



Synthesis and Characterization of Heterocyclic Compounds Derived from Schiff base Glycerol Triester

Marwa Abdulameer Mseer^{1*}, Khudheyer Jawad², Yahya Al-Khafaji³

Abstract

Heterocyclic compounds were prepared from Schiff bases triester derivatives, the first step was included, p-aminobenzoic acids convert to p-amino benzoyl chloride in the presence of thionyl chloride then glycerol was added to form triesters compound A. second step reaction of triester product with the 4-nitrobenzaldehyde, and 3-amino benzaldehyde to produce M1, and M2. The third step. Involve reacted Schiff bases triester derivatives to give heterocyclic compounds M1S, M1A, M2P, and M2K. The structure of all compounds is monitored by (TLC), and identified by many techniques ¹HNMR, FT-IR, and melting point.

Key Words: Schiff Bases Triester, Heterocyclic, 1, 3 Oxazepine.

DOI Number: 10.14704/nq.2021.19.9.NQ21141

NeuroQuantology 2021; 19(9):88-96

88

Introduction

Glycerol esters are the most common and diverse group of glycerol derivatives. They are found in the animal and of plants, especially vegetables as natural glycerides, oils, and fats. Glycerol and fatty acids are used to make a variety of glycerides. Inorganic acid esters are also present. The number of possible esters is enormous because glycerol has three hydroxyl groups, each of which can be esterified with almost any combination of acid radicals. The past few years have seen a great deal of progress in the esterification of glycerol, which yields a multitude of useful products (Pagliaro, Rossi and Pagliaro, 2008), such as (Pouilloux, Métayer and Barrault, 2000; Tewari and Bunk, 2001; Swati L Pandhare, Dongare and Umbarkar, 2015; Arshad *et al.*, 2018; Keogh, Tiwari and Manyar, 2019; Kong *et al.*, 2019). There are many

researcher that have studied the applications of Schiff base ester compounds as in ester (Nawaz *et al.*, 2009; Singh *et al.*, 2015; Hagar *et al.*, 2019), especially derived from heterocyclic rings offer numerous advantages in the development of novel compounds with biologically active properties. Nitrogen, oxygen, and sulfur are the most common heteroatoms (Fonkui *et al.*, 2018). Schiff bases have been extensively studied due to their structural diversity, selection and sensitivity to metal atoms, structural similarity with biological compounds found in nature, and the presence of the (-N = CH-) group (azomethine) that contribute to the understanding of biological transformations and elemental reactions (Gao and Zheng, 2002).

Corresponding author: Marwa Abdulameer Mseer

Address: ^{1,2,3}Department of Chemistry, College of Science, University of Babylon, Iraq.

¹E-mail: marwaabdulameer86@gmail.com

²E-mail: khudheyer_1965@gmail.com

³E-mail: sci.yahya.alkhafaji@uobabylon.edu.iq

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 10 July 2021 **Accepted:** 18 August 2021



The current study aims to synthesis Heterocyclic compounds 1, 3 oxazepine and tetrazole by Schiff bases derivatives. Heterocyclic compounds are cyclic compounds that contain at least one carbon atom and at least one non-carbon element. Homocyclic compounds are rings with only one heteroatom, and heterocycles are monocyclic compounds' counterparts.

Heterocyclic compounds are formed when oxygen, nitrogen, sulphur, or an atom of a related element is substituted for a carbon atom in an organic ring structure (Al-Masoudi *et al.*, 2006). It is well known that heterocyclic compounds with an azole nucleus are important pharmacophores that can be found in a wide range of pharmaceutical agents, are involved in a wide range of biochemical processes, and have a wide range of pharmacological activities. These heterocyclic compounds are an important part of organic chemistry; they are abundant in nature and play an important role in living cell metabolism. For Their practical applications span fields as diverse as medicine, agriculture, photochemistry, biocidal formulation, and polymer science, among others (Ravindra *et al.*, 2006). Some applications of cyclic compounds are mentioned in (Lamberth and Dinges, 2012; Ali *et al.*, 2018; Ma *et al.*, 2018; Ahmed, Ali and Khadom, 2019; Al-lami and Salom, 2019; Mahesh, Karpagam and Pandian, 2019; Pathan *et al.*, 2020).

Experimental

1. Materials and Methods

FT-IR spectra were measured an (FTIR-Affinity-1 SHIMADZU) in the range of (400 - 4000) cm⁻¹ using KBr disk. Proton Nuclear Magnetic Resonance (¹H-NMR) spectra were recorded on VARIAN, Ultra Sheild 300 MH Z in Iran, using DMSO as a solvent in Iran. The melting points were determined by using a Stuart melting point apparatus (SMP30, England) in the University of Babylon.

The reaction endpoint was followed by Thin-layer chromatography (TLC), aluminum plates coated with a 0.25mm layer of silica gel (Fluka) and the visualization was performed using iodine. All chemicals were used directly without further purification and it's were purchased from THOMAS BAKER, Analar R, Hayman Kimia, MACRON, CHEM-LAB.

2. Synthesis

Esterification of Glycerol (compound A)

A (4.114 g, 30.00 mmol) from p-aminobenzoic acid was taken in a 100 mL round-bottomed flask with 50 mL of benzene. Slowly added (4.35 mL, 60.00 mol) of SOCl₂ with stirred at room temperature for 30 min. Then (10 mmol) of glycerol was added. The reaction mixture was refluxed at (90–110 °C) for 6 hours. After reaction completion, the solvent was evaporated under vacuum at 100°C by a rotator evaporator. The obtained product was washed with petroleum ether and dioxane. Precipitate product an off-white solid (A).

Synthesis of Schiff bases Triester

In a 100 mL round-bottomed flask, (0.89g, 2.00 mmol) of compound A, and (6mmol) each of (0.90g of 4-nitrobenzaldehyde), and (0.72g of 3-amino benzaldehyde), were dissolved with (35 ml) ethanol and a few drops of GAA, and the mixed solution was stirred for (6-9) hours at (75-100° C). TLC was used to monitor the mixture, rotator evaporator was used to remove the solvent under reduced pressure. The solid precipitate that resulted in compounds M1 and M2 was dried in a desiccator at 80°C. ethanol was used to re-crystallize (Mehetre, Deshmukh and Bhosale, 2019)(Okey *et al.*, 2020).

TLC (Petroleum ether 3:2 Chloroform).

