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Ionic Sal-SGD Schiff bases as new synergetic chemotherapeutic candidates: Synthesis, metalation with Pd(II) and *in vitro* pharmacological evaluation.

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Contents:

1. Synthesis and characterization of the key starting materials

1.1 Materials

Chemicals were obtained from the following suppliers and used without further purification: salicylaldehyde (Sal), 2-*iso*-propylphenol (2-^{i}PrPhOH), 1,2-dimethylimidazole (1,2-$(Me)_2$-Im), 2-Methylpyridine (2-picoline, Pic), Quinoline (Qn) and anhydrous magnesium dichloride ($MgCl_2$) (Sigma–Aldrich), paraformaldehyde ($(CH_2O)_n$) (Roth), 1-butylimidazole (1-^{n}Bu-Im) (Alfa Aesar), triethyl amine (Et_3N) and anhydrous zinc chloride ($ZnCl_2$) (GRÜSSING GmbH) and Palladium(II) chloride ($PdCl_2$) and sulfaguanidine (SG) (Acros).

1.2 Instrumentation

Elemental analyses for C, H, N and S were performed with a Perkin–Elmer 263 elemental analyzer. FT-IR spectra were recorded on a BRUKER Tensor-37 FT-IR spectrophotometer in the range 400–4000 cm^{-1} as KBr discs or in the 4000-550 cm^{-1} region with 2 cm^{-1} resolution with an ATR (attenuated total reflection) unit (Platinum ATR-QL, Diamond). For signal intensities the following abbreviations were used: br (broad), sh (sharp), w (weak), m (medium), s (strong), vs (very strong). NMR-spectra were obtained with a Bruker Avance DRX200 (200 MHz for ^{1}H) or Bruker Avance DRX500 (500 MHz for ^{13}C) spectrometer with calibration to the residual proton solvent signal in DMSO-d_6 (^{1}H NMR: 2.52 ppm, ^{13}C NMR: 39.5 ppm), $CDCl_3$ (^{1}H NMR: 7.26 ppm, ^{13}C NMR: 77.16 ppm) against TMS with δ = 0.00 ppm. Multiplicities of the signals were specified s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). The mass spectra of the synthesized sal-imidazolium, saldach-imidazolium chlorides and their complexes were acquired in the linear mode for positive ions on a BRUKER Ultraflex MALDI-TOF instrument equipped with a 337 nm nitrogen laser pulsing at a repetition rate of 10 Hz. The MALDI matrix material (1,8-dihydroxy-9(10H)-anthracenone (dithranol, DIT) ($C_{14}H_{10}O_3$, M= 226.23)) was dissolved in chloroform at a concentration of 10 mg/mL. MALDI probes were prepared by mixing compound solutions (1 mg/mL in CH_2Cl_2) with the matrix solution (1:10, v/v) in a 0.5 mL Eppendorf® micro tube. Finally 0.5 µL of this mixture was deposited on the sample plate dried at room temperature and then analyzed. The molar conductance 10^{-3} M solution of various salts has been measured at ambient temperature with a digital conductivity meter (S30 SevenEasy™ conductivity, Mettler-Toledo Electronics, LLC, Polaris Parkway, Columbus). The overall accuracy of the conductance measurements was found to be ± 0.2%.

1.2 3-isopropylsalicylaldehyde (**1**)

