Supporting Information for

External Oxidant-Free Cross-Coupling: Electrochemically Induced Aromatic C−H Phosphonation of Azoles with Dialkyl-H-Phosphonates Under Silver Catalysis

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Experimental

General Considerations

Reactions were carried out under ambient atmosphere. Yields refer to purified and spectroscopically pure compounds. NMR experiments were carried out with Bruker spectrometers AVANCE-400 and AVANCE-500. Chemical shifts are reported on the δ (ppm) scale relative to the residual solvent signals for 1H and to external H_3PO_4 (0 ppm) for ^{31}P NMR spectra. Mass spectra were recorded in EI mode using ThermoQuest TRACE MS. Preparative chromatography BUCHI system including Pump Module C-601, ELS Detector C-605, Fraction Collector C-660, Control Unit C-620, Sepacore Control Package and software program were used for products isolation.

ESR experiments: Oxygen was removed from liquid samples by three cycles of "freezing in liquid nitrogen—evacuation—thawing" and after the last cycle the electrolysis cell was filled with gaseous helium. The material of the auxiliary electrode was platinum, the reference electrode was Ag/AgCl equipped with a bridge of a carbon slate-pencil, and a gold wire 0.5 mm in diameter served as a working electrode. Electrochemical experiments were carried out in DMF at 293 K using 0.1 M Bu_4NBF_4 as a supporting electrolyte; the potential sweep E(t) being 0.1 V s^{-1}. In experiments with spin trap, an equimolar to Fe complex amounts of N-tert-butyl-α-phenylnitrone (PBN) was added to solution. The measurements were carried out on an apparatus program complex including an analog electrochemical system with a potentiostat and a PWR-3 programmer, an ELEXSYS E500 ESR spectrometer of the X-range, and an E14-440 analog-to-digital and digital-to-analog modulus (L-Card), a fourth-generation computer, and a unique three-electrode helical cell. ESR spectra were simulated using the WinSim 0.96 program (developed by NIEHS).

Cyclic voltammetry: Cyclic voltammograms of all compoundes have been recorded in CH_3CN ($AgP(O)(OEt)_2$ in mixture of pyridine and CH_3CN (1:10)) with 0.003 mol×dm-3 substrate concentration, Bu_4NBF_4 was used as a supporting electrolyte (0.1 mol× dm-3) and a glassy carbon electrode as a working electrode (8 cm2), auxiliary electrode was platinum rod. All potentials are referenced against the Ag/AgCl, 10-2 M. Cyclic voltammograms registration was performed with BASi Epsilon potentiostate (USA).

Preparative electrolyses were carried out using a B5-49 dc source at a current strength of 100 mA h–1 in 30-mL three-electrode cell. The potential of the working electrode was detected by a V7-27 dc voltmeter. $Ag/AgNO_3$, 10^{-2} M in CH_3CN was a reference electrode. The working surface of the platinum cylindrical cathode used as a working electrode was 20.0 cm^2. A ceramic plate with the pore size 900 nm was used as a membrane. A platinum grid served as an cathode, and the catholyte was a saturated solution of the $PyHBF_4$ in the CH_3CN. Purified anhydrous solvents were stored under a dry argon atmosphere. The supporting salt [Bu4N]BF4 was prepared by mixing an aqueous solution of $[Bu_4N]OH$ and HBF_4 until the neutral pH value of the indicator. The precipitate formed ($[Bu_4N]BF_4$) was filtered off, doubly recrystallized from ethanol, and dried in a vacuum desiccator at 100°C for 48 h. All reagents (azoles, silver salts or oxide (Acros Organics or Alfa Aesar) were used without further purification.

General electrolysis procedure

0.04 mmol of silver salt, 4.2 mmol of azole, 4.2 mmol of dialkylphosphorus acid in 30 ml of acetonitrile were placed into electrochemical cell. Electrolysis was carried out in galvanostatic mode with simultaneous control of the working electrode potential in cell with separation of anodic and cathodic departments and with stirring in magnetic stirrer and continuous argon current. The saturated solution of $PyHBF_4$ in acetonitrile was placed into cathode space.

2.5 F of electricity per one mole of the initial azole was passed through the electrolyte. The electrolysis time is 2 hours usually. At the end of electrolysis the reaction mixture was evaporated on rotary evaporator, then treated with equimolar quantity of base t-BuOK or Na_3PO_4 (or other, see Table 1) (this stage is not carried out in case of electrolysis in the presence of base), washed with water solution and extracted with benzene (3x40 ml). After separation, the organic layer was dried over $MgSO_4$ within 24 hours, then the solvent was removed. The residue was purified through passing through chromatographic column with silica gel (hexane-ethyl acetate).

Diethylbenzoxazole-2-ylphosphonate **1**, yellow oil [1]. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.45 (d, J = 7.9 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 8.1 Hz, 1H), 6.88 (t, J = 8.0 Hz, 1H), 4.14 (dq, J = 7.1 Hz, J = 8.6 Hz, 4H), 1.36 (t, J = 7.0 Hz, 6H) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -1.14 (s) ppm. ESI-MS: m/z = 256.05 [M+H]+.

Diethylbenzothiazole-2-ylphosphonate **2**, yellow oil [1]. ^1H NMR (400 MHz, $(CD_3)_2CO$, δ): 8.28 (d, J = 7.5 Hz, 1H), 8.13 (d, J = 7.7 Hz, 1H), 7.77 (t, J = 7.1 Hz, 1H), 7.70 (t, J = 8.1 Hz, 1H), 4.19 (dq, J = 6.9 Hz, J = 9.2 Hz, 4H), 1.37 (t, J = 6.9 Hz, 6H) ppm. ^{31}P NMR (162 MHz, (CD3)2CO): δ = 4.79 (s) ppm. ESI-MS: m/z = 272.1 [M+H]+.

Diisopropyl-benzoxazole-2-ylphosphonate **3**, yellow butter [1]. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.79 (d, J = 6.9 Hz, 1H), 7.59 (d, J = 7.14 Hz, 1H), 7.382 (m, 2H), 4.72 (m, 2H), 1.36 and 1.35 (two d, J = 6.17 и J = 6.18 Hz, 12H) ppm. ^{31}P NMR (162 MHz, CDCl3): δ = -2.59 (s) ppm. ESI-MS: m/z = 284.2 [M+H]+.

Diethyl-3-methyl-1-H-indole-2-ylphosphonate **4**, yellow powder [2]. ^1H NMR (400 MHz, $(CD_3)_2CO$, δ): 10.46 (br s, 1H), 9.05 (d, J = 5.04 Hz, 1H), 8.79 (d, J = 8.12 Hz, 1H), 8.59 (t, J = 7.91 Hz, 1H), 8.05 (t, J = 5.97 Hz, 1H), 4.15 (dq, J = 7.07 Hz, J = 9.17 Hz, 4H), 2.05 (s, 3H), 1.32 (t, J = 7.05 Hz, 6H) ppm. ^{31}P NMR (162 MHz, CDCl3): δ = 10.008 (s) ppm. ESI-MS: m/z = 268.2 [M+H]+.

