

## FULL PAPER

# Phosphomolybdic acid immobilized chitosan/Fe<sub>3</sub>O<sub>4</sub>: an efficient catalyst for *n* alkylation of anilines

Mahdi Ghanimati<sup>a</sup> | Masumeh Abdoli Senejani<sup>a,\*</sup> | Mohammad Ali Bodaghifard<sup>b</sup> | Tahereh Momeni Isfahani<sup>a</sup>

<sup>a</sup>Department of Chemistry, Arak Branch, Islamic Azad University, Arak, Iran

<sup>b</sup>Department of Chemistry, Faculty of Science, Arak University, 38156-88349, Arak, Iran

In this work, phosphomolybdic acid immobilized on chitosan/Fe<sub>3</sub>O<sub>4</sub> as a green catalyst was used for the Hofmann *N*-alkylation of aniline derivatives with alcohols. H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub>/chitosan/Fe<sub>3</sub>O<sub>4</sub> (PMo/Chit/Fe<sub>3</sub>O<sub>4</sub>) was prepared from the phosphomolybdic acid, chitosan, and Fe<sub>3</sub>O<sub>4</sub> MNPs. Several secondary amines were synthesized from primary arylamines with electron-donating, electron-withdrawing groups, and alcohols in good to excellent yields. The catalyst could be separated using an external magnet and recovered without reducing its catalytic activity. The optimization of the reaction conditions was evaluated using the response surface method (RSM), involving the Box-Behnken design matrix. The simple procedure, only one byproduct (i.e., water), good to excellent yields, easy separation of the catalyst, short reaction times, and environmentally benign conditions were some advantages of this method.

**\*Corresponding Author:**

Masumeh Abdoli Senejani

Email: [mabdoli@iau-arak.ac.ir](mailto:mabdoli@iau-arak.ac.ir)

Tel.: +98 9183486925

**KEYWORDS**

Hofmann *N*-alkylation; heterogeneous catalyst; heteropolyacids; chitosan; design of experiment; green chemistry

**Introduction**

*N*-alkylation of amines is of a great importance in synthetic organic chemistry because of biological activities and industrial importance of products [1,2]. Alkylation of amines with alcohols using borrowing hydrogen or “hydrogenautotransfer” strategies is an environmentally friendly and useful method for preparation of amines. This method prevents waste salt formation, and the only byproduct is water [3-10]. Heteropoly acids (HPAs) belong to the category of non-volatile polyoxometalates with special molecular architectures that have remarkable properties such as strong Brønsted acidity, high stability toward humidity, easy to handle, proper redoxpotentials, high thermal stability,

environmental friendly, and low corrosiveness [11,12]. Heteropoly acids as potential solid acids are green catalysts in the synthesis of many organic compounds [13-15].

Due to the limited specific surface area, high solubility in polar solvents, and recycling performance of HPAs, supporting of HPA catalysts is important. In recent years, heterogenization of HPA catalysts, through immobilization onto the surface of modified materials has been received considerable attention [16-18]. Magnetic nanoparticles (MNPs) has received a lot of attention in case of the magnetization of solid phase [19-21]. In addition, MNPs are commonly used as potential support for the heteropoly acid catalysts because of easy separation from the

reaction mixture using an external magnet and increasing the area of contact between the reactant particles [18-24]. Chitosan is a biodegradable and available polymer and can be modified easily to synthesize magnetic composite adsorbents [25,26]. The chitosan coordinating sites for binding onto  $\text{Fe}_3\text{O}_4$  magnetic nanoparticles are amino and hydroxyl groups in glycosidic residue [27, 28]. In recent years, magnetic HPA-chitosan nanocomposites were used as a catalyst in some organic reactions [29,30]. Therefore, in the present study,  $\text{H}_3\text{PMo}_{12}\text{O}_{40}$  was immobilized into the network of the chitosan with the magnetic  $\text{Fe}_3\text{O}_4$  cores and used as a magnetically recoverable catalyst for N-alkylation of amines. In addition, the design of experimental technique was used to determine the optimal conditions for the reaction times and yields. A three-level Box-Behnken design (BBD) was used in this research to investigate the effects of the amount of catalyst, temperature, and the molar ratio of amine to alcohol. Box Behnken design is extremely effective in the same setting as the central composite design [31].

## Experimental

### General

All the solvents and reagents were purchased from the Sigma-Aldrich and Merck KGaA (Darmstadt, Germany) and used without any purification. Melting points were determined using an electrothermal 9200 apparatus.  $^1\text{H}$ NMR spectra was recorded on a 400-MHz Bruker AQS 500-AVANCE spectrometer using TMS as an internal standard and DMSO as the solvent. IR spectra were recorded from KBr disk on the FT-IR Bruker Tensor 27. Elemental analyses were performed using a Perkin-Elmer 2400 Series II CHNS/O analyzer. Agilent 5973A Series operating at 70 eV ionization energy, was used for GC-MS analyses. Most of the products were known and identified by comparison of their melting

points with those reported for authentic samples.

### Preparation and characterization of $\text{PMo/Chit/Fe}_3\text{O}_4$

$\text{H}_3\text{PMo}_{12}\text{O}_{40}$ /chitosan/ $\text{Fe}_3\text{O}_4$  nanoparticles were synthesized by a simple method [30]. Primarily, 0.5 g of  $\text{Fe}_3\text{O}_4$  MNPs, 0.5 g of chitosan and 50 mL of acetic acid solution (0.05 M) were sonicated and heated at 40 °C. Then, 12 mL of glutaraldehyde aqueous solutions (4 wt%) was added and stirred. The mixture was heated for 60 min at 40 °C and then 60 min at 60 °C. Subsequently, 20 mL phosphomolybdic acid solution (0.045 g.mL<sup>-1</sup>) was added and stirred at 60 °C for 4 h. The resulting solid was centrifuged at 4000 rpm, washed with deionized water and ethanol and dried under vacuum at 60 °C for 8 h to give the pure catalyst.

### General procedure for N-alkylation of aniline derivatives using $\text{PMo/Chit/Fe}_3\text{O}_4$

A mixture of amine (1.2 mmol), alcohol (1 mmol), and  $\text{PMo/Chit/Fe}_3\text{O}_4$  (0.06 g) was stirred at 60 °C in 15 mL  $\text{H}_2\text{O/EtOH}$  (1:1) for an appropriate time. The progress of the reaction was followed by TLC (Petroleum ether/ethyl acetate, 7/1). After completion of the reaction, the catalyst was separated using an external permanent magnet. The crude product was purified by recrystallization from  $\text{CH}_2\text{Cl}_2$  to give a pure product.

