Development of New Thiazole Complexes as Powerful Catalysts for Synthesis of Pyrazole-4-Carbonitrile Derivatives under Ultrasonic Irradiation Condition Supported by DFT Studies

Mahmoud Abd El Aleem Ali El-Remaily,* Tarek El-Dabea, Mohammed Alsawat, Mohamed H. H. Mahmoud, Alia Abdulaziz Alfi, Nashwa El-Metwaly,* and Ahmed M. Abu-Dief*

Cite This: ACS Omega 2021, 6, 21071−21086

ABSTRACT: In this study, we are interested in preparing Fe(III), Pd(II), and Cu(II) complexes from new thiazole derivatives. All syntheses were elaborately elucidated to estimate their molecular and structural formulae, which agreed with those of mononuclear complexes. The square-planer geometry of Pd(II) complex (MATYPd) was the starting point for its use as a heterocatalyst in preparing pyrazole-4-carbonitrile derivatives 4a−o using ultrasonic irradiation through a facile one-pot reaction. The simple operation, short-time reaction (20 min), and high efficiency (97%) were the special advantages of this protocol. Furthermore, this green synthesis strategy was advanced by examination of the reusability of the catalyst in four consecutive cycles without significant loss of catalytic activity. The new synthesis strategy presented remarkable advantages in terms of safety, simplicity, stability, mild conditions, short reaction time, excellent yields, and use of a H2O solvent. This catalytic protocol was confirmed by the density functional theory (DFT) study, which reflected the specific characteristics of such a complex. Logical mechanisms have been suggested for the successfully exerted essential physical parameters that confirmed the superiority of the Pd(II) complex in the catalytic role. Optical band gap, electrophilicity, and electronegativity features, which are essential parameters for the catalytic behavior of the Pd(II) complex, are based mainly on the unsaturated valence shell of Pd(II).

1. INTRODUCTION

Heterocyclic compounds of pyrazoles class are known by their importance in pharmaceutical targets and medicinal interest. Organic derivatives enriched by S and/or N atoms have a broad spectrum of biological activities such as antimicrobial, antioxidant;1,2 anti-HIV, anticancer,3 anticonvulsant,4 antimalarial, anti-inflammatory,5 and antidepressant.6 The ultrasonic state increases the rate of organic changes in mild conditions that otherwise require strict pressure and temperature conditions.7 Ultrasonic irradiation is also used to promote the formation, growth, and implosive collapse of bubbles in a liquid8 by various synthesis reactions. Initiated by cavitation, bubble collapse causes high stresses, extreme local heating, and very short lifetimes. Cavitation acts as a way of focusing the sound's scattered energy.9,10 Ultrasound irradiation can cause several reactions by providing activation energy, in contrast to traditional heating that provides thermal energy in the macro system.10b Other benefits of ultrasound irradiation include high product yields, low reaction times, minimization of side products,10b and nontoxic and environment-friendly solvents,11 saving money and energy.

Previously variable methods involved synthesis of many pyrazole-4-carbonitrile derivatives via the one-pot multicomponent reaction (MCR) among arylaldehydes, malononitrile, and phenylhydrazine using appropriate catalysts.12 The significance of such compounds and relevance of such timely topics in organic synthesis were the use of ionic liquids13 and the need for green reaction approaches.14 The benefit of pyrazoles in drug designing has continuously trapped the pursuit for novel and advanced methods.15 Therefore, a novel protocol with a good and inexpensive catalyst demanding short reaction times is well desired.16,17

In any of the abovementioned previous studies, pyrazole-4-carbonitrile derivatives catalyzed by new Pd(II) complexes under mild conditions have not been reported. Coinciding with outlined strategies and continuation of our work, we intended to achieve another success in the catalytic history of Pd(II) complexes by synthesizing bioactive heterocyclic compounds via multicomponent reactions. Because of the the merits of being environmentally benign, readily accessible, and cost-effective,
the Pd(II) complex seems to be a promising reusable catalyst in facile one-pot synthesis of pyrazole-4-carbonitrile derivatives 4a–o through a three-component coupling reaction (involving an aromatic aldehyde, malononitrile, and phenylhydrazine) under mild conditions. All products were isolated in distinguished yields within a short time. The catalytic reactivity of the selected complex was enhanced by the computational features of the DFT/B3LYP method.
2. EXPERIMENTAL SECTION

2.1. Chemicals and Techniques. All utilized materials and solvents implemented in this study were available from Sigma-Aldrich or Alfa Aesar and used as obtained. The characterization of the devices used and measurement conditions are stated in Supporting Information (part 1), while other conditions are listed in the discussion part, separately.

2.2. Synthesis of the MATY Ligand. 2,4-Thiazolidinedione (10 mmol in 10 mL of hot EtOH) was reacted with a mixture of 4-anisaldehyde, malononitrile (10 mmol in 10 mL of hot EtOH), and piperidine (20 mmol). The resulting solution was refluxed for 2 h. The product was separated out by filtration and its purity was checked by TLC. MATY: 2-amino-6-oxo-3-(piperidinylamidino)-4-(4-methoxyphenyl)-6,7-dihydro-pyran-2,3-diones, molecular formula C_{19}H_{21}NOS (386), m.p.: 233 °C. Color: pale yellow. Anal. calc’d (%): C 59.12, H 5.71, N 14.53; found (%): C 59.06, H 5.7, N 14.50. Solubility: ethanol. IR (KBr pellet, cm\(^{-1}\)):
- ν(C=O) 1711, ν(C–N) 1684, ν(C–H) 2931, 2859, 2713, 1683, ν(NH) 3429 (C=O), 3324 (NH), and
- ν(C–O) 1255 cm\(^{-1}\).

2.3. Synthesis of Metal Ion Complexes. An ethanolic solution of thiazole derivative (MATY) was reacted with an equimolar ratio of MATY and Pd(OAc)\(_2\) to yield a complex, molecular formula C_{23}H_{30}N_{4}O_{8}SPd (628.4), decom.t.: 285 °C. Color: brown.Anal. calc’d (%): C 41.92, H 5.77, N 8.55; found (%): C 41.97, H 5.77, N 8.51.

2.4. Kinetic and Thermodynamic Parameters’ Calculations. To identify the thermal stability of the tested complexes under the impact of a constant heating rate, TGA was introduced. Besides, the metal percentage in the composition is also involved. Furthermore, the thermal system is kinetically governed and kinetic or thermodynamic factors (\(E, A, \Delta S, \Delta H\) and \(\Delta G\)) can be assessed using the Coats–Redfern method.\(^{19,20}\)

\[
\log\left[\frac{\log(\alpha)}{T^2}\right] = \log\left[\frac{AR}{\alpha E^*}\left(1 - \frac{2RT}{E^*}\right)\right] - \frac{E^*}{2.303RT}
\]

From the left part of the above equation and the \(1/T\) value, \(A\) and \(E^*\) can be attained from the intercept and slope, respectively. Then, the thermodynamic parameters (\(\Delta H^*, \Delta S^*,\) and \(\Delta G^*\)) can be calculated by applying the following relations. \(\Delta S^* = 2.303R\log(\Lambda/K_\alpha T)\) and \(\Delta H^* = E^* - RT\) and \(\Delta G^* = \Delta H^* - T\Delta S^*\).

2.5. Stoichiometry and Formation Constants of Complexes in Solution. By implementing Job’s method of dissolving the sample in various proportions (10% of total, 20% of total, 30% of total, etc.), we studied the stoichiometry and stability of the complexes in the solution state, which may agree with the values in their solid form. Homogenized and clear solutions prepared (M and L) were left to balance, and then the absorbance was taken and plotted versus either ([L]/[L] + [M]) or ([L]/[M]). From spectrophotometric analyses, the consistency parameter (K\(_f\)) of the complexes formed in solution was calculated by the continuous variation route, according to the relation\(^{8,23}\): \(K_f = AAm/(1 - A/Am)^2\), where [Am], [A], and [C] are the absorbance at optimum consistency of the complex, the absorption value along both sides of the absorption curve, and the molar concentration of the metal, respectively.

