

Mortar-Pestle and Microwave Assisted Regioselective Nitration of Aromatic Compounds in Presence of Certain Group V and VI Metal Salts under Solvent Free Conditions

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ABSTRACT

Solvent-free Mortar-pestle (grinding) and microwave-assisted nitration reactions (MWANR's) underwent smoothly in the presence of group V and VI metal salts with high regio-selectivity for anilides, moderately- and non-activated aromatic compounds. The reactions were conducted under solvent-free conditions, which afforded good to excellent yields. The observed reaction times in MW assisted conditions are in the range of only few minutes.

Keywords: Nitration; Mortar-Pestle; Microwave-Assisted Nitration; Ammonium Molybdate; Potassium Chromate; Sodium Tungstate; Bismuth Nitrate; Sodium Bismuthate

1. Introduction

Nitro aromatic compounds are extensively used as chemical feed stocks for a wide range of materials such as dyes, pharmaceuticals, perfumes, and plastics. Therefore, nitration of organic compounds has been a long, very active and rewarding area of research and is the subject of a large body of literature [1-4]. More specifically the nitration of benzene and toluene is one of the most important routes to substituted aromatics in the production of chemical intermediates. The introduction of a nitro group into an aromatic ring is commonly performed in strongly acidic polar media [3-9] by means of mixed acid (a mixture of nitric acid, sulfuric acid, and water), which leads to excessive acid waste streams and added expense. Separation of the products from the acid is often a difficult and energy consuming process that habitually implies a basic aqueous work-up. Moreover, sulfuric acid is corrosive and is dangerous to transport and handle. The above mentioned disadvantages of the commercial manufacturing process currently used have led to a substantial effort to develop viable alternatives. Quite often either metal nitrates or metal nitrates supported on silica, alumina or clay [10-26] have been used as catalysts in the alternate methods of nitration to overcome the problems of classical nitration. In recent past Bismuth (III) compounds have received particular attention as low toxicity reagents and catalysts for various organic transformations [11,12].

In recent past, increasing attention has been paid to the

'green chemistry' processes that reduce or eliminate the use or generation of hazardous substances [13]. As a result "Atom-economy" of chemical reactions has become one of the most important key concepts of green and sustainable chemistry [14-24]. Synthetic chemists have tried and still are trying to achieve these goals by developing several valuable and distinctive techniques [25] to achieve these goals. Solvent free organic synthesis has been of great interest in recent years [26,27]. Elimination of volatile organic solvents in organic synthesis is one of the most important goals in green chemistry. Solvent free organic reactions make synthesis simpler, save energy and prevent solvent wastes, hazards and toxicity. In this part of our work we aimed at to explore solvent free nitration methods such as (a) grinding the solvent free reactants in a mortar with a pestle [28-34] and (b) conducting micro wave assisted nitration reactions [35-43].

Microwaves are a form of electromagnetic radiation. When molecules with a permanent dipole are placed in an electric field, they become aligned with that field. If the electric field oscillates, then the orientations of the molecules will also change in response to each oscillation. Most microwave ovens operate at 2.45 GHz wavelength, at which oscillations occur 4.9×10^9 times per second. Molecules subjected to this microwave radiation are extremely agitated as they align and realign themselves with the oscillating field, creating an intense internal heat that can escalate as quickly as 10°C per second. Non-polar molecules such as toluene, carbon tetrachloride, diethyl ether and benzene are microwave inac-

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tive, while polar molecules such as DMF, acetonitrile, dichloromethane, ethanol and water are microwave active. This technique proved to be excellent in cases where traditional heating has a low efficiency because of poor heat transmission and, hence, local overheating is a major inconvenience. The most important advantage of microwave-enhanced chemistry is the reduction in the reaction times. Reactions that require hours or days of conventional heating may often be accomplished in minutes under microwave heating. Moreover, reactions are not only faster, but proceed with higher purity and, consequently, higher yields.

The proposed work is taken in three different stages 1) conventional stirring/reflux conditions in solvent phase 2) grinding the reactants in a mortar with a pestle under solvent-free conditions. 3) using microwave irradiation under solvent-free conditions to save energy.

2. Experimental Details

2.1 Materials and Methods

All chemicals used were of analytical grade. All the reagents and substrates used were of laboratory reagent grade, which were obtained from E-Merck, SDfine chemicals or Alfa Aesar. Doubly distilled water (distilled over alkaline KMnO_4 and acid dichromate in an all glass apparatus) was used whenever required. Solvents were HPLC grade and used as such.

Laboratory model microwave reactor (CEM – 908010, bench mate model, 300 W equipped with temperature, pressure and microwave power control units) was used for microwave assisted reactions in this study.

2.2. Typical Experimental Procedure for Nitration of Organic Compounds under Conventional Conditions

The following procedure is a representative reaction. Phenol (0.094 ml, 1 mmol) and metal salt (394 mg, 1 mmol) were taken in chloroform (10 ml). Then 69% HNO_3 (0.063 ml, 1 mmol) was added and reaction mixture was stirred at room temperature for 3hrs, after the completion of reaction as indicated by TLC, the reaction mixture was filtered off and washed with water, organic layer was separated out dried over sodium sulphate and evaporated under vacuum. The crude product was purified by chromatography using ethyl acetate: hexane (3:7) as eluent to get p-nitrophenol m.p 113°C (lit.mp. 114°C) yield 85% as major product.

2.3. Typical Experimental Procedure for Solvent-Free Nitration of Organic Compounds by Grinding the Reactants in a Mortar with Pestle

A mixture of the aromatic compound (1 mmol), few

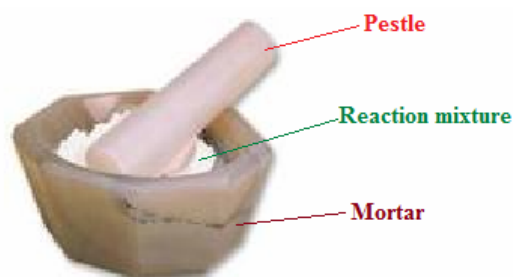
drops of HNO_3 (1 mmol) and metal salt (1 mmol) was ground in a mortar with a pestle at room temperature, till a slurry was observed (**Figure 1**). Progress of the reaction was monitored with TLC. Upon completion of the reaction, the reaction mixture was treated with sodium thiosulfate; the organic layer was diluted with dichloromethane (DCM), and separated from aqueous layer. Crude product was purified by column chromatography using ethyl acetate hexane as eluent. The products were identified by characteristic spectroscopic data ((**Figures S.1 to S.9** in Supplementary Data).

