



International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: www.ijrpns.com



SYNTHESIS OF SOME N-ACYL SULPHONAMIDES FOR PHARMACOLOGICAL SCREENING

**S. Bhavna Priyasri^{*1}, P. Balakrishna Reddy², Lakamsani Vyshnavi³, Bussu Rajani³,
Bhimavarapu Ramya Reddy³**

^{*1}Department of Pharmaceutical Engineering, New Jersey Institute of Technology, New Jersey, U.S.A.

²Department of Chemistry and Environmental Science, New Jersey Institute of Technology, New Jersey, USA.

³Department of Pharmacy, P.S.G College of Pharmacy, Coimbatore, Tamil Nadu, India.

ABSTRACT

A new method has been developed for the synthesis of some N-acyl sulphonamides in the presence inexpensive and bench top reagents. The main aim of this study includes synthesis of some N-acyl sulphonamides by using acid chlorides. Various aromatic sulphonamides are reacted with acid chlorides i.e. isothalyl chloride, terythalyl chloride in the presence of base (NaHCO₃). It is a green colour reaction where the synthesis is carried out under the solvent free conditions. Totally 8 compounds of n-acyl sulphonamides were synthesized. The compounds were isolated by TLC. Structures of the synthesized compounds were confirmed by IR spectroscopy and molecular weights were confirmed by MASS spectroscopy.

KEYWORDS

Aromatic sulphonamides, Isothalyl chloride, Terythalyl chloride, IR spectroscopy, Mass spectroscopy and TLC.

Author for Correspondence:

Bhavna Priyasri S,
New Jersey Institute of Technology,
New Jersey, U.S.A.

Email: bhavnapriyasri@gmail.com

INTRODUCTION

N-acyl sulphonamides have received attention due to their diverse biological activities as precursors of therapeutic agents of diverse biological activities, as precursors of therapeutic agents for Alzheimer's disease, as antibacterial inhibitors of tRNA synthetases, as prostaglandin F1a sulphonamides for the potential treatments of osteoporosis, as antagonist for angiotensin II, and as Leukotriene D4-receptors^{1, 2}.

The most practical methods for the N-acylation of sulfonamides are the reaction of parent sulphonamide with acyl chlorides or anhydrides in the presence of trialkylamine, pyridine or alkali hydroxide³. Another approach is direct coupling of sulphonamides with carboxylic acids utilizing condensing reagents such as carbodiimide (DCC, EDC), and N, N'-carbonyldiimidazole^{1,4}. Recently, Katritzky *et al.* reported N-acylation of sulphonamides using N-acyl benztriazole as acylating agent^{5, 6}. Few reports on this transformation under acidic conditions do not systematically examine the scope and the limitations of the reactions. Acylation of sulphonamides with conc. H₂SO₄ in the carboxylic acid anhydride as a solvent or in acetonitrile are among these methods^{4, 7}. However, most of these methods have some disadvantages including occurrence of side reactions especially formation bis-acylated byproducts, vigorous reaction condition and tedious work up, use of expensive or unavailable reagents and solvents, long reaction times and low yield of products⁷. Thus, there is still demand for developing new mild methods for N-acylation of sulphonamides in the presence of inexpensive and bench top reagents.

The principle behind the reaction involved in our synthesis of N-acyl sulphonamides is Schotten Bauman reaction. The various aromatic sulphonamides are reacted with acid chlorides in the presence of base. Our reaction scheme was a green one where the synthesis is carried out in the absence of solvent.

METHOD

All the chemicals used were of chemically pure grade. The main reaction was performed under solvent free conditions.

Scheme 1

General Procedure

4grms of sodium bicarbonate was ground in a motar for 10min and add 2mmols of parent sulphonamide then stir it in a magnetic stirrer until it attains a temperature 70°C. Then 2mmol of isophthalyl chloride was added and stirred in a magnetic stirrer

for 1hour. Water was added to the reaction mixture and filtered. To the filtrate dil. HCl was added till precipitation was complete. The precipitate was filtered, washed with water and dissolved in sufficient quantity of ethyl acetate. Small quantity of anhydrous sodium sulphate was added to remove the traces of moisture present and filtered. The filtrate was evaporated and recrystallized from ethyl acetate and toluene (Table No.1 and Figure No.1).

