CHAPTER 3

SYNTHESIS OF POLY(ALLYLMORPHOLINE *N*-OXIDE) GRAFTED SILICA MAGNETIC NANOPARTICLES

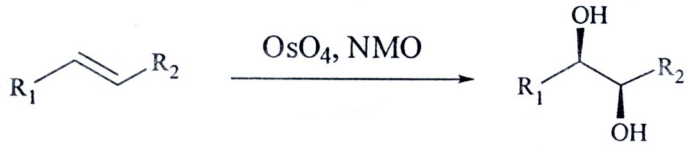
3.1 Introduction

3.1.1 *N*-Methylmorpholine *N*-Oxide (NMO)

N-Methylmorpholine *N*-Oxide (NMO) is an heterocyclic tertiary amine oxide which can be regarded as the most important amine *N*-oxide in organic synthesis [98]. The most prominent feature of NMO is the highly polar N-O group in which the highest electron density is located at oxygen atom. Thus the most frequent application of NMO in organic synthesis is their use as a mild oxidant or as co-oxidant [99-105]. While the other amine oxide, *N*,*N*,*N*-triethylamine-*N*-oxide (TMANO) [106], quinuclidine *N*-oxide (QNO) [107] and 4-Dimethylaminopyridine *N*-oxide (DMAP *N*-oxide) [108] are less important.

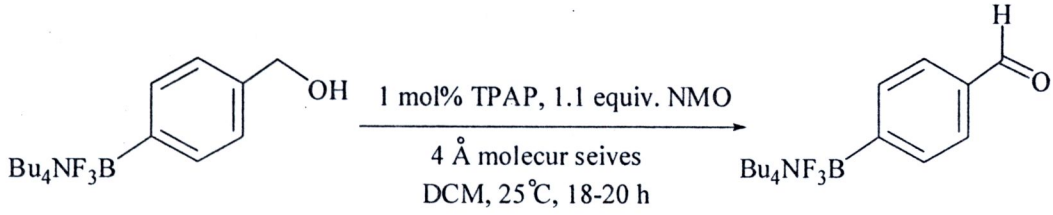
In *cis*-dihydroxylation of olefins, NMO was often used as cooxidant with osmium tetroxide (OsO_4) due to the high cost and toxicity of OsO_4 (Scheme 3.1) [99-102]. This reagent give high yield and do not require cumbersome workups in comparison with other *cis*-dihydroxylation reagents such as potassium permangante ($KMNO_4$), iodine silver acetate, or OsO_4 in the presence of barium pechlorate of

hydrogenperoxide (H_2O_2) [99]. In addition, NMO generally gives a faster reaction rate and it is easily prepared.



Scheme 3.1 Upjohn dihydroxylation

Besides OsO_4, other oxidants such as tetrapropylammonium perruthenate, TPAP, can be used catalytically in the presence of NMO [109, 110]. The TPAP reagent can be rendered catalytic if suitable co-oxidants are added, of which NMO is most effective. The efficient aerobic oxidation of primary and secondary alcohols to corresponding aldehyde or ketone using catalytic amounts of TPAP was reported [111-114]. For example, the report of Molander and Petrillo presented NMO along with TPAP was employed in oxidation reaction of tetra-*n*-butylammonium (TBA) trifluoroborate (Scheme 3.2). This protocol showed superior oxidation efficiency than that oxidation using Swern oxidation and Dess-Martin Periodinane conditions [112]. The representative applications of NMO are summarized in Table 3.1.



Scheme 3.2 Oxidation of TBA trifluoroborate using NMO/TPAP system

Table 3.1 Summary of the representative appilcations of NMO

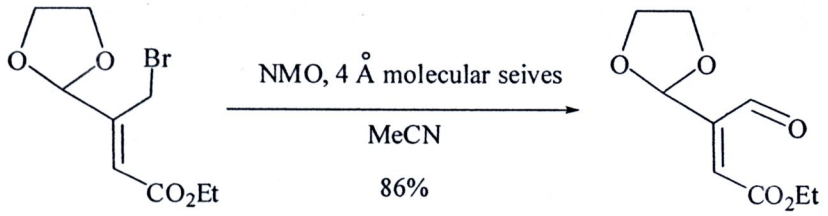
Reaction	Condition	Ref.
Oxidative removal of *O*- and *N*-allyl protecting groups	NMO (3 equiv.), OsO_4 (8 mol%), dioxane-water (10:1), 60 °C	[115]
Cyclization of 1,2,4-triazenes	NMO (12 equiv.), TPAP (1 equiv.), MeCN, rt, 12 h	[116]
cis-Dihydroxylation of olefins	NMM (27 mol%), OsO_4 (2 mol%),TEAA (2 equiv.), flavin (5 mol%), acetone-water (10:1), rt	[117]
Conversion of olefins to carbonyl compounds	NMO (3 equiv.), TPAP (5 mol%), 4 °A molcular sieves, DCM, rt	[111]
Dihydroxylation of a variety of polyenes	NMO (2.2 equiv.), OsO_4 (0.4 mol%), $PhB(OH)_2$ (2.2 equiv), DCM, rt	[102]
Dihydroxylation of Ene-Ester	NMO (3 equiv.), OsO_4 (5 mol%), acetone:water (8:1), rt	[118]
Oxidation of Stigmasterol methyl ether	NMO (13 equiv.), OsO_4 (4 mol%), THF-*t*-BuOH-water (7:4:1),rt	[105]
Dihydroxylation of cyclic allylic alcohols	NMO (4 equiv.), OsO_4 (5 mol%), acetone:water (4:1), rt	[100]
cis-Dihydroxylation of monoterpenes	NMO (1 equiv.), OsO_4 (0.27 mol%), pyridine, *t*-BuOH-water (5:1), rt, Ar(g)	[119]
cis-Dihydroxylation of olefins	NMM (0.5 equiv.), OsO_4 (1 mol%), *m*CPBA (4 equiv.), TEAA (1.3 equiv), acetone-water (3:1), rt	[120]

Table 3.1 Summary of the representative appilcation of NMO (continued)

