

## *Supplementary Information*

# Synthesis of $\alpha$ -amino phosphonates catalyzed by bifunctional cyclohexane derived thiourea organocatalyst

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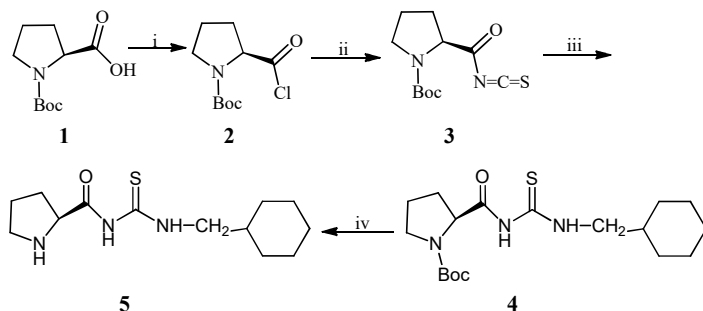
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### **General method for the synthesis of Organocatalyst(S)-N-((cyclohexylmethyl) carbamothioyl) pyrrolidine-2-carboxamide (NCCPC):**

General synthesis procedure for compound (1–5) has been taken from our previously published work (Kasralikar, H. M., Jadhavar, S. C., & Bhusare, S. R. (2019). Highly asymmetric aldol reaction of cyclohexanone and aromatic aldehydes catalyzed by bifunctional cyclohexane derived thiourea organocatalyst. *Asian Journal of Green Chemistry*, 3, 201-215). A solution of Boc-L-proline (0.1 mol) in anhydrous 1,2-dichloroethane is refluxed for 3 hr with thionyl chloride (0.2 mol). The solvent and the excess thionyl chloride are removed by reduced pressure distillation. The raw obtained (S)-tert-butyl 2-(chlorocarbonyl)pyrrolidine-1-carboxylate (10 mmol) is dissolved in anhydrous acetone (30 mL), added to a solution of ammonium thiocyanate (10 mmol) in dry acetone and refluxed for 1 hr. The ammonium chloride obtained, was removed by filtration and cyclohexylmethyl amine (10 mmol) dissolved in anhydrous acetone is added while stirring. The mixture is heated under reflux for 1 hr. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2×20 mL) and the combined organic layer was washed with brine (20 mL) dried over MgSO<sub>4</sub>, and filtered. The solvent was removed under vacuo. The resulting crude product, i.e. (S)-tert-butyl 2-(aminoN-(cyclohexylmethyl)methanethiocarbamoyl)pyrrolidine-1-carboxylate was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and added TFA (2 mL) dropwise with stirring for 1 hr at 0°C. After the consumption of the starting material as indicated by TLC analysis, the reaction mixture was diluted with H<sub>2</sub>O (10 mL) and the resulting solution was adjusted to pH≈7 with aqueous NaHCO<sub>3</sub>. The reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2×20 mL), the combined organic layer was washed with brine, dried over MgSO<sub>4</sub>, filtered, and the solvent was removed in vacuo. The purification of residue by column chromatography (EtOAc/hexane, 1:4) afforded 70–75% of 5 as yellow solid.

## Synthesis of organocatalyst:



**Scheme 1: Reaction Conditions and Reagents:** i) SOCl<sub>2</sub>, C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub>, reflux, 3hrs; ii) NH<sub>4</sub>SCN, acetone, reflux, 1hr; iii) Cyclohexylmethanamine, acetone, reflux, 1hr; iv) MDC, TFA, Stir, 1hr, 70-75%.

