Spectral, thermal, antimicrobial studies for silver(I) complexes of pyrazolone derivatives

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Abstract

Background: Synthesize new complexes of Ag(I) to enhance efficacy or stability and also, pharmacological activities on the operation of pyrazolone's biological properties.

Results: Efficient and high yielding pathways starting from the versatile and readily available 3-methyl-1-phenyl-5-pyrazolone by Knoevenagel condensation of a sequence of 4-arylidene-3-methyl-1-phenyl-5-pyrazolone derivatives (2a-c) have been formed by the reaction of various substituted aromatic aldehydes. Used as ligands to synthesize Ag(I) chelates. Synthesized compounds and their complexes have been characterized by elemental analysis, magnetic and spectroscopic methods (IR, 13C, 1HNMR, mass) and thermal analysis. The spectrophotometric determinations suggest distorted octaedral geometry for all complexes. Both ligands and their metal complexes have also been tested for their antibacterial and antifungal efficacy.

Conclusions: Newly synthesized compounds have shown potent antimicrobial activity. The results showed that the complex’s high activity was higher than its free ligands, and that Ag(I)-L3 had the highest activity.

Keywords: Pyrazolones, Ag(i) complexes, Knoevenagel condensation, Antimicrobial activity

Introduction

Pyrazolone chemistry began in 1883 when Ludwig Knorr first reacted to phenyl hydrazine with aceto-acetate ester. As pyrazolones were discovered as binding components for azo dyes in the late 1800s, they rapidly increased in importance. Today, pyrazolone is still an significant trade precursor to dyes and pharmaceuticals. Pyrazolone is a biologically important scaffold associated with different pharmacological activities such as antimicrobials [1–5], anti-inflammatory [6], analgesic [7], antidepres- sant [8], anticonvulsant [9], anti diabetic [10], antihyperlipidemic [11, 12], antiviral [13, 14], anti-tuberculosis [15, 16], antioxidant [17, 18] and anticancer [19, 20]. For several years, the preparation of pyrazolone and its derivatives has attracted significant attention from organic and medicinal chemists, as they belong to a class of compounds with promising results in medicinal chemistry. The heterocycles condensed to the pyrazole ring are an important source of bioactive molecules [21, 22]. Compounds containing both pyrazole and other essential heterocyclic active structural units usually demonstrate more remarkable biological activity. A number of condensed pyrazole derivatives have been reported as four-fold antibacterial agents against Gram-positive and Gram-negative bacteria compared to general pyrazole compounds [23, 24]. A digit of antimicrobial active silver(I) complexes have the capacity to disrupt microbrial transpiration as well as block tyrosinase synthesis and are extremely cytotoxic to cancer cells [24]. Massive attention in silver ions (Ag(I)) as a broad spectrum antimicrobial has upped the size and importance of in vitro
biocompatibility research [25]. Silver ions are toxic to many bacteria, viruses, algae and fungi. Silver-based medicines have been widely used for this task for decades [26]. The objective of this study is to display the synthesis and characterization of three Ag(I) pyrazolone complexes in an attempt to verify the mode of coordination and the biological properties of the final complexes.

Results and discussion

Synthesis and formulation

A sequence of derivatives of 4-arylidene-3-methyl-1-phenyl-5-pyrazolone (4-(4-dimethylamino benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2a) L1, 4-(4-Thiophene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2b) L2, 4-(4-methoxy benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2c) L3) is synthesized by condensing 3-methyl-1-phenyl-5-pyrazolone with substituted aromatic aldehydes as shown in Scheme 1 [27]. Three Ag(I) complexes have been prepared with the L1, L2, L3 ligands as shown in Scheme 2. Based on physicochemical and spectral data (IR and ¹HNMR), structure of the synthesized compounds (2a-c, Ag(I) complexes) has been evaluated.

Infrared spectra

KBr disks registered mid-infrared spectra of L1, L2, L3 and their metal complexes. As expected, with changes in band intensities and wave numbers, the absorption bands characteristic of L1, L2, L3 acting as a monodentate unit are observed in the complexes. The proposed structures of the complexes must be considered prior to determining the assignments of the infrared spectra. Here, Ag(I) ion interacts with these monodentate ligands forming monomeric structure complexes in which the Ag(I) ion is four coordinated (Scheme 2) [27–30].

The complexes of three ligands with Ag(I) contain only one plane of symmetry and therefore the complexes that belong to Cs symmetry and show 159 vibrational fundamentals, and all vibrations are distributed between movements of the types A1 and A1', all of which are monodegenerate, infra-red and Raman active. The free ligand infrared spectrum shows bands at 1496, 1508 and 1550 cm⁻¹ due to the stretching vibration of hydrazono (C=N) groups [31]. Comparing the Ag(I) IR spectrum with the free ligand spectrum, the transfer of (C=N) from O\[O\]O\[O\]O\[O\]+ NH₂NH₂ Ph to Acetic acid /sod.acetate results in OHC-CH₃ and OHC-OCH₃ groups to lower frequency values (1512, 1515, 1523 and 1527 cm⁻¹) and the change in strength of (C=N) from

