

# Article

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**ACS** Catalysis

# Inclusion of peripheral basic groups activates dormant cobalt-based molecular complex for catalytic $H_2$ evolution in water

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# ABSTRACT

The protein scaffold plays a key role during the enzymatic catalysis for metalloenzymes. Here we have rationally designed an enzyme-inspired outer coordination sphere in the form of protic functionalities, such as natural amino acid derived carboxylic acid and phenolic-OH groups, on the fringe of the cobalt-salen like complexes. This inclusion has enabled electrocatalytic H<sub>2</sub> evolution for an otherwise inactive cobalt-salen like core. The complexes containing peripheral carboxylic acid groups exhibited unique pH-switchable catalytic H<sub>2</sub> production that is connected with the  $pK_a$  of the carboxylic acid group (~ 4.0), suggesting the crucial involvement of the carboxylate group during the catalytic activity. The one- and two-dimensional NMR results of

the complexes have indicated the presence of possible hydrogen bonding network, generated by those protic groups in aqueous solution. These results highlight that an inactive metal complex can be activated for specific small molecule activation via rational inclusion of outer coordination sphere functionalities.

#### **KEYWORDS**

Electrocatalytic H<sub>2</sub> Production • Cobalt-Salen like complexes • pH-switchable outer coordination sphere • Enzyme-inspired catalyst design• Water soluble H<sub>2</sub> production catalysts

# Introduction

Hydrogen is considered as one of the top candidates for energy carrier for the efficient use of renewable energy resources.<sup>1-6</sup> In recent years, substantial research has been done in the quest for an efficient and sustainable catalytic system for  $H_2$  production from a widely abundant source like water.<sup>7,8</sup> Hitherto, platinum and hydrogenase enzymes have emerged as the best catalysts for efficient  $H_2$  production.<sup>9</sup> However, the low abundance of the precious platinum and the chemical sensitivity of the hydrogenase have restricted their large-scale usage.<sup>10–13</sup> Despite the shortcomings, hydrogenase enzyme active site has remained as the inspiration for developing biomimetic  $H_2$  production catalysts.<sup>14–21</sup> However, most of those structural models were inactive or poorly active for  $H_2$  production despite closely imitating the enzyme active site. The absence of the crucial protein environment around the metallocenter is believed to the prime reason behind this catalytic inactivity.<sup>22–24</sup> In recent years, different research groups have incorporated proteins and smaller peptides around synthetic metallocenter to induce active catalysis on the metal center highlighting the importance of the outer coordination sphere during the design of synthetic hydrogenase models.<sup>25–31</sup> However, the fragile nature of the proteins has raised stability

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issues for long-term usage of synthetic metallopeptides in acidic conditions. In a different approach, some research groups have developed rather robust catalysts by introducing only the minimal and essential feature of the protein scaffold around metalloporphyrin, and nickel bis(diphosphine) core.<sup>32–36</sup> Despite the improved reactivity of both set of complexes upon outer coordination sphere feature inclusion, their long-term stability in acidic water, especially in aerobic condition, is still uncertain.

The cobalt-salen (Co-salen) complexes are stable under broad pH conditions in aqueous oxygenic solutions, though, they are primarily known for  $O_2$  binding and ring opening reactions for epoxides.<sup>37–39</sup> Recently, research groups of Du and Wang have reported photocatalytic H<sub>2</sub> production by Co-salen complex; however, the detailed electrochemical behavior of the complex and the possible nature of H<sub>2</sub> production catalysis (homogeneous or heterogeneous) have not been probed yet.<sup>40,41</sup> In this work, we have developed four Co-salen like complexes varying peripheral protic functionalities (*Scheme I*). Natural amino acid phenylalanine was embedded in one of the complexes to position carboxylic acid (-COOH) groups in the periphery. The Inclusion of tyrosine ensured the presence of a phenolic-OH group along with the -COOH as



Scheme 1. Reaction scheme for the salen ligand  $(L_n)$  and Co-Salen like complex  $(C_n)$ 

outer coordination sphere feature in another complex. Two control complexes were prepared for each of those complexes, containing peripheral benzylamine and tyramine, respectively, where, the -COOH groups are absent. The experimental data suggested that the Co-salen like core gets activated for H<sub>2</sub> evolution in aqueous solution only in the presence of protic functionalities such as -COOH and phenolic-OH. The order of  $H_2$  production was as following: tyrosine  $\approx$ phenylalanine > tyramine. The –COOH group binds to the metal center in its deprotonated form, and that leads to unique pH-activated  $H_2$  production by the Co-salen like complexes only below pH 4.0, which is the  $pK_a$  of the peripheral –COOH group. The NMR data have also indicated the possible formation of hydrogen bonding network by the fringe protic functionalities around the complexes in water, which is vital for triggering catalytic H<sub>2</sub> production by the otherwise inactive Co-salen like core. This project has illustrated that the incorporation of interactive peripheral basic functionalities can induce electrocatalytic  $H_2$  production in water for otherwise inactive Co-salen like complexes. Thus, the inclusion of basic functionalities in outer coordination sphere can be used as a common strategy, which can not only improve the moderate catalysts but also spark life into dormant metal complexes, especially for small molecule activating reactions that involve exchange of protons.

## **Experimental Section**

Salicylaldehyde (98%), MES hydrate ( $\geq$ 99.5%) and L-tyrosine ( $\geq$ 98%) were purchased from Sigma-Aldrich. Benzylamine (98%), Tyramine hydrochloride (98%) and L-phenylalanine (98%) were purchased from Avra Synthesis Private Ltd, India. Hydrochloric acid and sulphuric acid were purchased from SD fine chemicals limited India. Sodium Hydroxide (AR grade), Sodium Hydroxide (AR grade) and Sodium sulphate anhydrous (AR grade), N, N-Dimethylformamide (HPLC grade) was purchased from Finar Chemicals Private Ltd, India. Tetrabutylammonium Page 5 of 43

