Electronic Supplementary Material (ESI) for Faraday Discussions.

Supporting Information for

Site-selective methylene C-H oxidation of an alkyl diamine enabled by supramolecular recognition using a bioinspired manganese catalyst

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1. Materials and Methods

1.1. Materials

Reagents and solvents used were of commercially available reagent quality unless stated otherwise. Solvents were purchased from SDS, Aldrich, Scharlab and Fluorochem. Sigma-Aldrich HPLC-grade acetonitrile was employed for oxidation reactions.

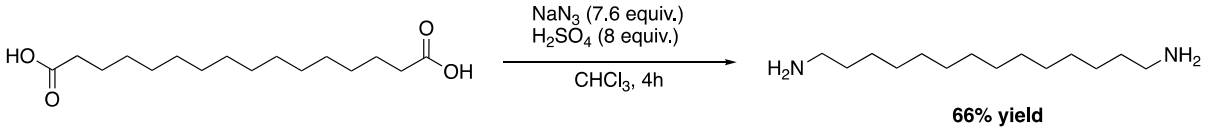
1.2. Instrumentation

^{1}H-NMR and ^{13}C-NMR were performed with a Bruker Ultrashield ASCEND Nanobay spectrometer. NMR titrations and NOESY experiments were performed with a Bruker Ultrashield ADVANCE III400. Spectra were referenced to the residual solvent peaks. Mass spectrometry was performed by electrospray ionization in a Bruker Esquire 6000 Ion trap mass spectrometer using acetonitrile as mobile phase. Samples were introduced into the mass spectrometer ion source by direct infusion through a syringe pump. Chromatographic analysis of the reaction was performed on an Agilent GC-7820-A (Agilent HP-5) column and a flame ionization detector. GC-MS analysis were performed on an Agilent 7890A gas chromatograph (HP-5MS column, 30 m x 0.25 mm, 0.25 μm, Agilent J&W) interfaced with an Agilent 5975X mass spectrometer. NH_3 was used as the ionization gas.

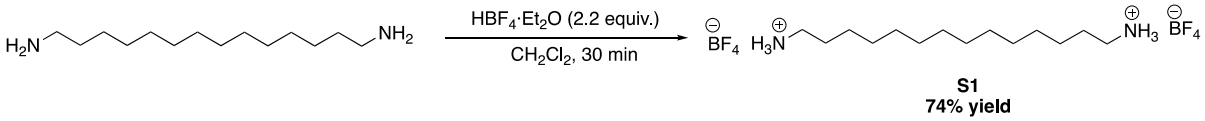
2. Synthesis of the catalysts

The complexes [Mn(OTf)$_2$(pdp)],[1] [Mn(OTf)$_2$(^{CR}pdp)],[1] [Zn(OTf)$_2$(pdp)][3] and [Zn(OTf)$_2$(^{CR}pdp)][4] were prepared according to the reported procedures.

3. Synthesis of the substrate (S1)



1,14-tetradecandiamine was prepared following a procedure inspired by J. Pinnavaia and co-workers[5] and B. Paulus, C. A. Schalley and co-workers.[6] 1,16-hexadecandioic acid (305.0 mg, 1.07 mmol, 1 equiv.) were solved in 20 mL of $CHCl_3$ (0.06M). Under N_2 atmosphere, 4.5 mL of concentrated H_2SO_4 (8.56 mmol, 8 equiv.) were slowly added and the mixture was heated to 55ºC. Then 500.0 mg of NaN_3 (8.13 mmol, 7.6 equiv.) were added in small portions during 2 hours under vigorous stirring. The reaction mixture was stirred for two additional hours. The crude was cooled to room temperature and moved to an extraction funnel and the acidic phase was collected in an H_2O/ice vessel to make the product precipitate. The solid was filtered and solved in 2M NaOH until pH = 11. The aqueous phase was extracted with $CHCl_3$ (5 x 50 mL) and the combined organic phases were dried over anhydrous $MgSO_4$, filtered and the solvent was removed under vacuum to afford the diamine as a white solid (155.0 mg, 0.680 mmol, 66% yield). The product was used in the next step without further purification. Spectral data match those previously reported.[7] ^{1}H-NMR (400 MHz, $CDCl_3$) δ, ppm: 2.68 (t, *J* = 7.0 Hz, 4H), 1.47 (br, 4H), 1.45-1.41 (m, 4H), 1.30-1.24 (m, 20H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ, ppm: 42.3, 33.7, 29.6, 29.6, 29.6, 29.5, 26.9.



1,14-tetradecandiamimium tetrafluoroborate **(S1)** was prepared following a procedure inspired by Olivo *et al.*[2] 1,14-tetradecandiamine (155.0 mg, 0.680 mmol, 1 equiv.) was solved in 2 mL of CH_2Cl_2 (0.5 M) and cooled to 0ºC. After 5 minutes of stirring, 570 µL of a 2.63 M CH_2Cl_2 solution of $HBF_4{\cdot}Et_2O$ (1.496 mmol, 2.2 equiv.) were added dropwise. The mixture was stirred for 30 minutes at 0ºC. The solvent was removed and the solid was washed with diethyl ether (8 mL) under stirring for 5 minutes. The supernatant was removed and the washing process was repeated twice and the solid obtained was dried under vacuum. Recrystallization with CH_3CN affords **S1** as a crystalline white solid (202.0 mg, 0.500 mmol, 74% yield). ^{1}H-NMR (400 MHz, CD_3CN) δ, ppm: 6.10 (t, *J* = 51.1 Hz, 6H), 2.98-2.88 (m, 4H), 1.67-1.52 (m, 4H), 1.42-1.18 (m, 20H). ^{13}C-NMR (100 MHz, CD_3CN) δ, ppm: 40.3, 29.4, 29.3, 29.1, 28.7, 26.6, 25.8.

