Oxidative Chlorination of Aromatic Compounds in Aqueous Media

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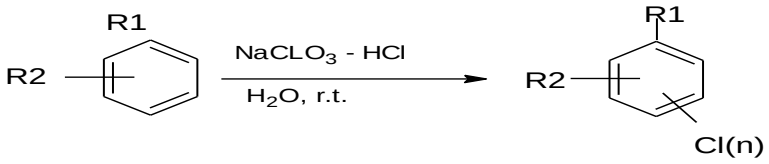
Abstract- An efficient method for the synthesis of chlorinated arenes is disclosed. The method involves the use of NaClO3 as oxidant and HCl as chlorinating agent in aqueous medium under mild conditions to chlorinate the aromatic compounds in good to excellent yields (75-96%). The reagent system is efficient, organic solvent-free and easy to handle.

Index Terms- Halogenation, Chlorination, Arenes, Sodium Chlorate, Aqueous medium, Oxidative Chlorination.

I. INTRODUCTION

Chlorination of arenes is a prominent organic reaction with wide laboratory use and industrial applications. The introduction of chlorine onto aromatic ring is an important synthetic transformation because chlorinated compounds are recognized as versatile starting materials and additives in the production of high quality insecticides, fungicides, herbicides, dyes, pharmaceutical etc. therefore, there are several known methods available in the literature that have been developed for the chlorination of aromatic compounds. A common method to introduce chlorine atom into organic substrates, whether they are free radical processes or polar additions to olefinic groups or electrophillic substitution on aromatic ones, involves the use of molecular chlorine which has high vapor pressure or are gasses at room temperature and 1 atm pressure. The dihalogens are corrosive, poisonous, and can be dangerous to handle, methods that require their transport and manipulation are difficult. Generally, the chlorination of arenes can be accomplished by using chlorinating agents such as t-butyl hypochlorite in presence of zeolites, metal chloride-H_2O_2 in acid aqueous medium, m-chloroperbenzoic acid/HCl/DMF. Sulfuryl chloride, acetyl chloride in presence of ceric ammonium nitrate, $SnCl_4$/$Pb(OAC)_4$, HCl-H_2O_2 under microwave conditions, N-chlorosuccinimide, etc.

Analyzing these literature data, one can see that the most promising example of chlorination include a one pot synthesis where elemental chlorine is generated in-situ by the use of haloacids in the presence of an oxidizing agent. Oxidative chlorination has emerged as an environmentally-benign process via the in-situ formation of molecular chlorine from the oxidation of chloride with suitable oxidants. Therefore, mono and biphasic oxidative process based on generating the chlorine from concentrated HCl in presence of oxidant has been developed. Chlorination of aromatic rings by HCl using H_2O_2, t-BHP and sodium perborate as oxidizing agents have already been attempted. However, these methods involved the use of organic solvents which have serious environmental impacts and also having disadvantages of long duration, high temperature and use of catalyst. Also, recently Podgorsek et al. have used HCl/H_2O_2 to transform aryliodides into aryliodine (III) dichlorides in the presence of trifluoroethanol which act not only as reaction medium but also as activator of hydrogen peroxide for oxidation of HCl into molecular chlorine. But, trifluoroethanol which is used in this system is toxic and harmful solvent and is recommended to avoid the long term contact with skin. One of the key principles of green chemistry is the elimination of solvent in chemical processes or the replacement of hazardous solvent with environmentally-benign solvents. Water is the most promising solvent because it is readily available, non-flammable, non-toxic and could offer the easy separation of reagents or catalysts from many organic products. Earlier the chlorination of substituted acetanilide (aromatic compounds) in acid-aqueous medium was carried out by jerzy et al. by using metal chloride-hydrogen peroxide system. The drawbacks of this method are use of large amount of acid (HNO_3) and chlorinating agent (NaCl) with poor yield and selectivity. Our present method overcomes all above limitations. Also, $NaClO_3$ is low cost, easy to handle than H_2O_2, t-BHP and has better solubility in water than sodium perborate, thus, making it a useful reagent for carrying out reaction in water. By considering these advantages of $NaClO_3$ it has been successfully employed as a convenient oxidant for oxidative chlorination in water. Also a perusal of the literature revealed that earlier Moon et al. have used $NaClO_3$/HCl in aqueous acetic acid to chlorinate activated arenes and α-position of ketones. The earlier system has limitations of use of acetic acid as solvent, poor selectivity, low yield and long reaction time (20 h). However, our present method is free from use of organic solvent, have low reaction time (upto 3 h) and good yield (75-96%) of chlorinated product (Scheme 1).



R^1 = OH, NH_2, NHCOMe, NHCOPh, CHO, COOH, CN
R^2 = H, OH, Cl, Br, NO_2

Scheme 1. Oxidative chlorination of aromatic substrates in water

Objective:

Chlorination is an important reaction of organic chemistry because of wide variety of uses of chloro-substituted organic compounds in fine chemicals and pharmaceutical intermediates. Therefore, large number of methods are available in the prior art for chlorination of organic compounds. However, most of these methods involved the use of organic solvents which have serious environmental impacts and also having disadvantages of long duration, high temperature and use of catalyst, so there is need for the development of a method which is efficient, free from organic solvent, cost effective and easy to handle. Also, one of the key principles of green chemistry is the elimination of solvent in chemical processes or the replacement of hazardous solvent with environmentally-benign solvents. Water is the most promising solvent because it is readily available, non-flammable, non-toxic and could offer the easy separation of reagents or catalysts from many organic products. Therefore, in our present study, a method has been developed for the chlorination of aromatic compounds using $NaClO_3$/HCl in aqueous medium. The present system uses the water as reaction media and also provides the chlorinated aromatic products in good to high yields (75-96%) under the mild conditions. Also, this system is cost effective, efficient and easy to handle.

II. Materials and Methods

Materials and instrumentation

Starting materials and other reagents were obtained from commercial suppliers and used without further purification. Granular and scaly substrates were crushed to fine powder using mortar and pestle. HPLC analyses were concluded using Waters 2695 instrument with PDA detector, column C_{18} (250 mm x 4.6 mm x 5 µ), solvent system 70% CH_3OH + 30% H_2O,flow rate 1 Ml/min. HPLC purity is reported by area% NMR spectra were obtained in DMSO and $CDCl_3$ on a Bruker Avance II 400 NMR spectrometer; the chemical shifts were reported in ppm, ^1H NMR (relative to TMS referenced as 0.00 ppm) and ^{13}C NMR (relative to DMSO referenced as 39.50 ppm). GC.MS analyses were carried out using Agilent GC (Model 5893) with Chemstation software; column-HP5-MS, 30 m x 0.25 mm x 0.25 micron; detector- mass range- 14 amu to 650 amu; flow- 2 ml/min (constant flow); injector temp- 270 ˚C; detector temp-300 ˚C; injection volume-1 microliter of 5 % solution in methanol. Mass spectra were recorded on Micromass uattro Micro APCI ion source. Quattro Micro API triple quadrupole MS equipped with a standard APCI ion source.

General procedure for the chlorination of aromatic compounds

Monochlorination:

An aqueous solution of $NaClO_3$ (0.005 mol) in water (8-10 Ml) was added to a fine powder of aromatic substrate (0.01 mol) taken in a 10-0 ml round-bottom flask equipped with a magnetic stirring bar at room temperature. After that HCl (2 ml) was added dropwise for 15 minutes. The reaction completion was monitored with thin layer chromatography (TLC). After completion of the reaction, 5 ml of water was added to separate the product;product was filtered, and dried in oven. The structures of products were confirmed by ^1H NMR, mass spectra and were compared with authentic samples.

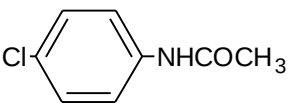
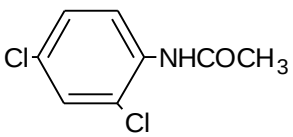
Dichlorination

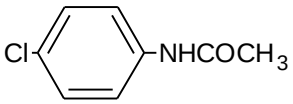
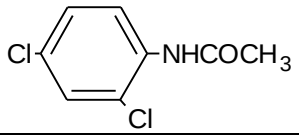
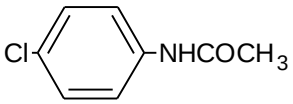
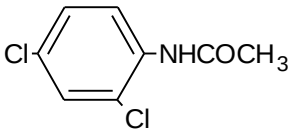
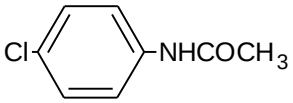
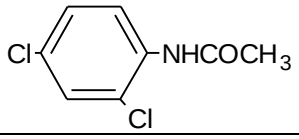
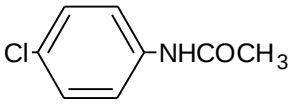
Process for the synthesis of dichlorinated product was same as that given in monochlorination, except 0.01 mol of $NaClO_3$ and 4 ml of HCl was used wrt 0.01 mol of substrate.

