Synthesıs and Characterızatıon of New Trıazole and Coumarın-Derived Heterocyclıc Compounds Part I

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(Received on 10th October 2018, accepted in revised form 7th March 2019)

Summary: Synthesis of ethyl ester of acetic acid containing 5-oxo-[1,2,4] triazole ring **(2)** was achieved by the condensation of 3-substituted-4-amino-1*H*-1,2,4-triazol-5(4*H*)-one **(1)** with ethyl bromoacetate in basic medium. Compound **2**, was then further reacted with hydrazine hydrate to form acid hydrazide, which is 2-(4-amino-3-substituted-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl)acetohydrazide **(3)**. Compound 3 was later treated with three different diverse coumarin aldehydes **(6, 12, 18)** resulted in the formation of arylidene hydrazides as *cis–trans* conformers **(7, 8, 13, 14, 19, 20)**. In conclusion, we synthesized 1,2,4-triazole Schiff bases derived from the condensation of 3-substituted-4-amino-1,2,4-triazole-5-on and formylhydroxy-4-methylcoumarin derivatives, which have been characterized by, spectroscopic measurements (IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis).

Keywords: Synthesis, 1,2,4-triazole, Coumarin aldehydes, Schiff bases.

Introduction

Coumarin (1,2-benzopyrone or 2H-1-benzopyran-2-one) and the derivatives of it are omnipresently distributed in nature and several of them were found to exhibit diverse and useful biological activities [1, 2]. Increasing number of reports shows that natural and synthetic coumarins have drawn tremendous attention due to their numerous therapeutic applications, as well as being as precursors in medicinal drug synthesis. Research have been shown that coumarin compounds possess anti-oxidative [3, 4], anti-inflammatory [5, 6], cardioprotective [7], antimicrobial [8, 9], antitumoral [10, 11], enzymatic inhibition [12, 13], anticoagulant [14] and anti-human immunodeficiency virus (HIV) [15, 16] activities. There is a high impact of the substitution on biological activities of synthetic coumarin derivatives. Most importantly these substitutions, on the coumarin nucleus, are quite important for predicting structure-activity relationship (SAR) studies and analysis designing and development of novel coumarin derivatives.

Furthermore, hydroxycoumarins are also known to be powerful chain-breaking anti-oxidants which can prevent free radical reactions by scavenging reactive oxygen species [17, 18]. It was earlier also reported that coumarin and its active metabolite, 7-hydroxycoumarin, have demonstrated growth-inhibitory activity in human cancer cell lines, such as A549 (lung), ACHN (renal), H727 (lung), MCF-7 (breast) and HL-60 (leukemia) also having anti-proliferative activity in case of prostate cancer, malignant melanoma and metastatic renal cell carcinoma in clinical trials [19-22].

In addition to that, compounds incorporating 1,2,4-triazole rings have also been shown to be anti-tumor agents [23]. Numerous reports have appeared from literature describing antimicrobial [24], antiradiation [25], and antiparasitic [26] properties of the thiazole ring also. Various 1,2,4-triazoles and N-bridged heterocycles derived from then are found to be assiated with diverse pharmacological activity [27]. The 1,2,4-triazole nucleus has recently been incorporated into a wide variety of therapeutically interesting drugs including Hl/H2 histamine receptor blockers, choline esterase active agents, CNS stimulants antianxiety agents and sedative [28].

On the other hand Schiff base compounds and their complexes are widely applied in enantioselective cyclopropanation of styrenes [29], asymmetric addition of cyanide to aldehydes [30], asymmetric aziridination of olefins [31], enantioselective epoxidation [32], regio-selective ring opening of epoxides [33] and these also find their usage as a membrane in ion selective electrode [34]. The metal complexes of Schiff bases also crutial in versatile catalytic reactions for the synthesis of organic compound, degradation of organic compounds, in radiopharmaceuticals [35], their tendency to reversibly bind oxygen and photochromic properties [36]. Likewise, Schiff bases were also reported as to be exhibiting the variety of biological actions due to azomethine linkage, which

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cause various antibacterial, herbicidal, antifungal, clinical and analytical activities [37].

As discussed, coumarin nucleus is found widely in natural products which shows number of pharmacological activities. Coumarin derivatives also form components of important drugs having several properties There are excellent monographs and review articles [38] describing the synthetic reactions, structure and properties of coumarin. Futhermore coumarins are also applicable, beyond the medicinal uses, such as fixative of perfumes, sweetener, natural oil enhancer such as lavender, a food additive in combination with vanillin, a flavor/ odor tobacco stabilizer [39**]**, an odor masker in rubber and paints.

Owing to the limitless applications, coumarins have been subject of intense investigations with reference to their synthesis and biological activity evaluations of their derivatives. We therefore are interested to further synthesize and evaluate characterization of new novel triazole and coumarin-derived heterocyclic compounds in order to step one more in the exploration of the biologically active compound. Keeping in view, as per observation and articles, the synthesis of complex hybrid molecules by the combination of many different pharmacophores into one frame may produce the potentially interesting bio-active profiles.

Chemistry

In the present study, compound **2** was synthesized via the nucleophilic attack of N-1 on 5-oxo-[1,2,4] triazole ring on bromine-bearing C atom of ethyl bromoacetate [40]. Later on, compound **3** was produced from the reaction of compound **2** with hydrazine hydrate (Fig. 1). Compound **3** was then reacted with three different diverse coumarin aldehydes **(6, 12, 18)** which resulted in the formation of arylidene hydrazides as its *cis-trans* isomer **(7, 8, 13, 14, 19, 20)** (Fig. 2-4). Keeping in view the coordination ability of Schiff bases as reported by the survey of the literature, that no work has been carried out over the synthesis of metal complexes with Schiff bases derived from 3-substituted-4-amino-1,2,4-triazole 5-on and 8-formyl-7-hydroxy-4-methyl coumarin. These Schiff bases have varied co-ordination abilities. This nature of the Schiff bases has attracted our attention and research is carried out for utilizing Schiff bases as ligands and to study the ligands and their metal complexes from a structural point of view.

