Computer Aid Screening for Potential Antimalarial Choroquinone Compounds as Covid 19 Utilizing Computational Calculations and Molecular Docking Study

¹Asmaa Aboelnaga, ²Asmaa M. Fahim and ^{1,3}Taghreed H. EL-Sayed

¹Department of Chemistry, Faculty of Women of Arts, Science and Education, Ain Shams University, Heliopolis, Egypt ²Departments of Green Chemistry, National Research Center, Dokki, P.O. Box.12622 Cairo, Egypt ³Departments of Chemistry, Faculty of Science, Taibah University, Yanbu, Saudi Arabia

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Corresponding Author: Asmaa Aboelnaga Department of Chemistry, Faculty of Women of Arts, Science and Education, Ain Shams University, Heliopolis, Egypt Email: asmaa.aboelnaga@women.as u.edu.eg

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Asmaa M Fahim Departments of Green Chemistry, National Research Center, Dokki, P.O. Box.12622 Cairo, Egypt Email: asmaamahmoud8521@hotmail. com Abstract: Click reaction of 4,7-dichloroquinoline (1)with thiosemicarbazide (2) to afford the corresponding 2-(7-chloroquinolin-4-yl)thiosemicarbazide (3) utilized ultrasonic irradiation which can cyclized easily with ethylacetoacetate to give the 3-(7-chloroquinolin-4ylamino)-tetrahydro-6-methyl-2-thioxopyrimidin-4(1*H*)-one (4) via nucleophilic substitution reaction. The synthesized compounds was examined *in vitro* antimalarial activity with $IC_{50} = 11.92$, 25.37 µg/mL against chloroquinone drug. Furthermore, the theoretical investigation of most active compounds CQT and CQP utilizing of DFT/B3LYP/6-311G(d) and HF/6-311G(d) basis's set and evaluated their physical characters, bond length, bond angles, dihedral angles, also its HOMO-LUMO energy gap was 3.77 eV which indicate the reactivity of CQP. Moreover, the molecular docking studies of these synthesized compounds showed small energy affinity against SARS-CoV-2 main protease (PDBID: 6lu7) and crystal structure of thermoplasma acidophilum (PDBID: 1q2w) and shorter bond length. All these parameters could be considered with different extent to significantly affect the binding affinity of these compounds to the active protein sites for further biological evaluation on Covid-19.

Keywords: Covid 19, Novel Chloroquinone Compounds, Antimalarial Activity, Computational Studies, Docking Interaction

Introduction

In December 2019, several cases of pneumonia of an unknown etiology appeared in Wuhan, Hubei Province, China. Later, a novel coronavirus was identified in a bronchoalveolar lavage fluid sample from the Wuhan Seafood Market through the use of metagenomic nextgeneration sequencing technology (Yang and Wang, 2020; Wu *et al.*, 2020a). On February 11, 2020, the International Committee on Taxonomy of Viruses (ICTV) named the virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This is the seventh member of the coronavirus family that can infect humans after the appearance of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The World Health Organization classified the coronavirus pneumonia epidemic caused by SARS-CoV-2 as a public health emergency of international concern on January 30, 2020 (Zhao *et al.*, 2010; Zhou *et al.*, 2020). A thorough program, including surveillance, diagnostics, clinical treatment, research and the development of vaccines and drugs, is crucial to win the battle against COVID-19 and other infectious diseases (Yang and Wang, 2020). Etiology of SARS-COV-2 Corona viruses are not new infectious pathogens in the world. The first described coronavirus was isolated from chickens in 1937 (Ludwig and Zarbock, 2020). In the mid-1960s the first human coronaviruses were first identified (Steardo *et al.*, 2020). The Corona virus family



can be divided into four genera: α , β , γ and δ , as per the genome structure and phylogenetic analysis of (Fehr Perlman, 2015). coronaviruses and The coronaviruses of the α and β mainly infect mammals and humans, while the coronaviruses of the γ and δ typically infect birds (Rodriguez-Morales et al., 2020; Guo et al., 2020). The pathogen that is causing the pandemic is related to the Acute Respiratory Syndrome Coronavirus (SARS-CoV), which caused another back outbreak in 2003 (Sjödin et al., 2020; Mirza and Froeven, 2020). As of yet, there are no effective treatments or targeted therapeutics against the virus. Because of that, the scientific community is striving to investigate many different mechanisms to interfere with the virus' metabolism. Consequently, in recent clinical trials against COVID-19 several antiviral drugs used with patients with similar viral infections to antimalarial drugs, such chloroquine (I), quinine (II) and amodiaquine (III) in malaria treatment is common (dos Santos Chagas et al., 2019; Kwofie et al., 2020). Also the hydroxychloroquine (IV) has approved drug for malaria disease treatment via the FDA was explored as a medication for SARS-CoV-2. As displayed in Figure 1 (Yao et al., 2020; Liu et al., 2020). Previous reports have shown that. the chloroquine and hydroxychloroquine can inhibit the Coronavirus (COVID-19) by altering the pH at the surface of the cell membrane. This can inhibit the attachment of the virus to the cell membrane. Furthermore, it can prevent nucleic acid replication, glycosylation of viral proteins, virus assembly, new virus particle delivery, virus release and other mechanisms to obtain its antiviral effects (Grimstein et al., 2019).

The theoretical DFT calculations and the conformational analyses can result in a great contribution to drug discovery by reducing financial costs and saving time (especially for emerging diseases such as COVID-19 and speeding up analyses of target interactions with drug candidates (Gimeno et al., 2019). As a result, different computational studies have been published to help better understand the mechanism of M-pro and try to inhibit its function (Mirza and Froeyen, 2020; Ton et al., 2020; Kong et al., 2020; Tang et al., 2020; Chen et al., 2020; Liu and Wang, 2020; Adem et al., 2020; Yoshino et al., 2020; Hosseini and Amanlou, 2020; Bzówka et al., 2020a; 2020b; Khaerunnisa et al., 2020; Xu et al., 2020).

In this investigation, we concern in our work of theoretical determination of the molecular geometry of synthesized materials 2-(7-chloroquinolin-4-yl)thiosemicarbazide (3) (*CQT*) and 3-(7-chloroquinolin-4-ylamino)-tetrahydro-6-methyl-2-thioxopyrimidin-

4(1*H*)-one (Aboelnaga and EL-Sayed, 2018) (4) (*CQP*) which exhibited excellent antimalarial activity against chloroquinone drug. Our stimulation was focused on confirmation of our compounds and comparison with 4,7-dichloroquinoline from physical properties, bond length, bond angles utilizing DFT/B3LYP/6-311G(d) and HF/6-311G(d) basis set (Hagar *et al.*, 2020; Arif *et al.*, 2020; Wu *et al.*, 2020b). Furthermore, the molecular docking studies of these compounds against target main protease (Mpro) of SARS-CoV-2: Mpro (PDBID: 6lu7) and crystal structure of thermoplasma acidophilum (PDBID: 1qw2) to know the binding interaction energy and interaction hydrogen bonding between our compounds and the different protein's sites.



Fig. 1: Some of antimalarial dugs attached to quinolone ring

Results and Discussion

Chemistry

The nucleophilic substitution reaction 4.7dichloroquinoline (1) with thiosemicarbazide (2) utilizing ultrasonic irradiation for 30 min at room temperature to afford the corresponding 2-(7chloroquinolin-4-yl) thiosemicarbazide (3) as Click reaction as displayed in Fig. 2. The obtained compound was investigated via spectral data as; the spectrum of IR of the was displayed vibrational bands at amino and NH group at $v = 3390 \text{ cm}^{-1}$, $v = 3150 \text{ cm}^{-1}$; respectively, while the NH bending vibration was showed at v = 1585 cm⁻¹. Furthermore, the ¹HNMR of the investigated novel thiosemicarbazide was showed signals at $\delta 8.89$ due to N = CH, quinolone and singlet signal of NH_2 at $\delta 8.20$. The mass spectrum showed a peak at m/z 252 corresponding to its molecular ion (Aboelnaga and EL-Sayed, 2018).

The reactivity of 2-(7-chloroquinolin-4yl)thiosemicarbazide (3) with ethylacetoacetate utilizing ultrasonic irradiation for 40 min at 90°C to afford the corresponding 3-(7-chloroquinolin-4-ylamino)tetrahydro-6-methyl-2-thioxopyrimidin-4(1*H*)-one (4). The spectral data confirmed the obtained compound where its FT-IR spectroscopy showed stretching NH at v 3110 cm⁻¹ and bending vibration at 1587 cm⁻¹, also the C = O band showed at 1674 cm⁻¹ while the C = S appeared at 1211 cm⁻¹. The ¹HNMR was assigned the doublet signals of N = CH quinolone at δ 8.20 ppm and aromatic regions ranges between δ 7.15-7.85 ppm. The mass spectrum of the revealed compound showed *m*/*z* = 318 (Aboelnaga and EL-Sayed, 2018).

Computational Studies

Molecular Orbital Calculations

The π -effects properties have an important contribution to biological systems that binding to the active site of a protein receptor so the most active optimized molecular structures of 2-(7-Chloroquinolin-4-yl)thiosemicarbazide (3) (CQT) and 3-(7-chloroquinolin-4-ylamino)-tetrahydro-6-methyl-2-

thioxopyrimidin-4(1*H*)-one (4) (CQP) is demonstrated in Fig. 3 and selected bond lengths, bond angles and dihedral angles are scheduled in Table 3 calculated through B3LYP/6-311G (d) The molecular structure of these compound were not planar (Akl *et al.*, 2020; Fahim and Ismael, 2019; Trott and Olson, 2010). The optimized structures of CQT (3), x ray of 4,7-dichloroquinoline (Hema *et al.*, 2015) and CQP (4) as showed in Table 1 and Fig. 3.



Fig. 2: (a) Ultrasonic reaction of 4,7-dichloroquinoline (1) with thiosemicarbazide (2); (b) Reactivity of 2-(7-chloroquinolin-4-yl) thiosemicarbazide (3) with ethylacetoacetate

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Fig. 3: The optimized geometry, numbering system and moiety of Compounds CQT (3), X ray of 4,7-dichloroquinoline (Fahim and Shalaby, 2019) and CQP(4), utilizing of DFT/B3LYP/6-311(G)-d

The optimized structure of compound CQT (3) have a different bond lengths, bond angles and dihedral angles utilizing B3LYP/6-311G(d), HF/6-311G(d). Comparing the theoretical data with the crystallographic data 4,7dichloroquinoline (Hema et al., 2015) indicated slightly alteration in the optimized bond lengths and bond angles. It was noticed that N₁₆-C₁₁ of CQT (3) measured 1.37286Å, 1.30236Å of HF/6-311G(d), B3LYP/6-311G(d); respectively while the x-ray of N1A-C9A (1.379 (10)Å) which the bond length of the quinolone was compatible with HF theory, but the other bonds such as C_5-C_6 (1.7600Å), (1.4023Å) for HF/6-311G(d), B3LYP/6-311G(d); respectively where it is compatible with C_2A-C_3A (1.432 (12)Å). Furthermore, the bond angles of CQT (3) such as N₁₆-C₁₁-C₁₂ (120.8622°), (120.5236°) for HF/6-311G(d), B3LYP/6-311G(d) while the x ray bond of $C_6A-C_5A-C_{10}A$ (120.2 (8)°) which is more nearest to B3LYP/6-311G(d), also Cl₁₇-C₆-C₅ (120.64566°), (122.0236°) and the C₃A-C₄A-Cl₁A (119.5 (7)°). Moreover, the dihedral angles of attached thiosemicarbazide H₂₀-N₁₉-N₁₈-C₂₂ (-109.7568°), (- 108.235°) and N₁₉-N₁₈-C₂₂-S₂₃(126.7877^{\circ}), (128.2365^{\circ}) for HF and DFT/B3LYP basis set which meant that this group out of plane and more reactive but the dihedral angle N_{16} -C₄-C₃-C₉ (-0.00075°), (-0.00072°) which compatible with the x-ray $C_9A-N_1A-C_2A-C_3A$ (0.9(12)°) as shown in Table 1.