To a stirred mixture of dry anhydrous magnesium dichloride (9.52 g, 100 mmol) and dry paraformaldehyde (4.50 g, 150 mmol) in dry ACN (200 ml) was added dry triethylamine (26.1 ml, 185 mmol) dropwise and the mixture was stirred at room temperature for 15 min under nitrogen atmosphere. 2-Isopropylphenol (6.80 g, 50.0 mmol) was then added dropwise, resulting an opaque, light pink mixture. This solution was heated at gentle reflux temperature under nitrogen for ca. 3 h, during which time the color of the reaction mixture changes from light pink to orange. The solution was allowed to cool to room temperature then 200 mL of 1 N HCl was added followed by stirring for 30 min. The product was extracted with diethyl ether (5 x/75 ml portions) and the ether fractions collected together and washed with 1 N HCl (2 x 100 mL) and saturated NaCl(aq) (3 x/100 ml portions). The ether layer was dried over anhydrous $MgSO_4$ followed by filtration. Volatiles were removed under reduced pressure to yield the corresponding salicylaldehyde, usually contaminated with the starting phenol. The crude product which was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (90 : 10) mixture as the eluent to give pure 3-isopropylsalicylaldehyde (6.84 g, 83 %) as a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.45 (s, 1 H, Ar-O**H**), 9.89 (s, 1 H, Ar-**H**C=O), 7.50 (dd, J_2 = 7.51 Hz, J_1 = 1.61 Hz, 1 H, Ar-**H**), 7.41 (dd, , J_2 = 7.72 Hz, J_1 = 1.68 Hz, 1 H, Ar-**H**), 7.01 (t, J_2 = 7.61 Hz, J_1 = 7.61 Hz, 1 H, Ar-**H**), 3.43 ($m_{(7)}$, 1 H, C**H**$(CH_3)_2$), 1.30 (d, J = 6.94 Hz, 6H, CH(C**H$_3$)$_2$**). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 196.45 (H**C**=O), 160.03 (**C**-OH), 136.79 (**C**, Ar), 133.21 (**C**H, Ar), 130.86 (**C**H, Ar), 120.34 (**C**, Ar), 119.51 (**C**H, Ar) , 26.31 (**C**H$(CH_3)_2$), 21.98 (CH(**C**H$_3$)$_2$).

1.3 5-chloromethyl-2-hydroxybenzaldehydes (**2**a,b)

They were synthesized from the corresponding salicylaldehydes according to the modified chloromethylation procedure [S1]. In a typical synthesis, (15.2 mmol) of salicylaldehydes were treated with para-formaldehyde (1.0 g, 33.3 mmol) and zinc chloride (0.2 g, 1.46 mmol) in 11 ml of concentrated hydrochloric acid. The mixture was vigorously stirred under $HC1_g$ atmosphere for 24-72 h at 313 K. The reaction mixture was extracted several times with diethyl ether (3x15 mL). Then the collected ether fractions were washed by 2x10 mL 5% aqueous $NaHCO_3$ solution, 2x10 mL brine, 5x10 mL milli-Q water and dried over anhydrous $MgSO_4$. After filtration and removal of the volatiles under reduced pressure, the obtained product was characterized and used in the next step without further purification.

5-Chloromethyl-2-hydroxybenzaldehyde (**2a**): Isolated as white needles (15.2 g, 62.0 % yield). FTIR (ATR, cm^{-1}): 3240 (m, br, *v* OH), 3120 (m, br, v_{asym} CH, Ar), 3050 (m, br, v_{sym} CH, Ph), 2876 (m, sh, *v* CH_2), 1659 (vs, sh, *v* C=O), 1578, 1489, 1437 (s, sh, *v* C=C_{arom} + *v* C-H bend), 1338 (m, sh, *v* CH_2), 1252 (s, sh, *v* CH_2Cl), 1150 (s, sh, *v* HCC, Ar), 772 (s, sh, *v* C–Cl). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.07 (s, 1H, Ar-O**H**) 9.90 (s, 1H, Ar-**H**C=O), 7.57 (m, 2H, 2 x Ar-**H**), 7.00 (d, 1H, J_{HH} = 8.34 Hz, Ar-**H**), 4.60 (s, 2H, C**H$_2$**-Ar).

