FULL PAPER



Hofmann *N*-alkylation of aniline derivatives with alcohols using ferric perchlorate immobilized on SiO₂ as a catalyst through Box–Behnken experimental design

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Funding information Islamic Azad University–Arak Branch An efficient method for the N-alkylation of poorly nucleophilic amines using ferric perchlorate immobilized on SiO₂ as a catalyst is described. $Fe(ClO_4)_3$ was prepared from mixing iron(III) hydroxide and perchloric acid and adsorbed on silica gel. The catalyst was characterized using various techniques. The supported ferric perchlorate ($Fe(ClO_4)_3/SiO_2$) revealed high efficiency and selectivity for N-alkylation of aromatic amines with alcohols to provide alkylated amines. Various secondary amines were synthesized from primary amines and alcohols in good to excellent yields, with water as the only by-product. The optimization of the reaction conditions was investigated using the response surface method, and involving the Box-Behnken design matrix. The conditions for optimal reaction yield and time were: amount of catalyst = 0.34 mmol, temperature = 60° C and molar ratio of amine to alcohol = 1.2. The catalyst was recovered and reused for five cycles without a considerable decrease in catalytic activity. The stability of the recycled catalyst was investigated. The proposed method has numerous advantages including procedure simplicity, short reaction times, low cost, good to excellent yields, reusability of the catalyst and mild and environmentally benign conditions.

KEYWORDS

amines, design of experiment, Fe(ClO₄)₃/SiO₂, heterogeneous catalyst, Hofmann N-alkylation

1 | INTRODUCTION

Organic compounds with nitrogen atoms such as amines play a significant role in natural products, dyes and pharmaceuticals.^[1,2] Therefore, various methods have been developed recently for catalysed organic reactions including the formation of a carbon–nitrogen bond because of the biological properties and industrial applications of amines.^[3–5] The most common route is *N*-alkylation of amines with alkyl halides which produces a mixture of amines and ammonium halides and leads to low selectivity and problems involving product separation and purification. Furthermore, this method is harmful to the environment due to untreated toxic alkyl halides and undesired waste.^[6,7] Alkylation of amines with alcohols instead of alkyl halides is an environmentally friendly and efficient method for synthesizing *N*-substituted amines because water is the only by-product.^[8-10]

Ferric perchlorate is a transition metal Lewis acid that acts as an inexpensive, easily available, odourless, nontoxic, reusable and stable catalyst in many organic reactions. The adsorption of ferric perchlorate onto silica gel generates a stable non-hygroscopic material.^[11] In recent years, ferric perchlorate immobilized on silica gel as a

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heterogeneous catalyst has been used in organic syntheses.^[12–14] So, for the development of a greener and milder procedure, herein we report a convenient method for Nalkylation of amines with alcohols using a catalytic amount of ferric perchlorate immobilized on silica gel $(Fe(ClO_4)_3/SiO_2).$

The experimental design technique was used to determine the optimal conditions for reaction times and yields. The Box-Behnken design (BBD) is a robust experimental design method that involves fitting a model by polynomial equation techniques under the response surface method design. This method is well shown in the visualization of response curve versus independent variables or factors.^[15] This design was applied for the estimation of various parameters affecting yield and time in the Nalkylation of amine derivatives, and then the optimum conditions were determined.

2 **RESULTS AND DISCUSSION**

In continuation of our studies of mild and green synthesis of heterocyclic compounds,^[16–20] herein we report a new, efficient and environmentally friendly method for the synthesis of N-alkylated amines using $Fe(ClO_4)_3/SiO_2$ as catalyst (Scheme 1).

First, $Fe(ClO_4)_3$ was prepared by mixing iron(III) hydroxide and perchloric acid and adsorbed on silica gel (Scheme 2). The resulting $Fe(ClO_4)_3/SiO_2$ was characterized using Fourier transform infrared (FT-IR) spectroscopy, X-ray diffraction (XRD), field emission scanning electron microscopy (SEM), thermogravimetric analysis (TGA) and energy-dispersive X-ray (EDX) analysis.

