Hg(II) Complexes Constructed from Indazole Ligands as New Heterogeneous Catalyst for the Biginelli/Transesterification Reaction: Synthesis and Quantum-Chemical Investigations

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ABSTRACT: *The present work deals with the synthesis, spectral characterization, DFT calculations, and catalytic activity of the new Hg(II) complexes derived from indazole ligands. The o-amino-ketones were obtained from the reduction of 6H-isoxazolo[4,3-e]indazoles as new heterocyclic ligands. Coordination of the ligands to Hg(II) cation led to the formation of new Hg(II) complexes. The IR, mass, and NMR spectra as well as the elemental analyses confirmed the structures of the new complexes. Furthermore, the DFT calculations at the B3LYP/6-311+G(d,p) level were used to gain further insight into the geometry of Hg(II) complexes. The catalytic activity of Hg(II) complexes as heterogeneous catalysts were studied for the synthesis of biologically active 3,4-dihydropyrimidin-2(1H)-one C5 ester (DHPMs), using classical Biginelli reaction followed by transesterification transformation. The results showed that the presented method gave the products good to excellent yields at reduced reaction time, which might be owing to the increased reactivity of the reactants on the surface area of Hg(II) complexes.*

KEYWORDS: *Hg(II) complex; DFT; Heterocycle ligand; Coordination; Biginelli reaction; Catalyst.*

INTRODUCTION

Biginelli reaction is one of the most imperative types of multicomponent reaction and it offers a simple method to construct a *N*-heterocyclic scaffold such as 3,4-dihydropyrimidin-2(*1H*)-one (DHPMs) was described by the Italian chemist Pietro Biginelli in 1893, involves a one-pot cyclocondensation of an aliphatic or arylaldehyde, a β-ketoester, and urea under strongly acidic conditions [1]. DHPMs have shown important pharmacological properties such as the integral backbones of several calcium channel blockers [2], antihypertensive agents [3], treatment of Alzheimer's disease [4] alpha-1a-antagonists [5], and neuropeptide Y (NPY) antagonists [6]. The increasing attention to the synthesis of DHPMs *via the* Biginelli reaction has demanded the development of new catalysts for the reason that traditional Biginelli reaction regularly suffers from insensitive reaction conditions, usage of harmful and non-volatile solvents, low yield, low selectivity, the requirement of high temperature, extended reaction time, etc [7-9]. Therefore, the discovery of milder and more practical routes for the synthesis of dihydropyrimidin-2(1H)-ones

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by the Biginelli reaction continues to attract the attention of researchers. On the other hand, coordination of ligands towards Hg(II) has assumed importance since, evidence for new classes of metal-binding motifs in enzymes, transcription factors, and regulatory proteins emphasizes the need for structural insights on local Hg(II) coordination environments [10]. Moreover, Hg(II) complexes are widely used as antibacterial [11], antifungal [12] and anticancer agents [13-15]. Hg(II) complexes are also employed as polymerization catalysts [16], precursors for metal sulfide nanoparticles [17], molecular material with interesting properties [18], and reagents in organic synthesis [19]. On the other hand, indazole scaffolds have been successfully incorporated into novel drug leads and therapeutic agents [20]. Much attention has been focused on indazoles as anticancer and antitumor agents [21, 22] and their therapeutic applications have been recently reviewed [23].

In this research, two new Hg(II) complexes derived from indazole ligands were synthesized and then characterized by both analytical and spectroscopic methods. Density Functional Theory (DFT) calculations were also used to provide the optimized geometries and structural parameters of the studied compounds. Furthermore, an efficient, facile, and convenient procedure was reported for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one C5 ester derivatives in the presence of the catalytic amount of Hg(II) complexes as a new heterogeneous catalyst under thermal and solvent-free conditions *via* Biginelli/Transesterification multicomponent reactions.

EXPERIMENTAL SECTION

Equipment and Materials

Melting points were measured on an Electrothermal type-9100 melting-point apparatus. The percentage of the Hg(II) was obtained by using a Hitachi 2-2000 atomic absorption spectrophotometer. Elemental analysis was performed on a Thermo Finnigan Flash EA micro analyzer. The mass spectrum was recorded on a Varian Mat, CH-7 at 70 eV, and ESI mass spectrum was measured using a Waters Micromass ZQ spectrometer. The FT-IR spectra were recorded on potassium bromide pellets using a Tensor 27 spectrometer and only noteworthy absorptions were listed. The ^{13}C NMR (75 MHz) and ^{1}H NMR (300 MHz) spectra were obtained on a Bruker Avance DRX-300 spectrometer. Chemical shifts were reported in ppm downfield from TMS as an internal standard; the coupling constant is given as *J* value in Hz. All solvents were dried according to standard procedures. Compounds **2a,b** [24] and **4a,b** [25] were obtained according to the published methods. Other reagents were commercially available.

Computational methods

All of the density functional theory (DFT) calculations have been performed by employing Gaussian 03 software package [26]. The B3LYP hybrid functional [27] and the 6-31+G(d,p) basis set were used, except for the Hg atom, where the LANL2DZ basis set [28] was employed. The geometry of the complex was fully optimized, which has no imaginary frequency in the frequency calculation. The sum of the electronic energies and the zero-point corrections (E+ZPE) were considered in the calculation of the electronic energies, which were obtained from the frequency calculations. The Polarizable-Continuum Model (PCM) [29] was employed to consider the solvent effects.