Diethyl-4-methyl-2-acetylthiazole-5-ylphosphonate **5**, yellow powder. ^{1}H NMR (400 MHz, ($CDCl_3$, δ): 4.14 (dq, J = 7.0 Hz, J = 9.1 Hz, 4H), 2.68 (s, 3H), 2.52 (s, 3H), 1.35 (t, J = 7.0 Hz, 6H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 190.54 (c), 174.00 (c), 165.82 (c), 151.60 (d, J_{CP} 141.4 Hz), 64.00 (t, J_{CH} 120.1 Hz), 26.15 (q, J_{CH} 129.8 Hz), 19.85 (q, J_{CH} 128.4 Hz), 16.68(q, J_{CH} 127.9 Hz). ^{31}P NMR (162 MHz, ($CDCl_3$): δ = 12.8 (s) ppm. ESI-MS: m/z = 278.1 [M+H]+. Calculated (%): C 43.32, H 5.77, N 5.05, P 11.19. $C_{10}H_{16}NO_4PS$. Found (%): C 42.64, H, 5.43, N 5.15, P 11.41.

Diisopropyl-4-methyl-2-acetylthiazole-5-ylphosphonate **6**, light yellow powder. ^{1}H NMR (400 MHz, ($CDCl_3$, δ): 4.08 (m, 2H), 2.69 (s, 3H), 2.54 (s, 3H), 1.22 (d, J = 6.4 Hz, 12H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 190.74 (c), 174.00 (c), 165.79 (c), 154.61 (d, J_{CP} 143.1 Hz), 44.33 (d, J_{CH} 142.3 Hz), 26.16 (q, J_{CH} 129.3 Hz), 21.25 (q, J_{CH} 127.2 Hz), 16.65(q, J_{CH} 128.5 Hz). ^{31}P NMR (162 MHz, ($CDCl_3$: δ = 0.21 (s) ppm. ESI-MS: m/z = 308.4 [M+H]+. Calculated (%): C 47.21, H 6.56, N 4.59, P 10.16. $C_{12}H_{20}NO_4PS$. Found (%): C 46.61, H 6.04, N 6.47, P, 10.38.

Silver diethyl phosphonate, $AgP(O)(OEt)_2$, white powder [3]. The mixture of 2.3 g Ag_2O (10 mmol) and 2.58 ml $HP(O)(OEt)_2$ in 50 ml benzene was reflux with a Dina-Stark's apparatus until the end of the water separation. The solvent was then removed by rotary evaporation. The product diluted with ether to afford white powder of silver diethyl phosphonate, yield 86%. ^{1}H NMR (400 MHz, CD_3CN, δ): 3.86 (m, 4H), 1.21 (t, J = 7.05 Hz, 6H) ppm. ^{31}P NMR (162 MHz, pyridine): δ = 107.7 (s) ppm.

Simulation of catalytic cycle steps

The phosphonation using $AgP(O)(OEt)_2$ as phosphorus precursor

1. 2.0 mmol of silver phosphonate, 2.0 mmol of benzoxazole, in 20 ml of acetonitrile were placed into the flask. This mixture was stirred during 24 hour. The solvent was evaporated and stillage residue in $CDCl_3$ was analyzed by NMR ^{31}P and ^{1}H. All reagents remained unchanged; no products of benzoxazole phosphorylation were detected.

2. 2.0 mmol of silver phosphonate, 2.0 mmol of benzoxazole, in 20 ml of acetonitrile were placed into electrochemical cell. Electrolysis was carried out as usually, in galvanostatic mode with simultaneous control of the working electrode potential at the oxidation potential of $AgP(O)(OEt)_2$ (1.1V ref Ag/AgCl) in cell with separation of anodic and cathodic departments and with stirring in magnetic stirrer and continuous argon current. After 2F electricity the reaction mixture was analyzed by NMR ^{31}P and and ^{1}H and elaborated as usually with *t*-BuOK as a base, the product of benzoxazole phosphonation was isolated using by Buchi preparative chromatography. $AgP(O)(OEt)_2$ was completely consumed, and the only phosphorous product is diethylbenzoxazole-2-ylphosphonate **1**.

3. To understand the mechanism of the process and to detect the possible reaction intermediates, the reaction mixture was analyzed during electrolysis after passing 0F, 1F, 2F and 2.5 F by NMR ^{31}P and ^{1}H. In each case, the starting conditions for the synthesis were as described in the General electrolysis procedure part. Prior to electrolysis, this mixture was stirred during 24 hour, but no conversion products were detected. The dynamics of the NMR ^{31}P spectra is shown in Fig. 8 SI. The isolation of the products was carried out with the help of Buchi preparative chromatography and their nature was confirmed by a complex of the above methods. No product with an open cycle of benzoxazole was isolated or fixed (expectative δ_P 17.67 ppm for diethyl (phenylimino)methylphosphonate [4]). The benzoxazole phosphonate **1** yield increased and reached a maximum after passing through electrolyte 2.5 F. ESR study of reaction mixtures confirms the absence of Ag^{2+} at all stages of synthesis.

4. To clarify the possible formation of an intermediate with the open benzoxazole cycle, the benzoxazole and $HP(O)(OEt)_2$ reaction with the addition of AcOH was investigated under similar conditions described for amination reactions [5]. After stirring for 24 hours at 60^0C, no external changes are observed, and in the ^{31}P spectrum only the signal of the original $HP(O)(OEt)_2$ (with decoupling and without decoupling from protons) is present. That is, there is no phosphorylation, there is no product with a cycle opening or without opening the cycle.

References

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2. H. Wang, X. Li, F. Wu, B. Wan, *Synthesis*, 2012, **44**, 941.
3. P. P.Winkler, P.Peringer, *Transition Met. Chem*. 1982, 7, 313.
4. E. Balint, A. Tajti, A. Dzielak, G. Hagele, G. Keglevich, *Beilstein Journal of Organic Chemistry* 2016, **12**, 1493.
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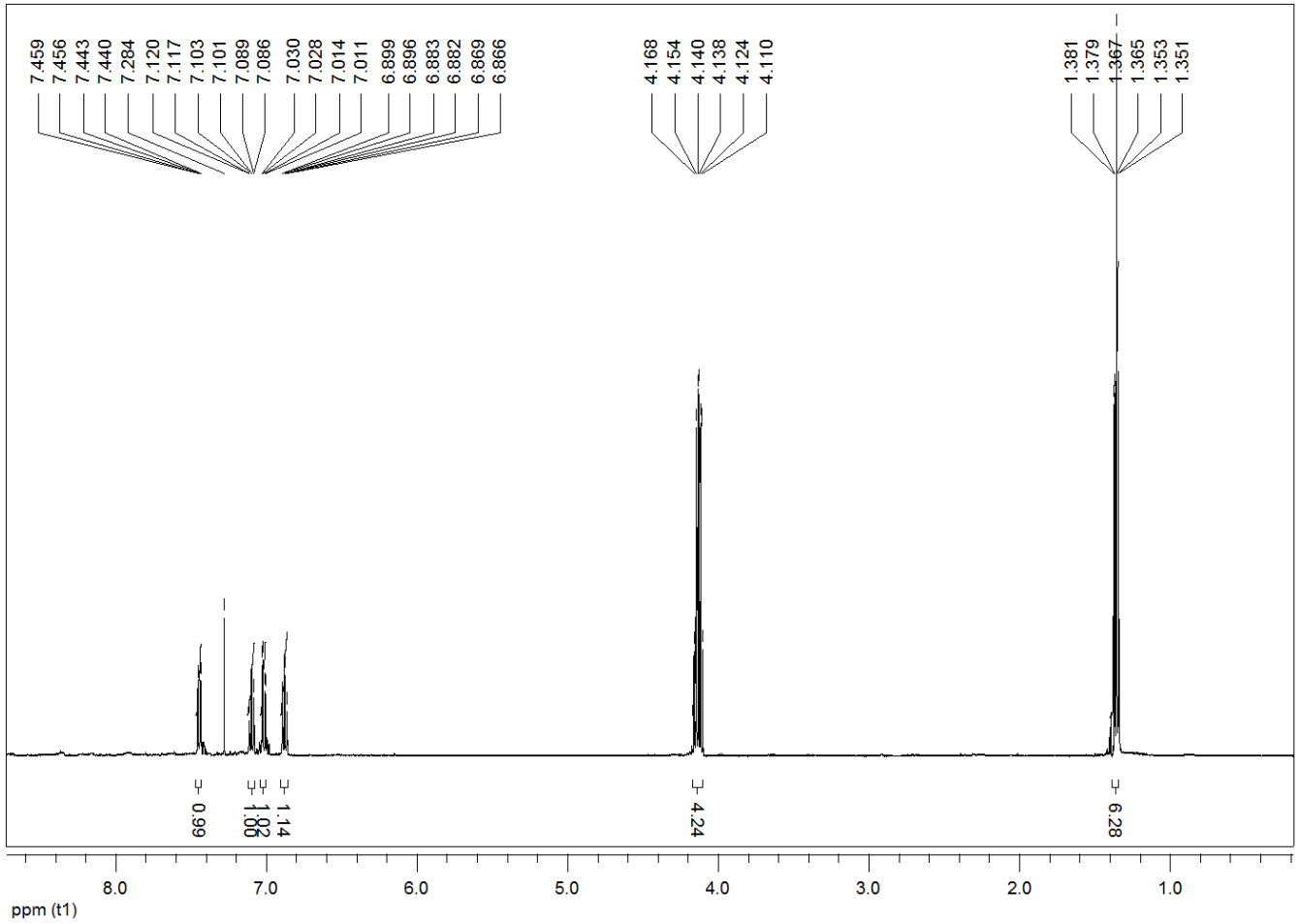
Figure S1. ^{1}H, ^{31}P, NMR spectra in $CDCl_3$ of **1**.

