Enantiospecific Synthesis of Nepetalactones by One-Step Oxidative NHC Catalysis

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[†] X-ray crystallography

Supporting Information

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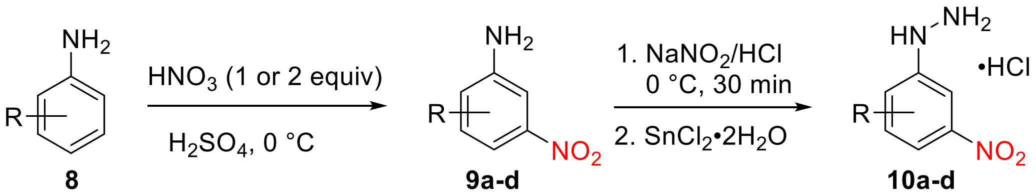
1. General

Nuclear magnetic resonance (^1H, ^{13}C) spectra were recorded on a Bruker Avance 300 instrument (^1H: 300.13 MHz, ^{13}C: 75.46 MHz) at ambient temperature. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) or solvent residual signals. The following abbreviations were used for chemical shift multiplicities in ^1H NMR spectra: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet. IR spectra were recorded on a Shimadzu IR Affinity-1 FT-IR spectrometer. GC-MS analyses were done on a *Hewlett Packard* HP 6890 Series Plus gas chromatograph, injector and autosampler, HP 5973 Series mass-selective detector operated in electron-impact (EI) mode with an ionization energy of 75 eV and all other parameters set at autotune values, using H_2 as carrier gas and a HP-5 MS column (30 m x 0.25 mm ID, 0.25 μm film thickness): temperature program (Std 50): 50 °C, 5 min; 20 °C/min to 280 °C, 280 °C, 10 min, unless otherwise stated. ESI-mass spectra were measured on an Agilent 1100 Series LC/MSD instrument with a G1312A binary pump, G1313A autosampler and G1956A mass-selective detector. GC analyses were done on an Agilent 6890N Network gas chromatograph, injector and autosampler, and flame ionization detector, using N_2 as carrier gas. Elemental analyses were performed using an Elementar Vario EL elemental analyzer. Optical rotations were recorded on an Anton Paar MCP 200 polarimeter. Melting points were determined on a Büchi apparatus and are uncorrected.

(*S*)-(−)-β-Citronellol (Merck), (*R*)-(+)-β-citronellol (Sigma Aldrich), 2,4,6-trimethylaniline (Alfa Aesar), 2,6-diisopropylaniline (Alfa Aesar), 2,6-dimethylaniline (Sigma Aldrich), 2,6-diethylaniline (Sigma Aldrich), fuming nitric acid (90%, Acros), 3-nitrophenylhydrazine hydrochloride (TCI), triethyl orthoformate (Acros), chlorobenzene (Acros), and HCl in dioxane (ca. 4 M, TCI) were purchased from the suppliers indicated and used as received. Diisopropyl ethyl amine (DIPEA) was distilled over CaH_2 under Ar. Anhydrous THF and MeCN were dried over Na/benzophenone and CaH_2, respectively, and distilled under Ar.

2. Synthesis of the nitrophenylhydrazines 10



2.1 General procedure 1 (GP-1) for the nitration of anilines to give 9:[1]

In a three-necked round-bottom flask, a solution of aniline **8** (150 mmol, 1.0 equiv) in conc. H_2SO_4 (100 mL) was cooled in an ice-salt bath. Fuming nitric acid (90%, *d* = 1.5, 1.0 or 2.0 equiv) was slowly added dropwise, the internal temperature was controlled not to exceed 10 °C. After the addition was complete, stirring of the reaction mixture was continued in the ice bath for 1 h. The mixture was then poured into ice (ca. 500 mL) and cooled down in an ice-water bath. The mixture was made slightly basic by slow addition of NaOH (6 N), keeping the temperature below 25 °C. The resulting

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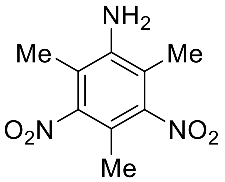
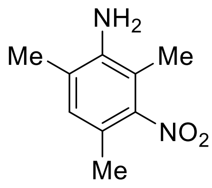
[1] (a) Noelting, E.; Stoecklin, L. *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 564–572. (b) Bergman, J.; Sand, P. *Tetrahedron* **1990**, *46*, 6085–6112.

precipitate (except for **9d**, see below) was collected by suction filtration, washed with water and dried to give **9**, which was used in the next step without further purification.



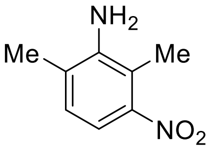
9a

2,4,6-Trimethyl-3,5-dinitroaniline (9a). According to GP-1, this product was obtained from the reaction between 2,4,6-trimethylaniline (20.3 g, 150 mmol, 1.0 equiv) and 90% nitric acid (15.0 mL, 300 mmol, 2.0 equiv) in conc. H_2SO_4 (100 mL) at 0 °C for 1 h and then at rt for 1h. After filtration, the product **9a** was obtained as a yellow-brown powder (19.4 g, 86 mmol, 57%), which was used in the next step without further purification; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 5.74$ (s, 2H, NH_2), 2.02 (s, 6H, 2xCH_3), 1.94 (s, 3H, CH_3).; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 150.1$ (ArC), 145.2 (2xArC), 113.2 (2xArC), 105.0 (ArC), 12.6 (2xCH_3), 11.3 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3499 (w), 3410 (m), 2988 (w), 2884 (w), 1632 (m), 1510 (s), 1475 (m), 1362 (s), 1076 (m), 862 (m), 804 (m), 669 (m); GC-MS: t_R (Std 50) = 14.1 min, $m/z = 225$ (M^+, 100%), 208, 191, 178, 162, 148, 132, 120, 106, 91, 77, 65, 54.



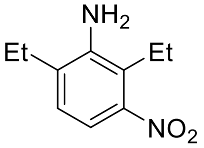
9b

2,4,6-Trimethyl-3-nitroaniline (9b). According to GP-1, this product was obtained from the reaction between 2,4,6-trimethylaniline (20.3 g, 150 mmol, 1.0 equiv) and 90% nitric acid (7.0 mL, 150 mmol, 1.0 equiv) in conc. H_2SO_4 (100 mL) at 0 °C for 1 h. After filtration, the product **9b** was obtained as a yellow powder (26.3 g, 146 mmol, 97%), which was used in the next step without further purification; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.82$ (s, 1H, ArH), 3.67 (s, 2H, NH_2), 2.16 (s, 6H, 2xCH_3), 2.05 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 141.5$ (ArC), 130.0 (ArCH), 123.8 (ArC), 117.7 (ArC), 112.7 (ArC), 17.6 (CH_3), 16.6 (CH_3), 12.3 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3414 (m), 3350 (w), 2928 (w), 2862 (w), 1632 (m), 1508 (s), 1474 (m), 1358 (s), 1306 (m), 1049 (m), 851 (m), 800 (m); GC-MS: t_R (Std 50) = 12.5 min, $m/z = 180$ (M^+, 100%), 163, 150, 135, 118, 108, 91, 77, 65, 54.



9c

2,6-Dimethyl-3-nitroaniline (9c). According to GP-1, this product was obtained from the reaction between 2,6-dimethylaniline (30.0 g, 247 mmol, 1.0 equiv) and 90% nitric acid (12.5 mL, 270 mmol, 1.1 equiv) in conc. H_2SO_4 (180 mL) at 10-15 °C for 1 h. After filtration, the product **9c** was obtained as a yellow powder (36.4 g, 219 mmol, 89%), which was used in the next step without further purification; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.16$ (d, $J = 8.2$ Hz, 1H, ArH), 7.01 (d, $J = 8.2$ Hz, 1H, ArH), 3.79 (br s, 2H, NH_2), 2.28 (s, 3H, CH_3), 2.23 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 144.2$ (ArC), 127.7 ArCH), 126.3 (ArC), 115.2(ArC), 113.4 (ArCH), 18.1 (CH_3), 12.9 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3485 (w), 3421 (m), 3389 (w), 3350 (m), 2980 (w), 2951 (w), 2914 (w), 2851 (w), 1638 (m), 1593 (m), 1508 (s), 1458 (m), 1350 (s), 1321 (s), 1277 (m), 1219 (m), 1042 (m), 868 (m), 802 (s), 741 (s); GC-MS: t_R (Std 50) = 12.4 min, $m/z = 166$ (M^+, 100%), 149, 136, 121, 104, 94, 77, 65, 51.



9d

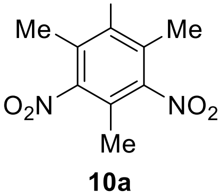
2,6-Diethyl-3-nitroaniline (9d). According to GP-1, this product was obtained from the reaction between 2,6-diethylaniline (22.4 g, 150 mmol, 1.0 equiv) and 90% nitric acid (7.0 mL, 150 mmol, 1.0 equiv) in conc. H_2SO_4 (100 mL) at 0 °C for 1h. After basicification with NaOH, the mixture was extracted with EtOAc. The combined organic layers were washed with water, brine, dried over Mg_2SO_4, and filtered. After removal of the solvent, the product **9d** was obtained as a yellow oil (29.1 g, 150 mmol, 100%), which was used in the next step without further purification; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16 (d, *J* = 8.3 Hz, 1H, ArH), 7.02 (d, *J* = 8.3 Hz, 1H, ArH), 3.95 (s, 2H, NH_2), 2.66 (q, *J* = 7.5 Hz, 2H, CH_2), 2.55 (q, *J* = 7.5 Hz, 2H, CH_2), 1.30 (t, *J* = 7.4 Hz, 3H, CH_3), 1.28 (t, *J* = 7.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4 (ArC), 143.2 (ArC), 132.2 (ArC), 125.8 (ArCH), 121.0 (ArC), 113.6 (ArCH), 24.6 (CH_2), 20.7 (CH_2), 12.5 (CH_3), 12.4 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3497 (w), 3410 (m), 2968 (m), 2938 (w), 2876 (m), 1732 (w), 1626 (m), 1512 (s), 1468 (m), 1431 (m), 1344 (s), 1955 (m), 814 (s), 735 (m) cm^{-1}; GC-MS: t_R (Std 50) = 13.1 min, *m/z* = 194 (M^+, 100%), 177, 162, 149, 135, 117, 108, 91, 77, 65, 51.

2.2 General procedure 2 (GP-2) for the synthesis of hydrazines 10 from 9:

In a three-necked round-bottom flask equipped with an overhead stirrer, a suspension of aniline **9** (1.0 equiv) in conc. HCl (ca. 2 mL/mmol) was cooled in an ice-salt bath. A solution of $NaNO_2$ (1.1 equiv) in water (ca. 0.18 mL/mmol) was added dropwise, keeping the internal reaction temperature below 5 °C. After the addition was complete, stirring of the reaction mixture was continued in the ice bath for 30 min. A solution of $SnCl_2{\bullet}2H_2O$ (2.5 equiv) in conc. HCl (ca. 0.25 mL/mmol) was added dropwise such that the temperature stayed below 5 °C. After completion of the addition, stirring of the reaction mixture was continued at 0 °C for 1 h and then at rt for 24 h. The precipitate was collected by suction filtration, and washed with 4N HCl (Important note: the product is soluble in water!) and then with Et_2O, providing the hydrazine hydrochloride **10•**HCl, which can be used in the next step without further purification.

To obtain the free hydrazine **10**, a suspension of the hydrochloride salt **10•**HCl in water (ca. 1 mL/mmol) was treated with cold 10% NaOH (aq.) at 0 °C until slightly basic. After stirring at 0 °C for 1 h, the solid was collected by suction filtration and washed with water and Et_2O to give the free hydrazine **10**, which was used in the next step without further purification. The product should be stored at temperature below 4 °C.

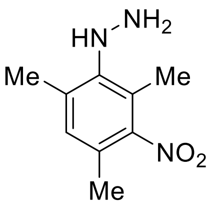
2,4,6-Trimethyl-3,5-dinitrophenylhydrazine (10a). According to GP-2, the reaction of **9a** (13.5 g, 60.0 mmol, 1.0 equiv) in conc. HCl (100 mL) with a solution of $NaNO_2$ (4.5 g, 66.0 mmol, 1.1 equiv) in water (15 mL), followed by the addition of a solution of $SnCl_2{\bullet}2H_2O$ (33.8 g, 149.8 mmol, 2.5 equiv) in conc. HCl (50 mL) yielded **10a•**HCl (12.1 g, 43.7 mmol, 73%) as a yellow solid: ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.21 (br s, 3H, NH_3), 7.38 (br s, 1H, NH), 2.38 (s, 6H, 2xCH_3), 2.14 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 149.9 (2xArC), 141.1 (ArC), 130.2 (2xArC), 119.4 (ArC), 13.5 (2xCH_3), 12.2 (CH_3).



10a

10a•HCl (9.8 g, 35.4 mmol) was treated with NaOH to give **10a** (8.2 g, 34.1 mmol, 96%) as a beige solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.30 (s, 1H, NH), 4.35 (s, 2H, NH_2), 2.20 (s, 6H, 2x CH_3), 2.02 (s, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5 (ArC), 149.2 (2xArC), 121.6 (2xArC), 111.5 (ArC), 13.8 (2xCH_3), 11.9 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3352 (w), 3327 (w), 2980 (w), 2901 (w), 1520 (s), 1389 (m), 1360 (m), 1294 (w), 1142 (w), 1070 (w), 1016 (w), 866 (m), 779 (m),679 (m); GC-MS: t_R (Std 50) = 14.6 min, *m/z* = 240 (M^+, 100%), 224, 206, 189, 178, 160, 149, 131, 117, 105, 91, 77, 65, 51.

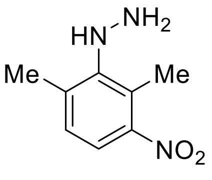
2,4,6-Trimethyl-3-nitrophenylhydrazine (10b). According to GP-2, the reaction of **9b** (13.5 g, 74.9 mmol, 1.0 equiv) in conc. HCl (120 mL) with a solution of $NaNO_2$ (5.7 g, 82.6 mmol, 1.1 equiv) in water (15 mL), followed by the addition of a solution of $SnCl_2•2H_2O$ (42.4 g, 187.5 mmol, 2.5 equiv) in conc. HCl (50 mL) yielded **10b•**HCl (17.0 g, 73.4 mmol, 98%) as a yellow solid: ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 9.97 (br s, 3H, NH_3), 7.21 (s, 1H, ArH), 7.00 (br s, 1H, NH), 2.45 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.20 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ = 150.3 (ArC), 139.2 (ArC), 138.4 (ArC), 130.7 (ArCH), 127.3 (ArC), 126.9 (ArC), 18.0 (CH_3), 16.4 (CH_3), 12.9 (CH_3).



10b

10b•HCl (16.0 g, 69.1 mmol) was treated with NaOH to give **10b** (10.5 g, 53.8 mmol, 78%) as a pale yellow solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.03 (s, 1H, ArH), 6.17 (br s, 3H, $NHNH_2$), 2.33 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.13 (s, 3H, CH_3) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5 (ArC), 142.9 (ArC), 135.0 (ArC), 130.4 (ArCH), 124.1 (ArC), 123.8 (ArC), 18.1 (CH_3), 16.2 (CH_3), 13.1 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3358 (w), 3291 (m), 3181 (w), 2972 (w), 2934 (w), 1607 (w), 1512 (s, br), 1460 (m), 1375 (m), 1360 (s),1277 (m), 1123 (s), 887 (s), 837 (m), 779 (s), 743 (s).; GC-MS: *t*$_R$ (Std 50) = 13.1 min, *m/z* = 195 (M$^+$, 100%), 179, 161, 149, 132, 117, 106, 91, 77, 65, 53.

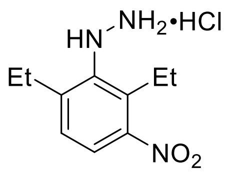
2,6-Dimethyl-3-nitrophenylhydrazine (10c). According to GP-2, the reaction of **9c** (17.0 g, 102.3 mmol, 1.0 equiv) in conc. HCl (150 mL) with a solution of $NaNO_2$ (7.7 g, 111.6 mmol, 1.1 equiv) in water (15 mL), followed by the addition of a solution of $SnCl_2•2H_2O$ (59.1 g, 261.9 mmol, 2.5 equiv) in conc. HCl (75 mL) yielded **10c•**HCl (14.7 g, 67.5 mmol, 66%) as a beige solid; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 10.04 (s, 3H, NH_3), 7.74 (d, *J* = 8.4 Hz, 1H, ArH), 7.34 (d, *J* = 8.4 Hz, 1H, ArH), 7.11 (s, 1H, NH), 2.52 (s, 3H, CH_3), 2.49 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ = 149.4 (ArC), 142.4 (ArC), 141.5 (ArC), 130.3 (ArC), 129.3 ArCH), 122.9 (ArCH), 19.1 (CH_3), 14.5 (CH_3).



10c

10c•HCl (10.0 g, 46.0 mmol) was treated with NaOH to give **10c** (6.5 g, 35.9 mmol, 78%) as a beige solid; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 7.37 (d, *J* = 7.6 Hz, 1H, ArH), 7.14 (d, *J* = 7.5 Hz, 1H, ArH), 6.10 (br s, 1H, NH), 6.10 (br s, 2H, NH_2), 2.37 (s, 6H, 2xCH_3); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ = 149.6 (ArC), 148.7 (ArC), 134.7 (ArC), 128.1 (ArCH), 124.0 (ArC), 117.2 (ArCH), 18.6 (CH_3), 14.6 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3350 (w), 3300 (m), 3181 (w), 2976 (w), 1591 (w), 1516 (s), 1354 (s), 1283 (m), 1258 (m), 1126 (m), 1047 (m), 912 (m), 835 (m), 812 (m), 793 (m), 743 (m); GC-MS: *t*$_R$ (Std 50) = 13.0 min, *m/z* = 181 (M$^+$, 100%), 165, 147, 134, 119, 106, 91, 77, 65, 51.

2,6-Diethyl-3-nitrophenylhydrazine hydrochloride (10d•HCl). According to GP-2, the reaction of **9d** (13.6 g, 70.0 mmol, 1.0 equiv) in conc. HCl (100 mL) with a solution of $NaNO_2$ (5.3 g, 76.8 mmol, 1.1 equiv) in water (15 mL), followed by the addition of a solution of $SnCl_2•2H_2O$ (39.6 g, 175.5 mmol, 2.5 equiv) in conc. HCl (50 mL) yielded **10d•**HCl (14.9 g, 60.6 mmol, 87%) as a cream coloured solid: ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 10.08 (s, 3H, NH_3), 7.75 (d, *J* = 8.4 Hz, 1H, ArH), 7.38 (d, *J* = 8.5 Hz, 1H, ArH), 7.00 (s, 1H, NH), 2.88 (m, 4H, 2xCH_2), 1.20 (t, *J* = 7.5 Hz, 3H, CH_3), 1.13 (t, *J* = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ = 148.6 (ArC), 146.9 (ArC), 140.9 (ArC), 135.0 (ArC), 127.2 (ArCH), 122.9 (ArCH), 23.9 (CH_2), 20.6 (CH_2), 15.1 (CH_3), 14.1

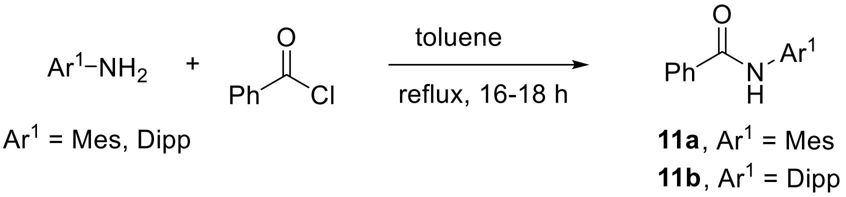


10d•HCl

(CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3277 (w), 2974 (m), 2876 (m), 2662 (w), 1601 (m), 1522 (s), 1462 (m), 1356 (m), 1119 (w), 883 (w), 839 (m), 797 (m), 741 (m); ESI-MS (positive): *m/z* = 210 (M^+-Cl, 100%).

3. Synthesis of the triazolium salts 13-19

3.1 Synthesis of the benzamides 11



N-(2,4,6-Trimethylphenyl)benzamide (11a): 2,4,6-Trimethylaniline (32.0 mL, 228 mmol, 1.0 equiv) was dissolved in toluene (200 mL, HPLC grade). Benzoyl chloride (30.0 mL, 260 mmol, 1.1 equiv) was added dropwise at room temperature. The resulting suspension was refluxed for 16 h under a drying tube containing $CaCl_2$. The reaction mixture was cooled down in an ice-bath and water (20 mL) was added. The resulting suspension was stirred for 30 min. The solid was collected by suction filtration and washed with EtOAc, affording the benzamide **11a** as a colorless solid (52.44 g, 219 mmol, 96 %); mp 207-208 °C (lit.[2] 205-206 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.68 (s, 1H, NH), 7.99-8.01 (m, 2H, PhH), 7.52-7.57 (m, 3H, PhH), 6.93 (s, 2H, ArH), 2.26 (s, 3H, CH_3), 2.15 (s, 6H, 2xCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.0 (C=O), 135.6 (ArC), 135.3 (2xArC), 134.5 (ArC), 132.7 (ArC), 131.4 (ArCH), 128.4 (2xArCH), 128.3 (2xArCH), 127.5 (2xArCH), 20.5 (CH_3), 18.0 (2xCH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3269 (m), 2949 (w), 2916 (w), 1638 (s), 1601 (m), 1578 (m), 1514 (s), 1485 (s), 1308 (m), 1292 (s), 1223 (m), 1074 (m), 1028 (m), 851 (s), 802 (m), 710 (s), 687 (s), 665 (s); GC-MS: t_R (Std 50) = 15.1 min, *m/z* = 239 (M^+, 100%), 134, 105, 91, 77, 51.

N-(2,6-Diisopropylphenyl)benzamide (11b): 2,6-Diisopropylaniline (37.6 g, 212 mmol, 1.0 equiv) was dissolved in toluene (200 ml, HPLC grade). Benzoyl chloride (26.0 mL, 226 mmol, 1.1 equiv) was added dropwise at room temperature. The resulting suspension was refluxed for 18 h under a drying tube containing $CaCl_2$. The reaction mixture was cooled down in an ice-bath and water (20 mL) was added. The resulting suspension was stirred for 30 min. The solid was collected by suction filtration and washed with hexane, affording the benzamide **11b** as a colorless solid (53.2 g, 189 mmol, 89 %); mp 264-265 °C (lit.[3] 265.4.-265.6 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, J = 7.6 Hz, 2H, ArH), 7.61 – 7.46 (m, 3H, ArH), 7.38 – 7.31 (m, 2H, ArH+NH), 7.23 (d, J = 7.6 Hz, 2H, ArH), 3.14 (hept, J = 6.9 Hz, 2H, 2xCH), 1.22 (d, J = 6.9 Hz, 12H, 4xCH_3)**;** ^{13}C NMR (75 MHz, DMSO-d_6): δ = 166.1 (C=O), 146.2 (2xArC), 134.4 (ArC), 132.8 (ArC), 131.4 (ArCH), 128.4 (2xArCH), 127.6 (2xArCH), 127.5 (ArCH), 122.9 (2xArCH), 28.2 (2xCH), 23.5 (CH_3), 23.3 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3262 (w), 2963 (m), 1639 (s), 1518 (s), 1487 (s), 1458 (m), 1285 (s), 1256 (m), 797 (m), 745 (m), 692 (s), 658 (m); GC-MS: t_R (Std 50) = 14.6 min, *m/z* = 281 (M^+), 264, 238 (100%), 223, 208, 176, 160, 146, 130, 117, 105, 91, 77, 51.

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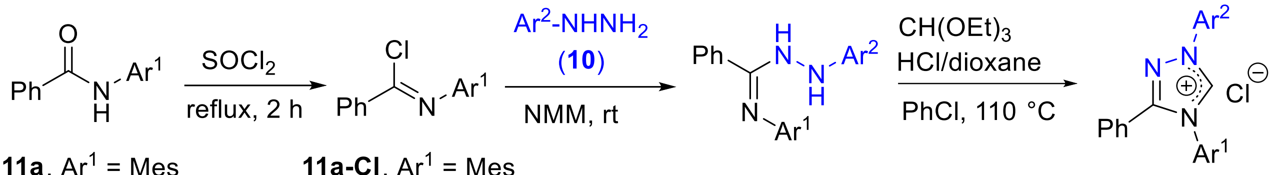
[2] Fan, W.; Yang, Y.; Lei, J.; Jiang, Q.; Zhou, W. *J. Org. Chem.* **2015**, *80*, 8782–8789.

[3] Gong, C.; Ding, H.; Lu, C.; Zhao, B.; Yao, Y. *Dalton Trans.* **2017**, *46*, 6031-6038.

3.2 General procedure 3 (GP-3) for the three-step synthesis of triazolium salts



11a, Ar^1 = Mes
11b, Ar^1 = Dipp

11a-Cl, Ar^1 = Mes
11b-Cl, Ar^1 = Dipp

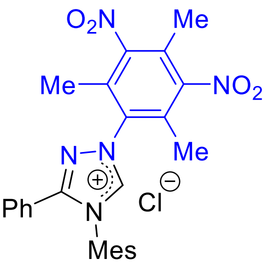
12

13-19

The benzamide **11** (1.0 equiv) was refluxed in $SOCl_2$ (excess) for 2h. The excess of $SOCl_2$ was distilled off in vacuo and colleccted in a trap cooled with liquid nitrogen. The residue was further dried in high vacuum to give the corresponding benzimidoyl chloride, which was used in the next step without further purification. The imidoyl chlorides **11a-Cl** and **11b-Cl** were also prepared on large scale and stored below 4°C for use in the next step.

The hydrazine **10** (1.0 equiv) or **10**•HCl (1.2 equiv) and dry THF were added to the benzimidoyl chloride (1.0 eqiuv) under Ar atmosphere. The mixture was cooled in an ice bath, followed by the addition of *N*-methylmorpholine (NMM, 1.1-1.8 equiv). The reaction mixture was stirred at 0 °C for 30 min and then at rt for 24 h. The volatiles were removed on a rotary evaporator. The residue was diluted with water and extracted with DCM. The combined organic layers were washed with water, brine, dried over Na_2SO_4, and filtered. After removal of the solvent, the crude product **12** was directly subjected to the final ring closing step.

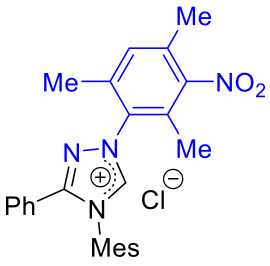
To the crude **12**, in a round-bottom flask, was successively added chlorobenzene, triethyl orthoformate, and anhydrous HCl (4 M in dioxane, 1-2 equiv). The reaction flask was immersed in an oil bath at 110 °C, and the mixture was stirred open to air for 1-16 h. The reaction mixture was then concentrated on a rotary evaporator at 60°C. The residue was washed with Et_2O by vigorously stirring for 1 h and the Et_2O phase was removed. The residue was further triturated with EtOAc with vigorous stirring for at least 2 h. The resulting solid was collected by suction filtration and washed with EtOAc (trituration with EtOAc can be repeated several times), furnishing the desired triazolium salt (**13-19**).



