Comparison of click-capable oxaliplatin and cisplatin derivatives to better understand Pt(II)-induced nucleolar stress

Andres S. Guerrero[a], Paul D. O'Dowd[b,c], Hannah C. Pigg[a], Katelyn R. Alley[a], Darren M. Griffith[b,c], and Victoria J. DeRose[a]

[a] Department of Chemistry and Biochemistry, University of Oregon, Eugene, OR USA
[b] Department of Chemistry, Royal College of Surgeons in Ireland, Dublin, Ireland
[c] SSPC, Synthesis and Solid State Pharmaceutical Centre, Ireland

Supplemental Information

***Caution**

Azides (organic and/or salts) should be handled with care and every precaution should be taken as they are explosive and a known neurotoxin. No issues with azides were encountered in this work.

*Average Coefficient of Variation (NPM1 relocalization assay) – **1,3-Pt, azido-Pt, 1, 2,** and **3***

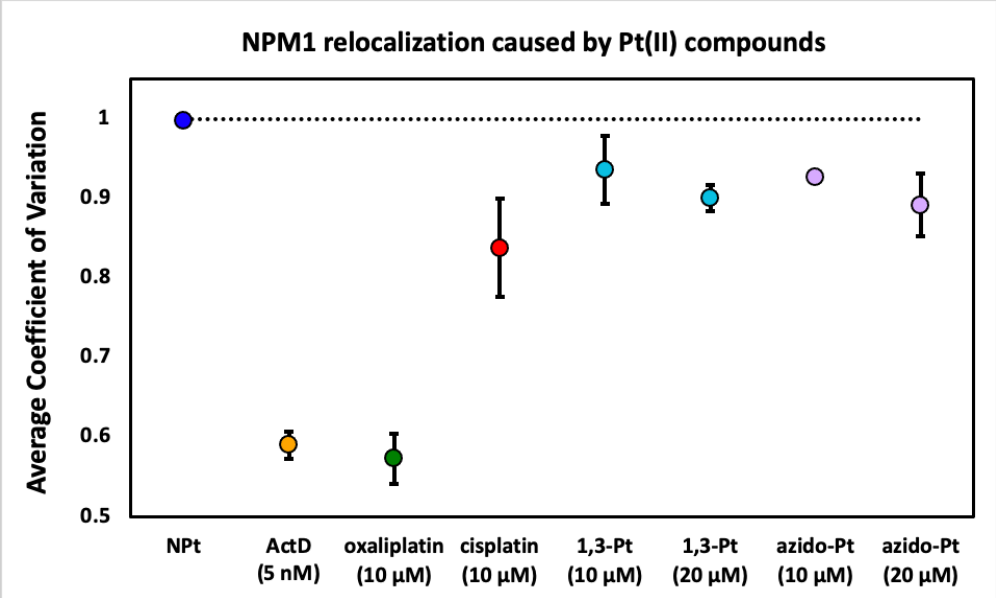


Figure S1. Average Coefficient of Variation (CV) quantification of NPM1 relocalization induced by **1,3-Pt** and **azido-Pt**. Treatment conditions indicated (either 10 or 20 µM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment; CV calculations, and boxplot presentation as described in the Experimental Section. For each treatment data set, average of CV of 3 trials along with std.

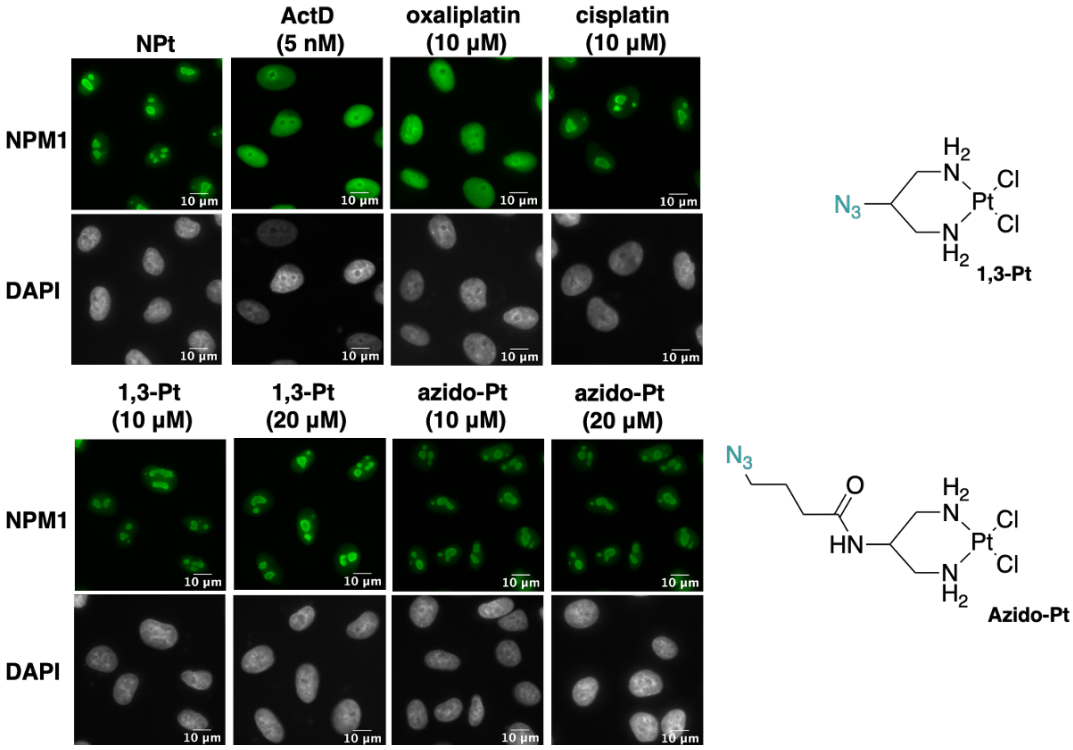


Figure S2. Supplementary A549 cell images of NPM1 relocalization induced by **1,3-Pt** and **azido-Pt.** Treatment conditions indicated (either 10 or 20 µM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment.

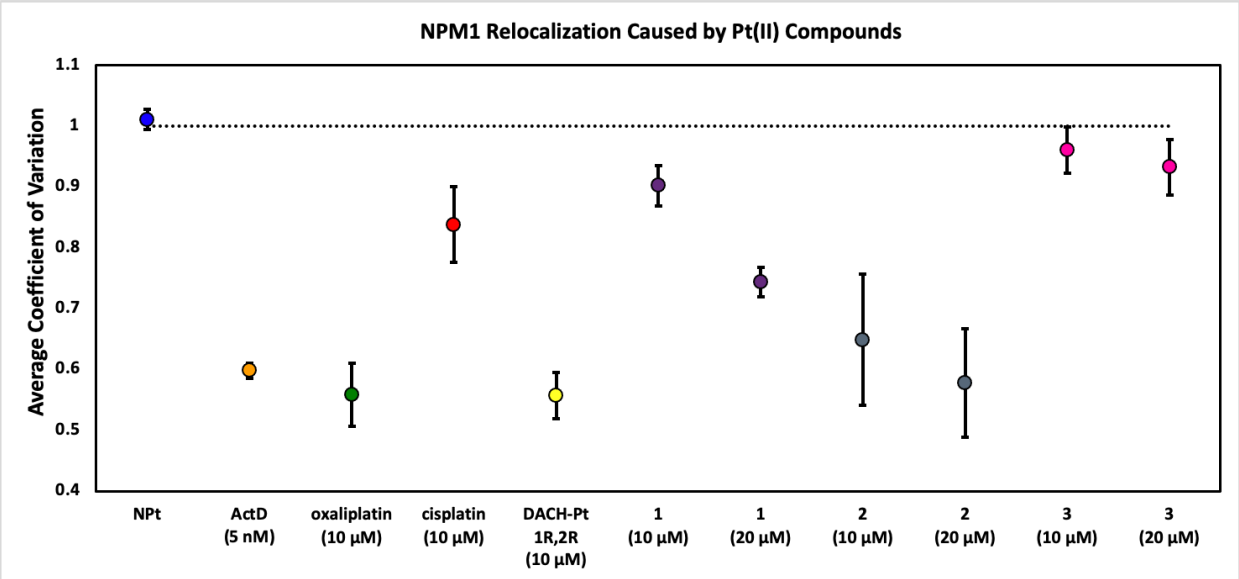


Figure S3. Average Coefficient of Variation (CV) quantification of NPM1 relocalization induced by **1, 2,** and **3**. Treatment conditions indicated (either 10 or 20 µM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment; CV calculations, and boxplot presentation as described in the Experimental Section. For each treatment data set, average of CV of 3 trials along with std.

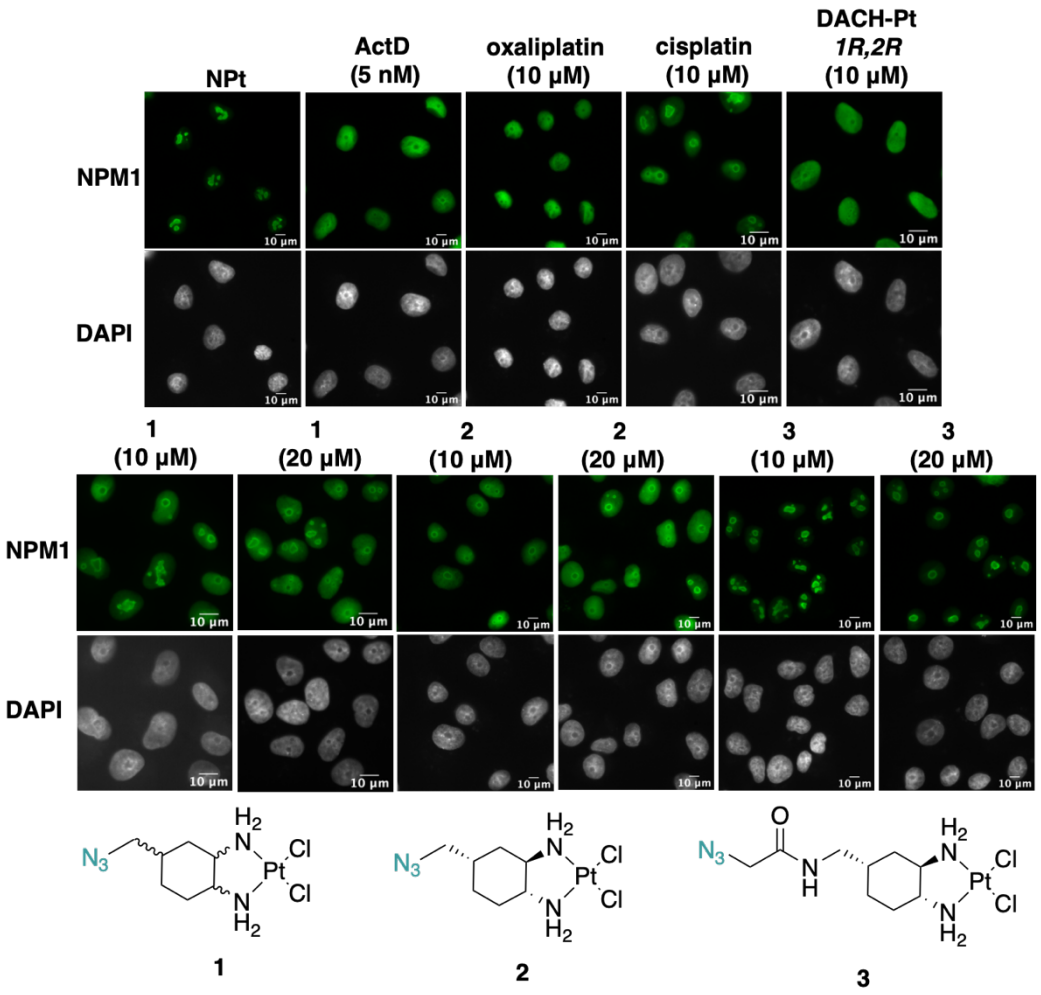


Figure S4. Supplementary A549 cell images of NPM1 relocalization induced by **1, 2,** and **3**. Treatment conditions indicated (either 10 or 20 µM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment.

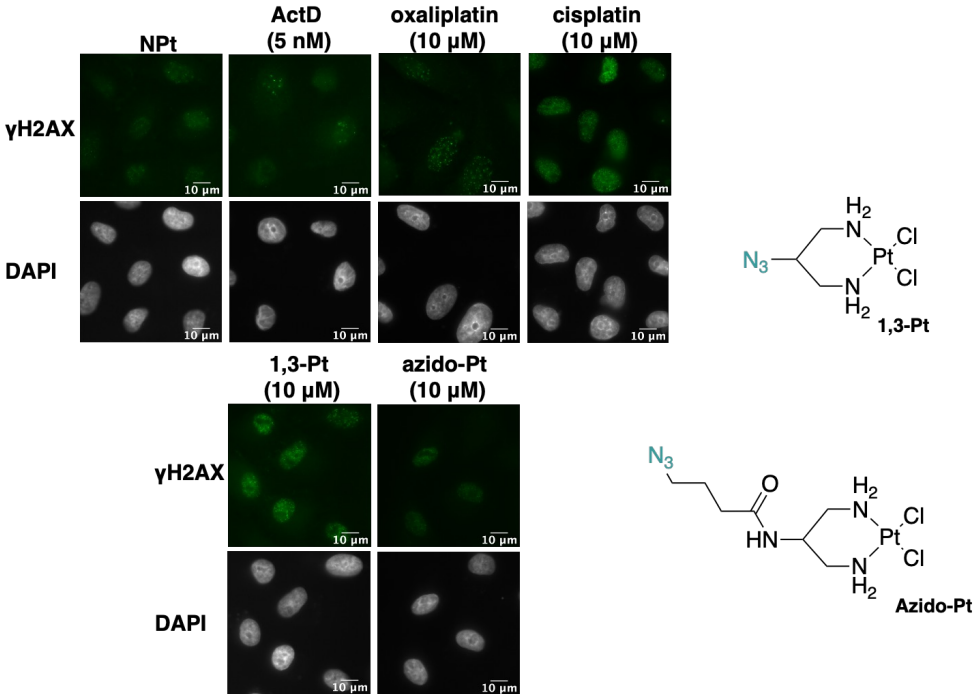


Figure S5. Supplementary A549 cell images of γH2AX induced by **1,3-Pt** and **azido-Pt**. Treatment conditions indicated (10 μM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment.