### Selected spectroscopic data

#### N-(diphenylmethyl)aniline (1)

IR (KBr):  $\tilde{\nu}$ =3379 (N-H), 3026 (C-H aromatic), 2925 (CH aliphatic), 1597 and 1494 (C=C aromatic), 1269 cm<sup>-1</sup> (C-N);  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ , 25 °C, TMS):  $\delta$ =7.65-7.70 (m, 10H, Ar-H), 7.07-7.20 (m, 5H, Ar-H), 5.86 (s, 1H, C-H), 4.45 ppm (brs, 1H, N-H); Anal Calcd. for  $\text{C}_{19}\text{H}_{17}\text{N}$ : C 87.99, H 6.61, N 5.40, Found: C 87.80, H 6.80, N 5.38.

*N*-(diphenylmethyl)-4-Chloroaniline (2)

IR (KBr):  $\tilde{\nu}$ =3295 (N-H), 3059 (C-H aromatic), 2953 (CH aliphatic), 1664 and 1488 (C=C aromatic), 1264 (C-N), 758  $\text{cm}^{-1}$  (C-Cl);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , 25°C, TMS):  $\delta$ =7.20-7.32 (m, 10H, Ar-H), 7.02 (d, 2H,  $J$ =6.4 Hz, Ar-H), 6.79 (d, 2H,  $J$ =6.4 Hz, Ar-H), 5.78 (s, 1H, C-H), 3.82 ppm (brs, 1H, N-H); Anal Calcd. for  $\text{C}_{19}\text{H}_{16}\text{ClN}$ : C 77.68, H 5.49, N 4.77, Cl 12.07, Found: C 77.31, H 5.80, N 4.78, Cl 12.09.

*N*-(diphenylmethyl)-4-Nitroaniline (3)

IR (KBr):  $\tilde{\nu}$ =3404 (N-H), 3077.97 (C-H aromatic), 2911 (CH aliphatic), 1599 and 1463 (C=C aromatic), 1508 and 1303 ( $\text{NO}_2$ ), 1279  $\text{cm}^{-1}$  (C-N);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , 25°C, TMS):  $\delta$ =7.27-7.39 (m, 10H, Ar-H), 7.13 (d, 2H,  $J$ =6.4 Hz, Ar-H), 6.67 (d, 2H,  $J$ =6.4 Hz, Ar-H), 5.36 (s, 1H, C-H), 3.86 ppm (brs, 1H, N-H); Anal Calcd. for  $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_2$ : C 74.98, H 5.30, N 9.20, O 10.51, Found: C 75.01, H 5.27, N 9.18.

*N*-(1-phenylethyl) 4-bromo aniline (6)

IR (KBr):  $\tilde{\nu}$ = 3385 (N-H), 3026 (C-H aromatic), 2925 (C-H aliphatic), 1596 and 1493 (C=C aromatic), 1269 (C-N), 697  $\text{cm}^{-1}$  (C-Br);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , 25°C, TMS):  $\delta$ =7.50-7.55 (m, 5H, Ar-H), 7.23 (d, 2H,  $J$ =8.4 Hz, Ar-H), 6.83 (d, 2H,  $J$ =8.4 Hz, Ar-H), 4.28 (q, 1H,  $J$ =6.9 Hz, C-H), 3.89 (brs, 1H, N-H), 1.64 ppm (d, 3H,  $J$ =6.9 Hz  $\text{CH}_3$ ); Anal Calcd. for  $\text{C}_{14}\text{H}_{14}\text{BrN}$ : C 60.89, H 5.11, N 5.07, Br 28.93, Found: C 60.80, H 5.22, N 5.07, Br 28.90.

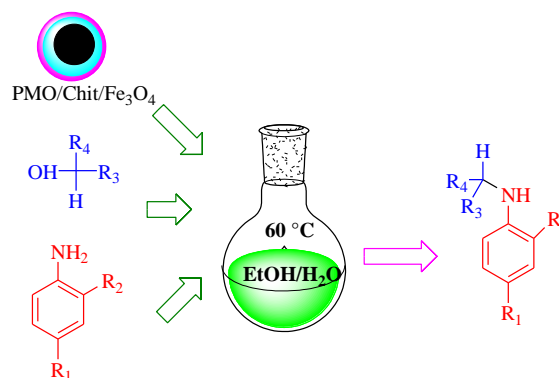
*N*-((4-chlorophenyl)phenylmethyl) 4-bromo aniline (15)

IR (KBr):  $\tilde{\nu}$ = 3382 (N-H), 3030 (C-H aromatic), 2924 (C-H aliphatic), 1618 and 1489 (C=C aromatic), 1284 (C-N), 818 (C-Cl), 701  $\text{cm}^{-1}$  (C-Br);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , 25°C, TMS):  $\delta$ =7.32-7.59 (m, 11H, Ar-H), 6.56

(m, 2H, Ar-H), 5.82 (s, 1H, C-H), 3.00 ppm (brs, 1H, N-H). Anal Calcd. for  $\text{C}_{19}\text{H}_{15}\text{BrClN}$ : C 61.36, H 4.06, Br 21.27, Cl 9.53, N 3.77, Found: C 60.17, H 4.01, Br 20.16, Cl 9.95, N 4.07.

## Results and discussion

As a part of ongoing research into the efficient synthesis of heterocyclic compounds [32-36], in the present study, we describe a green and effective procedure for the N-alkylation of aromatic amines with alcohols using  $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ /chitosan/ $\text{Fe}_3\text{O}_4$  (Scheme 1).



$\text{R}_1 = \text{H, Br, NO}_2, \text{Cl, CN, OCH}_3$ ;  $\text{R}_2 = \text{H, NO}_2$ ;  $\text{R}_3, \text{R}_4 = \text{Me, Ph, p-CIPh}$

**SCHEME 1** N-alkylation of aniline derivatives using  $\text{PMo/Chit/Fe}_3\text{O}_4$  as an efficient catalyst

At first, the reaction of aniline (1 mmol) and benzhydrol (1 mmol) in the presence of 0.05 g of the catalyst in various solvents at 60 °C was selected as a model reaction (Table 1). The results indicated that, among all,  $\text{C}_2\text{H}_5\text{OH/H}_2\text{O}$  (1:1) is the most effective solvent.

