

Supplementary Information

Annulated Pyridines as Highly Nucleophilic and Lewis-Basic Catalysts for Acylation Reactions

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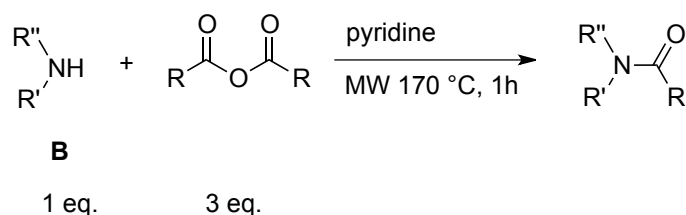
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1. Experimental part

General information

All air and water sensitive manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques. Calibrated flasks for kinetic measurements were dried in the oven at 120 °C for at least 12 hours prior to use and then assembled quickly while still hot, cooled under a nitrogen stream and sealed with a rubber septum. All commercial chemicals were of reagent grade and were used as received unless otherwise noted. Acetonitrile (Acros >99.9%, extra dry), was purchased and used without further purification. CDCl₃ was refluxed for at least one hour over CaH₂ and subsequently distilled. ¹H and ¹³C NMR spectra were recorded on Varian 300 or Varian INOVA 400 and 600 machines at room temperature. All ¹H chemical shifts are reported in ppm (δ) relative to TMS (0.00); ¹³C chemical shifts are reported in ppm (δ) relative to CDCl₃ (77.16). ¹H NMR kinetic data were measured on a Varian Mercury 200 MHz spectrometer at 23 °C. HRMS spectra (ESI-MS) were carried out using a Thermo Finnigan LTQ FT instrument. IR spectra were measured on a Perkin-Elmer FT-IR BX spectrometer mounting ATR technology. Reactions utilizing microwave technology were conducted in a CEM Discover Benchmate microwave reactor (model nr. 908010). Analytical TLC's were carried out using aluminum sheets silica gel Si 60 F254. 9-Azajulolidine (**3**) was obtained from TCI China (CAS.nr.: 6052-72-8), purity: > 97.0 % (GC).

General procedure 1 (amino acylation)



In a flame dried 10 mL microwave-vial compound **B** (1 eq.) was dissolved in pyridine (2 mL/ mmol **B**) and the according anhydride (3-3.5 eq. per NH group) was added. For more nucleophilic compounds it is necessary to perform the handling under inert gas atmosphere, thus an arrangement that figure S1 shows was invented. The tubing can be connected to a high vacuum pump. After stirring the solution for 10 min under nitrogen at room temperature the reaction mixture was heated for 1 h in a microwave reactor at 170 °C (200 W). After cooling the reaction mixture was quenched with methanol and the solvents were removed in vacuo (the usage of a big flask accelerates the removal of pyridine). The residue was taken in DCM and washed with saturated K₂CO₃ solution. The waterous phase was extracted three times with DCM and the combined organic extracts were dried over MgSO₄ and concentrated under vacuum. The crude mixture was purified by column chromatography.

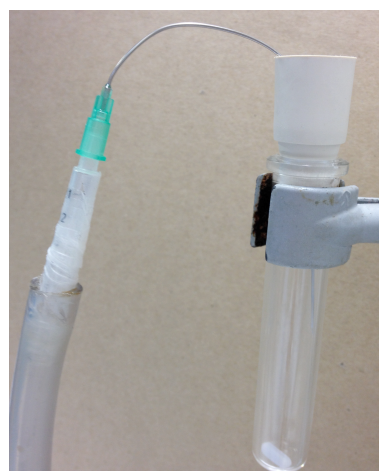
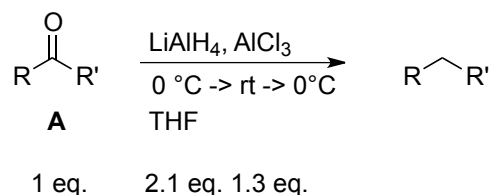


Figure S1. Arrangement for working under inert gas with 10 mL microwave-vials.

General procedure 2 (reduction with LiAlH₄/AlCl₃)



A flame dried Schlenk flask was charged with dry THF (5mL/mmol substrate **A**). At 0 °C LiAlH₄ (2.1 eq. per carbonyl group) was added in portions and followed by the slow and portion wise addition of AlCl₃ (1.3 eq. per carbonyl group). The reaction mixture was stirred for 20 minutes at room temperature. To that solution the substrate **A** (1 eq.) in dry THF (5 mL/mmol substrate) was added drop wise at -10 °C. The reaction was stirred at -10 °C until the disappearance of starting material (TLC/GC) but for most compounds a reaction time of one hour was sufficient. For benzylic carbonyl groups elevated temperatures (room temperature or reflux) and longer reaction times (2.5 h to 8 h) sometimes turned out to be more efficient in terms of product yield but the exact conditions will be mentioned in detail in the experimental part. The reaction was quenched by pouring the mixture onto ice-cold water (5mL/mmol substrate) and saturated K₂CO₃ (5mL/mmol substrate) solution (it is important to adjust to pH=12-14, in case add more K₂CO₃). In that way the crude mixture was subjected to filtration over a Celite plug using vacuum (the optimized arrangement to obtain higher yields than previously published^[5] can be found in figure S2, notice that a separation funnel can be attached directly with the NS 29 joint). The plug was washed with excess DCM and ethyl acetate. The resulting phases were separated by a separation funnel and the waterous phase was washed three times with DCM and ethyl acetate. The combined organic phases were washed with saturated K₂CO₃ solution and dried over MgSO₄. After evaporation of the organic solvent the crude product was purified by column chromatography.

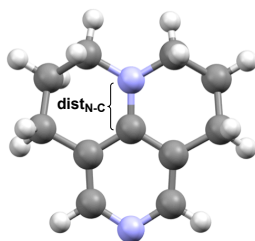


Figure S2. optimized arrangement for filtration over Celite.

Catalyst synthesis

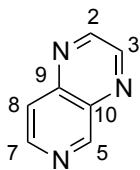
9-Azajulolidine (**3**)

Since the discovery of 9-azajulolidine **3** (TCAP) in 2003 by *Steglich et al.*^[2] different methods for its synthesis were published yet^[5,6,8,9]. The different synthesis strategies are summarized in the recently published review by *David et al.*^[3] Nowadays **3** is also commercially available (TCI China). The crystal structure below was obtained after recrystallization (from ethyl acetate) of commercially available 9-azajulolidine.



	dist _{N-C} /pm	d _(abcd)
crystal structure	137.5	12.7°
calculated best conf.	138.8	12.9°

Pyrido[3,4-*b*]pyrazine (**8**)



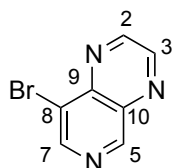
Under a constant nitrogen flow 2.50 g (22.9 mmol) 3,4-diaminopyridine **7** were dissolved in 40 mL ethanol. After the addition of 3.1 mL (27 mmol, $\rho = 1.256$ g/mL) glyoxal (40 wt.-% in water) the reaction mixture was submitted to a microwave reactor. After a reaction time of one hour at 110°C (70 W) the solvent was evaporated and the product **8** was obtained in quantitative yield (3.01 g) as a bright yellow solid.

¹H-NMR (300 MHz, CDCl₃): $\delta = 7.91$ (dd, ⁴J = 0.83 Hz, ³J = 5.8 Hz, 1 H, H-7), 8.81 (d, ³J = 5.8 Hz, 1 H, H-8), 8.92 (d, ³J = 1.8 Hz, 1 H, H-3), 8.99 (d, ³J = 1.8 Hz, 1 H, H-2), 9.53 (d, ⁴J = 0.8 Hz, 1 H, H-5).

¹³C-NMR (75 MHz, CDCl₃): δ = 120.5 (CH, C-8), 137.5 (C_q, C-10), 144.3 (C_q, C-9), 145.6 (CH, C-7), 146.4 (CH, C-3), 148.4 (CH, C-2), 153.6 (CH, C-5).

In line with published data^[9]

8-Bromopyrido[3,4-*b*]pyrazine (**9**)



A solution of 6.90 g (52.6 mmol) **8** in 280 mL CH₃CN was stirred in the dark. To this solution 10.3 g (57.9 mmol) *N*-bromosuccinimide were added in portions under nitrogen atmosphere. After stirring the orange solution at room temperature over night cold Et₂O was added and it was filtered from the brown precipitation (for small scale synthesis). Evaporation of the solvent and repeated column chromatography (until the NMR shows no signal of the succinimide that was formed during the reaction) on silica gel (EtOAc/Isohexan/NEt₃/Et₂O, 20:15:1:1.5) yielded 5.74 g (52 %) of **9** as pale solid.

R_f: 0.53 (silica, EtOAc/Isohexan/NEt₃, 20:15:1).

mp: 110.9 - 111.8 °C.

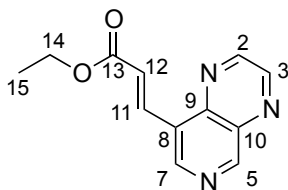
¹H-NMR (300 MHz, CDCl₃): δ = 8.96 (d, ³*J* = 1.8 Hz, 1 H, H-3), 9.02 (s, 1 H, H-7), 9.08 (d, ³*J* = 1.8 Hz, 1 H, H-2), 9.44 (s, 1H, H-5).

¹³C-NMR (75 MHz, CDCl₃): δ = 120.5 (C_q, C-8), 139.7 (C_q, C-10), 144.1 (C_q, C-9), 148.0 (CH, C-3), 149.8 (CH, C-7), 150.4 (CH, C-2), 154.7 (CH, C-5).

IR (ATR): ν̄ (cm⁻¹) = 1734 (w), 1578 (m, C=C stretching vibration), 1561 (w, C=C stretching vibration), 1548 (w, C=C stretching vibration), 1466 (m), 1428 (m), 1373 (m), 1256 (m), 1180 (m), 1103 (m), 1012 (m, C-Br), 969 (vs), 826 (m), 806 (m).

HRMS (EI): calculated for: C₇H₄N₃Br [M⁺] 208.9589, found: 208.9581.

(*E*)-Ethyl 3-(pyrido[3,4-*b*]pyrazin-8-yl)acrylate (**10**)



A flame dried pressure tube was charged with 10 mL dry CH₃CN, 46.9 mg (2.6 mol%, 0.21 mmol) Pd(OAc)₂, 159 mg (6.5 mol-%, 0.53 mmol) P(*o*-tolyl)₃, 0.76 mL (0.67 eq., 5.39 mmol, ρ = 0.72 g/mL) NEt₃, 1.69 g (8.05 mmol) **9** and 1.48 mL (1.70 eq, 13.69 mmol, ρ = 0.924 g/mL) ethyl acrylate. The solution was heated for 20.5 h to 120 °C. After cooling to room temperature the solvent was evaporated and the crude mixture was purified by column chromatography on silica (gradient of Isohexan/EtOAc 1:1 to 1:9). The product **10** was obtained in 65 % yield (1.20 g) as yellow solid.

R_f: 0.43 (silica, Isohexane/EtOAc, 1:1).

mp: 147.9 - 150.6 °C.

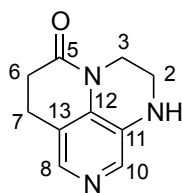
¹H-NMR (300 MHz, CDCl₃): δ = 1.36 (t, ³J = 7.1 Hz, 3 H, H-15), 4.31 (q, ³J = 7.1 Hz, 2 H, H-14), 7.11 (d, ³J = 16.3 Hz, 1 H, H-12), 8.47 (dd, ³J = 16.3 Hz, ³J = 0.7 Hz, 1 H, H-11), 8.99 (d, ³J = 1.7 Hz, 1 H, H-3), 9.03 (s, 1 H, H-7), 9.07 (d, ³J = 1.7 Hz, 1 H, H-2), 9.52 (s, 1 H, H-5).

¹³C-NMR (75 MHz, CDCl₃): δ = 14.1 (CH₃, C-15), 60.7 (CH₂, C-14), 123.8 (CH, C-12), 126.6 (C_q, C-8), 136.3 (CH, C-11), 137.3 (C_q, C-10), 143.1 (C_q, C-9), 146.1 (CH, C-7), 146.6 (CH, C-3), 148.3 (CH, C-2), 155.3 (CH, C-5), 165.9 (CH, C-13).

IR (ATR): ν̄ (cm⁻¹) = 3401 (w), 2956 (m, C-H stretching vibration), 2918 (s, C-H stretching vibration), 2850 (m, C-H stretching vibration), 1723 (vs, C=O), 1638 (m, C=N), 1566 (w, C=C stretching vibration), 1466 (w), 1442 (w), 1394 (w), 1375 (w), 1324 (s), 1275 (m), 1220 (vs), 1191 (s), 1178 (s), 1134 (w), 1028 (w), 979 (w), 912 (m, C-H deformation vibration (oop), alkene), 880 (w), 828 (w), 726 (w).

HRMS (EI): calculated for: C₁₂H₁₂O₂N₃ [M+H]⁺ 230.0930, found: 230.0925.

2,3,6,7-Tetrahydropyrazino[3,2,1-*ij*][1,6]naphthyridine-5(1H)-on (**11**)



In a flame dried 2L Schlenk flask 1.91 g (8.33 mmol) of **10** were dissolved in 350 mL ethanol. To this solution 0.50 g of palladium on charcoal (10 %) were added. The flask was purged three times with hydrogen and the solution turned slowly purple. The reaction was conducted under hydrogen atmosphere at room temperature for 8 hours (too long reaction times will hydrogenate the pyridine ring and thus should be avoided). The black solution was filtered through Celite and the residue was washed with ethanol, ethyl acetate and dichloromethane. After removal of the solvents the crude product was purified twice by column chromatography using neutral aluminum oxide (CHCl₃/MeOH 40:1). The product **11** was obtained as brown solid in 88 % yield (1.39 g).

R_f: 0.50 (neutral aluminum oxide, CHCl₃/MeOH 40:1).

mp: 158.6 - 163.5 °C.

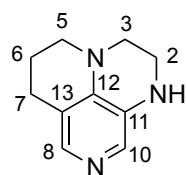
¹H-NMR (300 MHz, CDCl₃): δ = 2.64 – 2.73 (m, 2 H, H-6), 2.88 (dd, ³J = 6.2 Hz, ³J = 8.7 Hz, 2 H, H-7), 3.33 – 3.42 (m, 2H, H-2), 3.90 –3.99 (m, 2 H, H-3), 4.08 (s, br, 1 H, N-H), 7.77 (s, 1 H, H-9), 7.86 (s, 1 H, H-11).

¹³C-NMR (75 MHz, CDCl₃): δ = 21.7 (CH₂, C-7), 30.6 (CH₂, C-6), 39.1 (CH₂, C-3), 39.3 (CH₂, C-2), 119.1 (C_q, C-8), 129.8 (C_q, C-12), 130.2 (C_q, C-13), 135.3 (CH, C-11), 138.2 (CH, C-9), 168.0 (C_q, C-5).

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3323 (w, br, N-H stretching vibration), 2967 (w, C-H stretching vibration), 2934 (w, C-H stretching vibration), 2854 (w, C-H stretching vibration), 1659 (s, C=O), 1587 (s, C=C stretching vibration), 1496 (s), 1461 (m), 1378 (s), 1346 (s), 1304 (s), 1264 (m), 1233 (s), 1196 (s), 1153 (s), 1119 (m), 1090 (m), (1075 (m), 1032 (m), 908 (s), 865 (m), 842 (m), 776 (m), 690 (vs, C-H deformation vibration (oop), aromatic).

HRMS (EI): calculated for: C₁₀H₁₁ON₃ [M+H]⁺ 190.0980, found: 190.0975.

1,2,3,5,6,7-Hexahydropyrazino[3,2,1-*ij*][1,6]naphthyridine (**12**)



The reduction was conducted according to general procedure 2 applying 0.25 g (1.32 mmol) of starting material **11**. The crude mixture was purified by column chromatography on silica gel (EtOAc/NEt₃/MeOH 10:1:1) yielding the product as a yellow solid in 96 % yield (0.22 g).

R_f: 0.17 (silica, EtOAc/NEt₃/MeOH 10:1:1).

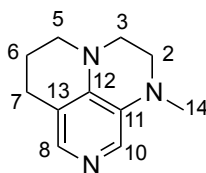
¹H-NMR (300 MHz, CDCl₃): δ = 1.90 – 2.04 (m, 2H, CH₂), 2.66 (t, ³J = 6.4 Hz, 2H, CH₂), 3.10 – 3.23 (m, 2H, CH₂), 3.23 – 3.35 (m, 2H, CH₂), 3.34 (s, 2H, CH₂), 7.46 – 7.60 (m, 2H, CH_{Ar}).

¹³C-NMR (75 MHz, CDCl₃): δ = 20.7, 23.7, 39.2, 48.1, 49.0, 115.0, 127.9, 129.2, 136.4, 139.5.

IR (ATR): ν̄ (cm⁻¹) = 3191 (w, br, N-H stretching vibration), 3015 (w, C-H stretching vibration), 2923 (s), 2850 (s), 2754 (s), 2680 (s), 1704 (s), 1655 (s), 1628 (s), 1569 (vs), 1457 (s), 1333 (vs), 1250 (s), 1209 (s), 1169 (s), 1123 (s), 1070 (s), 1055 (s), 1026 (s), 958 (w), 942 (w), 905 (s), 869 (s), 853 (s), 741 (vs).

HRMS (EI): calculated for: C₁₃H₁₃N₃ [M]⁺ 175.1109, found: 175.1106.

1-Methyl-1,2,3,5,6,7-hexahydropyrazino[3,2,1-*ij*][1,6]naphthyridine (**4a**)



In a 80 mL microwave-vial 0.88 g (5.03 mmol) of **12** were added to 12.54 mL of formic acid and 4.27 mL (37 % solution) of formaldehyde. The mixture was heated in a microwave

reactor for 36 hours at 110 °C and 110 W. After completion the reaction mixture is quenched by careful addition of NaOH (32 %) at 0 °C until pH=12. The reaction mixture is stirred together with excess EtOAc for at least 20 min. The mixture is extracted three times with EtOAc and two times with DCM and the combined organic layers dried over MgSO₄. The crude reaction mixture was purified twice by column chromatography on basic Alox (Brockmann 3) (CHCl₃/MeOH 40:1) and recrystallized from ethyl acetate/isohexane and yielded 61 % (0.58 g) of **4a** as white crystalline solid.

R_f: 0.45 (bas. Alox, EtOAc/NEt₃/MeOH 10:1:1).

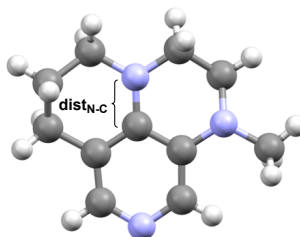
mp: 47.1 - 49.3 °C.

¹H-NMR (300 MHz, CDCl₃): δ = 1.80 – 2.08 (m, 2H, CH₂), 2.66 (t, ³J = 6.4 Hz, 2H, CH₂), 2.83 (s, 3H, CH₃), 3.08 – 3.28 (m, 4H, CH₂ x 2), 3.27 – 3.46 (m, 2H, CH₂), 7.53 (s, 1H, CH_{Ar}), 7.58 (s, 1H, CH_{Ar}).

¹³C-NMR (75 MHz, CDCl₃): δ = 21.1, 23.8, 39.1, 48.0, 48.5, 49.1, 114.3, 130.1, 130.8, 138.1, 140.9.

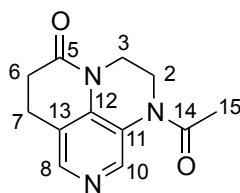
IR (ATR): ν̄ (cm⁻¹) = 3255 (w, br), 3037 (w), 2942 (s), 2833 (s), 2810 (s), 2781 (w), 1578 (vs), 1522 (vs), 1469 (vs), 1430 (s), 1374 (s), 1358 (s), 1331 (vs), 1312 (vs), 1223 (vs), 1124 (vs), 1035 (vs), 986 (s), 906 (s), 869 (s), 852 (vs), 769 (vs), 745 (vs), 652 (s).

HRMS (EI): calculated for: C₁₁H₁₅N₃ [M]⁺ 189.1266, found: 189.1262.



	dist _{N-C} /pm	r ₂ /pm	d _(abcd)
crystal structure	137.3	140.0	1.0°
calculated best conf.	139.4	140.6	2.1°

1-Acetyl-2,3,6,7-tetrahydropyrazino[3,2,1-*ij*][1,6]naphthyridin-5(1*H*)-one (**13b**)



The acylation of was conducted following general procedure 1 applying 0.70 g (3.70 mmol) of **11** and 1.23 mL (12.98 mmol, 3.5 eq.) acetic anhydride. The crude mixture was purified by column chromatography on silica (EtOAc/Net₃/MeOH 10:1:1) giving **13b** in 96 % (0.82 g) yield as yellow foam.

R_f: 0.17 (silica, EtOAc/NEt₃/MeOH 10:1:1).

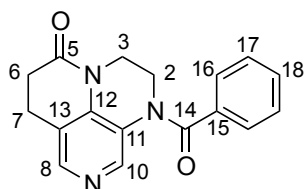
¹H-NMR (300 MHz, CDCl₃): δ = 2.32 (s, 3H, CH₃), 2.75 (t, ³*J* = 7.6 Hz, 2H, CH₂), 2.99 (t, ³*J* = 7.6 Hz, 2H, CH₂), 3.92 (d, ³*J* = 5.0 Hz, 4H, CH₂ x 2), 8.17 (s, 1H, CH_{Ar}, H-8), 8.27 – 8.67 (m, 1H, CH_{Ar}, H-10).

¹³C-NMR (75 MHz, CDCl₃): δ = 21.8, 22.4, 30.6, 42.5, 119.3, 123.3, 136.0, 144.0, 144.7, 168.5 (C=O), 168.6 (C=O).

IR (ATR): ν̄ (cm⁻¹) = 3525 (w, br), 2960 (w), 2892 (w), 2359 (w), 2337 (w), 1679 (vs, C=O), 1584 (s), 1495 (s), 1366 (vs), 1325 (vs), 1195 (s).

HRMS (EI): calculated for: C₁₂H₁₃N₃O₂ [M]⁺ 231.1008, found: 231.1002.

1-Benzoyl-2,3,6,7-tetrahydropyrazino[3,2,1-*ij*][1,6]naphthyridin-5(1*H*)-one (**13c**)



The amino acylation was conducted according to general procedure 1 applying 0.29 g (1.53 mmol) of compound **11** and 1.04 g (4.60 mmol, 3 eq.) benzoic anhydride. Purification of the crude product on basic aluminum oxide (DCM/MeOH 40:1) yielded the product in 82 % yield (0.37 g) as a light brown solid.

R_f: 0.78 (silica, EtOAc/NEt₃/MeOH 10:1:1).

mp: 171.8 - 175.9 °C.

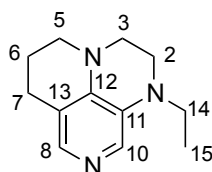
¹H-NMR (300 MHz, CDCl₃): δ = 2.75 (t, ³J = 7.4 Hz, 2 H, H-6), 2.96 (t, ³J = 7.5 Hz, 2 H, H-7), 3.90 – 4.06 (m, 4 H, H-2, H-3), 7.28 – 7.51 (m, 5 H, H-16, H-17, H-18), 8.02 (s, 2 H, H-9, H-11).

¹³C-NMR (75 MHz, CDCl₃): δ = 21.5 (CH₂, C-7), 30.3 (CH₂, C-6), 41.0 (CH₂), 41.9 (CH₂), 118.7 (C_q, C-13), 122.7 (C_q, C-11), 127.9 (CH, C-16, C-17, C-18), 128.3 (CH, C-16, C-17, C-18), 130.9 (CH, C-16, C-17, C-18), 133.6 (C_q, C-15), 134.4 (C_q, C-12), 143.4 (CH, C-8), 144.0 (CH, C-10), 168.1 (C_q, C-5), 168.5 (C_q, C-14).

IR (ATR): ν̄ (cm⁻¹) = 3370 (w), 3059 (w), 2925 (w, C-H stretching vibration), 2852 (w, C-H stretching vibration), 1681 (s, C=O), 1648 (s, C=O), 1585 (s, C=C stretching vibration), 1496 (s, C=C stretching vibration), 1458 (m, C-H deformation vibration), 1447 (m, C-H deformation vibration), 1434 (m, C-H deformation vibration), 1372 (vs), 1329 (vs), 1260 (s), 1241 (s), 1195 (s), 1184 (s), 1160 (s), 1120 (s), 1086 (m), 1034 (m), 1006 (m), 968 (w), 913 (m), 888 (s), 843 (w), 789 (m), 717 (vs, C-H deformation vibration (oop), Aromat), 697 (vs), 666 (m).

HRMS (EI): calculated for: C₁₇H₁₅O₂N₃ [M⁺] 293.1164, found: 293.1158.

1-Ethyl-1,2,3,5,6,7-hexahydropyrazino[3,2,1-ij][1,6]naphthyridine (**4b**)



The reduction was done following general procedure 2 applying 0.74 g (3.20 mmol) of **13b**. The crude mixture was purified by repeated column chromatography on silica gel (EA: NEt₃ 10:1) and yielded the product **4b** as a white solid in 81 % (0.53 g) yield.

R_f: 0.45 (silica, EtOAc/NEt₃ 10:1).

mp: 63.2 – 64.5 °C.

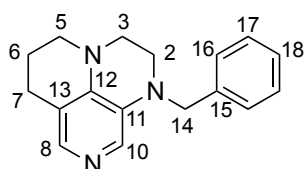
¹H-NMR (300 MHz, CDCl₃): δ = 1.16 (t, ³J = 7.1 Hz, 3H, CH₃), 2.01 – 2.91 (m, 2H, CH₂), 2.67 (t, ³J = 6.4 Hz, 2H, CH₂), 3.17 (dd, ³J = 6.9 Hz, ³J = 4.4 Hz, 2H, CH₂), 3.23 – 3.34 (m, 6H, CH₂ x 3), 7.55 (s, 1H, CH_{Ar}), 7.59 (s, 1H, CH_{Ar}).

¹³C-NMR (75 MHz, CDCl₃): δ = 10.1, 21.2, 23.8, 45.0, 45.2, 47.7, 49.2, 114.8, 129.3, 130.2, 138.1, 140.2.

IR (ATR): ν̄ (cm⁻¹) = 2954 (m), 2837 (m), 1578 (m), 1566 (m), 1513 (s), 1470 (s), 1429 (m), 1369 (m), 1343 (vs), 1316 (s), 1274 (m), 1204 (s), 1162 (s), 1091 (s), 938 (m), 879 (s), 795 (s), 766 (s), 747 (s).

HRMS (EI): calculated for: C₁₂H₁₇N₃ [M]⁺ 203.1422, found: 203.1418.

1-Benzyl-1,2,3,5,6,7-hexahydropyrazino[3,2,1-ij][1,6]naphthyridine (**4c**)



According to general procedure 2 1.33 g (4.53 mmol) of the starting material was submitted to react. Purification of the crude mixture twice on basic aluminum oxide (EtOAc/NEt₃/MeOH 10:1:1) and once on silica gel (EtOAc/NEt₃/MeOH 10:1:1) yielded the product **4c** as a brown oily substance (0.67g, 56 %).

R_f: 0.67 (silica, EtOAc/NEt₃/MeOH 10:1:1).

¹H-NMR (400 MHz, CDCl₃): δ = 1.88 – 2.06 (m, 2 H, H-6), 2.67 (t, ³J = 6.4 Hz, 2 H, 7-H), 3.18 (dd, ³J = 6.8 Hz, ³J = 4.4 Hz, 2 H, H-5), 3.23 – 3.35 (m, 4 H, H-2, H-3), 4.36 (s, 2 H, H-14), 7.16 – 7.38 (m, 5 H, H-16, H-17, H-18), 7.56 (d, ³J = 5.7 Hz, 2 H, H-8, H-10).

¹³C-NMR (100 MHz, CDCl₃): δ = 21.5 (CH₂, C-6), 24.2 (CH₂, C-7), 46.6 (CH₂, C-2), 48.1 (CH₂, C-3), 49.6 (CH₂, C-5), 55.5 (CH₂, C-14), 115.1 (C_q, C-13), 127.4 (CH, C-18), 127.6 (CH, C-16), 128.9 (CH, C-17), 130.4 (C_q, C-11), 130.6 (C_q, C-10), 138.1 (C_q, C-15), 138.3 (C_q, C-12), 140.6 (C_q, C-8).

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3086 (w, C-H stretching vibration, aryl), 3060 (w, C-H stretching vibration, aryl), 3029 (w, C-H stretching vibration, aryl), 2930 (w, C-H stretching vibration), 2841 (w, C-H stretching vibration), 1647 (w), 1582 (m, C=C stretching vibration), 1515 (s, C=C stretching vibration), 1495 (m), 1469 (C-H deformation vibration), 1437 (C-H deformation vibration), 1452 (C-H deformation vibration), 1350 (s), 1325 (m), 1293 (m), 1255 (m), 1231 (m), 1196 (m), 1156 (s), 1109 (m), 1066 (m), 1038 (w), 1028 (w), 977 (w), 907 (s), 725 (vs, C-H deformation vibration (oop), aryl), 697 (vs, C-H deformation vibration (oop), aryl).

HRMS (EI): calculated for: C₁₇H₁₉N₃ [M⁺] 265.1579, found: 265.1568.

3,4,5-Triaminopyridines

The core structure **14** of the 3,4,5-triaminopyridines was synthesized from **20** according to the published procedures of *David et al.*^[8].

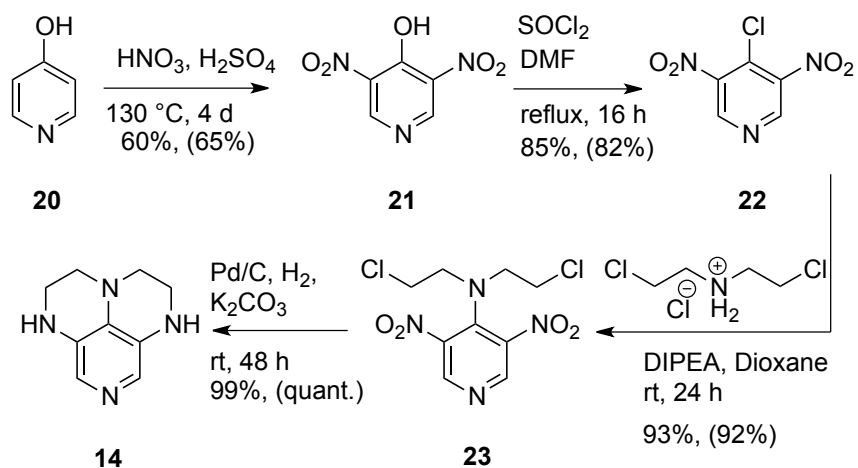


Figure S3. Published synthesis of **14** starting with 4-hydroxypyridine **20**^[8] (own yields are given in brackets).

Catalyst **5a** was synthesized through established procedures by *David et al.*^[8] (own yields are given in brackets).

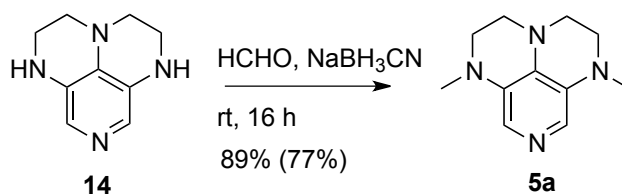
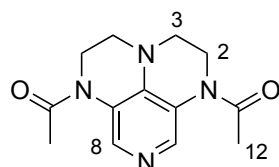


Figure S4. Synthesis of **5a**.

1,1'-(2,3,4,5-Tetrahydro-1,3a,6,8-tetraazaphenylene-1,6-diyl)diethanone (**5f**)



The acylation was performed according to general procedure 1 applying 0.36 g (2.04 mmol) of starting material **14**. After purification by column chromatography using silica gel (EtOAc/NEt₃/MeOH 10:1:1) the product was obtained as a pale brown solid in 88 % (0.47 g) yield.

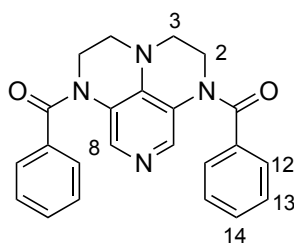
¹H-NMR (200 MHz, CDCl₃): δ = 2.29 (s, 6H, CH₃ x 2, H-12), 3.29 – 3.52 (m, 4H, CH₂ x 2, H-3), 3.93 (t, ³J = 5.2 Hz, 4H, CH₂ x 2, H-2), 8.01 (s, br, 2H, CH_{ar}, H-8).

¹³C-NMR (100 MHz, CDCl₃): δ = 22.4, 37.6, 45.8, 48.5, 121.2, 134.3, 140.6, 168.9.

HRMS (EI): calculated for: C₁₃H₁₆N₄O₂ [M]⁺ 260.1273, found: 260.1267.

In line with published data.^[8]

(2,3,4,5-Tetrahydro-1,3a,6,8-tetraazaphenalene-1,6-diyl)bis(phenylmethanone) (**15c**)



The acylation was performed according to general procedure 1 applying 1.50 g (8.51 mmol) of starting material **14** and 6 eq. of benzoic anhydride (11.6 g, 51.1 mmol) in a 80 mL microwave vial. After purification by column chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 10:1) the product was obtained as an ocher colored solid in 85 % (2.76 g) yield.

R_f: 0.30 (basic Alox, EtOAc/NEt₃ 10:1).

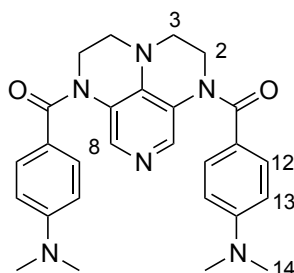
¹H-NMR (300 MHz, CDCl₃): δ = 3.47 – 3.71 (m, 4H, CH₂ x 2, H-3), 3.98 – 4.22 (m, 4H, CH₂ x 2, H-2), 7.27 – 7.47 (m, 10H, CH_{ar}, H-12 x 4, H-13 x 4, H-15 x 2), 7.56 (dt, ³J = 4.4 Hz, ³J = 1.8 Hz, 1H), 7.89 – 8.21 (m, 1H).

¹³C-NMR (75 MHz, CDCl₃): δ = 49.0, 121.4, 128.1, 128.2, 128.5, 130.9, 133.0, 134.5, 140.3, 169.0.

HRMS (EI): calculated for: C₂₃H₂₄N₄ [M]⁺ 356.2001, found: 356.1994.

In line with published data.^[8]

(2,3,4,5-Tetrahydro-1,3a,6,8-tetraazaphenalene-1,6-diyl)bis((4-(dimethylamino)phenyl) methanone) (**15d**)



The acylation was performed according to general procedure 1 applying 0.25 g (1.42 mmol) of starting material **14** and 6 eq. of 4-(dimethylamino)benzoyl chloride (1.56 g, 8.51 mmol). After purification by column chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 10:1) the product was obtained as brown solid in 90 % (0.60 g) yield.

R_f: 0.60 (basic Alox, EtOAc/NEt₃/MeOH 10:1:1).

mp: 243.2 -244.1 °C.

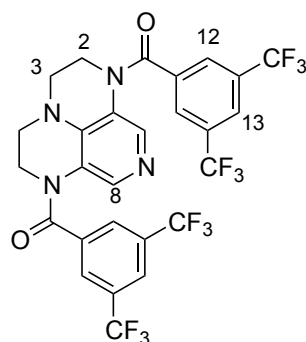
¹H-NMR (600 MHz, CDCl₃): δ = 2.97 (s, 12H, CH₃ x 4, H-14), 3.53 (t, ³J = 5.2 Hz, 4H, CH₂ x 2, H-3), 4.02 – 4.10 (m, 4H, CH₂ x 2, H-2), 6.50 – 6.59 (m, 4H, CH_{ar}, H-13), 7.32 – 7.41 (m, 4H, CH_{ar}, H-12), 7.53 (³J = 19.7 Hz, 2H, CH_{ar}, H-8).

¹³C-NMR (150 MHz, CDCl₃): δ = 40.0, 40.4, 40.1, 110.8, 120.8, 122.2, 130.8, 132.2, 139.8, 152.0, 162.1.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2871 (w), 1644 (s), 1629 (s), 1594 (vs), 1525 (s), 1444 (w), 1361 (vs), 1332 (vs), 1242 (s), 1123 (m), 946 (w), 887 (w), 819 (s), 764 (m).

HRMS (EI): calculated for: C₂₇H₃₀N₆O₂ [M]⁺ 470.2430, found: 470.2421.

(2,3,4,5-Tetrahydro-1,3a,6,8-tetraazaphenalene-1,6-diyl)bis((3,5-bis(trifluoromethyl)phenyl) methanone) (**15e**)



The acylation was performed according to general procedure 1 applying 0.60 g (3.40 mmol) of starting material **14** and 6 eq. of 3,5-(bistrifluoromethyl)benzoyl chloride (5.65 g, 20.40 mmol) in 30 mL pyridine (80 mL microwave vial). After purification by column

chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 10:1 → EtOAc/NEt₃ 10:1) the product was obtained as beige powder in 80 % (1.80 g) yield.

mp: 239.8 – 240.2 °C.

¹H-NMR (300 MHz, CDCl₃): δ = 3.67 (t, ³J = 5.2 Hz, 4H, CH₂ x 2, H-3). 4.11 (t, ³J = 5.2 Hz, 4H, CH₂, H-2), 7.49 (s, br, 2H, CH_{ar}, H-8), 7.88 (s, 4H, CH_{ar} x 4, H-12), 7.94 (s, 2H, CH_{ar} x 2, H-13).

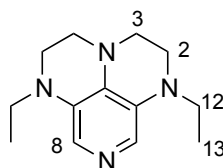
¹³C-NMR (75 MHz, CDCl₃): δ = 48.8, 120.5 (d), 124.4, 124.5, 128.0, 128.6, 132.1 (q), 133.1, 136.7, 140.9, 165.4.

¹⁹F-NMR (282 MHz, CDCl₃): δ = - 63.1.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3016 (w), 1675 (m), 1663 (m), 1602 (m), 1543 (w), 1404 (w), 1366 (m), 1301 (vs), 1232 (m), 1163 (s), 1123 (vs), 902 (m), 681 (s).

HRMS (EI): calculated for: C₂₇H₁₆F₁₂N₄O₂ [M]⁺ 656.1082, found: 656.1060.