2.4. Typical Experimental Procedure for Microwave Assisted Nitration (MWANR) of Organic Compounds

The microwave reactor used was of CEM make, which was equipped with temperature, pressure and microwave power control units. An oven-dried microwave vial was charged with a mixture containing aromatic compound, metal nitrate and few drops of nitric acid and silica gel slurry, and irradiated in a microwave (power input 140 W) at 150°C for few minutes. After completion of the reaction, as ascertained by TLC, the reaction mixture was treated with sodium thiosulfate; the organic layer was diluted with dichloromethane (DCM), and separated from aqueous layer. Crude product mixture was purified with ethyl acetate DCM mixture. The purity was checked with TLC. The products were identified by characteristic spectroscopic data (**Figures S.1 to S.9** in Supplementary Data)

3. Results & Discussion

Data presented in **Tables 1 to 5** represent certain group - V metal salts (bismuth nitrate (BN), sodium bismuthate (SB)) and certain group - VI B metal salts such as potassium chromate (PCR), ammonium molybdate (AMB) and sodium tungstate (STG)) which are used as catalysts to on-set nitration of non-active and moderately active aromatic



Solvent free Organic Synthesis by Grinding the Reaction mixture in a Mortar with a Pestle

Figure 1. Grinding the reactants in a mortar with a pestle under solvent-free conditions.

Table 1. Microwave assisted ammonium molybdate mediated regio selective nitration of anilides, non-activated and moderately activated organic compounds under mild acid conditions.

S.N	Substrate (AMB catalyst)	Conventional			Solvent Free Grinding			MWANR		
		Time /h	Yield (%)		Time /h	Yield (%)		Time /min	Yield (%)	
			Para	Ortho		Para	Ortho		Para	Ortho
1	Phenol	8	80	10	3.0	76	10	8	82	10
2	4-Chloro Phenol	8	-	85	3.5	-	82	8	-	86
3	4-Nitro Phenol	7	-	84	3.5	-	80	7	-	86
4	4-Amino Phenol	7	-	80	3.5	-	78	7	-	82
5	Aniline	8	74	20	4.0	70	20	8	76	10
6	Acetanilide	8	90	-	4.0	85	-	8	94	-
7	2-Chloro Acetanilide	6	100	-	3.0	92	-	6	100	-
8	4-Chloro Acetanilide	6	-	99	3.0	-	86	6	-	99
9	4-Nitro Acetanilide	6	-	97	3.0	-	90	6	-	98
10	3-Nitro Acetanilide	6	65	25	3.0	62	20	6	68	20
11	4-Methyl Acetanilide	6	-	92	3.0	-	88	6	-	94
12	4-Flouro Acetanilide	6	-	96	3.0	-	90	6	-	96
13	4-Bromo Acetanilide	6	-	94	3.0	-	90	6	-	95
14	4-Hydroxy Acetanilide	6	-	87	3.0	-	82	6	-	88
15	Benzanilide	6	86	12	3.0	82	10	6	87	10
16	2-Chloro Benzanilide	6	86	-	3.0	82	-	6	87	-
17	4-Chloro Benzanilide	6	-	92	3.0	-	88	6	-	92
18	4-Nitro Benzanilide	6	-	88	3.0	-	86	6	-	88
19	Chloro Benzene	6	82	12	3.0	80	10	6	84	12
20	Toluene	6	74	20	3.0	72	15	6	76	15
21	Ethyl Benzene	6	83	12	4.0	80	10	8	84	10

Table 2. Microwave assisted potassium chromate catalyzed regio selective nitration of anilides, non-activated and moderately activated organic compounds under mild acid conditions.

S.N.	Substrate (PCR Catalyst)	Conventional			Solvent Free Grinding			MWANR		
		Time /h	Yield (%)		Time /h	Yield (%)		Time /min	Yield (%)	
			Para	Ortho		Para	Ortho		Para	Ortho
1	Phenol	9	78	09	4.5	76	08	9	80	10
2	4-Chloro Phenol	9	-	81	4.5	-	78	9	-	82
3	4-Nitro Phenol	8	-	80	4.0	-	78	8	-	82
4	4-Amino Phenol	8	-	79	4.0	-	76	8	-	82
5	Aniline	9	83	11	4.5	80	10	9	85	11
6	Acetanilide	9	86	-	4.5	84	-	9	88	-
7	2-Chloro Acetanilide	7	90	-	3.5	88	-	7	92	-
8	4-Chloro Acetanilide	6	-	90	3.0	-	88	6	-	91
9	4-Nitro Acetanilide	7	-	88	3.0	-	86	6	-	90
10	3-Nitro Acetanilide	7	65	25	3.0	62	20	6	68	20
11	4-Methyl Acetanilide	7	-	86	3.0	-	84	6	-	88
12	4-Flouro Acetanilide	7	-	89	3.0	-	86	6	-	89
13	4-Bromo Acetanilide	7	-	85	3.0	-	84	6	-	86
14	4-Hydroxy Acetanilide	7	-	81	3.0	-	78	6	-	82
15	Benzanilide	7	83	14	3.0	80	10	6	84	10
16	2-Chloro Benzanilide	7	82	-	3.0	80	-	6	84	-
17	4-Chloro Benzanilide	7	-	90	3.0	-	88	6	-	92
18	4-Nitro Benzanilide	7	-	86	3.0	-	84	6	-	86
19	Chloro Benzene	7	80	11	3.0	78	10	6	82	10
20	Toluene	7	70	16	3.0	68	15	6	74	12
21	Ethyl Benzene	7	80	09	3.0	78	08	6	82	10

Table 3. Microwave assisted sodium tungstate catalyzed regio selective nitration of anilides, non-activated and moderately activated organic compounds under mild acid conditions.

S.N	Substrate (STG catalyst)	Conventional			Solvent Free Grinding			MWANR		
		Time /h	Yield (%)		Time /h	Yield (%)		Time /min	Yield (%)	
			Para	Ortho		Para	Ortho		Para	Ortho
1	Phenol	7	82	12	4.0	80	12	7	84	10
2	4-Chloro Phenol	7	-	88	4.0	-	82	7	-	89
3	4-Nitro Phenol	6	-	89	3.5	-	84	6	-	90
4	4-Amino Phenol	6	-	86	3.5	-	86	6	-	88
5	Aniline	7	80	11	4.0	78	10	7	82	10
6	Acetanilide	7	90	-	4.0	90	-	7	91	-
7	2-Chloro Acetanilide	5	99	-	3.0	95	-	5	99	-
8	4-Chloro Acetanilide	5	-	98	3.0	-	98	5	-	98
9	4-Nitro Acetanilide	5	-	97	3.0	-	97	5	-	98
10	3-Nitro Acetanilide	6	66	25	3.5	65	20	6	68	25
11	4-Methyl Acetanilide	5	-	94	3.0	-	92	5	-	95
12	4-Flouro Acetanilide	5	-	97	3.0	-	95	5	-	98
13	4-Bromo Acetanilide	5	-	96	3.0	-	94	5	-	97
14	4-Hydroxy Acetanilide	6	-	89	3.5	-	85	6	-	90
15	Benzanilide	5	87	08	3.0	84	08	5	88	08
16	2-Chloro Benzanilide	6	88	-	3.5	86	-	6	90	-
17	4-Chloro Benzanilide	5	-	94	3.0	-	92	5	-	95
18	4-Nitro Benzanilide	6	-	90	3.5	-	79	6	-	92
19	Chloro Benzene	6	83	14	3.5	80	10	6	84	14
20	Toluene	6	76	18	3.5	75	15	6	78	18
21	Ethyl Benzene	5	85	10	3.0	83	10	5	86	10

Table 4. Microwave assisted bismuth nitrate catalyzed regio selective nitration of anilides, non-activated and moderately activated organic compounds under mild acid conditions.