General procedure for the synthesis of ligands 5a,b

To a solution of **4a**,**b** (10 mmol) in EtOH (100 mL) and HCl (2 M, 5 mL), iron powder (2.25 g, 40 mmol) was added with stirring. Then, the mixture was refluxed for 6 h and then poured into water. The precipitate was collected by filtration, washed with water, and air-dried to give crude **5a**,**b**. The product was purified by crystallization from ethanol to give yellow needles **5a,*b*.**

(5-Amino-1-propyl-1H-indazol-4-yl)(phenyl)methanone (**5a, L1**)

mp.: 145–147 °C; Yield: 81%, IR (ν, cm^{-1}): 3332, 3275 (NH_2), 1642 (C=O). ^{1}H NMR ($CDCl_3$, δ, ppm): 0.98 (t, *J* = 7.5 Hz, 3H, CH_3), 1.83–1.89 (m, 2H, CH_2), 4.12 (t, *J* = 7.5 Hz, 2H, NCH_2), 4.35 (br s, 2H, NH_2), 7.03 (d, *J* = 8.7 Hz, 1H, Ar H), 7.21 (d, *J* = 8.7 Hz, 1H, Ar H), 7.35–7.39 (m, 5H, Ar H), 8.02 (s, 1H, Ar H); ^{13}C NMR ($CDCl_3$, δ, ppm): δ 12.1, 25.4, 47.4, 110.7, 115.5, 115.9, 123.4, 125.6, 127.9, 129.1, 129.4, 133.8, 135.1, 141.6, 196.5 (C=O). MS (m/z) 279 (M^+). Anal. Calcd for $C_{17}H_{17}N_3O$ (279.3) %: C, 73.10; H, 6.13; N, 15.04. Found (%): C, 72.87; H, 6.11; N, 15.37.

(5-Amino-1-butyl-1H-indazol-4-yl)(phenyl)methanone (**5b, L2***)*

m.p.: 137-139 °C. Yield: 74%. IR (ν, cm^{-1}): 3335, 3276 (NH_2), 1645 (C=O). ^{1}H NMR ($CDCl_3$, δ, ppm): 0.91 (t, *J* = 7.5 Hz, 3H, CH_3), 1.24–1.31 (m, 2H, CH_2), 1.81–1.86 (m, 2H, CH_2), 4.41 (br s, 2H, NH_2), 4.46

(t, *J* = 6.9 Hz, 2H, NCH_2), 7.02 (d, *J* = 8.9 Hz, 1H, Ar H), 7.24 (d, *J* = 8.9 Hz, 1H, Ar H), 7.33–7.37 (m, 5H, Ar H), 8.00 (s, 1H, Ar H); ^{13}C NMR ($CDCl_3$ δ, ppm): 14.0, 21.2, 33.4, 45.6, 110.5, 115.5, 116.5, 123.6, 125.2, 127.4, 128.8, 129.7, 134.1, 135.3, 142.1, 196.2 (C=O). MS (m/z) 293 (M^+). Anal. Calcd for $C_{18}H_{19}N_3O$ (293.4) %: C, 73.69; H, 6.53; N, 14.32. Found (%): C, 73.48; H, 6.50; N, 14.53.

General procedure for the synthesis of the complexes 6a,b

Hg(II) acetate (0.64 g, 2 mmol) was added to the yellow solution of ligand **5a,b** (4 mmol) in aqueous methanolic solution (30 mL, MeOH: H_2O, 10:90). The reaction continued for another 4 h at rt. After concentration at reduced pressure, the precipitate was collected by filtration, washed with water, following with cold EtOH and acetone respectively, and then air dried to give complexes **6a,b.** More purification was obtained by crystallization from EtOH.

$[Hg(L1)_2](CH_3COO)_2.2(H_2O)$ (**6a**): m.p. > 300 ºC (decomp). IR (ν, cm^{-1}): 3486 (OH), 3358, 3261 (NH_2), 1633 (C=O ligand), 1725 (C=O anion). ^1H NMR (DMSO-d_6 δ, ppm): 0.89 (t, *J* = 7.5 Hz, 6H, CH_3), 1.72–1.82 (m, 4H, CH_2), 2.21 (s, 6H, $\underline{CH_3}COO$) 4.12 (t, *J* = 7.5 Hz, 4H, NCH_2), 6.14 (br s, 4H, NH_2), 6.82 (d, *J* = 7.8 Hz, 2H, Ar H), 7.42 (d, *J* = 7.8 Hz, 2H, Ar H), 7.51–7.60 (m, 10H, Ar H), 7.85 (s, 2H, Ar H), 13.25 (br s, 4H, H_2O), ESI-MS (+) m/z (%): 760 $[Hg(L1)_2]^{2+}$. Anal. Calcd for $C_{38}H_{44}HgN_6O_8$ (913.4) %: C, 49.97; H, 4.86; N, 9.20; Hg, 21.96. Found (%): C, 50.29; H, 4.91; N, 8.94; Hg, 22.19.