Results and Discussion:

In present work, the chlorination was first tried on 4-chloroacetanilide by using $NaClO_3$ (0.01 mol),NaCl (0.03 mol) and H_2SO_4 (1 mL) in water (Table 1, Entry 1). The chlorinating reagent is thus generated in-situ in the reaction mixture by oxidizing NaCl using $NaClO_3$ as an oxidizing agent in acidic medium.

Table 1. Screening of optimum reaction conditions for oxychlorination using different reagent systems in aqueous media.

Entr Entry	Reagent System	Reaction Conditions	Starting Material	Product	Yield[a] (%)
1.	NaCl/$NaClO_3$/ H_2SO_4[b]	2 h at r.t.			87

2.	HCl/$NaClO_3$[c]	2 h at r.t.			95
3.	HCl/$NaIO_4$[d]	4 h at r.t.			16
4.	HCl/H_2O_2[e]	4 h at r.t.			22
5.	HCl/ $NaBO_3.3H_2O$[t]	4 h at r.t.		-------	---

[a] Isolated yields
[b] Conditions: Substrate, 0.01 mol;NaCl, 0.03 mol; $NaClO_3$, 0.005 mol; H_2SO_4, 1 Ml;H_2O, 8Ml
[c] Conditions: Substrate, 0.01 mol;$NaClO_3$, 0.005 mol; HCl, 2 Ml;H_2O, 8Ml
[d] Conditions: Substrate, 0.01 mol;$NalO_4$, 0.005 mol; HCl, 2 Ml;H_2O, 8Ml
[e] Conditions: Substrate, 0.01 mol;HCl.2Ml;H_2O_2, 3Ml; H_2O.8Ml
[f] Conditions: Substrate, 0.01 mol;$NaBO_3.3H_2O$,0.01 mol; HCl, 2 Ml; H_2O, 8 ML

Later on, HCl was tried instead of NaCl and H_2SO_4, which acts as a chlorine source as well makes the reaction mixture acidic (Table 1, Entry 2). Results of table 1 show that the chlorinated product obtained in better yield when HCl was used in place of NaCl and H_2SO_4. Chlorination was also tried in water bu using various oxidants such as sodium periodate. H_2O_2 (30%) and sodium perborate (Table 1). The results suggest that very little amount of product is formed in case of $NaIO_4$ (13%) and H_2O_2 (21%) and no product was formed with sodium perborate. Therefore, it is found experimentally that sodium chlorate and HCl gave the best results in aqueous medium.

Effect of surfactant:

Ionic and non ionic surfactants were used to study the effect of surfactant on the yield and reaction time. It was observed that surfactant improves the distersion of aromatic substrates in water and also improves the texture of product but there was no effect on yield and reaction time.

Effect of concentration of HCl

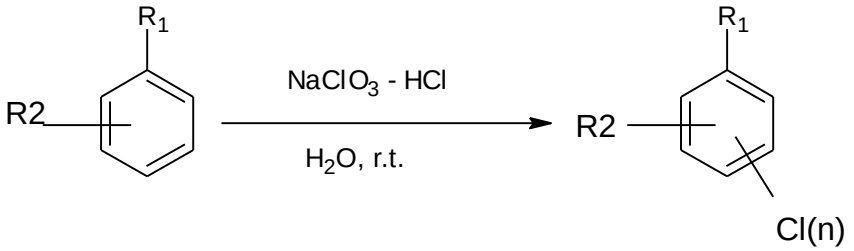
The amount of HCl from 2 ml to 1.5 ml, the yield of 2,4-dichloroacetanilide get decreased upto 70%. Also, depression in melting point reveals that underchlorinated product was formed due to decrease in the amount of HCl. On further decreasing the amount of HCl from 1.5 ml to 1 ml, no product was obtained. It was observed that the yield and menting point of 2.4-dichloroacetanilide became stagnant on increasing the amount of HCl from 2 ml to 2.4 ml. hence, the ideal amount of HCl is 2 ml.

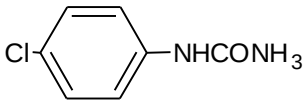
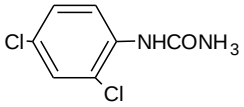
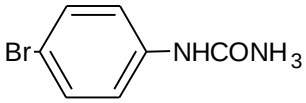
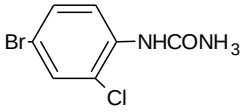
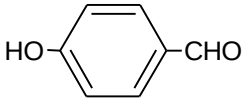
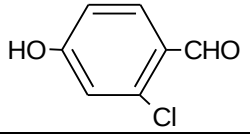
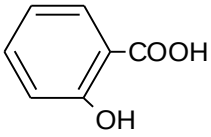
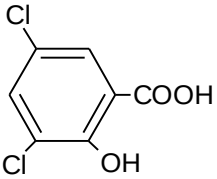
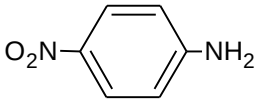
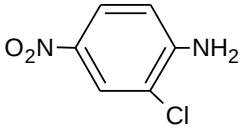
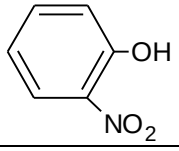
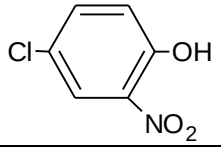
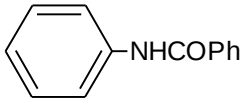
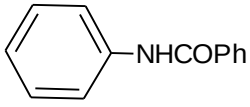
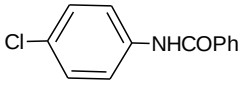
Effect of concentration of $NaClO_3$

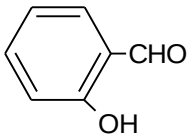
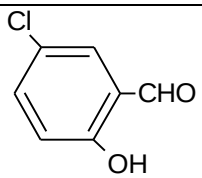
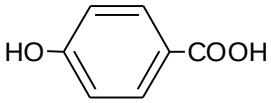
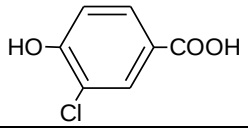
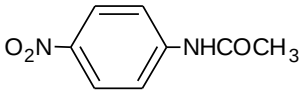
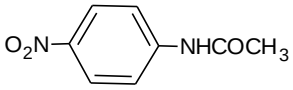
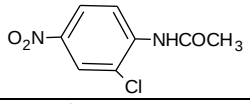
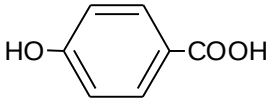
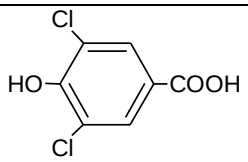
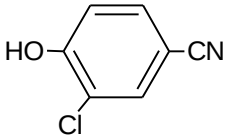
Decreasing in sodium chlorate ($NaClO_3$) concentration from 0.005 mol to 0.0033 mol resulted in decrease of the yield of 2,4-dichloroacetanilide. Melting point of product was also not within the desired range due to underchlorination of 4-chloroacetanilide in the presence of 0.0033 mol of $NaClO_3$. While increasing the concentration of $NaClO_3$ from 0.005 to 0.015 mol, there was no effect on these both parameters. Therefore, it was concluded experimentally that 2 Ml of HCl and 0.005 mol of $NaClO_3$ afforded the best yield of chlorinated product. The dichlorination can also be performed by increasing the amount of HCl along with the amount of $NaClO_3$.

To show the general application of the method, it was applied to a variety of aromatic compounds to give corresponding chlorinated products in good yields. The results of this investigation are tabulated in table 2. It is evident from the results that all aromatic substrates were chlorinated within 1.5-3.0 h in good yields. 2,4-dichloroacetanilide (Table 2, Entry 1) was obtained in best yield (95%) from 4-chloroacetanilide within 2 h at room temperature and having an HPLC purity of 96.8% (Table 3, Entry 1). 4-Nitroacetanilide showed no reactivity up to 4 h at room temperature (25˚C) while at slightly higher temperature (45˚C), 2-chloro-4-nitroacetanilide was obtained in good yield (75%) within 3 h of reaction (Table 2, Entry 3,4). Earlier Jerzy et al. has synthesized 2-chloro-4-nitroacetanilide from 4-nitroacetanilide in poor yield (32%) along with fornation of 2,6-dichloro-4-nitroacetanilide (68%) at 50˚C.3-chloro-4-hydroxybenzaldehyde which is used as an intermediate in organic syntheses was obtained in 86% yield (Table 1, Entry 13) with an HPLC purity of 98.38%. 5-chlorosalicylic acid (Table 1, Entry 14) which is used as intermediate of pesticide, medicine and dyes was obtained in 82% within 1.5 h at room temperature from salicylic acid. This compound was also synthesized by H.A.Muathen using $SnCl_4/Pb(OAc)_4$ in ethyl acetate in 77% yield.

Table 2. Oxidative chlorination of aromatic compounds in aqueous medium.



