

# Magnetic nanoparticle-supported proline as a recyclable and recoverable ligand for the CuI catalyzed arylation of nitrogen nucleophiles

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## General Remarks

Reagents were purchased from Aldrich Chemical and are used as received. Magnetic nanoparticles<sup>1</sup> and *tert*-butyl (2*S*, 4*R*)-*N*-*boc*-4-propargyloxyproline<sup>2,3</sup> were synthesized according to literature methods. IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR were recorded on a Bruker Avance (300 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C) using CDCl<sub>3</sub> as a solvent and tetramethylsilane as an internal standard. Chemical shifts ( $\delta$ ) are reported in ppm and the coupling constants (*J*) are given in Hertz (Hz). Full spectroscopic and spectrometric characterization is provided only for the new compounds. X-ray diffraction patterns (XRD) of all materials were recorded in air at room temperature using a Philips PW3020 diffractometer with a Cu-K $\alpha$  radiation source ( $\lambda = 1.54056 \text{ \AA}$ ) at 45 KV voltage and 40 mA current. Thermogravimetric analysis experiments were carried out on a TA instrument Q500 TGA under air at constant heating rate of 10 °C min<sup>-1</sup> up to 800 °C. Approximately 12-20 mg sample was used for each experiment. The TEM samples were prepared by suspending the magnetic nanoparticles in acetone followed by sonication for several minutes. One drop of the dilute magnetic nanoparticles/acetone suspension was placed on a carbon-coated holey TEM copper grid and was dried in air. The dried grid was then loaded into a double tilt sample holder. The sample was then examined with a Philips CM20 STEM equipped with a Gatan UltraScan 1000 CCD camera and an energy dispersive X-ray spectrometer: INCA Energy TEM 200. TEM images were taken at 200KV.

### Preparation of 3-azidopropylphosphonic acid **1**

To a pre-cooled (-5 °C) solution of diethyl 3-azidopropylphosphonate<sup>4</sup> (1.10 g, 5 mmol) in CH<sub>3</sub>CN (20 ml), trimethylbromosilane (3.25 ml, 25 mmol) was added dropwise in 10-15 min. The reaction mixture was stirred for 24 h at 20-30 °C. After completion of the reaction, the solvent was evaporated and residue was dissolved in methanol-water mixture (9:1, 10 ml), stirred for 24 h at room temperature and co-evaporated with dry toluene at reduced pressure to give **1** in quantitative yield.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 1.91 (m, 4H), 3.41 (m, 2H), 8.75 (bs, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 21.99, 22.03 (d, *J* = 4 Hz), 22.99 and 24.35 (d, *J* = 136 Hz), 51.25 (d, *J* = 18 Hz). <sup>31</sup>P NMR (100 MHz, CDCl<sub>3</sub>): δ = 23. IR (cm<sup>-1</sup>): 2912, 2873, 2854, 2094, 1446, 1409, 1350, 1247, 1112, 973, 925, 763, 750, 725, 703.

### Preparation of azide functionalized magnetic nanoparticles MNP-1

A 1:1 mixture of magnetic nanoparticles<sup>1</sup> and **1** in chloroform was ultrasonicated for 2 h. The nanoparticles were separated by magnetic decantation using an external magnet and washed 3 times with methanol and dried under reduced pressure to give azide functional magnetite **MNP-1** as a dark brown powder. The loading was determined to be 2.3 mmol g<sup>-1</sup> by elemental analysis.

IR (cm<sup>-1</sup>): 2920, 2858, 2092, 1415, 1363, 1384, 1232, 1108, 1058, 1012, 993, 927, 853, 779, 715.

### Procedure for the copper catalyzed conjugation of *tert*-butyl-*N*-*boc*-4-propargyloxyproline with MNP-1

Azide functionalized magnetite **MNP-1**, 500 mg (1.15 mmol of **1** at the surface) and *tert*-butyl-*N*-*boc*-4-propargyloxyproline (442 mg, 1.35 mmol) were suspended in a mixture of *tert*-butyl alcohol-water (5 ml, 1:1). Sodium ascorbate (10 mol %) was added, followed by the copper (II) sulphate pentahydrate (1.5 mol %). Triethylamine (2 equiv.) was added and the reaction mixture was stirred in air at room temperature for 24 h. The solvent was evaporated and co-evaporated with dry methanol at reduced pressure to give a brown coloured powder which was washed 3 times with ether and dried under vacuum

to give the magnetic nanoparticles **MNP-2** as a brown powder. These magnetic nanoparticles were soluble in dichloromethane, methanol and acetonitrile but insoluble in ether and water.