Until today, imine bond containing compounds have been synthesized intensively because of their biological activities. Furthermore, the compounds contaning arylidene–hydrazide structure may exists as E/Z geometrical isomers about –C=N double bond and cis-trans isomer of amide (Fig. 5) [40]. According to the literature [41] imine containing compounds are present in the high percentage in dimethyl-D_6 sulfoxide solution in the form of geometrical E isomer about –C=N double bond. The Z isomer could be stabilized in less polar solvents because of intramolecular hydrogen bonding. In the present study, dimethyl-D_6 sulfoxide solution were used to produce spectral data and no signal belonging to Z isomer was found. Apart from that, cis-trans isomers of E isomer were also detected in the dimethyl-D_6 sulfoxide solution of compounds **7, 8, 13** and **14, 19, 20.**

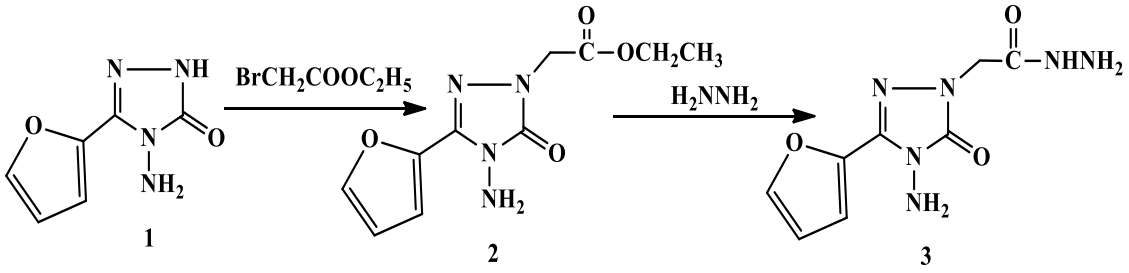

Fig. 1: Synthetic pathway for the preparation of compound **3.**

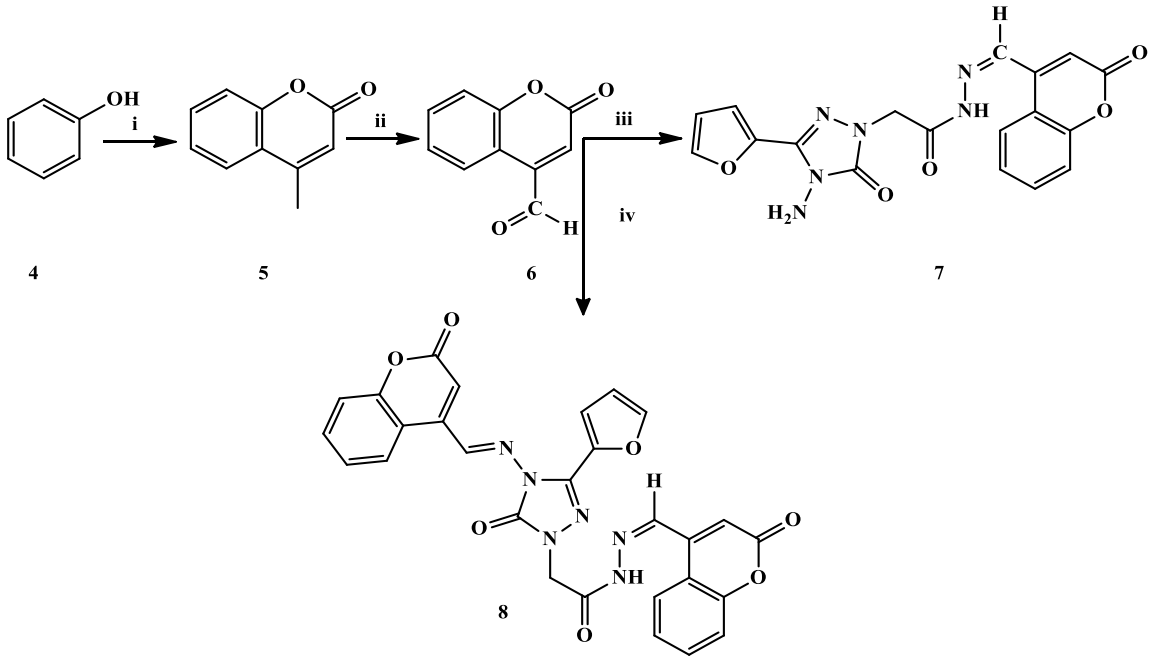

Fig. 2: Synthesized Schiff bases compounds. Reagents and conditions: (i) ethyl acetoacetate, 98% H_2SO_4 (ii) glacial acetic acid, hexamine, 85-90 ºC, 5 hrs, (iii) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:1 ratio, reflux 8 hrs, EtOH/HCl, (iv) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:2 ratio, reflux 16 hrs, EtOH/HCl