1,6-Diethyl-1,2,3,4,5,6-hexahydro-1,3a,6,8-tetraazaphenalene (**5b**)



The reduction was performed according to general procedure 2 applying 0.18 g (0.69 mmol) of starting material **15b**. After purification by column chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 20:1 → EtOAc/NEt₃/MeOH 10:1:3) the product was obtained as white solid in 95 % (0.15 g) yield.

mp: 258.2 – 260.3 °C.

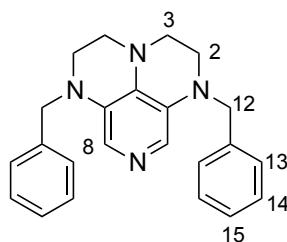
¹H-NMR (600 MHz, CDCl₃): δ = 1.13 (t, ³J = 7.1 Hz, 6H, CH₃ x 2, H-13), 3.26 (q, ³J = 7.1 Hz, 4H, CH₂ x 2, H-12), 3.29 – 3.33 (m, 4H, CH₂ x 2, H-3), 3.47 (dt, ³J = 8.1 Hz, 3.6 Hz, 4H, CH₂ x 2, H-2), 7.18 (s, 2H, CH_{ar}, H-8).

$^{13}\text{C-NMR}$ (150 MHz, CDCl_3): $\delta = 10.0, 43.5, 45.4, 47.7, 113.7, 128.7, 132.6$.

HRMS (EI): calculated for: $\text{C}_{13}\text{H}_{20}\text{N}_4$ $[\text{M}]^+$ 232.1688, found: 232.1682.

In line with published data.^[8]

1,6-Dibenzyl-1,2,3,4,5,6-hexahydro-1,3a,6,8-tetraazaphenalene (**5c**)



The reduction was performed according to general procedure 2 applying 2.20 g (5.72 mmol) of starting material **15c**. After purification by column chromatography using basic Alox (Brockmann 3, EtOAc/ NEt_3 20:1 \rightarrow EtOAc/ NEt_3 /MeOH 10:1:3) and recrystallization in EtOAc/Isohexane the product was obtained as white crystals in 78 % (1.59 g) yield.

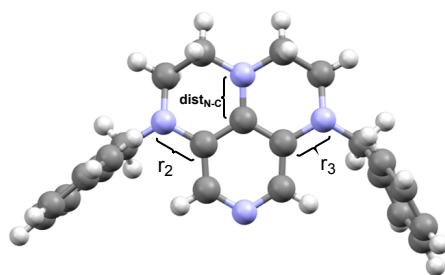
R_f : 0.66 (silica, EtOAc/ NEt_3 /MeOH 10:1:1).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 3.20 - 3.33$ (m, 4H, $\text{CH}_2 \times 2$, H-3), 3.37 (dt, $^3J = 8.1$ Hz, 5.0 Hz, 4H, $\text{CH}_2 \times 2$, H-2), 4.41 (s, 4H, $\text{CH}_2 \times 2$, H-12), 7.18 – 7.38 (m, 10H, $\text{CH}_{\text{ar}} \times 10$, H-13, H-14, H-15), 7.44 (s, 2H, $\text{CH}_{\text{ar}} \times 10$, H-8).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 46.7, 47.6, 55.5, 125.6, 126.7, 127.1, 127.3, 128.6, 130.3, 138.2$.

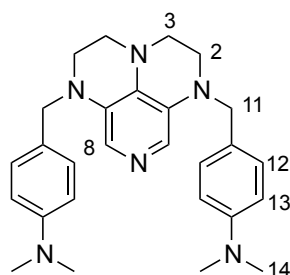
HRMS (EI): calculated for: $\text{C}_{23}\text{H}_{24}\text{N}_4$ $[\text{M}]^+$ 356.2001, found: 356.1994.

In line with published data.^[8]



	dist_{N-C} /pm	r₂ /pm	r₃ /pm	d_(abcd)
crystal structure	137.7	140.2	141.7	11.4°
calculated best conf.	140.4	141.0	141.0	21.1°

4,4'-((2,3,4,5-Tetrahydro-1,3a,6,8-tetraazaphenalene-1,6-diyl)bis(methylene))bis(*N,N*-dimethylaniline) (**5d**)



The reduction was performed according to general procedure 2 at room temperature over night applying 0.23 g (0.49 mmol) of starting material **15d**. After repeated purification by column chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 20:1 → EtOAc/NEt₃/MeOH 10:1:1) the product was obtained as pale yellow solid in 33 % (0.07 g) yield.

R_f: 0.40 (basic Alox, EtOAc/NEt₃ 10:1).

mp: 100.1 – 100.9 °C.

¹H-NMR (300 MHz, CDCl₃): δ = 2.93 (s, 12H, CH₃ x 4, H-14). 3.25 (td, ³*J* = 5.5 Hz, ³*J* = 2.7 Hz, 8H, CH₂ x 4, H-2, H-3), 4.30 (s, 4H, CH₂, H-11), 6.55 – 6.81 (m, 4H, CH_{ar}, H-13), 7.18 (d, ³*J* = 8.8 Hz, 4H, CH_{ar}, H-12), 7.53 (s, 2H, CH_{ar}, H-8).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 40.7, 45.8, 47.6, 54.8, 112.8, 125.5, 125.6, 127.0, 128.6, 130.4, 149.9$.

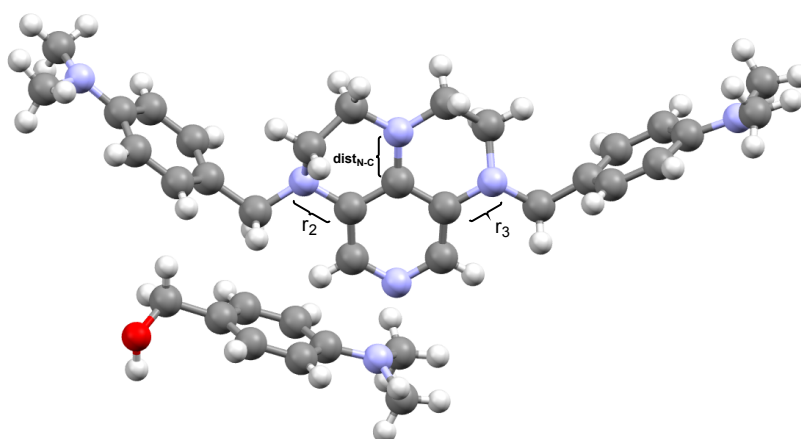
IR (ATR): $\bar{\nu}$ (cm^{-1}) = 2820 (br, m), 1612 (s), 1565 (s), 1521 (vs), 1441 (m), 1341 (vs), 1222 (s), 1156 (vs), 1125 (s), 1063 (m), 1041 (w), 945 (m), 920 (w), 798 (vs), 743 (m).

HRMS (EI): calculated for: $\text{C}_{27}\text{H}_{34}\text{N}_6$ $[\text{M}]^+$ 442.2845, found: 442.2831.

A recrystallization with EtOAc/Isohexane yielded bright yellow crystals. The crystal structure contains the catalyst with an 4-(dimethylamino)benzoyl adduct.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 2.93$ (d, $^3J = 3.4$ Hz, 18H, $\text{CH}_3 \times 6$), 3.12 – 3.40 (m, 8H, $\text{CH}_2 \times 4$), 4.28 (s, 4H, $\text{CH}_2 \times 2$), 4.57 (s, 2H, CH_2), 6.62 – 6.83 (m, 6H, CH_{ar}), 7.29 – 7.06 (m, 6H, CH_{ar}), 7.50 (s, 2H, CH_{ar}).

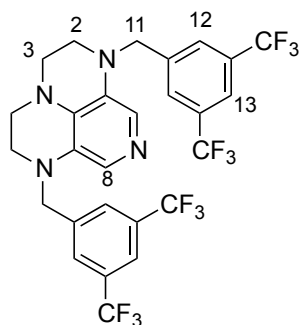
$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 40.7, 40.7, 45.7, 47.6, 54.7, 65.2, 112.6, 112.8, 125.2, 127.1, 128.6, 128.7, 129.1, 130.4, 149.9, 150.3$.



	$\text{dist}_{\text{N-C}}/\text{pm}$	r_2/pm	r_3/pm	$d_{(abcd)}$
crystal structure	136.8	141.4	141.5	1.76°
calculated best conf.	140.5	141.0	141.0	21.0°

In the best conformer both benzylic substituents point downwards whereas in the crystal structure they point up. This could be due to packing effects in the crystal. Conformation **7** shows the same orientation for the benzylic substituents and is 1.6 kJ/mol higher in energy. Conformation **16** shows a pyramidalisation angle of 0.2° but a different orientation of the benzylic substituents and is 11.4 kJ/mol higher in energy.

1,6-Bis(3,5-bis(trifluoromethyl)benzyl)-1,2,3,4,5,6-hexahydro-1,3a,6,8-tetraazaphenalene (**5e**)



The reduction was performed according to general procedure 2 applying 1.38 g (2.10 mmol) of starting material **15e**. After purification by column chromatography using basic Alox (Brockmann 3, EtOAc/NEt₃ 10:1) the product was obtained as skin colored powder in 77 % (1.02 g) yield.

R_f: 0.67 (silica, EtOAc/NEt₃/MeOH 10:1:1).

mp: 207.1 – 208.3°C.

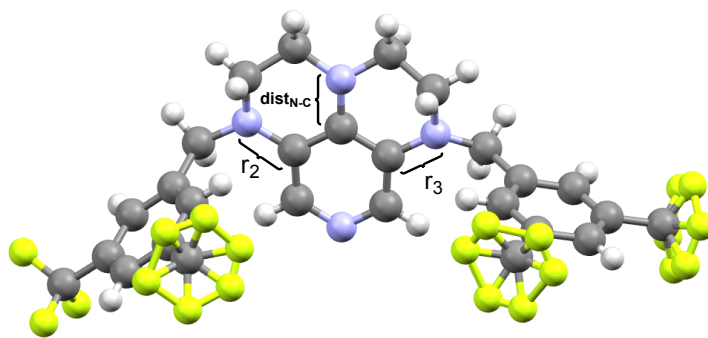
¹H-NMR (600 MHz, CDCl₃): δ = 3.43 (m, 8H, CH₂ x 4, H-2, H-3), 4.50 (s, 4H, CH₂ x 2, H-11), 7.30 (s, 2H, CH_{ar}), 7.75 (s, 4H, CH_{ar}, H-12), 7.78 (s, 2H, CH_{ar}).

¹³C-NMR (100 MHz, CDCl₃): δ = 47.3, 47.4, 55.5, 119.1, 121.4, 121.8, 124.6, 125.8, 127.1, 127.8, 129.6, 132.1 (q), 141.2.

¹⁹F-NMR (282 MHz, CDCl₃): δ = -62.9.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2857 (w), 1622 (w), 1571 (s), 1525 (m), 1443 (w), 1370 (m), 1352 (s), 1274 (vs), 1236 (m), 1162 (s), 1120 (vs), 1094 (vs), 1004 (w), 907 (s), 825 (s), 707 (s), 681 (s).

HRMS (EI): calculated for: C₂₇H₂₀F₁₂N₄ [M]⁺ 628.1496, found: 628.1492.



	$\text{dist}_{\text{N-C}}/\text{pm}$	r_2/pm	r_3/pm	$d_{(abcd)}$
crystal structure	138.5	140.4	138.9	20.3°
calculated best conf.	140.2	141.1	140.3	18.0°

In the best conformer of the calculated structure the substituents in 3- and 5- position are not the same like the crystal structure. One substituent directs to the back and one to the front. The conformer found to be most similar to the crystal structure is conformer **5** in which both benzylic substituents point to the front. The $d_{(abcd)}$ angle is 20.6° and it is just 1 kJ/mol higher in energy.

Synthesis of catalyst **18**

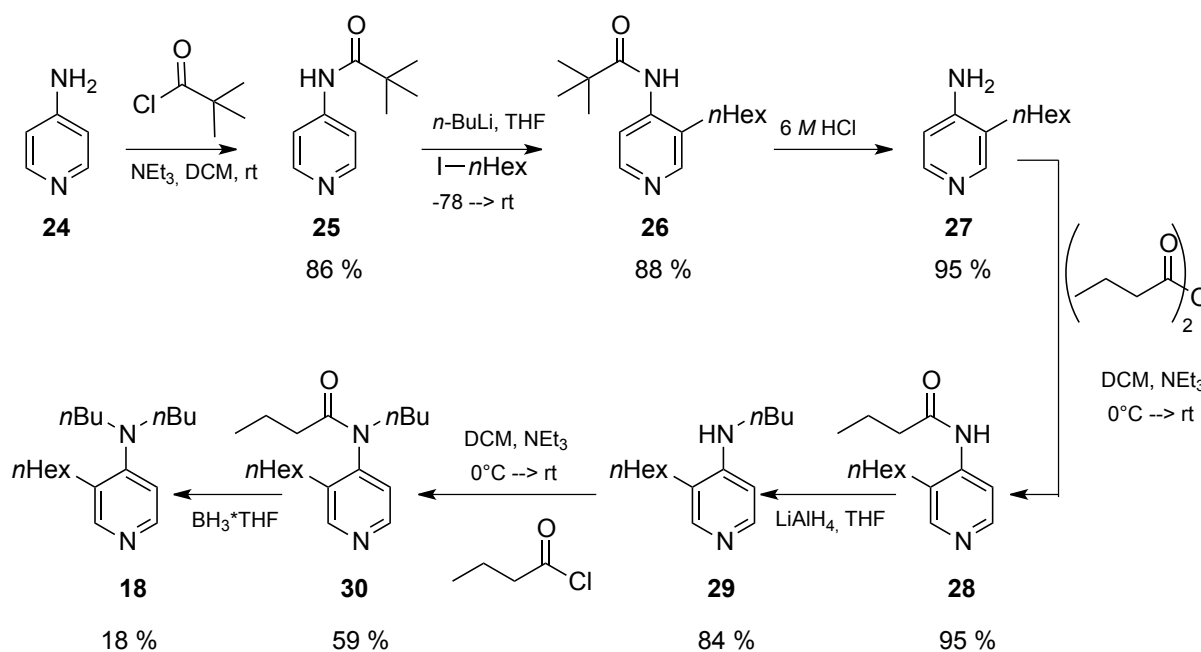
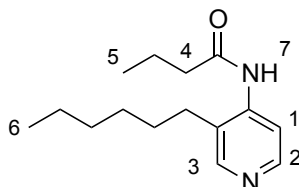


Figure S5. Synthesis of catalyst **18**.

Compound **27** was synthesized according to a previously published strategy by *Held et al.*^[10]

N-(3-Hexylpyridin-4-yl)butyramide (**28**)



Compound **27** 0.60 g (3.37 mmol) was dissolved in NEt₃ 0.70 mL (1.5 eq., 5.01 mmol) and 8 mL DCM. At 0 °C butyric anhydride 0.55 mL (3.37 mmol) in 2 mL DCM was added slowly via a dropping funnel. After stirring for one hour at 0°C the reaction mixture was stirred at room temperature over night. The reaction mixture was washed three times with sat. NaHCO₃ and three times with DCM. The combined organic layers were dried over MgSO₄ and the solvent was distilled off at reduced pressure. Column chromatography (silica, EtOAc/iH 9:1) gave **28** as a pale brown solid in 95 % (0.80 g).

R_f: 0.47 (silica, EtOAc/iH 9:1).

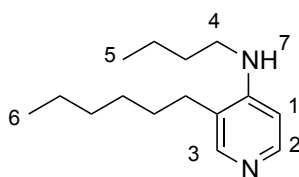
¹H-NMR (200 MHz, CDCl₃): δ = 0.89 (s, 3H), 1.02 (t, ³J = 7.4 Hz, 3H), 1.24 – 1.49 (m, 6H), 1.50 – 1.71 (m, 2H), 1.77 (dd, ³J = 14.9 Hz, ³J = 7.4 Hz, 2H), 2.40 (t, ³J = 7.4 Hz, 2H), 2.48 – 2.64 (m, 2H), 7.20 (s, br, 1H, NH, H-7), 8.16 (d, ³J = 5.6 Hz, 1H, H-1), 8.33 (s, 1H, H-3), 8.39 (d, ³J = 5.6 Hz, 1H, H-2).

¹³C-NMR (100 MHz, CDCl₃): δ = 13.6, 13.9, 18.8, 22.5, 28.5, 29.0, 39.1, 29.2, 29.3, 29.6, 31.5, 31.9, 39.9, 114.5, 124.7, 142.6, 148.9, 150.6, 171.4.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3252 (w, br, NH), 2957 (m), 2924 (s), 2854 (m), 1672 (s, C=O), 1577 (vs), 1503 (vs), 1463 (s), 1412 (s), 1377 (m), 1311 (m), 1282 (s), 1193 (s), 1075 (m), 990 (w), 908 (m), 834 (m), 730 (v), 699 (m).

HRMS (EI): calculated for: C₁₅H₂₄N₂O [M+H]⁺ 249.1967, found: 249.1959.

N-Butyl-3-hexylpyridin-4-amine (**29**)



In a flame dried three necked Schlenk flask LiAlH_4 62 mg (1.63 mmol) were stirred in THF. Compound **28** 0.30 g (1.21 mmol) was dissolved in THF and added slowly via a dropping funnel at 0 °C in 15 min. After stirring for additional 15 min at room temperature the reaction mixture was refluxed for three hours. The reaction was quenched with EtOAc and the solvent removed under reduced pressure. After addition of DCM to the residue it was filtered over Celite and directly subjected to column chromatography using silica (EtOAc 100 %). A yellow oily substance was obtained in 84 % (0.23 g) yield.

R_f: 0.17 (silica, EtOAc 100%).

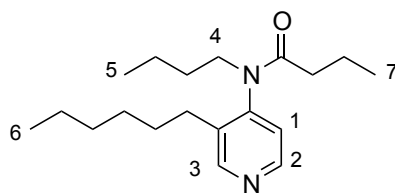
¹H-NMR (300 MHz, CDCl_3): δ = 0.90 (s, 3H), 0.99 (t, 3J = 7.3 Hz, 3H), 1.18 – 1.76 (m, 12H), 2.35 – 2.48 (m, 2H), 3.19 (dd, 3J = 12.4 Hz, 3J = 7.0 Hz, 2H), 4.05 (s, br, 1H, NH), 6.45 (d, 3J = 5.7 Hz, 1H, H-1), 8.03 (s, 1H, H-3), 8.16 (d, 3J = 5.6 Hz, 1H, H-2).

¹³C-NMR (75 MHz, CDCl_3): δ = 13.8, 14.0, 20.2, 22.6, 28.0, 28.3, 29.2, 31.3, 31.6, 42.5, 104.5, 120.6, 148.5, 148.7, 151.2.

IR (ATR): $\bar{\nu}$ (cm^{-1}) = 3152 (w, br, NH), 3140 (w), 2955(m), 2926 (s), 2857 (m), 1596 (vs), 1573 (s), 1519 (s), 1464 (m) 1332(m), 1222 (w), 1189 (s), 1067 (m), 919 (w), 811 (s), 724 (m), 611 (m).

HRMS (EI): calculated for: $\text{C}_{15}\text{H}_{26}\text{N}_2$ $[\text{M}]^+$ 234.2096, found: 234.2086.

N-Butyl-*N*-(3-hexylpyridin-4-yl)butyramide (**30**)



In a oven dried Schlenk tube the starting material **29** 0.28 g (1.19 mmol) was dissolved in dry DCM. After the addition of NEt_3 0.49 mL (3.57 mmol) the slightly yellow reaction mixture was cooled to 0 °C and butyryl chloride 0.28 mL (2.2 eq., 2.61 mmol) was added drop wise. The reaction mixture was stirred at room temperature over night. After the disappearance of starting material (TLC) the solvent was removed under reduced pressure and the orange residue was directly subjected to column chromatography (silica, IH/EtOAc/ NEt_3 10:2:1) and yielded the product **30** in 59 % (0.21 g).

R_f: 0.52 (silica, IH/EtOAc/ NEt_3 10:2:1).

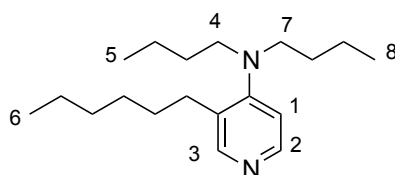
¹H-NMR (300 MHz, CDCl_3): δ = 0.87 (ddd, ³*J* = 22.8 Hz, ³*J* = 11.0 Hz, ³*J* = 5.9 Hz, 10H), 1.15 – 1.72 (m, 13H), 1.72 – 2.00 (m, 2H), 2.44 – 2.61 (m, 2H), 2.95 – 3.10 (m, 1H), 4.04 – 4.23 (m, 1H), 7.00 (d, ³*J* = 5.1 Hz, 1H), 8.50 (d, ³*J* = 5.1, 1H), 8.63 (s, 1H).

¹³C-NMR (100 MHz, CDCl_3): δ = 13.7, 13.8, 13.9, 18.6, 20.1, 22.5, 28.2, 29.4, 29.8, 29.9, 31.5, 36.3, 48.4, 124.0, 135.7, 148.6, 148.7, 152.6, 171.9.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2958 (s), 2929 (s), 2872 (m), 1756 (w), 1663 (vs, C=O), 1583 (s), 1559 (m), 1491 (m), 1458 (m), 1397 (s), 1283 (m), 1214 (m), 1137 (m), 838 (w), 731 (w), 616 (w).

HRMS (EI): calculated for: $\text{C}_{19}\text{H}_{32}\text{N}_2\text{O}$ [M]⁺ 304.2515, found: 304.2496.

N,N-Dibutyl-3-hexylpyridin-4-amine (**18**)



In an flame dried Schlenk flask $\text{BH}_3 \cdot \text{THF}$ 4.80 mL (4.80 mmol) is stirred and **30** 0.30 g (0.98 mmol) in 2 mL dry THF is added dropwise. The reaction mixture was refluxed for 16

hours and quenched by the slow addition of water. The mixture was poured onto 60 mL of 6M HCl and extracted with CHCl₃. After making the waterous phase under ice cooling slowly basic (pH=12) with NaOH it was extracted again with CHCl₃. After drying the organic phase over MgSO₄ the solvent was removed under reduced pressure and the crude mixture purified by column chromatography (silica, IH/EtOAc/NEt₃ 10:2:1). The product was obtained as colorless oil in 18 % (51 mg) yield.

R_f: 0.68 (silica, CHCl₃/MeOH 10:1).

¹H-NMR (300 MHz, CDCl₃): δ = 0.86 (dd, ³J = 8.2 Hz, ³J = 6.4 Hz, 9H), 1.13 – 1.36 (m, 10H), 1.43 (ddd, ³J = 11.8 Hz, ³J = 8.4 Hz, ³J = 6.0 Hz, 4H), 1.60 (dd, ³J = 15.2 Hz, ³J = 7.5 Hz, 2H), 2.52 – 2.62 (m, 2H), 2.95 – 3.07 (m, 4H), 6.80 (d, ³J = 5.5 Hz, 1H), 8.21 (d, ³J = 5.5 Hz, 1H), 8.26 (s, 1H).

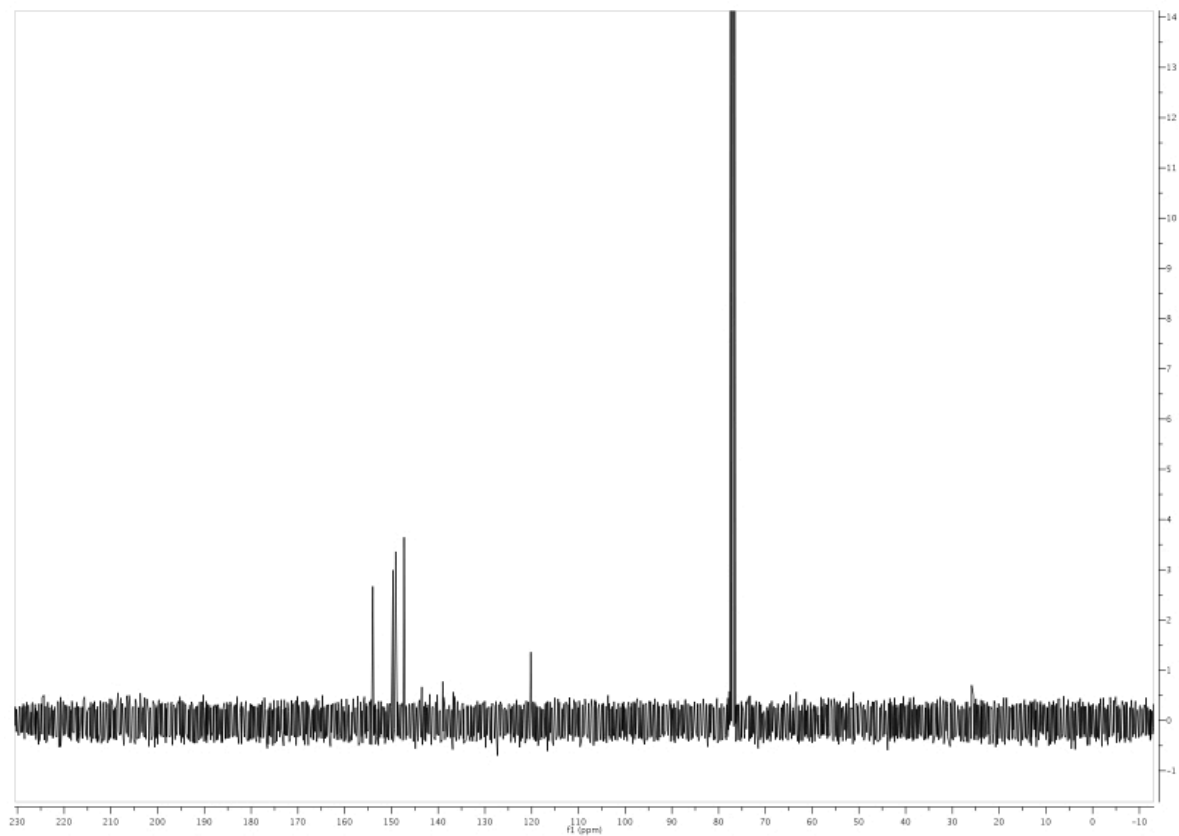
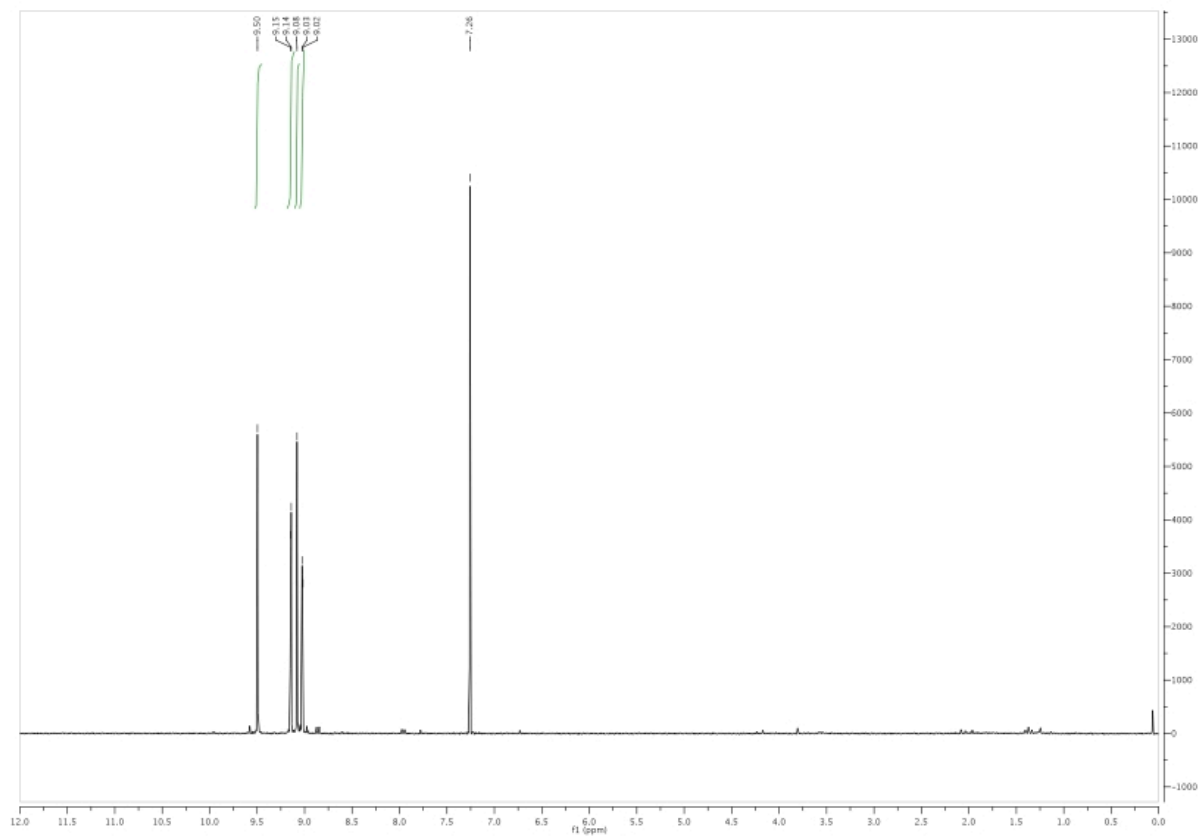
¹³C-NMR (75 MHz, CDCl₃): δ = 13.8, 14.0, 20.3, 22.6, 29.2, 29.3, 29.6, 29.7, 31.6, 52.2, 115.1, 131.3, 147.5, 151.5, 156.8.

IR (ATR): ν̄ (cm⁻¹) = 2957 (s), 2930 (s), 2860 (m), 2354 (w), 1623 (w), 1585 (s), 1492 (m), 1465 (m), 1376 (m), 1166 (m), 1117 (m), 927 (m), 828 (m), 731 (m).

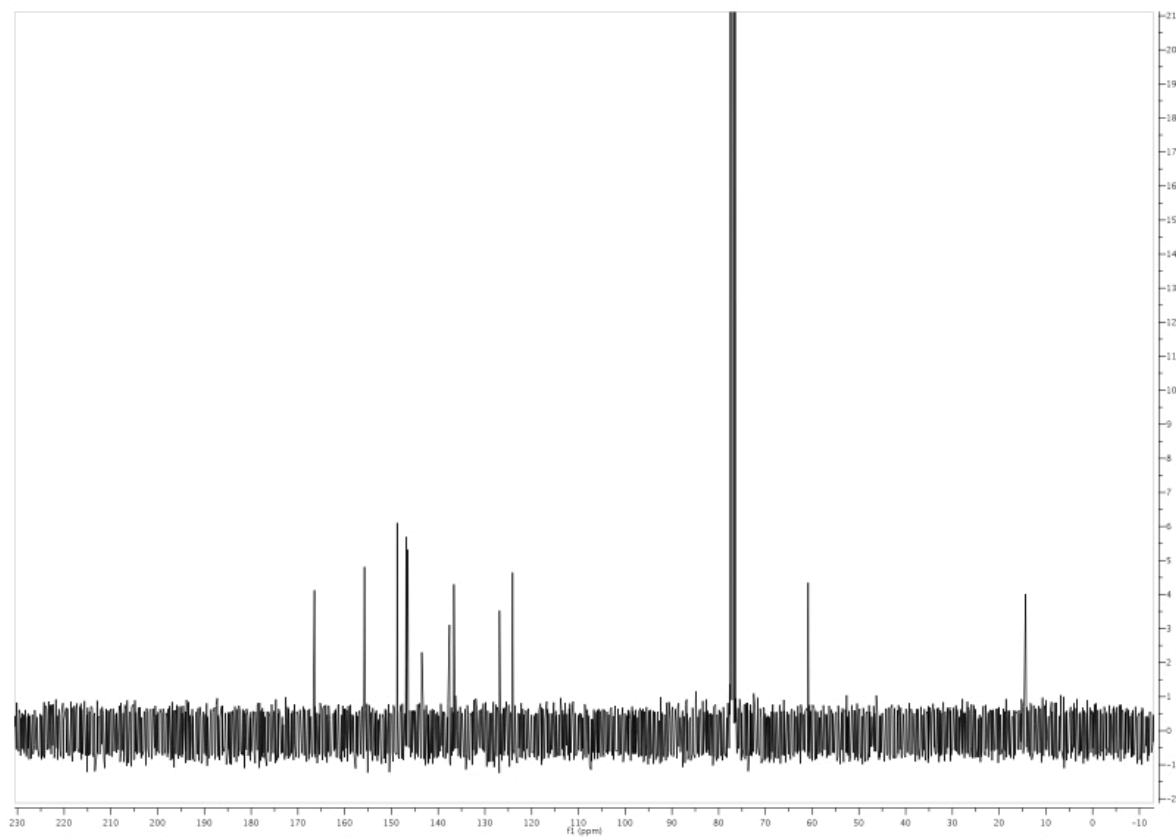
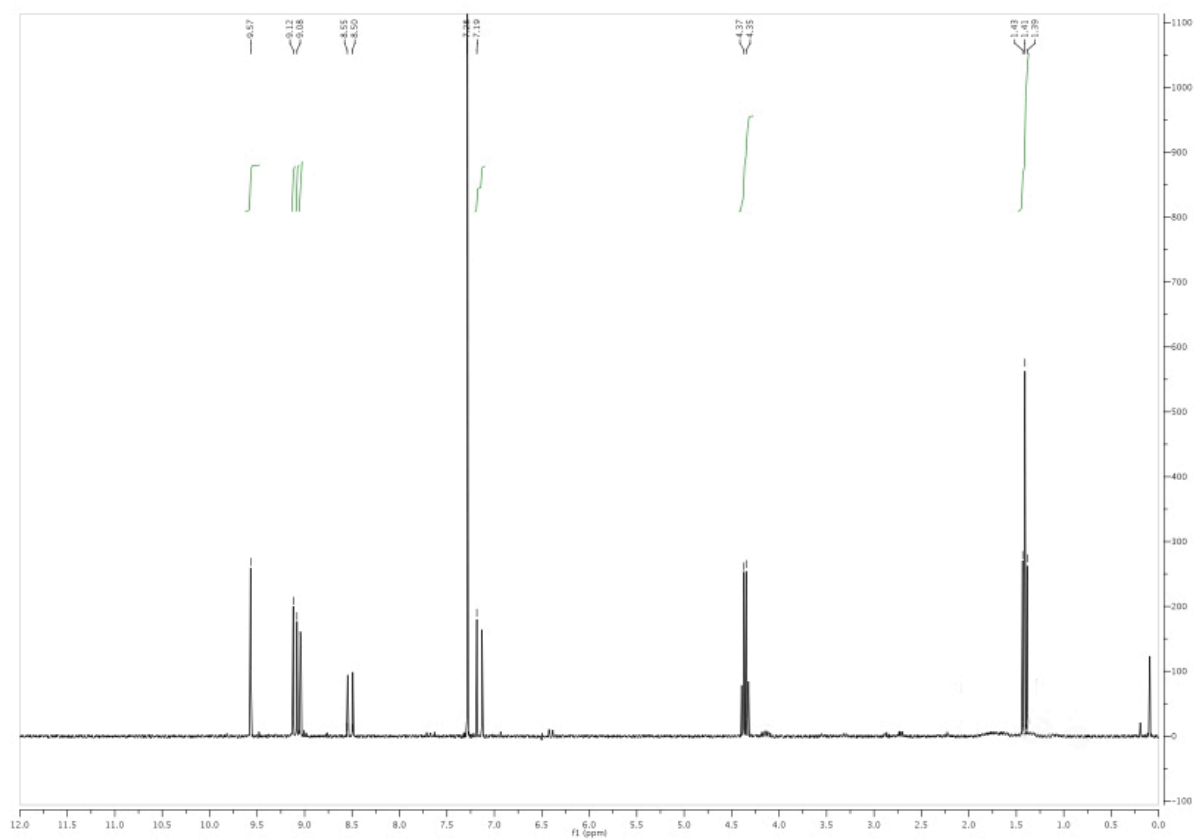
HRMS (EI): calculated for: C₁₉H₃₄N₂ [M]⁺ 290.2722, found: 290.2711.