Scheme 2

General Procedure

4grms of sodium bicarbonate was ground in a motar for 10min and add 2mmols of parent sulphonamide then stir it in a magnetic stirrer until it attains a temperature 70°C. Then 2mmol of terephthalyl chloride was added and stirred in a magnetic stirrer for 1hour. Water was added to the reaction mixture and filtered. To the filtrate dil. HCl was added till precipitation was complete. The precipitate was filtered, washed with water and dissolved in sufficient quantity of ethyl acetate. Small quantity of anhydrous sodium sulphate was added to remove the traces of moisture present and filtered. The filtrate was evaporated and recrystallized from ethyl acetate and toluene (Table No.2 and Figure No.2).

RESULTS AND DISCUSSION

Melting points

The melting points for the synthesized compounds are as follows (Table No.3).

Thin Layer Chromatography

The progress of the reactions was monitored by TLC and the products were isolated in good to high yield after an easy work-up (Table No.4).

IR Spectroscopy

The compounds were characterized by IR spectroscopy. The IR spectral data confirmed the proposed structure of N-acyl sulphonamides.

Figure No.3: P-toluene sulphonamide + isothalyl chloride

- N-H(amide) stretch at 3230 cm⁻¹
- C=O(amide)stretch at 1682 cm⁻¹
- S=O asymmetric stretch at 1334 cm⁻¹
- S=O symmetric stretch at 1166 cm⁻¹

Figure No.4: Benzene sulphonamide + isothalyl chloride

- N-H(amide)stretch at 3300 cm⁻¹
- C=O(amide)stretch at 1701 cm⁻¹
- S=O asymmetric stretch at 1350 cm⁻¹
- S=O symmetric stretch at 1170 cm⁻¹

Figure No.5: Chlorbenzene sulphonamide + isothalyl chloride

- N-H(amide)stretch at 3250 cm⁻¹
- C=O(amide)stretch at 1710 cm⁻¹
- S=O asymmetric stretch at 1350 cm⁻¹
- S=O symmetric stretch at 1170 cm⁻¹

Table No.1: Synthesized of compound of N-Acy1 Sulphonamides from isophthalyl chloride

S.No	Compound	R ¹	R ²
1	1	H	H
2	2	CH ₃	H
3	3	H	CH ₃
4	4	Cl	H

Table No.2: Synthesized of compound of N-Acy1 Sulphonamides from terephthalyl chloride

S.No	Compound	R ¹	R ²
1	5	H	H
2	6	CH ₃	H
3	7	H	CH ₃
4	8	Cl	H

Table No.3: The melting points for the synthesized compounds

S.No	Compound	IUPAC Name	MP ^o C
1	1	1-N,3-N-bis(benzene sulphonyl) benzene-1,3-dicarboxamide	186
2	2	1-N,3-N-bis(p-toluene sulphonyl) benzene-1,3-dicarboxamide	155
3	3	1-N,3-N-bis(o-toluene sulphonyl) benzene-1,3-dicarboxamide	143
4	4	1-N,3-N-bis[(4-chlorobenzene) sulphonyl] benzene-1,3-dicarboxamide	205
5	5	1-N,4-N-bis(benzene sulphonyl) benzene-1,4-dicarboxamide	205
6	6	1-N,4-N-bis(p-toluene sulphonyl) benzene-1,4-dicarboxamide	200
7	7	1-N,4-N-bis(o-toluene sulphonyl) benzene-1,4-dicarboxamide	240
8	8	1-N,4-N-bis[(4-chlorobenzene) sulphonyl] benzene-1,4-dicarboxamide	247

Table No.4: P-toluene sulphonamide + isothalyl chloride

S.No	Chloroform: Ethanol	Synthesized compound	Reference sample
1	9:1	0.45	0.85
2	8:2	0.90	0.79
3	4:6	0.80	0.81