The presence of Si, Fe, Cl and O atoms was confirmed using EDX analysis (Figure 1). The XRD pattern of the



SCHEME 1 *N*-Alkylation of aniline derivatives using $Fe(ClO_4)_3/$ SiO₂ as catalyst



FIGURE 1 EDX pattern of Fe(ClO₄)₃/SiO₂

synthesized catalyst is shown in Figure 2. There is a broad diffraction peak at around 25° which corresponds to the amorphous SiO₂ matrix. The characteristic peaks at $2\theta = 33^{\circ}$ and 35° confirm the supporting of FeClO₄ on the SiO₂ surface. The surface morphology of synthesized $Fe(ClO_4)_3/SiO_2$ was investigated using SEM (Figure 3). The SEM image revealed a homogenous powder structure for the catalyst.

TGA/DTA was used to investigate the thermal stability of the $Fe(ClO_4)_3/SiO_2$ catalyst (Figure 4). The weight loss (20.87%) at temperatures below 300°C can be due to the loss of adsorbed water and surface hydroxyl groups on silica gel support. It is obvious from the TGA/DTA curves that the catalyst is stable even at high temperature.

The FT-IR spectrum of synthesized $Fe(ClO_4)_3/SiO_2$ is shown in Figure 5. The spectrum displays a band at 1629 cm^{-1} corresponding to the stretching vibrational mode of H-O-H adsorbed layer. Furthermore, stretching vibration bands in the range $3100-3600 \text{ cm}^{-1}$ are attributed to both symmetric and asymmetric modes of O-H bonds. The spectrum displays characteristic asymmetric stretching bands at 1094 cm⁻¹ and symmetric stretching bands at 960, 807 and 464 cm⁻¹ for the Si-O-Si group.

For the optimization of the reaction conditions, the Nalkylation of aniline (1 mmol) with benzhydrol (1 mmol) in the presence of 0.4 g of the catalyst was selected as a model reaction. Selected results from our experiments are presented in Table 1. An initial optimization indicates that chloroform is more suitable than other solvents. In



FIGURE 2 XRD pattern of Fe(ClO₄)₃/ SiO₂





addition, it was found that $Fe(ClO_4)_3/SiO_2$ is an efficient catalyst to give the product in excellent yield and short reaction time.

2.1 | Statistical Analysis and Model Fitting

Herein, a three-level 15-run BBD using Design-Expert 7.0.0 Trial software (Stat-Ease Inc., Minneapolis) was used to analyse the effect of various reaction parameters, namely molar ratio of amine to alcohol, temperature and amount of catalyst, on the *N*-alkylation of aniline with

benzhydrol. In this regard, Table 2 presents the level of parameters, experimental design matrix and results. The input factors and levels were applied to the reaction optimization process. This process was: (A) the molar ratio (1, 1.2 and 1.4), (B) the amount of catalyst (0.15, 0.3 and 0.45 g) and (C) the temperature (30, 45 and 60°C). The response function (y) was a greater yield and a shorter reaction time for *N*-alkylation of aniline.

In order to obtain the optimum conditions, the BBD was used for optimization. The examined variables were distinguishable, and the interconnections between them were analysed.

Response surface methodology and the BBD were applied to create the coupled effect of the three factors on the reaction process and to define optimal values for the system. The results obtained from the BBD are presented in Tables 3 and 4. The quality of the proposed model was evaluated by analysis of variance (ANOVA) at 95% confidence level. Regarding the ANOVA test results, the process parameters with a *p*-value of less than 0.05 are deemed to be significant and have important effects on the yield and time of the synthesis. The results that showed B, C, BC, A^2 and B^2 are very significant in the model.