S.N	Substrate (BN Catalyst)	Conventional			Grinding			MWANR		
		Time /h	Yield (%)		Time /h	Yield (%)		Time /min	Yield (%)	
			Para	Ortho		Para	Ortho		Para	Ortho
1	Phenol	8	80	10	4.0	78	09	7	82	12
2	4-Chloro Phenol	8	-	85	4.0	-	81	7	-	88
3	4-Nitro Phenol	7	-	84	3.5	-	80	6	-	89
4	4-Amino Phenol	7	-	80	3.5	-	79	6	-	86
5	Aniline	8	74	20	4.0	73	11	7	80	10
6	Acetanilide	8	90	-	4.0	86	-	7	92	-
7	2-Chloro Acetanilide	6	100	-	3.0	90	-	5	99	-
8	4-Chloro Acetanilide	6	-	99	3.0	-	90	5	-	98
9	4-Nitro Acetanilide	6	-	97	3.0	-	88	5	-	97
10	3-Nitro Acetanilide	6	65	29	3.5	64	25	6	66	25
11	4-Methyl Acetanilide	6	-	92	3.0	-	86	5	-	94
12	4-Flouro Acetanilide	6	-	96	3.0	-	89	5	-	97
13	4-Bromo Acetanilide	6	-	94	3.0	-	85	5	-	96
14	4-Hydroxy Acetanilide	6	-	87	3.5	-	82	6	-	89
15	Benzanilide	6	86	12	3.0	83	14	5	87	08
16	2-Chloro Benzanilide	6	86	-	3.5	82	-	6	88	-
17	4-Chloro Benzanilide	6	-	92	3.0	-	90	5	-	94
18	4-Nitro Benzanilide	6	-	88	3.5	-	86	6	-	90
19	Chloro Benzene	6	82	16	3.5	80	11	6	83	14
20	Toluene	6	74	20	3.5	70	16	6	76	15
21	Ethyl Benzene	6	83	12	3.0	80	09	5	85	10

Table 5. Microwave assisted sodium bismuthate catalyzed regio selective nitration of anilides, non-activated and moderately activated organic compounds under mild acid conditions.

S.N	Substrate (SB Catalyst)	Conventional			Solvent free			MWANR		
		Time /h	Yield (%)		Time /h	Yield (%)		Time /min	Yield (%)	
			Para	Ortho		Para	Ortho		Para	Ortho
1	Phenol	8	80	10	4.0	78	09	7	82	12
2	4-Chloro Phenol	8	-	85	4.0	-	81	7	-	88
3	4-Nitro Phenol	7	-	84	3.5	-	80	6	-	89
4	4-Amino Phenol	7	-	80	3.5	-	79	6	-	86
5	Aniline	8	74	20	4.0	73	11	7	80	10
6	Acetanilide	8	90	-	4.0	86	-	7	90	-
7	2-Chloro Acetanilide	6	100	-	3.0	90	-	5	99	-
8	4-Chloro Acetanilide	6	-	99	3.0	-	90	5	-	98
9	4-Nitro Acetanilide	6	-	97	3.0	-	88	5	-	97
10	3-Nitro Acetanilide	6	65	29	3.5	62	20	6	66	25
11	4-Methyl Acetanilide	6	-	92	3.0	-	86	5	-	94
12	4-Flouro Acetanilide	6	-	96	3.0	-	89	5	-	97
13	4-Bromo Acetanilide	6	-	94	3.0	-	85	5	-	96
14	4-Hydroxy Acetanilide	6	-	87	3.5	-	81	6	-	89
15	Benzanilide	6	86	12	3.0	83	14	5	87	08
16	2-Chloro Benzanilide	6	86	-	3.5	82	-	6	88	-
17	4-Chloro Benzanilide	6	-	92	3.0	-	88	5	-	94
18	4-Nitro Benzanilide	6	-	88	3.5	-	86	6	-	90
19	Chloro Benzene	6	82	16	3.5	80	11	6	83	14
20	Toluene	6	74	20	3.5	70	16	6	76	18
21	Ethyl Benzene	6	83	12	3.0	80	09	5	85	10

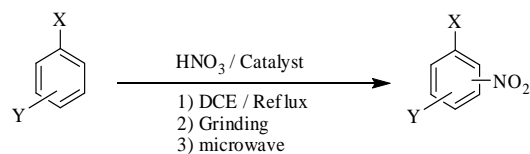
compounds, under conventional and non-conventional conditions. Solvent-free grinding and microwave assisted methods were chosen as non-conventional techniques. Traditional nitration reactions underwent smoothly with moderate to long reaction times (6 to 8 hours) with good yields with good regioselectivity (**Scheme 1**).

However, the active aromatic compounds such as carbonyl compounds underwent within hour affording high yields of the corresponding mono nitro derivatives (**Tables 6 to 10**) with high regioselectivity (**Scheme 1**). The reactions were clean, no attack being observed on the alkyl portion of the ketones. In marked contrast to ordinary nitration using mixed acid, which predominantly lead to meta- substitutions. In the absence of metal salts, the nitration did not proceed.

Solid state reaction occurred more efficiently and more selectively than the corresponding solution phase reactions, since molecules in the crystal are arranged tightly and regularly [34]. In present work grinding technique appears to be superior since it is eco-friendly, high yielding, requires no special apparatus, non-hazardous, simple and convenient. Rate accelerations could be explained due to the conversion of mechanical energy (kinetic energy exerted due to grinding) into heat energy, which becomes driving force for better activation of molecules. The kinetic energy supplied during grinding

can have several effects on a crystalline solid [28-34] including: heating, reduction of particle size (with concomitant increase in surface area and the generation of fresh surfaces), formation of defects and dislocations in crystal lattices, local melting and even phase changes to alternative polymorphs. Collisions between crystals during grinding can also lead to local deformations and potentially melting. Importantly, grinding also provides mass transfer, *i.e.* it is a sort of 'stirring'.

The dramatic acceleration and increased purity and yields of microwave assisted reactions make them attractive to the increased demands in industry and, in particular, for combinatorial drug discovery. In addition to being energy efficient, the possibility of employing milder and less toxic reagents and solvents, or even solvent-free



Catalyst = $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$; K_2CrO_4 ; $\text{Na}_2\text{WO}_4\cdot 2\text{H}_2\text{O}$, BiNaO_3 , BiN_3O_9
 where X = OH, NH_2 , NHCOPh , NHCOCH_3 , CHO, COCH₃, COPh, COOH,
 Y = EWG or EDG

Scheme 1. Nitration of organic compounds catalysed by group V and VI metal salts under solvent free conditions.

Table 6. Microwave Assisted Potassium Chromate catalysed Nitration of Carbonyl and Related Compounds under mild acid conditions.