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tetrafluoroborate was purchased from TCI Chemicals India Private Ltd. All the chemicals were used as received without further purification. All solvents used in this project were distilled before their use. Millipore ultrapure water (resistivity of 18.2 M $\Omega$ .cm at 25°C) was used for preparing all the aqueous solutions in this project. <sup>1</sup>H NMR spectra were recorded on Bruker Avance III Ascent FT 500 MHz Spectrometer. Tetramethylsilane (TMS) was used as an internal standard in CDCl<sub>3</sub> while the solvent signal was used for referencing in  $(CD_3)_2SO$  (d<sup>6</sup>-DMSO). UV-Visible spectra were recorded on Jasco V-750 spectrophotometer using quartz cuvette with 1cm path length. Infrared spectra were recorded on Perkin Elmer Spectrum Two spectrometer. The Mass data were recorded on Waters Synapt-G2S ESI-Q-TOF mass spectrometer. Electrochemical experiments were performed at room temperature under N2 atmosphere using Metrohm Autolab PGSTAT 101 potentiostat along with 1 mm glassy carbon disc working electrode, Pt-wire counter electrode and Ag/AgCl (in saturated KCl) as a reference electrode. All the cyclic voltammetry data reported in this work was internally referenced against  $[Fe(CN)_6]^{3-/4-}$  couple  $[E^0_{Fe(CN)_6]_{3-/4-}} = +0.360$  V vs. standard Hydrogen Electrode (SHE)] in aqueous medium. All the potential values reported in this work are referenced against standard Hydrogen Electrode (SHE) unless otherwise mentioned. Buffer solutions of pH 3-6 were prepared by using 2-(N-Morpholino)ethanesulfonic acid hydrate (MES hydrate) buffer. pH 2 and pH 1 solutions were prepared by adding an adequate amount of 18 M sulphuric acid in water. Tetrabutylammonium tetrafluoroborate and anhydrous sodium sulphate were used as a supporting electrolyte in organic solvents and buffer solutions, respectively. Before each run glassy carbon working electrode was polished using a slurry of 0.05 µm alumina power in Milli-Q water. Circular dichroism (CD) studies were carried out using Jasco J-815 CD spectrometer using quartz cuvette with 1mm path length. Data showed in this article is average of 5 runs. CD

studies for C2 and C4 were performed in buffered solution of different pH. Spectroelectrochemistry was performed at room temperature in buffered solution using Avantes starline Avaspec-2048 spectrophotometer. The sample was placed in a quartz cuvette (3.5 mL volume, 1cm path length) placed in an external sample holder connected to the light source and detector via optical fibres. The system was further connected to the Metrohm Autolab PGSTAT 101 using a 3 mm glassy carbon rod as working electrode, Pt wire as counter electrode, and Ag/AgCl (in saturated KCl) as a reference electrode. Bulk electrolysis was also performed using Metrohm Autolab PGSTAT 101. The bulk electrolysis setup includes a four-neck glass vessel (Volume 150 ml including the headspace), coiled 23 cm Pt wire as counter electrode, Ag/AgCl (in saturated KCl) as a reference electrode, and reticulated vitreous carbon or plastic-chip electrode prepared from graphite powder- and poly(methyl methacrylate) as the working electrode. 75 ml of 0.5 mM C4 and 0.25 mM of C2 in aqueous buffer solutions were used, respectively, during their chrono-coulometric experiments. The pH titrations of Co-salen like complexes were performed using Thermo Scientific Orion Star A111 pH meter in aqueous media.

# Synthesis of ligands:

*Salen-benzylamine ligand (L1):* Ligand L1 was synthesized as per the reported procedure.<sup>42</sup> Methanolic solution of salicylaldehyde (0.01 mol, 1.2 ml) was added dropwise to a solution of benzylamine (0.01 mol, 1.3 ml) with continuous stirring. The color of the solution turned yellow after the addition and the mixture solution was allowed to stir for 24 hours at room temperature. The progress of the reaction was monitored using thin layer chromatography using 30 % ethylacetate and hexane mixture as a mobile phase. After 24 hours, the solvent was evaporated under reduced pressure and washed subsequently with hexane (3 times) and chilled ether (2 times) and dried under vacuum to obtain yellow colored solid product.

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Yield: 55% (1.46 g). Mass Data: [M]<sup>+</sup>: Calculated: 212.1; Experimental: 211.9; NMR data <sup>1</sup>H
NMR (500 MHz, CDCl<sub>3</sub>) δ (ppm) = 4.82 (s, 2H, -CH<sub>2</sub>), 6.87-6.98 (m, 2H, Ar-H), 7.26-7.36 (m, 7H, Ar-H), 8.45 (s, 1H, -CH=N), 13.40 (s, 1H, -OH).

Salen-tyramine ligand (L3): Ligand L3 was synthesized via a modified version of the reported procedure.<sup>43</sup> L3 ligand was prepared by adding (0.01 mol, 106.4  $\mu$ L) salicylaldehyde dropwise to a solution of (0.01 mol, 173.6 mg) tyramine hydrochloride in methanol containing (0.01 mol, 40 mg) sodium hydroxide with continuous stirring. The color of the solution turned colorless to yellow following the addition. The reaction mixture was allowed to reflux at 70°C for about four hours where the reaction progress was monitored by thin layer chromatography. After completion of the reaction the solvent was removed under reduced pressure and the solid residue was washed with ethyl acetate and hexane (8:2) mixture. Then, the product was dried under vacuum and a light yellow colored powdered product was obtained.

Yield: 56% (137 mg). Mass Data: [M]<sup>+</sup>: Calculated: 241.4; Experimental: 241.8; NMR data <sup>1</sup>H NMR (500 MHz, CDCl3) δ (ppm) = 2.93 (t, J=7Hz, 2H, -CH2), 3.80 (t, J=6.9Hz, 2H, -CH2), 6.75-7.31 (m, 8H, Ar-H), 8.19 (s, 1H, -CH=N).

Salen-phenylalanine and Salen-tyrosine ligand (L2 and L4): For the preparation of amino acid containing ligands L2 and L4, first sodium hydroxide (0.01 mol, 40 mg) was dissolved in methanol, along with one equivalent amount of L-amino acids (tyrosine or phenylalanine, 0.01 mol, 165.2 mg phenylalanine and 122.2 mg tyrosine) with continuous stirring until the amino acids were dissolved completely. Then a methanolic solution of salicylaldehyde (0.01 mol, 106.4  $\mu$ L) was added to the reaction mixture drop wise and the color of the solution changed from colorless to yellow. Then the reaction mixture was refluxed at 70°C four hours. Then the reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure using a rotatory evaporator. A yellow colored solid product was obtained which was further washed with chilled ethanol and dried under vacuum.