Entry	Starting Material	Reaction Conditions	Product	Yield[a] (%)	Mp °C (lit.)
1.		2 h, r.t.		95[b]	145(143-146)
2.		2 h, r.t.		93[b]	152(151-152)
3.		4 h, r.t.		82[b]	130(128-132)
4.		2 h, r.t.		83[c]	222(221-224)
5.		2 h, r.t.		90[b]	107(107-110)
6.		2 h, r.t.		84[b]	83(85-87)
7.		3 h, r.t.	--------	Complex Mixture	---
8..		1.5h, r.t.		93[b]	190(192-193)

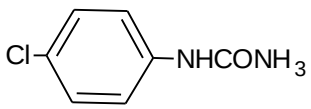
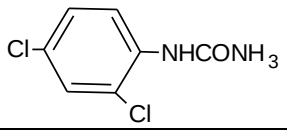
9.		1.5h, r.t.		85[b]	100(99-103)
10.		1.5h, r.t.		82[b]	166(168-170)
11.		4 h, r.t.	----	---	---
12.		3 h, 45 °C		75[b]	138(138-139)
13.		4 h, r.t.		86[c]	264(264-266)
14.		1.5h, r.t.		82[b]	149(150)

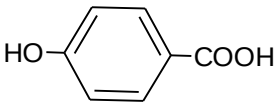
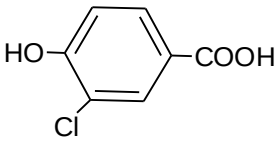
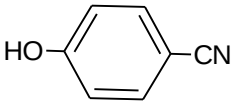
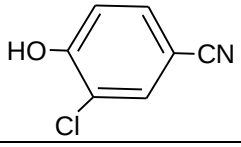
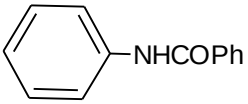
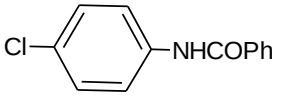
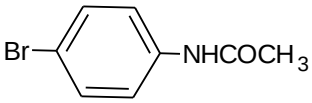
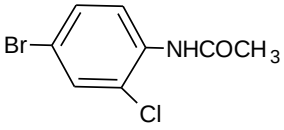
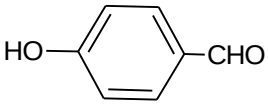
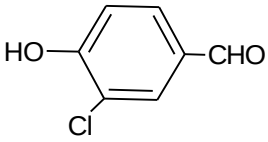
[a] Isolated yields
[b] Monochlorination: Substrate, 0.01 mol; $NaClO_3$, 0.005 mol; HCl, 2mL; H_2O, 8-10 mL.
[c] Dichlorination: Substrate, 0.01 mol; $NaCLO_3$, 0.01 mol; HCl, 4mL; H_2O, 8-10 mL.

In case of benzanilide, a mixture of substrate and product (underchlorinated product) was formed at room temperature within 3 h (Table 1, Entry 7) but at slightly higher temperature (40˚C), para-substituted product was obtained within 1.5 h (Table 1. Entry 8) with an HPLC purity of 95.23% which is an industrially-important compound.

3-chloro-4-hydroxybenzoic acid (Table 1, Entry 10) was obtained in 82 % yield and purity of 98.01%. Mukhopadhyay et al. prepred this compound with poor conversion (53%) at 45˚C in 4 h using H_2O_2 and aqueous HCl. An important pharmaceutical intermediate 3-chloro-4-hydroxybenzonitrile (Table 1. Entry 14) was prepared from 4-hydroxybenzonitrile within 1.5 h in 82% yield (98.8% purity by HPLC). 3,5-dichloro 4-hydroxybenzonitrile was synthesized from the dichlorination of 4-hydroxybenzonitrile in 85% yield at room temperature within 2 h, which is widely used as a pesticide. Highly activated aromatic compounds like aniline and phenol undergo oxidation rather than chlorination by this method. However, the substituted anilines and phenols were chlorinated in good yields at room temperature.

Table 3. Selectivity of products in the chlorination of various aromatic substrates

Entry	Substrate	Product	Yield[a] (%)	Product Purity[b] (%)	
				Main Product	Others
1.			97	96.90	3.10

2.			83	98.30	1.70
3.			85	98.50	1.50
4.			93	97	3.00
5.			95	96.35	3.65
6.			82	98.20	1.80

[a] Isolated yield
[b] Purity determined by HPLC

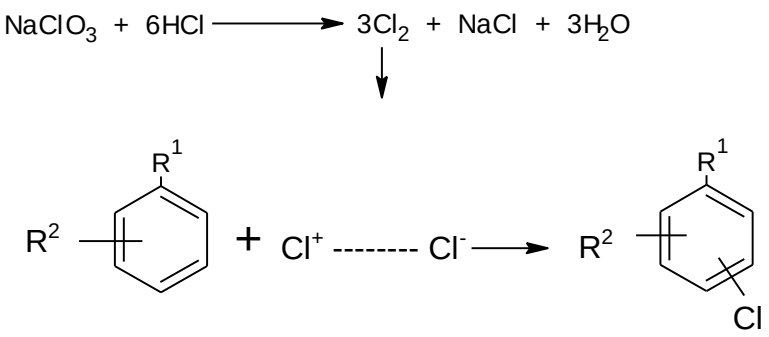
Encouraged by the results of activated arenes, same system, i.e.,$NaClO_3$/HCl using water as reaction media was also tried for the chlorination of deactivated arenes such as benzoic acid and nitrobenzene. However, the present system failed to chlorinate the deactivated aromatic compounds at 60˚C and 80˚C even after 20 h. Therefore, this system can be used to chlorinate activated arenes in good yield under mild conditions.

Mechanism:

It is evident from literature that in case of oxychlorination it is possible to oxidize the chloride under acidic conditions to obtain HOCl and/or Cl_2; these oxidized species then react in-situ with substrates such as arenes to yield chlorinated product. Therefore, under certain conditions either Cl_2 or HOCl can be main chlorinating agents or both can act concurrently to yield chlorinated product. However, it has been reported recently that at very low pH (Ph < 3) Cl_2 serves as an active chlorinating agent while at higher pH (3-6.5) HOCl is the active chlorinating species.

$$Cl_2 + H_2O \underset{\text{at pH <3}}{\overset{\text{at pH 3 - 6.5}}{\rightleftharpoons}} HOCl + H^+ + Cl^- \quad (1)$$

The Ph of our reaction medium is very low (Ph < 1) so the active chlorinating species may be Cl_2 rather than HOCl. Also, from rate data and relative reactivities studies it has been identified that Cl_2 is much more reactive chlorinating agent than HOCl and addition of large amount of acid or lowering the Ph of the reaction will suppress the hydrolysis of Cl_2 to HOCl (eq.1). Therefore, it can be concluded that $NaClO_3$ will oxidize the chloride to form chlorine and due to higher reactivity of Cl_2 it will serve as an active chlorinating species which furnishes the Cl^+ ion to accomplish a rapid chlorination of substrates (Scheme 2). Theoretically, one equivalent of chlorate generates three equivalents of chlorinating agent; however, this was not accorded precisely by experimental results.



Scheme 2. Plausible Mechanism of Oxidative Chlorination

Characterization of Representative Chlorinated Aromatic Compounds:

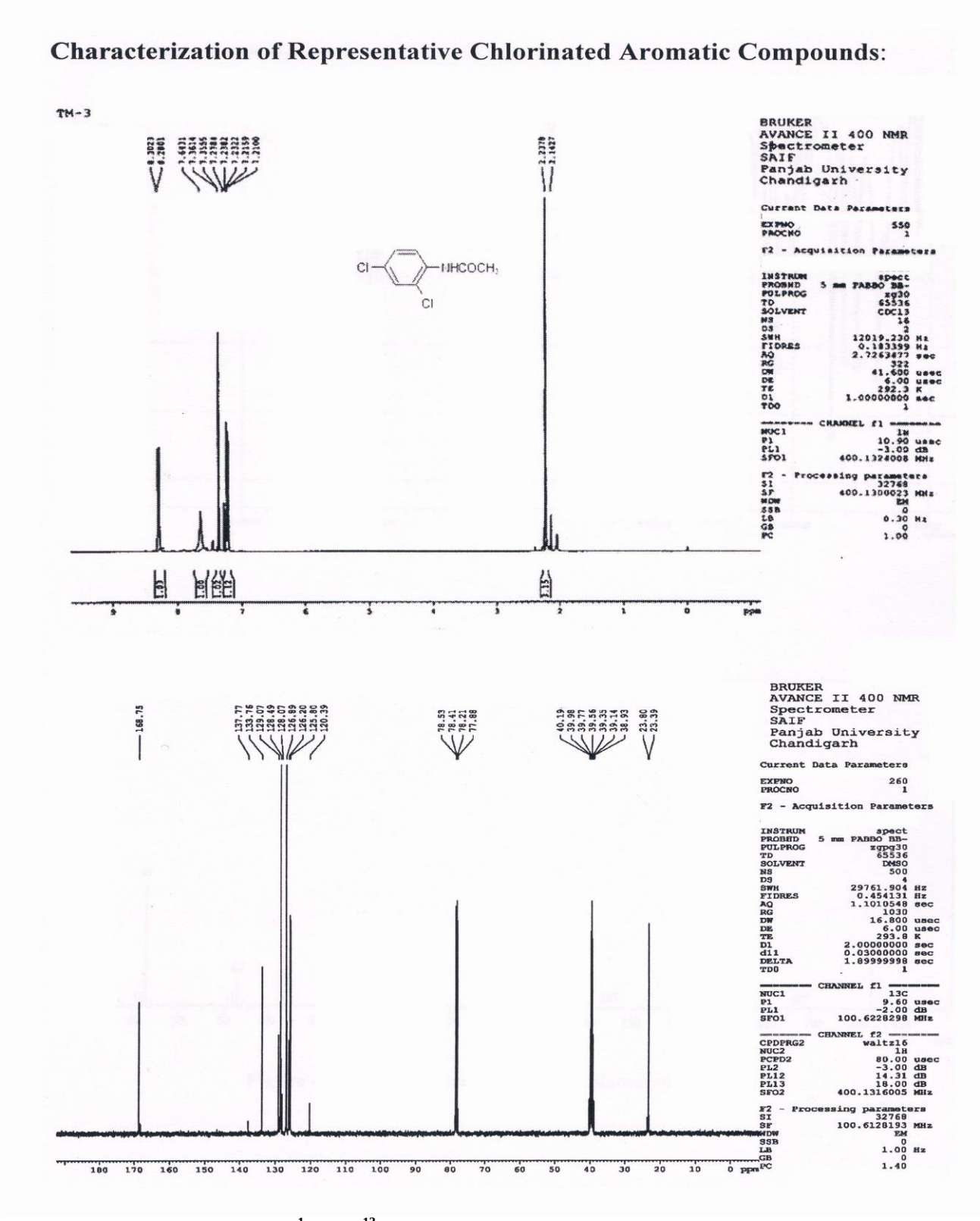


Figure 1. ^{1}H and ^{13}C-NMR spectra of 2,4-dichloroacetanilide (1)

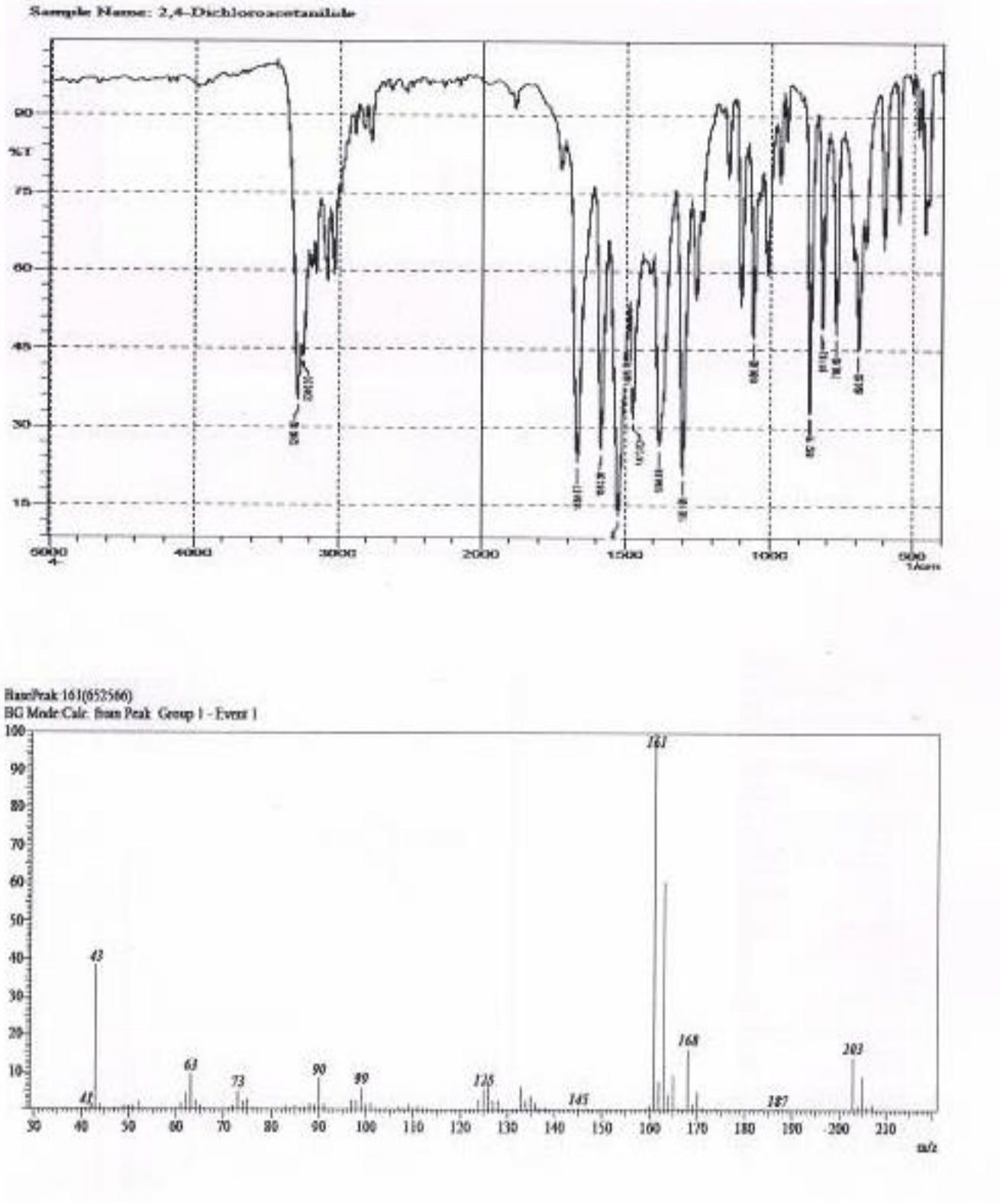
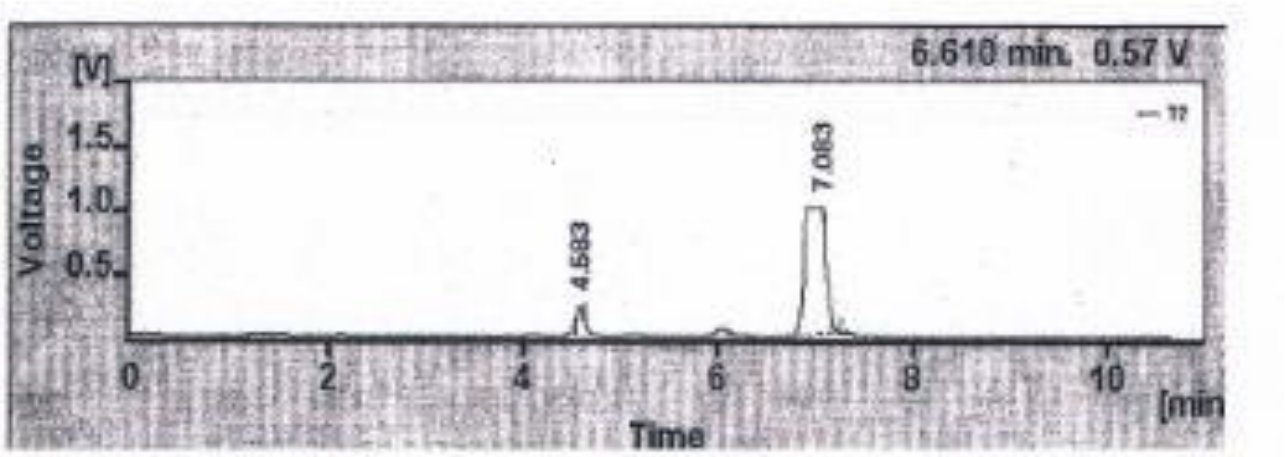


Figure 2. IR and mass spectra of 2,4-dichloroacetanilide (1)



Result Table

	Retention Time [min]	Area [mV s]	Height [mV]	Area [%]	Height [%]	Width [min]
1	4.583	366.441	101.983	2.2	9.4	0.07
2	7.063	14798.283	980.399	97.8	90.6	0.24
	Total	15167.724	1082.324	100.0	100.0	

Figure 3. HPLC chromatogram of 2,4-dichloroacetanilide (1)