Also the optimized of CQP (4) and illustrated the bond lengths, angles and dihedral angles as displayed in

Table 1 and Fig. 3. The bond lengths of tetrahydro-6methyl-2-thioxopyrimidin-4(1H)-one were utilizing B3LYP/6-311G (d), HF/6-311G (d) theory level. The bond length of N_{17} - N_{25} (1.4700Å) (1.5912Å), (C_{19} - S_{23}) (1.56640Å) (1.3526Å) for HF and B3LYP/6-311G(d), respectively which they were mostly same included that the more delocalization of charges on tetrahydro-6methyl-2-thioxopyrimidin-4(1H)-one with fixed bond length, while the smallest difference in bond length between theoretical and experimental of chloroquinone ring such as for C₂₂-C₂₁ for theoretical and for C₅B-C₆B of experimental was (0.0135Å) for DFT method. Also the largest difference between experimental and calculated DFT bond angles is C5-C6-Cl16 and C3B-C4B-Cl₁B (1.3764°). Therefore, the difference of bond angles of (S₂₆-C₁₉-N27), (C₁₉-N₂₇-H₂₃) between HF and DFT/B3LYP is (1.22508°), (3.24341°). Additionally, the dihedral angles of tetrahydro-6-methyl-2thioxopyrimidin-4(1H)-one (N27-C22-C28-H29), (N17-N25-C₁₉-N₂₇) was taken a negative charges which were out of plane of chloroquinone and give stability of this moiety, also the dihedral of chloroquinone were compatible the theoretical and experimental $(C_6 - C_5 - C_4 - N_{15})(-$ 179.0236°), $(C_7B-C_8B-C_9B-N_1B)$ (-178.5 (7)°) as displayed in Table 1. From the previous results it was noticed that the B3LYP/6-311G (d) more compatible with the confirmed structure and there are lowest difference between them (Farag and Fahim, 2019; Fahim and Shalaby, 2019; Dacrory and Fahim, 2020).

Table 1: Designated optimized bond length Å and bond angle degrees dihedral angle degrees of Compound CQT (3) X-ray of 4,7-dichloroquinoline and CQP(4) using B3LYP/6-311G(d)

