Power System Technology
ISSN:1000-3673

Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

Synthetic Development, Characterization and Antibacterial Activity of N-Substituted Derivatives of Procaine Sulfonamide

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Abstract

A new series of N-substituted Procaine sulfonamide derivatives (2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate) (**3a)** was synthesized and their antibacterial activity was assessed. The 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate (**3a)** was produced by reacting benzene sulphonyl chloride **(2a)** with 2-(diethylamino) ethyl 4-aminobenzoate (**1a**) in the presence of 10% Na_2CO_3**.** The parent compound was used further for the synthesis of N-alkyl/aralkyl-(2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate) **(5ac-ah**) by the interaction of lithium hydride and aralkyl/alkyl halides (**5c-h**) in polar aprotic media**.** The synthesized compounds were subjected against different strains of bacteria containing Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi, and

Power System Technology
ISSN:1000-3673

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Bacillus subtilis in comparison to conventional Ciprofloxacin to check their antibacterial activity and it was found that strong activity was shown by the compound **3a** against Salmonella typhi. The derivative **5ac** do not show inhibition activity against any bacteria except S. typhi. While compound **5ae** was found to be a strong inhibitor of complete strains of bacteria, containing Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Bacillus subtilis with MIC values 9.52±1.00, 10.58±2.96, 11.75±3.42, 8.02±3.29 respectively but showed moderate inhibition against Salmonella typhi. EI-MS, IR and ^{1}H-NMR spectral data was used to confirm the structures of the synthesized sulfonamide derivatives.

Keywords: Procaine, Benzene-sulfonyl chloride, antibacterial activity, Procaine sulfonamide

1. INTRODUCTION

Sulfonamides have been used as drug since 1968 and are among the most commonly prescribed antibiotics in the world. Sulfonamides are sulfanilamide derivatives that have a SO_2NH_2 moiety in their structure[1]. Gram (+ve) and (-ve) bacteria were found to be resistant to the sulfonamides, which were shown to be effective remedies. Any modification to the ring of the benzene sulfonamide results in a decrease or loss of activity[2]. Alfred Einhorn synthesized procaine in 1905, and it was first used as Novocain in medicine[3]. Numerous biochemical and cellular functions, including DNA methylation[4], oxidative phosphorylation[5], metabolic structure and function, membrane conductivity[6], and monoamine oxidase activity[7], are impacted by procaine and its metabolites. Furthermore, it was noted that procaine at high concentrations (20 mM) prevents bacteria from repairing their DNA[8]. A common local anesthetic used in neurological treatment is procaine. There have also been several other documented medical applications of procaine to treat conditions like antibacterial effect[9], overweight, depressive disorders, inflammatory conditions, and even cancer[10]. Its biological effect has been well investigated for many years[11]. It reversibly inhibits the conduction of impulses along excitable membranes, such as nerve axons, that use sodium channels as their principal source of action potential creation. Clinical applications exist for this activity, which blocks pain perception in particular body parts[12]. In the form of uncharged molecules, procaine enters tissues and acts as a cation inside cells[13]. Procaine usually has a short duration of action and might cause cardiac or neurological damage. In certain instances, it may even exhibit allergic signs[14]. Sulfonamide are the weak acids and are usually solvable in basic aqueous medium of solutions[15]. Sulfonamides have many biological activities like anticancer [16], antiepileptics[17], anti-bacterial [18], anti-viral[19], antifungal[20] and neurotoxicity actions[21]. Different sulfonamides have been employed in drugs as: Sulfisoxazole, Sulfamethoxazole anaphylactic shock, hepatitis, serum sickness, interstitial nephritis, pneumonia[22]. Its side effects caused fever, myocarditis, blood dyscrasia and many allergic reactions[23]. In a simple method of synthesis of sulfonamides, the alkyl/aralkyl/aryl amines attack on sulfonyl halides nucleophilically to produce sulfonamides[22] or aryl sulfonyl

