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Synthesis and structure elucidation of a novel mixed-ligand Cu(II)

Schiff base complex and its catalytic performance for the synthesis

of 2-amino-4H-pyrans and tetrahydro-4H-chromenes

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Abstract

A novel quinazoline Schiff base ligand, 3-((5-bromo-2-hydroxy-3-methoxybenzylidene)amino)-2-methylquinazolin-4(3H)-one [HL] and its mixed-ligand Cu(II) complex [Cu(L')(Imi)], [L']= 2-acetamido-N-(5-bromo-2-oxidobenzylidene) benzohydrazonate, [Imi]= imidazole, were synthesized and characterized by elemental analysis, FT-IR and UV–Vis spectrometry and conductivity measurements. The structure of [HL] and its Cu(II) complex have been accomplished by single crystal X-ray diffraction. The Hirshfeld surface analysis has also been performed to evaluate intermolecular interactions. All experimental results confirmed that in this complex Cu(II) central atom is coordinated by the donor atoms of deprotonated Schiff base ligand and nitrogen of imidazole. Furthermore, the catalytic activities of this complex have been investigated on the electrophilic reaction of malononitrile along with aldehydes, ethyl acetoacetate and dimedone in ethanol solution in order to obtain 2-amino-4H-pyrans and tetrahydro-4H-chromenes, respectively

Keywords: Cu(II) schiff base complex, crystal structure, hirshfeld analysis, catalytic activity, 2amino-4H-pyrans and tetrahydro-4H-chromenes

Introduction

The synthesize of Schiff base ligands are relatively easy and they can be used in a wide range of substition reaction [1]. In addition, their properties may be improved or modified by coordination to various transition metal ions [2]. It has been demonstrated that even a small change in the ligand structure can considerably change the properties of the corresponding complex. Schiff

base complexes containing imine groups are of significant interest [3-4]. For example, the properties of copper complexes have been investigated and it was found these complexes have applications in various research areas, including artificial photosynthesis, proteasome inhibitors, anticancer agents, different catalytic process such as liquid phase oxidation of organic substrates [5-7]. Accordingly, synthesis of novel copper complexes with improved activities in various applications have been attracted much attention [8-9].

Multicomponent reactions (MCRs) have recently gained new dimensions in the field of designing methods to produce elaborate libraries of biologically active compounds [10]. Among these compounds, 4H-pyrans and 4H-chromenes are heterocyclic compounds with biological and pharmacological activities including anti-allergic, spasmolytic, diuretic, anti-cancer, and anti-anaphylactic properties [11].

Due to the mentioned applications of 4H-pyrans and 4H-chromenes, development of suitable methods for the synthesis of their derivatives have attracted considerable attention [12-15]. Accordingly, the present work was amid to synthesize and characterize an efficient catalyst for the synthesis of 2-amino-4H-pyrans and tetrahydro-4H-chromenes (Scheme 1) in ethanol as a green reaction medium. This catalyst was a Cu(II) complex composed of a Schiff base derived from the reaction between para-boromo salicylaldehyde and 2-methyl-3-amino-quinazoline.



Scheme 1: [Cu(L')(Imi)] catalyzed one pot synthesis of 2-amino-4H-pyrans and tetrahydro-4H-chromenes in ethanol.

Materials and method

All chemicals and solvents were of analytical reagent grade and were used as received without further purification. Microanalyses for C, H and N were determined on a Thermo Finnigan Flash Elemental Analyzer 1112EA. Melting points were measured on an Electrothermal Apparatus-9100. Infrared spectra were determined by using KBr disk on a FTIR spectrophotometer Shimadzu model 8400s in the region 400-4000 cm⁻¹. Electronic spectra were recorded in ethanol solutions on UV-Vis spectrophotometer spectro Scan 80D in 200-800 nm range. Nuclear Magnetic Resonance spectrum (¹H-NMR) for the ligand was recorded on a Bruker AMX 300 spectrometer with tetramethylsilane as an internal standard. Molar conductance measurement was made by means of a Metrohm 712 Conductometer in EtOH.

Synthesis of 3-((5-bromo-2-hydroxybenzylidene)amino)-2-methylquinazolin-4(3H)-one [HL]

In a solution of 2-methyl-3-amino-quinazoline (1 mmol, 175 mg) in 10 ml methanol was added 5-bromo-2-hydroxy benzaldehyde (1 mmol, 201 mg). The resulting yellow solution was refluxed for ca. 45 min. Crystals were obtained by slow evaporation of solution, washed with cold ethanol and dried in a desiccator over silica gel.

