Journal Pre-proof

Molecular structure of 1,4-bis(substituted-carbonyl)benzene: A combined experimental and theoretical approach

Ezzat Khan, Muhammad Khalid, Zarif Gul, Adnan Shahzad, Muhammad Nawaz Tahir, Hafiz Muhammad Asif, Sumreen Asim, Ataualpa Albert Carmo Braga

PII: S0022-2860(19)31742-9

DOI: https://doi.org/10.1016/j.molstruc.2019.127633

Reference: MOLSTR 127633

To appear in: Journal of Molecular Structure

Received Date: 29 September 2019

Revised Date: 19 December 2019

Accepted Date: 20 December 2019

Please cite this article as: E. Khan, M. Khalid, Z. Gul, A. Shahzad, M.N. Tahir, H.M. Asif, S. Asim, A.A.C. Braga, Molecular structure of 1,4-bis(substituted-carbonyl)benzene: A combined experimental and theoretical approach, *Journal of Molecular Structure* (2020), doi: https://doi.org/10.1016/j.molstruc.2019.127633.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2019 Published by Elsevier B.V.



Journal Pre-proof

The Reaction between terephthaloyl dichloride and 2-aminopyrazol derivatives give corresponding compounds 1,4-phenylenebis(1H-pyrazol-1-yl)methanone (1), 1,4-phenylenebis(3-methyl-1H-pyrazol-1-yl)methanone (2) and 1,4-phenylenebis(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3). All compounds are crystalline and their structures were confirmed by single crystal X-ray diffraction. Detailed DFT calculations for compounds were also carried out.



Molecular structure of 1,4-Bis(substituted-carbonyl)benzene: A combined Experimental and Theoretical Approach

Ezzat Khan,^{a*} Muhammad Khalid,^d* Zarif Gul,^a Adnan Shahzad,^b Muhammad Nawaz Tahir,^c Hafiz Muhammad Asif,^d Sumreen Asim,^d Ataualpa Albert Carmo Braga^e

^aDepartment of Chemistry, University of Malakand, Chakdara, Lower Dir, Khyber Pakhtunkhwa, 18800, Pakistan.

^bInstitute of Chemical Sciences, University of Swat, Khyber Pakhtunkhwa, Pakistan.

^cDepartment of Physics, University of Sargodha, 40100 Punjab, Pakistan.

^dDepartment of Chemistry, Khwaja Farid University of Engineering & Information Technology, Rahim Yar Khan-64200, Pakistan

^eDepartamento de Química Fundamental, Instituto de Química, Universidade de São Paulo, Av. Prof. Lineu Prestes, 748, São Paulo, 05508-000, Brazil

*Corresponding authors, E-mail adresses: <u>ekhan@uom.edu.pk</u> (Ezzat Khan) and <u>khalid@iq.usp.br (</u>Muhammad Khalid)

Abstract

The reaction of pyrazole derivatives (pyrazole (Pz), 3-methylpyrazole (MPz) and 3,5dimethylpyrazole (DMPz)) with terephthaloyl dichloride (TD) in the presence of Et₃N afforded the desired products. 1,4-bis(pyrazolylcarbonyl)benzene (1), 1,4-bis(3methylpyrazolylcarbonyl)benzene (2) and 1,4-bis(3,5-dimethylpyrazolylcarbonyl)benzene (3). Good quality crystals were isolated and diffraction data for single crystal were collected which revealed that compounds 1-3 are monoclinic with space group P21/n, C2/c and P21/c, respectively. These compounds were obtained as a result of C-N coupling reaction between the acid chloride and pyrazol derivatives with the intent to explore their structure in solution as well as solid state. Density function theory (DFT) calculations using B3LYP and CAM-B3LYP functionals with 6-311G(d,p) basis set were performed to explore geometric and electronic properties of compounds. The Root Mean Square Error (RMSE) has also been calculated for the values of geometric parameters, indicating a good agreement with experimental findings. Moreover, frontier molecular orbitals (FMOs) and natural bond orbitals (NBOs) analyses were carried out through B3LYP/6-311G(d,p) level of theory. The linear polarizability (*a*) values of nonlinear optical (NLO) analysis were calculated with the same level of theory and basis set as FMO but under different solvent conditions. Time Dependent Density Functional Theory (TD-DFT) study of these pyrazole substituted derivatives was performed aiming to investigate UV-Visible behavior. The stability of molecule has been additionally analyzed by Hirshfeld surface analysis in addition to NBO analysis. The calculated HOMO and LUMO energies from FMO assisted in calculating global reactivity parameters (Chemical hardness, chemical softness, electronegativity, EA, IP and electrophilicity). Natural population analysis (NPA) and Molecular electrostatic potential (MEP) were also performed to obtain insights about the reactivity of compounds **1-3**. Theoretical calculations indicate that these compounds have considerable low reactivity and can be used for development of coordination chemistry under optimum conditions.

Key words: C-N coupling reactions; terephthaloyl dichloride; x-ray diffraction; Time Dependent Density Functional Theory; FMOs; NBOs.

Journal

1. Introduction

There is enormous interest in developing chemistry of acid chlorides and primary or secondary amines. Primarily the reaction between acid chloride derivatives was carried out with ammonia at low temperature under various reaction conditions and afterwards the same technique was extended to saturated and unsaturated homologues [1]. This strategy leads to the formation of amides which allow for simple and green operating procedure [2]. Pyrazole derivatives are easily accessible [3], they possess various active reaction cites, accommodate a variety of functional groups [4] and act as starting precursors in many reactions [5,6]. The NH function in the 5-membered ring is of particular importance and the acidic nature of this group led to a number of products for potential applications such as N-C coupling reactions for synthesis of carbonyl derivatives [7,8].

On the other hand, acid chlorides for instance terephthaloyl dichloride is an active ingredient in the synthesis of polymeric material. It has been reported that thiourea derivatives containing terephthaloyl group are active antimicrobial agents [9]. On the basis of acid chloride functional group at *para* position with respect to each other, this compound is suitable candidate to bridge several molecules for a variety of applications [10].

Keeping in view a very rich chemistry of pyrazole derivatives and terephthaloyl dichloride and in continuation to our previous work [8], Scheme 1, we carried out reactions between these two with the intent to design multidentate ligands for possible polynuclear coordination chemistry. The reaction of terephthaloyl dichloride with Pz, MPz and DMPz afforded compounds **1-3**, respectively. These compounds were isolated in crystalline form from their respective solutions and their structures were determined by single crystal X-ray diffraction. The compounds were explored theoretically using B3LYP and CAMB3LYP functionals with 6-311G(d,p) basis set from data obtained by diffraction analyses. The Root Mean Square Error (RMSE) has also been calculated for the geometric parameter data which disclosed a good agreement between experimental and calculated structural parameters. Moreover, FMOs and NBOs analyses were carried out to DFT method using B3LYP and CAM-B3LYP functional with 6-311G(d,p) basis set. The linear polarizability (α) values of nonlinear optical (NLO) analysis were calculated with the same level of theory but under different solvent conditions. The Hirshfeld surface of compounds **1-3** was calculated in order to determine the stability of these derivatives. The calculated E_{HOMO} and E_{LUMO} were helpful in determining the global reactivity

parameters such as chemical hardness, softness, electronegativity, EA (electron affinity), IP (ionization potential) and electrophilicity. The stability and electronic properties of compounds **1-3** are elaborated on the basis of insights obtained through DFT calculations.



Scheme 1: Compounds obtained by the reaction of acid chlorides with respective amines to afford new precursors as a result of N-C bond formation.

2. Material and methods

2.1 General

Reactions were carried out in toluene (dried over benzophenone/Na), products were obtained in reasonable quantity and were stored under aerobic conditions for prolonged period of time. Trimethylamine (Et₃N) was distilled prior to use. Other chemicals such as, pyrazole (pz), 3-methylpyrazole (MPz), 3,5-dimethylpyrazole (DMPz) and terephthaloyl dichloride (TD) were purchased from Sigma Aldrich and were used without further purification. Melting point of compounds were uncorrected, measured by BIO-COT STUART-SMP10, Japan in sealed capillary tubes. The FT-IR (ATR method, 400-4000 cm⁻¹) were recorded by SHIMADZU model 8400s. ¹H- and ¹³C-NMR were recorded on Bruker 300 MHz, in deuterated chloroform at room temperature. The X-ray diffraction data were collected for compounds **1-3**, at room temperature (Bruker kappa APEXII CCD diffractometer, graphite-monochromator, Mo-K α radiation, λ = 0.71073 Å). Resolution of structures and their refinements were accomplished by SIR97 [11], SHELXL-97 [12], WinGX [13] and PLATON [14] programs.