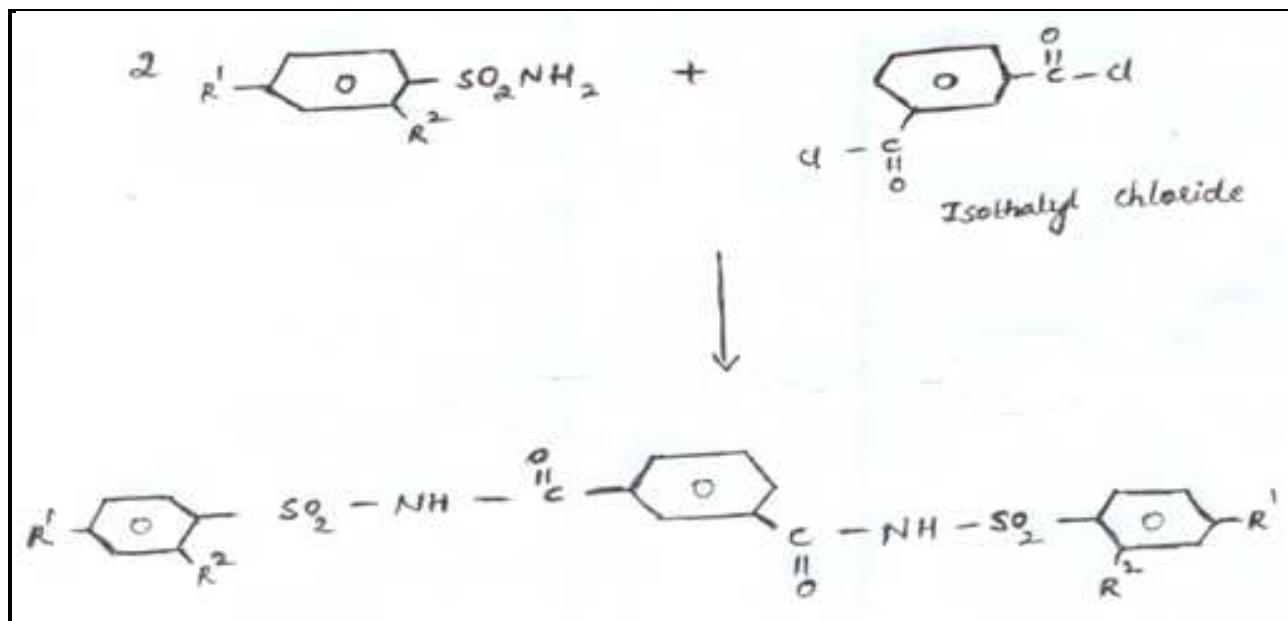


Figure No.1: Synthesis of N-Acyl Sulphonamides from isophthalyl chloride

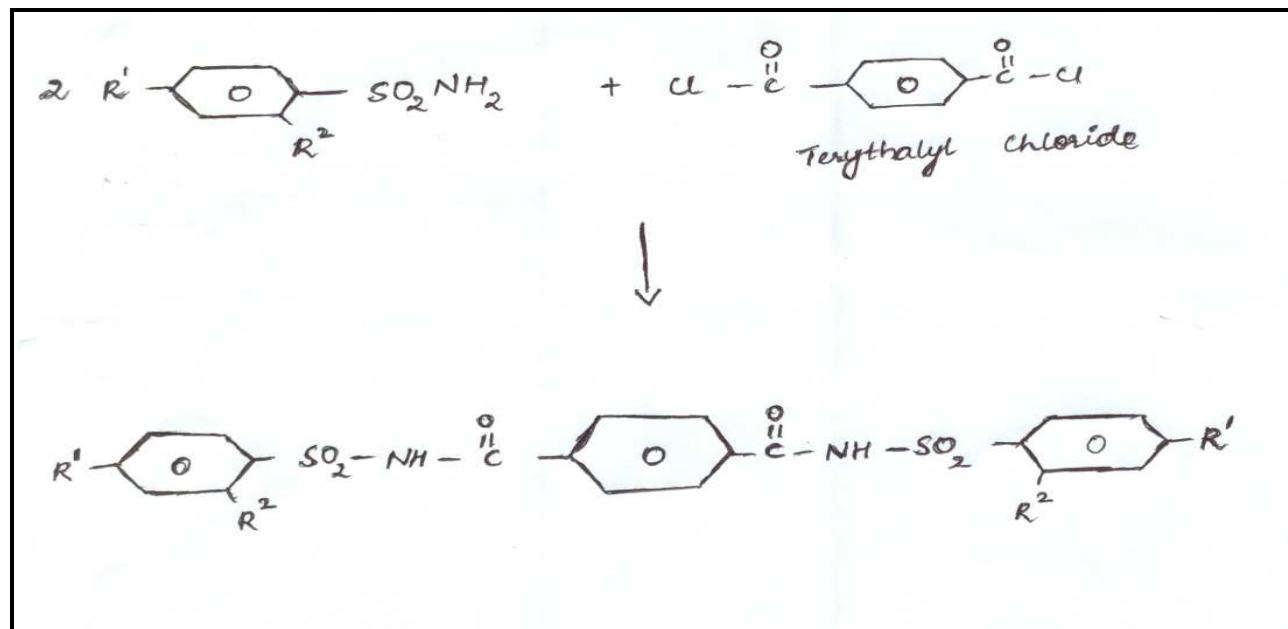


