UGC MAJOR RESEARCH PROJECT

FINAL REPORT

(F. No: 42-343/2013 (SR) dated 21.03.2013)

Synthesis, electronic properties and non-linear optics of some picrate derivatives and their antimicrobial screening

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UNIVERSITY GRANTS COMMISION

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NEW DELHI-110 002.

PERFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE MAJOR RESEARCH PROJET

1	Title of the Project	:	Synthesis, electronic properties and non-linear optics of some picrate derivatives and their antimicrobial screening.
2	Name and Address of the Principal Investigator	:	**Dr. G. RAJARAJAN** Assistant Professor Department of Chemistry Annamalai University, Annamalainagar-608 002.
3	Name and Address Institution	:	Annamalai University, Annamalainagar-608 002.
4	U.G.C. Approval Letter No and Date	:	F. No: 42-343/2013 (SR) dated 21.03.2013
	U.G.C. Extension Letter No and Date	:	F. No: 42-343/2013 (SR) dated 25.05.2016
5	Date of Implementation	:	01.04.2013
6	Tenure of the Project	:	01.04.2013 – 31.03.2017
7	Total Grant allocated	:	**8,28,533.00**
8	Total grant Received		1st Instalment : Rs. 4,70,800.00/- 2nd Instalment : Rs.2.82,560.00/- Total**:** Rs. 7,53,360.00
9	Final expenditure		Rs. **7,44,860.00/-**

10 Objectives of the project

It is proposed

- To synthesis a series of novel 3*t*-pentyl-2*r*,6*c*-diarylpiperidine-4-ones and their oximes, semicarbazones and picrate derivatives.
- To characterize the compounds by using Uv-Vis, fluorescence, IR, ^{1}H, ^{13}C NMR, 2D NMR, mass and CHN analysis.
- To determine the degree of activity against various bacterial and fungal species.
- To investigate the HOMO-LUMO energies by theoretically (Guassian-03W).
- To study the hyperpolarisability(NLO) for all picrate derivatives.
- To study their thermal stability by TGA, by considering their application in opto electronics field**.**
- To do computational studies by using Guassian-03 package to supplement the experimental results.
- To study their donar-acceptor interaction (NBO) analysis.

11. Whether Objectives Were Achieved: YES

12. Achievements from the projects

- A series of new 3*t*-pentyl-2*r*,6*c*-diarylpiperidin-4-one semicarbazones (**1-5),** 3*t*-butyl-2*r*,6*c*-diarylpiperidin-4-on-1-ium picrates (**6-11**), 3-alkyl-,3,5-dialkyl-2,6-di(thiophen-2-yl)piperidin-4-on-1-ium picrate and their derivatives (**12-23**), *N*-chloroacetyl-3-alkyl-,3,5-dialkyl-2*r*,6*c*-diphenyl/di(thiophen-2-yl)piperidin-4-one (**24-28**) 3-alkyl, 3,5,-dialkyl-2,6-di(naphthalene-1-

yl)piperidin-4-one **(29-35),** 3-pentyl 2,6-di(furan-2-yl) piperidin-4-one **(36)** and 2-phenyl-4,5-diphenyl-1*H*-imidazol-3-ium picrates (**37-41**) have been synthesized and characterized by elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectral techniques. Among these, the five representative compounds were determined by Single crystal XRD analysis. The results reveal that the further confirm synthesised compounds

- Some compounds such as 3*t*-pentyl-2*r*,6*c*-diarylpiperidin-4-one semicarbazones and *N*-chloroacetyl-3-alkyl-,3,5-dialkyl-2*r*,6*c*-diphenyl/di(thiophen-2-yl)piperidin-4-ones are biologically active.
- Synthesised compounds such as 3*t*-butyl-2*r*,6*c*-diarylpiperidin-4-on-1-ium picrates , 3-alkyl-,3,5-dialkyl-2,6-di(thiophen-2-yl)piperidin-4-on-1-ium picrate and their derivatives *N*-chloroacetyl-3-alkyl-,3,5-dialkyl-2*r*,6*c*-diphenyl/di(thiophen-2-yl)piperidin-4-one and2-phenyl-4,5-diphenyl-1*H*-imidazol-3-ium picrates are suitable for NLO materials.

❖ Structure of all synthesized compounds were optimised by computational methods(B3LYP). From optimised parameters Mulliken and MEP analyses clearly explain that negative regions are associated with N24 and O27 atoms. The synthesised compounds are the best candidate for the stabilizing ICT process.

