Proceedings of the Pakistan Academy of Sciences: Part A
Physical and Computational Sciences 59(2): 31-42 (2022)
Copyright © Pakistan Academy of Sciences
ISSN (Print): 2518-4245; ISSN (Online): 2518-4253
https://doi.org/10.53560/PPASA(59-2)615

Pakistan Academy of Sciences

Research Article

Economical Synthesis of Nitrophenols under Controlled Physical Parameters

Shabbir Hussain[1], Muhammad Ameen Ahmad[2], Muhammad Ahmad[3], Asma Nisar[4], Amina Asghar[3], Muhammad Suleman[5], Samra Barkaat[5], Muhammad Riaz[6], Muhammad Nasir[7]

[1]Institute of Chemistry, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan.
[2]Department of Chemistry, Lahore Garrison University, DHA Phase VI, Lahore, Pakistan.
[3]Department of Chemistry, DSNT, University of Education Lahore, Pakistan.
[4]Faculty of Engineering, Universiti Malaysia Sabah, Kota Kinabalu, Malaysia.
[5]Department of Chemistry, Riphah International University, Faisalabad Campus, Pakistan.
[6]Department of Basic and Applied Chemistry, Faculty of Science and Technology University of Central Punjab, Lahore, Pakistan.
[7]Department of Chemistry, GC University Faisalabad, Faisalabad, Pakistan

Abstract: Current studies were performed to find an economical path for the synthesis of nitrophenols which are plant growth regulators (PGR) and are applied to crops for better agricultural production. The study discourages the involvement of costly surfactants such as CTAB, TBAB, H-β and γ-alumina catalysts in commercial production of nitrophenols. This synthesis requires the lower number of chemicals, less time and does not involve the advance instruments. Phenol and its derivatives were selectively nitrated into o/p nitrophenols economically by controlling only the physical parameters, i.e., dilution of nitric acid, reaction time and reaction temperature. The synthesised products were characterised by RP-HPLC and gas chromatography. The reaction between 98% phenol and 32.5% nitric acid at a temperature of 20°C (±2°C) required only 1 hour for optimum yield (91%) of nitrophenols with 77% ortho and 14% para selectivity and was found to have the most suitable route for economical production. The investigated synthetic path is relatively clean and environmentally friendly as it does not involve catalysts and solvents, like the conventional processes. This process may be adopted for commercialisation and industrial level production of nitrophenols for agricultural purposes.

Keywords: Phenol, Nitration, Nitrophenols, o/p-selectivity, Yield, Economical

1. INTRODUCTION

Nitrophenols are synthetic chemicals or plant hormones which are effective at very low concentrations to regulate plant growth. They are organic compounds (instead of nutrients) that stimulate the physiological processes of the plant and improve their metabolic processes [1]. In industries, the nitration of aromatics are widely studied and utilised [2] for agricultural and medicinal purposes. Since it is necessary to use mixed acids such as concentrated nitric acid and sulfuric acid, the nitrification processes in general are not environmentally friendly and lead to significant discharge of acid wastes [3, 4]. Many nitration processes involve the use of conc. nitric acid, acid anhydrides, sulfonic acids, metal nitrates [5] and nitrogen oxides [6]. Nitration of phenolic compounds with conc. nitric acid also leads to the formation of many by-products including 2,4-dinitro and 2,4,6-trinito (picric acid) at high temperature [7]. The ordinary yields of the nitrophenols by direct nitration do not exceed than 60% due to side reactions [8]. Therefore, by using suitable catalysts,

---

Received: May 2021; Accepted: 29 June 2022
*Corresponding author: Muhammad Riaz <muhammad.riaaz@ucp.edu.pk>

proper reaction conditions and controlled physical parameters, the side reactions can be overcome [9]. Phenols can be nitrated by using the mixtures of dilute nitric acid and sulfuric acid in a suitable ratio (e.g., 1:42) [10]. However, these mixtures are less selective for the formation of the desired isomers i.e., o-nitrophenol and p-nitrophenol [11]. The use of fuming acids is not recommended for nitration because such acids may generate large amounts of fumes in the environment during the course of a reaction [12]. Attempts are being made to reduce the quantities of spent acids and to increase selectivity by replacing the catalysts with the appropriate solvents. The nitration of phenol over solid acid catalysts is an easy procedure for quantitative separation of products as compared to the conventional processes. Nitration of industrial aromatics commonly involves drug synthesis [13]. By using a mixture of nitric acid and sulfuric acid, most of phenolic reactions give mainly ortho isomers with some quantities of para compounds. Zeolite-based solid acid catalysts have also been employed in industries for economical production of nitrophenols; these catalysts include silica-supported sulfuric acid and p-toluene sulfonic acid [4], heteropolyacids [14], silica chloride [15] and nanosized tungsten oxide supported on sulfated SnO2 [16]. Regioselectivity of *o/p* nitrophenols was also successively investigated by using simple phenols with 2,4,6 trichloro thiazine [1,3,5]; this process is considered novel for green chemistry [17, 18]. The mechanism of nitration has been extensively investigated and different reviews have been published [19]. Concentrated nitric acid and sulfuric acid have been used for nitration of benzene, alkylbenzene and fragrance compounds [20]. Numerous nitration methodologies were developed for mild nitration-active aromatic compounds such as phenol and pyrroles [21]. Ferric nitrate, copper nitrate and vanadium nitrate were also used to increase the required conversion and selectivity [22]. The regioselectivity of phenol can be improved with silica-supported solid acid catalysts and is considered a noble approach for minimising the side reactions [23]. An excellent pathway for regioselective synthesis of nitrophenols from phenol and its derivative was observed by chelation of o-nitrophenol with carbon-carbon atoms [24]. The metals like Ru [25, 26], Rh [27] and Pd [28] were also employed for selective *o/p* nitration of phenol derivatives. However, less attention have been given towards the use of first row transition metals for nitration purposes [29]. Nitrophenols also exist in various forms in gas phase clouds and rainwater in the atmosphere [30]. The rate of nitration reaction in aqueous phase is more favorable as compared to that in the gaseous phase [31]. It has been experimentally confirmed that some atmospheric species split into nitrate radicals in aqueous phase of atmosphere in the presence of UV irradiations [32] and nitrogen dioxide ($NO2^+$) [33], nitrous acid (HONO) [34], nitrate (NO_3^-) and nitrite (NO_2^-) [35]. The other two nitrating reagents N_2O_5 and Cl-NO_2 are proposed for atmospheric region potential [36]. Hurdles of regioselective nitration can be resolved by ipso-nitration which involves the organo-metallic reagents for demetalation [37, 38]. Currently *ipso*-nitration has been reported by using tert-butyl nitrite as the nitrating agent [39]. Historically, the procedures for phenolic nitration have many troubles including low selectivity, difficulty to handle *etc*. [40].