The polynomial regression model was utilized to fit the terms of coded values (A, B, C) with yield (%) and reaction time as the response value using the following equations:

$$y(Time) = +333.33 - 2.5A - 128.75B - 88.75C - 2.5AB$$

-12.5AC + 55.0BC + 28.33A² + 120.83B² - 4.17C²
R² = 0.9987 Adjusted R² = 0.9964
 $y(yield) = +87.33 + 1.12A + 13.62B + 13.25C - 1.75AB$
+1.50AC + 3.00BC - 8.04A² - 11.04B² - 13.29C²
R² = 0.9965 Adjusted R² = 0.9903



FIGURE 4 TGA and DTA curves of Fe(ClO₄)₃/SiO₂



FIGURE 5 FT-IR spectrum of Fe(ClO₄)₃/SiO₂

TABLE 1 Optimization of reaction condit	ions
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Entry	Catalyst	Condition	Time (h)	Yield (%)
1	_	CHCl ₃ /reflux	6	_
2	$Fe(ClO_4)_3$	CHCl ₃ /reflux	5	80
3	Fe(ClO ₄) ₃ /SiO ₂	CHCl ₃ /reflux	4.5	87
4	Fe(ClO ₄) ₃ /SiO ₂	Solvent-free/25°C	6	_
5	Fe(ClO ₄) ₃ /SiO ₂	Solvent-free/60°C	4.5	60
6	Fe(ClO ₄) ₃ /SiO ₂	Solvent-free/120°C	4.5	60
7	Fe(ClO ₄) ₃ /SiO ₂	CH ₂ Cl ₂ /reflux	4.5	78
8	Fe(ClO ₄) ₃ /SiO ₂	EtOH/reflux	4.5	75

TABLE 2 Experimental factors, levels and results for Box-Behnken design

			Levels		
Factor	Unit	Symbol	Low (-1)	Central (0)	High (+1)
Molar ratio	_	А	1	1.2	1.4
Catalyst amount	g	В	0.15	0.3	0.45
Temperature	°C	С	30	45	60

Independent variables

	A		B		<u>C</u>		Dependent variable, time (min)		Dependent variable, yield (%)	
Run	Coded level	Actual level	Coded level	Actual level	Coded level	Actual level	Experimental	Predicted	Experimental	Predicted
1	-1	1	0	0.3	-1	30	440	436.25	55	53.13
2	-1	1	-1	0.15	0	45	610	611.25	50	51.75
3	0	1.2	-1	0.15	+1	60	430	435	60	59.62
4	-1	1	+1	0.45	0	45	350	358.75	82	82.5
5	0	1.2	+1	0.45	-1	30	360	355	60	60.37
6	+1	1.4	-1	0.15	0	45	620	611.25	58	57.5
7	0	1.2	-1	0.15	-1	30	720	722.5	40	39.12
8	+1	1.4	0	0.3	-1	30	450	456.25	51	52.38
9	0	1.2	0	0.3	0	45	335	333.33	87	87.33
10	+1	1	0	0.3	+1	60	290	283.75	78	76.63
11	0	1.2	0	0.3	0	45	330	333.33	87	87.33
12	0	1.2	0	0.3	0	45	335	333.33	88	87.33
13	+1	1.4	+1	0.45	0	45	350	348.75	83	81.25
14	+1	1.4	0	0.3	+1	60	250	253.75	81	81.88
15	0	1.2	+1	0.45	+1	60	290	287.5	92	92.88

where *y* is the predicted response as reaction time and yield; *A*, *B* and *C* are molar ratio, amount of catalyst and temperature, respectively; and *AB*, *AC* and *BC* are the interaction coefficients of these factors.

The correlation coefficients (R^2) of the two equations are 0.9987 and 0.9965, which indicate a good linearity. Three-dimensional response surfaces and contour curves can be applied for monitoring the effect of two factors on the response reaction time and yield, which are demonstrated in Figures 6 and 7. Figures 6 and 7 present the optimal experimental conditions in terms of dark blue and dark red for reaction time and yield, respectively. The reaction time of *N*-alkylation of aniline decreases with increasing temperature. Also, the yield increases with increasing temperature. As can be observed, the level at the centre of the amount of catalyst and molar ratio is the best level of the plots. The optimum conditions for the minimum reaction time of 240 min (4 h) and maximum yield of 92% are: molar ratio of amine to alcohol = 1.18-1.2, amount of catalyst = 0.34 mg and temperature = 58.29° C-(reflux condition). To demonstrate the conclusions, four-time reactions were done using these optimal experimental conditions. Figure 8 and Table 5 present the optimal synthesis conditions.