In the next step, the effect of different types of catalysts on the model reaction in  $\text{C}_2\text{H}_5\text{OH/H}_2\text{O}$  (1:1) at 65 °C was studied (Table 2). As shown in Table 2, the presence of a catalyst is essential for N-alkylation of aniline derivatives with alcohols. Also,  $\text{PMo/Chit/Fe}_3\text{O}_4$  is more suitable than the other catalysts.

**TABLE 1** The effect of various solvents on the model reaction

Entry	Solvent	Time (h)	Yield (%)
1	----	5	65
2	H <sub>2</sub> O	5	78
3	C <sub>2</sub> H <sub>5</sub> OH	5	77
4	CH <sub>3</sub> CN	5.5	75
5	CH <sub>2</sub> Cl <sub>2</sub>	5.5	71
6	C <sub>2</sub> H <sub>5</sub> OH/H <sub>2</sub> O (1:1)	4	91
7	C <sub>2</sub> H <sub>5</sub> OH/H <sub>2</sub> O (2:1)	5	76
8	C <sub>2</sub> H <sub>5</sub> OH/H <sub>2</sub> O (1:2)	5	80

**TABLE 2** The effect of various catalysts on the model reaction

Entry	catalyst	Time (h)	Yield (%)
1	Fe(ClO <sub>4</sub> ) <sub>3</sub>	7	78
2	Sulfamic acid	6.5	75
3	p-Toluenesulfonic acid	6.5	70
4	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub>	6	76
5	PMo/Chit/Fe <sub>3</sub> O <sub>4</sub>	4	91
6	----	6	---

*Statistical analysis and the model fitting*

To assess the effect of various reaction parameters such as the amount of catalyst, temperature, and the molar ratio of amine to alcohol on the N-alkylation of aniline derivatives with alcohols, a three-level 15-run Box-Behnken design method was used by utilizing Design-Expert 7.0.0 Trial software (Stat-Ease Inc., Minneapolis). The level of

parameters, the experimental design matrix and results are shown in Table 3. The input parameters in the reaction process optimization include: A) the molar ratio (i.e., 1, 1.2, and 1.4), B) the amount of catalyst (i.e., 0.02, 0.04, and 0.06 g), and C) temperature (25, 45, and 65°C). The response function (y) was a greater yield and a shorter reaction time for N-alkylation of aniline.

**TABLE 3** The experimental factors, levels, and results for the Box-Behnken design

Factors	Unit	Symbol	levels							
			Low (-1)	Central (0)	High (+1)					
Molar ratio	---	A	1	1.2	1.4					
Catalyst amount	g	B	0.02	0.04	0.06					
Temperature	°C	C	25	45	65					
Independent variables										
			A		B	C	Dependent variable (Time/min)		Dependent variable (Yield/%)	
Run	Coded levels	Actual levels	Coded levels	Actual levels	Coded levels	Actual levels	Experimental	Predicted	Experimental	Predicted
1	-1	1.00	0	0.04	-1	25.00	480	495	50	50.38
2	0	1.20	-1	0.02	-1	25.00	510	500.63	47	47.75
3	0	1.20	0	0.04	0	45.00	250	243.33	77	77.33
4	0	1.20	+1	0.06	+1	65.00	180	189.38	94	93.25
5	0	1.20	+1	0.06	-1	25.00	360	350.63	65	65
6	+1	1.40	0	0.04	+1	65.00	270	255	85	84.63
7	+1	1.40	+1	0.06	0	45.00	300	305.63	86	87.13
8	+1	1.40	0	0.04	-1	25.00	450	453.75	55	53.88
9	+1	1.40	-1	0.02	0	45.00	300	305.63	70	70.38

10	0	1.20	-1	0.02	+1	65.00	270	279.38	79	79
11	0	1.20	0	0.04	0	45.00	240	243.33	78	77.33
12	-1	1.20	0	0.04	+1	45.00	240	243.33	77	77.33
13	-1	1.00	0	0.06	-1	45.00	240	234.37	82	81.63
14	0	1.00	0	0.04	0	65.00	315	311.25	78	79.13
15	+1	1.00	0	0.02	+1	45.00	480	474.38	68	66.88

The BBD method also was applied to investigate the interaction of three factors on the yield and reaction times, and the obtained results are summarized in Tables 4 and 5. The analysis of variance (ANOVA) test at 95% confidence level was used to estimate the quality of the proposed model. The results of the ANOVA test demonstrated that the process factors with a p-value of less than

0.05 should be considered significant which could have substantial effects on the time and yield of the reaction. The results revealed that A, B, C, A<sup>2</sup>, B<sup>2</sup>, and C<sup>2</sup>, were statistically significant. A second-order polynomial model for time and yield based on significant levels and actual values were proposed by the Equations 1 and 2.

**TABLE 4** Analysis of variance (ANOVA) for Box–Behnken quadratic model for the reaction time of N-alkylation of aniline

Source	SS <sup>a</sup>	Df <sup>b</sup>	MS <sup>c</sup>	F-value	p-Value	Remark
Model	2571.52	9	285.72	192.62	< 0.0001	significant
A-molar ratio	40.5	1	40.5	27.3	0.0034	
B-Amount of catalyst	496.12	1	496.12	334.47	< 0.0001	
C-Temperature	1770.12	1	1770.12	1193.34	< 0.0001	
AB	1	1	1	0.67	0.449	
AC	1	1	1	0.67	0.449	
BC	2.25	1	2.25	1.52	0.2729	
A <sup>2</sup>	23.85	1	23.85	16.08	0.0102	
B <sup>2</sup>	10.78	1	10.78	7.26	0.043	
C <sup>2</sup>	224.16	1	224.16	151.12	< 0.0001	
Residual	7.42	5	1.48			
Lack of Fit	6.75	3	2.25	6.75	0.1318	not significant
Pure Error	0.67	2	0.33			
Cor Total	2578.93	14				

$$Y(\text{yield}) = 77.33 - 2.254A + 7.87B + 14.88C + 0.5AB + 0.5AC - 0.75BC - 2.54A^2 + 1.71B^2 - 7.79C^2$$

$$R^2 = 0.9971 \quad R^2\text{-Adj} = 0.9919 \quad (\text{equation 1})$$

$$Y(\text{time}) = 243.33 - 24.38A - 60B - 95.63C + 60AB - 3.75AC - 15BC + 67.71A^2 - 18.96B^2 - 67.71C^2$$