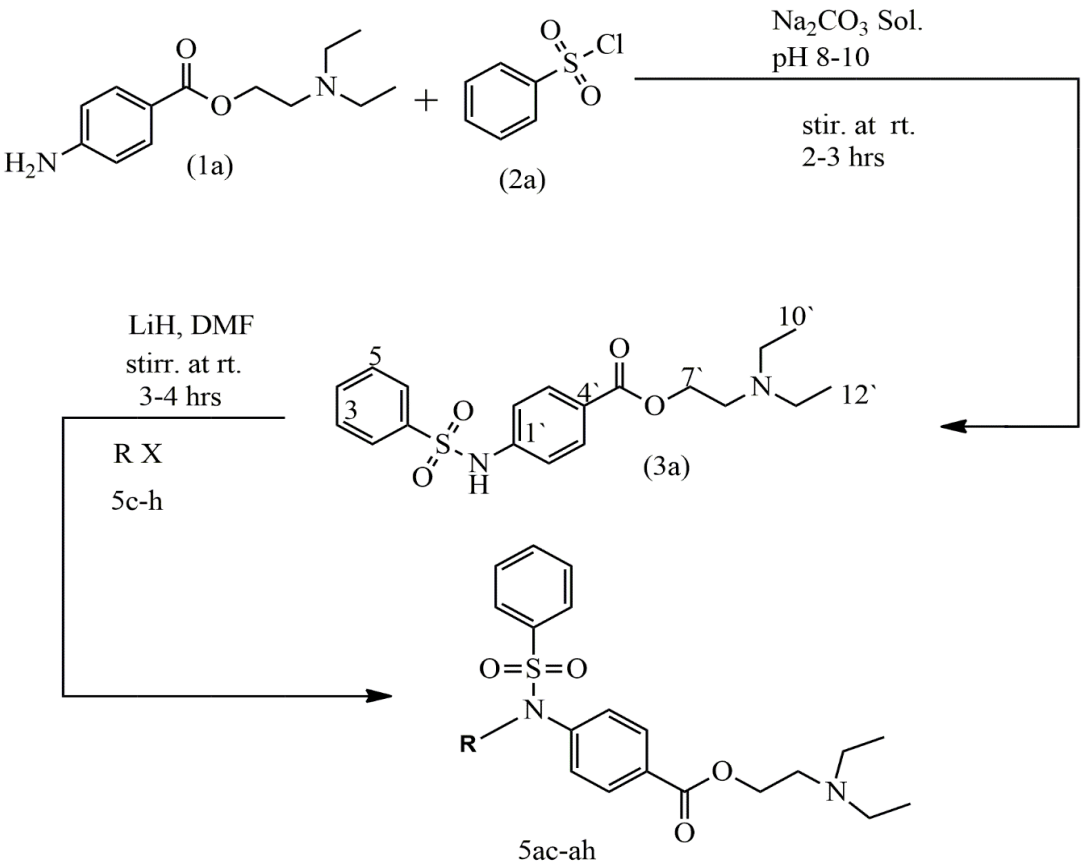
Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

azides can be reduced to sulfonamides[23]. Literature survey and medicinal importance of sulfonamides bring us to investigate antibacterial activity of these newly formed molecules derived from Procaine sulfonamide (**3a)** and their structures were established by using different spectral method such as ^{1}H-NMR, EI-MS and IR spectral data. For more information see[23-27].

2. EXPERIMENTAL

2.1. General

Various alkyl/aryl/aralkyl electrophiles, procaine, benzene sulfonyl chloride, and some important reagents buy from Sigma Aldrich and Merck. TLC method was used to check the purity of the synthesized derivatives by using organic solvents i.e.; chloroform and n-hexane in 3:7 ratios. TLC silica gel plates G-25UV_{254} was used for the visualize the compounds under UV lamp using ceric sulphate solution. On Gallonkamp equipment using an open capillary tube, the parent compound melting points and its derivatives were noted and no changes were found in M.P. of these compounds. A jasco320-A spectrophotometer with its wave number in cm^{-1} was used to measure

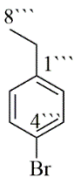
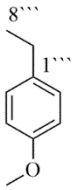
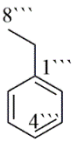
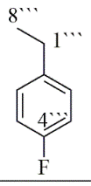


Scheme 1: Synthesis of N-Substituted derivatives of Procaine Sulfonamide

Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

the infrared spectra with KBr pellets method and JEOL JMS-600H apparatus used to conclude the mass spectra of all synthesized molecules. On a Bruker spectrometer, the parent compound and various derivative were individually dissolved in $CDCl_3$-d_1, the temperature was kept 25°C at 400 MHz to take the ^{1}H-NMR spectra.