Current studies were performed to introduce an economical path for nitrophenol synthesis by controlling only the physical parameters, i.e., nitric acid concentration, reaction time and temperature. This investigation may reduce the cost of nitrophenols which are plant growth regulators (PGR) and are applied to crops for better agricultural yield. The study discourages the use of costly surfactants such as (CTAB, TBAB, H-β and γ-alumina catalysts) which are commonly used for commercial production of nitrophenols. This synthesis requires fewer chemicals and less time and does not involve the advance instruments.

2. MATERIALS AND METHODS

IHigh purity analytical grade reagents as phenol, substituted phenols and nitrating agents were purchased from Sigma Aldrich, Germany and employed in experiments without any additional purification. High purity analytical standards namely o-nitrophenol and p-nitrophenol (Chem service USA) having purities of 99.5% and 99.8%, respectively were used for quantification purposes. The concentrated nitric acid and its various dilutions (65%, 50%, 40% & 32.5%) were used. The dilution of nitric acid was performed with a specified volume of distilled water. The reaction temperature during various time intervals was also specified. Special focus was made to control the internal temperature of the reaction by the circulation of cooled water and dilution of a nitrating agent around the reactor bath during the course of the reaction.

2.1 Sample preparation for GC

A specific quantity of sample was taken and diluted in 10 mL of 0.1% BHT solution and introduced into the GC system.

2.2 General synthetic procedure

Nitrating agent in concentrated and various diluted forms (65%, 50%, 40% & 32.5%) was added into the phenol substrate. The nitrating agent's flow and the reaction mixture's temperature were maintained with an adjustable flow meter and cooled water circulation. The color of the reaction matrix was initially yellowish; it was then changed to reddish brown, indicating the consumption of phenol. The product was extracted with dichloromethane and ethanol; the contents were dried in a heating oven for quantification purposes with RP-HPLC and gas chromatography.

2.3 Economical Synthesis

A series of experiments were performed with different concentrations of nitrants at different temperatures. The experiment was conducted with 32.5% (w/v) dilute nitric acid in a batch reactor. For this experiment, 5.0 g of phenol was taken into a reaction vessel and a controlled burette added 8.21 g of nitric acid solution. The reaction vessel was equipped with a stirrer (speed 200-1500 rpm, temperature controller +5°C-380°C, platform 15.5 x 15.5 cm and electrical power 230 V / 60 Hz). A burette probe monitored the flow of dilute acid. The mixture was stirred thoroughly during the reaction. At the first drop of acid addition, the brown-red vapors were formed which raised the temperature of the mixture upon further addition. The slow addition of acid was continued until thick viscous nitrophenol was precipitated in the reaction vessel. The product was collected in another beaker after separation by a separatory funnel for analytical purposes. The post-treatment of the reaction was carried out with dichloromethane and the solvent was evaporated in an oven at 60°C. A tuned thermocouple was used to monitor the temperature rise. It is therefore important to carry out the reaction at low temperature for safety, and it is also important that the reactor must be connected to the cooling system from the outside in order to control the reaction temperature during all the experiments. The extracted product was examined with RP-HPLC with Lc-20AT pump, LC solution software, and C-18 analytical column having dimensions (250mm x 4.6mm) with particle size 5.0µm (Technokroma C-18).

2.4 Chromatographic Conditions of RP-HPLC and Gas chromatography

All the experiments were performed on RP-HPLC and confirmed with gas chromatographs; the following conditions (Table 1) were adopted to identify and quantify the synthesised product.

3. RESULTS AND DISCUSSIONS

Experiments 1-12 were performed for selective nitration (at ortho and para positions) of phenols. Various electrophilic reagents and conditions were employed for these reactions commonly known as electrophilic aromatic substitutions. Table 2 shows important parameters for the nitration of concentrated phenol with nitric acid reagent (Experiments 1-3). Figure 1 displays the chromatogram of the nitration products of experiment 1. It was observed (Table 2) that *o/p* selectivity and %age conversion was lower in experiments 1-3. Moreover, the product yield was found to depend upon the reaction time. Four different peaks were observed in the chromatogram (Figure 1); the peaks at 2.630 and 4.489 minutes correspond to p-nitrophenol and o-nitrophenol, respectively as determined by analytical standards under the same conditions. However, the two peaks (1.202 and 1.418 minutes) observed very early on the left side of chromatogram were not verified; they definitely, belong to the formation of 2,4,6-trinitrophenol (picric acid) or other side product. The %age conversion of substrate to *o/p* isomers is influenced by these two peaks (on extreme left side of chromatogram); larger peaks will result in the less formation of desired isomers (ortho and para) and vice versa. The experiment 1 (Table 2) gives 33% conversion (p-nitro 18% and o-nitro 13%) within 30 minutes. This conversion was increased to 37% and 38% under the identical conditions by increasing the reaction time to 40 and

60 minutes, respectively.

The conversion of substrate phenol into *o/p* nitrophenols was also investigated by using dilute nitric acid (dilution was done with chilled water) at different temperatures (Tables 3-5). By using 50% nitric acid at various temperature (40°C, 30°C and 20°C with ±2°C), the overall yield of *o/p*-nitrophenols was increased to 55% (Table 3). Some phenol quantity was also left unreacted as observed from the chromatogram against working standards. Phenol has hydroxyl group which is more hydrophilic than the phenyl group, and as a result, the phenol remains in an interfacial state. This way, the phenolic ring's ortho position becomes activated at a specific temperature. This active site (ortho carbon atom) of the ringed structure can attack the nitronium ion more favorably as compared to the para position. However, other isomers such as di and tri-nitrophenols may also be synthesised as by-products during these reactions.

By varying the concentration of nitric acid solution to 40% and performing the experiments with the same quantity of phenol (5g of 98% phenol) at 40°C, 30°C and 20°C; the yields of *o/p* nitrophenols was increased to 54%, 66% and 72%, respectively (Table 4, experiments 7-9). Moreover, there was comparatively higher phenol consumption than the previous experiments, 4-6. The higher consumption of substrate ultimately enhanced the yield of end product i.e., nitrophenol. At 40°C, the initial peak was prominent in the chromatogram; this peak was reduced by lowering the reaction temperatures to 30°C and 20°C. The product yield was improved by lowering the temperature to 20°C (Exp. 7-9); a high yield with *o/p* of 72% was achieved at 20°C as compared to the 30°C and 40°C. It was concluded that low temperature is favorable for the conversion of phenol to para nitrophenol. While maintaining the importance of physical parameters during the reaction, the yield was increased by diluting nitric acid.