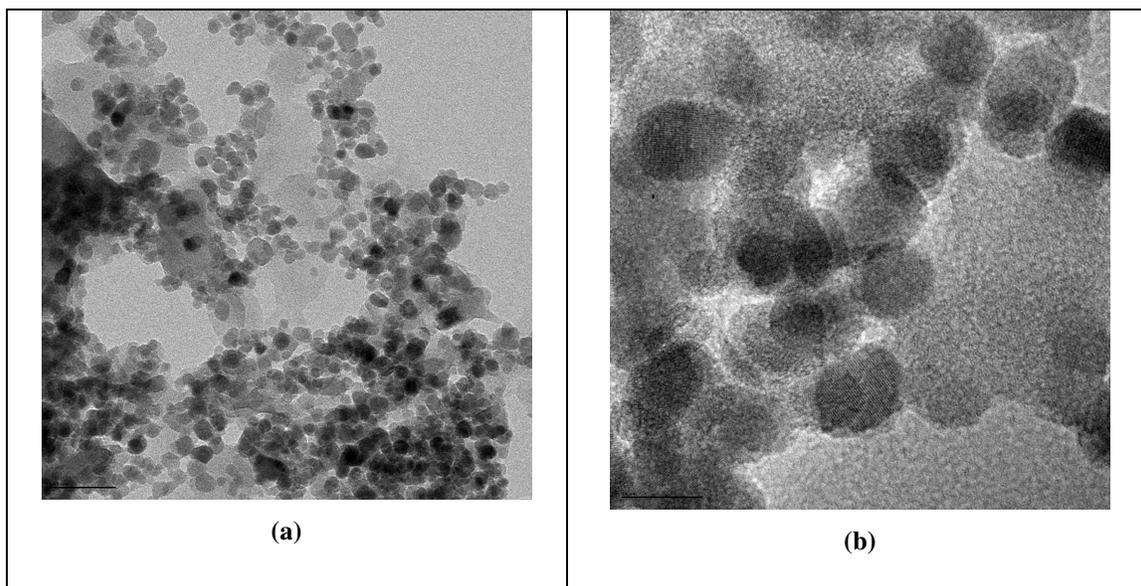
IR ( $\text{cm}^{-1}$ ): 2977, 2933, 2875, 1737, 1693, 1477, 1456, 1394, 1365, 1315, 1299, 1253, 1218, 1147, 1118, 1043, 993, 935, 910, 838, 769, 730, 696.