Synthesis of Heterocyclic Compounds

1. Synthesis of 1, 3 Oxazepines Compound M1S

A (1.00 mmol), of (0.80 g, compound M1), with (0.30g, 3.00 mmol) of succinic anhydride, in a 250 mL round bottom flask was dissolved with (30 ml) THF was used as a solvent. The reaction mixture was refluxed with stirring for (22-24) hours at (90-100°C). The mixture was tracked by TLC. A rotator evaporator evaporated the solvent under vacuum at 100°C. The product was sticky (gummy) and was washed with petroleum ether, ethanol, and chloroform, respectively, filtered off, to get rid of the gummy state, a solid precipitate appeared compound M1S. The resulting precipitate was dried in a desiccator at 80°C.

2. Synthesis of Tetrazoles Compound M1A

In a 50 mL round bottomed flask, (0.089g, 1.00 mmol) of compound M4 with (0.19g, 3mmol) of Sodium azide was dissolved with 25 ml THF. The reaction mixture was refluxed at (85-100°C) for



(22-24) hours with stirring. TLC was used to track the mixture. A rotator evaporator evaporated the solvent under vacuum at 100°C. The solid precipitate compound M1A was then dried at 80°C in a desiccator. The obtained product was chloroform washed and filtered. TLC (Petroleum ether 3:2 Chloroform).

3. Synthesis of 1, 3 Oxazepines Compound M2P

A (1.00 mmol), of (0.70 g, of compound M2), with (0.44 g, 3.00 mmol) of phthalic anhydride, in a 50 mL round bottomed flask was dissolved with (25 ml) dioxane. At (85-100°C), the reaction mixture was refluxed for (19-21) hours with stirring. The mixture was tracked by TLC. The solvent was evaporated under vacuum at 100°C by a rotator evaporator. The product was washed with chloroform. A rotator evaporator evaporated the solvent under vacuum at 100°C. The solid precipitate that resulted compound M2P was dried in a desiccator at 80°C. TLC (acetone 3:1 petroleum ether).

4. Synthesis of 1, 3 Oxazepines Compound M2K

A Compound K was prepared by using (0.47g, 0.60 mmol) of compound M2 with (0.12g, 1.80 mmol) of malic anhydride, in a 100 mL round bottomed flask dissolved in (35 ml) dioxane. The reaction mixture

was refluxed at (85-100°C) for (22-24) hours. TLC was used to track the mixture. A rotator evaporator evaporated the solvent under vacuum at 100°C. The solid precipitate compounds M2K was dried in a desiccator at 80°C. The obtained products were filtered off after being washed with ethanol for k1 and dioxane for K2. TLC (Acetone 3:1 petroleum ether).

The physical properties for all the above compounds below are shown in table 1.

3. Result and Discussion

The compound glycerol ester compound A was synthesized in advance according to the modified procedure^[15]. The glycerol ester is confirmed by FT-IR (Fig 1) and ¹H-NMR. Infrared was employed to characterize it shows of ester peak at ν (1703 cm^{-1} C=O ester), (C-H aromatic, 3229 cm^{-1}), (C-H aliph, 2658 cm^{-1}), (C=C aromatic ring, 1245 cm^{-1}), (C-O ester, 1171 cm^{-1}), (C-N amine, 1171 cm^{-1}). Also gave a peak at (3359 and 3458) evidence to form ester amine.

The ¹H-NMR spectrum for compound A (Fig 2) appeared the following characteristic signals (ppm): (Solvent 2.5ppm), (2 – 2.5 ppm, 2H, -C-NH₂), (3.5 ppm, 2H, -O-CH₂-), (7- 8 ppm, aromatic protons).

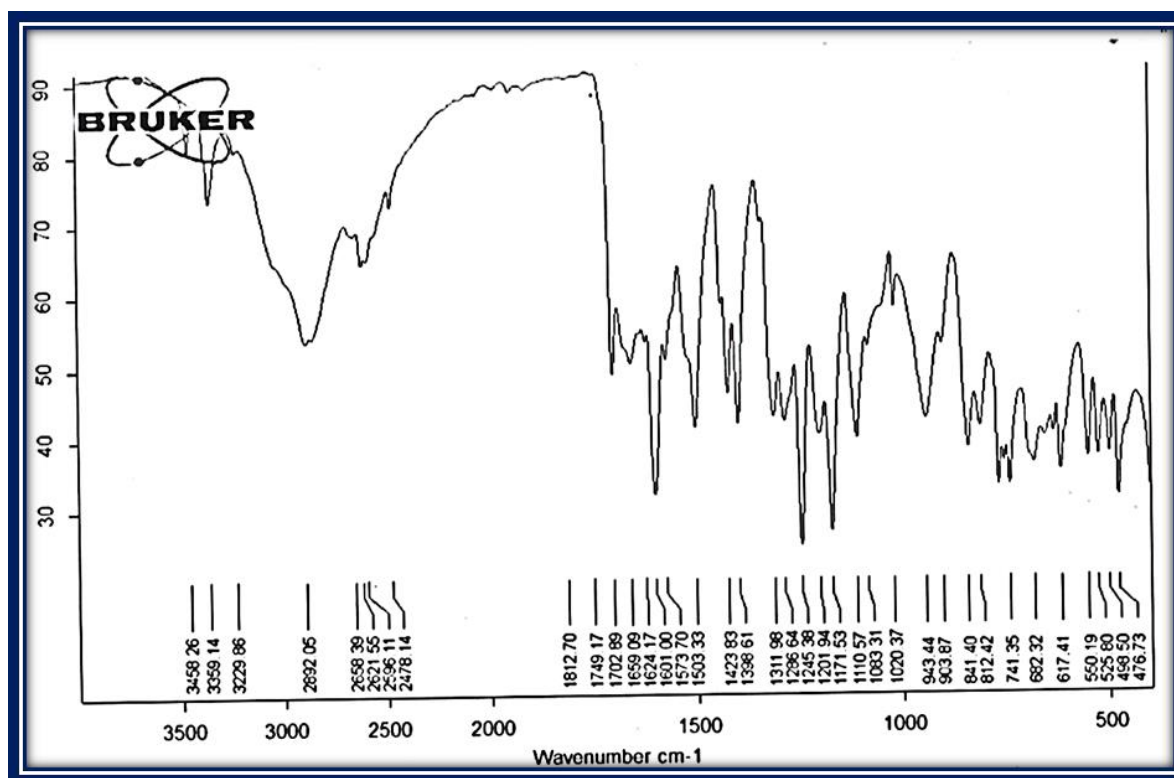


Fig. 1 FTIR Spectrum of Ester Compound A.