2. ^1H NMR spectra of new compounds

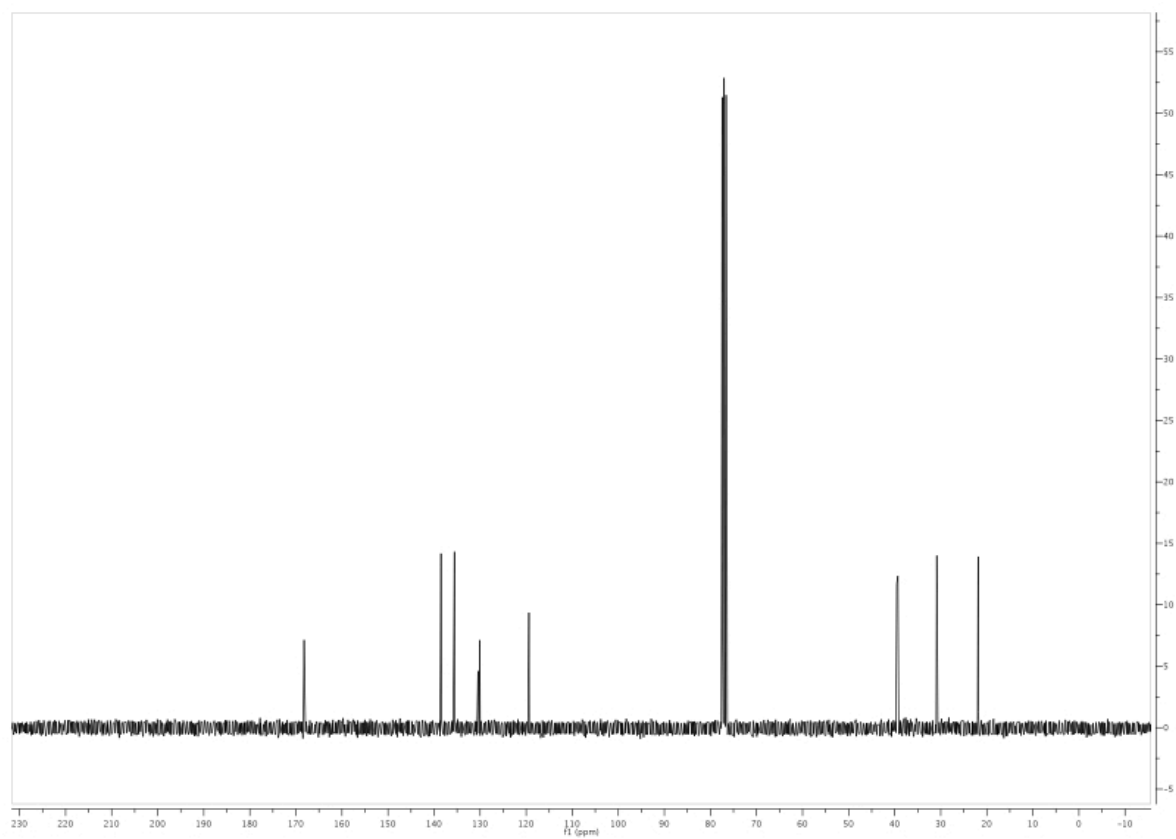
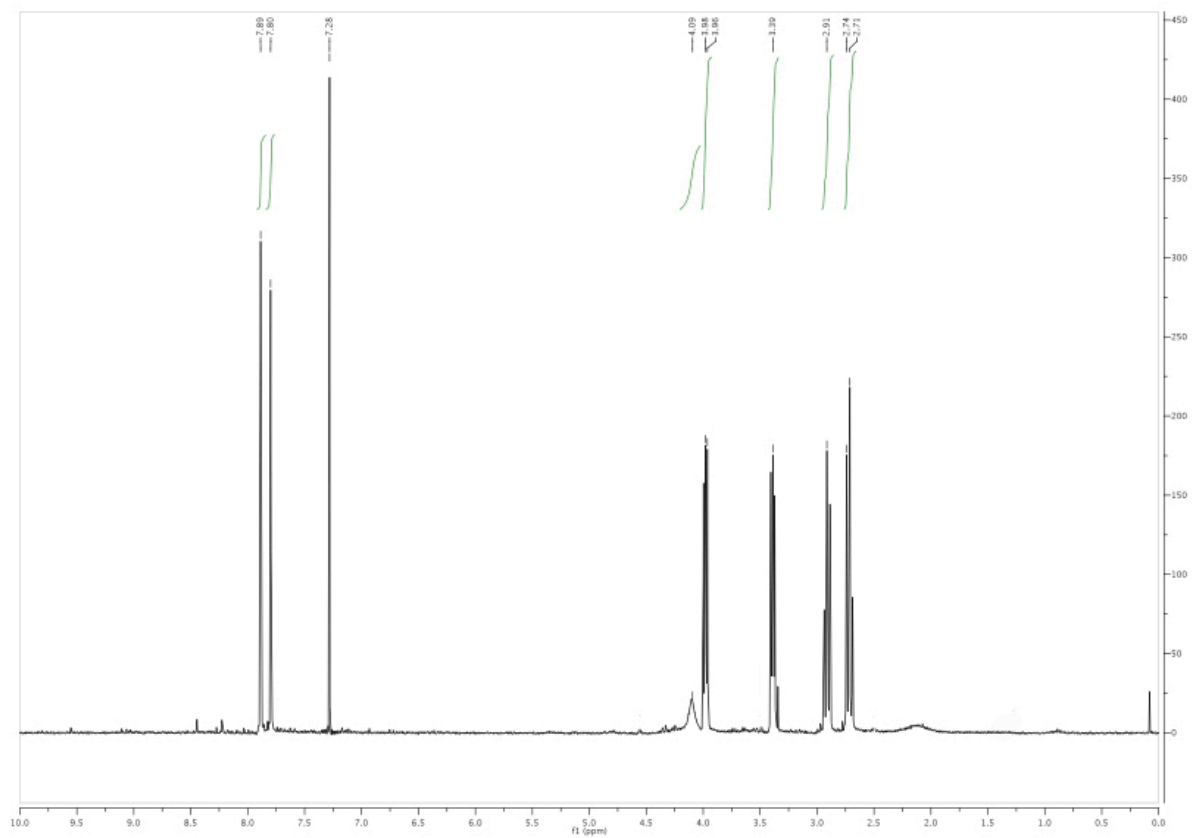
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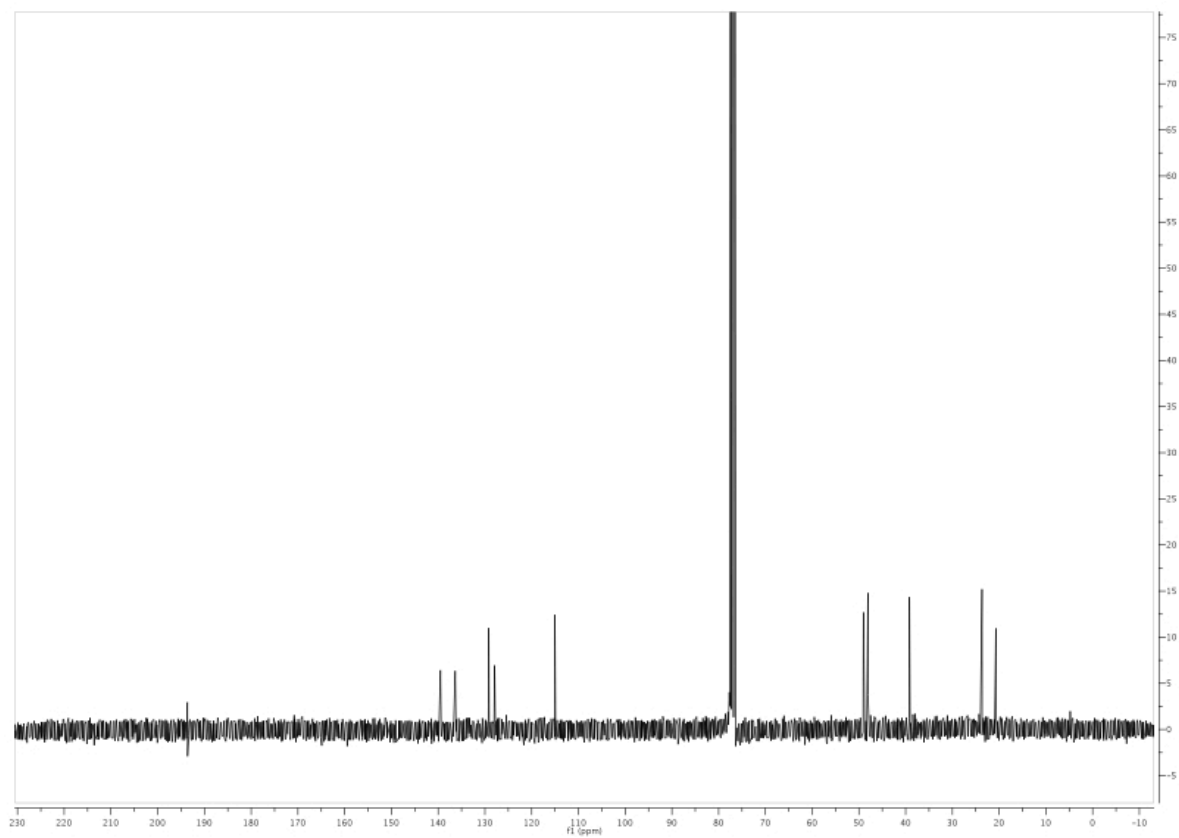
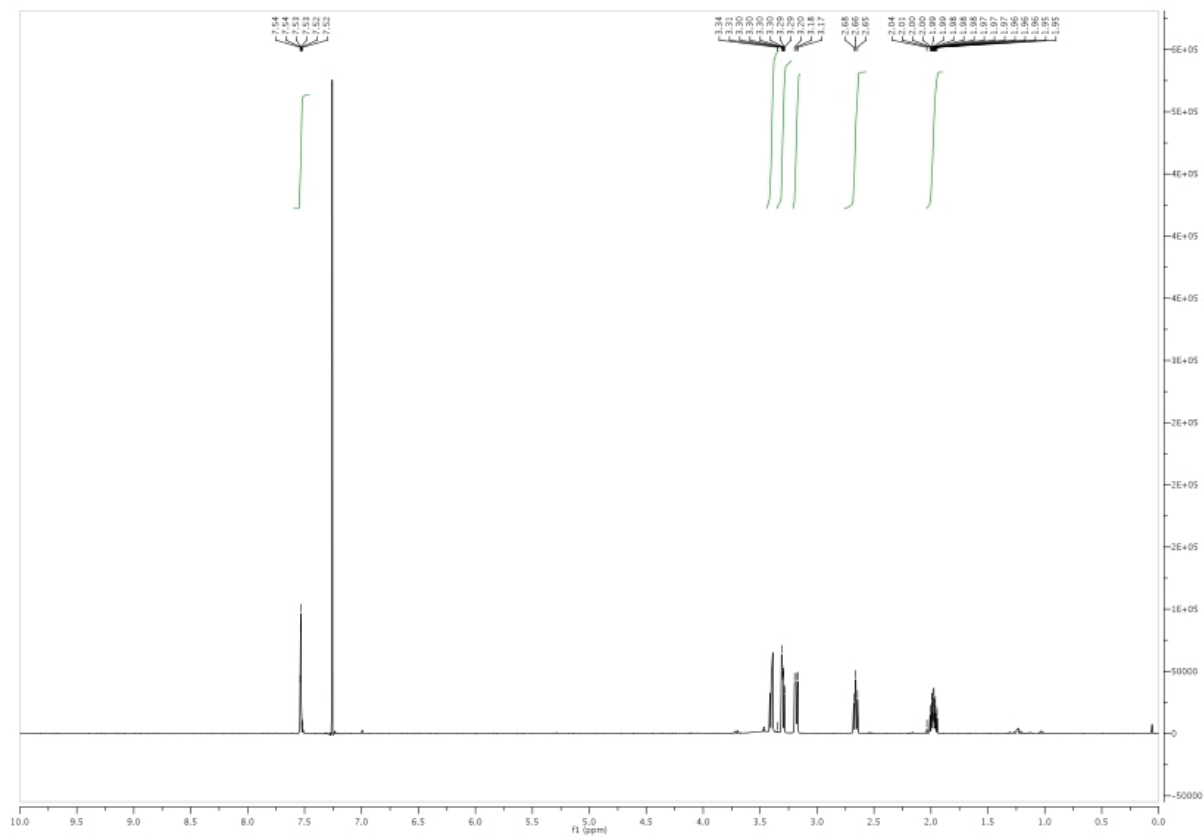
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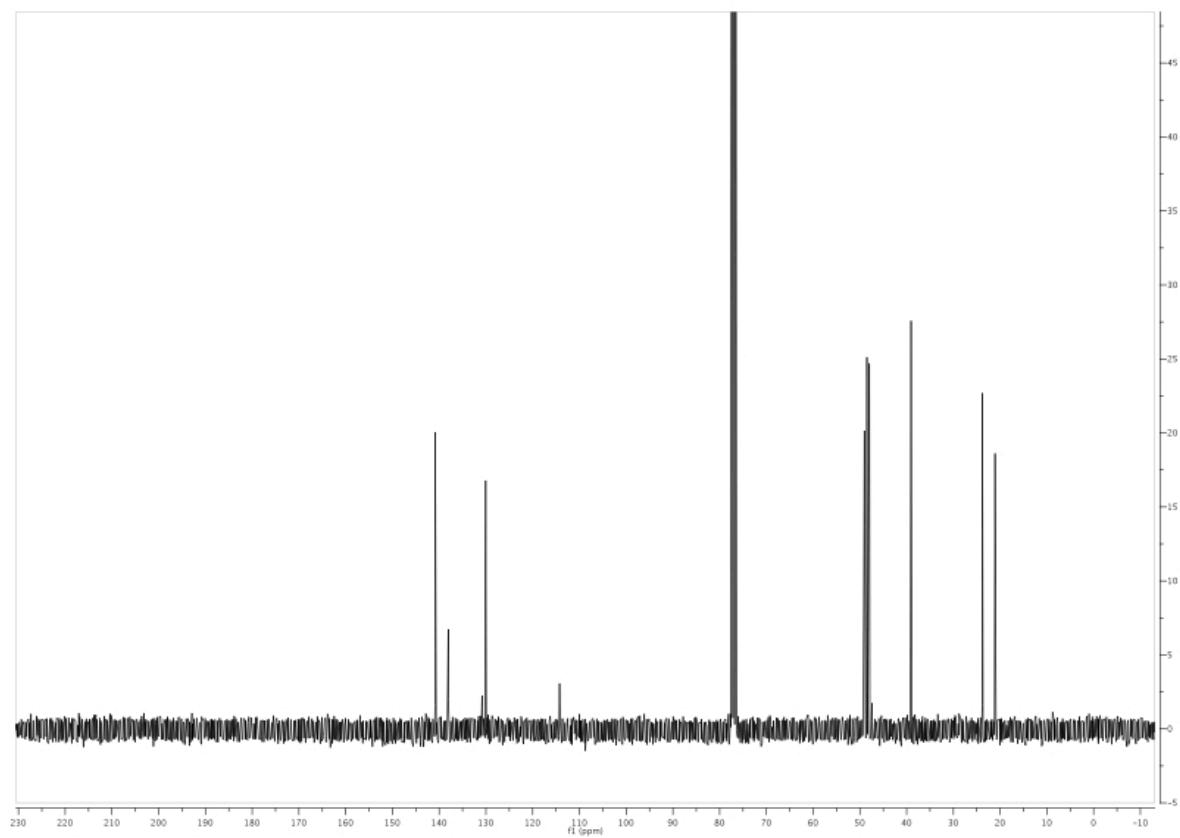
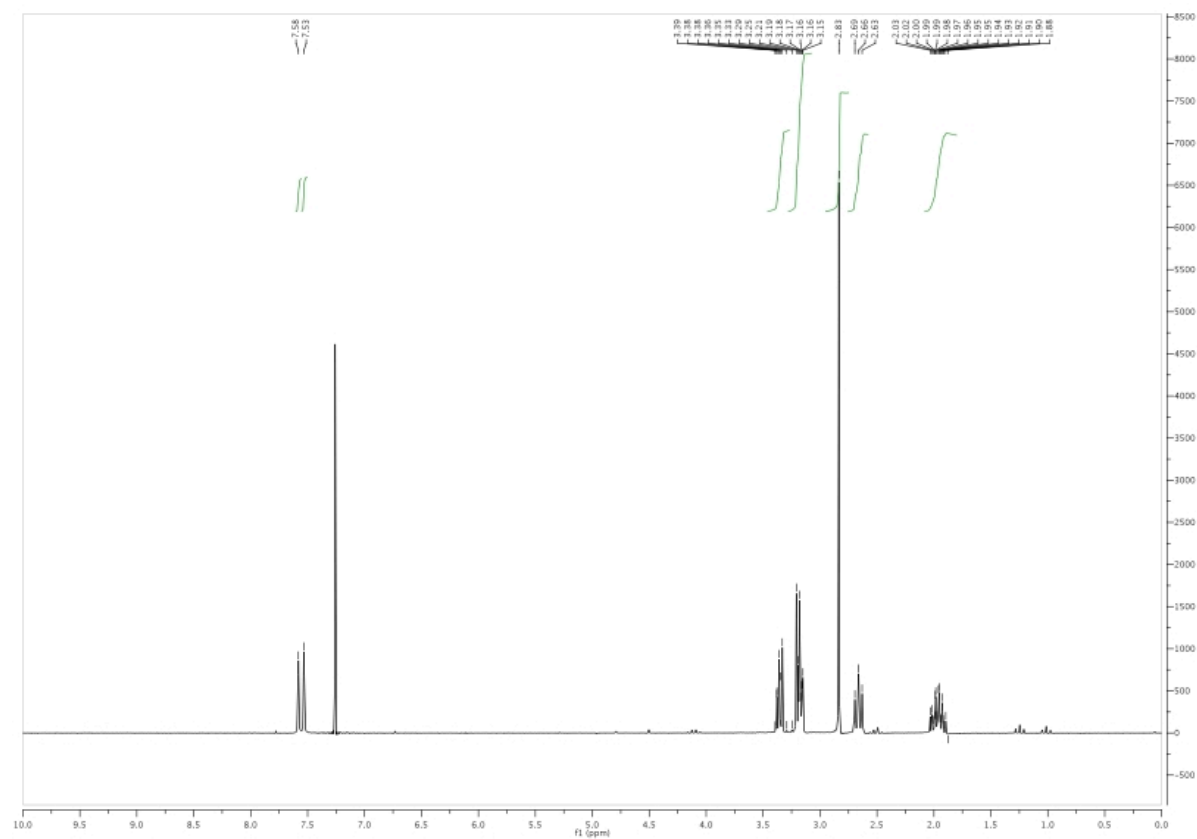
11:



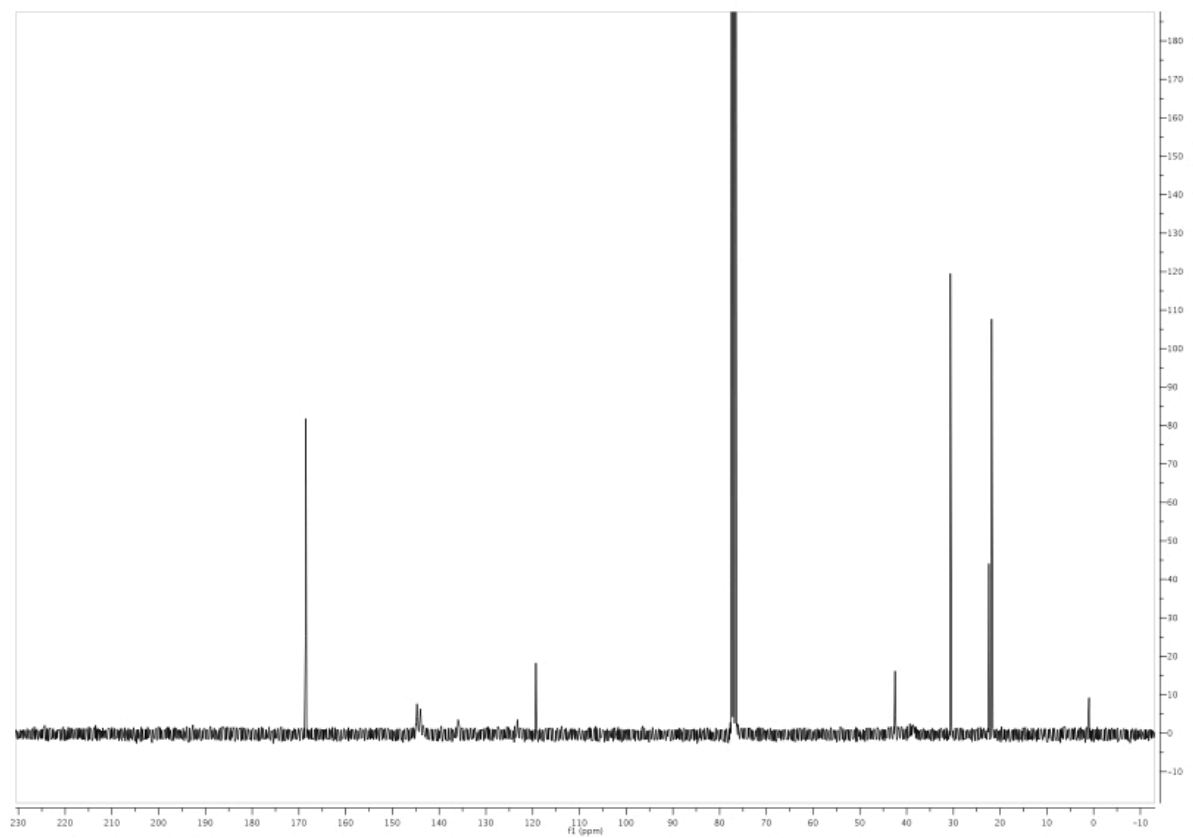
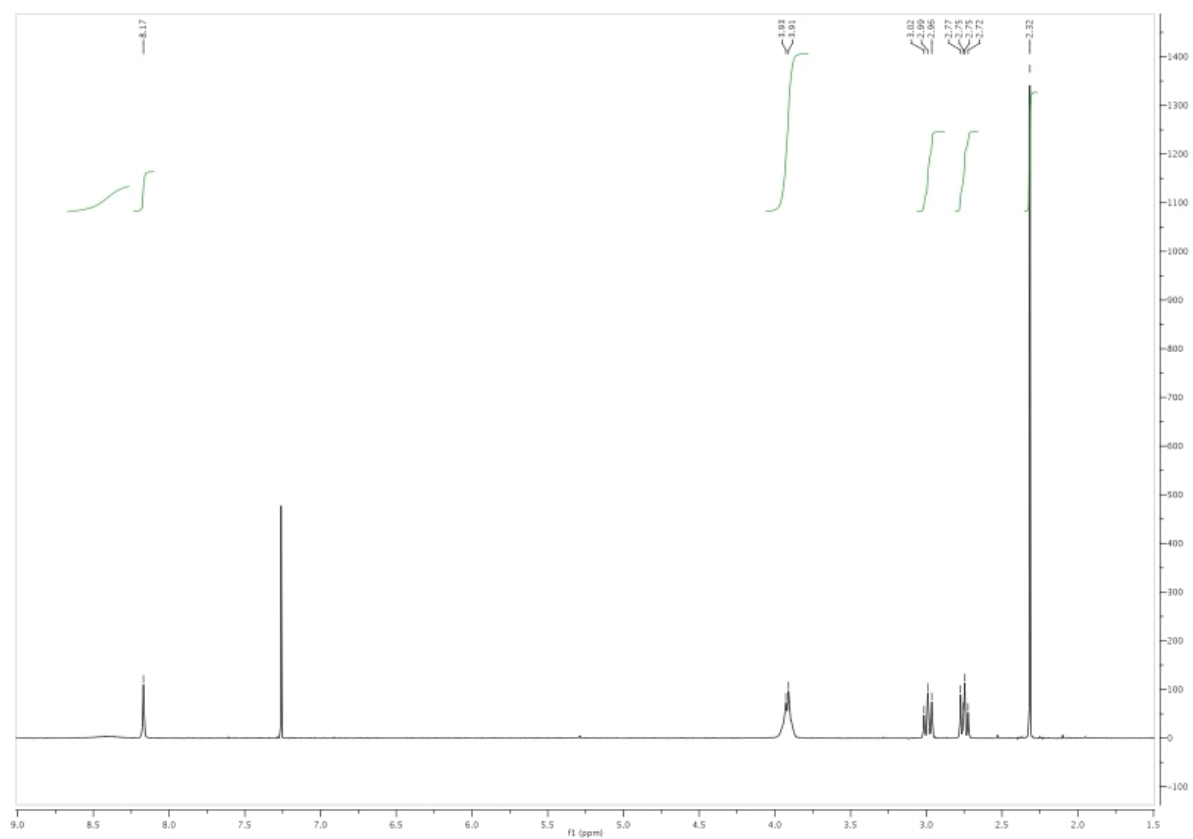
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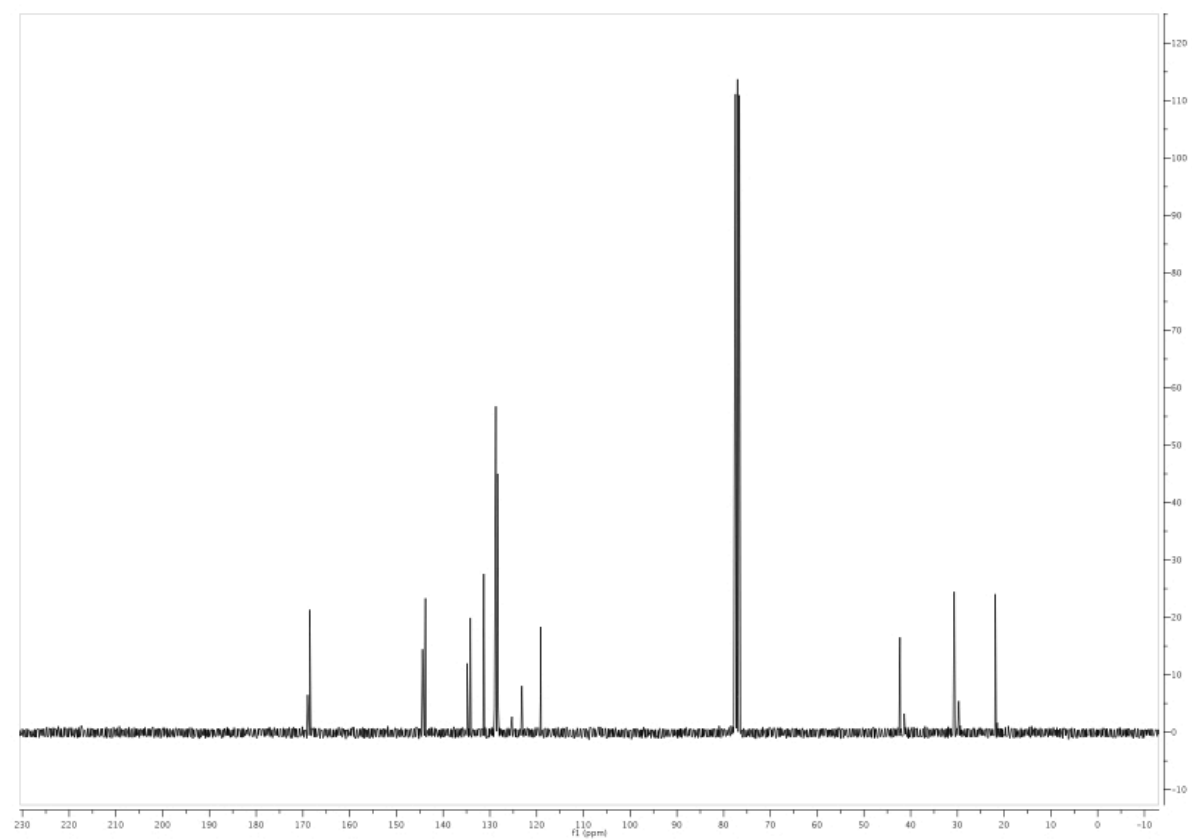
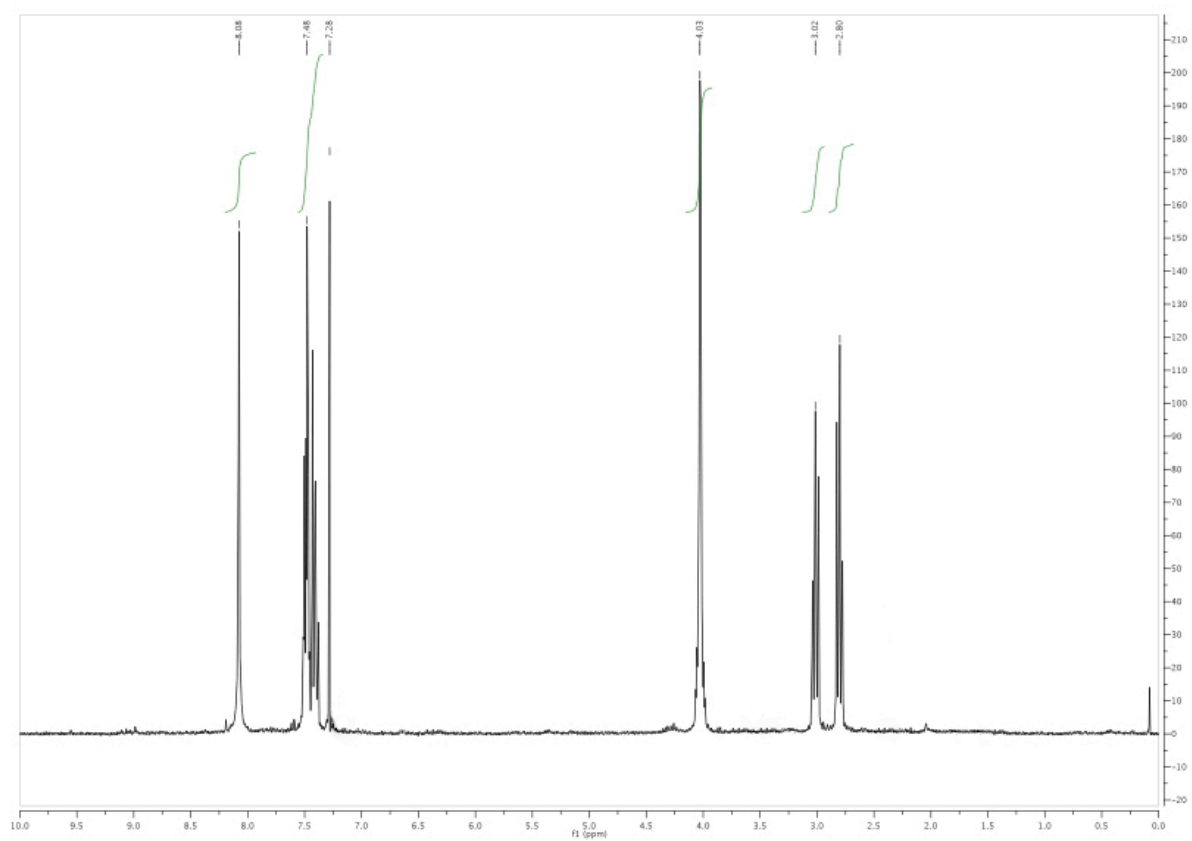
4a:



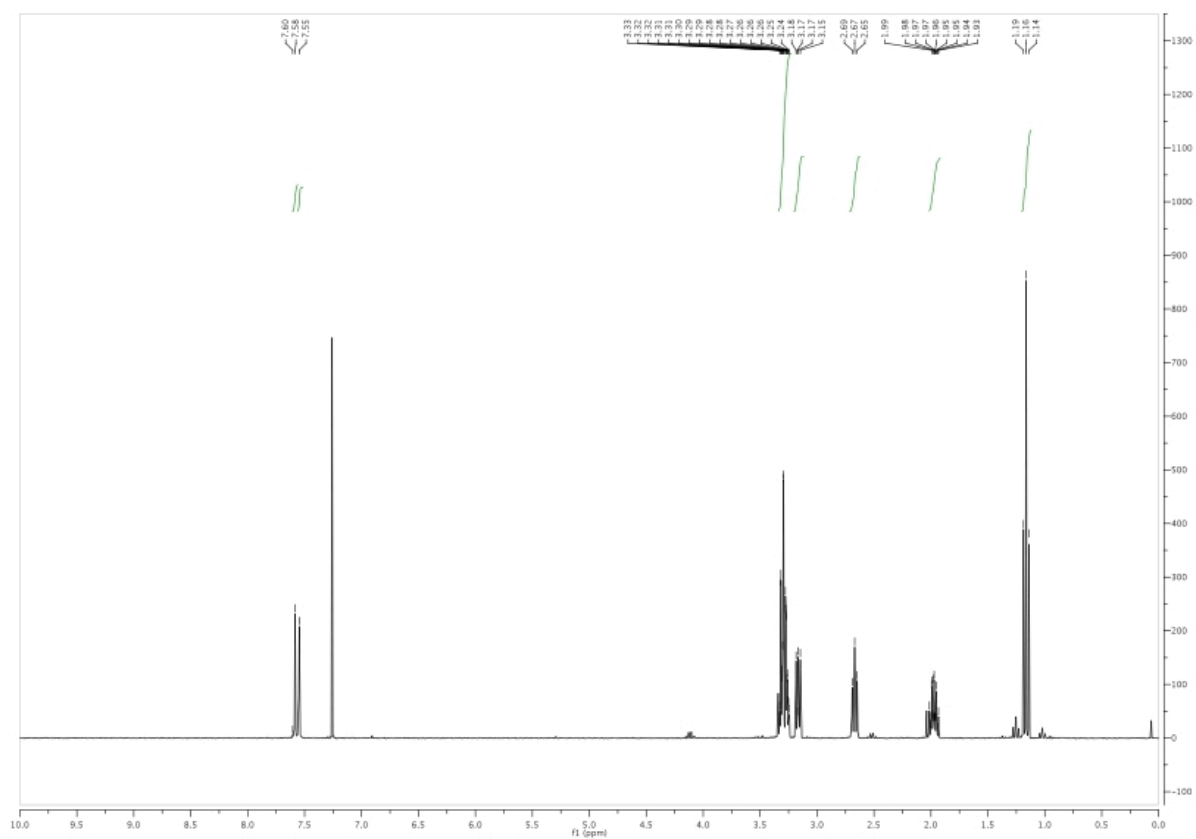
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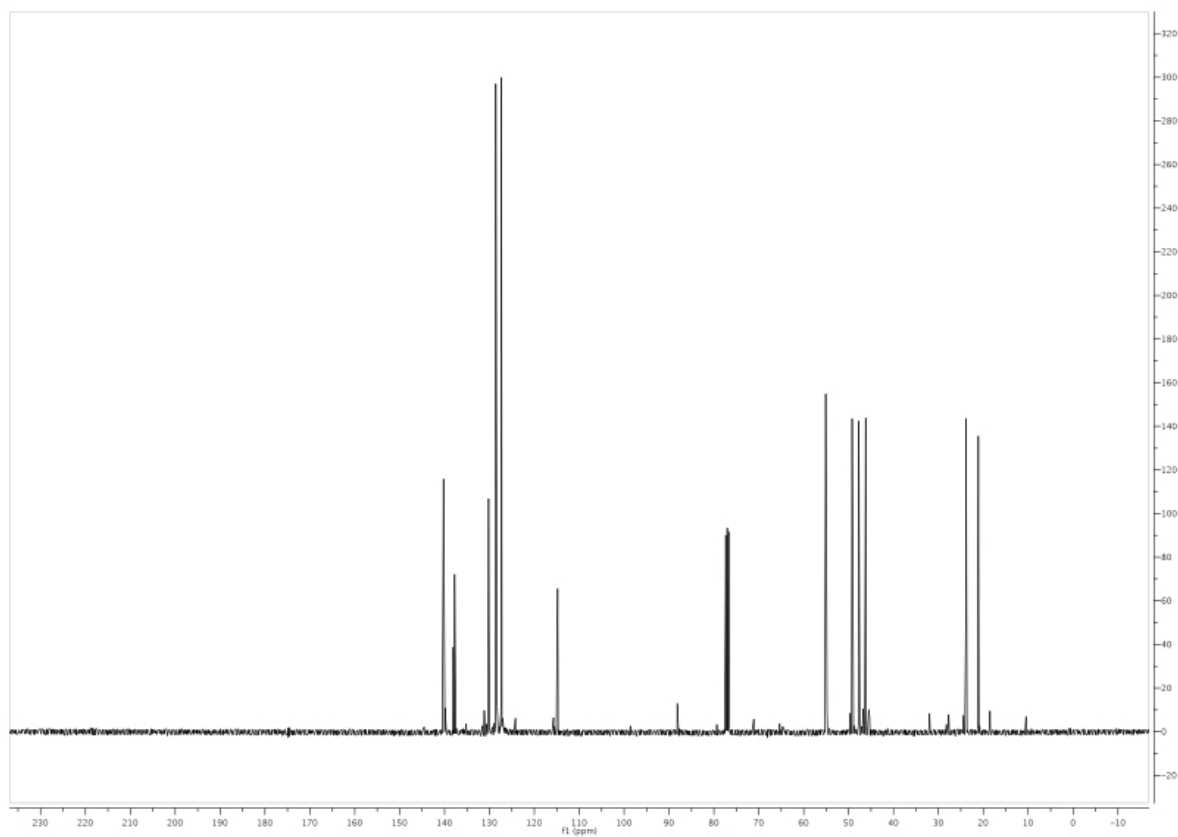
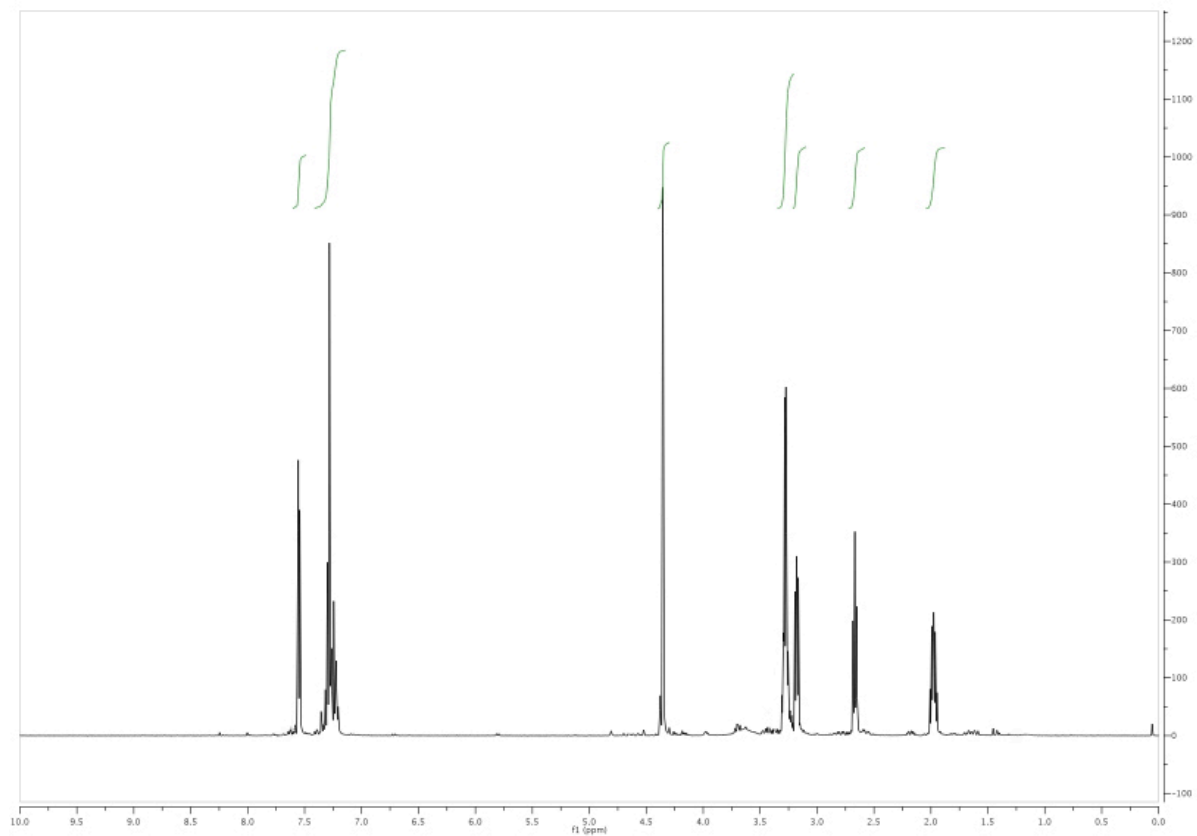
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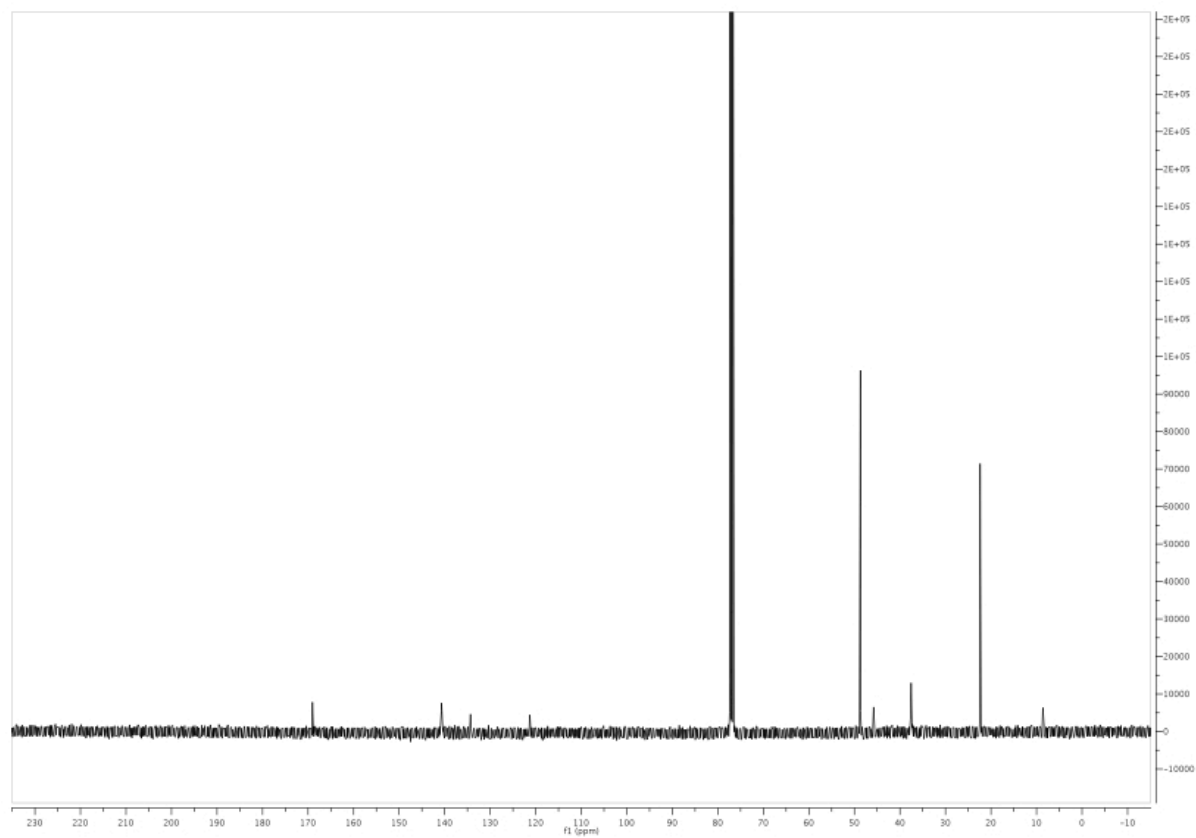
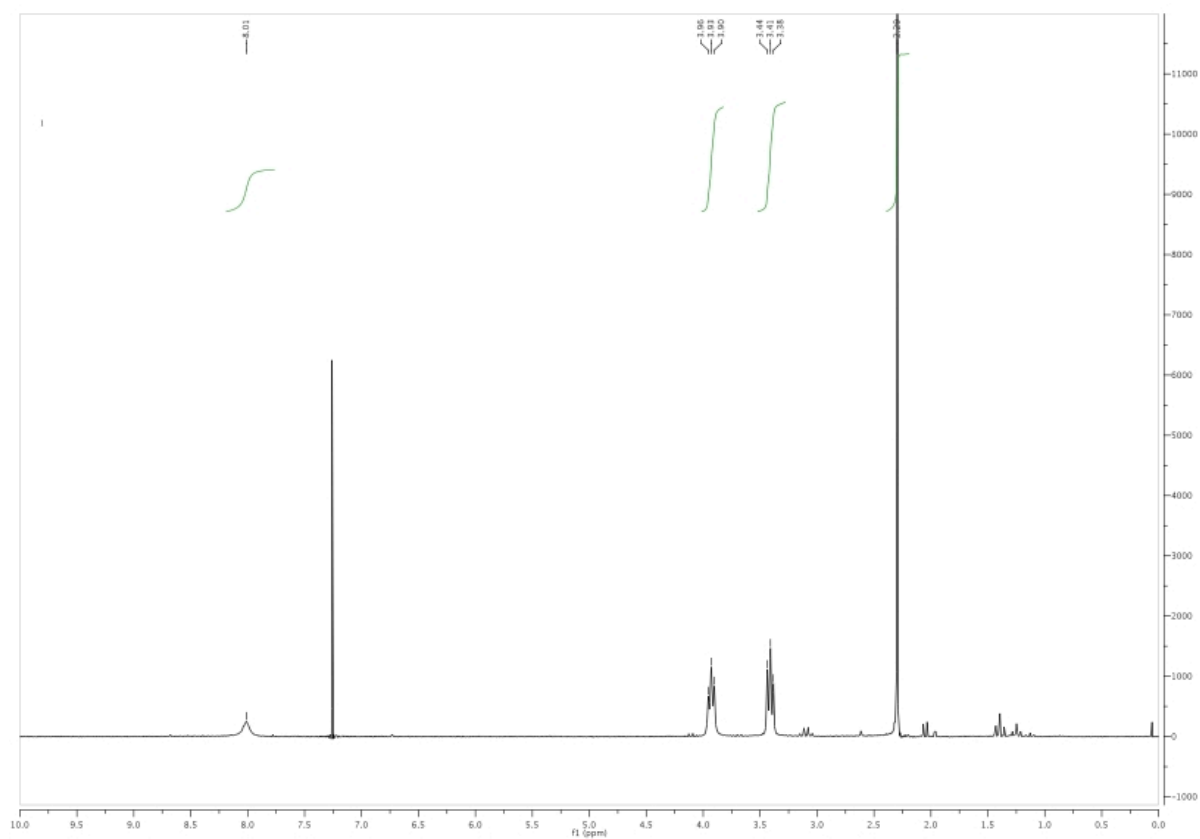
4b



