A single molecule multi analyte chemosensor differentiates among Zn$^{2+}$, Pb$^{2+}$ and Hg$^{2+}$: Modulation of selectivity by tuning of solvents

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Instruments\textsuperscript{1} and Reagents.

All reactants and reagents were commercially available and were used without further purification unless otherwise indicated. Solvents used were purified and dried by standard methods. All reactions were carried out under dry nitrogen atmosphere in flame-dried glassware, unless otherwise noted. Melting points were recorded with Buchi B-545 Melting Point Apparatus. The structures of the compounds were determined by 1D and 2D nuclear magnetic resonance spectroscopy and other spectroscopic techniques. \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were recorded with 400 MHz Jeol and 500 MHz Bruker instruments. Chemical shifts are reported in $\delta$ values relative to an internal reference of tetramethylsilane (TMS) for the solvent peak. The solvents for the spectroscopy experiments were of the spectroscopic grades and were free from any fluorescent impurities. Double distilled water was used for the spectroscopy experiments. The solutions of metal ions were prepared from Al(NO$_3$)$_3$·9H$_2$O, LiClO$_4$·3H$_2$O, NaClO$_4$, KClO$_4$, Ba(NO$_3$)$_2$·4H$_2$O, Mn(ClO$_4$)$_2$, Fe(ClO$_4$)$_2$·xH$_2$O, Co(ClO$_4$)$_2$·6H$_2$O, Cd(NO$_3$)$_2$, AgNO$_3$, Hg(NO$_3$)$_2$, Pb(ClO$_4$)$_2$, Ca(ClO$_4$)$_2$·4H$_2$O, Cu(ClO$_4$)$_2$·6H$_2$O, Ni(ClO$_4$)$_2$ and Zn(ClO$_4$)$_2$·6H$_2$O in MeOH and H$_2$O. IR data were obtained with a Bruker-Optics-Alpha-T spectrophotometer. UV spectra were recorded with a Hitachi U-4100 UV-vis spectrophotometer. Fluorescence measurements were carried out with Horiba Jobin Yvon (Fluoromax-3). Mass spectrometry data were obtained from an Acquity\textsuperscript{TM} ultra performance LC. pH data were recorded with a Sartorius Basic Meter PB-11 calibrated at pH 4, 7 and 10. Fluorescence imaging was carried out using an Olympus IX51 inverted microscope with UV excitation. Reactions were monitored by thin layer chromatography using Merck plates (TLC Silica Gel 60 F$_{254}$). Developed TLC plates were visualized with UV light (254 nm/366 nm). Silica gel (100 ~ 200 mesh, Merck) was used for column chromatography. Yields refer to the chromatographically and spectroscopically pure compounds, unless indicated.

\textsuperscript{1} All experimental data were obtained using the instrument facilities at IISER Kolkata.
Scheme S1. Preparation of compound 1.

3,5-bis(bromomethyl)-2-hydroxybenzaldehyde (3)

To a mixture of salicylaldehyde (0.50 g, 4.09 mmol) and paraformaldehyde (0.37 g, 12.27 mmol) in glacial acetic acid (1.50 mL), 33% HBr in acetic acid, 55 °C, 20h, 70%

Synthesis.

Compounds \(2^1\), \(4^2\), \(5^3\) were synthesized according to the literature procedure.

3,5-bis(bromomethyl)-2-hydroxybenzaldehyde (3)