$$R^2 = 0.9934 \quad R^2\text{-Adj} = 0.9815 \quad (\text{equation 2})$$

Where A, B, and C are molar ratios, the amount of catalyst, and temperature, respectively; AB, AC, and BC are the interaction coefficient of these factors, and Y is the predicted response as the reaction time and yield. The values of the correlation coefficient (R<sup>2</sup>) for the time and yield were found to be 0.9934 and 0.9971, respectively, demonstrating a good correlation between the observed results and the predicted regression. In order to analyze the influence of three reaction parameters, 1) the amount of catalyst, 2) temperature, 3) the molar ratio of amine to alcohol, and interaction between

them, on the reaction time and yield, three-dimensional response surface method and the corresponding contour curves are shown in Figures 1 and 2. The dark blue and the dark red areas in these figures, show the optimal experimental conditions for obtaining the maximum yield and minimum time, respectively. The results of Box–Behnken design method for N-alkylation of aniline derivatives indicated that the optimal condition for the minimum reaction time of 180 min (3 hours) and maximum yield of 93% is A= 1.2, B= 0.06 g, and C= 60.26 °C (almost 60°C) (Figure 3). To investigate the

validity of the model, the optimum conditions were utilized in four experiments (Table 5). The results revealed that the predicted values

were in good agreement with the experimental results.

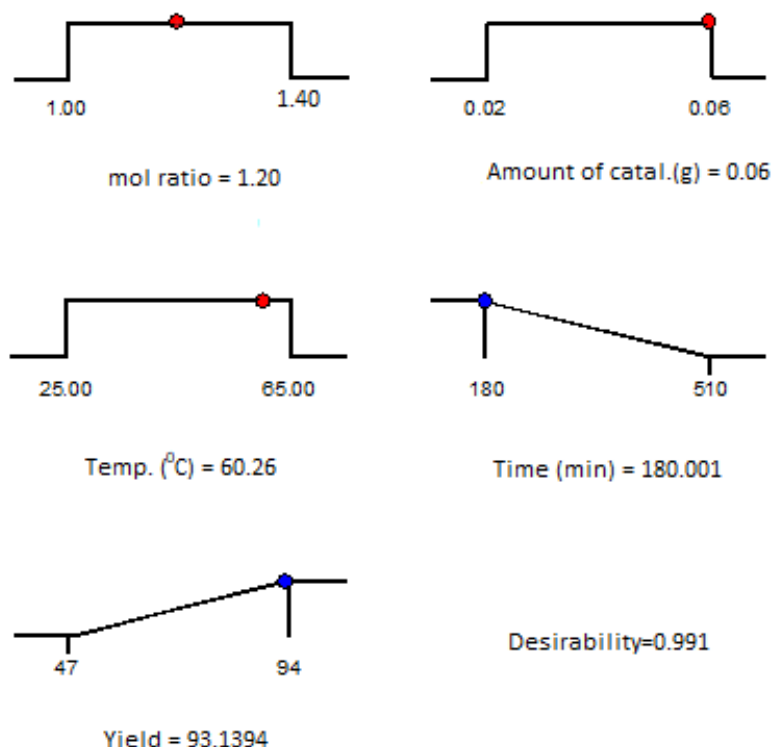
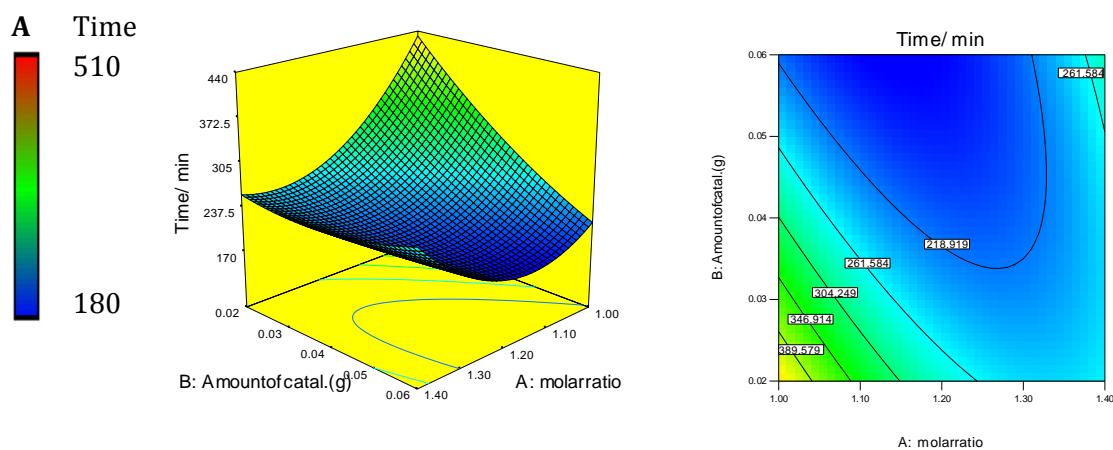


FIGURE 3 Optimized process conditions

TABLE 6 The result of N-alkylation of aniline in optimal conditions

Approach	Factors			Response	
	molar ratio	Catalyst amount(g)	Temperature (°C)	Time (min)	Yield(%)
predicted	1.20	0.06	60.26	180	93.14
Experimental	1.20	0.06	60.00	180±0.47 <sup>a</sup>	92.66±0.5 <sup>a</sup>