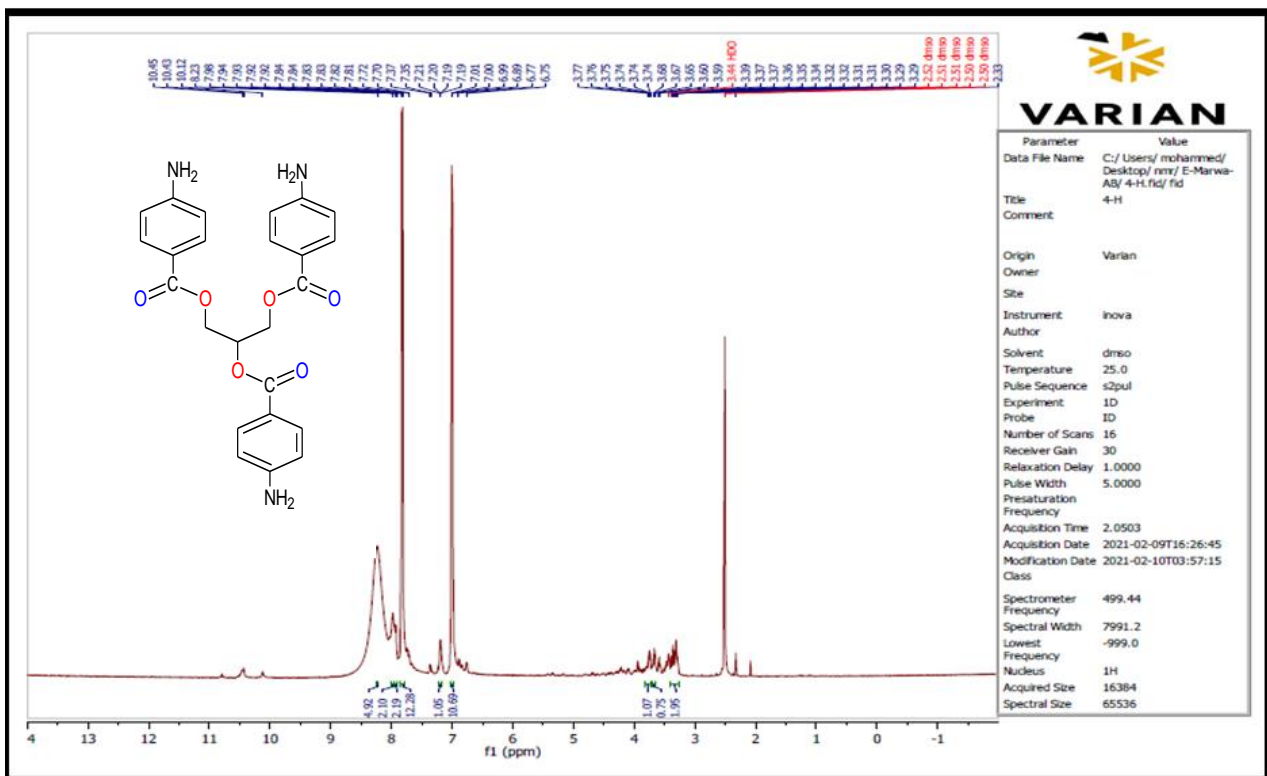


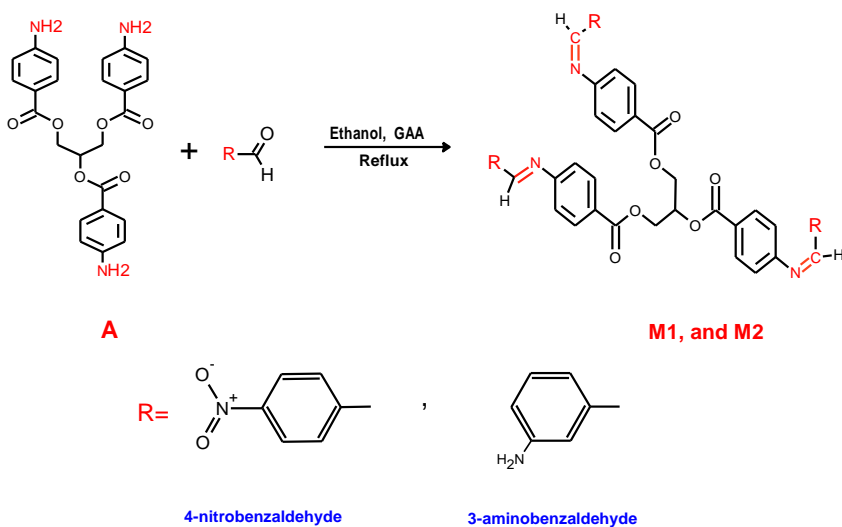
Fig. 2. The ¹H NMR Spectrum of Compound A.

Table 1. Physical properties and other characteristics for the synthesized compounds.

Comp. symbol	Molecular Formula	Color	M.P° C	Yield %	Rf cm	M.wt
A	C ₂₄ H ₂₃ N ₃ O ₆	Off white	155-158	80	0.59	449.455
M1	C ₄₅ H ₃₂ N ₆ O ₁₂	Yellow	158-160	90	0.46	848.768
M2	C ₄₅ H ₃₈ N ₆ O ₆	Black shiny	213-214	75	0.40	758.819
M1S	C ₅₇ H ₄₇ N ₃ O ₁₈	Greenish brown	240-241	85	0.72	1061.998
M1A	C ₄₅ H ₃₅ N ₁₅ O ₁₂	Dark brown	223-224	65	0.61	977.852
M2P	C ₆₉ H ₅₀ N ₆ O ₁₅	Shiny Brown	174-176	70	0.73	1203.16
M2K	C ₅₇ H ₄₄ N ₆ O ₁₅	Dark brown shiny	151-125	78	0.63	1052.99

The product of the glycerol ester contains three active amine group that was used to produce a series of tri Schiff bases by adding two aldehydes compound (scheme 1), and the ratio used to

conduct the reaction is 3 moles for every one mole of glycerol ester in the presence of glacial acetic acid as a catalyst and ethanol.



Scheme 1. Synthesis of Schiff base Compounds (M1, and M2).