To improve selectivity of *o/p* nitrophenols, the strength of nitric was further reduced to 32.5% solution and experiments 10-12 were performed (Table 5); it increased the *o/p* conversion to 65%, 75% and 91% at temperatures of 40°C, 30°C and 20°C, respectively. Again, the decrease of temperature has resulted in the rise of nitrophenol yield. The *o/p* ratio was also significantly improved from 0.75 to 5.69 by lowering the temperature from 40°C to 20°C, respectively (Table 5). Overall, the selectivity of isomers was highly affected by internal temperature of the reaction

Table 1. Specific conditions for identification and quantification of synthesised product

RP-HPLC		GC	
Parameters	**Specifications**	**Parameters**	**Specifications**
Mobile phase	Acetonitrile: Water	Column	TRB-5
Proportion	40:60 (0.02M KH_2PO_4)	Dimension	30m x 0.25mm x 0.25µm
Flow	1.0 ml/min	Column Temperature	110°C
Injection volume	10µl	Inlet	Spilt injection (1:50)
Temperature	Ambient	Carrier gas:	Hydrogen/ Air
Wavelength	254 nm	Detector type	FID
Detector	UV-detector	Detector temperature	340°C

Table 2. Experimentations with concentrated materials

Exp. no	Phenol (98%) (g)	Nitric acid (65%) (g)	Reaction time	Conversion (%)	Selectivity (%)		
					o-nitro	*p-nitro*	*o/p ratio*
1	5.0	5.0	30 min	33	13	18	0.722
2	5.0	5.0	40 min	37	21	16	1.313
3	5.0	5.0	45 min	38	23	15	1.533

*__Reaction condition:__ substrate as concentrated phenol (98% purity) and nitric acid (65% purity) as well as dilution of the nitrating agent. So, the current studies clarified that the strength of nitric acid strongly affects the conversion as well as selectivity of nitrophenol isomers. Figure 2 (A and B) displays the chromatograms for experiments 11 (at 30°C) and 12 (at 20°C). The results of experiment 12 are especially interesting. Here, the reaction mixture was agitated for one hour at 20°C and chromatographic study of the products mixture was performed by RP-HPLC. It was surprisingly noted that the nitrophenol conversion was 91% with 14% o-isomer and 77% (Table 5). It was concluded that this was a right economical process for the synthesis of nitrophenols by controlling the physical parameters during the course of reaction. The variation of the temperature may explicit the net conversion of phenol or phenolic compound. However, a very small amount of unreacted phenol was also noticed as initial peaks in the chromatograms of experiments 10-12 (Figure 2). Also, the intensity of these initial peaks (which may ultimately affect the net yield of the desired product) was reduced in the chromatogram in going from the experiment 11 (at 30°C, Figure 2A) to 12 (at 20°C, Figure 2B). In all of above experiments (1-12), the yields of the *o/p* nitrophenols were also calculated against pure analytical standards (having 99.9% purity). Figure 2 shows the chromatogram of high purity analytical standards of p-nitrophenol and o-nitrophenol. The analytical standards were also run on RP-HPPC under the same conditions as applied for experimental measurements.

Table 3. Experiments with 50% nitric acid strength (w/v)

Exp. No	Temp. of reaction mixture	Phenol (98%)	Dil. HNO_3 (50%)	Dilution scheme		Reaction time	Conversion	Selectivity (%)		
		(g)	(g)	Water (g)	65% N.A (g)	(min)	(%)	*ortho* nitro	*para* nitro	*o/p* ratio
4	40 °C	5	6.5	1.5	5	40	44	25	15	1.66
5	30 °C	5	6.5	1.5	5	40	50	33	17	1.94
6	20 °C	5	6.5	1.5	5	40	55	35	20	1.75

Table 4. Experiments with 40% nitric acid strength (w/v)

Exp. No.	Temp. of reaction mixture	Phenol (98%)	Dil. HNO_3 (40%)	Dilution scheme		Reaction time	Conversion	Selectivity (%)		
		(g)	(g)	Water (g)	65% N.A (g)	(min)	(%)	*ortho* nitro	*para* nitro	*o/p* ratio
7	40 °C	5	8.1	3.1	5	50	54	24	30	0.80
8	30 °C	5	8.1	3.1	5	50	66	32	34	0.94
9	20 °C	5	8.1	3.1	5	50	72	37	35	1.05

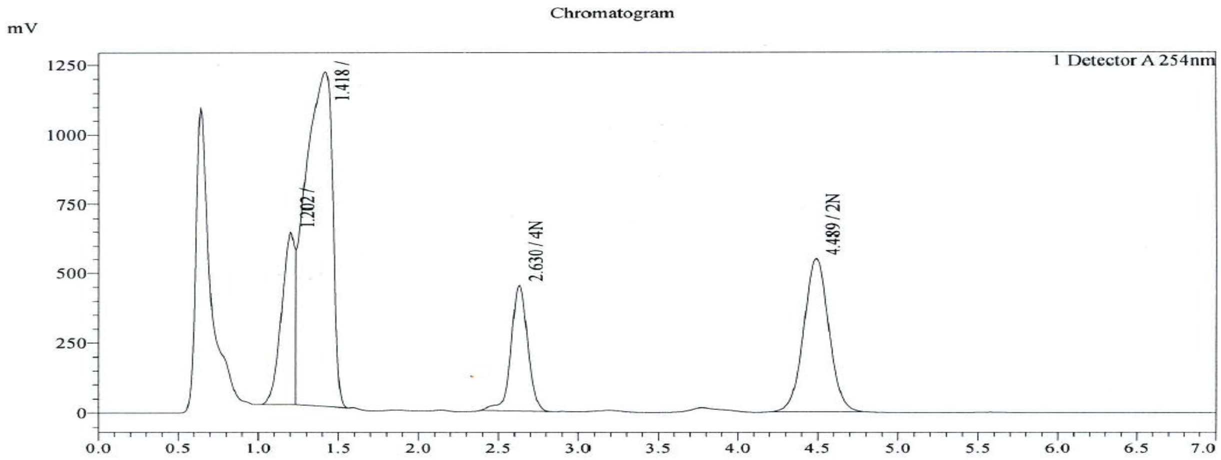

Fig. 1. Chromatogram for nitration of phenol with conc. nitric acid in 30 min (Exp 1)

Table 5. Experiments with 32.5% nitric acid strength (w/v)

Exp. No.	Temp. of reaction mixture (±2)	Phenol (98%)	Dil. HNO_3 (32.5%)	Dilution scheme		Reaction time	Conversion	Selectivity (%)		
		(g)	(g)	Water (g)	65% N.A (g)	(min)	(%)	*ortho* nitro	*para* nitro	*o/p* ratio
10	40 °C	5	10.8	5.8	5	1 hr	65	30	35	0.75
11	30 °C	5	10.8	5.8	5	1 hr	75	50	25	1.43
12	20 °C	5	10.8	5.8	5	1 hr	91	77	14	5.69