13

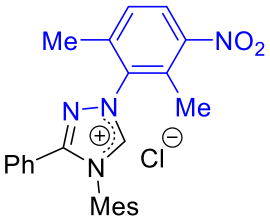
1-(2,4,6-Trimethyl-3,5-dinitrophenyl)-4-(2,4,6-trimethylphenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (13). According to GP-3, the pre-formed **11a-Cl** (5.1 g, 20.0 mmol, 1.0 equiv) was condensed with **10a** (4.8 g, 20.0 mmol, 1.0 equiv) in the presence of NMM (2.9 mL, 26.0 mmol, 1.3 equiv) in THF (50 mL), followed by the reaction with $CH(OEt)_3$ (10.0 mL, 60.0 mmol, 3.0 equiv) and HCl/dioxane (4 M, 7.5 mL, 30.0 mmol, 1.5 equiv) in PhCl (8.0 mL) at 110 °C for 16 h. After several triturations with EtOAc, **13** was obtained as a brown solid (1.0 g, 2.0 mmol, 10%): mp 266-267 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.57 (s, 1H, NCHN), 7.63 (s, 1H, ArH), 7.48 (s, 4H, ArH), 7.12 (s, 2H, ArH), 2.40 (s, 3H, CH_3), 2.33 (s, 9H, 3xCH_3), 2.15 (s, 6H, 2xCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7 (ArC), 150.6 (ArC), 149.7 (NCHN), 142.9 (ArC), 133.9 (ArC), 133.7 (ArCH), 133.0 (ArC), 130.8 (2xArCH), 130.7 (ArC), 129.8 (2xArCH), 127.7 (2xArCH), 127.4 (ArC), 126.5 (ArC), 121.5 (ArC), 21.3 (CH_3), 18.0 (2xCH_3), 14.2 (2xCH_3), 13.5 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2974 (w), 2901 (m), 1605 (w), 1535 (s), 1485 (m), 1449 (m), 1358 (m), 1233 (m), 1038 (m), 868 (m), 723 (m), 691 (s); ESI-MS (positive): *m/z* = 472 (M$^+$-Cl, 100%); elemental analysis calcd (%) for $C_{26}H_{26}N_5O_4Cl•0.5H_2O$: C, 60.41; H, 5.26; N, 13.55; found: C, 60.58; H, 5.27; N, 13.80.

1-(2,4,6-Trimethyl-3-nitrophenyl)-4-(2,4,6-trimethylphenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (14). According to GP-3, **11a** (4.8 g, 20.0 mmol, 1.0 equiv) was reacted with $SOCl_2$ (6.0 mL), condensed with **10b** (4.8 g, 20.0 mmol, 1.0 equiv) in the presence of NMM (2.4 mL, 22.0 mmol, 1.1 equiv) in THF (50 mL), followed by the reaction with $CH(OEt)_3$ (10.0 mL, 60.0 mmol, 3.0 equiv) and HCl/dioxane (4 M, 7.5 mL, 30.0 mmol, 1.5 equiv) in PhCl (8.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **14** was obtained as a cream colored solid (3.2 g, 7.0 mmol, 35%): mp 274-275 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.61 (s, 1H, NCHN), 7.59 (t, *J* = 7.1 Hz, 1H, ArH), 7.54 – 7.37 (m, 4H, ArH), 7.28 (s, 1H, ArH), 7.09 (s, 2H, ArH), 2.45 (s, 3H, CH_3), 2.39 (s, 6H, 2xCH_3), 2.22 (s, 3H, CH_3), 2.16 (br s, 6H, 2xCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1 (ArC), 150.4 (ArC), 149.1 (NCHN), 142.6 (ArC), 137.9 (ArC), 134.0 (ArC), 133.8 (ArC), 133.3 (ArCH), 132.0 (ArCH), 130.7(2xArCH), 129.7 (2xArCH), 127.6 (2xArCH), 127.5 (ArC), 121.9 (ArC), 21.3 (CH_3), 18.2 (CH_3), 18.0 (2xCH_3), 17.7 (CH_3), 13.5 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2996 (w), 2913 (w), 2685 (w), 2641 (w), 1601 (w), 1551 (m), 1530 (s), 1478 (m), 1448 (m), 1366 (m), 1329 (w), 1252 (m), 1219 (m), 1157 (w), 1038 (m), 843 (m), 781 (m), 723 (s), 691 (s); ESI-MS (positive): *m/z* = 427 (M^{+}-Cl, 100%); elemental analysis calcd (%) for $C_{26}H_{27}N_4O_2Cl$: C, 67.45; H, 5.88; N, 12.10; found: C, 67.31; H, 6.12; N, 11.94.

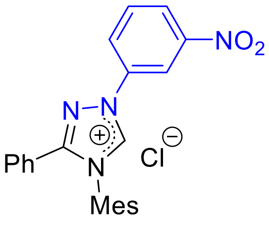


14

1-(2,6-Dimethyl-3-nitrophenyl)-4-(2,4,6-trimethylphenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (15). According to GP-3, the pre-formed **11a-Cl** (2.6 g, 10.0 mmol, 1.0 equiv) was condensed with **10c** (1.8 g, 10.0 mmol, 1.0 equiv) in the presence of NMM (1.3 mL, 12.0 mmol, 1.2 equiv) in THF (30 mL), followed by the reaction with $CH(OEt)_3$ (5.0 mL, 30.0 mmol, 3.0 equiv) and HCl/dioxane (4 M, 3.8 mL, 15.0 mmol, 1.5 equiv) in PhCl (5.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **15** was obtained as a beige solid (0.45 g, 1.0 mmol, 10%): mp 198-199 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.58 (s, 1H, NCHN), 8.14 (d, *J* = 8.5 Hz, 1H, ArH), 7.60 (t, *J* = 7.0 Hz, 2H), 7.55-7.40 (m, 5H, ArH), 7.11 (s, 2H, ArH), 2.51, 2.46, and 2.40 (each s, 3x3H, 3xCH_3), 2.23 and 2.12 (each br s, 2x3H, 2xCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3 (ArC), 149.1 (NCHN), 148.5 (ArC), 142.7 (ArC), 141.7 (ArC), 134.9 (ArC), 134.1 (ArC), 133.4 (ArCH), 131.4 (ArC), 130.8 (2xArCH), 129.7 (3xArCH), 127.8 (ArCH), 127.7 (2xArCH), 127.5 (ArC), 121.8 (ArC), 21.3, 18.7, 17.99, 14.94.; IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3292 (w), 2968 (w), 2735 (w), 1605 (w), 1551 (m), 1518 (s), 1487 (m), 1445 (m), 1350 (s), 1225 (w), 1036 (w), 980 (m), 853 (m), 833 (m), 768 (m), 723 (s); ESI-MS (positive): *m/z* = 413 (M^{+}-Cl, 100%); elemental analysis calcd (%) for $C_{25}H_{25}N_4O_2Cl \bullet 0.5H_2O$: C, 65.57; H, 5.72; N, 12.23; found: C, 65.18; H, 5.82; N, 11.88.

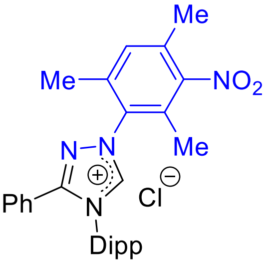


15



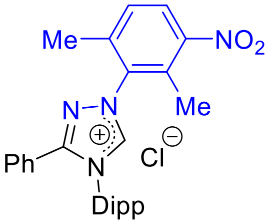
16

4-(2,4,6-Trimethylphenyl)-1-(3-nitrophenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (16). According to GP-3, the pre-formed **11a-Cl** (5.3 g, 21.0 mmol, 1.0 equiv) was condensed with 3-nitrophenylhydrazine hydrochloride (4.8 g, 25.0 mmol, 1.2 equiv) in the presence of NMM (4.1 mL, 37.0 mmol, 1.8 equiv) in THF (50 mL), followed by the reaction with CH(OEt)$_3$ (8.0 mL, 48.0 mmol, 2.3 equiv) and HCl in dioxane (4 M, 6.2 mL, 24.8 mmol, 1.2 equiv) in PhCl (6.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **13** was obtained as a cream colored solid (4.2 g, 10.0 mmol, 48%): mp >300 °C; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 13.85 (s, 1H, NCHN), 9.60 (d, J = 7.6 Hz, 1H, ArH), 9.16 (s, 1H, ArH), 8.40 (d, J = 7.7 Hz, 1H), 7.88 (t, J = 8.1 Hz, 1H, ArH), 7.70-7.42 (m, 5H, ArH), 7.10 (s, 2H, ArH), 2.40 (s, 3H, CH$_3$), 2.17 (s, 6H, 2xCH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 153.9 (ArC), 148.8 (ArC), 145.4 (NCHN), 142.6 (ArC), 135.7 (ArC), 134.3 (2xArC), 133.3 (ArCH), 132.0 (ArCH), 130.7 (2xArCH), 129.67 (2xArCH), 127.9 (2xArCH), 127.4 (ArCH), 125.2 (ArCH), 121.9 (ArC), 115.7 (ArCH), 21.3 (CH$_3$), 18.2 (2xCH$_3$); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2996 (w), 2909 (w, br), 2866 (w), 2370 (w), 1605 (w), 1551 (m), 1524 (s), 1491 (m), 1460 (m), 1449 (m), 1344 (s), 1254 (m), 1183 (w), 1057 (w), 986 (m), 897 (m), 858 (m), 752 (m), 735 (m), 720 (s); ESI-MS (positive): m/z = 385 (M$^+$-Cl, 100%); elemental analysis calcd (%) for $C_{23}H_{21}N_4O_2Cl$: C, 65.63; H, 5.03; N, 13.31; found: C, 65.20; H, 5.07; N, 13.12.



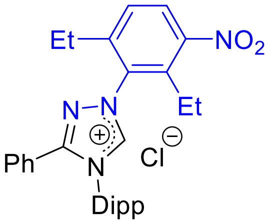
17

4-(2,6-Diisopropyl)phenyl)-1-(2,4,6-trimethyl-3-nitrophenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (17). According to GP-3, **11b** (5.6 g, 20 mmol, 1.0 equiv) was condensed with **10b** (4.8 g, 20 mmol, 1.0 equiv) in the presence of NMM (2.4 mL, 22.0 mmol, 1.1 equiv) in THF (50 mL), followed by the reaction with CH(OEt)$_3$ (10.0 mL, 60 mmol, 3.0 equiv) and HCl/dioxane (4 M, 7.5 mL, 30 mmol, 1.5 equiv) in PhCl (8.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **17** was obtained as a cream colored solid (3.2 g, 6.4 mmol, 32%): mp 235-236 °C; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 13.77 (s, 1H, NCHN), 7.66 (t, J = 7.8 Hz, 1H, ArH), 7.62 – 7.53 (m, 1H, ArH), 7.50 – 7.36 (m, 6H, ArH), 7.30 (s, 1H, ArH), 2.43 (s, 3H, CH$_3$), 2.39 (s, 3H, CH$_3$), 2.38 (m, 2H, 2xCH), 1.35 (br d, J = 6.0 Hz, 6H, 2xCH$_3$), 1.00 (d, J = 6.8 Hz, 6H, 2xCH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 154.6 (ArC), 150.5 (ArC), 149.5 (NCHN), 144.7 (ArC), 137.8 (ArC), 133.8 (ArC), 133.3 (ArCH), 133.0 (ArCH), 132.0 (ArCH), 129.5 (2xArCH), 128.0 (2xArCH), 127.6 (ArC), 127.3 (ArC), 125.6 (2xArCH), 121.9 (ArC), 29.5 (2xCH), 24.7 (2xCH$_3$), 22.6 (2xCH$_3$), 18.2 (CH$_3$), 17.8 (CH$_3$), 13.5 (CH$_3$); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2968 (m), 2602 (m), 1605 (w), 1585 (w), 1526 (s), 1445 (m), 1368 (m), 1221 (w), 1059 (m), 945 (w), 845 (m), 783 (m), 752 (m), 694 (m); ESI-MS (positive): m/z = 469 (M$^+$-Cl, 100%); elemental analysis calcd (%) for $C_{29}H_{33}N_4O_2Cl \bullet H_2O$: C, 66.59; H, 6.74; N, 10.71; found: C, 66.51; H, 6.53; N, 10.69.



18

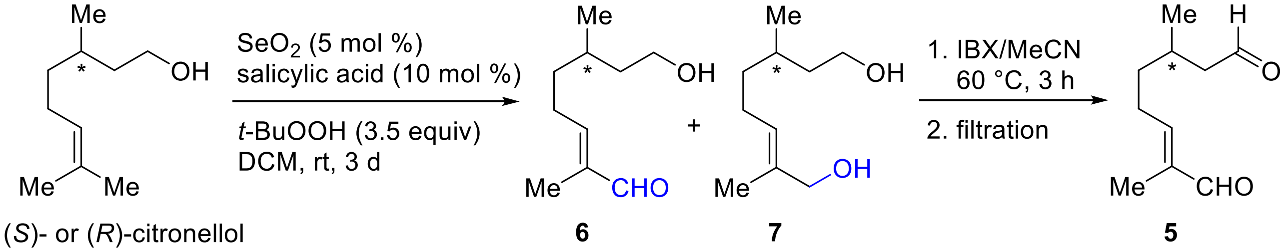
4-(2,6-Diisopropyl)phenyl)-1-(2,6-dimethyl-3-nitrophenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (18). According to GP-3, the pre-formed **11b-Cl** (2.6 g, 10.0 mmol, 1.0 equiv) was condensed with **10c** (1.8 g, 10.0 mmol, 1.0 equiv) in the presence of NMM (1.3 mL, 12.0 mmol, 1.2 equiv) in THF (30 mL), followed by the reaction with CH(OEt)$_3$ (5.0 mL, 30.0 mmol, 3.0 equiv) and HCl/dioxane (4 M, 3.8 mL, 15.0 mmol, 1.5 equiv) in PhCl (5.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **18** was obtained as a beige solid (1.5 g, 3.0 mmol, 30%): mp 242-243 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 14.03 (s, 1H, NCHN), 8.16 (d, J = 8.5 Hz, 1H, ArH), 7.67 (t, J = 7.8 Hz, 1H, ArH), 7.57 (t, J = 7.2 Hz, 1H, ArH), 7.54 – 7.34 (m, 7H), 2.51 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.43 (m, 2H, 2xC*H*Me_2), 1.39 and 1.34 (2x br d, J = 6.3 Hz, 6H, 2xCH_3), 1.03 (br s, 6H, 2xCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8 (ArC), 149.5 (NCHN), 148.4 (ArC), 144.7 (ArC), 141.6 (ArC), 134.9 (ArC), 133.4 (ArCH), 133.1 (ArCH), 131.4 (ArC), 129.7 (ArCH), 129.6 (2xArCH), 128.0 (2xArCH), 127.8 (ArCH), 127.3 (ArC), 125.6 (2xArCH), 121.6 (ArC), 29.5 (2xCH), 24.7 (2xCH_3), 22.5 (2xCH_3), 18.6 (CH_3), 14.9 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] =2965 (m), 2872 (w), 2581 (m), 1601 (w), 1587 (w), 1549 (m), 1522 (s), 1447 (m), 1342 (s), 1211 (m), 936 (m), 851 (m), 814 (m), 775 (m), 721 (s), 687 (s); ESI-MS (positive): *m/z* = 455 (M^+-Cl, 100%); elemental analysis calcd (%) for $C_{28}H_{31}N_4O_2Cl$: C, 68.49; H, 6.36; N, 11.41; found: C, 68.29; H, 6.08; N, 11.13.



19

1-(2,6-Diethyl-3-nitrophenyl)-4-(2,6-diisopropyl)phenyl)-3-phenyl-1*H*-1,2,4-triazol-4-ium chloride (19). According to GP-3, the pre-formed **11b-Cl** (2.6 g, 10.0 mmol, 1.0 equiv) was condensed with **10d**•HCl (2.9 g, 11.8 mmol, 1.2 equiv) in the presence of NMM (1.3 mL, 12.0 mmol, 1.2 equiv) in THF (50 mL), followed by the reaction with $CH(OEt)_3$ (5.0 mL, 30.0 mmol, 3.0 equiv) and HCl/dioxane (4 M, 2.5 mL, 10.0 mmol, 1.0 equiv) in PhCl (5.0 mL) at 110 °C for 1 h. After several triturations with EtOAc, **19** was obtained as a cream colored solid (1.3 g, 2.5 mmol, 25%): mp 235-236 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 14.27 (s, 1H, NCHN), 8.15 (d, J = 8.6 Hz, 1H, ArH), 7.65 (t, J = 7.8 Hz, 1H), 7.60 – 7.48 (m, 2H), 7.48 – 7.33 (m, 6H), 2.86-2.32 (m, 6H, 2xCH_2 and 2xCH), 1.42 – 1.24 (m, 12H, 4xCH_3), 1.01 (d, J = 6.7 Hz, 6H, 2xCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4 (ArC), 150.3 (NCHN), 148.2 (ArC), 147.2 (ArC), 144.7 (ArC), 136.7 (ArC), 134.2 (ArC), 133.4 (ArCH), 133.1 (ArCH), 129.6 (2xArCH), 128.4 (ArCH), 128.1 (3xArCH), 127.3 (ArC), 125.6 (2xArCH), 121.8 (ArC), 29.6 (2xCH), 25.1 (CH_2), 24.8 (2xCH_3), 22.6 (CH_3), 22.5 (CH_3), 22.1 (CH_2), 14.8 (CH_3), 13.9 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2970 (m), 2872 (w), 2554 (m), 2467 (w), 1587 (w), 1547 (m), 1522 (s), 1466 (m), 1354 (m), 1059 (m), 818 (m), 777 (m), 723 (s), 691 (s); ESI-MS (positive): *m/z* = 483 (M^+-Cl, 100%); elemental analysis calcd (%) for $C_{30}H_{35}N_4O_2Cl$: C, 69.42; H, 6.80; N, 10.79; found: C, 69.20; H, 6.61; N, 10.57.

4. Synthesis of 8-oxocitronellal (5) from citronellol



For the synthesis of **5**, a modification of a procedure described by Hofferberth and co-workers was employed.[4] (*S*)-Citronellol (10 g, 64.0 mmol, 1.0 equiv) was added to a mixture of SeO_2 (0.36 g,

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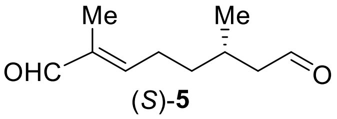
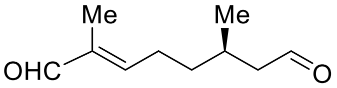
[4] Fischman, C. J.; Adler, S.; Hofferberth, J. E. *J. Org. Chem.* **2013**, *78*, 7318–7323.

3.3 mmol, 5 mol%), salicylic acid (0.92 g, 6.7 mmol, 10 mol%), *t*-BuOOH (70% in H_2O, *d* = 0.94, 30 mL, 219 mmol, 3.4 equiv), and DCM (20 mL). The reaction mixture was stirred at rt for 3d, diluted with toluene (50 mL) and evaporated on a rotary evaporator. The residue was diluted with Et_2O (200 mL), washed with 10% NaOH (6 x 25 mL) and brine, dried over anhyd $MgSO_4$, and filtered. After removal of the solvent, the resulting pale yellow oil (10.8 g), containing a mixture of (*S*)-**6** and (*S*)-**7**, was purified by passing it though a short pad of silica gel. First, by eluting with EtOAc/*c*Hex, 1:4, less polar impurities of R_f ca. 0.6 (EtOAc/Hex, 1:1) were removed. Then, using EtOAc/*c*Hex, 3:1 as eluent, a mixture of (*S*)-**6** and (*S*)-**7** was obtained [R_f = 0.32 and 0.13 (EtOAc/Hex, 1:1), 7.7 g, 45.0 mmol, 70%].

To this mixture of (*S*)-**6** and (*S*)-**7** (45.0 mmol, 1.0 equiv) in dry MeCN (100 mL) was added IBX (22.0 g, 78.6 mmol, 1.8 equiv). The suspension was stirred at 60 °C for 3 h, cooled down to rt, and diluted with EtOAc (100 mL). The solid was filtered off with a glass frit and washed with EtOAc, affording IBA which can be oxidized to IBX in 86% yield with Oxone, following the procedure described by Santagostino and co-workers.[5] The filtrate was concentrated on a rotary evaporator and purified by column chromatography on silica (EtOAc/*c*Hex, 1:9) to give (*S*)-**5** (6.2 g, 36.9 mmol, 58%) as a pale yellow oil: R_f = 0.63 (EtOAc/Hex, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.78 (t, *J* = 2.0 Hz, 1H, CHO), 9.40 (s, 1H, CHO), 6.48 (td, *J* = 7.3, 1.3 Hz, 1H, C=CH), 2.40 (m, 4H, $2xCH_2$), 2.14 (m, 1H, CH), 1.75 (s, 3H), 1.63-1.36 (m, 2H, CH_2), 1.03 (d, *J* = 6.7 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1 (CHO), 195.1 (CHO), 153.8 (CH), 50.8 (CH_2), 35.2 (CH_2), 27.7 (CH), 26.4 (CH_2), 19.6 (CH_3), 9.2 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2959 (m), 2922 (m), 2716 (w), 1721 (m), 1682 (s), 1643 (m), 1406 (m), 1381 (m), 1242 (m), 1067 (m), 1005 (m), 868 (w), 816 (w); GC-MS: t_R (Std 50) = 11.0 min, *m/z* = 168 (M$^+$, trace), 139 (100%), 124, 109, 97, 79, 69, 55.

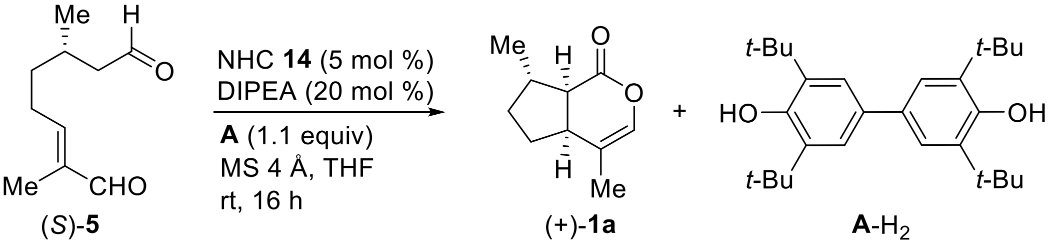

(*S*)-**5**

(*R*)-**5** was prepared in the same manner as described for (*S*)-**5** starting from (*R*)-citronellol (0.97 g, 5.8 mmol), providing (*R*)-**5** in 55% yield (0.54 g, 3.2 mmol) as a pale yellow oil.


(*R*)-**5**

5. One-step synthesis of nepetalactones (1a) from 5

5.1 Procedure for the oxidative NHC-catalyzed transformation of 5 to 1a



(*S*)-**5** (1.7 g, 10.0 mmol, 1.0 equiv) was added, under an Ar atmosphere, to a mixture of the triazolium salt **14** (0.24 g, 0.5 mmol, 5 mol%), the oxidant **A** (4.4 g, 10.8 mmol, 1.1 equiv), DIPEA (34.0 µl, 2.0 mmol, 20 mol%), and powdered MS 4 Å (1.0 g) in dry THF (25 mL). After stirring at rt for 16 h (to ensure full conversion), the reaction mixture was concentrated on a rotary evaporator. The

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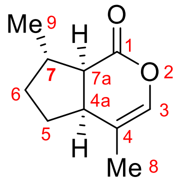
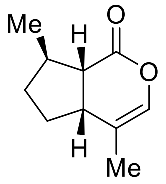
[5] Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537–4538.

residue was diluted with EtOAc/*c*Hex (1:3) and filtered through a short pad of silica. The filtrate was evaporated under reduced pressure to dryness. MeOH (30 mL) was added to the residue and the resulting suspension was stirred for 30 min, followed by the addition of H_2O (10 mL) to precipitate more of **A**-H_2/**A**. The solid was collected by suction filtration and washed with MeOH/H_2O (3:1), affording **A**-H_2/**A** (4.3 g, quant) as a light brown solid.

The filtrate was evaporated under reduced pressure and extracted with DCM (addition of brine to aid good phase separation). The combined organic phases were dried over anhyd Na_2SO_4, filtered, and concentrated by rotary evaporation. The resulting pale yellow oil was purified by the Kugelrohr distillation (0.2 mbar/oven temperature 100 °C) to give (+)-**1a** (1.4 g, 8.4 mmol, 84%) as a colorless oil: ds > 99% (GC on HP-5), ee = 97% (chiral GC on Lipodex E), $[\alpha]^{20}_{D}$ +21.9 (c 0.25, Et_2O) [lit.[6] +20.6 (c 0.24, Et_2O; >95% ee]; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.17 (m, 1H, H3), 2.76 (q, *J* = 7.7 Hz, 1H, H4a), 2.55 – 2.26 (m, 2H, H7a+H7), 2.04 (m, 1H, H5), 1.90 (m, 1H, H6), 1.63 (m, 3H, H8), 1.56 (m, 1H, H5), 1.23 (m, 1H, H6), 1.20 (d, *J* = 6.5 Hz, 3H, H9); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9 (C=O), 133.5 (CH), 115.3 (C_q), 49.3 (CH), 40.7 (CH), 39.7 (CH), 33.0 (CH_2), 30.9 (CH_2), 20.2 (CH_3), 15.5 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (m), 2870 (w), 1746 (s), 1686 (m), 1454 (w), 1337 (m), 1198 (m), 1125 (s), 1028 (m), 878 (m), 826 (w); GC-MS: t_R (Std 50) = 10.7 min, *m/z* = 166 (M^+, 100%), 151, 138, 123, 109, 95, 81, 67, 53.



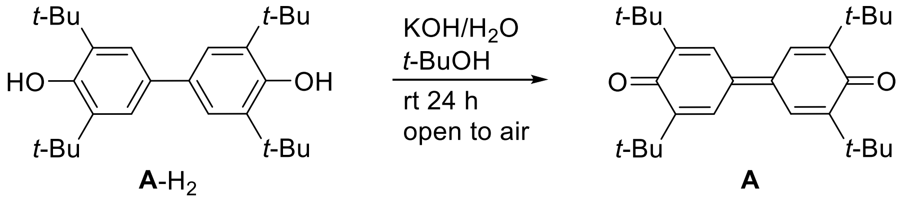
(+)-**1a**



(−)-**1a**

(−)-**1a** was prepared in the same manner as described for (+)-**1a** starting from (*R*)-5 (340 mg, 2.0 mmol), providing (−)-**1a** (266 mg, 1.6 mmol, 80%) as a colorless oil: ds > 99% (GC on HP-5), ee > 99% (chiral GC on Lipodex E), $[\alpha]^{20}_{D}$ −22.4 (c 0.25, Et_2O) [lit.[4] −21.0 (c 0.24, Et_2O; >95% ee].