1



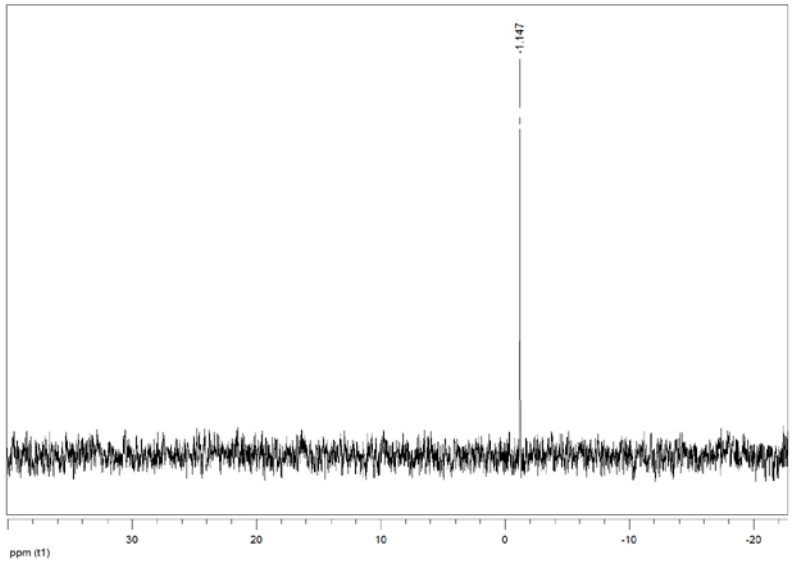
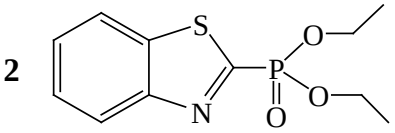
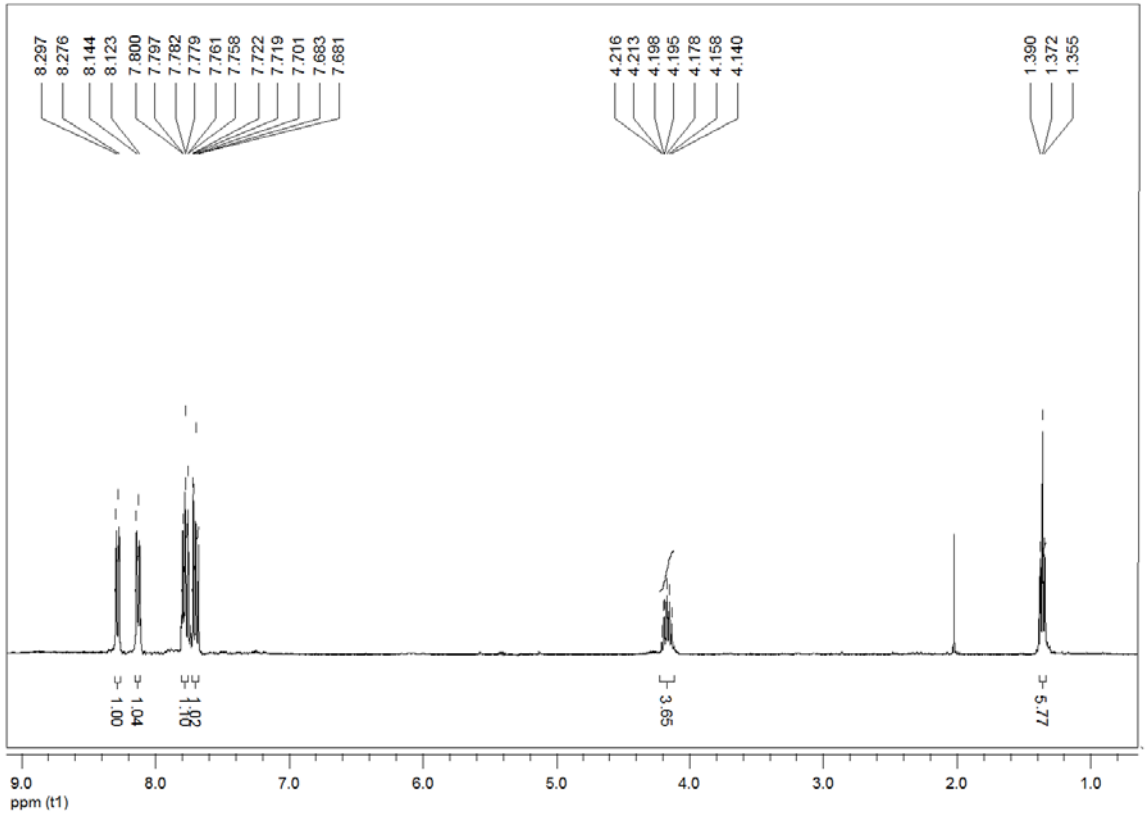


Figure S2. ^{1}H, ^{31}P, NMR spectra in $(CD_3)CO$ of **2**.

