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SYNTHESIS, STRUCTURAL ANALYSIS, & ANTIMICROBIAL EVALUATION OF ANILIDE, & THEIR DERIVATIVES OF AROMATIC ALDEHYDE

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ABSTRACT

This work presents the tailoring, characterization, and biological applications of anilide derivatives with aromatic aldehydes. Anilides are an important class of industrially organic compounds with diverse pharmacological activities such as antibacterial, anthelmintic, antifungal, Anti-inflammatory and many more. The potential of biological activity of anilide is enhanced with increasing heteroatom in the compound. These biological activities are showed more potential with having semi-carbazone moiety. TLC monitors the reaction's progress and competition of reaction. The structures of the synthesised compounds were analysed using spectral data from IR and ^{1}H-NMR, which revealed the expected frequencies and signals. The synthesized compounds (2a-2e) were investigated for anti-biological activity by agar well diffusion method. Compound [2c] showed excellent activity while compound [2e] exhibited moderate activity against *Staphylococcus aureus* bacterial stains.

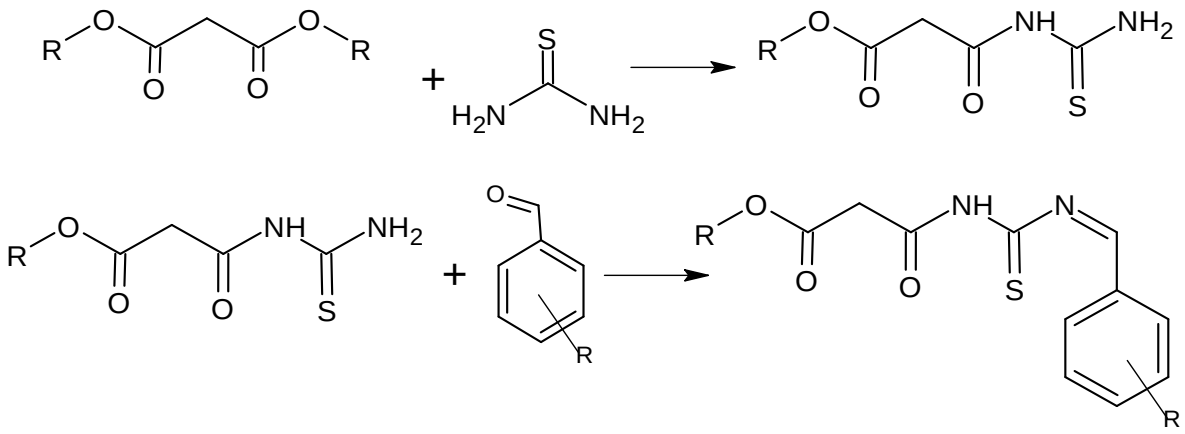
KEYWORDS: Anilide, Azomethine moiety, IR, ^{1}H-NMR, Antimicrobial Evaluation.

INTRODUCTION

The pharmacological activity of anilide compounds spans a wide range, including antibacterial, antifungal, antiviral, anticancer, anti-tuberculosis, anti-malarial, and anti-inflammatory effects.[1-6] The synthesis and biological activities of anilide derivatives have been extensively studied.[7] Anilide is a significant group of compounds; Some analogues are

synthesised and tested for many activities, and have diverse properties such as antimicrobial, insecticidal, herbicidal, and many more. Substitution of sulfur resulted in greatly reduced activity.[8]

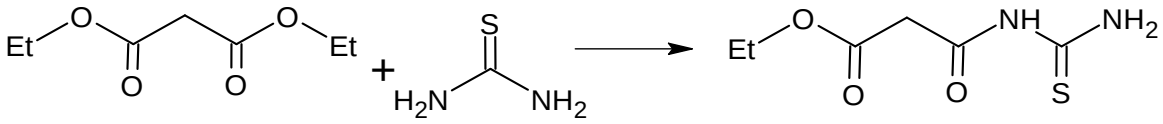
Hetero atoms such as sulphur, nitrogen, oxygen substituents with the anilde moiety resulted in greatly increases the activity.[9] The presence of C=S and C=N moiety in the compounds favours pharmacological and other activity.[10] In this work, we report the synthesis of anilide derivatives bearing azomethine moiety, and their characterization by IR, ^{1}HNMR and Mass spectral data. We predict the potentials of these compounds as drug on *Staphylococcus aureus* and *Escherichia coli* bacterial species.