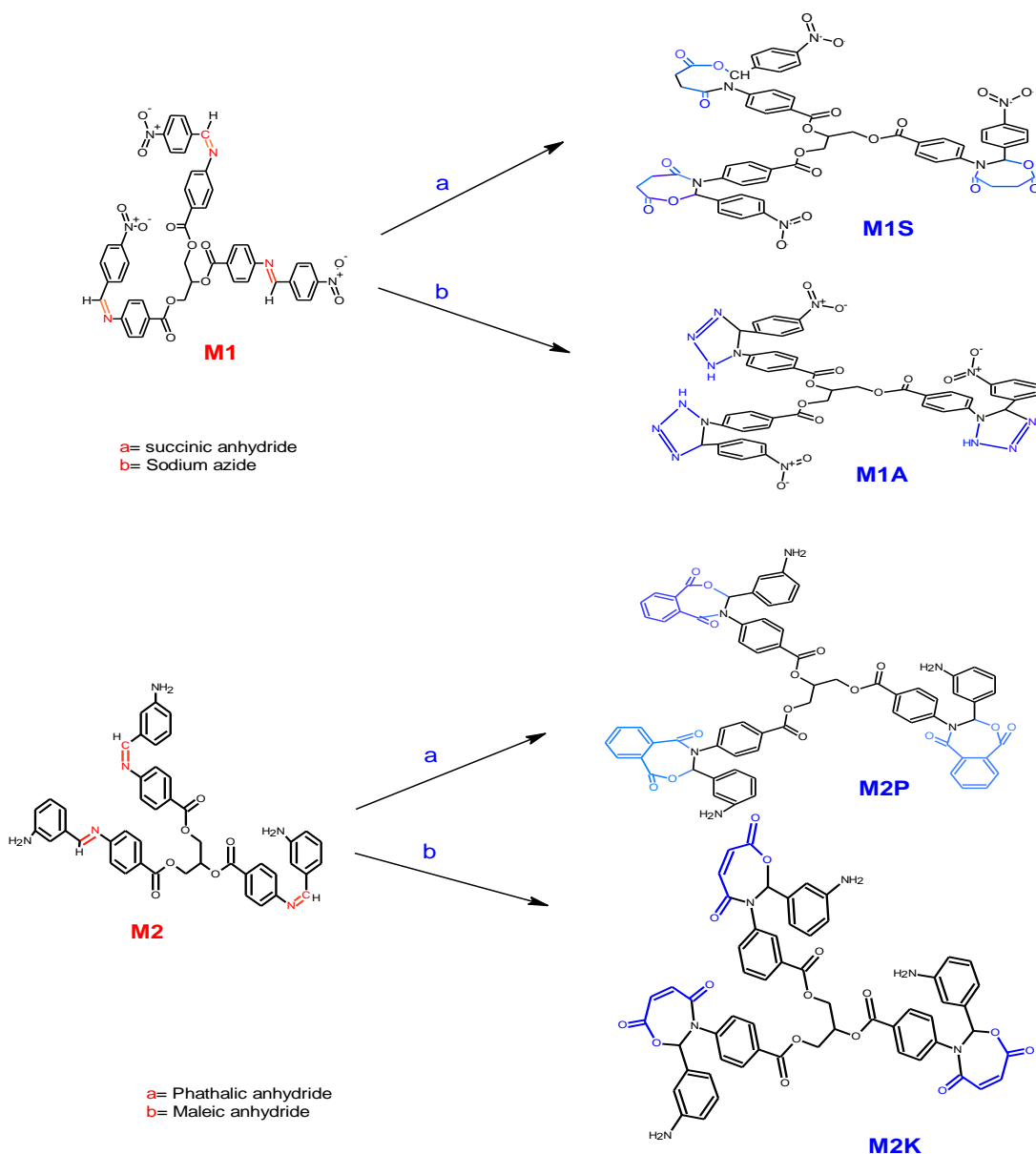
The FT-IR spectrum of Schiff base Compounds M1, and M2 (scheme 2) It appeared that the peaks at (3359 and 3458) belong to the amine group in compound (A) disappeared in all the compounds prepared for Schiff bases.

The FT-IR spectrum of compound M1 (fig 3) appeared the following bands ν_{max} : (C=N, 1600 cm^{-1}), (C=C aromatic, 1516 cm^{-1}), (C-H aliphatic, 2960 cm^{-1}), (C-H aromatic, 3016 cm^{-1}), (C=O ester, 1691 cm^{-1}), (C-O ester, 1246 cm^{-1}).

The FT-IR spectrum of compound M2 (fig 4) appeared the following bands ν_{max} : (C=N, 1597 cm^{-1}),

(C=C aromatic, 1510 cm^{-1}), (C-H aliphatic, 2939 cm^{-1}), (C-H aromatic, 3053 cm^{-1}), (C=O ester, 1690 cm^{-1}), (C-O ester, 1257 cm^{-1}).

Also the 1H -NMR spectrum for compound M1 (Fig 5) appeared the signal that belongs to the azomethine proton confirm the formation of Schiff bases, the following characteristic signals (ppm): (Solvent 2.5ppm), (4.3 ppm, 2H, -O-CH₂-), (7- 9 ppm, aromatic protons) (10.2 ppm, 1H, azomethine).