3-iso-propyl-5-chloromethyl-2-hydroxybenzaldehydes (**2**b): It is obtained as faint yellow crystals (3.00 g, 93%). FTIR (KBr, cm^{-1}): 3510 (m, br, $\nu_{(O-H)}$), 3075 (m, br, $\nu_{asym(C-H)}$, Ar), 3030 (m, br, $\nu_{sym(C-H)}$, Ar), 2971 (m, sh, $\nu_{(CH_3)}$), 2869 (m, sh, $\nu_{(CH_2)}$), 1647 (vs, sh, $\nu_{(C=O)}$), 1446, 1385 (s, sh, $\nu_{(C=C_{Ar} + C\text{-}H_{bend})}$), 1320 (m, sh, $\nu_{(CH_2)}$), 1266 (s, sh, $\nu_{(Ar\text{-}O)}$), 690 (s, sh, $\nu_{(C–Cl)}$). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.47 (s, 1 H, Ar-O**H**), 9.92 (s, 1 H, Ar-**H**C=O), 7.49 (dd, J_2 = 10.37, J_1 = 2.37 Hz, 2 H, 2 x Ar-**H**), 4.64 (s, 2 H, C**H$_2$**-Ar), 3.41 ($m_{(7)}$, 1 H, C**H**$(CH_3)_2$), 1.30 (d, J = 6.92 Hz, 6 H, CH(C**H$_3$)$_2$**). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 196.93 (H**C**=O), 159.80 (**C**-OH), 138.42 (**C**, Ar), 134.42 (**C**H, Ar), 131.59 (**C**H, Ar), 129.21 (**C**, Ar), 120.29 (**C**, Ar), 46.19 (**C**H_2-Ar), 26.86 (**C**H$(CH_3)_2$), 22.58 (CH(**C**$H_3)_2$).

1.4 Ionic liquids-based salicylaldehydes (**Sal-ILs**, **3a-e)**

To a vigorously stirred solution of N-heterocyclic derivatives (21.39 mmol) in dry toluene (25 mL) at room temperature was added the solution of chloromethyl- salicylaldehyde **2** (4.15 g, 19.50 mmol) in dry toluene (25 mL), drop-wise over 30 min, under nitrogen atmosphere. The resulting solution was stirred under nitrogen atmosphere at 60 °C for 24 h. After cooling, the isolated products were washed intensively with 2 x 5 mL dry toluene, several with ether (5x10 mL), to remove the unreacted materials, and dried under vacuum to give the desired products which used for the following preparations without further purification.

3-(3-Formyl-4-hydroxybenzyl)-2-methylpyridinium chloride (**3**a): Obtained as pale yellow solid (91 %). FTIR (KBr, cm^{-1}): 3385 (m, br, $\nu_{(O-H)}$), 2959 (m, sh, $\nu_{asym(C-H)}$, CH_3), 2884 (m, sh, $\nu\,CH_2$), 1661 (vs, sh, $\nu_{(C=O)}$), 1573, 1485, 1455 (s, sh, $\nu_{(C=C_{Ar} + C\text{-}H_{bend})}$), 1149 (s, sh, $\nu_{(H\text{-}C=C + H\text{-}C=N)_{bend}}$, Py). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 10.83 (s, 1H, Ar-O**H**) 10.30 (s, 1H, Ar-**H**C=O), 9.15 (d, J = 2.10 Hz, 1H, Py-**H**), 8.68 (m, 2H, Py-**H**), 7.84 (d, 1H, J =1.39 Hz, Py-**H**), 7.75 (d, J_{HH} = 1.41 Hz, 1H, Ar-**H**), 7.38 (m, 2H, 2 x Ar-**H**), 5.45 (s, 2H,-C**H$_2$**-Ar), 2.73 (s, 3H, C**H$_3$**). ESI MS: In positive mode peaks at m/z 228.10 (100 %, $[C_{14}H_{14}NO_2]^+$, M – Cl) a.m.u.

3-(3-Formyl-4-hydroxybenzyl)-quinolinium chloride (**3**b): Obtained as dark yellow solid (86 %). FTIR (KBr, cm^{-1}): 3369 (m, br, $\nu_{(O-H)}$), 1666 (vs, sh, $\nu_{(C=O)}$), 1574, 1487, 1453 (s, sh, $\nu_{(C=C_{Ar} + C\text{-}H_{bend})}$), 1156 (s, sh, $\nu_{(H\text{-}C=C + H\text{-}C=N)_{bend}}$, Py). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.22 (s, 1H, Ar-O**H**) 10.59 (s, 1H, Ar-**H**C=O), 9.14 (d, J = 7.31 Hz, 1H, Py-**H**), 8.70 (m, 2H, Py-**H**), 8.51 (m, 2H, Ar-**H**), 8.26 (m, 2H, Ar-**H**), 7.59 (s, 1H, Ar-**H**), 7.19 (m, 2H, 2 x Ar-**H**), 5.58 (s, 2H,-C**H$_2$**-Ar). ESI MS: In positive mode peaks at m/z 264.23 (69 %, $[C_{17}H_{14}NO_2$, M – Cl$]^+$) a.m.u.