5.2 Procedure for the oxidation of recovered A-H2 to A



For the recycling of **A**-H_2 to **A**, a modification of the literature known synthesis of **A** from 2,6-di-*tert*-butylphenol was applied.[7] A 250 mL Erlenmeyer flask was charged with **A**-H_2/**A** (13.5 g, 32.9 mmol, 1.0 equiv, recovered from the oxidative NHC-catalyzed transformation of **5** to **1**), *t*-BuOH (120 mL) and an aqueous solution of KOH (6.5 g, 115.9 mmol, 3.5 equiv) in H_2O (15 mL). The brown-yellow suspension was stirred vigorously open to air at rt for 24 h, resulting in a red-brown suspension. H_2O (30 mL) was added and stirring of the mixture was continued for 10 min. The solid was collected by suction filtration and washed with water to give the product as a red-brown powder (12.9 g, 96%). Further purification by recrystallization from toluene/EtOH (1:2) furnished **A** (12.1 g, 29.6 mmol, 90%) as red-brown crystals with a purple reflex; 97% purity, contaminated with 3% **A**-H_2

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[6] Sakurai, K.; Ikeda, K.; Mori, K. *Agric. Biol. Chem.* **1988**, *52*, 2369–2371.

[7] Carrera, M.; de la Viuda, M.; Guijarro, A. *Synlett* **2016**, *27*, 2783–2787.

(by NMR); mp 241-242 °C [lit.[3] 243.1-244 °C (corrected)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (s, 4H, ArH), 1.37 (s, 36H, $12xCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.4 (C=O), 150.4 (C_q), 136.1 (C_q)), 126.0 (ArCH), 36.0 (CMe_3), 29.6 (CH_3); IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3208 (w), 2957 (m), 2907 (m), 2864 (m), 1638 (w), 1601 (s), 1566 (m), 1481 (m), 1456 (m), 1360 (s), 1260 (s), 1088 (s), 1040 (s), 934 (m), 897 (s), 881 (s), 843 (m), 818 (m), 797 (m), 747 (w).

6. HPL chromatograms for the determination of the enantiomeric composition of citronellol

The enantiomeric composition of citronellol was determined from the corresponding benzoyl ester. A small vial was charged with citronellol (23.4 mg, 0.15 mmol, 1.0 equiv) and pyridine (20.0 µL, 0.25 mmol, 1.7 equiv). Benzoyl chloride (20.0 µL, 0.17 mmol, 1.1 equiv) was added and the resulting white suspension was stirred at rt for 30 min. The reaction was quenched by adding 1 N HCl and diluted with hexanes. Aliquots of the organic phase were withdrawn, filtered through a plug of silica gel and washed with hexanes for HPLC analysis. The NMR data of the analyzed 3,7-dimethyloct-6-en-1-yl benzoate were identical to the literature.[8]

HPL chromatograms were acquired on a VWR Hitachi Chromaster HPLC equipped with Chiracel OD-H column. Conditions: solvent, 0.5% 2-propanol in hexanes; flow rate, 0.5 mL/min; oven temp, 18.0 °C; detector, UV @ 230 nm; t_R of (*R*)-enantiomer = 11.6 min and t_R of (*S*)-enantiomer = 12.4 min.

(*S*)-3,7-dimethyloct-6-en-1-yl benzoate derived from (*S*)-citronellol was 97% ee.
(*R*)-3,7-dimethyloct-6-en-1-yl benzoate derived from (*R*)-citronellol was >99% ee.

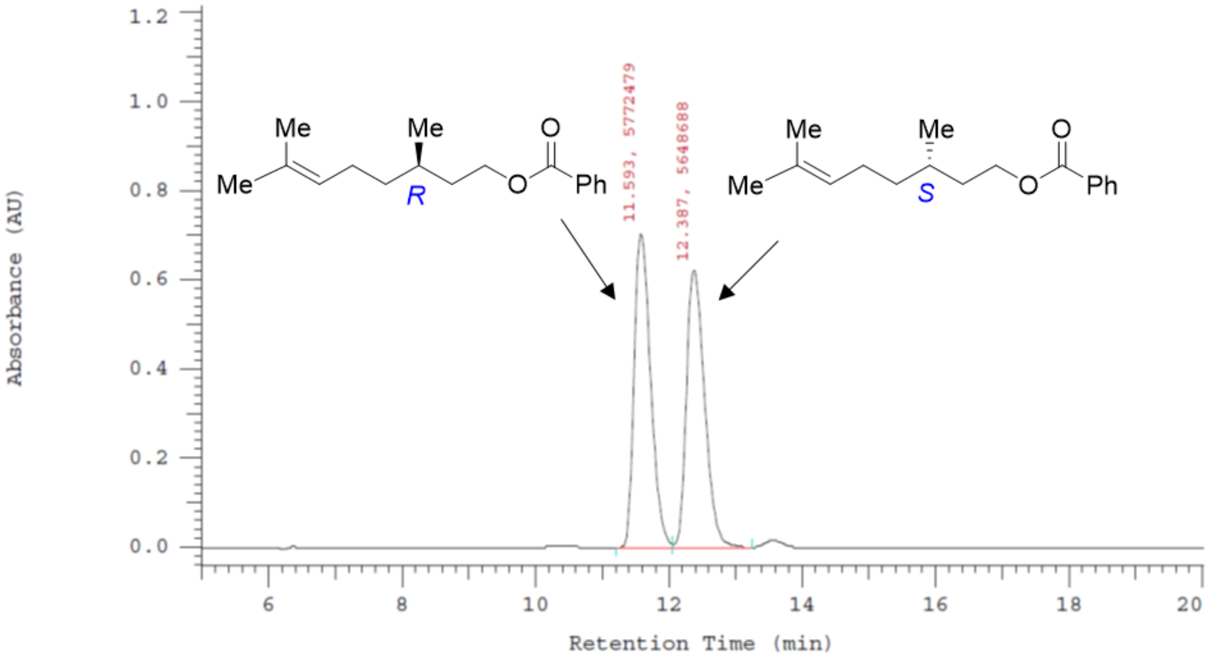

Figure S1. HPL chromatogram of *rac*-3,7-dimethyloct-6-en-1-yl benzoate.

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[8] Ye, D.; Liu, Z.; Chen, H.; Sessler, J. L.; Lei, C. *Org. Lett.* **2019**, *21*, 6888–6892.

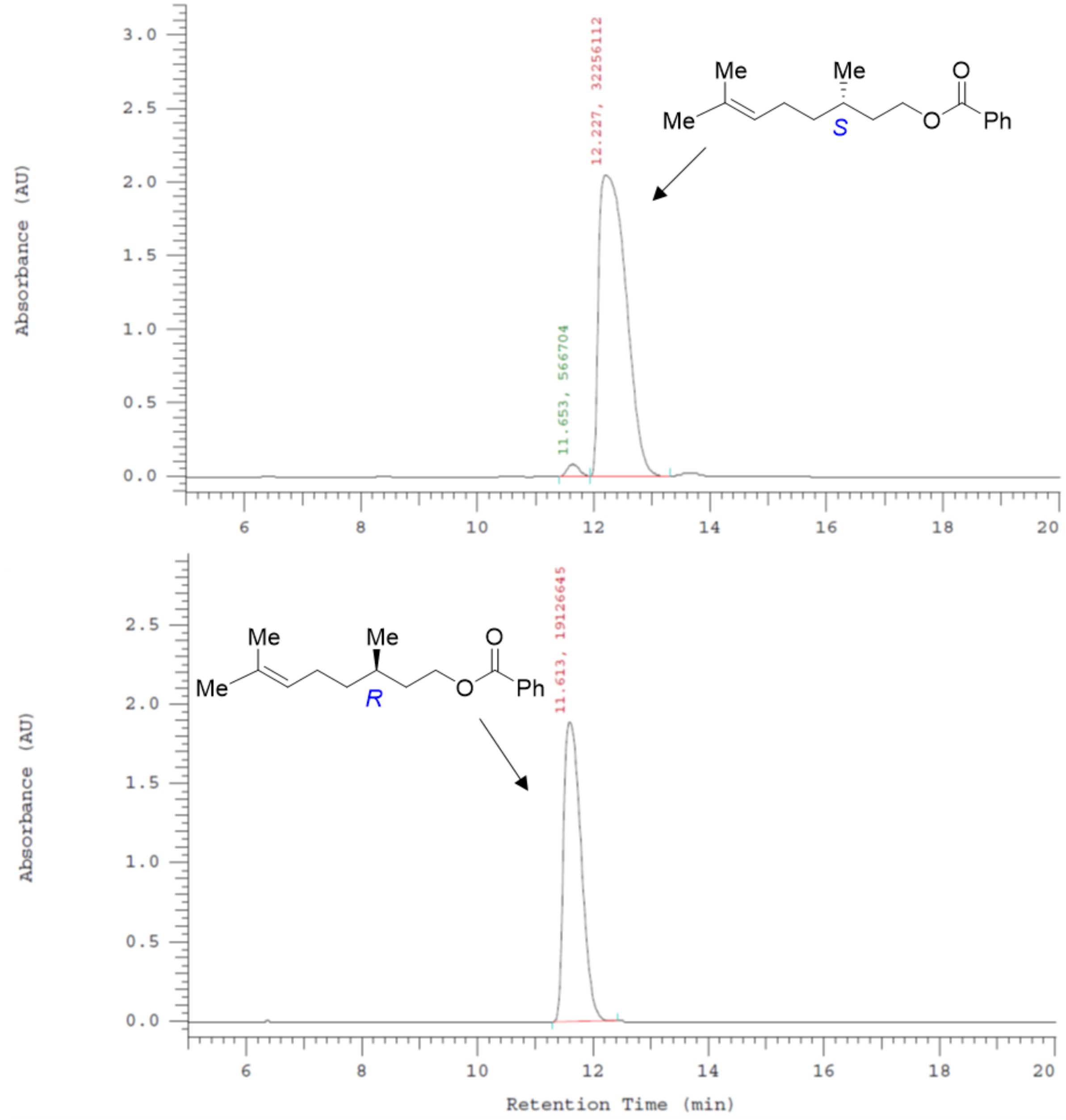
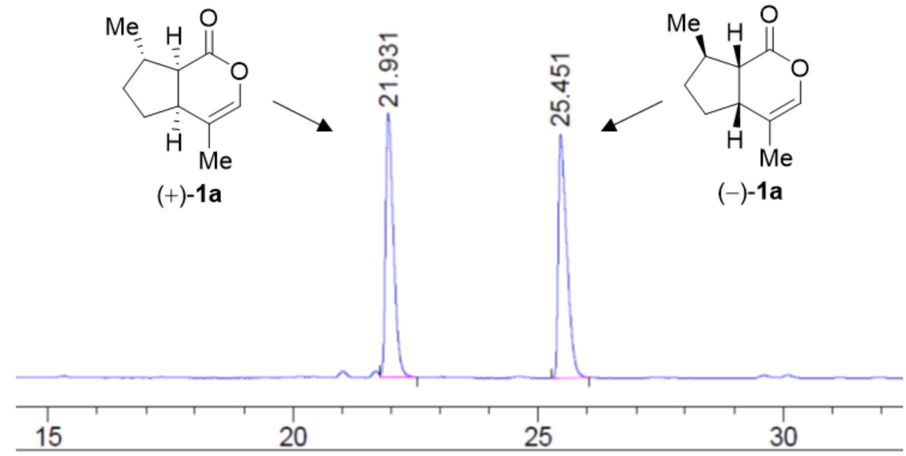


Figure S2. HPL chromatograms of (*S*)- and (*R*)-3,7-dimethyloct-6-en-1-yl benzoate derived from commercial (*S*)- and (*R*)-citronellol, respectively.

7. Gas chromatograms for the determination of the enantiomeric composition of 1a

Column: Lipodex-E; conditions: 80 °C, 2 min; 5 °C/min to 120 °C, 5 min; 1 °C/min to 135 °C, 5 min; 10 °C/min to 190 °C, 10 min; flow (N_2), 1.0 mL/min; t_R of (+)-**1a** = 21.9 min and t_R of (+)-**1a** = 25.5 min.



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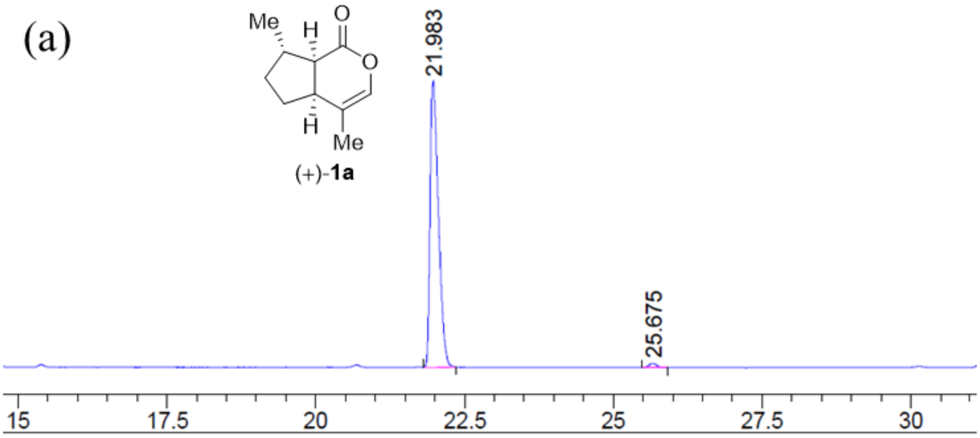
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [pA*s]       [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  21.931 VB    0.1496  360.28516   31.93756 50.17911
   2  25.451 BB    0.1657  357.71320   29.44718 49.82089
```

Figure S3. Gas chromatogram of *rac*-**1a**.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  21.983 BB    0.1385  342.33350   34.88972 98.50420
   2  25.675 BB    0.1359    5.19838 5.51847e-1  1.49580
```

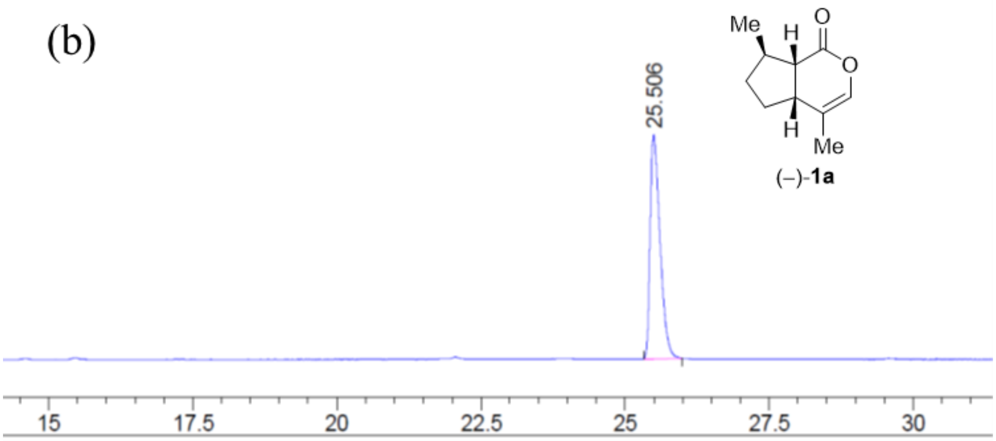


Figure S4. Gas chromatograms of (+)-**1a** (a) and (−)-**1a** (b).