Reaction Scheme: [01]

EXPERIMENT

[A] Synthesise of ethyl 3-(carbamothioylamino)-3-oxopropanoate



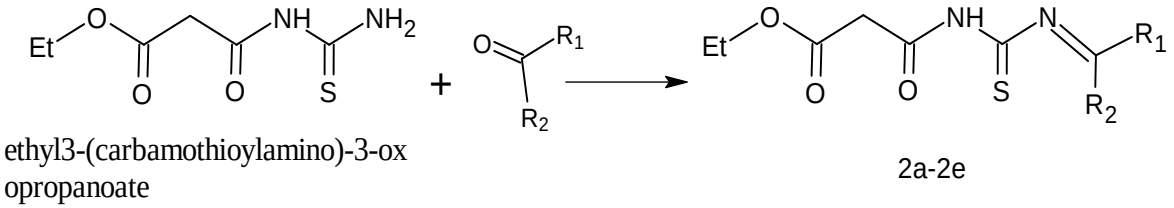
diethyl propanedioate thiourea ethyl-3-(carbamothioylamino)-3-oxo propanoate

Reaction Scheme: [02]

Preparation of **ethyl 3-(carbamothioylamino)-3-oxopropanoate;** A mixture of diethylpropanediote (0.01mol) and thiourea (0.01 mol), were taken in ethanol and refluxed the whole reaction mixture on water both for 3 hr. after refluxing the reaction mixture cooled at room temperature and recrystallized in ethanol. The progress of reaction was monitored by TLC. Melting point of synthesized compound were taken in open capillary.

[B] Synthesis of ethyl 3-oxo-3-({[(*Z*)-phenylmethylidene]carbamothioyl}amino) propanoate [2a]

Preparation of **ethyl 3-(carbamothioylamino)-3-oxopropanoate;** A mixture of **ethyl 3-(carbamothioylamino)-3-oxopropanoate** (0.01mol) and benzaldehyde (0.01 mol), were taken in round bottom flask and add few drops of glacial acid as catalyst. The reaction mixture heated on water bath for 5 hr. after refluxing the reaction mixture poured in ice cooled water. The progress of reaction was monitored by TLC. Melting point of synthesized compound were taken in open capillary.



ethyl3-(carbamothioylamino)-3-oxopropanoate

2a-2e

Reaction Scheme[03]

The other compounds, coded [2b-2e], were synthesised using the same method as [2a].

Table 01: Derivatives of aldehydes used in the synthesis.

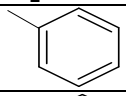
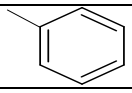
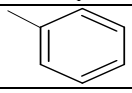
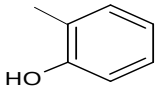
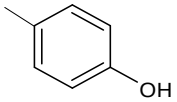
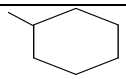
Com. Code	R_1	R_2	Name of synthesized compounds
[2a]	**-H**		ethyl 3-oxo-3-({[(*Z*)-phenylmethylidene]carbamothioyl}amino)propanoate
[2b]			ethyl 3-{[(diphenylmethylidene)carbamothioyl]amino}-3-oxopropanoate
[2c]	**-H**		ethyl 3-({[(*Z*)-(2-hydroxyphenyl)methylidene]carbamothioyl}amino)-3-oxopropanoate
[2d]	**-H**		ethyl 3-({[(*Z*)-(4-hydroxyphenyl)methylidene]carbamothioyl}amino)-3-oxopropanoate
[2e]	**-H**		ethyl 3-({[(*Z*)-cyclohexylmethylidene]carbamothioyl}amino)-3-oxopropanoate

Table 02: Physicochemical properties of compounds code [2a-2e].