Reaction	Condition	Ref.
Dihydroxylation of potassium alkyl- and aryltrifluoroborates	NMO (1.0-1.5 equiv.), OsO_4 (1.3 mol %), acetone/*t*-BuOH/water mixture (18:1:1), rt	[112]
cis-Dihydroxylation of olefins	NMO (1.5 equiv.), Os Encat (5 mol%), acetone-water (10:1), rt	[103]
Asymmetric dihydroxylation of olefins	NMO (1.5 equiv.), OsO_4 (1 mol%), (QN)PHAL (2.5 mol%), ionic liquid, acetone-water (10:1), 20 °C	[121]

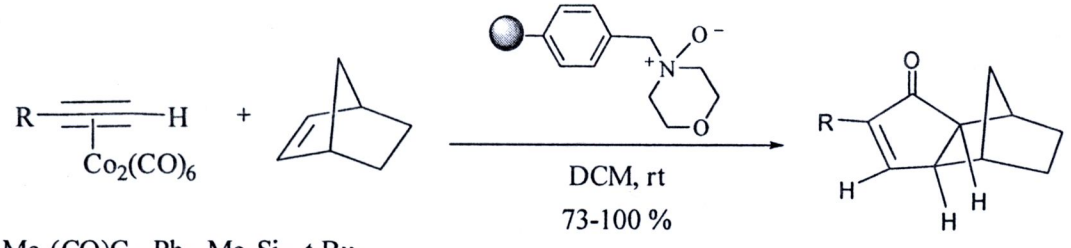
Although most reports on NMO involve its applications as co-oxidant, NMO itself can be used directly as an oxidant in the oxidation of benzylic halides to the corresponding aldehydes and ketones For example, cinnamyl bromide is converted to cinnamaldehye by stirring the activated halide with NMO in acetonitrile (Scheme 3.3) [122]. This reagent can oxidize a halide in the presence of a double bond.

In order to develop production process based on cleaner technologies, various polymer-supported catalysts and reagents have been developed [123]. One of the key advantages of immobilizing a catalyst or reagent on a solid support is the ease of separation from the product mixture at the end of a reaction, the greatly simplified work-up needed, recoverable achievement and recyclability [124].



Scheme 3.3 Oxidation of cinnamyl bromide with NMO

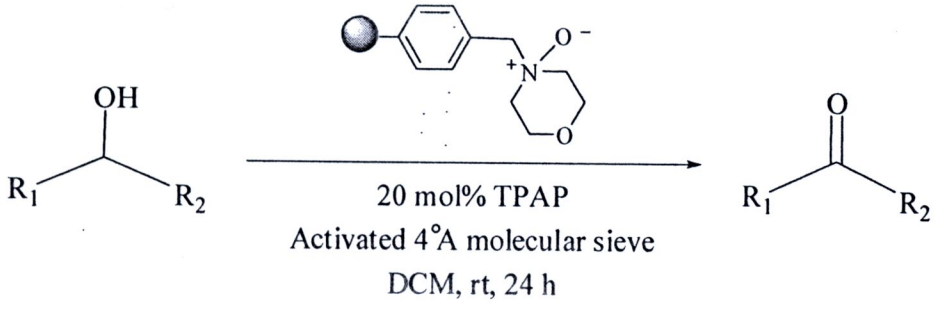
Generally, an excess amount of NMO (3-5 mole equiv.) is often used in reactions resulting in the presence of amine by-products which require to be removed and are normally discarded. In this respect, a high loading polymer supported NMO has been prepared by oxidation of polymer supported morpholine using *m*CPBA [125]. The polymer supported NMO was utilized as an economical and efficient promoter in the Pauson-Khand (P-K) cyclisation reaction (Scheme 3.4). In all cases, use of the resin resulted in good to excellent yields of cyclopentenone products and the resin was readily recycled.



R = $Me_2(CO)C$-, Ph-, Me_3Si-, *t*-Bu-

Scheme 3.4 P-K reactions of a range of alkynes with norbornene promoted by the polymer supported NMO

In another attempt, high load polymer supported NMO was prepared using the commercially available polymer supported morpholine based resin [126]. Oxidation of the attached morpholine was readily achieved with *N*-phenylsulfonyloxaziridine (Davis's reagent) or *m*CPBA. The supported NMO was applied as a co-oxidant with TPAP in oxidation of alcohols (Scheme 3.5). The resin gave rise to high product yields and showed good chemoselectivity for activated alcohol systems. The resins could be readily recycled without loss in activity.



Scheme 3.5 Oxidation of alcohol to corresponding aldehydes or ketones using TPAP and polymer supported NMO

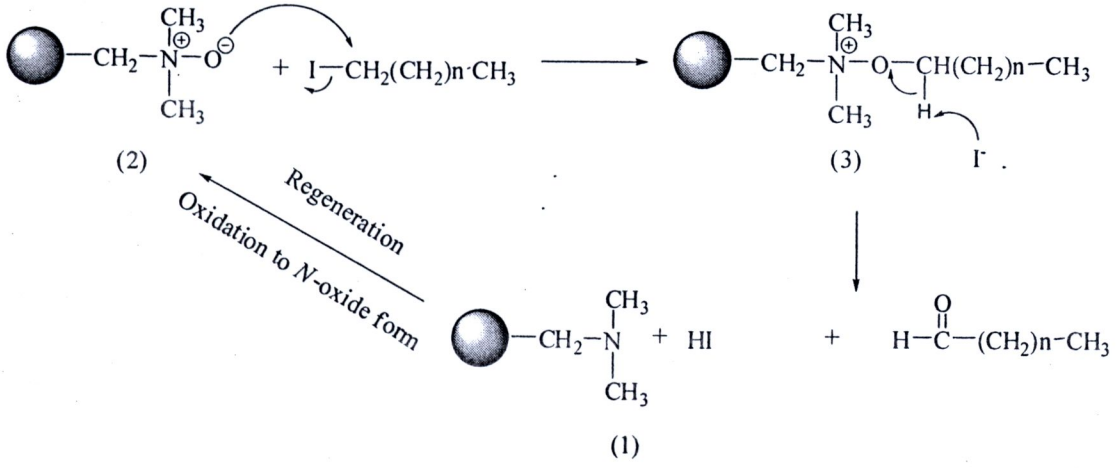
3.1.2 Oxidation of organic halides

The oxidation of organic halides to the corresponding aldehydes or ketones is a well known organic synthetic transformation in both laboratory and industrial synthetic chemistry. In many cases, direct oxidation of organic halides to aldehydes and ketones affords a more convenient synthesis than the oxidation of the corresponding alcohols [127]. The classical method for a conversion constitutes the Hass–Bender reaction [128], which involves *O*-alkylation of the nitronate anion

followed by decomposition of the resulting intermediate. This method is only satisfied for para-substituted substrates. Sommelet reaction [129] is another classic method for this transformation. The first step of this process is the reaction of hexamine with the alkyl halide to form a quaternary salt, which upon hydrolysis gives a primary amine, formaldehyde and ammonia (the Delepine reaction). Hydrolysis of the aldimine derived from reaction between formaldehyde and ammonia, gives the aldehyde. This reaction is generally possible with active halides such as benzylic halides, allylic halides, α-halo ketones and primary iodides. Other notable to accomplish this conversion is Krőhnke reaction [130] involves converting the halide to the pyridinium salt with *p*-*N*,*N*-dimethylnitroso-aniline to give a nitrone, which is hydrolyzed in aqueous acid to the carbonyl compounds.