2.2 Syntheses of 1,4-bis(pyrazolylcarbonyl)benzene (1), 1,4-bis(3-

methylpyrazolylcarbonyl)benzene (2) and 1,4-bis(3,5-dimethylpyrazolylcarbonyl)benzene (3)

1. Following the literature procedure [8], toluene solution of pyrazole (2.30 mL, 28.0 mmol) was prepared followed by addition of triethylamine (4.0 mL, 28.0 mmol). The resulting

solution was allowed to stir for ca. 10 min. Stoichiometric amount of terephthaloyl dichloride (3.00 g, 14.0 mmol) in toluene (20 mL) was dropwise added over a time of 20 min and reaction contents were left stirring overnight. Precipitates of ammonium salt, [Et₃NH]Cl were obtained, washed with copious amount of water and the chloroform (organic) phase was collected followed by slow evaporation at room temperature. After five days colorless needle-like crystals appeared, were separated from the mother liquor and structure for a single crystal was confirmed by X-ray diffraction. m.p. = 161-163°C, Yield = 80%; ¹H-NMR & (ppm) = 8.60 (d, 2H, CH-Pz), 8.24-8.26 (m, 4H, Ph), 7.82 (d, 2H, CH-Pz), 6.58 (2, 2H, CH-Pz); ¹³C-NMR & (ppm) = 110.6, 127.9, 129.2, 145.5, 134.3, 162.9; FT-IR (ATR) ν (cm⁻¹) = 1725 (CO), 1564 (CN).

2. Terephthaloyl dichloride (1.500 g, 7.0 mmol), 3-methylpyrazole, MPz (1.15 mL, 14.0 mmol) and two equivalents of Et₃N. Crystals were grown in toluene solution. m.p. = 178-180°C, Yield = 82%; ¹H-NMR & ppm) = 8.45 (d, 2H, CH-Pz), 8.23-8.26 (m, 4H, Ph), 6.52 (d, 2H, CH-pz), 2.36 (s, 6H, Me); ¹³C-NMR & ppm) = 12.0, 109.1, 128.8, 135.0, 137.9, 149.2, 164.7; FT-IR (ATR) ν (cm⁻¹) = 1728 (CO), 1556 (CN).

3. 3,5-dimethylpyrazole (2.30 mL, 28.0 mmol), slight excess of triethylamine (4.50 mL, > 28 mmol) and terephthaloyl dichloride (3.12 g, 14.0 mmol). Crystals of the proposed compound were grown in its chloroform solution. m.p. = 184-186°C, Yield = 86%; ¹H-NMR δ (ppm) = 2.23 (s, 6H, Me), 2.60 (s, 6H, Me), 6.12 (s, 2H, CH), 7.84-7.91 (m, 4H, Ph); ¹³C-NMR δ (ppm) = 13.2, 14.0, 111.0, 129.1, 134.8, 141.5, 147.6, 165.4; FT-IR (ATR) ν (cm⁻¹) = 1723 (CO), 1560 (CN).

2.3 Computational studies

Quantum chemical calculations for compounds **1-3** were carried out with the help of DFT employing Gaussian 09 program package [15]. The SC-XRD data were used to build the structure of compounds and the geometries were optimized. The complete geometrical optimization was carried out without symmetry restrictions by applying DFT/B3LYP/6-311G (d,p) and DFT/CAM-B3LYP/6-311G (d,p) levels of theory [16]. The frequency analysis based on DFT/B3LYP/6-311G (d,p) and DFT/CAM-B3LYP/6-311G (d,p) levels of theory was used for further confirmation of stability associated with optimized geometries. The NBO analysis was also accomplished with the help of DFT/B3LYP/6-311G (d,p) level of theory at the same basis set [17]. The NLO analysis was performed at B3LYP/6-311G (d,p) level of theory. The FMOs, MEP and

the photophysical characteristics of compounds were determined employing TD-DFT/B3LYP/6-311G (d,p) level of theory. The Hirshfeld surface analysis was conducted from their original Crystallographic Information Files (CIF). Global reactivity parameters (GRP) were calculated using the energies of FMOs and their respective energy gaps with the help of the given equations, as discussed in the preceding text. The EA (electronic affinity, represented by *A* in the equation) and IP (ionization potential, represented by *I*) values were calculated using equations 1 and 2, respectively [18].

$$I = -E_{HOMO}$$
 Equation 1

$$A = -E_{LUMO}$$
 Equation 2

Hardness (η) and electronegativity (X) were attained using equations 3 and 4 [19].

$$\eta = \frac{I-A}{2}$$
Equation 3
$$X = \frac{I+A}{2}$$
Equation 4

The chemical potential (μ) was calculated as below.

$$\mu = \frac{E_{HOMO} + E_{LUMO}}{2}$$
 Equation 5

The magnitude of electrophilicity (*a*) was calculated according Equation 6, which explain the relation amongst energy variation and maximum electron transferred [20-22].

$$\omega = \frac{\mu^2}{2\eta}$$
 Equation 6

For calculating the value of softness (σ) equation 7 was used.

$$\sigma = \frac{1}{2\eta}$$
 Equation 7

All input files were organized with the help of Gaussview 5.0. Avogadro [23], Gauss view 5.0 [24], Gauss Sum [25], Argus Labs [26], Crystal Explorer [27] and Chemcraft [28] programs. Moreover, same softwares were employed for the interpretation of the output files.

3. Results and discussion

3.1. General chemistry

Compounds 1-3 (Scheme 2, below) were synthesized as per literature protocol [7,8] with the intent to explore their coordination chemistry with certain metal ions. When they were treated with salts of Pd and Cu, extensive hydrolysis of the ligand was observed and only complexes containing pyrazolyl ligands were obtained [29]. This study reveals that such compounds undergo hydrolysis in the presence of metal salt and are converted into corresponding acids and starting pyrazolyl moieties.





Scheme 3: Cu(II) complexes of 3-methylpyrazole where the ligands adopts itself as 5methylpyrazole due to H exchange between two nitrogen atoms for the purpose to minimize steric bulk near metal ion for efficient connectivity.

Compounds 1-3 were synthesized with the intent to explore their coordination chemistry. Treatment of compound 2 with CuCl₂ salt under reflux condition for three hours, afforded a dinuclear copper (II) complex 4, Scheme 3. The formation of the complex was confirmed in some solvents with varying polarity such as EtOH, MeOH and CH₃Cl. Literature survey reveals that complex 4 has been synthesized in a different way [6a]. When 3-methylpyrazole was treated with CuCl₂ under identical conditions, compound 5 was exclusively obtained [5]. These reactions with copper (II) chloride salt did not allow further reactions to explore their coordination chemistry. The hydrolysis of structurally analogues compounds was used as a tool for the synthesis of coordination polymers with Cu(II) ion [8a] where as in this study we did not isolate structurally novel complexes.

3.1.1. Structure description of 1,4-phenylenebis(1H-pyrazol-1-yl)methanone, 1

Crystal of suitable dimensions of compound 1 (shown in Figure 1) were selected and the data were collected at room temperature. Structural parameters pertaining to crystal structure determination and refinements are summarized in Table 1. The data indicate that compound 1 is monoclinic with space group $P2_1/n$. The C=O groups at *para* position of the phenylene ring are oriented in a *trans* manner with respect to each other. The pyrazolyl and the respective carbonyl moiety are coplanar while both the pyrazolyl rings across phenylene are arranged in the space in a trans manner. Groups around C4 are arranged in trigonal manner and angles around it are collectively equal to 360° ($\angle 01 - C4 - N1119.1(2), \angle 01 - C4 - C4$ C5 122.2(2) and $\angle N1 - C4 - C5$ 118.7(18)). The bond lengths around C4 are C4-O1 1.206(2), C4-N1 1.402(2), C4-C5 1.487(3) Å (for comparison of bond lengths and angles see Table 2) indicating that electron density is partially delocalized resulting in a comparatively shorter bond length between C4 and C5 as compared to the reported structurally related compound [8a]. All other bond lengths are within the expected regions. Pyrazolyl groups of the molecule are co-planar with respect to each other while they are considerably twisted against the phenylene ring (torsion angle N1C4C5C6 44.8° and N1C4C5C7 139.08°). The co-planarity in compound 1 in solid state is probably attributed to intermolecular interactions as shown in Figure 2. These intermolecular interactions also called secondary interactions are responsible to arrange molecules in 2D supramolecular fashion. Separation distance between H of C6 and N2 (H6-N2) is 2.701 Å, which is actually separation between two parallel layers. The molecules in a parallel layer are linked through O1-H1 type hydrogen bonding with a distance of 2.388 Å.



Figure 1: Molecular structure of compound 1, partial numberings are shown and hydrogen atoms are omitted for clarity reasons. Selected bond lengths and angels are summarized in Table 2 also see Table S1 for more details.



Figure 2: Supramolecular 2D arrangements of molecules of compound **1**, linked together with the help of non-covalent interactions.