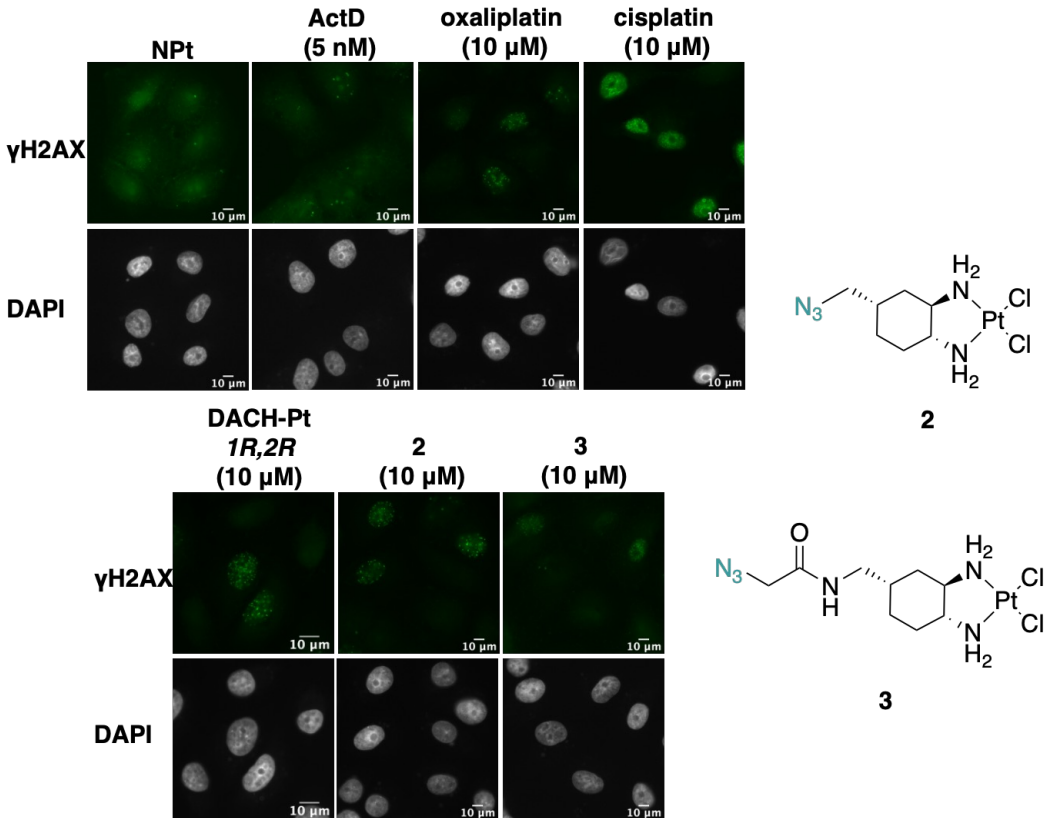
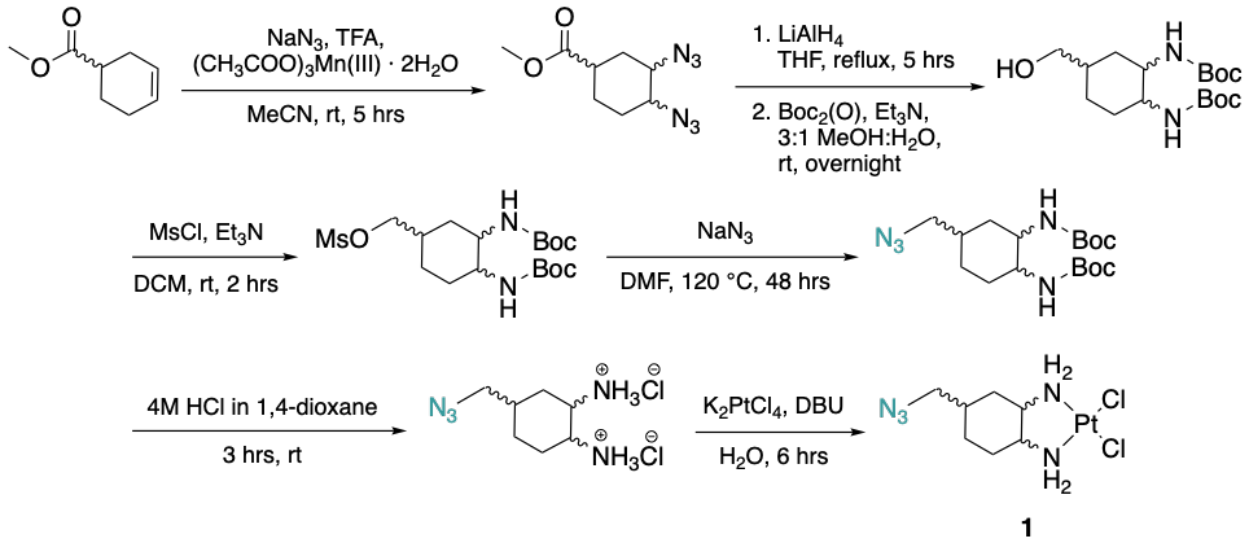


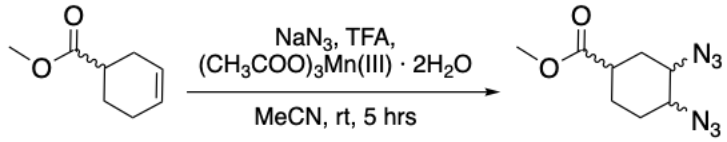
Figure S5. Supplementary A549 cell images of γH2AX induced by **2,** and **3.** Treatment conditions indicated (10 μM for Pt(II) compounds, 5nM for ActD) in A549 cells at 24 hr treatment.

*Expanded synthesis procedure of **1**, **2**, and **3***

Complete synthetic route of **1**



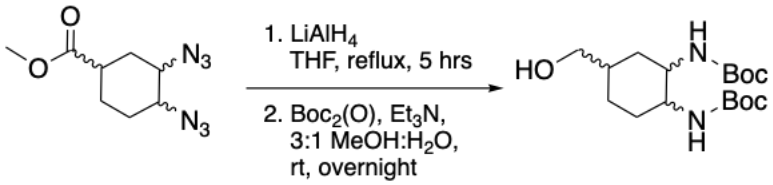
((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) Methyl 4-carboxylate-1,2-cyclohexanediazide



Synthesized as previously reported.[1, 2]

(*3S, 3R*) Methyl 3-carboxylate-1-cyclohexene (1.1 g, 7.9 mmol) solution in trifluoroacetic acid (12 mL) was added to a solution of manganese(III) acetate dihydrate (5.0 g, 18.7 mmol) and sodium azide (2.5 g, 39.7 mmol) in acetonitrile (150 mL) under N_2 at 0 °C and brought back to rt. After addition, temperature was brought to room temperature and stirred for 5 hrs. $NaHSO_3$ (10% w/v) was added to reaction and stirred for 15 minutes. Product was extracted using ethyl acetate (3 x 50 mL), organic layer was combined and neutralized with sat. sodium bicarbonate (3 x 50 mL), washed with brine (3 x 50 mL) and dried over anhyd. sodium sulfate to obtain crude ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) methyl 4-carboxylate-1,2-cyclohexanediazide (1.2 g, 69% yield).

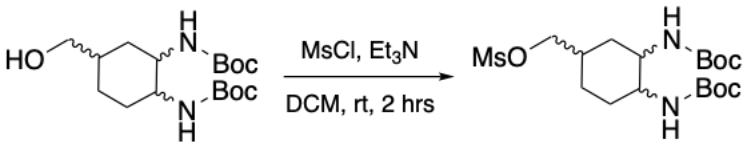
((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-tert-butyl 4 methanol-1,2-dicarbamatecyclohexane



((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) Methyl 4-carboxylate-1,2-cyclohexanediazide (1.0 g, 4.5 mmol) was added to a solution of $LiAlH_4$ (1.4 g, 36.3 mmol) in anhyd. THF (80 mL) at 0 °C under N_2. Reaction was brought to room temperature and refluxed for 5 hrs. Reaction was brought to 0 °C and dI water was used to quench any unreacted $LiAlH_4$. Reaction mixture was vacuum filtered with celite, and dried completely using rotovap to obtain a white solid. The white solid was dissolved in a 3:1 mixture of methanol (60 mL): water (20 mL), triethylamine (2 mL) was added, and excess di-*tert*-butyl di-

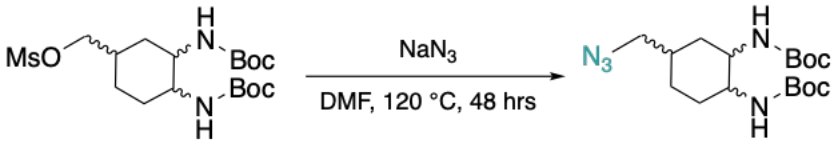
carbonate (4 mL, 17.4 mmol) was added and stirred at room temperature overnight. Reaction was completely dried using rotovap to obtain a crude mixture. Mixture was purified using column chromatography (80%:20% ethyl acetate: petroleum ether) and dried under vacuum overnight to obtain ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methanol-1,2-dicarbamatecyclohexane as a white solid (0.8 g, 48% yield). ^{1}H NMR (500 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 4.90 (d, J = 8.4 Hz, 2H), 3.39 – 3.26 (m, 2H), 1.96 (s, 1H), 1.84 (dt, J = 7.0, 2.9 Hz, 1H), 1.71 (s, 1H), 1.67 (s, 1H), 1.55 (q, J = 4.2 Hz, 1H), 1.42 (d, J = 2.1 Hz, 18H), 1.24 (ddd, J = 12.8, 7.7, 3.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 156.58, 79.5, 63.7, 54.8, 51.0, 35.7, 33.1, 28.5, 28.2, 25.5.

<u>((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methyl(methanesulfonate)-1,2-dicarbamatecyclohexane</u>



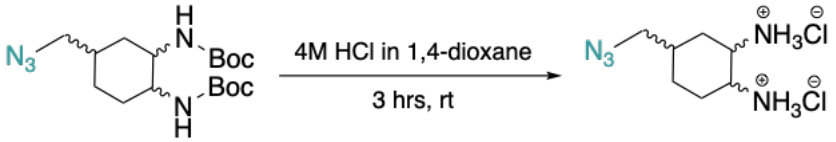
((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methanol-1,2-dicarbamatecyclohexane (0.6 g, 1.9 mmol) was dissolved in dichloromethane (80 mL) along with triethylamine (2 mL). Methanesulfonyl chloride (1.5 mL, 16.2 mmol) was added dropwise to reaction mixture at and stirred at 0 °C. Reaction was brought back to room temperature and stirred for 2 hrs. Reaction mixture was washed with dI water (3 x 50 mL), washed with brine (3 x 50 mL) and dried over sodium sulfate to obtain a crude oil. Crude product was purified using column chromatography (60% ethyl acetate: 40% petroleum ether) and dried under vacuum overnight to obtain ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methyl(methanesulfonate)-1,2-dicarbamatecyclohexane as a slight orange solid (0.5 g, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 4.94 – 4.83 (m, 2H), 4.06 – 4.00 (m, 2H), 3.45 – 3.34 (m, 2H), 3.03 (s, 3H), 2.24 (s, 1H), 1.98 (d, J = 13.7 Hz, 1H), 1.89 (d, J = 4.5 Hz, 1H), 1.77 (d, J = 12.3 Hz, 1H), 1.42 (d, J = 2.9 Hz, 18H), 1.26 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 156.3, 156.2, 79.46, 70.69, 54.35, 50.61, 37.32, 32.87, 32.70, 28.35, 27.87, 24.63.

<u>((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methylazido-1,2-dicarbamatecyclohexane</u>



((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methyl(methanesulfonate)-1,2-dicarbamatecyclohexane (0.5 g, 1.1 mmol) and sodium azide (0.3 g, 4.9 mmol) was dissolved in DMF (30 mL) and stirred at ~ 120 °C for 48 hrs. Reaction mixture was allowed to cool down to room temperature, extracted with ethyl acetate (3 x 50 mL), washed with dI water (3 x 50 mL), washed with brine (3 x 50 mL) and dried over anhyd. sodium sulfate to obtain a crude yellow oil. Crude product was purified using column chromatography (20% ethyl acetate: 80% petroleum ether) and dried under vacuum overnight to obtain ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-*tert*-butyl 4-methylazido-1,2- dicarbamatecyclohexane as would oily residue (0.2 g, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 4.99 – 4.74 (m, 2H), 3.52 – 3.21 (m, 4H), 2.04 (s, 1H), 1.97 – 1.85 (m, 2H), 1.72 – 1.66 (m, 1H), 1.59 (s, 1H), 1.46 (s, 1H), 1.43 (d, J = 6.7 Hz, 18H), 1.33 (d, J = 8.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 156.2, 79.5, 79.4, 54.7, 54.5, 50.2, 33.9, 33.0, 28.4, 27.5, 25.7.