In the Kornblum reaction, organic halide is refluxed in DMSO along with base to form an aldehyde [131]. In this reaction, the nucleophilic oxyanion of DMSO attacks the benzylic halide in an S_N2 reaction and displaces the halide to form an alkoxysulfonium salt. The base often abstracts a benzylic proton to form the aldehyde. However, this condition is invariably associated with certained limitations in term of long reaction times, poor yields, harmful to the environment, high temperature, etc. Another attention has been paid to the adding of co-operative oxidant such as amine *N*-oxide[106, 132, 133] which occasionally called "Ganem oxidation" [106]. Based on Ganem oxidation, the combination of *N*,*N*,*N*-triethylamine-*N*-oxide (TMANO) and DMSO was used in the oxidation of various alkyl and allylic halide to generate aldehyde in good yield at low reaction temperature [106].

Frechet and co-workers used five fold excess of the polymeric *N*-oxide for the oxidation of 1-bromoheptane and benzyl chloride to yield 87% and 95% of corresponding aldehydes at 70-80 °C [132]. The plausible mechanism of alkyl iodide oxidation was present as shown in Scheme 3.6. The highest electron density is located at oxygen atom of *N*-oxide part of tertiary amine *N*-oxide makes them a good nucleophilic site. In a first step, nucleophilic displacement of iodide by the *N*-oxide functionalities of polymer (2) results in the formation of polymer-bound intermediate (3). This intermediate then reacts immediately with base to undergo elimination, with formation of the aldehyde and the polymeric amine (2).



Scheme 3.6 Oxidation mechanism of oxidation reaction of organic halide using solid supported tertiary amine *N*-oxide [132].

Recently, Kaur and Dhiman reported oxidation of aliphatic and aromatic halides by *N*-oxide functionalities supported on 4-vinyl pyridine grafted cellulose

(CellO-g-poly(4-VP) *N*-oxide). The percentage yields of the corresponding aldehydes from 1-bromoheptane and benzyl chloride were 60% and 53.4% under reaction times of 38 h and 18 h, respectively [134].

In this present study, a new type of oxidizing reagent for organic halide oxidation were synthesized using aminopropyl magnetic silica which was followed by grafting with NMO polymeric chain to poly(allylmorpholine *N*-oxide) grafted on magnetic silica nanoparticles (M-NMOs). The effective loading of synthesized M-NMOs involving the oxidation of benzyl halides were examined by compare its activity with standard NMO reagent. Moreover, the solvent effect in the oxidation of benzyl halide to benzaldehyde was also investigated.

3.2 Experimentals

3.2.1 Chemicals

Acetic acid (AcOH), $C_2H_4O_2$, assay 100%, BDH, England

Acetonitrile (MeCN), C_2H_3N, analytical grade, RCI Labscan, Thailand

Acrylic acid (AA), $C_3H_4O_2$, assay >99%, Fluka, Switzerland

Allyl chloride, C_3H_5Cl, assay 99.9%, BDH, England

Ammonium solution (NH_4OH), NH_5O, assay 30%, Carlo Erba, Italy

3-Aminopropyltriethoxysilane (APTES), $C_9H_{23}NO_3Si$, assay 98%, Sigma–Aldrich, Germany

Azobisisobutyronitrile (AIBN), $C_8H_{12}N_4$, assay 98%, Aldrich, Germany

Benzoyl peroxide (Bz_2O_2), $C_{14}H_{10}O_4$, assay ≥ 97%, Fluka, Switzerland

Benzyl bromide (BnBr), C_7H_7Cl, assay ≥ 98%, Fluka, France

Benzyl chloride (BnCl), C_7H_7Br, assay >99%, Merck, Germany

Bromobenzene, C_6H_5Br, assay 99%, Aldrich, U.S.A.

Chloroform-d, $CDCl_3$, assay 99.8% atom D, Aldrich, U.S.A.

meta-Chloroperoxybenzoic acid (*m*CPBA), $C_7H_5ClO_3$, assay ≤ 77%, Aldrich, Germany

Dichloromethane (DCM), CH_2Cl_2, commercial grade, Fluka, Switzerland

Diethyl ether, $C_4H_{10}O$, assay 99%, Labscan, Ireland

4-Dimethylaminopyridine (DMAP), $C_7H_{10}N_2$, assay ≥98%, Fluka, Switzerland

Dimethylformamide (DMF), C_3H_7NO, assay 97%, Carlo Erba, Italy

Dimethyl sulfoxide (DMSO), C_2H_6OS, assay 99.9%, Labscan, Ireland

1,4-Dioxane, $C_4H_8O_2$, assay > 98%, BDH, England

Ethanol (EtOH), C_2H_6O, commercial grade, Fluka, Switzerland

Ethyl acetate (EtOAc), $C_4H_8O_2$, commercial grade, Fluka, Switzerland

Ferric chloride ($FeCl_3 \cdot 6H_2O$), assay 97%, Carlo Erba, Italy

Hexane, C_6H_{14}, assay >99%, QreC, New Zealand.

Hydrogen peroxide, H_2O_2, assay 30%, Northern Chemical and Glassware Limited, Thailand

Iron(II) sulphate ($FeSO_4 \cdot 7H_2O$), assay 99%, POCH, Poland

Methanol (MeOH), CH_4O, commercial grade, Fluka, Switzerland

Methyl morpholine *N*-Oxide, (NMO), $C_5H_{11}NO_2$, assay 97%, Aldrich, Germany

Montmorillonit K-10, Aldrich, Germany

N, *N*'-Diisopropyl carbodiimide (DIC), $C_7H_{14}N_2$, assay 991%, Sigma, U.S.A.