Yield: 84%. M.p.: 121 °C. Anal. Calc. for C₁₆H₁₂BrN₃O_{2.22} (361.71 g mol⁻¹): C, 53.13; H, 3.34; N, 11.62. Found: C, 53.19; H, 3.34; N, 11.68%. FT-IR (KBr, cm⁻¹): *v*(OH) 3453, *v*(C-H_{aromatic}) 2924-2998, *v*(C=O) 1679, *v*(C=N) 1608, *v*(C=C ring) 1480, *v*(C–O) 1255. ¹H NMR (300 MHz,

DMSO-d₆, 25 °C, ppm) d: δ = 10.88 (s, 1H, OH), 9.14 (s, 1H, CH=N), 6.96 – 8.27 (m, 7H, aromatic CH). UV/Vis (EtOH) λ_{max} , nm (log ε , L mol⁻¹ cm⁻¹): 235 (4.75), 310 (4.34).

Synthesis of Imidazole 2-acetamido-N-(5-bromo-2-oxidobenzylidene) benzohydrazonate Copper(II) [Cu(L')(Imi)]

A solution of [HL] (0.1 mmol, 35 mg) and CuNO₃.6H₂O (0.1 mmol, 30 mg) in methanol (5 ml) was refluxed for 30 min. Imidazole (0.3 mmol, 0.02 g) was added to the resulting green solution, which was further refluxed for an additional 10 min. After cooling, the solution was filtered and left to stand overnight. Reddish crystals suitable for crystallography appeared in the mother liquor after 1 day.

Yield: 62%. M.p.: 329 °C. Molar conductance (10^{-3} M, DMSO): 11 ohm⁻¹ cm² mol⁻¹. Anal. Calc. for C₁₉ H₁₆ Br Cu N₅ O₃ (505.82 g mol⁻¹): C, 45.12; H, 3.19; N, 13.85. Found: C, 45.10; H, 3.15; N, 13.90%. FT-IR (KBr, cm⁻¹): *v*(NH) 3308, *v*(NH_{imidazole}) 3142, *v* (C-H_{aromatic}) 2863-3027, *v*(C=O) 1677, *v*(C=N) 1588, *v*(C=C ring) 1471, *v*(C-O) 1251, *v*(Cu-O) 522, *v*(Cu-N) 460. UV/Vis (EtOH) λ_{max} , nm (log ε , L mol⁻¹ cm⁻¹): 235(4.84), 301(4.43), 395(4.37), 615(3.00)

Crystal structure determination

The diffraction data of [HL] were collected at 120 K on a Gemini Ultra diffractometer (Agilent Technologies) equipped with an Atlas S2 CCD detector, mirror-collimated CuK α radiation (λ = 1.54184Å) from a sealed X-ray tube, and the CryoJet 5 cooling system. Data collection and data processing were done with CrysAlis PRO software including absorption correction, which combined the analytical correction based on the crystal shape and correction by spherical harmonic functions (the ABSPACK procedure). The structure was solved by program Superflip

[16], and refined by program Jana2006 by full matrix least squares on F^2 . All non-hydrogen atoms were refined using harmonic refinement. All hydrogen atoms present in the structure model were discernible in difference Fourier maps and could be refined to reasonable geometry. According to common practice, H atoms bonded to C were kept in ideal positions with C-H = 0.96 Å while the position of H atom bonded to O2 was refined using an O-H restraint 0.820(1) Å. In both cases $U_{iso}(H)$ was set to 1.2 $U_{eq}(C,O)$. The hydrogen atoms of weakly occupied water molecule (s.o.f. 22%) could be recognized in the difference electron density maps as faint maxima but their refinement was unreliable; therefore, they are absent it the structure model. The diffraction data of [Cu(L')(Imi)] were collected at 100K in the CACTI (Universidade de Vigo) at low temperature using a Bruker D8 Venture with a CMOS Photon 100 detector and Mo-Ka radiation ($\lambda = 0.71073$ Å) equipped with a CryoStream 800 system. The software APEX3 [17] was used for collecting frames of data, indexing reflections, and the determination of lattice parameters, SAINT [17] for integration of intensity of reflections, and SADABS [17] for scaling and empirical absorption correction. The crystallographic treatment of [Cu(L')(Imi)]was performed with the Oscail program [18], using the SHELXT program [19] for structure solution and SHELXL program [20] for a full matrix least squares refinement on F^2 . Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in idealized positions and refined with isotropic displacement parameters. The Squeeze program [21] was used to eliminate the reflections caused by a disordered MeOH solvent. Details of crystal data and structural refinement for both compounds are given in Table S1. PLATON (version 21116) [22] was used for obtain some geometrical parameters of the cif file and for perform the Bond Valence Analysis on [Cu(L')(Imi)].