2





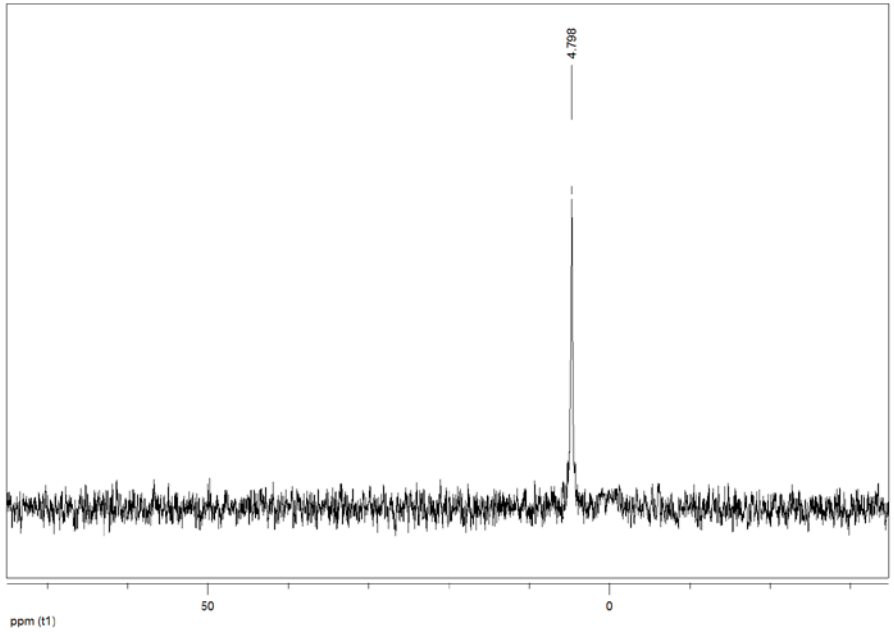
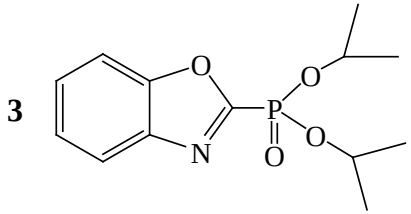
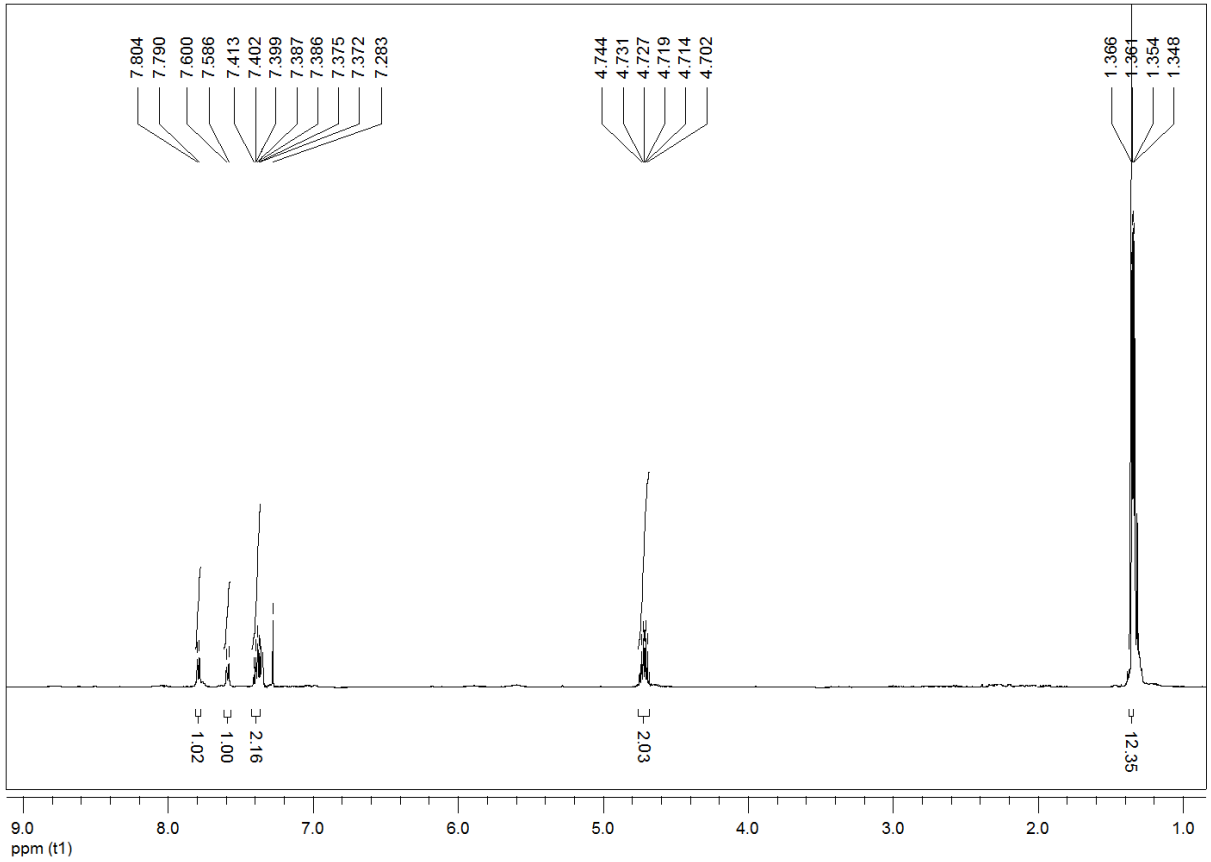


Figure S3. ^{1}H, ^{31}P, NMR spectra in $CDCl_3$ of **3**.

