

Acid-functionalized dissymmetric salen ligands and their manganese(III) complexes[☆]

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Abstract—Acid-functionalized symmetric and dissymmetric salen-type ligands were synthesized via a novel self-protection step in a quantitative yield. This synthetic method allows one to quickly prepare salen-based dissymmetric chiral compounds with tailorable coordinating properties. Therefore, this approach provides a blueprint for synthesizing and evaluating a new class of acid-functionalized salen ligands that can be used as chiral building blocks for a wide range of catalysts and coordination polymers with chemically tailorable properties.

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Salen ligands are important components of many types of catalysts, metal–organic-frameworks (MOFs), and coordination polymers.^{1–6} MOFs, in particular, have been the focus of many recent studies due to their encapsulating properties and potential applications in magnetism, catalysis, sensing, mixture separations, molecular electronics, and small molecule transport.^{7–10} MOFs have been made from a combination of many types of metal ions and polyfunctional ligands, and the salen ligand has been the focus of several researchers in this field because of its utility in catalysis. In this regard, pyridine functionalized salens have been the building block of choice, primarily because of the ease in which one can prepare such ligands.⁴

Acid-functionalized salens are also outstanding targets as building blocks for MOF structures because of the wealth of inorganic coordination chemistry that takes advantage of the carboxylate moiety. However, at present, there are no methods for preparing such ligands. In this regard, both symmetrically and dissymmetrically functionalized ligands are desirable. The desymmetrization of the salen core would create the possibility for a

greater structural variation in the resulting catalysts and infinite coordination polymers, allow for the systematic optimization of both the steric and electronic properties of the ligand, and create better ways of controlling polymerization in the context of the infinite coordination polymer structures (different functionality allows one to use different metals in the polymerization process). Indeed, it has been reported that metal complexes derived from unsymmetrical salen ligands sometimes exhibit better enantioselectivities when compared with their symmetric counterparts.^{11,12} Herein we report the first general synthetic approach for the preparation of acid-functionalized symmetric and dissymmetric salen ligands via self-protected intermediates. Note that this method does not need deliberate and time consuming protection or deprotection steps for the synthesis of the dissymmetric salen ligands as do previous stepwise approaches.^{13,14} These ligands can be easily metalated with Mn(III) in the salen core to form precursors that have the appropriate peripheral functionality for metal coordination driven polymerization (not studied in this manuscript).

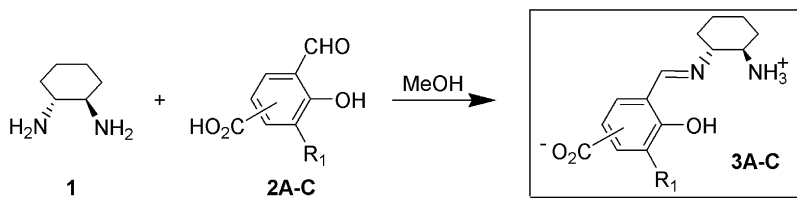
Our strategy takes advantage of the condensation of (1*R*,2*R*)-(–)-1,2-diaminocyclohexane **1** with acid-functionalized salicylaldehyde **2A–C** to form the self-protected zwitterionic intermediates **3A–C** (Scheme 1).¹⁵ Compounds **3A–C** precipitate during the reaction, allowing one to easily isolate these intermediates in near quantitative yields. The precipitates were collected by

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Scheme 1. Synthesis of self-protected zwitterionic intermediates.