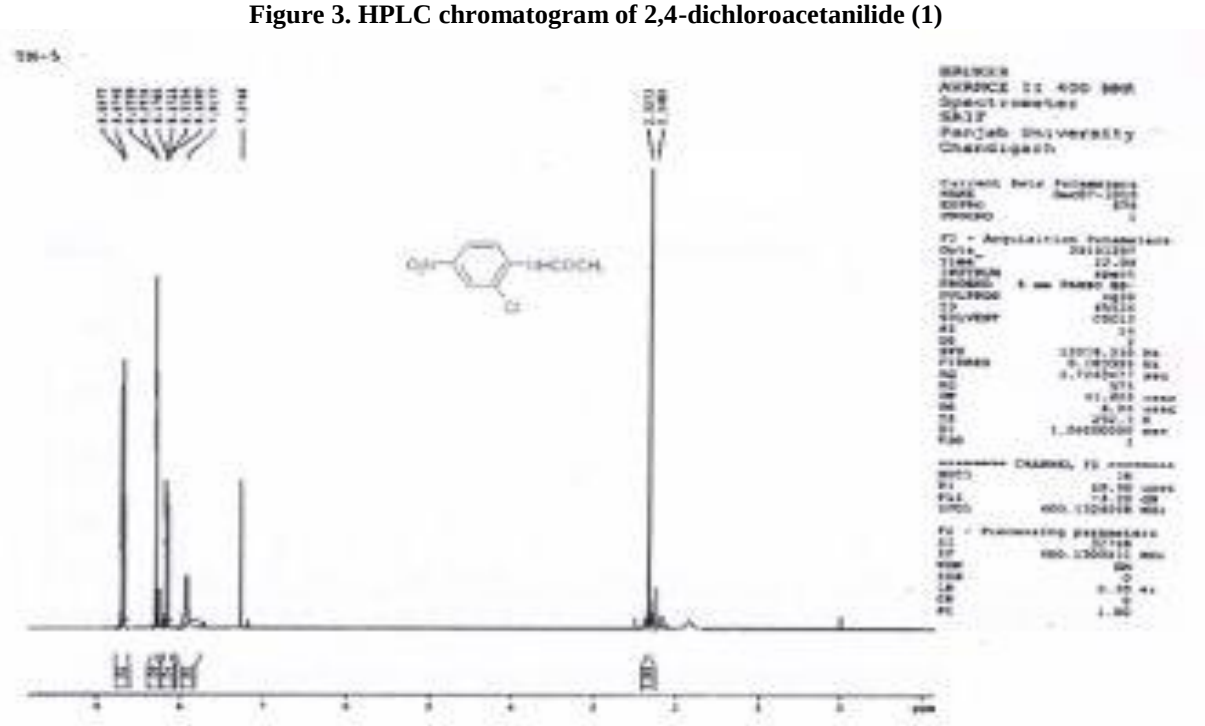


Figure 4. ^{1}H-NMR spectra of 2-chloro-4-nitroacetanilide (4)

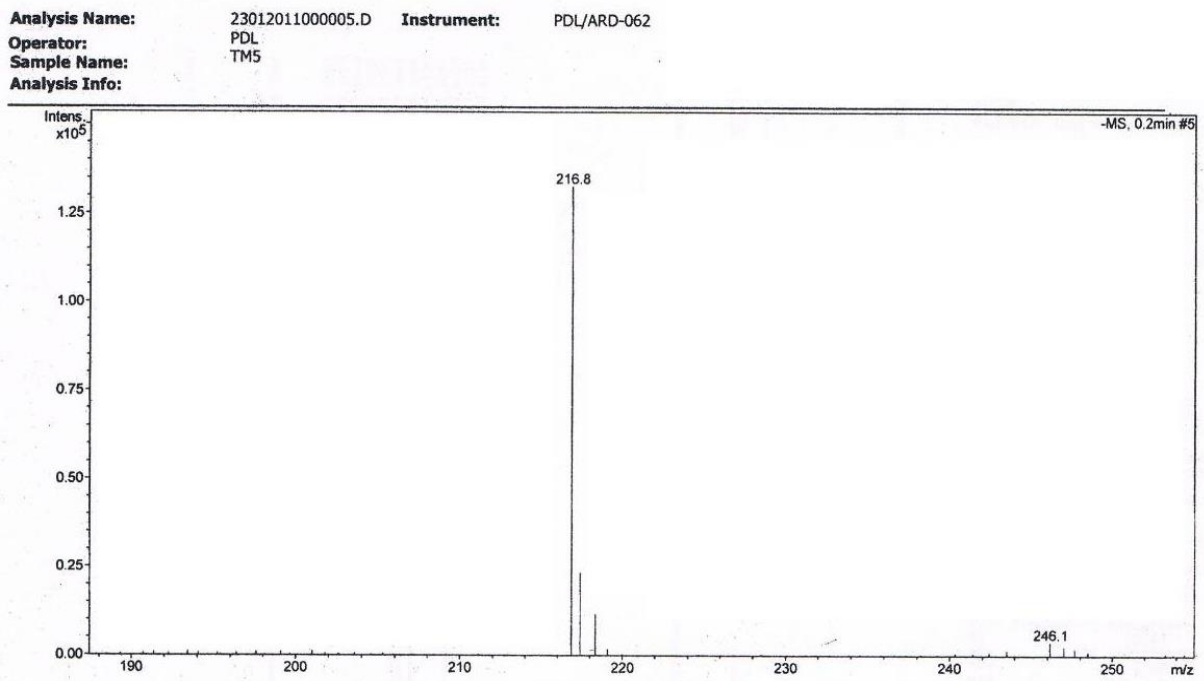


Figure 5 Mass spectra of 2-chloro-4-nitroacetanilide (**4**)

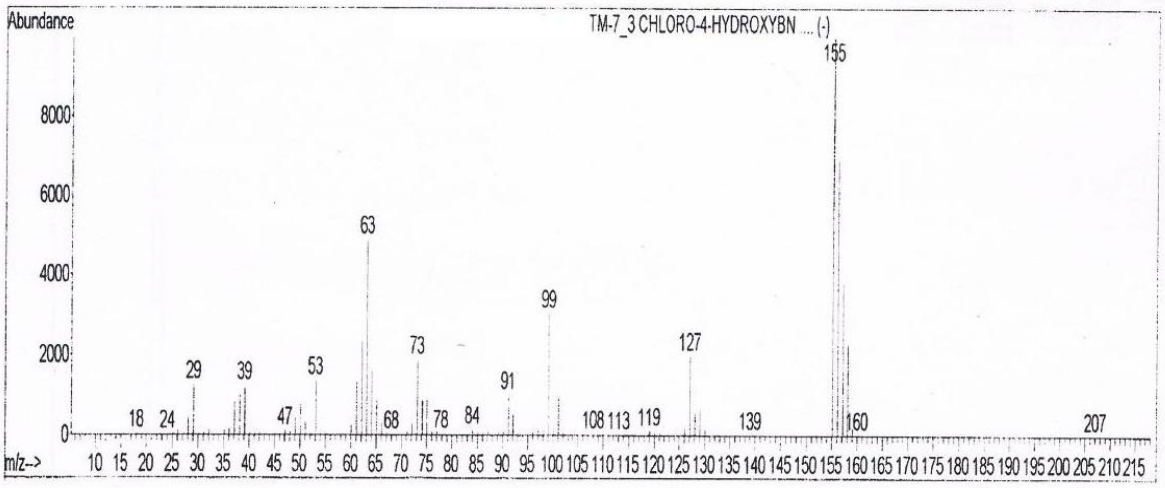


Figure 6. Mass spectra of 3-chloro-4-hydroxybenzaldehyde (5)