Scheme 2. Synthesis of Tetrazol, and Oxazepines Compound

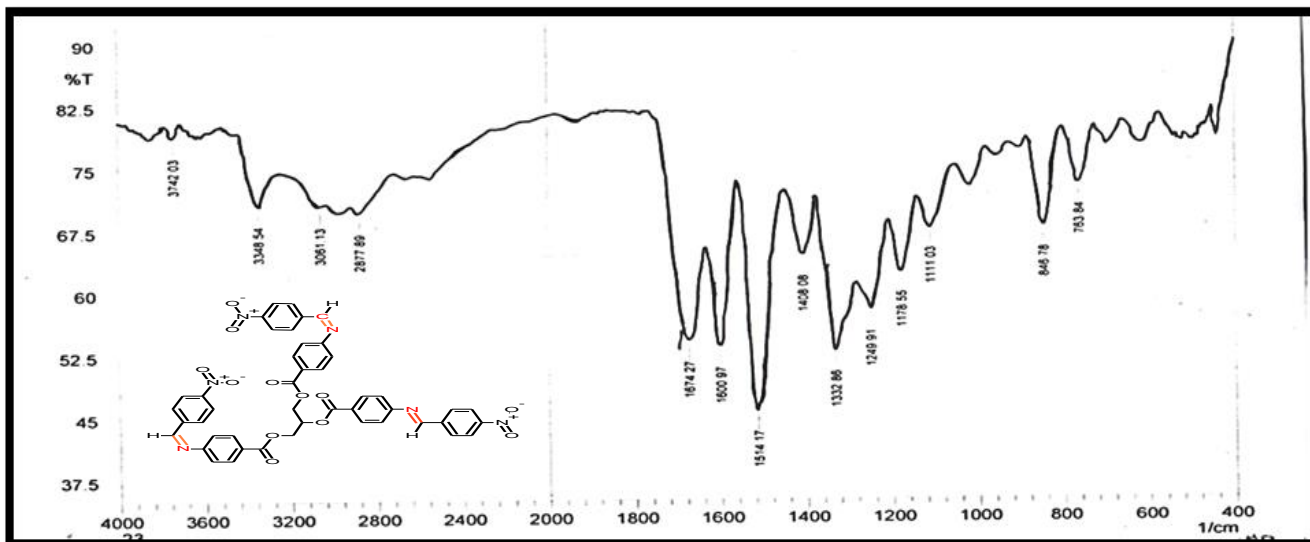


Fig. 3. The FTIR spectrum of compound M1

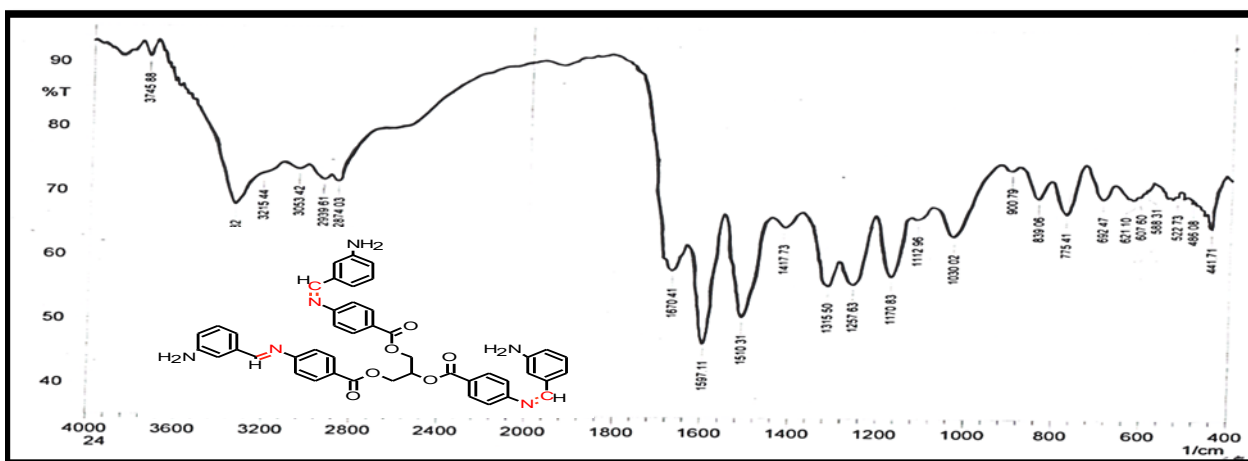


Fig. 4. The FTIR spectrum of compound M2

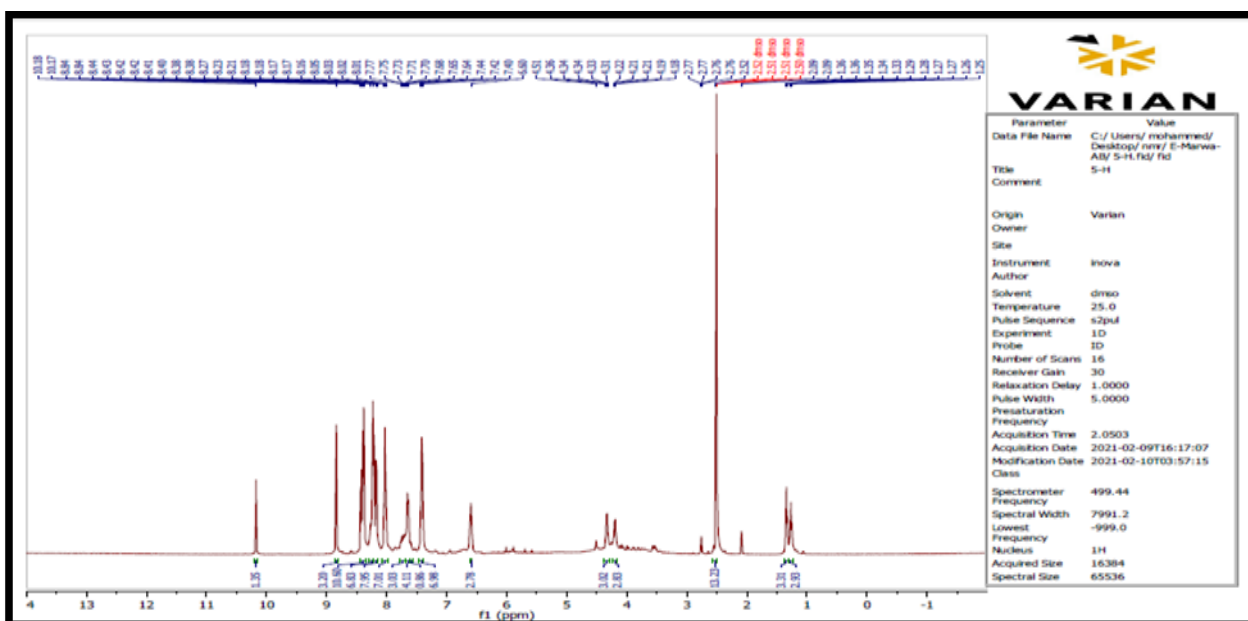


Fig. 5. The ¹H NMR spectrum of compound M1.



The FT-IR spectra of the synthesized 1, 3-Oxazepine showed a disappearance of the azomethine band reported at ν (1600–1650 cm^{-1}) which is evidence of azomethine group breaking. The spectra also were showed the appearance of two new bands belong to the carbonyl of lactone and lactam which consider good evidence for the formation of Oxazepines.

The FT-IR spectrum of compound M1S (fig 6) was appeared the following bands ν_{max} : (C=O lactone, 1687 cm^{-1}), (C=O lactam, 1604 cm^{-1}), (CH aromatic, 3059 cm^{-1}), (CH aliph, 2879 cm^{-1}), (C-N, 1247 cm^{-1}), (cyclic C=C, 1500 cm^{-1}), (aromatic C=C, 1408 cm^{-1}), ((NO₂) asy 1518 cm^{-1} , sym 1338 cm^{-1}).

The FT-IR spectrum of compound M1A (fig 7) appeared the following bands ν_{max} : (N-H, 3363 cm^{-1}), (N=N, 1600 cm^{-1}), (C-N, 1170 cm^{-1}), (N-N, 1103 cm^{-1}), (C=O ester, 1701 cm^{-1}), (C=C aromatic, 1521 cm^{-1}).