Entry	Substrate	Product	Conventional	Grinding	MWANR
			R.T (100min)	R.T (60min)	R.T (6min)
			Yield (%)	Yield (%)	Yield (%)
1a	Benzaldehyde	4-Nitro benzaldehyde	81	80	88
1b	4-Hydroxy benzaldehyde	4-Hydroxy-3-nitro benzaldehyde	80	78	86
1c	2,6-Dichloro benzaldehyde	2,6-Dichloro-4-nitro benzaldehyde	79	78	84
1d	4-Chloro benzaldehyde	4-Chloro-3-nitro benzaldehyde	80	78	89
1e	Salicylaldehyde	2-Hydroxy-5-nitro benzaldehyde	76	75	79
1f	3,4-Dimethoxy Benzaldehyde	3,4-Dimethoxy-5-nitro- benzaldehyde	80	78	89
1g	Acetophenone	4-Nitro acetophenone	77	75	86
1h	Benzophenone	4-Nitro benzophenone	80	76	87
1i	4-Hydroxy acetophenone	4-Hydroxy-3-nitro Acetophenone	79	78	88
1j	2,4-Dihydroxy acetophenone	5-Nitro-2,4-dihydroxy Acetophenone	78	75	86
1k	2-Amino benzophenone	2-Amino-5-nitro Benzophenone	83	78	89
1l	Benzoic acid	4-Nitro benzoic acid	81	78	89
1m	2-Chlorobenzoic acid	2-Chloro-4-nitro benzoic acid	82	76	91
1n	Salicylic acid	2-Hydroxy-5-nitro benzoic acid	80	75	90
1o	Benzoyl chloride	4-Nitrobenzoyl chloride	80	76	89
1p	Methylbenzoate	4-Nitromethyl benzoate	83	78	90
1q	Benzamide	4-Nitro Benzamide	81	76	88
1r	<i>p</i> -Toluene sulphonic acid	3-Nitro- <i>p</i> -toluene sulphonic acid	80	74	87
1s	Nitrobenzene	1,3-Dinitro benzene	82	76	86

Table 7. Microwave assisted ammonium molybdate catalysed nitration of carbonyl and related compounds under mild acid conditions.

Entry	Substrate	Product	Conventional	Grinding	MWANR
			R.T (100min)	R.T (60min)	R.T (6min)
			Yield (%)	Yield (%)	Yield (%)
1a	Benzaldehyde	4-Nitro benzaldehyde	85	78	88
1b	4-Hydroxy benzaldehyde	4-Hydroxy-3-nitro benzaldehyde	84	76	86
1c	2,6-Dichloro benzaldehyde	2,6-Dichloro-4-nitro benzaldehyde	82	74	84
d	4-Chloro benzaldehyde	4-Chloro-3-nitro benzaldehyde	86	78	89
1e	Salicylaldehyde	2-Hydroxy-5-nitro benzaldehyde	78	70	80
1f	3,4-Dimethoxy Benzaldehyde	3,4-Dimethoxy-5-nitro- benzaldehyde	84	78	89
1g	Acetophenone	4-Nitro acetophenone	82	75	86
1h	Benzophenone	4-Nitro benzophenone	82	76	87
1i	4-Hydroxy acetophenone	4-Hydroxy-3-nitro Acetophenone	82	76	88
1j	2,4-Dihydroxy acetophenone	5-Nitro-2,4-dihydroxy acetophenone	80	72	86
1k	2-Amino benzophenone	2-Amino-5-nitro benzophenone	84	74	89
1l	Benzoic acid	4-Nitro benzoic acid	86	78	89
1m	2-Chlorobenzoic acid	2-Chloro-4-nitro benzoic acid	88	78	91
1n	Salicylic acid	2-Hydroxy-5-nitro benzoic acid	82	74	88
1o	Benzoyl chloride	4-Nitrobenzoyl chloride	84	75	89
1p	Methylbenzoate	4-Nitromethyl benzoate	86	80	90
1q	Benzamide	4-Nitro benzamide	84	74	88
1r	<i>p</i> -Toluene sulphonic acid	3-Nitro- <i>p</i> -toluene sulphonic acid	82	74	87
1s	Nitrobenzene	1,3-Dinitro benzene	84	78	86

Table 8. Microwave assisted sodium tungstate catalysed nitration of carbonyl and related compounds under mild acid conditions.

Entry	Substrate	Product	Conventional	Grinding	MWANR
			R.T (75min)	R.T (40min)	R.T (4min)
			Yield (%)	Yield (%)	Yield (%)
1a	Benzaldehyde	4-Nitro benzaldehyde	81	76	82
1b	4-Hydroxy benzaldehyde	4-Hydroxy-3-nitro benzaldehyde	80	72	81
1c	2,6-Dichloro benzaldehyde	2,6-Dichloro-4-nitro benzaldehyde	79	70	84
1d	4-Chloro benzaldehyde	4-Chloro-3-nitro benzaldehyde	80	72	85
1e	Salicylaldehyde	2-Hydroxy-5-nitro benzaldehyde	76	70	79
1f	3,4-Dimethoxy Benzaldehyde	3,4-Dimethoxy-5-nitro- benzaldehyde	80	72	82
1g	Acetophenone	4-Nitro acetophenone	77	70	80
1h	Benzophenone	4-Nitro benzophenone	80	72	84
1i	4-Hydroxy acetophenone	4-Hydroxy-3-nitro acetophenone	79	72	81
1j	2,4-Dihydroxy acetophenone	5-Nitro-2,4-dihydroxy acetophenone	78	75	84
1k	2-Amino benzophenone	2-Amino-5-nitro benzophenone	83	78	85
1l	Benzoic acid	4-Nitro benzoic acid	81	76	85
1m	2-Chlorobenzoic acid	2-Chloro-4-nitro benzoic acid	82	78	85
1n	Salicylic acid	2-Hydroxy-5-nitro benzoic acid	80	76	83
1o	Benzoyl chloride	4-Nitrobenzoyl chloride	80	75	85
1p	Methylbenzoate	4-Nitromethyl benzoate	83	78	86
1q	Benzamide	4-Nitro benzamide	81	76	82
1r	p-Toluene sulphonic acid	3-Nitro-p-toluene sulphonic acid	80	75	82
1s	Nitrobenzene	1,3-Dinitro benzene	82	78	86

Table 9. Microwave assisted sodium bismuthate catalysed nitration of carbonyl and related compounds under mild acid conditions.