13. Summary of the findings

- A series of new 3*t*-pentyl-2*r*,6*c*-diarylpiperidin-4-one semicarbazones (**1-5),** 3*t*-butyl-2*r*,6*c*-diarylpiperidin-4-on-1-ium picrates (**6-11**), 3-alkyl-,3,5-dialkyl-2,6-di(thiophen-2-yl)piperidin-4-on-1-ium picrate and their derivatives (**12-23**), *N*-chloroacetyl-3-alkyl-,3,5-dialkyl-2*r*,6*c*-diphenyl/di(thiophen-2-yl)piperidin-4-one (**24-28**) 3-alkyl, 3,5,-dialkyl-2,6-di(naphthalene-1-yl)piperidin-4-one **(29-35),** 3-pentyl 2,6-di(furan-2-yl) piperidin-4-one **(36)** and 2-phenyl-4,5-diphenyl-1*H*-imidazol-3-ium picrates (**37-41**) have been synthesized and characterized by elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectral techniques. HSQC spectrum has been recorded for compound **1**. Some compounds have been recorded to UV-vis-NIR, fluorescence, mass, single crystal XRD and TG-DTA analyses. The spectral data confirm the formation of compounds **1-41.**
- The compounds **1-5** and **18-21** were tested for antibacterial and antifungal activities by serial dilution method. *Ciprofloxacin* and *Cetramazole* were used as standard drugs for antibacterial and antifungal activity, respectively. The compounds **2** and **4** exhibited excellent activity against *S. aureus* and *V. cholera*, respectively. As seen in from fungal results, compounds **2**, **5, 20 & 21** were the most active against the investigated fungal strains. Based on the results, the presence of substituent at C-2 and C-6 positions of piperidin-4-one ring led to a significant variation in the antimicrobial activity.
- Docking study has been carried out for compounds **1-5** and **18-22** using Topoisomerase II protein. In this study, compounds **4** and **21** docking score showed close binding interactions with standard drug *Ciprofloxacin*.
- Hirshfeld surface analysis has been employed for compounds **12** and **15** to assist better understanding of the possible diverse interactions within the crystal. The fingerprint plots derived from Hirshfeld surface show

different types of intermolecular interactions and their relative significance with respect to each other.

- ❖ The optical properties of compounds **6-11** are explained based on the UV-vis-NIR and fluorescence spectral data. The TG-DTA results reveal that all of the compounds **6-11** exhibit excellent thermal stabilities with decomposition temperatures ranging from 174 to 187 °C. SHG study reveals **9** as a suitable contender for NLO properties.

- ❖ From the computational analysis of synthesized compounds **1-41**, we conclude the following observations,

  - ✓ From optimized structural parameters, piperidine ring essentially adopt a chair conformation, with all substituents oriented in equatorial positions as evident from the torsional angles N1–C2–C3–C4 ≈ -55.00 and -51.99 and
    N1–C6–C5–C4 ≈ 52.00 and 54.81° by B3LYP and XRD, respectively.
  - ✓ In the molecular optimized structure, the semicarbazone analogue is nearly planar with the dihedral angle (N24-N25-C26-N28) around 12.00° by B3LYP and adopts an *E* configuration with respect to the C4=N24 bond.
  - ✓ Mulliken and MEP analyses clearly explain that negative regions are associated with N24 and O27 atoms. Thus, it is predicted that the nitrogen and oxygen atoms will be preferred electrophilic reaction site. Positive regions are located on the C4 carbon atom indicating possible site for nucleophilic reaction.
  - ✓ The result of molecular orbital composition analysis of compounds **1-41** revealed that the ΔE gap could be lowered upon modifying the phenyl core. Among these, compound **4,11 , 23,27,38,40** and **41** are the best candidate for the stabilizing ICT process.

- ✓ The calculated hyperpolarizability compare with reported values of similar derivatives. Among these compounds **4, 11**,23, **27, 38, 40** and **41** are good candidate for future nonlinear optical studies.

❖ . Single crystal XRD analysis of compound **9, 12, 21, 24, 27 38.40** an**d 41,** reveal that the compounds crystallizes in the monoclinic system with space group P_{21}/n. The single crystal X-ray data confirm the transfer of protons from picric acid (O2) to piperidin-4-one ring (N1) and the molecular structure is influenced by N-H···O and C-H···O intramolecular hydrogen bonds.