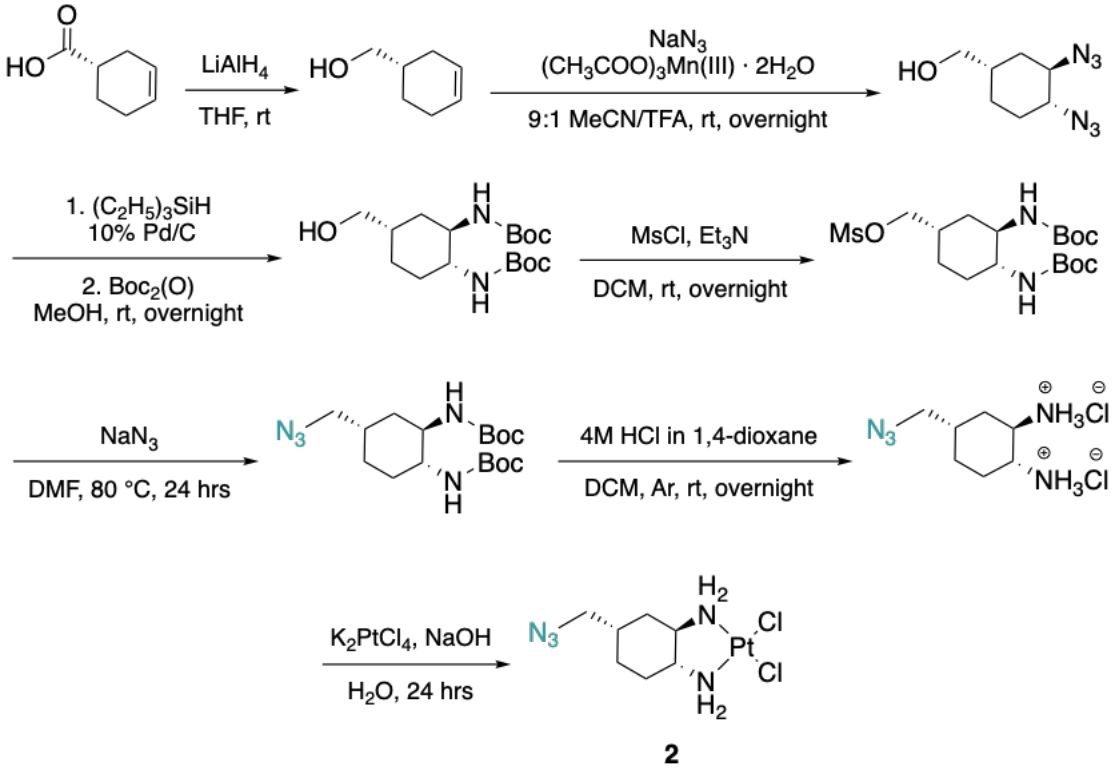
<u>((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) 4-methylazido-1,2-cyclohexanediaminium dihydrochloride</u>



4M HCl in 1,4-dioxane (5 mL) was added to ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) di-tert-butyl 4-methylazido-1,2- dicarbamatecyclohexane (0.2 g, 0.6 mmol) and stirred for 3 hrs at room temperature. Reaction was dried using rotovap at ~60 °C for 1 hr and dried under vacuum overnight obtain ((*1R, 2R, 4S*)/(*1S, 2S, 4R*), (*1R, 2R, 4R*)/(*1S, 2S, 4S*)) 4-

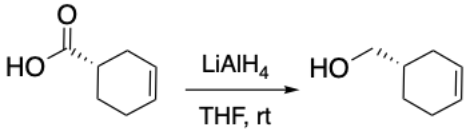
methylazido-1,2-cyclohexanediaminium dihydrochloride as an oily residue (0.2 g, quant.). ^{1}H NMR (500 MHz, DMSO-d_6) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 8.66 (s, 6H), 3.71 – 3.69 (m, 1H), 3.67 – 3.66 (m, 1H), 3.49 (d, J = 4.9 Hz, 1H), 3.47 – 3.45 (m, 1H), 2.07 (ddt, J = 13.9, 7.0, 3.4 Hz, 1H), 2.01 – 1.86 (m, 2H), 1.75 (dddt, J = 17.8, 10.2, 7.9, 3.4 Hz, 2H), 1.53 (dtd, J = 27.5, 9.0, 8.4, 4.5 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) (*1R, 2R, 4S*)/(*1S, 2S, 4R*): δ 53.3, 49.1, 47.1, 30.5, 28.2, 22.9, 22.8; (*1R, 2R, 4R*)/ (*1S, 2S, 4S*): δ 72.2, 70.5, 60.2, 43.6, 28.2, 22.9, 22.8

Complete synthetic route of **2**



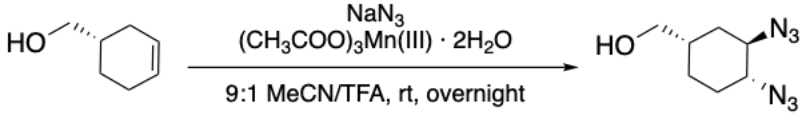
2

(*1S*) 3-cyclohexene-1-methanol



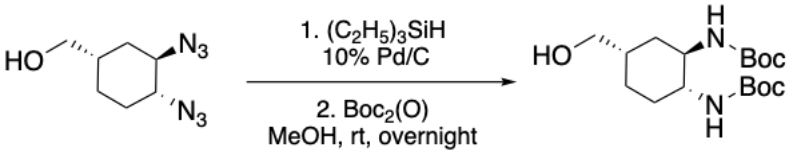
Lithium aluminum hydride (7.3 g, 190.0 mmol) was added in portions to anhydrous tetrahydrofuran (250 mL) under an argon atmosphere at 0 °C. A solution of (*1S*) 3-cyclohexene-1-carboxylic acid (20.0 g, 160.0 mmol) in anhydrous tetrahydrofuran (50 mL) was then added dropwise to this mixture. Following addition, the reaction mixture was allowed to warm to room temperature and stirred for 3 hours. After stirring, the mixture was diluted with diethyl ether and cooled to 0 °C. dI water (7 mL), 15% aqueous sodium hydroxide (7 mL) and dI water (21 mL) were then added consecutively to quench any unreacted lithium aluminum hydride. The reaction mixture was allowed to warm to room temperature and stirred for 15 minutes. Anhydrous sodium sulphate was then added and the reaction mixture stirred for a further 15 minutes. The resulting slurry was filtered under vacuum and the filtrate diluted with dI water (150 mL). The organic layer was separated off and the aqueous phase washed with diethyl ether (3 x 150 mL). The organic phases were combined, dried over anhydrous sodium sulfate and the solvent removed under vacuum to yield the product as a colorless oil of (*1S*) 3-cyclohexene-1-methanol (17.0 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.64 (m, 2H), 3.51 (m, 2H), 2.34 (s, 1H), 2.10-2.01 (m, 3H), 1.80-1.66 (m, 3H), 1.29-1.19 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 127.2, 126.0, 67.7, 36.3, 28.2, 25.3, 24.7. FT-IR vmax (cm^{-1}): (OH) 3323, (=C-H) 3022, (C-H) 2912, (C-H) 2837, (C=C) 1652, (C-O) 1023. MS(ESI+) [M+Na]+: m/z calcd for $C_7H_{12}NaO$: 135.1, found: 135.1. [α]21D -94.7 (c 3.0, MeOH) (lit. [α]D -96.0 (c 3.0, MeOH)).[3]

(*1R, 2R, 4S*) 4-methanol-1,2-cyclohexanediazide



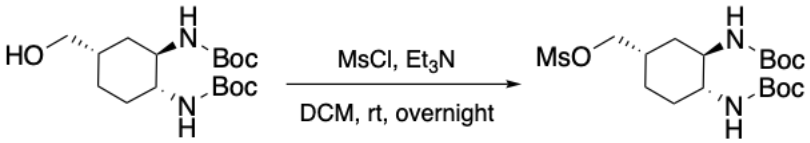
(*1S*) 3-cyclohexene-1-methanol (10.0 g, 89.0 mmol) in trifluoroacetic acid (50 mL) was added to a mixture of manganese(III) acetate dihydrate (71.7 g, 268.0 mmol) and sodium azide (29.0 g, 446.0 mmol) in acetonitrile (450 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and then stirred overnight under an argon atmosphere. After stirring, an aqueous sodium hydrogen sulfite solution (39% v/v, 100 mL, 375.0 mmol) was added to the mixture and the reaction stirred for a further 15 minutes. The reaction mixture was subsequently abstracted with dichloromethane (3 x 150 mL). The organic layers were combined, washed with a saturated sodium carbonate solution (3 x 10 mL), saturated sodium chloride solution (2 x 10 mL) and dried over anhydrous sodium sulfate. The solvent was removed under vacuum to give a crude mixture of the (*1R, 2R, 4S*) and (*1S, 2S, 4S*)-isomers (approx. 80:20 ratio). These isomers were separated from one another by column chromatography (60:40 petroleum ether: ethyl acetate) to yield (*1R, 2R, 4S*) 4-methanol-1,2-cyclohexanediazide as a colorless oil (9.1 g, 52%). (*1R, 2R, 4S*)-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (td, 1H, 5.4, 4.3 Hz), 3.55 (td, 1H, 5.5, 3.8 Hz), 3.51 (d, 2H, 6.5 Hz), 1.92-1.82 (m, 2H), 1.78-1.67 (m, 4H), 1.57 (ddd, 1H, 14.3, 8.9, 4.2 Hz), 1.49-1.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.2, 61.0, 59.9, 34.3, 29.1, 25.0, 23.5. FT-IR νmax (cm^{-1}): (OH) 3332, (-C-H) 2929, (-N=N=N) 2087, (C-N) 1251. (*1S, 2S, 4S*)-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.52-3.44 (m, 2H), 3.25 (td, 1H, 4.3, 10.7 Hz), 3.12 (td, 1H, 4.3, 10.8 Hz), 2.15-2.08 (m, 2H), 1.90-1.79 (m, 2H), 1.60-1.50 (m, 1H), 1.44-1.20 (m, 1H), 1.17-0.96 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.9, 64.8, 64.3, 38.6, 33.8, 30.1, 26.9. FT-IR νmax (cm^{-1}): (OH) 3336, (C-H) 2931, (C-H) 2866, (-N=N=N) 2088, (C-N) 1252.

(*1R, 2R, 4S*) di-*tert*-butyl 4-methanol-1,2-dicarbamatecyclohexane



Triethylsilane (81.4 mL, 510.0 mmol) was added slowly to a solution of (*1R, 2R, 4S*) 4-methanol- 1,2-cyclohexanediazide (5.0 g, 025.0 mmol), di-*tert*-butyl di-carbonate (14.1 mL, 61.0 mmol) and 10% Pd/C (20% by wt.) in methanol (100 mL) under an argon atmosphere. An empty balloon was attached to the flask and the reaction mixture stirred overnight at room temperature. After stirring, the reaction mixture was filtered over celite to remove the Pd/C suspension, and the solvent removed under vacuum. The product was purified by column chromatography (100% petroleum ether to 80:20 petroleum ether: ethyl acetate) to yield (*1R, 2R, 4S*) di-tert-butyl 4-methanol-1,2-dicarbamatecyclohexane as a white solid (5.5 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.09 (d, 1H, 7.9 Hz), 5.03 (d, 1H, 8.1 Hz), 3.41-3.25 (m, 2H), 1.98 (d, 1H, 12.9 Hz), 1.91 (s, 1H), 1.77-1.74 (m, 1H), 1.66 (d, 1H, 13.0 Hz), 1.51-1.44 (m, 2H), 1.36 (s, 18H), 1.31-1.27 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 79.4, 63.3, 54.5, 50.9, 35.5, 33.1, 28.4, 28.0, 25.5. FT-IR *ν*max (cm^{-1}): (OH) 3339, (C-H) 2977, (C-H) 2931, (C=O) 1683, (N-H) 1518, (C-N) 1246, (C-O) 1163. MS (ESI$^+$) [M+Na]$^+$: m/z calcd for $C_{17}H_{32}N_2NaO_5$: 367.2, found: 367.0.

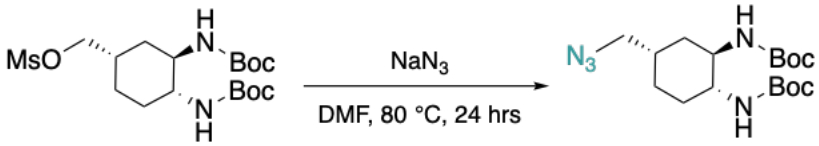
(*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(methanesulfonate)-1,2-dicarbamatecyclohexane



Methanesulfonyl chloride (1.4 mL, 174.0 mmol) was added dropwise to a solution of (*1R, 2R, 4S*) di-*tert*-butyl 4-methanol-1,2-dicarbamatecyclohexane (5.0 g, 145.0 mmol) and triethylamine (4.0 mL, 290.0 mmol) in dichloromethane (50 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and then stirred overnight under an argon atmosphere. After stirring, water (50 mL) was added to the reaction mixture and the product extracted with dichloromethane (3 x 50 mL). The organic layers were combined, washed with a saturated sodium chloride solution (2 x 20 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the product purified by column chromatography (60:40 ethyl acetate: petroleum ether) to yield (*1R, 2R, 4S*) di-tert-butyl 4- methyl(methanesulfonate)-1,2-dicarbamatecyclohexane as a white solid (5.9 g, quant.) ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.91 (d, 1H, 5.6 Hz), 4.81 (d, 1H, 6.5 Hz), 4.21 (dt, 2H, 16.6, 9.5 Hz), 3.44-3.34 (m, 2H), 3.03 (s, 3H), 2.23 (s, 1H), 1.98 (d, 1H, 13.4 Hz), 1.90 (dd, 1H, 13.4, 3.1 Hz), 1.78 (m, 1H), 1.63-1.54 (m,

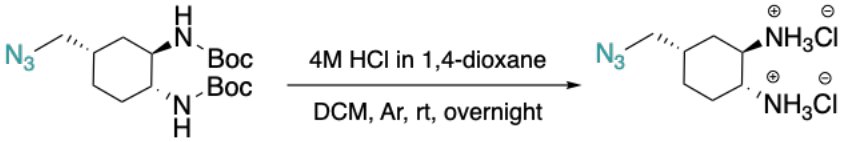
1H), 1.41 (s, 18H), 1.36-1.32 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 156.3, 79.6, 70.7, 54.3, 50.8, 37.5, 33.0, 32.8, 28.5, 27.6, 24.8. FT-IR vmax (cm^{-1}): (N-H) 3376, (C-H) 2977, (C-H) 2934, (C=O) 1690, (N-H) 1514, (S=O) 1351, (C-O) 1166. MS(ESI+) [M+Na]+: m/z calcd for $C_{18}H_{34}N_2NaO_7S$: 445.2, found: 445.0.