2.6. Molecular Modeling Study. Using Materials Studio package,\(^{24}\) geometry optimization was executed for the ligand and its complexes to assess the mode of bonding and structural stability. This modeling was carried out by the DMOL3 program using the DFT method, which was adjusted at the DNP basis set.\(^{25}\) The method was used without constraints under the exchange-correlation functional of Becke3–Lee–Yang–Parr (B3LYP) using GGA and RPBE functions.\(^{26}\) The positive value of frequency is the indicator for the suitability of the optimized structures. Time-dependent DFT (TD-DFT) was proceeded by implementing a polarizable continuum model. Also, using the integral equation formalism variant (IEF-PCM), which was executed at the B3LYP level, we studied the properties of ground or excited states.\(^{27}\)

2.7. Heterogeneous MATYPd Complex Catalyzed the Synthesis of Pyrazole-4-Carbonitrile Derivatives 4a–o.

In a rounded flask, aqueous solutions of aromatic aldehyde 1 (1 mmol), malononitrile 2 (1 mmol), phenylhydrazine 3 (1 mmol), and MATYPd complex (0 mol %) were mixed in 30 mL of H\(_2\)O under stirring (at 25 °C), and then at 20 kHz frequency and 40 W power at 80 °C; the sound was applied for the desired acceptable time (Scheme S2). After finishing the reaction according to the thin-layer chromatography test (TLC), the reaction mixture was allowed to cool to room temperature and the catalyst was filtered. The organic material was extracted with ethyl acetate (3×10 mL), and pyrazole-4-carbonitrile derivatives 4a–o combined with the organic phase were washed with water, dried over anhydrous Na\(_2\)SO\(_4\), and concentrated under reduced pressure. The resulting solid product was filtered and recrystallized from 10 mL of ethanol to give a pure product, which was first elucidated by its melting point and then characterized by IR and NMR spectra.

2.7.1. Catalyst Recovery and Reuse. Using a heterogeneous catalytic process, the MATYPd catalyst was easily separated by filtration and could be reused many times by the same efficacy approximately. The filtered complex was washed with ethanol.
and bi-distilled water. After drying at 90 °C (for 3 h), the catalyst was recycled for another run under typical reaction conditions.

2.7.2.2. **Compound 4b.** White solid (M. P. = 107°–109° C), IR (KBr) cm⁻¹ = 3314, 2366, 1595, 1244; ¹H NMR (400 MHz, DMSO-d₆) δ = 3.77 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 6.71 (t, J = 7.6 Hz, 2H, ArH), 6.59 (d, J = 8.76, 2H, ArH), 6.93 (d, J = 8.00, 2H, ArH), 7.19 (t, J = 7.84, 2H, ArH), 7.57 (d, J = 8.76 Hz, 2H, ArH), 7.81 (s, 2H, NH₂); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 130.63, 144.93, 143.44, 137.43, 128.10, 127.38, 127.10, 119.14, 111.41, 112.66, 99.98, 59.33, 55.35; EIMS (m/z) 290 (M)+.

2.7.2.3. **Compound 4c.** Brown solid (M. P. = 131°–133° C), IR (KBr) cm⁻¹ = 3482, 3411, 3120, 2830, 2545, 2233, 1650; ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 7.80–7.83 (m, 1H), 6.74 (s, 1H), 7.57–7.60 (m, 2H), 7.23–7.26 (m, 1H), 7.10 (d, J = 7.6, 2H), 7.01 (m, 1H), 6.89–6.93 (m, 2H), 6.85 (t, 1H) 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 150.03, 140.71, 134.33, 137.51, 137.42, 129.04, 127.31, 128.44, 118.92, 112.90, 113.44, 56.01; EIMS (m/z) 290 (M)+.

2.7.2.4. **Compound 4d.** White solid (M. P. = 121°–123° C), IR (KBr) cm⁻¹ = 3291, 2344, 1593, 1255; ¹H NMR (400 MHz, DMSO-d₆) δ = 3.79 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 6.71 (t, J = 7.2 Hz, 1H, ArH), 6.99 (d, J = 8.1, 1H, ArH), 7.05 (t, J = 6.6, 3H, ArH), 7.21 (t, J = 7.8, 2H, ArH), 7.47 (s, 2H, NH₂), 8.11 (s, 1H, ArH); ¹³C NMR (100 MHz, CDCl₃) δ: 55.65, 60.82, 111.86, 112.03, 113.33, 118.71, 124.14, 129.07, 131.76, 145.19, 146.32, 152.64.

2.7.2.5. **Compound 4e.** Brown solid (M. P. = 142°–144° C), IR (KBr) cm⁻¹ = 33055, 2348, 1601, 1254; ¹H NMR (400 MHz, DMSO-d₆) δ = 6.76 (t, J = 7.6 Hz, 1H, v), 7.11 (d, J = 8.3, 2H, ArH), 7.27–7.32 (m, 3H, ArH), 7.36 (t, J = 8.0, 1H, ArH), 7.45 (d, J = 7.9 Hz, 2H, ArH), 8.02 (d, J = 8.8 Hz, 1H, ArH), 8.23 (s, 2H, NH₂); ¹³C NMR (100 MHz, CDCl₃) δ: 112.16, 119.27, 125.79, 127.33, 129.05, 129.14, 129.66, 131.14, 131.91, 132.89, 144.81; HRMS of [C₁₆H₁₂ClN₄ + H⁺] (m/z): 295.0866; Calcd.: 295.08.

2.7.2.6. **Compound 4f.** White solid (M. P. = 128–130° C), IR (KBr) cm⁻¹ = 3461, 3382, 3131, 2522, 2251, 1662; ¹H NMR (400 MHz, CDCl₃) δ = 7.67 (s, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.29–7.34 (m, 2H), 7.16 (d, J = 7.6 Hz, 2H), 6.94 (t, J = 7.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 154.25, 143.42, 142.11, 142.31, 140.31, 130.00, 129.02, 127.23, 126.14, 119.40, 116.53.

2.7.2.7. **Compound 4g.** Yellow oil, IR (KBr) cm⁻¹ = 3462, 3410, 3141, 2542, 2221, 1650; ¹H NMR (400 MHz, CDCl₃) δ = 7.88–7.97 (m, 2H), 7.65 (s, 1H), 7.57–7.60 (m, 2H), 7.25–7.27 (m, 2H), 7.13 (d, J = 7.7, 1H), 6.91–6.95 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ = 157.55, 145.91, 140.01, 136.22, 138.45, 130.58, 129.01, 128.32, 127.41, 119.30, 116.56, 115.67, 113.35.

2.7.2.8. **Compound 4h.** Rose solid (M. P. = 162–164° C), IR (KBr) cm⁻¹ = 3304, 2355, 1598; ¹H NMR (400 MHz, DMSO-d₆) δ = 6.76 (t, J = 7.3 Hz, 1H, ArH), 7.04 (d, J = 8.0, 2H, ArH), 7.22 (t, J = 7.8, 2H, ArH), 7.55 (q, J = 7.9, 4H, ArH), 7.79 (s, 2H, NH₂); ¹³C NMR (100 MHz, CDCl₃) δ = 112.01, 118.95, 120.63, 127.41, 129.09, 131.51, 134.10, 135.09, 145.11; HRMS of [C₁₆H₁₄BrN₄ + 2H⁺] (m/z): 340.144; Calcd.: 340.146.