Immentes DTF Compound COTA Parameters DTF OTF GRood HF 6-311060 6-311060 Kay (future and Shaleby, 2019) Cr-G 1.3230 GLACA 1.7248 HF-G-C2 119.00273 118.2311 CAAAACA 127.28 Cr-G 1.33301 L4.2201 GLACA 1.7248 HF-G-C2 118.0685 114.2320 N.ACAACA 127.2 (a) Cr-G 1.33301 L4.201 GLACAA 1.379 (b) C-G-C 119.00238 11.0230 N.ACAACA 117.2 (a) Cr-G 1.3396 N.ACAA 1.339 (b) C-G-C-C 120.0386 11.0230 C.ACAACAA 119.2 (c) Cr-G 1.03365 C-AA-HAA 0.9900 C-G-C-C, 120.3506 120.2 (c) C.ACAACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	Bond Length	Å		Bond Angles(°)						
of bond HFic B13. YP K-ray of boot B13. YP Compound CQT15 T Grad-GA 1720. (B) 112.211 C_ANIA-GA 1172. (B) C-C; 1.2320 1.42210 CyAC-GA 1738. (B) H-C-C2 120.4670 113.2211 C_AANIA-GA 1172. (B) C-C; 1.3337 1.4230 CyAC-GA 173.910 H-C-C2 120.4570 112.211 CyAC-GA-GA 119.217 C-C; 1.3337 1.3236 CyAC-GA 1.3371(1) C-C-C2 120.4556 120.256 C/AC/AA-GA 119.217 C-G, 1 1.3000 L.1258 C/A/CA 1.337(1) C-C-C2 120.4566 120.256 C/A/CA/AA 120.11 C/A/CA	Parameters		DFT/			Parameters		DFT/		
lengths 311G40 6-311G40 (Fahlm and Shaleby, 2019) angles HF 6-311G40 K-ang (Tahlm and Shaleby, 2019) Gr, G. 1.27230 C1, AC, A. 1.272180 C1, AC, A. 1.12011 CA, AA, AC, AA 1.122, B) Gr, G. 1.2721 L3368 CA, AC, A. 1.32311 CA, AA, AC, AA 1.127, C) Gr, G. 1.37334 L37825 N, AC, A. 1.373101 C-C, C- 1.199588 119.3271 CA, CA, CA, AB, AC, A 1.172, C) Gr, G. 1.137025 CA, AC, AA, LA322 C, C-, C-, C, C, 120.21034 112.02350 CA, CA, CA, AB, AD, O'S000 C, C-, C-, C, 121.210301 121.22352 CA, AC, AC, AL, L322 CA, CA, AL, L320 C, C-, C-, C, L12.1270101 121.2326 CA, CA, CA, L326, C1, L320, C1, C-, C-, C, 121.210301 121.2326 C3, C-, C-, AL, L320 C, C-, C-, L12.1270101 121.2325 CA, CA, CA, L320, C1, C-, C-, C, 121.210301 121.2326 CA, C-, C-, AL, L320, C1, C-, C-, C-, 121.210301 121.2326 CA, C-, C-, AL, L320, C1, C-, C-, C-, 121.210301 121.2326 CA, C-, C-, AL, L320, C1, C-, C-, C-, 121.210301 121.2326 CA, C-, C-, AL, L320, C1, C-, C-, C-, 120.21034 110.	of Bond	HF/6-	B3LYP/	X-ray		of Bond		B3LYP/		
Compound CQT(3) C-C-C 12328 C-C-C 12328 C-C-C 124372 13728 C-C-C 124372 13728 C-C-C 124372 13728 C-C-C 124372 13728 C-C-C 124373 13728 13728 C-C-C 124373 13728 13728 1382 C-C-C 124373 1372 1372 1382 14 237 14 237 1 24 24 24 2 2 2 2 2 2 2 2 2 2 2 2 2 2	lengths	311G(d)	6-311G(d)	(Fahim and Shala	by, 2019)	angles	HF	6-311G(d)	X-ray (Fahim and Sha	laby, 2019)
C-C 12500	Compound C	CQT(3)	1 27280	C A C A	1 720 (9)		110.00272	110 2211	CANACA	117.2 (8)
Ci-C. 142172 13866 NiA-CA 13387(1) Hic-CC 18.06088 1105250 NiA-CAA 1179 Ci-C. 13734 137325 NiA-CAA 1337 (1) Ci-C. 1105252 Ci-AC-CAA 1137 (1) Ci-C. 110033 12564 Ci-AC-CA 1132 (1) Ci-C-C. 1121304 112320 Ci-AC-CAA 1132 (1) Ci-C-C. 1121304 112320 Ci-AC-CAA 1132 (1) Ci-AC-CA 1132 (1)	$C_1 - C_2$	1.29280	1.37280	ClipA-C7 A	1.720 (8)	$H_7-C_1-C_2$	120 64767	121 5232	$V_2A-IN_1A-C_9A$ $N_1A-C_2A-C_2A$	117.2 (8)
C-Cic 1.37334 1.37625 NiA-CiA 1.379 (10) C-CiC C	C3-C4	1.42172	1.3896	N1A-C2A	1.328 (11)	$H_7 C_1 C_2$ H8-C2-C3	118.60685	116.2580	N1A-C2A-H2AA	117.9
C-C.G. 1.70000 1.4023 C:A:CA 1.432 (12) C-C:C.G. 120.4593 116.98 CIA:CA:CA 117.7 () C-Ha 1.40031 1.2866 C:A:HA 0.360 C;-G:C. 120.4586 112.0236 C:A:CA:CA 112.12 C-Ha 1.4203 1.2365 C:A:CA 1.342 (11) C;-C:C. 121.350 C:A:CA:CAI 114.12 C:A:CA 1.1382 C:A:CA:CA 1.1384 1.1384 1.1384 C:A:CA:CA 1.1384 <td>C₄-C₅</td> <td>1.37334</td> <td>1.37625</td> <td>N₁A-C₉A</td> <td>1.379 (10)</td> <td>C_2-C_3-C_4</td> <td>119.09588</td> <td>119.5232</td> <td>C5A-C10A-C9A</td> <td>119.3 (7)</td>	C ₄ -C ₅	1.37334	1.37625	N ₁ A-C ₉ A	1.379 (10)	C_2 - C_3 - C_4	119.09588	119.5232	C5A-C10A-C9A	119.3 (7)
C+Clip 1.10021 1.07856 C:A-ElsA 0.9500 Cl:-C-C 1.20.64566 120.205 C:A-C:A-ElSA 121.1 C-Hia 1.00351 1.2544 C:A-C.A 1.32216 C:A-CA 1.32236 C:A-CA 1.32236 C:A-CA 1.32210 C:A-CA 1.32236 C:A-CA 1.32236 C:A-CA 1.32210 C:A-CA 1.32236 C:A-CA 1.32236 C:A-CA 1.32236 C:A-CA 1.32236 C:A-CA 1.32210 C:A-CA 1.32236 C:A-CA 1.32336 C:A-CA 1.32336 C:A-CA 1.32336 C:A-CA 1.32336 C:A-CA 1.32337 C:A-CA 1.32411 N:N-N:H-H 1.938054 1.992.55 C:A-CA 1.32377 N:N-Ha 1.40000 1.3325 C:A-HA A 1.43211 N:N-N:HA 1.992.55 C:A-CA	C5-C6	1.76000	1.4023	C_2A-C_3A	1.432 (12)	C4-C5-C6	120.45593	116.9875	C4A-C3A-C2A	117.7 (7)
C-H ₀ 1.1003 1.2564 C.ACAA 1.362 (11) CC-C, 1 12.1304 11.2523 C.A-CIAA-CIAA 1164 (7) C-K ₀ 1.21230 1.02552 C.A-H ₀ AA 0.9500 CC-C, 12.12300 121523 C.A-CAA-CIAA 119.10 (10) N = C_1 1.2128 1.30523 C.A-C ₀ AA 1.422 (11) CN ₁ C, 12.0.3500 120.253 C.A-CA-CAA-CIAA 119.10 (10) N = C_1 1.2123 1.23012 C.A-CAA 1.340 (12) CN ₁ C, 12.0.3500 119.801 C.OA-CAA-CIAA 119.10 (10) N = C_1 1.2124 1.3953 C.A-CAC AA 1.412 (11) CN ₁ C, 12.0.3500 120.253 C.A-CA-CAA 121.20 (10) CC-N ₁ 1.21230 C.A-CAA-AA 1.0550 1.2C-N ₁ 10.947 11 1.1525 C.A-CA-HAA 129.9 CC-N ₁ 1.41023 1.23012 C.A-CAA 1.417 (12) N.N ₁ N ₁ H ₁ 119.8850 110.2525 C.A-CA-CAA (13.12.6) C.N ₁ N ₁ 1.47000 1.0252 CA-HAA 0.9500 CR-C-N ₂ 1.4123 10.0252 CC-CA 1.434 (11) H.N ₁ N ₂ N ₂ -C ₂ 4.19850 109.2525 C.A-CA-CAA (13.12.6) N ₂ -N ₂ 1.50640 1.3261 CA-C ₁ AA 0.9500 CC-C ₁ N ₂ 1.47000 1.2351 CA-C ₁ AA 0.9500 CC-C ₁ N ₂ 1.47000 1.2351 CA-C ₁ AA 0.9500 CC-C ₁ N ₂ 1.47000 1.2351 CA-C ₁ AA 1.422 (11) N. ₁ N ₂ N ₂ -H ₁ H ₁ N ₂ -N ₂ 1.56640 1.2561 CC-C ₁ A-C ₂ A 1.422 (11) N. ₁ N ₂ N ₂ -H ₁ H ₂ Dibicdra1 angles (⁷) H ₂ N ₂ -N ₂ 1.56640 1.2561 CC-C ₁ A-C ₂ A 1.422 (11) N. ₁ N ₂ N ₂ -H ₁ 10.2578 1.2578 C.A-CA ₂ CAA 118.8 (6) CC-C ₄ A-CAA 118.8 (6) CC-C ₄ A-CAA 118.8 (6) CC-C ₄ A-CAA 118.8 (6) CC-C ₄ A-CAA 118.8 (6) CC-C ₄ C-C ₄ A 1.138 (10) CC-C ₂ C-C ₂ -199.9916 1.4852 C.G-B-CAB 1.769 (10) N ₁ N ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.769 (10) N ₁ N ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.769 (10) N ₁ N ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.769 (10) CN ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.438 (10) N ₂ -C ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.438 (10) N ₂ -C ₂ -C ₂ -199.9916 1.4852 C.G-B-CAB 1.438 (10) N ₂ -C ₂ -C ₂ -199.9916 1.19255 C.B-CAB 1.449 (9) CN ₂ -C ₂ -C ₂ 1.999.912 1.19285 C.B-CB-CAB 1.449 (9) CN ₂ -C ₂ -C ₂ 1.999.913 1.21521 CB-CACA,CAA1778 (7) CC-CAB-CAB 1.4452 C.B-CAB 1.438 (10) N ₂ -C ₂ -C ₂ -N ₂ 1.999.912 1.19285 C.B-CB-C	C6-Cl17	1.10021	1.07856	C ₂ A-H ₂ AA	0.9500	Cl17-C6-C5	120.64566	122.0236	C ₄ A-C ₃ A-H3AA	121.1
C-H ₀ 1.42293 1.28265 C.AC.Ma 1.422 (11) CCC.ha 12.15001 12.2320 C.AC.A.C.10A (12.12.8) CN. 1.37286 1.30255 C.AC.A. 1.428 (11) CCNa 120.3667 1.203.667 1.203.667 1.203.671 (10.4C.AC.1.4.120.4.16) NC. 1.37281 1.30256 C.AC.A. 1.420 (11) NCL. 120.3667 1.203.561 C.10AC.AC.1.4 119.4 (6) NC. 1.37284 1.30256 C.AC.A. 1.420 (11) NCL. 120.3667 1.203.526 C.AC.A.A.C.A.(11) 12.2 (2) CP. 1.37284 1.30255 C.AC.A. 1.427 (12) NNC.1. 120.3667 1.203.526 C.AC.AC.A.(8) 124.2 (8) CP. 1.37284 1.30251 C.AC.A. 1.417 (12) NNC.1. 120.3667 1.105236 C.AC.AC.A.(8) 124.2 (8) CN. 1.37294 1.30251 C.AC.A. 1.417 (12) NNC.1. 120.3667 1.105236 C.AC.AC.A.(8) 124.2 (8) CN. 1.47000 1.30261 C.AC.A. 1.364 (11) HN.SC.2. 41.98304 10.2326 C.AC.AC.A. (18.9 (7) NNH. 1.4000 1.30251 CAC.A. 1.364 (11) HN.SC.2. 41.98305 10.2325 C.AC.AC.A. (18.9 (7) CNE. 1.56640 1.2652 CC.C.A. 1.252 (11) N. _{N.NH.B} C. 41.97370 CC.AC.A. C.A. 118.8 (6) CAC.AC.A. 118.8 (7) HNCC 179.7578 1.203.55 C.AC.AC.A. 0.9 (12) HNCC 179.7596 1.4232 (2) CCC 179.9568 1.063.270 NCCC 179.9564 1.423 (17) NCC 109.7580 1.00252 CC.AC.AA. 123.7 (7) NCCC 179.956 1.4252 CBC.B 1.734 (8) SCNT.H 12.001052 121.2355 CC.AC.AC.AA. 11.8 (8) (7) HNCCC 179.9758 1.10622 N.BC.B. 116.3 (7) NCCCC199.7596 1.1022 S.CA.NC.AC.AA. (17).4 (7) NCCC110.9756 1.1248 (10) NCCC. 110.9759 1.20120 CCC.A199.77 (12).2325 CBN.BC.B. 116.3 (7) NCCL. 120.986 1.1658 (13.411) NCCC. 110.9759 1.20120 CCAAAAAAAAAAAAA.	C5-H10	1.10033	1.2564	C ₃ A-C ₄ A	1.362 (11)	C5-C4-C3	119.21034	117.0236	C4A-C10A-C9A	116.4 (7)
$ \begin{array}{c} C+C_{n} & 1.3228 \\ C+N_{n} & 1.37285 \\ C+N_{n} & 1.37285 \\ C+N_{n} & 1.37285 \\ C+C_{n} & 1.3700 \\ 1.3355 \\ C+C_{n} & 1.3700 \\ 1.3955 \\ C+C_{n} & 1.3700 \\ 1.3952 \\ C+C_{n} & 1.3700 \\ C+C_{n} & 1.3700 \\ 1.3952 \\ C+C_{n} & 1.421(11) \\ C+C_{n} & 1.3916 \\ C+C_{n} & 1.3917 \\ C+C_{n} & 1.3918 \\ C+C_{n} & 1.3916 \\ C+C_{n} & 1.3917 \\ C+C_{n} & 1.3918 \\ C+C_{n} &$	C ₂ -H ₈	1.42203	1.02365	C ₃ A-H ₃ AA	0.9500	$C_5-C_4-C_3$	121.73001	121.5230	C3A-C4A-C10A	121.2 (8)
$ \begin{array}{c} Crive 1.51286 \\ 1.51286 \\ 1.5128 \\ Crive 1.12728 \\ 1.2023 \\ Crive 1.12728 \\ Crive 1.1278 \\ Crive 1.12728 \\ Crive 1.12788 \\ Crive 1.1278 \\$	C ₃ -C ₉	1.42208	1.389523	$C_4A-C_{10}A$	1.422 (11)	$C_5-C_4-N_{16}$	120.54903	120.0251	C3A-C4A-CIIA	119.5 (7)
Cu-C ₁ 1.41623 1.23012 CA-HEAA 109500 Cu-C ₁ -R ₁ 109.47 115.325 CA-CA-CA-HAA 119.9 0 Cu-C ₁ -C ₁ 1.47000 1.0325 CA-CA-A 1.471(12) Nu-R-H ₂ 119.88051 112.5256 CA-CA-A 1.8452 CA-CA-A 1.8452 CA-CA-CA-CA 1.8452 CA-CA-CA-CA 1.84161 Nu-N ₁ 1.95452 CA-CA-CA-CA 1.84171 Nu-N ₁ -N ₁ 1.0000 1.30552 C-CA-CA 1.421(11) Nu-N ₁ -N ₂ -H ₂ 1.98051 109.2365 C-A-CA-CA 1.8456 (CA-CA-CA-CA 1.818.66 (CA-CA-CA-CA) 1.82.365 (CA-CA-CA-CA) 1.82.365 (CA-CA-CA-CA) 1.82.365 (CA-CA-CA-CA) 1.82.365 (CA-CA-CA-CA) 1.82.367 (CA-CA-CA-CA) 1.82.46 (IIIII) (IIII	C_4 -IN16	1.37286	1.30230	C5A-C6A	1.346(12) 1.420(11)	C_4 - N_{16} - C_{11}	120.30087	120 5236	C10A-C4A-C11A	119.4 (0)
Cip-Ci 13294 139853 CA-CyA 1417 (12) Nig-Nig-Hin 119.88054 CO-CA-CA-CA (28) 124.2 (8) Nig-Nig 140000 1.30261 CA-CA-CA 1.364 (11) His-Nig-Cr_2 41.98580 109.2365 CA-CA-CA 120.5 (7) Nig-Nig 1.40000 1.23251 CA-CA-A 1.364 (11) Hig-Nig-Cr_2 41.98580 109.2365 CA-CA-CA 1.21.7 (8) Nig-Nig-Hig 1.0000 1.23251 CA-Ca-A 1.422 (11) Hig-Nig-Nig-Hig CA-CA-CA 1.81.6 (6) CA-CA-CA 1.81.8 (7) CA-CA-CA 1.81.8 (7) CA-CA-CA 1.81.8 (6) CA-CA-CA 1.81.8 (7) CA-CA-CA 1.82.3 (7) CA-CA-CA 1.81.8 (7) CA-CA-CA-	C11-C12	1 41623	1 23012	CsA-HsAA	0.9500	C12-C9-N18	109 47	116 325	C6A-C5A-H5AA	119.9
C _N N ₈ 1.47000 1.0325 C _A -R _A A 0.9500 S _D -C _D -N ₂ 109.47117 115.4552 C _A -C _A -C _A A 1.108.8 N _B +H ₁ 1.0000 1.33652 C _F -R _A A 1.9500 1.98.2762 41.98580 109.2365 C _A AC _A C _A A 1.108.8 N ₂ -H ₂ 1.0000 1.2351 C _A -C _B A 1.422 (11) N ₁ -N ₁ -H ₂ 41.98580 109.2365 C _A AC _A C _A A 1.18.6 (6) C ₂ -S ₂₃ 1.56640 1.56640 1.56640 1.56640 1.422 (11) N ₁ -N ₁ -N ₁ -N ₁ -N ₂ -P ₂ 1.06.7588 -108.255 C _A A-C _A A-C _A A 1.18.9 (8) (N ₁ -A_C _A A-C _A A) 1.06.758 1.08.255 C _A A-C _A A-C _A A 1.73.8 (7) N ₁ A-C _A A-C _A A 1.73.8 (7) N ₁ A-C _A A-C _A A-C _A A 1.73.8 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.8 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.6 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.6 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.6 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.6 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.6 (7) N ₁ A-C _A A-C _A A-C _A A 1.78.7 (7) N ₁ A-C _A	C12-C9	1.37294	1.39853	C6A-C7A	1.417 (12)	N18-N19-H21	119.88054	120.5236	$C_{4}A-C_{10}A-C_{5}A(8)$	124.2 (8)