3





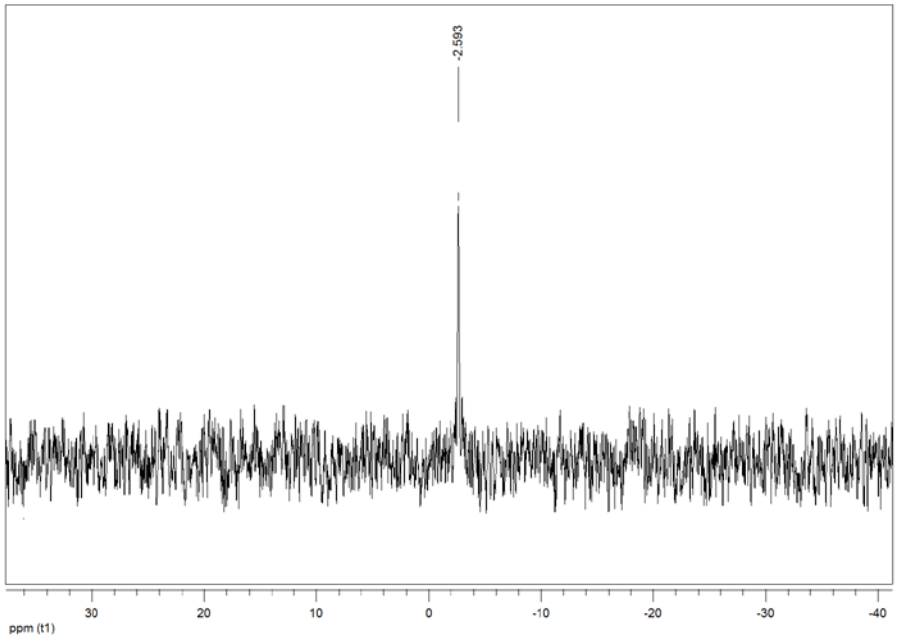
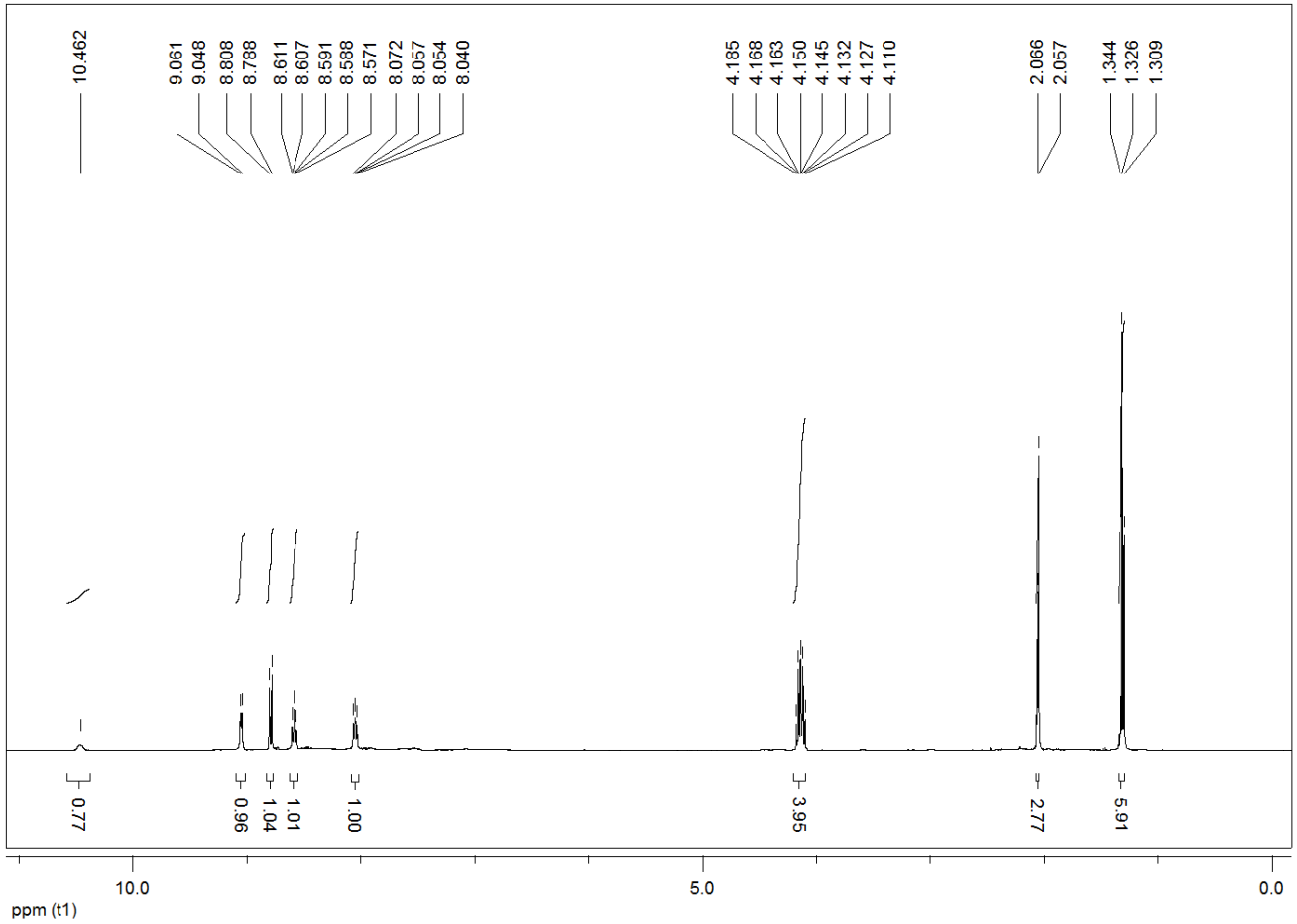


Figure S4. ^{1}H, ^{31}P, NMR spectra in $(CD_3)CO$ of **4**.

4