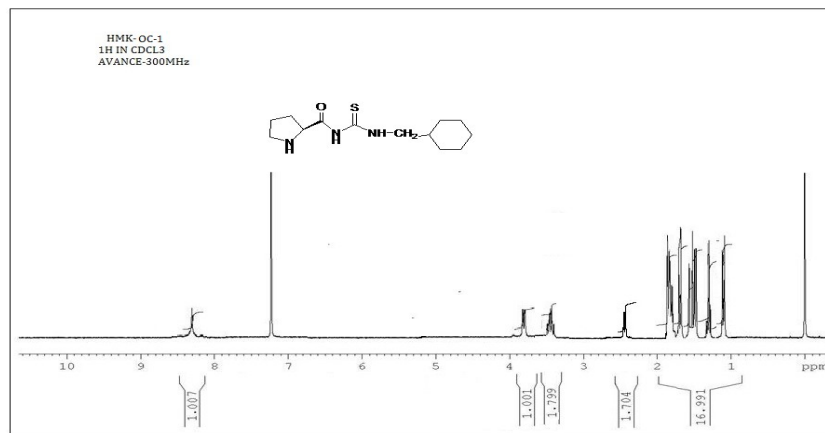
**Characterization data for organocatalyst (S)-N-((cyclohexylmethyl) carbamothioyl) pyrrolidine-2-carboxamide (NCCPC):** Yellowish Solid; **M.P. (°C):** 132°C; **Optical rotation**  $[\alpha]_D^{25}$ : -60.5° (c 0.4, CHCl<sub>3</sub>); **<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** δ 8.30 (s, 1H NH), 3.80 (t, 1H), 3.45 (t, 2H), 2.5 (s, 2H), 1.2-1.9(m, 17H); **<sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>):** δ 184.45, 174.24, 77.25, 77.0, 76.3, 62.0, 49.2, 44.9, 40.0, 37.0, 32.0, 26.8, 22.0; **GC-MS:** *m/z* 269 (M<sup>+</sup>); **Elemental Analysis:** Anal. Calcd for C<sub>13</sub>H<sub>23</sub>N<sub>3</sub>OS: C, 57.96; H, 8.61; N, 15.60; O, 5.94; S, 11.90; Found C, 57.45; H, 8.30; N, 15.50; O, 5.10; **HPLC:** 99.00% *ee*. [Enantiomeric purity is determined by chiral HPLC Systems using chiral column Whelk-O1 (25 cm x 4.6 mm), EtOAc / Hexane (80/20), Flow rate 1.0 mL /min, λ = 254; *t<sub>R</sub>* (minor) = 14.2 min, *t<sub>R</sub>* (major) = 20 min].

## Experimental details for Organocatalyst

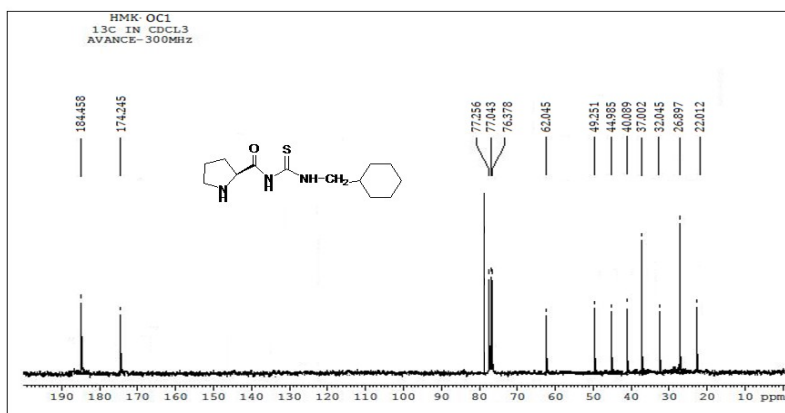
All solvents were used as commercial anhydrous grade without further purification. Aluminium sheets 20 x 20cm, Silica gel 60 F<sub>254</sub>, Merck grade was used for thin layer chromatography to determine progress of reaction. The column chromatography was carried out over silica gel (80–120 mesh). Optical rotations were measured on a Polax-2L digital polarimeter. Melting points were determined in open capillary tube and are uncorrected. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker 300 MHz spectrometer in CDCl<sub>3</sub> solvent. Mass spectra were taken on Polaris-Q Thermoscientific GC-MS. Enantiomeric purity is determined on PerkinElmer Series 200 HPLC Systems with chiral HPLC [Whelk-O1 (25 cm x 4.6 mm), EtOAc/Hexane (20/80), Flow rate 1.0 mL/min, λ = 254 nm]

# <sup>1</sup>H NMR, <sup>13</sup>C NMR, GC-MS spectra and HPLC chromatogram of compound

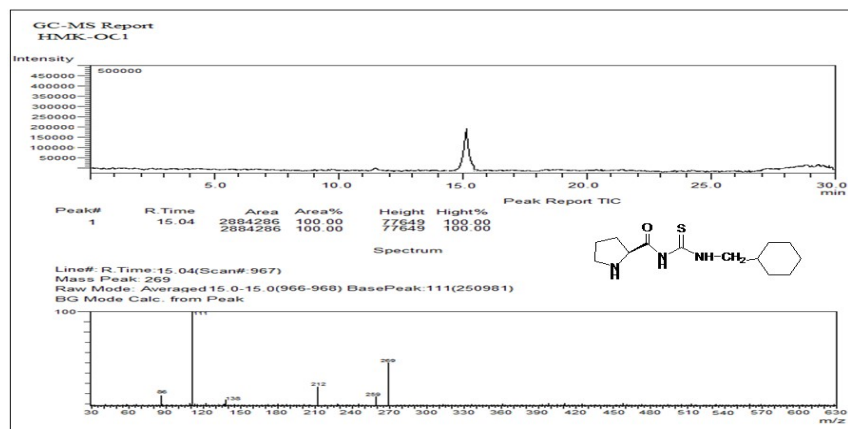
## <sup>1</sup>H-NMR spectra of NCCPC Organocatalyst