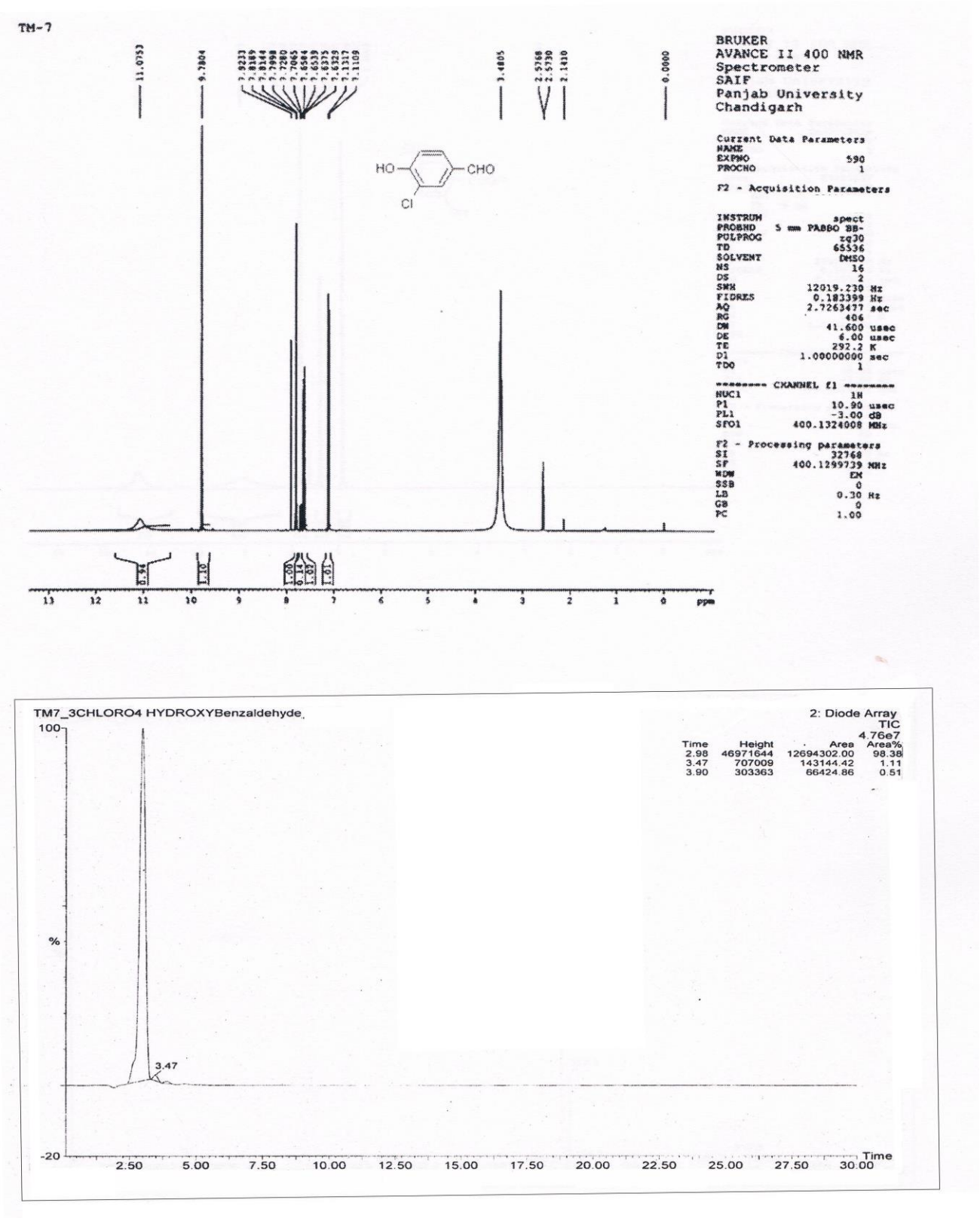


Figure 7. ^{1}H-NMR spectra and HPLC chromatogram of 3-chloro-4 hydroxybenzaldehyde (5)

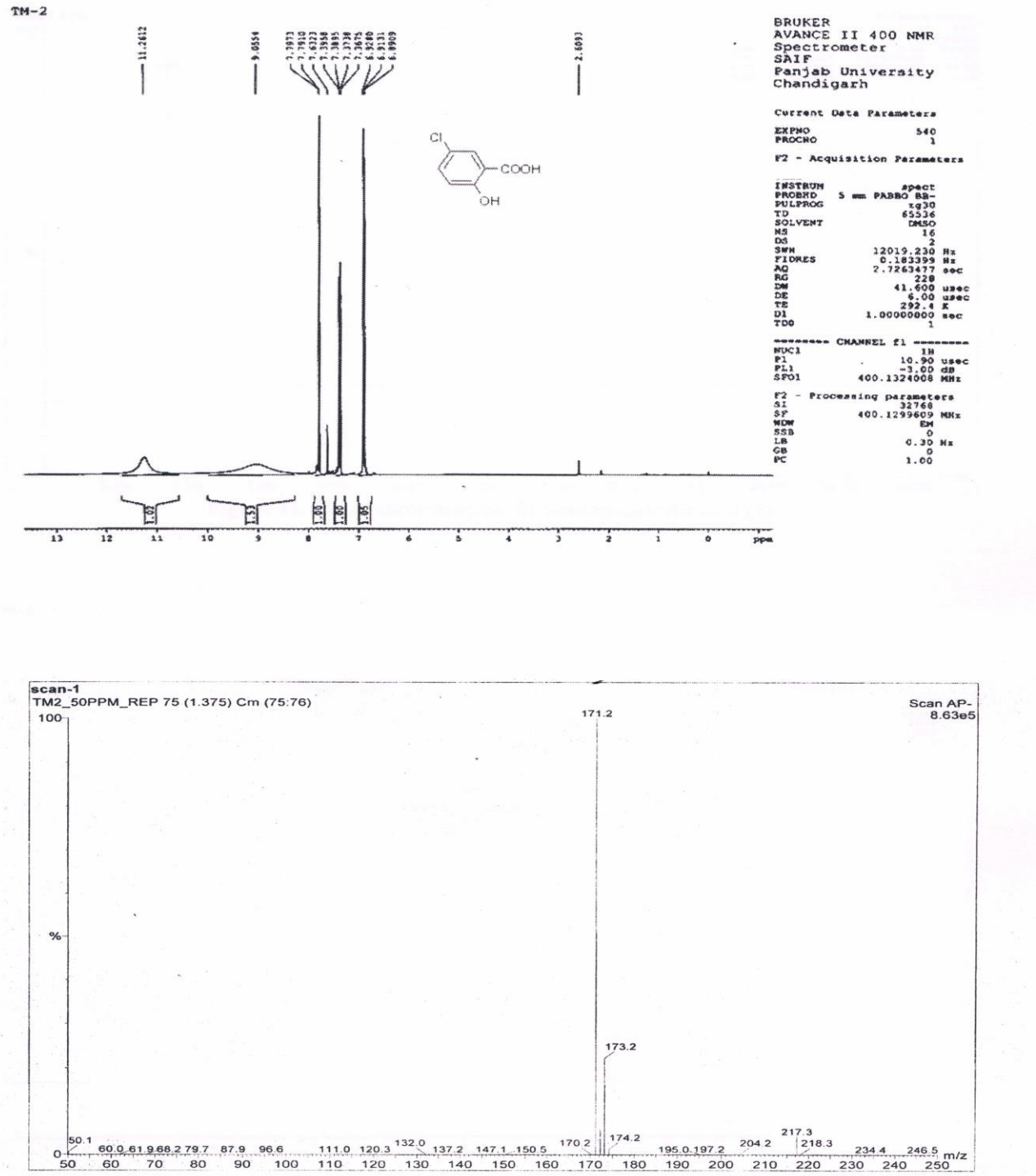


Figure 8. ^{1}H-NMR spectra and mass spectra of 5-chlorosalicylic acid (6)

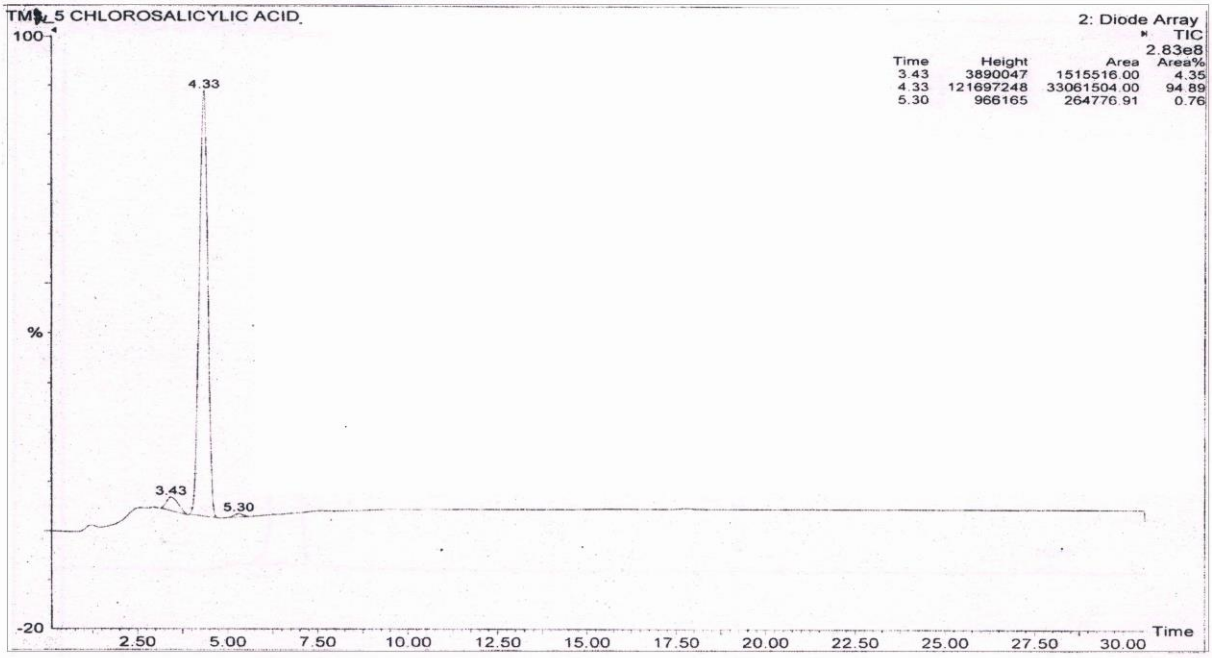


Figure 5 HPLC chromatogram of 5-chlorosalicylic acid (**6**)