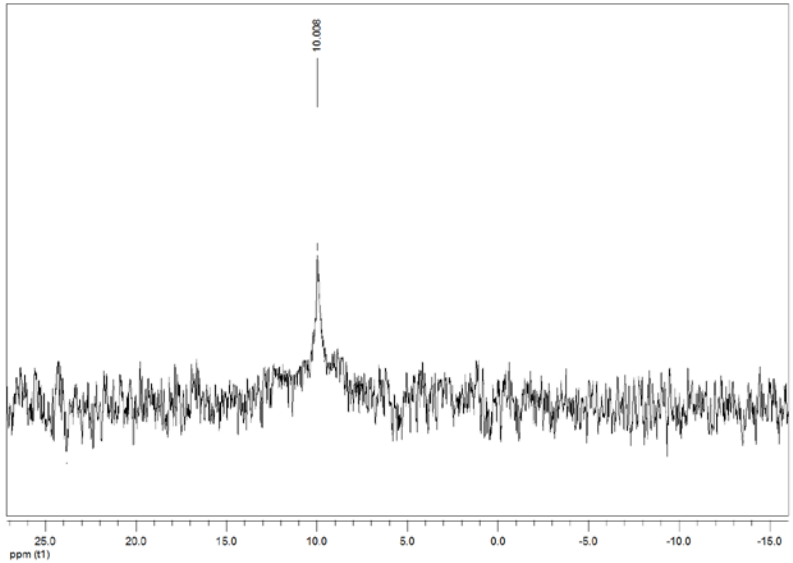
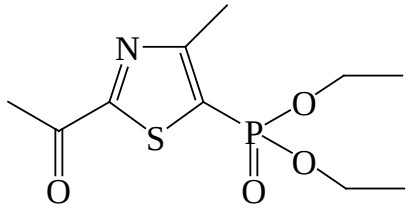
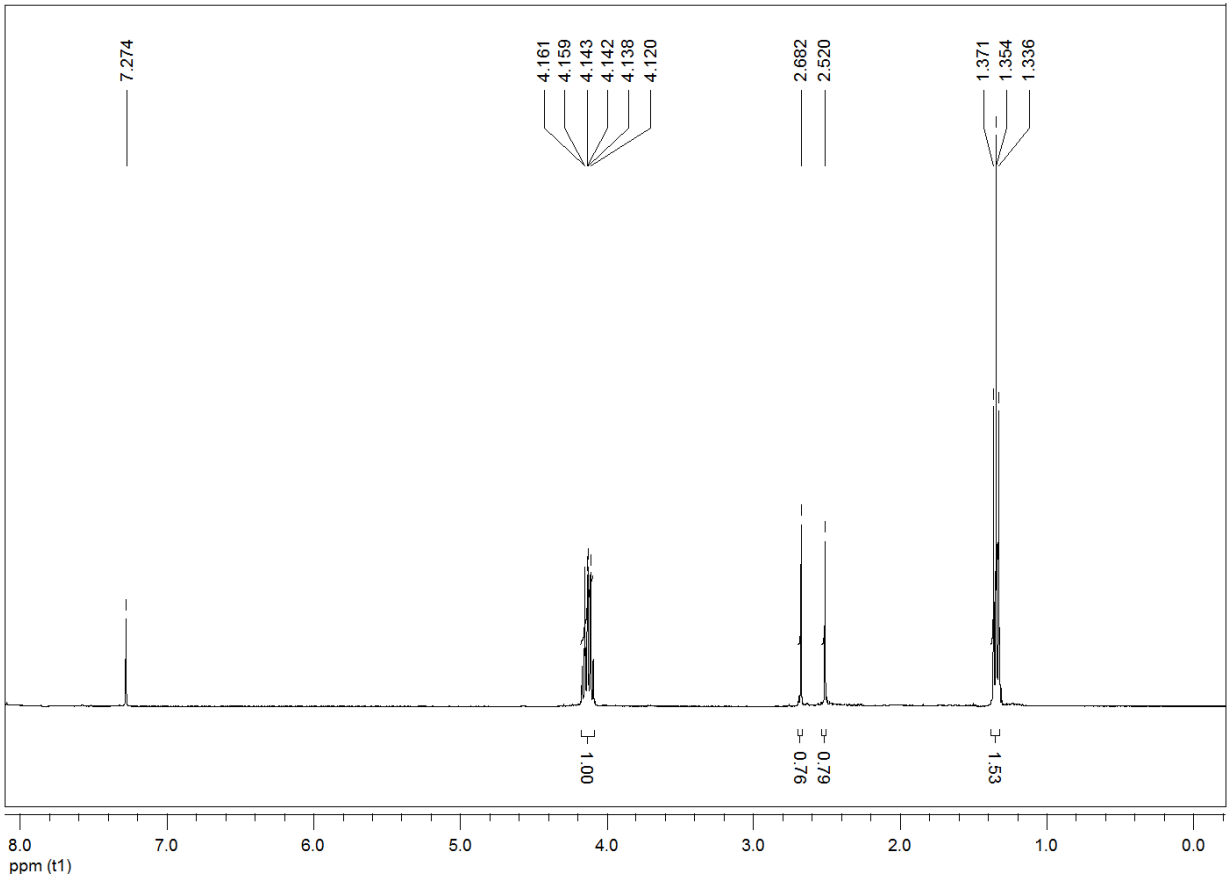
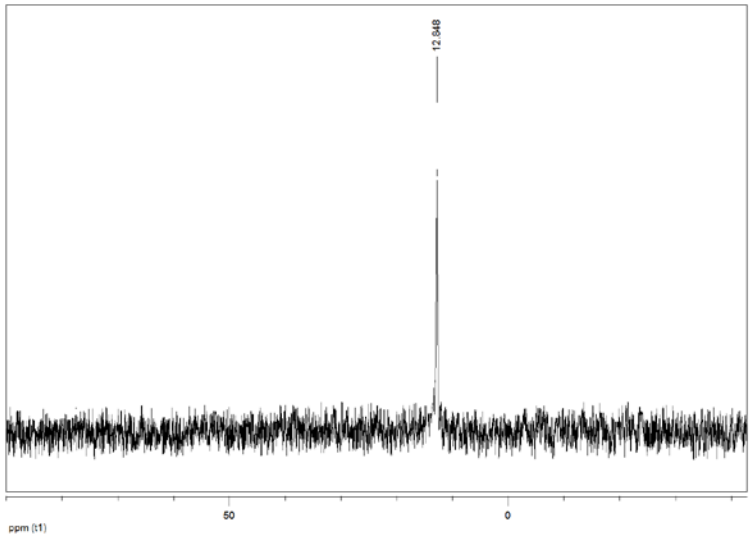