The FT-IR spectrum of compound M2P (fig 8) was appeared the following bands ν_{max} : (C=O lactone, 1656 cm^{-1}), (C=O lactam, 1599 cm^{-1}), (CH aromatic, 3192 cm^{-1}), (CH aliph, 2933 cm^{-1}), (C-N, 1253 cm^{-1}), (cyclic C=C, 1512 cm^{-1}), (aromatic C=C, 1558 cm^{-1}).

The FT-IR spectrum of compound M2K (fig 9) was appeared the following bands ν_{max} : (C=O lactone, 1599 cm^{-1}), (C=O lactam, 1589 cm^{-1}), (CH aromatic, 3055 cm^{-1}), (CH aliph, 2866 cm^{-1}), (C-N, 1238 cm^{-1}), (cyclic C=C, 1516 cm^{-1}), (aromatic C=C, 1525 cm^{-1}).

The ¹H-NMR spectrum for compound M2K (fig 10) disappear the signal that attributed for azomethine proton also appeared the following characteristic signals (ppm): (Solvent, 2.5ppm), (10-11 ppm, 1H, phenolic OH), (7.5-8 ppm, O-CH-N), (7 - 8 ppm, aromatic protons), (6.3 ppm, 2H -C-NH₂), (3.5-4 ppm O-CH₂-), (2.6 - 3 ppm =CH-CO).