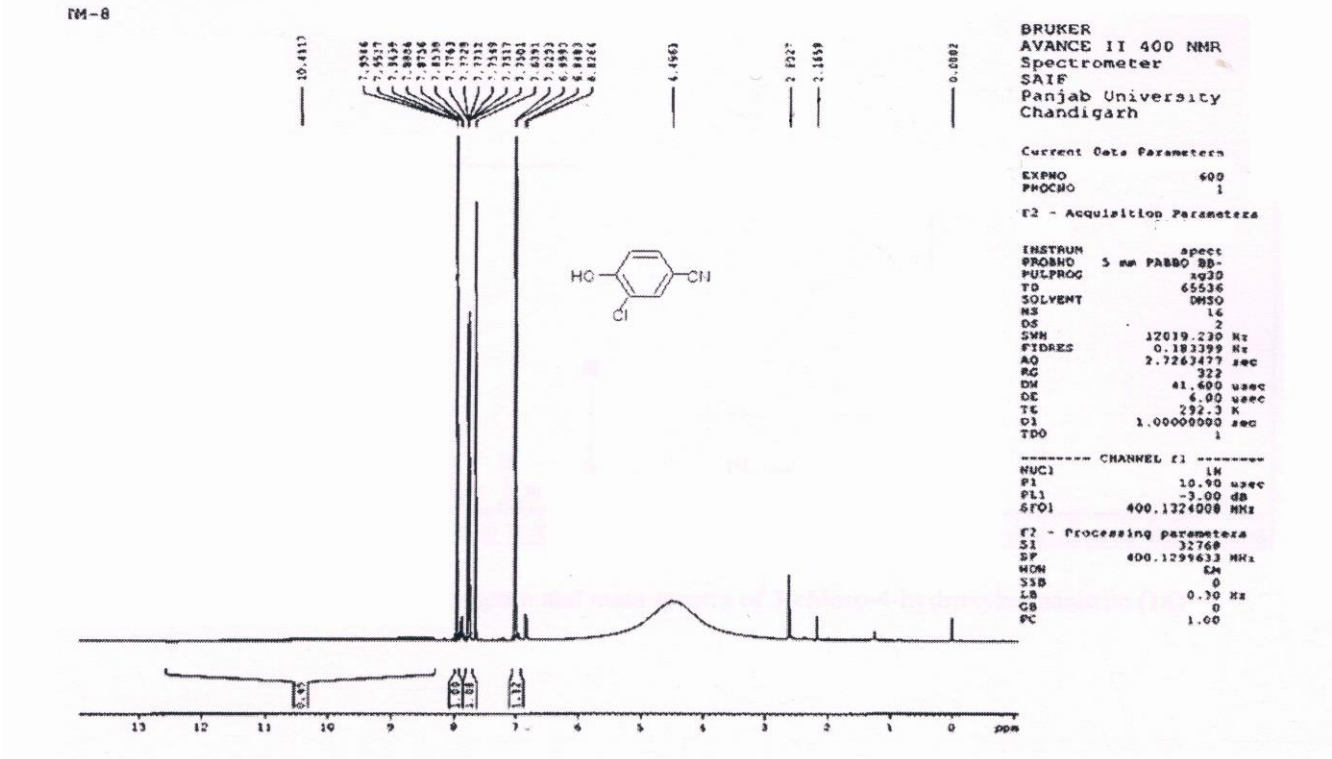


Figure 9. ^{1}H-NMR of 3-chloro-4-hydroxybenzonitrile (16)

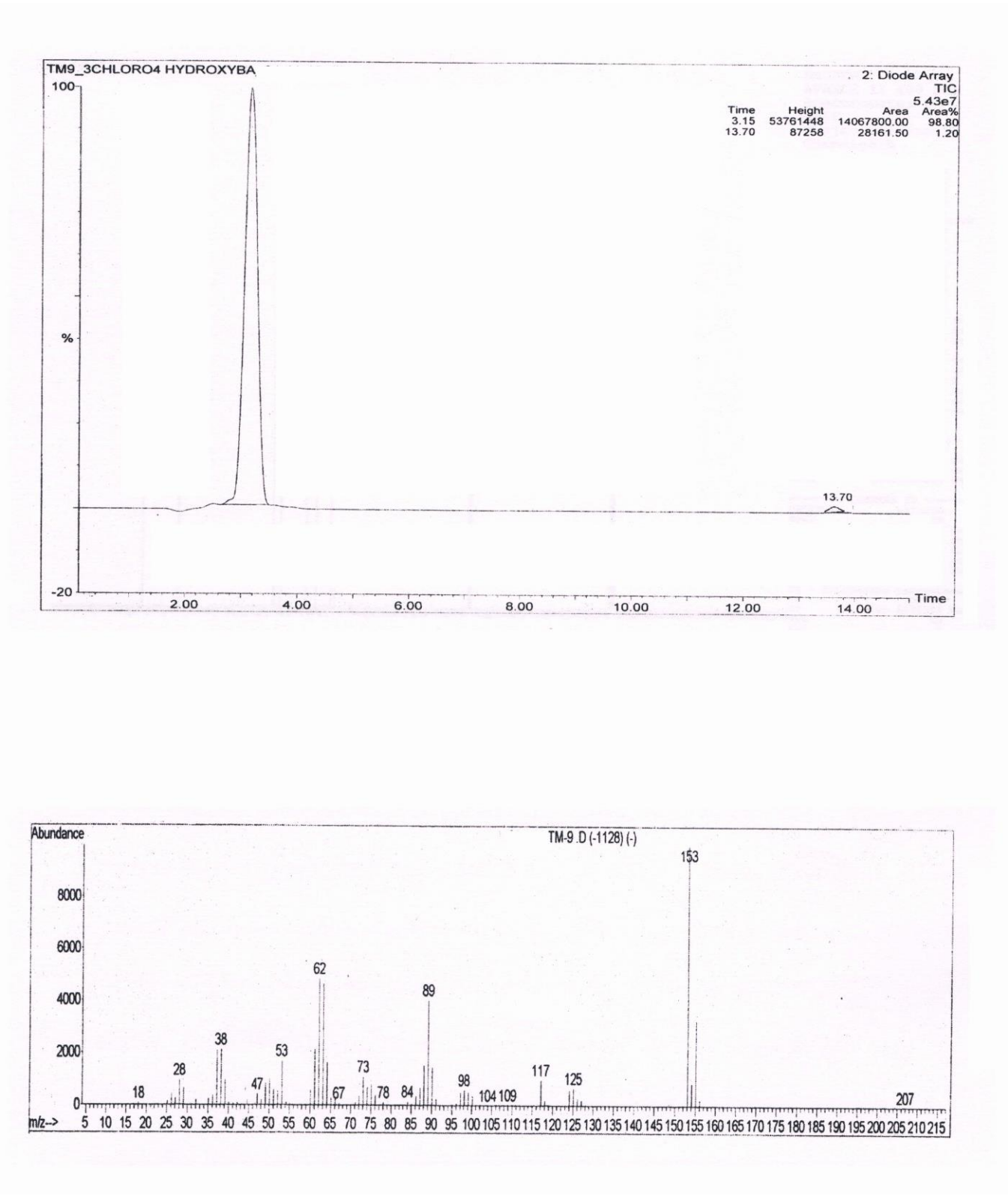


Figure 10. HPLC chromatogram and mass spectra of 3-chloro-4-hydroxybenzonitrile (16)