Figure S5. ^{1}H, ^{31}P, ^{13}C NMR spectra in CD_3Cl of **5**.

5







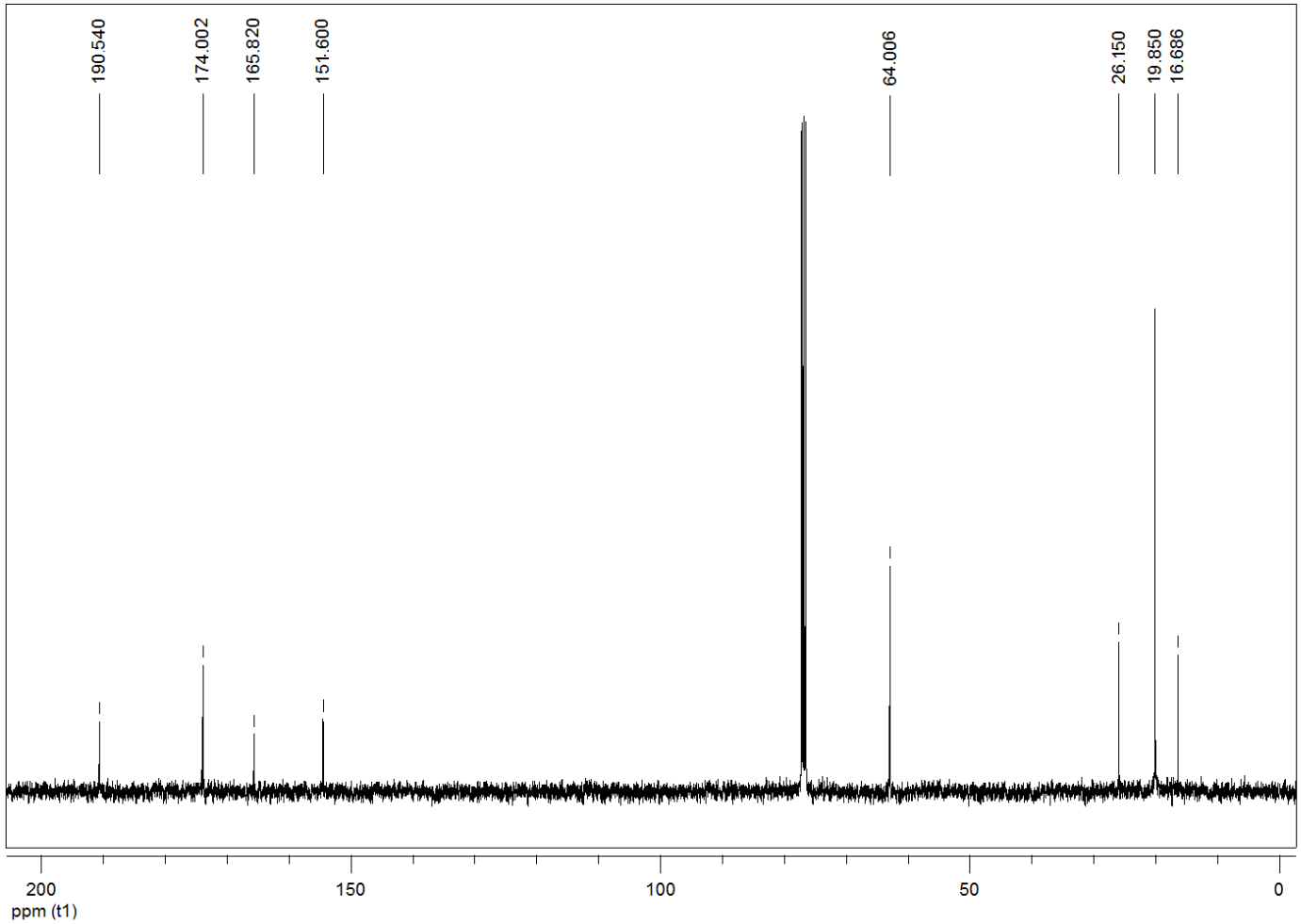
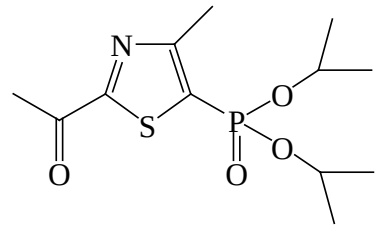
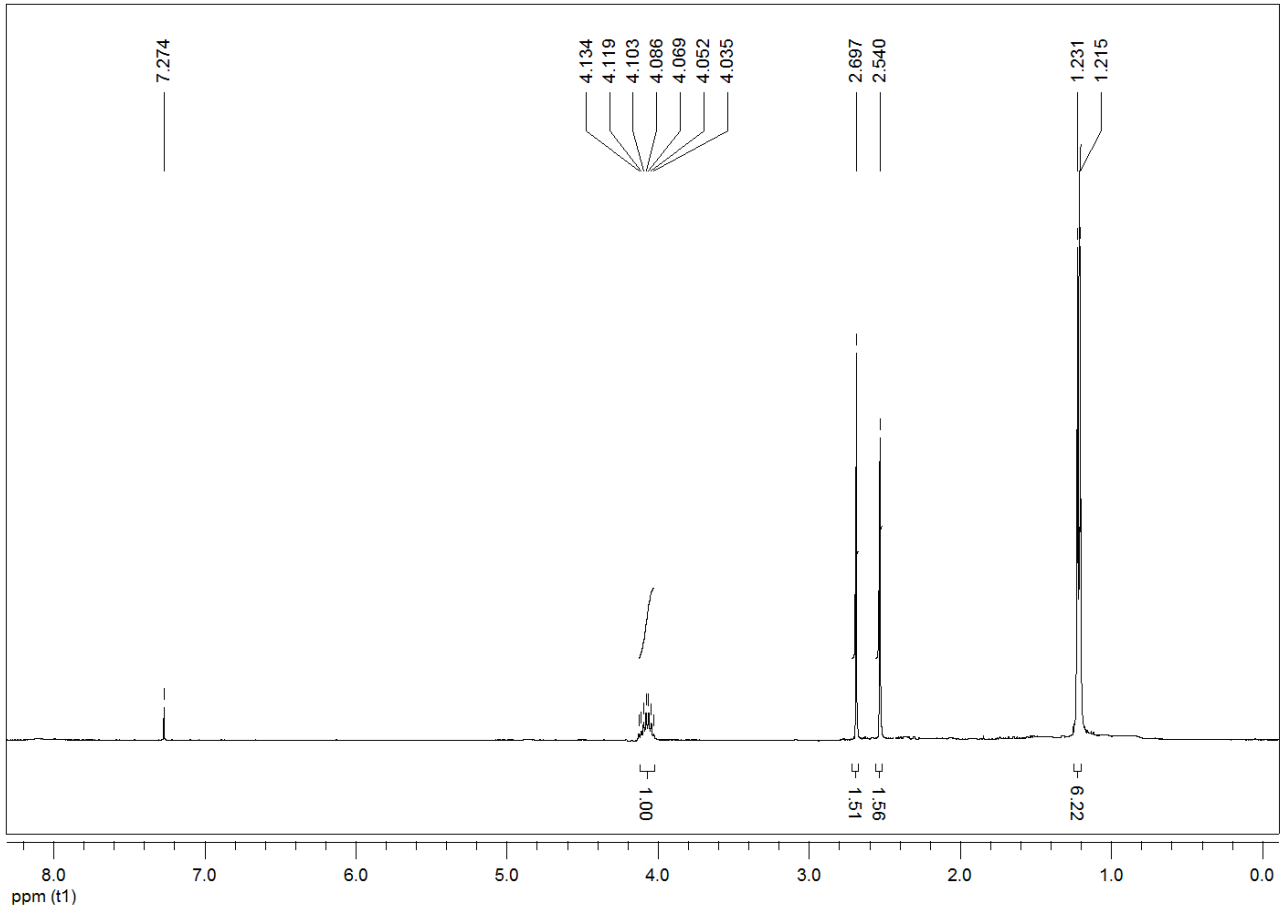
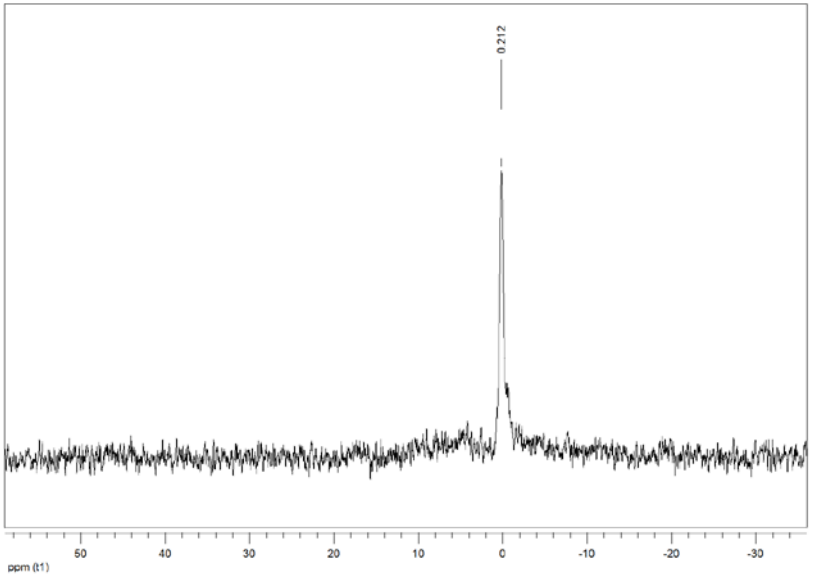

190.540
174.002
165.820
151.600
64.006
26.150
19.850
16.686
200
150
100
50
0
ppm (t1)

Figure S6. ^{1}H, ^{31}P, ^{13}C NMR spectra in CD_3Cl of **6**.