### **Procedure for the deprotection of tert-butyl groups from magnetically supported proline**

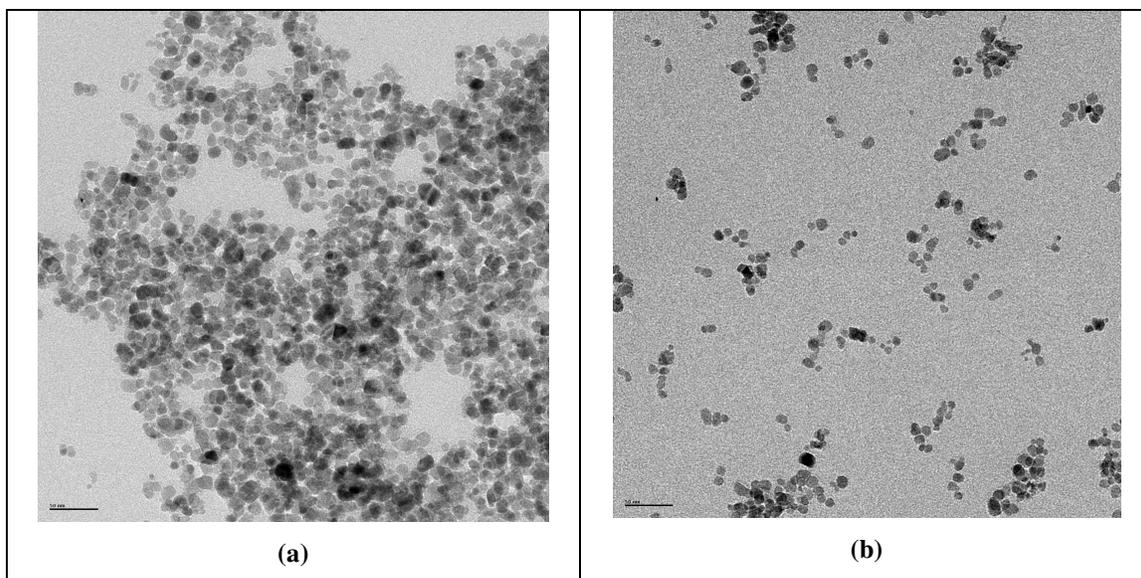
Magnetite nanoparticles **MNP-2** were dissolved in the mixture of dichloromethane-trifluoroacetic acid (1:1) and stirred overnight. The particles were separated by magnetic decantation using external magnet and sequentially washed with DCM, MeOH (with 5 %  $\text{Et}_3\text{N}$ ), water and finally with acetone to give a brown powder which was dried in vacuum to give the **MNP-3**. Elemental analysis shows the catalyst loading as  $2 \text{ mmol g}^{-1}$ .

IR ( $\text{cm}^{-1}$ ): 2970, 2939, 1620, 1446, 1361, 1317, 1288, 1215, 1199, 1114, 1043, 943, 898, 838, 771, 696.

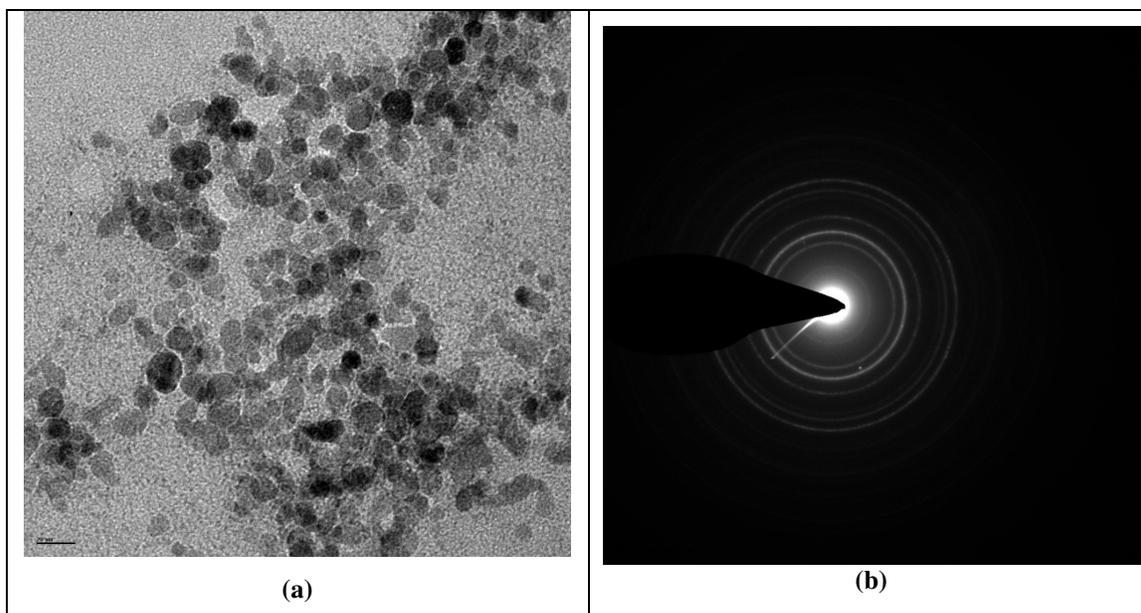
### **Characterization of MNP-1, MNP-2 and MNP-3**



**Fig. S-1** TEM images of azide functionalised  $\text{Fe}_3\text{O}_4$  nanoparticles **MNP-1** (Scale bar- image a: 50 nm and image b: 10 nm)