![Scheme 1](image-url)  
Scheme 1 Synthesis of 4-arylidene-3-methyl-1-phenyl-5-pyrazolone derivatives
medium to strong (Fig. 1 and Table 1) which confirms that the ligand molecule coordinated with metal ions through the hydrazon nitrogen atom [31]. A medium wide band for the $\text{H}_2\text{O}$ stretching vibrations of coordinated water molecules at 3379, 3364, and 3364 cm$^{-1}$ [31]; The stretching vibrations $\nu(\text{C-H})$ of phenyl groups and $-\text{CH}_3$ units in these complexes are assigned as a number of bands in the region 3066–3100 cm$^{-1}$ [11, 12]. The $\nu(\text{C}═\text{O})$ vibration appears in the region of 1666–1685 cm$^{-1}$. The spectra of the isolated solid complexes revealed a number of new bands of different intensities for $\nu(\text{M–N})$. The $\nu(\text{Ag–N})$ bands observed at 813, 837 cm$^{-1}$ for Ag(I)-L$_1$, at 748, 794 cm$^{-1}$ for Ag(I)-L$_2$ and at 759, 779 cm$^{-1}$ for Ag(I)-L$_3$ (Table 1) which are absent in the spectrum of free three ligands [30–32]. The coordinating water in the three complexes are characterized by the appearance of $\nu(\text{Ag–O})$ at 577, 515, 544 cm$^{-1}$. Also the stretching vibrations at 813, 792, 779 cm$^{-1}$ assigned to $\nu(\text{Ag OH}_2)$, sponsored coordinating water participation [32]. The suggested structural formulas are defined in Scheme 2 on the basis of the IR tests.

**Scheme 2** The coordination mode of Ag (I) with three ligand

**UV-Visible Spectra**

The application of ultraviolet spectroscopy is more general and can be useful for all chelate structural determinations as they are all absorbed in this region [33]. Electronic absorption spectra confirmed the development of metal ligand complexes. Electronic absorption spectra L$_1$ for Ag(I), L$_2$ for Ag(I) and L$_3$ for Ag(I). Complexes within the spectrum of wavelengths between 200 and 800 nm are described in Additional file 1: Table S1 and Fig. 2. The free three-ligand UV spectrum (L$_1$, L$_2$ and L$_3$) displays bands at 281, 297 and 297 nm that are assigned respectively to $\pi-\pi^*$ transitions at 330 nm. The modification of the reflectance band to higher (bathochromic shift) and lower values (hypochromic shift) and the appearance of new bands for complexes has resulted in the release of three ligands’ complex actions towards metal ions. Complexes also present bands within the range 410–480 nm which can be due to the transition of ligand–metal charges for three ligands [34, 36]. The molar absorptivity ($\varepsilon$) values of the prepared metal
complexes under investigation were determined (Additional file 1: Table S1) using the relation: $A = \varepsilon cl$, where, $A =$ absorbance, $c = 1.0 \times 10^{-3} \text{ M}$, $l =$ length of cell (1 cm) [22]. The values of 10Dq (difference between $t_{2g}$ and $e_g$) for the complexes were calculated by using the following Eq. $10Dq = E = h\nu$, where $E =$ energy, $h =$ blank constant $= 6.626 \times 10^{-34} \text{ J}.\text{sec}$, $c = 3 \times 10^{10} \text{ cm/sec}$, $\nu =$ wave number $\text{cm}^{-1}$ the data listed in Additional file 1: Table S1.

The $^1H$ NMR spectra
Suggested structure of the isolated Ag(I) complexes confirm about the efficiency of $^1H$ NMR spectra. Compared to the one of their complexes (Additional file 1: Table S2), the $^1H$ NMR spectra of new free three ligands in DMSO-$d_6$. The $^1H$ NMR spectra of L$_1$ and its metal complex shown in (Fig. 3a, b), the proton of (–CH–Ar) group observed in $\delta$: 9.66 ppm and the protons of aromatic ring of (s, 9H, Aromatic–H) observed at $\delta$: 7.14–7.97 ppm also the values of protons of -CH aliphatic observed in the range $\delta$: 3.03–3.33 ppm (s, 6H, –N (CH$_3$)$_2$), the proton of (s, 3H, –CH$_3$) group observed in $\delta$ 2.28 ppm, no major differences were observed as opposed to the Ag(I) complex except that the signal is observed in 3.46 ppm due to H$_2$O molecules [36]. This supports the hypothesis that L$_1$ interacts as a monodentate ligand bound to the Ag(I) ion through the hydrazono nitrogen group. [37].
Table 1 Infrared frequencies (cm\(^{-1}\))\(^a\) and tentative assignments\(^b\) for (A) \(L_1\), (B) \([\text{Ag}(L_1)_2(\text{H}_2\text{O})_2]\text{NO}_3\), (C), \(L_2\) (D) \([\text{Ag}(L_2)_2(\text{H}_2\text{O})_2]\text{NO}_3\), (E) \(L_2\) and (F) \([\text{Ag}(L_3)_2(\text{H}_2\text{O})_2]\text{NO}_3\)