14. CONTRIBUTION TO THE SOCIETY

- 3-alkyl-2,6-diarypiperidone semicarbozone , oxime and N-chloroacetyl derivatives play key role in the biological and medicinal field. So they are useful to society.
- Hyperpolarizability values piperidone picrate derivatives are high. Hence, All the compounds are suitable NLO materials.
- Docking study has been carried out piperidone derivatives using Topoisomerase II protein. In this study, compounds docking score showed close binding interactions with standard drug *Ciprofloxacin*. Hence, they play key role in the biological systems.
- The results of molecular orbital composition analysis of compounds revealed that the ΔE gap could be lowered upon modifying the phenyl core and are the best candidate for the stabilizing ICT process.

15. Whether any Ph.D. Enrolled/Produced out of the Project

Produced : YES
Candidate Name : M. AROCKIA DOSS
Awarded on : 22-5-2017

16. <u>List of publications</u>

1. M. Arockia doss, **G. Rajarajan**, V. Thanikachalam, S. Selvanayagam, B. Sridhar, Synthesis, single crystal X-ray, spe ctroscopic (FT-IR, UVevis, fluorescence, 1H &13C NMR), computational (DFT/B3LYP) studies of some imidazole based picrates, J. Mol. Struct., 1158 (2018) 277-285.
2. M. Arockia doss, S. Savithiri, **G. Rajarajan**, V. Thanikachalam, Synthesis, spectral, stereochemical and biological evaluation of (E)-2-(3-pentyl-2,6-diarylpiperidin- 4-ylidene)-N-phenylhydrazinecarbothioamide derivatives, Phosphorus, Sulfur, and Silicon and the Related Elements, 192 (2017) 1264-1270.
3. M. Arockia doss , **G. Rajarajan**, V. Thanikachalam, S. Selvanayagam, B. Sridhar, Synthesis, spectroscopic (UV-Vis, FT-IR and NMR), single crystal XRD of 3,5-diethyl -2,6-di(thiophen-2-yl)piperidin-4-on-1-ium picrate: A comprehensive experimental and computational study, J. Mol. Struct., 1128 (2017) 268-278.
4. M. Arockia doss, S. Amala, **G. Rajarajan**, V. Thanikachalam, Synthesis, Spectral (Uv-Vis, FT-IR and NMR), Molecular structure, NBO, HOMO-LUMO and NLO Analysis of Some 3t-pentyl-2r,6cdiarylpiperidin-4-one Semicarbazones, Can. Chem. Trans. 4(3) (2016) 398-414.
5. M. Arockia doss, **G. Rajarajan**, V. Thanikachalam, Molecular Structure, Spectroscopic (UV-Vis, FT-IR and NMR), Conformational Aspects of Some 3t-pentyl-2r,6c-diphenyl/di(thiophen-2-yl)piperidin-4-ones and their Oximes: A Comprehensive Experimental and DFT Study, Can. Chem. Trans. 4(2) (2016) 226-243.
6. S. Savithiri, M. Arockia doss**, G. Rajarajan**, V. Thanikachalam, Molecular structure, vibrational spectral assignments (FT-IR and FT-Raman), UV-Vis, NMR, NBO, HOM O-LUMO and NLO properties of 3t-pentyl-2r,6c-diphenylpiperidin-4-one picrate based on DFT calculations, J. Mol. Struct., 1105 (2016) 225-237.
7. M. Arockia doss, S. Savithiri, S. Vembu, **G. Rajarajan**, V. Thanikachalam, Synthesis, Spectral characterization of some 3-alkyl-2,6-di(naphthalen-1-yl)piperidin-4-one and oxime derivatives and their screening for Antimicrobial properties, Can. Chem. Trans. 2 (2015) 261-274.

8. M. Arockia doss, S. Savithiri, **G. Rajarajan**, V. Thanikachalam, C. Anbuselvan, Synthesis, electronic structure investigation of 3-pentyl-2,6-di(furan-2- yl)piperidin-4-one by FT-IR, FT-Raman and UV–Visible spectral studies and ab initio/DFT calculations, Spectrochim. Acta Part A, 151 (2015) 773–784.

9. M. Arockia doss, S. Savithiri, **G. Rajarajan**, V. Thanikachalam, H. Saleem, Synthesis, spectroscopic (FT-IR, FT-Raman, UV and NMR) and computational studies on 3t-pentyl-2r,6c diphenylpiperidin-4-one semicarbazone, Spectrochim, Acta Part A, 148 (2015) 189-202.