Figure No.2: Synthesis of N-Acyl Sulphonamides from terephthalyl chloride

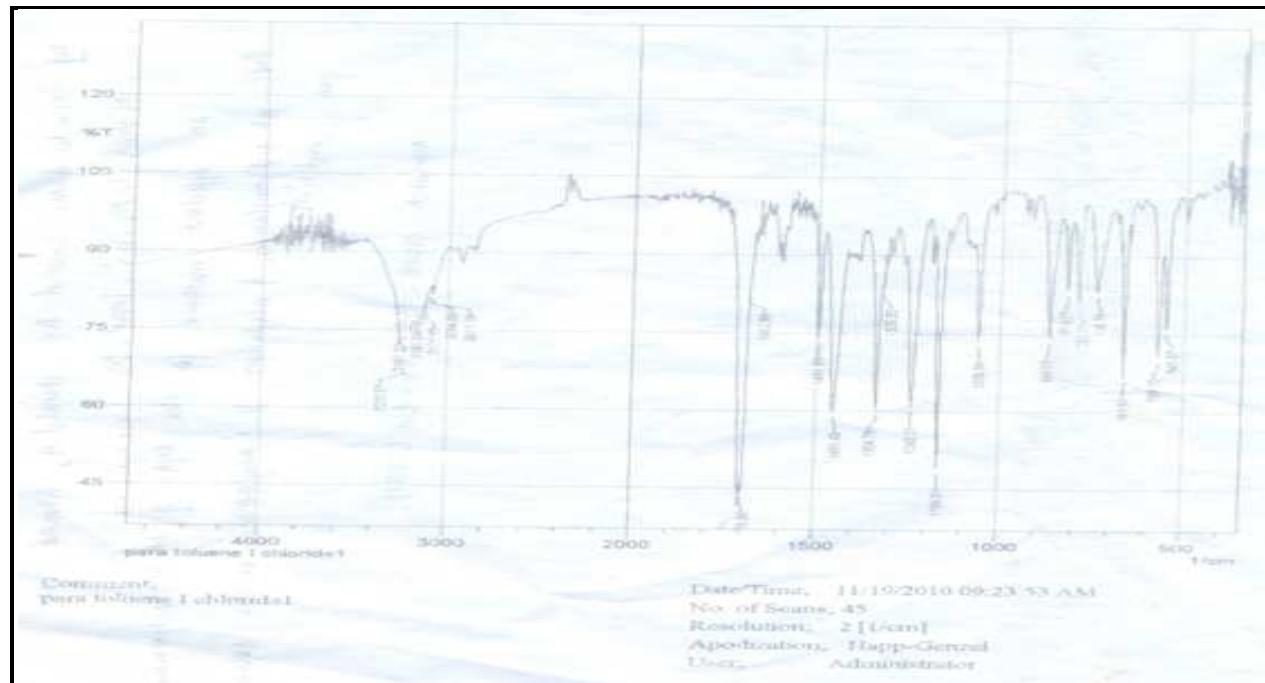


Figure No.3: IR spectrum of p-toluenesulphonamide + isothalyl chloride