Table 1. Zwitterionic intermediates and their spectroscopic and analytical characterization data

Ligand precursor	Intermediate (Yield)	Analytical data
 2A	 3A (95%)	$^1\text{H NMR}$ ($\text{CD}_3\text{OD}/\text{K}_2\text{CO}_3$): δ 1.15–1.33 (br m, 4H, $-\text{CH}_2-$), 1.40 (s, 9H, $-\text{C}(\text{CH}_3)_3$), 1.46–1.88 (br m, 4H, $-\text{CH}_2-$), 2.66 (m, 1H, $-\text{CH}-$), 2.88 (m, 1H, $-\text{CH}-$), 7.48 (s, 1H, Ar-H), 7.51 (s, 1H, Ar-H), 7.54 (d, 2H, Ar-H), 7.88 (d, 2H, Ar-H), 8.55 (s, 1H, $-\text{CH}=\text{N}-$). MS (ESI, m/z): $\text{M}^+ = 394.05$ (Calcd for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_3 = 394.23$). Elemental Anal. Calcd for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_3$ CH ₃ OH: C, 71.68; H, 7.86; N, 6.82. Found: C, 71.31; H, 7.60; N, 6.87
 2B	 3B (98%)	$^1\text{H NMR}$ ($\text{CD}_3\text{OD}/\text{K}_2\text{CO}_3$): δ 1.18–1.41 (br m, 8H, $-\text{CH}_2-$), 2.99 (m, 2H, $-\text{CH}-$), 6.78 (d, 1H, Ar-H), 7.96 (d, 1H, Ar-H), 8.47 (s, 1H, Ar-H), 9.02 (s, 1H, $-\text{CH}=\text{N}-$). MS (ESI, m/z): $(\text{M}+\text{H})^+ = 263.45$ (Calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_3 = 263.14$). Elemental Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3 \cdot 1/3\text{H}_2\text{O}$: C, 62.67; H, 7.01; N, 10.44. Found: C, 62.89; H, 6.74; N, 10.14
 2C	 3C (77%)	$^1\text{H NMR}$ ($\text{DMSO}-d_6$): δ 1.30–1.73 (br m, 8H, $-\text{CH}_2-$), 2.93 (m, 1H, $-\text{CH}-$), 3.06 (m, 1H, $-\text{CH}-$), 7.27 (s, 1H, Ar-H), 7.31 (d, 1H, Ar-H), 7.36 (s, 1H, Ar-H), 8.55 (s, 1H, $-\text{CH}=\text{N}-$). MS (ESI, m/z): $(\text{M}+\text{H})^+ = 263.71$ (Calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_3 = 263.14$). Elemental Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 63.89; H, 6.66; N, 10.49

filtration and washed with hot methanol ($\sim 50^\circ\text{C}$), which in all cases gave analytically pure compounds (Table 1).

The formation of the self-protected zwitterionic intermediate **3C** was confirmed by a single crystal X-ray diffraction study (Fig. 1). Single crystals of **3C** suitable