To a mixture of salicylaldehyde (0.50 g, 4.09 mmol) and paraformaldehyde (0.37 g, 12.27 mmol) in glacial acetic acid (1.50 mL), 33% HBr in acetic acid (2.80 mL, 16.40 mmol) was added at room temperature under N\(_2\). The reaction mixture was stirred at 55°C for 20h and cooled to room temperature. The reaction mixture was poured slowly into ice cold water (100 mL) with vigorous stirring whereupon a white precipitate was formed. The precipitate was dissolved in methylenechloride (30 mL) and washed with saturated NaHCO\(_3\) solution (20 mL x 2). The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and the volatiles were removed.
under reduced pressure. The desired compound on chromatography (hexane/EtOAc) yielded compound 3 as a white solid (0.60 g, 70%, m.p. 99-100 °C). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 11.55 (s, 1H, -ArO\(\text{H}\)), 9.88 (s, 1H, -ArCHO), 7.64 (s, 1H, -Ar\(\text{H}\)), 7.57 (s, 1H, -Ar\(\text{H}\)), 4.55 (s, 2H, -CH\(_2\)Br), 4.48 (s, 2H, -CH\(_3\)Br). \(^13\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 195.9, 159.2, 138.2, 134.3, 129.5, 127.0, 120.4, 31.8, 25.8. FT-IR (KBr, cm\(^{-1}\)) 3360 (br), 3160, 2935, 1665, 1279, 1151. ESI-MS e/z calcd for C\(_9\)H\(_8\)Br\(_2\)O\(_2\) [M+H] 308.9, found 308.9.

2-(2-oxo-2H-chromene-3-carboxamido)ethanaminium 2,2,2-trifluoroacetate (6)

[Compound 6 was obtained in three steps from compound 5]

2-oxo-2H-chromene-3-carbonyl chloride (6a).

To a stirred solution of compound 5 (2.0 g, 10.53 mmol) in dichloromethane (10 mL), oxalyl chloride (2.0 mL, 21.0 mmol) and a catalytic amount of DMF was added at 0°C. The reaction mixture slowly turned clear with gentle effervescence. The mixture was allowed to react for 4h at room temperature. The reaction mixture was concentrated under reduced pressure. The crude product was co-distilled with toluene. The intermediate acid chloride was dried under high vacuum to obtain brown solid which was used directly in the subsequent step without further purification.

tert-butyl 2-(2-oxo-2H-chromene-3-carboxamido) ethylcarbamate (6b).

The acid chloride of 5 (0.65 g, 3.12 mmol) dissolved in dichloromethane (5 mL) was added dropwise to a solution of compound 2 (0.50 g, 3.12 mmol) in dichloromethane (5 mL) and triethyl amine (0.86 mL, 6.24 mmol) at 0°C over a period of 30 minutes. The reaction mixture was stirred for another 12h at room temperature. The organic layer was extracted with dichloromethane (30 mL x 2) and washed with water (20 mL). It was then dried over Na\(_2\)SO\(_4\) and the solvent was removed under reduced pressure. The residue on chromatography (hexane/dichloromethane, 50:50, v/v) yielded the desired compound 6b as a pale yellowish solid (0.78 g, 75%) mp 140-141 °C (reported: 142-143 °C). The \(^1\)H NMR spectral data is in close agreement with the literature values.\(^4\) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.87 (br, 1H, -NHCOAr), 8.76 (s, 1H, -Ar\(\text{H}\)), 7.56 (m, 2H, -Ar\(\text{H}\)), 7.26 (m, 2H, -Ar\(\text{H}\)), 5.10 (br, 1H, -
NHBoc), 3.47 (t, 2H, J = 5.50 Hz, -CH_2NHCOAr), 3.27 (t, 2H, J = 5.00 Hz, -CH_2NHboc), 1.31 (s, 9H, -t-Bu). ESI MS e/z 233 (M+H).

Boc deprotection: 2-(2-oxo-2H-chromene-3-carboxamido)ethanaminium 2,2,2-trifluoroacetate (6)

Trifluoroacetic acid (0.30 mL, 2.42 mmol) in dichloromethane (5 mL) was added to a solution of compound 6b (0.20 g, 0.60 mmol) dissolved in dichloromethane (15 mL) over a period of 10 min at 0°C. The solution was stirred for another 4h at room temperature. The solvent was removed under reduced pressure. The compound 6 thus obtained as a trifluoroacetic acid salt was used in the subsequent step without further purification.