Table 1: Different alkyl/aryl/aralkyl (5c-h)

Compd. No.	-R	Compd. No.	-R
(5c)	1‴ -CH2-CH3	(5f)	
(5d)	1‴ -CH2-CH2-CH3	(5g)	
(5e)		(5h)	

2.2. Procedure for the synthesis of parent compound (3a)

Procaine (2-(diethylamino) ethyl-4-aminobenzoate) 2.13 g (0.00905 mol) added in 50ml round bottom flask containing 15 mL distilled water. The pH of reaction mixtures between 8 to 10 was kept by the addition of 5ml sodium carbonate. After stirring for at least 25 min then 3.27 grams of benzene sulfonyl Chloride (0.00905 mol) gently introduced in reaction mixture. Stirring was done continuously for 2-3 hours. Reaction progress was examined with the help of TLC plate by employing suitable system of solvents and UV lamp. When single spot appears on TLC plate few drops of hydrochloric acid was added in solution with vigorous hand shaking, in order to maintain the pH of the reaction mixture between 4 to 6. The product (3a) precipitated out were collected after filtration and dried. Scheme 1 illustrate the synthesis of 3a compound (2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate).

Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

2.2.1. 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate (3a)

Off white gummy solid; M.F: $C_{19}H_{24}N_2O_4S$**;** M.W: 376.4g/mol; m.p 145°C, Percentage Yield: 85 %; IR stretching (KBr) ν_{max} cm^{-1}: 3400 (N-H), 1346 (S=O), 1290 (Carbon nitrogen group), 1690 (Carbonyl), 1590 (Aromatic alkene group), 1180 (ether group), 2916 (Ar C-H); ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): δ_H (ppm) 7.91 (d, J = 9.03, 2H, for H-2 and H-6) , 7.62 (t, J = 8.05, 2H, H-3 and H-5), 6.71 (t, J = 6.55, 1H, H-4), 7.09 (d, J = 8.25, 2H, H-2` and H-6`), 7.64 (d, J = 6.88, 2H, for H-3` and H-5`), 4.30 (t, J = 6.89, 2H, H-7`), 3.15 (t, J = 6.89, 2H, H-8`), 3.01 (q, J = 7.16, 4H, H-9` & H-11`), 1.02 (t, J = 8.16, 6H, H-10` and H-12`); The EI-MS (m/z) ratio: 378.67 $[M+2]^+$, 376.67 $[M]^+$, 361.22 $[M\text{-}CH_3]^+$, 141.25 $[M\text{-}C_{13}H_{19}N_2O_2]^+$, 86.43 $[M\text{-}C_{14}H_{12}NO_4S]^+$, 77.01 $[M\text{-}C_{13}H_{18}N_2O_4S]^+$.

2.3. Methodology for the synthesis of derivatives consisting of alkyl/aryl/aralkyl-2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate (3ac to 3ah).

0.48 g (0.001275 mol) of 3a was measured and added in a round bottom flask. Reaction media solvent dimethyl formamide (DMF) 5 mL was added. Then LiH 0.004g (0.50 mmol) was added in the flask. The electrophiles (0.001275 mol) of alkyl/aryl/aralkyl as shown in table.1 (5c-h) were added to the flask with continues stirring for 3–4 hours. The compounds purity was confirmed by TLC until a single spot was appeared. The precipitate was obtained then washed with water to carry out additional recrystallization.

2.3.1. 2-(diethylamino) ethyl 4-(N-ethylphenylsulfonamido) benzoate (5ac)