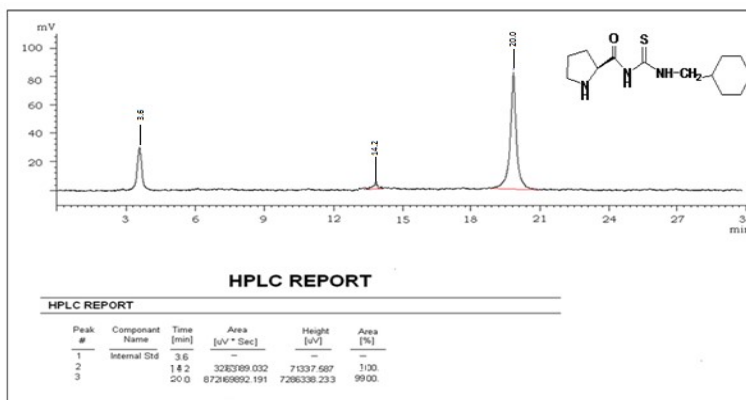
## <sup>13</sup>C-NMR spectra of NCCPC organocatalyst



## GC-MS spectra of NCCPC organocatalyst



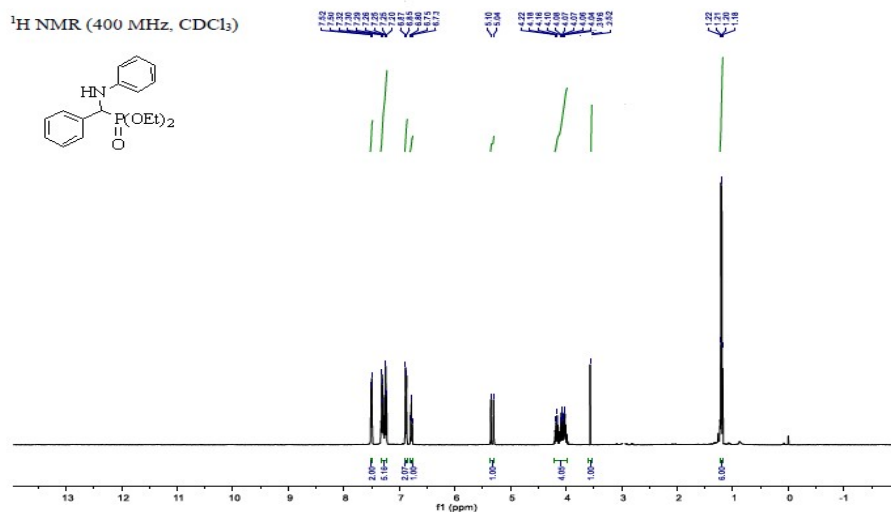
## HPLC chromatogram of NCCPC organocatalyst



## Experimental details for Phosphonate derivatives

All solvents were used as commercial anhydrous grade without further purification. Aluminium sheets 20 x 20cm, Silica gel 60 F<sub>254</sub>, Merck grade was used for thin layer chromatography to determine progress of reaction. Melting points were determined in open capillary tube and are uncorrected. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded on a Bruker AV-400 MHz and 126 MHz spectrometer in CDCl<sub>3</sub> solvent. Mass spectra were taken on Polaris-Q ThermoScientific MS. Characterization of Synthesized compounds

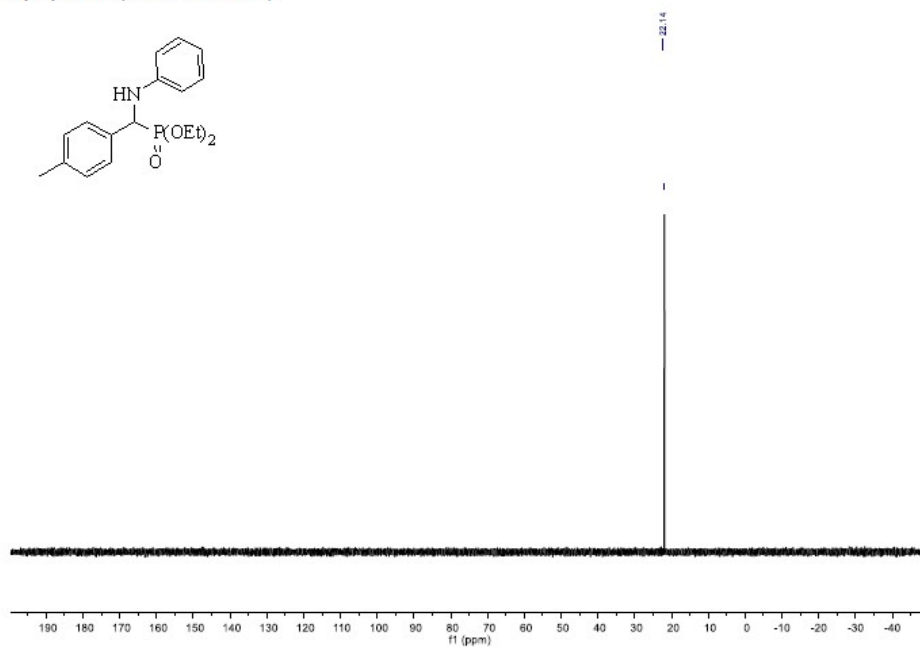
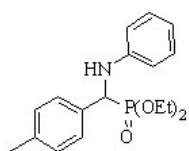
### 1) <sup>1</sup>H NMR, <sup>13</sup>C-NMR, <sup>31</sup>P-NMR Spectra for 9a