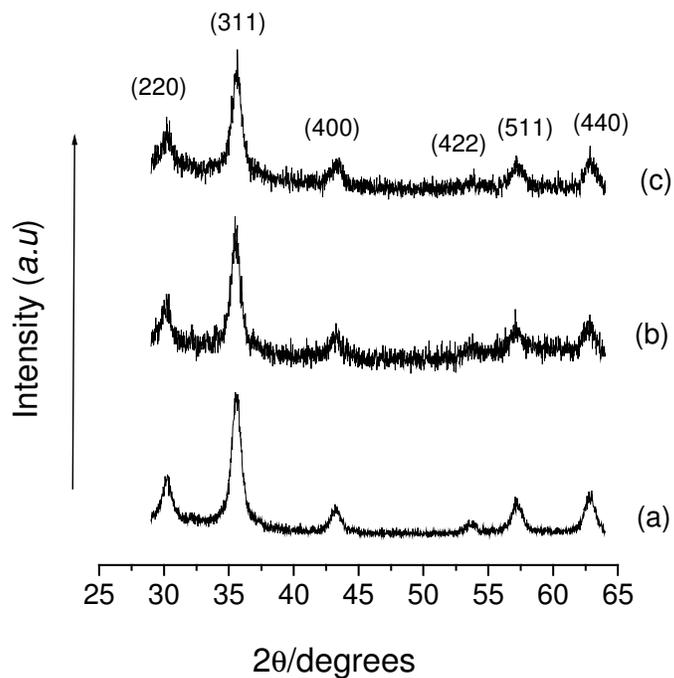


**Fig. S-2** TEM images of  $\text{Fe}_3\text{O}_4$  nanoparticles MNP-2 (Scale bar-image a: 50 nm and image b: 50 nm)



**Fig. S-3** (a) TEM image of  $\text{Fe}_3\text{O}_4$  nanoparticles MNP-3 (Scale bar-image a: 20 nm) and (b) Selected area electron diffraction (SAED) pattern.

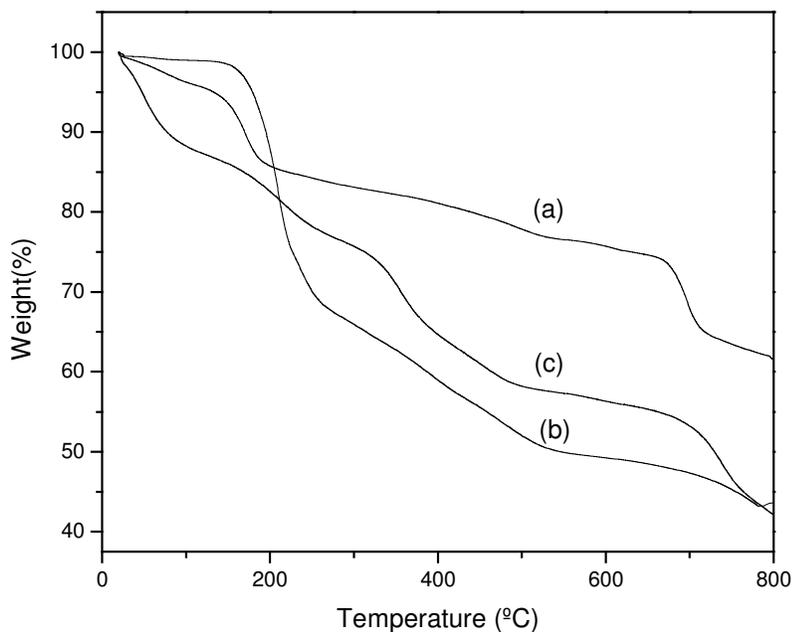
Fig. S-3 a shows the TEM images of the synthesized proline loaded magnetite nanoparticles. The average particle size (from counting ~50 particles) was  $16 \pm 2$  nm. The selected area electron diffraction pattern (Fig. S-3 b) of the MNP-3 shows a characteristic polycrystalline diffraction pattern of magnetite particles.