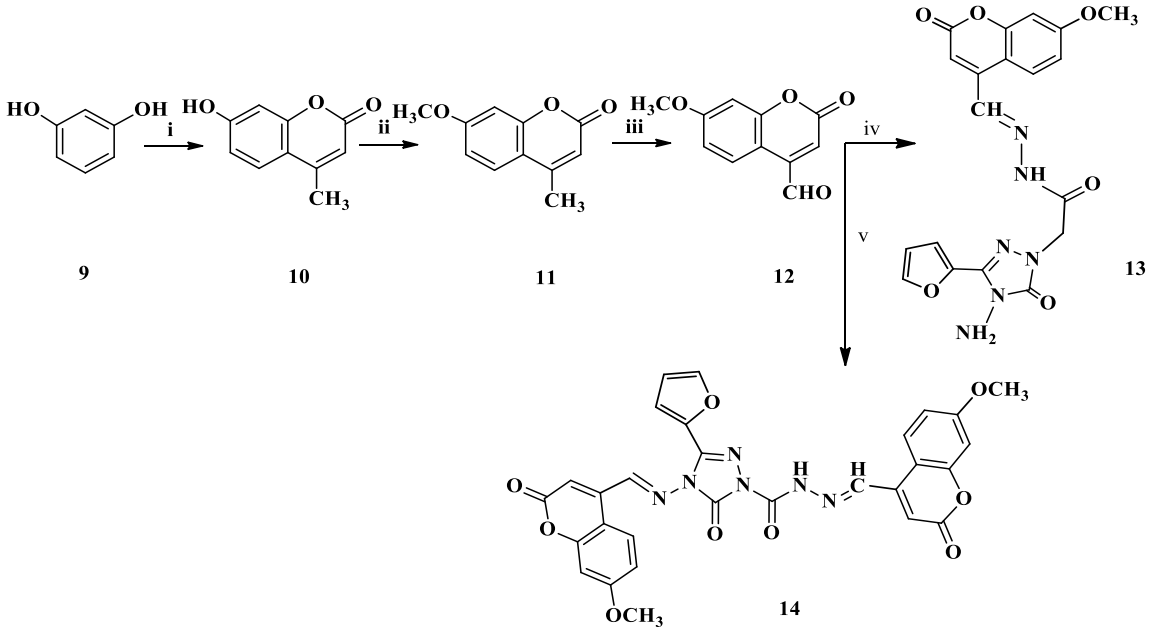

Fig. 3: Synthesized Schiff bases compounds. Reagents and conditions: (i) ethyl acetoacetate, 98% H_2SO_4 (ii) CH_3Cl, K_2CO_3, acetone (iii) glacial acetic acid, hexamine 85-90 ºC for 5 hrs, (iv) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:1 ratio, reflux 8 hrs, EtOH/HCl, (v) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:2 ratio, reflux 16 hrs, EtOH/HCl.

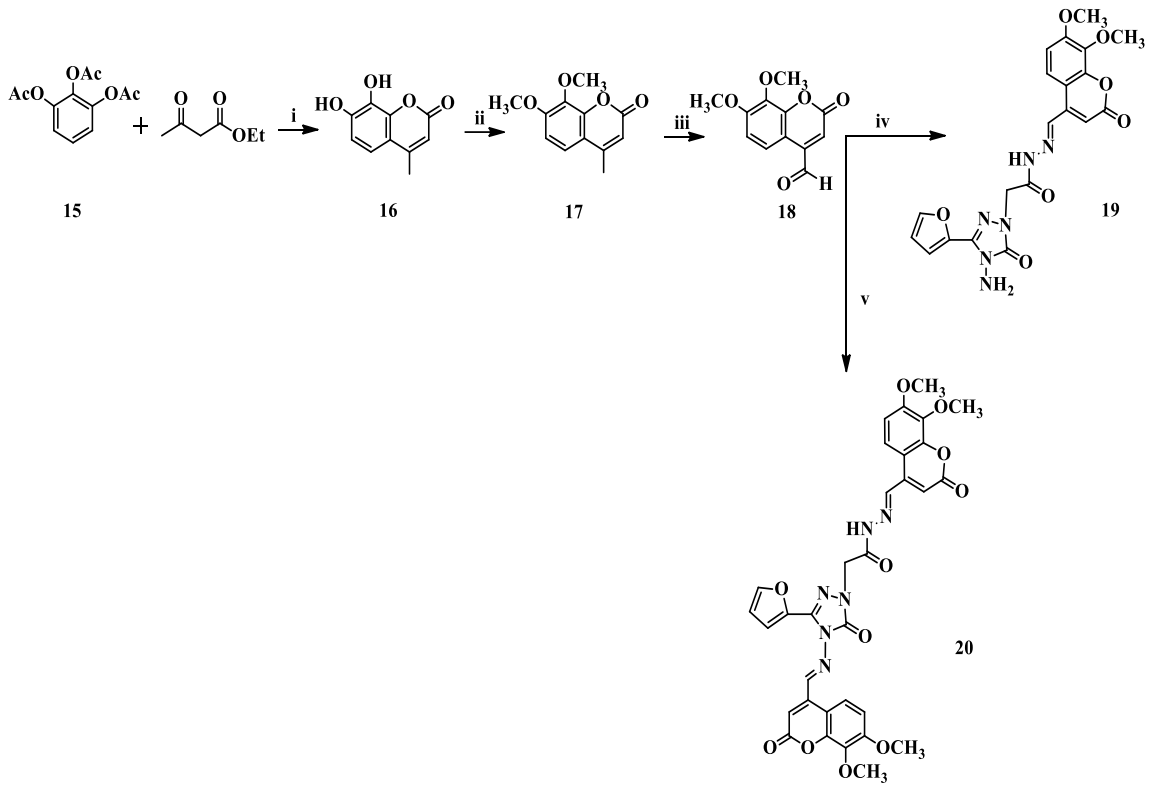

Fig. 4: Reagents and conditions: (i) $HClO_4$, 25-60 ºC, 6-8 hrs; (ii) CH_3Cl, K_2CO_3, acetone; (iii) glacial acetic acid, hexamine 85-90 ºC for 5 hrs, (iv) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:1 ratio, reflux 8 hrs, EtOH/HCl, (v) compound 3 and formyl-hydroxy-4-methyl coumarin derivatives was used in 1:2 ratio, reflux 16 hrs, EtOH/HCl