| A | B | C | D | E | F | Assignments |
|---|---|---|---|---|---|-------------|
| - | 3370\(_w\) | - | 3364\(_{mn}\) | - | 3364\(_{mn}\) | ν(O–H), coordinate \(\text{H}_2\text{O}\) |
| 3100\(_v\) | 3100\(_v\) | 3066\(_w\) | 3100\(_v\) | 3099 | 3100 | ν(C–H); aromatic |
| 2900 | 2900 | 2890 | 2885 | 2901 | 2900 | ν(H–H); aliphatic |
| 1670\(_{mn}\) | 1666\(_v\) | 1681\(_i\) | 1685\(_{sh}\) | 1678\(_m\) | 1678\(_m\) | ν(\(\text{C}–\text{C}\)); aromatic |
| 1550\(_i\) | 1523\(_s\) | 1496\(_i\), 1408\(_m\) | 1527\(_{rs}\) | 1508\(_i\) | 1520\(_i\) | ν(\(\text{C}–\text{N}\)); aromatic |
| 1400\(_{m}\) | 1410\(_i\) | - | 1381 | - | 1427\(_{vw}\) | ν(\(\text{C}=\text{O}\)); aromatic |
| 1319\(_i\) | 1319\(_i\) | 1300\(_i\) | 1311\(_i\) | 1311\(_{sh}\) | 1311\(_i\) | Δ\(_s\)(CH\(_3\)); aromatic |
| - | 1188\(_i\) | - | 1165\(_{mn}\) | - | 1172\(_i\) | ν(NO\(_3\)); aromatic |
| 1122\(_i\) | 1122\(_i\) | 1130\(_m\) | 1104\(_{sv}\) | 1110\(_w\) | 1130\(_{mn}\) | ν(\(\text{C}–\text{N}\)); aromatic |
| 1018\(_w\) | 1018\(_w\) | - | - | - | - | ν(\(\text{C}–\text{N}\)); aromatic |
| - | - | 1056\(_w\) | 1099\(_{sh}\) | - | - | ν(\(\text{C}–\text{N}\)); aromatic |
| 954\(_w\) | 995\(_w\) | 991\(_w\) | 941\(_{vw}\) | 988\(_w\) | 985\(_w\) | ν(CH\(_2\)); phenyl |
| 943\(_vw\) | 943\(_vw\) | 921\(_w\) | 910\(_w\) | 938\(_i\) | 965\(_sh\) | ν(CH\(_3\)); aromatic |
| - | 813\(_m\) | - | 792\(_m\) | - | 779\(_m\) | ν(\(\text{Ag}–\text{OH}\)); aromatic |
| - | 577\(_w\) | - | 515\(_w\) | - | 544\(_w\) | ν(\(\text{Ag}–\text{O}\)); aromatic |
| - | 524\(_w\) | - | 498\(_w\) | - | 488\(_w\) | ν(\(\text{Ag}–\text{N}\)); aromatic |

\(^a\) s = weak, w = strong; sh = shoulder, v = very, br = broad, \(^b\) ν = stretching and δ = bending

The \(^1\)H NMR spectra of \(L_2\) and its Ag(I) complex shown in (Fig. 3c, d), the proton of (= CH-Ar) group observed in δ: 8.25 ppm and, the protons of aromatic ring of (s, 8H, Aromatic–H) observed at δ: 7.39–7.91 ppm [38]. The proton of (s, 3H, –CH\(_3\)) group observed in δ 2.30 ppm, no major variations were noticed as opposed to the Ag(I) series. This supports the assumption that \(L_3\) reacts via the hydrazono nitrogen group as a monodentate ligand bound to the Ag(I) ion. The \(^1\)H NMR spectra of \(L_3\) and its Ag(I) complex shown in (Fig. 3 (E, F), the proton of (= CH-Ar) group observed in δ: 8.71 ppm and, the protons of aromatic ring of (s, 9H, Aromatic–H) group observed in δ: 8.71 ppm, no major variations were noticed as opposed to the Ag(I) series. This supports the assumption that \(L_3\) reacts as a mononitrogenate ligand bound to the Ag(I) ion via the hydrazono nitrogen group.

**Thermal studies**

The thermal degradation of ligand \((L_2)\) began at 190 °C and decay occurs at various temperatures at 310, 544 °C at one stage (Additional file 1: Fig. S1a). This step is accompanied by a net weight loss of 92.36 percent, equivalent to the predicted 92.07 percent. Corresponding to the loss of \(8\text{C}_2\text{H}_2+\text{NH}_3+\text{CO}+\text{N}_2\) molecule and 95.65 KJ mol\(^{-1}\) (endothermic) activation energy. The residue value decomposes at a height of 800 °C and the actual losing weight at this point is 7.64 percent, close to the estimated 7.86 percent equal to 2C. The \([\text{Ag}(L_2)_2(\text{H}_2\text{O})_2]\text{NO}_3\) complex decomposed in two steps (Additional file 1: Fig. S1b), The first one begins at a limit of 189 °C and is followed by a 33.78 percent weight loss leading to a 9C\(_2\text{H}_2+2\text{H}_2\text{O}\) loss similar to the estimated value of 33.06 percent with an activation energy of 34.37 KJ mol\(^{-1}\). The second step occurs at 366 and 562 °C followed by a weight loss of 52.79 percent; equivalent to a value of \(8\text{C}_2\text{H}_2+4\text{HCN}+\text{NO}+2\text{N}_2\text{O}\), potentially similar to the measured value of 53.798 percent. The residue value proceeds at 931 °C and the overall weight loss from this stage is 13.47 percent, referring to Ag, similar to the 13.14 percent estimated value (Table 2).

The ligand \((L_2)\) degrades at 273, 475 °C. This stage is followed by a complete loss of weight of 86.70 percent, close to 86.56 percent of the estimated value (Additional file 1: Fig. S1c). Equivalent to \(6\text{C}_2\text{H}_2+\text{SO}+\text{N}_2\) loss and 31.93 KJ mol\(^{-1}\) (endothermic) activation energy. Decomposition of the residual value occurs at 771 °C and the real weight loss from this stage is 13.30 percent, similar to the estimated value of 13.43 percent corresponding to 3C. The \([\text{Ag}(L_2)_2(\text{H}_2\text{O})_2]\text{NO}_3\) complex decomposes at two levels of decay (Additional file 1: Fig. S1d), the first phase occurs at 99 °C and is followed by a weight loss of 2.08 percent relating to the removal of \(\text{H}_2\text{O}\), activation energy of 79.28 KJ mol\(^{-1}\). The second step of decomposition occurs at temperature is 203, 528 and is accompanied by a weight loss of 75.90%; corresponding to the value of \(10\text{C}_2\text{H}_2+4\text{HCN}+2\text{H}_2\text{O}+\text{SO}_2+\text{SO}_2+\text{SO}_2\) theoretically, close to the calculated value 76.404%.
The Residue value decomposition occurs at maximum 881 °C and the actual weight loss from this step is 23.35%, corresponding to Ag + 6C, close to the calculated value 23.596%.