<sup>a</sup> Mean±SD



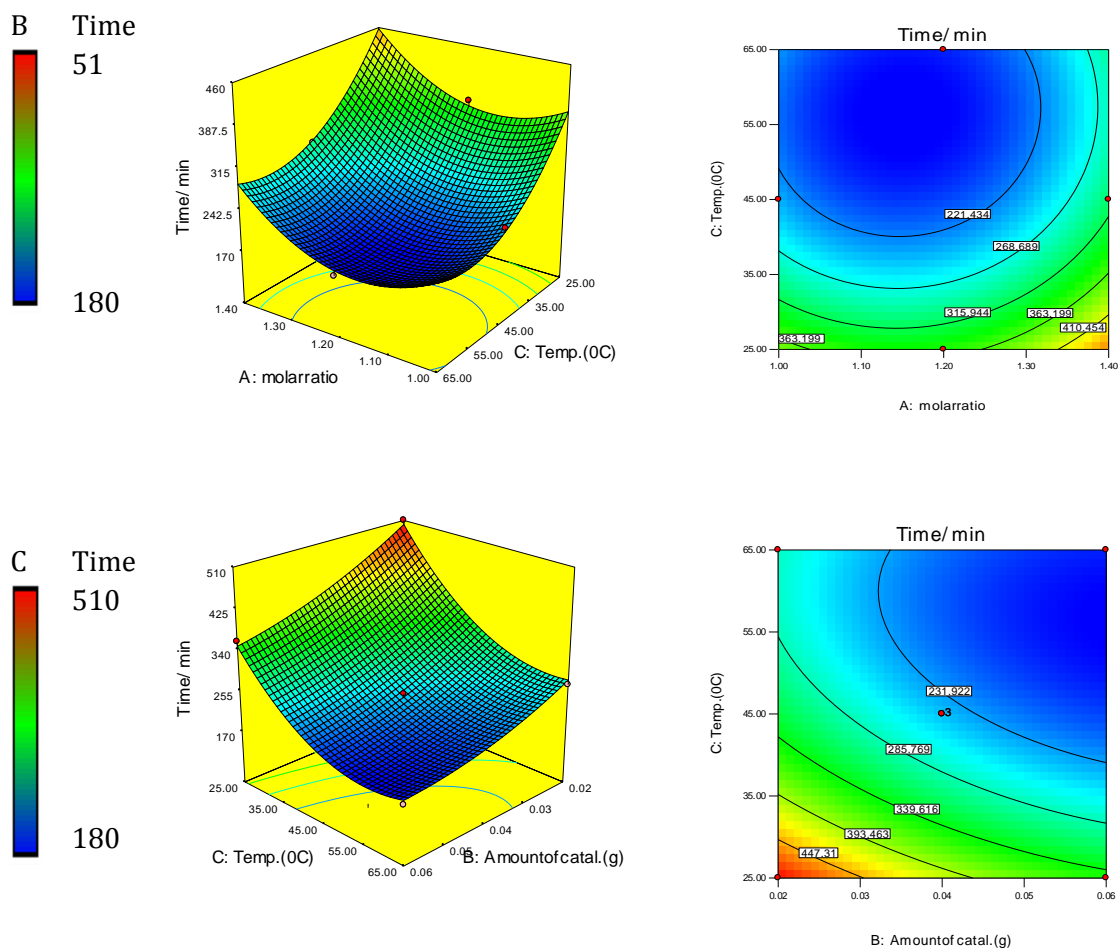
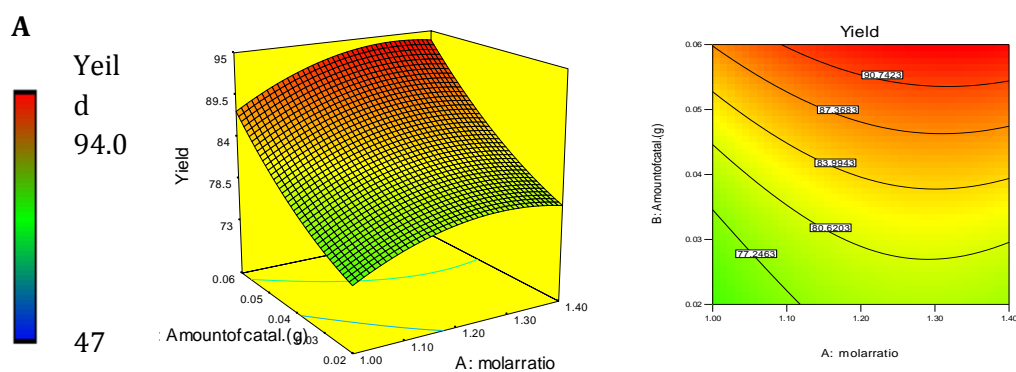
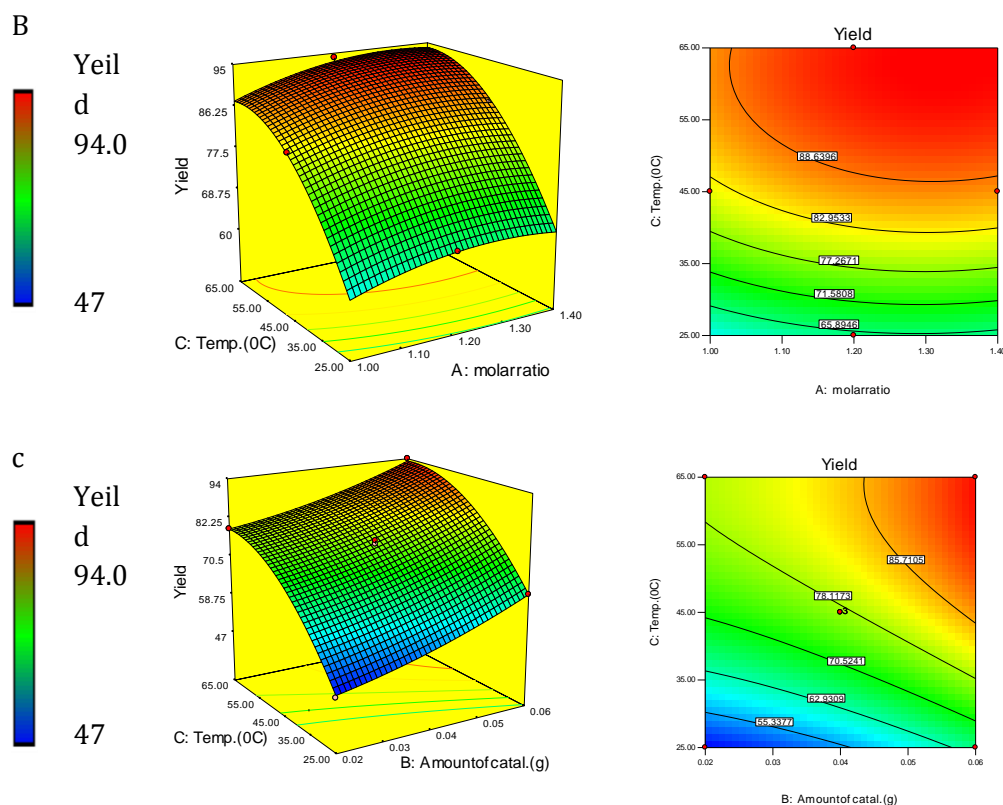


FIGURE 1 Response surface and contour plots corresponding to the prediction of the reaction time for N-alkylation of aniline





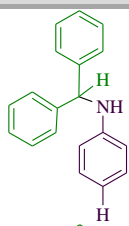
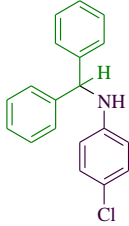
**FIGURE 2** Response surface and contour plots corresponding to the prediction of the yield for N-alkylation of aniline

