Indian Journal of Heterocyclic Chemistry
Vol. 33 - Number 02 (Apr-Jun 2023) 257-269
https://connectjournals.com/01951.2023.33.257
https://doi.org/10.59467/IJHC.2023.33.257

ISSN (Print) : 0971-1627
ISSN (Online) : 2456-4311

Synthesis, Spectral, and Computational Studies of 2-Cyano-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acrylamide

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ABSTRACT Synthesis of 2-cyano-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acrylamide (**5**), a pyrazole-based acrylamide, was achieved by the reaction of 1,3-diphenyl-2-carboxaldehyde with cyanoacetamide in aqueous polyethylene glycol – 400, a green medium. Computational studies of molecule **5** were performed using the B3LYP method with 6-311++G(d,p) basis set. The optimized structural parameters showed good agreement with the experimental data. The calculated (normal modes, predicted from DFT) and experimental vibrational frequencies matched well with each other. The complete assignments have been made on the basis of the potential energy distribution of the vibrational modes. ^{1}H and ^{13}C chemical shifts were calculated by the GIAO method and the results were compared with the experimental data. The other parameters, such as dipole moment, polarizability, first-order hyperpolarizability, E_{HOMO}, and E_{LUMO}, have also been computed.

KEYWORDS C=C bond formation, Cyanoacetamide, E_{HOMO}-E_{LUMO}, Electrostatic potential, Pyrazole.

How to cite this article: Iniyaval, S., Krishnan, K.G., Malathi, S. and Ramalingan, C. Synthesis, Spectral and Computational Studies of 2-Cyano-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acrylamide, *Indian J. Heterocycl. Chem.*, **2023**, *33*, 257–269. (https://doi.org/10.59467/IJHC.2023.33.257)

INTRODUCTION

Nitrogen-containing heterocycles are promising structural moieties for drug designing. Specifically, pyrazoles, a vital class of five-membered heterocyclic compounds composed of two nitrogens and three carbons at adjacent positions, are attractive targets of organic synthesis due to their pharmacological activity. Pyrazole-integrated molecules have been utilized in a diverse range of agrochemicals and pharmaceutical industries.[1,2] Further, pyrazole derivatives have been used as active intermediates in the construction of condensed heterocycles and signify an attractive model for combinatorial chemistry.[3] They are seldom found in nature may possibly be due to the complexity of the creation of nitrogen-nitrogen bonds by living organisms,[4] but still emergence of a plethora of research articles during the recent decades further implies the growing interest in medicinal as well as synthetic chemists in view of their extensive applications in various areas.[5-9]

The structural diversifications of the pyrazole ring system show a diverse range of bio-activities including antifungal,[10] antibacterial,[11] antiviral,[12] anticancer,[13-15] antidepressant,[16] antiglaucoma,[17] antitubercular,[18] and insecticidal.[19] On the other hand, various derivatives of pyrazole nucleus are utilized in supra-molecular chemistry,[20] polymer chemistry,[21] food industry,[22] and cosmetics as colorants and ultraviolet stabilizers while few of them exhibit liquid crystal properties.[23]

In general, the presence of certain functional groups in bio-pertinent scaffolds could either enhance or reduce their biological activities. There are several reports available in the literature which describe the nitrile group possessing molecules that support the predominance in their pharmaceuticals and continued clinical trials.[24] Those pharmaceuticals are characterized by their short triple-bond (polarized).[25] Further, the nitrile functionality plays an energetic role as an H-bond acceptor due to its electron richness/polarizability on the N- of the nitrile moiety. Besides, it is well known that amide moiety is one of the most important functional units in the aspect of biology.[26]

The widespread utility of organic molecules owning pyrazole, amide, and nitrile motifs reported in the literature

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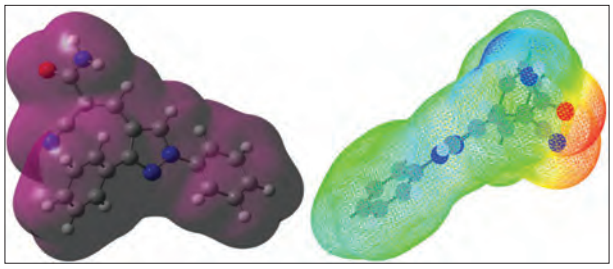

Figure 7: MEP surface total density and electrostatic potential model of compound 5

Table 8: NLO properties of compound 5

Dipole moment		Hyperpolarizability	
μ_x	−0.657	β_{xxx}	−37.249
μ_y	4.604	β_{xxy}	177.706
μ_z	−5.058	β_{xyy}	73.474
μ	6.871	β_{yyy}	30.716
Polarizability		β_{xxz}	−175.526
		β_{xyz}	−44.957
α_{xx}	−241.988	β_{yyz}	−40.528
α_{yy}	−255.484	β_{xzz}	70.746
α_{zz}	−270.884	β_{yzz}	66.037
α_{total}	6.223×10^{-23}	β_{zzz}	−85.252
α_0	−256.1184	β_0	3.641×10^{-30}

130.1, 129.4, 129.2, 128.5, 128.3, 119.8, 114.8, and 104.8.

Computational details

In the current investigation, DFT/B3LYP[42] at the 6–311++G(d,p) basis set has been followed to perform the optimization and vibrational frequencies of the title compound **5** using Gaussian 09 program.[43] The scaling factor[44,45] of 0.96 was utilized to bring theoretical and experimental frequencies to close proximity. DFT (time-dependent) with B3LYP/6-311++G(d,p) was utilized to calculate UV-Vis spectra in both solution and gas phases. B3LYP/6-311++G(2d,p) level using the GIAO method[46] was utilized to compute NMR chemical shifts.

CONCLUSION

A green synthetic protocol has been established to synthesize pyrazole-based acrylamide **5** from its corresponding pyrazole-based carbaldehyde **3** and cyanoacetamide using aqueous PEG-400 as a reaction medium. Computational studies have been carried out for molecule **5**. The computed structural parameters, IR frequencies, and NMR chemical shifts are in agreement with the experimental data. These results together with the other computed parameter including dipole moment, polarizability, first-order hyperpolarizability, E_{HOMO}-$_{LUMO}$ energy calculation, etc., imply that the pyrazole-based acrylamide **5** could serve as an effective intermediate for constructing effective NLO materials besides the construction of potent bio-pertinent chemical entities.

ACKNOWLEDGMENT

Financial assistance provided by the Indian Council of Medical Research (ICMR), New Delhi, India (No. 58/16/2013-BMS) is gratefully acknowledged.

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Received: 19 Apr 2023; Accepted: 29 Jun 2023