$[Hg(L2)_2]$ $(CH_3COO)_2.2(H_2O)$ (**6b**): mp > 300 ºC (decomp). IR (ν, cm^{-1}): 3484 (OH), 3357, 3269 (NH_2), 1630 (C=O). ^1H NMR (DMSO-*d6*,δ, ppm): 0.95 (t, *J* = 7.5 Hz, 6H, CH_3), 1.23–1.32 (m, 4H, CH_2), 1.85–1.91 (m, 4H, CH_2), 2.04 (s, 6H, $\underline{CH_3}COO$) 4.24 (t, *J* = 7.5 Hz, 4H, NCH_2), 6.19 (br s, 4H, NH_2), 6.83 (d, *J* = 7.8 Hz, 2H, Ar H), 7.41 (d, *J* = 7.8 Hz, 2H, Ar H), 7.53–7.64 (m, 10H, Ar H), 7.87 (s, 2H, Ar H), 13.58 (br s, 4H, H_2O),; ESI-MS (+) m/z (%): 788 $[Hg(L2)_2]^{2+}$. Anal. Calcd for $C_{40}H_{48}HgN_6O_8$ (941.3) %: C, 51.03; H, 5.14; N, 8.93; Hg, 21.31. Found (%): C, 50.81; H, 5.11; N, 9.29; Hg, 21.42.

Catalytic activity: Synthesis of 3,4-dihydropyrimidin-2(1H)-one C5 ester derivatives via Biginelli reaction via transesterification reaction

Tert-butyl acetoacetate **8** (1.0 mmol) and alcohol **10** (1.5 mmol) were finely mixed together and allowed to stir for 30 min at 110 ºC. The aryl aldehyde **7** (1.0 mmol), urea **9** (1.2 mmol), and catalytic amount (4.0 wt% of arylaldehyde) of Hg(II) complexes **6a,b** were added to the above mixture at room temperature/25 ℃ under stirring. The precursors were finely mixed together and allowed to mechanical stirring for 2 h/hour at 80°C (oil bath) till the reaction was completed. The reaction advancement was monitored by TLC. After the completion of reaction, it was cooled to room temperature and the catalyst was separated out by filtration. Then the resultant reaction mixture was washed with brine and extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was then purified by re-crystallization from EtOH and H_2O to afford 3,4-dihydropyrimidin-2(1*H*)-one C5 ester derivatives in high yield 81-92%. The structures of the products were confirmed from physical and spectroscopic data.

2-(dimethylamino)ethyl 6-methyl-2-oxo-4-(p-tolyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11a**)

mp.: 167-169°C [Lit mp. 168-170˚C][22]. ^1H-NMR (300MHz, $CDCl_3$): δ 2.20 (s, 6H), 2.31 (s, 3H), 2.32 (s, 3H), 2.42-2.44 (t, *J* = 5.8Hz, 2H), 4.12-4.13 (t, *J* = 5.8Hz, 2H), 5.37 (s, 1H), 5.61 (s, 1H), 7.11- 7.14 (d, *J* = 7.8Hz, 2H), 7.20-7.22 (d, *J* = 7.8Hz, 2H), 7.84 (s, 1H).

Prop-2-yn-1-yl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11d**)

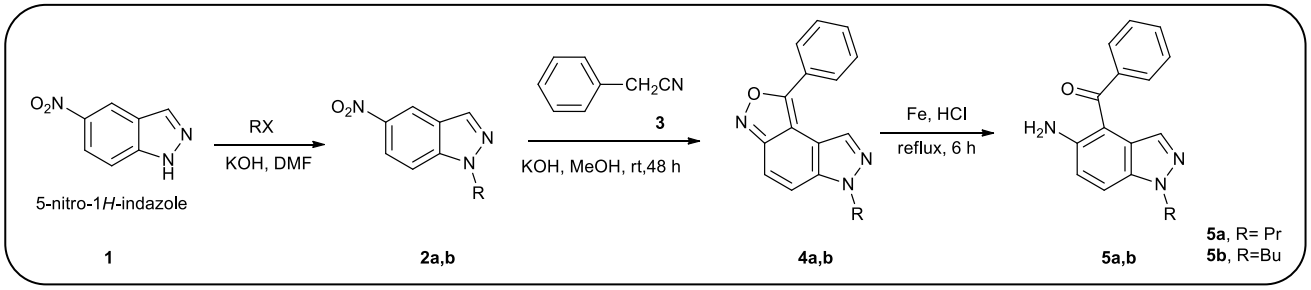
mp.: 181-183°C [Lit mp. 180-182˚C][22]. ^1H-NMR (300MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.41-3.43 (t,1H), 4.66 (s, 2H), 5.31-5.33 (d, 1H), 7.47-7.49 (d, *J* = 8.8 Hz, 2H), 7.89 (s, 1H), 8.21-8.23 (d, *J* = 8.7 Hz, 2H), 9.51 (s,1H).

Isopentyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11g**)

mp.: 167-169°C [Lit mp. 168-170˚C][22]. ^1H-NMR (300MHz, $CDCl_3$): δ 0.73-0.79 (d, 6H), 1.30-1.34 (m, 2H), 1.37-1.42 (m, 1H), 2.17 (s, 3H), 3.75 (s, 3H), 3.90-4.00 (m, 2H), 5.05-5.06 (d, 1H), 6.87-6.89 (d, *J* = 8.0 Hz, 2H), 7.10-7.12 (d, *J* = 8.0 Hz, 2H), 7.58 (s, 1H), 9.09 (s, 1H).

4-Methoxybenzyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11j**)

mp.: 179-181°C [Lit mp. 178-180˚C][22]. ^1H-NMR (300MHz, $CDCl_3$): δ 2.19 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 4.96-497



Scheme 1: Synthesis of the new ligands 5a,b.

(d, 2H), 5.11-5.13 (d, 1H), 6.78-6.82 (m, 4H), 7.11-7.17 (m, 4H), 7.62 (s, 1H), 9.06 (s, 1H).

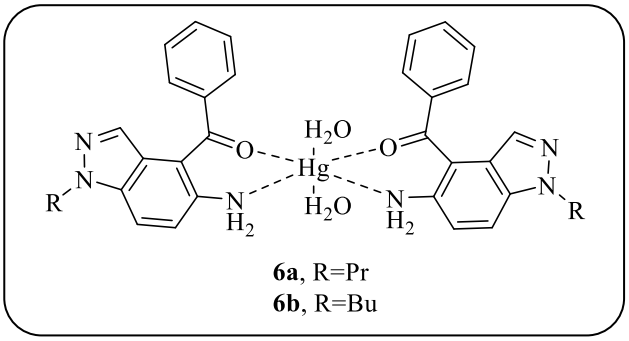
RESULTS AND DISCUSSION

Synthesis and structure of the new ligands 5a,b and complexes 6a,b

The process of the synthesis of novel complexes **6a,b** involves the following steps: 5-nitro-1*H*-indazole (**1**) was alkylated with propyl bromide and butyl bromide in KOH and DMF to produce the precursors 1-alkyl-5-nitro-1*H*-indazoles (**2a,b)** according to the published method [24]. The reaction of compounds **2a,b** with phenyl acetonitrile **3** led to the formation of 1-phenyl-6-propyl-6*H*-isoxazolo[4,3-*e*]indazole (**4a**) and 6-butyl-1-phenyl-6*H*-isoxazolo[4,3-*e*]indazole (**4b)** in basic MeOH solution [25]. The new heterocyclic ligands **5a,b** were obtained from the reduction of the compounds **4a,b** by Fe/HCl in EtOH in high yields (Scheme 1).

Structural assignments of the new compounds **5a,b** were based on their spectral and microanalytical (C, H, and N) data. For example, in the ^{1}H NMR spectrum of compound **5a**, the propyl group protons have appeared at δ 0.98 (t, *J* = 7.5 Hz, 3H, CH_3), 1.83–1.89 (m, 2H, CH_2) and 4.12 (t, *J* = 7.5 Hz, 2H, NCH_2). Also, NH_2 group protons can be seen at δ 4.35 ppm. Two doublet signals (δ = 7.03 and 7.21 ppm), a multiplet signal (δ = 7.35–7.39 ppm), and a singlet signal (δ = 8.02 ppm) were ascribed to eight protons of aromatic rings. Moreover, there are 15 different carbon atom signals in the ^{13}C NMR spectrum of compound **5a**. Furthermore, a broad absorption band at 3332 and 3275 cm^{-1} is assigned to NH_2 group, and the band at 1642 cm^{-1} is attributed to the C=O group in the FT- IR spectrum of compound **5a**. The results of mass spectroscopy (*m*/*z* 279 $[M]^+$) and elemental analysis support the structure of ligand **5a**.

Finally, the new Hg(II) complexes **6a,b** were obtained from the coordination of ligands **5a,b** to Hg(II) cation in aqueous methanolic solution (Scheme 2). The stoichiometry of the complexes **6a,b** (ML_2) was obtained by Job's method [30]. Nine aqueous methanolic mixtures of ligands (0.6 mM) and Hg(II) (0.6 mM) were prepared in the appropriate buffer at 25 ℃. Sodium perchlorate was added to give a constant ionic strength of 0.1 M. The volumes of ligand solution used varied from 9 to 1 mL and those of Hg(II) solution from 1 to 9 mL; the total volume was always 10 mL. The absorption spectra of the complexes were achieved immediately after mixing the ligands and Hg(II) solutions. Job's curve of equimolar solutions for the complex **6a** in aqueous methanolic solution can be found in Supplementary Data (Figs. S1).



Scheme 2: The structure of the new Hg(II) complexes 6a,b.