3-(3-formyl-4-hydroxybenzyl)-1,2-dimethylimidazolium chloride (**3**c): Obtained as of white solid, Yield (89 %). FTIR (KBr, cm^{-1}): 3373 (m, br, $\nu_{(O-H)}$), 1669 (vs, sh, $\nu_{(C=O)}$), 1547, 1455, 1399 (s, sh, $\nu_{(C=C_{Ar} + C\text{-}H_{bend})}$), 1274 (s, sh, $\nu\,\nu_{(Ar\text{-}O)}$), 1153 (s, sh, $\nu_{(H\text{-}C=C + H\text{-}C=N)_{bend}}$, Im). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 10.80 (s, 1 H, Ar-O**H**), 10.33 (s, 1 H, Ar-**H**C=O), 7.84 (d, J = 1.76 Hz, 1 H, N(1)CHC**H**N(3)), 7.67 (d, J = 2.01 Hz, 2 H, 2 x Ar-**H**), 7.55 (d, J = 1.69 Hz, 1 H, N(1)C**H**CHN(3)), 7.41 (m, 3H, 3 x Ar-**H**), 5.38 (s, 2H, N(3)-C**H$_2$**-Ar), 3.86 (s, 3 H, N(1)-C**H$_3$**), 2.60 (s, 3H, C(2)-

C**H$_3$**).^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 197.23, 160.18, 144.71, 137.45, 136.23, 131.03, 127.72, 122.80, 121.91, 120.13, 51.34, 35.39 and 22.16. MALDI-TOF MS, *m/z*: 231.21 [$C_{13}H_{15}N_2O_2$, M - Cl^-]$^+$.

3-(3-formyl-4-hydroxybenzyl)- 1-^{n}Butylimidazolium chloride (**3c**): Obtained as yellow solid (86%). FT-IR (KBr, cm^{-1}): 3359 (m, br, *ν* O-H), 2981 (m, sh, ν_{asym} CH_3), 2960 (m, sh, ν_{sym} CH_3), 2877 (m, sh, *ν* CH_2), 1657 (vs, sh, *ν* C=O), 1569, 1552, 1469 (s, sh, *ν* C=C_{arom} + *ν* C-H bend), 1149 (s, sh, *ν* HCC + *ν* HCN bending, Im), 850 (m, sh), 736 (m, sh), 679 (m, sh), 582 (m, sh). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.37 (s, 1H, Ph-**H**C=O) 10.30 (s, 1H, Ph-O**H**), 9.53 (s, 1H, -N(1)C**H**N(3)- Im), 7.88-7.86 (d, 2H, N(1)C**H**C**H-** Im), 7.74 (s, 1H, Ph-H), 7.66-7.64 (d, 1H, J_{HH} =6.99 Hz, Ph-H), 7.26.7.24 (d, 1H, J_{HH} =8.56 Hz, Ph-H), 5.40 (s, 2H, -N(3)-C**H$_2$**-Ph), 4.20-4.17 (t, J_{HH} = 7.06, 7.14 Hz, 2H, -N(1)C**H$_2$**), 1.79-1.73 ($m_{(5)}$, 2H, -N(1)CH_2C**H$_2$**), 1.27-1.19 ($m_{(6)}$, 2H, -C**H$_2$**CH_3), 0.89-0.86 (t, J_{HH} = 7.33, 7.38 Hz, 3H, -CH_2C**H$_3$**). ^{13}C NMR (500 MHz, $CDCl_3$) δ (ppm): 195.81, 159.04, 138.51, 136.10, 135.89, 130.96, 126.73, 123.23, 123.02, 116.77, 53.74, 48.13, 34.79, 19.44 and 13.40. MALDI-TOF MS, *m/z*: 259.2 [M - Cl]$^+$.