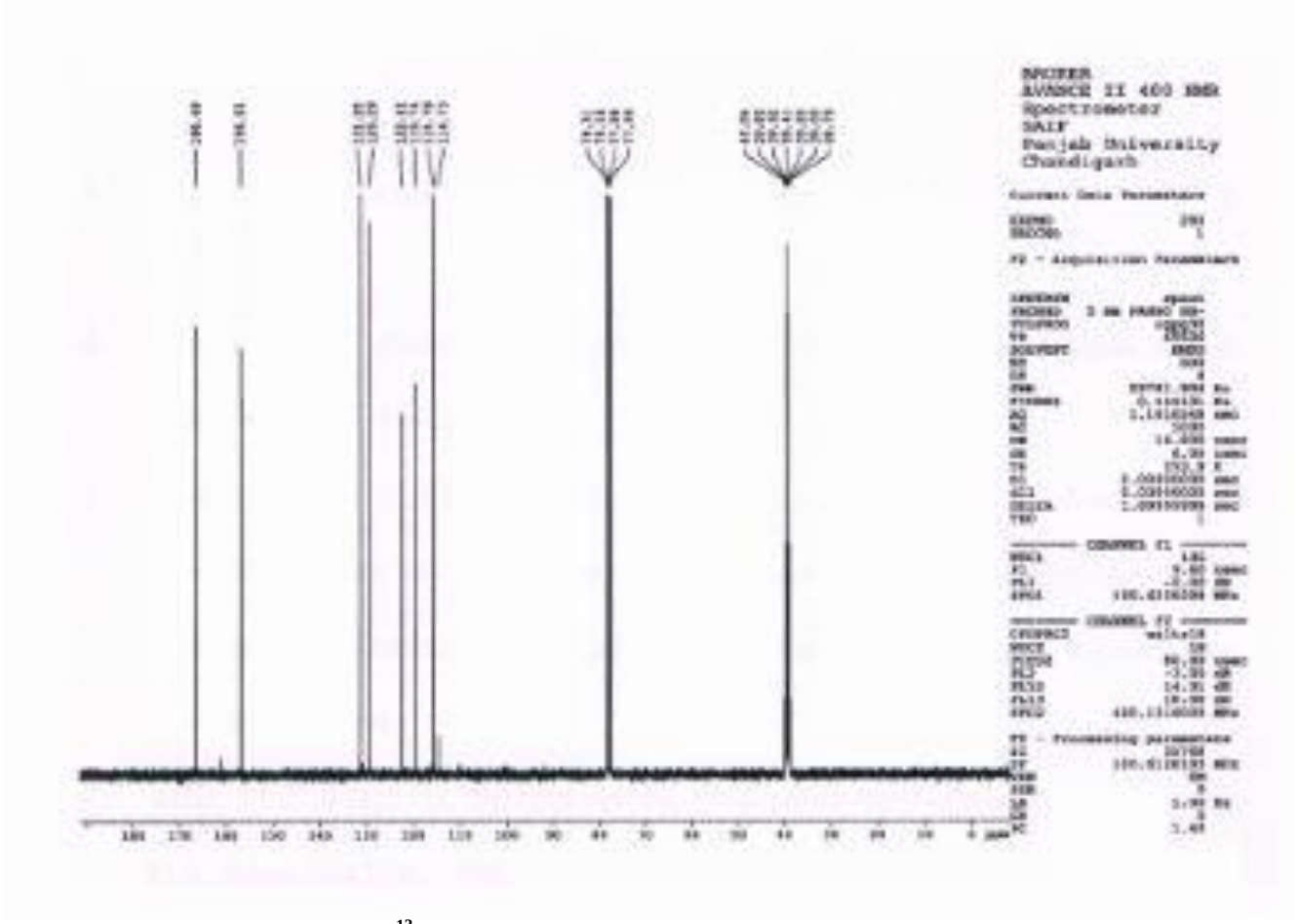


Figure 11. ^{13}C-NMR spectra of 3-chloro-4-hydroxybenzonitrile (16)

III. CONCLUSION

In conclusion , we have developed a practical method using sodium chlorate as an alternative to sodium periodate, sodium perborate and hydrogen peroxide in the oxidative chlorination of arenes using HCl in aqueous medium. The advantages of this method involves no use of organic solvent, mild reaction conditions and good yield of chlorinated product.

SPECTROSCOPIC DATA OF SOME CHLORINATED AROMATIC COMPOUNDS

2,4-Dichloroacetanilide (I): White needles;^{1}H NMR (400 MHz,$CDCl_3$) δ 2.23 (s,3H, CH_3), δ 7.36 (d, j = 2.36 Hz, 1H, Ar), δ 7.23 (dd, j = 8.88, 2.36 Hz, 1H, Ar), δ 7.64 (brs, 1H, NH), δ 8.30 (d, j = 8.88 Hz, 1H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO): 168.75, 133.76, 129.07, 128.49, 126.89, 126.20, 125.80, 23.39 ppm; MS: calcd. for $C_8H_7Cl_2NO$ $[M]^+$ 204.26, found 203.0 $[M-1]^+$.

4-Bromo-2-chloroacetanilide (2): White needles; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s,3H, CH_3), δ 7.51 (d, j = 2.20 Hz, 1H, Ar), δ 7.39 (dd, j = 8.84, 2.20 Hz, 1H, Ar), δ 7.59 (brs, 1H, NH), δ 8.27 (d, j = 8.84 Hz, 1H, Ar) ppm; MS: calcd. for $C_8H_7BrCINO$ $[M]^+$ 249, found 250 $[M+1]^+$.

2-Chloro-4-nitroacetanilide (4): Yellow powder; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (s,3H, CH_3), δ 8.68 (d, j = 9.24 Hz, 1H, Ar), δ 8.29 (d, j = 2.56 Hz, 1H, Ar), δ 8.16 (dd, j = 9.24,2.56 Hz, 1H, Ar), δ 7.91 (brs, 1H,NH) ppm; MS: calcd. For $C_8H_7CIN_2O_3$ $[M]^+$ 214.61, found 216.8 $[M+2]^+$.

3-Chloro-4-hydroxybenzaldehyde (5): Light brown powder; ^{1}H NMR (400 MHz, DMSO) δ 9.78 (s, 1H, CHO), δ 7.81 (d, j = 1.80 Hz, 1H, Ar), δ 7.64 (dd, j = 8.40, 1.80 Hz, 1H, Ar), δ 7.12 (d, j = 8.32 Hz, 1H, Ar) ppm; MS: calcd. For $C_7H_5ClO_2$ $[M]^+$ 156,5, found 155 $[M-1]^+$.

5-Chlorosalicylic acid (6): Whita crystals; ^{1}H NMR (400 MHz, DMSO) δ 9.05 (s, 1H, OH), δ 7.79 (d, j = 2.52 Hz, 1H, Ar), δ 7.38 (dd, j = 8.80, 2.52 Hz, 1H, Ar), δ 6.91 (d, j = 8.88 Hz, 1H, Ar) ppm; MS: calcd. for $C_7H_5ClO_3$ $[M]^+$ 172, found 171.

3,5-Dichlorosalicylic acid (7): Whita crystals; ^{1}H NMR (400 MHz, DMSO) δ 7.90 (d, j = 2.40 Hz, 1H, Ar), δ 7.79 (d, j = 2.40 Hz, 1H, Ar), ppm; MS: calcd. for $C_7H_4CI_2O_3$ $[M]^+$ 207.01, found 206 $[M-1]^+$.

4-Chloro-2-nitroaniline (8): Yellow Orange powder; ^{1}H NMR (400 MHz, DMSO) δ 7.90 (d, j = 2.42 , 1H, Ar), δ 7.28 (dd, j = 9.20, 2.24, 1H, Ar), δ 7.06 (d, j = 9.22, 1H, Ar) δ 7.55 (bs, 1H, NH_2) ppm; MS (APCI): calcd. for $C_6H_5CIN_2O_2$ $[M]^+$ 172.57, found 172 $[M]^+$.

2-Chloro-4-nitroaniline (9): Yellow powder; ^{1}H NMR (400 MHz, DMSO) δ 7.78 (d, j = 2.56 Hz , 1H, Ar), δ 7.65 (dd, j = 9.24, 2.56 Hz, 1H, Ar), δ 7.60 (d, j = 9.20 Hz, 1H, Ar) δ 3.85 (bs, 2H, NH_2) ppm; MS (APCI): calcd. for $C_6H_5CIN_2O_2$ $[M]^+$ 172.57, found 172 $[M]^+$.

4-Chloro-2-nitrophenol (10): Yellow needles; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, j = 9.20 , 1H, Ar), δ 7.86 (dd, j = 9.34, 2.44, 1H, Ar), δ 7.20 (d, j = 2.42, 1H, Ar) δ 10.82 (s, 1H, OH) ppm; MS (APCI): calcd. for $C_6H_4ClNO_3$ $[M]^+$ 173.56, found 173 $[M]^+$.

4-Chlorobenzanilide (12): White powder; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.81 (m, 9H, Ar), ppm; MS (APCI): calcd. for $C_{13}H_{10}ClNO$ $[M]^+$ 231, found 232 $[M+1]^+$.

5-Chlorosalicyladehyde (13): White powder; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H, CHO), δ 10.80 (s, 1H, OH), δ 6.90 (d, j = 8.84, 1H, Ar) δ 7.38 (dd, j = 8.84, 2.42, 1H, Ar) δ 7.48 (d. j = 2.42, 1H, Ar) ppm; MS (APCI): calcd. for $C_7H_5ClO_2$ $[M]^+$ 156.56, found 156 $[M]^+$.

3,5-Dichloro-4-hydroxybenzoic acid (15): White needles; ^{1}H NMR (400 MHz, DMSO) δ 11. (s, 1H, OH), δ 7.85 (s, 2H, Ar), ppm; MS: calcd. for $C_7H_4Cl_2O_3$ $[M]^+$ 207.01, found 206 $[M-1]^+$.

3-Chloro-4-hydroxybenzonitrile (16). White needles; ^{1}H NMR (400 MHz, DMSO) δ 7.12. (d, j = 8.48 Hz, 1H, Ar), δ 7.77 (dd, j = 8.44, 1.92 Hz, 1H, Ar),δ 7.95 (d, j = 1.88 Hz, 1H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO): 166.49. 156.91, 131.25, 129.29, 122.41, 119.74, 115.79 ppm; MS: calcd. for C_7H_4ClNO $[M]^+$ 153.56, found 153.

3,5-Dichloro-4-hydroxybenzonitrile (17): White needles; ^{1}H NMR (400 MHz, DMSO) δ 7.91 (s, 2H, Ar), ppm; MS: calcd. for $C_7H_3Cl_2NO$ $[M]^+$ 187, found 187 $[M]^+$.

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