Based on the IR, NMR, and mass spectra as well as the elemental analyses the Hg(II) complexes **6a,b** involve $C_{38}H_{44}HgN_6O_8$ and $C_{40}H_{48}HgN_6O_8$ formulas, where two **L** ligands as well as two aqua ligands are coordinated to the Hg^{2+} metal ion. For example, in the FT- IR spectrum of complex **6a** a broad absorption band at the range of 3300-3500 cm^{-1} is assigned to OH and NH_2 groups, and the band at 1626 cm^{-1} (compound **5a:** 1642 cm^{-1}) is ascribed to the C=O group. In the ^{1}H NMR spectrum of complex **6a**, the methyl group protons of acetate anion have appeared at δ 2.04 (s, 6H, CH_3). Shifted NH_2 group protons and H_2O ligand protons can also be seen at δ 6.14 and 13.25 ppm, respectively. Moreover, the results of mass spectroscopy

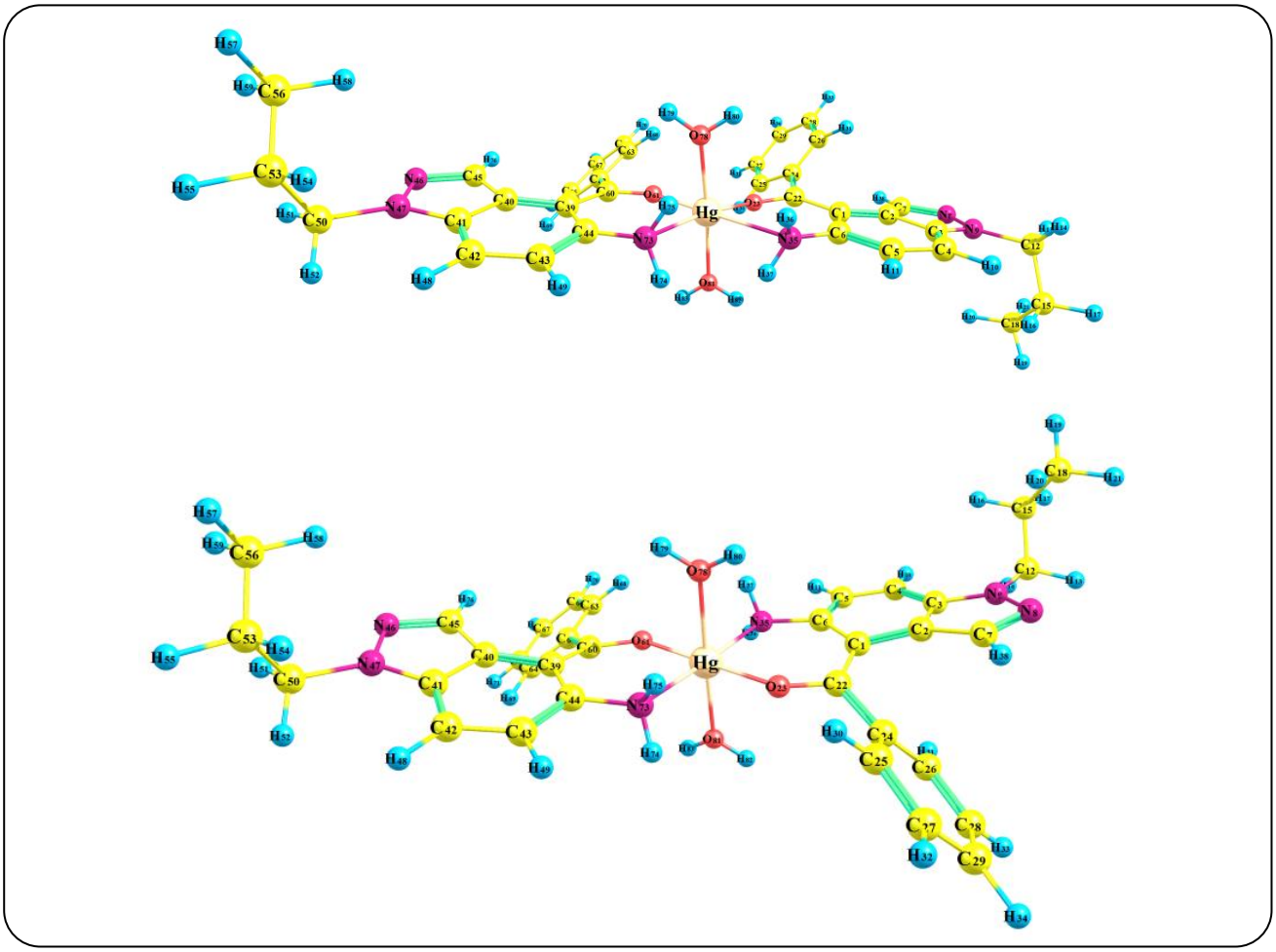


Fig. 1: Optimized geometries for the Cis (up) and Trans (down) isomers of the [HgL$_2$(H$_2$O)$_2$] complex 6a.

(ESI-MS (+) m/z (%): 760 $[Hg(L1)_2]^{2+}$) and elemental analysis confirm the proposed structure of complex **6a**.