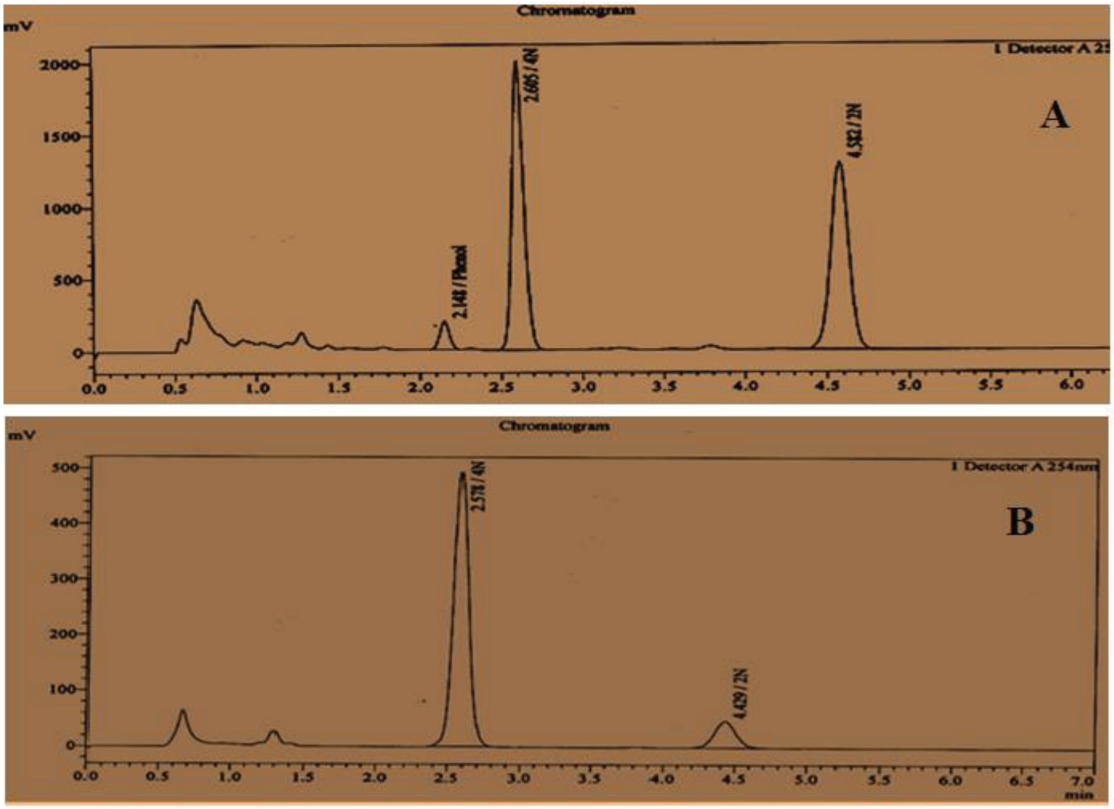

Fig. 2. (A-B): Chromatogram showing nitration of phenol with Dil. HNO_3 (32.5%) for 1 hr at 30°C (A) and 20°C (B)

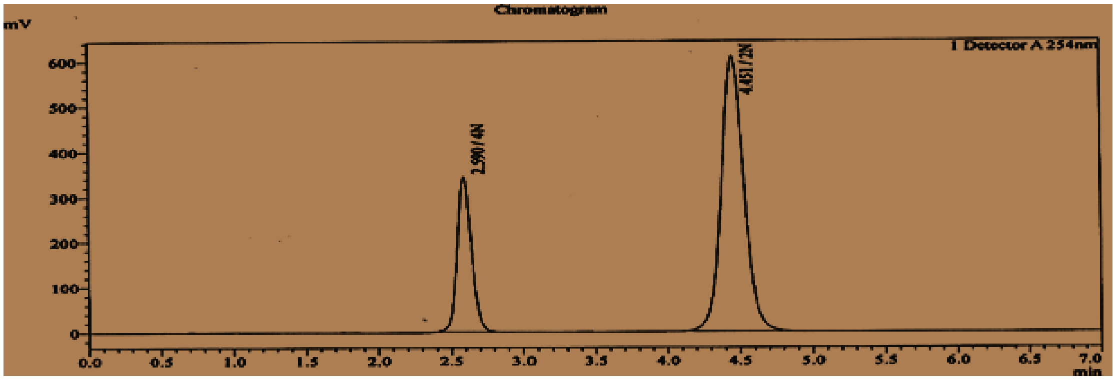

Fig. 3. Chromatogram of high purity analytical standards of *p*-nitrophenol and *o*-nitrophenol

As far as the regioselectivity is concerned, it was found through different experiments 1-12 that by lowering the temperature as well as the strength of nitric acid solution, the p-nitrophenol selectivity was increased because the nitronium ion attacks at the para position of the ring as the para position is far away from the hydroxyl group of ring. While at high temperature and high acid strength, it is very easy for nitronium ion to attack at ortho position of the ring structure. However, this selectivity may also be reversed by the use of catalysts i.e. CTAB, TBAB, NaBr etc as reported by different authors Chhatre et al [1993]. The selectivity of o-nitrophenol synthesis has been reported to be improved by carrying out the reaction under microemulsion conditions. It was suggested that the ratio of o-nitrophenol and p-nitrophenol is increased conversely with the decrease of initial phenol content. The solubility of phenol in the organic phase (isooctane) of microemulsion system is limited, and excess phenol is dissolved in the aqueous phase of microemulsion system. Apparently, the ratio of o-nitrophenol and p-nitrophenol is decreased [41]. It was suggested that the ratio of o-nitrophenol to p-nitrophenol was increased relatively when the concentration of HNO_3 was increased at constant concentration of phenol.

For comparison of results, the synthesis of nitrophenols was also investigated in the presence of smaller quantities of catalysts over substrate (phenol) and substituted phenol (4-chlorophenol); the obtained results are shown in Table 6 and Figures 4-6. In these experiments 13-15, H-β and γ-alumina (sigma Aldrich) catalysts were employed for selectivity and conversion of substrate (phenol) into *o/p* nitrophenols. The experiments were performed with dilute nitric acid and 0.50g catalyst quantity for 80 minutes reaction time at 24°C. It was concluded that there was good agreement for conversion of phenol to nitrophenol isomers with these catalysts. Also, it was noticed that both of the above discussed catalysts have characteristic potential for ortho-nitrophenol selectivity. With H-β catalyst (Table-6), there was 92% conversion with 78% o-nitrophenol and 14% para-nitrophenol selectivity. Similarly, with γ-alumina catalyst, there was overall conversion of 90% with 74% ortho-nitrophenol and 16% para-nitrophenol. Also, it was observed that conversion of substituted phenol into respective isomers was only 81% (Experiment 15, Table 6). No doubt, the catalysts play a very important role in the selectivity of isomers; however, comparing the results of experiments 13-15 with those of other experiments it can easily be understood that results of experiment 12 are much better. So, it can be concluded that raw materials and reaction conditions of experiment 12 are ideal, more environment friendly and more economical. Figure 7 displays the scheme for selected nitration reactions taking place in experiments 2, 6, 9 and 11-15 under various reaction conditions.