Yield: L2 : 44 % (120 mg); Mass Data:  $[M]^+$ : Calculated: 269.8; Experimental: 269.8; NMR data <sup>1</sup>H NMR (500 MHz, CDCl3)  $\delta$  (ppm) = 2.95 (dd, J=13.8, 9.5Hz, diastereotopic proton 1H, - CH2), 3.30 (dd, J= 13.8, 4.1Hz, diastereotopic proton 1H, -CH2), 3.88 (dd, J= 9.4, 4.1Hz, 1H, - CH), 6.68-7.24 (m, 9H, Ar-H), 8.12 (s, 1H, -CH=N).

Yield: L4: 49 % (140 mg); Mass Data:  $[M]^+$ : Calculated: 285.8; Experimental: 285.8; NMR data <sup>1</sup>H NMR (500 MHz, CDCl3)  $\delta$  (ppm) = 2.79 (dd, J= 13.8, 9.5 Hz, diastereotopic proton 1H, - CH2), 3.14 (dd, J= 13.8, 4Hz, diastereotopic proton 1H, -CH2), 3.73 (dd, J= 9.3, 4.1Hz, 1H, - CH), 6.13-7.18 (m, 8H, Ar-H), 7.94 (s, 1H, -CH=N).

*Synthesis of Complexes:* The following common procedure was used to synthesize the cobalt complexes (C1-C4) with prepared ligands (L1-L4), which is a modified version of the reported procedure for the preparation of analogous cobalt-salen complexes.<sup>44</sup> A methanolic solution of Cobalt (II) chloride hexahydrate (0.5 equivalents) was slowly added into the ligand (L1 or L2 or L3 or L4) solution in methanol in 1:1 ratio in the presence of air. After the addition of cobalt, the color of the solution turned green [in case of benzylamine (C1) and tyramine (C3)] or dark brown (in case of phenylalanine (C2) and tyrosine (C4)) from yellow colored ligand solution. The reaction mixture was stirred at room temperature for 4 hours. Then the solvent was removed under reduced pressure using a rotatory evaporator. The product was washed with cold ether and dried under vacuum to obtained powdered product. Yield and characterization results for the complexes were as following:

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C2: 31 %, Mass Data: [M-2Cl+CH3OH]<sup>+</sup>: Calculated: 625.1; Experimental: 624.7; NMR data <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ (ppm)= 4.5 (br, 4H, -CH<sub>2</sub>), 5.4 ppm (br, 2H, -CH), 6.5-8.4 (m, br, 20H, Ar-H and -CH=N);

C3: 51%; Mass Data:  $[M-2Cl+H]^+$ : Calculated: 539.1; Experimental: 538.9; NMR data <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm)= 2.7-3.0 (br, 8H, -CH<sub>2</sub>), 6.3-7.3 (m, br, 16H, Ar-H), 7.74, 8.0, 9.15, 9.33 ppm (s, 2H, phenolic -OH), and 7.9, 8.0, 9.0, 9.1(s, 1H,-CH=N) [Four different imine and phenolic-OH possibly due to both cis- and trans- isomer formation].

C4: 35%, Mass Data: [M-2Cl]<sup>-</sup>: Calculated: 625.4; Experimental: 625.3; NMR data: <sup>1</sup>H NMR of C4 (500 MHz, d<sup>6</sup>-DMSO) δ (ppm)= 4.1-4.7 (br, 6H, -CH<sub>2</sub> and -CH), 6.2-7.3 (m, br, 16H, Ar-H), 9.3 and 10.8 ppm (s, 2H, phenolic -OH), and 10.29 (s, 1H,-CH=N).

*pH titration experiment:* For the pH titration experiment for C2 and C4, an aqueous solution of the complexes were prepared (0.25 mM for C2 and 0.5 mM for C4). Then, sufficient amount of 0.1 M NaOH solution was added to the solution to make the pH of the solution ~13. The pH of the solution was measured by a pH meter (Thermo Scientific Orion Star A111). Then, 2  $\mu$ L of 0.1 M HCl was added to the solution with stirring and the pH of the solution was measured until it was stabilized (Figure S18). This last step was repeated until the pH of the solution stopped changing significantly even after the HCl addition.

Bulk electrolysis experiment: The bulk electrolysis experiments of complexes C2, C3 and C4 were performed in a four-neck glass vessel (Volume 150 ml including the headspace) where three of the necks were occupied with a coiled 23 cm Pt wire as counter electrode, Ag/AgCl (in saturated KCl) as a reference electrode, and reticulated vitreous carbon or plastic-chip electrode prepared from graphite powder- and poly(methyl methacrylate)<sup>45</sup> as working electrode, respectively. Last of the necks was closed with a 24/40 rubber septum, which was used for N<sub>2</sub> purging before the experiments and for headspace gas collection (via gas tight leur-lock Hamilton syringe). During the experiment, 75 mL of complexes (0.25 mM C2 or 0.5 mM C4) were added in the vessel, all the electrodes (along with a magnetic bead) were inserted along with rubber septum cap (in gas-tight manner) and the solution was purged with N<sub>2</sub> for 30 minutes. Then, the purging was stopped and the chrono-coulometric experiment was started at corresponding catalytic potentials (-0.8 V vs. SHE for C2 and -1.0 V vs. SHE for C4). The solution was continuously stirred with a magnetic stirrer during the experiment. The headspace gas was collected by a gas-tight leur-lock Hamilton syringe after 4200 s (for C2) and 5500 s (for C4), respectively, and they were analyzed via gas chromatography (GC) instrument (Figure S7 and S10). The GC was calibrated with a control gas mixture (49.5% $H_2$  in  $N_2$ ). Calculation of the current efficiency of C2 and C4 complex is shown in the SI.