(*1R, 2R, 4S*) di-*tert*-butyl 4-methylazido-1,2-dicarbamatecyclohexane



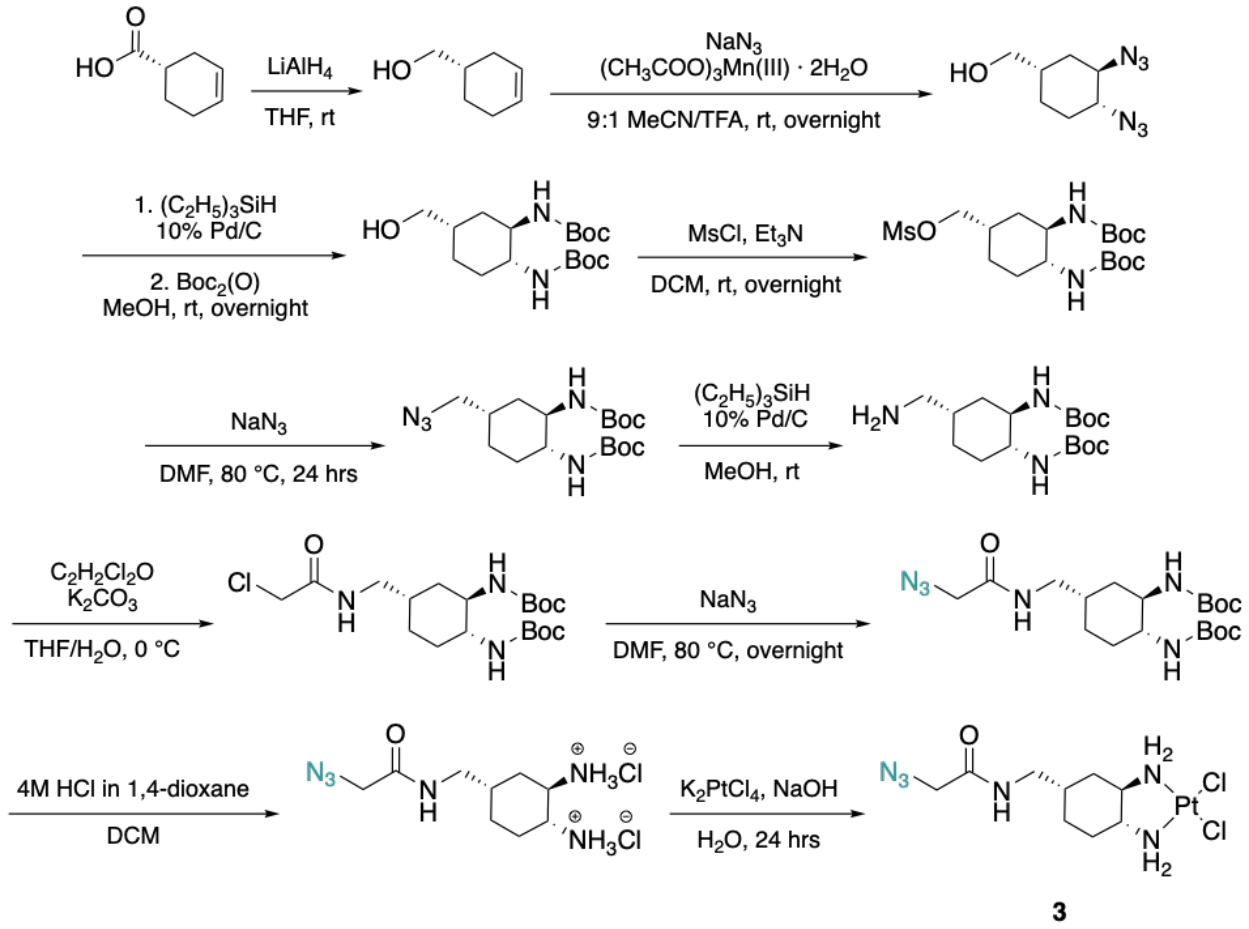
Sodium azide (1.3 g, 19.6 mmol) was added to a solution of (*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(methanesulfonate)-1,2-dicarbamatecyclohexane (2.0 g, 4.9 mmol) in anhydrous N,N- dimethylformamide (7.5 mL) under an argon atmosphere. The reaction mixture was heated to 80 °C and left to stir for 24 hours. Following stirring, the reaction mixture was allowed to cool to room temperature and water (50 mL) and dichloromethane (50 mL) added. The organic layer was separated off and then washed with a saturated sodium chloride solution (3 x 30 mL) and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the crude product purified by column chromatography (80:20 petroleum ether: ethyl acetate) to yield (*1R, 2R, 4S*) di-*tert*-butyl 4-methylazido-1,2- dicarbamatecyclohexane as a white solid (1.6 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 (d, 1H, 6.0 Hz), 4.80 (d, 1H, 6.4Hz), 3.45-3.29 (m, 4H), 2.04 (s, 1H), 1.91 (t, 2H, 14.2 Hz), 1.71 (d, 1H, 13.4 Hz), 1.61-1.52 (m, 1H), 1.48 (d, 1H, 4.9 Hz), 1.42 (s, 18H), 1.33 (m, 1H, 12.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 79.6, 79.5, 54.9, 53.3, 50.3, 34.1, 33.1, 28.5, 27.6, 25.8. FT-IR vmax (cm^{-1}): (N-H) 3314, (C-H) 2977, (-C-H-) 2932, (-N=N=N) 2096, (C=O) 1682, (N-H) 1515, (C-O) 1162. MS(ESI+) [M+Na]+: m/z calcd for $C_{17}H_{31}N_5NaO_4$: 392.2, found: 392.0.

(*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediammonium dihydrochloride



4M HCl in dioxane (5 mL, 20.0 mmol) was added to (*1R, 2R, 4S*) di-*tert*-butyl 4-methylazido-1,2-dicarbamatecyclohexane (2.0 g, 5.4 mmol) in anhydrous dichloromethane (10 mL). The reaction mixture was stirred at room temperature overnight and the resulting precipitate isolated by vacuum filtration. The solid was washed with anhydrous dichloromethane and dried overnight under vacuum, to yield (*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediammonium dihydrochloride as a white powder (1.0 g , 73%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.68 (s, 6H), 3.56-3.38 (m, 2H), 3.33-3.29 (m, 2H), 2.05 (s, 1H), 1.99-1.89 (m, 2H), 1.76-1.73 (m, 2H), 1.58-1.46 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 53.4, 49.1, 47.1, 30.5, 28.2, 22.9, 22.7. FT-IR vmax (cm^{-1}): (N-H) 2818, (-N=N=N) 2095, 1585 1519, 1492, 1268, 1017. MS(ESI+) [M2Cl+H]+:m/z calcd for $C_7H_{16}N_5$: 170.1, found: 170.0.

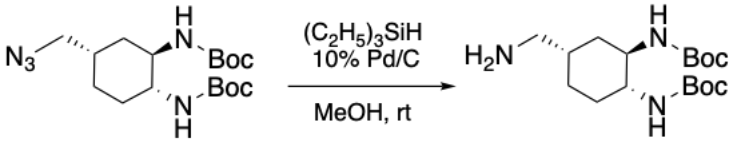
Complete synthetic route of **3**



3

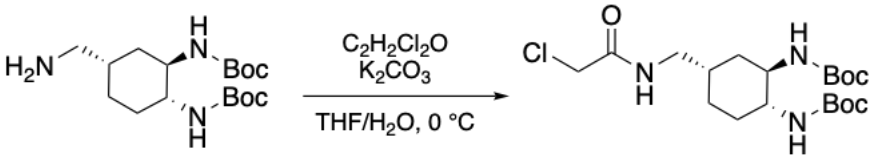
Synthetic procedure up until (*1R, 2R, 4S*) di-*tert*-butyl 4-methylazido-1,2-dicarbamatecyclohexane from **2**, was followed in the synthesis of **3**.

(*1R, 2R, 4S*) di-*tert*-butyl 4-methylamino-1,2-dicarbamatecyclohexane



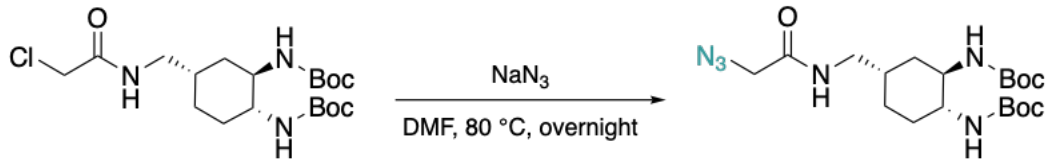
(*1R, 2R, 4S*) di-*tert*-butyl 4-methylazido-1,2-dicarbamatecyclohexane (2.6 g, 7.0 mmol) was dissolved in methanol (100 mL) and 10% Pd/C (0.3 g, 10% wt.) added under an argon atmosphere. To this was added triethylsilane (11 mL, 70.4 mmol) and the resulting mixture stirred at room temperature overnight. The next day, the flask was purged and refilled with Ar. The Pd/C was then separated off by filtering through celite and the solvent removed from the filtrate under reduced pressure. The resulting residue was purified by column chromatography (90: 10 dichloromethane: methanol + 2 drops NH_4OH) to give (*1R, 2R, 4S*) di-*tert*-butyl 4-methylamino-1,2-dicarbamatecyclohexane as a white solid. (1.9 g, 79%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 (d, 1H, 7.8 Hz), 4.86 (d, 1H, 7.8 Hz) ,3.46-3.39 (m, 1H), 3.32-2.20 (m, 1H), 2.77-2.65 (m, 2H), 1.97 (d, 1H, 13.2 Hz), 1.85-1.81 (m, 1H), 1.75 (s, 1H), 1.67 (d, 1H, 13.2 Hz), 1.57-1.44 (m, 4H), 1.41 (s, 18H), 1.35-1.30 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 79.4, 55.1, 50.6, 43.6, 36.6, 34.2, 28.5, 27.9, 26.2. FT-IR vmax (cm^{-1}): (N-H) 3319, (C-H) 2976, (C-H) 2934, (C-H) 2866, (C=O) 1699, (C=O) 1675, (N-H) 1511, (C-O) 1162. MS(ESI+) [M+H]+: m/z calcd for $C_{17}H_{34}N_3O_4$, calc.: 344.3, found: 344.0.

(*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(1-chloromethylamido)-1,2-dicarbamatecyclohexane



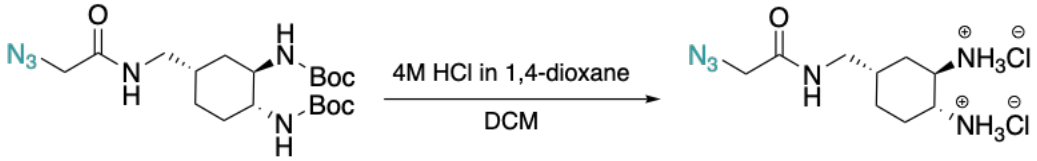
(*1R, 2R, 4S*) di-*tert*-butyl 4-methylamino-1,2-dicarbamatecyclohexane (2.5 g, 7.3 mmol) was dissolved in THF (30 mL) and added to a solution of potassium carbonate (4.0 g, 29.1 mmol) in water (10 mL). This mixture was placed in an ice bath and cooled to 0 °C. After stirring at 0 °C for 10 minutes, chloroacetyl chloride (2 mL , 21.8 mmol) in THF (5 mL) was added dropwise and the resulting mixture stirred at 0 °C for 2 hours. The reaction mixture was then allowed to warm to room temperature and the mixture extracted with ethyl acetate (3 x 50 mL). The organic layers were combined and washed with citric acid (5% w/v, 2 x 50 mL), sodium carbonate (sat. solution, 2 x 50 mL) and brine (2 x 25 mL). The organic layer was dried over anhydrous sodium sulfate and the solvent removed under reduced pressure to give (*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(1-chloromethylamido)-1,2-dicarbamatecyclohexane as a white solid that was used without further purification. (2.0 g , 66%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73 (s, 1H), 4.91 (m, 2H), 4.05 (s, 2H), 3.56-3.51 (m, 2H), 3.34-3.32 (m, 1H), 3.20-3.14 (m, 1H), 2.01 (s, 1H), 1.91-1.83 (m, 3H), 1.61-1.49 (m, 3H), 1.41 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 156.4, 79.5, 54.6, 50.6, 42.8, 41.3, 34.3, 33.2, 28.5, 27.6, 25.9. FT-IR vmax (cm^{-1}): (N-H) 3293, (C-H) 2976, (C-H) 2932, (C=O) 1698, (C=O) 1657, (N-H) 1530, (C-O) 1167. MS(ESI+) [M+Na]+: m/z calcd for $C_{19}H_{34}ClN_3NaO_5$.: 442.2, found: 442.2.

(*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(1-azidomethylamido)-1,2-dicarbamatecyclohexane



(*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(1-chloromethylamido)-1,2-dicarbamatecyclohexane (2.0 g, 4.8 mmol) was dissolved in anhydrous N,N-dimethylformamide (10 mL) under an argon atmosphere. To this was added sodium azide (1.2 g, 19.1 mmol) and the resulting mixture heated to 80 °C and left to stir overnight. dI water (30 mL) was then added to the reaction mixture and the product extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, washed with brine (4 x 50 mL) and dried over anhydrous sodium sulfate. The solvent was then removed under reduced pressure and the product purified by column chromatography (80: 20 ethyl acetate: petroleum ether) to give (*1R, 2R, 4S*) di-*tert*-butyl 4- methyl(1-azidomethylamido)-1,2-dicarbamatecyclohexane as a white solid. (1.5 g, 76%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (s, 1H), 4.91 (dd, 2H, 14.7, 7.9 Hz), 3.99 (s, 2H), 3.56-3.44 (m, 2H), 3.34-3.32 (m, 1H), 3.17-3.11 (m, 1H), 2.00 (s, 1H), 1.92-1.83 (m, 3H), 1.57-1.48 (m, 3H), 1.41 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 156.5, 156.4, 79.6, 54.5, 52.9, 50.7, 40.8, 34.2, 33.1, 28.5, 28.5, 26.0. FT-IR vmax (cm^{-1}): (N-H) 3305, (C-H) 2977, (C-H) 2932, (-N=N=N) 2104, (C=O) 1697, (C=O) 1661, (N-H) 1523, (C-O) 1166. MS(ESI+) [M+Na]+: m/z calcd for $C_{19}H_{34}N_6NaO_5$: 449.2, found: 448.9.