The thermal decay of L3 happens in two phases of degradation (Additional file 1: Fig. S1e), the first step arises at 291 °C and is followed by a weight loss of 70.55 percent leading to a loss of 8C2H2 similar to the measured value of 71.23 percent with activation energy of 35.31 kJ mol⁻¹. The second step occurs at 518 °C and is accompanied by a weight loss of 28.604%; corresponding to C2H2 + CO + 2HCN + 3NO2 theoretically, close to the calculated value 31.25%. The Residue remains at 677 °C and the actual weight loss is 17.76%, equal to Ag + 3C, close to the calculated value 18.15%.

### Kinetic data

The kinetic parameters (activation energy, E*, entropy, ΔS*, enthalpy, ΔH*, and Gibbs free energy, ΔG*) have been evaluated by using the two mentioned methods in the literature [39, 40] and shown in Additional file 1: Fig. S2 and listed in Table 3. The correlation coefficient for Arrhenius plots of thermal degradation stages were found to be in the range 0.943–0.985, revealing a good fit with linear function. The activation energies of decomposition were observed to be in the range 7.44–154.69 kJ mol⁻¹. The negative values of ΔS* indicate that the activation complex has a more ordered structure than the reactants or the reactions are slow. The positive ΔH* values postulate an endothermic nature of the formed complexes. The greater positive values of E* indicate that the processes involving in translational, rotational, vibrational states and a changes in mechanical potential.
Mass spectra

The principle of a mass spectrometer focuses on the separation of fragments of ions based on the distribution of these ions with the mass to charge ratio (m/z). The $L_1$, $L_2$, $L_3$ fragmentation patterns and their complexes were obtained from the mass spectra, and were in good agreement with the structure suggested. The $L_1$ showed molecular ion peak (M$^+$) with m/z = 305 (100%). The molecular ion peak [a] losses C$_6$H$_4$N to give fragment [b] at m/z = 261 (3.13%), then [b] losses C$_6$H$_4$ to give fragment [c] at m/z = 185 (2.98%) and [c] losses CH$_3$O to give [d] at m/z = 154 (0.66%). The molecular ion peak [a] losses C$_6$H$_4$ to give fragment [e] at m/z = 172 (29.92%) and this [e] losses C$_2$H$_2$O to give fragment [f] at m/z = 64 (2.08%) (Fig. 4). (Scheme 3). Fragmentation pattern of the complex [Ag(L$_1$)$_2$(H$_2$O)$_2$]NO$_3$ is given as an example in (Fig. 4), Additional file 1: Scheme S3. The molecular ion peak [a] appeared at m/z = 760 (35%) losses C$_{10}$H$_8$S$_2$ to give [b] at m/z = 532 (5%) and it losses C$_2$H$_2$O to give [c] at m/z = 470 (12%). The $L_3$ molecular ion peak [a] appeared at m/z = 292 (100%) losses CH$_3$O to give [b] at m/z = 261 (4%) then [a] losses C$_4$H$_2$ to give [c] at m/z = 185 (21.73%), molecular ion peak[c] loss CH to give [d] at m/z = 172 (6.8%) and molecular ion peak [d] losses CH$_3$O to give [e] at m/z = 141 (1.2%).(Fig. 4), Scheme 5. Fragmentation pattern of the complex [Ag(L$_3$)$_2$(H$_2$O)$_2$]NO$_3$ is given as an example in (Fig. 4), Additional file 1: Scheme S3. The molecular ion peak [a] appeared at m/z = 790 (65%) losses C$_6$H$_2$O$_2$to give [b] at m/z = 692 (2%), it losses C$_{12}$H$_2$ to give [c] at m/z = 540 (12.5%) and molecular ion peak [c] losses C$_2$H$_2$ to give [d] at m/z = 514 (25.3%) [42].

Biological activity studies

Antimicrobial studies

The antimicrobial efficacy of $L_1$, $L_2$, $L_3$ and their free ligand complexes are explored in this experiment. Studies were conducted on E. Coli ATCC11229, Coliform ATCC8729, S. aureus ATCC6538, and Salmonella typhi ATCC14028 and fungal species as A. niger and P. expansum screening was tested against and examination and evaluation of the prepared complexes [42]. The same results were reported for E. Coli ATCC11229 of Ag(I)-L$_2$ and Ag (I)-L$_1$ followed by Ag(I)-L$_3$ considers that the lowest findings are equivalent to those of other complexes. The effect of free ligands on this strain has been shown to be below its complex and can be organized according to the sensitivity of the strains $L_3$, $L_2$ and $L_1$ in the following ascending order. The effect of Ligands and their
Table 3 Thermal behavior and kinetic parameters determined using the Coats–Redfern (CR) and Horowitz–Metzger (HM) operated for L₁, L₂, L₃ and their complexes