3.1.2. Structure description of 1,4-phenylenebis(3-methyl-1*H*-pyrazol-1yl)methanone, 2

The solid state structure of compound 2 is depicted in Figure 3, while data pertaining to its structure refinements and solution are summarized in Table 1 and important structural parameters are shown in Table 2. The molecule is monoclinic bearing space group C2/c. geometry and orientation of various groups in the molecule are very close to each other with

negligible differences. The C4 is sp² hybridized with trigonal planar geometry. The bond lengths C4-O1 1.210(2), C4-N1 1.393(3) and C4-C2 1.484(3) Å are slightly different from compound **1**. It is evident that electron density is shifted towards pyrazolyl group thus making the C4-N1 bond slightly shorter and C4-O1 bond longer in comparison to compound **1**. Angles around C4 are also in support with the trigonal planar geometry ($\angle 01 - C4 - N1 119.62(19) \angle 01 - C4 - C2 122.66(19)$ and $\angle N1 - C4 - C2 117.73(16)^\circ$. In the same MePz (methylpyrazol) groups are coplanar with respect to each other as well as with respective CO group with slight deviation of 2.66°. Both the pyrazolyl moieties are twisted against phenylene ring (torsion angles N1-C4-C2-C3 55.51° and N1-C4-C2-C1 128.73°).

In establishing the supramolecular structure of the compound methyl group plays an important role. One of the H from CH_3 group makes an interaction with the CO group with a separation distance of 2.687 Å, affording a 2D architecture as depicted in Figure 4.



Figure 3: Molecular structure of compound **2**, hydrogen atoms and numbering of some structurally less important atoms are omitted for clarity reasons. Selected bond lengths and angles are represented in Table 2 and for more details see Table S2.



Figure 4: View of 2D supramolecular structure of compound 2, hanging contacts are deleted for clarity reasons.

3.1.3. Structure description of 1,4-phenylenebis(3,5-dimethyl-1*H*-pyrazol-1yl)methanone, 3

Solid state structure of compound **3** determined with the help of X-ray diffraction for its single crystal is given in Figure 5. Its crystal structure refinements and solution parameters are summarized in Table 1 and structural parameters in Table 2. The compound is monoclinic having identical space group as compound **1** ($P2_1/c$). Carbonyl (C=O) moieties are oriented in *trans* manner with respect to each other in a similar was as in compounds **1** and **2**. Carbonyl carbon (C6) is trigonal with angles around it, $\angle C7 - C6 - N2 \, 119.58, \angle C7 - C6 - O1 \, 1120.82$ and $\angle N2 - C6 - O1 \, 119.61^\circ$. These values are in agreement with trigonal planar geometry of the C7C6N2O1 fragment. The bond length C6-O1 1.215, C6-C7 1.499 and C6-N2 1.398 Å, indicate that C=O bond gradually elongates. The C6-N2 bond is least affected and C6-C7 bond becomes longer. These data indicate that the electron density is delocalized towards dimethypyrazolyl group along O1-C6-N2 fragment. In the molecule dimethylpyrazolyl groups are twisted by 163.85° with respect to DMP and by 28° with respect to the phenylene ring. The DMP and phenylene rings are mutually twisted by ca. 40°.

There are several short ranged intermolecular interactions in compound **3**, both Oxygen atoms of the carbonyl groups interact with CH of DMP (distance 2.619 Å), H of one molecule

also interact with p-electrons of DMP (distance 2.891 Å). The CH_3 protons of neighboring molecules also interact with each other, stabilizing two molecules at a distance of 2.821 Å. These interactions afford a 3D supramolecular structure of the compound.

Compound Names	1	2	3
Chemical Formula	$C_{14}H_{10}N_4O_2$	$C_{16}H_{14}N_4O_2$	$C_{18}H_{18}N_4O_2$
Mr	266.26	294.31	322.36
Crystal System	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_{1}/n$	C2/c	<i>P</i> 2 ₁ /c
Temperature(K)	296	296	296
a (Å)	3.9007(4)	3.9718(5)	4.1278(3)
b (Å)	11.0403(13)	15.299(3)	14.7281(12)
c (Å)	14.955(2)	12.0601(18)	13.1635(9)
eta(°)	96.407(9)	95.800(5)	94.682(4)
$V(\text{\AA}^3)$	640.02(13)	729.08(19)	
Z	2	2	2
Radiatio type	Μο/Κα	Mo/Ka	Mo/Ka
μ (mm ⁻¹)	0.10	0.09	0.09
Crystal size	0.39×0.20×0.15	0.35×0.15×0.14	0.40×0.20×0.18
Reflections measured	5614	6712	6660
Independent Reflections	1527	1738	1815
Observed Reflection $[I > 2\sigma(I)]$	894	943	1439
R _{int}	0.041	0.047	0.032
$(\sin\theta/\lambda)_{max}$ (Å ⁻¹)	0.659	0.660	0.649
$R[F^2>2\sigma(F^2)]$	0.058	0.050	0.044
$wR(F^2)$	0.139	0.132	0.126
S	1.02	1.01	1.06
No. of Reflections/parameters	1527/91	1738/101	1815/112
$\Delta \rho_{max}, \Delta \rho_{min} (e \text{\AA}^{-3})$	0.13, -0.16	0.14, -0.21	0.24, -0.22

 Table 1: Crystal structure determination and refinements of compounds 1-3.

Compound 1		Com	Compound 2 Compound				
Bond lengths							
C4-01	1.206(2)	C4-O1	1.210(2)	C6-O1	1.215(17)		
C4-N1	1.402(2)	C4-N1	1.393(3)	C6-N2	1.398(18)		
C4-C5	1.487(3)	C4-C2	1.484(3)	C6-C7	1.499(19)		
		Bonda	angles	(
01-C4-N1	119.1(2)	01-C4-N1	119.62(19)	01-C6-N2	119.61(13)		
01-C4-C5	122.2.(2)	O1-C4-C2	122.66(19)	01-C6-C7	120.82(13)		
C5-C4-N1	118.7 (18)	N1-C4-C2	117.73(16)	N2-C6-C7	119.58(12)		

Table 2: Summarized structural parameters of compounds **1-3**, bond length (Å) and bond angles (°).



Figure 5: Molecular structure confirmed by X-ray diffraction of compound **3**, hydrogen atoms are omitted for clarity, partial numbering is shown, for summarized structural features (bond lengths and angles) see Table 2, for more details see Table S3.

3.1.4. Molecular geometric parameters

The geometry of compounds **1-3** was optimized by using two different level of theories i.e., B3LYP and CAM-B3LYP with same basis set as 6-311G (d,p). The obtained parameters are tabulated in detail in Table S1-S3 (Supplementary Information) and graphical representation of molecular geometric parameters is presented in Figures 6, Figure S1 and S2, respectively.

Considering bond lengths, the experimental and calculated (DFT (B3LYP)) values, the identical value was found to be 1.498 Å for (C6-C7) and (C18-C19) in compound **3**. The least deviated values were found to be 0.002 Å for (C3-C9), (C8-C9), (N13-C19) and (C18-C19) in **1**, 0.002 Å for (O1-C7) and (O12-C18) in **2** and 0.001 Å for (C14-N22) in **3**. However, the most deviated values were 0.024 Å for (C2-C3) in **1**, 0.026 Å for (N2-C7) and (N13-C18) in **2** and 0.018 Å for (C3-C4) and (C15-C16) in **3** (Figure 6 and Figures S1, S2, respectively).

While considering bond lengths, comparing the XRD and the DFT (CAM-B3LYP) values, the least deviated values were found to be 0.002 Å for (C4-C10) and (N14-C20) in **1**, 0.001 Å for (N2-C8) and (N13-C19) in **2** and 0.001 Å for (C1-C2), (C7-C8), (C7-C9), (C13-C14), (C19-C20) and (C19-C21) in **3**. However, the most deviated values were 0.024 Å for (C1-C2) and (C11-C12) in **1**, 0.019 Å for (N2-N3), (N2-C7), (N13-N14) and (N13-C18) in **2** and 0.022 Å for (N10-N11) and (N22-N23) in compound **3**.

When considering bond angles, comparing the experimental and the DFT calculated (B3LYP) values, the identical values were found for (C2-C3-C9) and (C12-N13-C19) in compound **1**, (N3-C10-C9) and (N14-C21-C20) in **2** and (C8-C7-C9) and (C20-C19-C21) in compound **3**. The least deviated values were found to be 0.1° for (C2-C1-C8), (C5-C4-C10), (C5-C6-C17), (C7-C16-O15), (C12-C11-C18) and (O15-N14-C20) in compound **1**, 0.1° for (N3-C10-C11), (C9-C10-C11), (N14-C21-C22) and (C20-C21-C22) in **2** and 0.1° for (C3-C4-N11), (C7-C8-C21), (C7-C9-C20), (C8-C21-C19), (C9-C20-C19) and (C15-C16-N23) in **3**. However, the most deviated values were 2.8° for (C1-C8-C4) and (C11-C18-N14) in **1**, 2.8° for (C6-C5-C7) and (C17-C16-C18) in **2** and 1.1° for (C1-C2-C3), (C2-N10-N11), (C13-C14-C15) and (C14-N22-N23) in **3**.