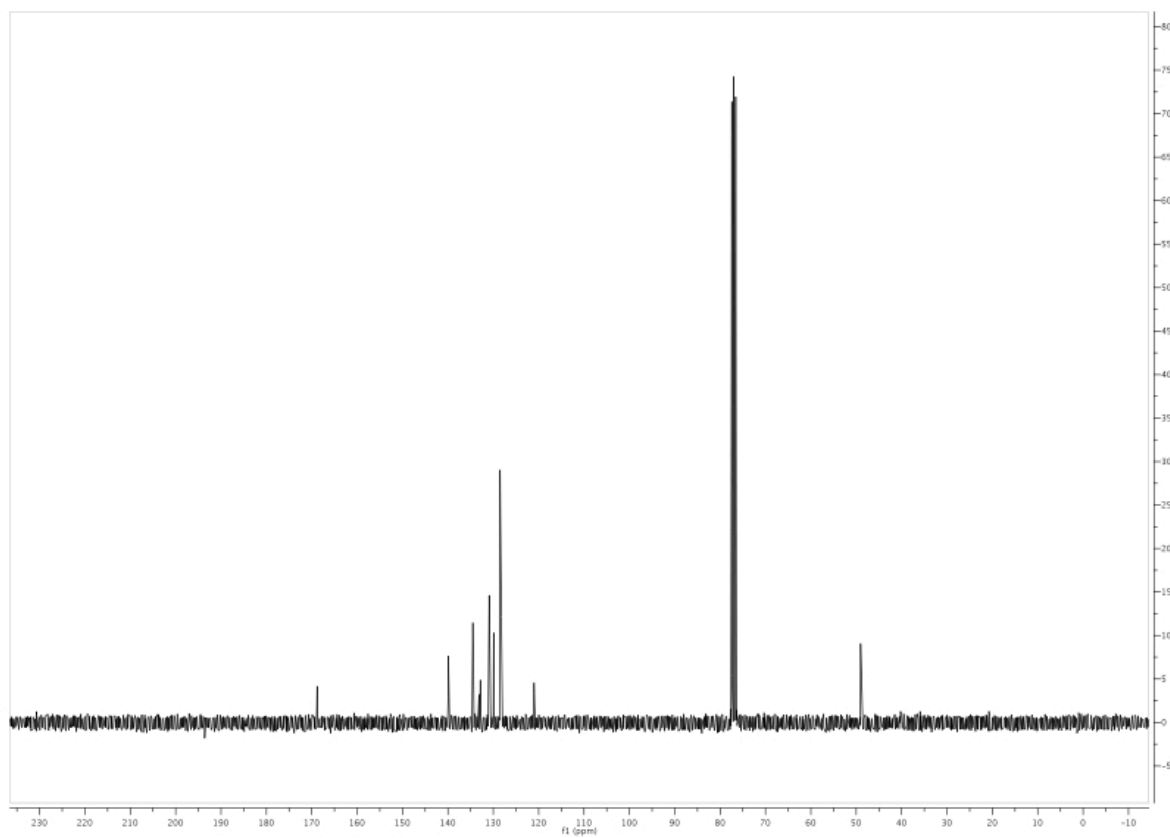
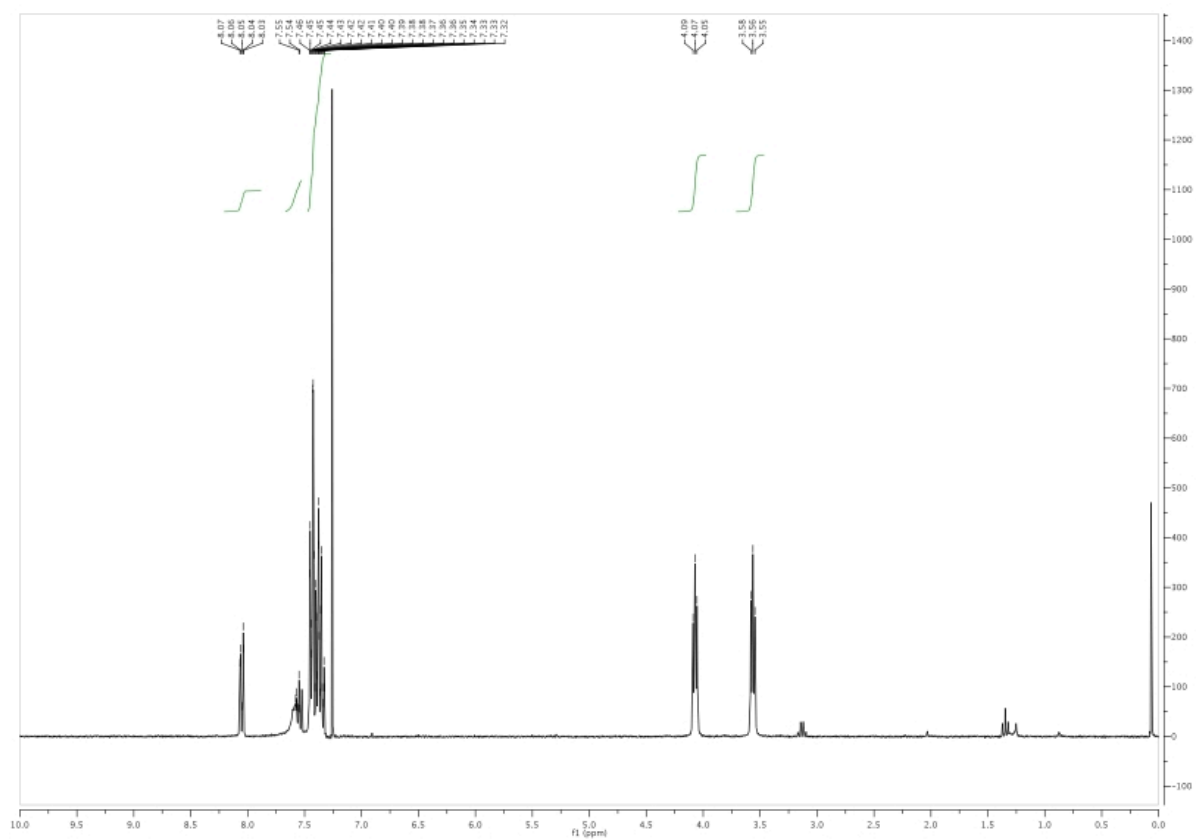
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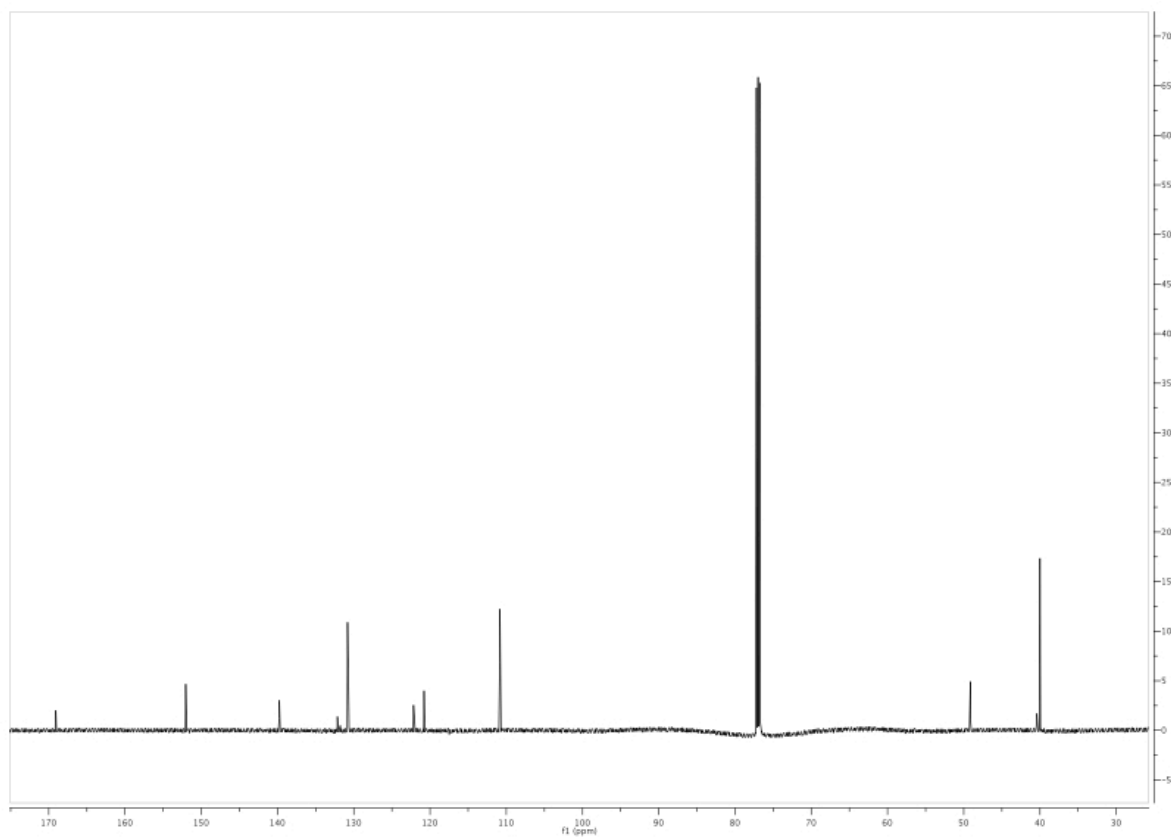
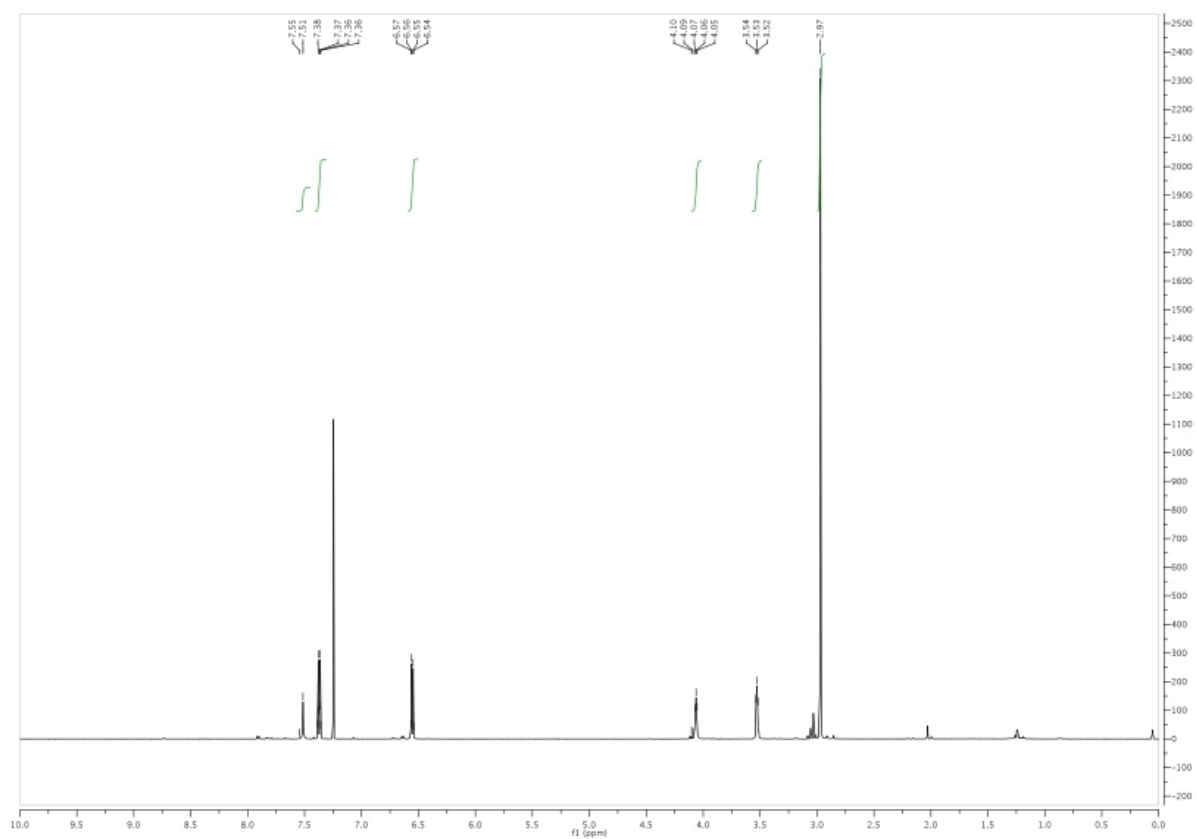
15b:



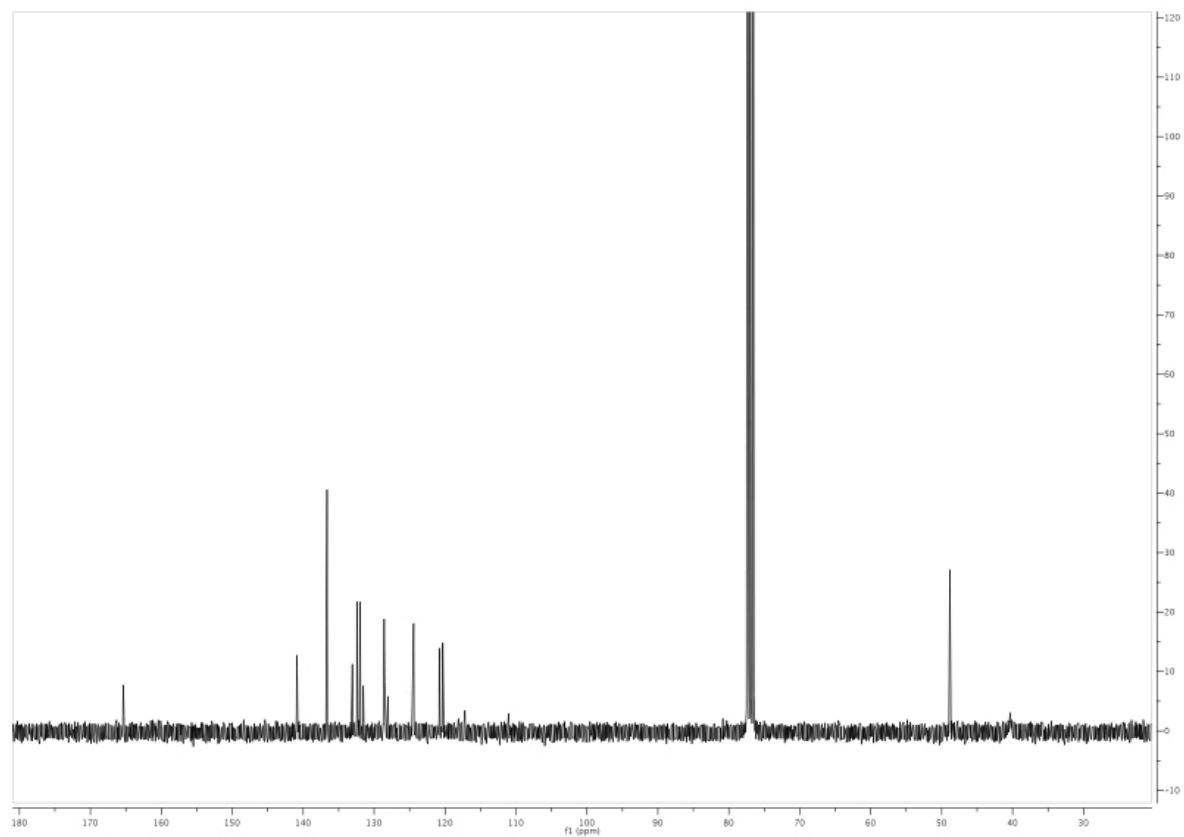
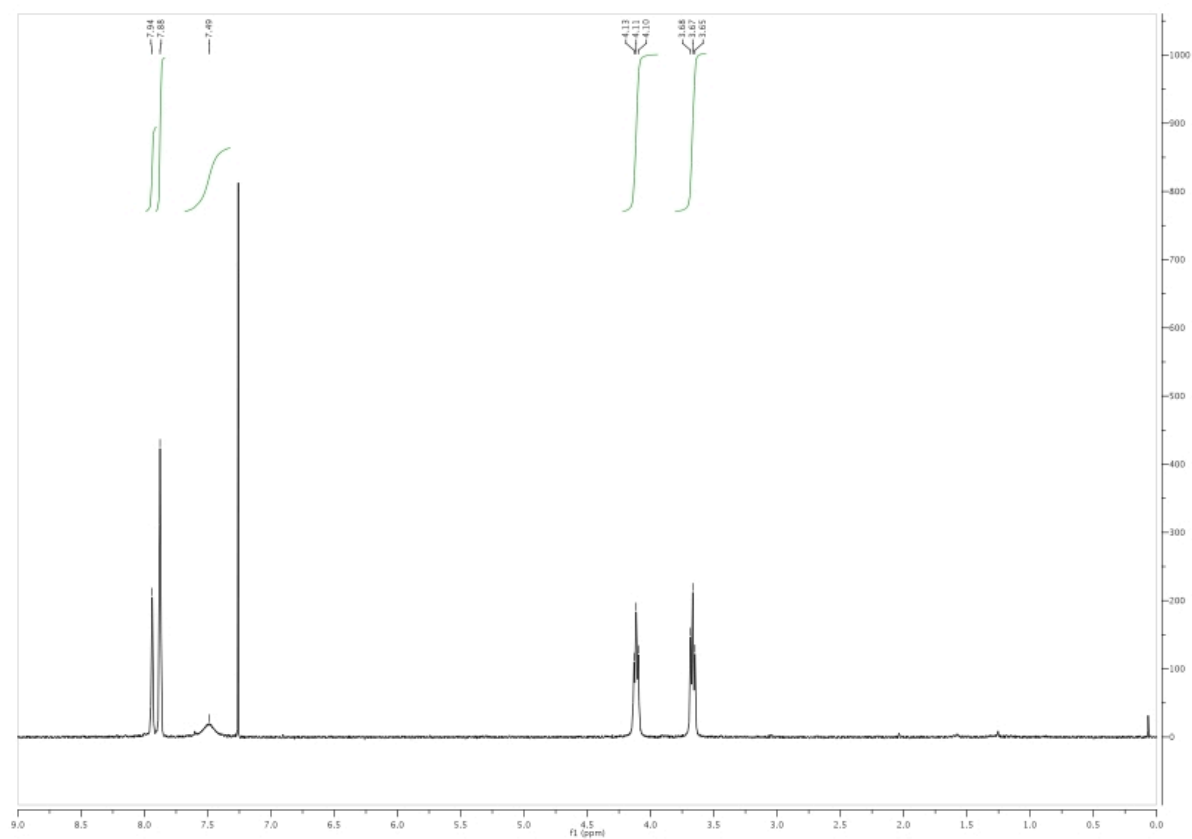
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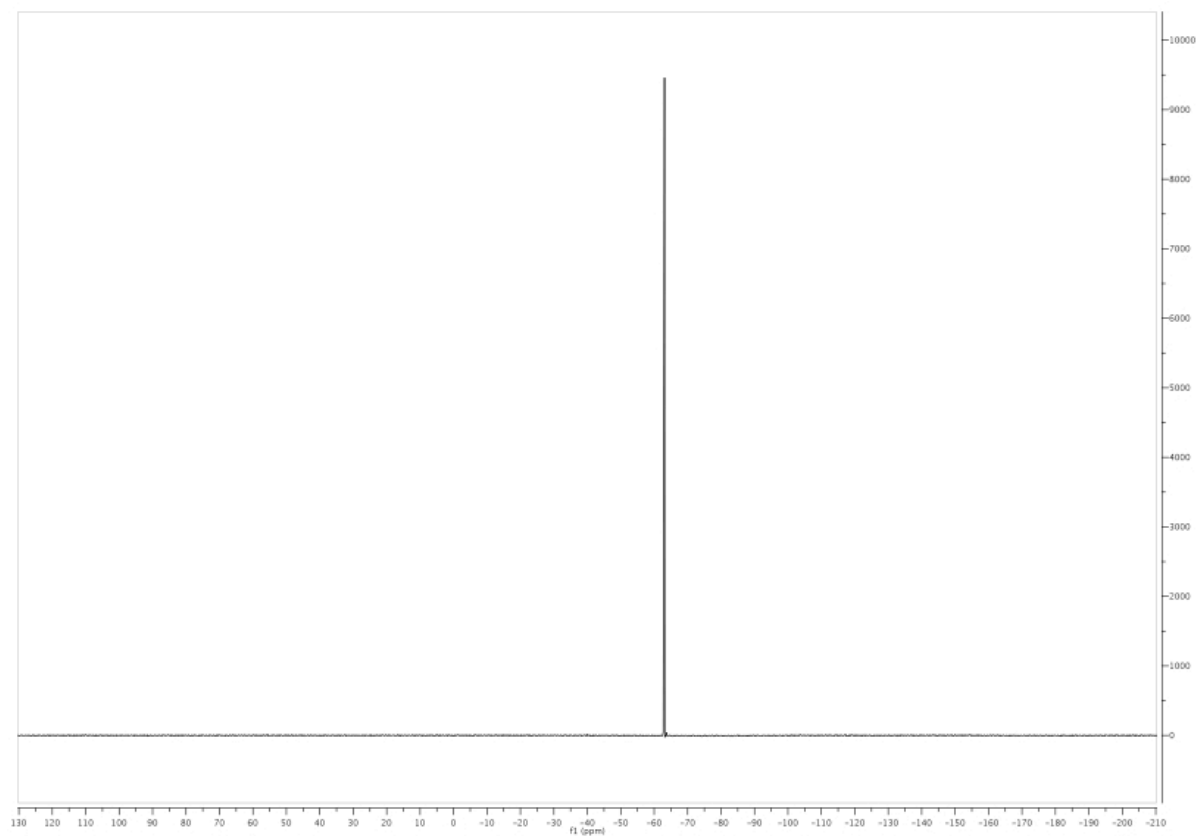


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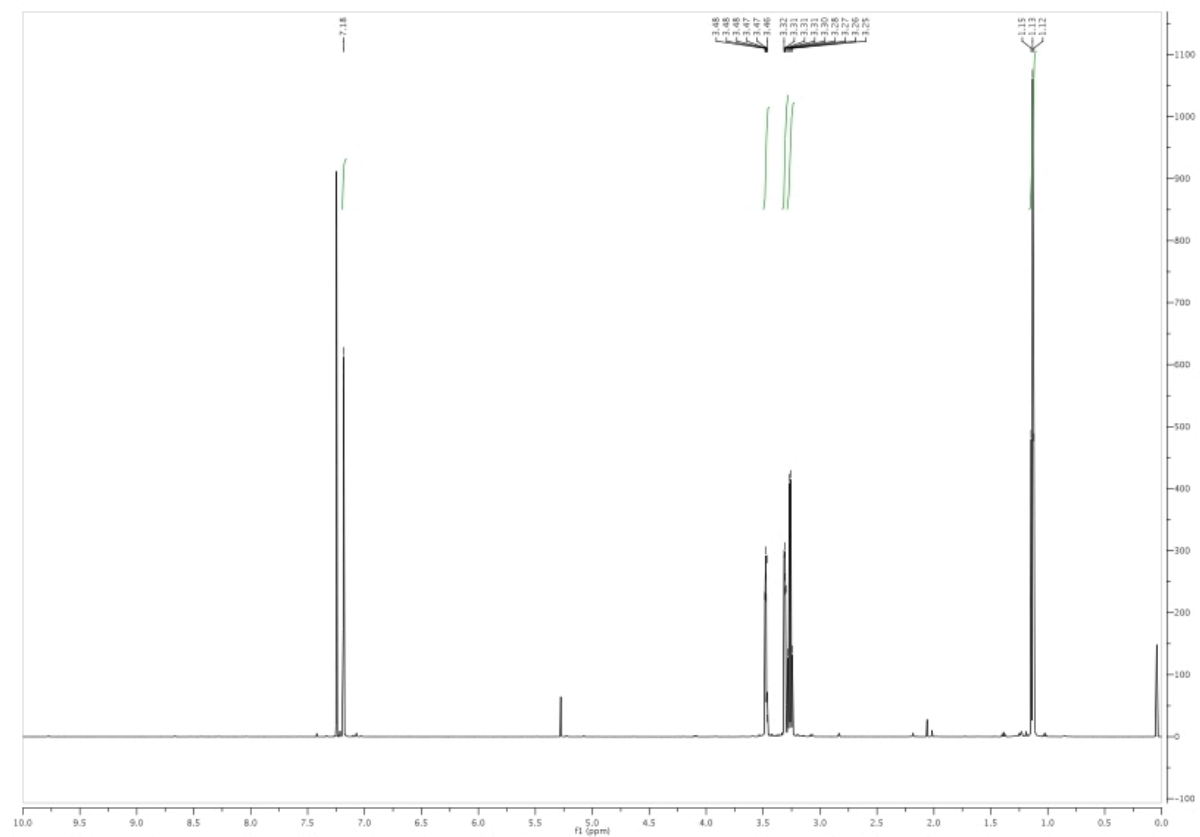


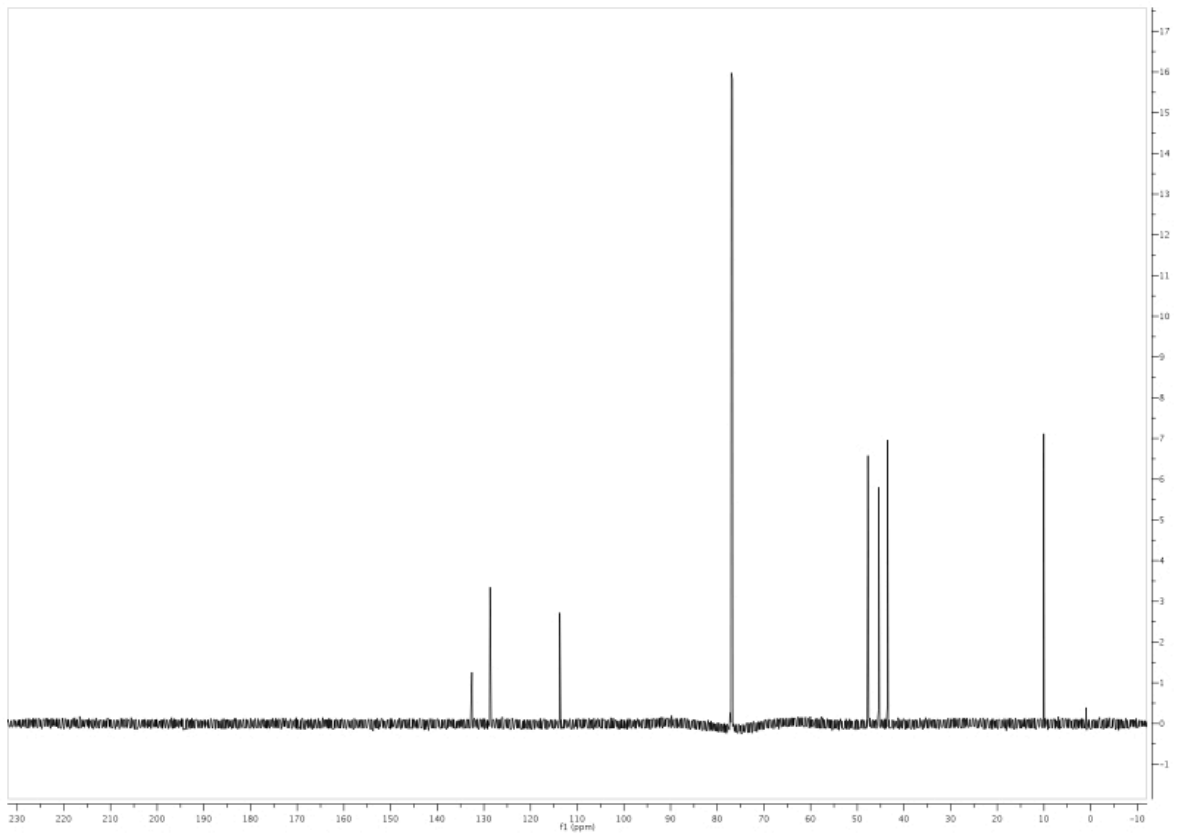
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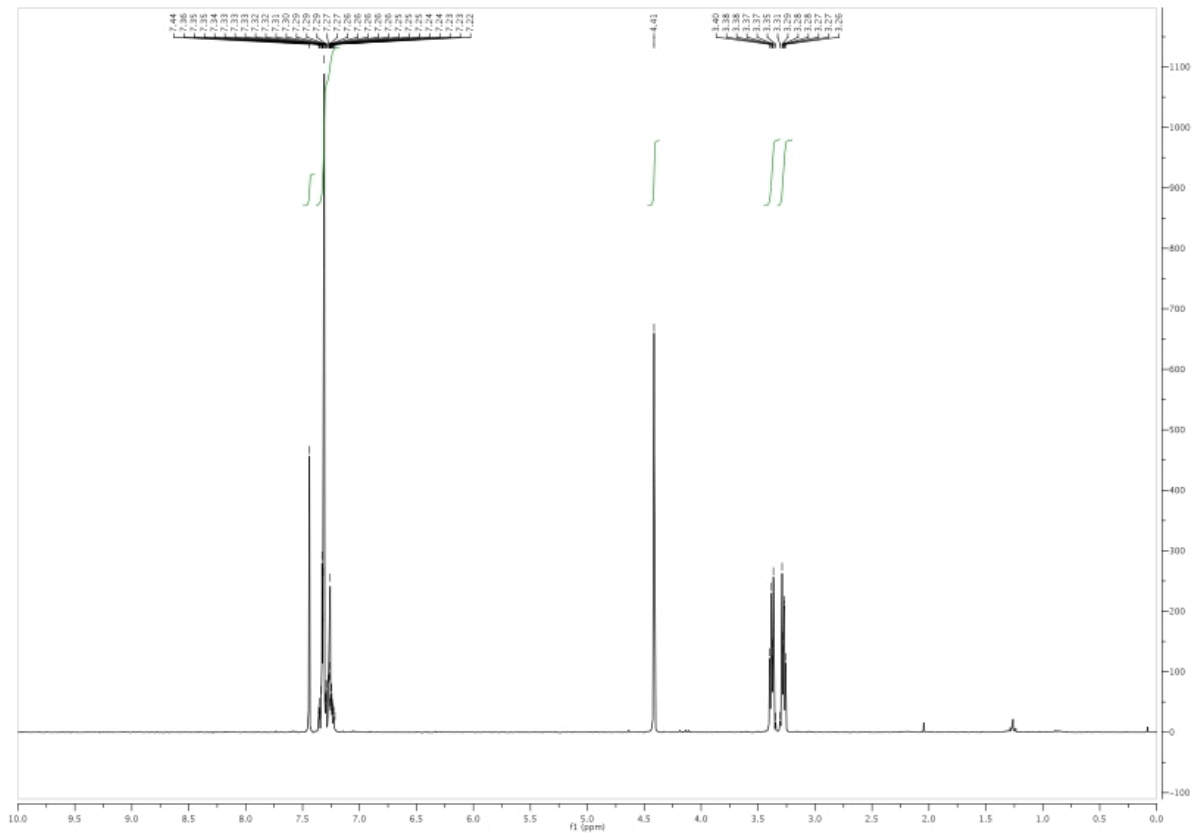