3.1 Factors affecting the synthesis and selectivity of nitrophenols

It was monitored through different experimentations that synthesis and selectivity of nitrophenol isomers was highly affected by dilution of nitric acid (Tables 2-5) and also in the presence/absence of catalysts (Table 6). When strength of nitric acid was increased from 32.5% to 65%, the conversion into *o/p* nitrophenol isomer was decreased from 91%, 75% and 65% (Table 5) into 38, 37 and 33 (Table 2) at temperatures of 20°C, 30°C and 40°C, respectively. By dilution of nitric acid from 65% to 50%, 40%, and 32.5%, the conversion of phenol to *o/p* nitrophenol was gradually increased (Tables 2-5). When 65% nitric acid was used for phenol nitration then di and tri-nitrophenol were also

Table 6. Synthesis of nitrophenols from phenol and substituted phenol in the presence of catalyst

Exp. No.	**Substrate Used**	**Temp. of reaction mixture (±2)**	**Wt. of substrate**	**Dil. HNO_3 (32.5%)**	**Catalyst Used**		**Reaction time**	**Yield**	**Selectivity (%)**		
			(g)	(g)	H-β (g)	γ-alumina (g)	(min)	(%)	*ortho* nitro	*para* nitro	*o/p* Ratio
13	Phenol	24°C	5	11	0.50	-	80	92	78	14	5.57
14	Phenol	24°C	5	11	-	0.50	80	90	74	16	4.69
15	4-chloro phenol	24°C	5	11	-	-	80	81	38	43	0.33

[*] **Reaction conditions:** Substrate phenol (5.0 gram); nitric acid (32.5%); temperature of reactions (24°C)

formed along with *o/p* nitrophenols. Experiments (No. 1-12) suggested that the nitric acid solution of 32.5% strength was the most suitable dilution for phenolic nitration as reflected from Figure 3 A & B. Figures 1 and 2 display the comparison between two chromatograms; one chromatogram (Figure 1) shows the effect of concentrated nitric acid on nitration while the other chromatogram (Figure 2) shows the effect of low temperature and dilute nitric acid on nitration of phenol.

3.2 Characterisation by Gas chromatography

The synthesised nitrophenols were characterised by gas chromatography. The *o/p*-nitrophenol standards with phenol substrate were employed with BHT (0.1%) solution as ISS (internal standard solution) for identification of the specific retention times of each isomer. The gas spectra with 32.5% nitric acid strength at 30°C and 20°C are displayed in Figures 8 and 9, respectively and corresponding data are summarised in Tables 7 and 8, respectively.

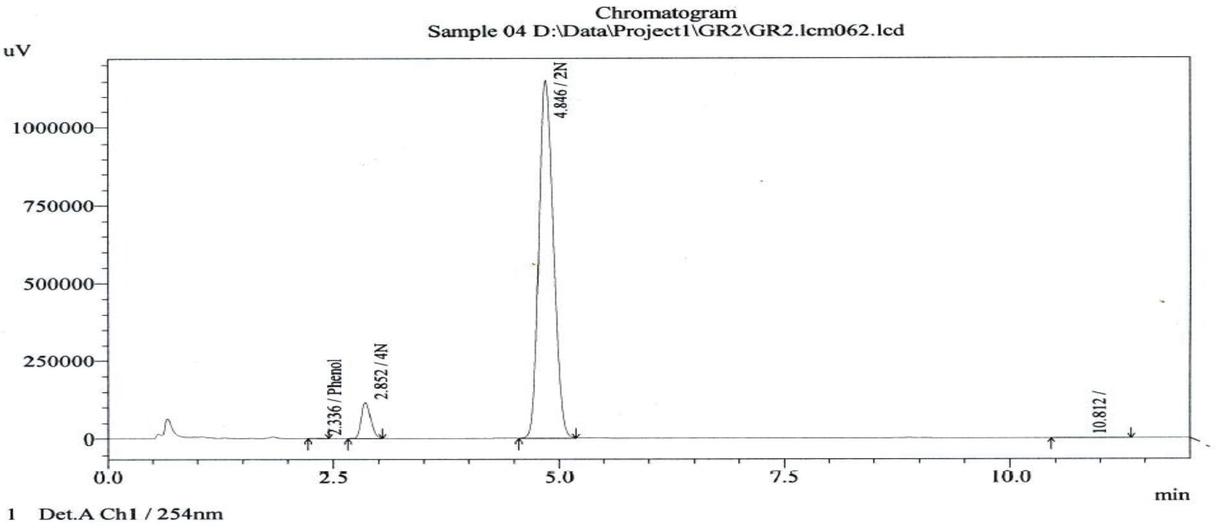

Fig. 4. Chromatogram for phenol nitration with 32.5% HNO_3 at 24°C in the presence of H-β

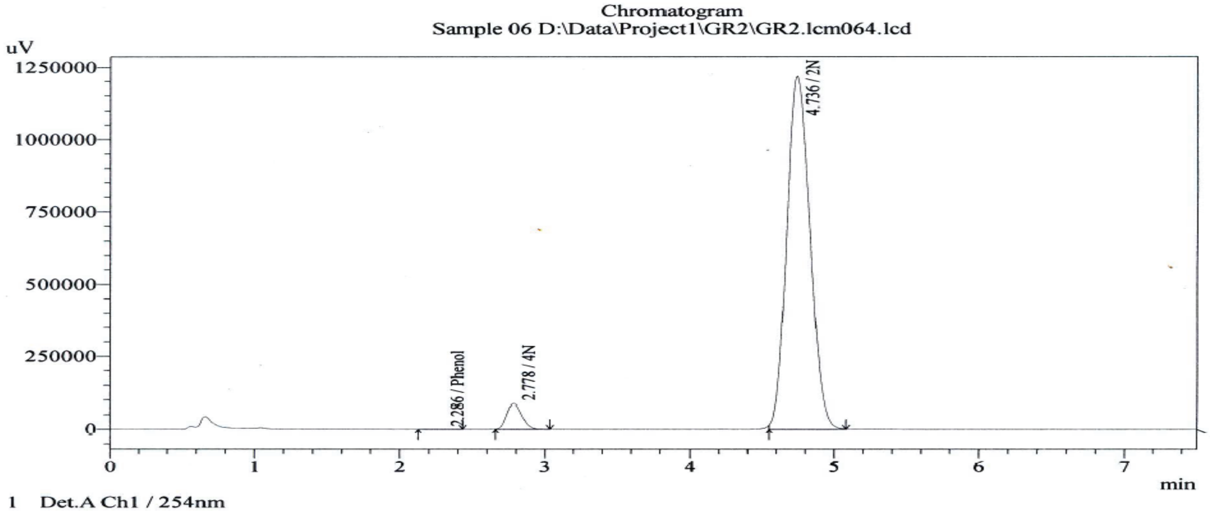

Fig. 5. Chromatogram for phenol nitration with 32.5% HNO_3 at 24°C in the presence of γ-alumina