3-(3-(iso-Propyl)-5-formyl-4-hydroxybenzyl)-1,2-dimethylimidazol-3-ium chloride **(3e)**: Obtained as pale yellow waxy solid which used for the following preparations without further purification, Yield (90 %). FT-IR (KBr, cm^{-1}): 3434 (m, br, $\nu_{(O-H)}$), 2967 (m, sh, $\nu_{(CH_3)}$), 1644 (vs, sh, $\nu_{(C=O)}$), 1537, 1464, 1401 (s, sh, $\nu_{(C=C_{Ar} + C-H_{bend})}$), 1270 (s, sh, $\nu_{(Ar-O)}$), 1153 (s, sh, $\nu_{(H-C=C + H-C=N)_{bend}}$, Im). ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 11.45 (s, 1 H, Ar-O**H**), 9.95 (s, 1 H, Ar- **H**C=O), 7.72 (s, br, 3 H, Ar-**H** and Im-**H**), 7.48 (s, br, 1 H, Ar-**H**), 5.57 (s, 2 H, N(3)-C**H$_2$**-Ar), 3.98 (s, 3 H, N(1)-C**H$_3$**), 3.31 ($m_{(7)}$, 1 H, C**H**$(CH_3)_2$), 2.86 (s, 3 H, C(2)-C**H$_3$**), 1.21 (d, *J* = 6.85 Hz, 6 H, CH(C**H$_3$**)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 197.76, 160.04, 144.69, 138.90, 133.76, 132.03, 124.61, 123.42, 122.07, 120.69, 52.02, 36.39, 26.97, 22.52 and 11.49. ESI MS: In positive mode peaks at m/z 273.16 (100%, $[C_{16}H_{21}N_2O_2]^+$) a.m.u. and in negative mode peak at m/z 34.97 (100%, $[Cl]^-$) a.m.u. HRMS $[C_{16}H_{21}N_2O_2]^+$ Calcd.: 273.1603 Found: 273.1597.

1.5 Anion metathesis: synthesis of salicylaldehyde-(1,2-dimethylimidazolium) hexafluoro-phosphate and tetrafluoroborate, H(^{i}Pr)sal(Me_2Im^+-X^-), (3f,g):

General method; To a solution of salicylaldehyde-(1,2-dimethylimidazolium) chloride **3a** (3.63 g, 11.75 mmol) in milli-Q water (50 mL) was added aqueous solution of HPF_6 (60 w % solution, 2.7 mL, 17.62 mmol)/ solid $NaBF_4$ (1.37 g, 12.43 mmol) portion-wise with vigorous stirring while cooling in ice bath over 1 h. After the addition was completed, the reaction was stirred at room temperature for 24 h. The solid product was filtered, washed with milli-Q water (to remove $NaBF_4$ or HPF_6- solution and any water-soluble impurities) until it was neutral. The final product was dried under vacuum at 40 °C for 24 h. Samples of the isolated products are fully characterized below.

3-(3-(iso-Propyl)-5-formyl-4-hydroxybenzyl)-1,2-dimethylimidazolium hexafluorophosphate (**3f**): Yield (94 %). FT-IR (KBr, cm^{-1}): 3436 (m, br, $\nu_{(O-H)}$), 2969 (m, sh, $\nu_{(CH_3)}$), 1644 (vs, sh, $\nu_{(C=O)}$), 1543, 1461, 1423 (s, sh, $\nu_{(C=C_{Ar} + C-H_{bend})}$), 1270 (s, sh, ν $\nu_{(Ar-O)}$), 1155 (s, sh, $\nu_{(H-C=C + H-C=N)_{bend}}$, Im), 838 (vs, sh, $\nu_{(PF_6^-)str}$), 743 (m, sh), 674 (m, sh), 558 (s, sh, $\delta_{(P-F)}$), 536 (m, sh). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.23 (s, 1 H, Ar-O**H**), 10.34 (s, 1 H, Ar-**H**C=O), 7.74 (d, J = 2.11 Hz, 1 H, N(1)CHC**H**N(3)), 7.67 (d, J = 2.10 Hz, 2 H, 2 x Ar-**H**), 7.60 (d, J = 2.32 Hz, 1 H, N(1)C**H**CHN(3)), 5.39 (s, 2H, N(3)-C**H$_2$**-Ar), 3.78 (s, 3 H, N(1)-C**H$_3$**), 3.31 ($m_{(7)}$, 1 H, C**H**$(CH_3)_2$), 2.66 (s, 3 H, C(2)-C**H$_3$**), 1.23 (d, J = 6.91 Hz, 6 H, CH(C**H$_3$**)$_2$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 197.13, 158.29, 144.92, 137.61, 133.88, 130.64, 126.33, 123.03, 121.31, 121.14, 50.31, 35.17, 26.31, 22.48 and 9.87. ^{31}P NMR (202 MHz, DMSO-d_6): -143.42 ppm (septet, $^2J_{PF}$ = 711.18 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): -7.28 ppm (doublet, $^1J_{PF}$ = 711.28 Hz). MALDI-TOF MS, *m/z*: 691.2 $[M{\cdot}{\sim}H_2O{\cdot}DIT + Na]^+$, 499.0 $[M{\cdot}DIT - PF_6^-]^+$ and 272.8 $[M - PF_6^-]^+$.