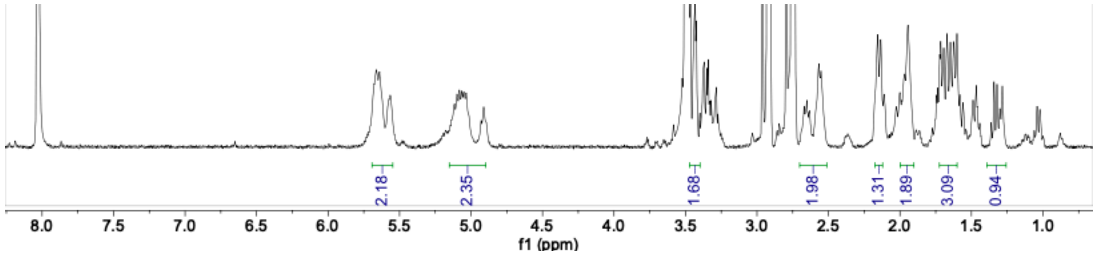
(*1R, 2R, 4S*) 4-methyl(1-azidomethylamido)-1,2-cyclohexaneammonium dihydrochloride



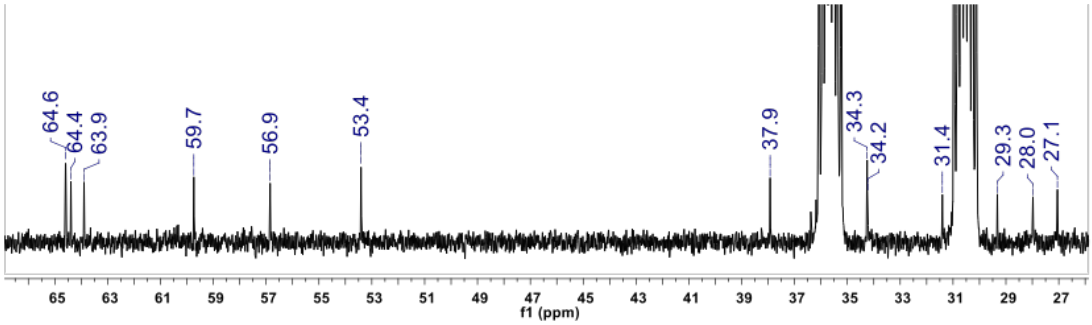
4M HCl in dioxane (9 mL, 35.2 mmol) was added to (*1R, 2R, 4S*) di-*tert*-butyl 4-methyl(1- azidomethylamido)-1,2-dicarbamatecyclohexane (1.5 g, 3.5 mmol) in anhydrous dichloromethane (10 mL). The reaction mixture was stirred at room temperature for 3 hours and the precipitated solid, isolated by vacuum filtration. The white solid was washed with anhydrous dichloromethane and dried overnight under vacuum, to yield (*1R, 2R, 4S*) 4-methyl(1-azidomethylamido)-1,2-cyclohexaneammonium dihydrochloride as a light-yellow powder (0.9 g , 85%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.66 (s, 6H), 8.38 (t, 1H, 5.6 Hz), 3.85 (s, 2H), 3.49 (s, 1H), 3.33 (s, 1H), 3.14-3.00 (m, 2H), 1.91-1.88 (m, 3H), 1.75-1.64 (m, 2H), 1.58-1.53 (m, 1H), 1.45-1.39 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.5, 50.7, 49.7, 47.5, 40.9, 30.8, 29.0, 23.3, 23.1. FT-IR ν_{max} (cm^{-1}): (N-H) 2849, (-N=N=N) 2116, 1592, 1558, 1509, 1414, 1130, 1034. MS (ESI+) [M-2Cl+H]+: m/z calcd for $C_9H_{19}N_6O$: 227.2, found: 227.0.

*SI NMR **1**, **2**, and **3** (^{1}H, ^{13}C, ^{195}Pt) DMF-d_7*

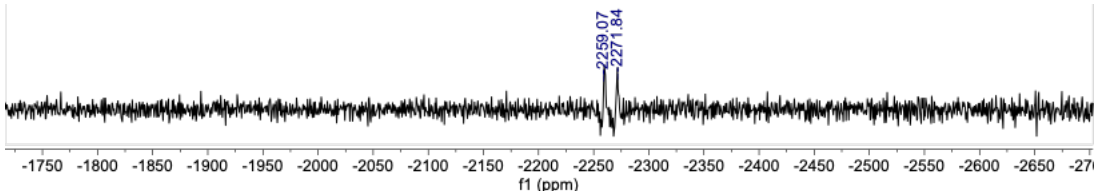
^{1}H NMR of **1**



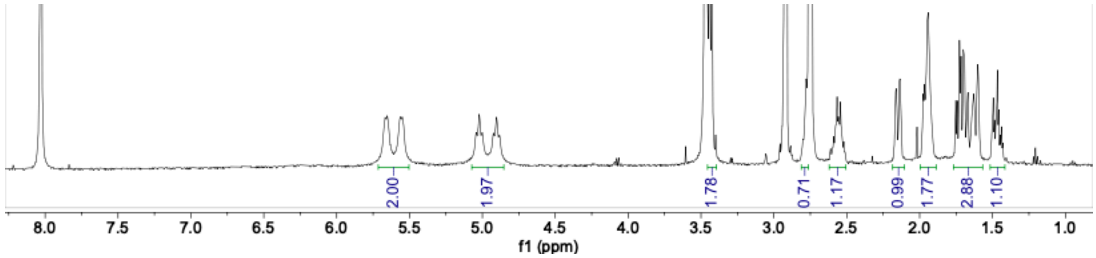
^{13}C NMR of **1**



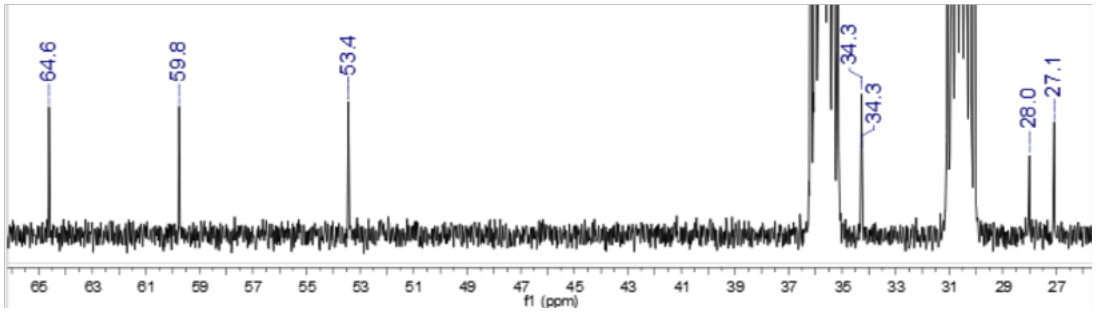
^{195}Pt NMR of **1**



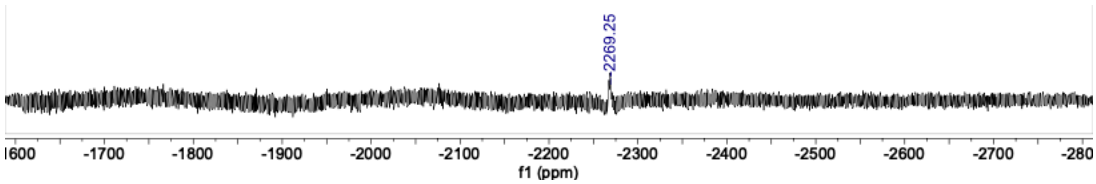
^{1}H NMR of **2**



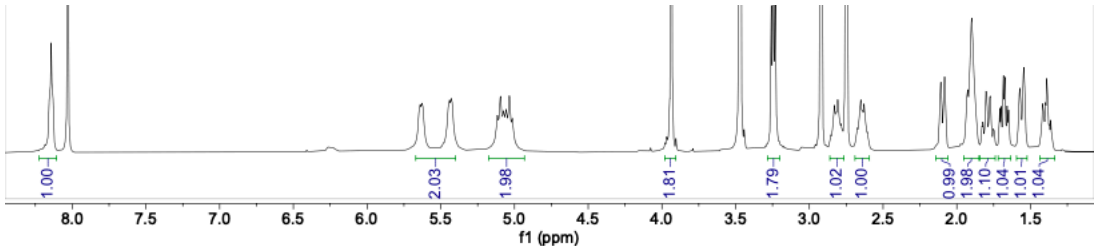
^{13}C NMR of **2**



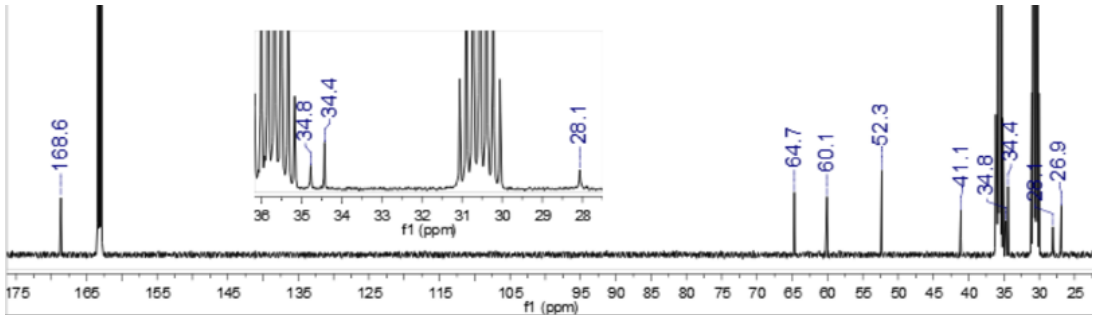
^{195}Pt NMR of **2**



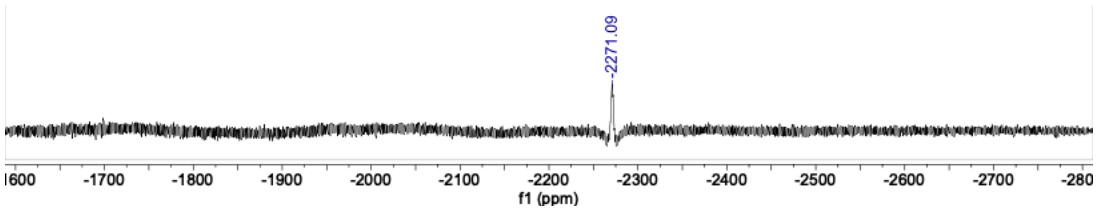
^{1}H NMR of **3**



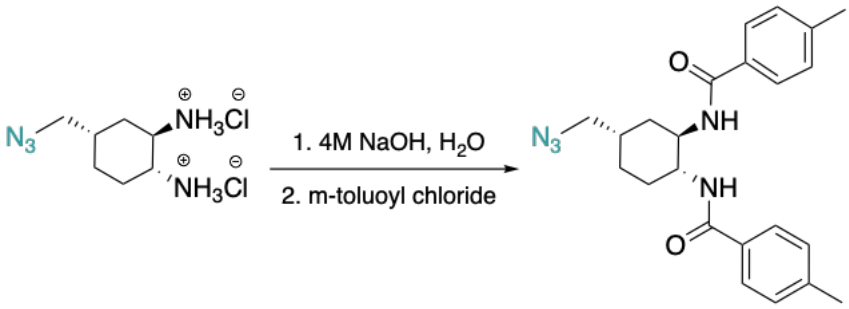
^{13}C NMR of **3**



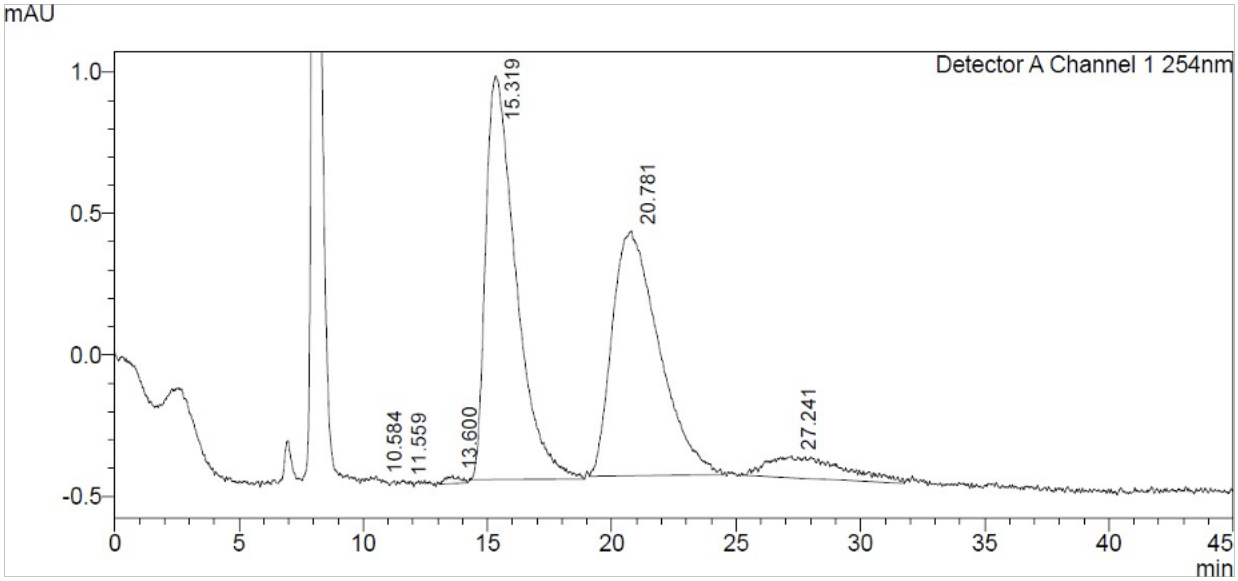
^{195}Pt NMR of **3**



*Chiral HPLC – ligand of **2** (1R, 2R, 4S) and (1R, 2R, 4S)/(1S, 2S, 4R)*

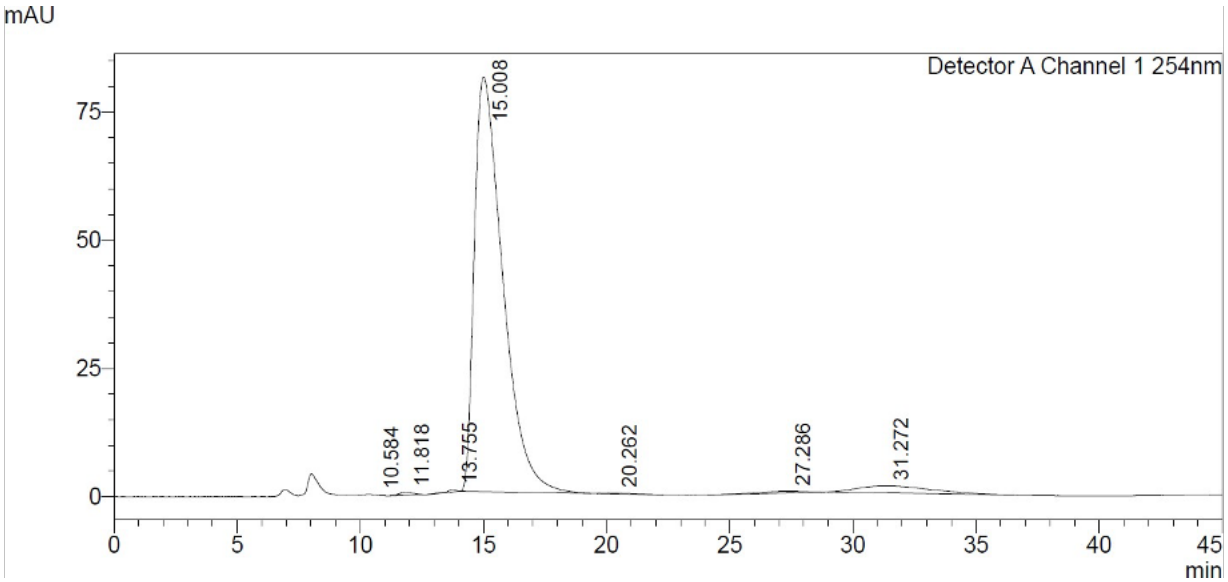


4M aqueous NaOH (80 µL, 0.3 mmol) was added to a suspension of (*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediaminium dihydrochloride (0.02 g, 0.1 mmol) in dichloromethane (2 mL) in a vial (shaken for 1 minute). *m*-toluoyl chloride (42 µL, 0.3 mmol) was then added and shaken at room temperature for 1 minute. The layers were separated and a portion (0.1 mL) was taken from the organic layer and added to *i*-PrOH (1.5 mL). Samples were analyzed by HPLC (Shimadzu SIL-20AHT HPLC instrument) using a CHIRALCEL OD-H column; size: 250 x 4.6 mm, I.D. particle size: 5 µm, detection method: UV-Vis wavelength for detection: 254 nm. Eluent: n-Hexane: isopropanol = 95:5 with 0.5 ml/min flow rate, oven temperature of 10 °C and injection volume of 5 µL. (1*R, 2R, 4S*)- isomer retention time = 15.008 min; (1*S, 2S, 4R*)- isomer retention time = 20.781 min.