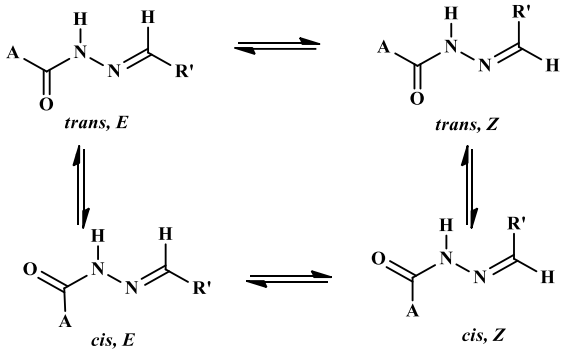

Fig. 5: E/Z geometrical isomers and cis-trans isomers of Schiff base.

Experimental

Gallenkamp melting point apparatus was used to measure the Melting points and remained uncorrected. Varian-Mercury 200 MHz spectrometer was used for ^{1}H-NMR and ^{13}C NMR spectra. Perkin-Elmer 1600 series FTIR spectrometer (potassium bromide pellets) were used to get IR. Combustion analysis data was obtained on a Carlo Erba 1106 elemental analyzer. Compound **1** was synthesized by a published method [40].

Table-1 to 4 contains Infrared spectral data, ^{1}HNMR data, ^{13} CNMR data and Elemental Analyses of all newly synthesized schiff bases (**7, 8, 13,14, 19, 20**)

Synthesis of compound 4-Amino-3-(2-furoyl)-5-oxo-4,5-dihydro-[1,2,4]triazol-1-yl-acetic acid ethyl ester **(2)**

The corresponding 3-alkyl-4-amino-5-oxo-4,5-dihydro-[1,2,4] triazole **(1)** (0.01 mol) was refluxed with equivalent amount of natrium in absolute ethanol for 2 h. Then, ethylbromoacetate (0.01 mol) was added and refluxed for an additional 5 h. After evaporating at 35–40 °C under reduced pressure, a solid appeared. This was recrystallized from an appropriate solvent to afford the desired compound **(2)**. Recrystallization from ethanol–water

(1:2), (yield: 1.64 g, 65.30%), m.p.153–154 °C. IR (KBr) (ν· cm^{-1}), 3390–3225 (νNH_2), 1736 (ester νC=O), 1714 (triazole νC=O), 1582 (νC=N), 1233 (νC–O); ^{1}H-NMR (DMSO-d_6) δ (ppm), 1.17 (t, 3H, –CH_3, *J* = 6.0 Hz), 4.10 (q, 2H, –OCH_2, *J* = 6.0 Hz), 4.52 (s, 2H, –NCH_2), 5.87 (s, 2H, NH_2), Ar-H [7.28 (d, 1H, *J* = 7.86 Hz), 7.63-7.75 (m, 1H), 7.95 (d, 1H, *J* =6.98 Hz]; ^{13}C NMR (DMSO-d_6) δ (ppm) 167.85 (exocyclic-C=O), 153.10 (triazole-C-$_5$),146.91 (triazole-C-$_3$), Ar C: [130.56 (CH), 129.43 (C), 128.22 (CH), 126.53 (CH)], 66.94 (–OCH_2), 65.43 (-NCH_2), 13.86 (–CH_3); Anal. calcd. (%) for ($C_{10}H_{12}N_4O_4$) 252.23 g/mol: C, 47.62; H, 4.80; N, 22.22. Found: C, 47.61; H, 4.86; N, 22.19.

Table-1: Infrared spectral data (cm^{-1}) of the newly synthesized Schiff base ligands.

Comp.	δC-O	δC=N	Hydrazide δC=O	Triazole δC=O	Coumarine δC=O	δNH +NH_2 /δNH	Ar-δOH
7	1053	1641,1500	1682	1716	1695	3357-3211	–
8	1041	1634,1547	1666	1705	1672	3302	3329
13	1043	1629,1544	1653	1717	1673	3284-3173	3329
14	1044	1636,1548	1651	1714	1702	3303	–
19	1238	1602,1569	1658	1726	1665	3286-3164	–
20	1274	1615,1542	1658	1704	1665	3296	–

Table-2: ^{1}HNMR data (DMSO-d_6) *d* (ppm) of the Schiff base ligands.

Comp.	-CH_3	-OCH_3	Aromatic-H	-NH_2	-NH	-OH
7	–	–	9.12 (s, 1H), 9.02-8.17 (m, 2H), 7.19-6.82 (m, 2H), 6.69-6.44 (m, 3H)	5.37 (s,2H)	10.37 (s,2H)	–
8	–	–	9.12 (s, 2H), 9.02-8.17 (m, 4H), 7.19 6.82 (m, 4H), 6.69-6.44 -(m, 3H)	–	10.68 (s,2H)	–
13	2.82 (s,3H)	–	8.78 (s, 1H), 8.50-8.43 (m, 1H), 7.82 -7.34 (m, 1H), 6.78-6.23 (m, 3H)	5.36 (s,2H)	10.29 (s,2H)	13.58 (s, 1H)
14	2.84 (s,3H)	–	8.78 (s, 2H), 8.50-8.43 (m, 2H), 7.82 -7.34 (m, 2H), 6.78-6.23 (m, 3H)	–	10.38 (s,2H)	13.58 (s, 2H)
19	–	3.40 (s,3H) 3.64 (s,3H)	9.12 (s, 1H), 8.17 (m, 1H), 6.82 (m, 1H), 6.69-6.50 (m, 3H)	5.28 (s,2H)	10.43 (s,2H)	–
20	–	3.44 (s,3H) 3.66 (s,3H)	9.12 (s, 2H), 8.17 (m, 2H), 6.82 (m, 2H), 6.69 -6.50 (m, 3H)	–	10.47 (s,2H)	–

Table-3: ^{13} CNMR data (DMSO-d_6) *d* (ppm) of the Schiff base ligands.