3. RESULTS AND DISCUSSION

3.1. Preliminary Properties. The analytical data obtained suggested the chemical formulae of Cu(II), Fe(III), and Pd(II)-thiazole complexes. The most fitted ratio was 1L:1M for all
colored complexes. All complexes were stable in air, non-hygroscopic, and insoluble in common solvents, but soluble in DMSO or DMF. Conductivity measurements exhibited values in the 5.12−24.85 (Ω cm−1 mol−1) range, which correspond to nonelectrolyte complexes.28

3.2. Infrared (IR) Spectroscopy. The IR spectra of the thiazole ligand (MATY) and its complexes were taken into account while using the KBr pellet technique over the 400−4000 cm−1 region to obtain information about the binding mode within the complexes (Figure S1). The MATY ligand presented a characteristic band of ν(NH) at 3402 cm−1. However, in MATYCu, MATYFe, and MATYPd complexes, the ν(NH) vibration was shifted to 3412, 3410, and 3429 cm−1, which indicates the coordination of the (NH) group with metal ions. Furthermore, the ligand spectrum exhibited bands at 3310−3220 cm−1 for ν(NH2) vibrations, which shifted to 3220, 3330, 3224, 3227, and 3429 cm−1 in the chelates, respectively. The peak at 1683 cm−1, which was assigned to the ν(C=O) vibration, was shifted to 1681, 1684, and 1682 cm−1 in the complexes, respectively. Moreover, the formation of MATYCu, MATYFe, and MATYPd complexes was determined by the presence of weak bands below 500 cm−1 corresponding to ν(M−O) and ν(M−N) vibrations.18 νas(OAc) and νs(OAc) in MATYCu and MATYPd complexes were assigned at 1500, 1270 cm−1 and 1480, 1270 cm−1, respectively, while νas(NO3) and νs(NO3) were assigned at 1530 and 1310 cm−1, respectively. The gap between two vibrations for both the acetate and nitrate groups (Δ = νas − νs) points to a monodentate mode of bonding for the acetate or nitrate anion.29

3.3. NMR Spectra. 1H NMR spectral data for MATY (Figure S3) and its MATYPd complex (Figure S4) were obtained in DMSO-d6 solvent. Signals of −NH and −NH2 protons were monitored to follow the effective synthesis of Pd(II) complex from [Pd(OAc)2] salt.31 A downfield shift of their signals was observed from 9.88 and 7.03 ppm in the MATY spectrum to 9.95 and 7.24 ppm in the MATYPd spectrum, respectively.18,30 Also, the 13C NMR spectrum of the ligand (Figure S2) displayed signals at 24.20, 25.86, 45.66, 51.18 (alph-C), 55.59 (OCH3), 56.38, 71.60, 114.63, 118.83, 129.59, 134.57, 152.47 (N−C=O, thiazol), 159.11 (N−C−O, pyran), 161.89 (N−C==NH), and 171.18 (C==O).

3.4. Electronic Spectroscopy. UV−Vis spectra of the thiazole ligand and its MATYCu, MATYFe, and MATYPd complexes were determined in DMF at 25 °C (Figure S5). The ligand spectrum exhibited an intense band at 295 nm, which is attributed to the n−π* transition inside C=No rC=O groups. For MATYCu, MATYPd, and MATYFe spectra, this band was slightly shifted to 310, 294, and 297 nm, respectively (Table S1). Also, the peaks at 397, 402, and 446 nm were attributed to the LMCT transitions, respectively. Besides, these complexes exhibited an intensity band around 730, 536, and 461 nm, assigned to the d−d transition, respectively. An irregular octahedral configuration was proposed for MATYFe and MATYCu complexes, whereas a square-planar geometry was proposed for the MATYPd complex.18,32 Using UV−Vis spectra, the optical band gap (Eg) can be calculated to measure the magnitude of separation between the valence band and the bottom of the conduction band. The lowest quantum (hν) used to raise an electron from its level and leave behind a positive hole despite the attraction forces in-between is the Eg value. A minimized band gap leads to overlapping of the conduction band with the valence band and the electrons have a high elasticity for excitation. The optical band gap that seems to be the separation between LUMO and

Figure 1. Optical band gap for (a) Cu(II), (b) Fe(III), and (c) Pd(II) complexes.
HOMO levels is an indicator of the activation energy values and semiconductor-like behavior.\textsuperscript{33} The $E_g$ value of a known semiconductor such as Si is 1.14 eV, which is considered low enough to clarify the extent of electron flexibility that is effective in catalytic behavior also. The values estimated for the studied complexes were 2.45, 2.54, and 2.65 eV for MATYPd, MATYFe, and MATYCu complexes, respectively. The value of the Pd(II)-thiazole complex reflects its effective catalytic role under lower activation energy as well as its promising semiconductor-like behavior. The values were estimated by using the following simple relations:\textsuperscript{33} $\alpha = 1/d \ln A$ (1), where $d$ is the cell width; $2 - \Delta h\nu = A(h\nu - E_g)^m$ (2), where $\alpha$ is the absorption coefficient and $A$ is the energy-independent constant. The direct or indirect transition was controlled by an $m$ value of 0.5 or 2, respectively; consequently, $\alpha$ values can be estimated from relation 1 and utilized in $(\Delta h\nu)^2$. Then, a relation was drawn between $(\Delta h\nu)^2$ and $h\nu$ (Figure 1), extrapolating the line for the first transition band to interact with the $x$-axis $[(\Delta h\nu)^2 = 0]$; $E_g$ value is the interacting point. Finally, the lower value reported for the MATYPd complex denotes its specific properties for solar cell, catalytic, and semiconductor uses.\textsuperscript{34}

3.5. Thermogravimetric and Kinetic Analysis. TGA curves for the tested complexes were obtained at a constant heating rate (5 °C min\textsuperscript{-1}) and under air atmosphere in the 25–800 °C range. Thermal data hypotheses are displayed in Table S2 and Scheme S1 to prove the proposed formulae and discriminate the connecting H\textsubscript{2}O molecules. All complexes exhibited the whole distortion up to four degradation steps extended to $\approx 750$ °C. The high thermal stability was documented after the first stage. This decrease indicates the involvement of crystal H\textsubscript{2}O molecules.\textsuperscript{35}

In each TGA curve, the kinetics and thermodynamic factors were evaluated over all degradation stages. The objective of this analysis is to evaluate the level of stability within the sphere of coordination and also the kinetic performance of the degradation reaction. The thermodynamic parameters are computed and listed in Table S2. In Coats–Redfern equations, fraction degradation functions ($\alpha$) at specific temperatures ($t$) were determined to measure the target parameters under a continual heating rate. The data lead directly to the following observations: the high activation energy ($E^*$, $-ve$) results signify a strong grade of bonding for such fragment; the values of ($\Delta S^*$) reflect the high-complexity degree in a nonspontaneous reaction.\textsuperscript{18,56,37}

3.6. Stoichiometry, Formation Constants, and pH Profile of the Complexes. By applying spectrophotometric methods (continuous variation and molar ratio), the most fitted stoichiometry of each metal chelate in solution was estimated (Figures S6 and S7). The stoichiometry was 1:1, in agreement with that proposed in solid form. The highest absorbance at a longer reaction time. But there was improved yield in the presence of the Pd(II) complexes, catalyst and ultrasonic irradiation environment, the yield of products was improved as clarified in Scheme 2. Series of aromatic aldehydes undergo electrophilic substitutions reactions are successfully synthesized in excellent yields as illustrated in Scheme 2.

3.7. Synthesis of Polysubstituted Pyrazole-4-Carbonitrile Derivatives 4a–6. The catalytic activity of Pd(II) complex was evaluated towards the synthesis of bioactive pyrazole-4-carbonitrile derivatives with ultrasonic irradiation conditions. In this context, a facile one-pot condensation reaction for three-component (1 mmol) of aromatic aldehyde 1, malononitrile 2 and phenylhydrazine 3, was designated as a model reaction. Through present experiments, improvement in condensation reaction was systemically studied based on the influence of catalyst dose, reaction-solvent, as well as different active Lewis acid catalysts.

In absence of catalyst and ultrasonic irradiation, the trace of the product was got at a longer reaction time. While ultrasonic irradiation was only used without a catalyst, the product was more efficient at a longer reaction time. But there was improved yield in the presence of the Pd(II) complexes, catalyst and ultrasonic irradiation environment, which appeared excellent after a short reaction period. In the presence of Pd(II) complexes and ultrasonic irradiation environment, the yield of products was improved as clarified in Scheme 2. Series of aromatic aldehydes undergo electrophilic substitutions reactions.
The efficiency of solvents was evaluated with the model reaction 4a. As indicated in Table 2, the polar protic solvents (MeOH, EtOH, AcOH, and H2O) were much better than aprotic solvents (DCM, DMF, THF, CH3CN, and CHCl3). The data reflect the much better solubility of the reactants in polar solvents. From Table 2, it is evident that the use of water as a solvent is obviously the best choice for the synthesis of pyrazole-4-carbonitrile derivatives 4a, which proceeded rapidly with the highest yield. This solvent is preferable because it is considered green, safe, and cheap in comparison with organic solvents.