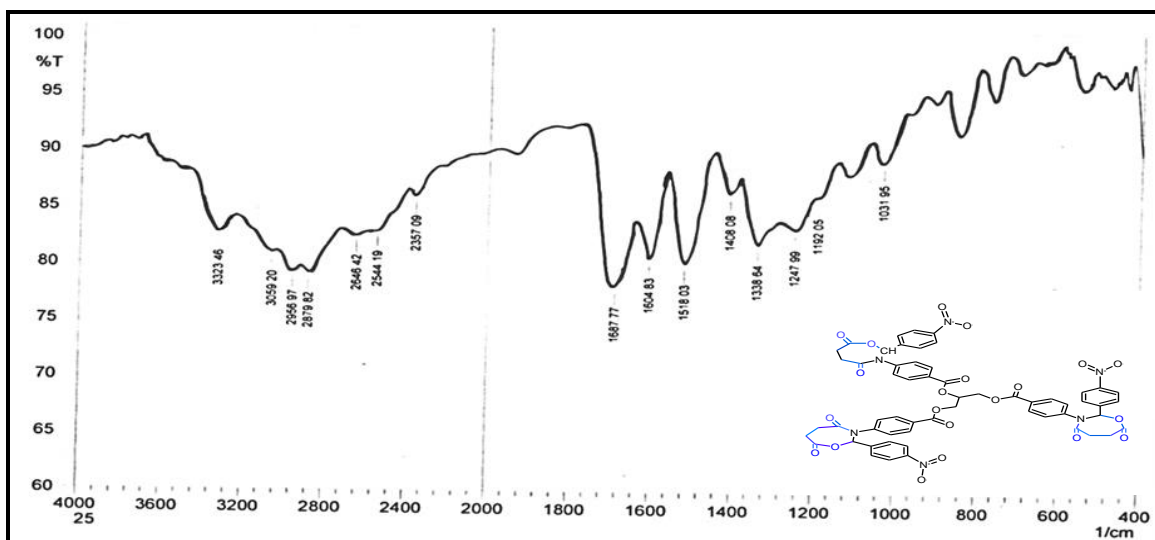


Fig. 6. FTIR Spectrum of Compound M1S

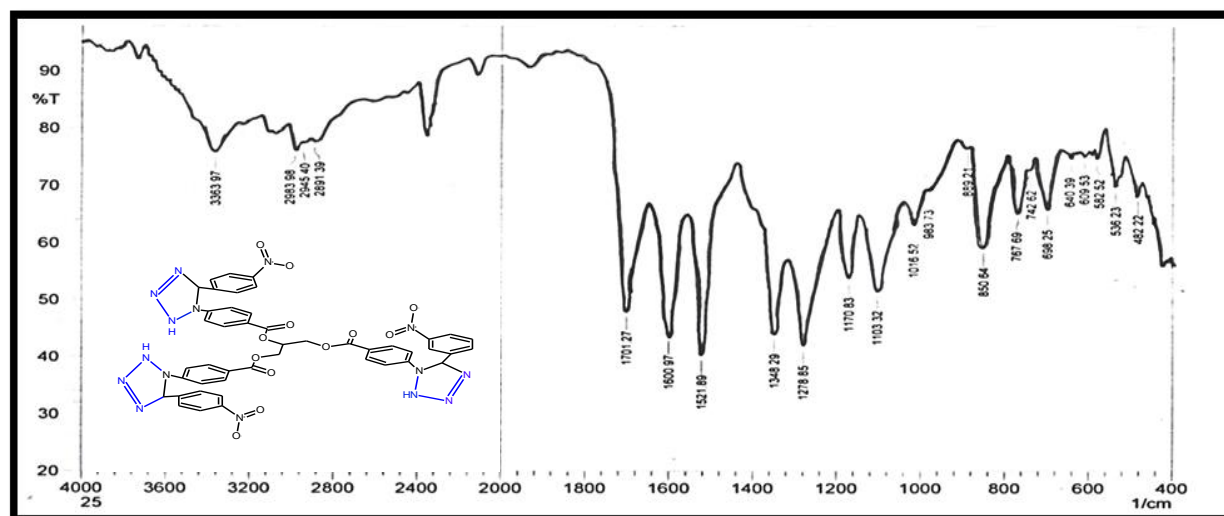


Fig. 7. FTIR Spectrum of Compound M2A

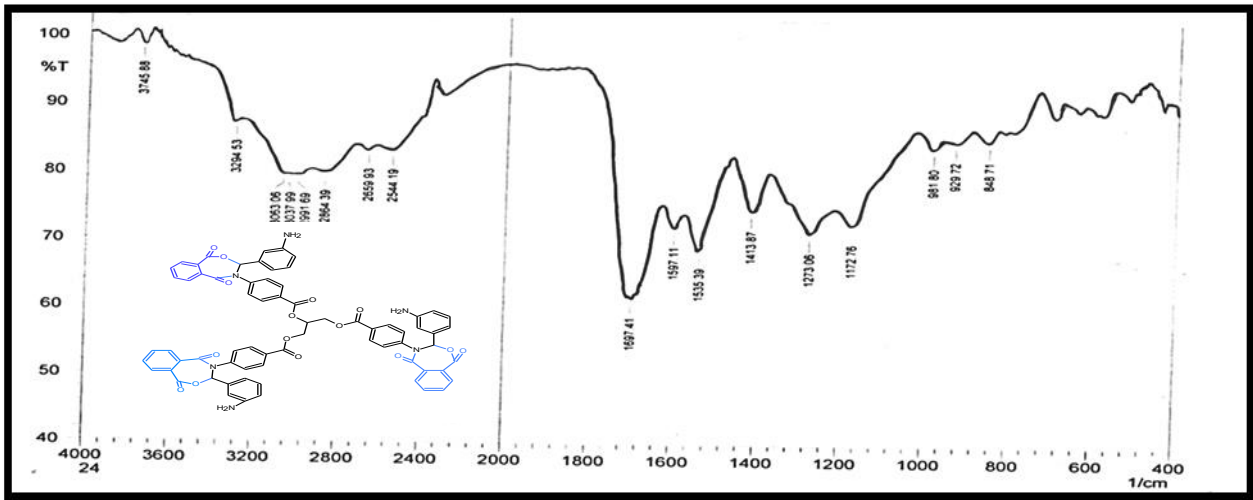


Fig. 8. FTIR spectrum of compound M2P.

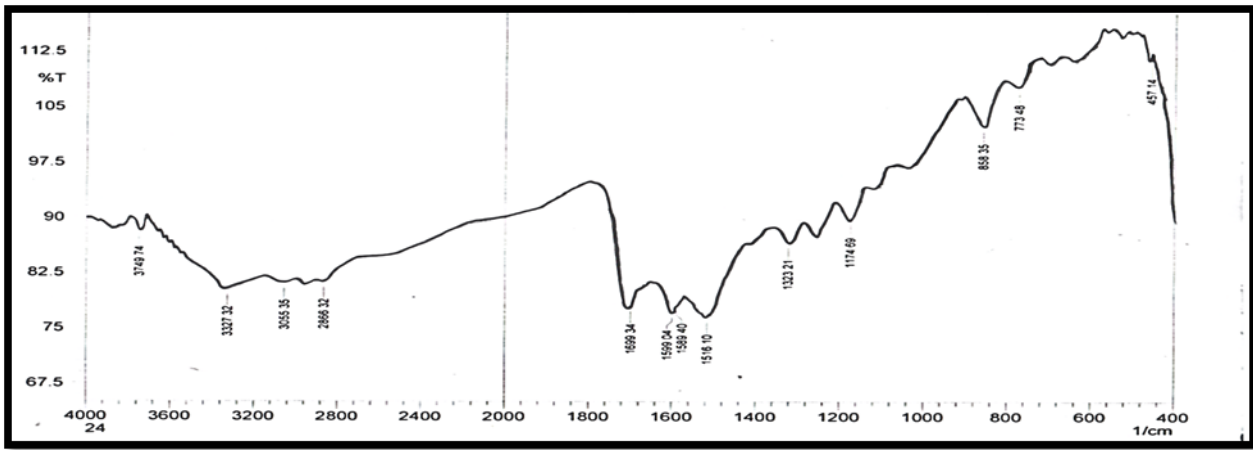


Fig. 9. FTIR Spectrum of Compound M2K.

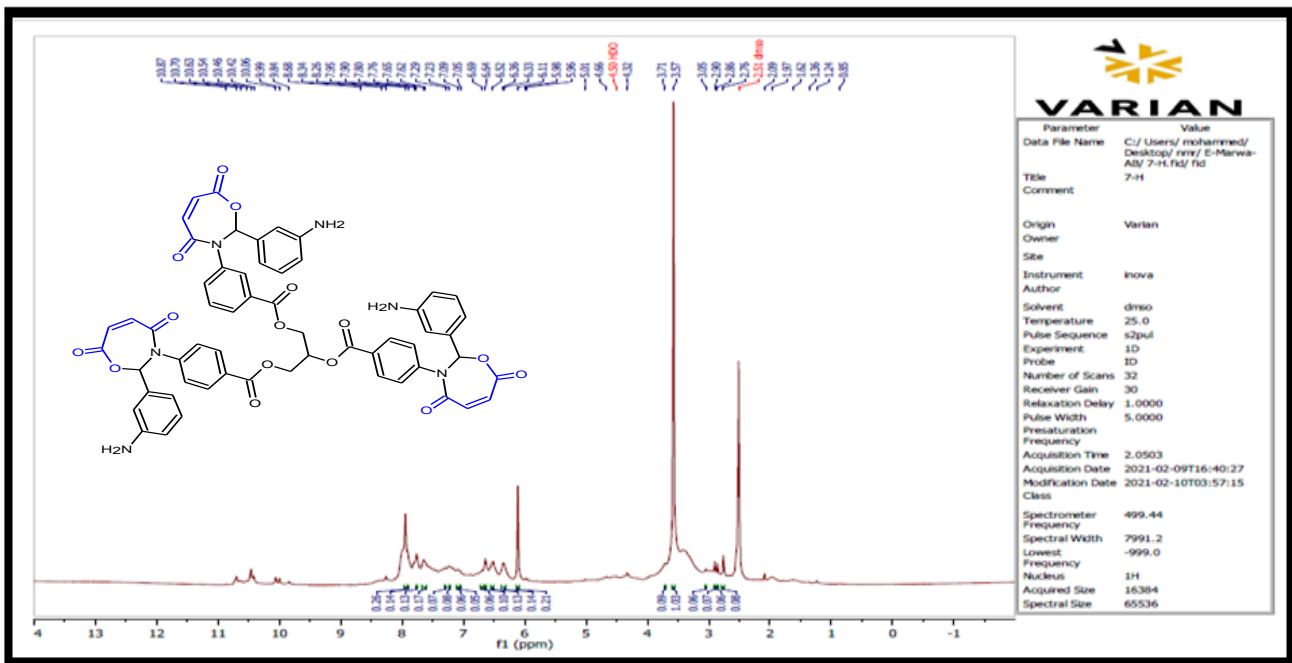


Fig. 10. ¹H NMR spectrum of compound M2K.



Conclusion

Syntheses two Schiff bases compounds by used acid-catalyzed Schiff bases have relatively higher yields than non-acid catalysts have been used as a starting materials for the prepare of some heterocyclic composite containing nitrogen or oxygen atom through the cycloaddition, some new heterocyclic have been synthesized All prepared compounds, are stable because they have a high melting point and are not affected by moisture.

Acknowledgments

We thank the University of Babylon, College of Science, Department of Chemistry. For their support.