Potassium bromide, KBr, assay 99%, BDH, England

Potassium cyanide, KCN, assay 97%, BDH, England

Potassium hydroxide, KOH, assay 85%, BDH, England

Pyridine, C_5H_5N, assay 99.5%, BDH, England

R.O. water, Department of Chemistry, Faculty of Science, Chiang Mai University, Thailand

Sodium bromide, NaBr, assay 99.5%, Rdh, U.S.A.

Sodium sulphate, Na_2SO_4, assay >99%, Fischer Scientific, U.S.

Triethylamine (Et_3N), $C_6H_{15}N$, assay 99%, Ajax Finechem, Australia

3.2.2 Instruments

UV/Vis Spectrophotometer (Perkin Elmer, Lambda 25), U.S.A.

Scanning Electron Microscope (SEM) (JEOL, JSM 6335F), Japan

Transmission electron microscopy (TEM) (JEOL, JEM 2010), Japan

Fourier Transform Infrared (FTIR) Spectrometer (Bruker, TENSOR 27), Germany

Magnetight™ Separation Stand (Novagen), Germany

Ultrasonic bath (Elma, S 30 H Elmasonic), Germany

Gas chromatography (Agilent, GC-6890A (G2163A)), U.S.A.

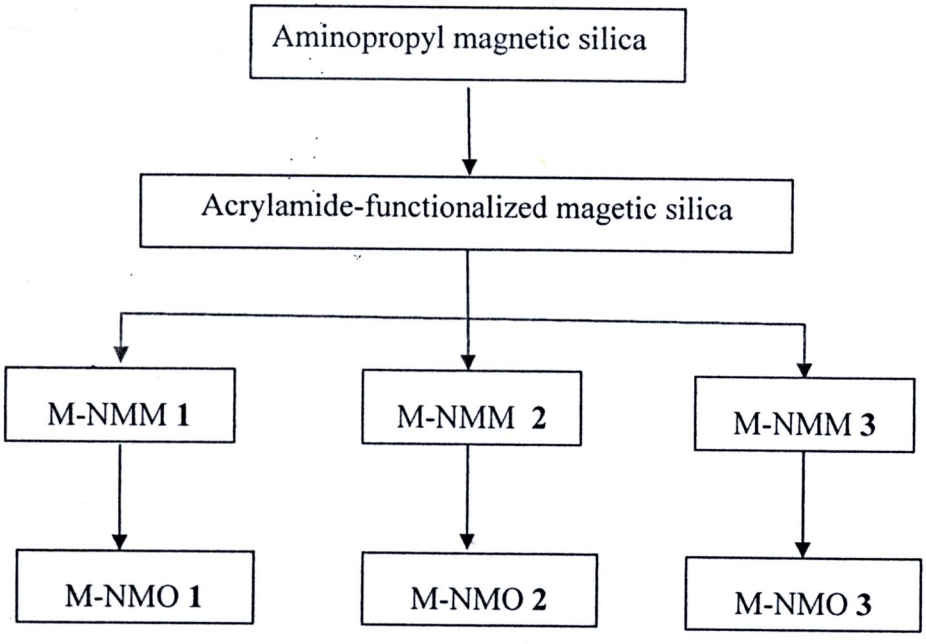
3.2.3 Synthesis of *N*-allylmorpholine monomer

N-allylmorpholine monomer was synthesized following previous report of Hachemaoui and Belbachir [135]. Briefly, the reactions were carried out in bulk (without solvent). Montmorillonite K-10 clays (3.0 g) was added to a solution of morpholine (9.18 g, 0.091 mol) and an allyl chloride (10.41 g, 0.136 mol), and the mixture was stirred at room temperature. After completion of the reaction, the solution was washed several times with DCM, the whole mixture was filtered and the clay-free material gave the salt of *N*-allylmorpholinium. After having prepared 100 ml of an aqueous solution of KOH (10%), one added to the ammonium salt by small quantities. The mixture was left under stirring overnight. A heterogeneous solution was obtained, the KCI precipitate was filtered off and the *N*-allylmorpholine was

extracted with diethyl ether. Two phases were separated by decantation, diethyl ether was evaporated to yield of allylmorpholine crude product. Finally, the crude product was purified by column chromatography (10%EtOAc/Hexane).

3.2.4 Synthesis of M-NMOs

The steps of synthesis of M-NMO were summarized in this following scheme.



Scheme 3.7 The steps of synthesis of of poly(allylmorpholine *N*-oxide) modified magnetic silica nanoparticles

3.2.4.1 Synthesis of acrylamide-functionalized magnetic silica nanoparticles

The acrylamide-functionalized magetic silica nanoparticles were synthesized by coupling method. Typically, 5.0 g of aminopropyl magnetic silicas were disperesed in 15 ml of a mixture of 4:1 (v/v) DCM:DMF by sonication for 15 min. At the same time, the a mixture of acrylic acid (0.476 g, 6.6 mmol), Et_3N (0.668 g, 6.6 mmol), DIC (0.833 g, 6.6 mmol) and DMAP (10 mg, catalytic amount) was prepared in 5 ml of same solvent at 0 °C. Then, the suspension of aminopropyl magnetic silicas was slowly added into that solution. A hole of reaction mixture was shaken for 3 h at room temperature. Completion of this reaction steps was monitored (qualitatively) using the ninhydrin test [76] (Table A.1). When primary amines were present on the beads, ninhydrin solution turned blue; otherwise, the color of the solution remained unchanged. The product nanoparticles were separated by Magnetight™ separation stand followed by washing of 4:1 (v/v) DCM:DMF (5 × 20 ml) and DCM (3 × 20 ml), then dried to powders at 50 °C for 16 h. The obtained product is coded as AA-Si-NPs.