### 3.7.3. Effect of Various Lewis Acid Catalysts

Recently, Pd(II) complexes have received considerable attention as a mild Lewis acid catalyst for an array of organic transformations. By the reaction of benzaldehyde 1, malononitrile 2, and phenylhydrazine 3 in the absence of catalyst and ultrasonic irradiation at the same condition, the trace product was obtained (Table 3, Scheme 2).
entry 1). While ultrasonic irradiation was only used without a catalyst, the product was more efficient at a longer reaction time (Table 3, entry 2). Various types of Lewis acids and Lewis bases such as AlCl₃, MgCl₂, FeCl₃·6H₂O, I₂, ZnBr₂, CuCl₂, CuO, Pd(OAc)₂, TiCl₄, PTSA, Et₃N, and TBABrc were tested in the selected reaction conditions. It was confirmed that the iron-soluble porphyrin catalyst was much better in comparison with all other Lewis acids due to its stability in water (Table 3, entries 3−14). When MATYCu, MATYFe, and MATYPd were tested (Table 3, entries 15−17), MATYPd was found to be the most effective catalyst, which afforded the desired product 4a by 97% yield (Table 3, entry 17). Use of MATYPd complex without ultrasonic irradiation at the same condition gave a lower yield (Table 3, entry 18).

3.7.4. Recycling of the Suggested Catalyst. The green and economic aspects of this synthetic protocol was further studied by examining the possibility of reusing the catalyst in the next runs of synthesis for derivatives. To do this, the progress of the model reaction at optimum conditions and in the presence of the MATYPd catalyst was repeated five times for synthesis of compound 4a, and there was found an inevitable loss of catalyst during the recovery process. The results summarized (Figure 3) show that the catalyst was reused for four consecutive cycles without a significant decrease in its activity, but during the next runs (5−8), a low catalytic activity was shown under the same conditions. IR spectra for the investigated MATYPd catalyst before and after the catalytic reaction are presented in Figure 4. It was noted that there is no notable change in the spectra of the investigated MATYPd catalyst after its recycling from the reaction medium.

3.7.5. Suggested Mechanism for the Investigated Catalytic Reaction. We proposed a plausible mechanism for the heterogeneous catalytic procedure to synthesize pyrazole-4-carbonitrile derivatives 4a−o.

| entry | catalyst (mol %) | yield (%) | conditions | solvent | time (min) | yield (%) |
|-------|-----------------|----------|------------|---------|-----------|----------|
| 1     | no catalyst     |          | water, 1 day | DCM     | 120       | 40       |
| 2     | no catalyst     |          | water, 1 h   | DCM     | 120       | 47       |
| 3     | AlCl₃ (10)      |          | water, 15 min | DCM     | 120       | 53       |
| 4     | MgCl₂ (10)      |          | water, 15 min | DCM     | 120       | 49       |
| 5     | FeCl₃·6H₂O (10) |          | water, 15 min | DCM     | 120       | 42       |
| 6     | I₂ (10)         |          | water, 15 min | DCM     | 120       | 47       |
| 7     | ZnBr₂ (10)      |          | water, 15 min | DCM     | 120       | 54       |
| 8     | CuCl₂ (10)      |          | water, 15 min | DCM     | 120       | 54       |
| 9     | CuO (10)        |          | water, 15 min | DCM     | 120       | 54       |
| 10    | Pd(OAc)₂ (10)   |          | water, 15 min | DCM     | 120       | 73       |
| 11    | TiCl₄ (10)      |          | water, 15 min | DCM     | 120       | 44       |
| 12    | PTSA (10)       |          | water, 15 min | DCM     | 120       | 54       |
| 13    | Et₃N (10)       |          | water, 15 min | DCM     | 120       | 67       |
| 14    | TBABr⁺ (10)     |          | water, 15 min | DCM     | 120       | 54       |
| 15    | MATYCu (10)     |          | water, 15 min | DCM     | 120       | 84       |
| 16    | MATYFe (10)     |          | water, 15 min | DCM     | 120       | 89       |
| 17    | MATYPd (10)     |          | water, 15 min | DCM     | 120       | 97       |
| 18    | MATYPd (10)     |          | water, 15 min | DCM     | 120       | 88       |

"Isolated yields based on 4a. bReaction conditions: 1a (1 mmol), 2 (1 mmol), and 3 (1 mmol) in water were heated at 80 °C under ultrasonic irradiation condition for 15 min.

| Table 1. Amounts of MATYPd Catalyst for the Synthesis of Pyrazole-4-Carbonitrile Derivatives 4a−o
| entry | catalyst (mol %) | yield (%) | conditions | solvent | time (min) | yield (%) |
|-------|-----------------|----------|------------|---------|-----------|----------|
| 1     | 3               | 16       | no US      | no catalyst | water, 1 day | trace   |
| 2     | 5               | 38       | no US      | no catalyst | water, 1 h | 49       |
| 3     | 6               | 57       | no US      | AlCl₃ (10) | water, 15 min | 42       |
| 4     | 7               | 77       | no US      | FeCl₃·6H₂O (10) | water, 15 min | 43       |
| 5     | 8               | 8        | no US      | I₂ (10) | water, 15 min | 51       |
| 6     | 9               | 5        | no US      | ZnBr₂ (10) | water, 15 min | 54       |
| 7     | 10              | 10       | no US      | CuCl₂ (10) | water, 15 min | 57       |
| 8     | 11              | 11       | no US      | CuO (10) | water, 15 min | 54       |
| 9     | 12              | 12       | no US      | Pd(OAc)₂ (10) | water, 15 min | 73       |
| 10    | 13              | 13       | no US      | TiCl₄ (10) | water, 15 min | 44       |
| 11    | 14              | 14       | no US      | PTSA (10) | water, 15 min | 67       |
| 12    | 15              | 15       | no US      | Et₃N (10) | water, 15 min | 64       |
| 13    | 16              | 16       | no US      | MATYCu (10) | water, 15 min | 84       |
| 14    | 17              | 17       | no US      | MATYFe (10) | water, 15 min | 89       |
| 15    | 18              | 18       | no US      | MATYPd (10) | water, 15 min | 97       |

"Isolated yields based on 4a. bReaction conditions: 1a (1 mmol), 2 (1 mmol), and 3 (1 mmol) in water were heated at 80 °C under ultrasonic irradiation condition for 15 min.

"Tetrabutylammonium bromide.

Figure 3. Recyclability of the MATYPd catalyst in the model reaction.

Figure 4. IR spectra of the MATYPd catalyst before and after the investigated catalytic reaction.
carbonitrile derivatives under the influence of the MATYPd catalyst using ultrasonic irradiation at mild conditions as depicted in Scheme 3. Enolization of malononitrile was improved in the presence of the catalyst and water, and the nucleophilic character of methylene carbon increased through a hydrogen bond. As a result, the Knoevenagel condensation and Michael addition produced intermediates I and II, respectively. Phenylhydrazine functioned as both a Brønsted base and a nucleophile in this catalyst-free system. Subsequently, annulation, tautomerization, and aromatization of intermediate II (B) yielded the final product.

3.8. Supporting Computations. 3.8.1. Quantitative Structural Activity Relationships (QSAR). QSAR parameter scan be done for the complexes under consideration using Hyper Chem (8.1) software after adjusting the geometry optimization requirements. The steps were started by adding H-atoms over the selected molecule, using the semiempirical (AM1) and force-field Molecular Mechanics (MM+) setups, and after that starting the energy minimization process. This structural optimization was executed without any restrictions according to the Polake−Ribiere conjugated gradient algorithm method. The parameters computed were surface area, hydration energy, reactivity, polarizability, and partition coefficient (log p), in order to clarify the features of these solid complexes (Table 4). Reactivity, polarizability, and surface area were the indicators for the surface properties of the solid compounds, which were significant in catalytic efficiency. According to their values, the properties of the Cu(II) complex were shown to be commonly superior to those of the Pd(II) or Fe(III) complexes. This superiority may be not effective, due to the octahedral configuration of the Cu(II) complex blocking perfectly the metal active sites and reducing the probability for extra coordination. However, the Pd(II) complex, due to its square-planar geometry, has a good chance for extra coordination and exceeded the number to five, which may have happened during the catalytic steps.