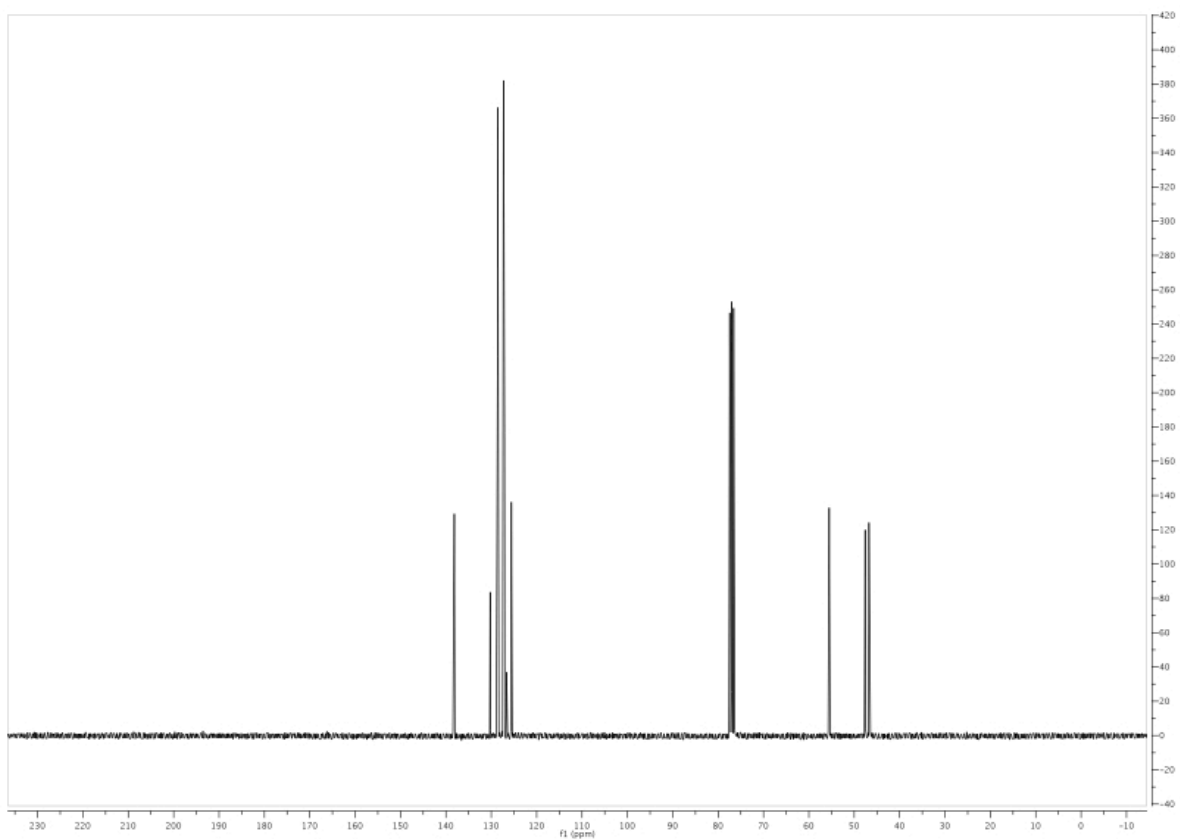
5b:



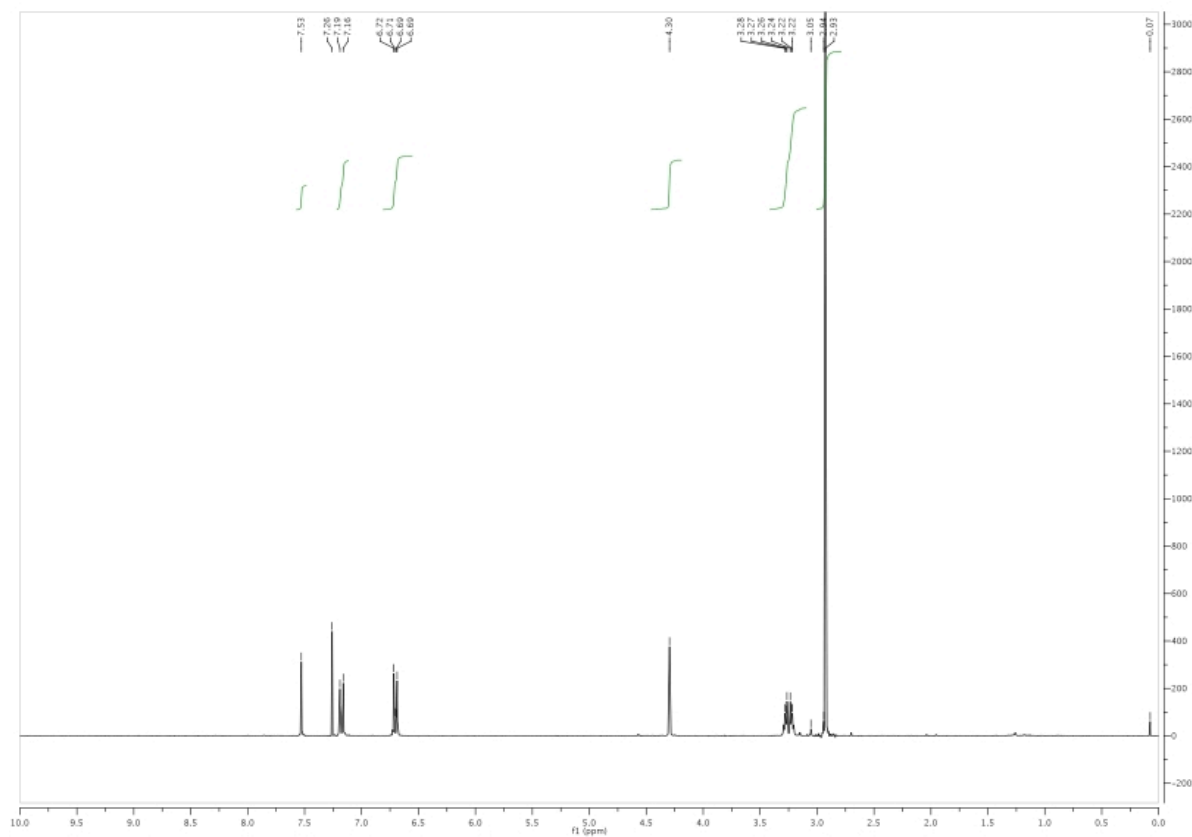


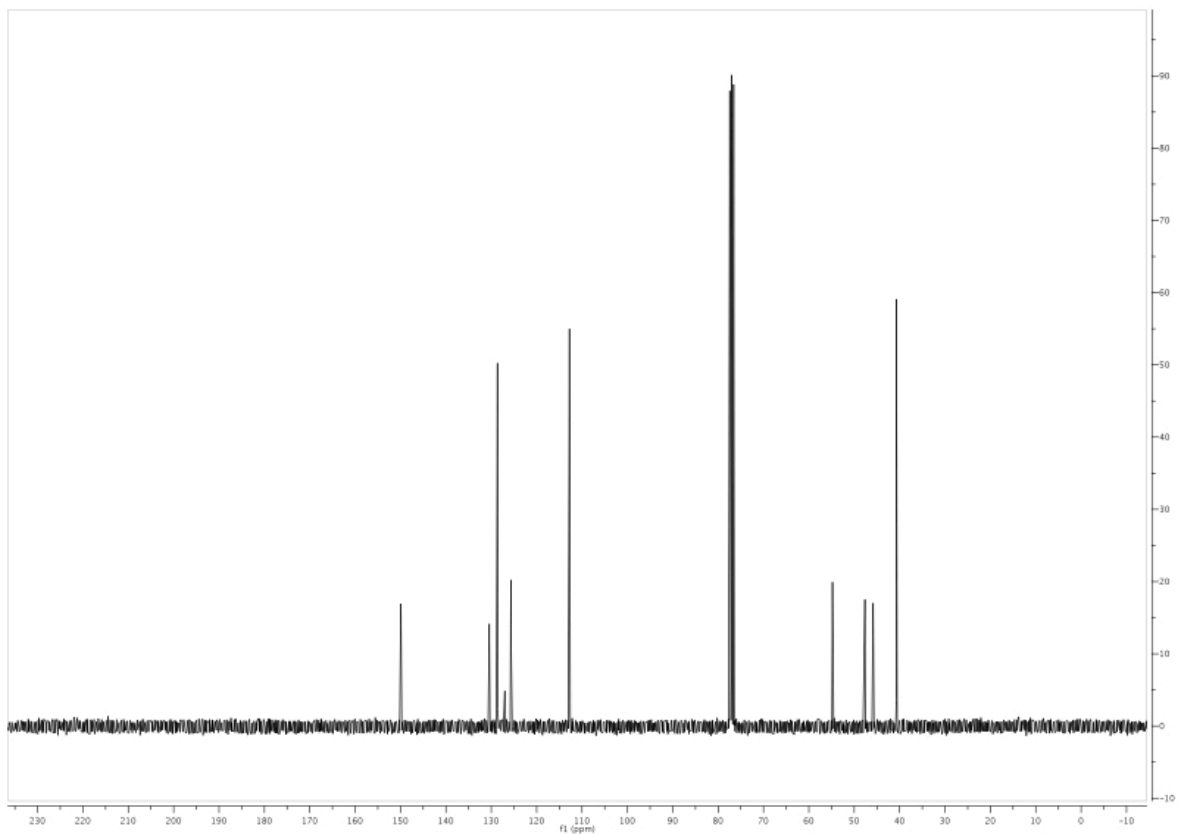
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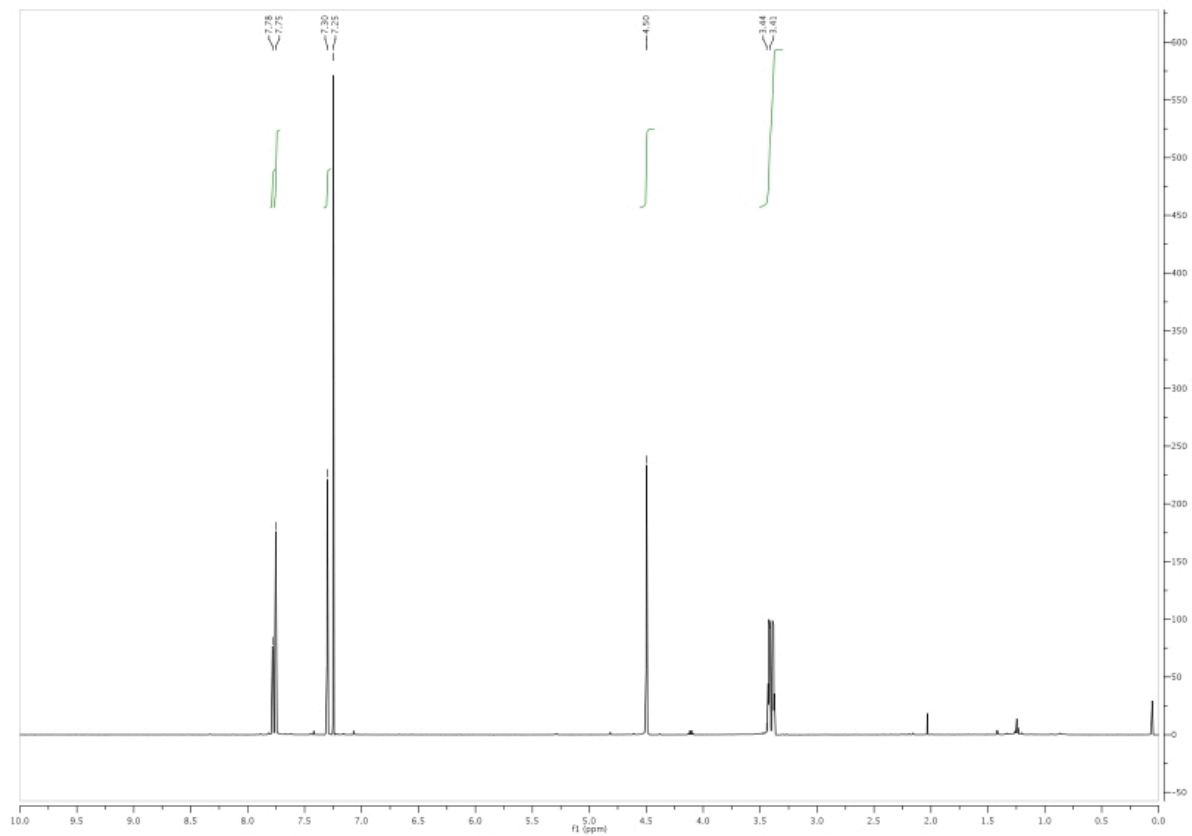


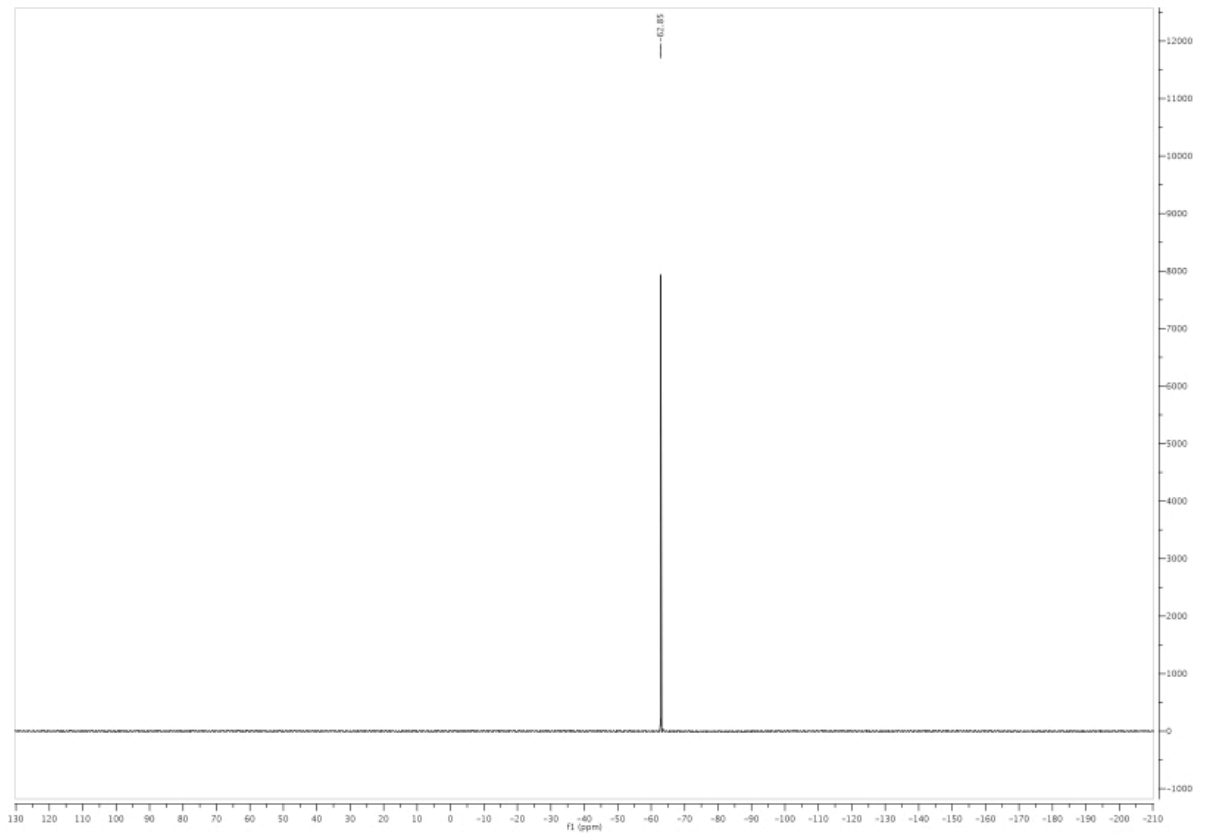
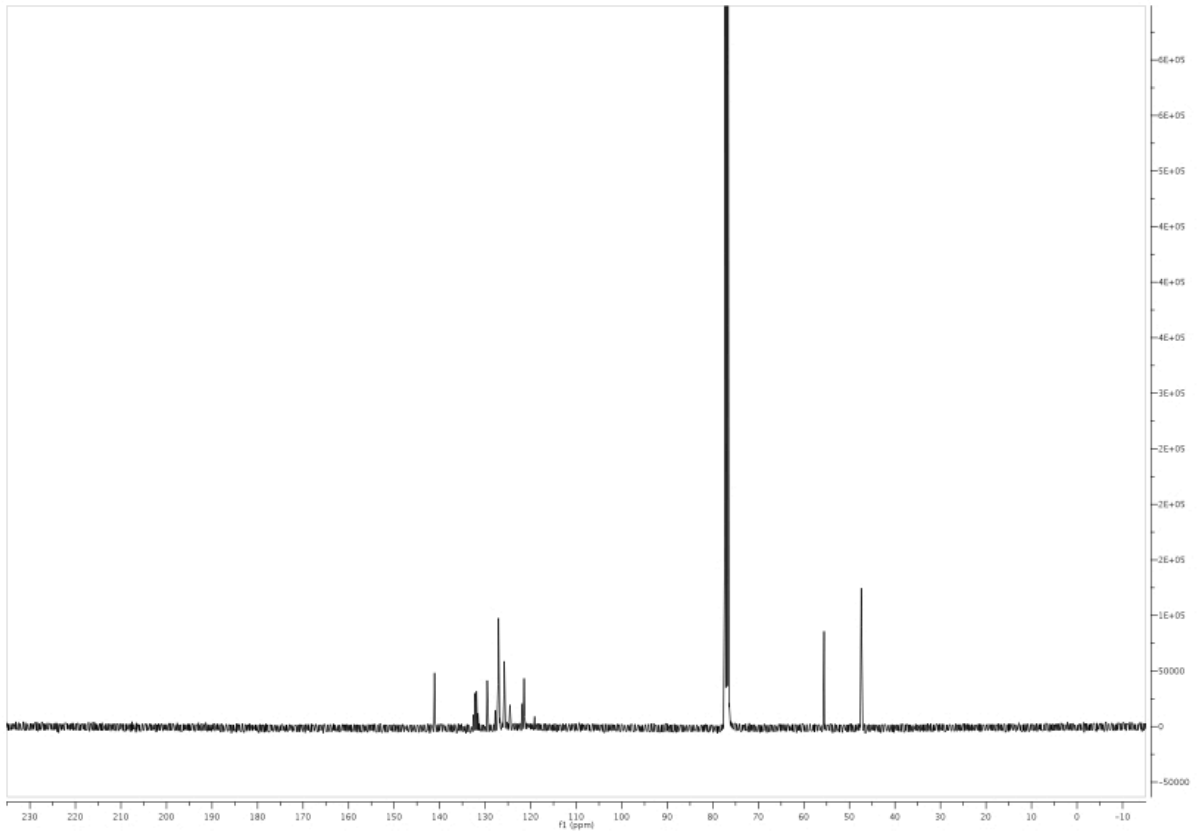
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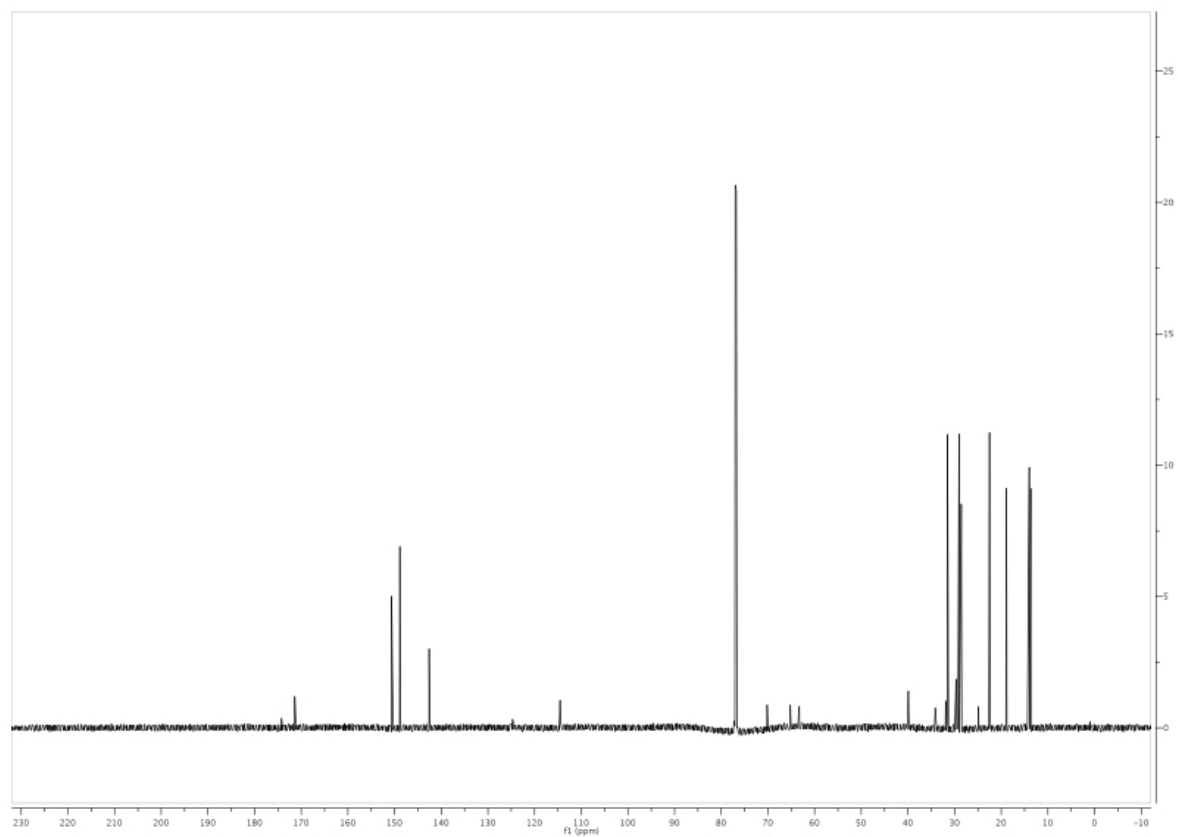
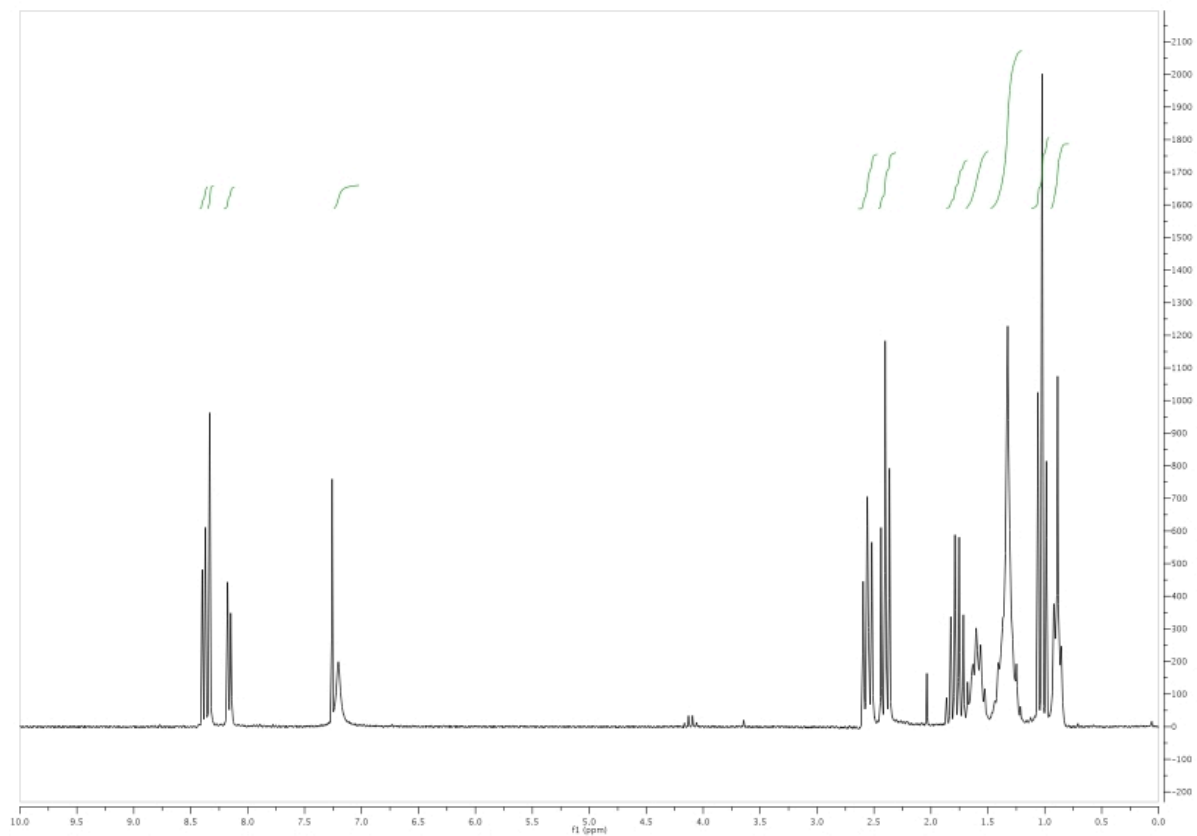


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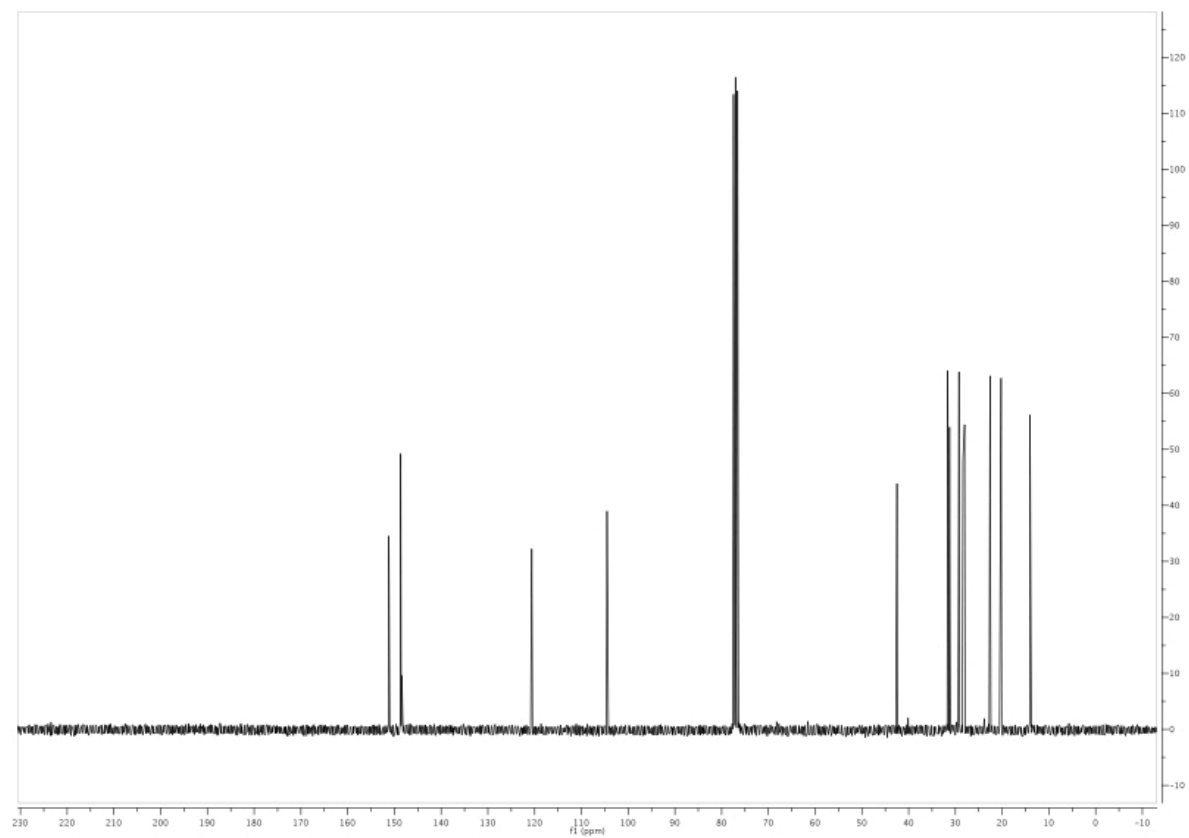
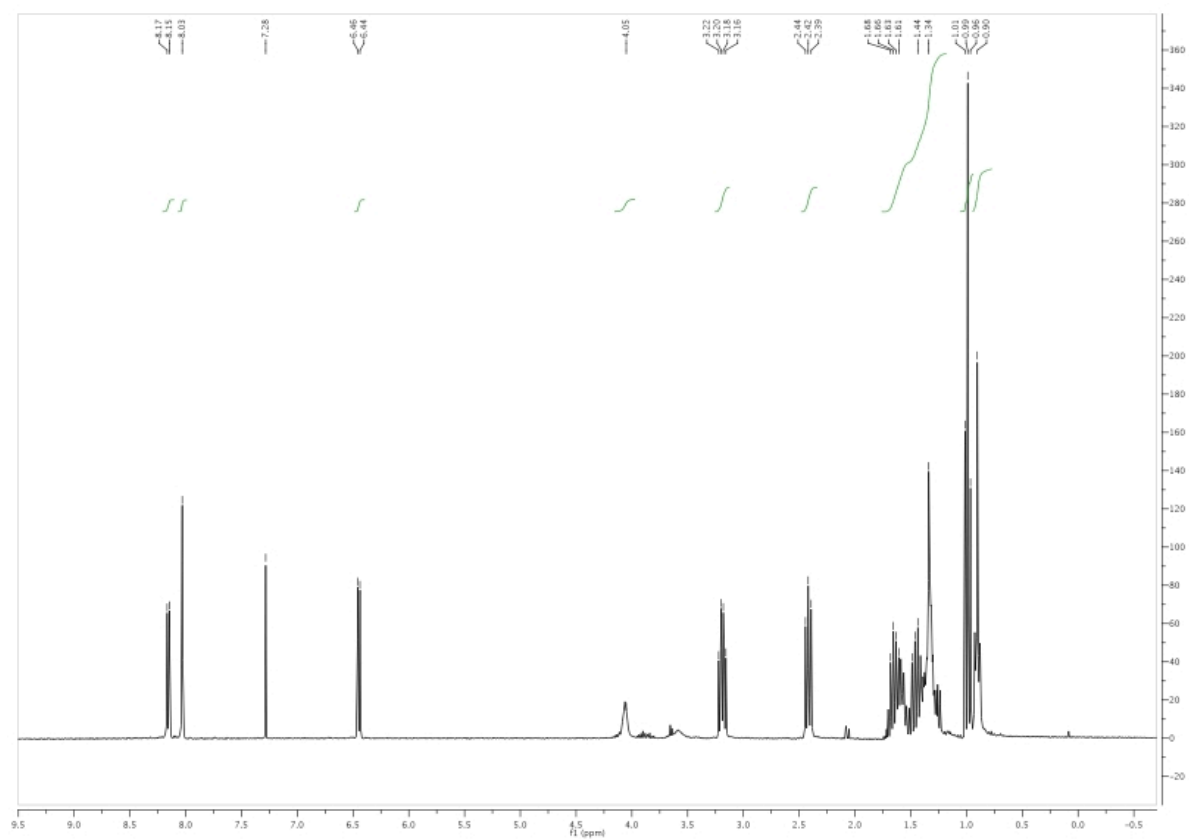




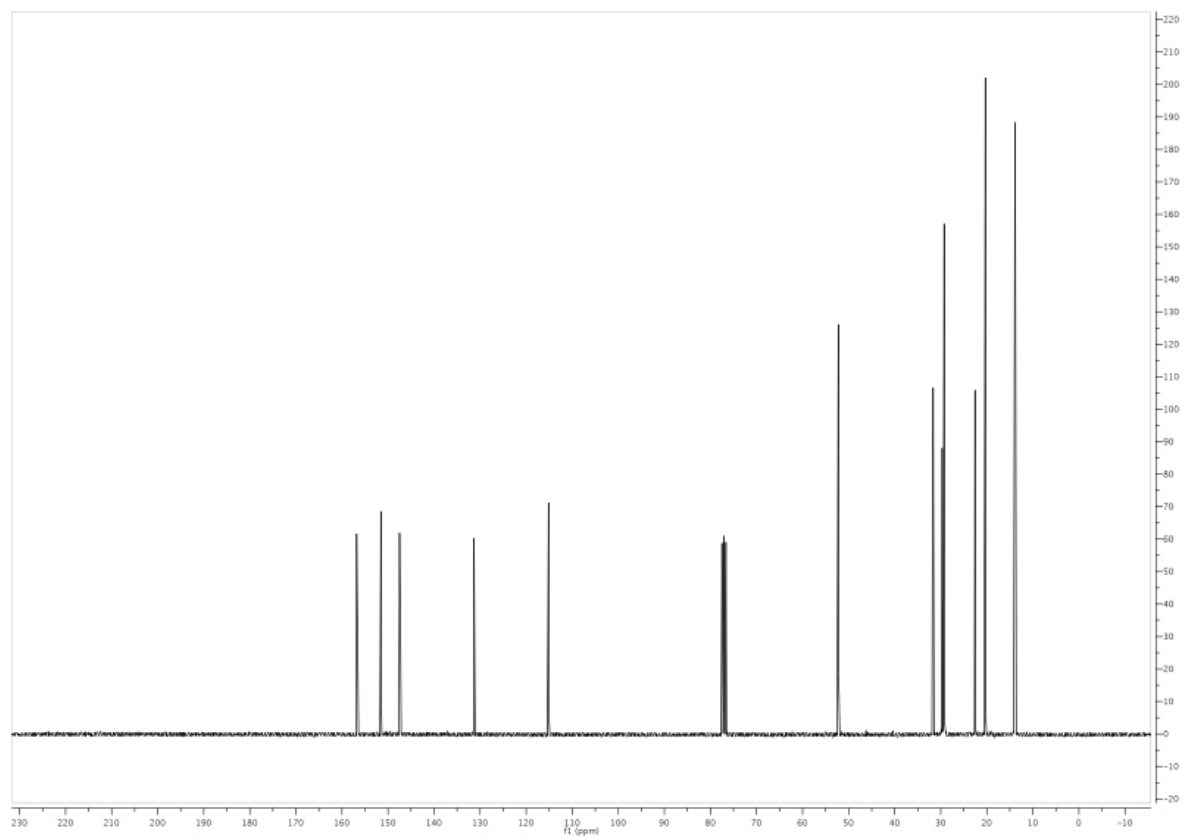
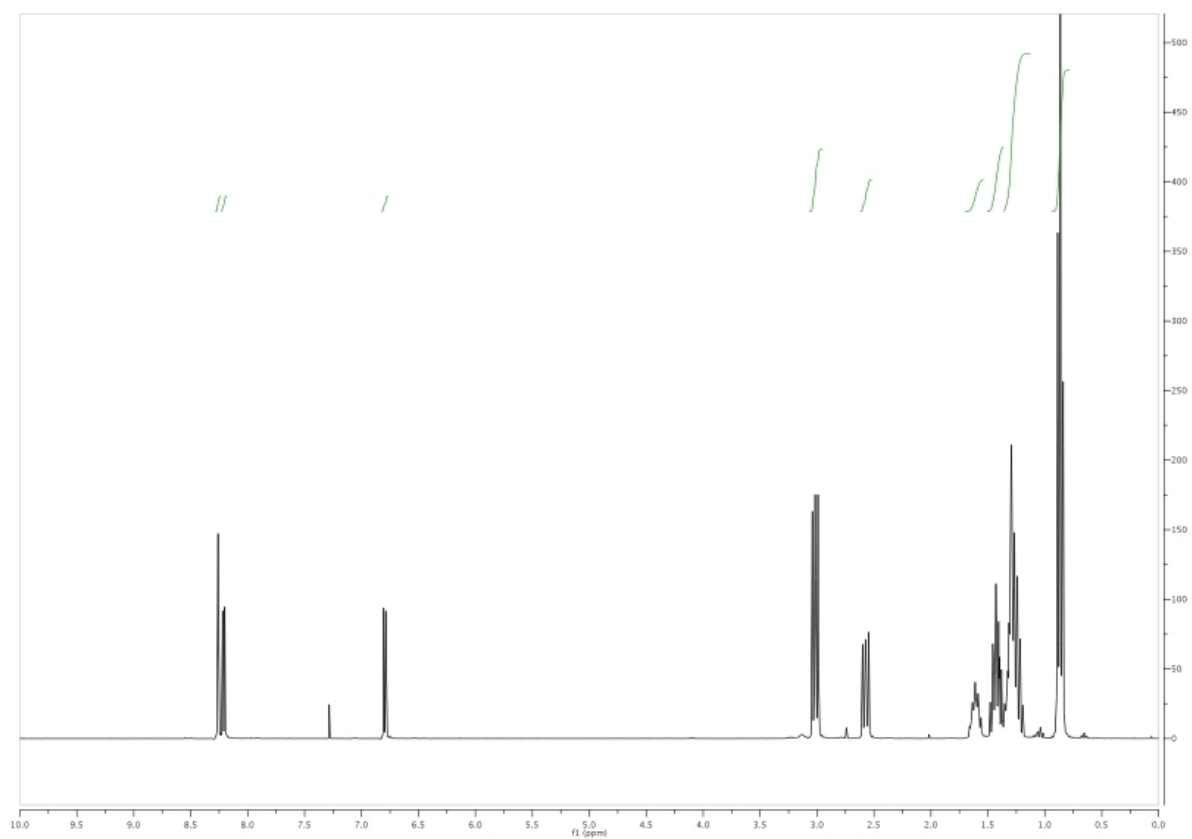
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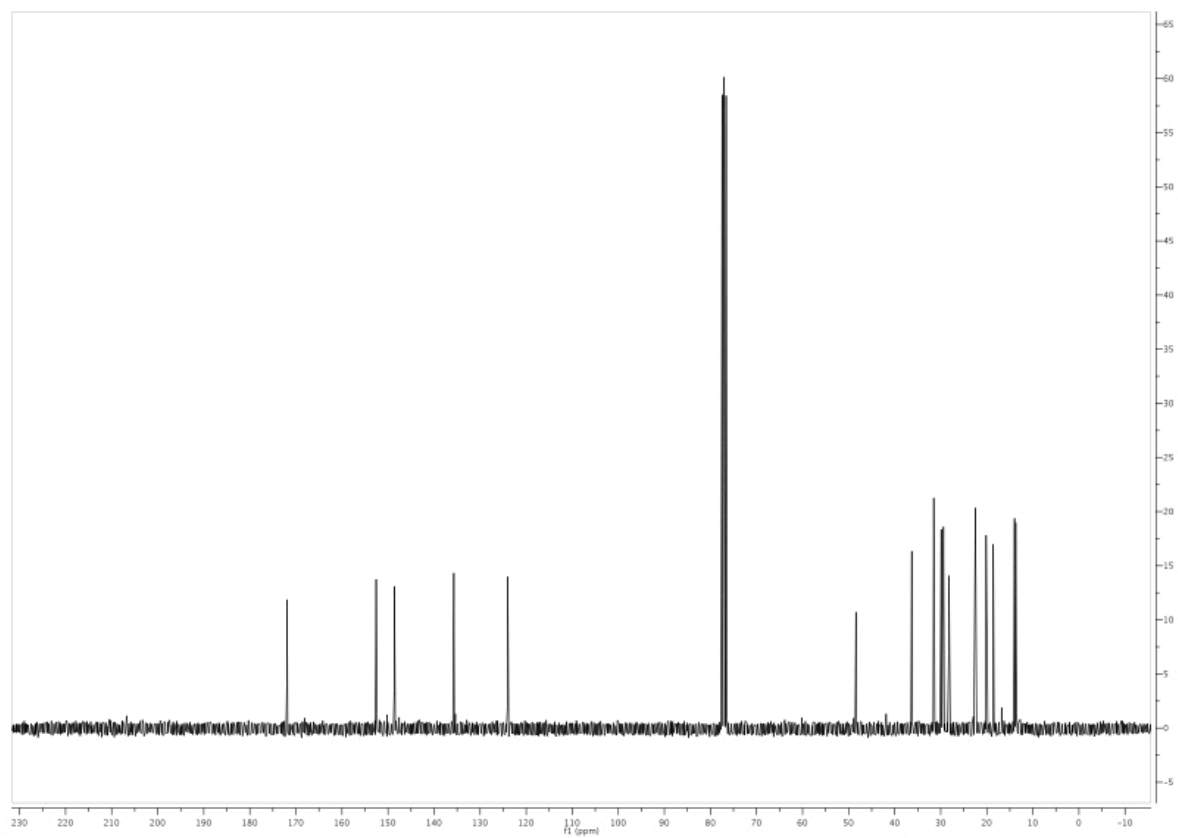
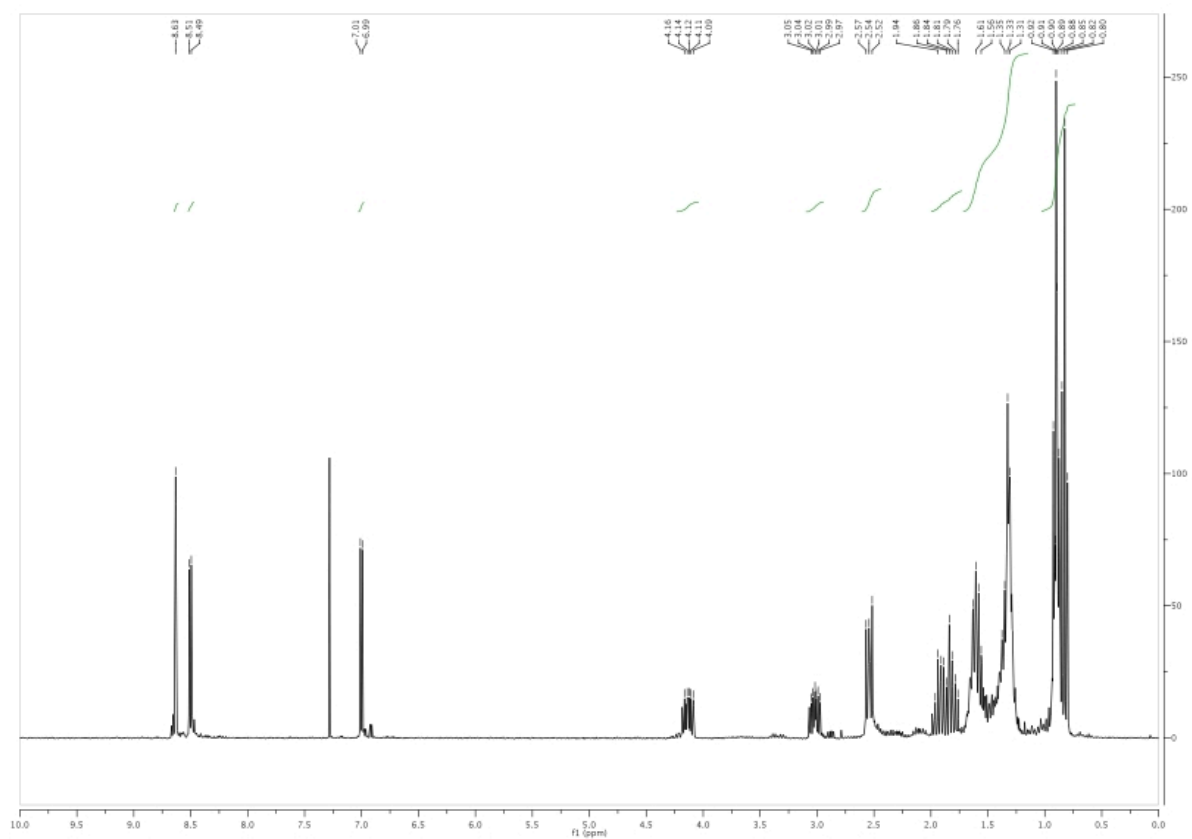
29:



30:

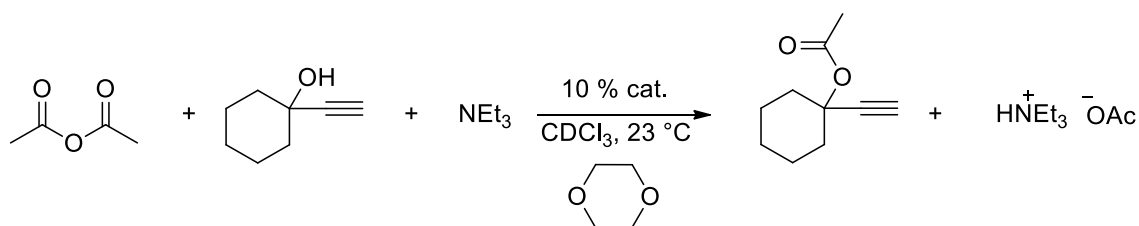


18:



3. Conduction and evaluation of kinetic measurements

The benchmark reaction (3) was carried out using stock solutions. The preparation of these stock solutions is carried out as follows: 3 mmol of the alcohol and 9 mmol triethylamine are mixed in a graduated 5 mL measurement flask. In the same way 6 mmol anhydride and 1.5 mmol dioxane (internal Standard) are mixed in another graduated 5 mL measurement flask. In a third graduated 5 mL measurement flask 0.3 mmol of the catalyst is weighed in. Now every graduated 5 mL measurement flask is filled up to 5 mL with freshly distilled CDCl₃ and sealed with a septum. After shaking the 5 mL measurement flasks 200 μL of every stock solution is transferred into an oven-dried and degassed NMR-tube. The concentrations of the stock solutions are: alcohol **16**: 0.6 M; anhydride: 1.2 M; triethylamine: 1.8 M; dioxane: 0.3 M; catalyst: 0.06 M.



Scheme S1. ¹H NMR benchmark reaction; acylation of a tertiary alcohol **16** in CDCl₃.

Concentrations used in the *benchmark reaction*: alcohol **16**: 0.2 M; anhydride: 0.4 M; triethylamine: 0.6 M; dioxane: 0.1 M; catalyst: 0.02 M.

Calculation of conversion:

$$\text{Conversion} = \left[\frac{4I_{\text{ester}}}{I_{\text{ester}} + I_{\text{anhydride}} + I_{\text{ammoniumacetate}}} \right] * 100 \%$$

The used abbreviations are: I_{ester} = Singlett of -CH₃ at 1.9 ppm; I_{dioxane} = Singlett of 4 -CH₂ groups at 3.6 ppm; $I_{\text{anhydride}}$ = Singlett of -CH₃ at 2.1 ppm; I_{alcohol} = Singlett of alkine proton at 2.3 ppm; $I_{\text{ammoniumacetate}}$ = Singlett of -CH₃ at 1.8 ppm.

Figure S6 shows a ^1H NMR of a kinetic measurement where the different substrates are designated to the chemical shifts.

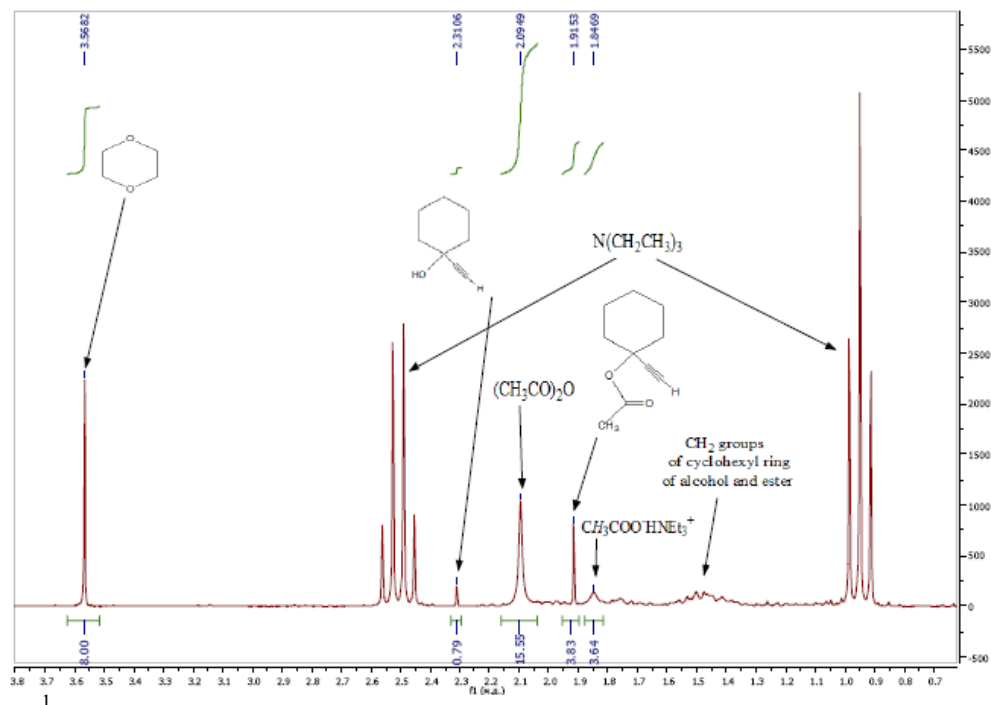


Figure S6. ^1H NMR (200 MHz) spectrum of reaction mixture for the benchmark reaction.

The experimental Data were fitted with a second order rate law:

The experimental Data were fitted with a second order rate law:

$$\text{conversion [\%]} = c_1 * \left(1 - \frac{1}{2 \exp(k(t - t_0)) - 1} \right) * 100$$

The resulting plot is depicted in figure S7 and finally the kinetic half-life time is calculated by the following formula:

$$t_{1/2} = \frac{\ln 1.5}{k_2[\text{ROH}]_0}$$

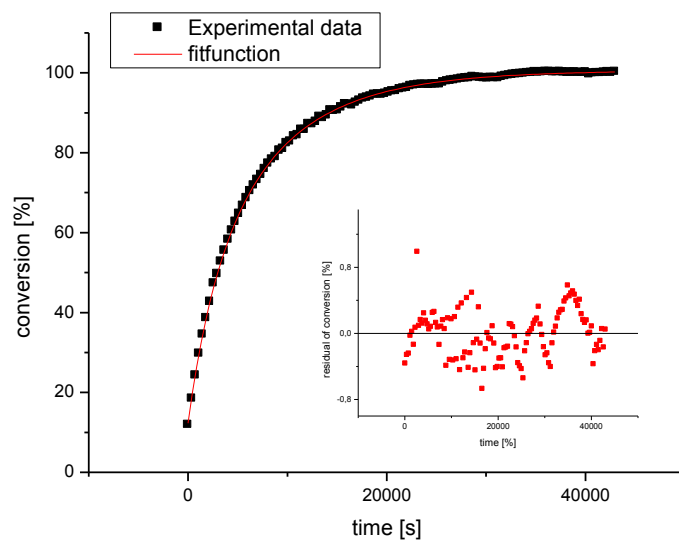
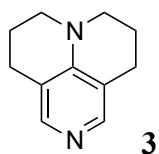


Figure S7. Results for the reaction of tertiary alcohol **16** and Ac₂O catalyzed by 10% **2** in CDCl₃.

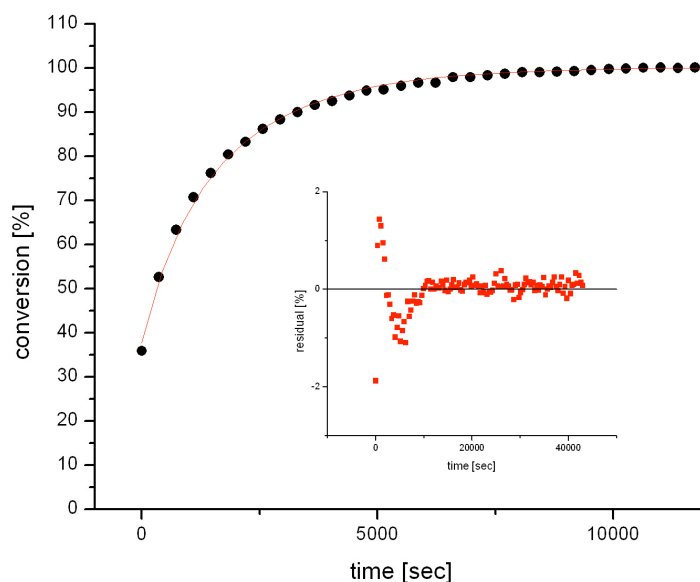
4. Data of kinetic runs

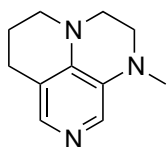
Kinetics of the reactions of catalysts **3,4a-c**, **5a-e** with alcohol **16** according to reaction 3. All time specifications are in minutes if not stated different. For every measurement the experimental data and the fit curve together with the residuals are depicted. The time window was chosen until the appearance of saturation at full conversion, depending on the speed of the catalyst. As the catalysts measured are too different in terms of activity it was not possible to compare the same time window for every catalyst. Every experiment was done at least twice and the resulting kinetic half-life times are given with standard deviations.

10 mol-% catalyst loading



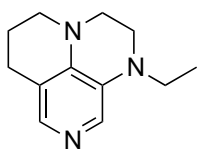
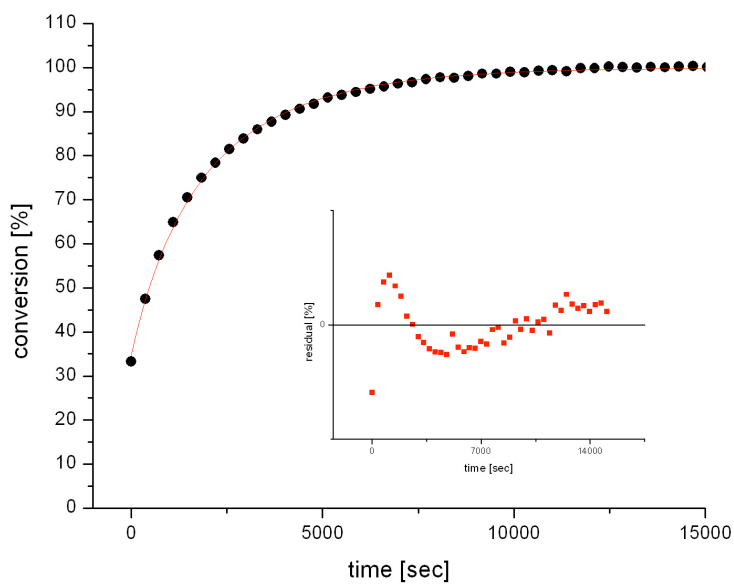
- 1) 15.1
 - 2) 14.2
- = 14.7 ± 0.5





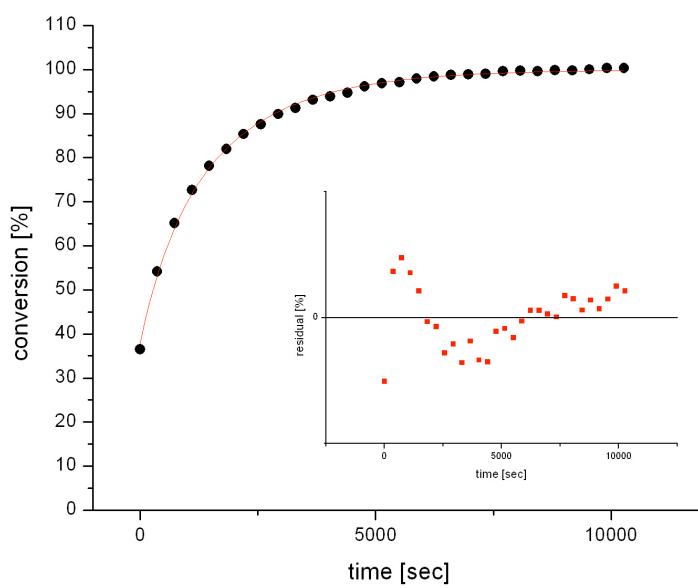
4a

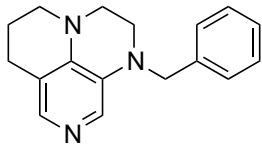
1) 18.8
2) 17.1
= 17.9 ± 0.9



4b

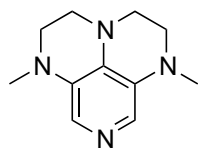
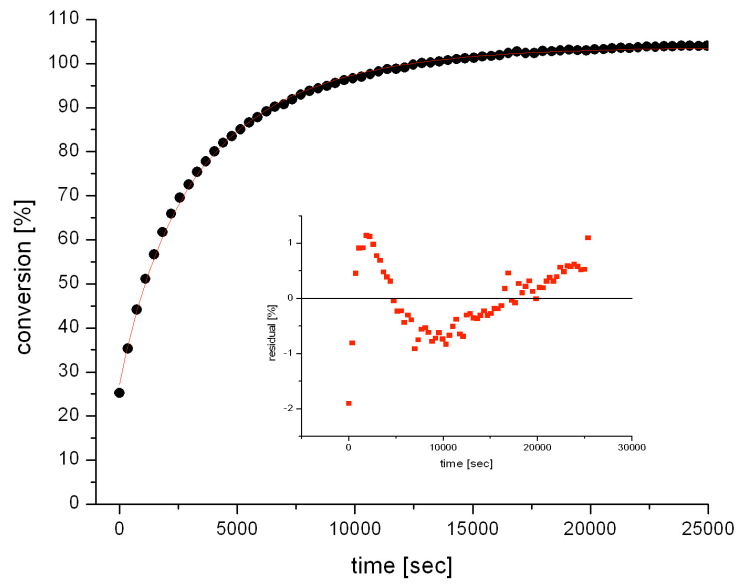
1) 13.4
2) 14.1
= 13.8 ± 0.4





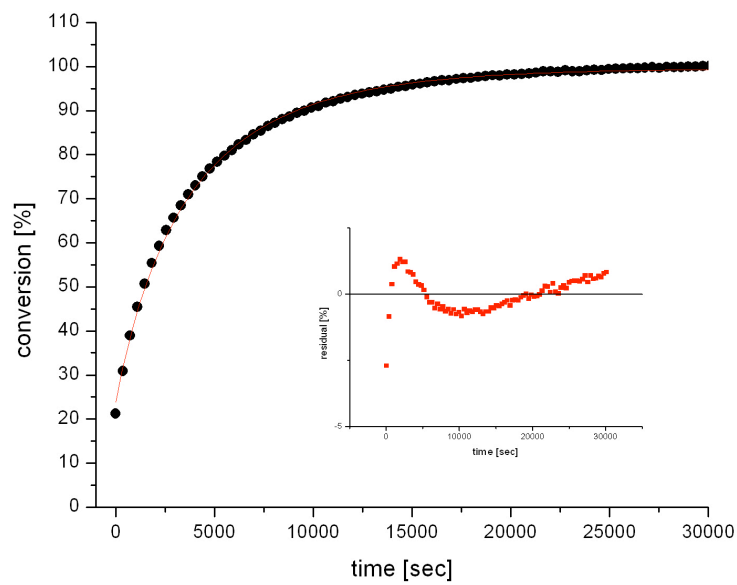
4c

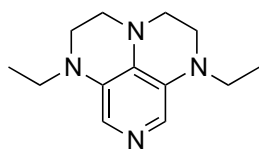
1) 34.1
2) 34.5
= 34.3 ± 0.2



5a

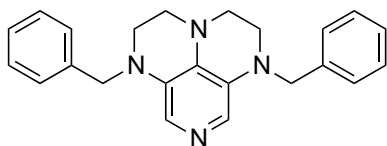
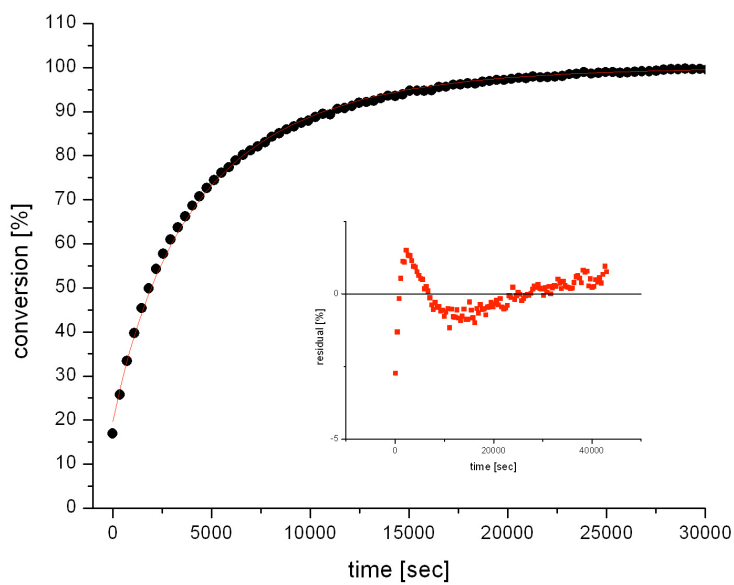
1) 36.1
2) 38.1
3) 39.8
= 38.0 ± 1.5





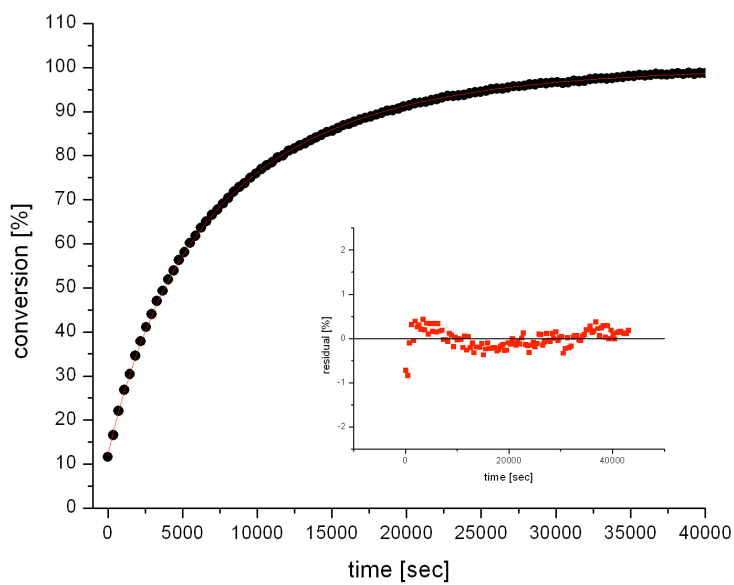
5b

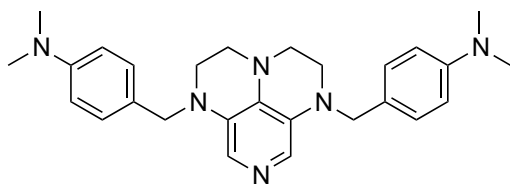
- 1) 44.9
 - 2) 44.9
 - 3) 41.6
 - 4) 45.3
- = 44.2 ± 1.5



5c

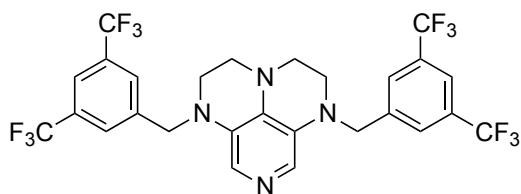
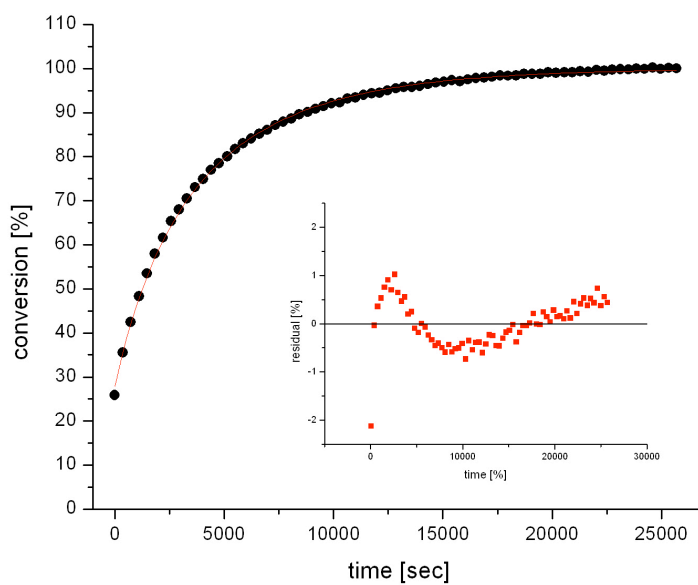
- 1) 62.3
 - 2) 68.5
- = 65.4 ± 3.1





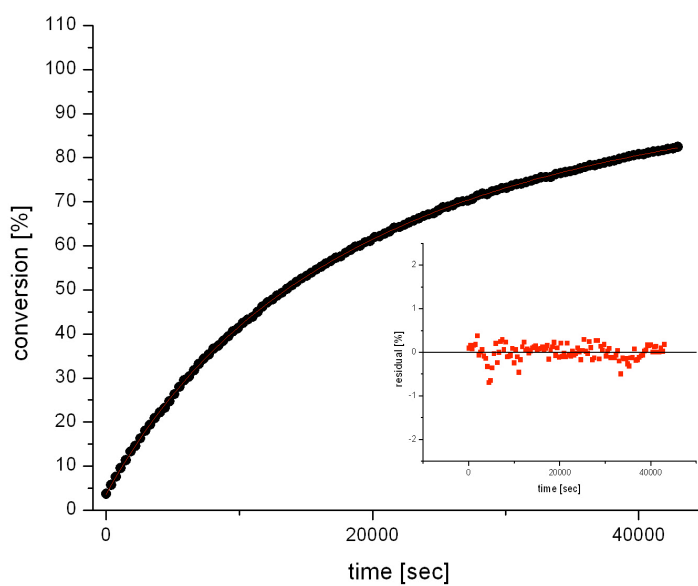
5d

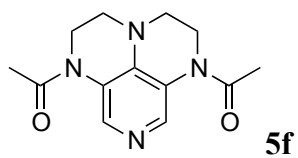
1) 39.4
2) 37.3
= 38.4 ± 1.0



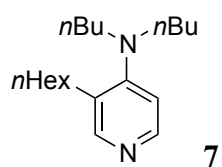
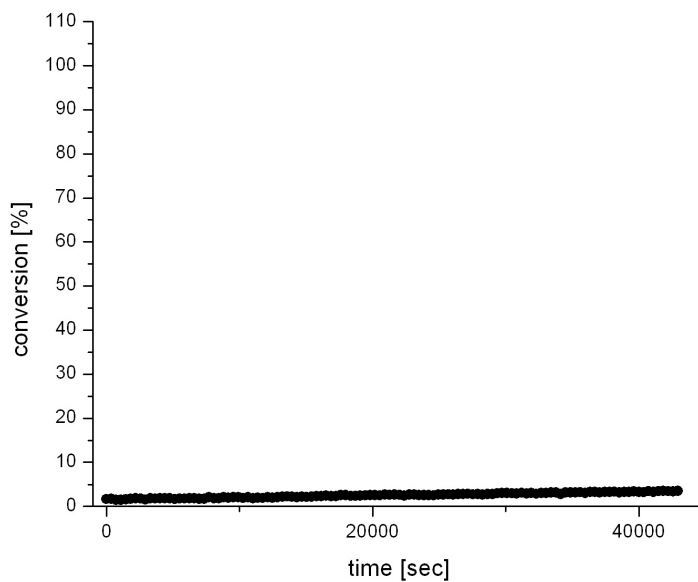
5e

1) 227.9
2) 226.8
= 227.3 ± 0.5

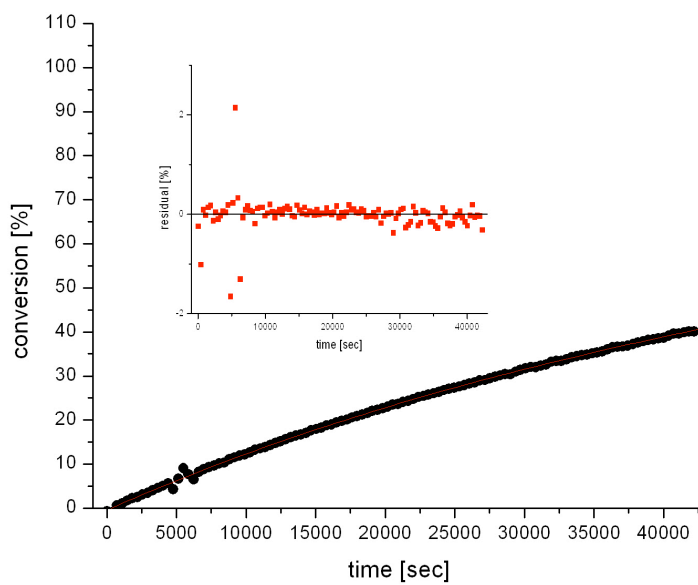




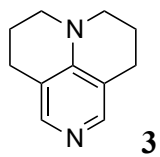
- 1) 13 % conversion after 12 h
- 2) 12 % conversion after 12 h
 ≥ 2880 min (extrapolated)



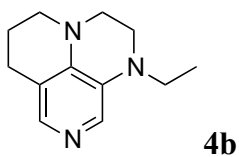
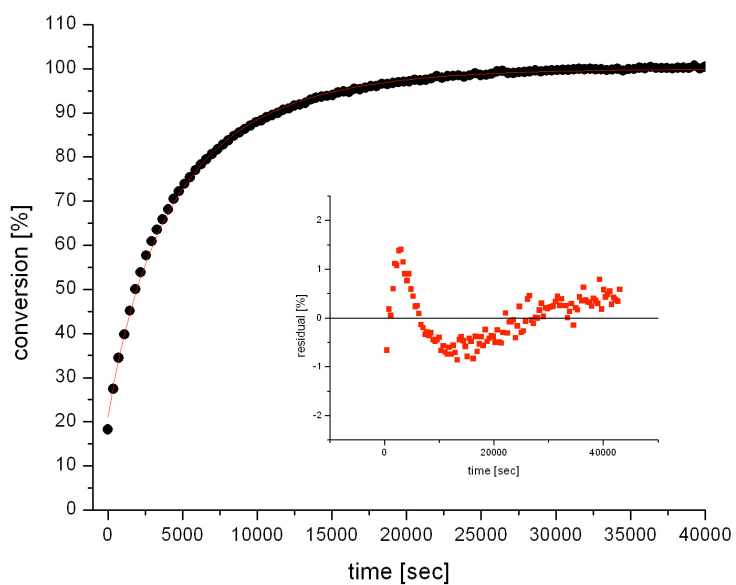
- 1) 818.2
- 2) 938.1
 $= 878.1 \pm 59.9$



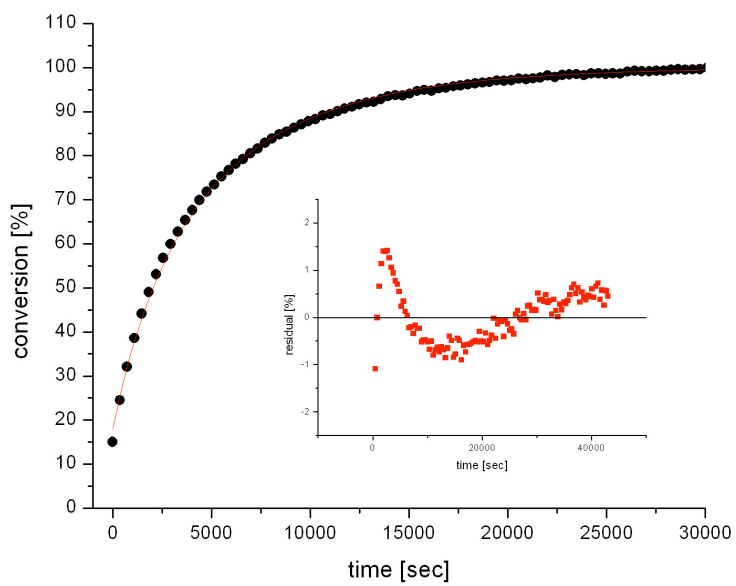
3 mol-% catalyst loading

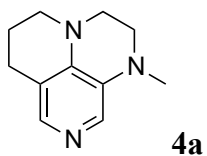


1) 46.7

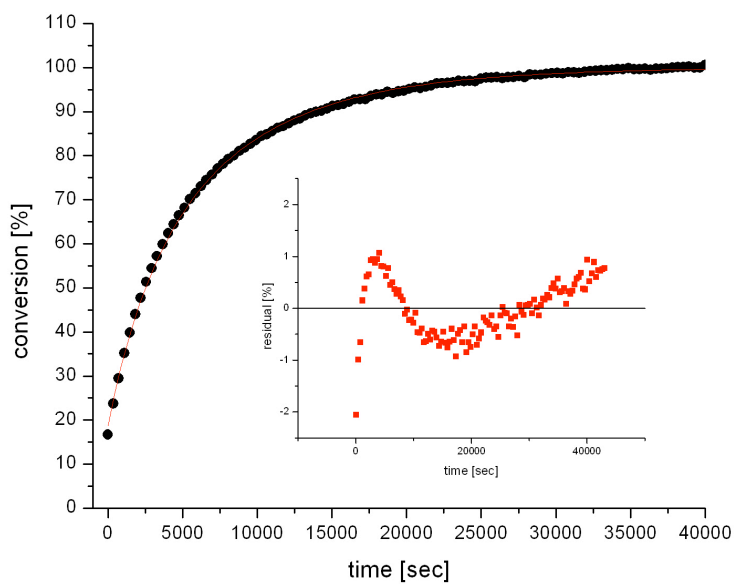


1) 45.9

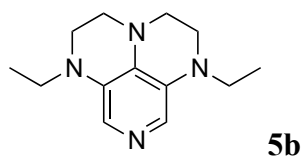




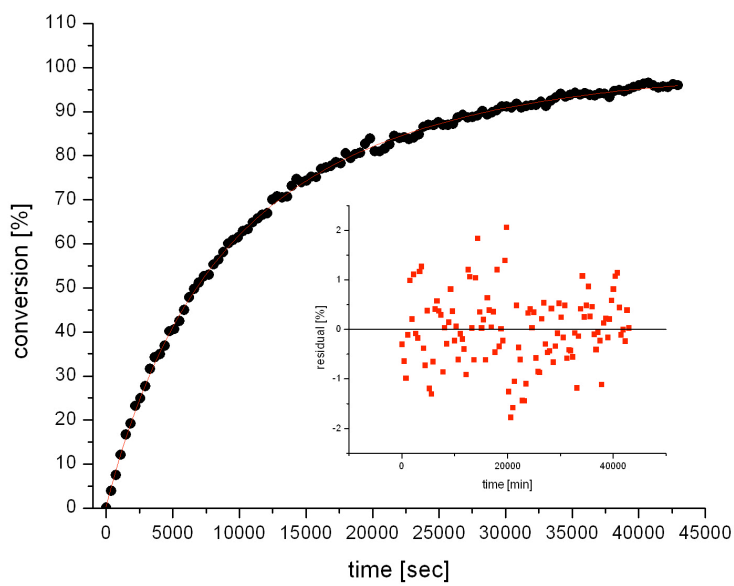
1) 57.4



Isobutyrylation



1) 113.9

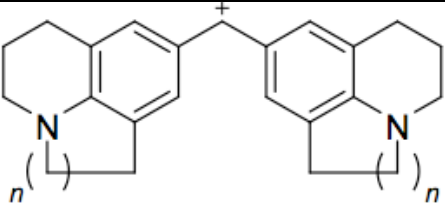
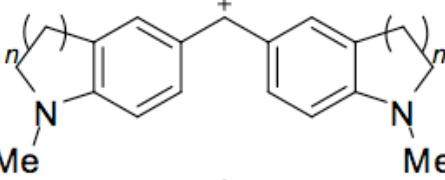
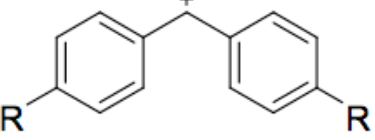


5. Measurement of *N*-parameters

The benzhydrylium tetrafluoroborates **E(a-f)**-BF₄^[20] (see Table S1) were synthesized as described in the literature. The kinetics of the reactions of the pyridines **2** and **3** with the benzhydrylium ions **E** were followed by UV/vis spectroscopy in acetonitrile at 20 °C using a stopped-flow spectrophotometer system (Applied Photophysics SX.18MV-R or Hi-Tech SF-61DX2). The kinetic runs were initiated by mixing equal volumes of acetonitrile solutions of the pyridines and the benzhydrylium salts.

The pyridines were used in large excess (over 6 equivalents) relative to the electrophiles **E** to ensure first-order conditions with $k_{\text{obs}} = k_2[\text{Nuc}]_0$. From the exponential decays of the absorbances at λ_{max} of **E**, the first-order rate constants k_{obs} (s⁻¹) were obtained by least-squares fitting to the single-exponential curve $A_t = A_0 \exp(-k_{\text{obs}}t) + C$. The slopes of plots of k_{obs} versus the concentrations of the nucleophiles yielded the second-order rate constants k_2 or k_2' (M⁻¹ s⁻¹). The nucleophilicity parameters *N* and *s_N* were determined from the linear plots of log k_2 against the electrophilicity parameters of the benzhydrylium ions **E** according to eq (2).

Table S1. List of the Reference Electrophiles **E Used in This Study.**

Reference Electrophile ^a		Abbreviation	<i>E</i> ^b
	<i>n</i> = 1	Ea (lil) ₂ CH ⁺	-10.04
	<i>n</i> = 2	Eb (jul) ₂ CH ⁺	-9.45
	<i>n</i> = 1	Ec (ind) ₂ CH ⁺	-8.76
	<i>n</i> = 2	Ed (thq) ₂ CH ⁺	-8.22
	R = <i>N</i> -pyrrolidino	Ee (pyr) ₂ CH ⁺	-7.69
	R = NMe ₂	Ef (dma) ₂ CH ⁺	-7.02

^a Counterion of the benzhydryl cations: BF₄⁻. ^b Electrophilicity parameters *E* were taken from ref.^[20]

Kinetic Experiments

Kinetics of the reactions of 4-(1-pyrrolidinyl)pyridine (2) with benzhydrylium ions (E)

Table S1. Rate constants for the reactions of 4-(1-pyrrolidinyl)pyridine (**2**) with (lil)₂CH⁺ BF₄⁻ (**Ea**) in CH₃CN (stopped-flow, 20 °C, λ = 631 nm).