N ₁₂ -N ₂₂ 1.4000 1.30261 C:A.C.A 1.364 (11) H ₂₂ -N ₂₂ -R ₂₁ 4.98580 109.2365 C:A.C.A.A 119.5 (7) C ₂₂ -N ₂₁ 1.47000 1.20325 C:A-L.(aA 0.9500 N ₁₂ -N ₁₂ -N ₁₂ C:A.C.A.C.(AA 119.5 (7) C ₂₂ -S ₂₃ 1.56640 1.56640 1.56640 1.66640 1.422 (11) V V C:A.C.(AA 118.6 (6) C ₂₂ -S ₂₃ 1.56640 1.56640 1.56640 1.56640 1.56640 1.37.8 (8) N ₁₁ -N ₁₂ -N	C9-N18	1.47000	1.0325	C ₆ A- H ₆ AA	0.9500	S23-C22-N24	109.47117	115.4562	C5A-C6A-C7A	120.5 (7)
Na-Ha, Car-Na 1.0000 1.39652 Car-CaA 1.421 (1) Nur-Ma; Nur-Ha; CBA-CaA-CaA 1195 (7) Nar-Ha; 1.0000 1.2351 CaA-CinA 1.422 (1) CaA-CinA 1.456 (6) Ca-Ca-CaA 1.56640 1.55640 1.56640 CaA-CinA 1.456 (6) Ci-AC-CaA-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (6) Ci-AC-CinA 1.816 (7) Immon-Mine-Ci2 1.99736 1.912.235 (7) CiAC-CiA-CiA 1.734 (7) Compound COP(4) Immon-Mine-Ci2 -109.756 -108.235 (7) CiAC-CiA-CiA 1.797 (7) Cin-Sign 1.56640 1.3526 Nig-CiB 1.734 (8) Sign-Cip-Nig-Ti2 CiAC-CiA-CiA-CiA 1.797 (7) Cin-Sign	N18-N19	1.4000	1.30261	C7A-C8A	1.364 (11)	H25-N24-C22	41.98580	109.2365	C5A-C6A-H6AA	119.8
C2:Na 1.47000 1.2325 Cr-HaA 0.9500 Ca-Ca Ca-Ca 1.7(8) C2:S3 1.56640 1.56640 L52640 L52640 Ca-Ca 1.82(1) Ca-Ca-Ca 1.85(6) C2:S3 1.56640 1.56640 L52640 L52640 Ca-Ca-Ca 1.85(6) Ca-Ca-Ca 1.82(1) Ca-Ca-Ca 1.82(1) Ca-Ca-Ca 1.85(6) Dihedral angles (*) Ha-Nu-Nu-C2:: -109.7560 -108.235 Ca-Ca-Ca-Ca 1.97(5) Ha-Nu-Nu-C2:: -109.7560 -108.235 Ca-Ca-Ca-Ca 1.97(7) Ca-Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.98.756 -108.235 Ca-Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca-Ca 1.97(7) Ca-Ca Ca-Ca-Ca 1.97(7) Ca-Ca 1.97(7) Ca	N19-H21	1.0000	1.39652	C ₈ -C ₉ A	1.421 (11)	N ₁₈ -N ₁₉ -H ₂₁			C8A-C9A-C10A	119.5 (7)
Na-HE 1.0000 L251 CA-CaA 1.422 (11) CAACaA 19.7 (7) Cg-Sg 1.56640 1.56640 1.56640 CA-CaA CAACaA 118.6 (6) Cg-Sg 1.56640 1.56640 CA-CaA Na-HE CAACaA 118.6 (6) Cg-Sg 1.6640 1.56640 Na-CA-CaA 118.6 (6) CA-CaA 118.6 (6) Cg-Sg 1.07756 -106.7568 -106.255 CAANA-CAA-CAA 173.3 (8) Ng-Na-Cg-Sg 1.67777 128.2365 C6A-CSA-CAA 178.6 (7) Hg-Na-Cg-Sg 2.67777 128.2365 C6A-CAA-CAA 178.6 (7) Ng-Sg-Cg 1.93516 1.4852 CgB-CB 1.769 (8) Cg-Na-G2N77 120.0152 179.4 (7) Ng-Cg 1.39516 1.4852 CgB-CB 1.769 (8) Cg-Na-G2N7 120.0152 CgB-CB 1.791 (7) Ng-Cg 1.39516 1.4852 CgB-CB 1.769 (8) Cg-Na-G2N 119.9911 10.231 CA-CA-CA-A 1.11 (1) Ng-Cg 1.39514 1.4255 NB-CB-B 1.36 (10) Ng-Cg-Cg 119.9911	C ₂₇ -N ₂₄	1.47000	1.20325	C8-H8AA	0.9500				C ₈ A-C ₇ A-C ₆ A	121.7 (8)
C2:>52: 1.50640 1.30640 CA-CA-CA 118.9.(8) C3:>52: 1.50640 1.30640 CA-CA-CA 118.9.(8) C4:CA-CA 118.9.(8) CA-CA-CA 118.9.(8) C4:CA-CA 123.37(7) CA-CA-CA 123.37(7) Dihedral angles (*) H:SN:NI;-C2:: -109.7568 -108.235 CA-NIA-CA-CA 0.9 (12) N:pN:NI;-C3:: -109.7568 -108.235 CA-CA-CA-CA 178.6 (7) H:SN:S:: C5:: -30: -63.2708 127.232 CA-CA-CA, CA-CA-A 178.6 (7) N:pN:NI: C4: C5: -109.0075 -000075 -000072 CA-CA-CA, CA-CA-A 178.6 (7) N:p-Ns: 1.4700 1.5912 CuB-CB 1.734 (8) Sp:-Cip-N27 120.01052 121.2356 CB-NIB-C3B 116.1 (7) N:p-Cs: 1.39543 1.4123 CuB-CB 1.734 (8) Sp:-Cip-N27 120.01052 121.2356 CB-NIB-C3B 124.9 (8) N:p-Cs: 1.39543 1.4123 CuB-CB 1.33 (1) Cip-N2-C2 119.99110 119.2365 CB-CB-CB 119.4 (8) Cip-Ca 1.39141 1.4256 N,B-CB 1.338 (10) N:	N ₂₄ -H ₂₅	1.0000	1.2351	$C_9A-C_{10}A$	1.422 (11)				$C8A-C/A-C_{12}A$	119.7 (7)
Сл. Сс. 100 Сл. С. С. А. На 100 6 NiA CA - Cia 173.38) NiA CA - Cia 179.4 (7) Compound CQP(4) NiA - Cia - Cia 179.4 (7) Nia Ca - Cia - 179.9736 NiA - Cia - Cia - 179.9736 Nia Ca - Cia - Cia - Cia - 179.9736 Nia Ca - Cia - Cia - Cia - 179.9736 Nia Ca - Cia - Cia - Cia - 179.9736 Nia Ca - Cia - Cia - Cia - 179.9736 Nia Ca - Cia - Cia - Cia - Cia - 179.9736 Nia Ca - Cia - 179.4 (7) Nia Ca - Cia - 179.4 (7) Nia Ca - Cia	C22-323	1.30040	1.30040						$C_{6}A-C_{7}A-C_{12}A$	118.0 (0)
NiA-Ca-Ca-Ca- 173-8 Dihedral angles (*) Dihedral angles (*) Hzs-Nic-Nic-Cz- 108.235 CGA-NiA-Ca-Ca-CA 186 (7) Hzs-Nic-Nic-Cz- 108.235 CGA-NiA-Ca-Ca-CA 186 (7) Hzs-Nic-Cz-2252 126.7877 Hzs-Nic-Cz-2252 126.7877 Hzs-Nic-Cz-27581 116.6729 Ormound CQP(4) 179.4 (7) Compound CQP(4) Nic-Ca-Cc-109926 Vin-Nic-S 14700 L-S2C CiB-CB L-S326 NiB-CB L-S327 CiB-CB-CiB L-S328 L-S326 L-S327 L-S326									C7A-C8A-H8AA	120.6
Na-Cya-Cya Na-Cya-Cya 123.3 (7) Dihedral angles (*) - </td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>N1A-C9A-C8A</td> <td>117.3 (8)</td>									N1A-C9A-C8A	117.3 (8)
Dihedral angles () Dihedral angles () Dihedral angles () Display Display <thdisplay< th=""> Display <thdisplay< th=""></thdisplay<></thdisplay<>									N1A-C9A-C10A	123.3 (7)
Hap-Nip-Nip-Cap 109,7568 -108,235 CA-NiA-CA-CAA 0.9 (12) Nip-Nip-Cap 126,2787 126,2877 128,2365 CA-CA-CAA-CAA 179,4 (7) Hap-Nip-Cap 116,67700 110,231 CAA-CAA-CAA 179,4 (7) Mip-Nip-Cap 116,67700 110,231 CAA-CAA-CIAA-CIAA 178,8 (7) Cap-Cap-Cap -179,9936 -179,5231 CAA-CIAA-CIAA-CIAA -171,88 (7) Cap-Cap Cap-Cap-Cap -179,9936 -179,5231 CAA-CIAA-CIAA-CIAA -171,111 Nip-Cap 1,35216 CIB-CaB 1,734 (8) Sag-Cip-N27 120,01052 121,2356 CB-NiB-CoB 116,3 (7) Nip-Cap 1,35216 NIB-CaB 1,313 (1) Cip-Nyr-Cap 119,99110 119,2365 CB-CB-CB 118,8 (8) Nip-Cap 1,39471 1,4256 NIB-CaB 1,338 (1) Cip-Nyr-Cap 119,99110 119,2365 CB-CB-CB 118,8 (8) Nip-Cap 1,39471 1,4256 NIB-CaB 1,338 (1) Cip-Nyr-Cap 119,99160 119,2556 C						Dihedral angles ((°)			
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $						H20-N19-N18-C22	-109.7568	-108.235	C9A-N1A-C2A-C3A	0.9 (12)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $						N ₁₉ -N ₁₈ -C ₂₂ -S ₂₃	126.7877	128.2365	C6A-C5A-C ₁₀ A-C ₄ A	178.6 (7)
$\begin{array}{c c c c c c c c c c c c c c c c c c c $						H ₂₅ -N ₂₄ -C ₂₂ -S ₂₃	-63.32708	127.232	$C_2A-N_1A-C_9A-C_8A$	179.4 (7)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $						$\Pi_{25} = \Pi_{24} = C_{22} = \Pi_{18}$	170 0036	170.231	C_7A - C_8A - C_9A - N_1A	-170.7(7)
$ \begin{array}{c} \text{Compound CQP(4)} \\ \text{Ni7-N25} & 1.4700 & 1.5912 & \text{Ci}_{1B}\text{C-LB} & 1.734 (8) & \text{Sae-Cige-N27} & 120.01052 & 121.2356 & \text{Ci}_{B}\text{-N}\text{B-C}\text{B} & 116.3 (7) \\ \text{Ni7-N25} & 1.39516 & 1.33526 & \text{N}_{B}\text{-C}\text{-B} & 1.769 (8) & \text{Ci}_{1e}\text{N}\text{N}\text{-H}\text{23} & 120.01279 & 121.2356 & \text{C}_{3B}\text{-C}\text{B} \text{-C}\text{B} & 124.9 (8) \\ \text{Cip-N27} & 1.39471 & 1.4256 & \text{N}_{B}\text{-C}\text{-B} & 1.313 (11) & \text{Cip-N27-C22} & 119.994110 & 119.2365 & \text{C}_{B}\text{-C}\text{B} \text{-H}\text{B}A & 117.6 \\ \text{Cip-N27} & 1.39471 & 1.4256 & \text{N}_{B}\text{-C}\text{-B} & 1.318 (11) & \text{Cip-N27-C22} & 119.994110 & 119.2365 & \text{C}_{B}\text{-C}\text{-B} \text{-H}\text{B}A & 120.6 \\ \text{N27-H23} & 1.09968 & 1.16595 & \text{C}_{B}\text{-H}\text{B}A & 0.9500 & \text{Ci}_{1}\text{-C}\text{-N}\text{-O}\text{-23} & 119.99117 & 119.869 & \text{C}_{B}\text{-C}\text{-B} \text{-L}\text{B} & 112.4 (6) \\ \text{C2s-C2s} & 1.54000 & 0.9965 & \text{C}_{B}\text{-H}\text{B}A & 0.9500 & \text{C}_{2}\text{-N}\text{-N}\text{N}\text{S} & 120.00800 & 121.5965 & \text{C}_{B}\text{-C}\text{-B} \text{-L}\text{B} & 117.9 (6) \\ \text{Ca-N13} & 1.42208 & 1.5032 & \text{C}_{B}\text{-C}\text{-B} & 1.438 (11) & \text{Ni}\text{-C}\text{-C}\text{-C12} & 120.0430 & 121.5621 & \text{Ci}_{B}\text{-C}\text{-B} \text{-C}\text{-B} & 119.7 (6) \\ \text{C2s-C12} & 1.39482 & 1.38652 & \text{C}_{B}\text{-C}\text{-B} & 1.437 (12) & \text{Ni}\text{-C}\text{-C}\text{-C12} & 120.86230 & 120.235 & \text{C}_{B}\text{-C}\text{-B} \text{-L}\text{B} & 117.9 (6) \\ \text{C2s-C12} & 1.39482 & 1.38652 & \text{C}_{B}\text{-C}\text{-B} & 1.470 (12) & \text{Ni}\text{-C}\text{-C}\text{-C2} & 119.0596 & 119.2356 & \text{C}_{B}\text{-C}\text{-B} \text{-L}\text{B} & 117.0 (8) \\ \text{C2s-C21} & 1.39482 & 1.38652 & \text{C}_{B}\text{-C}\text{-B} & 1.410 (11) & \text{C}_{2}\text{-C}\text{-C}\text{-L}\text{I} & 120.24558 & 120.2556 & \text{C}_{B}\text{-C}\text{-B} & 119.4 (6) \\ \text{C}_{2}\text{-C} & 1.47000 & 1.3652 & \text{C}_{B}\text{-C}\text{-B} & 1.490 (11) & \text{C}_{2}\text{-C}\text{-C}\text{-L}\text{I} & 120.256 & \text{C}_{B}\text{-C}\text{-B} & 123.7 (7) \\ \text{C}_{2}\text{-C} & 1.47000 & 1.3652 & \text{C}_{B}\text{-C}\text{-B} & 1.400 (11) & \text{C}_{2}\text{-C}\text{-C}\text{-L}\text{I} & 120.2556 & \text{C}_{B}\text{-C}\text{-B} & 119.4 (7) \\ \text{N}_{B}\text{-C}_{B}\text{-C}\text{-B} & 119.4 (7) \\ \text{N}_{B}\text{-C}_{B}\text{-C}\text{-B} & 119.4 (7) \\ \text{N}_{B}\text{-C}_{B}\text{-C}\text{-B} & 119.4 (7) & \text{N}_{B}\text{-C}_{B}\text{-C}\text{-B} & 119.4 (7) \\ \text{C}_{B}\text{-C}_{B}\text{-C}$						N16-C4-C3-C9	-0.00075	-0.00072	$C_3A-C_4A-C_{10}A-C_9A$	-11(11)
$\begin{split} N_{17}N_{25} & 1.4700 & 1.5912 & C_{11}B-C_{18} & 1.734 (8) & S_{16}C_{19}N_{27} + 120.01052 & 121.2356 & C_{18}B-N_{18}C_{18} & 116.3 (7) \\ N_{25}-C_{19} & 1.39516 & 1.4852 & C_{12}B-C_{78} & 1.769 (8) & C_{19}-N_{27}-H_{23} & 120.01052 & 121.2356 & C_{18}B-C_{28} & 124.9 (8) \\ C_{19}-N_{27} & 1.39471 & 1.4256 & N_{18}-C_{28} & 1.313 (11) & C_{19}-N_{17}-C_{22} & 119.99412 & 116.982 & N_{18}-C_{28}-H_{18}A & 120.6 \\ N_{27}-C_{22} & 1.39543 & 1.4123 & C_{28}-C_{28} & 1.418 (11) & C_{22}-C_{23}-C_{20} & 119.99110 & 119.2365 & C_{28}-H_{18}A & 120.6 \\ N_{27}-H_{23} & 1.09968 & 1.16595 & C_{28}-H_{18}A & 0.9500 & C_{21}-C_{29}-O_{22} & 120.00469 & 120.523 & C_{48}-C_{16}B & 121.4 (6) \\ C_{28}-H_{29} & 1.07000 & 0.9965 & C_{28}-H_{18}A & 0.9500 & C_{20}-N_{25}-N_{15} & 120.00300 & 121.5561 & C_{18}-C_{16}B & 121.4 (6) \\ C_{28}-H_{29} & 1.07000 & 0.9965 & C_{28}-H_{18}A & 0.9500 & C_{20}-N_{25}-N_{15} & 120.00300 & 121.5561 & C_{18}-C_{16}B & 121.4 (6) \\ C_{29}-C_{21} & 1.39482 & 1.3865 & C_{38}-C_{48} & 1.373 (12) & C_{12}-C_{12} & 120.86230 & 120.235 & C_{48}-C_{16}B & 121.7 (7) \\ C_{22}-C_{21} & 1.39482 & 1.3865 & C_{38}-C_{48} & 1.373 (12) & C_{12}-C_{15} & 119.0596 & 119.2356 & C_{38}-C_{48} - H_{19}A & 119.1 \\ C_{21}-C_{20} & 1.39514 & 0.96598 & C_{28}-H_{48}A & 0.9500 & C_{4}-C_{5}-C_{4} & 120.6554 & 120.2565 & C_{38}-C_{58} & 119.0 (11) \\ C_{2}-C_{3} & 1.25840 & 1.238652 & C_{48}-C_{48} & 1.410 (11) & C_{2}-C_{6}-C_{16} & 120.6554 & 120.2565 & C_{38}-C_{48}-H_{48}A & 121.5 \\ C_{39}-C_{30} & 1.3254 & C_{39}-C_{39} & 1.429 (10) & & & & & & & \\ C_{39}-C_{18}-C_{28}-C_{28} & 1.19.5 (7) & C_{38}-C_{48}-C_{48} & 115.7 (7) \\ C_{3}-C_{4} & 1.4187 & 1.39652 & C_{48}-C_{48} & 1.429 (10) & & & & & & \\ C_{3}-C_{4}-C_{38}-C_{48}-C_{48} & 119.4 (7) \\ C_{4}-C_{5} & 1.42203 & 1.3256 & C_{48}-C_{48} & 1.429 (10) & & & & & & & \\ N_{19}-C_{48}-C_{48}-C_{48} & 1.5 (1) \\ N_{17}-N_{25}-C_{19}-N_{27} & -0.90550 & & & & & & \\ C_{48}-C_{48}-C_{48}-C_{48} & 1.5 (1) \\ N_{17}-N_{25}-C_{19}-N_{29} & -0.90550 & & & & & & \\ C_{48}-C_{$	Compound C	CQP(4)								()