*Scanning Electron Microscopy (SEM) and Energy-Dispersive X-ray Spectroscopy (EDS) analysis:* Scanning electron microscopy (SEM) images were obtained using JEOL JSM7600F instrument. The images were obtained at an energy of 5 KeV at a working distance of 8 mm. The plastic-chip electrode prepared from graphite powder- and poly(methyl methacrylate) electrode was used for this experiment prior and after the bulk electrolysis experiment. Energy-dispersive X-

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ray spectroscopy (EDS) spectra is obtained in SEM mode with working distance of 15mm to align the EDS detector, at 15 KeV.

*Spectroelectrochemistry of C4 in aqueous media:* The change in the oxidation states of C4 in aqueous media was investigated via spectroelectrochemical technique. C4 exhibited two distinct reduction signals around -0.09 V and -0.30 V, respectively, at pH4. Chronocoulometric experiments were performed on compound C4 at pH4 buffered solution, where it was reduced electrochemically at -0.25 V and -0.50 V, respectively, over time and the gradual change in its optical spectra was monitored. The electrochemical reductions were performed at a slightly cathodic direction compared to the reduction peak maxima to ensure the complete reduction during chronocoulometry. The same experiment was performed for C4 at pH 2.0 at -0.4 V.

*Rinse Test:* The rinse test of the complex C2 and C4 were performed in acidic aqueous solution (pH 2.0) to figure out the nature of the catalytic  $H_2$  production reaction; i.e. whether it is heterogeneous or homogeneous. For this purpose, we have performed three consecutive runs for each sample. In the first run, a complete scan was recorded for the complex in the pH 2.0 solution, including the cathodic scan, where catalytic  $H_2$  production was observed (Figure S8). Then, the 1 mm diameter glassy carbon disc electrode (working electrode in this case) was thoroughly rinsed with water and polished with 0.25 micron alumina powder to remove any possible heterogeneous species formed on the electrode surface. Afterwards, a second run was performed in the same solution containing the complexes with the cleaned electrode. Here, this second run was stopped at a negative potential, close to the potential where the maximum catalytic  $H_2$  production was observed (Figure S13). Then, the working electrode was only rinsed with water (no polishing with alumina) and third voltammogram was recorded in a fresh acidic aqueous solution (pH 2.0), which did not contain any metal complex. Here the scan was started

at a negative potential, close to the potential where the maximum catalytic  $H_2$  production was observed (Figure S13). As the third run did not exhibit any significant catalytic  $H_2$  production, compared to the first two runs, it can be concluded that the catalytic  $H_2$  production is generated due to homogeneous catalytic pathway.

# Results

Optical and CD spectroscopy: The salen ligands L1-L4 were prepared by reacting salicylaldehyde with benzylamine, L-phenylalanine, tyramine, or L-tyrosine, respectively. The corresponding Co(III)-Salen like complexes (C1-C4) were prepared by separately adding the Co(II) ion to these ligands in the presence of aerial oxygen. All the complexes are soluble in organic solvent N,N'-dimethylformamide (DMF) but only C2 and C4 are soluble in water. The optical spectrum for all the complexes, recorded in DMF, commonly demonstrated three distinct electronic transitions. The strongest absorbance was observed around 270 nm region for the complexes ( $\varepsilon > 10000 \text{ M}^{-1}\text{cm}^{-1}$ ). This can be attributed to  $\pi - \pi^*$  transition from the aromatic moiety (Figure 1, Table S1), which was also observed for the free ligands (Figure S1).<sup>46</sup> Additionally, a broad feature was noticed for all the complexes in 300-450 nm region with moderate molar extinction coefficient values ( $\varepsilon \sim 4000 \text{ M}^{-1}\text{cm}^{-1}$ ) (Figure 1A, Table S1). This band is possibly due to the ligand (N and O lone pairs of the salen) to metal (vacant d orbitals of low spin cobalt (III) (d<sup>6</sup>) center) charge transfer (LMCT).<sup>46</sup> All these complexes also displayed a weak transition around 600-700 nm region ( $\varepsilon < 500 \text{ M}^{-1}\text{cm}^{-1}$ ), which are characteristic of the metal-based *d-d* transitions (Figure 1A (inset), Table S1).<sup>47</sup> These characteristic *d-d* transition bands were blue shifted for C2 and C4 compared to C1 and C3, possibly due to the influence of the COOH groups present in C2 and C4.

 Optical spectra of C2 and C4 were also recorded in aqueous solution with varying pH. Figure 1B exhibits the optical spectra for C4 that was recorded in aqueous solution at pH 2-6 (Table S2). No evident changes were observed in the optical signatures for  $\pi$ - $\pi$ \*, LMCT (Figure 1B) and *d*-*d* transitions (Figure S2) for C4 when the acidity of the solution was gradually changed



**Figure 1. (A)** Optical spectra of complexes C1 (black trace), C2 (red trace), C3 (blue trace), and C4 (green trace) recorded in DMF highlighting the  $\pi$ - $\pi$ \* and LMCT transitions in the UV-visible region. The d-d transitions of the complexes are shown in the inset. **(B)** Comparative optical spectra of C4 in aqueous solution at pH 2 (black trace), pH 3 (red trace), pH 4 (blue trace), pH 5 (green trace), and pH 6 (violet trace). **(C)** The CD spectra of the analogous solutions of C4 exhibiting difference in the negative LMCT band above 300 nm region.

from pH 6 to pH 2. Circular dichroism (CD) spectroscopy was utilized to further probe any pH - dependent spectral variations of C4 in aqueous solution. CD is a common technique for investigating the structural dynamics of optically active molecules.<sup>48,49</sup> In this case, the presence

of optically active L-tyrosine in the coordination sphere of C4 induces chirality into an otherwise achiral Co-salen like core. The CD spectrum of C4 at pH 6 solution displayed a positive band at 305 nm and a broad negative band at 360 nm (Figure 1C), which are presumably originated from the LMCT band, as suggested by the comparative optical spectra (Figure 1B&C). This CD activity confirmed that the Co-salen like core is connected to chiral L-Tyrosine possibly via the amine (via the Schiff base imine) and carboxylate groups. As the pH of the solution was gradually changed to pH 2, the negative CD band at 360 nm blue shifted significantly by 20 nm. C2 also demonstrated analogous alterations in the CD signal originated from the LMCT band around 300-350 nm region below pH 3 (Figure S3). On the other hand, C1 and C3 did not exhibit any detectable signal in CD spectroscopy due to the absence of any chiral component in the ligand structure (Figure S4). This data insinuates a peripheral amino acid induced structural change in the complex C2 and C4 beyond pH 3.

