Journal of Molecular Structure 1127 (2017) 597–610

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

Synthesis, molecular structure, DFT studies and antimicrobial activities of some novel 3-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-*1H*-imidazol-2-yl)-1*H*-indole derivatives and its molecular docking studies

D. Rajaraman [a], G. Sundararajan [a], N.K. Loganath [b], K. Krishnasamy [a, *]

[a] Department of Chemistry, Annamalai University, Annmalainagar 608 002, India
[b] Department of Studies and Physics, University of Mysore, Managangothri, India

ARTICLE INFO

Article history:
Received 22 February 2016
Received in revised form
8 August 2016
Accepted 9 August 2016
Available online 11 August 2016

Keywords:
Tetra substituted imidazole
XRD
DFT
Docking
Antimicrobial activity

ABSTRACT

A new series of 3-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1*H*-imidazol-2-yl)-1*H*-indole derivatives (**5a-5j**) are conveniently synthesized and characterized by IR, ^{1}H NMR and ^{13}C NMR spectral techniques. The compound **5f** was also confirmed by single crystal XRD analysis and optimized bond parameters were calculated by density functional theory (DFT) at B3LYP/6–31G (d, p) level. The optimized geometrical parameters obtained by DFT calculation are in good agreement with single crystal XRD data. The experimentally observed FT-IR and FT-Raman bands were assigned to different normal modes of the molecule. The stability and charge delocalization of the molecule were also studied by Natural Bond Orbital (NBO) analysis. The overlapping of atomic orbital along with their predicted energy is explained on the basis of HOMO–LUMO energy gap calculations. Molecular Electrostatic Potential map (MEP) was studied for predicting the reactive sites. The reported molecule used as a potential NLO material since it has high $\mu\beta_0$ value. The antibacterial activities of these derivatives were studied using molecular docking studies and it is compared with their experimental results.

1. Introduction

Imidazole is a class of very important heterocyclic compounds, which can be found in many natural products [1]. They are recognized to exhibit a large variety of important biological and pharmacological activities [2]. It has been reported that some imidazole derivatives can be used as herbicides, fungicides, growth regulators, potent angiotensin II receptor antagonist, glucagon receptor antagonist, anti-allergy, anti-tumor, anti-inflammatory, anti-bacterial, antioxidant and analgesic activities [3–13]. Compounds incorporating the imidazole scaffold are known as inhibitors of interleukin (IL)-1 and 5-lipoxygenase, 20-HETE synthase inhibitors, β-lactamase inhibitors, carboxypeptidase inhibitors, Heme oxygenase inhibitors, NOs inhibitors, p38 MAPK inhibitors, JNK, BRaf kinase, 5-LOX inhibitors and COX-2 inhibitors [14–22]. Imidazole, the N-heterocycle molecule has high electron-withdrawing ability, good coplanarity and good thermal stability which render it to be an ideal building block for nonlinear optical materials [23–25]. Imidazoles are also used as Plant growth regulators and therapeutic agents [26], dye super sensitized star cells (DSSCs) [27,28], nonlinear optics (NLO) [29,30] and organic light emitting diodes (OLED) [31,32]. Vibrational spectroscopy is a valuable tool for the elucidation of molecular structure and gives a dynamical image of the molecule. Vibrational spectroscopy has contributed appreciably to the growth of polymer chemistry, catalysis and reaction dynamics [33]. The present research work predominantly focused on the synthesis of 2-(4-chlorophenyl)-1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1*H*-imidazole and its FT-IR, FT-Raman vibrational spectral characterizations. To support our experimental investigation, theoretical calculation of vibrational analysis were studied using B3LYP/6-31G (d, p) level of theory [34]. In addition the intramolecular charge transfer, non-linear optical activity, frontier molecular orbital analysis and molecular electrostatic potential of the compound **5f** have been also studied. All the synthesized compounds were evaluated for their antibacterial and antifungal

* Corresponding author. Department of Chemistry, Annamalai University, Annamalainagar, 608 002, Tamilnadu, India.
E-mail address: krishnasamybala56@gmail.com (K. Krishnasamy).

http://dx.doi.org/10.1016/j.molstruc.2016.08.021
0022-2860/

screening on different strains of bacteria and fungi.