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	N ₁₇ -N ₂₅	1.4700	1.5912	$C_{11}B-C_4B$	1.734 (8)	S26-C19-N27	120.01052	121.2356	$C_2B-N_1B-C_9B$	116.3 (7)
	N ₂₅ -C ₁₉	1.39516	1.4852	$C_{12}B-C_7B$	1.769 (8)	C19-N27-H23	120.01279	123.2562	$N_1B-C_2B-C_3B$	124.9 (8)
	C19-S23	1.56640	1.3526	N_1B-C_2B	1.313 (11)	C19-N27-C22	119.99412	116.982	N ₁ B-C ₂ B-H ₂ BA	117.6
$\begin{split} & N_{27} - C_{22} & 1.39543 & 1.4125 & C_{2} - C_{3} & 1.418 & (11) & C_{22} - C_{21} - C_{30} & 120.00469 & 120.525 & C_{4} - C_{3} - E_{1} - B_1 & A & 120.6 \\ & N_{27} - H_{23} & 1.09968 & 1.16595 & C_{3} - E_{4} - B_{4} & 0.9500 & C_{21} - C_{20} - O_{22} & 119.99197 & 119.869 & C_{3} - C_{4} - C_{10} B & 121.4 & (6) \\ & C_{28} - H_{29} & 1.07000 & 0.9965 & C_{3} - E_{4} - B_{4} & 0.9500 & C_{21} - C_{20} - O_{22} & 119.99197 & 119.869 & C_{3} - C_{4} - C_{1} B & 117.9 & (6) \\ & C_{27} - C_{21} & 1.39482 & 1.3865 & C_{3} - C_{4} - B & 1.443 & (11) & N_{17} - C_{9} - C_{12} & 120.86230 & 120.235 & C_{3} - C_{4} - B & 121.7 & (7) \\ & C_{27} - C_{21} & 1.39482 & 1.3865 & C_{3} - C_{6} B & 1.443 & (11) & N_{17} - C_{9} - C_{12} & 120.36689 & 122.5695 & C_{3} - C_{6} - B + H_{5} A & 1.91 & 1 \\ & C_{21} - H_{24} & 1.09976 & 1.3265 & C_{3} - B_{-} - B & 1.410 & (11) & C_{5} - C_{6} - C_{11} & 120.36689 & 122.565 & C_{3} - C_{6} - B + H_{6} A & 12.15 & C_{2} - C_{20} & 1.25840 & 1.238652 & C_{6} - B_{-} - B_{6} & 1.410 & (11) & C_{5} - C_{6} - C_{16} & 120.0256 & C_{3} - C_{6} - B_{-} + H_{6} A & 12.32 & (7) & C_{17} - C_{9} & 1.47000 & 1.3652 & C_{6} - B_{-} - B_{6} & 1.439 & (10) & C_{5} - C_{6} - C_{16} & 120.05564 & 120.0236 & C_{3} - C_{6} - B & 119.8 & (6) & C_{9} - C_{3} & 1.420203 & 1.3256 & C_{7} - B_{-} - C_{8} & 1.379 & (12) & C_{7} - C_{9} - C_{16} & 1.20.6256 & 120.0236 & C_{3} - C_{7} - B_{-} & 19.9 & (6) & C_{9} - C_{7} - C_{9} & 1.4187 & 1.39652 & C_{6} - B_{-} - B_{6} & 1.439 & (11) & C_{7} - C_{6} - C_{16} & 120.0236 & C_{3} - C_{7} - C_{6} & 119.256 & C_{3} - C_{1} - C_{1} & 1.4187 & 1.39652 & C_{3} - B_{-} - B_{0} & 1.400 & (11) & C_{7} - C_{9} - C_{16} - B_{-} + B_{-} & A_{1} - A_{1} & A_{1} &$	C ₁₉ -N ₂₇	1.39471	1.4256	N ₁ B-C ₉ B	1.368 (10)	N ₂₇ -C ₂₂ -C ₂₈	119.98110	119.2365	$C_4B-C_3B-C_2B$	118.8 (8)
$\begin{split} & \begin{array}{c} N_{27} + R_{23} & 1.09968 & 1.16395 & C_{28} + R_{28} A & 0.9500 & C_{21} - C_{20} - V_{22} & 119.9917 & 119.869 & C_{38} - C_{46} - C_{16} B & 120.7 (7) \\ & \begin{array}{c} C_{22} - C_{28} & 1.54000 & 1.48852 & C_{38} - C_{48} & 1.338 (12) & O_{22} - C_{20} - N_{25} & 120.00800 & 121.5965 & C_{38} - C_{48} - C_{16} B & 121.4 (6) \\ & \begin{array}{c} C_{28} - R_{29} & 1.07000 & 0.9965 & C_{3} - R_{3} B A & 0.9500 & C_{20} - N_{25} & 120.00800 & 121.5962 & C_{48} - C_{16} B & 121.7 (7) \\ & \begin{array}{c} C_{21} - C_{21} & 1.39482 & 1.3865 & C_{48} - C_{68} B & 1.473 (12) & V_{17} - C_{72} & 120.36623 & 122.5695 & C_{48} - C_{48} B - H_{48} A & 119.1 \\ & \begin{array}{c} C_{21} - C_{20} & 1.399514 & 0.96598 & C_{38} - C_{48} B & 1.407 (12) & N_{15} - C_{4} - C_{3} & 119.0596 & 119.2356 & C_{38} - C_{68} - H_{68} A & 121.5 \\ & \begin{array}{c} C_{20} - O_{32} & 1.25840 & 1.238652 & C_{68} - C_{78} & 1.410 (11) & C_{5} - C_{6} - C1_{16} & 120.65564 & 120.0236 & C_{8} - C_{6} - B & 123.7 (7) \\ & \begin{array}{c} C_{3} - C_{4} & 1.41887 & 1.39652 & C_{68} - C_{18} B & 1.359 (12) & & & & & \\ C_{3} - C_{4} & 1.41887 & 1.39652 & C_{48} - C_{8} B & 1.359 (12) & & & & & \\ C_{3} - C_{4} & 1.41887 & 1.39652 & C_{48} - C_{8} B & 1.359 (12) & & & & & \\ C_{3} - C_{4} & 1.41887 & 1.39652 & C_{48} - C_{8} B & 1.400 (11) & & & & \\ C_{4} - N_{5} & 1.42203 & 1.42256 & C_{58} - C_{48} B & 1.429 (10) & & & & \\ N_{18} - C_{9} - C_{9} - C_{8} B & 119.4 (7) \\ C_{4} - C_{4} & 1.41827 & 1.42172 & & & & & \\ C_{4} - C_{5} & 1.37334 & 1.37334 & & & & \\ C_{4} - C_{5} & 1.37334 & 1.37334 & & & & \\ C_{6} - C_{116} & 1.7600 & 1.7600 & & & & & \\ N_{17} - N_{22} - C_{19} - S_{11} - 7_{19} - 7_{29} - 5_{29} - 5_{21} - 8_{8} - 5_{20} - 1_{28} - 1_{28} - C_{18} - 1_{28} - C_{18} B & 119.3 (7) \\ C_{5} - C_{6} & 1.37334 & 1.37334 & & & & \\ C_{6} - C_{16} - C_{18} - C_{18$	N ₂₇ -C ₂₂	1.39543	1.4123	C_2B-C_3B	1.418 (11)	C_{22} - C_{21} - C_{20}	120.00469	120.523	$C_4B-C_3B-H_3BA$	120.6
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	N27-H23	1.09968	1.10395	C_2B-H_2BA C_2B-C_4B	0.9500	C_{21} - C_{20} - O_{32}	119.99197	119.809	C_3B - C_4B - $C_{10}B$	120.7(7)
$ \begin{array}{c} C_{4} N_{15} \\ C_{4} N_{15} \\ C_{21} C_{22} \\ C_{21} \\ C_{22} C_{21} \\ C_{23} C_{48} \\ C_{48} N_{15} \\ C_{21} C_{22} \\ C_{21} C_{22} \\ C_{21} \\ C_{22} C_{21} \\ C_{22} C_{21} \\ C_{22} C_{21} \\ C_{23} C_{48} \\ C_{48} \\ C_{58} \\ C_{$	C22-C28	1.07000	0.9965	C2B-H2BA	0.9500	C20-N25-N17	120.00300	121.5905	$C_{10}B_{-}C_{4}B_{-}C_{11}B_{-}$	121.4(0) 117.9(6)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	C4-N15	1.42208	1.5032	C4B-C10B	1.443 (11)	N17-C9-C12	120.86230	120.235	C6B-C5B-C10B	121.7 (7)
$ \begin{array}{ccccc} C_{21}-H_{24} & 1.09976 & 1.3265 & C_{3}B-C_{10}B & 1.407 (12) & N_{15}-C_{4}-C_{3} & 119.0596 & 119.2356 & C_{3}B-C_{6}B-C_{7}B & 117.0 (8) \\ C_{21}-C_{20} & 1.39514 & 0.96598 & C_{3}B-H_{5}BA & 0.9500 & C_{4}-C_{5}-C_{6} & 120.4558 & 120.2565 & C_{3}B-C_{6}B-H_{6}BA & 121.5 \\ C_{20}-O_{32} & 1.25840 & 1.238652 & C_{6}B-C_{7}B & 1.410 (11) & C_{5}-C_{6}-C_{1_{16}} & 120.65564 & 120.0236 & C_{8}B-C_{7}B-C_{6}B & 123.7 (7) \\ C_{17}-C_{9} & 1.47000 & 1.3652 & C_{6}B-H_{6}BA & 0.9500 & & & & C_{8}B-C_{7}B-C_{12}B & 119.8 (6) \\ C_{9}-C_{3} & 1.42203 & 1.3256 & C_{7}B-C_{5}B & 1.359 (12) & & & & & & & & & & & & & & & & & & &$	C22-C21	1.39482	1.3865	C5B-C6B	1.373 (12)	C12-C11-N15	120.36689	122.5695	C6B-C5B-H5BA	119.1
$\begin{array}{cccccc} C_{21} C_{20} & 1.39514 & 0.96598 & C_{3}B-H_{5}BA & 0.9500 & C_{4}-C_{5}-C_{6} & 120.4558 & 120.2565 & C_{3}B-C_{6}B-H_{6}BA & 121.5 \\ C_{20}-O_{32} & 1.25840 & 1.238652 & C_{6}B-C_{7}B & 1.410 (11) & C_{5}-C_{6}-C1_{16} & 120.65564 & 120.0236 & C_{8}B-C_{7}B-C_{6}B & 123.7 (7) \\ C_{17}-C_{9} & 1.47000 & 1.3652 & C_{6}B-H_{6}BA & 0.9500 & & & & & & & & & & & & & & & & & & $	C21-H24	1.09976	1.3265	$C_5B-C_{10}B$	1.407 (12)	N ₁₅ -C ₄ -C ₃	119.0596	119.2356	C5B-C6B-C7B	117.0 (8)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	C_{21} - C_{20}	1.39514	0.96598	C5B-H5BA	0.9500	$C_4-C_5-C_6$	120.4558	120.2565	C5B-C6B-H6BA	121.5
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$C_{20}-O_{32}$	1.25840	1.238652	C_6B-C_7B	1.410 (11)	C5-C6-Cl16	120.65564	120.0236	$C_8B-C_7B-C_6B$	123.7 (7)
$\begin{array}{cccccccc} C_{9}C_{3} & 1.42203 & 1.3256 & C7B-C_8B & 1.359 (12) & C_6B-C_7B-C_2B & 116.5 (7) \\ C_{3}-C_4 & 1.41887 & 1.39652 & C_8B-C_9B & 1.400 (11) & C7B-C_8B-C_9B & 119.4 (7) \\ C_4+N_{15} & 1.42208 & 1.4236 & C_8B-H_8BA & 0.9500 & C_7B-C_8B-H_8BA & 120.3 \\ C_{11}-C_{12} & 1.41622 & 1.4235 & C_9B-C_{10}B & 1.429 (10) & N_{18}-C_{9B}-C_{18}B & 117.0 (7) \\ N_{15}-C_{11} & 1.37289 & 1.33256 & N_{1B}-C_9B-C_{10}B & 118.7 (7) \\ C_{4}-C_{5} & 1.42172 & 1.42172 & C_{8B}-C_{9B-C_{10}B & 118.7 (7) \\ C_{5}-C_{6} & 1.37334 & 1.37334 & C_{5B}-C_{10}B-C_{1B} & 119.4 (7) \\ C_{6}-C_{16} & 1.7600 & 1.7600 & & & & & & & & & & & & & & & & & & $	C17-C9	1.47000	1.3652	C ₆ B-H ₆ BA	0.9500				$C_8B-C_7B-C_{12}B$	119.8 (6)
$\begin{array}{ccccccc} C_{3}-C_{4} & 1.41887 & 1.39652 & C_{8}B-C_{9}B & 1.400 (11) & C_{7}B-C_{8}B-C_{9}B & 119.4 (7) \\ C_{4}-N_{15} & 1.42208 & 1.4236 & C_{8}B-H_{8}BA & 0.9500 & C_{7}B-C_{8}B-H_{8}BA & 120.3 \\ C_{11}-C_{12} & 1.41622 & 1.4235 & C_{9}B-C_{10}B & 1.429 (10) & N_{1}B-C_{9}B-C_{9}B & 117.0 (7) \\ N_{15}-C_{11} & 1.37289 & 1.33256 & N_{1}B-C_{9}B-C_{10}B & 118.7 (7) \\ C_{4}-C_{5} & 1.42172 & 1.42172 & C_{8}B-C_{9}B-C_{10}B & 118.7 (7) \\ C_{5}-C_{6} & 1.37334 & 1.37334 & C_{5}B-C_{10}B-C_{4}B & 119.3 (7) \\ C_{6}-C_{16} & 1.7600 & 1.7600 & & & & & & & & & & & & & & & & & & $	C ₉ -C ₃	1.42203	1.3256	C7B-C8B	1.359 (12)				$C_6B-C_7B-C_{12}B$	116.5 (7)
$\begin{array}{cccccccc} C_4 + N_15 & 1.42208 & 1.4230 & C_{8} B - R_{8} BA & 0.9300 & C_{7} B - C_{8} B - R_{8} BA & 120.3 \\ C_{11} - C_{12} & 1.41622 & 1.4235 & C_{9} B - C_{10} B & 1.429 (10) & N_{1} B - C_{9} B - C_{9} B & 117.0 (7) \\ N_{15} - C_{11} & 1.37289 & 1.33256 & N_{1} B - C_{9} B - C_{10} B & 118.7 (7) \\ C_{4} - C_{5} & 1.42172 & 1.42172 & C_{8} B - C_{10} B & 118.7 (7) \\ C_{5} - C_{6} & 1.37334 & 1.37334 & C_{3} B - C_{10} B - C_{4} B & 119.3 (7) \\ C_{6} - C_{16} & 1.7600 & 1.7600 & C_{5} B - C_{10} B - C_{4} B & 125.8 (7) \\ & & & & & & & & & & & & & & & & & & $	$C_3 - C_4$	1.41887	1.39652	C ₈ B-C ₉ B	1.400 (11)				C-B-C-B-L-BA	119.4 (7)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Cu-1N15	1.42208	1.4230	C8D-H8DA	1 429 (10)				UB-C8D-FI8DA	120.5
$\begin{array}{c} \label{eq:carbon} \labe$	N15-C11	1.37289	1.33256	C9D-C10D	1.727 (10)				N ₁ B-C ₉ B-C ₁₀ B	124.4 (7)
$\begin{array}{cccccccc} C_{3}C_{6} & 1.37334 & 1.37334 & 1.37334 & & & C_{5}B-C_{10}B-C_{9}B & 119,3 (7) \\ C_{6}-Cl_{16} & 1.7600 & 1.7600 & & & C_{5}B-C_{10}B-C_{4}B & 125.8 (7) \\ & & & C_{5}B-C_{10}B-C_{4}B & 125.8 (7) \\ & & & C_{5}B-C_{10}B-C_{4}B & 125.8 (7) \\ & & & C_{9}B-C_{10}B-C_{4}B & 114.9 (7) \end{array}$	C_4-C_5	1.42172	1.42172						C ₈ B-C ₉ B-C ₁₀ B	118.7 (7)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	C ₅ -C ₆	1.37334	1.37334						$C_5B-C_{10}B-C_9B$	119.3 (7)
$\begin{array}{c c} C_9B-C_{10}B-C_4B & 114.9\ (7) \\ \hline \\ Dihedral angles\ (^{\circ}) \\ N_{27}-C_{22}-C_{28}-H_{29} & -59.11679 & -80.3256 & C_9B-N_1B-C_2B-C_3B & 1.5\ (12) \\ N_{17}-N_{25}-C_{19}-S_{26} & -0.05197 & -0.02365 & C_2B-C_4B-C_1B & -179.5\ (6) \\ N_{17}-N_{25}-C_{19}-N_{27} & -179.97295 & -179.2356 & C_5B-C_6B-C_7B-C_{12}B & 179.9\ (6) \\ C_9-N_{17}-N_{25}-C_{20} & -90.85212 & -88.3625 & C_2B-N_1B-C_9B-C_8B & 178.4\ (7) \\ O_{32}-C_{20}-N_{25}-N_{17} & -0.00256 & C_7B-C_8B-C_9B-N_1B & -178.5\ (7) \\ C_8-C_8-C_4-N_{15} & 179.99158 & -179.0236 & C_6B-C_8B-C_9B & -178.5\ (7) \\ \end{array}$	C6-Cl16	1.7600	1.7600						C5B-C10B-C4B	125.8 (7)
$\begin{array}{c c c c c c c c c c c c c c c c c c c $									C_9B - $C_{10}B$ - C_4B	114.9 (7)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$						Dihedral angles ((°)			
$ \begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$						N27-C22-C28-H29	-59.11679	-80.3256	$C_9B-N_1B-C_2B-C_3B$	1.5 (12)
$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$						$N_{17}-N_{25}-C_{19}-S_{26}$	-0.05197	-0.02365	$C_2B-C_3B-C_4B-Cl_1B$	-179.5 (6)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$						$N_{17}-N_{25}-C_{19}-N_{27}$	-1/9.9/295	-1/9.2356	$C_5B-C_6B-C_7B-C_{12}B$	1/9.9 (6)
$C_{32}-C_{21}-1125-1117 - 0.00234 - 0.00230 - C_{12}-C_{32}-C_{$						022-C20 Nor No-	-90.85212	-00.3023	C2D-INID-C9B-C8B	1/0.4 (/) -178 5 (7)
						C6-C5-C4-N15	179.99158	-179.0236	C6B-C5B-C10B-C0B	-1.7 (11)