3.8.2. Global Reactivity and Electrostatic Potential Maps. The DFT method was implemented in the DMOL3 program using the Becke3−Lee−Yang−Parr (B3LYP) exchange-correlation functional under the DNP basis set due to its flexibility and consistency. This study was used to optimize the geometries of MATY and its complexes to realize their comparative features and confirm the MATY binding mode. Significant computational parameters were extracted (Table 5) to discriminate between them regarding their catalytic efficiency. An electrostatic potential map was drawn for all optimized structures to clarify the attacking behavior of the functional groups. The best geometry obtained for the MATY ligand points to the perfect positions of the coordinating sites (N20 and N19). Also, the geometry of the complexes showed normal bond lengths, and the bonds do not suffer any unfavorable strain (Figure 5). This emphasizes the mode of coordination proposed from practical analyses. Electrophilicity (ω), absolute softness (σ), global softness (S), and electronegativity (χ) indexes were calculated to have a clear view about some properties (Table 5).

Table 4. QSAR Parameters for the Tested Complexes

| parameters            | Fe(III) | Pd(II) | Cu(II) |
|-----------------------|---------|--------|--------|
| surface area (Å)      | 638.49  | 719.35 | 761.51 |
| volume (Å)            | 1319.54 | 1329.55| 1338.0 |
| hydration energy (kcal/mol) | −31.40  | −13.75 | −21.01 |
| log p                 | −8.16   | −0.87  | −1.85  |
| reactivity (Å)        | 134.15  | 131.91 | 134.31 |
| polarizability (Å)    | 50.00   | 50.55  | 50.57  |

Scheme 3. Suggested mechanism for the synthesis of pyrazole-4-carbonitrile derivatives and the catalytic role of MATYPd by ultrasonic irradiation
The softness property appeared to be distinguished for the MATYPd complex. This reflects the elasticity of such a complex, which is preferable for interaction with biological systems. The high electrophilicity and electronegativity values of the MATYPd complex denote its susceptibility for acquiring electrons from any donor species. This capacity depends on the unsaturated electronic configuration of the Pd atom, which pushed for extra coordination to reach saturation (18 e\textsuperscript{−}).

The lower energy-gap values ($\Delta E = E_{\text{LUMO}} - E_{\text{HOMO}}$) of the complexes, particularly for the MATYPd complex, indicate the ease of electronic transitions and low activation energy barrier, which are preferred in a catalytic application. Other molecular parameters were computed to measure the stability of the complexes under study (Table 6). The MATYPd complex is less stable due to its high energy content, which suggests its ability for extra bonding to complete the electron count of the palladium valence shell. Frontier orbitals were established on optimized geometries, to recognize the groups that are responsible for coordination and electronic transitions (Figure 6).

Electrostatic potential maps (MEP) were established (Figure 7) to clarify the electronic distribution over the functional groups. Nucleophilic, electrophilic, and neutrality features could be easily indicate by such maps. Red, blue, and green colors were the indicators used for discrimination between the three features, respectively. The nucleophilic property of N19 and N20 was clearly noticed and mainly improved in the complexes due to M → L charge transfer.

Table 5. Estimated Physical Parameters (eV) according to Frontier Energy Gaps

| compound  | $E_{\text{H}}$ | $E_{\text{L}}$ | $E_{\text{H}} - E_{\text{L}}$ | $\rho$ | $\eta$ | $S$ (eV\textsuperscript{−}) | $\omega$ | $\sigma$ (eV) |
|-----------|----------------|----------------|-------------------------------|-------|-------|-----------------|-------|------------|
| MATY      | −0.1868        | −0.1100        | 0.0768                        | 0.1484| 0.0384| 0.0192          | 0.2868| 26.0417    |
| MATYCu    | −0.1798        | −0.1444        | 0.0354                        | 0.1621| 0.0177| 0.0089          | 0.7415| 56.4334    |
| MATYFe    | −0.0619        | −0.0270        | 0.0349                        | 0.0444| 0.0175| 0.0087          | 0.0565| 57.2902    |
| MATYPd    | −0.1463        | −0.1198        | 0.0265                        | 0.1330| 0.0133| 0.0066          | 0.6683| 75.4717    |

Table 6. Molecular Parameters of the MATY Ligand and Its Complexes

| compounds                   | MATYPd | MATYCu | MATY |
|-----------------------------|--------|--------|------|
| total energy (Ha)           | −1580.591392 | −2416.144023 | −2204.070170 | −2642.515338 |
| sum of atomic energies (Ha) | −1572.1156181 | −2403.6396360 | −2192.2986133 | −2630.9706630 |
| kinetic energy (Ha)         | −10.7121247 | −18.0085026 | −17.2035576 | −20.4028446 |
| electrostatic energy (Ha)   | −3.9931612 | −2.9883189 | −2.4260780 | 0.5258222 |
| exchange-correlation energy (Ha) | 3.6028155 | 4.8463313 | 4.5024046 | 4.7095150 |
| spin polarization energy (Ha) | 2.6266963 | 3.6461037 | 3.3556744 | 3.6223828 |
| binding energy (Ha)         | −8.4757741 | −11.6576227 | −11.3715566 | −11.5446746 |
| dipole moment (Debye)       | 5.4926  | 4.4641  | 6.4713  | 16.6801   |

Figure 5. Optimized geometry of the investigated (a) MATY ligand, and (b) MATYCu, (c) MATYPd, and (d) MATYFe complexes.

Figure 6. Molecular parameters of the MATY ligand and its complexes.

Figure 7. Electrostatic potential maps (MEP) for the MATY ligand and its complexes.
3.8.3. Theoretical Bases for Catalytic Behavior. The catalytic behavior of the MATYPd complex is estimated based on the following features:

1. The reduced band-gap value \( \Delta E = E_{\text{LUMO}} - E_{\text{HOMO}} = 0.0265 \text{ eV} \) estimated denotes the flexibility of the valence electrons and lower required activation energy for a catalytic role.

2. The unsaturated valence shell of the central atom in a complex (16 e\(^{-}\)−1) reflects its instability and reactivity toward acquiring electrons to reach saturation (18 e\(^{-}\)−1), which may be attributed to the extra-coordinate bond. Consequently, a computational study assumes importance in supporting the catalytic mechanism, which is based mainly on the logical hypotheses regarding how the catalytic processes have happened. The suggested reaction pathway has proceeded through the formation of five conformers (A–E). Such conformers were optimized by the DFT/B3LYP method under the 6-31G** basis set to confirm this mechanism opportunity through the stability of the assumed conformers and the possibility for their formation (Scheme 4). The MATYPd catalyst \( (E = -6938 \text{ au}) \) has a lower energy content, which is increased after its interaction (Compound A) with starting materials such as benzaldehyde and malononitrile \( (E = -2112.8 \text{ au}) \). Four sequenced conformers appeared with the following formation energies: \(-836.82, -835.30, -836.85, \) and \(-835.69 \text{ au} \) for conformers B–E, respectively. These values reflect their closeness to each other in stability degree, which gives credibility for the suggested mechanism pathway.

4. CONCLUSION

Three thiazole complexes were prepared and characterized to establish their chemical forms. The ligand behaved as a neutral bidentate toward the mononuclear central atom (1:1 molar ratio) within the complexes. Octahedral geometry was suggested for Fe(III) and Cu(II) complexes, while Pd(II) complex (MATYPd) appeared to have a square-planar geometry. Pd(II) complex was successfully developed by a facile and efficient
method for synthesis of pyrazole-4-carbonitrile derivatives using ultrasonic irradiation. This was achieved by reaction of aromatic aldehyde 1 (1 mmol), malononitrile 2, and phenylhydrazine 3 in the presence of catalyst by ultrasonic irradiation at mild conditions. The catalytic activity of MATYPd in a three-component reaction approach for the aromatization of pyrazole-4-carbonitrile derivatives was achieved by the green way (in H₂O). The higher catalytic activity of the complex is ascribed to its high acidity and water tolerance. Also, the superiority of using MATYPd toward the synthesis of pyrazoles is compared with other Lewis acids and Lewis bases. All reactions were carried out in H₂O within 15–30 min to afford the products with high to excellent yields. Computational parameters asserted the properties of the Pd(II) complex, which may be effective in catalytic application because of its reduced optical band gap and electrophilicity. The mechanism of the catalytic process was
suggested and supported by the DFT/B3LYP method. This simple, economical, and green procedure may be applied to industry in the future.