Hirshfeld surface analysis

The Hirshfeld surfaces for HL and for [Cu(L')(Imi)]were calculated using the Crystal Explorer v.3.1 program package and the 2D fingerprint was prepared using the same software, by using reciprocal interactions, that is, both X...Y and Y...X interactions were included in the fingerprints [23]. For them, two distances d_e (the distance from the point to the nearest nucleus external to the surface) and d_i (the distance to the nearest nucleus internal to the surface) where considered. The drawn surfaces were determined from the normalized contact distance, d_{norm}, defined as the sum of the normalised by the van der Waals radius of the atom involved d_i and d_e. [24]. In the input used for HL, we omitted the weakly occupied (22%) oxygen atom of the water molecule because we think it cannot affect the packing. On the other hand, in the input used for [Cu(L')(Imi)]we added oxygen, carbon and calculated hydroxyl hydrogen of the solvent MeOH. Position of oxygen atom was calculated by riding methods. . The surfaces were calculated on the dimeric unit, since we think this is the "molecule" to be considered.

General procedure for the synthesis of 2-amino-4 H -Imirans (1a-6a) and tetrahydro-4Hchromenes (1b-6b) derivatives

An aromatic aldehydes (1 mmol), malononitrile (1 mmol), ethyl acetoacetate or dimedone (1 mmol) and Schiff base complex as a catalyst (20 mg) were placed in 10 ml round-bottom flask. The reaction mixture was stirred at 50 °C until the reaction was completed. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the catalyst was separated by filtration then washed with acetone and after drying were used in the next reaction without loss

of activity. The precipitate was separated by filtration, washed thoroughly with ethyl acetat to yield the product. Recrystallization was carried out in EtOH/H₂O.

Result and discussion

General aspects

There are a few reports about quinazoline-based metal Schiff base complexes. Spectroscopic data of these reports suggest that the ligand act as a monobasic tridentate or neutral bidentate complexing agent [25, 26]. Surprisingly, we found that this class of ligands can be hydrolyzed during the complexation, and so, can act as a dibasic chelating agent [27]. In the present work a similar mechanism was observed for the coordination of Cu(II) by 3-((5-bromo-2-hydroxybenzylidene)amino)-2-methylquinazolin-4(3H)-one as illustrated in Fig 1.

Characterization

Infrared Spectroscopic Analysis

In the FTIR spectrum of the ligand, an absorption band was appeared at 3453 cm⁻¹ corresponding to OH group [28]. However, this peak was not observed in the spectrum of the complex, which is indicative of the deprotonation of the oxygen atom which is due to the coordination to the metal ion. Also, HL revealed vibrations of C=O and C=N bands at 1679 and 1608 cm⁻¹, respectively [29]. In the spectrum of the complex, the band of v(C=N) was observed at 1588 cm⁻¹. So, a red shift was occurred compared with the ligand spectrum suggesting that the azomethine nitrogen was coordinated to the metal ion [30]. Additionally, the vibration of C=O in the complex spectrum was appeared at 1677 cm⁻¹ which is due to hydrolysis of the ligand during the complexation process. Also, a red shift of 4 cm⁻¹ was observed in v(C-O) in the complex

spectrum in comparision with the free ligand spectrum confirming the coordination of the ligand to the Cu(II) ion center through the phenolic oxygen atom [31]. In the complex spectrum, the stretching vibrations of N-H of the amide and imidazole moieties were appeared at 3308 and 3102 cm⁻¹ and those of Cu-O and Cu-N were observed at 522 cm⁻¹ and 460 cm⁻¹, respectively.