3-(3-(iso-Propyl)-5-formyl-4-hydroxybenzyl)-1,2-dimethylimidazolium tetrafluoroborate (**3g**): Yield (92%). FT-IR (KBr, cm^{-1}): 3467 (m, br, $\nu_{(O-H)}$), 1645 (vs, sh, $\nu_{(C=O)}$), 1544, 1463, 1392 (s, sh, $\nu_{(C=C_{Ar} + C-H_{bend})}$), 1271 (s, sh, $\nu_{(Ar-O)}$), 1156 (s, sh, $\nu_{(H-C=C + H-C=N)_{bend}}$, Im), 1063 (vs, sh, $\nu_{(BF_4^-)str}$). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.24 (s, 1 H, Ar-O**H**), 10.03 (s, 1 H, Ar-**H**C=O), 7.74 (d, J = 2.10 Hz, 1 H, N(1)CHC**H**N(3)), 7.67 (d, J = 2.05 Hz, 2 H, 2 x Ar-**H**), 7.60 (d, J = 2.20 Hz, 1 H, N(1)C**H**CHN(3)), 5.40 (s, 2 H, N(3)-C**H$_2$**-Ar), 3.78 (s, 3 H, N(1)-C**H$_3$**), 3.31 ($m_{(7)}$, 1 H, C**H**$(CH_3)_2$), 2.66 (s, 3 H, C(2)-C**H$_3$**), 1.23 (d, J = 6.91 Hz, 6 H, CH(C**H$_3$**)$_2$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 197.23, 158.30, 144.93, 137.59, 133.90, 130.70, 126.33, 122.92, 121.30, 121.09, 50.31, 35.16, 26.31, 22.47 and 9.80. ^{19}F NMR (470 MHz, DMSO-d_6): -148.69 ppm (singlet). MALDI-TOF MS, *m/z*: 499.2 $[M{\cdot}DIT - BF_4^-]^+$ and 273.0 $[M - BF_4^-]^+$.

1.6 Antimicrobial susceptibility

The plate-hole diffusion method was employed for the determination of antimicrobial activities against the gram (+), gram (−) bacterial and fungal organisms. Broth micro-dilution method was used to determine the MICs (minimum inhibitory concentrations) for the free ligands and their complexes in H_2O against test organisms. All the tests were performed in duplicate and repeated twice. Modal values were selected. Each microorganism was seeded in tube with nutrient broth (NB) (1 cm^3) which was then homogenized in the tubes with 9 cm^3 of melted (45 ^oC) nutrient Agar (NA). The homogeneous suspensions were poured into Petri dishes and holes of 4 mm diameter were done in the cool medium. After cooling these holes, 100 µL of the investigated compounds solutions, with serial concentrations, were applied using a micropipette with the pathogens to be tested against. The plates were incubated for 72h hours at 37 °C for bacteria and 28 °C for fungi, after that the clear zone around the wells was measured as inhibition zones and the diameter of these zone of inhibition (mm) were measured accurately. The antibacterial activities were observed and measured using a transparent meter rule and recorded if the zone of inhibition was ≥10 mm [S2]. Ampicillin, Antibacterial, and Amphotericin B, Antifungal, were employed as standard drugs

2. Tables Captions

Table S1: Structure of literature complex from CSD

Table S2: Assignment of the vibrations from IL-Sal-SGD Schiff bases (**4a-g**) and their palladium(II) complexes (**5a-g**).