Comp.	-C=O	-C=N	Triazol C-5/ C-3	Arom-C	-OCH_3	-CH_3
7	160.81	157.95	151.85/ 146.54	152.08 (CH), 150.42 (2CH), 149.93 (C), 133.13 (2CH), 132.96 (C), 114.94 (C).	–	–
8	160.97	156.83	151.15/ 145.92	153.92 (C), 153.65 (2CH), 152.07(CH), 150.42 (2CH), 150.27(2CH), 149.93(2C), 147.84 (2CH), 147.59(CH), 144.33 (C), 144.27 (2CH),143.08 (CH), 133.15 (C), 130.33 (C), 118.04 (C).	–	–
13	161.30	155.83	153.10/ 146.41	152.11 (C), 150.42 (CH), 144.33 (CH), 133.14 (CH), 132.96 (C), 116.17 (C), 113.03 (C), 111.61(C).	–	21.18
14	161.44	159.37	153.61/ 146.92	153.23 (2C),152.95 (2CH),151.33 (2C), 151.05 (2CH),150.75 (2CH), 147.84 (2C), 147.50 (CH), 143.54 (CH), 130.48 (2C), 130.05 (2CH), 118.70 (2CH), 112.38 (2C), 110.23 (C), 110.18 (2C).	–	21.06
19	160.18	158.23	154.46/ 144.80	117.52 (C), 116.12 (C), 115.32 (CH), 113.05 (CH), 112.54 (CH), 111.61 (C), 111.38 (C), 107.05 (C).	55.58 54.97	–
20	161.25	159.65	153.05/ 144.77	153.02 (2C), 152.95 (2CH), 152.67 (2C), 151.02 (2CH), 150.27 (2CH), 149.73 (2C), 147.84 (CH), 144.33 (2C), (CH), 133.15 (2C), 130.33 (CH), 124.76 (CH), 118.04 (C).	55.87 55.18	–

Table-4: Analytical Data of New Ligands.

			Elemental Analyses- Calcd. (Found)		
Comp.	% Yield	M.p. °C	C	H	N
7	73	281-283	54.82 (54.87)	3.58 (3.56)	21.32 (21.35)
8	61	266-268	61.20 (61.23)	3.11 (3.14)	15.29 (15.25)
13	72	239-241	53.76 (53.83)	3.80 (3.85)	19.81 (19.76)
14	51	237-239	60.10 (60.12)	3.30 (3.34)	14.50 (14.51)
17	83	131-133	65.45 (65.44)	5.49 (5.49)	-
18	81	142-144	61.54 (61.57)	4.30 (4.32)	-
19	70	220-222	52.86 (52.82)	3.99 (3.96)	18.50 (18.55)
20	53	219-221	59.02 (59.05)	3.46 (3.40)	13.76 (13.70)

Synthesis of compound 4-Amino-3-(2-furoyl)-5-oxo-4,5-dihydro-[1,2,4]triazol-1-yl-acetic acid hydrazide **(3)**

A solution of the corresponding compound **2** (0.01 mol) in *n*-butanol was refluxed with hydrazine hydrate (0.025 mol) for 4 h. After cooling to room temperature, a white solid appeared. This was recrystallized from an appropriate solvent to afford the desired product **(3).** Recrystallization from ethanol (yield: 1.73 g, 72.58%), m.p. 202–203 °C. IR (KBr) (ν, cm^{-1}), 3303–3167 (ν NH + $2NH_2$), 1726 (triazole νC=O), 1658 (hydrazide νC=O), 1569 (νC=N); ^{1}H-NMR (DMSO-d_6) δ (ppm) 4.22 (s, 2H, –NCH_2), 4.62 (s, 2H, –NH_2), 6.25 (d, 2H, –NH_2), Ar-H [7.31 (d, 1H, J =7.86 Hz), 7.65-7.70 (m, 1H), 7.88 (d, 1H, J =6.98 Hz), 10.58 (t, 1H, –NH); ^{13}C NMR (DMSO-d_6) δ (ppm) 165.92 (exocyclic-C=O), 153.22 (triazole-C_5), 146.10 (triazole-C_3), Ar C: [131.04 (CH), 130.58 (C), 130.48 (CH), 129 71 (CH)], 66.10 (–CH_2); Anal.calcd. (%) for ($C_8H_{10}N_6O_3$) 238.21 g/mol: C, 40.33; H, 4.23; N, 35.28. Found: C, 40.31; H, 4.27; N, 35.34.

General Method for Synthesis of 4-Methyl coumarin derivatives **(5, 10, 16)**

4-methylcoumarin **(5)**, 4-Methyl-7-hydroxycoumarin **(10)** and 4-Methyl-7,8-dihydroxycoumarin **(15)** were synthesized using a published methods [42, 43 and 44] respectively. The synthesis route of these compounds are presented in **Fig 2**.

General Method for Synthesis of 4-formyl coumarin derivatives **(6, 11, 12, 16, 17, 18)**

4-formylcoumarin **(6)**, 4-methyl-7-metoxycoumarin **(11)**, 4-formyl-7metoxycoumarin **(12)** and 4-methyl-7,8-dihydroxycoumarin **(16)** were synthesized literature methods [42-44] respectively. The synthesis route of these compounds are presented in **Fig (2-4)**.