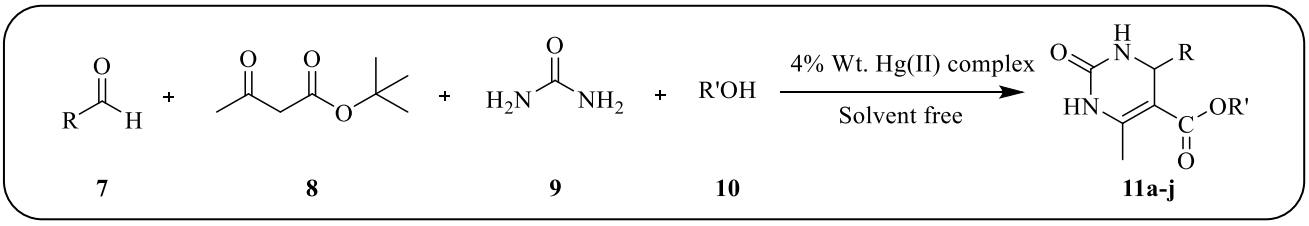
On the other hand, the structure of the complexes could exist as two different isomers, *Cis* and *Trans*. In the *Cis* and *Trans* isomers of the complex, corresponding donating atoms of two **L** ligands lie on the same side and opposite side to each other, respectively. For example, optimized geometries for the *Cis* and *Trans* isomers of the [Hg**L**$_2$(H$_2$O)$_2$] complex **6a** have been shown in Fig. 1.

The calculated PCM energies showed that the *Trans* isomer of the [Hg**L**$_2$(H$_2$O)$_2$] complex **6a** is more stable than the *Cis* one by 217.83 kJ.mol^{-1}. This large energy difference between the *Cis* and *Trans* isomers demonstrates that the methanol solution of the synthesized [Hg**L**$_2$(H$_2$O)$_2$] complex involves only the *Trans* isomer. Also, the Gibbs free energy difference (ΔG) between the *Cis* and *Trans* isomers of the complex is the favorite of the Trans isomer. The calculated ΔG value in the methanol solution of the complex is 229.42 kJ.mol^{-1}. Based on this large ΔG value, the amount of the *Cis* isomer is predicted to be negligible in the methanol solution of the [Hg**L**$_2$(H$_2$O)$_2$]. Selected structural parameters of the *Trans* isomer of the [Hg**L**$_2$(H$_2$O)$_2$] complex **6a** are listed in Table 1. For comparison, reported structural parameters for the free **L** ligand **5a** are gathered in Table 1.

In the optimized geometry of complex **6a**, the **L** species acts as a bidentate ligand, and coordinates to the Hg^{2+} ion *via* the carbonyl oxygen and nitrogen atom of the amine group. The O23, O61, N35, and N73 are donating atoms of two **L** ligands **5a**, which occupy four coordination positions of the square plane. The calculated dihedral angles prove that the four coordinating atoms of two ligands as well as the Hg^{2+} metal ion are in the same plane (Table 1). The O78 and O81 atoms of two H_2O ligands occupy two other coordinative positions of the octahedral complex. Coordination of the O23, O61, N35

Table 1: Important structural parameters of the $[HgL_2(H_2O)_2]$ complex 6a together with the free L ligand 5a.

Species	L	$[HgL_2(H_2O)_2]$		L	$[HgL_2(H_2O)_2]$		L	$[HgL_2(H_2O)_2]$
Bond length (ppm)			Angle (°)			Dihedral angle (°)		
C22-O23	123.4	131.2	O23-C22-C1	121.6	124.3	O23-C22-C1-C6	-26.5	-22.6
O1-H16	194.6	-	C22-C1-C6	119.6	124.7	C22-C1-C6-N35	2.1	6.8
C22-C1	147.7	144.1	C1-C6-N35	122.4	122.1	C24-C22-C1-C2	-29.4	-21.7
C1-C6	142.3	144.2	C6-N35-H36	133.9	132.7	Hg-O23-C22-C1	-	23.5
C6-N35	137.0	146.5	O78-Hg-O81	-	177.9	O23-N35-O61-N73	-	2.1
N35-H36	101.0	102.2	O23-Hg-O61	-	178.4	O23-N35-O61-Hg	-	-1.1
Hg-O23	-	199.6	O23-Hg-N35	-	88.7	O61-Hg-O23-C22	-	-142.3
Hg -O78	-	255.0	N35-Hg-N73	-	176.7	O78-Hg-O23-C22	-	-99.2
Hg -N35	-	217.2	Hg-O23-C22	-	132.4	O81-Hg-N73-C43	-	-89.7
C22-C24	150.3	149.1	Hg-N35-C6	-	124.3	C1-C2-C7-N8	-177.8	-177.6
C1-C2	146.2	146.1	C1-C2-C7	135.7	135.2	C2-C7-N8-N9	0.03	0.04
C7-N8	133.0	133.0	C7-N8-N9	105.9	106.0	C7-N8-N9-C12	178.6	177.7
N8-N9	136.3	136.1	N8-N9-C12	120.1	120.3	N8-N9-C12-C15	98.7	98.5



Scheme 2. Synthesis of 3,4-dihydropyrimidin-2(1H)-one C5 ester derivatives using

and N73 atoms to the Hg^{2+} ion increases the C22-O23, C6-N35, C60-O61 and C44-N73 bond lengths. The calculated structural parameters are consistent with the reported data for similar compounds [31].