Off white powder; M.F: $C_{21}H_{28}N_2O_4S$; M.W: 404.53 g/mol; m.p 151°C, Percent Yield: 81%; stretching frequency ν_{max} IR (KBr) in cm^{-1}: 1342 (S=O), 1279 (Caron-Nitrogen bond), 1684 (C=O), 1587 (aromatic alkene functional group), 1176 (C-O-C ether group), 2910 (C-H), ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): δ_H (ppm) 7.89 (d, J = 8.02, 2H, H-2 and H-6), 6.98 (t, J = 8.02 ,2H, H-3 and H-5), 8.71 (t, J = 7.53, 1H, H-4), 6.71 (d, J = 8.19, 2H, H-2` and H-6`), 7.68 (d, J = 6.87, 2H, H-3` and H-5`), 4.30 (t, J = 6 .88, 2H, H-7`), 3.15 (t, J = 6.88, 2H, H-8`), 3.01 (q, J = 7.15, 4H, H-9` and H-11`), 1.03 (t, J = 7.15, 6H, for H-10` & H-12`), 3.25 (q, J = 8.11, 2H, H-1```), 2.15 (t, J = 7.16, 3H, H-2```); The EI-MS (m/z) ratio: 406.76 $[M+2]^+$, 404.76 $[M]^+$, 141.03 $[M\text{-}C_{15}H_{23}N_2O_2]^+$, 86.43 $[M\text{-}C_{16}H_{16}NO_4S]^+$, 77.01 $[M\text{-}C_{15}H_{22}N_2O_4S]^+$.

2.3.2. 2-(diethylamino) ethyl 4-(N-propyl phenyl sulfonamido) benzoate (5ad)

Light brown powder; Molecular Formula: $C_{22}H_{30}N_2O_4S$**;** Molecular weight: 418.55g/mol; Yield: 85%;m.p 155°C, stretching frequency ν_{max} IR (KBr) in cm^{-1}: 1278 (Carbon nitrogen bond), 1683 (carbonyl group), 1175 (Ether functional group), 2909 (C-H), 1586 (aromatic alkene), 1341 (Sulphonyl group); ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): (ppm)

Power System Technology
ISSN:1000-3673
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δ_H 7.81 (d, J = 8.03, 2H, H-2 and H-6), 7.62 (t, J = 8.05, 2H, H-3 andH-5), 7.71 (t, J = 7.54, 1H, H-4), 6.73 (d, J = 8.2, 2H, H-2` and H-6`), 7.68 (d, J = 7.89, 2H, H-3` and H-5`), 4.30 (t, J = 6.89, 2H, H-7`), 3.15 (t, J = 6.89, 2H, H-8`), 3.01 (q, J = 7.14, 4H, H-9` and H-11`), 1.02 (t, J = 6.14, 6H, H-10`& H-12`), 3.21 (q, J = 8.11, 2H, H-1```), 1.57 (t, J = 6.16, 3H, H-2```),, 1.96 (t, J = 7.67, 3H, H-3```); The EI-MS (m/z) ratio: 420.77 $[M+2]^+$, 418.77 $[M]^+$, 141.45 $[M-C_{16}H_{25}N_2O_2]^+$, 86.4 $[M-C_{17}H_{18}NO_4S]^+$, 77.01 $[M-C_{16}H_{25}N_2O_4S]^+$

2.3.3. 2-(diethylamino) ethyl 4-(N-benzylphenylsulfonamido) benzoate (5ae)

Greenish solid; M.F: $C_{26}H_{30}N_2O_4$; M.W: 466.60 g/mol; Yield: 75%; m.p 159°C, stretching frequency ν_{max} IR (KBr) in cm^{-1}: 1286 (Carbon nitrogen bond), 1682 (carbonyl group), 1177 (ether group), 2909(C-H), 1589 (aromatic alkene functional group), 1344 (S=O); ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): (ppm) δ_H 7.91 (d, J = 8.01, 2H, H-2 and H-6), 7.62 (t, J = 8.01, 2H, H-3 and H-5), 7.71 (t, J = 7.54, 1H, H-4), 6.71 (d, J = 8.19, 2H, H-2` and H-6`), 7.68 (d, J = 6.88, 2H, H-3` and H-5`), 4.35 (t, J = 6.89, 2H, H-7`), 3.16 (t, J = 6.99, 2H, H-8`), 3.08 (q, J = 7.15, 4H, H-9` and H-11`), 1.07 (t, J = 7.16, 6H, for H-10` & H-12`), 7.29 (d, J = 7.16, 2H, H-2``` and H-6```), 7.40 (t, J = 7.72, 2H, H-3``` & for H-5```), 7.30 (t, J = 7.73, 1H, H-4```), 2.80 (s, 2H, H-7```), 3.50 (t, J = 6.92, 2H, H-8```); The EI-MS (m/z) ratio: 468.23 $[M+2]^+$, 466.23 $[M]^+$, 141.43 $[M-C_{20}H_{25}N_2O_2]^+$, 86.43 $[M-C_{19}H_{23}NO_4S]^+$, 77.01 $[M-C_{20}H_{25}N_2O_4S]^+$.