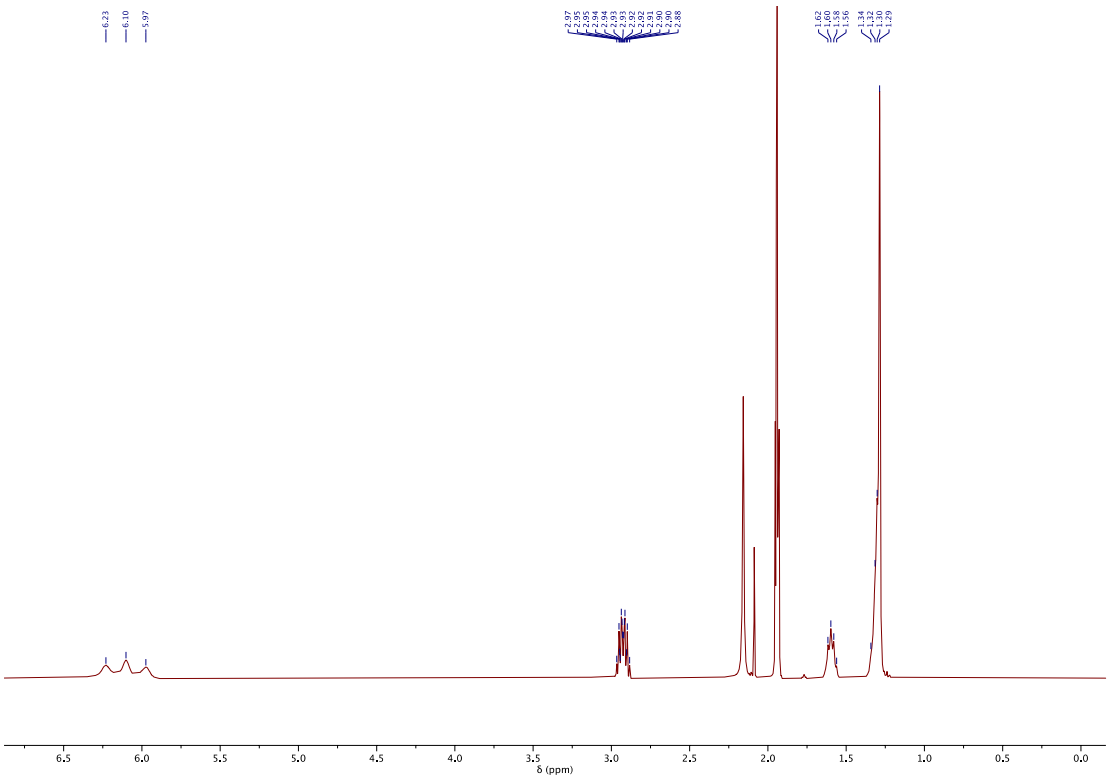


Figure S1. ^{1}H-NMR spectrum (400 MHz, CD_3CN) of **S1**.