Physical Characterization

Moreover, the physical calculation boundaries of compound CQT (3) and CQP (4), like, absolute electronegativities (χ), global Softness (S), absolute

hardness, (η) absolute softness (σ), chemical potentials (*Pi*), global electrophilicity (ω) and additional electronic charge, (ΔN_{max}), were tabulated in Table 2 according to the Equations (2-8) and DFT/B3LYP/6-31G(d) used to optimize it (Dacrory and Fahim, 2020). The molecular

structure of these compounds was not planar. The potential activities presented in the precursor compounds COP (4) due to presence of tetrahydro-6-methyl-2thioxopyrimidin-4(1H)-one which increased the activity and more stability rather than COT (3) due to resonance of electrons and stability of ring attached to chloroquinone, Another point of view, The π isoelectronic structures of compound CQT (3) and CQP (4) utilizing DFT/B3LYP/6-311G(d) and HF/6-311G(d) basis set, whereas the difference in COT between two basis set (160 eV) (≈3800 kcal/mol), but the CQP (4) difference was (182.126 eV) (≈4199.92 kcal/mol) which these difference indicate the stability of CQP (4). Moreover, the dipole moment (μ) difference for HF and B3LYP/6-311G(d) basis sets for CQT (3) through (2.9217D) and COP (4) was (1.3353D) which indicate that the easily charge separation of CQP(4) (Atkins and De Paula, 2011) as shown in Table 2:

$$\Delta E = E_{LUMO} - E_{HOMO} \tag{1}$$

$$\chi = \frac{-\left(E_{LUMO} + E_{HOMO}\right)}{2} \tag{2}$$

$$\eta = \frac{\left(E_{LUMO} - E_{HOMO}\right)}{2} \tag{3}$$

$$\sigma = 1/\eta \tag{4}$$

$$Pi=-X$$
 (5)

$$S = 1/2\eta \tag{6}$$

$$\omega = Pi^2 / 2\eta \tag{7}$$

$$\Delta N_{\rm max} = -Pi / \eta \tag{8}$$

The absolute electronegativities (χ) which concept that designates the affinity of an atom to attract a mutual pair of electrons, the value of (χ) for CQT (3) was (5.798 eV) (\approx 133.71286 kcal/mol) and CQP (4) was (1.1574351 eV) (\approx 26.69107 kcal/mol), which confirm that the higher value of thiosemicarbazide CQT (3) which attract the atoms of ethylacetoacetate to form the tetrahydro-6-methyl-2-thioxopyrimidin-4(1*H*)-one (Yamamoto *et al.*, 1998).