Entry	Substrate	Product	Conventional	Grinding	MWANR
			R.T (75min)	R.T (40min)	R.T (4min)
			Yield (%)	Yield (%)	Yield (%)
1a	Benzaldehyde	4-Nitro benzaldehyde	82	75	88
1b	4-Hydroxy benzaldehyde	4-Hydroxy-3-nitro benzaldehyde	78	72	86
1c	2,6-Dichloro benzaldehyde	2,6-Dichloro-4-nitro benzaldehyde	84	78	84
1d	4-Chloro benzaldehyde	4-Chloro-3-nitro benzaldehyde	86	76	89
1e	Salicylaldehyde	2-Hydroxy-5-nitro benzaldehyde	75	70	79
1f	3,4-Dimethoxy Benzaldehyde	3,4-Dimethoxy-5-nitro- benzaldehyde	82	75	89
1g	Acetophenone	4-Nitro acetophenone	78	72	86
1h	Benzophenone	4-Nitro benzophenone	82	75	87
1i	4-Hydroxy acetophenone	4-Hydroxy-3-nitro acetophenone	80	74	88
1j	2,4-Dihydroxy acetophenone	5-Nitro-2,4-dihydroxy acetophenone	78	72	86
1k	2-Amino benzophenone	2-Amino-5-nitro benzophenone	82	75	89
1l	Benzoic acid	4-Nitro benzoic acid	81	74	89
1m	2-Chlorobenzoic acid	2-Chloro-4-nitro benzoic acid	82	75	91
1n	Salicylic acid	2-Hydroxy-5-nitro benzoic acid	80	72	90
1o	Benzoyl chloride	4-Nitrobenzoyl chloride	82	75	89
1p	Methylbenzoate	4-Nitromethyl benzoate	81	74	90
1q	Benzamide	4-Nitro benzamide	80	74	88
1r	p-Toluene sulphonic acid	3-Nitro-p-toluene sulphonic acid	84	78	87
1s	Nitrobenzene	1,3-Dinitro benzene	82	75	86

Table 10. Microwave assisted bismuth nitrate catalysed nitration of carbonyl and related compounds under mild acid conditions.

Entry	Substrate	Product	Conventional	Grinding	MWANR
			R.T (90min)	R.T (60min)	R.T (6min)
			Yield (%)	Yield (%)	Yield (%)
1a	Benzaldehyde	4-Nitro benzaldehyde	88	80	90
1b	4-Hydroxy benzaldehyde	4-Hydroxy-3-nitro benzaldehyde	86	78	88
1c	2,6-Dichloro benzaldehyde	2,6-Dichloro-4-nitro benzaldehyde	84	86	88
1d	4-Chloro benzaldehyde	4-Chloro-3-nitro benzaldehyde	89	80	90
1e	Salicylaldehyde	2-Hydroxy-5-nitro benzaldehyde	79	72	82
1f	3,4-Dimethoxy Benzaldehyde	3,4-Dimethoxy-5-nitro- benzaldehyde	89	80	90
1g	Acetophenone	4-Nitro acetophenone	86	78	88
1h	Benzophenone	4-Nitro benzophenone	87	79	88
1i	4-Hydroxy acetophenone	4-Hydroxy-3-nitro acetophenone	88	80	90
1j	2,4-Dihydroxy acetophenone	5-Nitro-2,4-dihydroxy acetophenone	86	78	88
1k	2-Amino benzophenone	2-Amino-5-nitro benzophenone	89	80	90
1l	Benzoic acid	4-Nitro benzoic acid	89	80	90
1m	2-Chlorobenzoic acid	2-Chloro-4-nitro benzoic acid	91	81	92
1n	Salicylic acid	2-Hydroxy-5-nitro benzoic acid	90	81	92
1o	Benzoyl chloride	4-Nitrobenzoyl chloride	89	80	90
1p	Methylbenzoate	4-Nitromethyl benzoate	90	81	92
1q	Benzamide	4-Nitro benzamide	88	80	90
1r	p-Toluene sulphonic acid	3-Nitro-p-toluene sulphonic acid	87	79	88
1s	Nitrobenzene	1,3-Dinitro benzene	86	78	87

systems, offers a further advantage of this heating technology. In order to check for a possible specific (not purely thermal) microwave effect, CEM model benchmate microwave oven was used [44]. Under conventional conditions an increase in temperature increases only fraction of activated molecules. At any given time temperature on the surface of the reaction vessel is greater than the internal temperature, and heat energy is transferred to the reaction mixture via thermal conduction. However, in MW assisted reactions microwave radiation is directly transferred to reactant species. Reaction mixture absorbs microwave energy, which probably causes super heating followed by the formation of bulk activation molecules (Figures 2). Regarding the goal of a general interpretation of specific microwave effects, we can assume that these will be favorable if the polarity of the transition state is increased during the reaction (microwave materials interactions are enhanced with polarity) [45]. This should therefore be the case for reactions in which the transition state (TS) is more polar than the ground state (GS) (**Figure 3**) [46,47].

4. Conclusion

In conclusion, we have demonstrated that mortar-pestle (grinding) and micro wave-assisted nitration reactions (MWANR's) underwent smoothly in the presence of

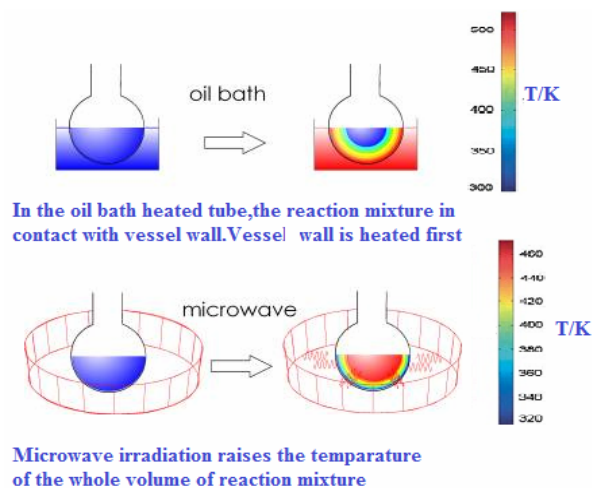


Figure 2. Microwave Assisted Nitration (MWANR) of Organic compounds.

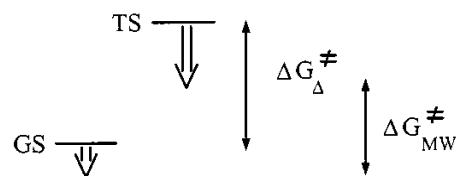


Figure 3. Relative stabilization of transition state (TS) and ground state (GS) by dipole-dipole interactions with electromagnetic field if TS is more polar than GS.

group V and VI metal salts for the first time. These methods have several advantages over existing methods such as region-selectivity, high yields, simple procedure, and short reaction times. It is noteworthy to mention here that if the ortho position is engaged, p-nitro derivatives are obtained while o-nitro derivatives are obtained when para position is engaged. In case of MWANR of aromatic carbonyl and related compounds the effect of microwaves is extremely high. The observed reaction times are in the range of 3 - 5 minutes.

5. Electronic Supplementary Material

Figures S.1 to S.9 in Supplementary Data indicate certain spectroscopic results of nitration products.