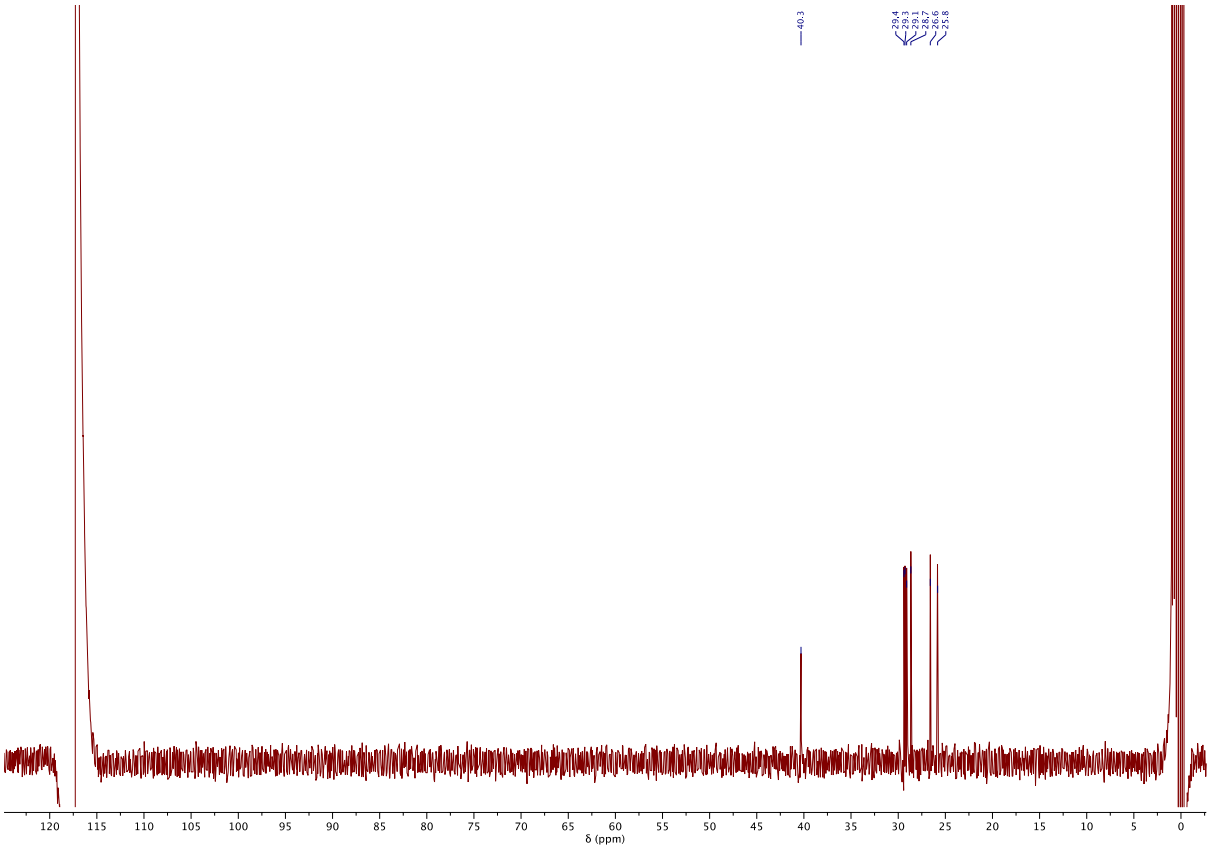


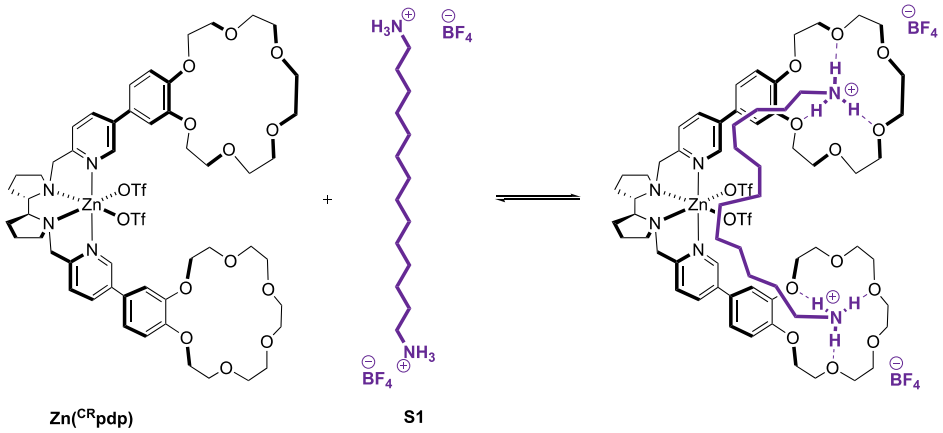
Figure S2. ^{13}C-NMR spectrum (100 MHz, CD_3CN) of **S1**.

4. NMR titration

4.1. General procedure

0.5 mL of a 1 mM CD_3CN catalyst solution of were introduced in an NMR tube and analyzed by ^{1}H-NMR. Then, portions of a CD_3CN solution containing substrate (5 mM) and catalyst (1 mM) were periodically added and analyzed after each addition. When 1 equiv. of substrate was added, a NOESY experiment was conducted (mixing time d_8=0.8 seconds). After the acquisition the titration was finished following the same procedure.

4.2. Titration of *(S,S)*-Zn(CRpdp) with S1



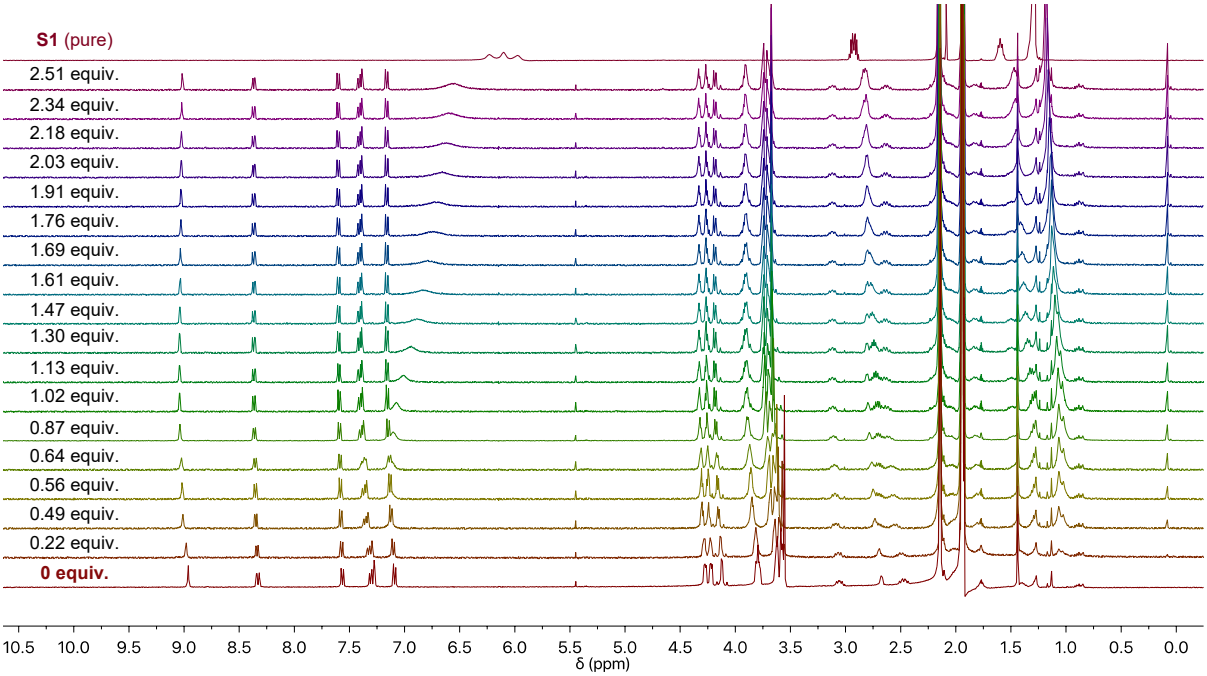


Figure S3. Titration of ***(S,S)*-Zn(CRpdp)** (1 mM) with **S1** in CD_3CN at 25ºC.