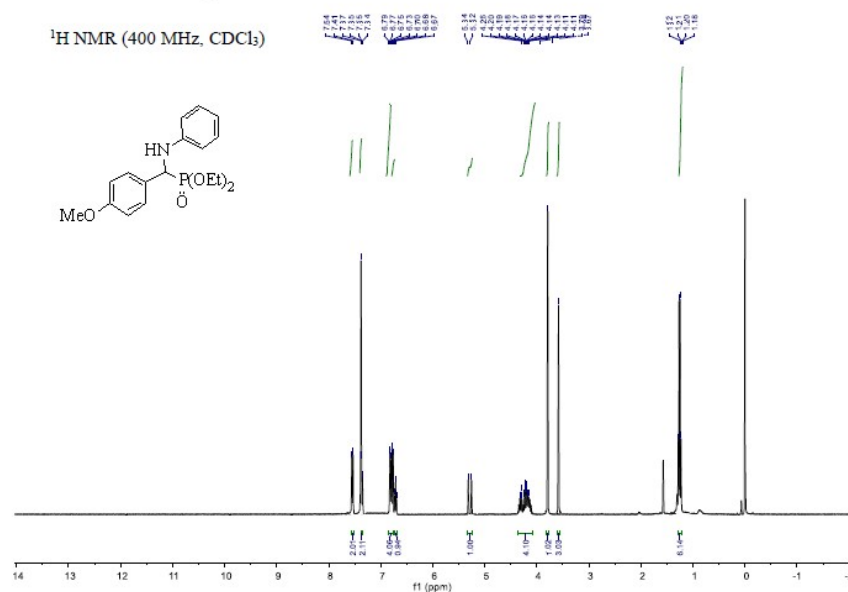
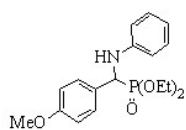


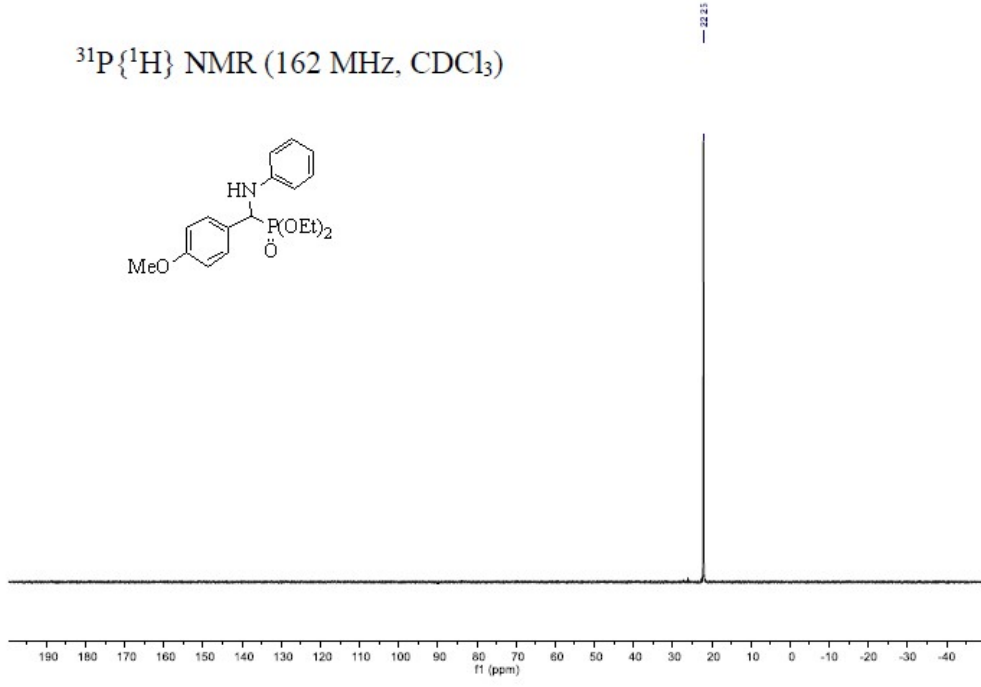
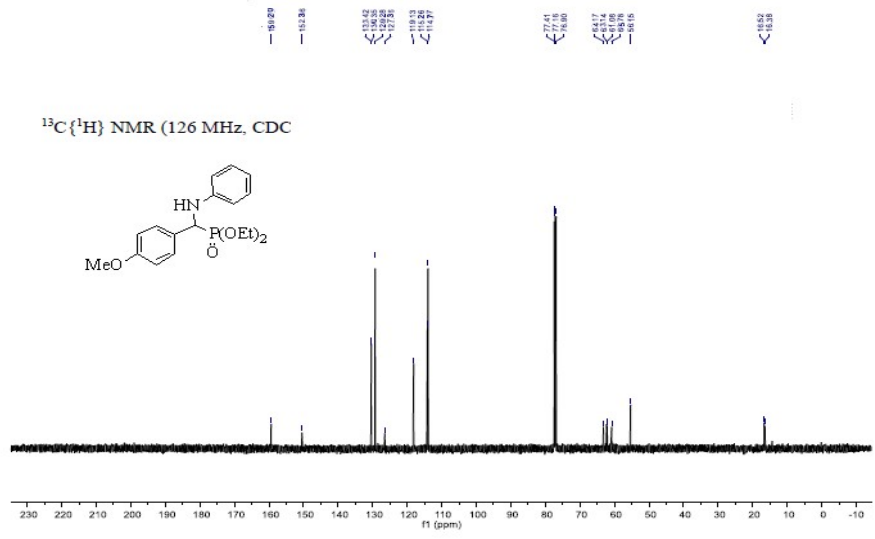
$^{31}\text{P}\{^1\text{H}\}$  NMR (162 MHz,  $\text{CDCl}_3$ )