[Ea] ₀ /M	[2] ₀ /M	[2] ₀ /[Ea] ₀	k _{obs} /s ⁻¹
7.51 × 10 ⁻⁶	1.51 × 10 ⁻⁴	20	5.02 × 10 ⁻¹
7.51 × 10 ⁻⁶	3.02 × 10 ⁻⁴	40	9.01 × 10 ⁻¹
7.51 × 10 ⁻⁶	4.52 × 10 ⁻⁴	60	1.28
7.51 × 10 ⁻⁶	6.03 × 10 ⁻⁴	80	1.73
7.51 × 10 ⁻⁶	7.54 × 10 ⁻⁴	100	2.14
$k_2 = 2.72 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$			

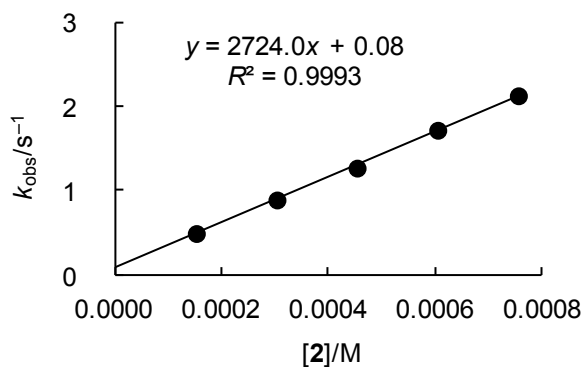


Table S2. Rate constants for the reactions of 4-(1-pyrrolidinyl)pyridine (**2**) with (ind)₂CH⁺ BF₄⁻ (**Ec**) in CH₃CN (stopped-flow, 20 °C, λ = 616 nm).

[Ec] ₀ /M	[2] ₀ /M	[2] ₀ /[Ec] ₀	k _{obs} /s ⁻¹
7.55 × 10 ⁻⁶	1.51 × 10 ⁻⁴	20	2.93
7.55 × 10 ⁻⁶	3.02 × 10 ⁻⁴	40	5.76
7.55 × 10 ⁻⁶	4.52 × 10 ⁻⁴	60	8.56
7.55 × 10 ⁻⁶	6.03 × 10 ⁻⁴	80	1.15 × 10 ¹
$k_2 = 1.89 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$			

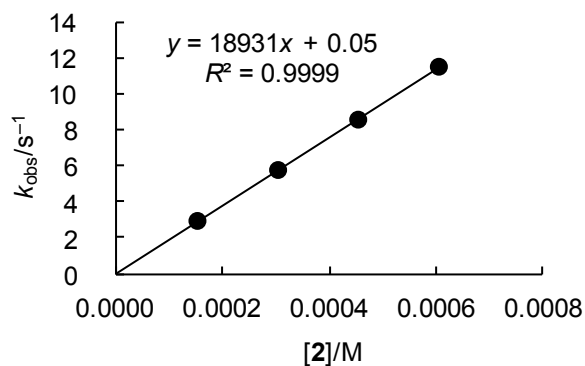


Table S3. Rate constants for the reactions of 4-(1-pyrrolidinyl)pyridine (**2**) with (pyr)₂CH⁺ BF₄⁻ (**Ee**) in CH₃CN (stopped-flow, 20 °C, λ = 616 nm).

[Ee] ₀ /M	[2] ₀ /M	[2] ₀ /[Ee] ₀	<i>k</i> _{obs} /s ⁻¹
7.65 × 10 ⁻⁶	1.50 × 10 ⁻⁴	20	2.32 × 10 ¹
7.65 × 10 ⁻⁶	2.25 × 10 ⁻⁴	29	3.41 × 10 ¹
7.65 × 10 ⁻⁶	3.01 × 10 ⁻⁴	39	4.51 × 10 ¹
7.65 × 10 ⁻⁶	3.76 × 10 ⁻⁴	49	5.50 × 10 ¹
7.65 × 10 ⁻⁶	4.51 × 10 ⁻⁴	59	6.58 × 10 ¹
<i>k</i> ₂ = 1.41 × 10 ⁵ M ⁻¹ s ⁻¹			

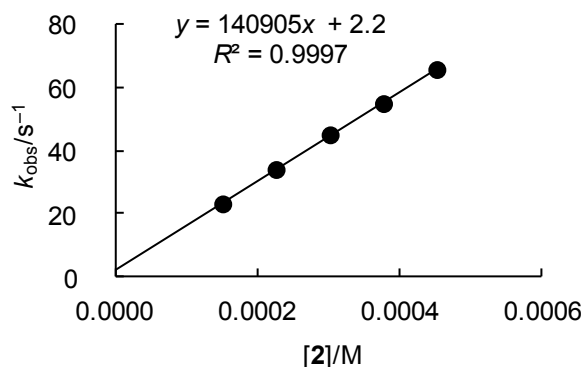


Table S4. Rate constants for the reactions of 4-(1-pyrrolidinyl)pyridine (**2**) with (dma)₂CH⁺ BF₄⁻ (**Ef**) in CH₃CN (stopped-flow, 20 °C, λ = 605 nm).

[Ef] ₀ /M	[2] ₀ /M	[2] ₀ /[Ef] ₀	<i>k</i> _{obs} /s ⁻¹
7.64 × 10 ⁻⁶	1.50 × 10 ⁻⁴	20	5.01 × 10 ¹
7.64 × 10 ⁻⁶	2.25 × 10 ⁻⁴	29	7.54 × 10 ¹
7.64 × 10 ⁻⁶	3.01 × 10 ⁻⁴	39	9.88 × 10 ¹
7.64 × 10 ⁻⁶	3.76 × 10 ⁻⁴	49	1.19 × 10 ²
7.64 × 10 ⁻⁶	4.51 × 10 ⁻⁴	59	1.40 × 10 ²
<i>k</i> ₂ = 2.97 × 10 ⁵ M ⁻¹ s ⁻¹			

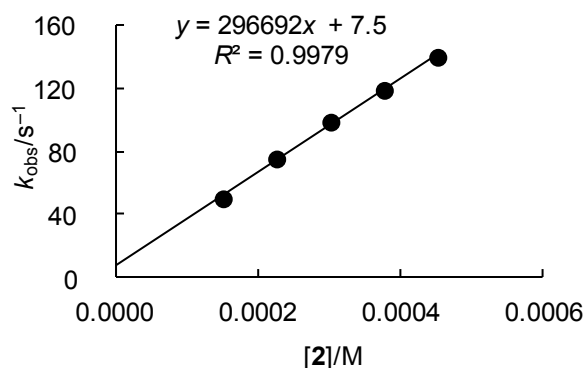
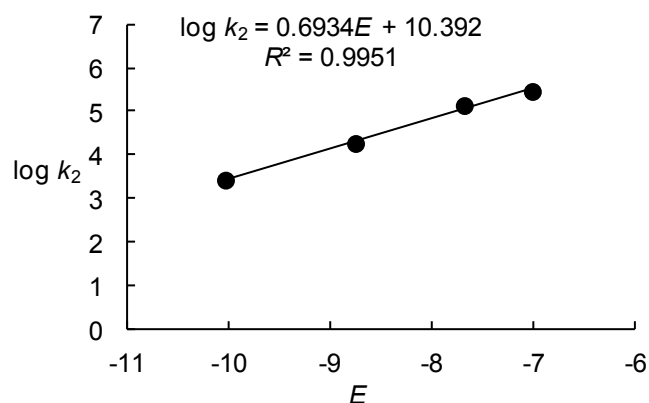


Table S5. Determination of the nucleophilicity parameters *N* and *s*_N for the 4-(1-pyrrolidinyl)pyridine (**2**) in CH₃CN.

Electrophile (<i>E</i>)	<i>k</i> ₂ /M ⁻¹ s ⁻¹	log <i>k</i> ₂
Ea (-10.04)	2.72 × 10 ³	3.43
Ec (-8.76)	1.89 × 10 ⁴	4.28
Ee (-7.69)	1.41 × 10 ⁵	5.15
Ef (-7.02)	2.97 × 10 ⁵	5.47
<i>N</i> = 14.99, <i>s</i> _N = 0.69		



Kinetics of the reactions of 9-azajulolidine (**3**) with benzhydrylium ions (**E**)^[20]

Table S6. Rate constants for the reactions of 9-azajulolidine (**3**) with (lil)₂CH⁺ BF₄⁻ (**Ea**) in CH₃CN (stopped-flow, 20 °C, λ = 631 nm).

[Ea] ₀ /M	[3] ₀ /M	[3] ₀ /[Ea] ₀	<i>k</i> _{obs} /s ⁻¹
6.92 × 10 ⁻⁶	1.36 × 10 ⁻⁴	20	8.33 × 10 ⁻¹
6.92 × 10 ⁻⁶	2.73 × 10 ⁻⁴	39	1.70
6.92 × 10 ⁻⁶	4.09 × 10 ⁻⁴	59	2.52
6.92 × 10 ⁻⁶	5.58 × 10 ⁻⁴	81	3.47
6.92 × 10 ⁻⁶	6.94 × 10 ⁻⁴	100	4.36
<i>k</i> ₂ = 6.30 × 10 ³ M ⁻¹ s ⁻¹			

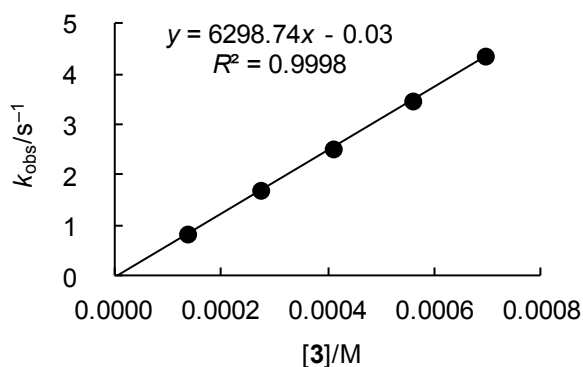


Table S7. Rate constants for the reactions of 9-azajulolidine (**3**) with (ind)₂CH⁺ BF₄⁻ (**Ec**) in CH₃CN (stopped-flow, 20 °C, λ = 616 nm).

[Ec] ₀ /M	[3] ₀ /M	[3] ₀ /[Ec] ₀	<i>k</i> _{obs} /s ⁻¹
7.17 × 10 ⁻⁶	1.36 × 10 ⁻⁴	19	6.00
7.17 × 10 ⁻⁶	2.73 × 10 ⁻⁴	38	1.20 × 10 ¹
7.17 × 10 ⁻⁶	4.09 × 10 ⁻⁴	57	1.75 × 10 ¹
7.17 × 10 ⁻⁶	5.58 × 10 ⁻⁴	78	2.36 × 10 ¹
7.17 × 10 ⁻⁶	6.94 × 10 ⁻⁴	97	2.94 × 10 ¹
<i>k</i> ₂ = 4.17 × 10 ⁴ M ⁻¹ s ⁻¹			

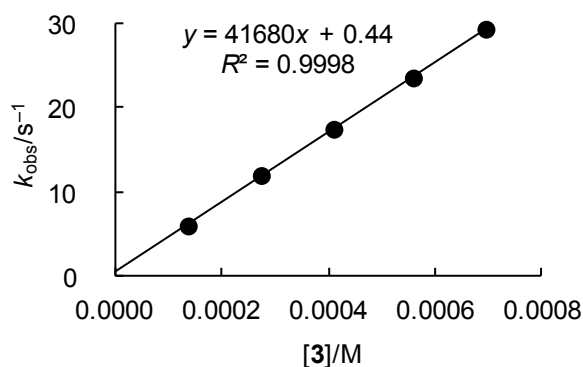


Table S8. Rate constants for the reactions of 9-azajulolidine (**3**) with (pyr)₂CH⁺ BF₄⁻ (**Ee**) in CH₃CN (stopped-flow, 20 °C, λ = 611 nm).

[Ee] ₀ /M	[3] ₀ /M	[3] ₀ /[Ee] ₀	<i>k</i> _{obs} /s ⁻¹
7.17 × 10 ⁻⁶	6.92 × 10 ⁻⁵	10	2.18 × 10 ¹
7.17 × 10 ⁻⁶	1.04 × 10 ⁻⁴	15	3.23 × 10 ¹
7.17 × 10 ⁻⁶	1.44 × 10 ⁻⁴	20	4.45 × 10 ¹
7.17 × 10 ⁻⁶	1.73 × 10 ⁻⁴	24	5.34 × 10 ²
7.17 × 10 ⁻⁶	2.13 × 10 ⁻⁴	30	6.52 × 10 ²
<i>k</i> ₂ = 3.03 × 10 ⁵ M ⁻¹ s ⁻¹			

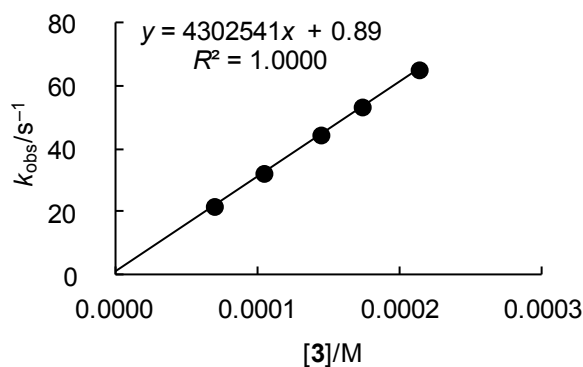


Table S9. Rate constants for the reactions of 9-azajulolidine (**3**) with (dma)₂CH⁺ BF₄⁻ (**Ef**) in CH₃CN (stopped-flow, 20 °C, λ = 605 nm).

[Ef] ₀ /M	[3] ₀ /M	[3] ₀ /[Ef] ₀	<i>k</i> _{obs} /s ⁻¹
7.06 × 10 ⁻⁶	6.92 × 10 ⁻⁵	10	4.63 × 10 ¹
7.06 × 10 ⁻⁶	1.04 × 10 ⁻⁴	15	7.01 × 10 ¹
7.06 × 10 ⁻⁶	1.44 × 10 ⁻⁴	20	9.55 × 10 ¹
7.06 × 10 ⁻⁶	1.73 × 10 ⁻⁴	25	1.14 × 10 ²
7.06 × 10 ⁻⁶	2.13 × 10 ⁻⁴	30	1.39 × 10 ²

$k_2 = 6.43 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$

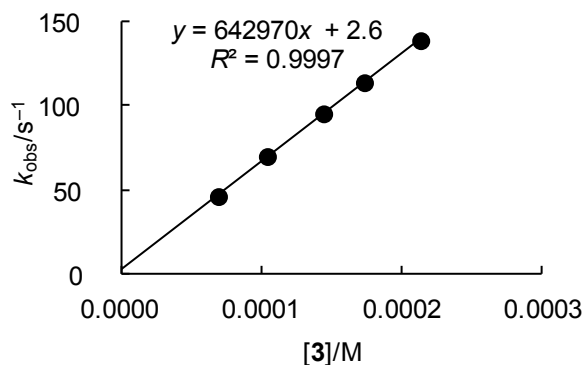
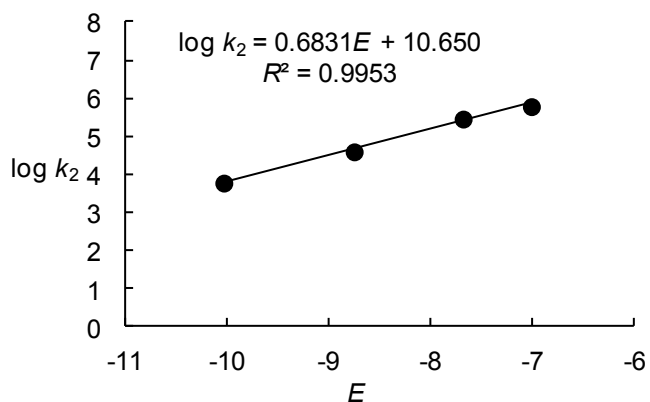


Table S10. Determination of the nucleophilicity parameters *N* and *s_N* for 9-azajulolidine (**3**) in CH₃CN.

Electrophile (<i>E</i>)	<i>k</i> ₂ /M ⁻¹ s ⁻¹	log <i>k</i> ₂
Ea (-10.04)	6.30 × 10 ³	3.80
Ec (-8.76)	4.17 × 10 ⁴	4.62
Ee (-7.69)	3.03 × 10 ⁵	5.48
Ef (-7.02)	6.43 × 10 ⁵	5.81

$N = 15.59, s_N = 0.68$



6. Solvent effects

We studied acylation reaction (3) in different solvents with commercially available **2** by means of ^1H NMR kinetics. The reaction of catalyst **2** in different solvents led with exception of THF and DMSO to full conversion for which the kinetic half-life times thus were extrapolated. For secondary non hindered alcohols Ishihara *et al.*^[16] found heptane being the best choice for running efficient and fast acylation reactions. We met solubility problems trying to perform the reaction in heptane leading to a tremendous increase in obtained half-life times. Additionally after some reaction time a precipitate formed which was found to be triethyl ammonium acetate as proofed by x-ray crystal structure analysis from the reaction mixture. The same was true for pure CCl_4 . In order to achieve a better solubility without loosing too much of the solvent characteristics we added 10 % CDCl_3 for the reaction in CCl_4 making it even possible to follow the reaction directly by ^1H NMR. Nevertheless the reaction mixture was still not 100 % homogeneous and thus it is not surprisingly that the reaction half-life time of **2** in 90/10 $\text{CCl}_4/\text{CDCl}_3$ is 1.5 times more slowly than in pure CDCl_3 (see Figure S8 and Table S11). In fact the solvent with the fastest turn over rates obtained in this study was CDCl_3 . The reaction in DCM is even 1.6 times more slowly although the solubility is here not a problem. For benzene we found an almost two-fold decrease in reaction speed compared to chloroform. From all the solvents tested showing full conversion the worst performance in terms of reaction speed showed acetonitrile. Compared to chloroform we obtain a 2.8 fold decrease in activity. Unfortunately these results are not reflected by any of the solvent descriptors like ET30, AN (Gutmann acceptor number) and DN (Gutmann donor number).^[21,22]

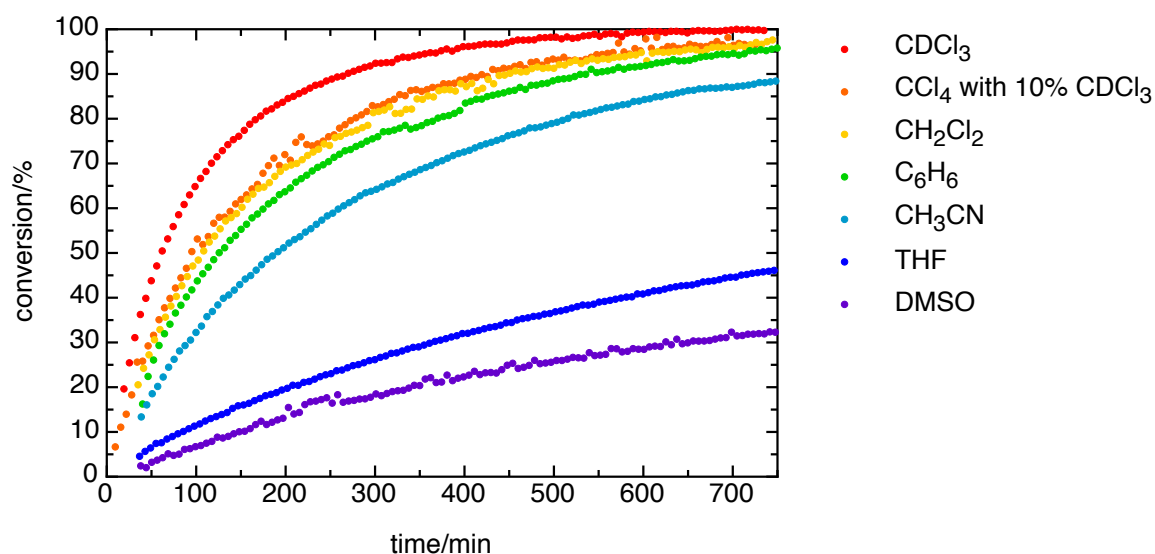


Figure S8. Conversion time plots for **2** for reaction (3) in CDCl_3 (red), CCl_4 with 10 mol-% CDCl_3 (orange), CH_2Cl_2 (yellow), benzene (green), CH_3CN (light blue), THF (dark blue), DMSO (magenta).

Table S11. Kinetic half life times for acylation reaction (3) in different solvents with ET30, AN and DN.

solvent	$t_{1/2}^{[b]}$	ET30 ^[f]	AN ^[g]	DN ^[g]
		[kcal/mol]	[kcal/mol]	[kcal/mol]
CDCl_3	67 ^[c]	39.1	23.1	4.0
CCl_4 ^[a]	100.3	32.4	8.6	0.0
CH_2Cl_2	109.2	40.7	20.4	1.0
benzene	128.6	34.3	8.2	0.1
CH_3CN	190.0	45.6	18.9	14.1
THF	800 ^[d]	37.4	8.0	20.0
DMSO	1125 ^[e]	45.1	19.3	29.8

[a] 90 % CCl_4 and 10 % CDCl_3 ; [b] Kinetic half-life times for benchmark reaction (3); [c] data from ref. 11; [d] linear extrapolation, 45 % conversion after 12 h; [e] linear extrapolation, 32 % conversion after 12 h. [f] data from ref. 22; [g] data from ref. 21.

7. Correlation plots

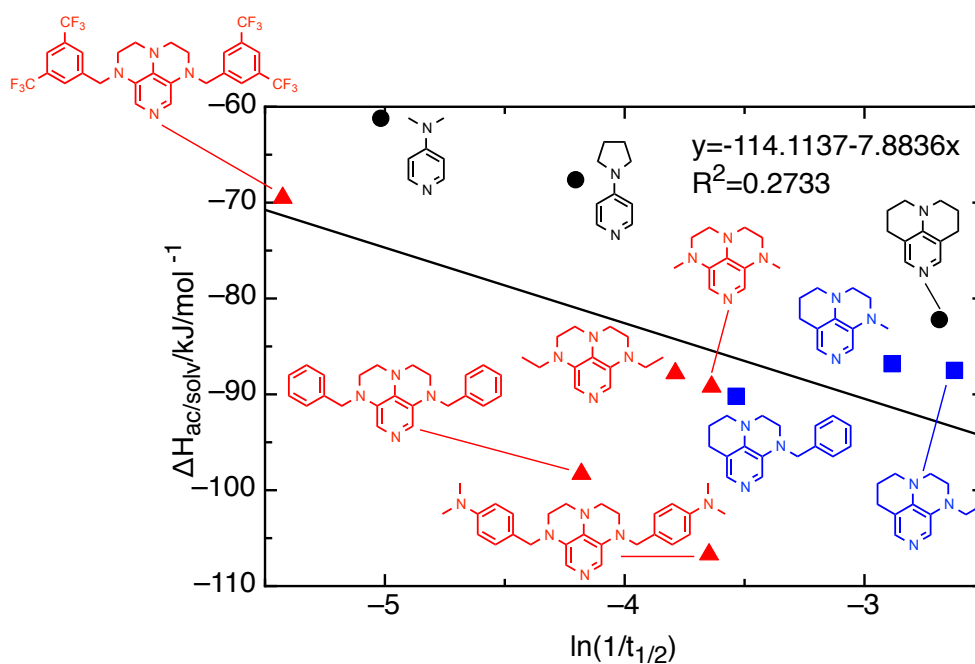


Figure S9. Correlation of affinity data (with PCM) with catalytic activity of 4-aminopyridines (black circles), 3,4-diaminopyridines (blue squares) and 3,4,5-triaminopyridines (red triangles).

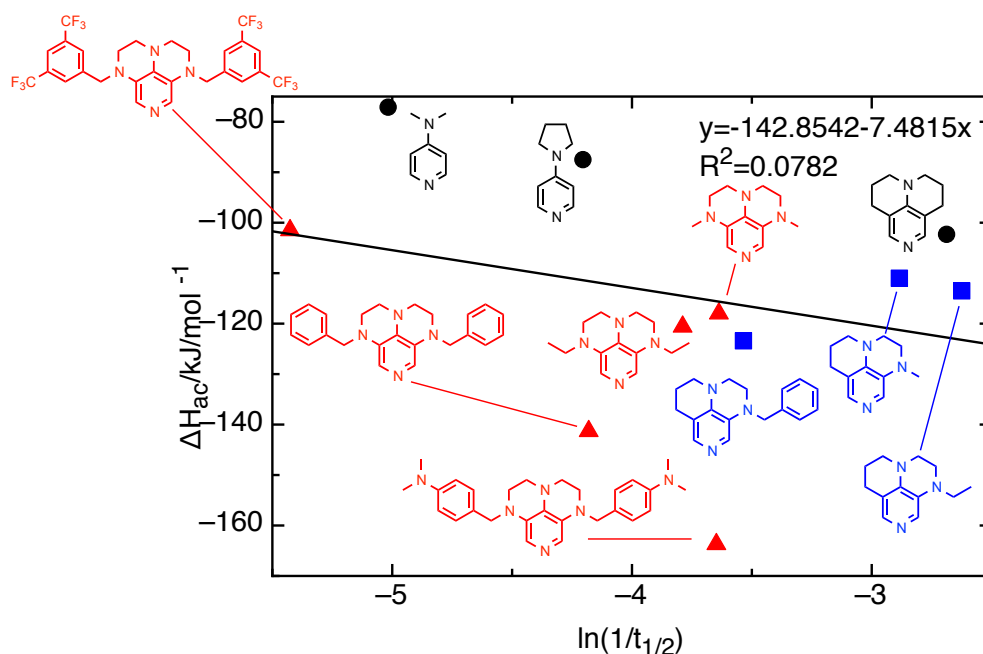


Figure S10. Correlation of affinity data (gas phase) with catalytic activity of 4-aminopyridines (black circles), 3,4-diaminopyridines (blue squares) and 3,4,5-triaminopyridines (red triangles).

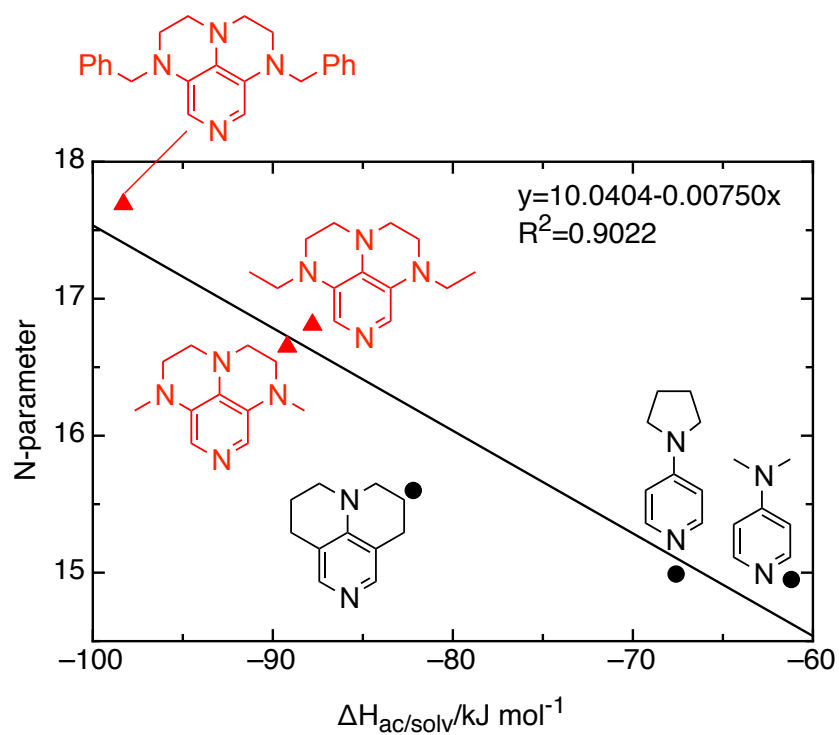


Figure S11. Correlation of N-parameters with acylation enthalpies ($\Delta H_{ac/solv}$) of 4-aminopyridines (black circles), and 3,4,5-triaminopyridines (red triangles).

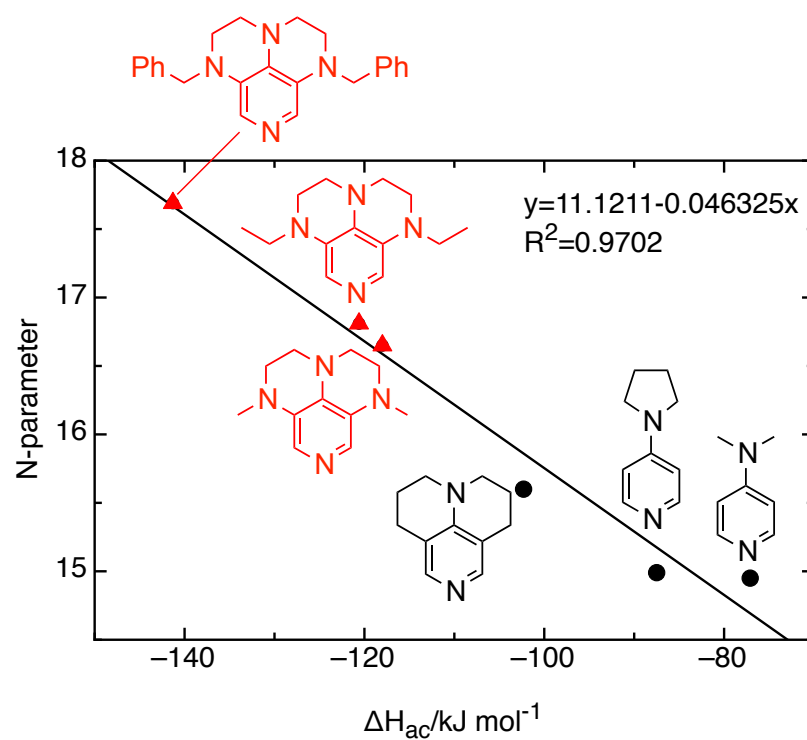


Figure S12. Correlation of N-parameters with acylation enthalpies in gas phase (ΔH_{ac}) of 4-aminopyridines (black circles), and 3,4,5-triaminopyridines (red triangles).

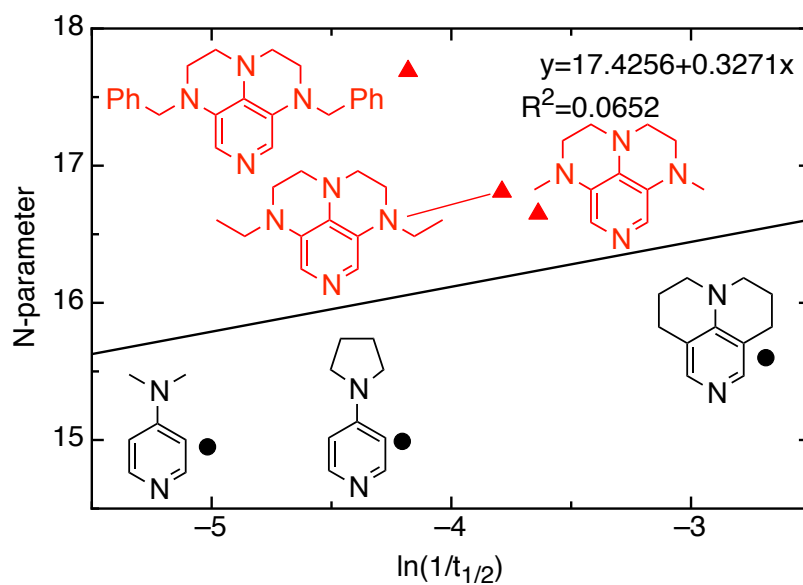


Figure S13. Correlation of N-parameters with kinetic data of 4-aminopyridines (black circles), and 3,4,5-triaminopyridines (red triangles).

8. Description of the QSAR parameters

Studies on the impact of input parameters for the QSAR program were tested with a larger set of catalysts depicted in Figure S14.

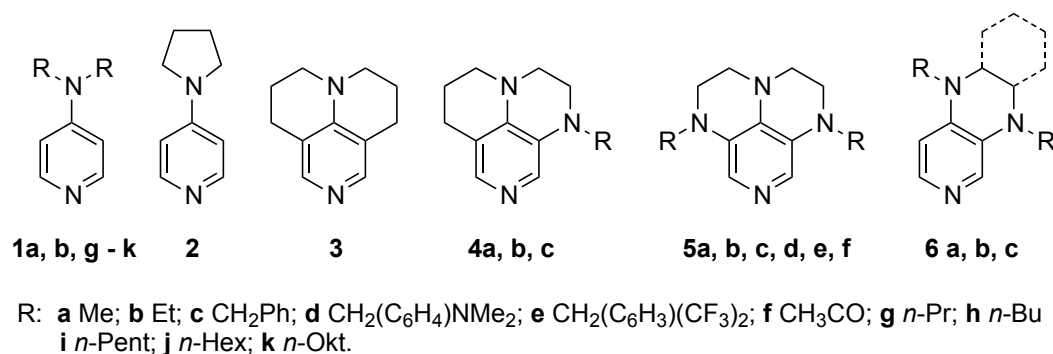


Figure S14. Catalysts used for the optimization of QSAR models.

The surveyed parameters are depicted in Figure S15. As descriptors we used the gas phase enthalpies (ΔH_{ac}), enthalpies including solvation terms in chloroform ($\Delta H_{ac/solv}$) the charge of the *ortho*-hydrogen atom of the free catalyst ($q_{ortho-H}$) and that of the pyridine nitrogen (q_N) and the bond distance ($dist_{N-C}$) between the nitrogen atom in 4-position and the pyridine carbon atom at the same position.

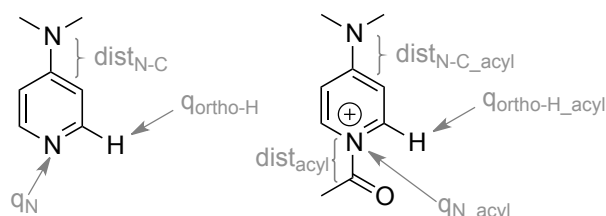


Figure S15. Depiction of the descriptors used for the QSAR models.

In Table S12 the number of input parameters was varied using ground state data of the free catalysts only. In one model the parameters of the free catalyst and that of the acylated catalyst according to Figure S15 were tested thus using 11 parameters (ΔH_{ac} , $\Delta H_{ac/solv}$, $q_{ortho-H}$, $dist_{N-C}$, q_N , $q_{ortho-H_acyl}$, $dist_{N-C_acyl}$, q_{N_acyl} and $dist_{acyl}$) in which the 2 $q_{ortho-H}$ charges of every catalyst were not averaged as usual, but taken separately ($R^2=0.916$, $Q^2=0.691$, (number of components: 4)). To understand the output parameters of the QSAR program these will be briefly described:

R^2 : Conventional R^2 value for the number of components used to create the model.

$$R^2 = 1 - \frac{SS_{err}}{SS_{tot}}$$

with: $SS_{tot} = \sum_i (y_i - y_{av})^2$; total sum of squares

$SS_{err} = \sum_i (y_i - f_i)^2$; sum of squares of residuals

and: $y_{av} = \frac{1}{n} \sum_i^n y_i$

- f_i : predicted values
- y_i : observed values

Q^2 : Crossvalidated R^2 value for the number of components used to create the model. To express the predictive power of the analysis, the cross-validated R^2 ($= Q^2$) is used. In cross-validation, one value is left out, a model is derived using the remaining data, and the model is used to predict the value originally left out. This procedure is repeated for all values, yielding Q^2 . Q^2 is normally (much) lower than R^2 and values greater than 0.5 already indicate significant predictive power.^[23]

$$Q^2 = 1.0 - \frac{\sum_y (y_{pred} - y_{actual})^2}{\sum_y (y_{actual} - y_{mean})^2}$$

- y_{pred} : a predicted value (depending on model)
- y_{actual} : an actual or experimental value
- y_{mean} : the best estimate of the mean of all values that might be predicted
- the summations are over the same set of y .

Number of components: the number of components that provided the largest value of Q^2 .

Table S12. Optimization of number of parameters used in the QSAR models.

Model-nr.	ΔH_{ac}	$\Delta H_{ac/solv}$	$q_{ortho-H}$	$dist_{N-C}$	q_N	R^2/Q^2 ^[a]
1 parameter						
1	✓					0.131/-0.047 (1)
2		✓				0.303/0.133 (1)
3			✓ ^{a2}			0.328/0.036 (1)
4			✓ ^{d3}			0.235/-0.065 (1)
5				✓		0.069/-0.109 (1)
2 parameters						
6	✓	✓				0.604/0.481 (2)
7	✓	✓ ^[b]				0.604/0.481 (2)
8		✓		✓		0.434/0.144 (2)
9		✓	✓ ^{a2}			0.705/0.604 (1)
10		✓	✓ ^{d3}			0.707/0.595 (2)
3 parameters						
11	✓	✓		✓		0.655/0.499 (3)
12	✓	✓	✓ ^{a2}			0.693/0.560 (2)
13	✓	✓	✓ ^{d3}			0.694/0.569 (2)
14		✓	✓ ^{a2}	✓		0.694/0.456 (2)
15		✓	✓ ^{d3}	✓		0.850/0.770 (3)
4 parameters						
16	✓	✓	✓ ^{a2}	✓		0.869/0.789 (3)
17	✓	✓	✓ ^{d3}	✓		0.852/0.764 (3)
5 parameters						
18	✓	✓	✓ ^{a2}	✓	✓ ^{a2}	0.917/0.861 (5)
19	✓	✓	✓ ^{d3}	✓	✓ ^{d3}	0.899/0.801 (5)

[a] in brackets the number of components is given; ✓^a: Mulliken charges; ✓^b: Chelpg charges; ✓^c: ESP charges from MOPAC; ✓^d: NPA charges; ¹: HF/6-31+G(2d,p); ²: HF/6-31G(d) with PCM model (PCM/UAHF/RHF/6-31G(d) solvation energies for chloroform); ³: HF/6-31G(d).