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Supplementary Data

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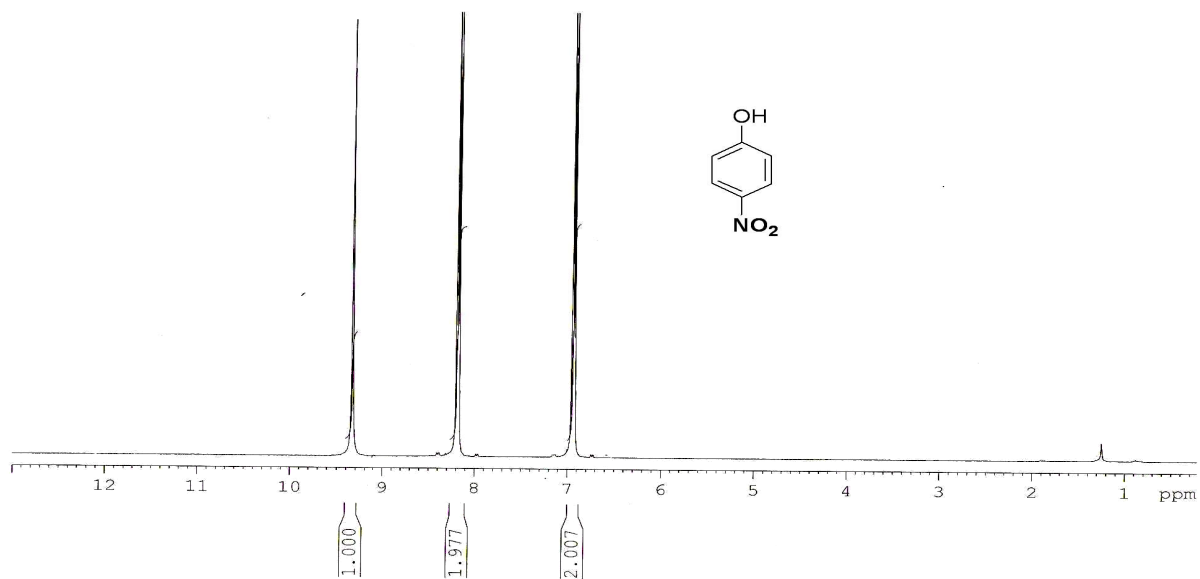


Figure S.1. HNMR Spectrum of 4-nitro phenol.

P1112-1008 N-008

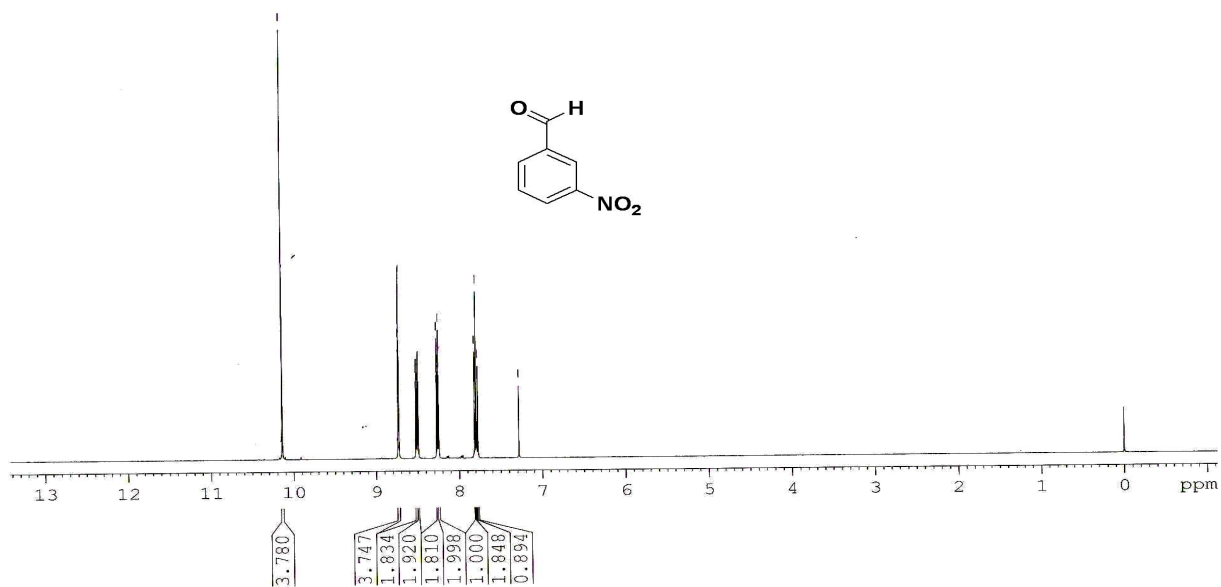


Figure S.2. HNMR Spectrum of 3-nitro benzaldehyde.

P1112-1008 N-009

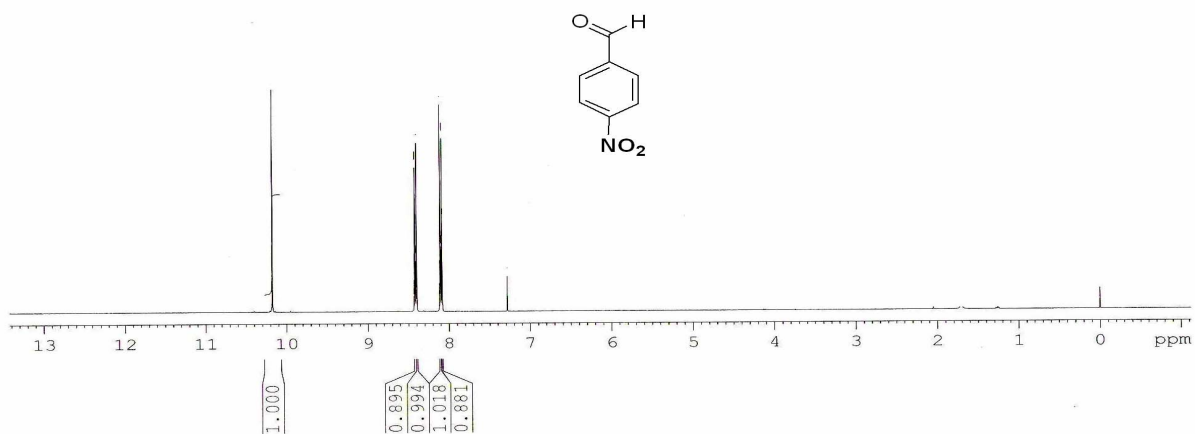


Figure S.3. HNMR Spectrum of 4-nitro benzaldehyde.