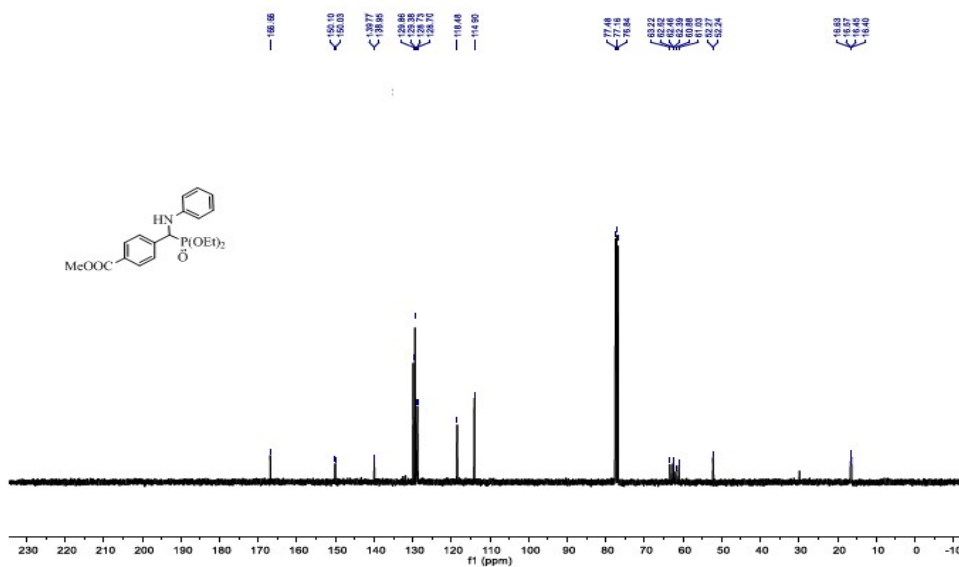
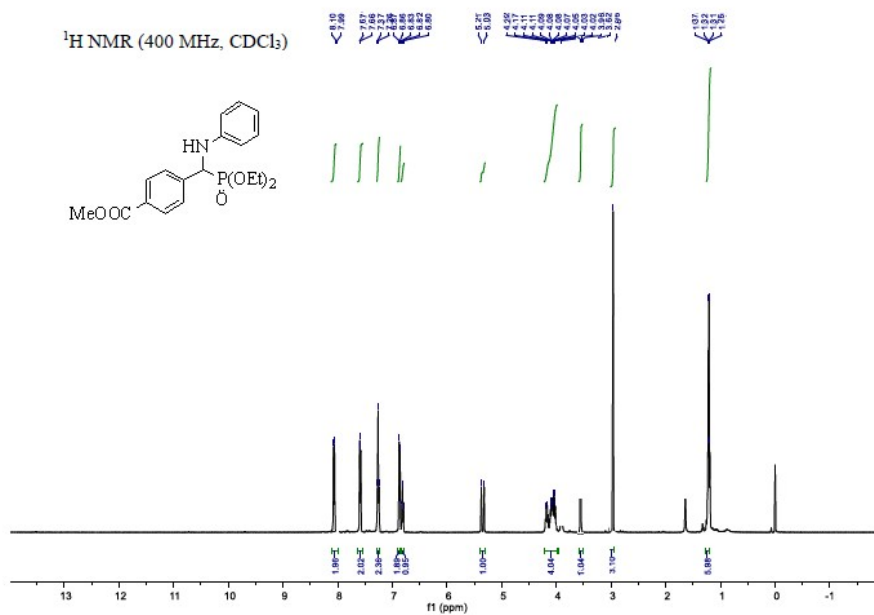
### 3) $^1\text{H}$ NMR, $^{13}\text{C}$ -NMR, $^{31}\text{P}$ -NMR Spectra for 9c