Table S1: Structure of literature complex from CSD

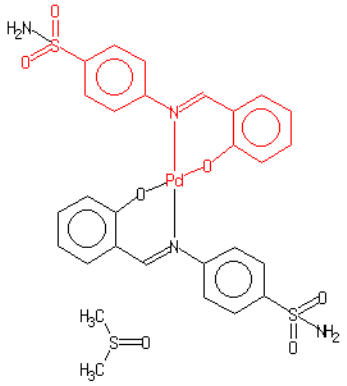
Entry	Structure	Reference
JAWHIZ		S3

Table S2 Assignment of the vibrations from IL-Sal-SGD Schiff bases (**4a-g**) and their palladium(II) complexes (**5a-g**).

Nr.	$\nu_{(O-H)}$	$\nu_{(NH_2)}$	$\nu_{(N-H)}$	$\nu_{(NH_3^+)}$	$\nu_{(C=N)}$	$\Delta\nu_{(C=N)}$	$\nu_{(SO_2)}$	$\nu_{(Ar-O)}$	$\Delta\nu_{(Ar-O)}$	$\nu_{(IL)}$
4a	3425	3356	3185	–	1617	–	1326	1263	–	1533, 700,
		3324	3152	–	1577	–		681	–	616, 556
5a	–	–	3202	3121	1627	+10	1321	1283	+20	1534, 698,
		–	3132	1493	1592	+14		706	+25	613, 555
4b	3419	3340	3192	–	1622	–	1323	1267	–	1535, 764,
		3308	3174	–	1579	–		679	–	562
5b	–	–	3177	3119	1645	+23	1319	1280	+23	1537, 765
		–	3131	1491	1580	+10		705	+26	560
4c	3419	3336	3200	–	1620	–	1328	1265	–	1535, 757
		3304	3135	–	1573	–		683	–	561
5c	–	–	3199	3111	1649	+29	1323	1282	+17	1536, 756
		–	3128	1494	1689	+16		707	+24	559
4d	3476	3434	3236	–	1623	–	1327	1270	–	1543, 760
		3354	3166	–	1581	–		682	–	557
5d	–	–	3195	3116	1645	+22	1318	1284	+14	1540, 763
		–	3142	1493	1592	+11		718	+36	557
4e	3436	3398	3201	–	1625	–	1326	1272	–	1539, 784
		3317	3154	–	1583	–		680	–	552
5e	–	–	3188	3115	1647	+22	1321	1283	+11	1538, 788
		–	3128	1492	1590	+7		715	+35	554
4f	3475	3459	3185	–	1624	–	1325	1270	–	1060, 1542,
		3359	3150	–	1578	–		684	–	773
5f	–	–	3201	3116	1644	+20	1320	1287	+17	1541, 1061,
		–	3134	1494	1596	+18		719	+35	770
4g	3479	3435	3236	–	1621	–	1325	1273	–	1539, 845,
		3344	3163	–	1580	–		682	–	776
5g	–	–	3185	3117	1650	+29	1322	1280	+17	1539, 845,
		–	3143	1493	1594	+14		716	+34	770

References

[S1] R .F. M. Elshaarawy and C. Janiak, *Eur. J. Med. Chem.,* 2014, **75**, 31-42.

[S2] A.J. Vlietink, L. Van Hoof, J. Totte, H. Laure, D.V. Berhe, P.C. Rwangabo, J. Mrukiyunmwami, J. Ethnopharm. 46 (1995) 31-47.

[S3] R. R. Coombs, M. K. Ringer, J. M.Blacquiere, J. C. Smith, J. S. Neilsen, Y.-S. Uh, J. B. Gilbert, L. J. Leger, H. Zhang, A. M. Irving, S. L. Wheaton, C. M. Vogels, S. A. Westcott, A. Decken and F. J. Baerlocher, *Transition Met. Chem.*, 2005, **30 (4)**, 411-418