Uv-vis absorption Spectral studies

In the Uv-vis spectrum of the ligand, the band appeared at 235 nm is attributed to π - π * transitions within the aromatic and quinoline rings. The n- π *transition of the C=N group is observed at 310 nm. In the spectrum of the Cu(II) complex similar features are observed. Appearance of an absorption peak at 395 nm with the epsilon value of log ε = 4.37 indicates the coordination of the ligand to the Cu²⁺ ion. This high epsilon value suggests that the corresponding band is a result of metal to ligand (MLCT) and ligand to metal (LMCT) charge transfer transitions. It has been illustrated that SP or distorted SP geometries have a characteristic band in the wavelength range of 550–660 nm which is related to $d_{xz}, d_{yz} \rightarrow d_{x^2-y^2}$ while TBP structures show an absorption peak around >800 nm originated from $d_{xz}, d_{x^2-y^2} \rightarrow d_{z^2}$. Since [Cu(L')(Imi)] shows a band at 652 nm, it can be concluded that the geometry of the Cu(II) complex is closer to SP [32].

X-ray Crystal structure

Figure 2 displays an ORTEP drawing of the asymmetric unit found in HL, showing the numbering scheme used. Some bond distances and angles are reported on Table S2_ at the Supplementary Material. Note that, as was mentioned in the experimental section, a molecule of water was found with a small occupancy factor (22%), and the hydrogen atoms of this molecule

could not be reliably refined. On the other hand, coordinates of the difference Fourier maxima indicated one hydrogen of water participates in a weak O1w-H...O1 hydrogen bond (Table S3). Therefore, we have included to the Figure 2 simulated positions of water hydrogen atoms. It is worth noting that, to the best of our knowledge, there are not any other (alkylideneamino)quinazolin-4-one compounds described in the literature (CCDC database, CSD version 5.37 (Feb. 2016 updated) [33]), although several 2,3-dihydroquinazolin-4-one derivatives [34] were described. HL is therefore planar in clear difference with the dihydroquinazolinone derivatives, and the distances and angles found in HL are related with the sp² character [35] of the carbon atoms in the rings. A detailed description of HL, together with its supramolecular behaviour and the Hirshfeld surface analysis is provided in the Supplementary Material.

Description of the Cu(II) complex [Cu(L')(Imi)]

Figure 3 displays an ORTEP drawing of the asymmetric unit found in [Cu(L')(Imi)], showing the numbering scheme used. In the Supplementary Material, Table S4 contains a selection of bond distances and angles. In the asymmetric unit, the Cu(II) atom is bonded by two oxygen atoms and one nitrogen atom of the tridentate salicylaldehyde-phenylhydrazonate ligand, and by another nitrogen atom from neutral imidazole molecule, forming a distorted square-planar coordination configuration. Noteworthy the presence of another molecule transformed by symmetry operation 1-x, 2-y, 1-z, which becomes parallel to the original one in such a way that the oxygen atom of the acetylimide substituent of the ligand is situated at only 2.678(2) Å from the copper atom. Both are sketched in Figure 4, and this behaviour contrast with the usual one found in the literature where dimers are constructed by using the phenolato oxygen atom [36,

37]. If this bond is considered, the compound is best defined as a dimeric one, where the copper atoms are square pyramid coordinated ($\tau = 0.13$) [38]. A detailed description of [Cu(L')(Imi)], together with its supramolecular behaviour and the Hirshfeld surface analysis is provided in the Supplementary Material.

Hirshfeld surface analysis

Hirshfeld surface analysis allows the visual representation of the interactions in crystal structures [39]. Several properties of intermolecular interactions can be visualized through mapping onto this surface: curvedness, shape index, d_{norm} , etc. In addition, all (d_i , d_e) contacts can be expressed in the form of a two dimensional plot, known as the 2D fingerprint plot [24, 40-41]. Opposite views of d_{norm} Hirshfeld surface analysis (see Supplementary Material for definitions) for HL are shown in Figure 5. In both cases, the neighbour molecule was also sketched to show the O-H…N interaction. Red spots indicate the intermolecular interactions, and they are found in the proximity of the phenolic group (hydrogen donor) and in the proximity of the acceptor nitrogen atom, and they produce the growing of the molecule in the zone axis ($\overline{1}$, 0, 1). The parameters of these hydrogen interactions are set out in Table S5. The plots of 2D fingerprint are included in the Supplementary Material.

In similar way, opposite views of d_{norm} Hirshfeld surface analysis for [Cu(L')(Imi)] are shown in Figure 6. As was stated in the experimental part, there is a molecule of solvent in the crystal, probably MeOH, but the quality of the data did not allow to model this molecule. However, since we were interested in participation of this solvent molecule in intermolecular interactions, a cif file was generated including those atoms. However, it seems that this molecule does not interact in a significant manner with the dimeric molecule of [Cu(L')(Imi)]. Red spots indicate the

intermolecular interactions, and they are found, as expected, in the proximity of the free N-H groups of the imidazole ligand, since this group is forming a classical hydrogen bond with the oxygen atom of the acetylimide moiety from a neighbour symmetry generated molecule. Detailed study of these surfaces is provided in the Supplementary Material and the supramolecular arrangement is related with it. Moreover, plots of 2D fingerprint are included in the Supplementary material.