**Fig. S-4 XRD pattern of (a) MNP-1, (b) MNP-2 and (c) MNP-3**

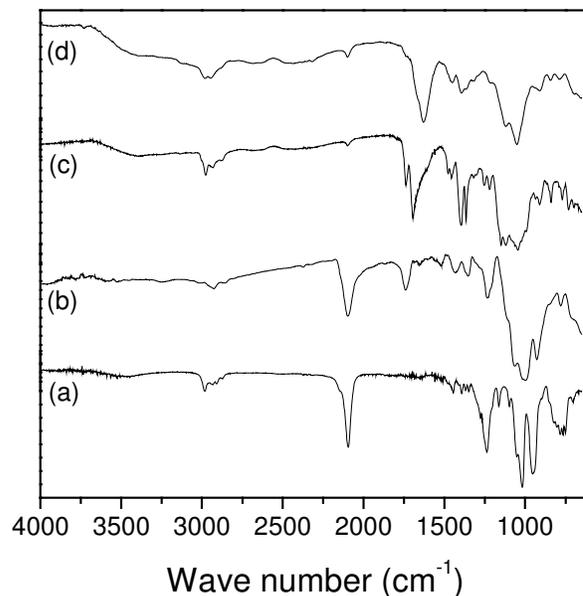
**Table S-1 Lattice parameters and interlayer spacing (in Å) from magnetic nanoparticles MNP-3**

Sample	(hkl)					
	1	2	3	4	5	6
Standard Fe <sub>3</sub> O <sub>4</sub> <sup>5</sup>	2.96	2.53	2.09	1.71	1.61	1.48
MNP-3	2.95	2.52	2.08	1.70	1.61	1.47



**Fig. S-5 TGA curves of (a) MNP-1, (b) MNP-2 and (c) MNP-3**

Fig. S-5 shows the TGA curves for the azide functionalised magnetite nanoparticles (a), magnetite nanoparticles after the click chemistry (b) and the proline ligand loaded magnetite nanoparticles (c). The azide functionalised nanoparticles were found to have a weight percentage loss of ~ 38 %, while for the proline loaded nanoparticle (**MNP-2** and **MNP-3**) this loss was ~56%. This clearly shows the high loading of organic materials on nanoparticles.



**Fig. S-6 FTIR spectra of azidophosphonic acid 1 (a) and magnetic nanoparticles MNP-1 (b), MNP-2 (c), MNP-3 (d).**

The FTIR spectrum of azide functionalised nanoparticles (Fig. S-5b) shows a stretching vibration at  $2092\text{ cm}^{-1}$  that is due to the asymmetrical modes of  $-\text{N}_3$  bonds. The values at  $2920\text{ cm}^{-1}$  and  $2858\text{ cm}^{-1}$  correspond to asymmetric and symmetric stretching of the  $\text{CH}_2$ -group. The band at  $1232\text{ cm}^{-1}$  is due to the  $\text{P}=\text{O}$  stretching indicating that the phosphonate group is connected to the  $\text{Fe}_3\text{O}_4$  surface through ionic bonds. Two broad bands at  $1058\text{ cm}^{-1}$  and  $1012\text{ cm}^{-1}$  are due to superimposed  $\text{Fe}-\text{O}-\text{P}$  and  $\text{P}=\text{O}$  stretching bands. After the click chemistry reaction of **MNP-1** with propargyloxypicolinate, the azide functional group band almost disappeared replaced by two new bands at  $1737\text{ cm}^{-1}$  and  $1693\text{ cm}^{-1}$  corresponding to carbonyl functionality of boc and *tert*-butyl ester groups, whereas bands at  $1395\text{ cm}^{-1}$  and  $1365\text{ cm}^{-1}$  are due to the two *tert*-butyl groups. After the deprotection of both *tert*-butyl groups of the proline ligand with TFA, the IR spectrum of **MNP-3** shows no *tert*-butyl groups. A new band appears at  $1620\text{ cm}^{-1}$  assigned to the  $-\text{COOH}$  functional group of the proline. Absorption bands at  $1446\text{ cm}^{-1}$  and  $1114\text{ cm}^{-1}$  were assigned to  $\text{P}-\text{CH}_2-$  and  $-\text{P}=\text{O}$ ,  $\text{Fe}-\text{O}-\text{P}=\text{O}$  stretching bands.

## References

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