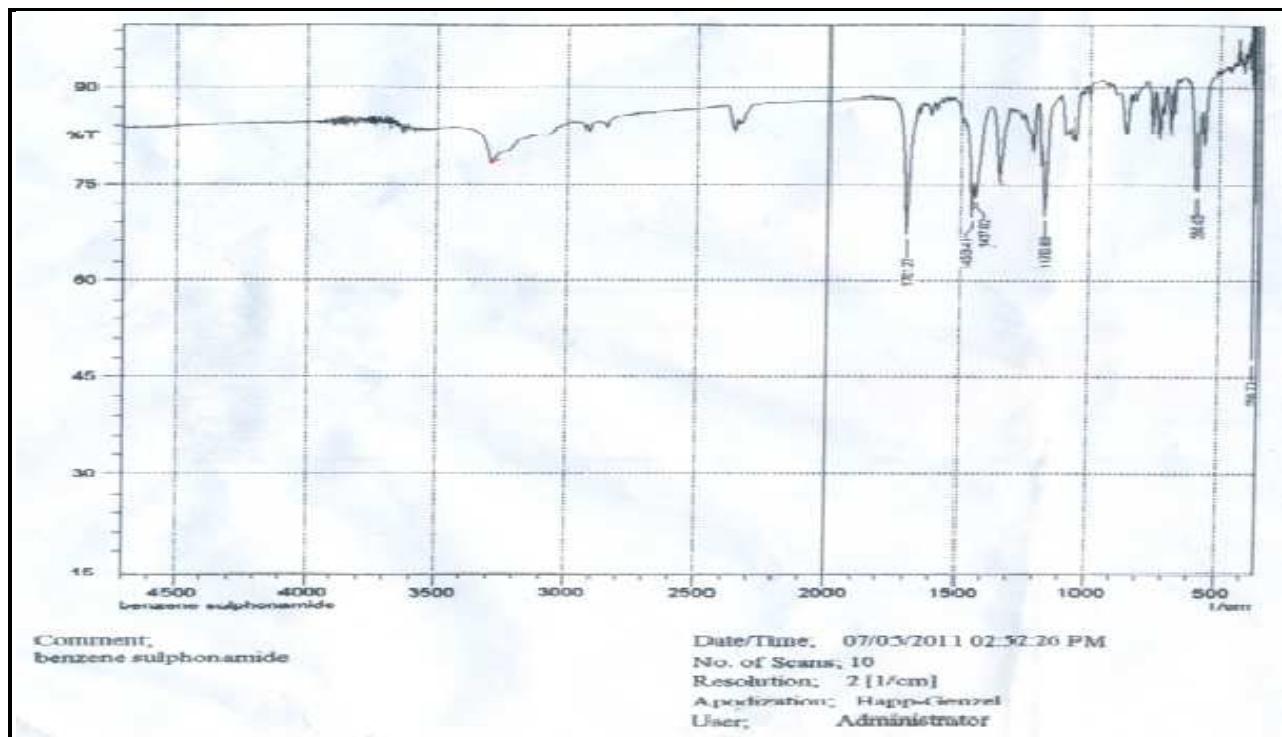


Figure No.4: IR Spectroscopy of benzene sulphonamide + isothalyl chloride

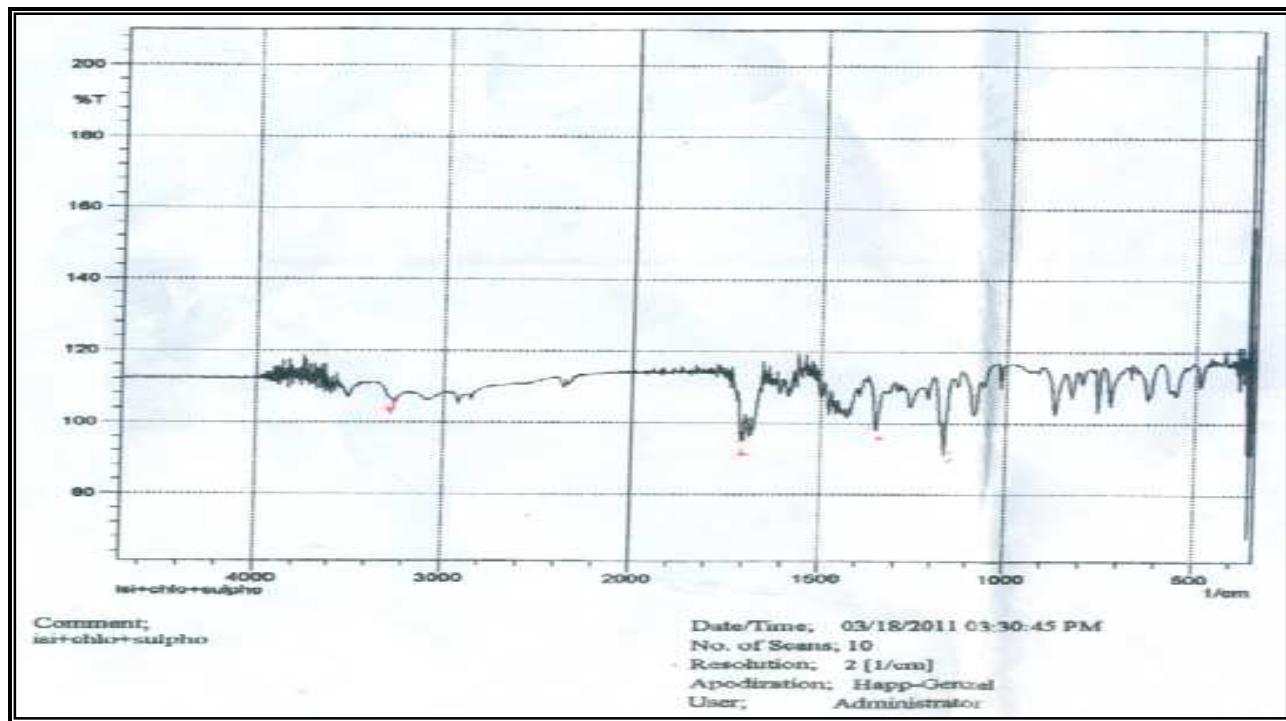