2. Experimental

2.1. General methods

TLC was carried out to monitor the course of the reaction and the purity of the product. Melting point of the synthesized compounds have been measured in open glass capillaries and were uncorrected **(Cole-Parmer)**. IR spectra were recorded in AVATAR-330 FT-IR spectrophotometer (Thermo Nicolet) and only noteworthy absorption levels (reciprocal centimeters) are listed. The FT-Raman spectrum of the compound **5f** was recorded on BRUKER: RFS27 spectrometer operating at laser 100 mW in the spectral range of 4000–50 cm^{-1}. FT-Raman spectral measurements were carried out from Sophisticated Analytical Instrument Facility (SAIF), Indian Institute of Technology (IIT), Chennai. The ^{1}H and ^{13}C NMR spectra at 400 and 100 MHz, respectively were obtained at room temperature using a Bruker 400 MHz NMR spectrometer (Bruker biospin, California, USA). All the chromatographic purifications were performed with silica gel (100–200 mesh) whereas all TLC (silica gel) was performed on silica gel coated (Merk Kiesel 60 GF 254, 0.2 mm thickness) sheets. All the chemicals and solvents are commercially obtained (Sigma-Aldrich, Merck) and used directly without any further purification.

2.2. Synthesis of 3-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1H-imidazol-2-yl)-1H-indole derivatives

A mixture of aromatic (or) heterocyclic aldehyde (1 mmol), benzil (1 mmol), 2-(3,4-dimethoxyphenyl)ethanamine (1 mmol) and ammonium acetate (2 mmol) with Y_2O_3/SO_4^{2-} (50 mg) as the catalyst [35] was taken in a round bottom flask and the reaction mixture was refluxed at the boiling point of ethanol (78 °C) and the completion of the reaction was monitored by thin layer chromatography (TLC) technique using benzene: ethyl acetate (8:2) as the eluent. The reaction mixture was then extracted with dichloromethane and the resultant material was purified by column chromatography.

2.2.1. 3-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1H-imidazol-2-yl)-1H-indole **(5a)**

White solid: m.p. 157–159 °C and yield 85%. IR (KBr) (cm^{-1}): 1601 (C=N stretching), ^{1}H NMR (δppm): 9.15 (s, NH proton), 7.16–7.87 (m, 15H aryl protons), 6.56 (d, H-12, $J = 8.4$ Hz), 6.20 (d, H-13, $J = 7.2$ Hz), 5.93 (s, H-9), 4.12 (t, H-7, $J = 6.8$ Hz), 3.77 (s, OCH_3), 3.56 (s, OCH_3), 2.47 (t, H-6, $J = 6.8$ Hz), (^{13}C NMR (δppm): 36.06 (C-6), 46.40 (C-7), 55. 89 & 55.60 (OCH_3), 110.99–147.67 (aromatic and ipso carbon), 148.78 (C=N carbon).

2.2.2. 1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-2-(thiophen-2-yl)-1H-imidazole **(5b)**

White solid: m.p. 151–154 °C and yield 89%. IR (KBr) (cm^{-1}): 1608 (C=N stretching), ^{1}H NMR (δppm): 7.12–7.71 (m, 13H aryl protons), 6.66 (d, H-12, $J = 8$ Hz), 6.37 (d, H-13, $J = 1.2$ Hz), 6.13 (s, H-9), 4.18 (t, H-7, $J = 7.2$ Hz), 3.84 (s, OCH_3), 3.78 (s, OCH_3), 2.68 (t, H-6, $J = 7.6$ Hz), ^{13}C NMR (δppm): 36.15 (C-6), 46.50 (C-7), 55. 92 & 55.63 (OCH_3), 111.20–147.88 (aromatic and ipso carbon), 148.96 (C=N carbon).

2.2.3. 1-(3,4-dimethoxyphenethyl)-2,4,5-triphenyl-1H-imidazole **(5c)**

White solid: m.p. 148–151 °C and yield 90%. IR (KBr) (cm^{-1}): 1598 (C=N stretching), ^{1}H NMR (δppm): 7.13–7.98 (m, 15H aryl protons), 6.60 (d, H-12, $J = 8$ Hz), 6.20 (d, H-13, $J = 1.2$ Hz), 6.01 (s, H-9), 4.11 (t, H-7, $J = 7.2$ Hz), 3.85 (s, OCH_3), 3.65 (s, OCH_3), 2.48 (t, H-6, $J = 7.2$ Hz), ^{13}C NMR (δppm): 36.17 (C-6), 46.41 (C-7), 55. 93 & 55.71 (OCH_3), 111.10–147.94 (aromatic and ipso carbon), 148.86 (C=N carbon).

2.2.4. 1-(3,4-dimethoxyphenethyl)-2-(4-(methylthio)phenyl)-4,5-diphenyl-1H-imidazole **(5d)**

White solid: m.p. 156–159 °C and yield 90%. IR (KBr) (cm^{-1}): 1601 (C=N stretching), ^{1}H NMR (δppm): 7.11–7.48 (m, 14H aryl protons), 6.61 (d, H-12, $J = 8$ Hz), 6.24 (d, H-13, $J = 8$ Hz), 6.00 (s, H-9), 4.10 (t, H-7, $J = 6.8$ Hz), 3.81 (s, OCH_3), 3.66 (s, OCH_3), 2.51 (CH_3), 2.47 (t, H-6, $J = 6.4$ Hz), ^{13}C NMR (δppm): 29.74 (CH_3), 36.13 (C-6), 46.53 (C-7), 55. 94 & 55.64 (OCH_3), 111.11–147.83 (aromatic and ipso carbon), 148.88 (C=N carbon).