8. NMR spectra

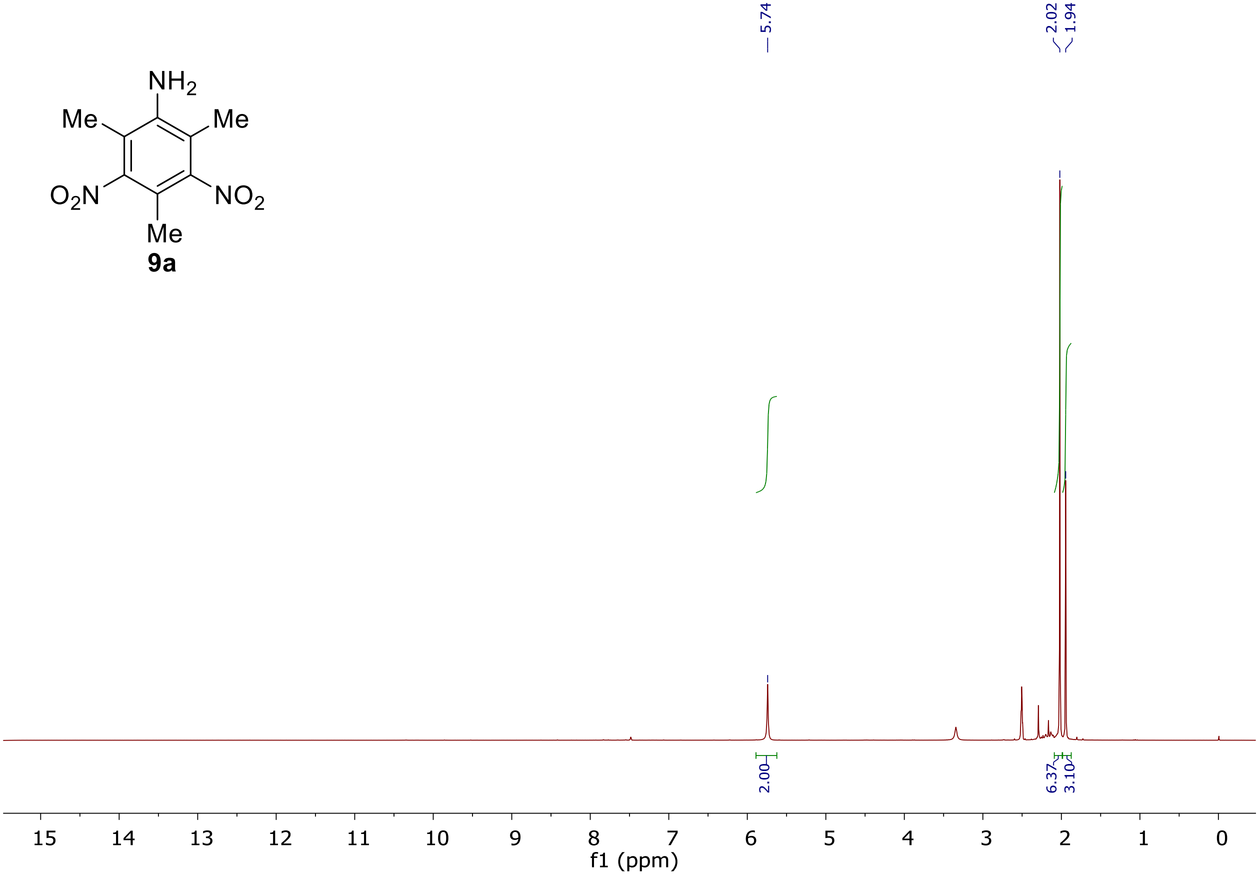


Figure S5. ^{1}H NMR (300 MHz, DMSO-d_6) of **9a**

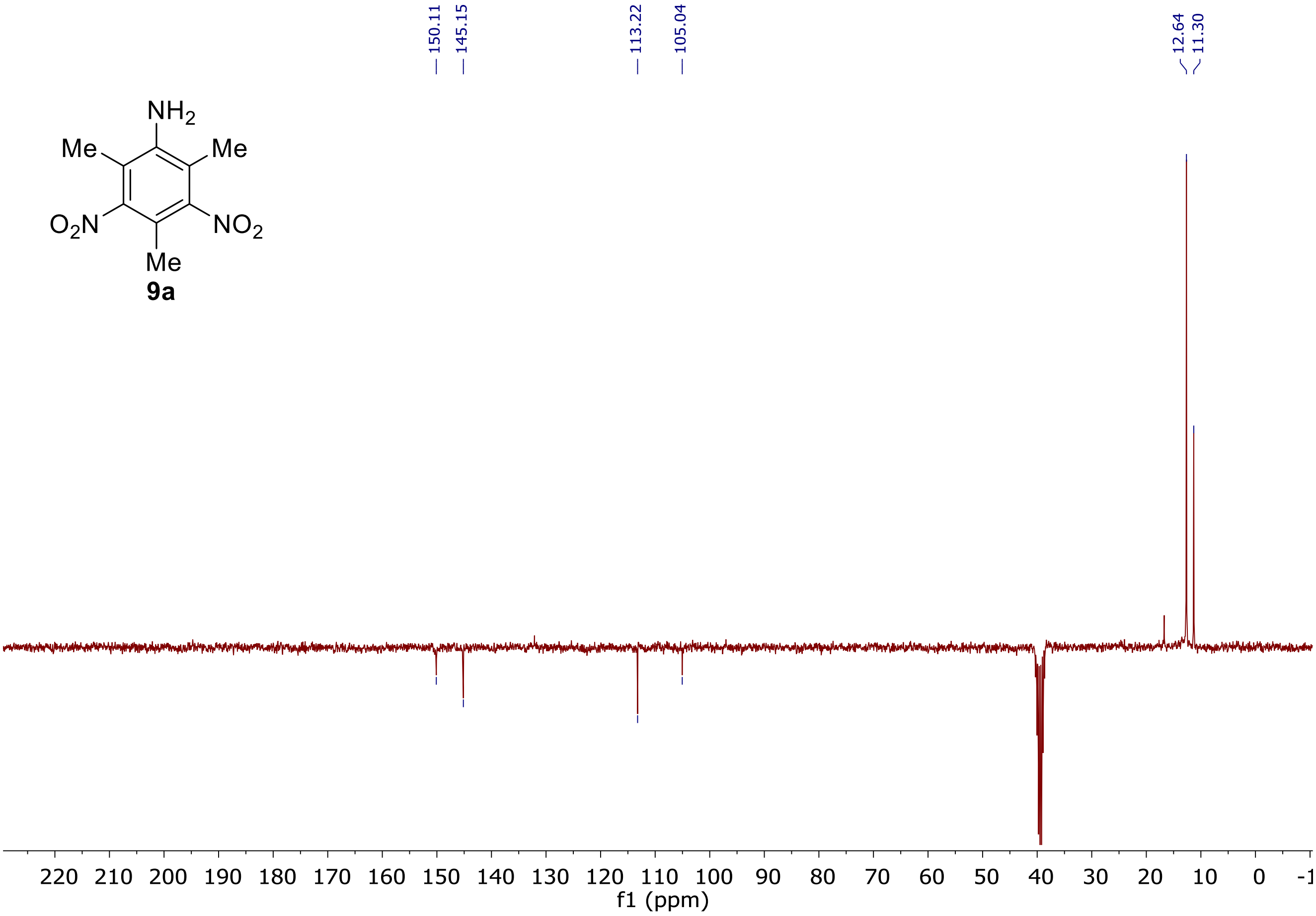


Figure S6. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **9a**

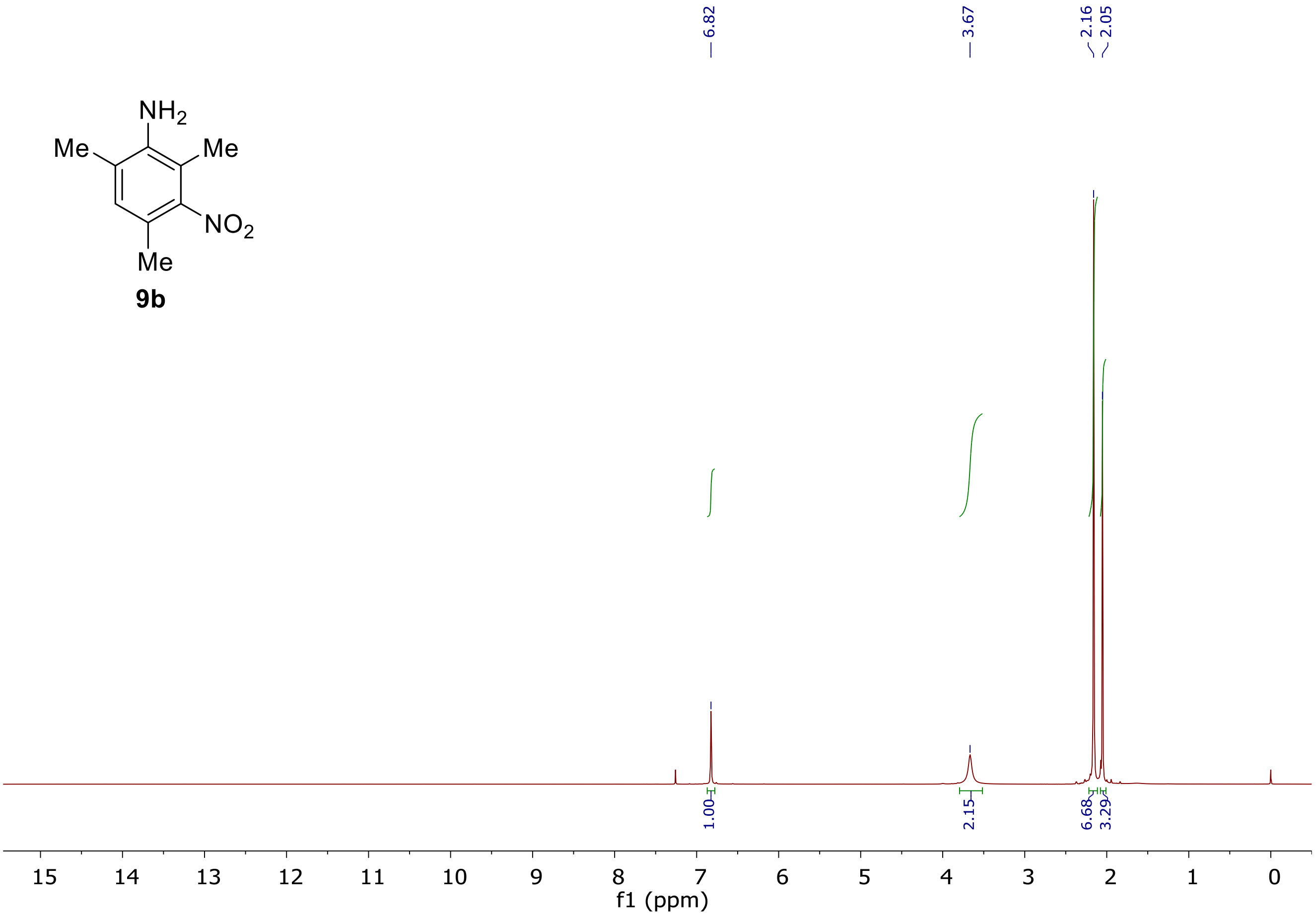


Figure S7. ^{1}H NMR (300 MHz, CDCl$_3$) of **9b**

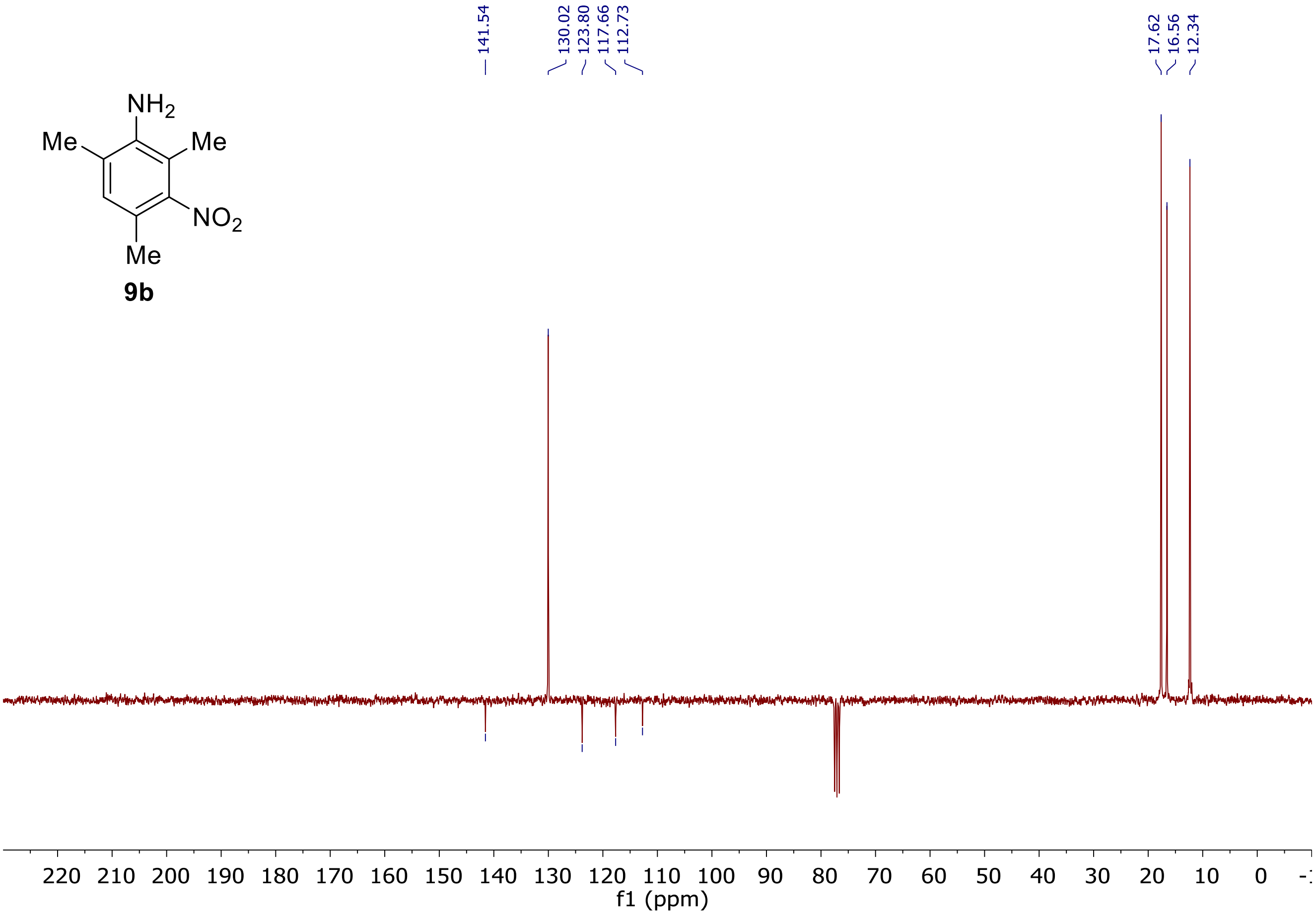


Figure S8. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **9b**

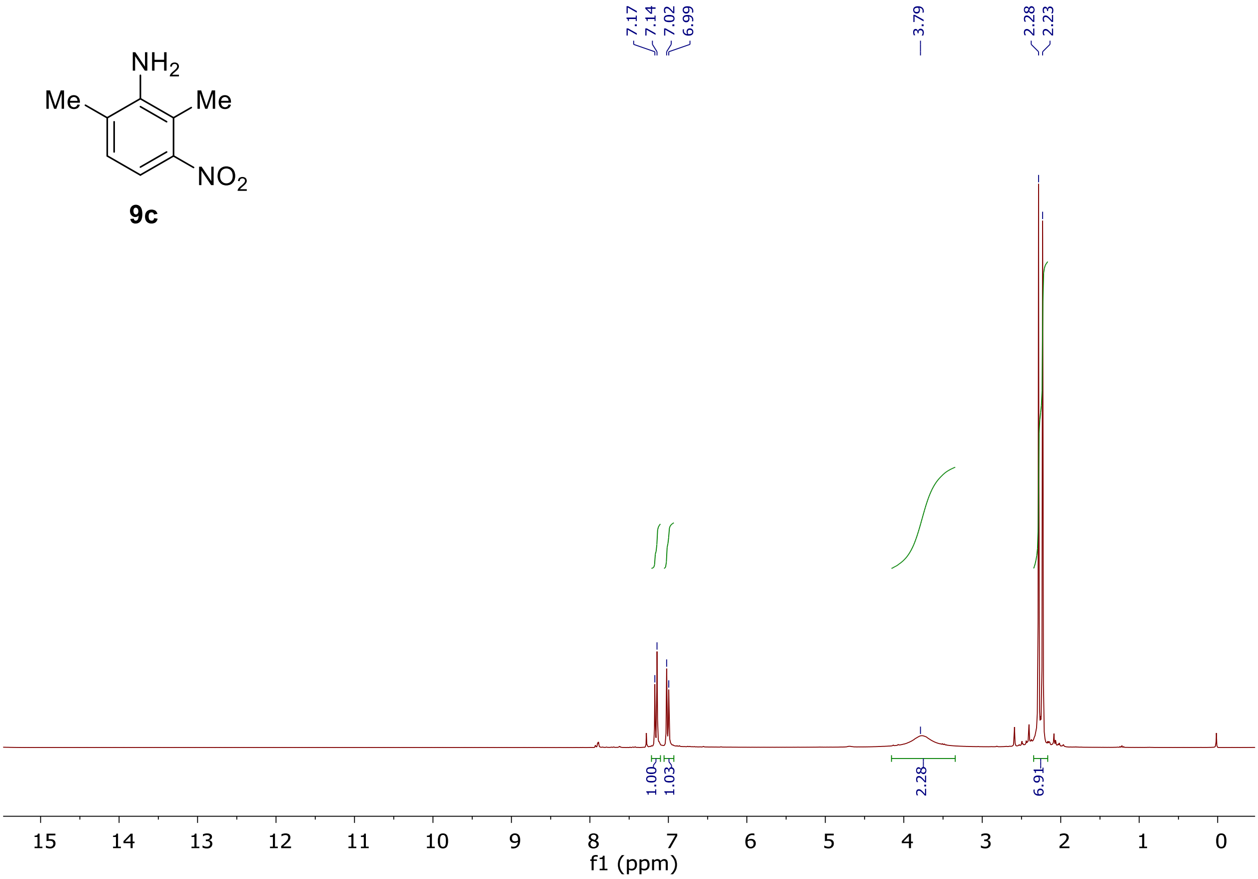


Figure S9. ^{1}H NMR (300 MHz, $CDCl_3$) of **9c**

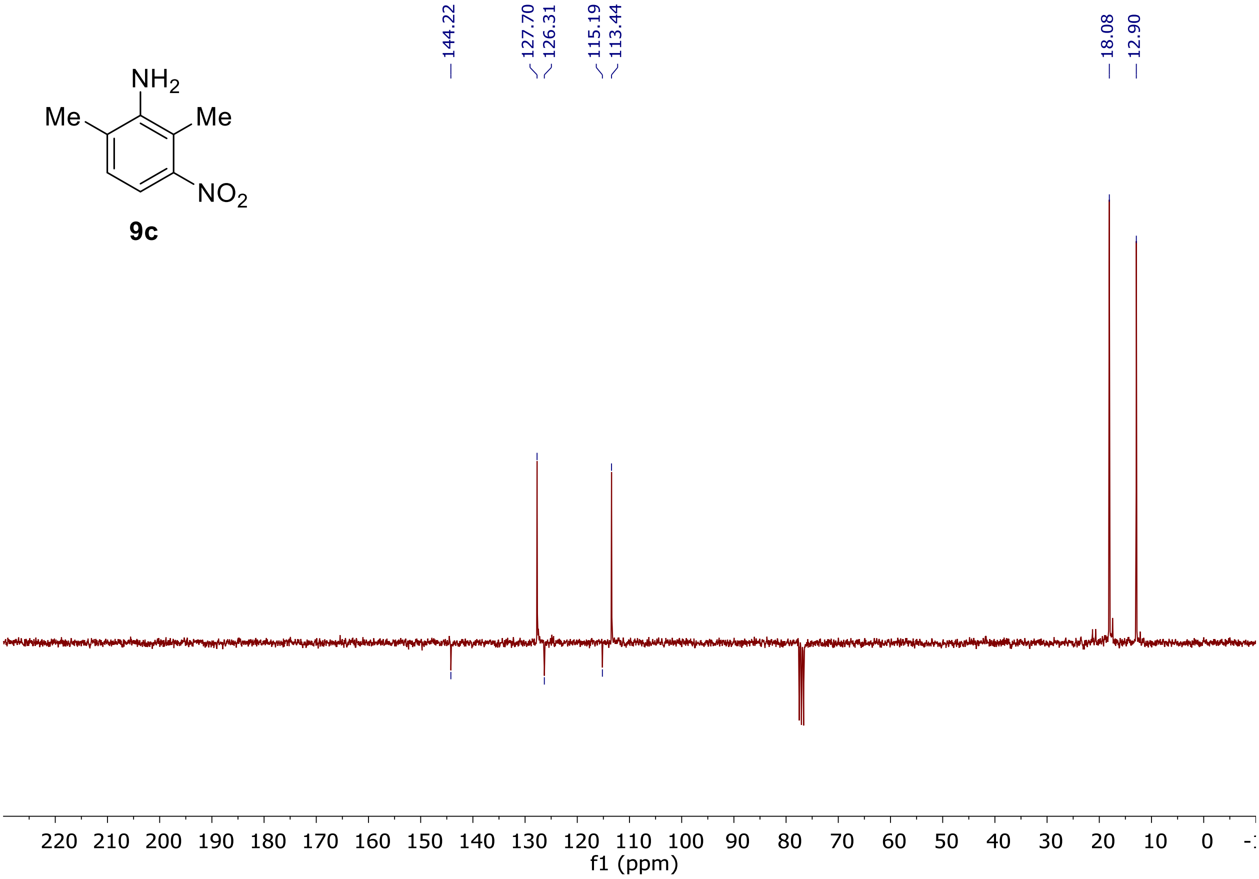


Figure S10. ^{13}C NMR (75 MHz, APT, $CDCl_3$) of **9c**

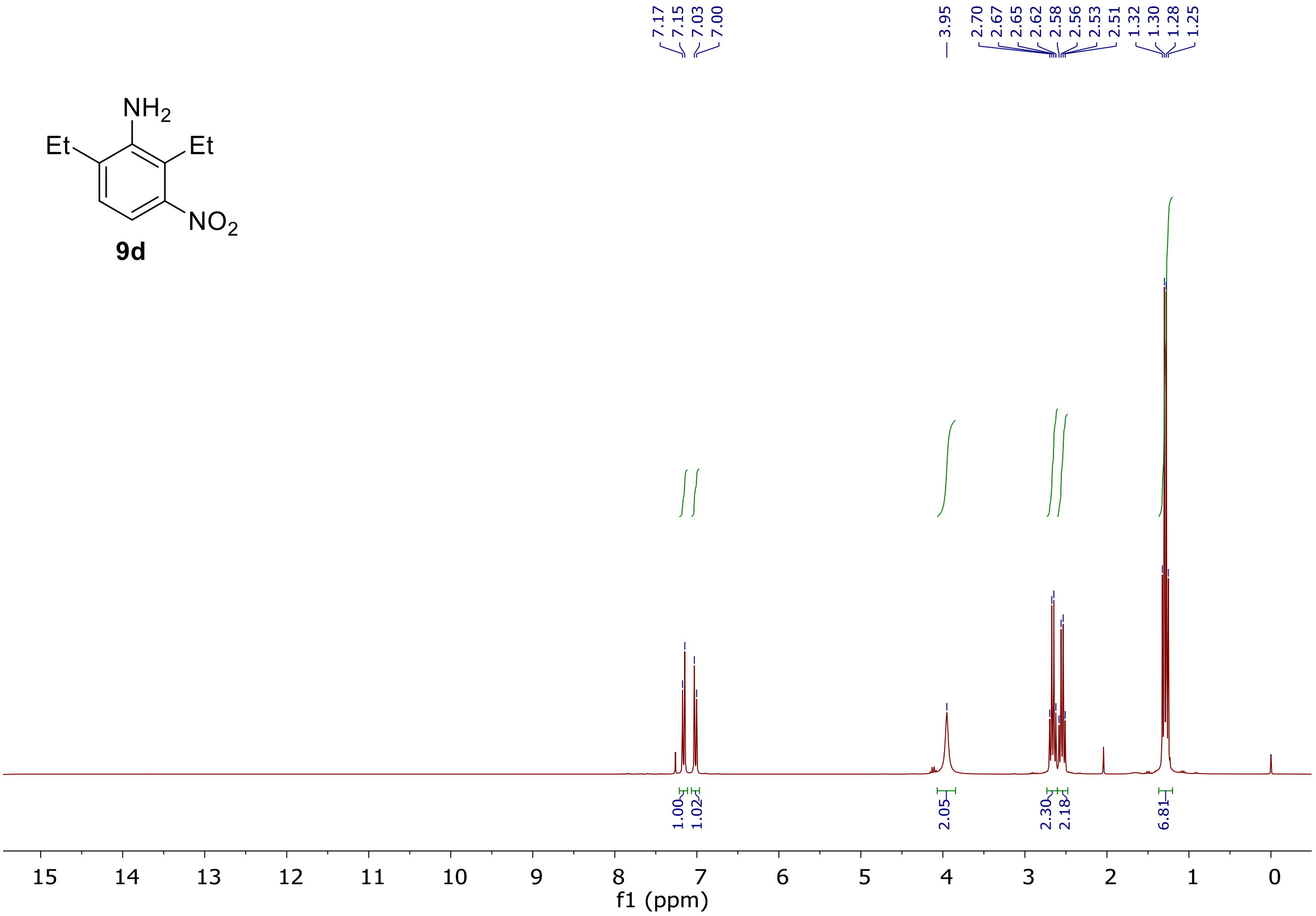


Figure S11. ^{1}H NMR (300 MHz, CDCl$_3$) of **9d**

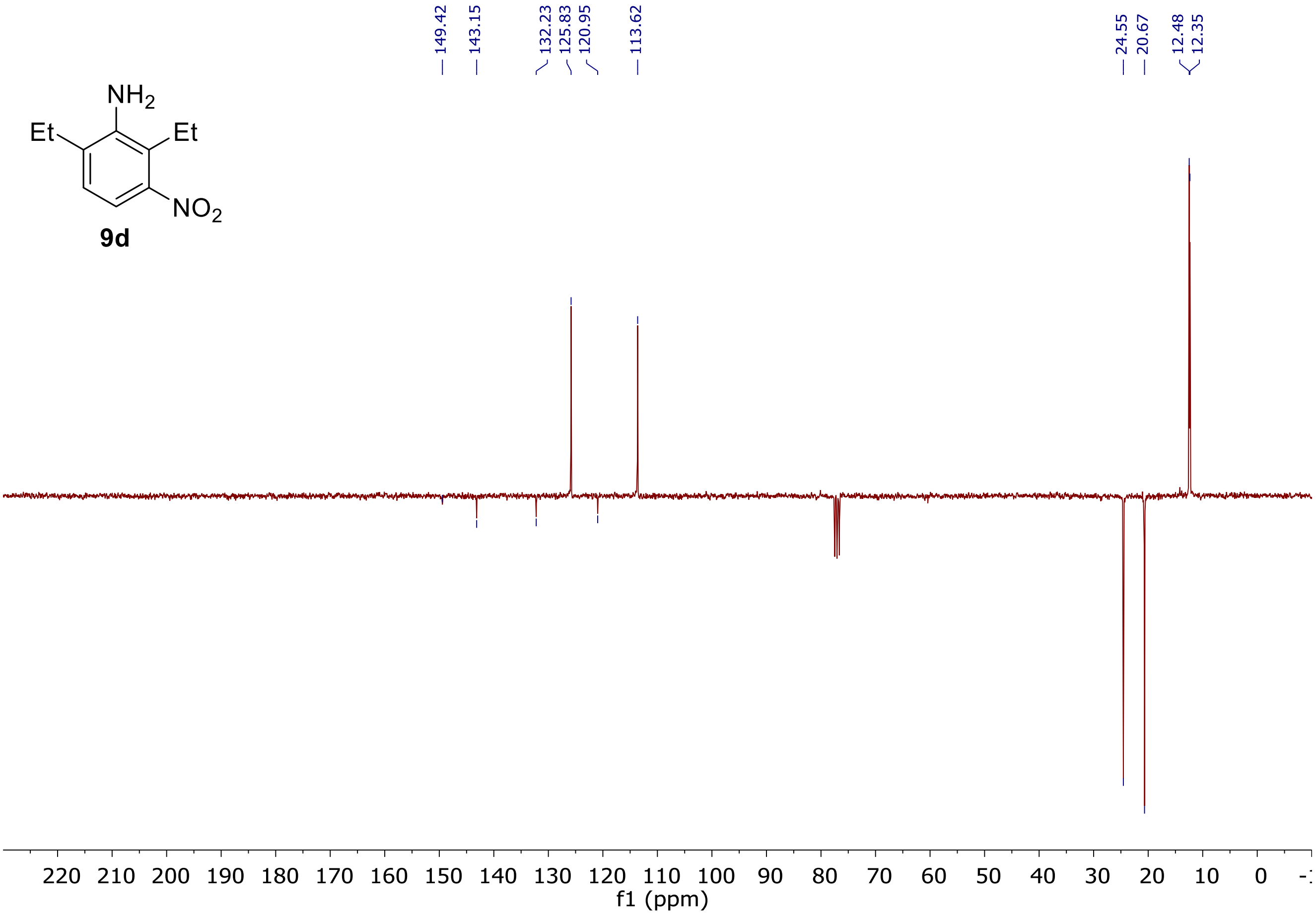


Figure S12. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **9d**

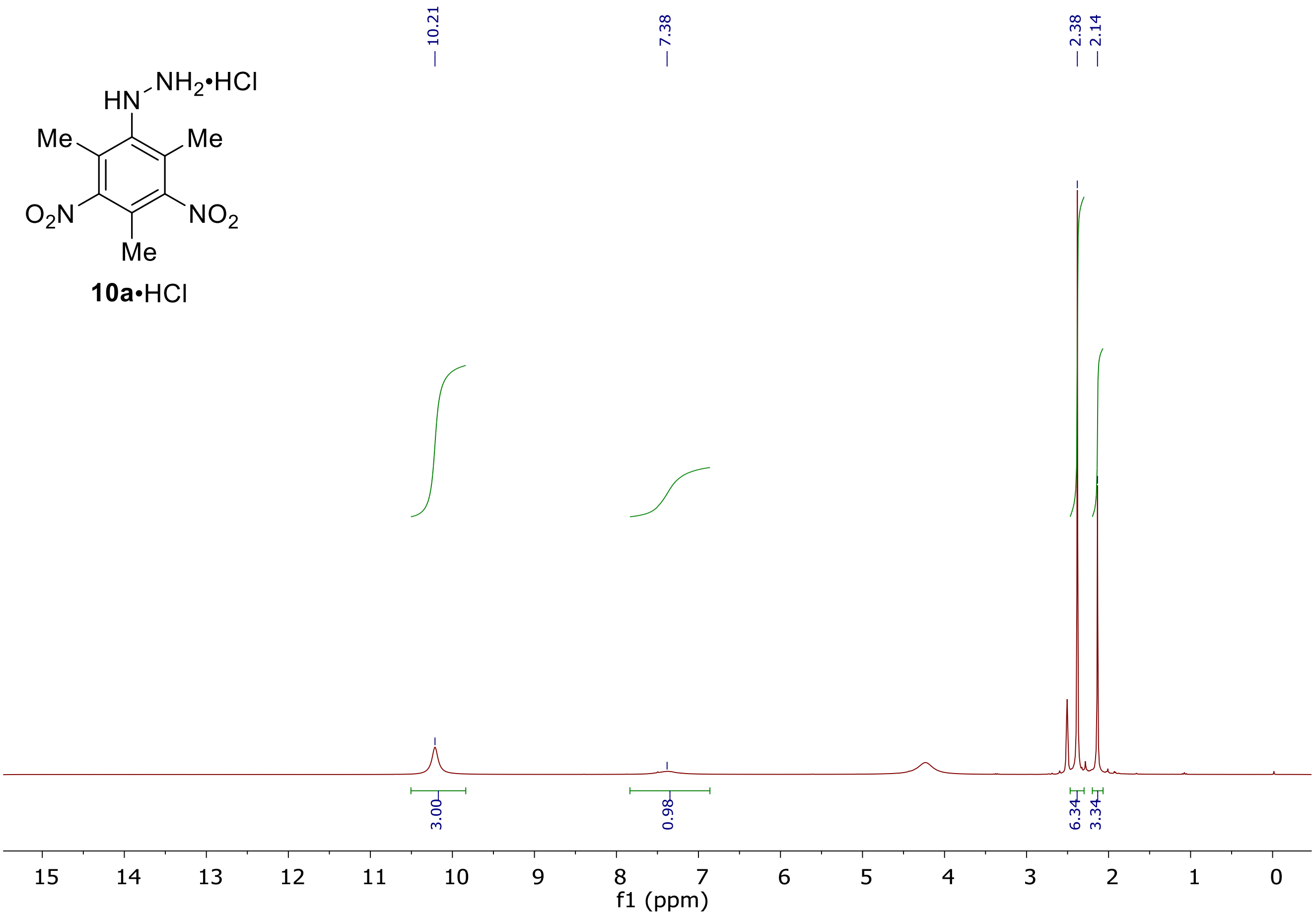


Figure S13. ^{1}H NMR (300 MHz, DMSO-d_6) of **10a**·HCl

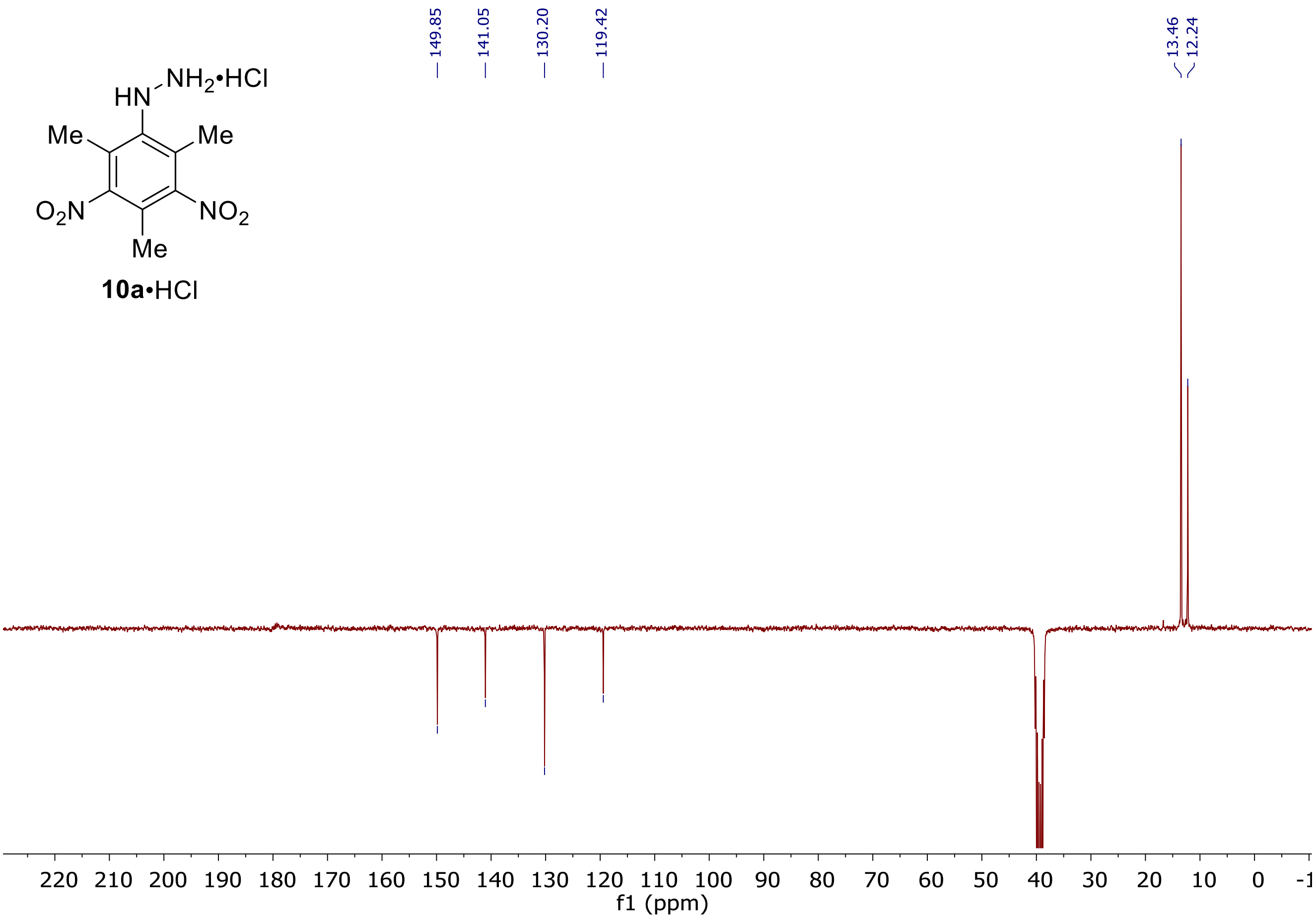
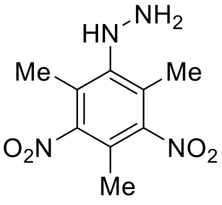