References

- Ahmed SK, Ali WB, Khadom AA. Synthesis and investigations of heterocyclic compounds as corrosion inhibitors for mild steel in hydrochloric acid. *International Journal of Industrial Chemistry* 2019; 10(2): 159-173.
- Al-lami N, Salom KJ. Pharmacological studies on some new 3-cyclic oxazepine-2-aryl imidazo (1, 2-a) pyridine derivatives. *Journal of Pharmaceutical Sciences and Research* 2019; 11(1): 125-130.
- Al-Masoudi IA, Al-Soud YA, Al-Salihi NJ, Al-Masoudi NA. 1, 2, 4-Triazoles: Synthetic approaches and pharmacological importance. *Chemistry of Heterocyclic Compounds* 2006; 42(11): 1377-1403.
- Ali I, Mukhtar SD, Hsieh MF, Allothman ZA, Alwarthan A. Facile synthesis of indole heterocyclic compounds based micellar nano anti-cancer drugs. *RSC advances* 2018; 8(66): 37905-37914.
- Arshad T, Sheikh HK, Kazmi MH, Farheen S, Sohail T, Lateef M. New bioactive triaryl triglyceride esters: Synthesis, characterization and biological activities. *Bangladesh Journal of Pharmacology* 2018; 13(4): 302-308.
- Fonkui TY, Ikhile MI, Ndinteh DT, Njobeh PB. Microbial activity of some heterocyclic Schiff bases and metal complexes: A review. *Tropical Journal of Pharmaceutical Research* 2018; 17(12): 2507-2518. <http://doi.org/10.4314/tjpr.v17i12.29>
- Gao WT, Zheng Z. Synthetic studies on optically active Schiff-base ligands derived from condensation of 2-hydroxyacetophenone and chiral diamines. *Molecules* 2002; 7(7): 511-516.
- Hassan AS, Askar AA, Nossier ES, Naglah AM, Moustafa GO, Al-Omar MA. Antibacterial evaluation, in silico characters and molecular docking of Schiff bases derived from 5-aminopyrazoles. *Molecules* 2019; 24(17): 3130. <http://doi.org/10.3390/molecules24173032>
- Keogh J, Tiwari MS, Manyar H. Esterification of glycerol with acetic acid using nitrogen-based brønsted-acidic ionic liquids. *Industrial & Engineering Chemistry Research* 2019; 58(37): 17235-17243.
- Kong PS, Pérès Y, Wan Daud WMA, Cognet P, Aroua MK. Esterification of glycerol with oleic acid over hydrophobic zirconia-silica acid catalyst and commercial acid catalyst: optimization and influence of catalyst acidity. *Frontiers in chemistry* 2019; 7: 205. <https://doi.org/10.3389/fchem.2019.00205>
- Lamberth C, Dinges J. *Bioactive heterocyclic compound classes: pharmaceuticals*. John Wiley & Sons 2012.
- Ma J, Wu G, Li S, Tan W, Wang X, Li J, Chen L. Magnetic solid-phase extraction of heterocyclic pesticides in environmental water samples using metal-organic frameworks coupled to high performance liquid chromatography determination. *Journal of Chromatography A* 2018; 1553: 57-66.
- Mahesh K, Karpagam S, Pandian K. How to design donor-acceptor based heterocyclic conjugated polymers for applications from organic electronics to sensors. *Topics in Current Chemistry* 2019; 377(3): 1-39.
- Mehetre AR, Deshmukh SR, Bhosale VN. '20 ARM JBCC 5 3 Synthesis, Characterization and Biological Study of Schiff Bases Derived from 4-Amino-3-Hydroxy Benzoic Acid', 3-7. *Journal of Biological and chemical Chronicles* 2019, 5(3): 79-82
- Nawaz H, Akhter Z, Yameen S, Siddiqi HM, Mirza B, Rifat A. Synthesis and biological evaluations of some Schiff-base esters of ferrocenyl aniline and simple aniline. *Journal of Organometallic Chemistry* 2009; 694(14): 2198-2203. <https://doi.org/10.1016/j.jorgchem.2009.02.032>
- Okey NC, Obasi NL, Ejikeme PM, Ndinteh DT, Ramasami P, Sherif ESM, Ebenso EE. Evaluation of some amino benzoic acid and 4-aminoantipyrine derived Schiff bases as corrosion inhibitors for mild steel in acidic medium: Synthesis, experimental and computational studies. *Journal of Molecular Liquids* 2020; 315. <https://doi.org/10.1016/j.molliq.2020.113773>
- Pagliaro M, Rossi M. Glycerol: properties and production. *The future of glycerol* 2010: 20-21.
- Pathan SI, Chundawat NS, Chauhan NPS, Singh GP. A review on synthetic approaches of heterocycles via insertion-cyclization reaction. *Synthetic Communications* 2020; 50(9): 1251-1285.
- Pouilloux Y, Métayer S, Barrault J. Synthesis of glycerol monooleate from octadecanoic acid and glycerol. Influence of solvent on the catalytic properties of basic oxides. *Comptes Rendus de l'Académie des Sciences-Series IIC-Chemistry* 2000; 3(7): 589-594. [https://doi.org/10.1016/S1387-1609\(00\)01171-3](https://doi.org/10.1016/S1387-1609(00)01171-3)
- Ravindra KC, Vagdevi HM, Vaidya VP, Basavaraj P. 'Synthesis, antimicrobial and antiinflammatory activities of 1, 3, 4-oxadiazoles linked to naphtho [2, 1-b] furan'. *Indian Journal of Chemistry -Section B (IJC-B)* 2006; 45B(11): 2506-2511.
- Singh RK, Pandey S, Saxena RC, Thakre GD, Atray N, Ray SS. Study of cystine schiff base esters as new environmentally benign multifunctional biolubricant additives. *Journal of Industrial and Engineering Chemistry* 2015; 26: 149-156. <http://doi.org/10.1016/j.jiec.2014.11.027>
- Kotbagi TV, Pandhare S, Dongare M, Umbarkar S. In situ Formed Supported Silicomolybdc Heteropolyanions: Efficient Solid Catalyst for Acetylation of Glycerol. *Journal of Environmental Analytical Chemistry* 2015; 2(5).
- Tewari YB, Bunk DM. Thermodynamics of the lipase-catalyzed esterification of glycerol and n-octanoic acid in organic solvents and in the neat reaction mixture. *Journal of Molecular Catalysis B: Enzymatic* 2001; 15(4-6): 135-145. [http://doi.org/10.1016/S1381-1177\(01\)00016-9](http://doi.org/10.1016/S1381-1177(01)00016-9)
- Fabio RA, Capri T, Buzzai C, Pittalà V, Gangemi A. Auditory and visual oddball paradigm evaluated through p300 in five girls with rett syndrome. *NeuroQuantology* 2019; 17(7): 40-49.