(5-formyl-4-hydroxy-1,3-phenylene)bis(methylene)bis(2-(2-oxo-2H-chromene-3-carboxamido)ethylcarbamodithioate) (1)

TFA salt 6 (0.20 g, 0.58 mmol) and K_2CO_3 (0.48 g, 3.46 mmol) in dioxane/water (1:1) (10 mL) was stirred for 5 minutes at 0°C. To it carbon disulfide (1.11 g, 0.88 mL, 14.5 mmol) was added and the mixture was stirred for another 10 min. Compound 3 (0.09 g, 0.26 mmol) dissolved in dioxane (2 mL) was subsequently added dropwise over a period of 15 minutes. The solution was allowed to attain room temperature (25°C) and was stirred for another 30 min. After complete disappearance of the starting material was observed by TLC, the solution was concentrated under reduced pressure. The yellowish solid thus obtained was dissolved in dichloromethane (20 mL) and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and the volatiles were removed under reduced pressure which on chromatography (dichloromethane/CH_3CN, 9:1, v/v) yielded compound 1 as a white solid (0.10 g, 58%). mp 181-182 °C. ^1H NMR (500 MHz, DMSO-d_6): δ 11.09 (br, 1H, -ArOH), 10.08 (br, 2H, -CONHCH_2), 9.99 (s, 1H, ArCHO), 8.87 (s, 2H, -ArH), 7.97 (m, 2H, -ArH), 7.72 (m, 4H, -ArH), 7.50 (s, 1H, -ArH), 7.48 (s, 1H, -ArH), 7.43 (m, 2H, -ArH), 4.47 (s, 2H, Ar-CH_2S-), 4.46 (s, 2H, ArCH_2), 3.75 (td, 4H, J = 5.0 Hz, -CH_2NHCO), 3.57 (td, 4H, J = 5.0 Hz, -CH_2NHCS). ^13C NMR (500 MHz, DMSO-d_6): δ 196.09, 195.98, 195.89, 161.48, 161.47, 160.10, 153.80, 147.51, 137.70, 134.06, 132.00, 130.20, 128.62, 125.52, 125.05, 120.85, 118.50, 118.32, 116.03, 46.53, 46.45, 37.49, 37.03, 32.17. UV-vis [MeOH; δ nm (ε M⁻¹ cm⁻¹)]: 280 (34800), 335 (19100); FT–IR (KBr, cm⁻¹): 3315, 3218, 1708, 1650, 1607, 1567, 1536. HRMS (ESI) calcd for C_{35}H_{30}N_{4}O_{8}S_{4}K⁺ 801.0584, found 801.0586
General Procedure for UV-Vis and Fluorescence Studies.

For absorption and emission spectra, stock solutions of the metal salts (1.0 mM) and the free chemosensor 1 (10 µM) were prepared in MeOH/ DMSO (99:1, v/v) and H₂O/DMSO (99:1, v/v) in presence of HEPES buffer pH = 7.0. All experiment were carried out with 10 µM solutions of 1 in MeOH/ DMSO, H₂O/DMSO mixture and various concentrations of the salt solutions in MeOH or H₂O. The absorption and emission spectra were recorded immediately except for the Hg²⁺ complex. Excitation was performed at 320 nm with all excitation and emission slit widths at 5.0 nm unless otherwise indicated.

**Figure (S1).** The electronic absorption spectra of 1 (10 µM) in MeOH/ DMSO (99:1, v/v) in the presence of Zn²⁺. Inset: Titration profile of 1 (10 µM) and Zn²⁺ (0 - 40 µM).
Figure (S2). The electronic absorption spectra of 1 (20 µM) in MeOH/ DMSO (99:1, v/v) in the presence of Hg$^{2+}$.

Figure (S3). The electronic absorption spectra of 1 (20 µM) in MeOH/ DMSO (99:1, v/v) in the presence of Pb$^{2+}$. 
Figure (S4). The electronic absorption spectra of 1 (10 µM) in water (H₂O/DMSO, 99:1, v/v) in the presence of Hg²⁺ (0 – 40 µM). Inset: Ratio of absorption [A₂₉₅/A₄₀₀] as a function of eqv. of Hg²⁺.

Figure (S5). Emission ratio at 495 and 410 nm of 1 (10 µM) in MeOH/ DMSO (99:1, v/v) induced by different metal cations (20 µM).
Figure (S6). Normalized fluorescence intensity of compound 1 (10 µM) in H₂O/DMSO (99:1, v/v) upon addition of different metal ions (20 µM) (orange bars) and fluorescence recovery by Hg²⁺ (20 µM) in the presence of other metal ions (50 µM) (violet bars).