2.3.4. 2-(diethylamino) ethyl 4-(N-(4-bromobenzyl) phenylsulfonamido) benzoate (5af)

Light Yellow powder; Molecular Formula: $C_{26}H_{29}BrN_2O_4S$; Molecular weight**:** 544.49g/mol; Yield: 81%; m.p 163°C, stretching frequency ν_{max} IR (KBr) in cm^{-1}: 1293 (Carbon nitrogen bond), 1696 (Carbonyl group), 1184 (ether group), 2920 (C-H), 1598 (aromatic alkene), 1350 (S=O); ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): (ppm) δ_H 8.12 (d, J = 8.02, 2H, H-2 and H-6), 8.62 (t, J = 8.99 ,2H, H-3 and H-5), 7.71 (t, J = 7.53 ,1H, H-4), 6.73 (d, J = 8.20, 2H, H-2` and H-6`), 7.68 (d, J = 6.89, 2H, H-3` and H-5`), 4.30 (t, J = 6.88, 2H, H-7`), 3.15 (t, J = 6.89, 2H, H-8`), 3.08 (q, J = 7.19, 4H, H-9` and H-11`), 1.02 (t, J = 7.15, 6H, H-10` and H-12`), 7.18 (d, J = 6.96, 2H, for H-2``` & H-6```), 7.92 (t, J = 5.90, 2H, H-3``` and H-5```), 2.80 (t, J = 6.98, 2H, H-7```), 3.51 (t, J = 6.96, 2H, for H-8```); The EI-MS (m/z) ratio: 546.87 $[M+2]^+$, 544.87 $[M]^+$, 464.23 $[M-Br]^+$, 141.32 $[M-C_{20}H_{24}BrN_2O_2]^+$, 86.43 $[M-C_{21}H_{17}BrNO_4S]^+$, 77.01 $[M-C_{20}H_{24}BrN_2O_4S]^+$

2.3.5. 2-(diethylamino) ethyl 4-(N-(4-methoxybenzyl) phenylsulfonamido) benzoate (3ag)

Yellowish Powder; M.F: $C_{27}H_{32}N_2O_5S$; M.W: 496.62 g/mol; Yield: 80%; m.p 164°C, stretching frequency ν_{max} IR (KBr) in cm^{-1}: 1280 (Carbon nitrogen bong), 1682 (Carbonyl group), 1173 (ether group), 2908 (C-H), 1583 (aromatic alkene functional group), 1341 (S=O);

Power System Technology
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^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): (ppm) δ_H 7.93 (d, J = 8.03, 2H, H-2 and H-6), 7.62 (t, J = 8.02 ,2H, H-3 and H-5), 7.74 (t, J = 7.54, 1H, H-4), 6.71 (d, J = 8.20, 2H, H-2` and H-6`), 7.69 (d, J = 6.89, 2H, H-3` and H-5`), 4.29 (t, J = 6.89, 2H, H-7`), 3.17 (t, J = 6.88, 2H, H-8`), 3.01 (q, J = 7.16, 4H, H-9` and H-11`), 1.08 (t, J = 7.19, 6H, H-10` and for H-12`), 7.27 (d, J = 7.67, 2H, H-2``` and H-6```), 6.99 (t, J = 7.66, 2H, H-3``` & H-5```), 2.87 (t, J = 7.16, 2H, H-7```), 3.47 (t, J = 7.15, 2H, H-8```). The EI-MS (m/z) ratio: 498.31 $[M+2]^+$, 496.33 $[M]^+$, 86.41 $[M\text{-}C_{23}H_{23}NO_5S]^+$, 141.34 $[M\text{-}C_{21}H_{27}N_2O_3S]^+$, 77.01 $[M\text{-}C_{21}H_{27}N_2O_5S]^+$