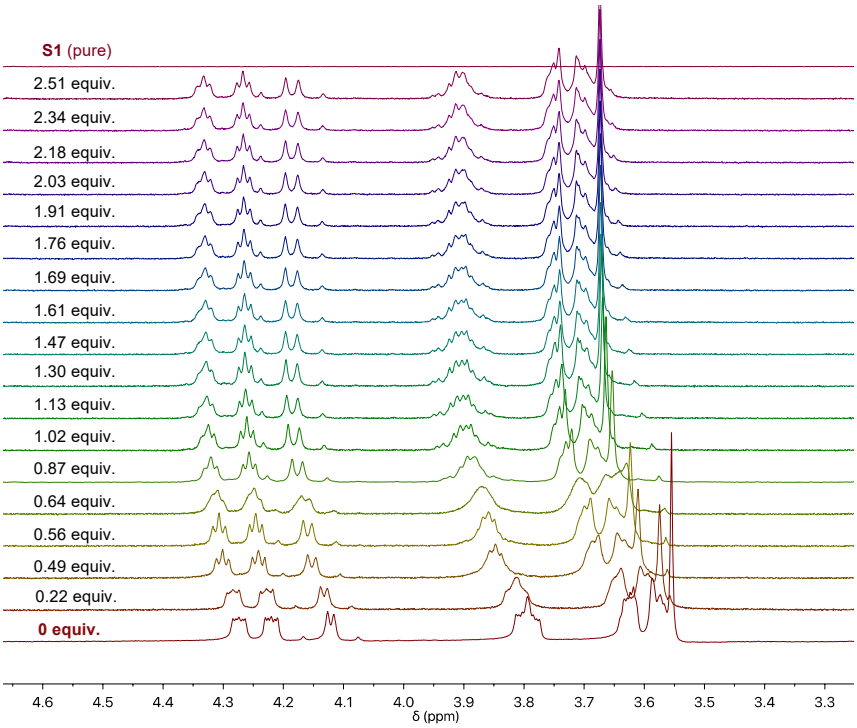


Figure S4. Downfield shift of the crown signals during the titration of ***(S,S)*-Zn(^CR^pdp)** (1 mM) with **S1** in CD_3CN at 25ºC (enlargement of crown region).

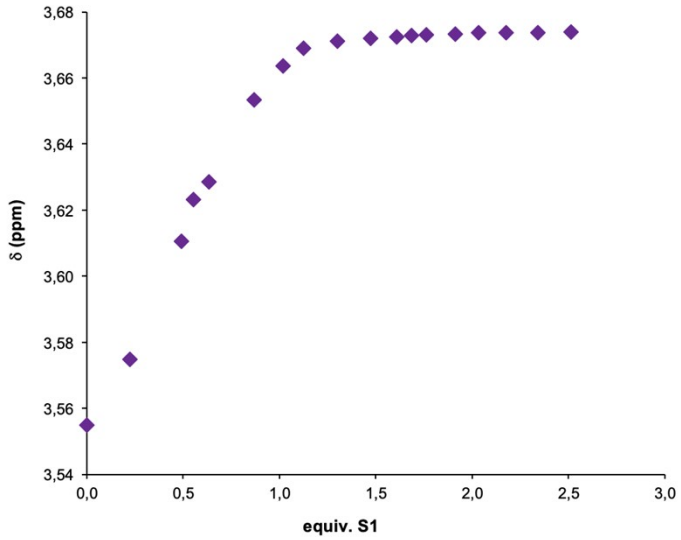


Figure S5. Titration curve of the above NMR experiments (Figure S3). A reliable binding constant could not be extracted, but anyway, this curve is consistent with the formation of 1:1 adducts at millimolar concentrations.