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2.2 | Utilizing Optimal Conditions

After the optimization of the reaction conditions, we studied the efficiency of $Fe(ClO_4)_3/SiO_2$ for the *N*-alkylation of aniline derivatives with a variety of benzyl alcohols under the optimized reaction conditions (Table 6). A variety of aniline derivatives with electron-

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TABLE 3 ANOVA for Box-Behnken quadratic model for reaction time of N-alkylation of aniline

Source	Sum of squares	Df	Mean square	F-value	<i>p</i> -value	Remark
Model	2.645×10^{5}	9	29389.07	430.08	< 0.0001	Significant
A, molar ratio	50.00	1	50.00	0.73	0.4314	
<i>B</i> , amount of catalyst	1.326×10^{5}	1	1.326×10^{5}	1940.67	< 0.0001	
C, temperature	63012.50	1	63012.50	922.13	< 0.0001	
AB	25.00	1	25.00	0.37	0.5717	
AC	625.00	1	625.00	9.15	0.0293	
BC	12100.00	1	12100.00	177.07	< 0.0001	
A^2	2964.10	1	2964.10	43.38	0.0012	
B^2	53910.26	1	53910.26	788.93	< 0.0001	
C^2	64.10	1	64.10	0.94	0.3773	
Residual	341.67	5	68.33			
Lack of fit	325.00	3	108.33	13.00	0.0723	Not significant
Pure error	16.67	2	8.33			
Cor total	2.648×10^{5}	14				

TABLE 4 ANOVA for Box–Behnken quadratic model for yield of N-alkylation of aniline

Source	Sum of squares	Df	Mean square	F-value	<i>p</i> -value	Remark
Model	4130.52	9	458.95	159.17	< 0.0001	Significant
A, molar ratio	10.13	1	10.13	3.51	0.1198	
B, amount of catalyst	1485.12	1	1485.12	515.07	< 0.0001	
C, temperature	1404.50	1	1404.50	487.11	< 0.0001	
AB	12.25	1	12.25	4.25	0.0943	
AC	9.00	1	9.00	3.12	0.1375	
BC	36.00	1	36.00	12.49	0.0167	
A^2	238.78	1	238.78	82.81	0.0003	
B^2	450.16	1	450.16	156.12	< 0.0001	
C^2	652.31	1	652.31	226.24	< 0.0001	
Residual	14.42	5	2.88			
Lack of fit	13.75	3	4.58	13.75	0.0686	Not significant
Pure error	0.67	2	0.33			
Cor total	4144.93	14				

donating as well as electron-withdrawing groups were *N*-alkylated with isopropanol, α -phenylethanol and diphenylcarbinol derivatives, using Fe(ClO₄)₃/SiO₂ as catalyst, in good to excellent yields and in short reaction times. However, the substituents had no considerable effect on the reaction times and yields.

A plausible mechanism for *N*-alkylation of aniline derivatives with alcohols using $Fe(ClO_4)_3/SiO_2$ is shown in Scheme 3. The dehydrogenation of alcohol gives the corresponding carbonyl compound. This oxidation process may be carried out via electron transfer between Fe(III) and Fe(II) ions in the presence of atmospheric



FIGURE 6 Response surfaces and contour plots to predict the reaction time for N-alkylation of aniline

oxygen. Then, the carbonyl compound undergoes condensation with an amine to give an imine intermediate. Finally, the product is created by adding hydrogen to imine and the $Fe(ClO_4)_3/SiO_2$ is recycled.