Figure S14. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10a**·HCl



10a

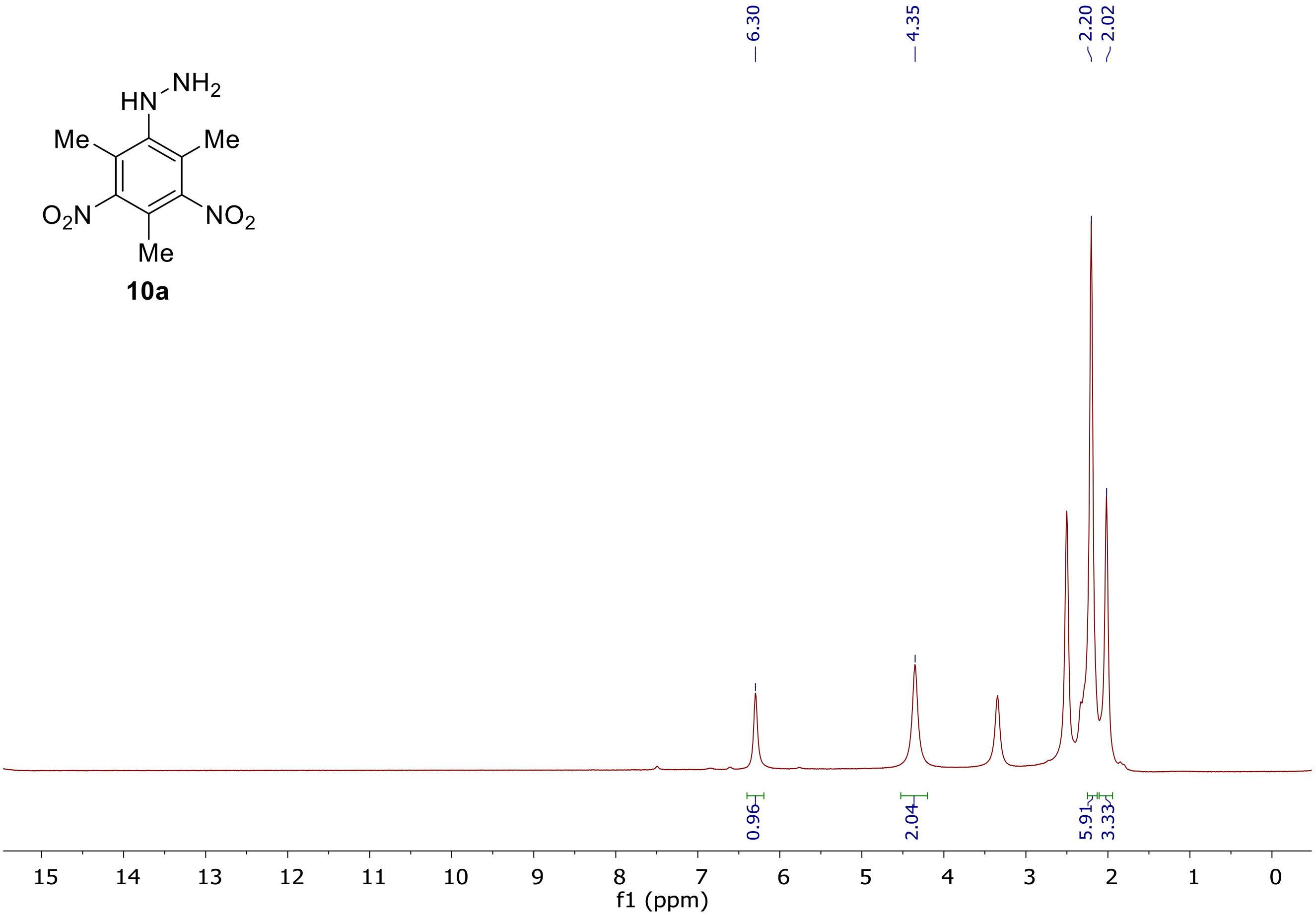
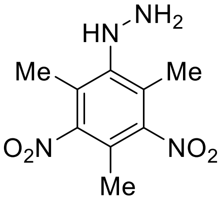