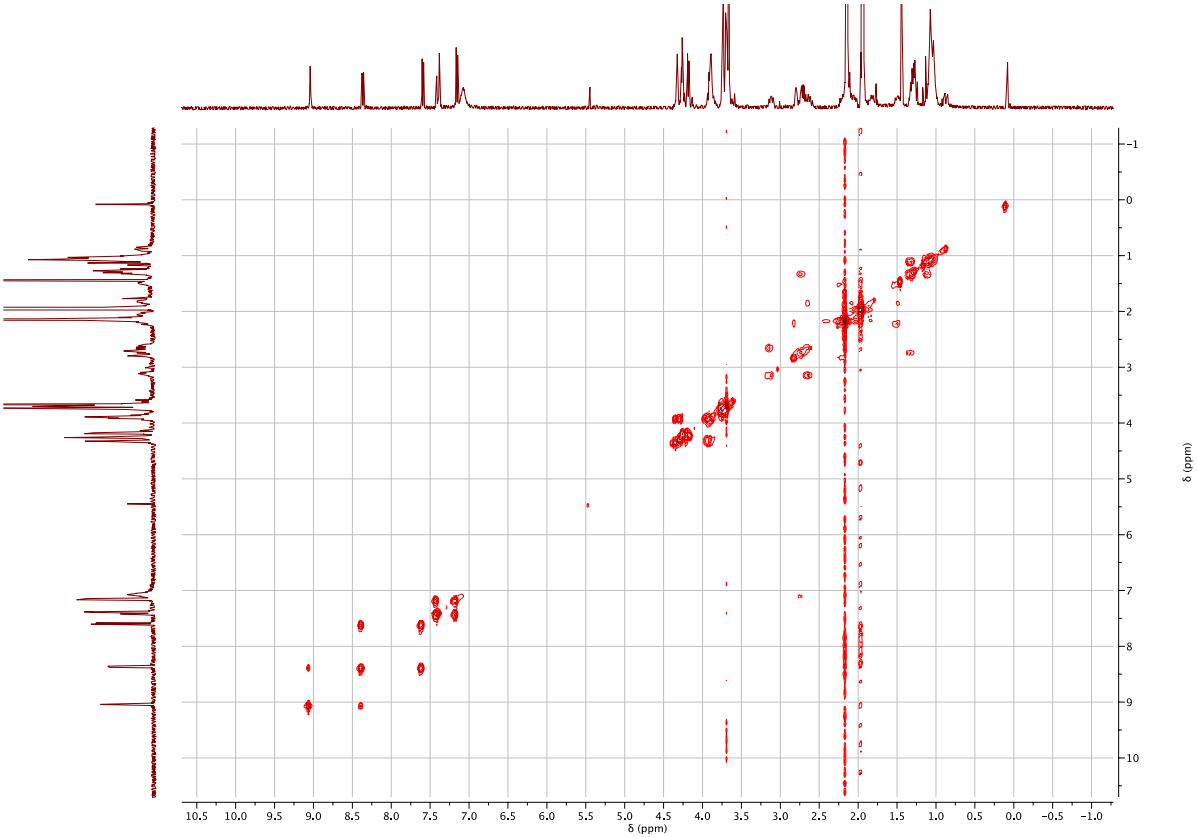


Figure S6. COSY spectrum of a 1:1 mixture of ***(S,S)*-Zn(^CRpdp)** : **S1** in CD_3CN (1 mM) at 25°C.

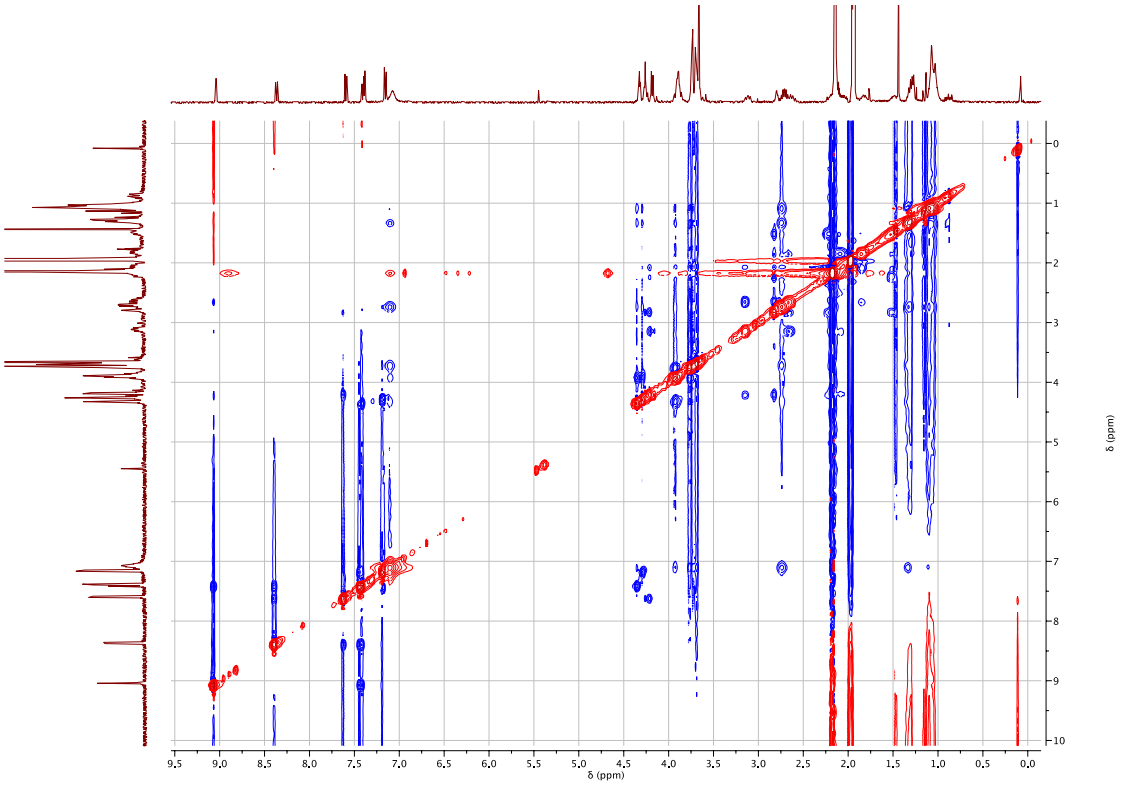


Figure S7. NOESY spectrum of a 1:1 mixture of ***(S,S)*-Zn(^CRpdp)** : **S1** in CD_3CN (1 mM) at 25°C (mixing time d_8=0.8s).