■ ASSOCIATED CONTENT

1 Supporting Information
The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c02811.

Reagents and instrumentation used in investigated study; thermogravimetric scheme for degradation of degradation steps for prepared complexes; IR, NMR, electronic spectra; Jop’s and molar ratio figures; Tables S1–S3 for electronic spectra, degradation steps and stability constants for complex formation (PDF)

■ AUTHOR INFORMATION

Corresponding Authors
Mahmoud Abd El Alem Ali Ali El-Remaisy — Department of Chemistry, Faculty of Science, Sohag University, 82524 Sohag, Egypt; orcid.org/0000-0002-3591-0077; Email: mreoliday@yahoo.com, mahmoud_ali@science.sohag.edu.eg

Nashwa El-Metwaly — Department of Chemistry, Faculty of Science, Umm Al-Qura University, 715 Makkah, Saudi Arabia; Department of Chemistry, Faculty of Science, Mansoura University, 35516 Mansoura, Egypt; orcid.org/0000-0002-0619-6206; Email: n_elmetwaly00@yahoo.com

Ahmed M. Abu-Dief — Department of Chemistry, Faculty of Science, Sohag University, 82524 Sohag, Egypt; Department of Chemistry, College of Science, Taibah University, 344 Madinah, Saudi Arabia; orcid.org/0000-0003-3771-9011; Email: ahmed_benzoic@yahoo.com

Authors
Tarek El-Dabea — Department of Chemistry, Faculty of Science, Sohag University, 82524 Sohag, Egypt
Mohammed Alsawat — Department of Chemistry, College of Science, Taif University, Taif 21944, Saudi Arabia
Mohamed H. H. Mahmoud — Department of Chemistry, College of Science, Taif University, Taif 21944, Saudi Arabia
Alia Abdulaziz Ali — Department of Chemistry, Faculty of Applied Science, Umm Al-Qura University, 715 Makkah, Saudi Arabia

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.1c02811

Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the Taif University Researchers Supporting Project Number (TURSP-2020/158), Taif University, Taif, Saudi Arabia. Also, the authors are deeply grateful to Sohag University in Egypt for supporting and facilitating this study.

■ REFERENCES

(1) Renuka, N.; Kariyappa, A. K. Synthesis and biological evaluation of novel formyl-pyrazoles bearing coumarin moiety as potent antimicrobial and antioxidant agents. Bioorg. Med. Chem. Lett. 2013, 23, 6406–6409.

(2) Kalaria, P. N.; Shalesh, P. S.; Dipak, K. R. Synthesis, identification and in vitro biological evaluation of some novel 5-imidazopyrazole incorporated pyrazoline and isoxazoline derivatives. New J. Chem. 2014, 38, 2902–3002.

(3) (a) El-Metwaly, N.; Katouh, H.; Aljuhani, E.; Alharbi, A.; Alkhathib, F.; Aljohani, M.; Alzahrani, S.; Alfaifi, M. Y.; Khedr, A. M. Synthesis and elucidation for new nanosized Cr (III)-pyrazolin complexes; crystal surface properties, antitumor simulation studies beside practical apoptotic path. J. Inorg. Organomet. Polym. 2020, 30, 4142–4154. (b) El-Metwaly, N.; Althagafi, I.; Khedr, A. M.; Al-Fahemi, J. H.; Katouh, H. A.; Hossan, A. S.; Al-Dawood, A. Y.; Al-Hazmi, G. A. Complexes-dyes and their usage in dyeing cotton to be special bandage for cancerous wounds. J. Mol. Struct. 2019, 1194, 86–103. (c) Althagafi, I.; El-Metwaly, N. M.; Farghaly, T. Characterization of new Pt (IV)–thiazole complexes: Analytical, spectral, molecular modeling and molecular docking studies and applications in two opposing pathways. Appl. Organomet. Chem. 2019, 33, No. e5099.

(4) Yang, J.; Gharagoozoo, P.; Yoo, J.; Ilyin, V. I.; Carter, R. B.; Nguyen, P.; Robledo, S.; Woodward, R. M.; Hogenkamp, D. J. 3-(4-Phenoxypyphenyl) pyrazoles: a novel class of sodium channel blockers. J. Med. Chem. 2004, 47, 1547–1552.

(5) El-Metwaly, N.; Farghaly, T. A.; Elghalban, M. G. Synthesis, analytical and spectral characterization for new VO (II)-triazole complexes; conformational study beside MOE docking simulation features. Appl. Organomet. Chem. 2020, 34, No. e5505.

(6) Bailey, D. M.; Hansen, P. E.; Hlavac, A. G.; Baizman, E. R.; Pearl, J.; DeFelice, A. F.; Feigenson, M. E. 3, 4-Diphenyl-1H-pyrazole-1-propanamine antidepressants. J. Med. Chem. 1985, 28, 256–260.

(7) (a) Eddingsaas, N. C.; Suslick, K. S. Light from sonication of crystal slurries. Nature 2004, 444, 163. (b) Khaligh, N. G.; Shirini, F. N-Sulfonic acid poly (4-vinylpyridinium) hydrogen sulfate as an efficient and reusable solid acid catalyst for one-pot synthesis of xanthene derivatives in dry media under ultrasound irradiation. Ultrason. Sonochem. 2015, 22, 397–403.

(8) Suslick, K. S. The chemical effects of ultrasound. Sci. Am. 1989, 260, 80–87.

(9) Allalyari, S.; Haghighi, M.; Ebadi, A.; Hosseinizadeh, S. Ultrasound assisted co-precipitation of nanostuctured CuO–ZnO– Al2O3 over HZSM-5: effect of precursor and irradiation power on nanocatalyst properties and catalytic performance for direct syngas to DME. Ultrason. Sonochem. 2014, 21, 663–673.

(10) (a) Ramazani, A.; Rouhani, M.; Joo, S. W. Catalyst-free sonosynthesis of highly substituted propanamide derivatives in water. Ultrason. Sonochem. 2016, 28, 393–399. (b) Xu, H.; Zeiger, B. W.; Suslick, K. S. Sonocatalytic synthesis of nanomaterials. Chem. Soc. Rev. 2013, 42, 2555–2567.

(11) (a) Jones, R. A.; Bean, G. P. The Chemistry of Pyrroles, 1st ed.; Academic: London, 1977; pp 1–5. (b) Sundberg, R. J. Comprehensive Heterocyclic Chemistry; In Katritzky, A. R.; Rees, C. W.; Bird, C. W.; Cheeseman, G. W. H., Eds.; Pergamon: Oxford, 1989; Vol. 4, pp 331–376. (c) Sundberg, R. J. Comprehensive Heterocyclic Chemistry II; In Katritzky, A. R.; Rees, C. W., Eds.; Pergamon: Oxford, 1996; Vol. 2, p 149.

(12) (a) Maddila, S.; Rana, S.; Pagadala, R.; Kankala, S.; Maddila, S.; Jonnalagadda, S. B. Synthesis of pyrazole-4-carbonitrile derivatives in aqueous media with CuO/ZrO2 as recyclable catalyst. Catal. Commun. 2015, 61, 26–30. (b) Srivastava, M.; Rai, P.; Singh, J.; Singh, J. An environmentally friendlier approach—ionic liquid catalysed, water promoted and grinding induced synthesis of highly functionalised pyrazole derivatives. RSC Adv. 2013, 3, 16994–16998. (c) Kiyani, H.; Bamdad, M. Sodium ascorbate as an expedient catalyst for green synthesis of polysubstituted 5-aminopyrazole-4-carbonitriles and 6-amino-1, 4-dihydropyran-2,3-5 pyrazole-5-carbonitriles. Res. Chem. Intermed. 2018, 44, 2761–2778. (d) Srivastava, M.; Rai, P.; Singh, J.; Singh, J. Efficient iodine-catalyzed one pot synthesis of highly functionalised pyrazoles in water. New J. Chem. 2014, 38, 302–307.