Catalytic activity of Hg(II) complexes 6a,b

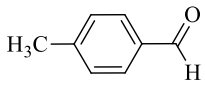
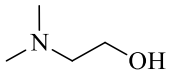
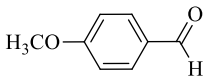
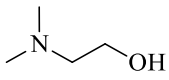
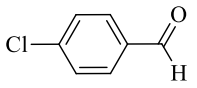
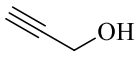
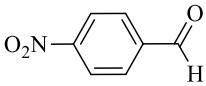
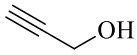
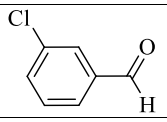
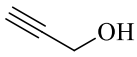
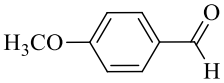
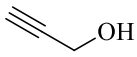
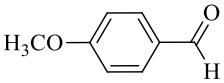
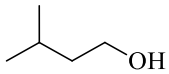
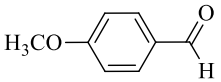
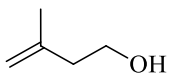
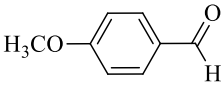
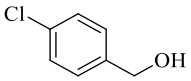
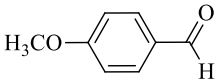
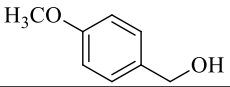
Forasmuch as the complexes **6a,b** can be considered as Lewis acid to activate the carbonyl groups in starting material, the different catalytic concentrations for the solvent-free synthesis of 3,4-dihydropyrimidin-2(1*H*)-one C5 ester derivatives using Hg(II) complex **6a** as the heterogeneous catalyst at 110 °C were studied (Scheme 2). To explore the practicability of the different catalytic concentrations, the reaction of 4-methoxybenzaldehyde (**7**), t-butyl-β-ketoester (**8**), urea (**9**) and propargyl alcohol was selected as representation reactants for the synthesis of corresponding dihydropyrimidinones (Table 2, entry 6) and unchanging the reaction time to 2 h.

Hg(II) complex *via* Biginelli/Transesterification multicomponent reactions.

It can be seen from Fig. 2 that a maximum conversion of 92% was achieved with 4.0 Wt.% to aldehyde for catalyst concentration. The observed increase in the percentage conversion with increasing catalyst concentration can be due to the availability of a more active site on the catalyst surface during the reaction circumstance of four-component Biginelli reaction followed by the transesterification process. However, a further increase in the catalyst concentration over 4.0 % might have resulted in the increase in viscosity of the system which in turn reduces the interaction between the catalyst and reaction medium.

To prove the generality of the protocol, the reaction was then extended with a variety of arylaldehydes and different alcohols bearing a diversity of functional groups.

Table 2: Synthesis of of 3,4-dihydropyrimidin-2(1H)-one C5 ester via Biginelli condensation followed by transesterification reaction[a].

Entry	Aldehyde/R	Alcohol/R'	Product	Yield/%[b]	M.p °C/Lit.[c] [32]
1			11a	87	167-169 (168-170)
2			11b	90	159-161 (158-160)
3			11c	91	174-176 (174-176)
4			11d	87	181-183 (180-182)
5			11e	81	155-158 (156-158)
6			11f	92	195-197 (194-196)
7			11g	91	167-169 (168-170)
8			11h	90	153-155 (152-154)
9			11i	89	199-201 (200-202)
10			11j	88	179-181 (178-180)

a) Reaction conditions: **7** (1.0 mmol), **8** (1.0 mmol), **9** (1.2 mmol) and **10** (1.5 mmol) at 110 °C using Hg(II) Complex **6a** under solvent-free condition.
b) Isolated yield.
c) The products were characterized by comparison of their spectroscopic and physical data with authentic samples synthesized by the procedure given in the references.