*Electrochemical properties:* Complexes C2 and C4 have exhibited appreciable aqueous solubility for exploring their electrochemical behavior in variable pH conditions in water. As shown in Figure 2A (inset), C4 exhibited two distinct irreversible reduction peaks centered at 0.09 V and -0.37 V at pH 6.0. These peaks can be recognized as stoichiometric Co(III/II) and Co(II/I) reductions as observed for analogous Co-diimine complexes such as Co(dimethylglyoxime)<sub>2</sub>.<sup>50</sup> These stoichiometric metal reduction signals are irreversible in nature



**Figure 2.(A)** Cyclic voltammograms of C4 recorded in aqueous solution at pH 1 (violet trace), pH 2 (orange trace), pH 3 (green trace), pH 4 (magenta trace), pH 5 (blue trace), and pH 6 (red trace). A control blank was recorded at pH 2 (black trace). The inset figure highlights the changes in the stoichiometric signals for C4 with pH. A 1 mm glassy carbon disc electrode, a Pt wire and Ag/AgCl in saturated KCl were used as working, counter, and reference electrodes, respectively, during this experiment. Scan rate during all the CVs were 0.1 V/s.

in aqueous solution. Similar results were also obtained by research groups of Coutsolelos and Delgadillo for cobalt imine complexes in water.<sup>51,52</sup> The Co(II/I) stoichiometric peak started shifting significantly to anodic direction with increasing acidity of the solution, while the position of the Co(III/II) peak fluctuated slightly towards the cathodic direction (Figure 2A inset, Table S3). At pH 2, the Co(III/II) and Co(II/I) peaks merged completely to a single two-electron reduction signal (Figure 2A), and it remained the same at pH 1. The generation of a single step

two electron transfer was also supported by the spectroelectrochemical data. At pH 4, when C4 was reduced at -0.25V (at a potential in between the two stoichiometric reduction signals for C4 at the same condition), it induced a gradual decrease (by ~25%) in the LMCT band at 370 nm, while the band around 300 nm remained the same (Figure S5, Table S2). While, the reduction of C4 at -0.5 V induced further depletion of the optical band at 370 nm (overall  $\sim 66\%$ ) along with a decrease of 300 nm band at the same solution of pH 4 (Figure S5). This data suggests a possible two-step reduction of the Co-N2O2 salen like core in C4 complex, which can be attributed to Co(III/II) and Co(II/I) oxidation state changes. However, the same compound C4 displayed a single reduction peak at -0.2 V in pH 2 solution (Figure S5). The chronocoulometric reduction of the compound at -0.4 V exhibited concurrent decrease in both the 300 nm and 370 nm optical bands (Figure S5). The resultant optical spectrum observed after this single reduction step for C4 at pH 2 solution is analogous to the spectrum recorded for the same compound after two subsequent reduction steps at pH 4. Thus, this data implies a solo-step two electron reduction at pH 2 for C4 complex, which can be attributed to possibly Co(III/I) oxidation state change. The Co(II/I) peak shifted  $\sim$ 30 mV/pH unit in the pH range of 3-6, which plausibly signifies the presence of a proton-coupled electron transfer (PCET) here before the merging it with Co(III/II) signal below pH 3 (Figure S6). Similar pH dependent unification of metal-based stoichiometric signals were observed earlier for Ni(P2N2)2 complexes containing similar peripheral COOH groups.<sup>35</sup> C4 did not exhibit any significant reductive catalytic response that can be attributed to homogeneous  $H_2$  production in aqueous solutions at pH > 3. However, it started displaying catalytic reduction current in water at pH 3 or below (Figure 2A). The onset potential and the potential at which maximum current  $(E_{cat})$  was observed are mentioned in Table S3. The bulk electrolysis data along with complementary gas chromatography (GC) also

suggested that H<sub>2</sub> gas is produced due to this catalytic activity by C4 with > 90% current efficiency (Figure S7-S8, SI). Thus this reductive catalytic response can be attributed to catalytic H<sub>2</sub> production by C4 in acidic aqueous solution. The catalytic H<sub>2</sub> production for C4 improved slightly as the pH of the solution was decreased gradually to pH 1 (Figure 2). An additional catalytic feature was noticed in the CV for C4 around -1.05 V at pH 1.0. This trait can be attributed to H<sub>2</sub> evolution via a different mechanism during the catalytic cycle. Analogous features were observed earlier for Ni-*bis*-(diphosphine) catalysts.<sup>53</sup> C2 also exhibited analogous shift of Co(II/I) signal (~30 mV/pH unit) and ultimate merging of stoichiometric Co(III/II) and Co(II/I) peaks in water with decreasing pH of the solution (Figure S9A-B, Table S4). The catalytic H<sub>2</sub> production signal by C2 was again observed only below pH 3 and the catalytic response was improved appreciably as the acidity of the solution is increased to pH 1 (Figure S9A, Table S4). Corresponding chrono-coulometric and GC experiments corroborated production of H<sub>2</sub> gas during the catalytic reduction with > 90% current efficiency (Figure S8, S10).