Figure S15. ^{1}H NMR (300 MHz, DMSO-d_6) of **10a**



10a

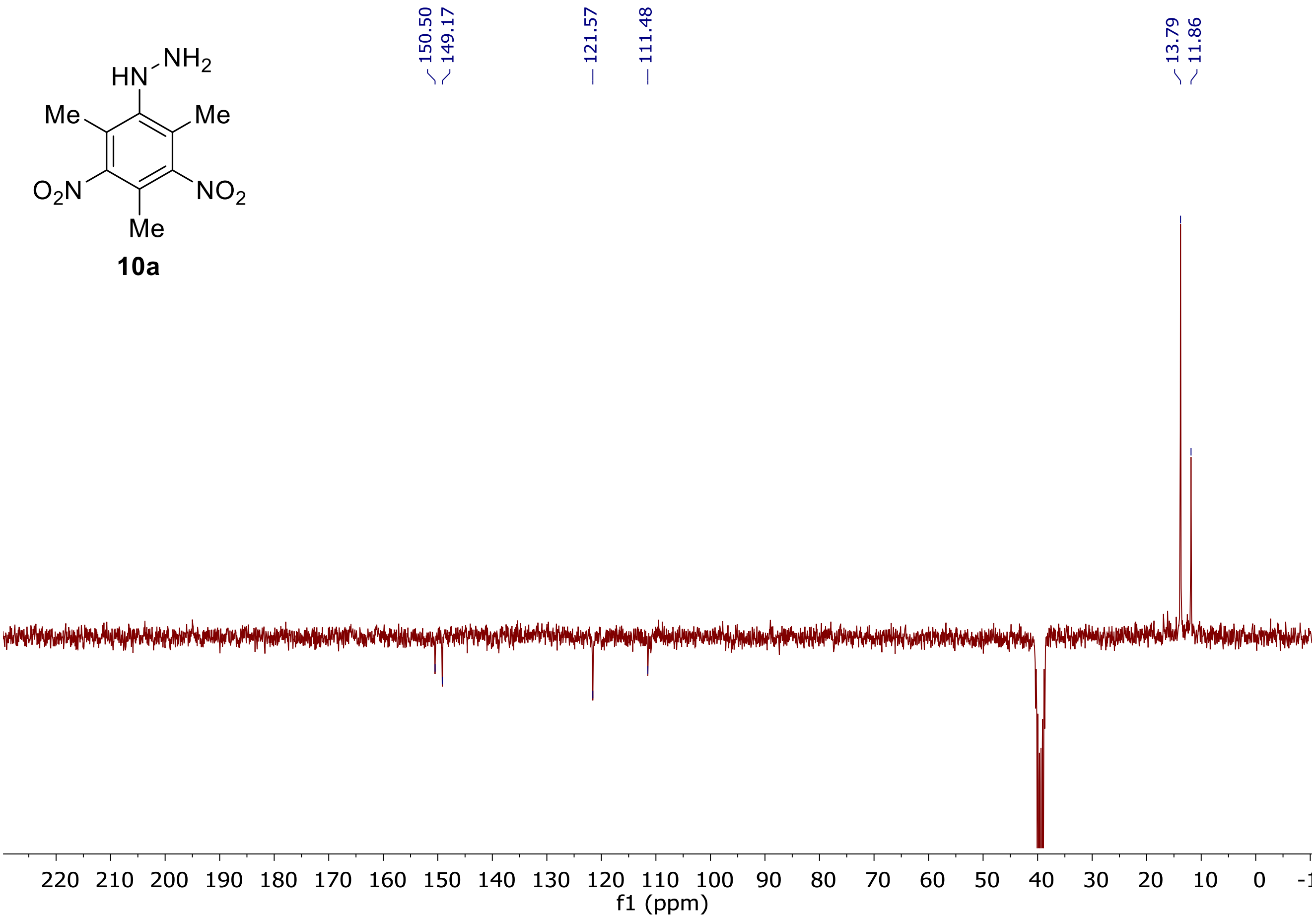


Figure S16. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10a**

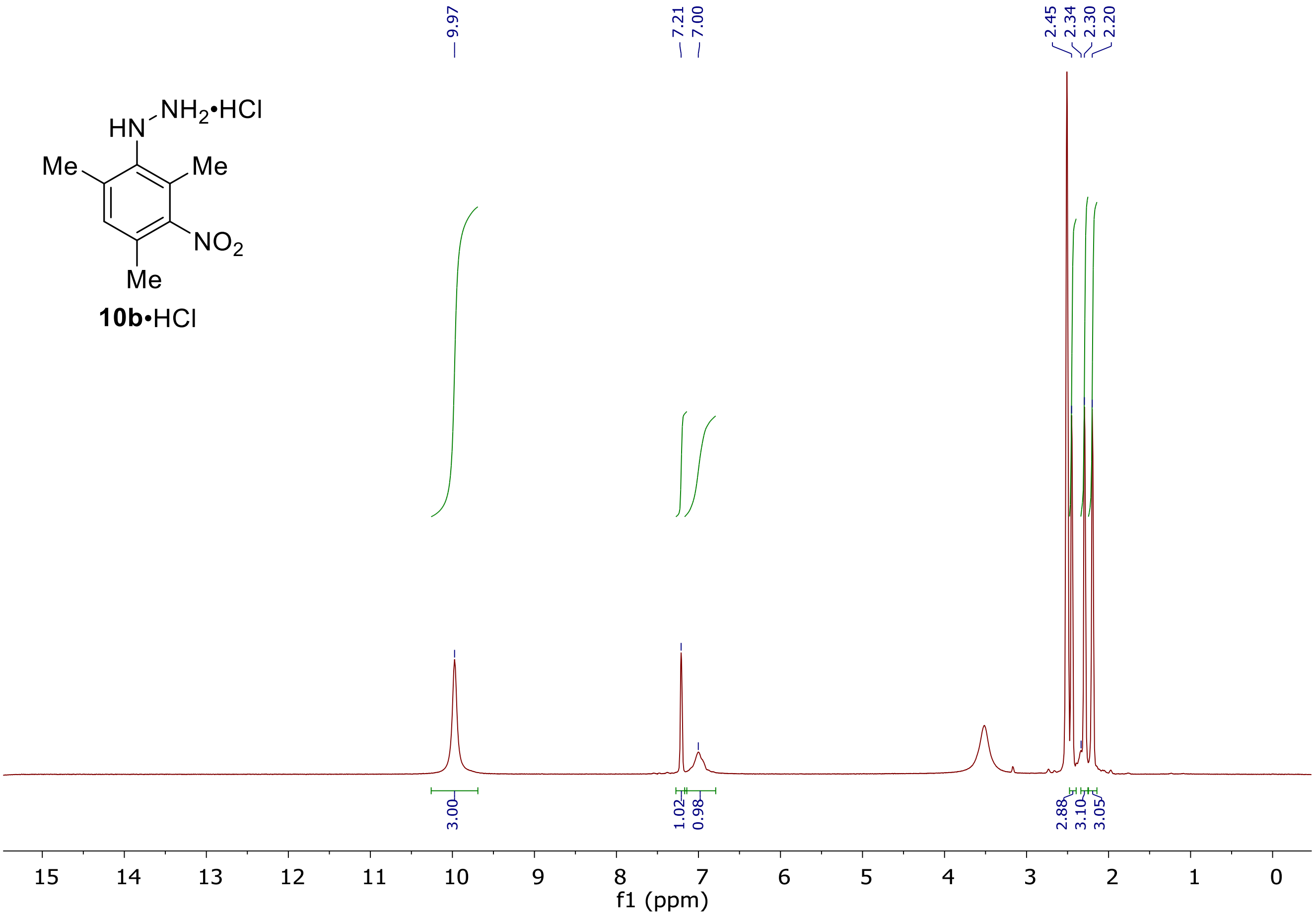


Figure S17. ^{1}H NMR (300 MHz, DMSO-d_6) of **10b**·HCl

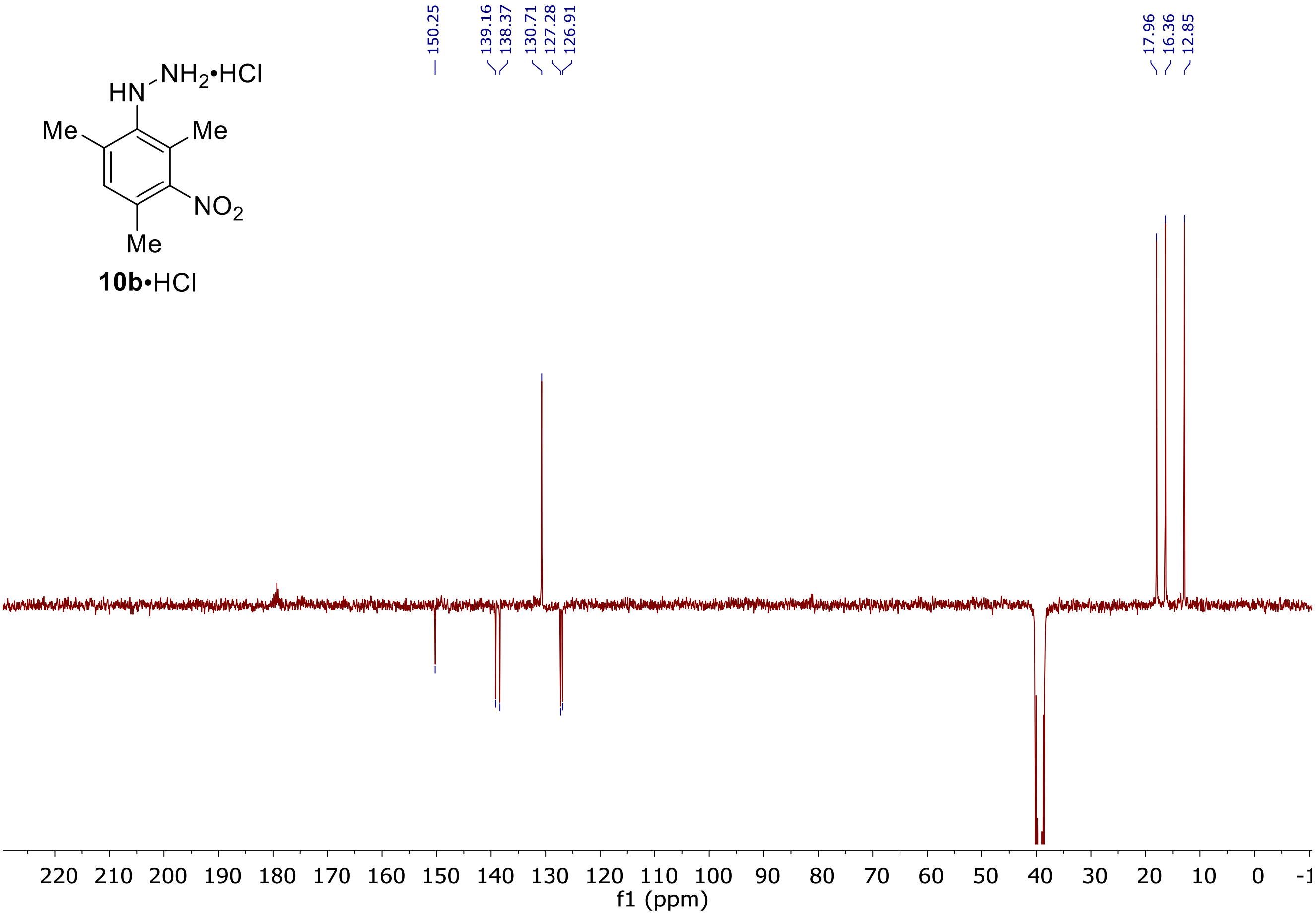


Figure S18. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10b**·HCl

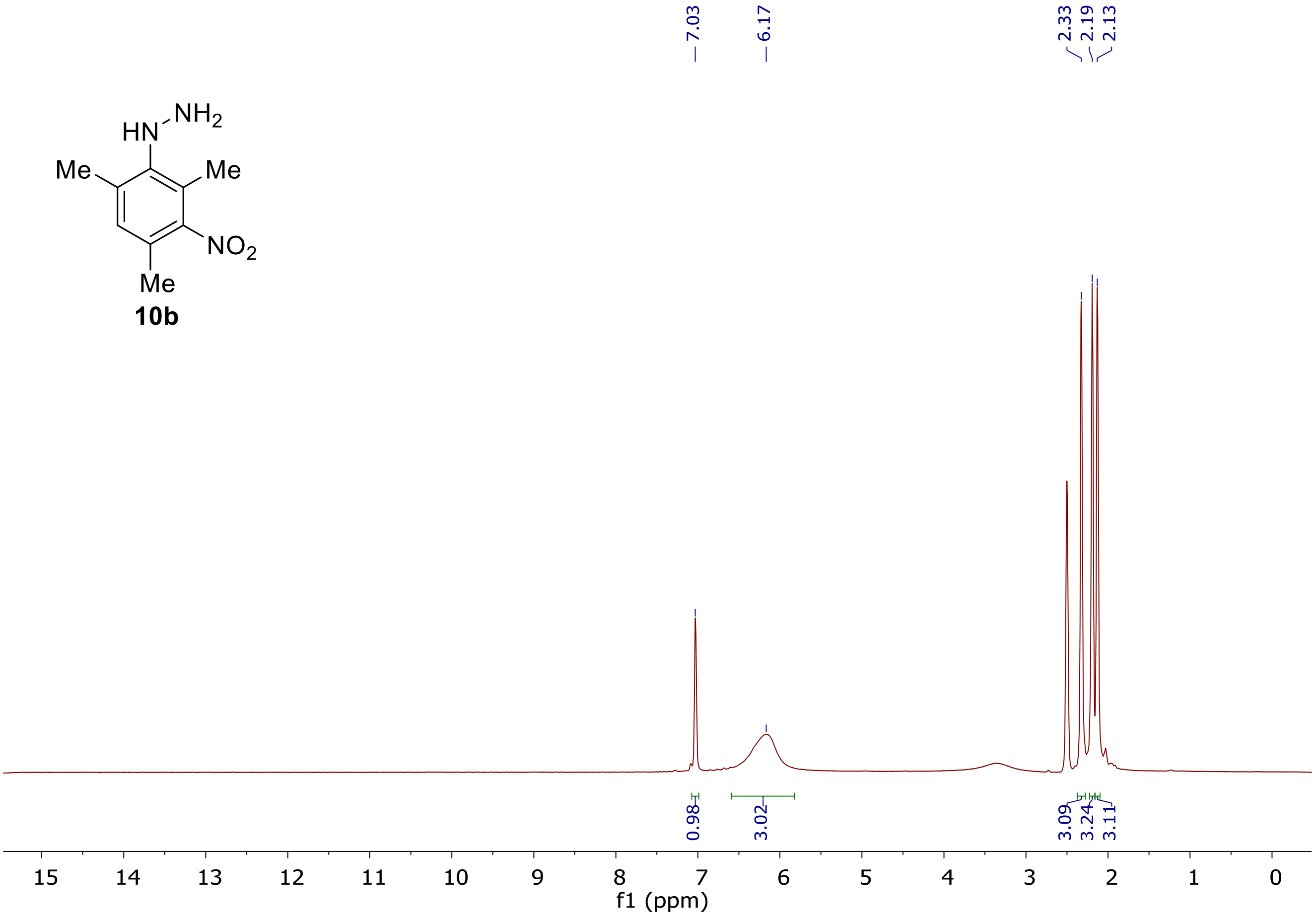


Figure S19. ^{1}H NMR (300 MHz, DMSO-d_6) of **10b**

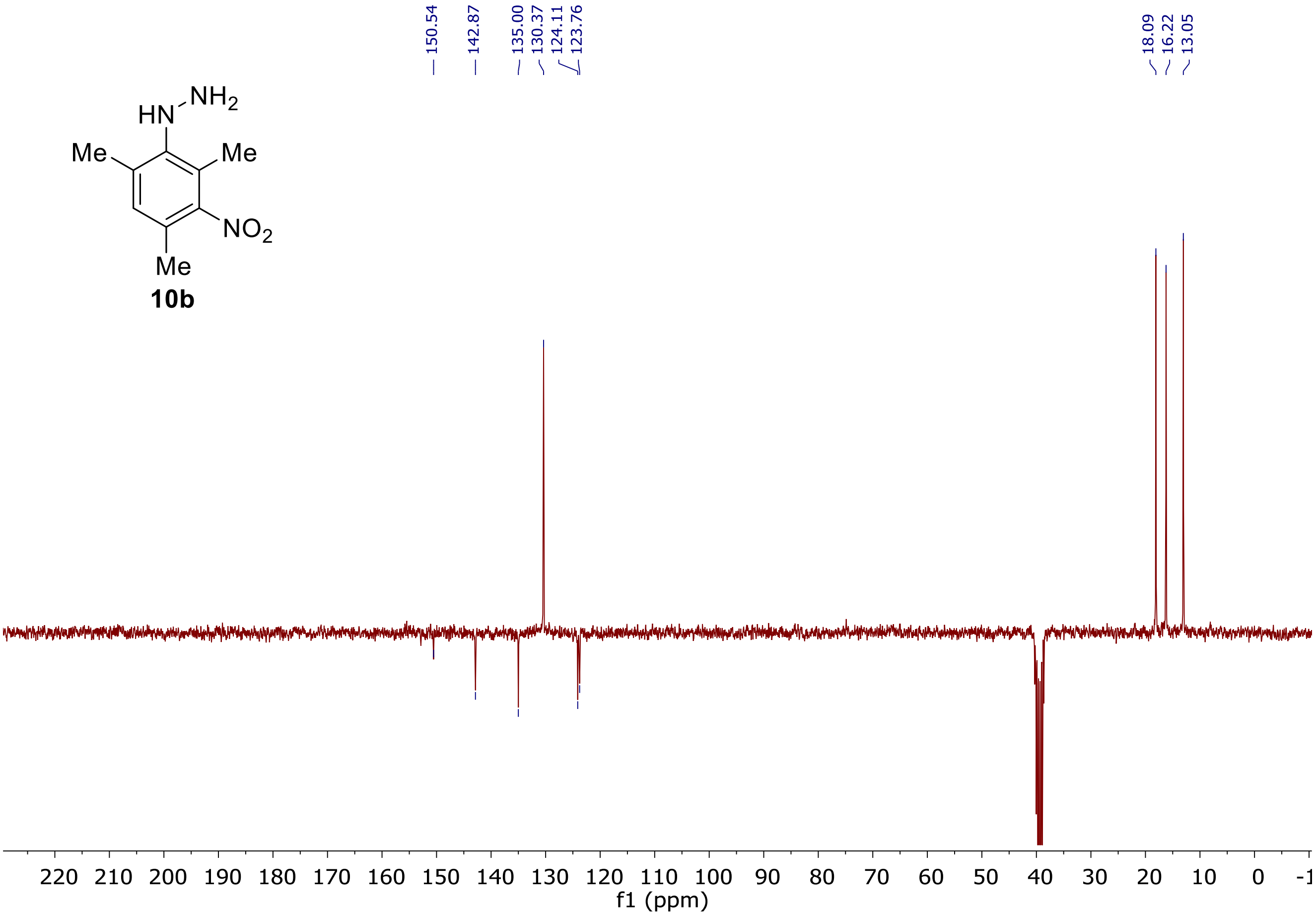


Figure S20. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10b**

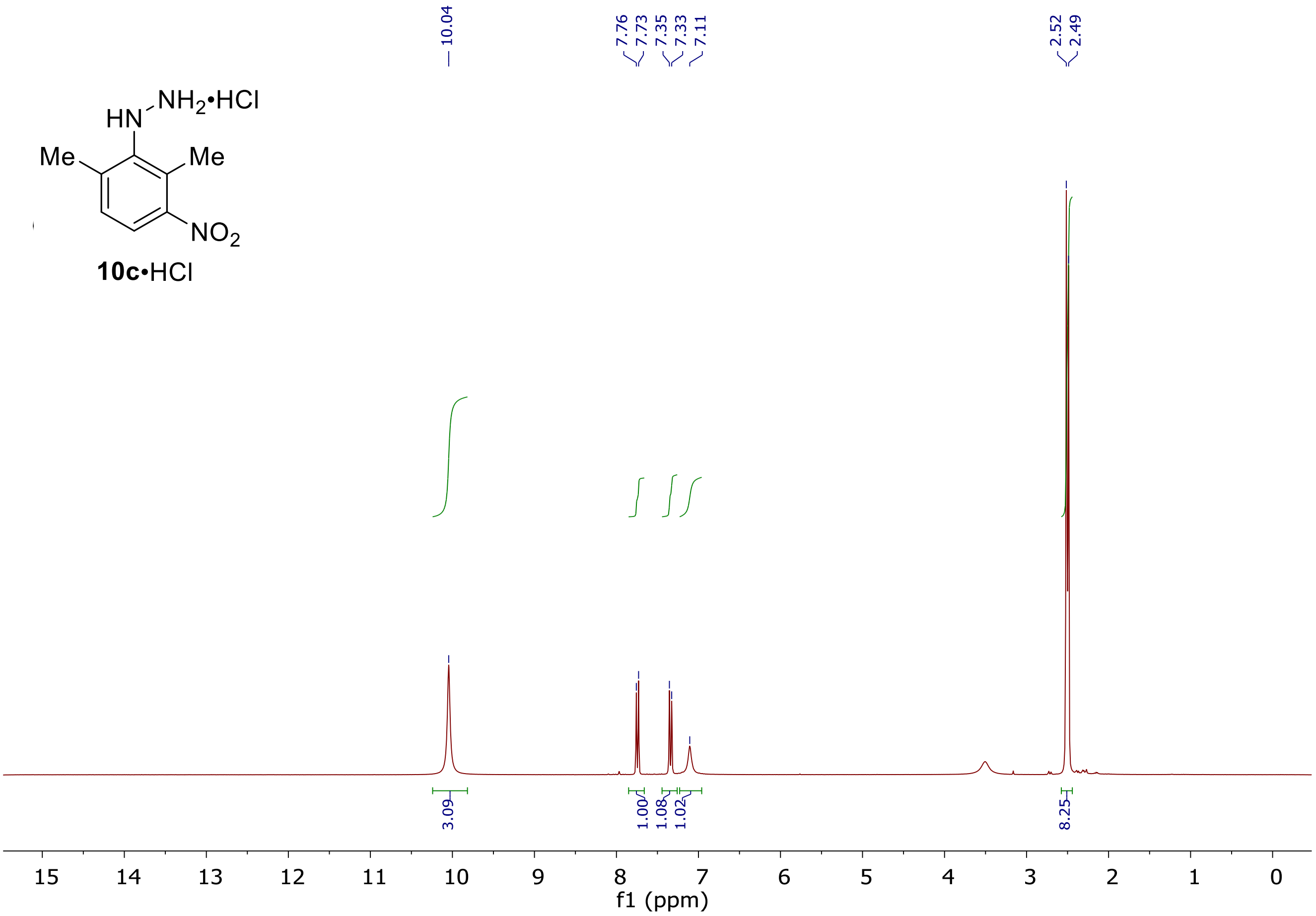


Figure S21. ^{1}H NMR (300 MHz, DMSO-d_6) of **10c**·HCl

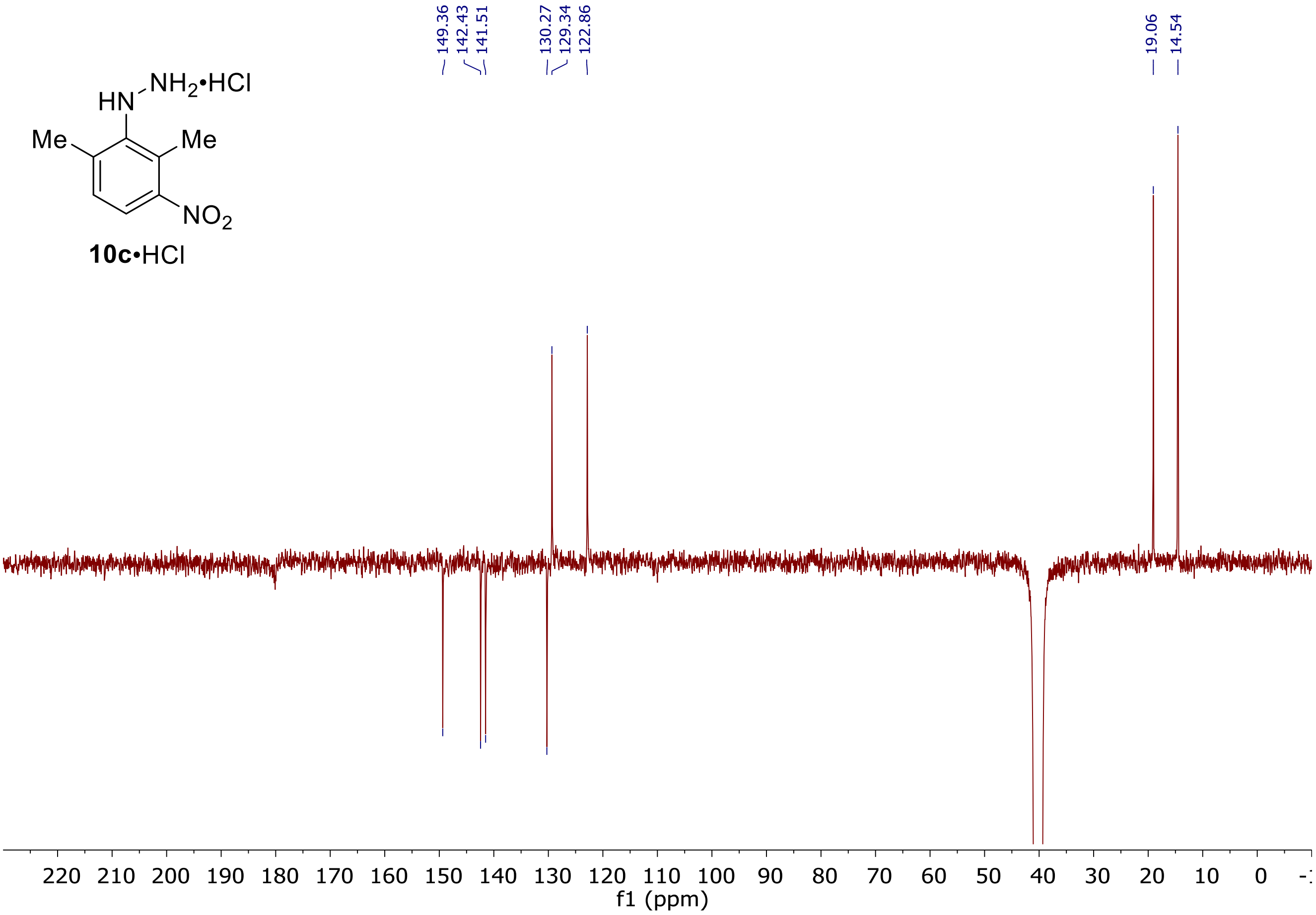


Figure S22. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10c**·HCl

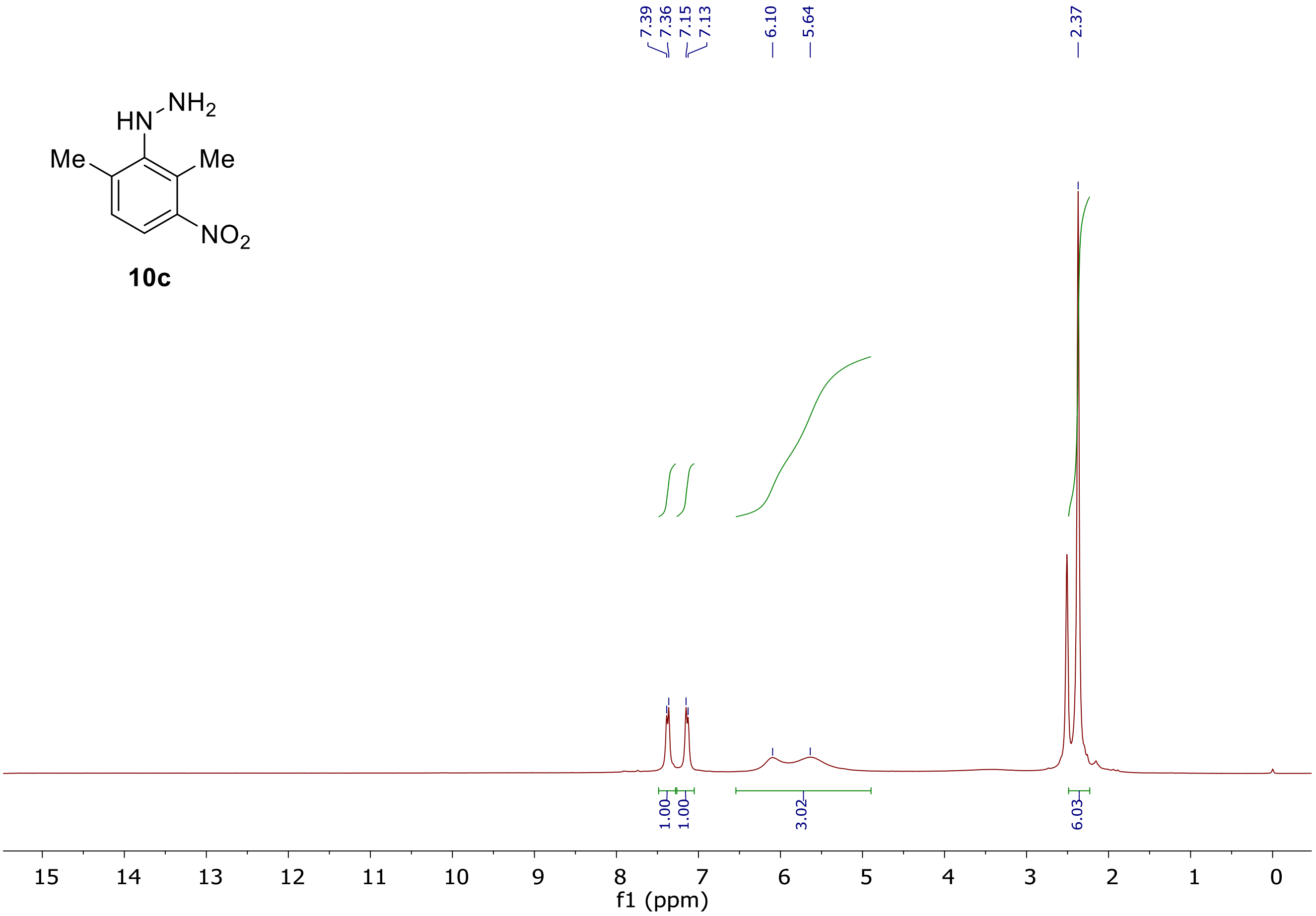


Figure S23. ^{1}H NMR (300 MHz, DMSO-d_6) of **10c**

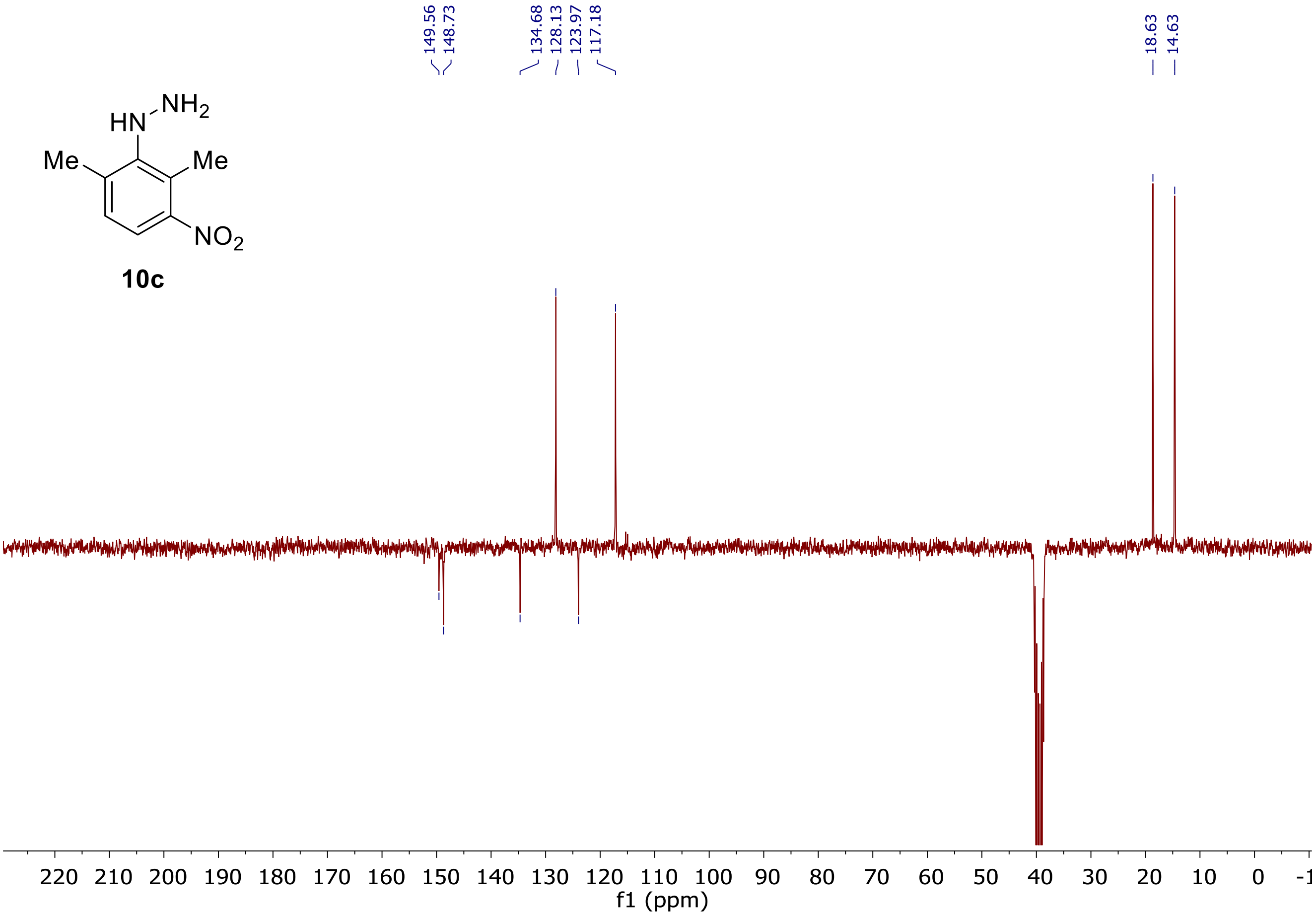