(e) Liu, P.; Pan, Y. M.; Xu, Y. L.; Wang, H. S. PTSA-catalyzed Mannich-type—cyclization—oxidation tandem reactions: one-pot synthesis of
1,3,5-substituted pyrazoles from aldehydes, hydrazines and alkynes. Org. Biomol. Chem. 2012, 10, 4696–4698.

(13) (a) Neohoritsis, C. G.; Zhao, T.; Doming, A. Tetrazoles via multicomponent reactions. Chem. Rev. 2019, 119, 1970–2042. (b) Safaei, H. R.; Khahtkhoda, T.; Shekouhy, M. A. New Highly Efficient Method for the Catalysis-Free Synthesis of Conjoined Twins 1, 6-Dioxaspiro Derivatives Through Double Reaction of Carbon Dioxide in One Reaction. ChemistrySelect 2018, 3, 6273–6278. (c) Elhamifar, D.; Kazempoor, S.; Karimi, A. Benine-functionalized liquid-based mesoporous organosilicas as a highly efficient nanocatalyst for the Knoevenagel condensation. Catal. Sci. Technol. 2016, 6, 4318–4326. (d) Mirbagheri, R.; Elhamifar, D.; Norouzi, M. Propylamine-containing magnetic ethyl-based organosilica with a core-shell structure: an efficient and highly stable nanocatalyst. New J. Chem. 2018, 42, 10741–10750. (e) Norouzi, M.; Elhamifar, D. Magnetic yolk-shell structured methylene and propylamine based mesoporous organosilica nano-composite: A highly recoverable and durable nanocatalyst with improved efficiency. Colloids Surf. A 2021, 615, No. 126226.