The electrochemical study of complexes C1 and C3 were performed in a DMF/water mixture solvent due to their aqueous insolubility. 1% and 2.5% DMF in water solutions were used for the study of C1 and C3, respectively. C1 exhibited only stoichiometric Co(III/II) and Co(II/I) signals without any significant catalytic response for homogeneous  $H_2$  production (Figure S11) even at acidic conditions (pH < 3). The stoichiometric signals for cobalt based reductions for C1 at pH 2.0 remained distinctly separated unlike to the merged cobalt signals for C2 and C4 (Figure S11). This feature possibly highlights the absence of PCET mechanism during electron transfer for C1. However, the stoichiometric Co(III/II) and Co(II/I) signals for C3 were merged at all conditions below pH 5.0 and the stoichiometric peak shifted to cathodic direction by ~65 mV/pH unit

(Figure S12). These observations again suggested that PCET mechanism is involved during the reduction of cobalt center, possibly via the phenolic OH group present in tyramine. C3 also showed significant catalytic response in the cathodic direction beyond -0.9 V at all aqueous solution below pH 6.0 (Figure S12A). The bulk electrolysis study of complex C3 demonstrated reductive charge accumulation with the following increasing order: pH 5 < pH 4 < pH 3 < pH 2 (Figure S8C). The corresponding GC study supported the formation of H<sub>2</sub> gas during the cathodic catalytic step for each of those solutions with > 90% current efficiency. The origin of this  $H_2$  production was probed carefully to exclude the possibility of heterogeneous  $H_2$ production, which was observed earlier for analogous cobalt complexes.<sup>54</sup> Here, the rinse test was performed in pH 2.0 aqueous solution, which exhibited homogeneous catalytic H<sub>2</sub> production for all the complexes (Figure S13, SI). Additionally, scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDS) were performed on the plastic chip electrode before and after the bulk electrolysis experiment for C4 at pH 1.0. The SEM and EDS data clearly demonstrated no deposition of cobalt based materials on the electrode following the electrolysis, supporting the homogeneous nature of the first catalytic H<sub>2</sub> production step (Figure S14). The stability of all the complexes during the catalytic process was also supported by the almost identical comparative optical spectra for the complexes C2-C4 before and after the chrono-coulometric experiments (Figure S15). Another catalytic response was observed for C2-C4 at further cathodic direction following this homogeneous H<sub>2</sub> production step. As illustrated in Figure S14, for C4 exhibited the additional catalytic response at -1.30 V beyond the homogeneous response at -1.0 V. To explore the nature of the additional catalytic feature, analogous rinse test was performed by extending the partial cathodic scan till -1.30 V. Rinse test

 of the unpolished electrode in a blank solution following this run confirmed the heterogeneous nature of this additional catalytic process at -1.30 V(Figure S16).

*Calculating*  $H_2$  *production turn over frequency (TOF) and overpotential:* The catalytic rate ( $k_{obs}$  or *TOF*) for the complexes were calculated by using the following equation (1):

$$\frac{i_{cat}}{i_p} = \frac{n}{0.4463} \left(\frac{RTk_{obs}}{Fv}\right)^{1/2} \quad \text{(Equation 1)}^{55-57}$$

Here  $i_{cat}$  and  $i_p$  are catalytic and stoichiometric current, respectively, n= number of electrons involved in this process, R = universal gas constant, T = temperature in degree K, F = 1 Faraday, and v = scan rate. On the other hand, the overpotential requirement of the catalyst was calculated as the difference between the potential of half maxima catalytic response ( $E_{\text{cat/2}}$ ) and equilibrium potential for H<sup>+</sup>/0.5 H<sub>2</sub> couple ( $E_{H^+/0.5H2}$ ) at a particular pH condition vs. SHE. The potential at which the catalytic H<sub>2</sub> evolution reaction (HER) wave started to shift significantly from the background current was determined as the onset potential. The calculation showed that C4 produces H<sub>2</sub> in aqueous solution at a rate of 178 s<sup>-1</sup> with an overpotential requirement of 780 mV at pH 3.0 (Table 1). The rate improved further in acidic solutions to 190 s<sup>-1</sup> (pH 2.0) and 277 s<sup>-1</sup> (pH 1.0), respectively, while the overpotential requirement gradually increased to 840 mV at pH 1.0 (Table 1). Analogously, C2 also displayed catalytic  $H_2$  production activity only below pH 4.0. The catalytic rates for H<sub>2</sub> production for C2 were similar to C4; however, the overpotential requirement was reduced significantly (by  $\sim 200 \text{ mV}$ ) (Table 1). However, the complex was unstable at pH 1.0, and the maximum catalytic response for C3 was recorded at pH 2.0, where it produces H<sub>2</sub> at a rate of ~ 160 s<sup>-1</sup> with an overpotential requirement of ~780 mV (Table 1).

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**Table 1.** Overpotential requirement (OP) and catalytic HER turnover frequencies (TOFs) of complexes C2, C3, and C4 in aqueous medium. All the TOFs are calculated at 1V/s.

nH	C	2	C34	1	C4			
pm	<b>TOF</b> (s <sup>-1</sup> )	OP (mV)	<b>TOF</b> (s <sup>-1</sup> )	OP (mV)	TOF(s <sup>-1</sup> )	OP (mV)		
1	255 (±11.01) <sup>b</sup>	670 (± 5)	unstable	unstable	277 (±23.5)	840 (± 5)		
2	190 (±10)	565 (± 5)	160 (±16.5)	780 (± 5)	190 (± 2.1)	775 (± 5)		
3	170 (± 20)	580 (± 5)	140 (± 5)	720 (± 5)	178 (±11.9)	780 (± 5)		
4	n.d. <sup>c</sup>	n.d.	126 (± 5.3)	680 (± 5)	n.d.	n.d.		
5	n.d.	n.d.	110 (± 5.6)	660 (± 5)	n.d.	n.d.		

<sup>a</sup>Recorded in 2.5% DMF in aqueous buffer mixture

<sup>b</sup>The error range is calculated from 3 independent runs for each sample

*<sup>c</sup>n.d.*: not detected

*NMR Spectroscopy:* Detailed <sup>1</sup>H NMR and two dimensional NMR spectroscopy was performed

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on the ligands (L3-L4) and complexes (C3-C4) to explore the role of the peripheral basic

functionalities on the overall proton trafficking around the complex. The comparative <sup>1</sup>H NMR data (recorded in d<sup>6</sup>-DMSO containing minute amount of water) of L4 and C4, clearly exhibited a significant change of phenolic –OH proton upon cobalt binding (Figure S17A). In the ligand stage, the phenolic –OH was broad in nature ( $\delta \sim 14.5$  ppm), which was transformed into two



**Figure 3.** (**A**) The NOESY spectra of C4 and (**B**) C3 in d<sup>6</sup>-DMSO at room temperature, recorded with 0.3 s mixing time. The cross peaks are connected by the dotted black line.