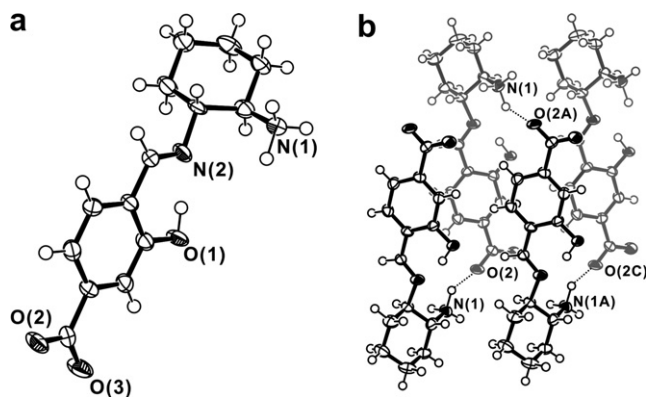
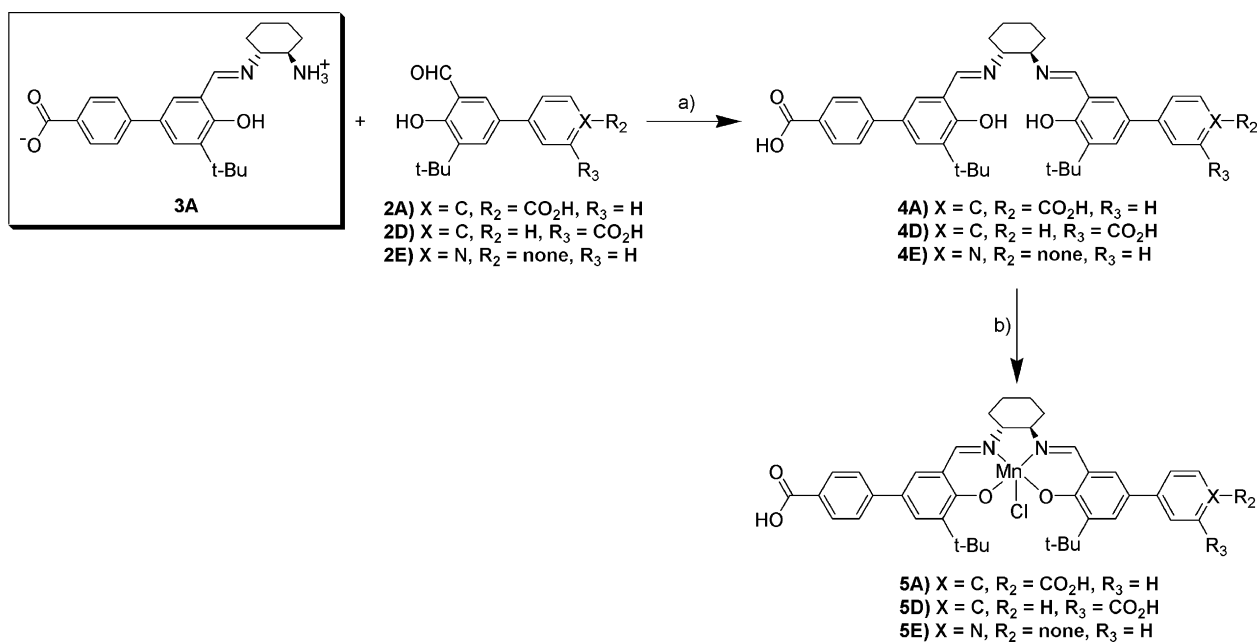


Figure 1. X-ray crystal structure of **3C** with thermal ellipsoids shown at 70% probability (two water molecules have been omitted for clarity): (a) asymmetric unit and (b) hydrogen-bonding scheme.

for X-ray analysis were taken directly from the precipitate. The solid-state structure is consistent with the proposed solution structure (Fig. 1a).¹⁶ As shown in Figure 1b, compound **3C** is zwitterionic and one hydrogen atom of the amine moiety exhibits a $\text{H}\cdots\text{O}$ distance (1.96 Å) consistent with a strong hydrogen bonding with the carboxylate ion of an adjacent molecule ($\text{N}\cdots\text{O} = 2.74$ Å). This results in the formation of a loosely coordinated one-dimensional helical polymer. The other two hydrogen atoms on the amine also exhibit $\text{H}\cdots\text{O}$ distances that are consistent with hydrogen bonds with two water molecules ($\text{N}\cdots\text{O}_{\text{avg}} = 2.78$ Å) included in the crystal (not shown).

The desired symmetric or dissymmetric salen-type ligand **4A–E** can be obtained by reacting one of the mono-substituted zwitterionic intermediate **3A–C** with an equivalent of a second salicylaldehyde **2A–E** in refluxing pyridine, respectively (Scheme 2).¹⁷ After a few min, the turbid reaction mixture became a clear yellow solution. Note that pyridine in this reaction is used both as a solvent and as a base. In all cases, the analytically pure product **4A–E** was isolated in a near quantitative yield by a simple evaporation of the solvent after the reaction (Table 2). The acid-functionalized symmet-



Scheme 2. Reagents and conditions: (a) pyridine, reflux; (b) Mn(OAc)₂·4H₂O, pyridine or EtOH, reflux; LiCl, air, reflux.