4.3. Control experiment using *(S,S)*-Zn(pdp)

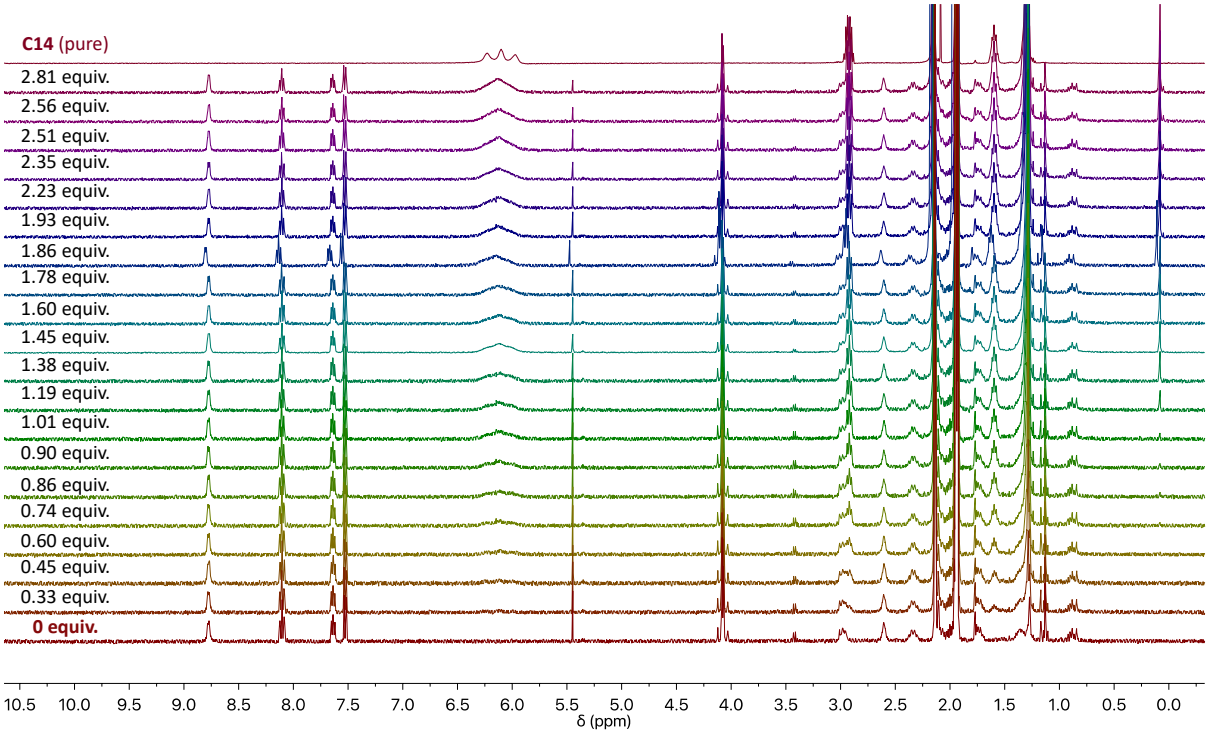


Figure S8. Titration of ***(S,S)*-Zn(pdp)** (1 mM) with **S1** in CD_3CN at 25ºC. Comments: Note that the signals of the complex and **S1** do not show any shift, indicating lack of interaction between the Zn complex and the protonated diamine.

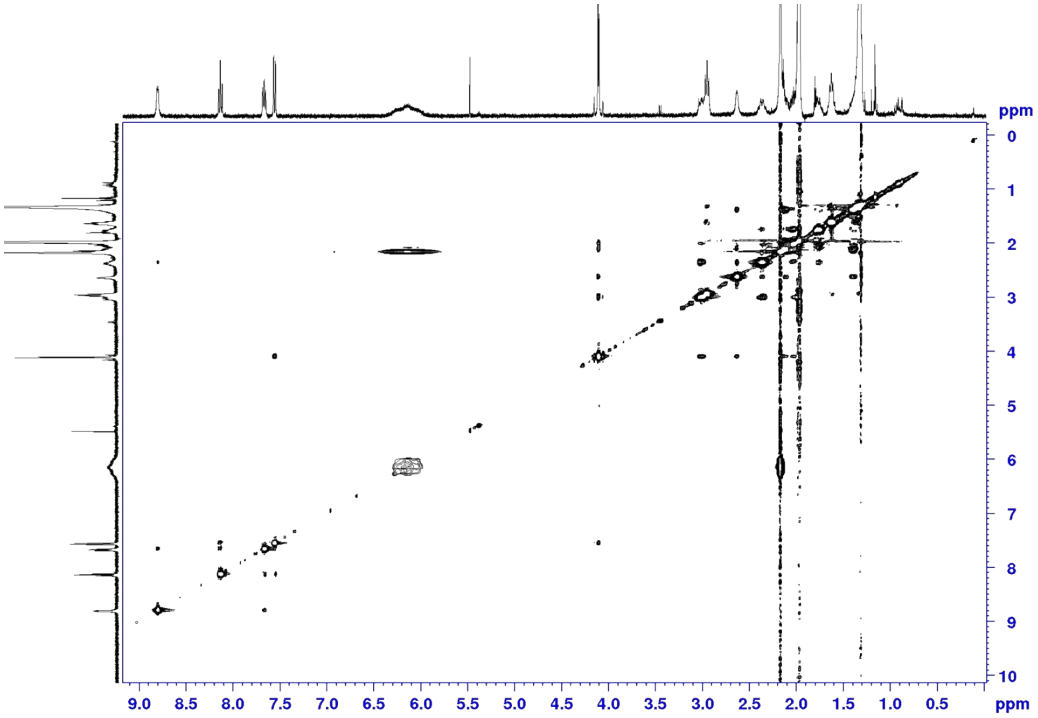
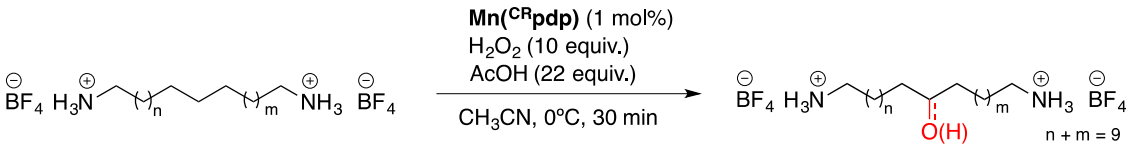


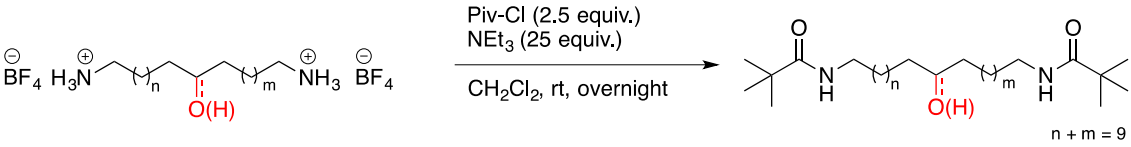
Figure S9. NOESY spectrum of a 1:1 mixture of ***(S,S)*-Zn(pdp)** : **S1** in CD_3CN (1 mM) at 25ºC (mixing time d_8=0.8s). There are no intermolecular correlations, indicating no binding between the complex and the substrate.