| Compounds                  | Decomposition range(K) | Tₛ(K) | Method | Parameter | E* (kJ mol⁻¹) | A (s⁻¹) | ΔS* (J mol⁻¹ K⁻¹) | ΔH* (kJ mol⁻¹) | ΔG* (kJ mol⁻¹) | R² | SD² |
|----------------------------|------------------------|-------|--------|----------|--------------|---------|------------------|---------------|---------------|----|-----|
| L₁                         | 673–905                | 817   | CR     |          | 95.65669368 x 10³ | 43.2844 | 88.863           | 442.497       | 0.970         | 0.187 |
| [Ag(L₁)₂(H₂O)₂]NO₃         | 373–573                | 462   | CR     |          | 34.3793.390 x 10² | 39.344  | 30.537           | 212.262       | 0.984         | 0.065 |
| L₂                         | 453–645                | 546   | CR     |          | 31.93137.451 | 37.3640 | 27.391           | 231.398       | 0.934         | 0.207 |
| [Ag(L₂)₂(H₂O)₂]NO₃·H₂O     | 689–881                | 801   | CR     |          | 79.2846618 x 10³ | 41.3475 | 72.624           | 403.817       | 0.945         | 0.220 |
| L₃                         | 438–630                | 564   | CR     |          | 35.3171.185 x 10² | 38.2948 | 30.627           | 246.610       | 0.960         | 0.182 |
| [Ag(L₃)₂(H₂O)₂]NO₃         | 365–685                | 497   | CR     |          | 15.3160.758  | 34.2002 | 11.183           | 181.158       | 0.981         | 0.089 |

*a Correlation coefficients of the Arrhenius plots and bStandard deviation
complexes on *Coliform* ATCC8729 showed that Ag(I)-L₂ is highly important, giving 25.12 mm respectively. Although the remaining complexes showed lower results than the L₂ complexes. The results obtained in Table 4 and Fig. 5 showed that lower activity on the same strain and these results ensured that free ligand complexes were more active than free ligand complexes. In gram+ve bacteria, *S. aureus* ATCC6538, Highly important antibacterial activity of metal complexes with L₁ followed L₃ complex. The lesser activity from ligand L₂ and its complex. The antibacterial activity of metal complexes on *Salmonella typhi* ATCC14028 showed a good activity against (gram−ve), that recorded the best results Ag(I)-L₃ > Ag(I)-L₁ > Ag(I)-L₂ respectively. The action of the free ligands on gram −ve bacteria has yielded results lower than their complexes which give respectively 12.6, 11.43 and 7.8 mm, L₃, L₁, L₂. The presence of different ligands and other complexes on both fungal strains of the testes, *A. niger* recorded that Ag(I)-L₃ showed a significant difference the highly results (20 ± 2.6) though free L₁ results showed less than its complex. Others did not show any activity against tested fungi (*A. niger*). The effect of various significant ligands and other complexes on *P. expansum* did not show any activity whereas the the highest broad spectrum of activity on the same test strain showed the best results on L₁ and its complexes [42].

Normal antibiotic efficacy of antimicrobials (AMC, CTX, NS, FU). The AMC mixture give the effective against *E. coli*, *Coliform*, *S. aureus* and NS high inhibitory activity on *A. niger*. Other antibiotics have shown no action on other microorganisms. Eventually, the bacterial strains showed a varied response to the three free ligands and their complex antimicrobial activity, but the results indicated that the high activity of ligand complexes was better than their free ligands. The two fungal strains are more resistant to synthesis ligands and their complexes than bacterial strains [42–46].

**Determination of MIC for the most sensitive organisms**

The artificial ligands and their complexes developed the biological efficacy towards the more resistant
bacteria and fungi (Table 5A–D) and Fig. 6). The order of The lowest MIC for in case of *E. coli* decrease in order: \( L_1 = \text{Ag (I)} \rightarrow L_3 \) (0.02 mg/100 mL) \( L_3 \)
(0.05 mg/100 mL) \( \text{Ag(I)} - L_3 = (0.1 \text{ mg/100 mL}) \) \( \text{Ag(I)} - L_2 = (0.07 \text{ mg/100 mL}) \) \( \text{Ag(I)} - L_1 = (0.02 \text{ mg/100 mL}) \) \( \text{Coliform} \) decrease in order: Ag(I) – L2 (0.02 mg/100 mL) > Ag(I) – L3 (0.07 mg/100 mL) > Ag(I) – L1 (0.1 mg/100 mL). \text{Salmonella typhi} \) showed that the amazing results of ligands and its complexes: L3 = Ag(I) – L2 = Ag(I) – L1 = (0.02 mg/100 mL) > Ag(I) – L3 (0.1 mg/100 mL), \text{S. aureus} \) order: L3 = Ag(I) – L2 = Ag(I) – L1 = (0.02 mg/100 mL) > Ag(I) – L3 (0.1 mg/100 mL), \text{A. niger} \) showed that the lowest MIC for the two strains measured at conc. 0.02 mg/100 mL. Table 5E, F and Fig. 6 data showed that the lowest MIC for the two strains measured at conc. 0.02 mg/100 mL. Although MIC at complex L3 was recorded by \text{A. niger}, the same result was recorded on Ag(I) – L3 at conc. 0.02 mg/100 mL. Ligand L3 and its complexes demonstrate the strongest MIC on \text{P. expansum}, although no behavior is displayed.
Table 5  (A) Of One-way ANOVA: *E. coli* vs MIC Compounds. (B) Of One-way ANOVA: Coliform versus MIC Compounds. (C) Of One-way ANOVA: *S. aureus* vs MIC Compounds. (D) Of One-way ANOVA: *Salm. typhi* vs MIC Compounds. (E) Of One-way ANOVA: *A. niger* vs MIC Compounds. (F) Of One-way ANOVA: *P.expansum* vs MIC Compounds