Table 2. Acid-functionalized salen ligands and their precursors

Intermediate	Aldehyde	Product	Yield (%)
3A	 2A	 4A	94
3B	 2E	 4B	99
3C	 2E	 4C	99
3D	 2D	 4D	91
3E	 2E	 4E	96

rical salen ligand **4A** can be synthesized alternatively by the reaction of (1*R*,2*R*)-(–)-1,2-diaminocyclohexane **1** with 2 equiv of 4-(3-hydroformyl-4-hydroxy-5-*t*-butylphenyl)benzoic acid **2A** in refluxing pyridine. Finally, the resulting salen-type ligands **4A–E** with acid functional groups can be metalated easily with Mn(OAc)₂/LiCl in air to form complexes **5A–E** using a literature procedure analogous to those used to synthesize (*R,R*)-(–)-1,2-cyclohexanediamine-*N,N'*-bis(3-*tert*-butyl-5-(4-pyridyl)salicylidene)Mn^{III}Cl (Scheme 2).^{4,18}

This work demonstrates that one can synthesize acid-functionalized symmetric and dissymmetric salen-type ligands via a novel self-protection step in a quantitative yield. This synthetic method allows one to quickly prepare salen-based dissymmetric chiral compounds with tailorable coordinating properties. Therefore, this approach provides a blueprint for synthesizing and evaluating a new class of acid-functionalized salen ligands that can be used as chiral building blocks for a wide range of MOFs with potentially tailorable asymmetric catalytic activity.