Figure No.5: IR Spectroscopy of chlorbenzene sulphonamide + isothalyl chloride

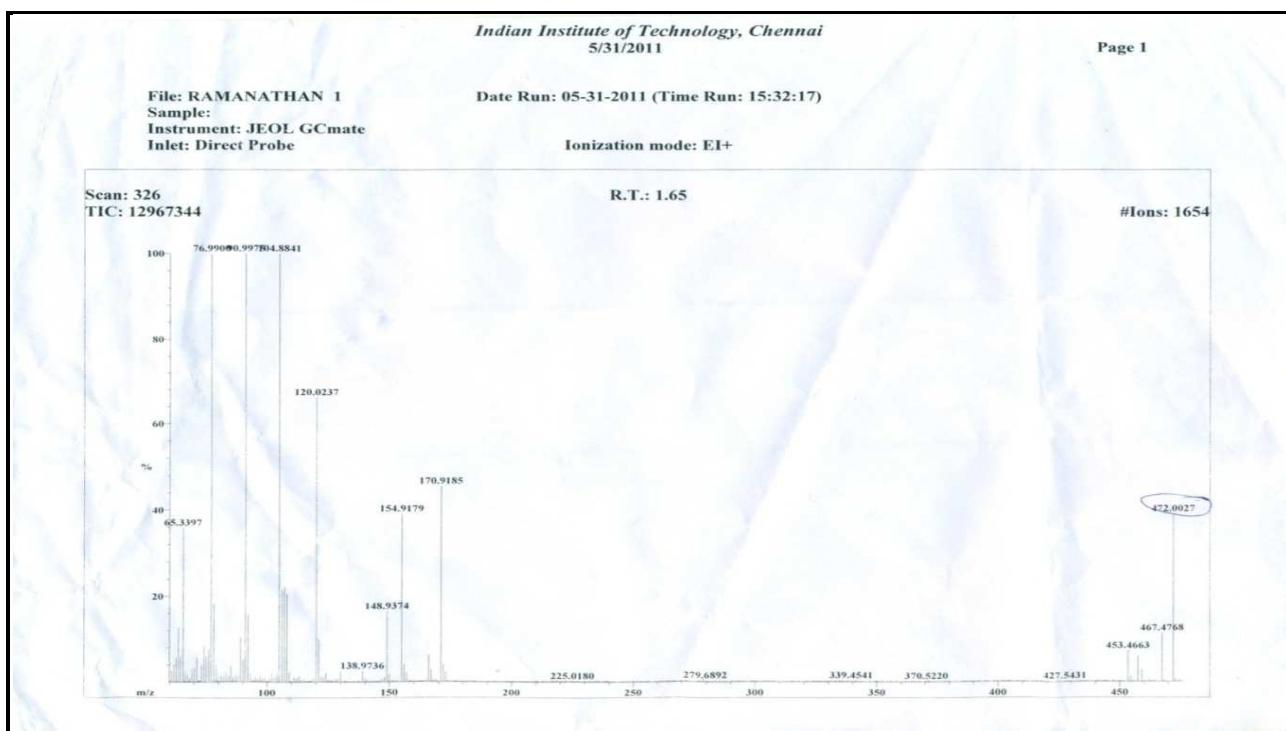


Figure No.6: Molecular weight peak of P-toluene sulphonamide + isothalyl chloride was shown at 472

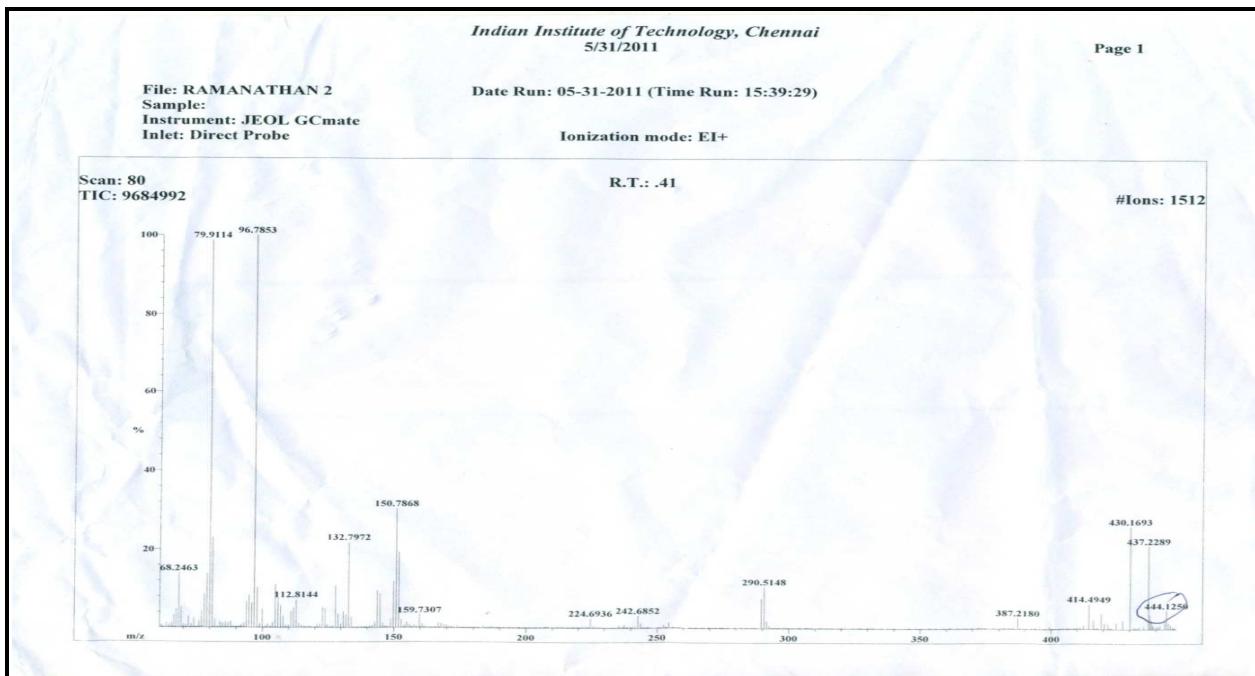


Figure No.7: Molecular weight peak of benzene sulphonamide + isothalyl chloride was shown at 444