5. Catalytic oxidation of S1

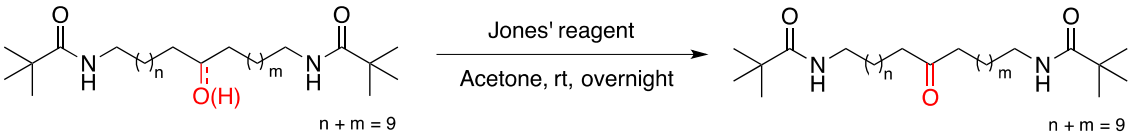
5.1. General procedures



General procedure for the oxidation of S1. A CH_3CN solution (200 μL, 0.1 M) of **S1** (7.8 mg, 0.0193 mmol, 1 equiv.) and **C1** (0.25 mg, 0.193 μmol, 1 mol%) was prepared in a 10 mL vial equipped with a stirring bar. 22 equiv. of AcOH (25 μL, 0.418 mmol) were then added to the solution. The resulting mixture was cooled to 0°C in an ice bath. 100 μL of H_2O_2 (from a 1.9 M solution in CH_3CN diluted from 50% in water, 0.193 mmol, 10 equiv.) were directly added by syringe pump over 30 minutes. At this point, the reaction was quenched with 2 mL of 2-propanol and the solvent was removed under reduced pressure. A known amount of 1,3,5-trimethoxybenzene (around 0.5 equiv.) were added in the vial as solid, the mixture was solved in CD_3CN and analyzed by ^{1}H-NMR to determine the conversion and yield of the reaction.

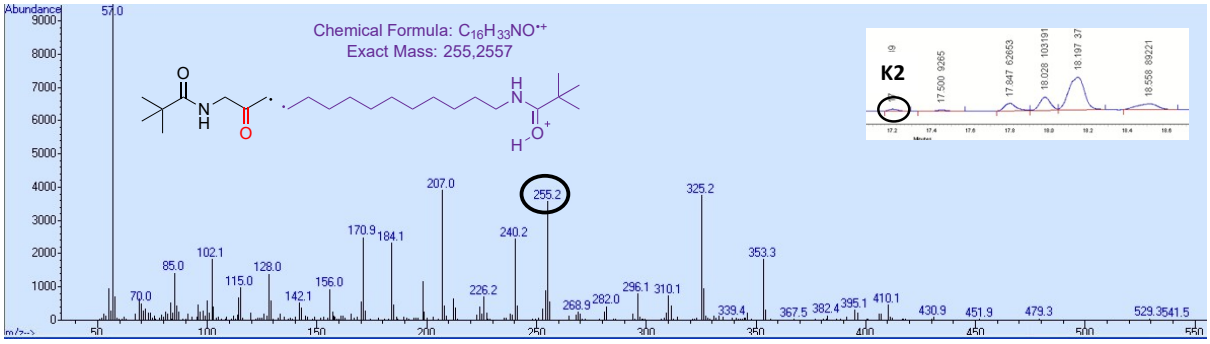


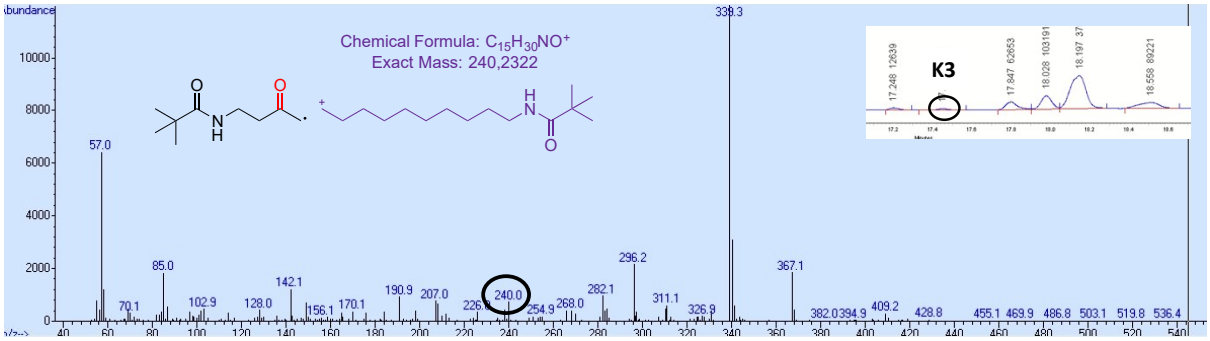
Derivatization of the reaction.[8] The contents of the NMR tube were evaporated under vacuum and the crude was solve in 2 mL of CH_2Cl_2. 70 μL of Et_3N (0.475 mmol, 25 equiv.) and 10 μL of pivaloyl chloride (0.0475 mmol, 2.5 equiv.) were added. The mixture was stirred at room temperature overnight and washed with a saturated solution of $NaHCO_3$ (2 mL) and 2M HCl (2 mL). The organic phase was filtered through an anhydrous $MgSO_4$ plug and directly injected in the GC to determine the selectivity of the reaction.