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- A mixture of (1*R*,2*R*)-(–)-1,2-diaminocyclohexane **1** (0.16 g, 1.37 mmol) and 4-(3-hydroformyl-4-hydroxy-5-*t*-butylphenyl)benzoic acid **2A** (0.40 g, 1.34 mmol) in methanol (50 mL) was heated to reflux for 1 h. The resulting precipitate was filtered and washed with hot methanol (~50 °C, 3 × 10 mL) and dried under vacuum to give a pale yellow solid **3A** (0.51 g, 95%).
- Selected X-ray crystallographic data of **3C**: C₁₄H₂₂N₂O₅, monoclinic, space group C2, *a* = 21.208(5) Å, *b* = 5.9408(13) Å, *c* = 12.526(3) Å, *β* = 105.933(4)°, *V* = 1517.5(6) Å³, *Z* = 4. A colorless plate type crystal was used to measure 6922 reflections at *T* = 153 K, of which 3481 were unique (*R*_{int} = 0.1131). Refinement proceeded to *wR*₂ = 0.1227 (all data), *R*₁ = 0.0561 and GOF = 0.808 [*I* > 2σ(*I*)]. Maximum residual electron density was 0.234 e Å⁻³. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as the supplementary publication number CCDC-623453. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
- A slurry of **3A** (0.31 g, 0.79 mmol) and 5-(4-pyridyl)salicylaldehyde **2E** (0.20 g, 0.79 mmol) in pyridine (20 mL) was heated to reflux for 1 h, which gave a clear yellow solution. The solvent was removed under reduced pressure and the resulting solid was sonicated with ether (10 mL). The solvent was evaporated and dried under vacuum to give an analytically pure yellow solid **4E** (0.48 g, 96%). Analytical data for compounds **4A–E** are as follows: Compound **4A**: ¹H NMR (DMSO-*d*₆): δ 1.34 (s, 9H, –C(CH₃)₃), 1.42–1.99 (br m, 4H, –CH₂–), 3.46 (br s, 1H, –CH–), 7.48 (s, 1H, Ar-*H*), 7.51 (s, 1H, Ar-*H*), 7.60 (d, 2H, Ar-*H*), 7.93 (d, 2H, Ar-*H*), 8.57 (s, 1H, –CH=N–), 12.89 (br s, 1H, –CO₂H), 14.41 (br s, 1H, –OH). HRMS (EI, *m/z*) M⁺ = 673.3341 (Calcd for C₄₂H₄₆N₂O₆ = 674.3356). Elemental Anal. Calcd for C₄₂H₄₆N₂O₆: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.39; H, 6.81; N, 4.15. Compound **4B**: ¹H NMR (pyridine-*d*₅): δ 1.55 (d, 9H, –C(CH₃)₃), 1.38–1.95 (br m, 8H, –CH₂–), 3.41 (br m, 2H, –CH–), 7.11 (d, 1H, Ar-*H*), 7.54 (m, 3H, Ar-*H*), 7.69 (m, 1H, Ar-*H*), 8.30 (m, 1H, Ar-*H*), 8.40 (dd, 1H, Ar-*H*), 8.59 (s, 1H, –CH=N–), 8.60 (s, 1H, –CH=N–), 8.79 (d, 1H, Ar-*H*), 8.82 (d, 1H, Ar-*H*), 14.40 (br s, 1H, –CO₂H), 14.79 (s, 1H, –OH), 14.82 (s, 1H, –OH). MS (ESI, *m/z*): [M–H][–] = 498.64 (Calcd for C₃₀H₃₂N₃O₄ = 498.24). Elemental Anal. Calcd for C₃₀H₃₃N₃O₄·1/4H₂O: C, 71.48; H, 6.70; N, 8.34. Found: C, 71.42; H, 6.54; N, 8.78. Compound **4C**: ¹H NMR (pyridine-*d*₅): δ 1.57 (s, 9H, –C(CH₃)₃), 1.37–1.88 (br m, 8H, –CH₂–), 3.40 (br m, 2H, –CH–), 7.41 (d, 1H, Ar-*H*), 7.52 (dd, 2H, Ar-*H*), 7.59 (d, 1H, Ar-*H*), 7.71 (d, 1H, Ar-*H*), 7.86 (d, 1H, Ar-*H*), 8.11 (s, 1H, Ar-*H*), 8.55 (s, 1H, –CH=N–), 8.59 (s, 1H, –CH=N–), 8.78 (dd, 2H, Ar-*H*), 13.79 (br s, 1H, –CO₂H), 14.80 (br s, 1H, –OH). MS (ESI, *m/z*): [M–H][–] = 498.41 (Calcd for C₃₀H₃₂N₃O₄ = 498.24). Elemental Anal. Calcd for C₃₀H₃₃N₃O₄·1/4H₂O: C, 71.48; H, 6.70; N, 8.34. Found: C, 71.45; H, 6.67; N, 8.41. Compound **4D**: ¹H NMR (DMSO-*d*₆): δ 1.33 (s, 18H, –C(CH₃)₃), 1.67–1.95 (br m, 8H, –CH₂–), 3.42 (br s, 2H, –CH–), 7.36–8.04 (m, 10H, Ar-*H*), 8.54 (br m, 2H, –CH=N–, 2H, Ar-*H*), 12.99 (br s, 2H, –CO₂H), 14.36 (br s, 2H, –OH). HRMS (EI, *m/z*) M⁺ = 673.3356 (Calcd for C₄₂H₄₆N₂O₆ = 674.3356). Elemental Anal. Calcd for C₄₂H₄₆N₂O₆: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.37; H, 6.81; N, 4.56. Compound **4E**: ¹H NMR (DMSO-*d*₆): δ 1.32 (s, 18H, –C(CH₃)₃), 1.66–1.94 (br m, 8H, –CH₂–), 3.35 (br m, 2H, –CH–), 7.48–7.60 (br m, 8H, Ar-*H*), 7.94 (br d, 2H, Ar-*H*), 8.51 (br m, 2H, –CH=N–, 2H, Ar-*H*), 12.95 (br s, 1H, –CO₂H), 14.38 (br s, 1H, –OH), 14.51 (br s, 1H, –OH). HRMS (EI, *m/z*): M⁺ = 631.3414 (Calcd for C₄₀H₄₅N₃O₄ = 631.3410). Elemental Anal. Calcd for C₄₀H₄₅N₃O₄·1/2H₂O: C, 74.97; H, 7.24; N, 6.56. Found: C, 74.82; H, 7.00; N, 6.516.
- The free base ligand **4E** (0.20 g, 0.31 mmol) and Mn(OAc)₂·4H₂O (0.086 g, 0.35 mmol) were combined with absolute EtOH (50 mL) and heated to reflux for 2 h under N₂ atmosphere. LiCl (0.041 g, 0.97 mmol) was then added and the resulting solution was refluxed for an additional hour in air before being cooled to room temperature. The solvent was removed under reduced