Catalytic activity

Initially, in order to optimize the reaction conditions, we used solvents in the three component reaction of ethylacetoacetate, malononitrile and benzaldehyde in the presence of [Cu(L')(Imi)] as a catalyst to investigate the effects of solvent in the preparation of ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (Table 1). In order to optimize the effect of catalyst loading to this reaction we noted that although the product could be formed with low catalyst loading (4 mol% of the [Cu(L')(Imi)]), the best outcome, in terms of yield and the reaction time, was obtained with 8 mol% of [Cu(L')(Imi)] (Table 2). In addition the effect of temperature on this reaction was investigated. It was found that the optimum temperature was 50 °C from the point of view of yield and reaction time. At higher temperatures, no further improvement on yield and reaction time was observed. On the other hand, the reaction did not proceed at room temperature. At 50 °C, the reaction proceeded smoothly and almost complete conversion of the reagent was observed (Table 1).

Using the optimal solvent and catalyst loading, various 4H pyran derivatives with different aldehydes were synthesized (Table 3). High yields were obtained; especially when aromatic

aldehydes were used containing electron withdrawing groups, much lesser reaction time was needed in comparison to electrophilic aromatic aldehydes.

In order to synthesize tetrahydro-4H-chromene derivatives, we replaced ethyl acetoacetate in the reaction with 5,5-dimethyl-1,3-cyclohexanedione. The reaction conditions for the synthesis of 2-amino-4 H –chromenes were optimized. For this purpose, dimedone, benzaldehye and malononitrile were used as model substrates. Table 4 and 5 gives the optimization obtained results. Under the optimal condition, different substrates containing electron donating and electron releasing groups were investigated. The reactions of all tested substrates were found to proceed smoothly in a procedure similar to the synthesis of 2-amino-4H-pyrans to give 2-amino-4 H -chromenes (Table 6). The recyclability of the Cu(II) complex was also evaluated using a series of three consecutive runs for 1a and 1b using the optimal conditions. No change was observed in the activity of the catalyst for up to three uses and the yields were as follows: (1a: 95%, 93%, 90%, 1b: 92%, 90%, 89%).

In order to show the efficiency and capability of the present method, our results were compared with some of the previously reported and published procedures for the synthesis of compound 1a and 1b. The results, are summarized in Tables S5 and S6, clearly show that the present procedure exhibits superiority over the other methods in terms of the yield, an easy work-up process, reaction time and also low temperature.

A plausible mechanism for the formation of 2-amino-4H-pyrans and tetrahydro-4H-chromenes is depicted in Fig. 7. In the first step of these reactions, 2-arylidenemalononitrile derivatives are synthesized from Knoevenagel condensation reaction (I). The electrophilic C=C double bond of 2-arylidenemalononitrile reacts with the methine of cyclic β -dicarbonyl compounds and the intermediate (II) is formed which tautomerizes to (III). Then, nucleophilic attack of the

negatively charged oxygen to the cyano (CN) moiety results in the formation of a new heterocycle as shown in the intermediate (IV). Finally, tautomerization of (IV) affords products 1a-2g. Herein, the catalytic activity of the Cu(II) complex was established for Knoevenagel condensation and Michael addition reactions. In these reactions, the central Cu²⁺ ion acts as a Lewis acid and coordinates respectively to the oxygen atom of the aldehyde carbonyl and the nitrogen atom of the cyano moiety. This coordination results in the polarization of the π -electrons of carbonyl and cyano groups. Finally, these groups are attacked by nucleophiles more easily (Fig. 7)

Conclusions

A novel tridentate quinazoline-Schiff base ligand [HL] and its mixed-ligand Cu(II) complex were synthesized and characterized by physico-chemical and spectroscopic methods including elemental analysis, FT-IR, ¹H NMR and UV-Vis spectra data. The structures of compounds were also determined by single crystal X-ray diffraction. In the title complex, positions around the central atom being occupied with donor atoms of HL and N donor atom of coordinated Imidazole. This complex was used as an efficient catalyst in the synthesis of 2-amino-4H-pyrans and tetrahydro-4H-chromenes. These reactions were carried out in EtOH as a solvent at 50 °C. In comparison to the previous methods high yields, low temperature and reusability of the catalyst with almost consistent activity are advantages of this procedure that make it more useful process compare to the existing methods.