P1112-1008 N-020

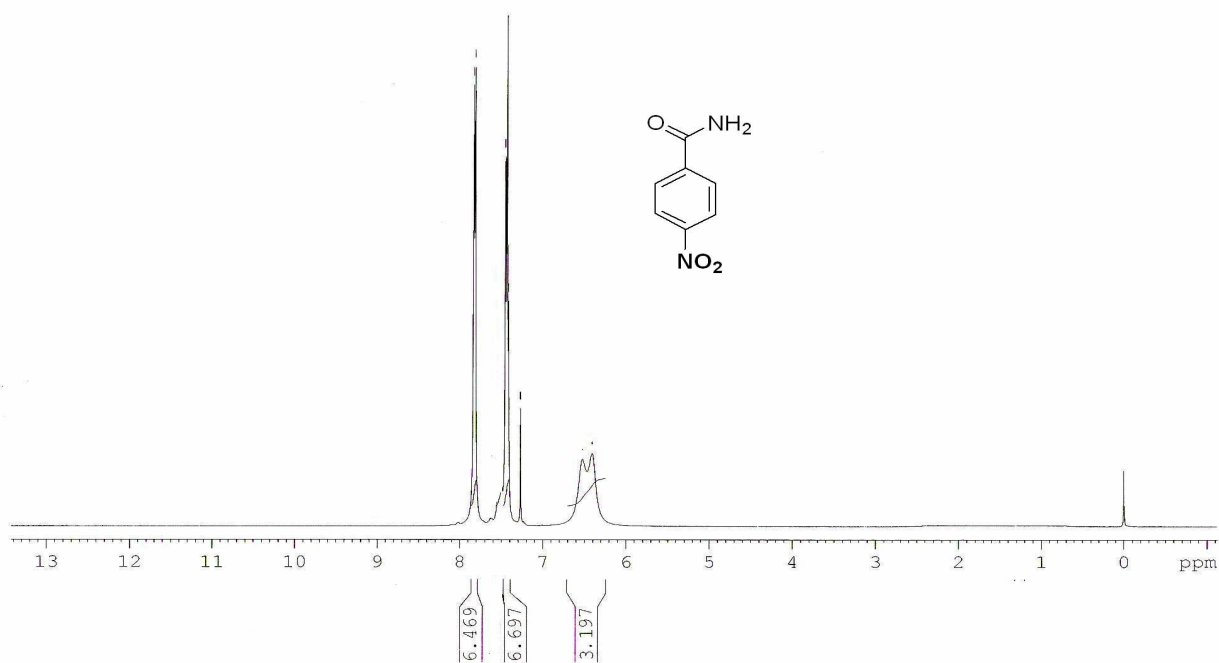


Figure S.4. HNMR Spectrum of 4-nitro benzamide.

P1112-1008 N-023

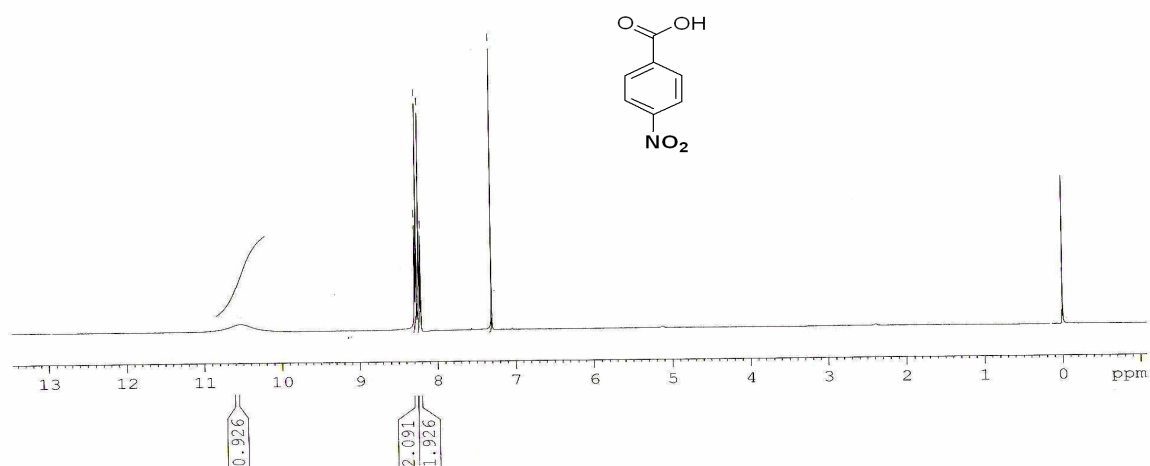


Figure S.5. HNMR Spectrum of 4-nitro benzoic acid.

P1112-1008 N-001

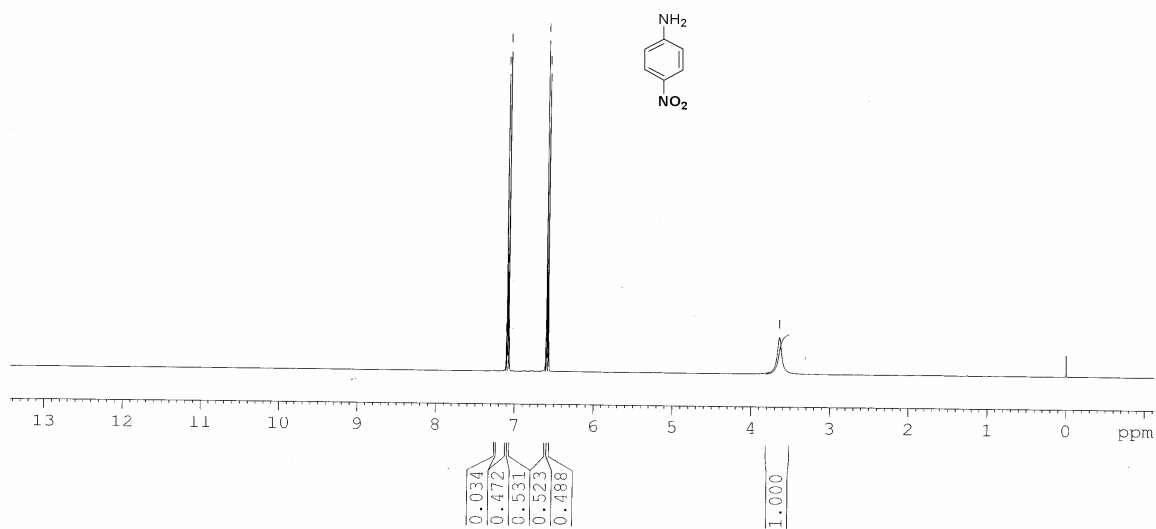


Figure S.6. HNMR Spectrum of 4-nitro aniline.

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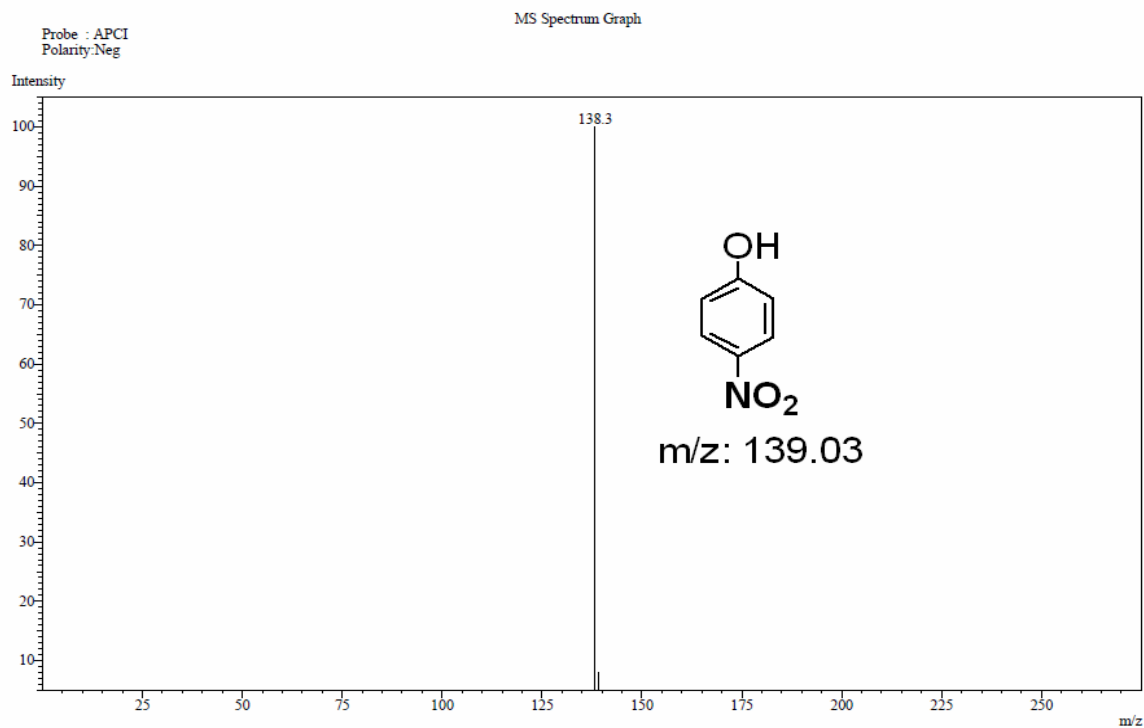