6







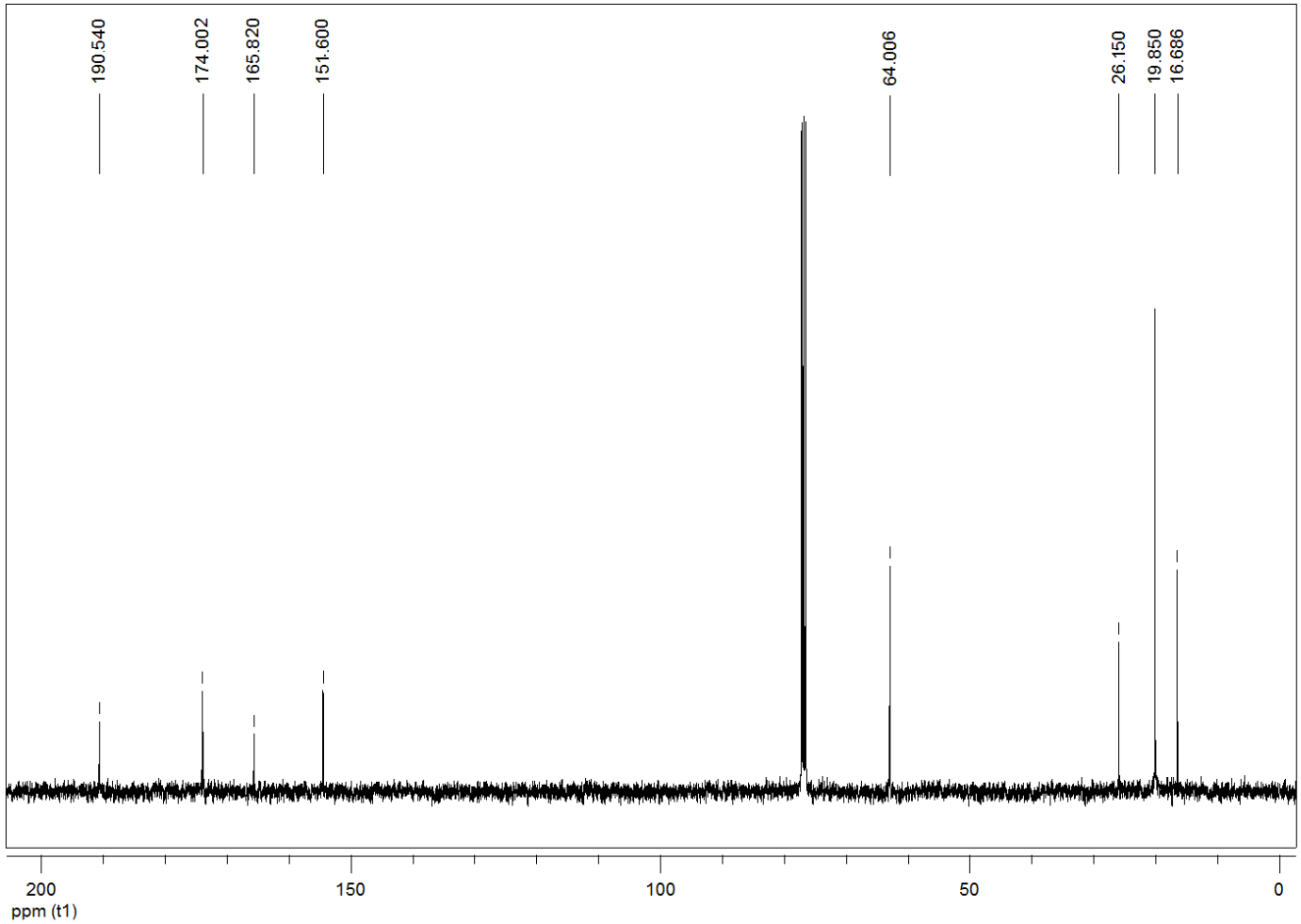
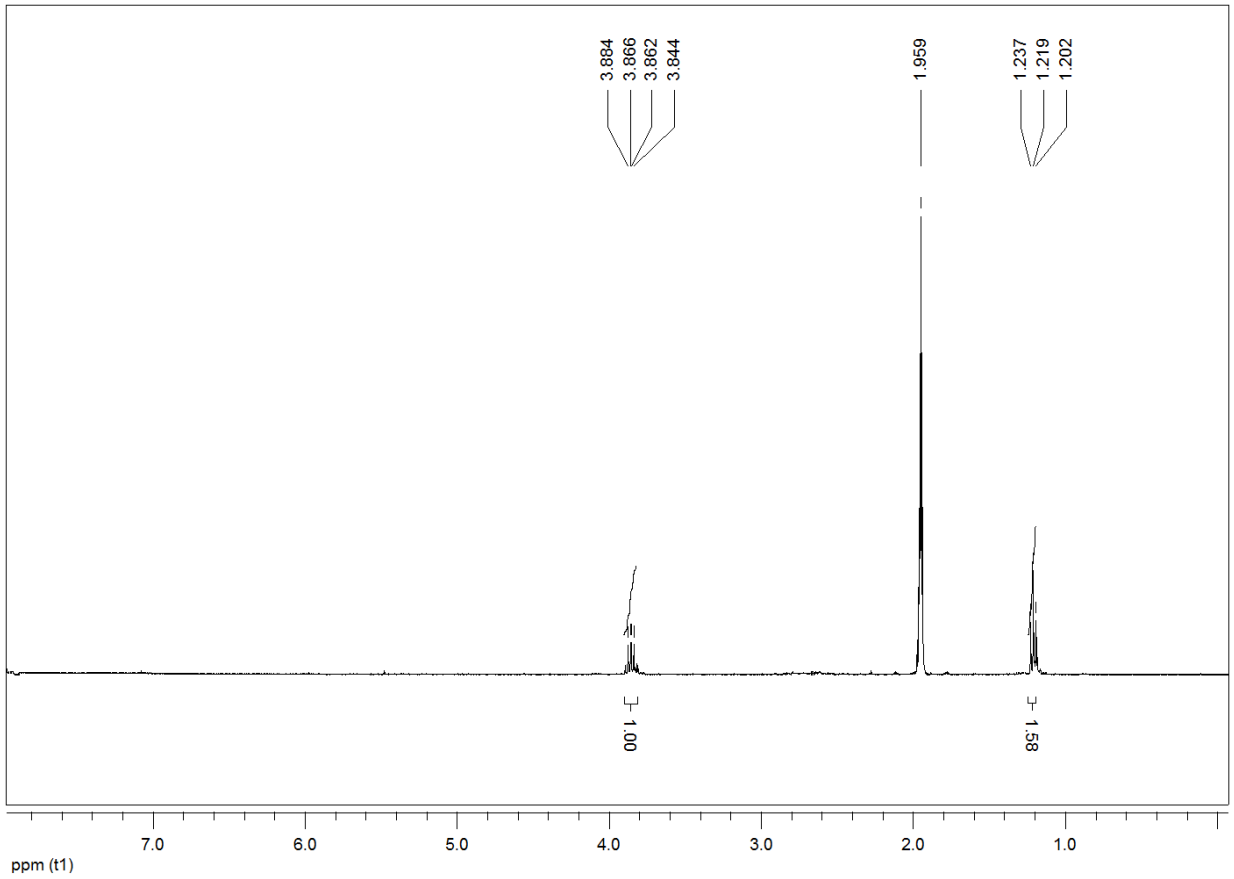

190.540
174.002
165.820
151.600
64.006
26.150
19.850
16.686
200
150
100
50
0
ppm (t1)

Figure S7. ^{1}H (in CD_3CN), ^{31}P (in pyridine), NMR spectra of **$AgOP(OEt)_2$**



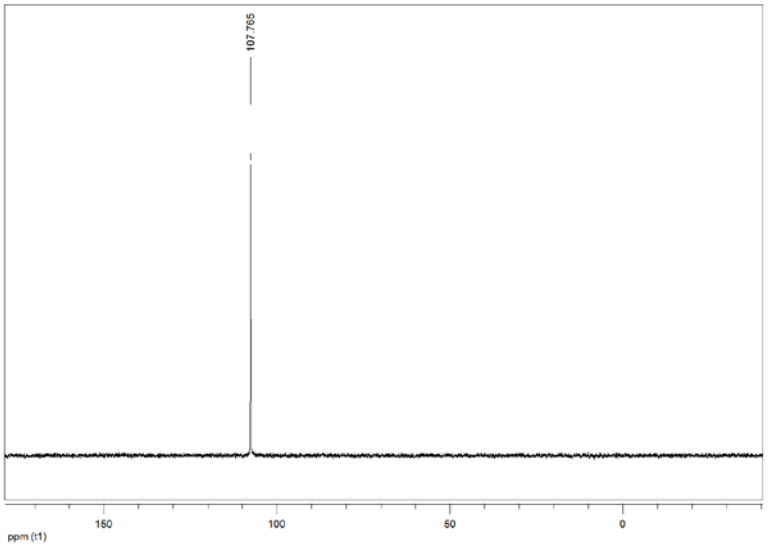


Figure S8. Dynamics of changes in the nature of phosphorus compounds before and during electrolysis, and also after treatment with a base using ^{31}P NMR spectroscopy. CH_3CN solution.