3.2.4.2 Synthesis of M-NMM 1

Poly(*N*-allylmorpholine) modified magnetic silica nanoparticles **1** or M-NMM **1** was synthesized following previously polymerization method which reported by Gao and co-workers [136]. Typically, AA–Si–NPs (5.0 g) were dispersed in 30 ml of MeCN by ultrasonic vibration for 15 min. Then, *N*-allylmorpholine (1.737 g,

13.66 mmol) and AIBN (0.022 g, 0.14 mmol) were added to the suspension of AA–Si–NPs. The mixed solution was polymerized at 60 °C for 24 h under purging with nitrogen and continued stirring. Resulting M-NMM **1** were washed repeatedly with MeCN (5 × 20 ml) and MeOH (2 × 20 ml), respectively. Finally, the product were washed with DCM (2 × 20 ml) then dried at 60 °C for 16 h. The obtained solid is coded as M-NMM **1**.

3.2.4.3 Synthesis M-NMM 2 and 3

M-NMM **2** and **3** were synthesized using same polymerization method which previously reported by Bicak and co-workers [137], but the difference is the amount of *N*-allylmorpholine monomer using in reaction. For M-NMM **2**, 10 equivalent of *N*-allylmorpholine monomer was used while M-NMM **3**, 20 equivalent of *N*-allyl morpholine monomer was used (the equivalent of *N*-allylmorpholine monomer was calculated from loading of the totally used AA–Si–NPs). Typical procedure, AA–Si–NPs were dispersed in 45.0 ml of 1,4-dioxane by ultrasonic vibration for 15 min. Then, *N*-allylmorpholine was mixed with the suspension of AA–Si–NPs in a 100 ml flask attached to a reflux condenser and a nitrogen inlet. To neutralize the allyl monomer, 1.0 ml of acetic acid was added to the solution. After that, the mixture was flushed with nitrogen and benzoyl peroxide (3 %mol) in 5 ml of 1,4-dioxane was added to the solution. The mixture was heated at 80°C for 24 h under N_2 protecting. At the end of this period, the mixture was cooled and the beads were separated by Magnetight™ separation stand followed by washing with 1,4-dioxane (5 × 20 ml).

And then, washed throughly with 20 ml of 10% NaOH solution. Finally, the product were washed repeatedly with MeCN (5 × 20 ml) and DCM (2 × 20 ml), respectively. Then dried to be powder at 60 °C for 16 h. The recovered materials are code as M-NMM **2** and M-NMM **3**.

3.2.4.4 Oxidation of M-NMM 1 and 2 to M-NMO 1 and 2

To oxidize the grafted polymeric NMM on the surface of modified magnetic silica nanoparticles to be NMO form, M-NMO **1** and **2** were prepared using the method as previously reported by Brown and co-workers [126]. Typically, 5.0 g of M-NMM was disperesed in 20 ml of DCM by ultrasonic condition for 15 min. Then, a two-fold excess of *m*CPBA in DCM was added and reaction mixture was further sonicated for 15 min and kept to continuously shake for 24 h at room temperature. The final product beads were separated by Magnetight™ separation stand followed by washing several times with DCM to remove of benzoic acid and residues of *m*CPBA. After that, M-NMO was washed with MeOH (2 × 20 ml) to make sure that unwanted residues were completely removed and washed again with DCM (2 × 20 ml) before dried at 60 °C for 16 h. The resulting materials are code as M-NMO **1** and M-NMO **2**.

3.2.4.5 Oxidation of NMM beads 3 to M-NMO 3

To prepare of the polymeric NMO modified magnetic silica nonoparticles, another method was attempted using commercially available H_2O_2. M-NMO **3** was transformed to *N*-oxide form via oxidation method using H_2O_2 condition as previously reported by VanRheenen and co-workers [138]. Typically, 4.0 g of M-NMM **3** was disperesed in of 20 ml of MeCN by ultrasonic condition for 15 min. Then, five-fold excess molar of H_2O_2 were dropwise into the reaction with continued stirring and then kept for further continueously stir at room temperature for 24 h. After reaction was finished, M-NMO was separated by Magnetight™ separation stand and washed several times with MeCN and follwed with water (1 × 20 ml) and MeOH (2 × 20 ml), respectively, to make sure that unwanted residues were completely removed. Finally, the product was washed with DCM (2 × 20 ml) before dried at 60 °C for 16 h. The final product is coded as M-NMO **3**.

3.2.5 Oxidation of benzyl halides to coresponding aldehydes using standard NMO reagent

Typical reaction procedure; the homogeneous reactions were conducted in a sealed reaction vessel to prevent loss of volatile compounds which might be produced in the reaction. Benzyl chloride (0.127 ml, 1.0 mmol), NMO (0.469 g, 4.0 mmol), NaBr (catalytic amount) and dimethylsulfoxide (DMSO) (2.0 ml) were mixed and sonicate for 10 min. In case of benzyl bromide as substrate, no NaBr catalyst

necessary. The reaction was monitored by thin layer chromatography by comparison with the starting material (10% EtOAc in Hexane). After reaction complete, the reaction mixture was poured into ice-cold, saturated aqueous NaCl (3 ml) and extracted 4 x 10 ml with diethyl ether. The combined ether layers were dried over anhydrous sodium sulfate then filtered off and concentrated. The residue was purified by column chromatography on 60–100 mesh silica gel to give the desired product.

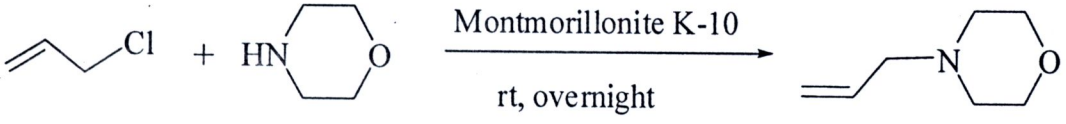
3.2.6 Oxidation of benzyl halides to coresponding aldehydes using M-NMOs

General procedure for the oxidation of organic halides to carbonyl compounds using benzyl chloride as an example: benzyl chloride (12.7 mg, 0.1 mmol) was taken in a reaction vessel along with M-NMO (300 mg) and catalytic amount of NaBr (in case of benzyl bromide, NaBr is unnecessary used). The above mixture was dissolved in 0.7 ml of solvent (DMSO, DMF, MeCN, THF, MeOH and toluene) and the mixture was reacted in ultrasonicate bath for 20 min. at setted temperature. The progress of the reaction was monitored by thin layer chromatography (10% EtOAc in hexane). The M-NMO was separated from reaction mixture by Magnetight™ separation stand and the supernatant was analysed by GC.