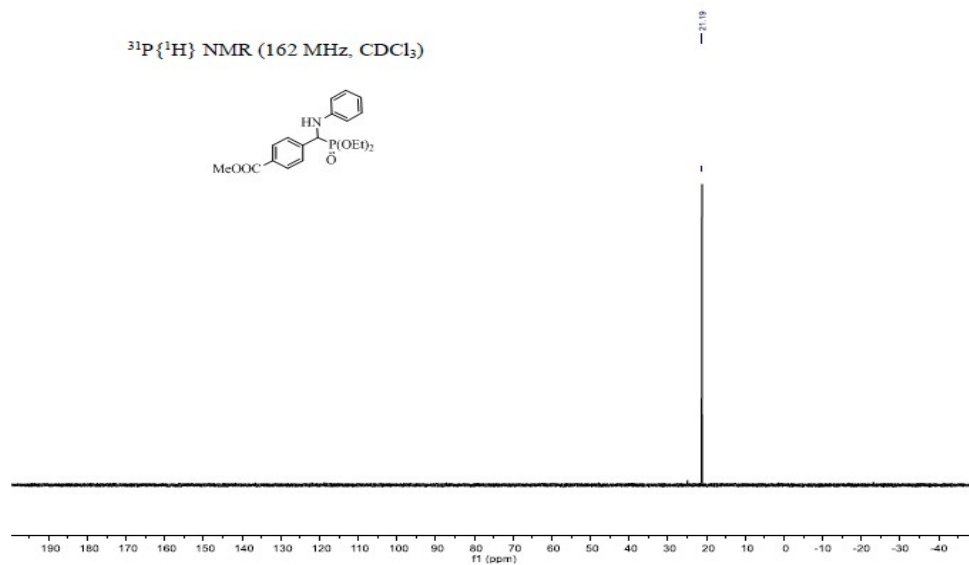
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