Figure (S7). Job's plots for 1:2 complexation of 1 with Zn²⁺ in MeOH/ DMSO (99:1, v/v) according to the absorption at 330 nm. The total concentration of the ligand and the metal was kept constant at 100 µM.
**Figure (S8).** Job's plots for 1:1 complexation of 1 with Pb$^{2+}$ in MeOH/DMSO (99:1, v/v) according to the emission at 410 nm. The total concentration of the ligand and the metal was kept constant at 8 µM.

**Figure (S9).** Job's plots for 1:1 complexation of 1 with Hg$^{2+}$ in H$_2$O/DMSO (99:1, v/v) according to the emission at 465 nm. The total concentration of ligand and metal remained constant at 8 µM.
$^1$H NMR titration method.

Stock solutions of 1 (1.0 mM) were prepared in (DMSO-d$_6$/CD$_3$OD), (DMSO-d$_6$/D$_2$O). Metal salts (10 mM) were separately prepared in CD$_3$OD, D$_2$O. The $^1$H NMR spectra were immediately recorded after addition of different eqv. of Zn$^{2+}$ with chemosensor 1. For Hg$^{2+}$, the data were recorded after 30 min addition of metal salts.

![Figure (S10). Partial $^1$H-NMR spectra changes of chemosensor 1 upon addition of Hg$^{2+}$ in D$_2$O/DMSO-d$_6$ (2:3, v/v).](image)

**Determination of association/dissociation constants.**

The dissociation constant ($K_d$) of Hg$^{2+}$ and Pb$^{2+}$ was determined from the fluorescence titration experiment using the following equation $^5$, $(F_i - F_0) = \Delta F = [M^{2+}](F_{\text{max}} - F_0)/(K_d + [M^{2+}]), M = \text{Hg}^{2+} \text{ or } \text{Pb}^{2+}$. $F_i$ is the observed fluorescence with different eqv. of $M^{2+}$, $F_0$ is the fluorescence for the free chemosensor 1, $F_{\text{max}}$ is the saturation value of the fluorescence intensity for the metal complexes. To obtain $Y = AX + B$ a linear equation, the reciprocal of $\Delta F$ was plotted against the reciprocal of the concentration of $M^{2+}$. $K_d$ was calculated from the ratio $A/B$.

The association constant of Zn$^{2+}$ was calculated from the fluorescence titration data using the following equation $^6$ $\ln[(F - F_0)/(F_\infty - F)] = n \ln[\text{Zn}^{2+}] + n \ln(K_{\text{asscn}}) \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots

In above equation, n refers to the number of zinc ions associating with each molecule of 1, $K_{\text{asscn}}$ refers to the association constant, $F_0$, F and $F_\infty$ refers to the fluorescence intensities solution of chemosensor 1 alone, 1 with any concentration of Zn$^{2+}$, and at high concentration of Zn$^{2+}$ ion.
Figure (S11). Plot of $\ln\left[\frac{(F-F_0)/(F_\infty-F)}{F-F_\infty}\right]$ against $\ln[Zn^{2+}]$; the stoichiometry of 1-Zn$^{2+}$ association, obtained directly from the slope, is $2.08 \equiv 2$. Following equation 1, the intercept gave an association constant of $7.07 \times 10^4$ M$^{-2}$.

Figure (S12). Benesi–Hildebrand plot for determination of binding constant Hg$^{2+}$ in MeOH/DMSO (99:1, v/v) with chemosensor 1. Association constant is $3.08 \times 10^5$ M$^{-1}$. 
Figure (S13). Benesi–Hildebrand plot for determination of binding constant of Pb\(^{2+}\) in MeOH/DMSO (99:1, v/v) with chemosensor 1. Association constant is 3.90 \times 10^5 M\(^{-1}\).