4-methyl-7,8-dimethoxycoumarin **(17)**

4-methyl-7, 8-dihydroxycoumarin **(16)** (3.84 g, 0.02 mol) was dissolved in 50 ml acetone. To it, anhydrous K_2CO_3 (5.5 g, 0.04 mol) was added. The reaction solition was refluxed for 10 min, then 5.80 g (0.04 mol) methyl iodide added, and continuosly refluxed for 6 h. The reaction mixture was filtered during heating [43]. White product was obtained by evaporating off the solvent from the filtrate. Recrystallization from ethanol (yield: 3.65 g, 82.95%), m.p. 131-133 °C. IR (KBr) cm^{-1} 3054 (νCH), 1704 (νC=O), 1620 (νC=C), 1148 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.36 (s, 3H, CH_3), 3.88, 3.90 (2s, 6H, 2 OCH_3), Ar–H [6.22 (s, 1H), 6.69 (d, 1H, *j* =8.54 Hz), 7.65 (d, 1H, *j* =8.54 Hz]; ^{13}C-NMR (DMSO-d_6) δ (ppm) 160.76 (-C=O), Ar–C [153.67 (CH), 148.13 (C), 143.44 (C), 131.52 (CH), 114.51 (C), 113.70 (C), 112.16 (C), 109.37 (CH)], 56.02 (-OCH_3), 55.68 (-OCH_3), 21.14 (-CH_3); Anal.calcd. (%) for ($C_{12}H_{12}O_4$) 220.42 g/mol: C, 65.45; H, 5.49. Found: C, 65.44; H, 5.49.

4-formyl-7,8-dimethoxycoumarin **(18)**

4-methyl-7,8-dimethoxycoumarin **(17)** (4.41 g, 0.02 mol) was dissolved in 50 ml dimethylbenzene during heating. To it, seleninic acid (3.8 g, 0.027 mol) was added. The reaction solution was refluxed for 20 h, and than filtered during heating to recycle selenium [43]. After the filtrate was cooled, yellow cristal product was separeted out. Recrystallization from ethanol (yield: 3.79 g, 81.00%), m.p. 142-144 °C. IR (KBr) cm^{-1} 3056 (νCH), 2952-2845 (νH-C=O),1709 (νC=O), 1622 (νC=C), 1146 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.88, 3.91 (2s, 6H, 2 OCH_3), Ar–H [6.41 (s, 1H), 6.63 (d, 1H, *j* =8.54 Hz), 7.46 (d, 1H, *j* =8.54 Hz]; 10.14 (s, 1H, -H-C=O); ^{13}C-NMR (DMSO-d_6) δ (ppm) 177.98 (-CH=O), 160.41 (-C=O), Ar–C [153.62 (CH), 148.98 (C), 144.20 (C), 132.17 (CH), 114.93 (C), 113.56 (C), 112.08 (C), 109.85 (CH)], 54.02 (-OCH_3), 53.75 (-OCH_3); Anal.calcd. (%) for ($C_{12}H_{10}O_5$) 234.20 g/mol: C, 61.54; H, 4.30. Found: C, 61.57; H, 4.32.

General Method for Synthesis of Schiff bases **(7, 13, 19 and 8, 14, 20)**

A mixture of 2-[4-amino-3-(2-furoyl)-5-oxo-4,5-dihydro-1H-1, 2, 4-triazol-1-yl] acetohydrazide **(3)** and 4-formyl coumarin derivatives **(6, 12, 18)** in 1:1 molar proportion in glacial acetic acid medium was refluxed for 8 h. After cooling, the mixture was poured into a beaker containing ice-water (100 mL). The precipitate formed was filtered. After drying in vacuo, [45] the product was recrystallized from ethanol to afford the desired products **(7, 13, 19)**.

The corresponding compound **(3)** was then added to a solution of compounds **(6, 12, 18)** in 1:2 molar proportion in glacial acetic acid (20 mL) and the mixture was refluxed for 16 hours. After cooling, the mixture was poured into a beaker containing ice-water (100 mL). The precipitate formed was filtered. After drying *in vacuo*, the product was recrystallized from 1:2 benzene-petroleum ether [46] to give the desired compounds **(8, 14, 20)**.

2-(4-amino-3-(furan-2-yl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl)-N'-((2-oxo-2H-chromen-4-yl) met--hylene)acetohydrazide **(7)**

(Yield 2.87 g, 72.84 %). M.p. 281-283 °C; IR (KBr) cm^{-1} 3357-3211(ν NH_2 + NH), 1716 (triazole νC=O), 1695 (coumarin νC=O), 1682 (exocyclic νC=O), 1641, 1500 νC=N), 1622 (νC=C), 1053 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.60 (s, 2H, CH_2), 6.20 (s, 2H, NH_2), Ar–H [6.44 (s, 1H), 6.55 (d, 1H, *j* = 8.64 Hz), 6.60-6.80 (m, 2H), 7.62 (d, 1H, *j* = 8.72 Hz), 8.66-8.92 (m, 2H), 9.12 (d, 1H, *j* = 6.98 Hz)], 8.64 (s, 1H, N=CH), 10.37 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 172.25 (exocyclic-C=O), 170.00 (N=CH), 166.90 (triazole-C=O), 160.81 (coumarin-C=O), 146.54 (triazole C=N), Ar–C [152.08 (CH), 150.42 (2CH), 149.93 (C), 145.62 (CH), 141.23 (CH), 133.13 (CH), 132.96 (C),114.94 (C), 113.76 (CH), 112.43 (C), 109.00 (CH)], 67.34 (-CH_2); Anal.calcd. (%) for ($C_{18}H_{14}N_6O_5$) 394.34 g/mol: C, 54.82; H, 3.58; N, 21.32. Found: C, 54.87; H, 3.56; N, 21.35.

