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Synthesis, Characterization and Antimicrobial Studies of Tosyl Esters of Carboxylic Acid

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Abstract- Tosyl esters of Indole acetic acid and Naphthalene acetic acid were prepared by treating the acids with *p*-toluenesulfonyl chloride in the presence of a strong base triethylamine. The synthesized compounds were identified by TLC technique. IR and ^{1}H-NMR spectral measurements were carried out to characterize and elucidate the structure of the synthesized compounds. Anti microbial activity on the synthesized compounds were studied by Agar well diffusion method. The result shows that the Tosyl esters are potentially active against Bacterial and Fungal strains.

Index Terms- Tosyl esters, Sulfonyl sulfur, TLC technique, Antimicrobial activity, Agar well diffusion method

I. INTRODUCTION

Esterification of carboxylic acids with alcohols and phenols are of considerable interest. The preparation of esters from their corresponding carboxylic acids is an important and well known transformation in organic synthesis. *p*-Toluenesulfonyl chloride (TsCl) is most widely used as a tosylating agent. It is more reactive than tosyl anhydride and *p*-toluene sulfonic acid. For the preparation of tosylates, generally TsCl is used in the presence of base such as pyridine or triethylamine[1]. The various methods of preparation of tosyl esters of phenols and aliphatic alcohols have been studied by many researchers [2-4]. Nucleophilic substitution reactions of benzenesulfionyl halides [5, 6], and substituted benzyl halides [7-9] has been extensively studied. In these reactions halides are displaced by nucleophile which occurs at sulfonyl sulfur.

The organo sulfur compounds received much attention of researchers due their wide range of application in biological and chemical applications. Sulfur containing drugs such as sulfonamides, sulfonyl ureas, 2- thio uracil, 6- mercapto purines etc., have extensive therapeutic usage. Some sulfur containing agrochemicals have useful biological activity. They used as insecticides, herbicides, fungicides and agaricides. Sulfonamide derivatives of azo dyes have high light stability, water solubility and fixation to fiber [10-12].

In view of the above, we report here the synthesis and characterization of tosyl esters of Indole acetic acid and Naphthalene acetic acid. Further, the synthesized compounds were subjected to antimicrobial studies.

II. EXPERIMENTAL SECTION

Materials and methods

Materials

All the chemicals such as *p*-toluenesulfonyl chloride, Indole acetic acid, Naphthalene acetic acid, triethylamine and acetonitrile were purified before use by recrystallization or distillation until their physical constants (melting/boiling) agreed well with the literature values [13,14]. FT-IR (KBr) spectra were recorded on Perkin Elmer RXI spectrophotometer and proton NMR spectra were recorded on a Bruker AMX 400 MHz NMR spectrometer using TMS as internal reference.

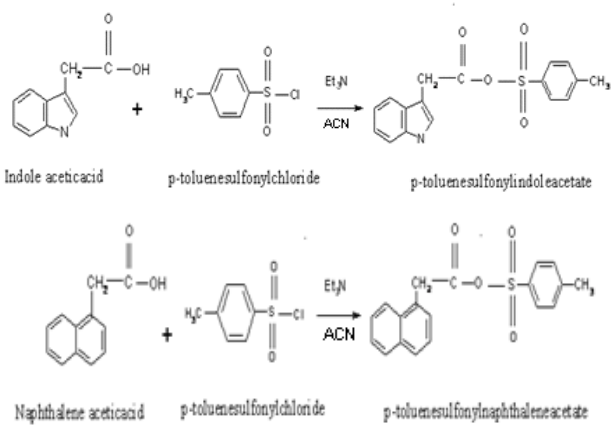
Experimental

Synthesis of compounds

Equal volumes of equimolar solution of *p*-toluenesulphonyl chloride (0.05 mol dm^{-3}, 25ml) and the mixture of Indoleaceticacid-Triethylamine (0.05 mol dm^{-3}, 25ml) in Acetonitrile were mixed thoroughly with constant stirring and kept overnight at about 30 ^{o}C. The solid product obtained was treated with ether. The upper and bottom layers were collected separately and dried over anhydrous Na_2SO_4. A solid product obtained from top layer was seperated. The bottom layer was completely evaporated in vacuum to get residue. TLC tests on both products using a mixture of methanol-ether as eluent, showed a single spot. The solid product obtained from the top layer (yield 54%) was identified as *p*-toluenesulfonylindoleacetate and the solid product obtained from the bottom layer (yield 40%) was identified as triethylammonium chloride from FT-IR (KBr) and ^{1}H ($CDCl_3$) spectral data. The schematic route of synthesis of tosyl esters of acids were given in Scheme 1.

The same procedure was adopted for the synthesis of *p*-toluenesulfonylnapthaleneacetate (yield 60%)

Scheme 1



Characterization of the synthesized compounds

Compound I:

***p*-toluenesulfonylindoleacetate**

IR (cm^{-1}): 3057 υ C- H(aromatic), 2914 υ C-H(aliphatic), 1691 υ (carbonyl), 1597 υ (N-H), 1510 υ (-C=C-), 1409 υ (C-Hbending), 1182 υ (S-O sym), 1327 υ (S-O asym), 977 υ (C-N aromatic), 729 υ (C-O-S).