3.3 Results and Discussions

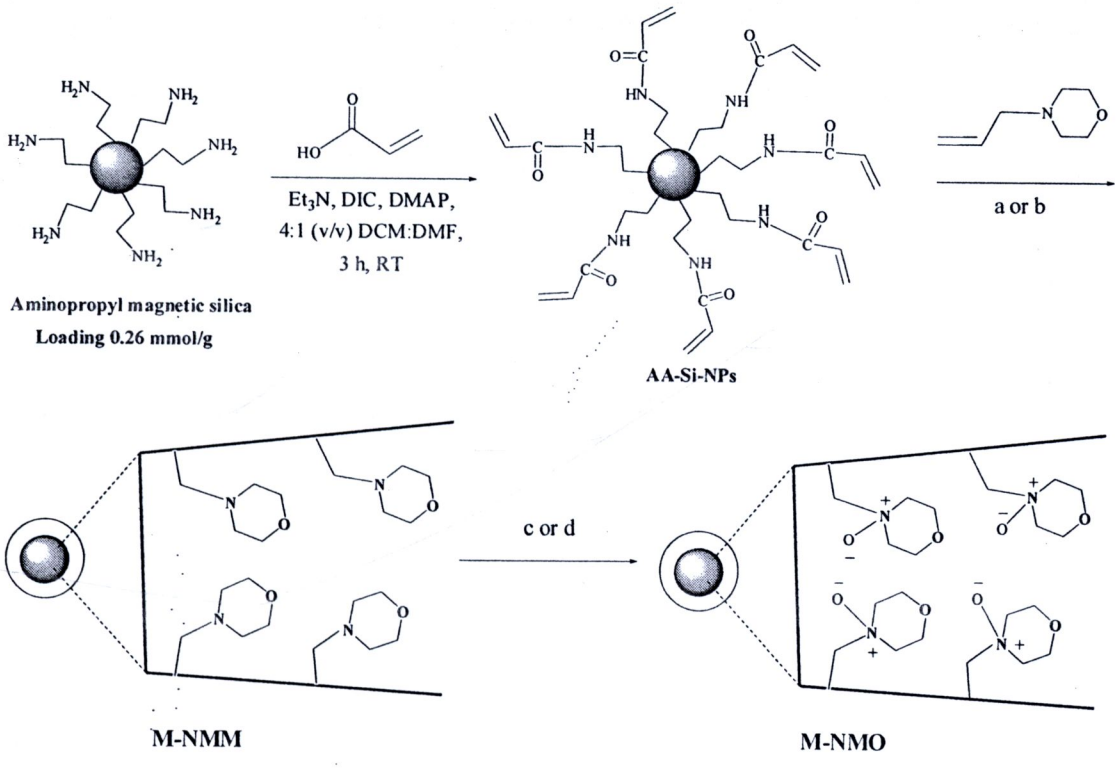
3.3.1 Synthesis and characterization of M-NMOs

N-allylmorpholine monomer was synthesis following previous report of Hachemaoui and Belbachir [135] as shown in Scheme 3.8. Allylchloride was reacted with morpholine under solvent less condition using Montmorillonite K-10 clays as a catalyst. After extraction and concentration, crude product was purified by column chromatography to generate allylmorpholine as yellow oil (3.740 g, 64.48%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.40 (t, 4H), 2.96 (d, 2H), 3.67 (t, 4H), 5.13 (dd, 2H), 5.81 (m, 1H).



Scheme 3.8 Synthesis reaction of allyl morpholine

The synthesis of poly(*N*-allymopholine *N*-oxide) grafted magnetic silica nanoparticles, M-NMOs, involved multisteps procedure as illustrated in Scheme 3.9. In the first step, aminopropyl magnetic silica nanoparticles were modified with acrylic acid to give acrylamide-functionalized MNPs, AA-Si-NPs. Polymeric NMM was then grafted on to their surface to yield M-NMMs. Subsequent oxidation of the NMM groups generated the required M-NMOs.



Scheme 3.9 Synthesis of poly(*N*-allymopholine) modified magetic silica nanoparticles (a) AIBN, MeCN, 80 °C, 24 h,under N_2; (b) Benzoylperoxide, AcOH, 1,4-dioxane, 80°C, 24 h, under N_2; (c) 2 equiv. *m*CPBA, DCM, rt, 24 h; (d) 5 equiv. H_2O_2, MeCN, RT, 24 h.

It is noted that slightly low loading (0.26 mmol/g) of aminopropyl magnetic silica nanoparticle was used in this study since it will be further modified with polymeric chain of allylmorpholine. This would presumably allows sufficient spaces on the surface of modified particles for polymeric chain growth. Nevertheless, no differences in both physical appearance and magnetism properties of aminopropyl magnetic silica were observed between this batch and the batch obtained in previous chapter.

Bicak and co-workers have been mentioned about the polymerization of *N*-allylmorpholine in previous reported [137]. They explained that the attempts at homopolymerization of *N*-allylmorpholine in different solvents with common peroxide initiators were always unsuccessful, as in the case of the well- known allyl monomers. Only small amounts of a waxy residue were obtained in aqueous solutions. Most probably, here the tertiary amino group acts as a trapping agent for peroxy radicals. Also, the allyl amine does not polymerize under ordinary conditions. In another way, Harrada and Hasegawa were the first to succeed in homopolymerizing allyl amine in phosphoric acid, to yield a polymer with a high molecular weight Presumably phosphoric acid prevents the oxidation of amino groups by blocking the nucleophilicity of the nitrogen atom involved. Therefore, high degree of *N*-allylmorpholine polymerization was occurred [139]. From this result, Bicak and co-workers therefore has transpired an idea to create polymerization condition with addition of acetic acid to give high yield of the required polymer [137].

In this work, both of conventional polymerization method and polymerization condition which reported by Bicak were applied to graft allylmorpholine on to AA-Si-NPs. Whilst two different conditions of oxidation were used to convert M-NMM to M-NMO. Theoretical loading was calculated from mole of allylmorpholine used in grafting reaction under the assumption that 100% conversion of allylmorpholine monomer are grafted on core surface. The synthesis conditions, percentage yield and characteristic of the obtained M-NMOs are shown in Table 3.2.