Peak #	Ret. Time	Area	Height	Peak % Area
1	10.584	0	0	0 %
2	11.559	0	0	0 %
3	13.600	1043	30	0.4 %
4	15.319	121278	1429	48.1 %
5	20.781	113474	867	45.0 %
6	27.241	16273	78	6.5%
Total		252068	2403	100%

Figure S6. Chiral HPLC chromatogram for mixed isomer (*1R, 2R, 4S*)/(*1S, 2S, 4R*) HPLC derivative. Peak at 8.1 min corresponds to unreacted *m*-toluoyl chloride**.**

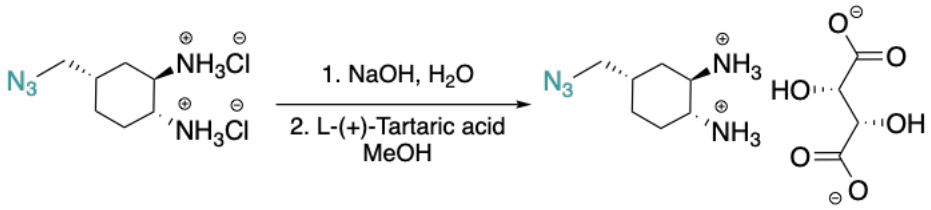


Peak #	Ret. Time	Area	Height	Peak % Area
1	10.584	0	0	0 %
2	10.818	22402	521	0.3 %
3	13.755	10282	298	0.1 %
4	15.008	6489677	80812	94.5 %
5	20.262	10983	110	0.2 %
6	27.286	45414	337	0.7 %
7	31.272	286285	1354	4.2%
Total		6865043	83533	100%

Figure S7. Chiral HPLC chromatogram for (*1R, 2R, 4S*)-HPLC derivative. Peak at 8.1 min corresponds to unreacted *m*-toluoyl chloride.

*Crystal structures of ligand and derivative of **2***

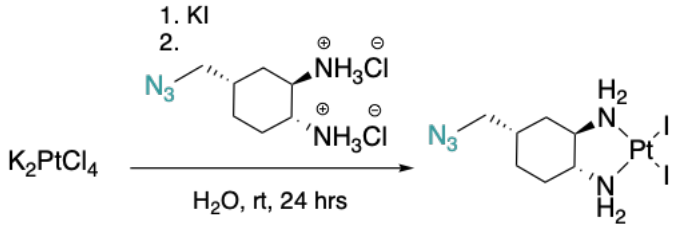
(*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediammonium-L-(+)-tartrate



(*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediammonium dihydrochloride (1.5 g, 6.2 mmol) was dissolved in dichloromethane (40 mL). To this was added sodium hydroxide solution (10% w/v) until a pH of 12 was reached. The reaction mixture was then stirred for 15 minutes. Following stirring, the mixture was diluted with dI water (10 mL) and the product extracted using ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous sodium sulphate and the solvent removed under vacuum. The resulting residue was dissolved in methanol and L-(+)-tartaric acid (1.1 g, 7.4 mmol) added. This mixture was stirred for 30 minutes at room temperature, resulting in the formation of a precipitate. This precipitate was isolated by vacuum filtration and dried overnight under vacuum to yield (*1R, 2R, 4S*) 4-methylazido- 1,2-cyclohexanediaminium-L-(+)-tartrate as a white solid (1.8 g, 90%). The product could be recrystallized in a water/methanol mixture to increase diastereomeric purity of the compound. ^{1}H NMR (400 MHz, D_2O): δ 4.32 (s, 2H), 3.65 (td, 1H, 8.4, 4.4 Hz), 3.54 (td, 1H, 8.3, 4.1 Hz), 3.44- 3.39 (m, 2H), 2.15-2.13 (m, 1H), 2.10-2.02 (m, 2H), 1.91-1.65 (m, 4H). ^{13}C NMR (100 MHz, D_2O): δ 179.1, 74.5, 53.7, 51.0, 48.7, 31.5, 29.8, 24.3, 23.9. FT-IR vmax (cm^{-1}): (OH) 3393, (C-H) 2938, (-N=N=N) 2090, 1639, 1563, 1506, 1389, 1109. MS(ESI+) [M-$C_4H_4O_6$+H]+: m/z calcd for $C_7H_{16}N_5$: 170.1, found: 170.0.

Single crystals suitable for X-ray crystallography were isolated through recrystallisation of (*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediaminium-L-(+)-tartrate) in a water/methanol mixture at 4 °C.

(*1R, 2R,* 4S) 4-methylazidoDACH-Pt-I_2

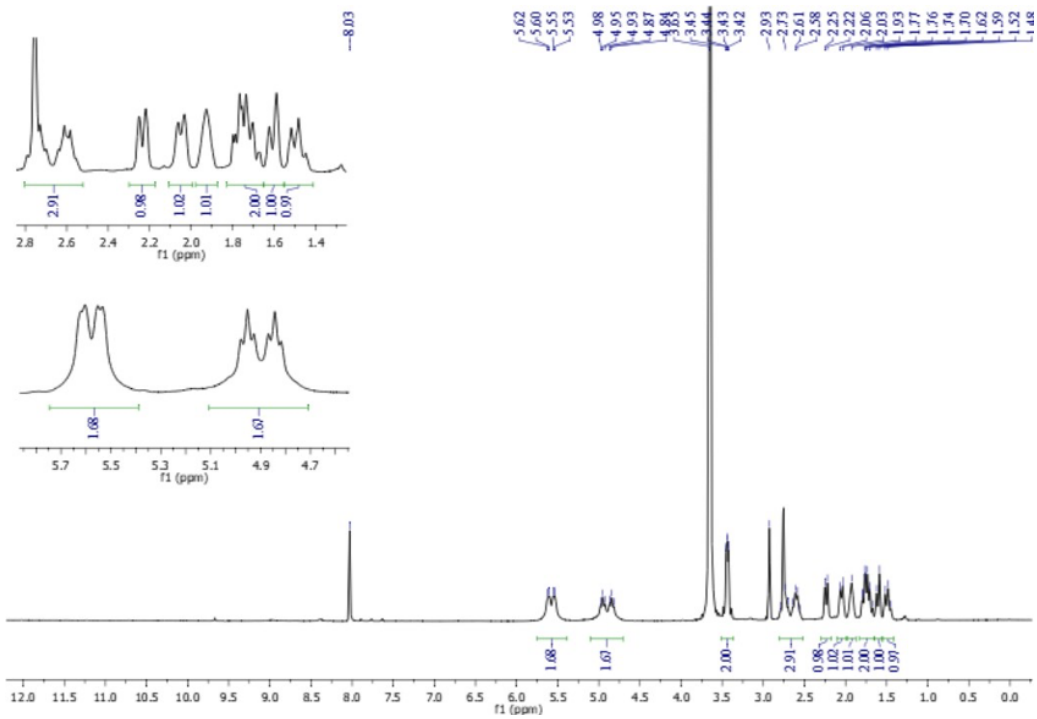


Potassium tetrachloroplatinate (0.8 g, 1.9 mmol) was dissolved in dI water (40 mL). To this was added a solution of potassium iodide (1.2 g, 7.3 mmol) in dI water (15 mL). The reaction mixture was stirred in the dark at room temperature for 15 minutes. Following stirring, a solution of (*1R, 2R, 4S*) 4-methylazido-1,2-cyclohexanediammonium dihydrochloride (0.5 g, 1.9 mmol) in dI water (10 mL) was added to the reaction mixture. The pH of the mixture was adjusted to ca. 7 using 10% sodium hydroxide solution and the resulting solution stirred in the dark at room temperature for 24 hours. The resulting precipitate was isolated by vacuum filtration, washed with dI water and dried overnight under vacuum to yield (*1R, 2R, 4S*) 4-methylazidoDACH-Pt-I_2 (derivative of **2**) as a light-yellow powder (0.8 g, 70%). ^{1}H NMR (400 MHz, DMF-d_7): δ 5.62-

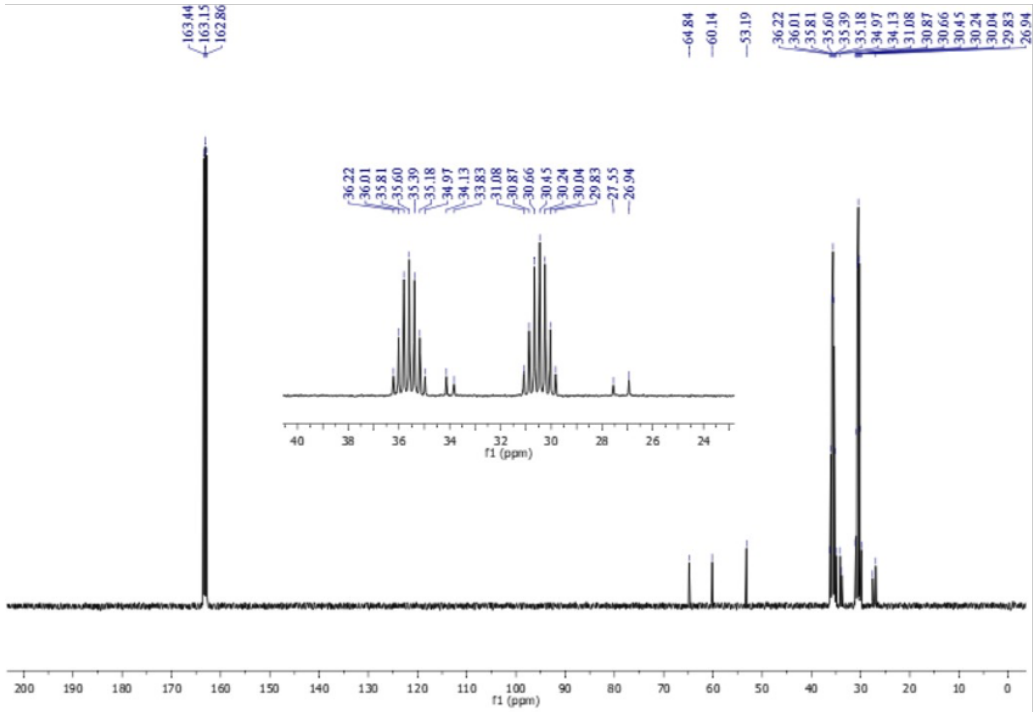
5.53 (m, 2H), 4.98-4.84 (m, 2H), 3.45-3.42 (m, 2H), 2.79-2.56 (m, 2H), 2.24 (d, 1H, 12.6 Hz), 2.05 (d, 1H, 11.3 Hz), 1.93 (s, 1H), 1.80-1.68 (m, 2H), 1.61 (d, 1H, 13.8 Hz), 1.52-1.45 (m, 1H). ^{13}C NMR (100 MHz, DMF-d_7): δ 64.8, 60.1, 53.2, 34.1, 33.8, 27.6, 26.9. FT-IR vmax (cm-1): (N-H) 3245, (N-H) 3184, (C-H) 2930, (C-H) 2863, (N=N=N) 2092, (N-H) 1553, 742.

Single crystals suitable for X-ray crystallography were isolated on leaving a saturated solution of (*1R, 2R, 4S*) 4-methylazidoDACH-Pt-I_2 in DMF with diethyl ether via slow vapor diffusion at room temperature.