The absolute hardness (η) which measure of the resistance to change in electron density around the molecule, CQT (3) difference between HF/6-311G(d) and DFT/B3LYP/6-31G(d) (2.1739519 eV) (\approx 50.13251 kcal/mol), also the CQP (4) different (3.1191 eV) (\approx 71.9258 kcal/mol) which the more electron density of CQP and stability of this compound (Yang and Parr, 1985).

Absolute softness (σ) indicate the interaction of the compound, the difference of CQT (3) (740.1817 eV) while CQP (4) was (244.0135 eV), the large difference for CQT indicate that the activity of CQT to react with ethylacetoacetate (Fahim *et al.*, 2020).

 Table 2: Ground state energies of compounds CQT (3) and CQP (4) utilizing DFT/B3LYP/6-311G(d) and HF/6-31G(d)and their physical parameters

 DFT/B3LYP/6-311G(d)
 HF/6-311G(d)

Compound CQT Compound CQP					Compound CQT	Compound CQP			
$E_{\rm T}$ (au)	-1464.32	216		-1692.634	E _T (au)	-1458.83632		-1685.9406	
$E_{\rm HOMO}$ (au)	-0.16212	2		-0.24111	E _{HOMO} (au)	-0.45510		-0.31274	
$E_{\rm LUMO}({\rm au})$	-0.10736	5		-0.10238	E _{LUMO} (au) -0.24055		1	0.05432	
Eg (eV)	1.49009	62		3.7750374	Eg (eV)	5.8382057		18.24796	
μ (D)	4.6871			8.9694	μ (D)	7.6088		10.3047	
χ (eV)	3.66646	39		4.67342172	χ (eV)	9.46480486		3.5159849	
η(eV)	0.74504	81		1.88751869	η(eV)	2.91910283		4.9941081	
σ(eV)	993.8419			392.2795	σ(eV)	253.6602097		148.26675	
P _i (eV)	-3.6664639		-4.67342172	$P_i(eV)$	-9.464804857		-3.5159849		
S(eV)	0.37252405		0.94369132	S(eV)	1.459551414		2.49705403		
ω(eV)	0.06763121107		0.027837261177	ω(eV)	0.0176574768		0.041688	0.04168867961	
ΔN_{max}	133.9102932		67.3727	ΔN_{max}	88.22752		19.157369		
Net charges	N ₁₈	-0.384	N_{17}	-0.465	Net charges	N ₁₈	-0.510	N_{17}	-0.544
	N ₁₉	-0.550	H_{18}	0.352		N ₁₉	-0.605	H_{18}	0.380
	H_{21}	0.295	N ₂₅	-0.497		H_{21}	0.335	N_{25}	-0.680
	C ₂₂	-0.119	C19	0.124		C ₂₂	-0.004	C19	0.320
	H ₂₀	0.330	S ₂₆	-0.018		H_{20}	0.377	S_{26}	-0.084
	S ₂₃	0.056	N ₂₇	-0.681		S ₂₃	0.186	N_{27}	-0.890
	N ₂₄	-0.679	H ₂₃	0.398		N ₂₄	-0.812	H ₂₃	0.449
			C ₂₂	0.390				C ₂₂	0.509
	^a Eg = $E_{\rm I}$	$UMO - E_{HOMO}$							

Table 3: The calculated Mullikar	and NBO charges of CQT (3) an	d CQP (4) utilizing DFT/ B3LYP/6-311G(d)

DFT/ B3LYP/6-311G(d)

Total Mu	llikan charges			NBO Charges				
Compound CQT		Compound	Compound COP		Compound CQT		Compound COP	
C1	-0.073	C1	0.079	C1	-0.228	C1	-0.221	
C_2	-0.062	C_2	-0.005	C_2	-0.186	C_2	-0.146	
C3	-0.191	C3	-0.072	C3	-0.087	C3	-0.094	
C_4	-0.434	C_4	0.116	C_4	0.202	C_4	0.177	
C5	-0.071	C5	-0.011	C5	-0.277	C5	-0.278	
C_6	-0.308	C_6	-0.294	C_6	-0.031	C_6	-0.018	
H_7	0.171	Cl ₁₆	0.003	H_7	0.221	Cl_{16}	-0.002	
H_8	0.176	H_{10}	0.189	H_8	0.232	H_{10}	0.240	
Cl ₁₇	-0.015	H_7	0.181	Cl ₁₇	-0.016	H_7	0.225	
H_{10}	0.173	H_8	0.195	H_{10}	0.217	H_8	0.195	
N16	-0.830	N15	-0.422	N16	-0.566	N15	-0.438	
H_{13}	0.341	C11	0.039	H_{13}	0.410	C11	0.053	
C11	-0.124	C12	-0.168	C11	-0.005	C12	-0.267	
H_{14}	0.176	C9	0.209	H_{14}	0.205	C 9	0.184	
C11	0.124	H_{13}	0.176	C11	-0.005	H_{13}	0.201	
C12	-0.129	H_{14}	0.185	C12	-0.223	H_{14}	0.226	
H_{15}	0.131	C ₁₂	0.168	H_{15}	0.217	C ₁₂	-0.267	
C9	0.342	N17	-0.465	C 9	0.148	N17	-0.457	
N18	-0.384	H_{18}	0.352	N18	-0.337	H_{18}	0.388	
N19	-0.550	N ₂₅	-0.497	N19	-0.614	N ₂₅	-0.457	
H_{21}	0.295	C19	0.124	H_{21}	0.332	C19	-0.270	
C ₂₂	-0.119	S ₂₆	-0.018	C ₂₂	0.158	S ₂₆	0.212	
H_{20}	0.330	N27	-0.681	H_{20}	0.352	N27	-0.137	
S ₂₃	0.056	H ₂₃	0.398	S ₂₃	-0.018	H ₂₃	-0.590	
N ₂₄	-0.679	C ₂₂	0.390	N ₂₄	-0.854	C ₂₂	0.270	
H ₂₅	0.325	C ₂₁	-0.298	H25	0.365	C21	0.335	
H ₂₆	0.336	C20	0.577	H_{26}	0.372	C20	0.578	
		O32	-0.396			O32	-0.577	
		H_{24}	0.204			H_{24}	0.249	
		H ₂₉	0.217			H ₂₉	0.216	
		H ₃₁	0.2220			H ₃₁	0.224	
		C ₂₈	0.610			C ₂₈	-0.596	
		C22	0.390			C22	0.772	

Mullikan and NBO Atomic Charges

Mullikan and NBO of compounds CQT (3) and CQP (4) were calculated utilized the DFT/B3LYP/6-311G(d) basis set as displayed in Table 5. For the compound the Mullikan charges of CQT(3) showed that $N_{16}(-0.830)$ and $N_{24}(-0.679)$ of more negative charges, while the $C_9(0.342)$, also the NBO charges of the same compound seemed at N₁₆(-0.566), N₂₄(-0.854) and C₉(0.148) which indicated that the N₁₆ and N₂₄ are the most electrophilic the thiosemicarbazide attached centers of to chloroquinoline moiety and the attached Carbon C9 of chloroquinone which act as nucleophilic susceptibility center which make stability of quinolone ring as displayed in Table 3. Furthermore, the Mullikan and NBO charges of CQP (4) compound showed the most electrophilic negative center of moiety of tetrahydro-6methyl-2-thioxopyrimidin-4(1*H*)-one moiety which attached to quinolone ring which showed the $N_{17}(-0.465)$,

 $N_{25}(\text{-}0.497),\ S_{26}(\text{-}0.018)$ and $N_{27}(\text{-}0.681)$ for Mullikan while $N_{17}(\text{-}0.457),\ N_{25}(\text{-}0.457),\ S_{26}(0.212)$ and $N_{27}(\text{-}0.137)$ which meant that the stability of thiopyrimidine moiety with quinolone ring (Ibrahim and Mahmoud, 2009).

Frontier Molecular Orbitals (FMO) and Molecular Electrostatic Potential Maps (ESP)

The electrical and optical properties can be inferred through chemical reactions and ultraviolet spectra, but FMO is an amazing guideline method for identifying these properties. Time-Dependent Functional Density Theory (TD-DFT) is used for studying FMO principles (Griffith and Orgel, 1957) The highest occupied HOMO molecular orbital acts as an electron donor and the LUMO lowest unoccupied molecular orbital acts as an electron acceptor مرجع. The energy difference between HOMOs and LUMOs related to the biological activity of the molecule (Dennington *et al.*, 2009). Additionally, it

helps in describing the molecule reactivity and kinetic stability. The high kinetic stability is due to the large energy gap between HOMO-LUMO (Gaussian09, 2009). Figure 6 illustrates the distributions and energy levels of the HOMO, LUMO and orbitals computed at the B3LYP/6-311G (d) level for CQT and CQP. The positive and negative phases were symbolized in red and green colors, respectively. As shown in Fig. 4, the HOMO of compound CQT was localized in the fused of quinolone ring and its LUMO was localized in the Natom of quinolone moiety, the value of the energy gap between the HOMO -LUMO is (1.49 eV). Furthermore, the HOMO and LUMO of CQP was localized on Sulphur atom of tetrahydro-6-methyl-2-thioxopyrimidin-4(1H)-one ring with difference in band energy (3.77 eV). This energy gap between HOMO-LUMO indicates the high excitation energies for a lot of excited states and reactivity of these compounds. Moreover, molecular reactivity and biological recognition interactions can be studied by the molecular Electrostatic Potential (ESP) that the nuclei and electrons of a molecule create in the surrounding space (Fukui, 1982). So, the 3-(7chloroquinolin-4-ylamino)-tetrahydro-6-methyl-2thioxopyrimidin-4(1H)-one (4) (CQP) designate a certain point then gather this to remaining surface, indicates that there is a uniform distribution of surface

contour to fused quinolone, whereas the methyl-2thioxopyrimidin-4(1*H*)-one moiety contains the C = Oand C = S which acts as electrophilic centers which induced more protonation and gave more reactivity in the biological interaction and in the binding sites of proteins in molecular docking (Schlegel, 1982) as demonstrated in Fig. 4.

Biological Investigation

Antimalarial Activity

The investigated compounds CQT (3) and CQP (4) were previously treated against action of *P. falciparum* as displayed in Table 4. The CQT and CQP showed higher antimalarial activity in yield for CQT with (80% yield, $IC_{50} = 25.37 \ \mu g/mL$) and CQP (87% yield, $IC_{50} = 11.92 \ \mu g/mL$) as shown in Table 4 and Fig. 5. The preliminary SAR study of CQP has focused on the influence of occurrence methyl-2-thioxopyrimidin-4(1*H*)-one moiety attached to chloroquinoline and make more polarizable of electrons and enhancing their antimalarial activities, while the CQT with low activity due to presence of NH₂ attached of C = S of thiosemicarbazide and more electrons center which increase the activity (Bawa *et al.*, 2010).