As noted before none of the descriptors for the pyridine nitrogen atom itself provided statistically significant predictive value^[18]. Thus we concentrated on the charge analysis of the *ortho*-hydrogen atom which plays a role in the transition state of DMAP catalyzed acetylation reactions due to the contacts to the acetate counterion^[24]. The Analysis has been performed for the best conformers of the free catalysts at the HF/6-31G(d) level of theory. We surveyed Mulliken, CHELPG (charges from electrostatic potentials using a grid based method) and NPA (natural population analysis) charges at two levels of theory and additionally one model that accounts for solvent effects. In Table S13 the different types of charges (Mulliken, CHELPG and NPA) were surveyed in combination with different basis sets and solvent models. It was found that the NPA charges are the charges of choice considering PCM effects in chloroform. They show the best correlation with the experiment but with still acceptable effects towards changes in basis set and solvation model. A screening of the optimum choice of combination in terms of best correlating parameter set combinations for the QSAR model led us to the following ones: we use averaged NPA charges ($q_{ortho-H}$) of the *ortho*-hydrogen atom to avoid getting too much parameters, as second we use the acylation enthalpies including a PCM solvation model ($\Delta H_{ac/solv}$) (= model-nr. 28a) and finally the N-C bond distance in 4-position ($dist_{N-C}$). It was found that having $\Delta H_{ac/solv}$ among the parameters the acylation enthalpies in the gas phase are redundant (compare models 6 and 7). Finally model 28a was applied to the catalysts surveyed herein. The important catalyst characteristics for catalysts **1 – 5** can be found in Table S14.

Table S13. Variation of different basis sets and solvation model in the QSAR study.

Model-nr.	ΔH_{ac}	$\Delta H_{ac/solv}$	$q_{ortho-H}$	$dist_{N-C}$	R^2/Q^2 [a]
HF/6-31+G(2d,p)					
20	✓	✓	✓ ^{a1}	✓	0.662/0.250 (3)
21	✓	✓	✓ ^{b1}	✓	0.665/0.423 (4)
22	✓	✓	✓ ^{d1}	✓	0.846/0.759 (3)
HF/6-31G(d) with PCM model					
23	✓	✓	✓ ^{a2}	✓	0.869/0.789 (3)
24	✓	✓	✓ ^{b2}	✓	0.684/0.431 (4)
25	✓	✓	✓ ^{d2}	✓	0.839/0.746 (3)
HF/6-31G(d)					
26	✓	✓	✓ ^{a3}	✓	0.862/0.759 (3)
27	✓	✓	✓ ^{b3}	✓	0.674/0.417 (4)
28	✓	✓	✓ ^{d3}	✓	0.852/0.764 (3)
28a		✓	✓ ^{d3}	✓	0.850/0.770 (3)
28b	✓		✓ ^{d3}	✓	0.800/0.682 (3)
28c	✓	✓		✓	0.655/0.499 (3)
28d	✓	✓	✓ ^{d3}		0.694/0.569 (2)

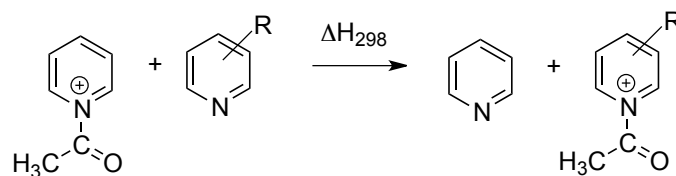
[a] in brackets the number of components is given; ✓^a: Mulliken charges; ✓^b: Chelpg charges; ✓^c: ESP charges from MOPAC; ✓^d: NPA charges; ¹: HF/6-31+G(2d,p); ²: HF/6-31G(d) with PCM model (PCM/UAHF/RHF/6-31G(d) solvation energies for chloroform); ³: HF/6-31G(d).

Table S14. QSAR input parameters of catalysts **1 – 5**.

catalyst	$\Delta H_{ac/solv}$ [kJ/mol]	$q_{ortho-H}$	$dist_{N-C}$ [Å]	$\ln(1/t_{1/2})$ exp.	$\ln(1/t_{1/2})$ pred.	residual
5d	-106.70	0.2227	1.4051	-3.6481	-3.6777	0.0297
5c	-98.30	0.2220	1.4044	-4.1805	-4.2015	0.0210
4c	-90.20	0.2162	1.3958	-3.5351	-3.5239	-0.0112
5a	-89.20	0.2137	1.3997	-3.6376	-3.3741	-0.2635
5b	-87.80	0.2112	1.4055	-3.7887	-3.3324	-0.4563
4b	-87.50	0.2109	1.3965	-2.6247	-2.9049	0.2802
4a	-86.80	0.2122	1.3939	-2.8848	-3.0640	0.1792
3	-82.20	0.2108	1.3884	-2.6879	-2.9600	0.2722
5e	-69.50	0.2171	1.4020	-5.4263	-5.6053	0.1790
2	-67.60	0.2150	1.3695	-4.2047	-3.9785	-0.2262
1	-61.20	0.2157	1.3787	-5.0173	-5.0132	0.0041

9. Theoretical methods and data

Acylation enthalpies



The conformational space of flexible pyridine derivatives has been searched using the MM3 force field and the systematic search routine implemented in MACROMODEL 9.7. Following a recently developed protocol for the calculation of cation affinity values,^[13] geometry optimizations have been performed in the gas phase at the B98/6-31G(d) level of theory. Thermal corrections to 289.15 K and 1 atm have been calculated at the same level of theory using the rigid rotor/harmonic oscillator model. Single point energies calculated at the MP2(FC)/6-31+G(2d,p) level have then been combined with thermal corrections obtained previously to calculate enthalpies (H_{298}) and free energies (G_{298}) at 298.15 K. In conformationally flexible systems enthalpies have been calculated as Boltzmann-averaged values over all available conformers within 30 kJ. Solvent effects in chloroform have subsequently been determined through PCM (polarized continuum solvation model) single points at the RHF/6-31G(d) level with UAHF radii. All quantum mechanical calculations have been performed with Gaussian 03.^[25]

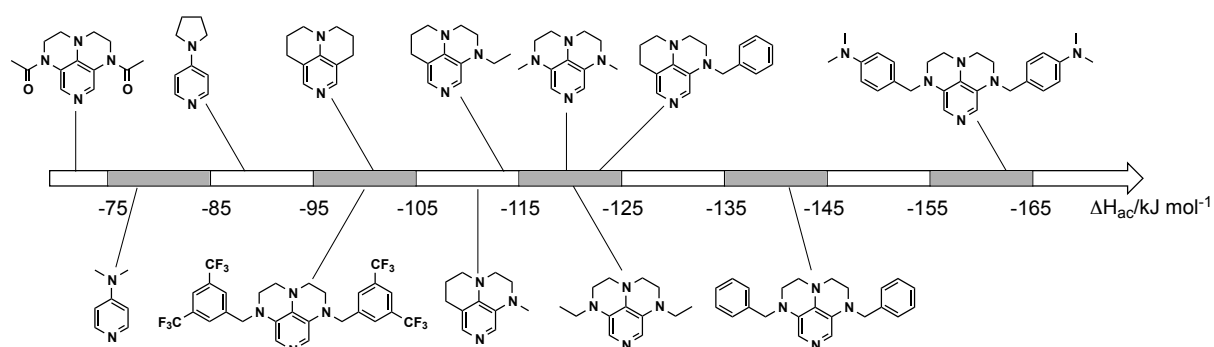


Figure S16. Acylation enthalpies in gas phase (ΔH_{ac}) for investigated catalyst.

Table S15. Calculated energies of conformers for catalysts **5d** and **5e**, as calculated at MP2/6-31+G(2d,p)//B98/6-31G(d) level with inclusion of solvent effects at PCM/UAHF/RHF/6-31G(d).

Conf	E _{tot} B98/6-31G(d)	H ₂₉₈ B98/6-31G(d)	E _{tot}	G _{solv.} kcal/mol	H ₂₉₈	H ₂₉₈
			MP2(FC)/6-31+G(2d,p)		MP2-5 with- out solvation	MP2-5 with solvation
Pyr						
1	-248.181767	-248.087628	-247.589433	-2.15	-247.495294	-247.498720
Pyr-Ac⁺						
1 ac	-401.140005	-400.991697	-400.215517	-34.07	-400.067209	-400.121503
5d						
5	-1377.273310	-1376.663857	-1373.974752	-4.1	-1373.365299	-1373.371832
13	-1377.275202	-1376.665689	-1373.975470	-3.66	-1373.365957	-1373.371790
6	-1377.274605	-1376.664862	-1373.975115	-3.86	-1373.365373	-1373.371524
7	-1377.275834	-1376.665975	-1373.975495	-3.66	-1373.365636	-1373.371468
4	-1377.273690	-1376.663737	-1373.974891	-3.87	-1373.364938	-1373.371105
9	-1377.274707	-1376.664933	-1373.974696	-3.74	-1373.364922	-1373.370882
17	-1377.273236	-1376.663538	-1373.974157	-3.95	-1373.364459	-1373.370754
12	-1377.273230	-1376.663530	-1373.973692	-3.84	-1373.363991	-1373.370111
16	-1377.271466	-1376.661683	-1373.973203	-4.19	-1373.363420	-1373.370097
1	-1377.273796	-1376.663774	-1373.974318	-3.59	-1373.364296	-1373.370017
14	-1377.273167	-1376.663416	-1373.973545	-3.79	-1373.363794	-1373.369834
10	-1377.271339	-1376.661621	-1373.972685	-3.82	-1373.362967	-1373.369055
11	-1377.271138	-1376.661331	-1373.971149	-3.97	-1373.361341	-1373.367668
5d-Ac⁺						
16 ac1	-1530.294965	-1529.630131	-1526.664562	-22.20	-1525.999728	-1526.035106
16 ac2	-1530.294965	-1529.630130	-1526.664559	-22.20	-1525.999724	-1526.035102
5 ac2	-1530.295110	-1529.630472	-1526.664628	-21.96	-1525.999990	-1526.034985
5 ac1	-1530.295110	-1529.630471	-1526.664631	-21.94	-1525.999992	-1526.034955
17 ac1	-1530.296435	-1529.631789	-1526.663844	-22.42	-1525.999198	-1526.034926
6 ac1	-1530.296646	-1529.632207	-1526.663833	-22.26	-1525.999395	-1526.034868
4 ac1	-1530.294758	-1529.629928	-1526.663378	-22.22	-1525.998548	-1526.033958
4 ac2	-1530.294058	-1529.629081	-1526.662531	-22.20	-1525.997554	-1526.032932
17 ac2	-1530.294001	-1529.629363	-1526.660669	-22.92	-1525.996031	-1526.032557
13 ac2	-1530.295345	-1529.631120	-1526.659805	-23.14	-1525.995580	-1526.032456
10 ac1	-1530.292983	-1529.628556	-1526.661485	-22.08	-1525.997058	-1526.032244
9 ac2	-1530.295304	-1529.630507	-1526.661509	-22.22	-1525.996712	-1526.032122
14 ac2	-1530.294637	-1529.630151	-1526.660755	-22.35	-1525.996269	-1526.031886
12 ac1	-1530.294709	-1529.629850	-1526.660820	-22.43	-1525.995961	-1526.031706
1 ac1	-1530.293105	-1529.628511	-1526.660863	-22.21	-1525.996269	-1526.031663
1 ac2	-1530.293106	-1529.628509	-1526.660850	-22.19	-1525.996252	-1526.031615
10 ac2	-1530.292720	-1529.627857	-1526.660741	-22.38	-1525.995878	-1526.031543
6 ac2	-1530.294302	-1529.629689	-1526.660586	-22.28	-1525.995973	-1526.031478
7 ac2	-1530.295415	-1529.630671	-1526.659513	-22.92	-1525.994769	-1526.031294

9	ac1	-1530.293625	-1529.628403	-1526.659251	-23.03	-1525.994028	-1526.030729
11	ac1	-1530.292285	-1529.627430	-1526.659789	-22.34	-1525.994934	-1526.030535
14	ac1	-1530.291865	-1529.627252	-1526.657030	-23.27	-1525.992417	-1526.029500
12	ac2	-1530.291866	-1529.627225	-1526.657040	-23.28	-1525.992399	-1526.029498

5e

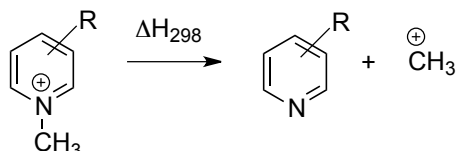
4		-2457.167590	-2456.680733	-2452.332600	3.2	-2451.845743	-2451.840643
5		-2457.167844	-2456.680186	-2452.332439	3.36	-2451.844781	-2451.839426
6		-2457.167475	-2456.679766	-2452.331402	3.23	-2451.843693	-2451.838545
16		-2457.166341	-2456.678411	-2452.331395	3.21	-2451.843465	-2451.838349
17		-2457.166909	-2456.678911	-2452.330841	3.13	-2451.842843	-2451.837855
9		-2457.167235	-2456.679336	-2452.330594	3.29	-2451.842695	-2451.837452
13		-2457.167124	-2456.679203	-2452.330138	3.22	-2451.842217	-2451.837086
7		-2457.167440	-2456.679606	-2452.329809	3.17	-2451.841976	-2451.836924
1		-2457.167009	-2456.679192	-2452.330928	4.02	-2451.843111	-2451.836705
12		-2457.165605	-2456.677618	-2452.329303	3.25	-2451.841315	-2451.836136
10		-2457.165057	-2456.677241	-2452.329585	3.69	-2451.841769	-2451.835888
11		-2457.164568	-2456.676750	-2452.328251	3.38	-2451.840433	-2451.835047
14		-2457.164693	-2456.676764	-2452.328819	4.31	-2451.840890	-2451.834022

5e-Ac⁺

16	ac2	-2610.166251	-2609.623431	-2604.998864	-21.36	-2604.456044	-2604.490083
5	ac1	-2610.166298	-2609.623448	-2604.998542	-20.87	-2604.455693	-2604.488951
5	ac2	-2610.166297	-2609.623466	-2604.998567	-20.83	-2604.455737	-2604.488931
17	ac1	-2610.166226	-2609.623203	-2604.996205	-22.35	-2604.453182	-2604.488799
4	ac1	-2610.165544	-2609.622795	-2604.997395	-21.23	-2604.454646	-2604.488478
17	ac2	-2610.163792	-2609.620806	-2604.993838	-23.25	-2604.450853	-2604.487904
6	ac1	-2610.166176	-2609.623211	-2604.995963	-21.74	-2604.452999	-2604.487643
4	ac2	-2610.163876	-2609.621009	-2604.995773	-21.54	-2604.452905	-2604.487232
13	ac2	-2610.163538	-2609.620761	-2604.991138	-24.10	-2604.448361	-2604.486767
10	ac2	-2610.164630	-2609.621812	-2604.996347	-20.60	-2604.453529	-2604.486357
7	ac2	-2610.163406	-2609.620521	-2604.990748	-23.97	-2604.447863	-2604.486062
9	ac1	-2610.162859	-2609.619973	-2604.992293	-22.99	-2604.449407	-2604.486044
9	ac2	-2610.163525	-2609.620553	-2604.992841	-22.43	-2604.449869	-2604.485613
1	ac1	-2610.162845	-2609.620878	-2604.994296	-20.71	-2604.452329	-2604.485333
12	ac2	-2610.162355	-2609.619464	-2604.991647	-22.93	-2604.448756	-2604.485297
10	ac1	-2610.163287	-2609.620400	-2604.994743	-20.95	-2604.451856	-2604.485242
6	ac2	-2610.163733	-2609.620763	-2604.993542	-21.67	-2604.450573	-2604.485106
12	ac1	-2610.163094	-2609.620210	-2604.992336	-22.34	-2604.449453	-2604.485054
11	ac2	-2610.161781	-2609.619016	-2604.992997	-21.73	-2604.450232	-2604.484861
14	ac2	-2610.165660	-2609.622534	-2604.995442	-20.31	-2604.452316	-2604.484682
1	ac2	-2610.162704	-2609.619830	-2604.994320	-20.74	-2604.451446	-2604.484497

MCA values

Methyl cation affinities have been calculated as the reaction enthalpy at 298.15 K and 1 atm pressure for the methyl cation detachment reaction shown below. This is in analogy to the mass spectrometric definition of proton affinities.



The geometries of all species have been optimized at the B98/6-31G(d) level of theory. The conformational space of flexible pyridines and phosphanes and the corresponding cations has been searched using the MM3* force field and the systematic search routine implemented in MACROMODEL 9.7. All stationary points located at force field level have then been reoptimized at B98/6-31G(d) level as described before. Thermochemical corrections to 298.15 K have been calculated for all minima from unscaled vibrational frequencies obtained at this same level. The thermochemical corrections have been combined with single point energies calculated at the MP2(FC)/6-31+G(2d,p)//B98/6-31G(d) level to yield enthalpies H_{298} at 298.15 K. In conformationally flexible systems enthalpies have been calculated as Boltzmann-averaged values over all available conformers. This procedure has recently been found to reproduce G3 methyl cation affinity values of selected small and medium sized organocatalysts within 4.0 kJ mol⁻¹.^[12] All quantum mechanical calculations have been performed with Gaussian 03.^[25]

Table S16. Calculated energies of conformers for catalysts **5d** and **5e**, as calculated at MP2/6-31+G(2d,p)//B98/6-31G(d) level.

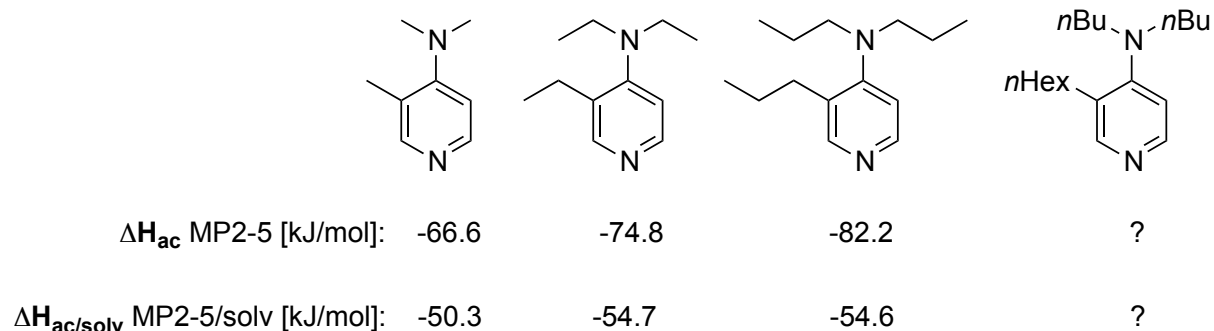
system	B98/6-31G(d)		MP2(FC)/6-31+G(2d,p)//B98/6-31G(d)	
	E_{tot}	H_{298}	E_{tot}	H_{298}
CH₃⁺				-39.316929
CH₃⁺	-39.462922	-39.427481	-39.352370	-39.316929
5d				-1373.365244
13	-1377.275202	-1376.665689	-1373.975470	-1373.365957
7	-1377.275834	-1376.665975	-1373.975495	-1373.365636
6	-1377.274605	-1376.664862	-1373.975115	-1373.365373
5	-1377.273310	-1376.663857	-1373.974752	-1373.365299

4	-1377.273690	-1376.663737	-1373.974891	-1373.364938
9	-1377.274707	-1376.664933	-1373.974696	-1373.364922
17	-1377.273236	-1376.663538	-1373.974157	-1373.364459
1	-1377.273796	-1376.663774	-1373.974318	-1373.364296
12	-1377.273230	-1376.663530	-1373.973692	-1373.363991
14	-1377.273167	-1376.663416	-1373.973545	-1373.363794
16	-1377.271466	-1376.661683	-1373.973203	-1373.363420
10	-1377.271339	-1376.661621	-1373.972685	-1373.362967
11	-1377.271138	-1376.661331	-1373.971149	-1373.361341
5d-Me⁺				-1412.934033
5	-1417.002909	-1416.350286	-1413.587226	-1412.934602
16	-1417.002349	-1416.348090	-1413.586624	-1412.932365
6	-1417.002907	-1416.349289	-1413.585385	-1412.931767
4	-1417.002170	-1416.348015	-1413.585639	-1412.931484
17	-1417.002443	-1416.348593	-1413.585095	-1412.931245
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13	-1417.002459	-1416.349150	-1413.583296	-1412.929987
9	-1417.001883	-1416.348114	-1413.583422	-1412.929653
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12	-1417.000884	-1416.347151	-1413.582214	-1412.928480
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4	-2457.167590	-2456.680733	-2452.332600	-2451.845743
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6	-2457.167475	-2456.679766	-2452.331402	-2451.843693
16	-2457.166341	-2456.678411	-2452.331395	-2451.843465
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13	-2457.167124	-2456.679203	-2452.330138	-2451.842217

7	-2457.167440	-2456.679606	-2452.329809	-2451.841976
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12	-2457.165605	-2456.677618	-2452.329303	-2451.841315
14	-2457.164693	-2456.676764	-2452.328819	-2451.840890
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4	-2496.874252	-2496.342261	-2491.921708	-2491.389717
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6	-2496.873089	-2496.341126	-2491.918499	-2491.386536
16	-2496.871852	-2496.339686	-2491.915361	-2491.383195
1	-2496.872148	-2496.340067	-2491.917211	-2491.385130
17	-2496.871731	-2496.339779	-2491.915537	-2491.383585
9	-2496.872230	-2496.341247	-2491.919008	-2491.388024
13	-2496.872709	-2496.340778	-2491.918212	-2491.386281
7	-2496.873773	-2496.341564	-2491.921623	-2491.389415
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12	-2496.872168	-2496.340021	-2491.919073	-2491.386926
14	-2496.873052	-2496.340681	-2491.918410	-2491.386039
11	-2496.871037	-2496.338911	-2491.917312	-2491.385186

Extrapolation of acylation enthalpies for catalyst **18**:

The calculation of the full conformational space of compound **18** would have included too many conformers for Boltzmann averaging. For that reason the acylation enthalpies in gas phase and in solvation (PCM model) were extrapolated (see Figure S17 and Scheme S1).



Scheme S1. Extrapolation of enthalpies in gas phase (ΔH_{ac} MP2-5) and solvation ($\Delta H_{ac/solv}$ MP2-5/solv) for catalyst **18**.

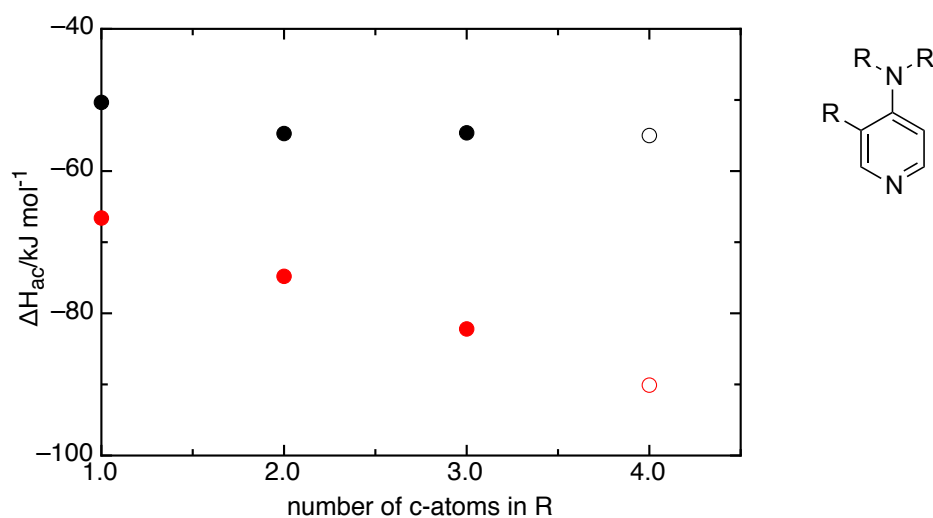


Figure S17. Extrapolation of ΔH_{ac} MP2-5 (red circles) and $\Delta H_{ac/solv}$ MP2-5/solv (black circles). The assumed values for the extrapolation are not filled.

Figure S17 shows that the gas phase enthalpies follow a rather linear correlation whereas the enthalpies with inclusion of the solvent model show a saturation effect. The gas phase enthalpy (ΔH_{ac} MP2-5) for **18** amounts up to -90.1 kJ/mol (after linear extrapolation) and the enthalpy in solution ($\Delta H_{ac/solv}$ MP2-5/solv) -55.0 kJ/mol (under the acceptance of a saturation effect; three data points were not sufficient to perform a non linear fit).

10. Literature

References 1-20 and additionally:

- [21] V. Gutmann, *Electrochimica Acta*. **1976**, *21*, 661.
- [22] a) C. Reichardt, *Chem. Rev.* **1994**, *94*, 2319 - 2358. b) C. Reichardt, G. Schäfer, *Liebigs Ann.* **1995**, 1579 - 1582. c) R. Eberhardt, S. Löbbecke, B. Neidhart, C. Reichardt, *Liebigs Ann. /Recueil* **1997**, 1195 - 1199. d) C. Reichardt, *Green Chem.* **2005**, *7*, 339 - 351.
- [23] <http://www.cmbi.ru.nl/edu/bioinf4/comfa-Prac/comfa.shtml>, 26.10.2012, 14:02 CET.
- [24] (a) V. Lutz, J. Glatthaar, C. Würtele, M. Serafin, H. Hausmann, P. R. Schreiner, *Chem. Eur. J.* **2009**, *15*, 8548 - 8557. (b) C. B. Fisher, S. Xu, H. Zipse, *Chem. Eur. J.* **2006**, *12*, 5779 - 5784.
- [25] Gaussian 03, Revision D.01, M. J. Frisch, G. W. Trucks, H.B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. S. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, **2004**.

11. Crystallographic Data

The crystal structure for compound **3** is in line with the already published one (CCDC 633500).

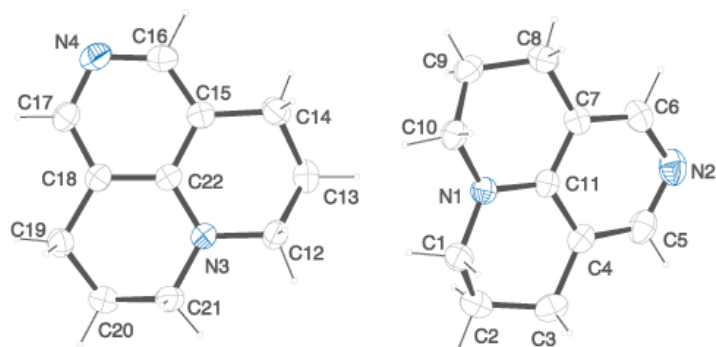


Table S 17. Crystallographic data of **4a**, CCDC-nr.: 914973.

4a	
net formula	C ₁₁ H ₁₅ N ₃
<i>M_r</i> /g mol ⁻¹	189.257
crystal size/mm	0.24 × 0.19 × 0.07
<i>T</i> /K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> /Å	9.0158(6)
<i>b</i> /Å	8.5738(6)
<i>c</i> /Å	25.5574(16)
α/°	90
β/°	94.298(4)
γ/°	90
<i>V</i> /Å ³	1970.0(2)
<i>Z</i>	8
calc. density/g cm ⁻³	1.27624(13)
μ/mm ⁻¹	0.079
absorption correction	none
refls. measured	5882
<i>R</i> _{int}	0.0770
mean σ(<i>I</i>)/ <i>I</i>	0.0942
θ range	3.28–24.15
observed refls.	1612
<i>x</i> , <i>y</i> (weighting scheme)	0.0956, 0
hydrogen refinement	constr
refls in refinement	3108
parameters	255
restraints	0
<i>R</i> (<i>F</i> _{obs})	0.0724
<i>R</i> _w (<i>F</i> ²)	0.1970
<i>S</i>	1.023
shift/error _{Tmax}	0.001
max electron density/e Å ⁻³	0.329
min electron density/e Å ⁻³	-0.184

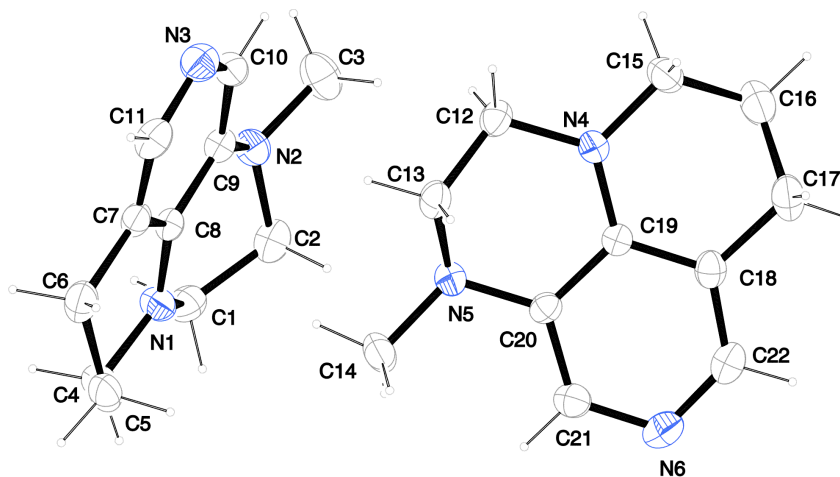


Table S 18. Crystallographic data of **5c**, CCDC-nr.: 914974.

5c	
net formula	C ₂₃ H ₂₄ N ₄
<i>M_r</i> /g mol ⁻¹	356.464
crystal size/mm	0.36 × 0.29 × 0.26
<i>T</i> /K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	<i>P</i> 1bar
<i>a</i> /Å	6.7771(7)
<i>b</i> /Å	10.1414(11)
<i>c</i> /Å	14.0005(14)
α/°	78.648(9)
β/°	77.902(9)
γ/°	83.399(9)
<i>V</i> /Å ³	919.74(17)
<i>Z</i>	2
calc. density/g cm ⁻³	1.2872(2)
μ/mm ⁻¹	0.078
absorption correction	'multi-scan'
transmission factor range	0.93079–1.00000
refls. measured	5113
<i>R</i> _{int}	0.0221
mean σ(<i>I</i>)/ <i>I</i>	0.0467
θ range	4.24–26.37
observed refls.	2885
<i>x</i> , <i>y</i> (weighting scheme)	0.0442, 0.2121
hydrogen refinement	constr
refls in refinement	3715
parameters	244
restraints	0
<i>R</i> (<i>F</i> _{obs})	0.0458
<i>R</i> _w (<i>F</i> ²)	0.1209
<i>S</i>	1.037
shift/error _{max}	0.001
max electron density/e Å ⁻³	0.173
min electron density/e Å ⁻³	-0.203

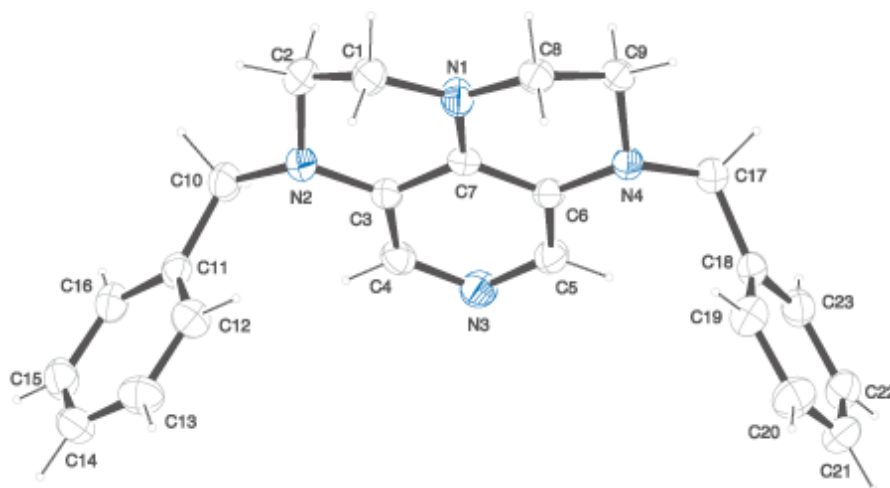


Table S 19. Crystallographic data of **5d**, CCDC-nr.: 914975.

5d	
net formula	C ₃₆ H ₄₇ N ₇ O
<i>M_r</i> /g mol ⁻¹	593.805
crystal size/mm	0.34 × 0.28 × 0.21
<i>T</i> /K	173(2)
radiation	MoKα
diffractometer	'KappaCCD'
crystal system	triclinic
space group	<i>P</i> 1bar
<i>a</i> /Å	10.7475(3)
<i>b</i> /Å	11.2640(3)
<i>c</i> /Å	15.6318(4)
α/°	96.177(2)
β/°	104.2366(18)
γ/°	114.7428(15)
<i>V</i> /Å ³	1617.53(7)
<i>Z</i>	2
calc. density/g cm ⁻³	1.21921(5)
μ/mm ⁻¹	0.076
absorption correction	none
refls. measured	10576
<i>R</i> _{int}	0.0293
mean σ(<i>I</i>)/ <i>I</i>	0.0402
θ range	3.37–25.52
observed refls.	4473
<i>x</i> , <i>y</i> (weighting scheme)	0.0701, 0.3613
hydrogen refinement	mixed
refls in refinement	5909
parameters	406
restraints	0
<i>R</i> (<i>F</i> _{obs})	0.0485
<i>R</i> _w (<i>F</i> ²)	0.1363
<i>S</i>	1.035
shift/error _{Tmax}	0.001
max electron density/e Å ⁻³	0.203
min electron density/e Å ⁻³	-0.210

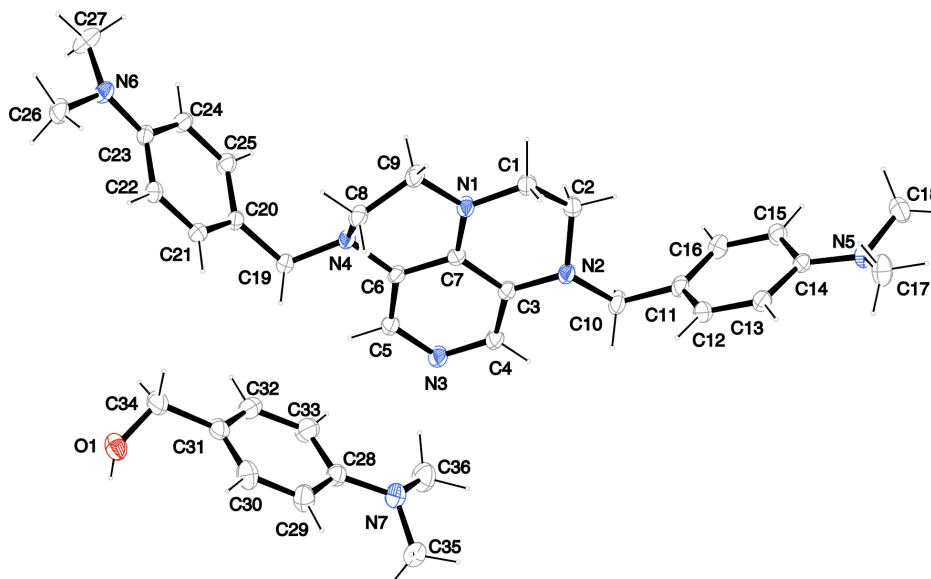
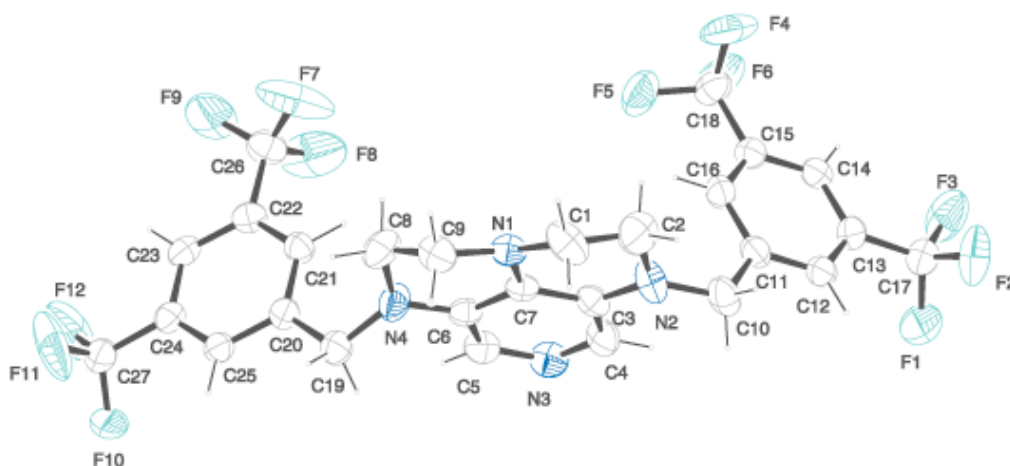


Table S 20. Crystallographic data of **5e**, CCDC-nr.: 914976.

5e	
net formula	C ₂₇ H ₂₀ F ₁₂ N ₄
<i>M_r</i> /g mol ⁻¹	628.456
crystal size/mm	0.31 × 0.18 × 0.13
<i>T</i> /K	173(2)
radiation	MoKα
diffractometer	'Oxford XCalibur'
crystal system	triclinic
space group	<i>P</i> 1bar
<i>a</i> /Å	8.7064(10)
<i>b</i> /Å	12.5447(14)
<i>c</i> /Å	13.4356(16)
α/°	63.787(11)
β/°	77.333(10)
γ/°	79.499(10)
<i>V</i> /Å ³	1278.3(3)
<i>Z</i>	2
calc. density/g cm ⁻³	1.6328(4)
μ/mm ⁻¹	0.159
absorption correction	'multi-scan'
transmission factor range	0.50690–1.00000
refls. measured	7083
<i>R</i> _{int}	0.0411
mean σ(<i>I</i>)/ <i>I</i>	0.0680
θ range	4.37–26.37
observed refls.	3382
<i>x</i> , <i>y</i> (weighting scheme)	0.1193, 1.1833
hydrogen refinement	constr
refls in refinement	5148
parameters	427
restraints	9
<i>R</i> (<i>F</i> _{obs})	0.0838
<i>R</i> _w (<i>F</i> ²)	0.2514
<i>S</i>	1.030
shift/error _{max}	0.002
max electron density/e Å ⁻³	0.642
min electron density/e Å ⁻³	-0.549



12. Archive Entries

5d_5

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5d-Ac⁺_16ac1

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5e_4

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eom=check guess=read\PCM of subdmap4_1 b98/6-31G(d) structures on 4p
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46186\C,0,-1.818300018,-0.9770506079,3.1163972395\C,0,-1.1306667546,-0
.2692936463,0.8933723163\C,0,-1.1898369823,0.6130995147,-0.2001448047\
C,0,0.8583270854,-0.0419202744,-0.9872431646\C,0,1.030816364,-0.990759
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5e-Ac⁺_16.ac2

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