Figure S24. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10c**

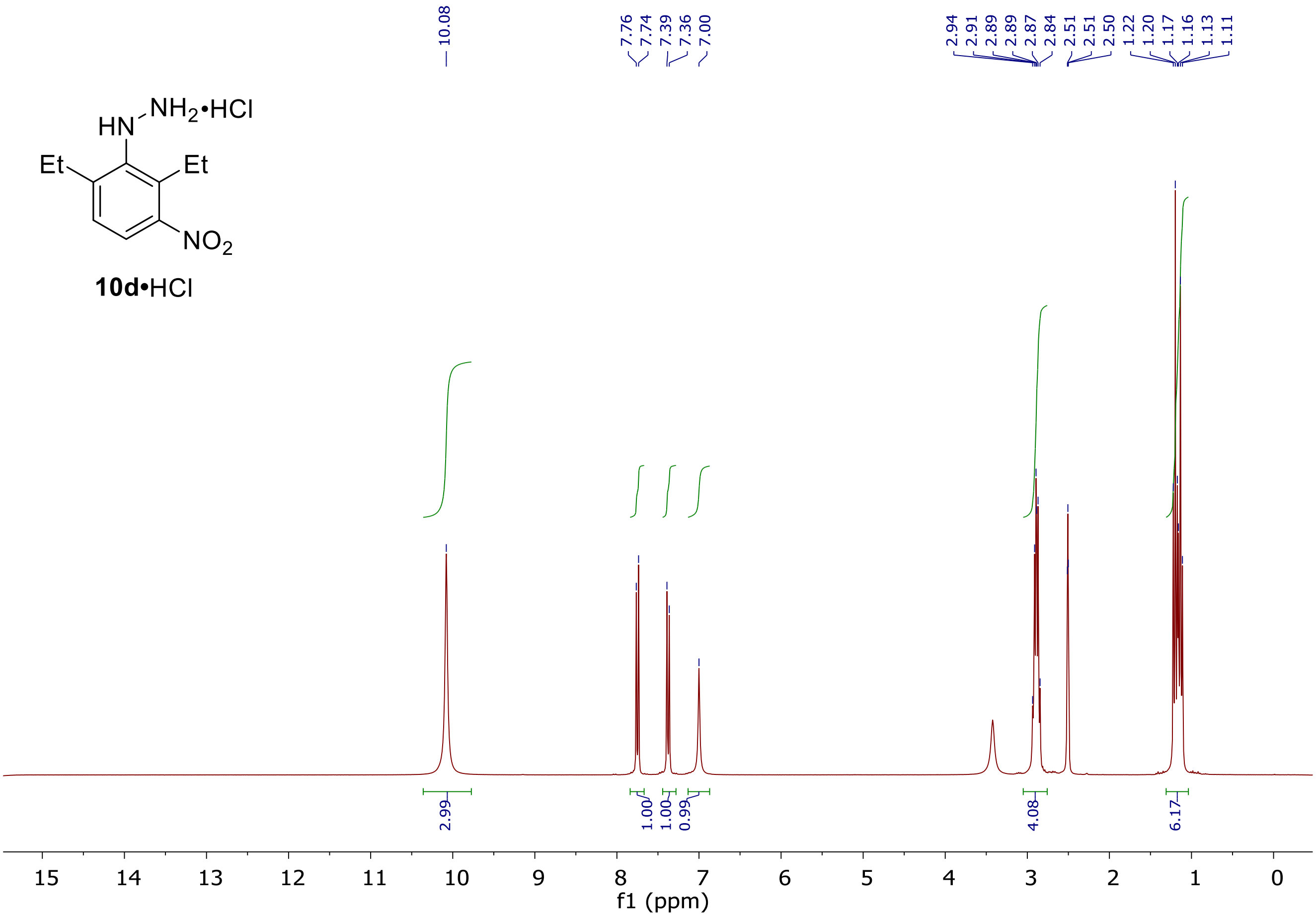


Figure S25. ^{1}H NMR (300 MHz, DMSO-d_6) of **10d**·HCl

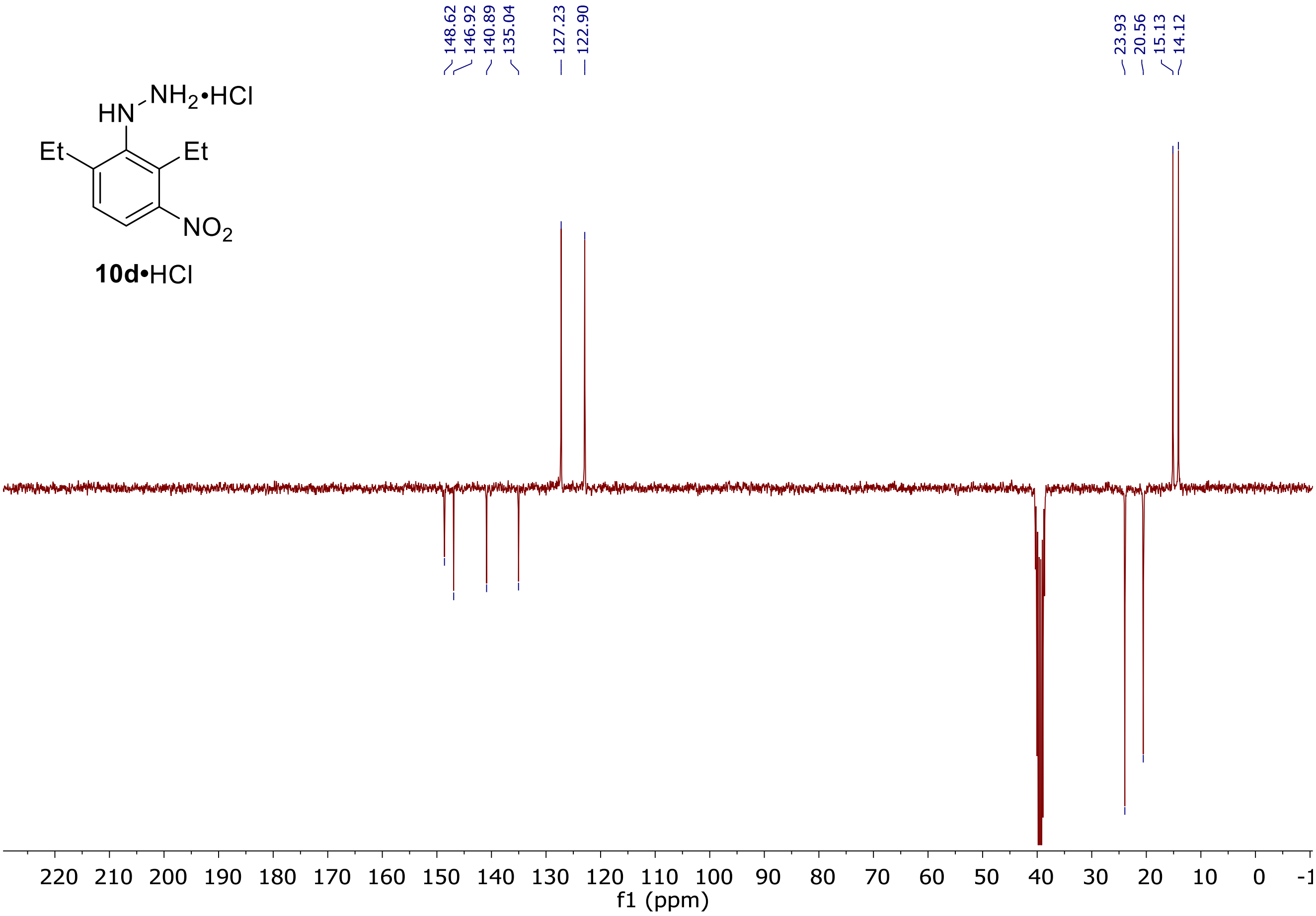


Figure S26. ^{13}C NMR (75 MHz, APT, DMSO-d_6) of **10d**·HCl

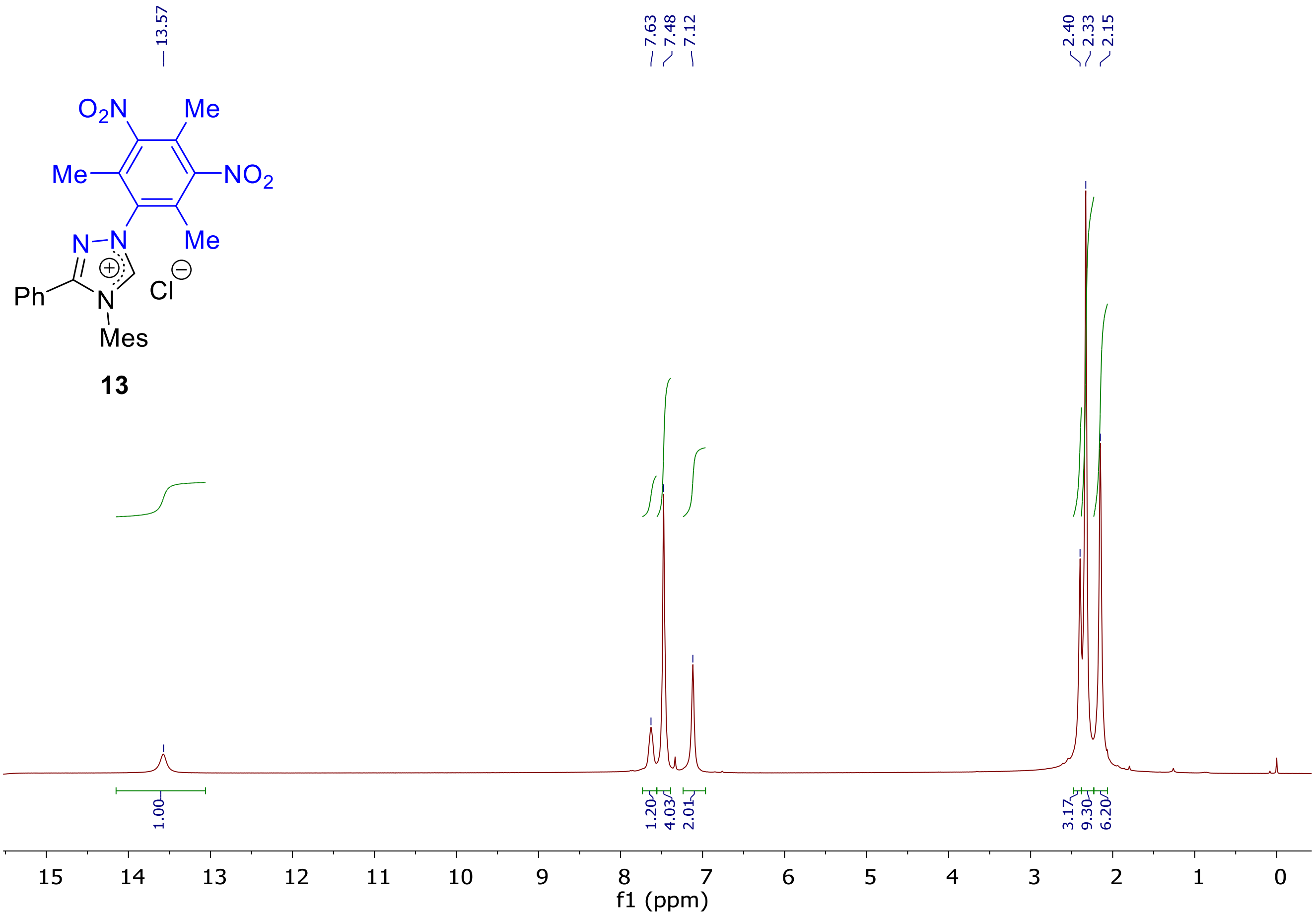


Figure S27. ^{1}H NMR (300 MHz, CDCl$_3$) of **13**

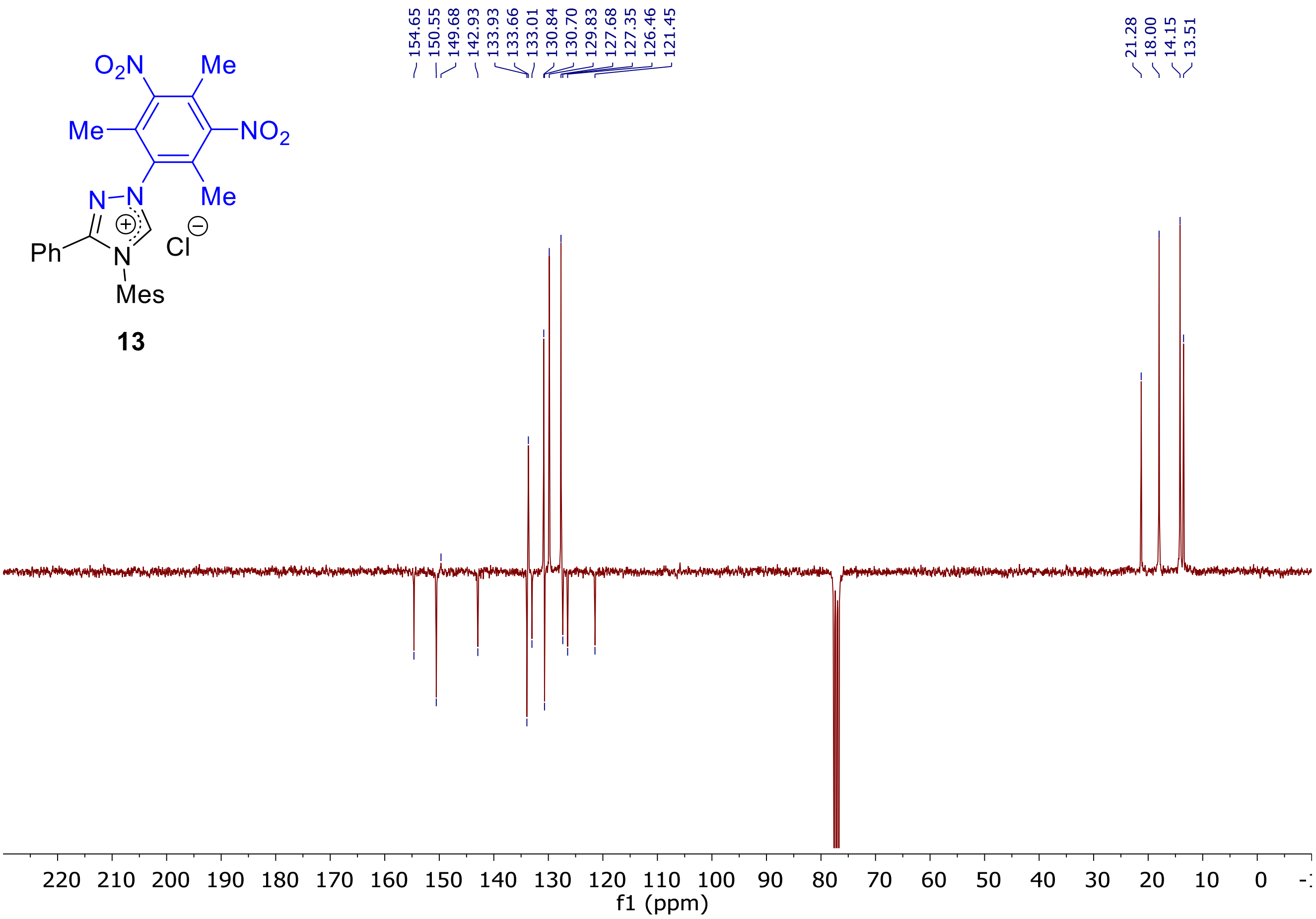


Figure S28. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **13**

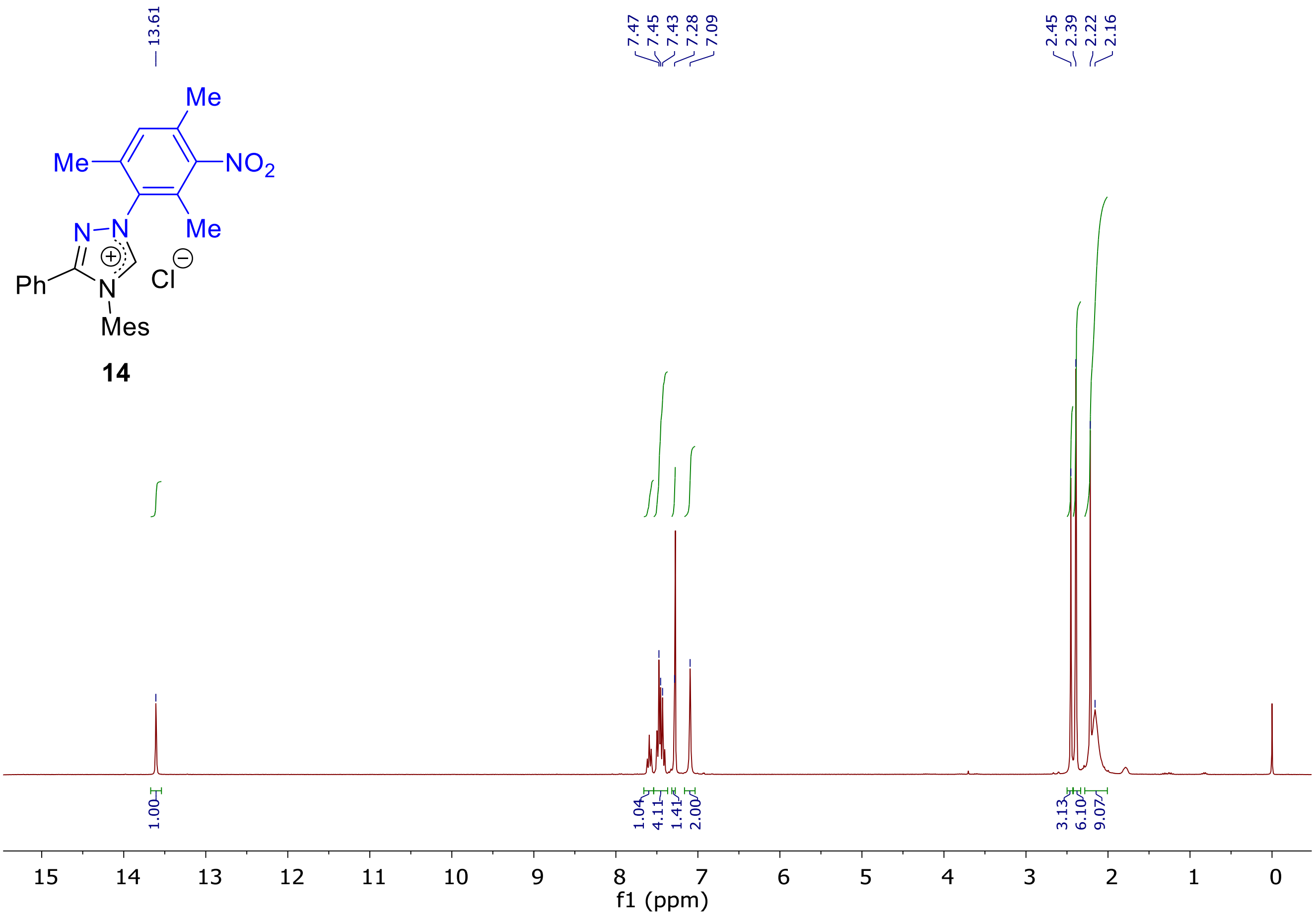


Figure S29. ^{1}H NMR (300 MHz, $CDCl_3$) of **14**

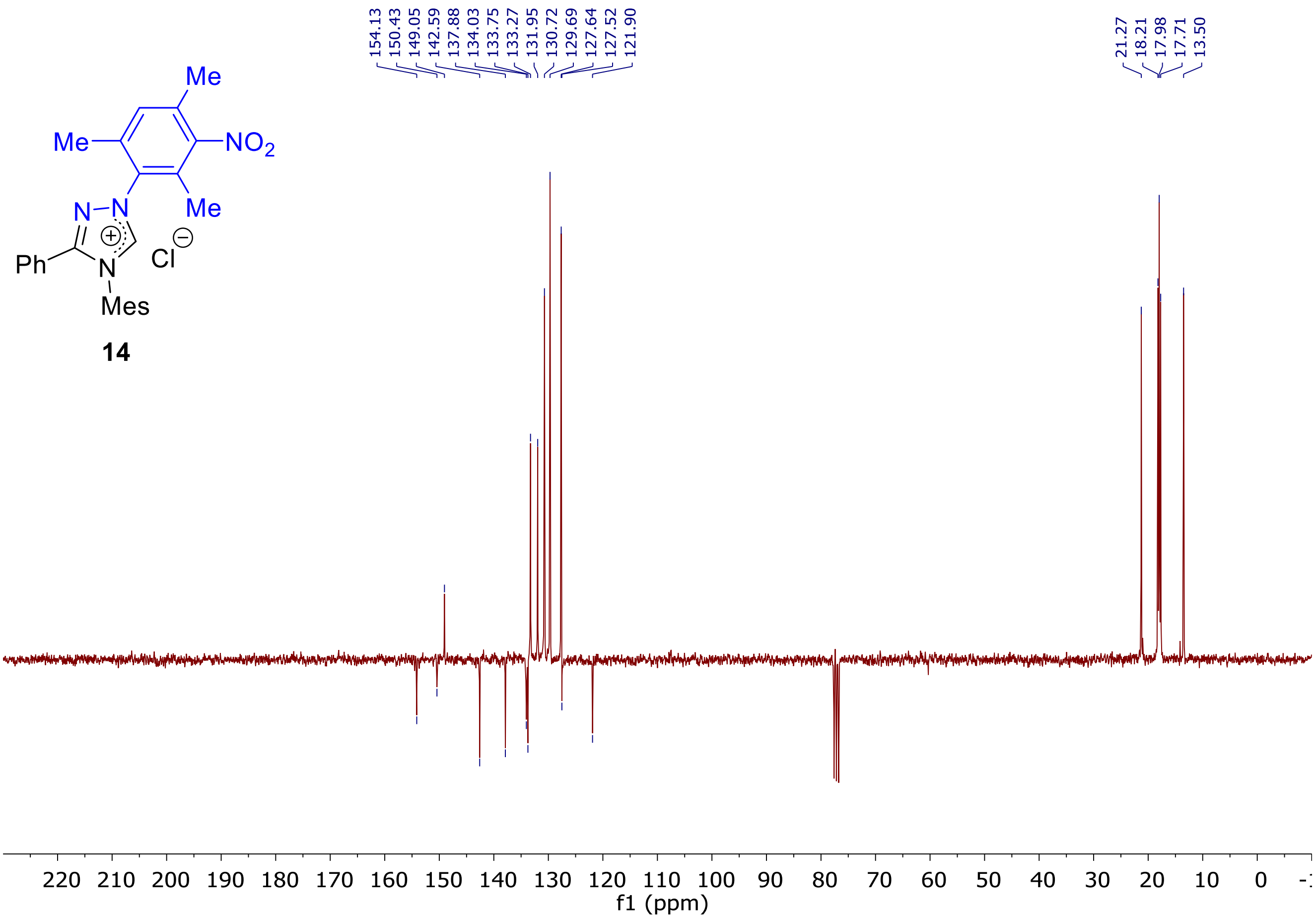


Figure S30. ^{13}C NMR (75 MHz, APT, $CDCl_3$) of **14**

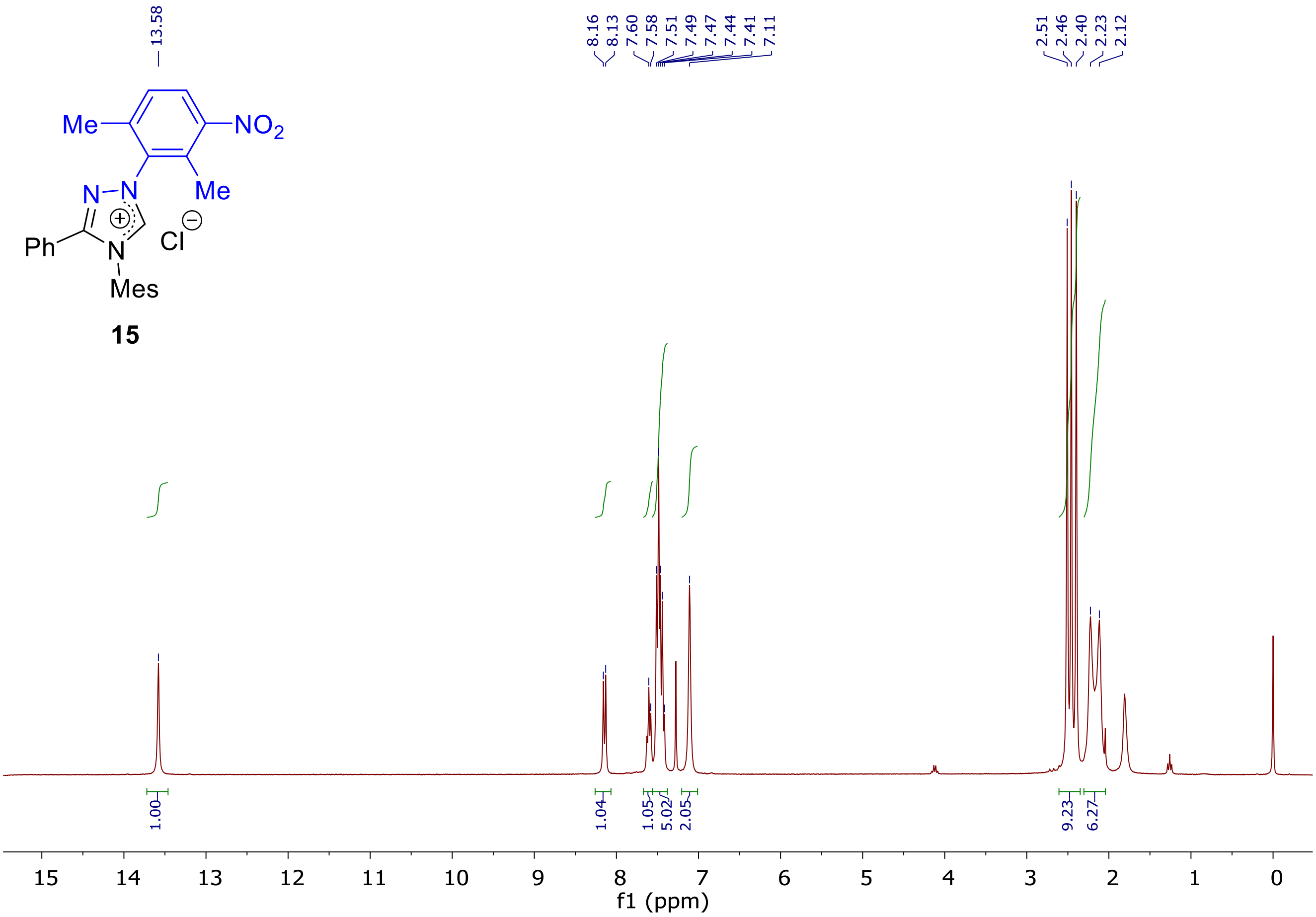


Figure S31. ^{1}H NMR (300 MHz, CDCl$_3$) of **15**

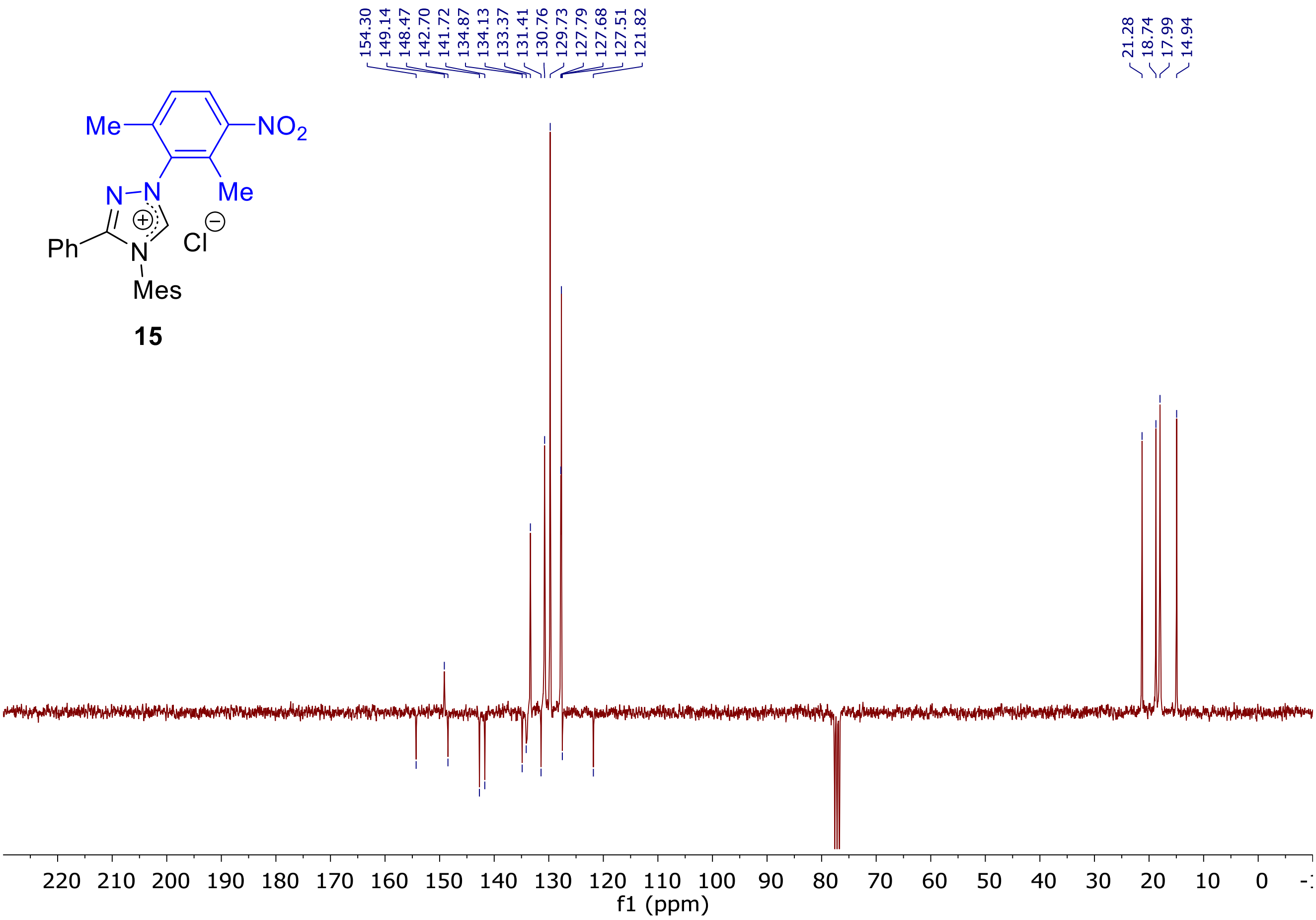


Figure S32. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **15**

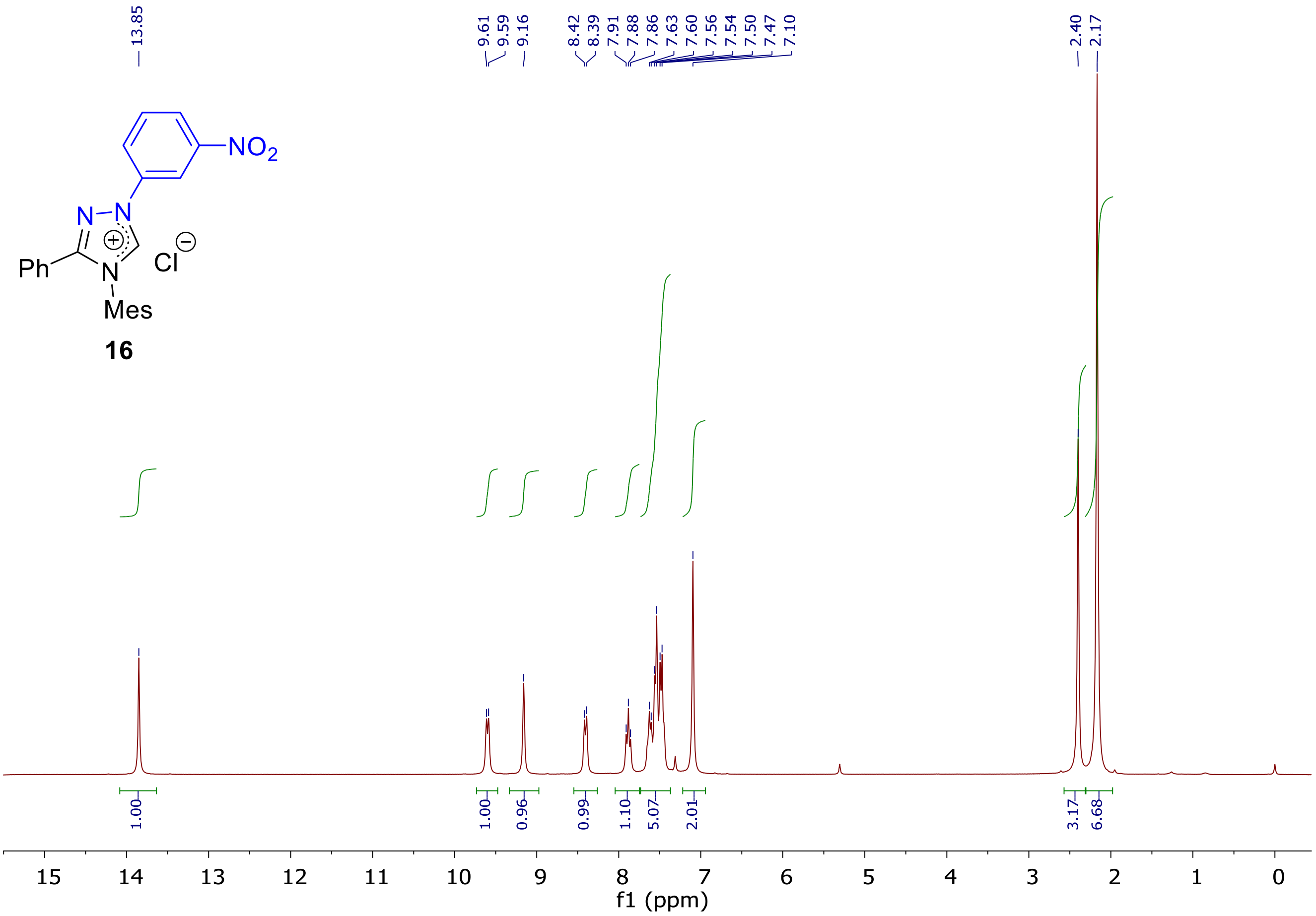


Figure S33. ^{1}H NMR (300 MHz, $CDCl_3$) of **16**