### *N*-Alkylation of anilines

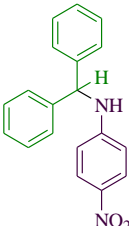
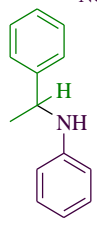
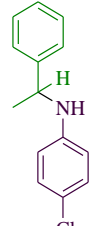
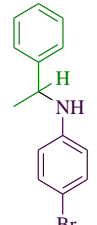
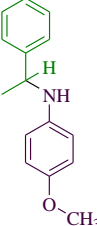
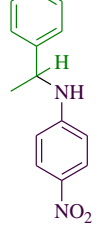
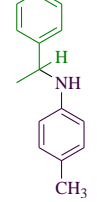
After optimization of reaction conditions, the capability of PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> as a catalyst for N-alkylation reaction of aniline derivatives with some alcohols was investigated under the optimized reaction conditions. The results are summarized in Table 7. As shown in Table 7, a variety of aniline derivatives with both electron-donating and electron-withdrawing

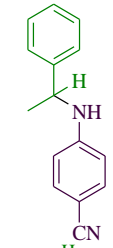
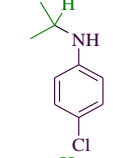
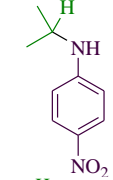
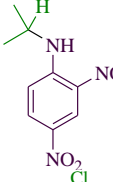
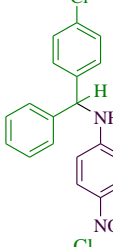
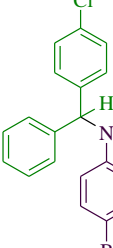
groups undergo *N*-alkylation with isopropanol,  $\alpha$ -phenylethanol, and diphenylcarbinol derivatives using PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> in good to excellent yields. In addition, aniline derivatives with electron-withdrawing groups decreased the reaction rate as the electron-rich anilines are better nucleophiles and facilitate the second step of the reaction mechanism.

**TABLE 7** The *N*-alkylation of aniline derivatives with alcohols using PMo/Chit/Fe<sub>3</sub>O<sub>4</sub>

Entry	Product	Time (h)	Yield <sup>a</sup> (%)	mp (Lit. mp) [Ref.](°C)
1		3	93	57-59 (58) [37]
2		4	91	76-78 (75) [38]



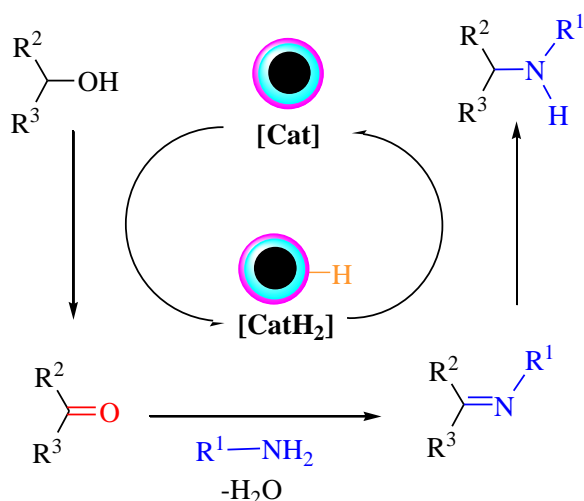
3		4	89	180-182 (182-183) [39]
4		3	90	50-52 (52) [40]
5		4.5	89	58-59 (58-60) [41]
6		4.5	90	69-71 (68-71) [41]
7		3	93	61-62 (61-63) [42]
8		5	85	102-103 (103) [43]
9		3	88	74-76 (75-76) [44]

10		4	89	97-98 (98-99) [45]
11		4	83	liquid (liquid)[46]
12		4.5	88	83-85 (82-84) [47]
13		5	85	91-93 (93-95) [48]
14		4	89	119-121 (120-121) [49]
15		5	86	84-86 (83-86) [50]

<sup>a</sup> Isolated yield

A plausible mechanism for N- alkylation of aniline derivatives with alcohols using PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> is shown in Scheme 2. The model reaction was investigated at the presence of chitosan, Fe<sub>3</sub>O<sub>4</sub> or PMO as the catalyst under the optimized reaction conditions and compared with the results obtained from PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> (Table 8). As seen in Table 8, the PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> is more suitable than the others and the PMO plays the main role of catalyst in this reaction. In this work, PMO was supported on the

magnetic chitosan, which boosted catalytic characteristic of PMO.



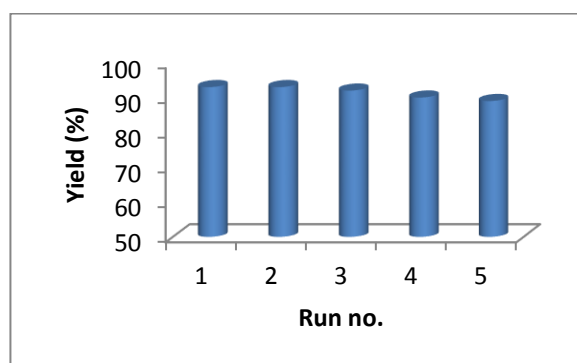
**SCHEME 2** A plausible mechanism for *N*-alkylation of aniline derivatives with alcohols using PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> as a catalyst

**TABLE 8** Results of *N*-alkylation aniline in the presence of chitosan, Fe<sub>3</sub>O<sub>4</sub>, PMO and PMo/Chit/Fe<sub>3</sub>O<sub>4</sub>

Entry	Catalyst	Time (h)	Yield (%)
1	PMO	4.5	83
2	Fe <sub>3</sub> O <sub>4</sub>	4.5	78
3	Chitosan	6	trace
4	PMo/Chit/Fe <sub>3</sub> O <sub>4</sub>	3	93

To verify the mechanism, the reaction mixture at the half-time and end of the reaction and designed control tests were analyzed by GC-Mass spectroscopy technique. Except for the main product, other significant byproducts were not found at the end of reaction. However, the oxidation of alcohol to ketone in reaction progress is confirmed. The benzhydrol in the absence of amine (aniline) in the reaction condition produced benzophenone. In the absence of benzhydrol as a starting material, aniline did not react with ethanol as a primary alcohol and co-solvent. These results prove *N*-alkylation of anilines through borrowing hydrogen mechanism. In addition, it was found that at the end of the reaction, ethanol as a co-solvent and alcohol substrate in the presence of an acidic catalyst did not produce other by-products.

To study the recyclability of PMo/Chit/Fe<sub>3</sub>O<sub>4</sub>, the catalyst was magnetically separated by an external magnet from the reaction mixture, washed three times with 5 ml of diethyl ether, dried, and reused in the synthesis of 4e for five times without a considerable loss in its catalytic activity (Figure 4).