The recyclability of $Fe(ClO_4)_3/SiO_2$ was investigated for *N*-alkylation of aniline (1.2 mmol) with benzhydrol (1 mmol) in the presence of 0.34 g of the catalyst under the optimized conditions. After completion of the reaction, the reaction mixture was filtered to separate the catalyst, which was washed two times with 20 ml of acetone and then dried at 70°C in an oven for 12 h. The recycled catalyst reused for five cycles without a considerable decrease in catalytic activity (Figure 9).

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Furthermore, the stability of the recycled catalyst was studied using FT-IR spectroscopy, XRD, SEM, EDX analysis and TGA. The results of XRD and SEM analyses of the recycled $Fe(ClO_4)_3/SiO_2$ showed shape and size identical to those of fresh catalyst (Figures 10 and 11). EDX analysis also indicates that the chemical composition of the recycled catalyst is almost unchanged after five reuses (Figure 12). The comparison of TGA/DTA curves for fresh and recycled catalyst shows that the thermal stability of



FIGURE 7 Response surfaces and contour plots to predict product yield for N-alkylation of aniline

the catalyst does not change after five reuses (Figure 13). So, the recovered catalyst had no obvious change in structure after five runs, as apparent from a comparison of analyses of fresh catalyst and recovered catalyst.

Finally, the efficiency of the method was compared with some other methodologies for the *N*-alkylation of amine derivatives with alcohols (Table 7). The results of this research prove the advantage of this procedure compared to previous methods with respect to the yields and times of reactions.

3 | EXPERIMENTAL

3.1 | General

Melting points were determined using an Electrothermal 9200 apparatus. ¹H NMR and ¹³C NMR spectra were recorded with a 400 MHz Bruker AQS 500-AVANCE spectrometer using dimethylsulfoxide (DMSO) as the solvent. FT-IR spectra were recorded with a Bruker Tensor 27 FT-IR spectrometer. Elemental analyses were



FIGURE 8 Optimized process conditions

performed using a PerkinElmer 2400 Series II CHNS/O analyser. EDX analysis and SEM micrographs of the synthesized catalyst were obtained using a Tescan Mira III. TGA and DTA curves were measured using a TGA/DSC 1 instrument at a heating rate of 10°C min⁻¹ from 25 to 1000°C under nitrogen atmosphere. Powder XRD patterns were obtained with a PANalytical X'Pert PRO MPD X-ray diffractometer using a Cu tube in the range $2\theta = 3-80^{\circ}$. All solvents and reagents were purchased from Aldrich or Merck with a high-grade quality and were used without any purification. All products were characterized using NMR and FT-IR spectra and compared with those of authentic samples.

3.2 | General Procedure for Preparation of Ferric Perchlorate

A mixture of $Fe(OH)_3$ (1.0 g, 9.3 mmol) and perchloric acid (3.7 g, 37.2 mmol) was heated under reflux conditions for 10 h. Then, the mixture was cooled to room temperature, and ferric perchlorate was precipitated. The

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TABLE 6 N-Alkylation of aniline derivatives with alcohols using $Fe(ClO_4)_3/SiO_2$

Entry	Product	Time (h)	Yield (%) ^a	M.p. (Lit.) (°C)
1	H H	4	92	56–58 (58) ^[21]
2	H H H CI	5	88	75–77 (75) ^[22]
3	H NH NO ₂	5	85	181–182 (182–183) ^[23]
4	H NH	4	86	51–53 (52) ^[8]
5	H NH CI	5.5	85	57–59 (58–60) ^[24]
6	The second secon	5	85	69–72 (68–71) ^[24]

(Continues)

TABLE 5 N-Alkylation of aniline under optimal conditions

	Factor		Dependent variabl	e, time (min)	Dependent variable, yield (%)		
Approach	Molar ratio	Amount of catalyst (g)	Temperature (°C)	Experimental (mean <u>+</u> SD)	Predicted	Experimental (mean ± SD)	Predicted
BBD	1.18-1.2	0.34	58.29-(reflux condition)	240 ± 2.5	240.012	92.25 ± 1.47	92.05