2-(4-amino-3-(furan-2-yl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl)-N'-((7-methoxy-2-oxo-2H-chromen-4-yl)methylene)acetohydrazide **(13)**

(Yield 3.07 g, 72.41 %). M.p. 239-241 °C; IR (KBr) cm^{-1} 3284-3173 (ν NH_2 + NH), 1717 (triazole νC=O), 1673 (coumarin νC=O), 1653 (exocyclic νC=O), 1629, 1544 νC=N), 1621 (νC=C), 1043 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.59 (s, 2H, CH_2), 3.89 (s, 3H, OCH_3), 6.16 (s, 2H, NH_2), Ar–H [6.44 (s, 1H), 6.82-7.19 (m, 2H), 7.34 (s, 1H), 8.70-8.90 (m, 2H), 8.95 (d, 1H, *j* = 6.98)], 8.56 (s, 1H, N=CH), 10.68 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 172.13 (exocyclic-C=O), 170.54 (N=CH), 164.51 (triazole-C=O), 161.30 (coumarin-C=O), 145.92 (triazole C=N), Ar–C [152.11 (CH), 150.42 (CH), 149.93 (C), 146.07 (CH), 144.33 (C), 142.50 (CH), 133.26 (CH), 132.00 (C),115.42 (C), 113.06 (CH), 112.49 (C), 111.74 (CH)], 66.82 (-CH_2), 55.80 (-OCH_3); Anal.calcd. (%) for ($C_{19}H_{16}N_6O_6$) 424.37 g/mol: C, 53.76; H, 3.80; N, 19.81. Found: C, 53.83; H, 3.85; N, 19.76.

2-(4-amino-3-(furan-2-yl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl)-N'-((7,8-dimethoxy-2-oxo-2H-chromen-4-yl)methylene)acetohydrazide **(19)**

(Yield 3.20 g, 70.48 %). M.p. 220-222 °C; IR (KBr) cm^{-1} 3286-3164 (ν NH2 + NH), 1726 (triazole νC=O), 1665 (coumarin νC=O), 1658 (exocyclic νC=O), 1602, 1569 νC=N), 1600 (νC=C), 1238 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.62 (s, 2H, CH_2), 3.87, 3.91 (2s, 6H, $2OCH_3$), 6.28 (s, 2H, NH_2), Ar–H [6.50 (s, 1H), 6.65-6.84 (m, 2H), 8.78-8.90 (m, 2H), 9.12 (d, 1H, *j* = 6.98 Hz)], 8.68 (s, 1H, N=CH), 10.43 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 170.07 (exocyclic-C=O), 168.00 (N=CH), 165.12 (triazole-C=O), 160.18 (coumarin-C=O), 144.80 (triazole C=N), Ar–C [151.06 (CH), 150.44 (CH), 148.16 (C), 147.39 (CH), 143.72 (C), 142.60 (CH), 133.88 (C), 131.46 (C),115.23 (C), 113.99 (CH), 112.08 (C), 109.56 (CH)], 66.05 (-CH_2), 56.09 (-OCH_3), 55.47 (-OCH_3): Anal.calcd. (%) for ($C_{20}H_{18}N_6O_7$) 454.39 g/mol: C, 52.86; H, 3.99; N, 18.50. Found: C, 52.82; H, 3.96; N, 18.55.

2-(3-(furan-2-yl)-5-oxo-4-((E)-((2-oxo-2H-chromen-4-yl)methylene)amino)-4,5-dihydro-1H-1,2,4-triazol-1-yl)-N'-((2-oxo-2H-chromen-4-yl)methylene)acetohydrazide **(8)**

(Yield 3.34 g, 60.84 %). M.p. 266-268 °C; IR (KBr) cm^{-1} 3302(νNH), 1716 (triazole νC=O), 1695 (coumarin νC=O), 1682 (exocyclic νC=O), 1641, 1500 νC=N), 1622 (νC=C), 1053 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.60 (s, 2H, CH_2), Ar–H [6.13 (s, 2H), 6.59-6.65 (m, 2H), 6.88-7-00 (m, 4H), 7.54-7.65 (m, 2H), 8.56-8.82 (m, 2H), 8.78 (d, 1H, *j* = 6.98 Hz)], 8.80, 8.84 (2s, 2H, 2 N=CH), 10.29 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 170.07 (exocyclic-C=O), 187.59, 164.86 (2 N=CH), 163.72 (triazole-C=O), 160.97 (coumarin-C=O), 145.92 (triazole C=N), Ar–C [152.35 (CH), 151.07 (CH), 150.64 (CH), 149.61 (C), 148.92 (2C), 147.56 (CH), 145.97 (CH), 145.62 (2CH), 143.29 (CH), 136.12 (C), 133.00 (CH), 132.24 (2C), 131.46 (C), 114.56 (CH), 113.76 (CH), 112.43 (CH), 109.00 (CH)], 64.47 (-CH_2); Anal.calcd. (%) for ($C_{28}H_{17}N_6O_7$) 549.49 g/mol: C, 61.20; H, 3.11; N, 15.29. Found: C, 61.23; H, 3.14; N, 15.25.