**FIGURE 4** The recoverability of PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> in the synthesis of *N*-(diphenylmethyl) aniline

Finally, a comparison of *N*-alkylation of aniline derivatives with alcohols using PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> with a range of other methodologies proved the efficiency of this method with respect to the yields and time of reactions (Table 9).

## Conclusion

PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> was synthesized from Phosphomolybdic acid, chitosan, and Fe<sub>3</sub>O<sub>4</sub> MNPs. The magnetic PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> as heterogeneous catalyst exhibited excellent catalytic activity in the *N*-alkylation of variety of aniline derivatives with electron-donating as well as electron-withdrawing groups using isopropanol,  $\alpha$ -phenylethanol and diphenylcarbinol via direct reductive amination. The optimization of the reaction conditions was evaluated using the response surface method (RSM) and adopting the Box-Behnken design matrix. The predicted values were found to be in good agreement with experimental results. The catalyst could be separated using an external magnet and

recovered without reducing its catalytic activity. The efficiency of the PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> is comparable with other catalysts for *N*-alkylation of amines. The simple experimental procedures, the very limited byproduct (only

water), good to excellent yields, easy separation, reusability of the catalyst, short reaction times, and environmentally benign conditions were distinctive advantages of this method.

**TABLE 9** A comparison of the efficiency of PMo/Chit/Fe<sub>3</sub>O<sub>4</sub> with the previous procedure for the *N*-alkylation of aniline derivatives using alcohols

Entry	Catalyst	Time (h)	Yield (%)	Condition[Ref.]
1	PMo/Chit/Fe <sub>3</sub> O <sub>4</sub>	3-5	83-93	H <sub>2</sub> O:EtOH, 60 °C [this work]
2	SnCl <sub>4</sub>	16-18	71-93	CH <sub>2</sub> Cl <sub>2</sub> , r.t. [49]
3	Ph <sub>2</sub> PdCl/imidazole/I <sub>2</sub>	0.25-48	50-94	CH <sub>2</sub> Cl <sub>2</sub> , reflux [2]
4	Pd/Fe <sub>2</sub> O <sub>3</sub>	2-28	72-99	Solvent free, 140-170 °C [51]
5	DBU <sup>a</sup> , CSA <sup>b</sup>	24	81-99	Trichloroacetonitrile, CH <sub>2</sub> Cl <sub>2</sub> , [41]
6	Iridium Complex/K <sub>2</sub> CO <sub>3</sub>	12-24	19-95	2,2,2-trifluoroethanol, 100 °C [4]
7	CsOH.H <sub>2</sub> O	24-28	26-95	Solvent free, air, 130-150 °C [52]
8	[Cp*IrCl <sub>2</sub> ] <sub>2</sub> /K <sub>2</sub> CO <sub>3</sub> <sup>c</sup>	17	69-95	Toluene, 110 °C [53]
9	In(OTf) <sub>3</sub>	4-24	37-99	H <sub>2</sub> O, 100 °C [38]

<sup>a</sup>1,8-diazabicyclo[5.4.0]undec-7-ene, <sup>b</sup>Camphorsulfonic acid, <sup>c</sup>Cp\* = pentamethylcyclopentadienyl

## Acknowledgments

The authors are thankful to the Arak Branch, Islamic Azad University for its lab supplies. We also appreciate Dr. Ali Ayati for his support.

## Orcid:

Mahdi Ghanimati: <https://orcid.org/0000-0001-8536-9218>

Masumeh Abdoli Senejani: <https://orcid.org/0000-0002-3677-7853>

Mohammad Ali Bodaghifard: <https://orcid.org/0000-0001-9732-4746>

Tahereh Momeni: <https://orcid.org/0000-0002-6648-9625>

## References

- [1] A. Ricci, *Amino group chemistry: from synthesis to the life sciences*, John Wiley & Sons, **2008**.
- [2] H.A. Wittcoff, B.G. Reuben, J.S. Plotkin, *Industrial organic chemicals*, John Wiley & Sons, **2012**.
- [3] M.H.S. Hamid, P.A. Slatford, J.M. Williams, *Adv. Synth. Catal.*, **2007**, *349*, 1555-1575.

[4] Q. Zou, C. Wang, J. Smith, D. Xue, J. Xiao, *Chem-Eur. J.*, **2015**, *21*, 9656-9661.

[5] Q. Xu, H. Xie, E.-L. Zhang, X. Ma, J. Chen, X.-C. Yu, H. Li, *Green Chem.*, **2016**, *18*, 3940-3944.

[6] G. Guillena, D.J. Ramón, M. Yus, *Chem. Rev.* **2010**, *110*, 1611-1641.

[7] S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann, M. Beller, *Chem. Cat., Chem.*, **2011**, *3*, 1853-1864.

[8] L. Chen, X.-P. Yin, C.-H. Wang, J. Zhou, *Org. Biomol. Chem.*, **2014**, *12*, 6033-6048.

[9] J. Muzart, *Tetrahedron*, **2005**, *61*, 4179-4212.

[10] E. Emer, R. Sinisi, M.G. Capdevila, D. Petruzzello, F. De Vincentiis, P.G. Cozzi, *J. Org. Chem.*, **2011**, 647-666.

[11] J.B. Moffat, *Metal-oxygen clusters: the surface and catalytic properties of heteropoly oxometalates*, Springer Science & Business Media, **2006**.

[12] I.V. Kozhevnikov, *Chem. Rev.*, **1998**, *98*, 171-198.

[13] A. Bordoloi, S. Sahoo, F. Lefebvre, S. Halligudi, *J. Catal.*, **2008**, *259*, 232-239.