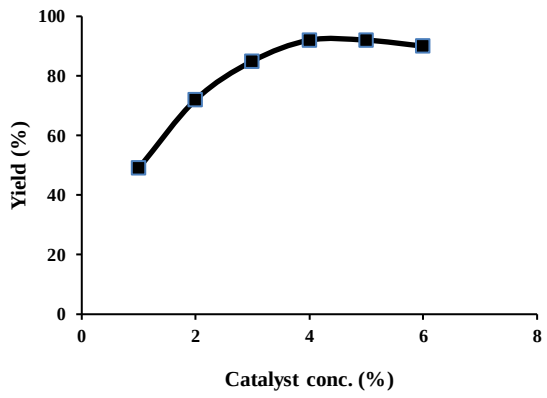
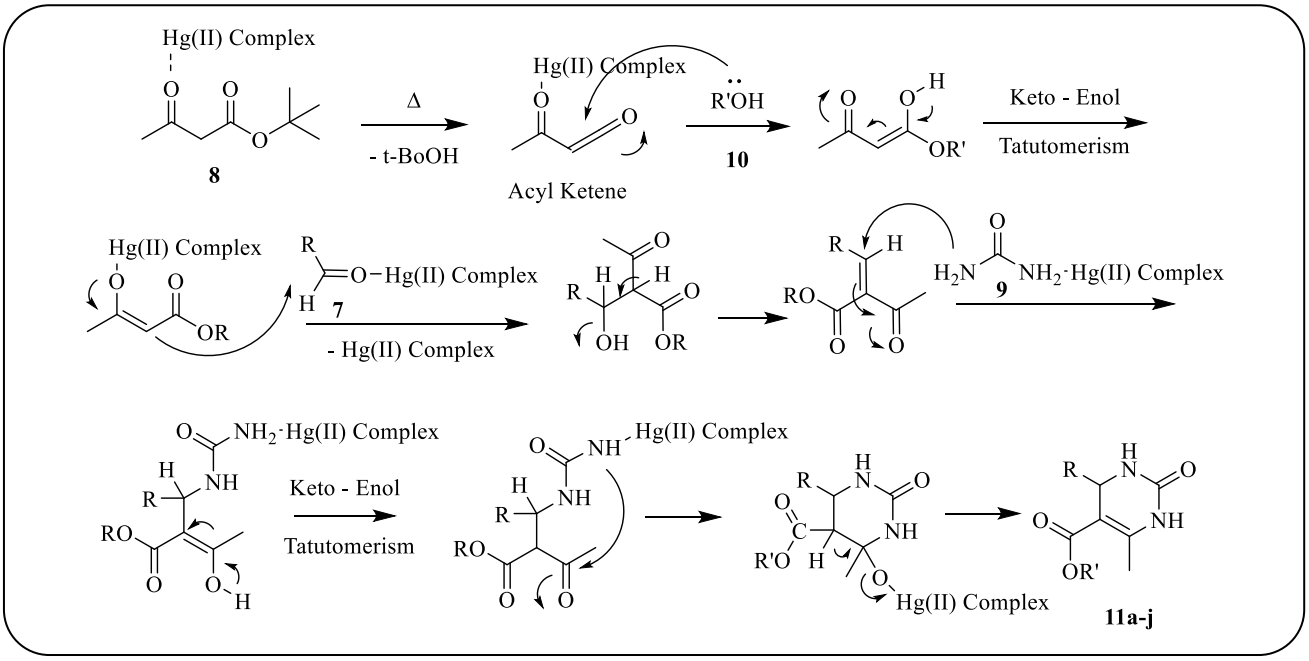


Fig. 2: Effect of catalyst concentration for the solvent-free synthesis of DHPMs using wt% Hg(II) Complex 6a.

As shown in the Table 2, the desired ring closure annulations of 3,4-dihydropyrimidin-2(1*H*)-one C5 ester ring was acquired in good to outstanding yields (81–92%). An additional important quality of this procedure is continued existence of a variety of functional groups, such as nitro, alkoxy, and halides under reaction circumstances. In all these cases, the reactions were clean and the products were obtained with a simple work-up in excellent to outstanding yields.

Hg(II) Complex **6b** was also employed as a catalyst for the reaction and the same results were obtained.

A reasonable reaction mechanism for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one C5 esters (DHPMs) using Hg(II) complexes **6a,b** was depicted in Scheme 3



Scheme 3: The multistep possible reaction mechanism for preparation of 3,4-dihydropyrimidin-2(1H)-one C5 ester by Biginelli reaction followed by transesterification.

according to the exceeding enlightenment and the literature proceedings. The used Hg(II) complex **6a,b** contains Lewis acid in addition to basic surface sites. Initially, in transesterification transformation, *tert*-butyl-β-ketoester (**8**) coordination with Hg(II) complex enhances the electrophilicity of their carbonyl carbon underwent transacetoacetylation through acetylketene intermediate to form β-ketoester with alcohol. Aldehyde (**7**) and β-ketoester with Hg(II) complex improve the electrophilicity of their carbonyl carbon. Then aldol-type condensation between aromatic aldehyde and β-ketoester forms the corresponding aldol-type product. In the next step, the electron-deficient sites present at the surface of the Hg(II) complex coordinate with the *N*-donor sites of urea (**9**) molecules and thus stabilize/ activate it for 1,4-addition reaction. This leads to the generation of adult products. Finally, cyclization of adult product by elimination of a water molecule results in the formation of DHPMs **11a-j**.

Comparing the efficiency of the present method with the previous methods confirmed that the presented method has numerous advantages, which include operational simplicity [32,33], short reaction time [34], and acceptable yields [35,36], does not need any chromatographic separation and a broad spectrum of substrate extent are the input features of this protocol.

CONCLUSIONS

Two new heterocyclic ligands (5-amino-1-propyl-1*H*-indazol-4-yl)(phenyl)methanone and (5-amino-1-butyl-1*H*-indazol-4-yl)(phenyl)methanone were obtained by the reduction of 1-phenyl-6-alkyl-6*H*-isoxazolo[4,3-*e*]indazoles. Then novel Hg(II) complexes were synthesized from the coordination of the ligands to Hg(II) cation. The structures of the ligands and complexes were confirmed by spectral and analytical data. The optimized geometries and structural parameters of Hg(II) complexes were also investigated by the DFT calculations at the B3LYP/6-311+G(d,p) level. The large energy difference between two isomers of Hg(II)complexes confirms that the complexes involve only the *Trans* isomer. Moreover, a simple, efficient, and robust one-pot procedure was presented for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one C5 ester derivatives by using a catalytic amount of Hg(II) complexes under thermal and solvent-free conditions. The noteworthy merits of this protocol are the straightforward operation, mild reaction conditions, no toxic solvents, and ease of work-up procedure.

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