Figure S.7. Mass Spectrum of 4-nitro phenol.

SAPALA ORGANICS PVT LTD

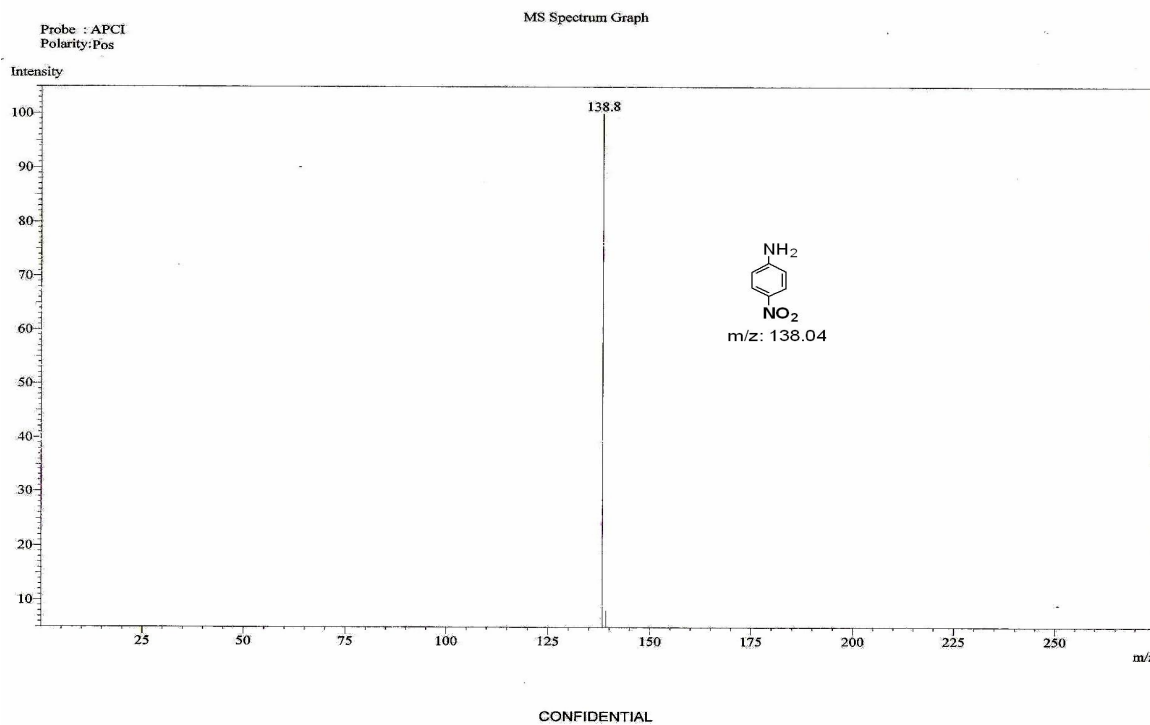


Figure S.8. Mass Spectrum of 4-nitro aniline.

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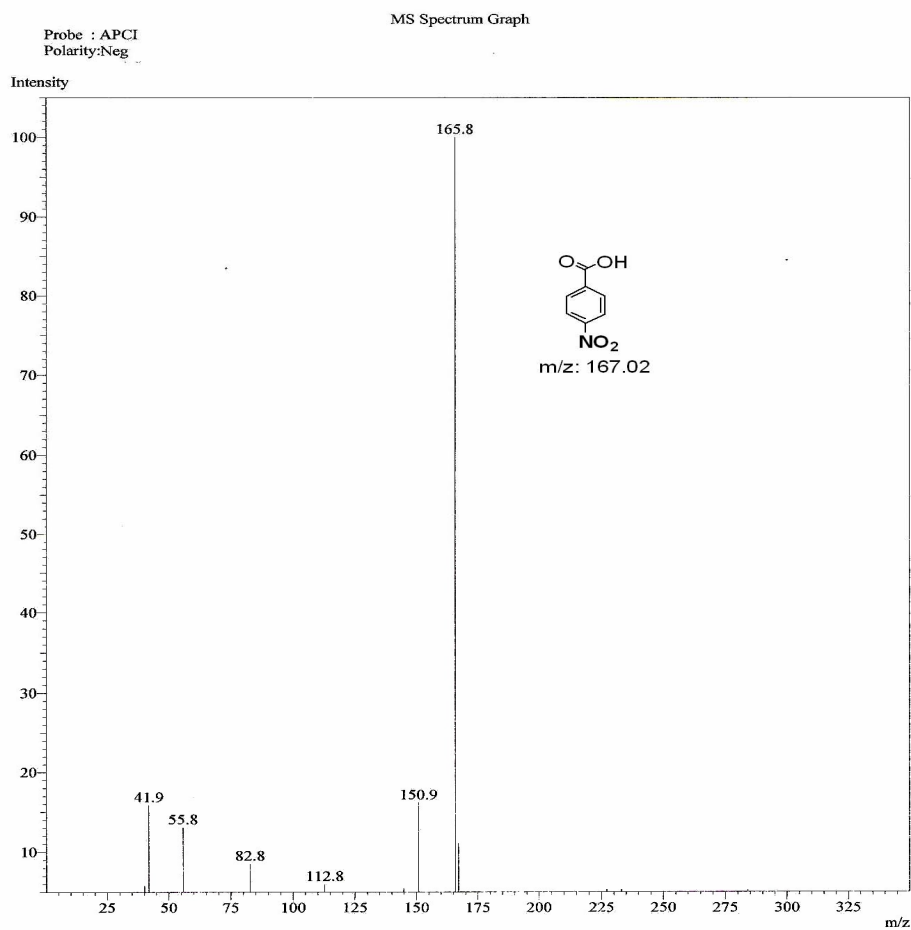


Figure S.9. Mass Spectrum of 4-nitro benzoic acid.