2.3.6. 2-(diethylamino) ethyl 4-(N-(4-fluorobenzyl) phenylsulfonamido) benzoate (5ah)

Brownish amorphous powder; M.F: $C_{26}H_{29}FN_2O_4S$; M.W:484.59 g/mol; Yield: 75%; m.p 160°C, stretching frequency ν_{max} IR (KBr) in cm^{-1}:1292 (Carbon nitrogen bond), 1691 (Carbonyl group), 1183 (ether group), 2918 (C-H), 1593 (aromatic alkene functional group), 1352 (S=O); ^{1}H-NMRchemical shift (400 MHz frequency, $CDCl_3$): δ_H (ppm) 7.91 (d, J = 8.03, 2H, H-2 and H-6), 7.62 (t, J = 8.03 ,2H, H-3 and H-5), 7.71 (t, J = 7.54 ,1H, H-4), 6.71 (d, J = 8.21, 2H, H-2` and H-6`), 7.68 (d, J = 6.89, 2H, for H-3` and H-5`), 4.30 (t, J = 6.87, 2H, H-7`), 3.15 (t, J = 6.89, 2H, H-8`), 3.01 (q, J = 7.16, 4H, for H-9` and H-11`), 1.02 (t, J = 7.16, 6H, H-10` and H-12`), 7.18 (d, J = 7.17, 2H, for H-2``` & H-6```), 6.94 (t, J = 6.99, 2H, for H-3```& H-5```), 3.83 (s, 1H, for H-4```), 3.80 (t, J = 6.0, 2H, H-7```), 4.50 (t, J = 6.02, 2H, H-8```); The EI-MS (m/z) ratio: 486.33 $[M+2]^+$, 484.33 $[M]^+$ 141.20 $[M\text{-}C_{20}H_{24}FN_2O_2]^+$, 86.4 $[M\text{-}C_{21}H_{17}FNO_4S]^+$, 77.01 $[M\text{-}C_{20}H_{24}FN_2O_4S]^+$

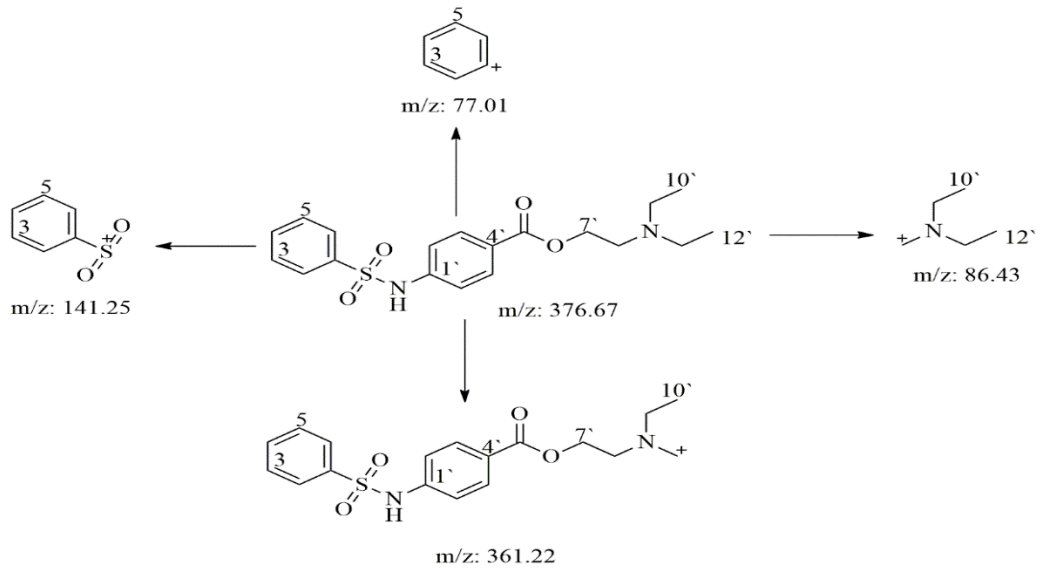

Figure 1: Mass Fragmentation of 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate (3a)

Power System Technology
ISSN:1000-3673
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2.4. Antibacterial Assays