^{1}H NMR of 4-methylazidoDACH-Pt-I_2 (derivative of **2**) in DMF-d_7



^{13}C NMR of 4-methylazidoDACH-Pt-I_2 (derivative of **2**) in DMF-d_7



*Properties of X-ray Crystal Structure of (L)-(+)-tartrate salt ligand of **2***

Table S1. Crystal data and structure refinement for the X-ray Crystal Structure of (L)-(+)-tartrate salt ligand of **2**

Identification code	tcd1762
Empirical formula	$C_{11.50}H_{25.30}N_5O_{7.65}$
Formula Weight	356.07
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	a = 18.1460(8) Å □= 90° b = 6.3721(3) Å □= 117.203(2)°. c = 16.6518(7) Å □ = 90°
Volume	1712.45(13) Å^3
Z	4
Density (calculated)	1.381 Mg/m^3
Absorption coefficient	0.991 mm^{-1}
E(000)	762
Crystal Size	0.36 x 0.1 x 0.05 mm^3
Theta range for data collection	2.984 to 70.060°
Index ranges	-22≤h≤22, -7≤k≤7, -20≤l≤20
Reflections collected	25857
Independent reflections	2878 [R(int) = 0.0645]
Completeness to theta = 67.679°	99.5 %
Absorption coefficient	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.5828
Refinement method	Full-matrix least-squares on F^2
Data/ restraints/ parameters	2878 / 35 / 259
Goodness-of-fit on F^2	1.070
Final R indices [I>2σ(I)]	R1 = 0.0678, wR2 = 0.1827
R indices (all data)	R1 = 0.0702, wR2 = 0.1863
Absolute structure parameter	0.1(4)
Largest diff. peak and hole	0.341 and -0.237 e.Å^{-3}

Table S2. Bond lengths [Å] and angles [°] for the X-ray Crystal Structure of (L)-(+)-tartrate salt ligand of **2**

C(4)-H(4A)	0.9900	C(9)-C(7)-C(6)	110.5(3)
C(4)-H(4B)	0.9900	C(9)-C(7)-H(7)	108.4
C(4)-C(5)	1.533(7)	N(8)-C(7)-C(6)	108.8(3)
C(4)-N(3)	1.489(7)	N(8)-C(7)-H(7)	108.4
C(5)-H(5)	1.0000	N(8)-C(7)-C(9)	112.3(3)
C(5)-C(6)	1.528(6)	C(7)-C(9)-H(9)	108.9
C(5)-C(12)	1.524(7)	C(11)-C(9)-C(7)	109.2(3)
C(6)-H(6A)	0.9900	C(11)-C(9)-H(9)	108.9
C(6)-H(6B)	0.9900	N(10)-C(9)-C(7)	111.5(3)

C(6)-C(7)	1.529(5)	N(10)-C(9)-H(9)	108.9
C(7)-H(7)	1.0000	N(10)-C(9)-C(11)	109.3(3)
C(7)-C(9)	1.527(5)	C(9)-C(11)-H(11A)	109.3
C(7)-N(8)	1.493(5)	C(9)-C(11)-H(11B)	109.3
C(9)-H(9)	1.0000	C(9)-C(11)-C(12)	111.7(4)
C(9)-C(11)	1.519(5)	H(11A)-C(11)-H(11B)	107.9
C(9)-N(10)	1.491(5)	C(12)-C(11)-H(11A)	109.3
C(11)-H(11A)	0.9900	C(12)-C(11)-H(11B)	109.3
C(11)-H(11B)	0.9900	C(5)-C(12)-C(11)	112.1(3)
C(11)-C(12)	1.531(6)	C(5)-C(12)-H(12A)	109.2
C(12)-H(12A)	0.9900	C(5)-C(12)-H(12B)	109.2
C(12)-H(12B)	0.9900	C(11)-C(12)-H(12A)	109.2
N(1)-N(2)	1.134(9)	C(11)-C(12)-H(12B)	109.2
N(2)-N(3)	1.224(8)	H(12A)-C(12)-H(12B)	107.9
N(8)-H(8A)	0.9100	N(1)-N(2)-N(3)	171.0(8)
N(8)-H(8B)	0.9100	N(2)-N(3)-C(4)	114.5(6)
N(8)-H(8C)	0.9100	C(7)-N(8)-H(8A)	109.5
N(10)-H(10A)	0.9100	C(7)-N(8)-H(8B)	109.5
N(10)-H(10B)	0.9100	C(7)-N(8)-H(8C)	109.5
N(10)-H(10C)	0.9100	H(8A)-N(8)-H(8B)	109.5
C(15)-C(16)	1.531(5)	H(8A)-N(8)-H(8C)	109.5
C(15)-O(13)	1.260(5)	H(8B)-N(8)-H(8C)	109.5
C(15)-O(14)	1.258(5)	C(9)-N(10)-H(10A)	109.5
C(16)-H(16)	1.0000	C(9)-N(10)-H(10B)	109.5
C(16)-C(18)	1.521(5)	C(9)-N(10)-H(10C)	109.5
C(16)-O(17)	1.426(5)	H(10A)-N(10)-H(10B)	109.5
C(18)-H(18)	1.0000	H(10B)-N(10)-H(10C)	109.5
C(18)-C(20)	1.532(5)	O(13)-C(15)-C(16)	118.9(4)
C(18)-O(19)	1.413(5)	O(14)-C(15)-C(16)	116.5(3)
C(20)-O(21)	1.256(5)	O(14)-C(15)-O(13)	124.7(4)
C(20)-O(22)	1.254(5)	C(15)-C(16)-H(16)	109.1
O(17)-H(17)	0.879(14)	C(18)-C(16)-C(15)	110.5(3)
O(19)-H(19)	0.881(14)	C(18)-C(16)-H(16)	109.1
C(25)-H(25A)	0.9800	O(17)-C(16)-C(15)	112.7(3)
C(25)-H(25B)	0.9800	O(17)-C(16)-H(16)	109.1

C(25)-H(25C)	0.9800	O(17)-C(16)-C(18)	106.2(3)
C(25)-O(24)	1.431(12)	C(16)-C(18)-H(18)	108.7
O(24)-H(24)	0.8400	C(16)-C(18)-C(20)	109.5(3)
C(27)-H(27A)	0.9800	C(20)-C(18)-H(18)	108.7
C(27)-H(27B)	0.9800	O(19)-C(18)-C(16)	110.1(3)
C(27)-H(27C)	0.9800	O(19)-C(18)-H(18)	108.7
C(27)-O(26)	1.451(12)	O(19)-C(18)-C(20)	111.0(3)
O(26)-H(26)	0.8400	O(21)-C(20)-C(18)	116.6(3)
O(23)-H(23A)	0.8715	O(22)-C(20)-C(18)	117.7(4)
O(23)-H(23B)	0.8720	O(22)-C(20)-O(21)	125.8(4)
O(28)-H(28A)	0.9830	C(16)-O(17)-H(17)	112(4)
O(28)-H(28B)	0.9830	C(18)-O(19)-H(19)	109(5)
		H(25A)-C(25)-H(25B)	109.5
H(4A)-C(4)-H(4B)	107.9	H(25A)-C(25)-H(25C)	109.5
C(5)-C(4)-H(4A)	109.2	H(25B)-C(25)-H(25C)	109.5
C(5)-C(4)-H(4B)	109.2	O(24)-C(25)-H(25A)	109.5
N(3)-C(4)-H(4A)	109.2	O(24)-C(25)-H(25B)	109.5
N(3)-C(4)-H(4B)	109.2	O(24)-C(25)-H(25C)	109.5
N(3)-C(4)-C(5)	112.0(4)	C(25)-O(24)-H(24)	109.5
C(4)-C(5)-H(5)	107.4	H(27A)-C(27)-H(27B)	109.5
C(6)-C(5)-C(4)	111.3(4)	H(27A)-C(27)-H(27C)	109.5
C(6)-C(5)-H(5)	107.4	H(27B)-C(27)-H(27C)	109.5
C(12)-C(5)-C(4)	112.6(4)	O(26)-C(27)-H(27A)	109.5
C(12)-C(5)-H(5)	107.4	O(26)-C(27)-H(27B)	109.5
C(12)-C(5)-C(6)	110.4(4)	O(26)-C(27)-H(27C)	109.5
C(5)-C(6)-H(6A)	109.2	C(27)-O(26)-H(26)	109.5
C(5)-C(6)-H(6B)	109.2	H(23A)-O(23)-H(23B)	104.2
C(5)-C(6)-C(7)	112.1(3)	H(28A)-O(28)-H(28B)	116.1
H(6A)-C(6)-H(6B)	107.9		
C(7)-C(6)-H(6A)	109.2		
C(7)-C(6)-H(6B)	109.2		
C(6)-C(7)-H(7)	108.4		

Table S3. Torsion angles [°] for the X-ray Crystal Structure of (L)-(+)-tartrate salt ligand of **2**

C(4)-C(5)-C(6)-C(7)	-71.8(5)	N(8)-C(7)-C(9)-N(10)	-58.9(4)

C(4)-C(5)-C(12)-C(11)	72.5(5)	N(10)-C(9)-C(11)-C(12)	-179.9(3)
C(5)-C(4)-N(3)-N(2)	55.4(7)	C(15)-C(16)-C(18)-C(20)	176.7(3)
C(5)-C(6)-C(7)-C(9)	-57.6(4)	C(15)-C(16)-C(18)-O(19)	54.4(4)
C(5)-C(6)-C(7)-N(8)	178.6(3)	C(16)-C(18)-C(20)-O(21)	-116.7(4)
C(6)-C(5)-C(12)-C(11)	-52.6(5)	C(16)-C(18)-C(20)-O(22)	62.9(5)
C(6)-C(7)-C(9)-C(11)	58.4(4)	O(13)-C(15)-C(16)-C(18)	-118.0(4)
C(6)-C(7)-C(9)-N(10)	179.4(3)	O(13)-C(15)-C(16)-O(17)	0.6(5)
C(7)-C(9)-C(11)-C(12)	-57.6(4)	O(14)-C(15)-C(16)-C(18)	61.7(5)
C(9)-C(11)-C(12)-C(5)	55.6(5)	O(14)-C(15)-C(16)-O(17)	-179.6(3)
C(12)-C(5)-C(6)-C(7)	54.0(5)	O(17)-C(16)-C(18)-C(20)	54.2(4)
N(3)-C(4)-C(5)-C(6)	-174.0(4)	O(17)-C(16)-C(18)-O(19)	-68.1(4)
N(3)-C(4)-C(5)-C(12)	61.4(5)	O(19)-C(18)-C(20)-O(21)	5.1(5)
N(8)-C(7)-C(9)-C(11)	-179.9(3)	O(19)-C(18)-C(20)-O(22)	-175.3(3)

Properties of X-ray Crystal Structure of diiodo [Pt(DACH)(I_2)] analogue of **2**

Table S4. Crystal data and structure refinement for the X-ray crystal structure of diiodo [Pt(DACH)(I_2)] analogue of **2**

Identification code	tcd2011
Empirical formula	$C_{10}H_{22}I_2N_6OPt$
Formula Weight	691.22
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 8.4825(4) Å □= 112.2786(14)° b = 10.3937(5) Å □= 91.4077(16)°. c = 11.4784(5) Å □ = 108.8135(14)°
Volume	873.87(7) $Å^3$
Z	2
Density (calculated)	2.627 Mg/m^3
Absorption coefficient	11.567 mm^{-1}
E(000)	632
Crystal Size	0.222 x 0.134 x 0.11 mm^3
Theta range for data collection	2.268 to 30.748°.
Index ranges	-12≤h≤12, -14≤k≤14, -16≤l≤16
Reflections collected	36469
Independent reflections	10735 [R(int) = 0.0316]
Completeness to theta = 67.679°	100.0 %
Absorption coefficient	Semi-empirical from equivalents
Max. and min. transmission	0.1617 and 0.0518
Refinement method	Full-matrix least-squares on F^2
Data/ restraints/ parameters	10735 / 136 / 386

Goodness-of-fit on F^2	1.083
Final R indices [I>2σ(I)]	R1 = 0.0336, wR2 = 0.0720
R indices (all data)	R1 = 0.0394, wR2 = 0.0745
Absolute structure parameter	0.031(12)
Extinction Coefficient	0.0025(2)
Largest diff. peak and hole	1.862 and -2.078 e.$Å^{-3}$

Table S5. Bond lengths [Å] and angles [°] for the X-ray crystal structure of diiodo [Pt(DACH)$(I)_2$] analogue of **2**

Pt(1)-I(1)	2.5865(15)	C(7)-C(2)-H(2)	108.3
Pt(1)-I(2)	2.5914(14)	C(7)-C(2)-C(3)	109.8(10)
Pt(1)-N(1)	2.087(16)	C(2)-C(3)-H(3A)	109.4
Pt(1)-N(8)	2.058(17)	C(2)-C(3)-H(3B)	109.4
N(1)-H(1A)	0.9100	C(2)-C(3)-C(4)	111.1(13)
N(1)-H(1B)	0.9100	H(3A)-C(3)-H(3B)	108.0
N(1)-C(2)	1.498(19)	C(4)-C(3)-H(3A)	109.4
N(8)-H(8A)	0.9100	C(4)-C(3)-H(3B)	109.4
N(8)-H(8B)	0.9100	C(3)-C(4)-H(4A)	109.1
N(8)-C(7)	1.499(18)	C(3)-C(4)-H(4B)	109.1
N(10)-N(11)	1.182(19)	C(3)-C(4)-C(5)	112.6(11)
N(10)-C(9)	1.475(19)	H(4A)-C(4)-H(4B)	107.8
N(11)-N(12)	1.146(19)	C(5)-C(4)-H(4A)	109.1
C(2)-H(2)	1.0000	C(5)-C(4)-H(4B)	109.1
C(2)-C(3)	1.51(2)	C(4)-C(5)-H(5)	107.3
C(2)-C(7)	1.502(14)	C(4)-C(5)-C(6)	111.0(12)
C(3)-H(3A)	0.9900	C(4)-C(5)-C(9)	113.1(12)
C(3)-H(3B)	0.9900	C(6)-C(5)-H(5)	107.3
C(3)-C(4)	1.52(2)	C(6)-C(5)-C(9)	110.5(12)
C(4)-H(4A)	0.9900	C(9)-C(5)-H(5)	107.3
C(4)-H(4B)	0.9900	C(5)-C(6)-H(6A)	109.6
C(4)-C(5)	1.529(17)	C(5)-C(6)-H(6B)	109.6
C(5)-H(5)	1.0000	H(6A)-C(6)-H(6B)	108.1
C(5)-C(6)	1.53(2)	C(7)-C(6)-C(5)	110.4(13)
C(5)-C(9)	1.538(19)	C(7)-C(6)-H(6A)	109.6
C(6)-H(6A)	0.9900	C(7)-C(6)-H(6B)	109.6
C(6)-H(6B)	0.9900	N(8)-C(7)-C(2)	109.4(10)
C(6)-C(7)	1.51(2)	N(8)-C(7)-C(6)	111.9(11)