- [14] S.K. Jana, Y. Kubota, T. Tatsumi, *J. Catal.*, **2008**, *255*, 40-47.
- [15] M. Keshavarz, M. Abdoli-Senejani, S. Hojati, M. Moosavifar, *Org. Prep. Proced. Int.*, **2017**, *49*, 549-556.
- [16] R. Tayebee, M.M. Amini, F. Nehzat, O. Sadeghi, M. Armaghan, *J. Mol. Catal. A-Chem.*, **2013**, *366*, 140-148.
- [17] R. Tayebee, M.M. Amini, M. Ghadamgahi, M. Armaghan, *J. Mol. Catal. A-Chem.*, **2013**, *366*, 266-274.
- [18] R. Tayebee, M.M. Amini, N. Abdollahi, A. Aliakbari, S. Rabiei, H. Ramshini, *Appl. Catal. A-Gen.*, **2013**, *468*, 75-87.
- [19] F. Ajormal, F. Moradnia, S. Taghavi Fardood, A. Ramazani, *J. Chem. Rev.*, **2020**, *2*, 90-102.
- [20] S. Sajjadifar, S. Rezayati, Z. Arzehgar, S. Abbaspour, M. Torabi Jafroudi, *J. Chin. Chem. Soc.*, **2018**, *65*, 960-969
- [21] Z. Arzehgar, A. Aydi, M. Mirzaei Heydari, *Asian J. Green Chem.*, **2018**, *2*, 281-298.
- [22] S. Shylesh, V. Schünemann, W.R. Thiel, *Angew. Chem. Int. Edit.*, **2010**, *49* 3428-3459.
- [23] J. Yuan, P. Yue, L. Wang, *Powder Technol.*, **2010**, *202*, 190-193.
- [24] B. Tanhaei, A. Ayati, F.F. Bamoharram, M. Lahtinen, M. Sillanpää, *J. Chem. Technol. Biot.*, **2016**, *91*, 1452-1460.
- [25] N. Rasouli, H. Salavati, M. Movahedi, A. Rezaei, *Chem. Methodol.*, **2017**, *1*, 74-86.
- [26] E. Doustkhaha, M. Heydarizadehb, Z. Fathic, H. Mohtashamb, S. Rostamniab, M. Hasani, *Chem. Methodol.*, **2019**, *3*, 626-634.
- [27] D.H.K. Reddy, S.-M. Lee, *Adv. Colloid Interface Sci.*, **2013**, *201*, 68-93.
- [28] W.Li, L. Xiao, C. Qin, *J. Macromol. Sci. A*, **2010**, *48*, 57-64.
- [29] A. Kong, P. Wang, H. Zhang, F. Yang, S. Huang, Y. Shan, *Appl. Catal. A-Gen.*, **2012**, *417*, 183-189.
- [30] A. Ayati, M.M. Heravi, M. Daraie, B. Tanhaei, F.F. Bamoharram, M.Sillanpaa, *J. Iran. Chem. Soc.*, **2016**, *13*, 2301-2308.
- [31] Y.-L. Li, Z.-X. Fang, J. You, *J. Agric. Food Chem.*, **2013**, *61*, 1464-1470.
- [32] M. Keshavarz, M. Abdoli-Senejani, S.F. Hojati, S. Askari, *React. Kinet. Mech.Cat.*, **2018**, *124*, 757-766.
- [33] N. Azizi, F. Abbasi, M. Abdoli-Senejani, *Chemistry Select*, **2018**, *3*, 3797-3802.
- [34] S.H. Siadatifard, M. Abdoli-Senejani, M.A. Bodaghifard, *Cogent Chem.*, **2016**, *2*, 1188435.
- [35] A. Mobinikhaledi, M.A. Bodaghifard, S. Asadbegi, *Mol. Divers.*, **2016**, *20*, 461-468.
- [36] M. Bodaghifard, A. Mobinikhaledi, S. Asadbegi, *Appl. Organomet., Chem.*, **2017**, *31*, e3557.
- [37] G. Wang, C. Chen, T. Du, W. Zhong, *Adv. Synth. Catal.*, **2014**, *356*, 1747-1752.
- [38] J.-M. Yang, R. Jiang, L. Wu, X.-P. Xu, S.-Y. Wang, S.-J. Ji, *Tetrahedron*, **2013**, *69*, 7988-7994.
- [39] H. Hikawa, Y. Mori, S. Kikkawa, I. Azumaya, *Adv. Synth. Catal.*, **2016**, *358*, 765-773.
- [40] N. Nowrouzi, M.Z. Jonaghani, *Can. J. Chem.*, **2012**, *90*, 498-509.
- [41] D.R. Wallach, P.C. Stege, J.P. Shah, J.D. Chisholm, *J. Org. Chem.*, **2015**, *80*, 1993-2000.
- [42] X. Zhu, X. Zhou, W. Zhang, *J. Chem. Res.*, **2015**, *39*, 390-393.
- [43] F. Han, L. Yang, Z. Li, C. Xia, *Adv. Synth. Catal.*, **2012**, *354*, 1052-1060.
- [44] D. Gülcemal, S.I. Gülcemal, C.M. Robertson, J. Xiao, *Organometallics*, **2015**, *34*, 4394-4400.
- [45] N. Sakai, N. Takahashi, Y. Ogiwara, *Eur. J. Org. Chem.*, **2014**, *2014*, 5078-5082.
- [46] Y. Motoyama, M. Taguchi, N. Desmira, S.H. Yoon, I. Mochida, H. Nagashima, *Chem. Asian J.*, **2014**, *9*, 71-74.
- [47] L.F. Kuyper, D.P. Baccanari, M.L. Jones, R.N. Hunter, R.L. Tansik, S.S. Joyner, C.M. Boytos, S.K. Rudolph, V. Knick, H.R. Wilson, J. *Med. Chem.*, **1996**, *39*, 892-903.
- [48] Y.-S. Feng, L. Mao, X.-S. Bu, J.-J. Dai, H.-J. Xu, *Tetrahedron*, **2015**, *71*, 3827-3832.
- [49] L. Li, A. Zhu, H. Yao, Y. Wei, D. Yang, J. Li, G. Zhang, *J. Chem., Res.*, **2010**, *34*, 511-513.
- [50] M. Ghanimati, M. Abdoli Senejani, T. Momeni Isfahani, M.A. Bodaghifard, *Appl. Organomet. Chem.*, **2018**, *32*, e4591.

- [51] Y. Zhang, X. Qi, X. Cui, F. Shi, Y. Deng, *Tetrahedron Lett.*, **2011**, *52*, 1334-1338.
- [52] X. Li, S. Li, Q. Li, X. Dong, Y. Li, X. Yu, Q. Xu, *Tetrahedron*, **2016**, *72*, 264-272.
- [53] K.-i. Fujita, Z. Li, N. Ozeki, R. Yamaguchi, *Tetrahedron Lett.*, **2003**, *44*, 2687-2690.

**How to cite this article:** Mahdi Ghanimati, Masumeh Abdoli Senejani\*, Mohammad Ali Bodaghifard, Tahereh Momeni Isfahani. Phosphomolybdic acid immobilized chitosan/Fe<sub>3</sub>O<sub>4</sub>: an efficient catalyst for n-alkylation of anilines. *Eurasian Chemical Communications*, 2020, 2(6), 688-701. **Link:** [http://www.echemcom.com/article\\_105234.html](http://www.echemcom.com/article_105234.html)