Supplementary data

Crystallographic data for the free proligand [HL] and [Cu(L')(Imi)] have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 1583955 & 1564391. Copies of this information may be obtained from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; email: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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Figure Captions:

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Fig. 1. Schematic diagram for hydrolysis processes.

Fig. 2. ORTEP drawing of [HL] (50% probability level). Hydrogen atoms in the water molecule

(22% occupancy factor) were drawn in simulated positions.

Fig. 3. ORTEP [50% probability level] drawing of [Cu(L')(Imi)].

Fig. 4. Dimer drawn of [Cu(L')(Imi)].

Fig. 5. Front and back views of d_{norm} mapped on the Hirshfeld surfaces for [HL].

Fig. 6. Front and back views of d_{norm} mapped on the Hirshfeld surfaces for [Cu(L')(Imi)]

Fig. 7. Proposed mechanism for formation of 2-amino-4H-pyrans and tetrahydro-4H-chromenes using [Cu(L')(Imi)] as catalyst.

















Fig. 7.

Solvent	Temperature	Time (min)	Isolated yield %
EtOH	R.T	70	75
EtOH	50	15	95
EtOH	Reflux	15	95
Acetonitrile	Reflux	60	80
Ethyl acetate	Reflux	55	75

Table 1. Optimization of times and yields in various solvents for the synthesis of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (1a)

Table 2. Optimization of the amounts of [Cu(L')(Imi)] charged as catalyst to the threecomponent synthesis ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (1a) at 50 °C.

A mount of astalyst		
Amount of catalyst	Time (min)	Isolated yield %
(mol%)		
0	115	35
4	40	80
8	15	95
12	15	95

5					
	Fntry	Aldehvde	Time(min)	Isolated	
	Lifti y	Thichyde	T mic(min)	yield %	\mathbf{X}
	1a	benzaldehyde	15	95	
	2a	4-chlorobenzaldehyde	18	90	
	3a	4-methoxybenzaldehyde	21	89	
	4a	3-nitrobenzaldehyde	18	89	
	5a	2,4-dichlorobenzaldehyde	17	91	
	6a	4-methylbenzaldehyde	20	88	

 Table 3. Three-component reaction of ethylacetoacetate (3b), malononitrile (2) and aromatic aldehydes.

Table 4. Optimization of times and yields in various solvents for the synthesis of 2-amino-4-phenyl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (1b)

Solvent	Temperature	Time (min)	Isolated yield %
EtOH	R.T	65	75
EtOH	50	20	92
EtOH	Reflux	20	92
Acetonitrile	Reflux	75	82
Ethyl acetate	Reflux	60	80

Table 5. Optimization of the amounts of [Cu(L')(Imi)] charged as catalyst to the three-
component synthesis of 2-amino-4-phenyl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-
3-carbonitrile (1b) at 50 °C.

Amount of catalyst		
$(mo^{10/2})$	Time (min)	Isolated yield %
(1110176)		
0	120	30
4	45	75
8	20	92
12	20	92

Entry	Aldehyde	Time(min)	Isolated yield	
			%	
1b	benzaldehyde	20	92	
2b	4-chlorobenzaldehyde	18	91	
3b	4-methoxybenzaldehyde	26	88	
4b	3-nitrobenzaldehyde	17	89	
5b	2,4-dichlorobenzaldehyde	19	90	
6b	4-methylbenzaldehyde	24	90	

Table 6. Three-component reaction of dimedone, malononitrile and aromatic aldehydes.

Synthesis and structure elucidation of a novel mixed-ligand Cu(II) Schiff base complex and its catalytic performance for the synthesis of 2-amino-4H-pyrans and tetrahydro-4H-chromenes

A novel mixed-ligand Cu(II) complex, [Cu(L')(Imi)] ,[L']= 2-acetamido-N-(5-bromo-2oxidobenzylidene) benzohydrazonate, [Imi]= Imidazole,was synthesized and fully characterized using spectroscopic and physicochemical techniques. The catalytic activities of the title complex was also investigated in the green synthesis of 2-amino-4H-pyrans and tetrahydro-4Hchromenes.

Synthesis and structure elucidation of a novel mixed-ligand Cu(II) Schiff base complex and its catalytic performance for the synthesis of 2-amino-4H-pyrans and tetrahydro-4H-chromenes

