2020

Datablock 2 - ellipsoid plot