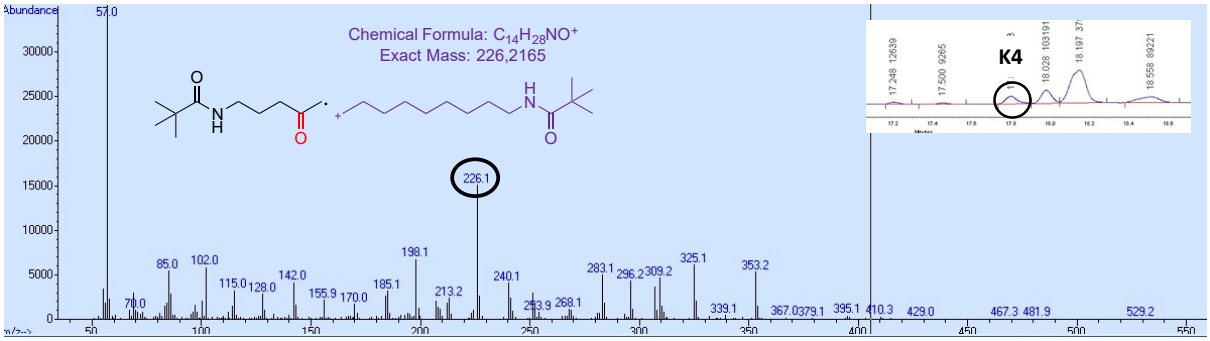


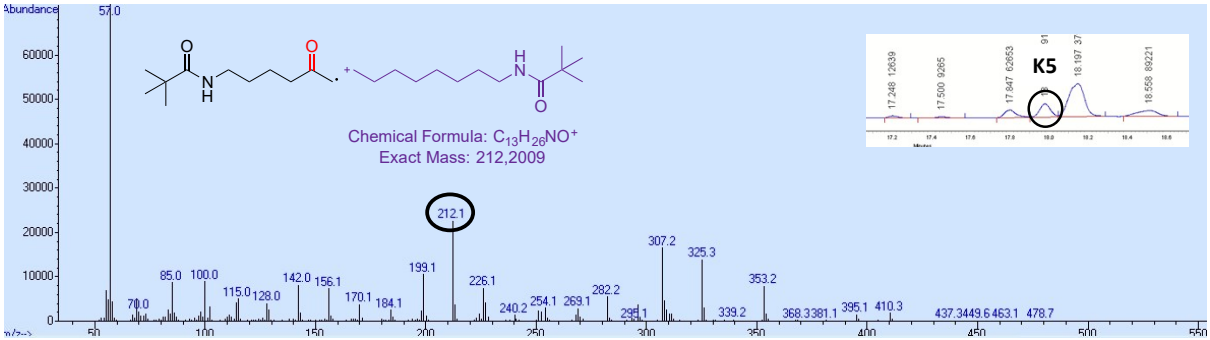
Jones' oxidation.[9] After derivatization, the solvent was removed under reduced pressure and the crude obtained was solved in 2 mL of acetone. 200 μL of Jones' reagent were added at 0°C and the mixture was stirred overnight at room temperature. The reaction crude is filtered through a Celite© plug and directly injected in the GC to determine the selectivity of the reaction.

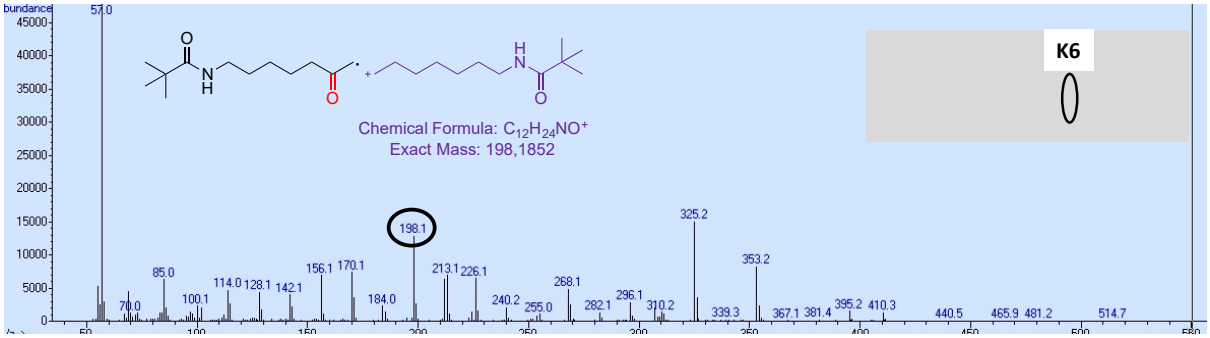
5.2. GC-MS fragmentation of the products










K6
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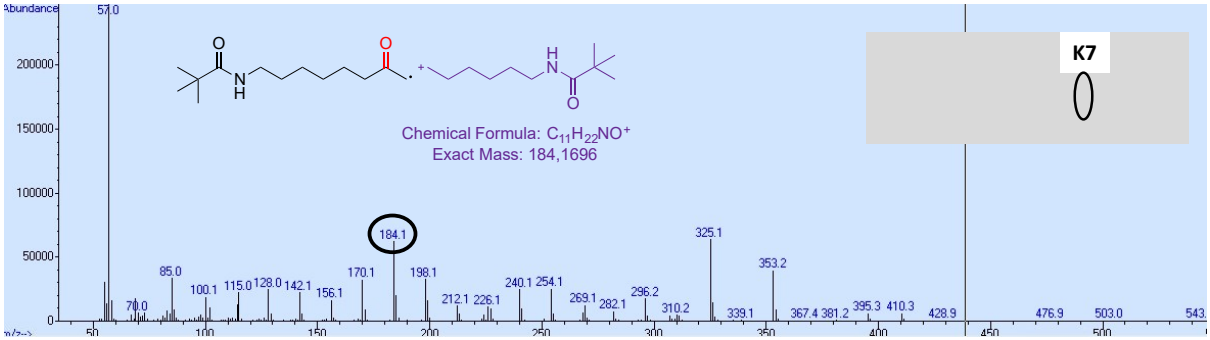
Exact Mass: 198,1852


K7
Chemical Formula: $C_{11}H_{22}NO^+$
Exact Mass: 184,1696

6. References

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