As shown in Table 3.2, the most distinctive physical appearance found in all samples of M-MNO is brown powder. The product yield of M-NMM **1** and M-NMM **2** are likely to same. In contrast, the product yield of M-NMM **3** was exhibited as lower than 50%. This can be evidantly indicated that *N*-allylmorpholine monomers that used to prepared the M-NMM **3** were not completely polymerized. After oxidation M-NMM to generate M-NMO, M-NMO **1** still produced excellent product yields as well as M-NMO **2**. While M-NMO **3** showed lower yield compared to other M-NMOs.

Table 3.2 Synthesis conditions, characteristic properties of M-NMOs

M-NMO	Polymerization		Oxidation		Theoretical loading (mmol/g)	Physical appearance
	Conditions	%Yield	Conditions	%Yield		
1	Allylmorpholine (10 eqiuv.) AIBN, MeCN, 60 °C, 24 h	74	2 equiv. *m*CPBA, RT, 16 h	99	2.7	Brown powder
2	Allylmorpholine (10 eqiuv.) Bz_2O_2, Dioxane/AcOH, 80 °C, 24 h	78	2 equiv. *m*CPBA, RT, 16 h	97	2.6	Brown powder
3	Allylmorpholine (17 eqiuv.) Bz_2O_2, Dioxane/AcOH, 80 °C, 24 h	45	3 equiv. H_2O_2, MeCN, RT, 16 h	89	8.2	Brown powder

FT-IR spectroscopy was used to characterize the chemical structure of the MNPs and the chemically modified magnetic silica nanoparticles. The stack plot of corresponding FT-IR spectra are shown in Fig. 3.1. A sharp and strong Fe-O stretching peak (~586 cm^{-1}) was observed for bulk MNPs and all surface modified samples, indicating that the main structure was not changed by the modification [66, 84]. The absorption bands at ~2910 cm^{-1} and 2990 cm^{-1} (C-H stretching), 1500-1600 cm^{-1} (N-H bending), 1075 cm^{-1} (Si-O stretching) of aminopropyl magnetic silica and all surface modified samples, indicated the presence of aminopropyl silane groups [66]. IR spectrum of AA-Si-NPs (Fig. 1c) showed the typical peak at 1620 cm^{-1} represented the stretching vibration of carbonyl and the absorption band at 1545 cm^{-1} relates to amino N-H bending vibration, confirming the presence of an acrylamide on the surface of aminopropyl magnetic silica [140]. Meanwhile, IR spectra of M-NMM and their corresponding M-NMO (Fig. 3.1 d-i) exhibited two dominated adsorption bands of morpholine at 1470 cm^{-1} and 1550 cm^{-1} confirming the existence of the NMM anchored groups [137]. However, there is no substantial difference in the IR absorption bands of M-NMM and M-NMO. This is because absorption bands of N-O group between *N*-Oxide and morpholine ring is unable to distinct.

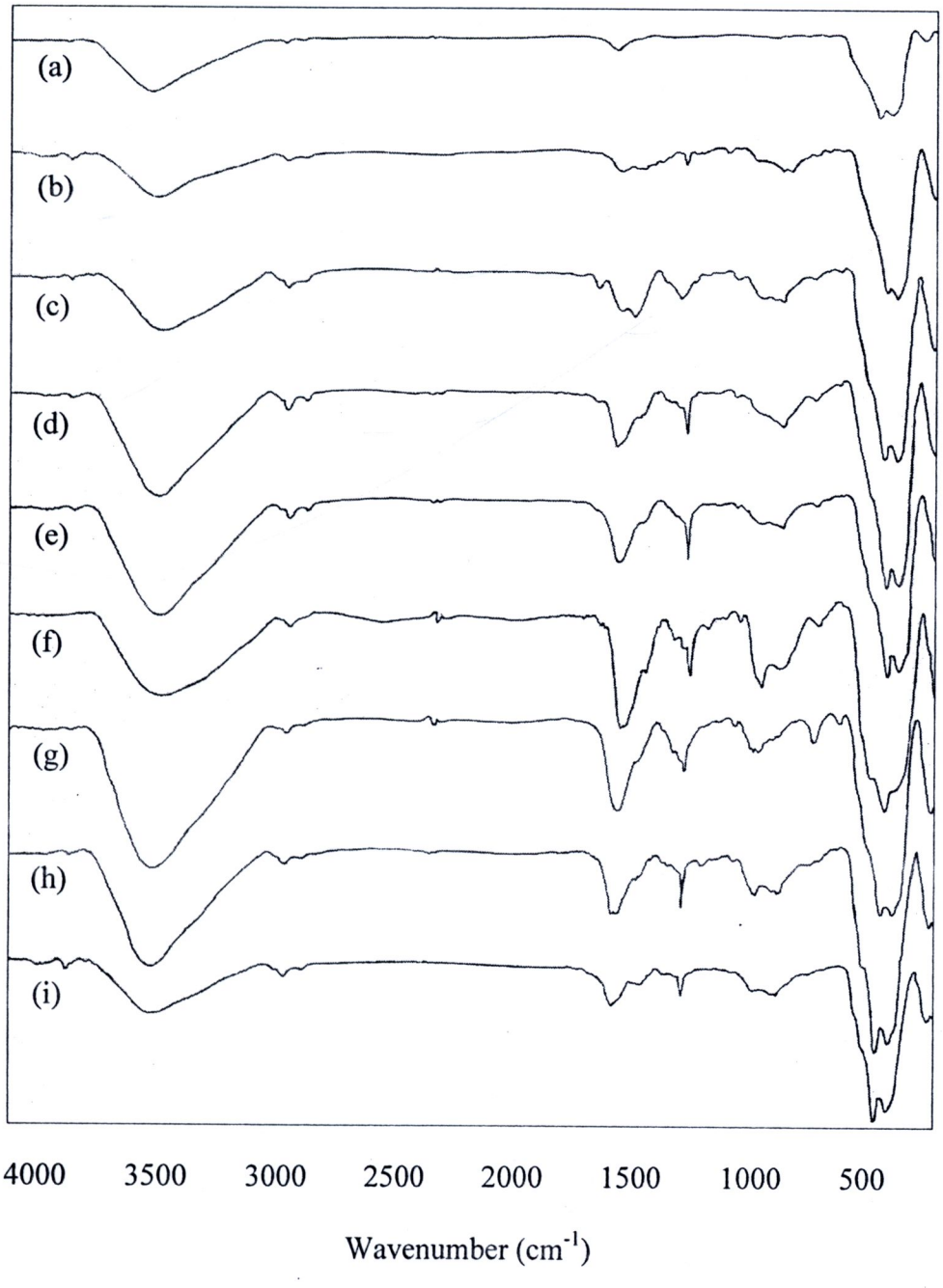


Figure 3.1 FT-IR spectrum of (a) MNPs, (b) aminopropyl magnetic silica, (c) AA-Si-NPs, (d) M-NMM **1**, (e) M-NMO **1**, (f) M-NMM **2**, (g) M-NMO **2**, (h) M-NMM **3**, (i) M-NMO **3**