(A)

| Compounds     | N | Mean | Grouping |
|---------------|---|------|----------|
| L₁            | 3 | 0.02 | A        |
| L₁/Ag(I)      | 3 | 0.02 | A        |
| L₃            | 3 | 0.05 | B        |
| L₁/Ag(I)      | 3 | 0.07 | B        |
| L₂            | 3 | 0.07 | B        |
| L₂/Ag(I)      | 3 | 0.10 | C        |

(B)

| Compounds     | N | Mean | Grouping |
|---------------|---|------|----------|
| L₁            | 3 | 0.02 | A        |
| L₁/Ag(I)      | 3 | 0.07 | C        |
| L₂            | 3 | 0.07 | C        |
| L₃            | 3 | 0.10 | D        |
| L₁/Ag(I)      | 3 | 0.10 | D        |
| L₂            | 3 | 0.10 | D        |

(C)

| Compounds     | N | Mean | Grouping |
|---------------|---|------|----------|
| L₁            | 3 | 0.05 | A        |
| L₁/Ag(I)      | 3 | 0.05 | A        |
| L₂            | 3 | 0.07 | B        |
| L₁/Ag(I)      | 3 | 0.10 | C        |
| L₁            | 3 | 0.10 | C        |
| L₂            | 3 | 0.10 | C        |

(D)

| Compounds     | N | Mean | Grouping |
|---------------|---|------|----------|
| L₁            | 3 | 0.02 | A        |
| L₁/Ag(I)      | 3 | 0.02 | A        |
| L₂            | 3 | 0.02 | A        |
| L₁/Ag(I)      | 3 | 0.05 | B        |
| L₂            | 3 | 0.05 | B        |
| L₁/Ag(I)      | 3 | 0.10 | C        |

(E)

| Compounds     | N | Mean | Grouping |
|---------------|---|------|----------|
| L₁            | 3 | 0.02 | A        |
| L₁/Ag(I)      | 3 | 0.02 | A        |
| L₂            | 3 | 0.0  | B        |
by the other compounds and their complexes. These findings ensured that the activity of synthetic ligands and their complexes on pathogenic bacteria and fungi demonstrated a minimum inhibitor concentration (MIC) for the most vulnerable pathogens. [42, 47, 48].

### Conclusion

Development and characterisation of three novel complexes of some replaced pyrazole derivatives as ligands (4-(4-dimethylamino benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2a) \( \text{L}_1 \), 4-(4-Thiophene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2b) \( \text{L}_2 \), 4-(4-methoxy benzylidene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2c) \( \text{L}_3 \) with Ag(I) was achieved using physicochemical and spectroscopic methods.. In the resulting complexes, \( \text{L}_1 \), \( \text{L}_2 \), and \( \text{L}_3 \) were bound by the nitrogen atom to the metal ion via ν(C=N). For the three ligands and their complexes, thermogravimetric kinetic parameters and their differential were evaluated using the Coats-Redfern and Horowitz-Metzger equations. Metal complexes exhibited higher inhibition against all tested microorganisms and pathogenic bacteria and fungi and were the most susceptible pathogens with a minimum inhibitory concentration (MIC).

### Methods

**Chemistry**

Analytical grade reagents, commercially available from multiple suppliers and used without further purification, were all the chemicals used in the complex preparation. Synthesized compounds and their complexes have been characterized by elemental analysis, magnetic and spectroscopic methods (IR, \(^{13}\)C, \(^{1}\)HNMR, mass) and thermal analysis using the known apparatuses [42].
Synthesis of the ligands

**Common 3-methyl-1-phenyl-5-pyrazolone synthesis technique (1)**

Pure ethyl acetoacetate (0.05 mol, 6.2 mL) was mixed with pure phenyl hydrazine (0.05 mol, 5 mL), 0.5 mL of acetic acid was added, according to known method [42]. Methyl phenyl pyrazolone was obtained as colorless crystals, 127 °C melting point and 83.6 percent yield [27].

**Specific method for preparing derivatives of 4-arylidene-3-methyl-1-phenyl-5-pyrazolone (2a-c)**

The oil bath heated a mixture of 1-aryl-3-methyl-5-pyrazolone (0.01 mol, 1.74 g) and replaced aromatic aldehydes (0.012 mol) at 150–160 °C for 2-4 hrs. TLC has tracked the progress of the reaction using ethyl acetate: hexane (9:1) as a solvent. The mixture was cooled, triturated and washed off with ether (20 mL). The colored residue was recrystallized from ethanol to provide the corresponding 4-arylidene-3-methyl-1-phenyl-5-pyrazolone (2a-c) as colored products, respectively [28].

4-[(4-dimethylamino benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2a) L1.
4-[(4-Thiophene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2b) L2.
4-[(4-methoxy benzylidene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2c) L3.

**4-(4-Dimethylamino benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2a)**

Brick Red, mp = 170 °C, yield 83% IR (KBr, ν, cm⁻¹): 3444 (OH), 1670 (C = O), and 1550 cm⁻¹. ¹H NMR (DMSO-d6, 300 MHz): δ = 2.28 (s, 3H, CH3), 3.03 (s, 6H, -N(CH3)2), 7.14 (s, 1H, =CH-Ar), 9.66 (d, 3H, Ar=H). Anal. Calcd for C19H19N3O (305.19): C, 74.23; H, 6.13; N, 13.35%.