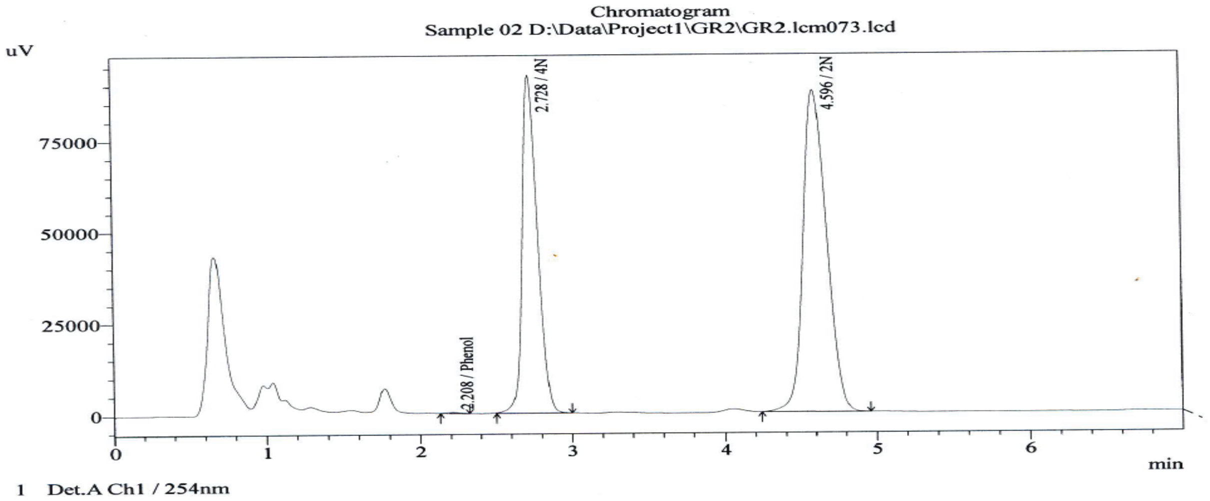

Fig. 6. Chromatogram for nitration of substituted phenol (4-chlorophenol) with 32.5% HNO_3 at 24°

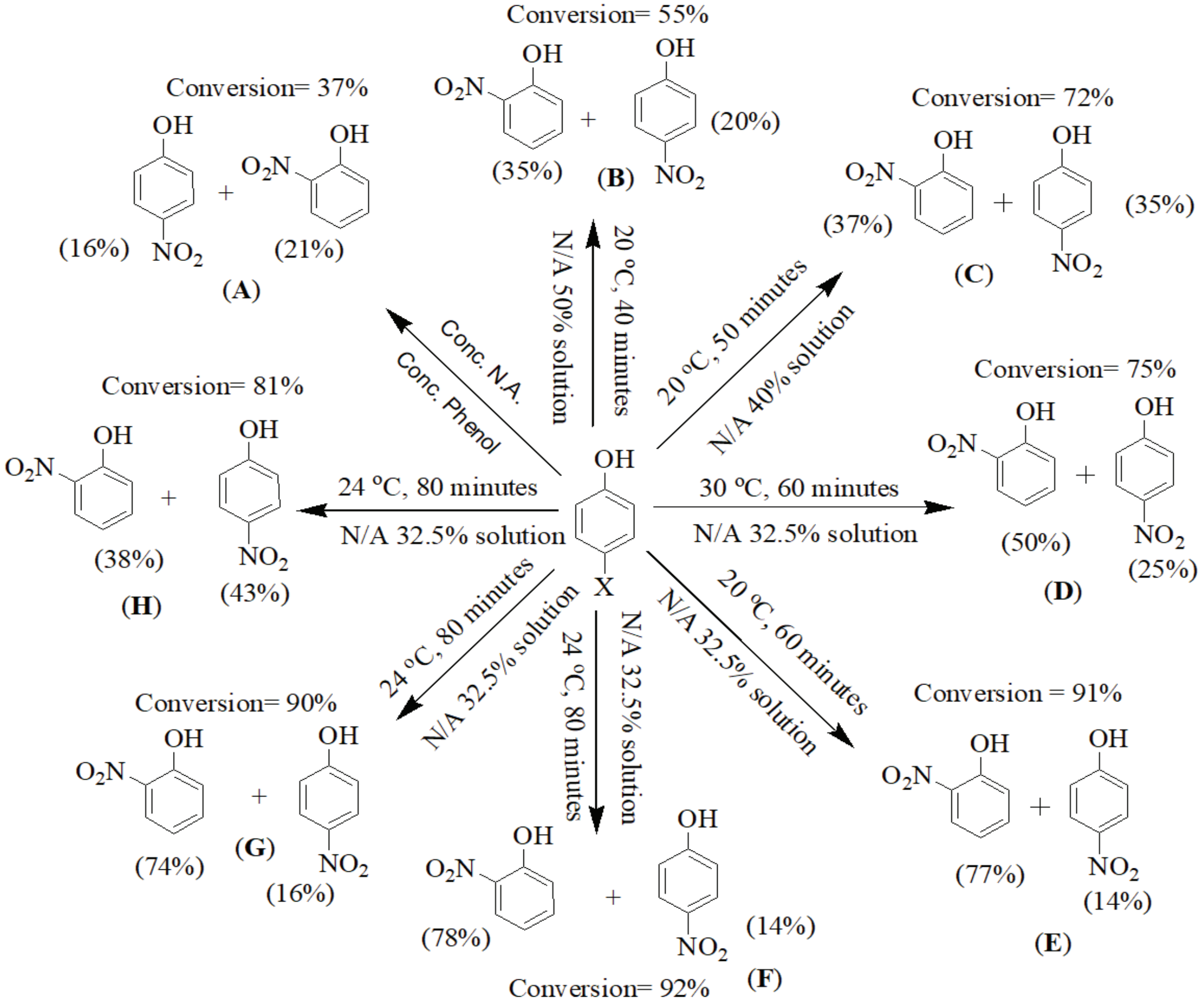

Fig. 7. Selective nitration reactions corresponding to experiments 2(**A**), 6(**B**), 9(**C**), 11(**D**), 12(**E**), 13(**F**), 14(**G**) and 15(**H**); X = H for experiments 1-14; X = Cl for experiment 15