^{1}H-NMR ($CDCl_3$) (ppm): 3.71 (s, 3H), 2.0 (d, 2H), 7.54 (d, 2H), 7.57 (d, 2H), 6.9-7.3 (m, 6H)

Compound II:

***p*-toluenesulfonylnapthaleneacetate**

IR (cm^{-1}): 3056 υ C-H(aromatic), 2958 υ C-H (aliphatic), 1710 υ (carbonyl), 1598 υ (-C=C-), 1302 υ (S-O asym), 1124 υ (S-O sym), 684 υ (C-S), 736 υ (C-O-S).

^{1}H-NMR ($CDCl_3$) ppm: 4.0 (s, 3H), 2.0 (s, 2H), 7.8 (d, 2H), 8.0 (d, 2H), 7.4 -7.5 (m, 7H)

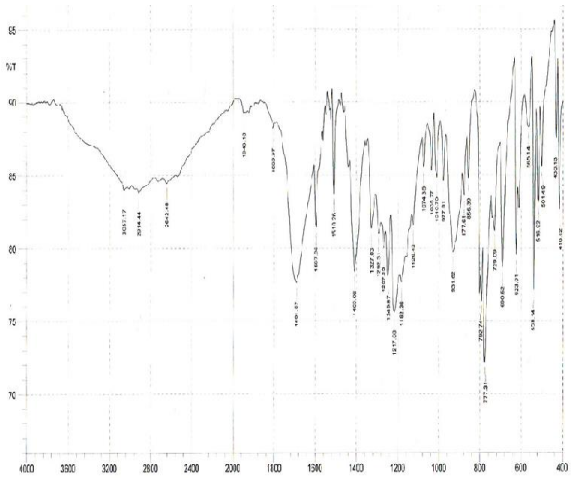


Figure 1: FTIR spectrum of p- Toluenesulfonylindoleacetate

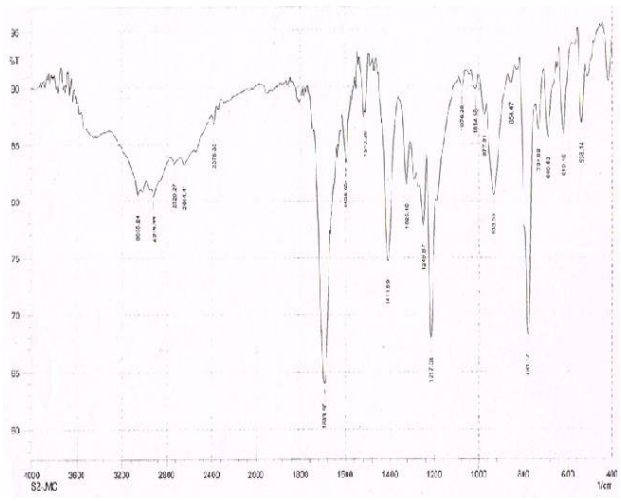


Figure 2: FTIR spectrum of *p*-Toluenesulfonylnaphthaleneacetate

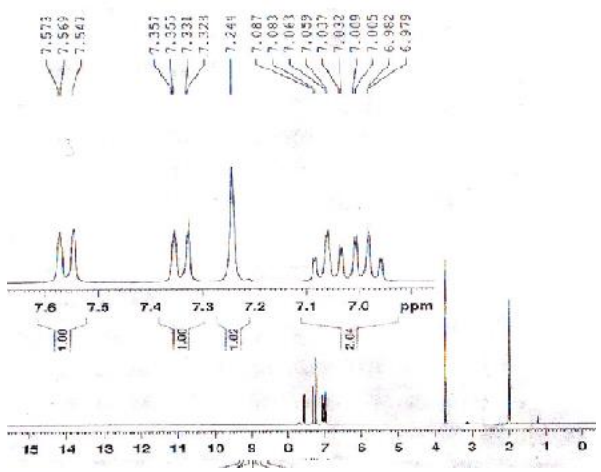


Figure 3: NMR spectrum of p- Toluenesulfonylindoleacetate

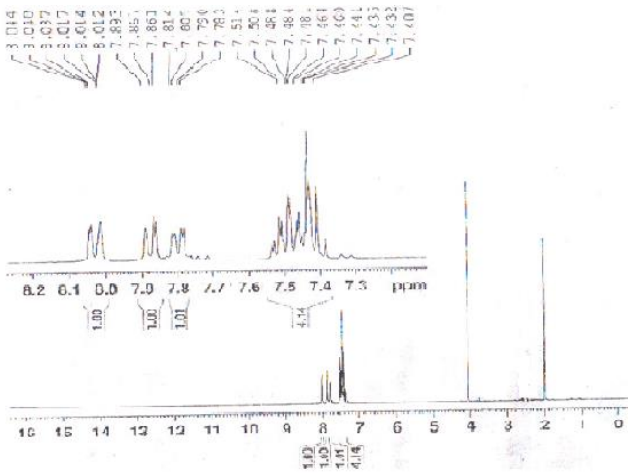


Figure 4: NMR spectrum of *p*-Toluenesulfonylnaphthaleneacetate

Anti microbial Screening

Different species of microorganisms have varying degrees of susceptibility to antimicrobials. Further, the pathogenic microbes may develop drug resistance to a particular type of antimicrobial agent on prolonged use. Hence, the antimicrobial sensitivity tests are very useful to determine the level of antimicrobial activity of a particular chemical compound on certain pathogenic microorganisms [15].