 C4) and (C11-C18-N14) in **1**, 2.7° for (C6-C5-C7) and (C17-C16-C18) in **2** and 1.2° for (C2-N10-N11) and (C14-N22-N23) in **3**.

The comparative analysis reveals that calculated bond angles and bond lengths are higher than SC-XRD values as reflected in Tables S1-S3 and Figures 6, S1, S2. However, in few cases the DFT values of bond angles and bond lengths were otherwise i.e., smaller than the XRD values. The disagreement between DFT and experimental findings is predominantly because of the medium effect (solid state and solution phase).



Figure 6: Comparative representation of Experimental and calculated bond lengths (Å) and bond angles (°) for compound **1**

For a fair comparison between the experimental and DFT study regarding optimization, error was further calculated with the help of equations 8-10;

Mean Absolute Deviation (MAD) =
$$\frac{\sum_{t=1}^{n} |EXP - DFT|}{n}$$
 Equation 8

Where, n is the total number of bond length or bond angle values considered, t is number of bond length or bond angle values, "EXP" is the experimental based bond length or bond angle value and "DFT" is the calculated bond length or bond angle value.

The mean absolute deviation (MAD) can be defined as the sum of absolute differences between the experimental and calculated study-based values divided by the total number of bond length or bond angle values taken.

Mean Square Error (MSE) =
$$\frac{\sum_{t=1}^{n} (EXP - DFT)^2}{n}$$
 Equation 9

Mean square error is usually utilized error metric. It penalizes huge errors due to squaring larger numbers consisting of a largest impact as compared to squaring smaller numbers.

Root Mean Square Error (RMSE) =
$$\sqrt{\frac{\sum_{t=1}^{n} (EXP - DFT)^2}{n}}$$
 Equation 10

The root mean square error (RMSE) can be calculated by taking the square root of MSE. It is the most commonly used error metric and had been especially considered for compounds **1-3**.

The RMSE approach is considered to be the most commonly used in structural calculations, so, the RMSE approach has also been adopted for our investigated systems as given in Table 3.

		1		2		3
Level of Theory	B3LYP	CAM- B3LYP	B3LYP	CAM- B3LYP	B3LYP	CAM- B3LYP
RMSE for bond lengths	0.0154	0.012	0.0146	0.0112	0.00855	0.00845
RMSE for bond angles	1.2295	1.266	1.516	1.5362	0.5472	0.5629

Table 3: Calculated standard error values for compounds 1-3.

The error calculations in terms of root mean square error gave an accurate comparison of both the level of theories being applied, B3LYP and CAM-B3LYP. Both the level of theories were in good agreement to one another.

3.1.5. Hirshfeld Surface Analysis

Moreover, to explore intermolecular interactions, Hirshfeld surface analysis for 1, 2 and 3 was performed [30-32]. The configuration of Hirshfeld surface for complete molecule of 1, 2 and 3 is shown in Figure 7. In Hirshfeld surface plot, strongest interactions are indicated by red colour, intermediate interactions are indicated by white colour and almost negligible intermolecular interactions are indicated by blue colour (shown in online version). Overall interactions of compound 1 are given in Figure 8.

Journal Pre-proof

The intermolecular interactions can also be explored with the utilization of twodimensional fingerprint plots, which can be decomposed to quantify the individual contributions of each intermolecular interaction involve in the structure. The overall two-dimensional fingerprint plots are shown in Figure 8 (compound 1) and Figure S3 and S4 (compound 2 and 3, respectively) [33-35]. These figures show the percent intermolecular contributions for various interatomic contacts to the Hirshfeld surface and percentage contributions of an atom in Hirshfeld surface with all other atoms present outside the surface to specify its role in crystal packing.



Figure 7: Hirshfeld surfaces mapped over d_{norm} in the range from -0.2799 to 1.2890 a.u., 0.0079 to 1.3088 a.u. and -0.0748 to 1.1368 a.u. for compounds 1, 2 and 3 (left to right). 1 a.u. of electron density = 6.748 eÅ⁻³





Figure 8: Two-dimensional fingerprint plots for compound 1.

Theoretical findings regarding crystal packing of compounds 1-3, show that the H^{...}H contacts appear to be the major contributor and was quantified as 38.3, 46.8 and 55.4%, respectively. The role of hydrogen atoms is very crucial in the overall stabilization of structure for these compounds and the percent contribution to intermolecular contacts is quite high. The smallest contribution towards intermolecular interactions was observed for oxygen atom of C=O group, its role in crystal packing was found as 1.3, 0.1 and 0%, respectively [36].

3.1.6. Natural Bond Orbital (NBO) Analysis

NBO analysis provides insights into intra- and inter-molecular interactions in filled and virtual orbitals. Evaluation of the donor-acceptor interactions within the NBO analysis was administered with the help of second-order Fock matrix [37]. For each donor (i) and acceptor (j), the stabilization energy $E^{(2)}$ associated with the delocalization $i \rightarrow j$ was assessed according to literature protocol, as given in equation 11 [38].

$$E^{(2)} = q_i \frac{\left(F_{i,j}\right)^2}{\varepsilon_j - \varepsilon_i}$$
 Equation 11

Where F(i,j) is the diagonal and ε_j and ε_i are the off-diagonal NBO Fock matrix elements and q_i is the donor orbital occupancy [39].

For finding out intra- and inter-molecular bonding and interaction among existing bonds, natural bond orbital (NBOs) analysis is an efficient tool and it additionally provides a convenient basis for investigating conjugative interactions or charge transfer in molecular systems [40,41]. The NBOs analyses were carried out for **1-3**, the obtained data are given in supplementary file (Table S4-S6, respectively). Selected values are represented in Table 4, and optimized structures with complete numbering scheme are shown in Figure S5-S7.

Entry	i	Туре	j (Acceptor)	Туре	$E(2)^{\mathrm{a}}$	$E(j) - E(i)^{b}$ [a.u.]	$F(i;j)^{c}$ [a.u.]
Entry	(Donor)						
	C1-C3	π	C5-N14	π^*	26.92	0.28	0.080
	C16-C18	π	C20-N29	π^*	26.92	0.28	0.080
	C5-N14	π	C1-C3	π^*	12.03	0.34	0.059
	C20-N29	π	C16-C18	π^*	12.03	0.34	0.059
1	C18-C20	д	C16-H17	∂^*	5.39	1.12	0.069
I	C3-C5	д	C1-H2	∂^*	5.39	1.12	0.069
	C5-N14	д	C7-N13	∂^*	5.03	1.21	0.071
	N13	LP(1)	C7-O15	π^*	37.49	0.29	0.099
	N28	LP(1)	C22-O30	π^{*}	37.49	0.29	0.099
	N14	LP(1)	C3-C5	∂^*	5.39	0.93	0.064
	C10-C12	π	N3-C14	π^*	27.21	20.29	0.082
	C28-C30	π	N21-C32	π^*	27.21	0.29	0.082
	C6-C7	π	C22-C24	π^{*}	21.19	0.28	0.069
2	C6-C7	π	O1-C9	π^{*}	18.20	0.26	0.065
2	N3-C14	д	C10- C12	∂^*	11.50	0.34	0.058
	C30-C32	д	C28-H29	∂^*	5.27	1.11	0.069
	N2	LP(1)	O1-C9	π^{*}	38.76	0.29	0.100
	N21	LP(1)	C30-C32	∂^*	6.06	0.92	0.067
	C6-C8	π	C5-N19	π^*	28.25	0.29	0.083
	C27-C29	π	C26-N40	π^{*}	28.25	0.29	0.083
3	C35-C38	π	C14-C15	π^{*}	21.19	0.28	0.069
	C9-H12	д	C8-N20	∂^*	7.64	0.93	0.076
	С30-Н33	д	C29-N41	∂^*	7.64	0.93	0.076

 Table 4: Representative values of NBOs analyses for 1, 2 and 3

C6-C8	д	C1-C5	∂^*	5.12	1.13	0.068
N20	LP(1)	C13-O21	∂^*	38.45	0.28	0.099
N41	LP(1)	C34-O42	π^{*}	38.45	0.28	0.099
N19	LP(1)	C5-C6	∂^*	5.91	0.93	0.067

^a $E^{(2)}$ represents "energy of hyper conjugative interaction (stabilization energy in kcal/mol)". ^bEnergy difference between *i* and *j* NBOs.

^cF(i;j) is the Fock matrix element between *i* and *j*.