CONCLUSION

In the current project we have synthesized some N-acyl sulphonamides and their structures were confirmed by IR spectrophotometric and Mass spectrum analysis. The compounds now would be subjected to further pharmacological screening, especially concerning those activities that our literature survey on N-acyl sulphonamides indicates.

ACKNOWLEDGEMENT

Authors were express our sincere thanks to the management of P.S.G College of Pharmacy, Coimbatore, Tamilnadu, India for providing the facilities and giving us an opportunity to do research in this campus. We are deeply indebted to Dr. Sivaram Hariharan, for his valuable guidance and untiring assistance throughout our research. We would like to thank Dr. Murgesan, Head of SAIF, IIT, Chennai for helping us in conducting mass spectrum analysis.

We sincerely thank Mr. R.Massah, Associate Professor of Organic Chemistry, Dept. of Chemistry, Islamic Azad University, Shahreza

Branch, Shahreza - 86145-311, Isfahan, Iran. Our thanks to all the teaching, non-teaching staff members and friends who rendered us support in time of need.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Hasegawa T, Yamamoto H. A practical synthesis of optically active (R)-2-Propylo acid: therapeutic agent for Alzheimer's disease, *Bull. Chem. Soc. Jpn*, 73(26), 2000, 423-28.
2. Banwell M G, Crasto C F, Easton C J, Forrest A K, Karoli T, March D R, Mensah L, Nairn M R O, Hanlon P J, Oldham M D, Yue W. Analogues of SB-203207 as inhibitors of tRNA synthetases, *Bioorg. Med. Chem. Lett*, 10(20), 2000, 2263-2266.
3. Wang Y, Soper D L, Dirr M J, DeLong M A, De B, Wos J A. The synthesis and human FP receptor binding affinity of 13,14-dihydro prostaglandin F1alpha sulfonamides: potential treatments for osteoporosis, *Chem. Pharm. Bull*, 48(9), 2000, 1332-7.

4. Chang L L, Ashton W T, Flangan K L, Chen T B, Malley O, Zingaro S S, Siegel G J, Kivlighn P K S, Lotti S D, Chang V J, Greenlee R S et al. Triazolinone biphenylsulfonamides as angiotensin II receptor antagonists with high affinity for both the AT1 and AT2 subtypes, *J. Med. Chem.*, 37(26), 1994, 4464-78.
5. Musser J H, Kreft A F, Bender R H W, Kubrak D M, Grimes D, Carlson R P, Hand J J. N-[(arylmethoxy)phenyl] carboxylic acids, hydroxamic acids, tetrazoles, and sulfonyl carboxamides. Potent orally active leukotriene D4 antagonists of novel structure, *Med. Chem.*, 33(1), 1990, 240-5.
6. Kondo K, Sekimoto E, Nakao J, Murakami Y. Studies on Development of Sufficiently Chemoselective N-Acylation Reagents: N-Acyl-N-(2,3,4,5,6-pentaurophenyl) methane sulfonamides, *Tetrahedron*, 56(7), 2000, 5843-56.
7. Kondo K, Sekimoto E, Miki K, Murakami Y. A versatile synthon for chemoselective N-acylation reagents, 2-fluoro- N-mesylaniline, *J. Chem. Soc., Perkin Trans*, 1(10), 1998, 2973-74.

Please cite this article in press as: Bhavana priyasri S. et al. Synthesis of some n-acyl sulphonamides for pharmacological screening, *International Journal of Research in Pharmaceutical and Nano Sciences*, 2(1), 2013, 115-123.