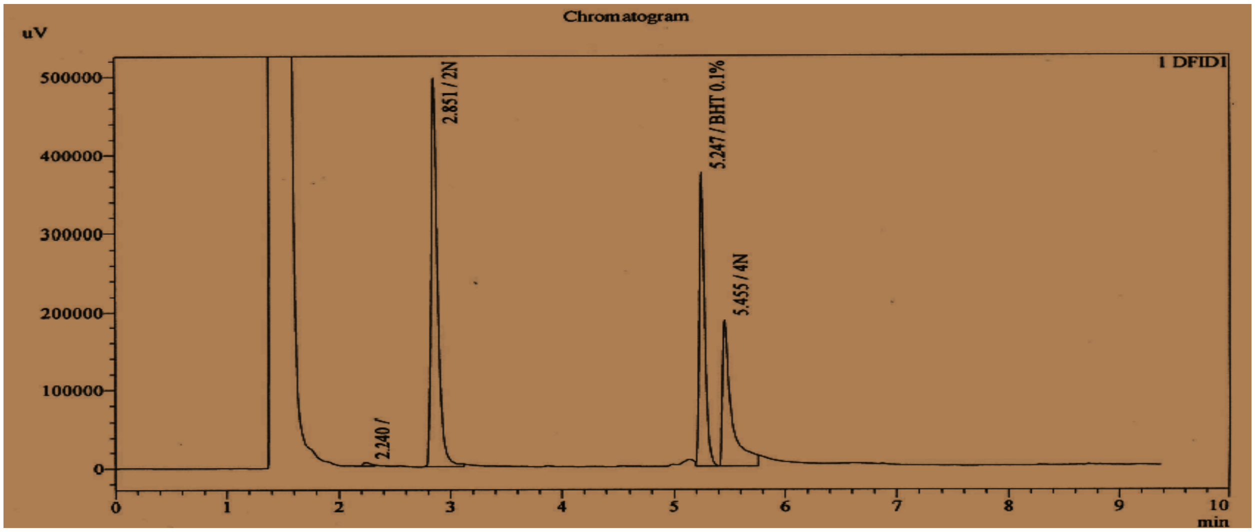

Fig. 8. GC Spectra (segregation peaks) with 32.5% nitric acid strength at 30°C

Table 7. Retention time and peak area (%) with GC capillary column using 32.5% nitric acid at 30°C

Sr. No	Retention time (minutes)	Substance	Peak area (%)
1	2.140	Phenol	7
2	2.851	*o*-nitrophenol	80
3	5.247	ISS (BHT 0.1%)	100
4	5.455	*p*-nitrophenol	13

Table 8. Retention time and peak area (%) with GC capillary column using 32.5% nitric acid at 20°C

Sr.No	Retention time (minutes)	Substance	Peak area (%)
1	2.105	Phenol	10
2	2.860	*o*-nitrophenol	15
3	5.263	ISS (BHT 0.1%)	100
4	5.525	*p*-nitrophenol	75

4. CONCLUSIONS

Phenol and its derivatives can selectively be nitrated into *o/p* nitrophenols by controlling only the physical parameters i.e., dilution of nitric acid, reaction time and reaction temperature. The reaction between 98% phenol and 32.5% nitric acid at a temperature of 20°C (±2°C) required only 1 hour for optimum (91%) yield of nitrophenols with 77% ortho and 14% para selectivity and was found most suitable route for economical production of nitrophenols. The investigated synthetic path is relatively clean and environmentally friendly as it does not involve catalysts and hazardous solvents, like the conventional processes. This process may be adopted for commercial production of nitrophenols which are plant growth regulators and are applied to crops for better agricultural production. The study discourages the use of costly surfactants such as (CTAB, TBAB, H-β and γ-alumina catalysts) which are traditionally used for commercial production of nitrophenols. This synthesis requires the lower number of chemicals, less time and does not involve the advance instruments.

5. CONFLICT OF INTEREST

There is no conflict of interest among the authors.

6. REFERENCES

1. L.G. Nickell, Plant Growth Regulators. *Chemical and Engineering News.* 56(41): 18-34 (1978).
2. G.A. Olah., R. Malhotra and S.C. Narang, *Nitration: methods and mechanisms, in Across Conventional Lines: Selected Papers of George A Olah Volume 2.* 2003, World Scientific. p. 975-979.
3. B.S. Furniss, *Vogel's textbook of practical organic chemistry.* 1989: Pearson Education India.
4. V. Anuradha., P. Srinivas., P. Aparna and J.M. Rao, p-Toluenesulfonic acid catalysed regiospecific nitration of phenols with metal nitrates. *Tetrahedron letters.* 47(28): 4933-4935 (2006).
5. C. Braddock, Award. Novel recyclable catalysts for

atom economic aromatic nitration. *Green Chemistry*. 3(2): G26-G32 (2001).