**4-(4-Thiophene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2b)**

Orange, mp = 125 °C, yield 74% IR (KBr, ν, cm⁻¹): 3448 (OH), 1681 (C = O), 1496 cm⁻¹ (C = N) and 1056 cm⁻¹(C = S). ¹H NMR (DMSO-d6, 300 MHz): δ = 2.30 (s, 3H, CH3), 7.39 (s, 1H, =CH-Ar), 8.25 (d, 3H, Ar=H). Anal. Calcd for C15H12N2O (268): C, 74.70; H, 4.47; N 10.44; S, 11.94; Found C, 74.23; H, 4.32; N, 10.21; S, 11.65%.

**4-(4-Methoxy benzylidene)-3-methyl-1-phenyl-1Hpyrazol-5(4H)-one (2c)**

Orange, mp = 122 °C, yield 82% IR (KBr, ν, cm⁻¹): 3444 (OH), 1678 (C = O), 1508 cm⁻¹ (C = N) and. ¹H NMR (DMSO-d6, 300 MHz): δ = 1.91 (s, 3H, CH3), 3.69 (s, 3H, -OCH3), 7.20 (s, 1H, =CH-Ar), 8.71 (d, 3H, Ar=H). Anal. Calcd for C18H16N2O2 (292): C, 73.97; H, 5.47; N 9.58; Found C, 73.78; H, 5.13; N, 9.34%.

**Synthesis of the complexes**

The brown solid complex [Ag(L1)2(H2O)]NO3 was prepared by adding 0.5 mmol (0.085 g) of AgNO3 in 20 ml of acetone to a stirred suspension solution 1 mmol (0.305 g) of L1 in 50 ml acetone. The reaction mixture was refluxed for 6 hrs, the precipitate was drained off, washed several times with acetone and dried under vacuum over anhydrous CaCl2. Dark brown [Ag(L2)2(H2O)]NO3:H2O, [Ag(L3)2(H2O)]NO3 solid complexes were prepared in the same manner as mentioned above.

[Ag(C19H19N3O)2(H2O)]NO3 (AgC38H42N7O7) complex
Brown; Yield: 85%; m.p.: 160 °C; M.Wt: 816.65; Elemental analysis for AgC38H42N7O7: found, C, 55.31; H, 4.99; N, 12.00; Ag, 13.14; Calcld, C 55.89; H, 4.67; N, 12.01; Ag, 12.21; A m = 115.75 S cm² mol⁻¹; IR (KBr, ν, cm⁻¹): 3450 mbr (OH), 1666 m (C = O), 1523vw cm⁻¹ (C = N) and 813w and 837w (M–N). ¹H NMR (DMSO-d6, 300 MHz): δ = 2.49 (s, 3H, CH3), 3.46 (s, 2H, H2O), 2.27–2.33 (s, 6H, –N(CH3)2), 9.67 (s, 1H, =CH-Ar), 7.14–7.97 (m, 4H, Ar=H).

[Ag(C15H12N2O)2(H2O)2]NO3 (AgC30H30N5O4S2) complex
Dark brown; Yield: 74%; m.p.: 125 °C; M.Wt: 760.59; Elemental analysis for AgC30H30N5O4S2: found, C, 47.22; H, 3.91; N, 9.15; Ag, 14.13; Calcld, C, 47.37; H, 3.98; N, 9.21; Ag, 14.18; A m = 135.50 S cm² mol⁻¹; IR (KBr, ν, cm⁻¹): 3444 m, br (OH), 1685 m (C = O), 1527vw cm⁻¹ (C = N), 1099 mm⁻¹ (C = S), 748w and 792w (M–N). ¹H NMR (DMSO-d6, 300 MHz): δ = 2.49 (s, 3H, CH3), 3.37 (s, 2H, H2O), 8.64 (s, 1H, =CH-Ar), 7.20–7.94 (d, 3H, Ar=H).

[Ag(C19H16N2O2)2(H2O)]NO3 (AgC36H32N4O9) complex
Dark brown; Yield: 90%; m.p.: 150 °C; M.Wt: 790.57; Elemental analysis for AgC36H32N4O9: found, C, 54.47; H, 4.11; N, 8.80; Ag, 13.60; Calcld, C, 54.69; H, 4.59; N, 8.86; Ag, 13.64; A m = 114.52 S cm² mol⁻¹; IR (KBr, ν, cm⁻¹): 3444 (OH), 1678 (C = O), 1520 cm⁻¹ (C = N), 759w and 779w (M–N). ¹H NMR (DMSO-d6, 300 MHz): δ = 2.33 (s, 3H, CH3), 3.31 (s, 3H, -OCH3), 8.42 (s, 1H, =CH-Ar), 7.18–7.46 (d, 3H, Ar=H).