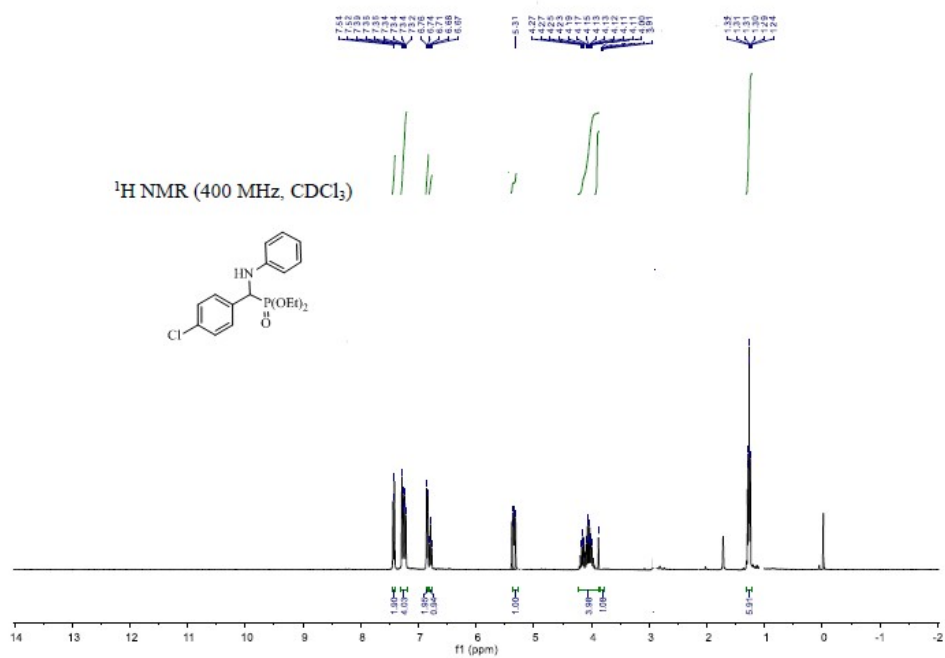


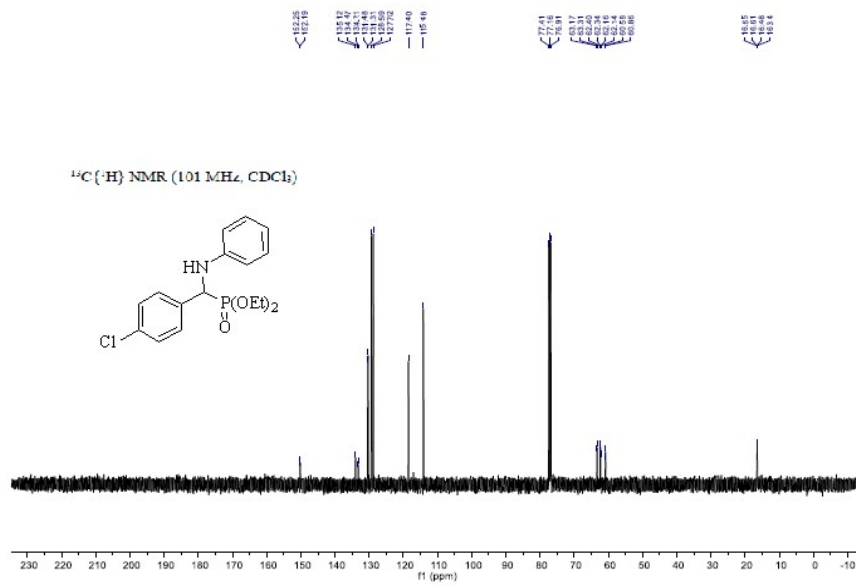
#### 4) $^1\text{H-NMR}$ , $^{13}\text{C-NMR}$ , $^{31}\text{P-NMR}$ Spectra for 9d





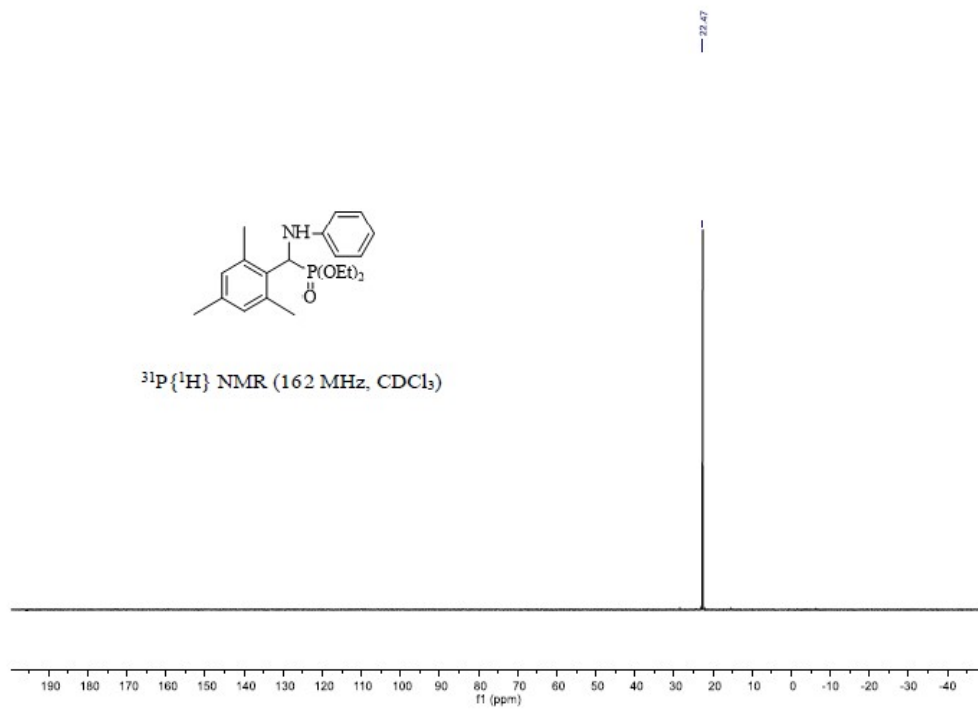
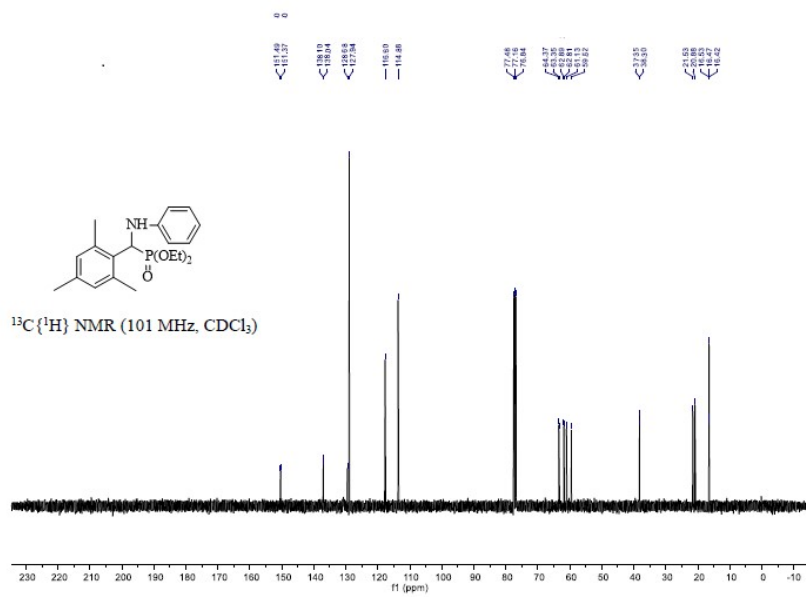
5)  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR,  $^{31}\text{P}$ -NMR Spectra for 9e