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TABLE 6 (Continued)



TABLE 6 (Continued)



^aIsolated yield.

produced pink crystals were filtered and washed with 5 ml of perchloric acid.^[36]

3.3 | General Procedure for Preparation of Fe(ClO₄)₃/SiO₂

A solution of 1.0 g of $Fe(ClO_4)_3$ in ethanol (10 ml) was added to a mixture of 10 g of silica gel (Kieselgel 40, 70–230 mesh; Merck) in ethanol (30 ml), and stirred magnetically at room temperature for 30 min. The solvent was evaporated, and then the brown powder was dried at 60°C in a vacuum drying cabinet for 1 h.^[14]

3.4 | General Procedure for N-Alkylation of Aniline Derivatives using $Fe(ClO_4)_3/SiO_2$

A mixture of amine (1.2 mmol), alcohol (1 mmol) and $Fe(ClO_4)_3/SiO_2$ (0.34 g) in CH₃Cl (15 ml) was stirred and heated under reflux conditions 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 reaction mixture was cooled to room temperature and filtered to isolate the catalyst. The crude product was recrystallized from dichloromethane to afford the pure compound.

3.5 | Selected Spectroscopic Data

3.5.1 | *N*-(Diphenylmethyl)aniline (entry 1)

FT-IR (KBr, ν_{max} , cm⁻¹): 3379 (N–H), 3026 (C–H aromatic), 2925 (C–H aliphatic), 1597 and 1494 (C=C aromatic), 1269 (C–N). ¹H NMR (300 MHz, CDCl₃, *δ*, ppm): 7.70–7.65 (m, 10H, Ar–H), 7.20–7.07 (m, 5H, Ar–H), 5.86 (s, 1H, C–H), 4.45 (brs, 1H, N–H).



SCHEME 3 Plausible mechanism for *N*-alkylation of aniline derivatives with alcohols using Fe(ClO₄)₃/SiO₂



FIGURE 9 Recyclability of Fe(ClO₄)₃/SiO₂ in the synthesis of *N*-(diphenylmethyl)aniline

3.5.2 | *N*-(Diphenylmethyl)-4chloroaniline (entry 2)

FT-IR (KBr, ν_{max} , cm⁻¹): 3295 (N–H), 3059 (C–H aromatic), 2953 (C–H aliphatic), 1664 and 1488 (C=C aromatic), 1264 (C–N), 758 (C–Cl). ¹H NMR (300 MHz,



250µm

FIGURE 10 SEM image of recycled Fe(ClO₄)₃/SiO₂

CDCl₃, δ , ppm): 7.32–7.20 (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 (brs, 1H, N–H).

3.5.3 | *N*-(Diphenylmethyl)-4-nitroaniline (entry 3)

FT-IR (KBr, ν_{max} , cm⁻¹): 3404 (N—H), 3077.97 (C—H aromatic), 2911 (C—H aliphatic), 1599 and 1463 (C=C aromatic), 1508 and 1303 (NO₂), 1279 (C—N). ¹H NMR (300 MHz, CDCl₃, δ , ppm): 7.39–7.27 (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 (brs, 1H, N—H).

3.5.4 | N-(1-Phenylethyl)-4-bromoaniline (entry 6)

FT-IR (KBr, ν_{max} , cm⁻¹): 3385 (N—H), 3026 (C—H aromatic), 2925 (C—H aliphatic), 1596 and 1493 (C=C aromatic), 1269 (C—N), 697 (C—Br). ¹H NMR (300 MHz, CDCl₃, δ , ppm): 7.55–7.50 (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 (d, 3H, J = 7.1 Hz, CH₃).