(14) (a) Salehi, N.; Mirjali, B. B. F. Green Synthesis of Pyrano [2, 3-c] pyrazoles and Spiro [indoline-3, 4'-pyrano [2, 3-c] pyrazoles] Using Nano-silica Supported 1, 4-Diazabicyclo [2.2. 2] octane as a Novel Catalytic. Org. Prep. Proc. Int. 2018, 50, 578–587. (b) Carvalho, R. B.; Joshi, S. V. Solvent and catalyst free synthesis of 3, 4-dihydropyrimidin- 2 (1 H)-ones/thiones by twin screw extrusion. Green Chem. 2019, 21, 1921–1924. (c) McDonald, E.; Keith, J.; Paul, A. B.; Drysdale, M. J.; Workman, P. Discovery and development of pyrazole-scaffold Hsp90 inhibitors. Curr. Top. Med. Chem. 2006, 6, 1193–1203. (d) Norouzi, M.; Elhamifar, D.; Mirbagheri, R. Phenylene-based periodic mesoporous organosilicas supported melamine: an efficient, durable and reusable organocatalyst. Microporous Mesoporous Mater. 2019, 278, 251–256. (e) Mofatolah, P.; Ziarani, G. M.; Elhamifar, D.; Badiei, A. A new yolk-shell hollow mesoporous nanocomposite, Fe3O4@SiO2@MCM41-IL/WO42- as a catalyst in the synthesis of novel pyrazole coumarin compounds. J. Phys. Chem. Solids 2021, 155, No. 110097. (f) Mousavi, F.; Elhamifar, D.; Kargar, S. Copper/IL-containing Nano-silica Supported 1, 4-Diazabicyclo [2.2. 2] octane as a Novel Catalyst with high reusability for synthesis of 1,2-dihydroquinoline derivatives. Appl. Organomet. Chem. 2019, 33, No. S005. (b) El-Remaily, M. A. E. A. A.; Abu-Dief, A. M.; Rafat, M. E. A. Robust Synthesis and Characterization for Superparamagnetic CoFe2O4 Nanoparticles as an Efficient and Reusable Catalyst for Synthesis of some Heterocyclic rings in aqueous medium. Appl. Organomet. Chem. 2016, 30, 1022–1029. (c) El-Remaily, M. A. E. A. A.; Soliman, A. M. M.; Elhady, O. M. Green Synthesis of TiO2 nanoparticles as an efficient heterogeneous catalyst with high reusability for synthesis of 1,2-dihydroquinoline derivatives. Appl. Organomet. Chem. 2021, 35, No. e6197. (e) El-Remaily, M. A. E. A. A. A.; Elhady, O. M. Green Bio-organic and Recoverable Catalyst Taurine (2-aminoethanesulfonic acid) for Synthesis of Bio-active Compounds 3,4-Dihydropyrimidin Derivatives in Aqueous Medium. ChemistrySelect 2020, 5, 6194–6198. (d) Ahmed, E. A.; Soliman, A. M. M.; Ali, A. M.; El-Remaily, M. A. A. Boosting the catalytic performance of zink linked amino acid complex as an eco-friendly for synthesis of novel pyrimidines in aqueous medium. Appl. Organomet. Chem. 2021, 35, No. e6238. (g) Shokr, E. K.; Kamel, M. S.; Abdel-Ghany, H.; El-Remaily, M. A. A. Optoelectronic characteristics of as-deposited, annealed and I2–Treated thin films of newly synthesized organic dye based on pyrrole [2, 3-b] pyrrole. Curr. Opin. Green Sustainable Chem. 2021, 4, No. 100090. (h) Hamad, H. A.; Nageh, H. H.; El-Bery, H. M.; Kasry, A.; Carrasco-Marin, F.; Elhady, O. M.; Soliman, A. M. M.; El-Remaily, M. A. A. Unveiling the exceptional synergism-induced design of Co-Mg-Al layered triple hydroxides (LTHs) for boosting catalytic activity toward the green synthesis of indol-3-yl derivatives under mild conditions. J. Colloid Interface Sci. 2021, 599, 227–244. (j) Shokr, E. K.; Kamel, M. S.; Abdel-Ghany, H.; El-Remaily, M. A. A. Optical characterization and effects of iodine vapor and gaseous HCl adsorption investigation of Novel Synthesized Organic dye Based on Thieno [2,3-b]bi phenone. Optik 2021, 243, No. 167385. (18) (a) Abu-Dief, A. M.; Metwaly, N. M.; Alzahrani, S. O.; Alkhatib, F.; AbuAlnaja, M. M.; El-Dabea, T.; El-Remaily, M. A. A. Synthesis and characterization of Fe (III), Pd (II) and Cu (II)-thiazole complexes; DFT, pharmacophore modeling, in-vitro assay and DNA binding studies. J. Mol. Liq. 2021, 326, No. 115277. (b) Alzahrani, S. O.; Abu-Dief, A. M.; Alkhatib, F.; El-Remaily, M. A. A.; Metwaly, N. M.; et al. Synthesis and structural elucidation for new pyranothiazole complexes: Biological screening and effects on DNA adsorption investigation of Novel Synthesized Organic dye Based on Thieno [2,3-b]biophene. Optik 2021, 243, No. 167385. (18) (a) Abu-Dief, A. M.; El-Metwaly, N. M.; Alzahrani, S. O.; Alkhatib, F.; AbuAlnaja, M. M.; El-Dabea, T.; El-Remaily, M. A. A. Synthesis and characterization of Fe (III), Pd (II) and Cu (II)-thiazole complexes; DFT, pharmacophore modeling, in-vitro assay and DNA binding studies. J. Mol. Liq. 2021, 326, No. 115277. (b) Alzahrani, S. O.; Abu-Dief, A. M.; Alkhatib, F.; El-Remaily, M. A. A.; Metwaly, N. M.; et al. Synthesis and structural elucidation for new pyranothiazole complexes: Biological screening and effects on DNA adsorption investigation of Novel Synthesized Organic dye Based on Thieno [2,3-b]biophene. Optik 2021, 243, No. 167385.
reversible Pd (II) thiazole catalyst accelerated by ultrasonic: Computational studies. Appl. Organomet. Chem. 2021, 35, No. e6320. (19) (a) Taakeyama, T.; Quinn, F. X. Thermal Analysis Fundamentals and Applications to Polymer Science; John Wiley and Sons: Chichester, 1994. (b) Abdel-Rahman, L. H.; Abu-Dief, A. M.; Mostafa, H.; Abdel-Mawgoud, A. A. H. Design and nonlinear optical properties (NLO) using DFT approach of new Cr (III), VO (II), and Ni (II) chelates incorporating tri-dentate imine ligand for DNA interaction, antimicrobials, anticancer activities and molecular docking studies. Arab. J. Chem. 2020, 13, 649–670. (c) Coats, A. W.; Redfern, P. Kinetic parameters from thermogravimetric data. Nature 1964, 201, 68–69. (20) Alkhathat, F.; Hameed, A.; Sayqal, A.; Bayazeed, A. A.; Alzahrani, S.; Al-Hmed, Z. A.; Zaky, R.; El-Metwaly, N. M.; et al. Green-synthesis and characterization for new Schiff-base complexes; spectroscopy, conductometry, Hirshfeld fields and biological assay enhanced by in-silico study. Arab. J. Chem. 2020, 13, 6327–6340. (21) Abd El-Lateef, H. M.; Abu-Dief, A. M.; Mohamed, M. A. Corrosion inhibition of carbon steel pipelines by some novel Schiff base compounds during acidizing treatment of oil wells studied by electrochemical and quantum chemical methods. J. Mol. Struct. 2017, 1170, 522–542. (22) Abd El-Lateef, H. M.; Abu-Dief, A. M.; Abdel-Rahman, L. H.; Sañudo, E. C.; Alqala-Alcalde, N. Electrochemical and theoretical quantum approaches on the inhibition of C1018 carbon steel corrosion in acidic medium containing chloride using some newly synthesized phenolic Schiff bases compounds. J. Electroanal. Chem. 2015, 743, 120–133. (23) Abdel-Rahman, L. H.; Abu-Dief, A. M.; Ismael, M.; Mohamed, M. A.; Hashem, N. A. Synthesis, structure elucidation, biological screening, molecular modeling and DNA binding of some Cu (II) chelates incorporating imines derived from amino acids. J. Mol. Struct. 2016, 1103, 232–244. (24) Modeling and Simulation Solutions for Chemicals and Materials Research, Materials Studio (version 5.0); Accelrys Software Inc.: San Diego, USA, www.accelrys.com, 2009. (25) Frisch, M. J.; Trucks, G. W.; Pople, J. A. Gaussian 09, Revision B.3; Gaussian Inc.: Pittsburgh, PA, 2009. (26) Hehre, W. J.; Radom, L.; Schleyer, P. V. R.; Pople, J. A. Ab Initio Molecular Orbital Theory; Wiley: New York, 1986. (27) Kessi, A.; Delley, B. Density functional crystal vs. cluster models as applied to zeolites. Int. J. Quantum Chem. 1998, 68, 135–144. (28) (a) Abdel-Rahman, L. H.; Adam, M. S. S.; Abu-Dief, A. M.; Mostafa, H.; Bawazeer, T. M.; El-Metwally, N. M.; et al. Electrochemical and quantum chemical methods. J. Mol. Liq. 2020, 319, 124665. (b) Abu-Dief, A. M.; El-Khatib, R. M.; Al-Johani, F.; Alzahrani, S. O.; Mahran, A.; Khalifa, M. E.; El-Metwaly, N. M. Synthesis and characterization of functional Zn (II), Ag (I) complexes of chlorobenzylidene Schiff base: Promising antioxidant and anticancer agents. Appl. Organomet. Chem. 2018, 32, No. e4527. (b) Abu-Dief, A. M.; El-Khatib, R. M.; Aljohani, F. S.; Alzahrani, S. O.; Mahran, A.; Khalifa, M. E.; El-Metwaly, N. M. S. in: 3-Di sulfonic Acid I mide A m id alume M a thalene Ni (II) and V O (II) Schiff base complexes, DNA-interaction, DFT, drug-likeness and molecular docking studies. J. Mater. Sci. 2021, 1242, No. 130693. (c) Alsalme, A. M.; Nafady, A.; Abdel-Rahman, L. H.; Abu-Dief, A. M.; Atlam, F. M.; Hassan Abdel-Mawgoud, A. A.; Alothman, A. M.; Alkhatib, F.; Hameed, A. M.; Alzahrani, S. O.; Mahran, A.; Khalifa, M. E.; El-Metwaly, N. M. S. in: 3-Di sulfonic Acid I mide A m id alume M a thalene Ni (II), Ag (I) complexes of chlorobenzylidene Schiff base: Promising antioxidant and anticancer agents. Appl. Organomet. Chem. 2018, 32, No. e4527. (b) Abu-Dief, A. M.; El-Khatib, R. M.; Aljohani, F. S.; Alzahrani, S. O.; Mahran, A.; Khalifa, M. E.; El-Metwaly, N. M. Synthesis and characterization for novel Zn (II), Pd (II), Ag (I) complexes of chlorobenzylidene Schiff base: Promising antioxidant and anticancer agents. Appl. Organomet. Chem. 2015, 3173. (c) J. Mole Struct. 2010, 987, 61–143. (d) Al-Bayazeed, A. A.; Bawazeer, T. M.; Al-Solimy, A. M.; El-Metwally, N. M. Copper–acetanilide complexes: synthesis, characterization, crystal structure, computational analysis and their application as heterogeneous catalysts for biodiesel synthesis from frying waste oils. Res. Chem. Intermed. 2020, 46, 4543–4562. (e) Shah, R. S.; Katouah, H.; Sedayo, A. A.; Aljohani, M.; Alzahrani, S. M.; Al-Mutairi, F. S.; Al-Hmed, Z. A.; Zaky, R.; El-Metwaly, N. M. Practical and computational studies on novel Schiff-base complexes derived from green synthesis approach: conductometry as well as in-vitro screening supported by in-silico study. J. Mol. Liq. 2020, 319, No. 114116. (f) Alshikhah, N. I.; Zare, A.; Sajadikhah, S. S.; Banaei, A. Novel dicationic ionic liquid as a highly effective and dual-functional catalyst for the synthesis of 3-methyl-4-arylmethylene-2H-pyrazol-3-yl phenyl} methanesulfonamides on mild steel in 1 M HCl: experimental and theoretical studies. RSC Adv. 2016, 6, 86782−86797. (g) El Adnani, Z.; Mcharfi, M.; Sfarra, M.; Benzakour, M.; Benjelloun, A. T.; Touhami, M. E. DFT theoretical study of 7-R-5-methylquinolin-2-(1H)-thiones (R = CH3, C3) as corrosion inhibitors in hydrochloric acid. Corros. Sci. 2013, 68, 223−230. (h) Al-Wasidi, A. S.; Al-Jafshar, N. M.; Al-Anazi, A. M.; Refat, M. S.; El-Metwally, N. M.; Ibrahim, H. K.; Abd El-Fattah, W.; Naglah, A. M.; Al-Omar, M. A.; Kalmouch, A. In: Methanol Solvent Synthesis of New Mn (II), Co (II), Ni (II) and Cu (II) Schiff Base of Aromatic β Amino
Acids: Spectroscopic, Thermal, Molecular Docking and Antimicrobial Studies. *Sci. Adv. Mater.* 2020, 12, 1137–1148.

(44) Al-nami, S. Y.; Aljuhani, E.; Althagafi, I.; Abumelha, H. M.; Bawazeer, T. M.; Al-Solimy, A. M.; Al-Ahmed, Z. A.; Al-Zahrani, F.; El-Metwaly, N. Synthesis and Characterization for new nanometer Cu (II) complexes, conformational study and molecular docking approach compatible with promising in vitro screening. *Arab. J. Sci. Eng.* 2021, 46, 365–382.

(45) Alkhatib, F.; Hameed, A.; Sayqal, A.; Bayazeed, A. A.; Alzahrani, S.; Al-Ahmed, Z. A.; Zaky, R.; El-Metwaly, N. M.; et al. Green-synthesis and characterization for new Schiff-base complexes; spectroscopy, conductometry, Hirshfeld properties and biological assay enhanced by in-silico study. *Arab. J. Chem.* 2020, 13, 6327–6340.