3-(furan-2-yl)-N'-((7-methoxy-2-oxo-2H-chromen-4-yl)methylene)-4-((E)-((7-methoxy-2-oxo-2H-chromen-4-yl)methylene)amino)-5-oxo-4,5-dihydro-1H-1,2,4-triazole-1-carbohydrazide **(14)**

(Yield 2.98 g, 51.47 %). M.p. 237-239 °C; IR (KBr) cm^{-1} 3303 (ν NH), 1714 (triazole νC=O), 1702 (coumarin νC=O), 1651 (exocyclic νC=O), 1636, 1548 νC=N), 1628 (νC=C), 1044 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.64 (s, 2H, CH_2), 3.80 (s, 6H, $2OCH_3$), Ar–H [6.40 (s, 2H), 6.56 (s, 1H), 6.82 (s, 1H), 7.54-7.65 (m, 2H), 6.65-8.00 (m, 2H), (m, 2H), 8.56 (d, 1H, *j* = 6.98 Hz)], 9.14, 9.20 (2s, 2H, 2N=CH), 10.38 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 170.00 (exocyclic-C=O), 164.12, 162.81 (2 N=CH), 163.57 (triazole-C=O), 161.44 (coumarin-C=O), 146.92 (triazole C=N), Ar–C [152.67 (CH), 151.02 (CH), 150.18 (CH), 149.05 (C), 148.51 (2C),

146.35 (CH), 145.13 (CH), 144.26 (CH), 141.31 (CH), 139.22 (C),135.54 (2C), 133.99 (CH), 132.15 (2C),114.48 (CH), 113.61 (CH), 112.77 (C), 109.64 (CH)], 65.89 (-CH_2), 55.80 (2 -OCH_3); Anal.calcd. (%) for ($C_{29}H_{19}N_6O_8$) 579.53 g/mol: C, 60.10; H, 3.30; N, 14.50. Found: C, 60.12; H, 3.34; N, 14.51.

N'-((7,8-dimethoxy-2-oxo-2H-chromen-4-yl)methylene)-2-(4-((E)-((7,8-dimethoxy-2-oxo-2H-chromen-4-yl)methylene)amino)-3-(furan-2-yl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl)acetohydrazide **(20)**

(Yield 3.25 g, 53.28 %). M.p. 219-221 °C; IR (KBr) cm^{-1} 3296 (νNH), 1704 (triazole νC=O), 1665 (coumarin νC=O), 1658 (exocyclic νC=O), 1615-1542, νC=N), 1610 (νC=C), 1274 (νC-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 3.61 (s, 2H, CH_2), 3.84 (s, 6H, 2OCH_3), 3.89 (s, 6H, 2OCH_3), Ar–H [6.45 (s, 2H), 6.87-6.99 (m, 2H), 7.52-7.68 (m, 2H), 8.60-8.72 (m, 2H), 8.92 (d, 1H, *j* = 6.98 Hz)], 8.85, 8.89 (2s, 2H, 2N=CH), 10.47 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 167,60 (exocyclic-C=O), 166.97, 164.45 (2 N=CH), 164.40 (triazole-C=O), 161.25 (coumarin-C=O), 144.77 (triazole C=N), Ar–C [153.02 (CH), 152.95 (CH), 150.27 (CH), 149.73 (2C), 147.84 (2C), 147.00 (CH), 146.12 (2C), 144.16 (CH), 143.25 (CH), 133.15 (C), 133.01 (CH), 130.33 (2C), 124.76 (CH), 118.04 (C), 115.18 (C), 111.83 (CH)], 67.00 (-CH_2), 56.21 (2 -OCH_3), 55.82 (2 -OCH_3); Anal.calcd. (%) for ($C_{30}H_{21}N_6O_9$) 610.52 g/mol: C, 59.02; H, 3.46; N, 13.76. Found: C, 59.05; H, 3.40; N, 13.70.

Results and Discussion

In the ^{1}H-NMR spectra of compound **(2)** additional signals derived from ester group were obtained at 4.52 (–NCH_2), 4.10 ppm (–OCH_2CH_3) and 1.17 ppm (–OCH_2CH_3) ppm with integration for two protons, two, and three protons, respectively. In the ^{13}C NMR spectra of these compounds, the signals related to the same groups were recorded at 65.43, 66.94, and 13.86 ppm, respectively. The ^{1}H-NMR spectra of compound **(3)** showed no signals for OCH_2CH_3 group; instead, new signals derived from hydrazide structure appeared at 6.25 ppm (–$NHNH_2$) and 10.29-10.68 ppm (–$NHNH_2$) integrating for two protons and one proton, respectively (controlled by changing with D_2O).In addition, the signals derived from –NH_2 group at position-4 on 5-oxo-[1,2,4] triazole ring resonated between 4.62–6.28 ppm integrating for two protons (exchangeable with D_2O). The IR spectra of acid hydrazide **(3)** showed an additional peak at 1736 cm^{-1} due to exocyclic-carbonyl function derived from hydrazide structure beside the endocyclic carbonyl peak at position-5 of [1,2,4] ring. The^{13}C NMR values of triazole-C-3 and triazole-C-5 are consistent with the literature [40].

Conclusion

The main idea of the present research work is to synthesize some novel Schiff bases to utilize as ligands and to study the ligands and their metal complexes from a structural point of view. These ligands with varius bonding interactions, tautomeric phenomena, potential variety of bonding modes and hydrogen bonding interactions, was expected to obtained stimulating results. This expectation became fruitful Metal chelates of Schiff bases hold exciting possibilities for the future concerning their wide applications viz. in designing new catalytic systems, in formulating new synthetic route, in developing new analytical reagents and in metal-based antimicrobial agents etc. In addition, the synthesis of a compound can be used in a selective extraction of the metal is of great importance for the environment and the metal industry. Hopefully, the results of this investigation would attract increased interest in this field.

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