Table 4: The invirto- antimalrial activity of CQT and CQP against plasmodium falciparum

IC ₅₀
25.37
11.92
0.18

CQ: Chlroquinone drug



Fig. 4: FMO and ESP of CQT and CQP at (TD-DFT) B3LYP/ 6-311G (d) basis sets

Molecular Docking Studies

A molecular modeling study was carried out to explain the cytotoxic activity profile demonstrated by the synthesized compounds. A conformational search using an implicit solvent model was accomplished for the prepared compounds; this was monitored by the refinement of the geometry of local minima through a Quantum-Mechanical (QM) (Morris et al., 2009). Consequently, adaptable docking of the compounds was cultivated in the crystal structure of the (PDBID: 6LU7 Version 2, 2.16 Å resolution, CQP (4) was stimulated with functions as a homo dimer (Jin et al., 2020) and leads that target main protease (Mpro) of SARS-CoV-2: Mpro is a key enzyme of coronaviruses and has a pivotal role in mediating viral replication and transcription, making it an attractive drug target for SARS-CoV-25,6 (Jo et al., 2020). The docking simulation of CQT and CQP with (PDBID: 6lu7) as shown in Table 5 and Fig. 6 to evaluate the binding interaction energy and the distance between protein's and it was shown that the (PDBID: 6lu7) attached to CQP with ($\Delta E = -14.4383$ Kcal/mol, 2.337Å) with Hydrogen bonding with amino acid Pro132 of NH

group rather than the COT attched with binding energy $(\Delta E = -12.2755 \text{ Kcal/mol}, 3.576\text{Å})$ and attched to chloroquinoline with Phe294. We identified a mechanismbased inhibitor (N3) through docking stimulation and determined that the crystal structure of Mpro of SARS-CoV-2 in complex with CQT and CQP. Through a combination of structure-based virtual and highthroughput screening, Furthermore, crystal structure of a protein of unknown function TA1206 from thermoplasma acidophilum (PDBID: 1qw2O) (Pathare et al., 2017) which contain of single unique chain 1qw2(A) (102 residues long) (Pathare et al., 2017). The compounds COT and CQP were docked with (PDBID: 1qw2) with binding interaction energy ($\Delta E = -6.66$, -13.61 kcal/mol); respectively and with short bond distance og CQP with 2.51Å with NH between chloroquinone and tetrahydro-6methyl-2-thioxopyrimidin-4(1H)-one ring which confirmed this H-proton the most active in mobilization of electrons and increase the biological evaluation of Compound CQP rather than CQT which its docking ability with (PDBID: 1qw2) with NH₂ groups and bond distance 3.21Å as shown in Table 5 and Fig. 6.

Table 5: Docking of CQT(3) and CQP(4) with (PDB ID: 6lu7) and (PDBID:1q2w):

I dole et Boening of eQ		51 01a (1 B B 1				
Compound	Energy affinity (kcal/mol)	Distance (Å)	Amino acids			
PDBID: 6lu7						
CQT	-12.2755	3.576	Gln110,Ph294,Asn 151, Ser158, Asp153 and Asn 133			
CQP	-14.4383	2.337	Pro132, Thr196, Asp153, Asn 133, Glu240 and Thr 198			
PDBID: 1q2w(Chain A)						
CQT	-6.6601	3.21	Pro108, His 246, GlnA107			
CQP	-13.6197	2.51	Pro A108, GluA240, HisA246 and Leu202			



Fig. 5: The antimalarial concentration of CQT (3) and CQP (4)



Fig. 6: Binding docking modes of CQT, CQP with (a) PDBID: 6lu7 and (b) PDBID:1qw2; respectively

Experimental

General Procedure

Melting points were measured with a Gallen Kamp melting point apparatus. Silica-gel-coated aluminum plates used to test the purity of the compounds. Infrared spectra (λ -cm⁻¹) were recorded on Bruker Vector (Germany) and on Mattson FT-IR 1000 (Cairo University, Egypt), using KBr disks. ¹H NMR spectra were recorded on Gemini 300 MHz, ¹³CNMR spectrometer, in DMSO-d₆ using dimethyl sulfoxide as a solvent and tetramethylsilane (TMS) as an internal standard (Chemical shift in δ , ppm); ¹³C NMR spectra were recorded on Gemini 50 MHz NMR spectrometer. Mass spectra were measured on GCO Finnigan MAT and Elemental analyses were performed at the micro analytical Center, Cairo University, Giza, Egypt. Biological activity was determined in a laboratory by the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Cairo, Egypt. All the chemicals were purchased from Sigma-Aldrich.

Synthesis of 2-(7-Chloroquinolin-4yl)Thiosemicarbazide (3)

An ethanolic solution of 4,7-dichloroquinoline (1) (0.196 g, 0.01 mol) with thiosemicarbazide (2) (0.096,

0.01 mole) were stirred in ultrasonic apertures at room temperature for 30 min, then monitoring TLC to know the reaction was finished then add CH₃Cl and washed with solution NaOH solution to afford the organic layer and aqueous layer. Then the crude poured on ice bath to afford 2-(7-chloroquinolin-4-yl)thiosemicarbazide (3): yellow soild which was washed with ether and dried. Yield: 80%; mp 278-280°C, Rf = 0.38 (1:2 EtOAcpetroleum ether); IR (KBr) cm^{-1} :3390-3266 (NH₂), 3150 (NH), 1615 (C = N), 1585 (NH_{bend}), 1235 (C-N), 1212 (C = S), 758 (C-Cl); ¹H NMR(300 MHz, DMSO d_{6}) δ 8.89(d, J = 5.48 Hz, 1H,N = CH, quinoline), 8.57(d, J = 8.48 Hz, 1H, Ar-H), 8.54(s, 1H, Ar-H), 8.26(d, J = 8.43 Hz, 1H, Ar- H), 8.20 (s, 2H, NH2), 8.10 (s, 1H, ArC-NH), 7.93(d, J = 5.42 Hz, 1H, Ar-H), 7.86 (s, 1H, NH); 13C NMR(50 MHz, DMSO-d₆) 181.22, 158.22, 155.72, 149.02, 148.14, 138.50, 128.42, 127.65, 120.03, 18.34. Mass spectra (M^{\pm}) m/z = 252. Anal. Calcd for C10H9ClN4S: C,47.53; H, 3.59; N, 22.17. Found: C, 47.33; H, 3.52; N, 22.09%.

Reactivity of 2-(7-Chloroquinolin-4yl)Thiosemicarbazide (3) with Ethyl Acetoacetate

Ultrasonic reaction of compound (3) (0.25 g, 0.01 mol) with ethylacetoacetate (2 mL, 0.01 mol) in water bath for 40 min at 90°C, the solid product was formed

and filtered to afford the corresponding product (4) and crystallized with EtOH 3-(7-chloroquinolin-4-ylamino)tetrahydro-6-methyl-2-thioxopyrimidin-4(1*H*)-one (4): Brown crystals which was washed with ether and dried. Yield: 87%; mp 250-252°C Rf = 0.48(1:2 EtOAcpetroleum ether); IR (KBr) cm^{-1} : 3110 (NH), 1674 (C = O), 1618 (C = N), 1587 (NH bend), 1237 (C-N), 1211 (C = S), 760(C-Cl) : 1H NMR(300 MHz, DMSO-d₆): δ 8.20 (d, J = 5.38 Hz,¹HN = CH quinoline) 8.10 (s, ¹H, NH); 7.85 (d, J = 8.32 Hz, ¹H, Ar-H), 7.82 (s, ¹H, Ar-H), 7.18 $(d, J = 5.38 \text{ Hz}, 1\text{H}, \text{Ar-H}), 7.15 (d, J = 5.38 \text{ Hz}, {}^{1}\text{H}, \text{Ar-H})$ H), 2.50 (s, 2H, CH₂), 2.17 (s, 3H, CH₃); ¹³C NMR (50 MHz, DMSO-d₆) δ 181.36,166.23, 156.96, 151.13, 149.15, 141.30, 138.57, 122.23, 119.52, 118.17, 115.31, 113.80, 91.21, 48.79. Mass spectra (M^{\pm}) m/z = 318. Anal. Calcd.for C14H11N4ClOS:C, 52.75; H, 3.48; N. 17.58. Found: C, 52.91; H, 3.32; N,17.71%.

Determination of Antimalarial Activity

Cultures of P. falciparum were measured according to a protocol from (Moloney et al., 1990; Trager and Williams, 1992). The percentage of Inhibition was studied the 50% inhibitory concentrations (IC₅₀) was measured and the data got from the inhibitordependent concentration growth curves were registered into plots with nonlinear retreating analysis from y-axis (inhibition %) to x-axis (inhibitor concentration) (Singh et al., 1997) P. falciparum isolate NF54 was maintained in continuous culture with gentamicin (40 µg/mL) in Petri dishes (5 cm in diameter) with a gaseous phase of 90% N₂, 5% O₂ and 5% CO₂, according to a protocol from (Molonev et al., 1990; Trager and Williams, 1992) P. falciparum parasites were cultured in human erythrocytes (blood group A+ at 10% (v/v) hematocrit) in RPMI 1640 medium (Sigma) supplemented with 25 mM HEPES, 20 mM sodium bicarbonate and 10% heat-inactivated human A+ plasma. The culture was routinely monitored through Geimsa staining of the thin blood smears. The parasitemia of the infected erythrocytes was determined in Giemsa-stained smears by light microscopy. Parasitemias and morphological changes detected in the cultures were scored visually with a 100-fold oilimmersion objective, counting at least 1000 erythrocytes to determine the percentage of the infected erythrocytes (Kaiser et al., 2003). Antimalarial activity assay: The experiments were performed in 96-well culture plates (Nunc); compounds were tested at two-fold dilutions in a dose-titration range of 500 to 2 µM. One hundred microliters of infected human red blood cell suspension (1% parasitemia, 4% hematocrit), with more than 90% of ring forms, were added to each well containing 100 mL of extracts pre-diluted in RPMI-1640. Test plates were incubated for 48 h. Parasite multiplication was determined microscopically after Giemsa staining and expressed as a percentage of the controls without test compounds. A drug-free control (methanol/water 50:50% v,v) was used in all experiments and CQ (0.01 μ M) was used as the standard reference drug. Parasitemia and stage distribution were estimated as triplicates daily from Giemsa-stained smears by counting 1000 erythrocytes (Noedl *et al.*, 2002).

Computational Procedures

Calculations of DFT with a hybrid functional B3LYP (Becke's three-parameter hybrid functional using the BLYP correlation functional) with the 6-311G(d) basis set and Hartree-Fock calculations with the 6-311G(d) basis set using the Berny method (Jamróz, 2013), were performed with the Gaussian 09 W program (Ditchfield, 1972). No symmetry constraints were applied during the geometry optimization. The harmonic vibrational frequencies were calculated at the same level of theory for the optimized structures to prove the optimized structures as true minimums and confirm that no imaginary frequency occurs. The wideranging assignments of the vibrational modes were accomplished on the basis of the Potential Energy Distribution (PED), calculated using Vibrational Energy Distribution Analysis (VEDA) program (Foresman and Frish, 1996).

Molecular Docking

The molecular model of innovative sulfonamide derivatives was fabricated using standard bond lengths and angles, with the AutoDock Vina and detected by Discovery Studio Client (version 4.2). Following geometry optimization, a systematic conformational examine was supported out to an RMS gradient of 0.01 Å, with energy minimization of the resultant conformations employing the Confirmation Examination module implemented in Auto Dock Vina. The experimental Structure of Mprofrom SARS-CoV-2 and discovery of its inhibitors (PDBID: 6lu7) (Jo et al., 2020) and Crystal structure of a protein of unknown function ta1206 from thermoplasma acidophilum (PDBID: 1qw2) (Pathare et al., 2017). Missing hydrogens were added to the enzyme and partial charges were considered. After removing the co-crystallized inhibitor, validation monitored by docking of the compounds were carried out by AutoDock Vina and viewed by Discovery Studio Client (version 4.2) (Morris et al., 2009). The goal protein was kept inflexible, while the ligands were disappeared permitted to determine the conformational space exclusive the enzyme cavity; Twenty dispersed docking simulations were run via default parameters and the confirmations were designated constructed on the arrangement of total statistics, E conformation and appropriate with the relevant amino acids in the binding pocket.

Conclusion

In this study, the synthesis of some novel chloroquinoline derivative using green methodology, the synthesized compounds were exhibited high antimalarial activities. The SAR relationship related to the most active compound was CQP (4) with $IC_{50} = 11.92 \mu g/ml$ and due to cyclized tetrahydro-6-methyl-2-thioxopyrimidin-4(1H)one ring attached to chlorine ring. The optimized molecular structure of compounds COT and COP utilizing of DFT/B3LYP/6-311G(d) and HF/6-311G(d) basis's set, approves their stability and the geometric parameters suggestions between the calculated and the experimental data values indicate that B3LYP basis set is better than the HF method in approximating bond lengths and in evaluating energy, Mullikan and NBO charges. Furthermore, the COT and COP were docked against (PDB ID: 6lu7) and (PDBID: 1q2w) and showed the NHhydrogen: 2.337Å of CQP with (Mpro) of SARS-CoV-2. So for further biological investigation we will test these compounds and other quinolone derivatives in treatment of SARS-Covid-19.

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Author's Contributions

Asmaa Aboelnaga: Preparation of organic compounds and main corresponding author.

Asmaa M. Fahim: Make theoretical studies and elucidation the main idea of manuscript.

Taghreed H. EL-Sayed: Synthesis the organic compounds and revise the manuscript.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues involved.

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