sharp signals (at  $\delta \sim 11.0$  and  $\delta \sim 9.3$  ppm) in the complex C4 (Figure S17A). The sharpening of the exchangeable phenolic –OH group in C4 suggests the possible involvement of the tyrosine side chain in robust hydrogen bonding network once the cobalt compound is formed. Similar changes in phenolic-OH proton NMR signals were also observed by Gerothanassis et al.<sup>58</sup> The two signals of phenolic –OH in C4 can be presumably attributed to the formation of transstructure of C4. Analogous changes in phenolic –OH <sup>1</sup>H NMR signal was also observed for the tyramine containing L3 and C3 compounds (Figure S17B). The two dimensional Nuclear Overhauser Effect Spectroscopy (NOESY) was also performed for complexes C3 and C4 in the same d<sup>6</sup>-DMSO to further explore the exchange properties of the phenolic –OH groups at room temperature. The NOESY data for C4 clearly demonstrated exchange of protons between the phenolic –OH groups and solvent water molecules. The two different phenolic –OH groups also

swapped protons among themselves that was evident from the appearance of cross peaks at 11.0 and 9.3 ppm (Figure 3A). Analogous cross peaks were observed for C3 at 9.5, 8.0, and 3.3 ppm, which signify the exchange of protons between the variable phenolic-OH groups and solvent water, respectively (Figure 3B). These results highlight the crucial role of phenolic –OH groups in the proton exchange phenomenon and possible formation of hydrogen bonding network around the complexes in presence of solvent water molecules.

#### Discussion

Here in this work, we have developed a series of complexes containing identical Co-salen like core with varying peripheral functionalities. The electrochemical experiments showed that incorporation of peripheral basic functionalities such as -COOH and/or phenolic -OH groups can induce catalytic H<sub>2</sub> production reactivity for the otherwise inactive Co-salen like core complexes in acidic aqueous solution. Complexes C2 and C4 exhibited catalytic H<sub>2</sub> production only below pH 4.0. This observation indicates to the plausible vital role of the -COOH group in the catalysis as the  $pK_a$  of carboxylic acid groups are generally documented in that range under analogous conditions.<sup>59</sup> The pH titration experiment with both C2 and C4 in aqueous solution revealed that both these complexes indeed have a  $pK_a \sim 4$ , possibly due to the -COOH functionality existing in the periphery (Figure S18). C4 also exhibited an additional  $pK_a \sim 11.2$ , presumably due to the presence of phenolic -OH functionality.<sup>59</sup> Interestingly, both these complexes showed an additional  $pK_a \sim 7$ , which is characteristic to the metal bound water molecule (Figure S18).<sup>60</sup> Thus, the pH switch around 4.0 can be attributed to the altered interaction between the cobalt core and the ligand moiety connected via -COOH group. This change in metal coordination was also monitored through the CD spectroscopy for C2 and C4. Both these complexes contained chiral amino acid based ligands that can induce chirality in the

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spectra (Figure 1C and S3B) demonstrated that the stark change in the metal-ligand interaction

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occurs only around pH 3, suggesting the crucial role of only carboxylic acid moiety in this pH

switch. The -COOH group coordination to metal is expected to be different in its protonated (-

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COO<sup>-</sup> group possibly binds directly as an axial ligand to the cobalt center above pH 4.0 in

aqueous solution. This strong axial bonding of COO<sup>-</sup> group to the cobalt center would close

down the catalytic cycle as the possible binding site of proton will be occupied (Figure 4). However, once the pH of the solution is switched below 4.0, the COO<sup>-</sup> gets protonated to -COOH. At this condition, the proton is expected to bind the basic cobalt(I) center outcompeting the relatively weaker  $\sigma$ -donor ligand -COOH. Additionally, the protonated COOH will act as a proton donor to the metal site to elevate the H<sub>2</sub> production catalysis. Interestingly, the pHswitchable catalysis was not observed for C3 that contains only phenolic –OH as basic functionality in the periphery. As the phenolic OH group has  $pK_a \sim 11.2$  (Figure S18), it is expected to be active for proton channeling to cobalt center even from neutral condition. This hypothesis deemed valid from the observation of catalytic H<sub>2</sub> production by C3 even from pH 5.0 (Figure S8 and S12). Thus, this pH-activated change between the primarily coordinating –



**Figure 4.** *pH switchable HER catalysis:* Changing the pH of the aqueous solution below 4.0 protonates the  $-COO^{-}$  group to -COOH functionality and activates the Co-salen core, present in C2 and C4 complexes, for hydrogen evolution reaction (HER) catalysis. The orange bubbles represent H<sub>2</sub> gas.

COO<sup>-</sup> group and the peripheral proton donating but non-coordinating COOH group tunes the pH–switchable H<sub>2</sub> production catalysis observed for C2 and C4 complexes.

The crucial role of the COOH group during the proton exchange is also supported by the PCET induced merging of the cobalt centered stoichiometric redox signals of Co(III/II) and Co(II/I), for both C2 and C4 complexes. Remarkably, this blending of the two different stoichiometric signals to a single two electron step occurred for C2 and C4, only below pH 4. Compound C3 comprises of only peripheral phenolic OH group around the Co-salen like core. Analogous merging of stoichiometric peaks was also detected for C3, however, at relatively higher pH compared to C2 and C4 complexes. This observation clearly indicates the influence of the outer coordination sphere basic functionalities on the redox properties of the metal active center.<sup>35</sup>

The existence of H<sub>2</sub> production activity for complexes C2, C3, and C4 also corroborates the effect of the peripheral basic functionalities on the catalytic activity of Co-salen like core, which is possibly regulated by the facile proton movement. In the case of C3, the proton conduit around the metal core is possibly generated by the phenolic –OH functionality in presence of water molecules. The <sup>1</sup>H NMR data and NOESY spectra of C3 indicate the possible existence of an active proton exchange network in the presence of phenolic –OH groups in the outer coordination sphere, where a rapid proton trafficking is possible via the Grotthuss mechanism (Figure S19).<sup>61,62</sup> Recently Savéant also highlighted the crucial role of proton relay channels on the elevated catalytic performance via amplified proton concentration in "the key-catalytic reactions".<sup>63</sup> During the catalysis, the reduced Co-salen like core possibly generates the cobalt-hydride species, a key intermediate for the H<sub>2</sub> production catalytic cycle.<sup>64</sup> The attempts of capturing the hydride species were unsuccessful in aqueous media. However, in d<sup>6</sup>-DMSO

solution, C4 exhibited the hydride signal in <sup>1</sup>H NMR spectroscopy at -2.8 ppm only in the presence of minute amount of water (Figure S20). The generation of the hydride species as an intermediate supports the existence of a  $H_2$  production catalytic cycle that is possibly influenced by the solvent water and the outer coordination sphere basic functionalities. The hydride peak disappeared after addition of 1 equivalent of trifluoroacetic acid (TFA) to the same C4 solution, indicating its exchangeable nature (Figure S20).