2.2.5. 1-(3,4-dimethoxyphenethyl)-2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole **(5e)**

White solid: m.p. 153–158 °C and yield 92%. IR (KBr) (cm^{-1}): 1597 (C=N stretching), ^{1}H NMR (δppm): 7.12–7.86 (m, 14H aryl protons), 6.97 (d, H-12, $J = 8$ Hz), 6.21 (d, H-13, $J = 8$ Hz), 6.02 (s, H-9), 4.08 (t, H-7, $J = 6.8$ Hz), 3.86, 3.80, 3.68 (s, OCH_3), 2.48 (t, H-6, $J = 6.4$ Hz), ^{13}C NMR (δppm): 55.94, 55.65, 5538 (OCH_3), 36.13 (C-6), 46.46 (C-7), 111.17–147.82 (aromatic and ipso carbon), 148.90 (C=N carbon).

2.2.6. 2-(4-chlorophenyl)-1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1H-imidazole **(5f)**

White solid: m.p. 160–163 °C and yield 80%. IR (KBr) (cm^{-1}): 1605 (C=N stretching), ^{1}H NMR (δppm): 7.12–7.86 (m, 14H aryl protons), 6.60 (d, H-12, $J = 8.4$ Hz), 6.24 (d, H-13, $J = 2$ Hz), 5.99 (s, H-9), 4.11 (t, H-7, $J = 7.2$ Hz), 3.82, 3.66 (s, OCH_3), 2.46 (t, H-6, $J = 7.2$ Hz), ^{13}C NMR (δppm): 55.94, 55.62 (OCH_3), 36.09 (C-6), 46.58 (C-7), 111.12–147.91 (aromatic and ipso carbon), 148.90 (C=N carbon).

2.2.7. 1-(3,4-dimethoxyphenethyl)-2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole **(5g)**

White solid: m.p. 157–159 °C and yield 82%. IR (KBr) (cm^{-1})1603 (C=N stretching), ^{1}H NMR (δppm): 7.08–7.89 (m, 14H aryl protons), 6.60 (d, H-12, $J = 8.4$ Hz), 6.24 (d, H-13, $J = 2$ Hz), 5.99 (s, H-9), 4.08 (t, H-7, $J = 7.2$ Hz), 3.81, 3.66 (s, OCH_3), 2.46 (t, H-6, $J = 7.2$ Hz), ^{13}C NMR (δppm): 55.93, 55.62 (OCH_3), 36.06 (C-6), 46.52 (C-7), 111.14–147.88 (aromatic and ipso carbon), 148.88 (C=N carbon).

2.2.8. 4-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1H-imidazol-2-yl)phenol **(5h)**

White solid: m.p. 159–1162 °C and yield 85%. IR (KBr) (cm^{-1}): 1598 (C=N stretching), ^{1}H NMR (δppm): 7.13–7.52 (m, 14H aryl protons), 6.60 (d, H-12, $J = 8.4$ Hz), 6.24 (d, H-13, $J = 2$ Hz), 5.99 (s, H-9), 4.05 (t, H-7, $J = 7.2$ Hz), 3.75, 3.59 (s, OCH_3), 2.43 (t, H-6, $J = 7.2$ Hz), ^{13}C NMR (δppm): 55.94, 55.62 (OCH_3), 36.09 (C-6), 46.58 (C-7), 111.12–147.91 (aromatic and ipso carbon), 148.90 (C=N carbon). 9.8 (s, hydroxyl proton).

2.2.9. 4-(1-(3,4-dimethoxyphenethyl)-4,5-diphenyl-1H-imidazol-2-yl)-N,N-dimethylaniline **(5i)**

White solid: m.p. 160–1163 °C and yield 80%. IR (KBr) (cm^{-1}): 1593 (C=N stretching), ^{1}H NMR (δppm): 7.11–7.52 (m, 14H aryl protons), 6.62 (d, H-12, $J = 8.4$ Hz), 6.29 (d, H-13, $J = 2$ Hz), 6.05 (s, H-9), 4.08 (t, H-7, $J = 7.2$ Hz), 3.80, 3.67 (s, OCH_3), 3.01 $(CH3)_2$, 2.51 (t, H-6, $J = 7.2$ Hz), ^{13}C NMR (δppm): 55.92, 55.66 (OCH_3), 36.15 (C-6), 46.46 (C-7), 40.41 $(CH3)_2$, 111.06–147.69 (aromatic and ipso carbon), 148.83 (C=N carbon).