In the present study Agar well disc diffusion technique has been used for determining the susceptibility of the bacterial strain (Staphylococus Aureus) and fungal strain (Aspergillus Niger) on the test compounds I and II. Two different media have been prepared and used in this study. (i) Nutrient Agar medium for cultivating bacteria and (ii) Rose Bengal Chloramphenicol agar medium for culturing fungal species. The Agar media were inoculated with test organism and solution of the test compounds 50µg/ml in sterile $CHCl_3$. Then a standard antibiotic disc (Tetracyclin against S.Aureus and Amphotericin against Aspergillus) was placed at the center of the agar plate. The plate with bacterial organism was incubated at 35-37 °C for about 24

hours. But the plate with fungal organism was incubated at the same temperature for 48 hours and the zone of inhibition was measured in mm. The results of antibacterial and antifungal screening on the test compounds are furnished in Table 1 .

Table 1: Antimicrobial activity of Tosylesters of Carboxylic acid

Test sample	Zone of inhibition (mm)			
	Bacterial strain (Staphylococus Aureus)		Fungal strain (Aspergillus Niger)	
	25µg/ ml	50µg/ ml	25µg/ ml	50µg/ ml
Compound I	23	32	10	19
Compound II	17	24	13	20
Tetracyclin	18	-	-	-
Amphotericin	-	-	13	-

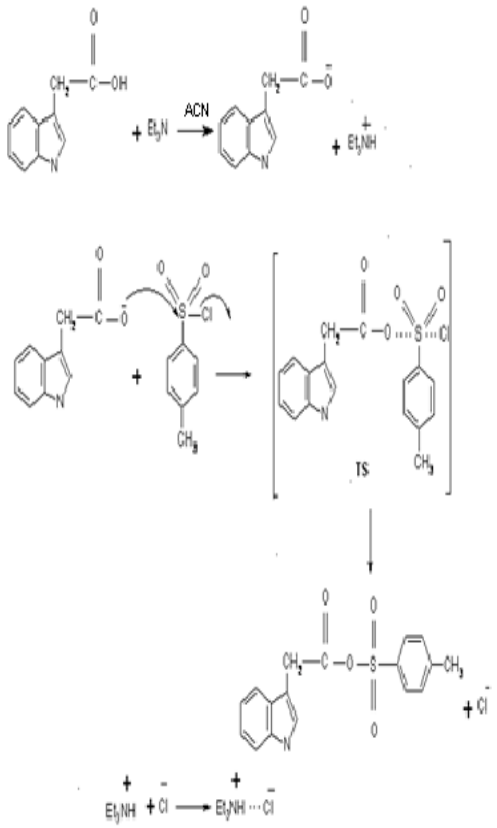
From the results of the antimicrobial activity it is observed that antimicrobial activity of the test samples increases with increase of their concentrations and also found that the synthesized compounds possess varied antimicrobial activities towards the microorganism with minimum inhibitory concentration.

III. RESULT AND DISCUSSION

Treatment of the Indole acetic acid or Naphthalene acetic acid with *p*-toluenesulfonyl chloride in the presence of a strong base triethylamine resulted in the formation of corresponding tosyl esters (Scheme I). Here, the strong base triethylamine abstract the hydrogen from the acid and thereby producing a nucleophile, which attacks the electron deficient sulfur center in *p*-toluenesulfonyl chloride that leads to the formation of tosyl esters. The synthesized tosyl esters were characterized by IR and ^{1}H-NMR spectral measurements. Spectral data confirms the structure of the synthesized compounds. Anti microbial activity on the synthesized compounds has been studied by Agar well diffusion method. From the result it was concluded that the compound I has high activity against the bacterial strain (Staphylococus Aureus) and compound II has high activity against the fungal strain (Aspergillus Niger) when compared with their standards.

Based on the spectral data it is concluded that the reaction may proceed through the following reaction path way.

Reaction path way



IV. CONCLUSION

Tosylesters of Indoleacetic acid and Naphthalene Acetic acid were synthesized and characteriazed by FT-IR and ^{1}H-NMR. The synthesized compounds were identified by TLC technique. From the spectral data the structure of the compounds were established. The bacterial strain Staphylococus Aureus and fungal strain Aspergillus Niger were used for antimicrobial screening. Based on the results, the newly synthesized compounds possess significant antimicrobial activity comparable to that of the standard drugs used.

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