Figure (S14). Benesi–Hildebrand plot for determination of binding constant Hg\(^{2+}\) in H\(_2\)O/DMSO (99:1, v/v) with chemosensor 1. Association constant is 1.2 \times 10^6 M\(^{-1}\).
Detection limit

The detection limit for the ions were calculated from the titration experiments following the reported method. For Hg$^{2+}$ in H$_2$O, the fluorescence intensity data at 415 nm were normalised between the minimum intensity found at zero eqv. of Hg$^{2+}$ and the maximum intensity found at 1 eqv. of Hg$^{2+}$ added. A linear curve was obtained from these normalised fluorescence intensity data and the intercept on the x-axis was considered as the detection limit. Thus the value obtained for the Hg$^{2+}$ was found to be 9.0 x 10$^{-9}$ (M).

For Pb$^{2+}$ the fluorescence intensity data at 410 nm were normalised between the minimum intensity found at zero eqv. of Pb$^{2+}$ and maximum intensity found at 1 eqv. of Pb$^{2+}$ added. A linear curve was obtained from these normalised fluorescence intensity data and the detection limit was obtained by the extrapolation of the straight line on the x-axis. Thus the value obtained for the Pb$^{2+}$ was found to be 1.6 x 10$^{-8}$ (M).

For Zn$^{2+}$ the absorption data at 400 nm was normalised between the minimum absorption observed at zero eqv. of Zn$^{2+}$ and maximum absorption found at 2.0 eqv. of Zn$^{2+}$ added. A linear curve was obtained from these normalised absorption data and the intercept on the x-axis was considered as the detection limit. Thus the value obtained for the Zn$^{2+}$ was found to be 5.8 x 10$^{-7}$ (M).

![Graph](image)

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Y = 0.479X + 2.984
R = 0.99

Figure (S15). Absorbance of chemosensor 1 in MeOH/DMSO (99:1, v/v) at each concentration of Zn$^{2+}$ added, normalized between the minimum absorbance was found at zero equiv of Zn$^{2+}$, and the maximum absorbance was found at 2.0 equiv of Zn$^{2+}$.
**Figure (S16).** Fluorescence intensity of chemosensor 1 in MeOH/DMSO (99:1, v/v) at each concentration of Pb²⁺ added, normalized between the minimum emission intensity was found at zero equiv of Pb²⁺, and the maximum intensity was found at 1.0 eqv. of Pb²⁺.

![Graph showing fluorescence intensity vs. log concentration of Pb²⁺](image1)

**Figure (S17).** Fluorescence intensity of chemosensor 1 in H₂O/DMSO (99:1, v/v) at each concentration of Hg²⁺ added, normalized between the minimum emission intensity was found at zero equiv of Hg²⁺, and the maximum intensity was found at 1.0 eqv. of Hg²⁺.

![Graph showing fluorescence intensity vs. log concentration of Hg²⁺](image2)
Preparation and imaging of cells

Hela S3 were grown in DMEM (Dulbecco's Modified Eagle Medium) supplemented with 10% FBS (fetal bovine serum), 100 units/ml penicillin and 100µg/ml streptomycin, at 37°C and 5% CO₂. Cells (0.4 X 10⁶ per mL) were plated on 12 mm cover slips and allowed to adhere for 24 hours. Hela S3 cell lines were exposed to Hg(NO₃)₂ (500 µM) in DMEM for 2h at 37°C. Subsequently, the cells were washed twice with PBS to remove the remaining Hg²⁺ ions, and incubated with 1 (10 µM) in PBS for 10 minutes at 25°C. It was followed by washing the cells using PBS to remove residual dye from the cells. Fluorescence imaging was carried out using an Olympus IX51 inverted microscope (20X objective lens) with UV excitation.
Figure (S19). HRMS of chemosensor [1+K⁺].
Figure (S20). ESI-MS of the complex \([1 + 2 \text{Zn}^{2+} + \text{H}_2\text{O} - 3\text{H}^+]\).

Figure (S21). ESI-MS of the complex \([1 + \text{Pb}^{2+} - \text{H}^+]\).
Figure (S22). ESI-MS of the complex [1 + Hg^{2+}].

Figure (S23). $^1$H-NMR spectra of 3.
Figure (S24). $^{13}$C-NMR spectra of 3
Figure (S25). $^1$H-NMR spectra of 6b
Figure (S26). $^1$H-NMR spectrum of 1
**Figure (S27).** $^{13}$C-NMR spectra of 1

**References**