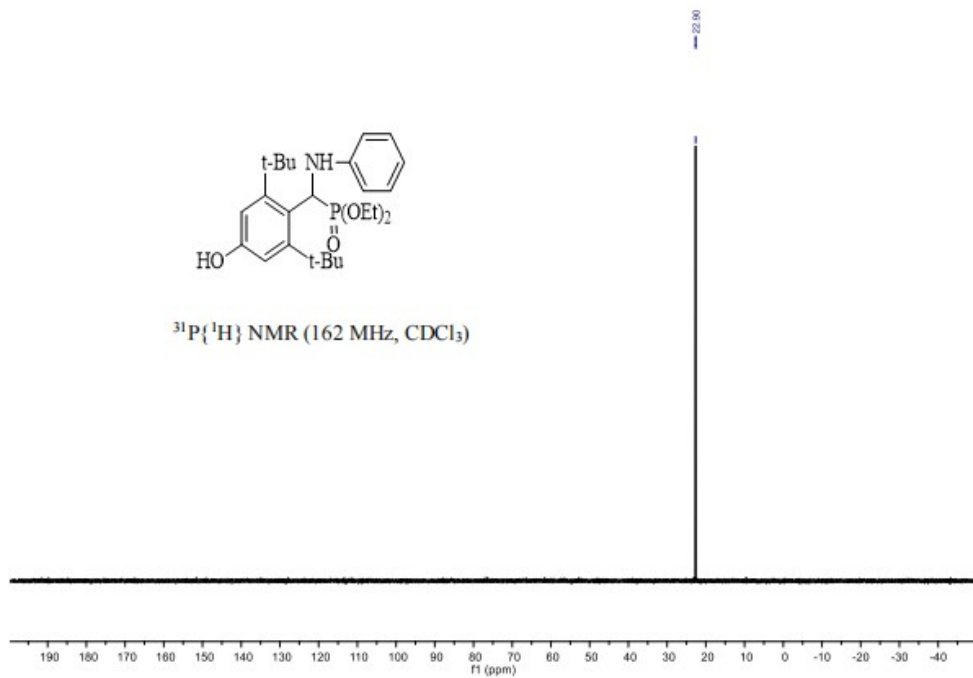
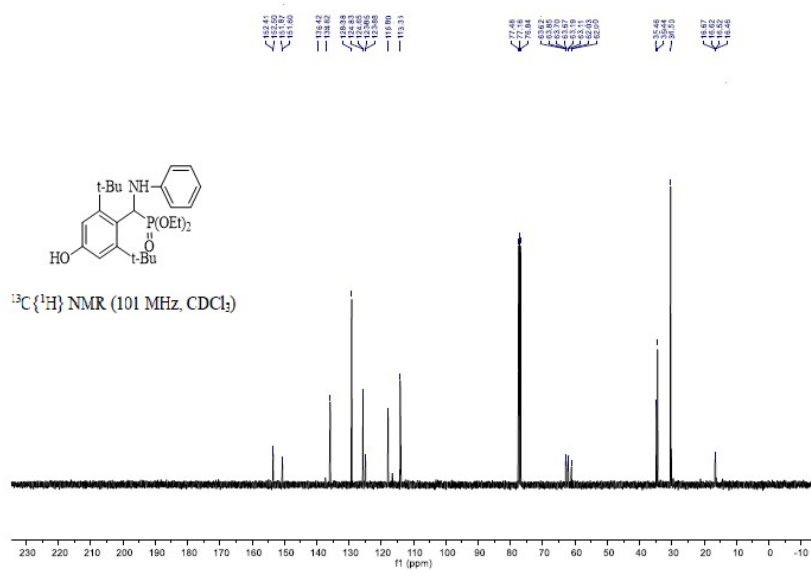




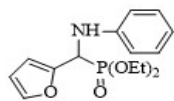












$^{31}\text{P}\{^1\text{H}\}$  NMR (162 MHz,  $\text{CDCl}_3$ )