SN	Parameter	[2a]	[2b]	[2c]	[2d]	[2e]
01	Mole. Formula	$C_{13}H_{14}N_2O_3S$	$C_{19}H_{18}N_2O_3S$	$C_{13}H_{14}N_2O_4S$	$C_{13}H_{14}N_2O_4S$	$C_{13}H_{20}N_2O_3S$
02	Molecular weight	278.32	394.42	294.32	294.32	284.37
03	Yield %	78.12	82.11	84.11	86.12	61.11
04	Melting Point	108 ^oC	122 ^oC	135 ^oC	138 ^oC	98 ^oC
05	RF Value (TLC)	0.76	0.58	0.62	0.64	0.81
06	Colour	Pale Yellow	Muddy	Muddy	Yellow	Pale Yellow

CHARACTERIZATION

All synthesised compounds are confirmed by IR and HNMR spectral data. In laboratory, thin layer chromatography (TLC) is used to check the purity of product and confirmation of completing of reaction.

[2a] ethyl 3-oxo-3-({[(*E*)-phenylmethylidene]carbamothioyl}amino)propanoate

FT-IR (KBr, cm^{-1}): 2782 (ν CH_3), 1644 (ν C=N), 3168 (ν NH), 760 (ν C=S), 2932 (ν C-H Aro.), 1426 (ν C=C Aro.).

^{1}H NMR (CDCl3) (ppm) δ: 1.1-1.5 (t, CH_3, 3H), 2.1-2.8 (q, CH_2, 2H), 4.8 (s, NH, 1H), 8.1 (s, HC=N, 1H), 6.8-7.6 (m, CH, 5H Aro.).

[2b] ethyl 3-{[(diphenylmethylidene)carbamothioyl]amino}-3-oxopropanoate.

FT-IR (KBr, cm^{-1}): 2781 (ν CH_3), 1652 (ν C=N), 3175 (ν NH), 758 (ν C=S), 2925 (ν C-H Aro.), 1406 (ν C=C Aro.).

^{1}H NMR (CDCl3) (ppm) δ: 0.8-1.6 (t, CH_3, 3H), 2.0-3.1 (q, CH_2, 2H), 5.1 (s, NH, 1H), 7.9 (s, HC=N, 1H), 6.9-7.8 (m, CH, 10H Aro.).

[2c]: ethyl 3-({[(*E*)-(2-hydroxyphenyl)methylidene]carbamothioyl}amino)-3-oxopropanoate

FT-IR (KBr, cm^{-1}): 2778 (ν CH_3), 1638 (ν C=N), 3169 (ν NH), 758 (ν C=S), 12918 (ν C-H Aro.), 1422 (ν C=C Aro.), 3342 (ν C-O.).

^{1}H NMR (CDCl3) (ppm) δ: 1.2-1.4 (t, CH_3, 3H), 3.0-4.1 (q, CH_2, 2H), 5.5 (s, NH, 1H), 7.7 (s, HC=N, 1H), 7.0-7.8 (m, CH, 4H Aro.), 9.2 (s, O-H, 1H).

[2d]: ethyl 3-({[(*E*)-(4-hydroxyphenyl)methylidene]carbamothioyl}amino)-3-oxopropanoate

FT-IR (KBr, cm^{-1}): 2767 (ν CH_3), 1641 (ν C=N), 3174 (ν NH), 754 (ν C=S), 2934 (ν C-H Aro.), 1413 (ν C=C Aro.), 3327 (ν C-OH).

^{1}H NMR (CDCl3) (ppm) δ: 1.2-1.5 (t, CH_3, 3H), 3.1-4.4 (q, CH_2, 2H), 5.7 (s, NH, 1H), 7.2 (s, HC=N, 1H), 6.2-7.8 (m, CH, 4H Aro.), 8.3 (s, O-H, 1H).