3.5.5 | *N*-((4-Chlorophenyl) phenylmethyl)-4-bromoaniline (entry 15)

FT-IR (KBr, ν_{max} , cm⁻¹): 3382 (N–H), 3030 (C–H aromatic), 2924 (C–H aliphatic), 1618 and 1489 (C=C aromatic), 1284 (C–N), 818 (C–Cl), 701 (C–Br). ¹H NMR (300 MHz, CDCl₃, δ , ppm): 7.59–7.32 (m, 11H, Ar–H), 6.56 (m, 2H, Ar–H), 5.82 (s, 1H, C–H), 3.00 (brs, 1H, N–H). ¹³C NMR (75 MHz, DMSO- d_6 , δ , ppm): 65.70, 114.03, 115.97, 124.45, 126.94, 127.86, 128.23, 131.64, 132.28, 138.41, 141.41, 148.78, 152.56. Anal. Calcd for C₁₉H₁₅BrClN (%): C, 61.36; H, 4.00; 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.



FIGURE 11 XRD pattern of recycled Fe(ClO₄)₃/SiO₂



FIGURE 12 EDX pattern of recycled Fe(ClO₄)₃/SiO₂

4 | CONCLUSIONS

In summary, ferric perchlorate adsorbed on silica gel was used as a heterogeneous catalyst for the *N*-alkylation of aniline derivatives using alcohols, with the only byproduct being water. A variety of aniline derivatives with electron-donating as well as electron-withdrawing groups undergo *N*-alkylation with isopropanol, α -phenylethanol and diphenylcarbinol derivatives using Fe(ClO₄)₃/SiO₂ in good to excellent yields and in short reaction times. High yields, simple conditions, and green and reusable catalyst are advantages of this method.



FIGURE 13 TGA and DTA curves of recycled $Fe(ClO_4)_3/SiO_2$

TABLE 7 Comparison of efficiency of various catalysts used in N-alkylation of aniline derivatives with alcohols

Entry	Catalyst	Time (h)	Yield (%)	Condition
1	Fe(ClO ₄) ₃ /SiO ₂	4–6	80-92	CHCl _{3,} reflux (this work)
2	Ph ₂ PCl/imidazole/I ₂	0.25-48	50-94	CH_2Cl_2 , reflux ^[8]
3	Montmorillonite	1–30	39–99	1,4-Dioxane, 150°C ^[7]
4	Iridium complex/K ₂ CO ₃	12–24	19–95	2,2,2-Trifluoroethanol, 100°C ^[9]
5	Pd/Fe ₂ O ₃	2–28	72–99	Solvent-free, 140–170°C ^[10]
6	CsOH·H ₂ O	24–28	26–95	Solvent-free, air, 130–150°C ^[33]
7	Au/TiO ₂	5-63	50–98	120°C, N ₂ (5 atm), toluene ^[34]
8	Ph ₂ CHBr	24	Trace to 96	Solvent-free, N ₂ , 120°C ^[35]

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REFERENCES

- S.-Y. Park, P. Fung, N. Nishimura, D. R. Jensen, H. Fujii, Y. Zhao, S. Lumba, J. Santiago, A. Rodrigues, T.-F. Chow, *Science* 2009, *324*, 1068.
- [2] S. A. Lawrence, Amines: Synthesis Properties and Applications, Cambridge University Press, Cambridge 2004.
- [3] S. Pisiewicz, T. Stemmler, A. E. Surkus, K. Junge, M. Beller, *ChemCatChem* 2015, 7, 62.
- [4] R. V. Jagadeesh, K. Murugesan, A. S. Alshammari, H. Neumann, M.-M. Pohl, J. Radnik, M. Beller, *Science* 2017, 358, 326.
- [5] Y. Hoshino, N. Ohtsuka, T. Okada, K. Honda, *Tetrahedron Lett.* 2016, 57, 5304.
- [6] R. N. Salvatore, C. H. Yoon, K. W. Jung, *Tetrahedron* 2001, 57, 7785.
- [7] K. Motokura, N. Nakagiri, T. Mizugaki, K. Ebitani, K. Kaneda, J. Org. Chem. 2007, 72, 6006.
- [8] N. Nowrouzi, M. Z. Jonaghani, Can. J. Chem. 2012, 90, 498.
- [9] Q. Zou, C. Wang, J. Smith, D. Xue, J. Xiao, Chem. Eur. J. 2015, 21, 9656.
- [10] Y. Zhang, X. Qi, X. Cui, F. Shi, Y. Deng, *Tetrahedron Lett.* 2011, 52, 1334.
- [11] P. Salehi, A. R. Motlagh, Synth. Commun. 2000, 30, 671.
- [12] F. K. Behbahani, A. Lotfi, Eur. Chem. Bull. 2013, 2, 694.
- [13] E. Najafi, F. Behbahani, Russ. J. Org. Chem. 2017, 53, 454.