3.3.2 Oxidation of benzyl halides to aldehydes with M-NMOs

In this study, the efficiency of the synthesized M-NMOs were investigated by comparing M-NMO activity to the activity of standard NMO reagent in the oxidation of benzyl bromide to aldehyde. Ultrasonication was applied in NMO oxidation in DMSO to aid the mixing and to accelarate the reaction rate [141]. The efficiency of synthesized M-NMOs will be reported in a term of the effective loading which defines as the capacity of the anchored NMO groups presented on surface of magnetic reagents that enable conversion of benzyl halides (X = Br, Cl) to benzaldehyde. Organic chloride is commonly known to be less reactive than the bromide derivatives and some catalysts or additives such as KI, KBr, NaBr are often required [132, 142, 143]. In this study, catalytic amount of NaBr (10 mol%) was thus added in the reaction mixture. Effective loading was estimated from the %yield of benzaldehyde using M-NMOs oxidant relative to that using standard NMO reagent. The equation for effective loading calculation was as followed:

$$\text{Effective loading (mmol g}^{-1}\text{ of support)} = \frac{\left(\frac{\text{Mol}_{\text{NMO}}}{\%\text{Yield}_{\text{NMO}}}\right) \times \%\text{Yield}_{\text{support}}}{\text{Wt}_{\text{support}}\ \text{(g)}}$$

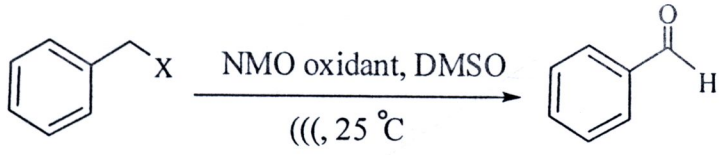
Where Mol_{NMO} is mole of standard NMO used in benzyl bromide oxidation

$\%\text{Yield}_{\text{NMO}}$ is percentage yield of oxidized product using standard NMO reagent

$\%\text{Yield}_{\text{support}}$ is percentage yield of oxidized product using M-NMO

and $Wt_{support}$ is weight (gram) of M-NMO used in the reaction

Table 3.3 Effective loading of M-NMOs in benzyl halide oxidation



Oxidant	X	Yield (%)	Effective loading (mmol/g)
NMO	Br	91[a]	-
NMO	Cl	92[a]	-
M-NMO 1	Br	4[b]	0.6
M-NMO 2	Br	14[b]	2.0
M-NMO 3	Br	9[b]	1.3
M-NMO 1	Cl	11[b]	1.6
M-NMO 2	Cl	15[b]	2.2
M-NMO 3	Cl	0[b]	0.0

[a]Reaction conditions: Benzyl halide (1.0 mmol), NMO (4.0 mmol), NaBr (10 %mol) and DMSO (2.0 ml), 25 °C, sonication times 10 min.

[b]Reaction conditions: Benzyl halide (0.1 mmol), M-NMO **2** (300 mg), NaBr (cat. amount) and DMSO (0.7 ml), 25 °C, sonication times 20 min.

Table 3.3 summarizes the effective loadings of synthesized M-NMOs. The efficiency of all synthesized M-NMOs were found to be different. Among them, M-NMO **2** provided the best effective loading in both benzyl chloride and benzyl bromide oxidations as compared to M-NMO **1** and M-NMO **3**. In contrast, M-NMO **3** gave somewhat low effective loading for benzyl bromide oxidation. When this M-NMO **3** was applied to oxidize benzyl chloride, the effective loading can be estimated as zero as no desired product was obtained. These results can be reasoned that polymerization and oxidation methods in the M-NMOs preparation seems to have a major influence on the activity of the supported reagents. Synthetic conditions used in M-NMM **2** preparation has been previously described by Bicak and co-workers for more effective polymerization of allylmorpholine comparing to conventional methods (conditions used in the synthesis of M-NMM **1**) which could presumably gave the support with high NMM functionality.

To study the effect of solvent, the oxidation of benzyl chloride using M-NMO **2** with various solvents (DMSO, DMF, MeCN, THF, MeOH and toluene) was investigated. As can be seen in Table 3.4, the reaction which was carried out in DMSO and DMF exhibited highest percentage yield of product while no significant difference of product yield was observed in other solvents. According to the proposed mechanism that the S_N2 mechanism is an essential feature of *N*-oxide oxidized organic halide [132, 134]. High polar aprotic solvent such as DMSO and DMF presumably stabilize polar transition state by solvation of accompanying cation rather than the

nucleophilic anion, resulting in the bare unsoivated anions have a greater nucleophilicity, and S_N2 reactions take place at correspondingly faster reaction rates.

Table 3.4 Effect of solvent on the oxidation of benzyl chloride by M-NMO[a]

Entry	Solvent	Dielectric constant	Yield (%)
1	DMSO	47	15
2	DMF	38	15
3	MeCN	37	8
4	THF	6.5	11
5	MeOH	33	10
6	Toluene	2.0	10

[a]Reaction condition: Benzyl chloride (0.013 ml, 0.1 mmol), M-NMO **2** (300 mg), NaBr (cat. amount) and DMSO (0.7 ml), 25 °C, sonication times 20 min.

It is known that DMSO acts as a good oxidizing agent in many organic transformations [144]. The results from this experiment indicated that DMSO is not the main oxidant in benzyl halides oxidation because the reaction can proceed in all solvents.

Nevertheless, all the synthesized M-NMOs gave unsatisfactory results in the direct oxidation of benzyl halides to benzaldehyde. This may be due to low loading capacity and the limit of kinetic in heterogeneous reaction. These problem can be

overcome by increasing amount of M-NMOs in the reaction. However, an economy issue should be concerned. Alternatively, the polymerization of *N*-allylmorpholine requires further improvement to provide higher degree of NMO functionalization.