[2e]: ethyl 3-({[(*Z*)-cyclohexylmethylidene]carbamothioyl}amino)-3-oxopropanoate

FT-IR (KBr, cm^{-1}): 2758 (ν CH_3), 1631 (ν C=N), 3168 (ν NH), 758 (ν C=S).

^{1}H NMR (CDCl3) (ppm) δ: 1.5-1.8 (t, CH_3, 3H), 2.9-3.1 (q, CH_2, 2H), 5.1 (s, NH, 1H), 8.1 (s, HC=N, 1H).

ANTIBACTERIAL ACTIVITY

The agar well diffusion method used to determine MIC (minimum inhibitory concentration) of synthesized compounds against *Staphylococcus aureus* and *Escherichia coli* bacterial strain. Streptomycin was employed during the test procedures as a stander drug. Tested compounds were found to be more sensitive toward *Staphylococcus aureus* (Gram-positive bacteria) as compare to *Escherichia coli* (Gram-negative bacteria) bacterial stains.

CONCLUSION

The anilides derivatives were successfully synthesized from the condensation reaction of ethyl-3-(carbamothioylamino)-3-oxopropanoate with various aldehyde and their structures were identified by NMR, and FTIR spectra. The anti-bacterial activity of the prepared compounds was tested against *Staphylococcus aureus* and *Escherichia coli* bacterial stains.

The compound coded [2c] and [2d] shows excellent activity against bacterial stains *Staphylococcus aureus* while compound [2e] show moderate activity against *Staphylococcus aureus*. All synthesized compounds show moderate activity against *Escherichia coli* bacterial stain.

REFERENCES

1. Barbara BC. (Anilides and Toluidides of 3β-Acetyloleanolic Acid). Natural Product Communications, 2011; 7(4): 507-510.
2. Naresh S, Moni S and Prem MSC. (Recent advances in the design and synthesis of Heterocycles as anti-tubercular agents). Future Medicinal Chemistry, 2010; 2(9): 1469-1500.
3. Altaf HP, Nasarul I. (Antimicrobial activity assessment of certain anilide derivatives: a DFT study). Nasarul Islam Int. J. Chem, 2012; 1(1): 71-79.
4. Anurag K, Arun N, Pradeep Kumar, Balasubramanian N. (Synthesis, antimicrobial evaluation and QSAR studies of gallic acid derivatives). Arabian Journal of Chemistry, 2017; 10: S2871-S2880.
5. Bhupender SR, Shrawan KS, Nidhi G, Roopali T and S.C Mehra. (Synthesis Characterization and Anti-Inflammatory Activities of Substituted Aniline Oxadiazolyl Derivatives). IJSRSET173467, 2017; (3)5: 290-295.

6. Ze Li Mansoora K, Zhigang Z, Carol BP, Richard JK, and Mark C. (Design, Synthesis, and Biological Evaluation of Antiviral Agents Targeting Flavivirus Envelope Proteins). J. Med. Chem, 2008; 51: 4660–4671.
7. Alaa MH, Ahmad AT, and Abdel Alim MA. (Design and Synthesis of New 8-Anilide Theophylline Derivatives as Bronchodilators and Antibacterial Agents). Arch Pharm Res, 2012; 35(08): 1355-1368.
8. Prateek P, Mousmee S. (Medicinal chemistry of anthranilic acid derivatives: A mini review). Drug development research, 2022; 18(13): 01-05.
9. Praveen KS, Andleeb A and M Kumar. (A Review: Medicinally Important Nitrogen Sulphur Containing Heterocycles). The Open Medicinal Chemistry Journal, 2020; 14: 49-64.
10. Siddiqui EJ, Azad I, Khan AR, Khan T. (Thiosemicarbazone Complexes as Versatile Medicinal Chemistry Agents: A Review). Journal of Drug Delivery and Therapeutics, 2019; 9(3): 689-703.