- [14] M. Heravi, F. Behbahani, J. Iran. Chem. Soc. 2007, 4, 375.
- [15] J. P. Maran, S. Manikandan, C. V. N. Ivetha, R. Dinesh, Arab. J. Chem. 2017, 10, S1145.
- [16] M. Keshavarz, M. Abdoli-Senejani, S. Hojati, M. Moosavifar, Org. Prep. Proced, Int. 2017, 49, 549.
- [17] N. Azizi, F. Abbasi, M. Abdoli-Senejani, *Mater. Chem. Phys.* 2017, 196, 118.
- [18] S. H. Siadatifard, M. Abdoli-Senejani, M. A. Bodaghifard, Cogent Chem. 2016, 2, 1188435.
- [19] A. Mobinikhaledi, M. A. Bodaghifard, S. Asadbegi, *Mol. Divers.* 2016, 20, 461.
- [20] M. A. Bodaghifard, A. Mobinikhaledi, S. Asadbegi, Appl. Organometal. Chem. 2017, 31, e3557.
- [21] G. Wang, C. Chen, T. Du, W. Zhong, Adv. Synth. Catal. 2014, 356, 1747.
- [22] J.-M. Yang, R. Jiang, L. Wu, X.-P. Xu, S.-Y. Wang, S.-J. Ji, *Tetrahedron* 2013, 69, 7988.
- [23] H. Hikawa, Y. Mori, S. Kikkawa, I. Azumaya, Adv. Synth. Catal. 2016, 358, 765.
- [24] D. R. Wallach, P. C. Stege, J. P. Shah, J. D. Chisholm, J. Org. Chem. 2015, 80, 1993.
- [25] X. Zhu, X. Zhou, W. Zhang, J. Chem. Res. 2015, 39.
- [26] F. Han, L. Yang, Z. Li, C. Xia, Adv. Synth. Catal. 2012, 354, 1052.
- [27] D. Gülcemal, S. I. Gülcemal, C. M. Robertson, J. Xiao, Organometallics 2015, 34, 4394.
- [28] N. Sakai, N. Takahashi, Y. Ogiwara, Eur. J. Org. Chem. 2014, 2014, 5078.
- [29] Y. Motoyama, M. Taguchi, N. Desmira, S. H. Yoon, I. Mochida, H. Nagashima, *Chem. Asian J.* 2014, 9, 71.
- [30] 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.
- [31] Y.-S. Feng, L. Mao, X.-S. Bu, J.-J. Dai, H.-J. Xu, *Tetrahedron* 2015, 71, 3827.
- [32] L. Li, A. Zhu, H. Yao, Y. Wei, D. Yang, J. Li, G. Zhang, J. Chem. Res. 2010, 34, 511.

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- [33] X. Li, S. Li, Q. Li, X. Dong, Y. Li, X. Yu, Q. Xu, Tetrahedron 2016, 72, 264.
- [34] L. He, X. B. Lou, J. Ni, Y. M. Liu, Y. Cao, H. Y. He, K. N. Fan, *Chem. Eur. J.* 2010, 16, 13965.
- [35] Q. Xu, H. Xie, E.-L. Zhang, X. Ma, J. Chen, X.-C. Yu, H. Li, Green Chem. 2016, 18, 3940.
- [36] B. Kumar, H. Kumar, M. Singh, Indian J. Chem. B 1991, 30, 460.

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