C(7)-H(7)	1.0000	N(8)-C(7)-H(7)	107.4
C(9)-H(9A)	0.9900	C(2)-C(7)-C(6)	112.9(11)
C(9)-H(9B)	0.9900	C(2)-C(7)-H(7)	107.4
Pt(2)-I(3)	2.5992(14)	C(6)-C(7)-H(7)	107.4
Pt(2)-I(4)	2.5894(14)	N(10)-C(9)-C(5)	113.3(12)
Pt(2)-N(13)	2.056(15)	N(10)-C(9)-H(9A)	108.9
Pt(2)-N(20)	2.039(15)	N(10)-C(9)-H(9B)	108.9
O(30)-C(31)	1.23(2)	C(5)-C(9)-H(9A)	108.9
N(13)-H(13A)	0.9100	C(5)-C(9)-H(9B)	108.9
N(13)-H(13B)	0.9100	H(9A)-C(9)-H(9B)	107.7
N(13)-C(14)	1.483(18)	I(4)-Pt(2)-I(3)	95.40(5)
N(20)-H(20A)	0.9100	N(13)-Pt(2)-I(3)	172.8(4)
N(20)-H(20B)	0.9100	N(13)-Pt(2)-I(4)	90.9(4)
N(20)-C(19)	1.488(19)	N(20)-Pt(2)-I(3)	90.9(4)
N(32)-C(31)	1.31(2)	N(20)-Pt(2)-I(4)	173.6(4)
N(32)-C(33)	1.47(2)	N(20)-Pt(2)-N(13)	82.9(6)
N(32)-C(34)	1.49(2)	Pt(2)-N(13)-H(13A)	109.8
C(14)-H(14)	1.0000	Pt(2)-N(13)-H(13B)	109.8
C(14)-C(15)	1.51(2)	H(13A)-N(13)-H(13B)	108.3
C(14)-C(19)	1.527(15)	C(14)-N(13)-Pt(2)	109.2(9)
C(15)-H(15A)	0.9900	C(14)-N(13)-H(13A)	109.8
C(15)-H(15B)	0.9900	C(14)-N(13)-H(13B)	109.8
C(15)-C(16)	1.51(2)	Pt(2)-N(20)-H(20A)	109.6
C(16)-H(16A)	0.9900	Pt(2)-N(20)-H(20B)	109.6
C(16)-H(16B)	0.9900	H(20A)-N(20)-H(20B)	108.1
C(16)-C(17)	1.531(19)	C(19)-N(20)-Pt(2)	110.5(9)
C(17)-H(17A)	1.0000	C(19)-N(20)-H(20A)	109.6
C(17)-H(17)	1.0000	C(19)-N(20)-H(20B)	109.6
C(17)-C(18)	1.54(2)	C(31)-N(32)-C(33)	122.9(15)
C(17)-C(21B)	1.52(3)	C(31)-N(32)-C(34)	121.6(16)
C(17)-C(21A)	1.52(2)	C(33)-N(32)-C(34)	115.4(14)
C(18)-H(18A)	0.9900	N(13)-C(14)-H(14)	108.6
C(18)-H(18B)	0.9900	N(13)-C(14)-C(15)	113.5(12)
C(18)-C(19)	1.53(2)	N(13)-C(14)-C(19)	106.5(10)
C(19)-H(19)	1.0000	C(15)-C(14)-H(14)	108.6

C(31)-H(31)	0.9500	C(15)-C(14)-C(19)	110.8(12)
C(33)-H(33A)	0.9800	C(19)-C(14)-H(14)	108.6
C(33)-H(33B)	0.9800	C(14)-C(15)-H(15A)	109.4
C(33)-H(33C)	0.9800	C(14)-C(15)-H(15B)	109.4
C(34)-H(34A)	0.9800	H(15A)-C(15)-H(15B)	108.0
C(34)-H(34B)	0.9800	C(16)-C(15)-C(14)	111.2(15)
C(34)-H(34C)	0.9800	C(16)-C(15)-H(15A)	109.4
C(21B)-H(21A)	0.9900	C(16)-C(15)-H(15B)	109.4
C(21B)-H(21B)	0.9900	C(15)-C(16)-H(16A)	108.9
N(13)-H(13A)	0.9100	C(15)-C(16)-H(16B)	108.9
N(13)-H(13B)	0.9100	C(15)-C(16)-C(17)	113.5(12)
N(13)-C(14)	1.483(18)	H(16A)-C(16)-H(16B)	107.7
N(20)-H(20A)	0.9100	C(17)-C(16)-H(16A)	108.9
N(20)-H(20B)	0.9100	C(17)-C(16)-H(16B)	108.9
N(20)-C(19)	1.488(19)	C(16)-C(17)-H(17A)	107.1
N(32)-C(31)	1.31(2)	C(16)-C(17)-H(17)	107.4
N(32)-C(33)	1.47(2)	C(16)-C(17)-C(18)	111.5(12)
N(32)-C(34)	1.49(2)	C(18)-C(17)-H(17A)	107.1
C(14)-H(14)	1.0000	C(18)-C(17)-H(17)	107.4
C(14)-C(15)	1.51(2)	C(21B)-C(17)-C(16)	117(5)
C(14)-C(19)	1.527(15)	C(21B)-C(17)-H(17)	107.4
C(15)-H(15A)	0.9900	C(21B)-C(17)-C(18)	106(4)
C(15)-H(15B)	0.9900	C(21A)-C(17)-C(16)	111(2)
C(15)-C(16)	1.51(2)	C(21A)-C(17)-H(17A)	107.1
C(16)-H(16A)	0.9900	C(21A)-C(17)-C(18)	112.6(17)
C(16)-H(16B)	0.9900	C(17)-C(18)-H(18A)	109.7
C(16)-C(17)	1.531(19)	C(17)-C(18)-H(18B)	109.7
C(17)-H(17A)	1.0000	H(18A)-C(18)-H(18B)	108.2
C(17)-H(17)	1.0000	C(19)-C(18)-C(17)	109.9(13)
C(17)-C(18)	1.54(2)	C(19)-C(18)-H(18A)	109.7
C(17)-C(21B)	1.52(3)	C(19)-C(18)-H(18B)	109.7
C(17)-C(21A)	1.52(2)	N(20)-C(19)-C(14)	107.9(9)
C(18)-H(18A)	0.9900	N(20)-C(19)-C(18)	113.3(11)
C(18)-H(18B)	0.9900	N(20)-C(19)-H(19)	108.1
C(18)-C(19)	1.53(2)	C(14)-C(19)-C(18)	111.3(11)

C(19)-H(19)	1.0000	C(14)-C(19)-H(19)	108.1
C(31)-H(31)	0.9500	C(18)-C(19)-H(19)	108.1
C(33)-H(33A)	0.9800	O(30)-C(31)-N(32)	125.3(16)
C(33)-H(33B)	0.9800	O(30)-C(31)-H(31)	117.3
C(33)-H(33C)	0.9800	N(32)-C(31)-H(31)	117.3
C(34)-H(34A)	0.9800	N(32)-C(33)-H(33A)	109.5
C(34)-H(34B)	0.9800	N(32)-C(33)-H(33B)	109.5
C(34)-H(34C)	0.9800	N(32)-C(33)-H(33C)	109.5
C(21B)-H(21A)	0.9900	H(33A)-C(33)-H(33B)	109.5
C(21B)-H(21B)	0.9900	H(33A)-C(33)-H(33C)	109.5
C(21B)-N(22B)	1.4671	H(33B)-C(33)-H(33C)	109.5
N(22B)-N(23B)	1.1816	N(32)-C(34)-H(34A)	109.5
N(23B)-N(24B)	1.1461	N(32)-C(34)-H(34B)	109.5
C(21A)-H(21C)	0.9900	N(32)-C(34)-H(34C)	109.5
C(21A)-H(21D)	0.9900	H(34A)-C(34)-H(34B)	109.5
C(21A)-N(22A)	1.4669	H(34A)-C(34)-H(34C)	109.5
N(22A)-N(23A)	1.1818	H(34B)-C(34)-H(34C)	109.5
N(23A)-N(24A)	1.1464	C(17)-C(21B)-H(21A)	109.6
O(25)-C(26)	1.22(3)	C(17)-C(21B)-H(21B)	109.6
N(27)-C(26)	1.30(2)	H(21A)-C(21B)-H(21B)	108.1
N(27)-C(28)	1.44(2)	N(22B)-C(21B)-C(17)	110(6)
N(27)-C(29)	1.42(3)	N(22B)-C(21B)-H(21A)	109.6
C(26)-H(26)	0.9500	N(22B)-C(21B)-H(21B)	109.6
C(28)-H(28A)	0.9800	N(23B)-N(22B)-C(21B)	116.6
C(28)-H(28B)	0.9800	N(24B)-N(23B)-N(22B)	172.0
C(28)-H(28C)	0.9800	C(17)-C(21A)-H(21C)	108.5
C(29)-H(29A)	0.9800	C(17)-C(21A)-H(21D)	108.5
C(29)-H(29B)	0.9800	H(21C)-C(21A)-H(21D)	107.5
C(29)-H(29C)	0.9800	N(22A)-C(21A)-C(17)	115(2)
		N(22A)-C(21A)-H(21C)	108.5
I(1)-Pt(1)-I(2)	95.65(5)	N(22A)-C(21A)-H(21D)	108.5
N(1)-Pt(1)-I(1)	91.3(4)	N(23A)-N(22A)-C(21A)	116.6
N(1)-Pt(1)-I(2)	171.5(4)	N(24A)-N(23A)-N(22A)	172.1
N(8)-Pt(1)-I(1)	174.2(4)	C(26)-N(27)-C(28)	119.8(18)
N(8)-Pt(1)-I(2)	89.3(4)	C(26)-N(27)-C(29)	121.7(19)

N(8)-Pt(1)-N(1)	83.9(6)	C(29)-N(27)-C(28)	118.5(16)
Pt(1)-N(1)-H(1A)	110.4	O(25)-C(26)-N(27)	129(2)
Pt(1)-N(1)-H(1B)	110.4	O(25)-C(26)-H(26)	115.7
H(1A)-N(1)-H(1B)	108.6	N(27)-C(26)-H(26)	115.7
C(2)-N(1)-Pt(1)	106.5(9)	N(27)-C(28)-H(28A)	109.5
C(2)-N(1)-H(1A)	110.4	N(27)-C(28)-H(28B)	109.5
C(2)-N(1)-H(1B)	110.4	N(27)-C(28)-H(28C)	109.5
Pt(1)-N(8)-H(8A)	109.8	H(28A)-C(28)-H(28B)	109.5
Pt(1)-N(8)-H(8B)	109.8	H(28A)-C(28)-H(28C)	109.5
H(8A)-N(8)-H(8B)	108.2	H(28B)-C(28)-H(28C)	109.5
C(7)-N(8)-Pt(1)	109.5(10)	N(27)-C(29)-H(29A)	109.5
C(7)-N(8)-H(8A)	109.8	N(27)-C(29)-H(29B)	109.5
C(7)-N(8)-H(8B)	109.8	N(27)-C(29)-H(29C)	109.5
N(11)-N(10)-C(9)	116.4(15)	H(29A)-C(29)-H(29B)	109.5
N(12)-N(11)-N(10)	172.4(17)	H(29A)-C(29)-H(29C)	109.5
N(1)-C(2)-H(2)	108.3	H(29B)-C(29)-H(29C)	109.5
N(1)-C(2)-C(3)	113.3(11)		
N(1)-C(2)-C(7)	108.7(10)		
C(3)-C(2)-H(2)	108.3		

Table S6. Torsion angles [°] for the X-ray crystal structure of diiodo [Pt(DACH)$(I)_2$] analogue of **2**

Pt(1)-N(1)-C(2)-C(3)	166.4(9)	N(13)-C(14)-C(19)-N(20)	-52.2(13)
Pt(1)-N(1)-C(2)-C(7)	43.9(11)	N(13)-C(14)-C(19)-C(18)	-177.1(11)
Pt(1)-N(8)-C(7)-C(2)	33.0(12)	C(14)-C(15)-C(16)-C(17)	52.8(19)
Pt(1)-N(8)-C(7)-C(6)	159.0(10)	C(15)-C(14)-C(19)-N(20)	-176.1(12)
N(1)-C(2)-C(3)-C(4)	-177.9(11)	C(15)-C(14)-C(19)-C(18)	59.0(15)
N(1)-C(2)-C(7)-N(8)	-51.7(14)	C(15)-C(16)-C(17)-C(18)	-51.8(17)
N(1)-C(2)-C(7)-C(6)	-177.1(12)	C(15)-C(16)-C(17)-C(21B)	70(3)
N(11)-N(10)-C(9)-C(5)	-89.1(19)	C(15)-C(16)-C(17)-C(21A)	74.6(18)
C(2)-C(3)-C(4)-C(5)	54.6(16)	C(16)-C(17)-C(18)-C(19)	53.1(16)
C(3)-C(2)-C(7)-N(8)	-176.2(12)	C(16)-C(17)-C(21B)-N(22B)	71(5)
C(3)-C(2)-C(7)-C(6)	58.3(15)	C(16)-C(17)-C(21A)-N(22A)	66(3)
C(3)-C(4)-C(5)-C(6)	-52.6(16)	C(17)-C(18)-C(19)-N(20)	-179.1(12)
C(3)-C(4)-C(5)-C(9)	72.3(15)	C(17)-C(18)-C(19)-C(14)	-57.3(15)

C(4)-C(5)-C(6)-C(7)	52.5(16)	C(17)-C(21B)-N(22B)-N(23B)	66(11)
C(4)-C(5)-C(9)-N(10)	68.5(16)	C(17)-C(21A)-N(22A)-N(23A)	56(5)
C(5)-C(6)-C(7)-N(8)	179.2(12)	C(18)-C(17)-C(21B)-N(22B)	-164(5)
C(5)-C(6)-C(7)-C(2)	-56.7(15)	C(18)-C(17)-C(21A)-N(22A)	-169(2)
C(6)-C(5)-C(9)-N(10)	-166.4(13)	C(19)-C(14)-C(15)-C(16)	-55.6(17)
C(7)-C(2)-C(3)-C(4)	-56.1(14)	C(33)-N(32)-C(31)-O(30)	-4(3)
C(9)-C(5)-C(6)-C(7)	-73.8(16)	C(34)-N(32)-C(31)-O(30)	175.5(17)
Pt(2)-N(13)-C(14)-C(15)	165.5(11)	C(21B)-C(17)-C(18)-C(19)	-75(5)
Pt(2)-N(13)-C(14)-C(19)	43.3(11)	C(21A)-C(17)-C(18)-C(19)	-72(2)
Pt(2)-N(20)-C(19)-C(14)	36.5(11)	C(28)-N(27)-C(26)-O(25)	-1(3)
Pt(2)-N(20)-C(19)-C(18)	160.2(10)	C(29)-N(27)-C(26)-O(25)	180(2)
N(13)-C(14)-C(15)-C(16)	-175.4(13)		

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