In a sterile 96-well microplate, the produced derivatives' anti-bacterial activity was assessed under aseptic circumstances. Gram (+ve) bacteria including Staphylococcus aureus & Bacillus subtilis as well as gram (-ve) bacteria like Escherichia coli, Salmonella typhi & Pseudomonas aeruginosa were all tested against these compound. This method is based on a specific principle that shows as the population of microorganisms grow, increase the broth medium's absorbance. Because of this, the derivatives were first diluted before being pumped into wells. Ager was used for the growth of bacterial culture supplement. These new bacterial cultures were examined additionally by dilution with nutrient broth then put into the wells (180 L) at 37°C temperature was maintained for 24 hours during incubation. With the use of a microplate reader instrument, the absorbance between 0.12 and 0.19 was maintained at 540 nm in order to observe the zone of inhibition. The well-volume microplates were precisely maintained at 200 L. The estimated absorbance was 540 nm, and the disparity between the samples and the absorbance test reflects the progress of the bacteria.

3. RESULTS AND DISCUSSION

The synthesis of a number of procaine sulfonamide derivatives was the main goal of the current study. The parent compound (**3a)** was synthesized by reacting **(2a)** benzene sulphonyl chloride with **(1a)** procaine (2-(diethylamino) ethyl-4-aminobenzoate). When procaine sulfonamide was combined with alkyl or aryl halides, N-alkyl/aryl/aralkyl substituted sulfonamide derivatives were produced. The compounds were found as powder and crystals form, and advanced spectral methods like EI-MS, ^{1}HNMR and IR were used to check their structure.

Escherichia coli, Salmonella typhi and Pseudomonas aeruginosa were among the five bacterial strains used to test the compound's anti-microbial properties, while Staphylococcus aureus and Bacillus subtilis were among the two gramme (+) strains.

3.1. Chemistry

This is a two-step synthesis in which the reactants are converted to parent molecules, 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate (3a), and the parent molecule was then coupled up with appropriate electrophiles to generate the derivatives. The spectroscopic findings, which were described in the experimental section, provided excellent evidence for the molecular configurations of all the produced molecules. In EI-MS spectra, the synthesized molecule 3a exhibited the [M]+ peak at m/z 376.67 as shown in figure 1. The occurrence of functional groups in the compound was established by the various bands in the infrared spectra of this compound (3a). Stretching of the S=O functional group was showing at 1346 cm-1. On the other hand, a carbonyl (C=O) stretching peak was revealed at 1180 cm^{-1}.

Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

Similar to this, aromatic ring (C=C) stretching in IR spectra exhibited a distinct band at 1590 cm^{-1}, and carbon nitrogen stretching was occurred at 1290 in units per centi meter. All bands above clearly demonstrated how these groups can be found in molecules. The presence of the procaine moiety and benzene ring in the parent compound (3a) was confirmed by proton NMR spectrum signals that showed both upfield and downfield. Due to the presence of sulfonyl group's electron-withdrawing effect on the aromatic ring, proton NMR spectra of compound displayed (3a) signals chemical shifts data in (ppm) of 7.91 (d, J = 9.03, for two H, H-2 and H-6), proton present at three & four position 7.62 (t, J = 8.05, 2H, H-3 and H-5), and for proton at position 6.71 (t, J = 6.55, one H, H-4) that appeared downfield. Presence of procaine benzene moiety coupled to electronegative atoms, such as oxygen and nitrogen, was confirmed by additional downfield signals in ppm at 7.09 (d, J = 8.25, two H, one is H-2` and other H-6`) and value 7.65 represent doublet having J value = 6.88 for two proton H-3` and H-5`. In the spectra upfield shift, signals at 4.30 (t, J = 6.89, 2H, H-7`), 3.15 (t, J = 6.89, 2H, H-8`), 3.01 (q, J = 7.16, 4H, H-9` and H-11`), and 1.02 (t, J = 8.16, 6H, H-10` and H-12`) verified the presence of the aliphatic region of procaine. The chemical structure of 3a, which was named as 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate, was supported by all of the spectrum data. Similarly, as mentioned in the experimental section, ^{1}H-NMR, IR, and mass spectrum data confirmed the structures of all synthesised compounds.