pressure, after which the precipitate was sonicated with water (20 mL). Product **5E** was isolated by filtration and dried under vacuum (0.21 g, 93%). Analytical data for compounds **5A–E** are as follows: Compound **5A**: IR (KBr pellet, cm^{-1}): 575 (w), 757 (w), 780 (w), 1174 (w), 1255 (m), 1313 (m), 1342 (m), 1384 (m), 1537 (m), 1603 (s), 1693 (w), 2951 (w). MS (ESI, m/z): $[\text{M}-\text{Cl}]^+ = 727.99$ (Calcd for $\text{C}_{42}\text{H}_{44}\text{MnN}_2\text{O}_6 = 727.26$). Elemental Anal. Calcd for $\text{C}_{42}\text{H}_{44}\text{ClMnN}_2\text{O}_6$: C, 66.10; H, 5.81; N, 3.67. Found: C, 66.41; H, 5.92; N, 3.77. Compound **5B**: IR (KBr pellet, cm^{-1}): 573 (w), 637 (w), 656 (w), 818(w), 1175 (w), 1274 (s), 1308 (s), 1343 (m), 1382 (m), 1437 (w), 1553 (m), 1598 (vs), 1944 (w). MS (ESI, m/z): $[\text{M}-\text{Cl}]^+ = 552.76$ (Calcd for $\text{C}_{30}\text{H}_{31}\text{MnN}_3\text{O}_4 = 552.52$). Elemental Anal. Calcd for $\text{C}_{30}\text{H}_{31}\text{ClMnN}_3\text{O}_4\text{Cl}\cdot 1/4\text{H}_2\text{O}$: C, 61.28; H, 5.31; N, 7.15. Found: C, 60.85; H, 5.31; N, 7.04. Compound **5C**: IR

(KBr pellet, cm^{-1}): 573 (w), 635 (w), 820 (w), 1272 (m), 1315 (w), 1344 (m), 1386 (s), 1423 (w), 1436 (w), 1553 (s), 1596 (vs), 2944 (w). MS (ESI, m/z): $[\text{M}-\text{Cl}]^+ = 552.83$ (Calcd for $\text{C}_{30}\text{H}_{31}\text{MnN}_3\text{O}_4 = 552.52$). Elemental Anal. Calcd for $\text{C}_{30}\text{H}_{31}\text{MnN}_3\text{O}_4\text{Cl}$: C, 65.21; H, 5.66; N, 7.61. Found: C, 65.53; H, 5.88; N, 7.72. Compound **5D**: IR (KBr pellet, cm^{-1}): 576 (w), 637 (w), 771 (w), 1269 (m), 1341 (m), 1310 (m), 1341 (m), 1390 (m), 1538 (m), 1611 (s), 1700 (w), 2949 (w). MS (ESI, m/z): $[\text{M}-\text{Cl}-\text{H}]^- = 726.07$ (Calcd for $\text{C}_{42}\text{H}_{43}\text{MnN}_2\text{O}_6 = 726.25$). Elemental Anal. Calcd for $\text{C}_{42}\text{H}_{44}\text{ClMnN}_2\text{O}_6$: C, 66.10; H, 5.81; N, 3.67. Found: C, 66.45; H, 6.08; N, 3.66. Compound **5E**: MS (ESI, m/z) = 719.37 (Calcd for $\text{C}_{40}\text{H}_{43}\text{ClMnN}_3\text{O}_4 = 719.23$). Elemental Anal. Calcd for $\text{C}_{40}\text{H}_{43}\text{ClMnN}_3\text{O}_4\cdot\text{H}_2\text{O}$: C, 65.08; H, 6.14; N, 5.69. Found: C, 65.26; H, 6.50; N, 5.73.