**Supplementary information**

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3. Anshu D, Ruby S, Dharmendra S et al (2010) Regioselective Synthesis of Diltiazem Analogue Pyrazol(4-3-c),1,5benzothiazepines and Antifungal Activity. Phosphorus Sulfur Silicon Relat Elem 185(12):2472–2479
4. Sureshkumar EV, Rao RM et al (2012) Synthesis, characterization and biological evaluation of novel pyrazole ring containing manchik derivatives. Der Pharma Chemica 4(2):707–713
5. Ouyang G, Chen Z, Cai XJ, Song BA et al (2008) Synthesis and antiviral activity of novel pyrazole derivatives containing oxime esters group. Bioorg Med Chem 16(22):9699–9707
6. Idrees GA, Aly OM, Abou-Rahma GEAA et al (2009) Design, synthesis and hypolipidemic activity of novel 2-(naphthalen-2-yl)oxypripionic acid derivatives as desmethyl fibrate analogues. Eur J Med Chem 44(10):3973–3980
7. Hu Y, Wei F, Zhou H et al (2006) Organic synthesis in ionic liquids: condensation of 3-Methyl-1-phenyl-5-pyrazole with carbonyl compounds catalyzed by ethyleneimmonium diacetate (EDDA). Chin Chem Lett 17:299–301
8. Umesh KBI, Rae KML, Nayaka MAH (2009) Antioxidant and Antimicrobial Activity of 5-methyl-2-(5-methyl-1,3-diphenyl-1H-pyrazole-4-carbonyl)-2,4-dihydro-pyrazol-3-one. Inter J Biomed Sci 5(4):359
9. Dongmei L, Liping S, Shaoj S et al (2007) Regioselective synthesis of 6-trifluoromethyl-1,4,5,6-tetrahydropyrazol(3,4-b)pyridin derivatives. J Fluorine Chem 128(8):952–957
10. Xiao-Liu L, Yong-Mei W, Bing T et al (1998) The solid-state microwave addition of 3-methyl-1-phenyl-5-pyrazol. J Heterocycl Chem 35(1):129–134
11. Mohd A, Shikhah K (2005) Synthesis and anti-inflammatory, analgesic, ulcerogenic and lipid peroxidation activities of 3,5-dimethyl pyrazoles, 3-methylpyrazol-5-ones and 3,5-disubstituted pyrazolines, Indian. J Chem 44B:2532–2537
12. Vijesh AM, Arun MI, Shikrishna I et al (2011) Synthesis of some new pyrazolone derivatives as potent antimicrobial agents. Der Pharma Chemica 3(4):454–463
13. Mohamed A, Gamal EAA, Alaa AH (2009) Synthesis of novel pyrazole derivatives and evaluation of their antidepressant and anticonvulsant activities. Eur J Med Chem 44(9):3480–3487
14. Mahinder TM, Rajesh TK, Vithal MK et al (2004) De novo design and synthesis of HIV-1 integrase inhibitors. Bioorg Med Chem 12(9):2317–2333
15. Das N, Verma A, Shrivastava PK (2008) Synthesis and biological evaluation of some new aryl pyrazol-3-one derivatives as potential hypoglycemic agents. Indian J Chem 47B(10):1553–1558
16. Manojkumar P, Ravikumar P, Ravi TK (2009) Subbucchettar, G. Synthesis of coumarin heterocyclic derivatives with antioxidant activity and in vitro cytotoxic activity against tumour cells. Acta Pharm 59:159–170
17. Rishikesh VA, Cendilukumar A, Gurubasavajewamy PM et al (2011) Pyrazolone part 3: Antibacterial activity of novel 4-substituted pyrazolone derivatives. Der Pharma Chemica 3(5):7–12
18. Bondock S, Rabie R, Etman HA, Fadda AA (2008) Synthesis and antimicrobial activity of some new heterocycles incorporating antipyrine moiety. Eur J Med Chem 43(10):2121–2129
19. Rostom SAF, El-Ashmawy IM, Abd El Razik HA et al (2009) Design and synthesis of some thiazolyl and thiadiazolyl derivatives of antipyrine as potential non-acidic anti-inflammatory, analgesic and antimicrobial agents. Bioorg Med Chem 17:882–895
20. Kucukguzel SG, Rollas S, Ertelzen H et al (2000) Synthesis, characterization and pharmacological properties of some 4-arylhydrazono-2-pyrazolino-S-one derivatives obtained from heterocyclic amines. Eur J Med Chem 35(7–8):761–771
21. Meng L, Bao-Xiang Z (2014) Progress of the synthesis of condensed pyrazole derivatives (from 2010 to mid-2013). Eur J Med Chem 85:311–340
22. Douglass FT, Favan KT (2011) Indole synthesis: a review and proposed classification. Tetrahedron 67:7195–7210
23. Demetrio R, Benedetta M, Maria VR (2015) Recent advanced in bioactive systems containing pyrazole fused with a five membered heterocycle. Eur J Med Chem 97:732–756
24. Frederick EB, Vera Prasad JVN, Allison LC et al (2007) Synthesis and SAR of novel conformationally-restricted oxazolidinones possessing Gram-positive and fastidious Gram-negative antibacterial activity. Part 1: substituted pyrazoles. J Bioorg Med Chem Lett. 17(16):4694–4698

Additional file 1: Table S1. UV-Vis spectral data of the free ligand L1, L2, L3 and their Agl(II)-complexes. Table S2. Selected 1H NMR data of L1, L2, L3 and its diamagnetic complexes. Fig. S1. TGA and DTG diagrams for a L1, b [Ag(L1)2(H2O)2]NO3, c L2, d [Ag(L2)2(H2O)2]NO3, e L3, and f [Ag(L3)2(H2O)2]NO3. Fig. S2. The diagrams of kinetic parameters of L1, L2, L3 and its diamagnetic complexes. Additional file 1: Scheme S1. Fragmentation pattern of [Ag(L2)2(H2O)2]NO3. Scheme S2. Fragmentation pattern of [Ag(L1)2(H2O)2]NO3. Scheme S3. Fragmentation pattern of [Ag(L3)2(H2O)2]NO3.