The probable transition consisting of enormous stabilization energies such as: π (C1-C3) $\rightarrow \pi^*(C5-C14)$ and $\pi(C16-C18) \rightarrow \pi^*(C20-N29)$ contain 26.92 kcal/mol each for compound 1, $\pi(C10-C12) \rightarrow \pi^*(N3-C14)$ and $\pi(C28-C30) \rightarrow \pi^*(N21-C32)$ has an energy value of 27.21 kcal/mol each for compound 2 and $\pi(C6-C8) \rightarrow \pi^*(C5-N19)$ and $\pi(C27-C29) \rightarrow \pi^*(C26-N40)$ each with 28.25 kcal/mol for compound 3. Other important transitions in these compounds pointing towards conjugation system are, $\pi(C5-N14) \rightarrow \pi^*(C1-C3)$ and $\pi(C20-N29) \rightarrow \pi^*(C16-C1)$ C18) in compound 1, $\pi(C6-C7) \rightarrow \pi^*(C22-C24)$ and $\pi(C6-C7) \rightarrow \pi^*(O1-C9)$ in compound 2 and π (C35-C38) $\rightarrow \pi^*$ (C14-C15) in compound 3 with stabilization energy values 12.03, 21.19 and 18.20 kcal/mol, respectively and 21.19 kcal/mol for 3. However, transitions such as π (C1-C3) $\rightarrow \pi^*(C5-C14)$, $\pi(C10-C12) \rightarrow \pi^*(N3-C14)$ and $\pi(C6-C8) \rightarrow \pi^*(C5-N19)$ demonstrated highest stabilization energies of 26.92, 27.21 and 28.25 kcal/mol, respectively in compounds 1-3 (see supporting information Table S4-S6). Among all calculated stabilization energies, these values were the leading one. The calculation of energy corresponds to $\pi \rightarrow \pi^*$ interactions is important to know about the existence of conjugation as well as charge transfer phenomenon in compounds. Electronic transitions i.e., $\pi(C20-N29) \rightarrow \pi^*(C16-C18)$, $\pi(C6-C7) \rightarrow \pi^*(O1-C9)$ and π (C35-C38) $\rightarrow \pi^*$ (C14-C15) consisting of 12.03, 18.20 and 21.19 kcal/mol are associated with least energy in 1-3, respectively. The interaction between the electron donor-acceptor moieties lead to least energies. In contrast to $\pi \rightarrow \pi^*$ the $\sigma \rightarrow \sigma^*$ transitions are associated with very weak donor (σ)-acceptor (σ^*) interactions energies. The σ (C18-C20) $\rightarrow \sigma^*$ (C16-C17), σ (C3-C5) $\rightarrow \sigma^*$ (C1-H2) transitions contained 5.39 kcal/mol each in compound 1, σ (N3-C14) $\rightarrow \sigma^*$ (C10-C12) contained 11.50 kcal/mol in 2 and $\sigma(C9-H12) \rightarrow \sigma^*(C8-N20)$ and $\sigma(C30-H33) \rightarrow \sigma^*(C29-H12) \rightarrow \sigma^*(C8-N20)$ N41) contained 7.64 kcal/mol each in 3, showing higher stabilization energies among all $\sigma \rightarrow \sigma^*$ interactions. The σ (C5-N14) $\rightarrow \sigma$ *(C7-C13) transition associated with 5.03 kcal/mol energy in 1, $\sigma(C30-C32) \rightarrow \sigma^*(C28-H29)$ with 5.27 kcal/mol energy in 2 and $\sigma(C6-C8) \rightarrow \sigma^*(C1-C5)$ with 5.12 kcal/mol in compound **3** were with least stabilization energy values (Table 4).

Interactions correspond to resonance were also observed in compounds 1-3, for example, LP1(N13) $\rightarrow \pi^*(C7\text{-}O15)$, LP1(N28) $\rightarrow \pi^*(C22\text{-}O30)$, LP1(N2) $\rightarrow \pi^*(O1\text{-}C9)$, LP1(N20) $\rightarrow \pi^*(C13\text{-}O21)$ and LP1(N41) $\rightarrow \pi^*(C34\text{-}O42)$ produced 37.49, 37.49, 38.76, 38.45 and 38.45 kcal/mol in 1-3 and were the highest values. While LP1(N14) $\rightarrow \sigma^*(C3\text{-}C5)$, LP1(N21) $\rightarrow \sigma^*(C30\text{-}C32)$ and LP1(N19) $\rightarrow \sigma^*(C5\text{-}C6)$ produced 5.39, 6.06 and 5.91 kcal/mol which exhibited least electron donating interactions energies in 1-3, respectively.

3.1.7. UV-Visible Analysis

The time dependent TD-DFT with B3LYP/6-311G (d,p) and CAM-B3LYP/6-311G (d,p) levels of theory were used for theoretical calculations of UV-Visible spectral analysis. The outcomes of UV spectrum of **1-3** are represented in Tables S7 and S8.

The theoretical results presented in Table S7 reveal that compound **1** gives absorbance at 274 and 297 nm with oscillator strength, f = 0.454 and 0.135, respectively. The same data for compound **2** was observed as 283 and 295 nm with f = 0.303 and 0.191, respectively. Similarly, **3** gave 278 and 291 nm with f values 0.317 and 0.175, respectively. The aforesaid excitations of **1-3** are allowed transitions however, the known prohibited transitions are 289 and 294 for **1**, 288 and 295 for **2** and 290 and 304 nm for **3** because they were found with zero magnitude of oscillator strengths.

Tabulated data for compounds 1-3 (Table S8) reveal that compound 1 exhibits wavelength 250 and 234 nm with associated f values 0.539 and 0.115, compound 2 gives values at 251 and 266 nm with f 0.681 and 0.097 in the same way and two values 247 and 264 nm with f = 0.673 and 0.091 were observed for compound 3. The aforesaid excitations are allowed transitions however, prohibited transitions are those with wavelength frequency of 235 and 269 (1), 237 and 268 (2) and 244 and 267 (3) because they possessed zero magnitude of oscillator strengths.

The calculated data represented in Tables S7 and S8 were based on B3LYP and CAM-B3LYP, respectively. These give an easy understanding of comparison that B3LYP calculations ended up with higher wavelengths and lower oscillator strengths while reverse was observed for CAM-B3LYP.

3.1.8. Vibrational Analysis

As it is discussed that the DFT studies were carried out with the intent to have a clear understanding of vibrational modes and stability (absence of imaginary frequency) for compounds **1**, **2** and **3** at B3LYP/6-311G(d,p) level of theory under solvent free conditions (gas phase). The number of atoms in **1**, **2** and **3** are 30, 36 and 42, respectively with symmetry point group C_1 . Their FT-IR spectra are given in Figures S8-S10 (Supplementary Information), the peaks observed corresponding to stretching frequencies of all-important bonds are within expected regions.

3.1.9. Natural Population Analysis (NPA)

The Mulliken atomic charges of compounds **1-3** were determined with Time Dependent DFT (TD-DFT) at B3LYP level of theory with basis set 6-311G (d,p) as presented in Figure 9 and Figures S11 and S12. Atomic charge transformation process normally takes place in reactions and the electrostatic potential on external surface has to be calculated through theory [42]. The bonding capacity and molecular confirmation are predicted on the basis of electronic charges of respective atoms. The data pertaining to Mulliken population [43] reveal that unequal distribution of electron density over the benzene ring is because of the presence of more electronegative atoms O and N in compounds **1-3**. Our concern is to describe the electron distribution over the crystal and to explore the reactivity of the figured charges in the quantum chemical approach [43].

Moreover, Mulliken population examination displays that there is no discrepancy in charge distribution over H-atoms. The positive charges over H-atoms are because of the negative charges of carbon atoms. The oxygen and nitrogen atoms present in entitled compounds containing high negative charges and they enforce a large negative charge on some carbon atoms because of resonance process.



Figure 9: Natural population analysis of compound **1**, see Figures S11 and S12 for compounds **2** and **3**.

3.1.10. Frontier Molecular Orbitals (FMOs)

The FMOs hold a significant place in the optical and electric properties and are used in interpreting the chemical stability of species [45-50]. The energy gap of FMOs is an appreciated parameter to get knowledge concerning the dynamic stability and chemical reactivity of species.

The HOMO/LUMO energies were obtained such as -7.36 /-2.61 eV, -7.24/-2.46 eV and -6.93/-2.24 eV respectively for **1**, **2** and **3**. A chemical system contains a greater energy difference between HOMO and LUMO orbitals might be less reactive as compared to that one which contains a smaller gap. For compounds **1**, **2** and **3**, the calculated HOMO-LUMO energy gap was 4.75, 4.79 and 4.69 eV respectively, indicating that the compound **3** has more reactivity than **1** and **2**.

Compounds	1		2		3		
MO(s)	Energy	ΔE	Energy	ΔE	Energy	ΔE	
НОМО	-7.36	4 75	-7.24	4 79	-6.93	4 69	
LUMO	-2.61	ч.75	-2.46	т.19	-2.24	1.07	
HOMO-1	-7.39	5.03	-7.26	5.06	-6.94	5 85	
LUMO+1	-1.46	5.95	-1.30	5.90	-1.09	5.65	
НОМО-2	-7.46	6.83	-7.32	6.79	-7.12	6.69	

Table 5: Frontier molecular orbitals energy calculated for compounds 1-3, units in eV.