3.2. Antibacterial Activity

Five strains of bacteria were subjected to antibacterial investigation, with Ciprofloxacin serving as standard drug. Against five bacterial strains, all of the synthesized complexes demonstrated high to normal antibacterial action. Strong activity was shown by the compound **3a** against Salmonella typhi. The derivative **5ac** do not show inhibition activity against any bacteria except S. typhi. While compound **5ae** was found to be a strong inhibitor of complete bacterial strains, comprising Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, having MIC values 11.75±3.42, 8.02±3.29, 9.52±1.00, 10.58±2.96 respectively. While this compound **5ae** shows moderate inhibition against Salmonella typhi. Except for Staphylococcus aureus, which had a MIC value of 16.81±2.50, compound **5ad** showed no inhibitory action against all of the bacterial strains. Only Salmonella typhi demonstrated inhibitory action for compound **5ac**, and it was discovered to be inactive for all other strains. With the exception of Pseudomonas aeruginosa, compound **5af** demonstrated modest inhibitory activity. All compounds MIC values are given in table-02.

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Table-02. MIC value & %age inhibition of antibacterial action

Compound	S. typhi (-)		E. coli (-)		P. aeruginosa (-)		B. subtilis (+)		S. aureus (+)	
	Percent Inhibition	Minimum inhibitory conc.	Percent inhibition	Minimum inhibitory conc.	Percent Inhibition	Minimum inhibitory conc.	Percent Inhibition	Minimum Inhibitory conc.	Percent Inhibition	Minimum inhibitory conc.
3a	74.53± 1.06	10.32± 2.13	72.14± 1.42	14.42± 3.20	67.14± 1.98	12.58±2. 09	59.32± 3.05	12.46±5. 01	63.66± 3.44	15.17±1. 14
5ac	60.54± 2.33	13.36± 3.65	57.53± 1.49	-	28.94± 6.00	_	53.32± 2.51	-	56.56± 1.54	-
5ad	47.58± 2.00	_	42.52± 2.43	_	21.04± 2.48	_	39.28± 2.32	_	56.70± 3.80	16.81±2. 50
5ae	82.73± 2.25	12.94± 5.00	78.94± 2.42	9.52±1. 00	75.76± 1.70	10.58±2. 96	68.77± 2.51	8.02±3.2 9	72.46± 3.15	11.75±3. 42
5af	76.94± 2.79	10.23± 1.31	76.16± 1.36	11.44± 1.60	53.14± 3.68	19.57±2. 98	57.05± 1.95	14.77±0. 54	62.01± 1.41	12.06±1. 35
5ag	64.94± 1.36	17.01± 1.83	71.13± 2.41	14.02± 5.00	55.06± 2.31	17.67±4. 62	57.32± 1.15	15.74±4. 70	59.59± 2.64	16.06±3. 34
5ah	53.50± 1.55	17.51± 3.00	52.15± 4.60	16.41± 1.20	45.85± 2.48	_	53.65± 3.59	15.45±4. 71	63.39± 4.34	12.15±5. 00
Ciprofloxacin	91.84± 0.05	9.21±2. 00	90.56± 1.47	8.92±1. 67	89.65± 1.11	9.02±0.1 4	90.94± 1.06	8.03±0.3 3	92.06± 2.34	8.37±1.0 4

4. CONCLUSION

Procaine sulfonamide and its derivatives were synthesized in the current study. The procaine drug and benzene sulphonyl chloride were combined to create the primary compound. Na_2CO_3, was utilized as a catalyst in this reaction to keep the pH in the range of 8 to 10. The reaction was conducted by stirring for three to four hours at room temperature. These procaine sulfonamide derivatives were made by reacting 2-(diethylamino) ethyl 4-(phenylsulfonamido) benzoate along with various alkyl/aryl halides in the occurrence of lithium hydroxide plus dimethylformamide. Well-yielding manufactured compounds exposed to additional analysis utilising IR, EI-MS and ^{1}H-NMR, spectroscopy. It was found that the produced compounds

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have important clinical applications. They exhibit strong anti-microbial properties and have demonstrated applications in biological research and pharmaceutical sectors.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

FUNDING DETAILS

This study did not get any financial provision.

CONFLICTS OF INTEREST

No authors have reported any competing interest.

Authors Contribution

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All authors have agreed to the published version of the manuscript.

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