6. J.H. Clark, *Chemistry of waste minimisation.* 2012: Springer Science & Business Media.
7. K. Holmberg, Organic reactions in microemulsions. *Current opinion in colloid & interface science.* 8(2): 187-196 (2003).
8. K. Smith., K. Fry., M. Butters and B. Nay, Para-selective mononitration of alkylbenzenes under mild conditions by use of benzoyl nitrate in the presence of a zeolite catalyst. *Tetrahedron letters.* 30(39): 5333-5336 (1989).
9. Y.V. Geletii., A.J. Bailey., J.J. Cowan., I.A. Weinstock and C.L. Hill, Highly efficient and stable catalyst for peroxynitrite decomposition. *Canadian Journal of Chemistry.* 79(5-6): 792-794 (2001).
10. A.I. Vogel, *A text-book of practical organic chemistry including qualitative organic analysis.* 2013: Longmans Green And Co; London; New York; Toronto.
11. T. Lopez., J. Moreno., R. Gomez., X. Bokhimi., J. Wang., H. Yee-Madeira., G. Pecchi and P. Reyes, Characterisation of iron-doped titania sol–gel materials. *Journal of Materials Chemistry.* 12(3): 714-718 (2002).
12. Z. Helwani., M. Othman., N. Aziz., J. Kim and W. Fernando, Solid heterogeneous catalysts for transesterification of triglycerides with methanol: a review. *Applied Catalysis A: General.* 363(1-2): 1-10 (2009).
13. R.P. Cheng., S.H. Gellman and W.F. DeGrado, β-Peptides: from structure to function. *Chemical reviews.* 101(10): 3219-3232 (2001).
14. Z. Xinqiang., H. Yantao., S. Xiaolei and W. Yanji, Structure and catalytic performance of H3PW12O40/SiO2 prepared by several methods. *Chinese journal of catalysis.* 28(1): 91-95 (2007).
15. M.A. Zolfigol., F. Shirini and A.G. Chogamarani, Silica chloride/$NaNO_2$ as a novel heterogeneous system for the nitration of phenols under mild conditions. *Phosphorus, Sulfur, and Silicon.* 178(9): 2019-2025 (2003).
16. A. Khder and A. Ahmed, Selective nitration of phenol over nanosized tungsten oxide supported on sulfated SnO2 as a solid acid catalyst. *Applied Catalysis A: General.* 354(1-2): 153-160 (2009).
17. G. Sharma., K.L. Reddy., P.S. Lakshmi and P.R. Krishna, 'In situ'Generated 'HCl'-An Efficient Catalyst for Solvent-Free Hantzsch Reaction at Room Temperature: Synthesis of New Dihydropyridine Glycoconjugates. *Synthesis.* 2006(01): 55-58 (2006).
18. M.A. Bigdeli., M.M. Heravi and G.H. Mahdavinia, Wet cyanuric chloride catalysed simple and efficient synthesis of 14-aryl or alkyl-14-H-dibenzo [a, j] xanthenes. *Catalysis Communications.* 8(11): 1595-1598 (2007).
19. N. Lankaster, liopis-Mestre, V. *Chem. Commun.* 2812 (2003).
20. D. Džober., D. Lankaster., M. Ivanji and S. Topalović, *Prodaja i upravljanje prodajom.* 2006: Clio.
21. K. Amani and F. Maleki, Catalytic effects of some Keggin-type heteropoly acids and polyoxometalates on selective nitration of phenols. *Journal of the Iranian Chemical Society*. 4(2): 238-243 (2007).
22. M.M. Heravi., K. Bakhtiari and F.F. Bamoharram, An efficient and chemoselective synthesis of acylals from aromatic aldehydes and their regeneration, catalysed by 12-molybdophosphoric acid. *Catalysis Communications.* 7(7): 499-501 (2006).
23. D.P. Sawant and S. Halligudi, Alkylation of benzene with α-olefins over zirconia supported 12-silicotungstic acid. *Journal of Molecular Catalysis A: Chemical.* 237(1-2): 137-145 (2005).
24. D. Alberico., M.E. Scott and M. Lautens, Aryl−aryl bond formation by transition-metal-catalysed direct arylation. *Chemical reviews.* 107(1): 174-238 (2007).
25. P.B. Arockiam., C. Bruneau and P.H. Dixneuf, Ruthenium (II)-catalysed C–H bond activation and functionalisation. *Chemical reviews.* 112(11): 5879-5918 (2012).
26. V.S. Thirunavukkarasu., S.I. Kozhushkov and L. Ackermann, C–H nitrogenation and oxygenation by ruthenium catalysis. *Chemical Communications.* 50(1): 29-39 (2014).
27. N. Schröder. *Wencel***-** *Delord J, Glorius FJ Am. in Chem.* Soc. 2012.
28. M. Anand., R.B. Sunoj and H.F. Schaefer III, Non-innocent additives in a palladium (II)-catalysed C–H bond activation reaction: insights into multimetallic active catalysts. *Journal of the American Chemical Society.* 136(15): 5535-5538 (2014).
29. K. Gao., P.-S. Lee., T. Fujita and N. Yoshikai, Cobalt-Catalyzed Hydroarylation of Alkynes through Chelation-Assisted C− H Bond Activation. *Journal of the American Chemical Society.* 132(35): 12249-12251 (2010).
30. M. Harrison., M. Heal and J. Cape, Evaluation of the pathways of tropospheric nitrophenol formation from benzene and phenol using a multiphase model.

Atmospheric Chemistry and Physics. 5(6): 1679-1695 (2005).

31. M.R. Heal., M.A. Harrison and N. Cape, Evaluation of the pathways of tropospheric nitrophenol formation from benzene and phenol using a multiphase model. (2005).
32. T. Umschlag., R. Zellner and H. Herrmann, Laser-based studies of NO 3 radical reactions with selected aromatic compounds in aqueous solution. *Physical Chemistry Chemical Physics.* 4(13): 2975-2982 (2002).
33. B. Barletta., E. Bolzacchini., S. Meinardi., M. Orlandi and B. Rindone, The NO3 radical-mediated liquid phase nitration of phenols with nitrogen dioxide. *Environmental science & technology.* 34(11): 2224-2230 (2000).
34. D. Vione., S. Belmondo and L. Carnino, A kinetic study of phenol nitration and nitrosation with nitrous acid in the dark. *Environmental chemistry letters.* 2(3): 135-139 (2004).
35. D. Vione., V. Maurino., C. Minero., M. Vincenti and E. Pelizzetti, Aromatic photonitration in homogeneous and heterogeneous aqueous systems. *Environmental Science and Pollution Research.* 10(5): 321-324 (2003).
36. B. Yuan., J. Liggio., J. Wentzell., S.-M. Li., H. Stark., J.M. Roberts., J. Gilman., B. Lerner., C. Warneke and R. Li, Secondary formation of nitrated phenols: insights from observations during the Uintah Basin Winter Ozone Study (UBWOS) 2014. *Atmospheric Chemistry and Physics.* 16(4): 2139-2153 (2016).
37. C.B. McPake., C.B. Murray and G. Sandford, Sequential Continuous Flow Processes for the Oxidation of Amines and Azides by using HOF MeCN. *ChemSusChem*. 5(2): 312-319 (2012).
38. J. Jacoway., G.N. Kumar and K.K. Laali, Aromatic nitration with bismuth nitrate in ionic liquids and in molecular solvents: a comparative study of Bi (NO3) 3• 5H2O/[bmim][PF6] and Bi (NO3) 3• 5H2O/1, 2-DCE systems. *Tetrahedron Letters.* 53(50): 6782-6785 (2012).
39. L. Ji., Z. Lin., M. Alcoutlabi and X. Zhang, Recent developments in nanostructured anode materials for rechargeable lithium-ion batteries. *Energy & Environmental Science.* 4(8): 2682-2699 (2011).
40. A. Lalitha and K. Sivakumar, Zeolite H-Y–Supported Copper (II) Nitrate: A simple and effective solid-supported reagent for nitration of phenols and their derivatives. *Synthetic Communications.* 38(11): 1745-1752 (2008).
41. A. Chhatre., R. Joshi and B. Kulkarni, Microemulsions as media for organic synthesis: selective nitration of phenol to ortho-nitrophenol using dilute nitric acid. *Journal of colloid and interface science.* 158(1): 183-187 (1993).