LUMO+2	-0.63		-0.53		-0.43	
НОМО-3	-7.59	711	-7.36	7.04	-7.17	6.04
LUMO+3	-0.48	/.11	-0.32	7.04	-0.23	0.94

HOMO: Highest Occupied Molecular Orbital and LUMO: Lowest Unoccupied Molecular Orbital



Figure 10: FMOs of compounds 1-3.

The electron density in HOMO of compound **1** is dispersed on the 1,4-bis((1*H*-pyrazol-1-yl)methyl)benzene fragment which is almost the whole structure except the carbonyl groups, in the same way compounds **2** offers 1,4-bis((1*H*-pyrazol-1-yl)methyl)benzene fragment to take up the electron density which is also almost the whole structure except the carbonyl groups and

methyl groups. However, it is different in case of 3, in which the electron density is dispersed on the 5-methyl-1*H*-pyrazole fragment which is a minor portion of the structure (Figure 11).

3.1.11. Global Reactivity Parameters (GRPs)

The GRPs such as *I* (Ionization potential), *A* (electron affinity), *X* (electronegativity), η (global hardness), μ (chemical potential), ω (global electrophilicity) and σ (global softness) were calculated using the FMOs energies for entitled compounds [50]. These chemical quantities can be seen in Table 6.

Compounds	I	<mark>A</mark>	X	η	μ	<mark>ω</mark>	σ
1	8.71	1.20	4.96	3.75	-4.96	3.27	0.13
2	6.93	2.24	4.59	2.34	-4.59	4.49	0.21
3	8.83	1.35	5.09	3.74	-5.09	3.46	0.13

Table 6: Global reactivity parameters (eV) of entitled derivatives 1, 2 and 3

In broad context, the electron donating and accepting capability of molecules is distinguished with the help of ionization potential and electron affinity values, respectively. The ionization potential values of 1-3 were established to be much greater than their electron affinity values. The chemically hardness values were found to be 3.75, 2.34 and $3.74 \ eV$ for 1, 2 and 3 respectively. However, the chemically softness values were found to be 0.13, 0.21 and $0.13 \ eV$ for 1, 2 and 3 respectively. These results indicate that investigated compounds have low reactivity and show a good agreement with NBO and SC-XRD findings.

3.1.12. Density of States (DOS)

The DOS of compounds 1-3 were determined by the Gauss Sum software and the results obtained therefrom are shown in Figure S13. The DOS spectrum provides enough informations in relation to the population analysis per orbital in a certain energy range (energy range of the spectrum is 0 to $-20 \ eV$). The CO groups and pyrazole rings are major contributors in high energy range of -8 to $-10 \ eV$, which is the highest contribution and has substantial influence on nonlinear optical properties of the material. The observation obtained are in close agreement with FMOs analysis where the maximum electron density is spread over pyrazole substituents [51].

3.1.13. Non-Linear Optical Properties (NLO)

Electronic properties are accountable for the strength of optical response which rely on the linear and nonlinear responses (polarizability, α and hyper polarizabilities, β and γ etc.) [52,54]. For the estimation of non-linear optical properties of **1-3**, these linear and nonlinear responses have to be evaluated. The $\langle \alpha \rangle$ values were calculated by the set of theory as described above. The average polarizability values of **1-3** accompanied by their major contributing tensors in three different ways, with no solvent effect, with ethanol and acetonitrile as solvent. However, our compounds are centrosymmetric, so, first hyper polarizabilities (β) values could not be calculated.

Solvent	Polarizability	1	2	3
	α_{xx}	304.516	339.12	356.079
None	α_{yy}	182.685	214.15	248.925
1,0110	α_{zz}	81.649	102.03	125.964
	α_{total}	189.616	218.43	243.656
	α_{xx}	371.086	413.62	431.296
Ethanol	α_{yy}	259.379	298.55	341.882
	α_{zz}	104.785	132.22	166.574
	α_{total}	245.083	281.46	313.251
	α_{xx}	372.296	415.061	432.780
Acetonitrile	α_{yy}	261.429	300.767	344.313
	α_{zz}	105.579	133.278	168.009
	atotal	246.434	283.036	315.034

Table 7: Dipole polarizabilities and major contributing tensors (a.u.) of compounds 1-3.

The data pertaining to the average $\langle \alpha \rangle$ values and their tensors are represented in Table 7. The dipole polarizabilities values obtained were 189.616, 218.43 and 243.656 a.u. for compounds 1-3, respectively. Where the compound 3 exhibited higher value than the other members of the 1 and 2. The HOMO/LUMO energy gap influences the molecular polarizability and has an inverse relationship with linear polarizability. The compounds with small energy gap endorse large linear polarizabilities. Compound 3 was found with smaller energy gap as compared to 1 and 2 (Table 5). Subsequently, it shows more linear polarizability values (Table 7).

3.1.14. Molecular Electrostatic Potential (MEP)

The 3D plot of total electron density is also called molecular electrostatic potential (MEP). The MEP is descriptor for elucidation of non-covalent interactions (NCIs) in molecules. The MEP, a plot of electrostatic potential and constant electron density surface, is taken for foreseeing sites and relative reactivity towards electrophilic or nucleophilic attack, in studies of biological recognition, interactions between homo- or heterosynthons and in correlation and prediction of scope of macroscopic properties. The color code is sorted from deep red to deep blue, where blue indicates a nominal concentration of electrons and high density of electrons is shown by red color in the figure. The charge contribution can be systematic in decreasing order as, red > orange > yellow >green > blue.

It further elaborates that negative zones (red and yellow) are supposed to be favorite sites for electrophilic attack and the positive zones (blue) can possibly allow nucleophilic attack. The Figure S14 indicates a negative potential restrained over O and N atoms, whereas positive region is located around H atoms for 1, 2 and 3.

4. Conclusion

Reaction between terethaloyl dichloride and pyrazole derivatives afford corresponding products as a result of N-C coupling. The computed bond lengths as well as bond angles are in close agreement with SC-XRD data. The error calculations of RMSE revealed that both CAM-B3LYP and B3LYP functionals are in good agreement with respect to each other. The NBOs analysis indicate that molecules are involved in the process of intra-molecular charge transfer. The Hirshfeld surface analysis of the compounds support higher molecular stability. Furthermore, NBOs based hyper conjugative interaction values were found with greater magnitude which endorses the same molecular stability fact. For compounds 1,2 and 3, the calculated HOMO-LUMO energy gap was 4.75, 4.79 and 4.69 eV, respectively, indicating that the compound 3 is more reactivity than 1 and 2. The band gap of compound 3 is slightly smaller than compounds 1 and 2 the smaller value is because of electron-donating ability of the attached methyl groups. The global reactivity parameters have been calculated using the energies of FMOs. The chemical hardness values of 1-3 were found greater as compared to their softness values which indicated that the investigated compounds have low reactivity and show a good agreement with NBOs and SC-XRD finding. Mutual comparison of compounds 1-3, indicates that compound **3** has highest $\langle \alpha \rangle$ values. The effect of solvent on the dipole polarizabilities of compounds was determined and the higher average polarizabilities $\langle \alpha \rangle$ values of **1-3** were found in acetonitrile than ethanol and free solvent conditions.

Acknowledgement

EK, ZG and AS acknowledge the financial support from Higher Education Commission of Pakistan under NRPU project No. 1488.

Supporting information

Supplementary information Figures and Tables pertaining to this work are given in a separate file, available in online version of this paper. Crystal data (CIFs) have been submitted to Cambridge Crystallographic Data Center CCDC No 19556722 (1), 1955620 (2) and 1955621 (3) these data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (+44) 1223-336-033; or E-mail: <u>deposit@ccdc.cam.ac.uk</u>.

Conflict of interest

Authors declare no conflict of interest

References

- N. O. Sonntag, The Reactions of Aliphatic Acid Chlorides. Chemical Reviews. 52 (1953) 237-416.
- T. W. Bousfield, K. P. Pearce, S. B. Nyamini, A. Angelis-Dimakis, J. E. Camp, Synthesis of amides from acid chlorides and amines in the bio-based solvent CyreneTM. *Green Chem.*, 21 (2019) 3675-3681.
- Selected References a) S. T. Heller, S. R. Natarajan, 1,3-Diketones from acid chlorides and ketones: a rapid and general one-pot synthesis of pyrazoles. Organic letters. 8 (2006) 2675-2678. b) S. Fustero, A. Simón-Fuentes, J. F. Sanz-Cervera, Recent advances in the synthesis of pyrazoles. A review. Organic Preparations and Procedures International. 41 (2009) 253-290. c) A. Keivanloo, M. Bakherad, S. Samangooei, Synthesis of 3, 5disubstituted-1H-pyrazoles from acid chlorides, alkynes, and hydrazine in the presence of silica-supported-zinc bromide. J. Chemical Research. 39 (2015) 484-486. d) B. F. Abdel-Wahab, R. E. Khidre, A. A. Farahat, Pyrazole-3 (4)-carbaldehyde: synthesis, reactions and biological activity. ARKIVOC i (2011) 196-245.