The relative catalytic H<sub>2</sub> production rate observed for the complexes were in the following order:  $C4 \sim C2 > C3$  (Table 1). This observation points out the differential effect of the basic functionalities (COOH and phenolic OH) on the reactivity of Co-Salen like core. It is evident from the results (Table 1) that the COOH group acts as a superior proton conduit during the catalysis as C2 exhibited better H<sub>2</sub> production rate than C3. The pH-switchable H<sub>2</sub> production for complexes C2 and C4, highlights that the catalytic activity is primarily controlled by -COOH group, even in the presence of phenolic OH functionality for these complexes. The cobalt based stoichiometric reductions (i.e. Co(III/II) and Co(II/I)) occurred at relatively anodic (positive) direction for C4 compared to C2 (Table S3 and S4), implying thermodynamically facile electron transfer to cobalt center in case of C4 in comparison to C2. However, the overpotential requirement for HER catalysis demonstrated the opposite trend and it was found that C4 requires  $\sim 200$  mV higher overpotential for the catalysis than C2 (Table 1). This feature may be attributed to the presence of peripheral phenolic -OH group in C4, which possibly creates a robust hydrogen-bonding network alongside the carboxylate/carboxylic acid group in presence of the solvent water molecules. This interaction will reduce the electron donor ability of -COO<sup>-</sup>/COOH towards Co-salen like core in C4 compared to C2. As a result, the reduction of the cobalt center will be thermodynamically easier for C4 compared to C2, which will be reflected with positively

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shifted stoichiometric reduction potentials. At the same time, this intricate hydrogen bonding will also stabilize the protons and may generate a larger energy barrier for proton shuttling during catalysis for C4. As a consequence the  $H_2$  production activity should require higher overpotential for C4 compared to C2.

# Conclusion

In this work, we have incorporated variable peripheral functionalities around a common Cosalen like core and probed the electrochemical behavior of the complexes in aqueous solution. The presence of basic functionalities (COOH and phenolic OH groups) in the fringe of the metallocenter has enabled catalytic homogeneous H<sub>2</sub> production for otherwise inactive Co-salen like complex. The COOH functionality plays a dual role as it can act an axial ligand in its basic form (COO<sup>-</sup>) when the pH of the solution is higher than the  $pK_a$  of the group (~4.0). At this situation, the COO<sup>-</sup> blocks the protons from accessing the reduced cobalt center to shut down catalytic H<sub>2</sub> production cycle. However, at pH below 4.0, the protonated COOH behaves as a relatively poor axial ligand and allows the proton to bind the electron rich reduced cobalt center to trigger the catalytic H<sub>2</sub> production. Here, the COOH group also acts as a proton conduit to improve the proton reduction activity by the Co-salen like complex. The phenolic OH group itself can also act as a peripheral basic functionality to play the role of a proton supplier to generate H<sub>2</sub> production; however, its influence is inferior compared to COOH group, as suggested by the faster H<sub>2</sub> production by C2 compared to C3 complex. When both the COOH and phenolic-OH group are present in the periphery, even then, COOH group outmanoeuvres phenolic OH group to regulate the activity as observed in the case of complex C4, as it is evident from the pH switchable catalytic activity for C4. The NMR studies suggested that the basic functionalities possibly generate an intricate hydrogen bonding network around the metal center

in the aqueous solution, which crucially controls the  $H_2$  production reaction efficiency, in terms of both the rate and overpotential requirements. Thus, here, we have activated an otherwise dormant Co-salen like core for homogeneous  $H_2$  production by strategic inclusion of basic peripheral functionalities, which can be triggered by pH modulation. This study showcases the prospects of inclusion of outer coordination sphere functionalities during catalysts design, which can pave the leeway for developing efficient catalysts for other small molecule activation reactions involving proton transfer steps.

#### ASSOCIATED CONTENT

#### Supporting Information.

The optical spectra of the complexes recorded in DMF, optical spectra of C4 in visible region in water at variable pH; pH titration data for C2 and C4 in water; comparative optical and CD spectra of C2 at variable pH in water; spectroelectrochemical data for C4 at variable pH in water; chronocoulometric and GC data for C2 and C4 in water; cyclic voltammetry data for C1, C2, C3 and C4 in aqueous or aqueous/ DMF-water mixture solution; rinse test results for C2, C3, and C4 in water; extended rinse test for C4 in water; comparative <sup>1</sup>H NMR data of L3, C3 and L4, C4 in d<sup>6</sup>-DMSO; SEM and EDS data for the working electrode before and after the bulk H<sub>2</sub> production; corresponding optical spectral data for C3; hydride NMR signal for C4 in in d<sup>6</sup>-DMSO; optical absorbance data in table of C1-C4 in DMF; optical absorbance data in table of C2 and C4 at variable pH in water is provided in the supporting information (PDF file format).

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# Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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# **ABBREVIATIONS**

CD: Circular Dichroism

DMF: N, N'- Dimethyl Formamide

EDS: Energy-dispersive X-ray spectroscopy

GC: Gas Chromatography

HER: Hydrogen Evolution Reaction

- LMCT: Ligand to Metal Charge Transfer
- NOESY: Nuclear Overhauser Effect Spectroscopy
- SHE: Standard Hydrogen Electrode
- SEM: Scanning Electron Microscopy
- TOF: Turn Over Frequency
- TFA: Trifluoroacetic acid

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# **TOC figure**