- a) C. F. Beam, D. C. Reames, C. E. Harris, L. W. Dasher, W. M. Hollinger, N. L. Shealy, R. M. Sandifer, M. Perkins, C. R. Hauser, New method for the preparation of 4-acylpyrazoles. Reaction of C (. alpha.), N dianions of phenylhydrazones with acid chlorides. J. Org. Chem. 40 (1975) 514-516. b) X. Chen, J. She, Z. C. Shang, J. Wu, P. Zhang, Room-temperature synthesis of pyrazoles, diazepines, β-enaminones, and β-enamino esters using silica-supported sulfuric acid as a reusable catalyst under solvent-free conditions. Syn. Commun. 25 (2009) 947-957. C) J. Wu, Q. Shi, Z. Chen, M. He, L. Jin, D. Hu, Synthesis and bioactivity of pyrazole acyl thiourea derivatives. Molecules 17 (2012) 5139-5150. d) R. D. Miller, O. Reiser, The synthesis of electron donor□acceptor substituted pyrazoles. J. Heterocycl. Chem. 30 (1993) 755-763.
- 5. a) Y. Akcamur, A. Sener, A. M. Ipekoglu, G. Kollenz, Functionalization and cyclization reactions of 4 benzoyl 1, 5 diphenyl 1H pyrazole 3 carboxylic acid. J. Heterocycl. Chem. 34 (1997) 221-224. b) A. G. Allah, M. W. Badawy, H. H. Rehan, M. M. Abou-Romia, Inhibition of corrosion of α-brass (Cu-Zn, 67/33) in acid chloride solutions by some amino pyrazole derivatives. J. Appl. Electrochem. 19 (1989) 928-932.
- a) I. D. Giles, J. C. DePriest, J. R. Deschamps, Effect of substitution and the counterion on the structural and spectroscopic properties of Cu(II) complexes of methylated pyrazoles. J. Coord. Chem. 68 (2015) 3611-3635. b) C. J. Vincent, I. D. Giles, J. R. Deschamps, Two Cu(II) complexes of 3, 4, 5-trimethyl-1H-pyrazole. Acta Cryst. E74 (2018) 357-362. c) S. O. Ojwach, J. Darkwa, Pyrazole and (pyrazol-1-yl) metal complexes as carbon–carbon coupling catalysts. Inorg. Chim. Acta. 363 (2010) 1947-1964.
- M. S. Mohlala, I. A. Guzei, J. Darkwa, S. F. Mapolie, Pyridine linker pyrazolyl palladium complexes: Synthesis, characterization and ethylene polymerization activity. J. Mol. Catal. A 241 (2005) 93-100.
- a) E. Khan, S. A. Khan, M. Zahoor, M. N. Tahir, A. Noor, A. A. Altaf, Cu(II) coordination polymers stabilized by pyridine-2, 6-dicarboxylate anion and pyrazole derivatives through ligand hydrolysis. J. Coord. Chem. 71 (2018) 2658-2673. b) E. Khan, S. A. Khan, A. Shahzad, A. Noor, Synthesis Characterization and DFT Calculations of 2, 5-Substituted Thiophene Derivatives. J. Chem. Crystallogr. 45 (2015) 238-243.
- 9. a) N. A. Mohamed, N. A. El-Ghany, Synthesis and antimicrobial activity of some novel terephthaloyl thiourea cross-linked carboxymethyl chitosan hydrogels. Cellulose. 19 (2012)

1879-1891. b) N. A. Mohamed, N. Y. Al-mehbad, Novel terephthaloyl thiourea crosslinked chitosan hydrogels as antibacterial and antifungal agents. International J. Bio. Macromol. 57 (2013) 111-117.

- 10. a) L. Y. Chu, S. H. Park, T. Yamaguchi, S. I. Nakao, Preparation of thermo-responsive core-shell microcapsules with a porous membrane and poly (N-isopropylacrylamide) gates. J. Memb. Sci. 192 (2001) 27-39. b) S. Konagaya, M. Tokai, Synthesis of ternary copolyamides from aromatic diamine (m phenylenediamine, diaminodiphenylsulfone), aromatic diamine with carboxyl or sulfonic group (3, 5 \Box diaminobenzoic acid, 2, 4 \Box diaminobenzenesulfonic acid), and iso or terephthaloyl chloride. J. Appl. Polym. Sci. 76 (2000) 913-920. c) G. Montaudo, C. Puglisi, F. Samperi, Mechanism of exchange in PBT/PC and PET/PC blends. Composition of the copolymer formed in the melt mixing process. Macromolecules 31 (1998) 650-661. d) H. Hirano, S. Watase, M. Tanaka, Linear polymers with sulfur in the main chain. II. Synthesis of polyesters by interfacial polycondensation of bis(4,4' hydroxyphenyl) sulfide with several aliphatic acid dichlorides and their properties. J. Appl. Polym. Sci. 91 (2004) 1865-1872. e) X. Tang, C. Zheng, Y. Chen, Z. Zhao, A. Qin, R. Hu, B. Z. Tang, Multicomponent tandem polymerizations of aromatic diynes, terephthaloyl chloride, and hydrazines toward functional conjugated polypyrazoles. Macromolecules. 49 (2016) 9291-9300. f) E. Mathiowitz, M. D. Cohen, R. Langer, Novel microcapsules for delivery systems. React. Poly. Ion Exchangers, Sorbents 6 (1987) 275-283.
- A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. Moliterni, G. Polidori, and R. Spagna, SIR97: a new tool for crystal structure determination and refinement, J. Appl. Crystallogr., 32 (1999) 115-119.
- G. M. Sheldrick, New features added to the refinement program SHELXL since 2008 are described and explained, Acta Crystallogr. 71 (2015) 3-8.
- J. L. Farrugia, WinGX suite for small-molecule single-crystal crystallography, J. Appl. Crystallogr. 32 (1999) 837-838.
- L. A. Spek, Structure validation in chemical crystallography, Acta Cryst. D65 (2009) 148-155.
- Gaussian 09, Revision A.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M.
 A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li,

M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

- J.-L. Calais, "Density-functional theory of atoms and molecules. R.G. Parr and W. Yang, Oxford University Press, New York, Oxford, 1989.
- 17. J. E. Carpenter, Extension of Lewis structure concepts to open-shell and excited- state molecular species, University of The Wisconsin Madison 1987.
- R. G. Parr, R. A. Donnelly, M. Levy, and W. E. Palke, "Electronegativity: The density functional viewpoint," J. Chem. Phys., 68 (1978) 3801–3807.
- 19. R. G. Parr and R. G. Pearson, "Absolute hardness: companion parameter to absolute electronegativity," J. Am. Chem. Soc. 105 (1983) 7512–7516.
- 20. P. K. Chattaraj, U. Sarkar, and D. R. Roy, "Electrophilicity Index," *Chem. Rev.*, 106 (2006) 2065–2091.
- P. K. Chattaraj and D. R. Roy, "Update 1 of: Electrophilicity Index," *Chem. Rev.*, 107 (2007) PR46–PR74.
- 22. R. G. Parr, L. v. Szentpály, and S. Liu, "Electrophilicity Index," J. Am. Chem. Soc., 121 (1999) 1922–1924.
- M. D. Hanwell, D. E. Curtis, D. C. Lonie, T. Vandermeersch, E. Zurek, G. R. Hutchison; Avogadro: An advanced semantic chemical editor, visualization, and analysis platform" *J. Cheminformatics* 4 (2012) 17.
- 24. GaussView, Version 6.1, Roy Dennington, Todd A. Keith, and John M. Millam, Semichem Inc., Shawnee Mission, KS, 2016.
- 25. N. M. O'Boyle, A. L. Tenderholt, K. M. Langner. J. Comp. Chem., 29 (2008) 839-845.
- 26. Argus Labs 4.0.1 Mark Thompson and Planaria Software LLC.

- CrystalExplorer (Version 3.1), S. K. Wolff, D. J. Grimwood, J. J. McKinnon, M. J. Turner, D. Jayatilaka, M. A. Spackman, University of Western Australia, 2012.
- 28. Chemcraft-graphical software for visualization of quantum chemistry computations. https://www.chemcraftprog.com
- 29. S. A. Khan, A. Noor, R. Kempe, H. Subhan, A. Shah, E. Khan, Syntheses, molecular structure, and electrochemical investigations of cobalt(II), copper(II), palladium(II), and zinc(II) complexes with 3-methylpyrazole. J. Coord. Chem. 67 (2014) 2425-2434.
- J. Zukerman-Schpector, S. D. Pedroso, L. S. Madureira, M. W. Paixão, A. Ali, E. R. T. Tiekink, 4-Benzyl-1-(4-nitro-phen-yl)-1H-1,2,3-triazole: crystal structure and Hirshfeld analysis, *Acta Cryst. E*73 (2017) 1716–1720.
- 31. H. Wang, Z. Yin, Crystal structure and Hirshfeld surface analysis of dibutyl 5,5'-(pentane-3,3-diyl)bis(1H-pyrrole-5-carboxylate), *Acta Cryst. E*75 (2019) 711–713.
- N.-P. Pook, A. Adam, M. Gjikaj, Crystal structure and Hirshfeld surface analysis of (μ-2-{4-[(carboxyl-atometh-yl)carbamo-yl]benz-amido}-acetato-κ2O:O')bis-[bis-(1,10phenanthroline-κ2 N,N')copper(II)] dinitrate N,N'-(1,4-phenyl-enedicarbon-yl)diglycine monosolvate octa-hydrate, *Acta Cryst. E*75 (2019) 667–674.
- 33. A. Ali, J. Zukerman-Schpector, M. Weber Paixão, M. M. Jotani, and E. R. T. Tiekink, 7-Methyl-5-[(4-methyl-benzene)-sulfon-yl]-2H,5H-[1,3]dioxolo[4,5-f]indole: crystal structure and Hirshfeld analysis, *Acta Cryst. E*74 (2018) 184–188.
- N. K. Sebbar, B. Hni, T. Hökelek, A. Jaouhar, M. L. Taha, J. T. Mague, E. M. Essassi, Crystal structure, Hirshfeld surface analysis and inter-action energy and DFT studies of 3-{(2Z)-2-[(2,4-di-chloro-phen-yl)methyl-idene]-3-oxo-3,4-di-hydro-2H-1,4-benzo-thia-zin-4-yl}propane-nitrile, *Acta Cryst. E*75 (2019) 721–727.
- M. N. Tahir, M. Ashfaq, A. F. de la Torre, J. Caballero, E. W. Hernández-Rodríguez, A. Ali, Rationalizing the stability and interactions of 2,4-diamino-5-(4-chlorophenyl)-6-ethylpyrimidin-1-ium 2-hydroxy-3,5-dinitrobenzoate salt," *J. Mol. Str.*, 1193 (2019) 185–194.
- H. Chebbi, S. Mezrigui, M. Ben Jomaa, M. F. Zid, Crystal structure, Hirshfeld surface analysis and energy framework calculation of the first oxoanion salt containing 1,3cyclohexanebis(methylammonium): [3-(azaniumylmethyl)cyclohexyl]methanaminium dinitrate, *Acta Cryst. E*74 (2018) 949–954.

- 37. D. G. Truhlar, P. Politzer, A. C. Society, Chemical applications of atomic and molecular electrostatic potentials : reactivity, structure, scattering, and energetics of organic, inorganic, and biological systems. New York : Plenum Press, 1981.
- 38. E. Isac Paulraj, S. Muthu, Spectroscopic studies (FTIR, FT-Raman and UV), potential energy surface scan, normal coordinate analysis and NBO analysis of (2R,3R,4R,5S)-1-(2-hydroxyethyl)-2-(hydroxymethyl) piperidine-3,4,5-triol by DFT methods, *Spectrochim Acta A*, 108 (2013) 38–49.
- 39. J. Liu, Z. Chen, S. Yuan, Study on the prediction of visible absorption maxima of azobenzene compounds, *J. Zhejiang Univ. Sci. B*, 6 (2005) 584–589.
- S. Subashchandrabose, A. R. Krishnan, H. Saleem, R. Parameswari, N. Sundaraganesan, V. Thanikachalam, G. Manikandan, Vibrational spectroscopic study and NBO analysis on bis (4-amino-5-mercapto-1, 2, 4-triazol-3-yl) methane using DFT method. Spectrochim. Acta Part A, 77 (2010) 877-84.
- C. James, A. A. Raj, R. Reghunathan, V. S. Jayakumar, I. H. Joe, Structural conformation and vibrational spectroscopic studies of 2,6-bis(p-N,N-dimethyl benzylidene)cyclohexanone using density functional theory, *J. Raman Spectrosc.* 37 (2006) 1381–1392.
- 42. R. S. Mulliken, Electronic Population Analysis on LCAO–MO Molecular Wave Functions.I," J. Chem. Phys., 23 (1955) 1833–1840.
- 43. L. Li, C. Wu, Z. Wang, L. Zhao, Z. Li, C. Sun, T. Sun, Density functional theory (DFT) and natural bond orbital (NBO) study of vibrational spectra and intramolecular hydrogen bond interaction of l-ornithine–l-aspartate. Spectrochim. Acta Part A 136 (2015) 338-46.
- J. A. Burrows, "Pauling, Linus. The nature of the chemical bond and the structure of molecules aid crystals. Ithaca: The Cornell University Press, 1939. P430
- 45. M. Khalid, M. Ali, M. Aslam, S. H. Sumrra, M. U. Khan, N. Raza, N. Kumar, M. Imran, Frontier molecular, Natural bond orbital, UV-Vis spectral stduy, Solvent influence on geometric parameters, Vibrational frequencies and solvation energies of 8-Hydroxyquinoline. Int. J. Pharm. Sci. Res. 8 (2017) 457-569.
- M. Srnec, E. I. Solomon, "Frontier Molecular Orbital Contributions to Chlorination versus Hydroxylation Selectivity in the Non-Heme Iron Halogenase SyrB2," J. Am. Chem. Soc., 139 (2017) 2396–2407.

- R. Jawaria, M. Hussain, M. Khalid, M. U. Khan, M. N. Tahir, M. M. Naseer, A. A. Braga,
 Z. Shafiq, Synthesis, crystal structure analysis, spectral characterization and nonlinear optical exploration of potent thiosemicarbazones based compounds: A DFT refine experimental study, *Inorg. Chem. Acta*, 486 (2019)162–171.
- M. Haroon, M. Khalid, T. Akhtar, M. N. Tahir, M. U. Khan, M. Saleem, R. Jawaria, Synthesis, spectroscopic, SC-XRD characterizations and DFT based studies of ethyl2-(substituted-(2-benzylidenehydrazinyl)) thiazole-4-carboxylate derivatives. J. Mol. Str. 1187 (2019) 164-71.
- M. Shahid, M. Salim, M. Khalid, M. N. Tahir, M. U. Khan, A. A. C. Braga, Synthetic, XRD, non-covalent interactions and solvent dependent nonlinear optical studies of Sulfadiazine-Ortho-Vanillin Schiff base: (E)-4-((2-hydroxy-3-methoxy- benzylidene) amino)-N-(pyrimidin-2-yl)benzene-sulfonamide, J. Mol. Str., 1161 (2018) 66–75.
- 50. K. Fukui, Role of Frontier Orbitals in Chemical Reactions, Science, 218 (1982) 747–754.
- L. Sznitko, J. Mysliwiec, K. Parafiniuk, A. Szukalski, K. Palewska, S. Bartkiewicz, A. Miniewicz, Amplified spontaneous emission in polymethyl methacrylate doped with 3-(1,1-dicyanoethenyl)-1-phenyl-4,5-dihydro-1H-pyrazole (DCNP), Chem. Phy. Lett., 512 (2011) 247-250.
- 52. Z. Peng and L. Yu, Second-Order Nonlinear Optical Polyimide with High-Temperature Stability, *Macromolecules*, 27 (1994) 2638–2640.
- E. M. Breitung, C.-F. Shu, and R. J. McMahon, Thiazole and Thiophene Analogues of Donor–Acceptor Stilbenes: Molecular Hyperpolarizabilities and Structure–Property Relationships, J. Am. Chem. Soc., 122 (2000) 1154–1160.
- N. Tsutsumi, M. Morishima, and W. Sakai, Nonlinear Optical (NLO) Polymers. 3. NLO Polyimide with Dipole Moments Aligned Transverse to the Imide Linkage, *Macromolecules*, 31 (1998) 7764–7769.

Research Highlights

- 2-Methylpyrazole, and its 3-methyl and 3,5-dimethyl-substituted derivatives react with • terephthaloyl dichloride through N-C coupling reaction.
- The resultant compounds are crystalline in nature and their X-ray Diffraction data were collected.
- Experimental data were reproduced theoretically by B3LYP and CAM-B3LYP of DFT with 6-311G(d,p) basis set.
- Theoretical data are in close agreement with the experimental findings.

Ezzat Khan supervised the Experimental work which was carried out in his Laboratory.

Zarif Gul and Adnan Shahzad, equally contributed in Experimental work during synthesis of compounds **1-3**.

Muhammad Nawaz Tahir collected x-ray diffraction data and solved and refined the solid state structures.

Muhammad Khalid, Hafiz Muhammad Asif, Sumreen Asim, and Ataualpa Albert Carmo Braga Carried out DTF studies of the compounds.

Journal Pression

Conflict of interest

Authors declare no conflict of interest

burnalprendio