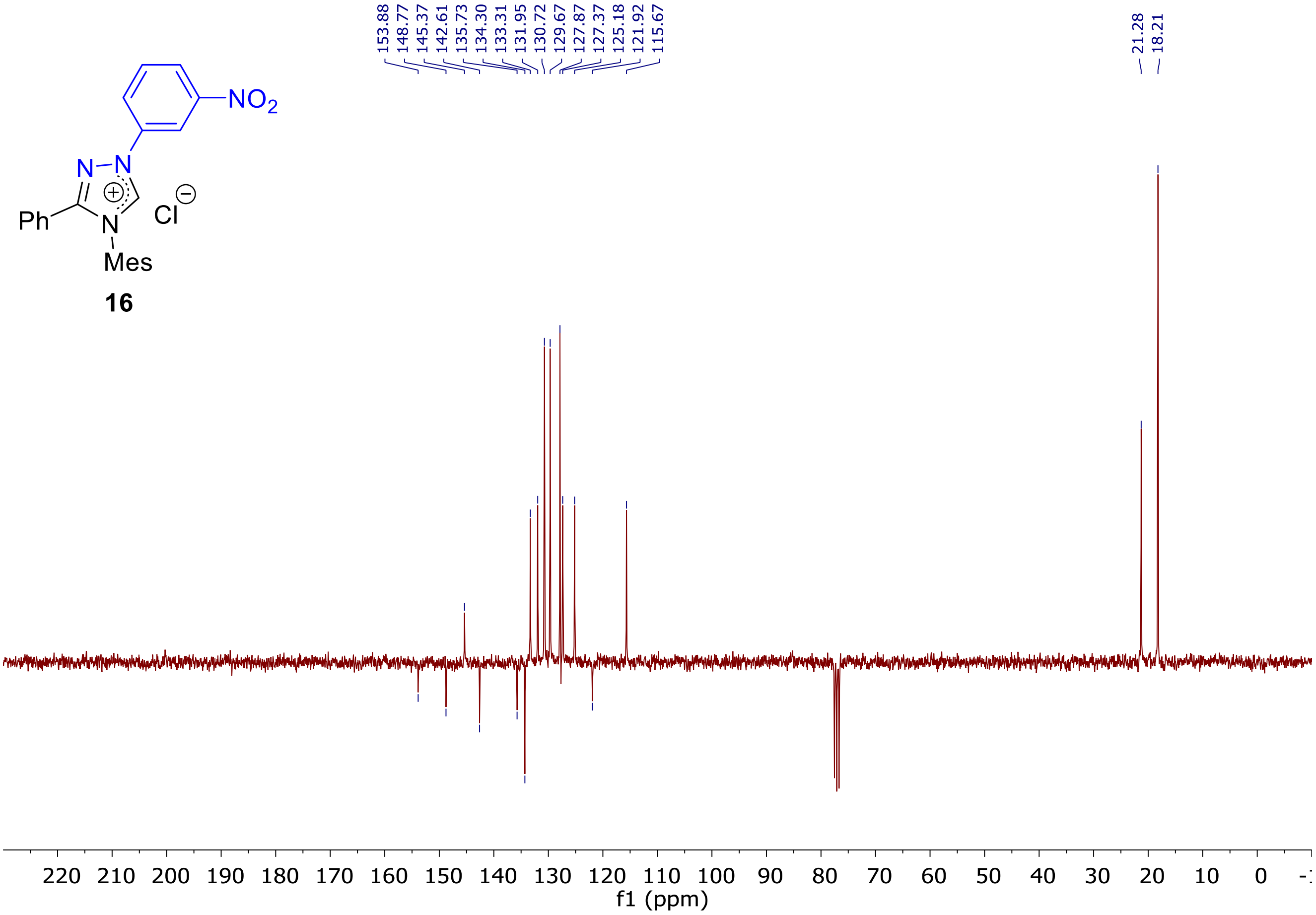


Figure S34. ^{13}C NMR (75 MHz, APT, $CDCl_3$) of **16**

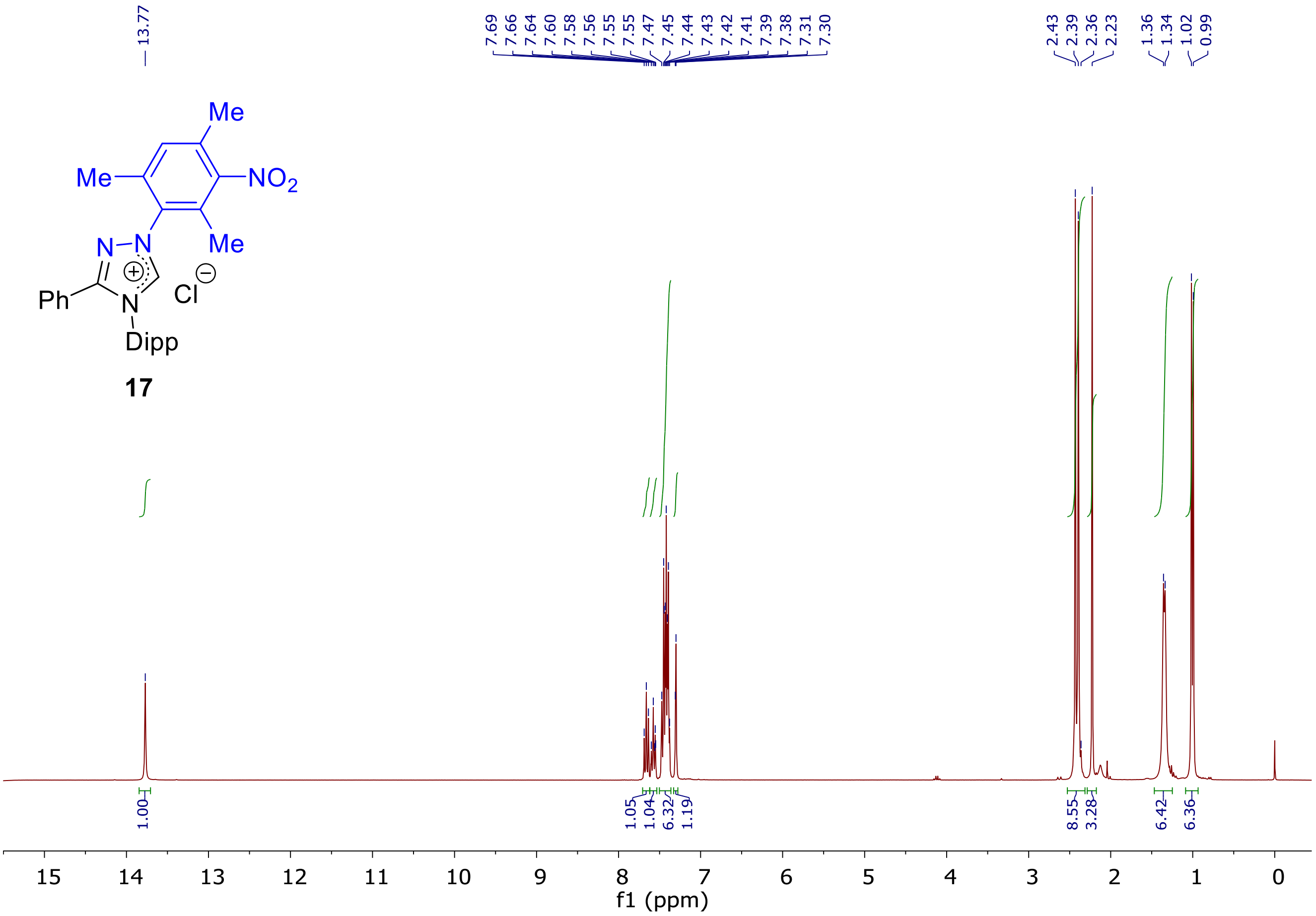


Figure S35. ^{1}H NMR (300 MHz, CDCl$_3$) of **17**

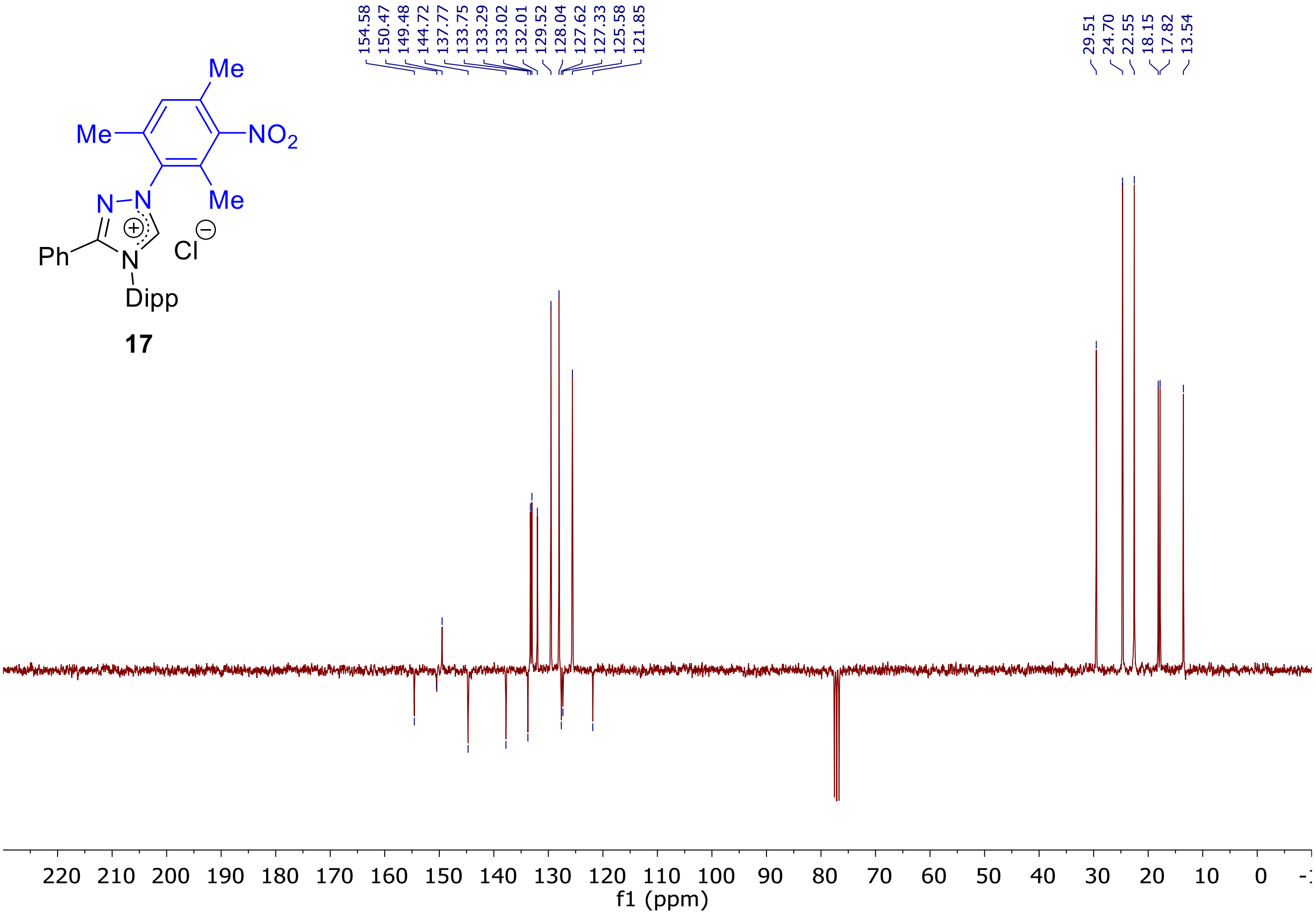


Figure S36. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **17**

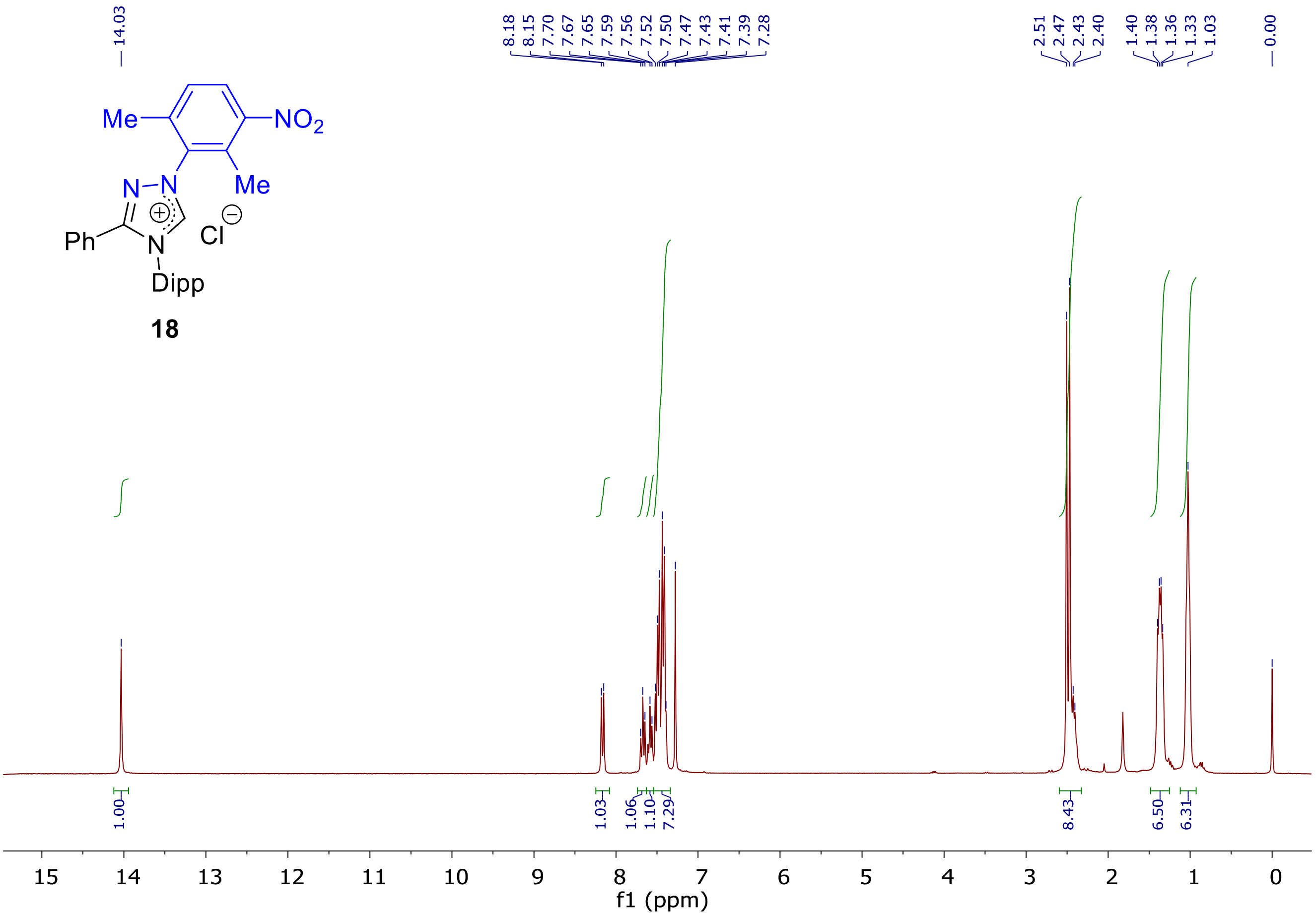


Figure S37. ^{1}H NMR (300 MHz, CDCl$_3$) of **18**

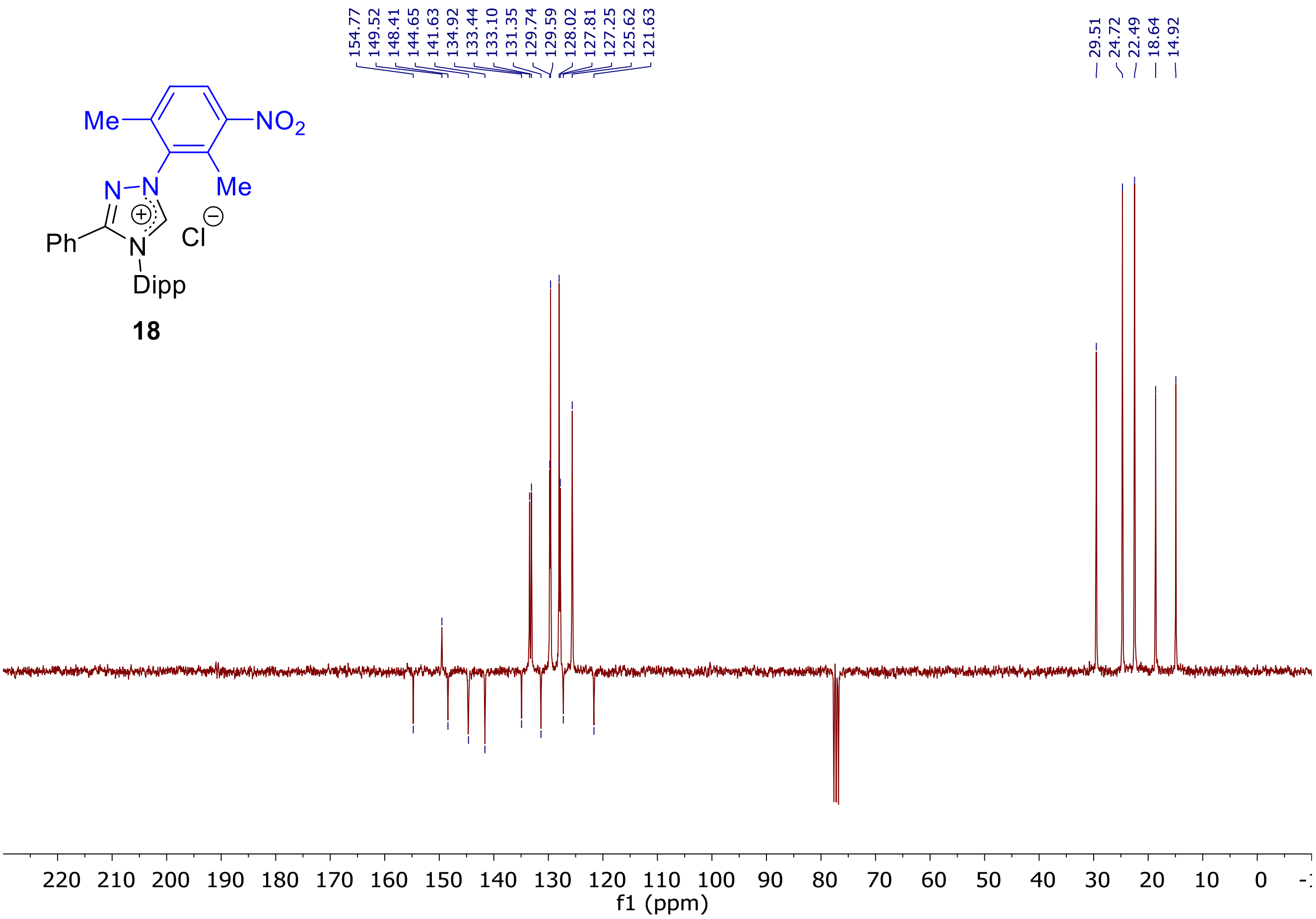


Figure S38. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **18**

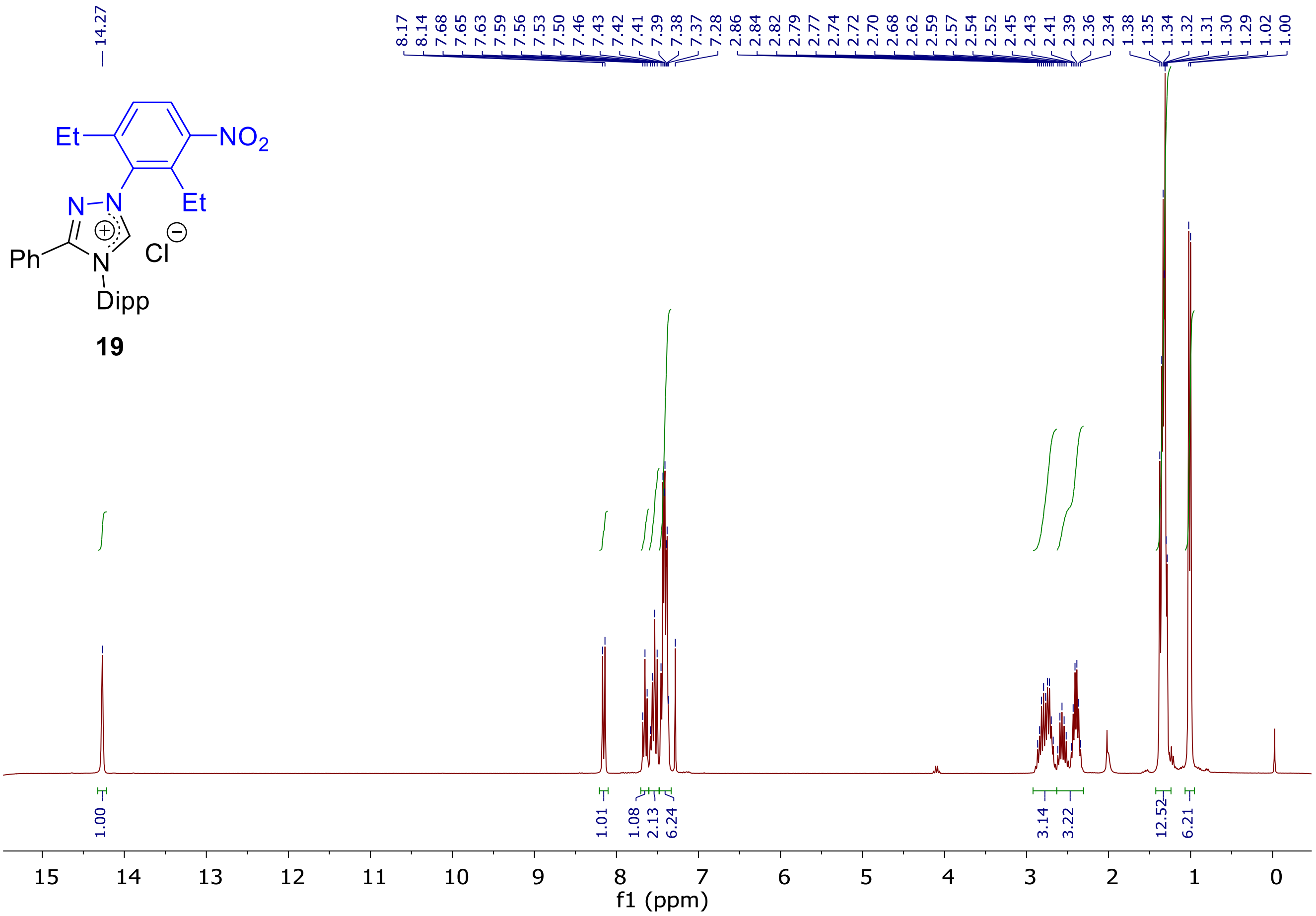


Figure S39. ^{1}H NMR (300 MHz, CDCl$_3$) of **19**

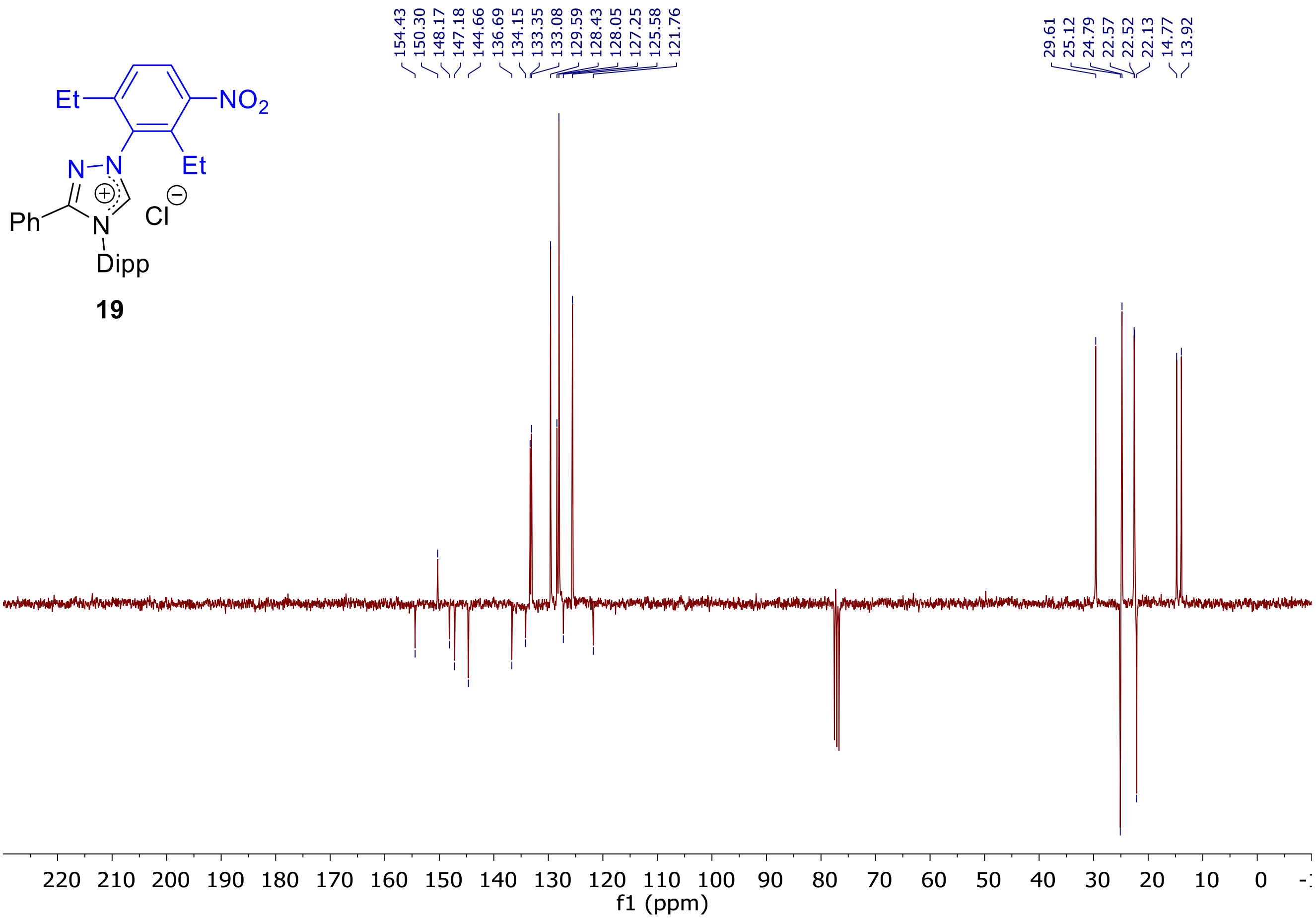


Figure S40. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of **19**

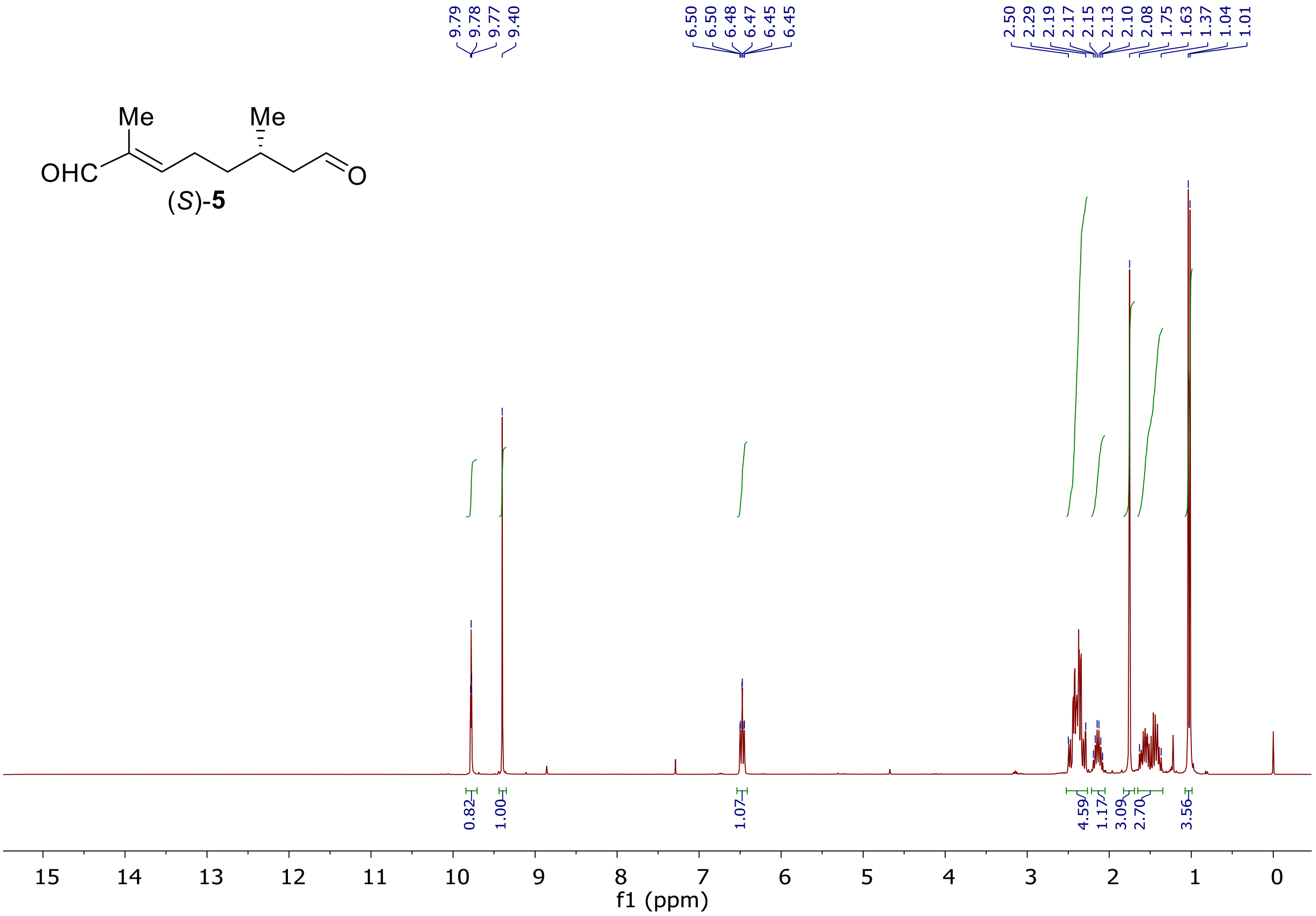


Figure S41. ^{1}H NMR (300 MHz, CDCl$_3$) of (*S*)-**5**

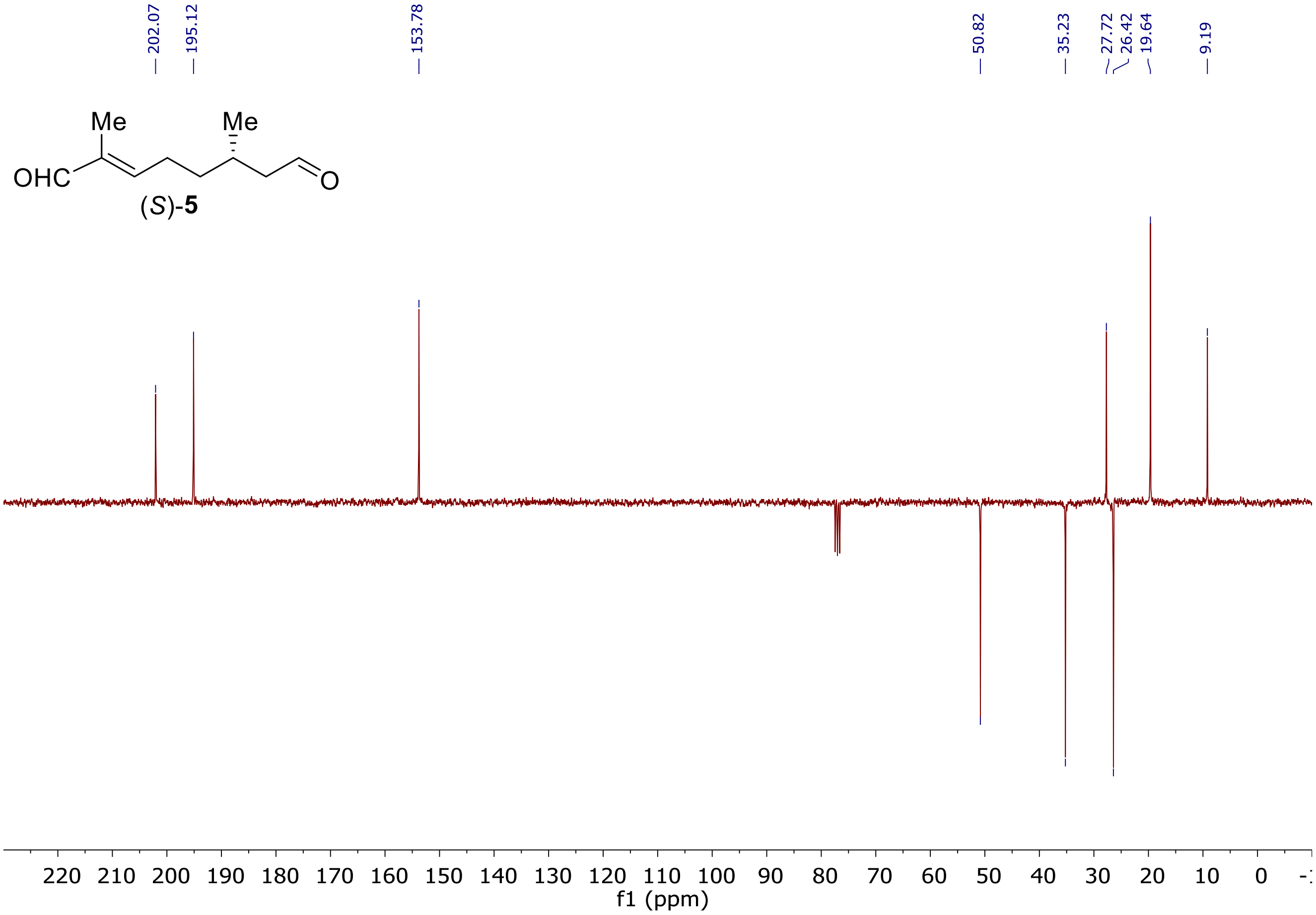


Figure S42. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of (*S*)-**5**

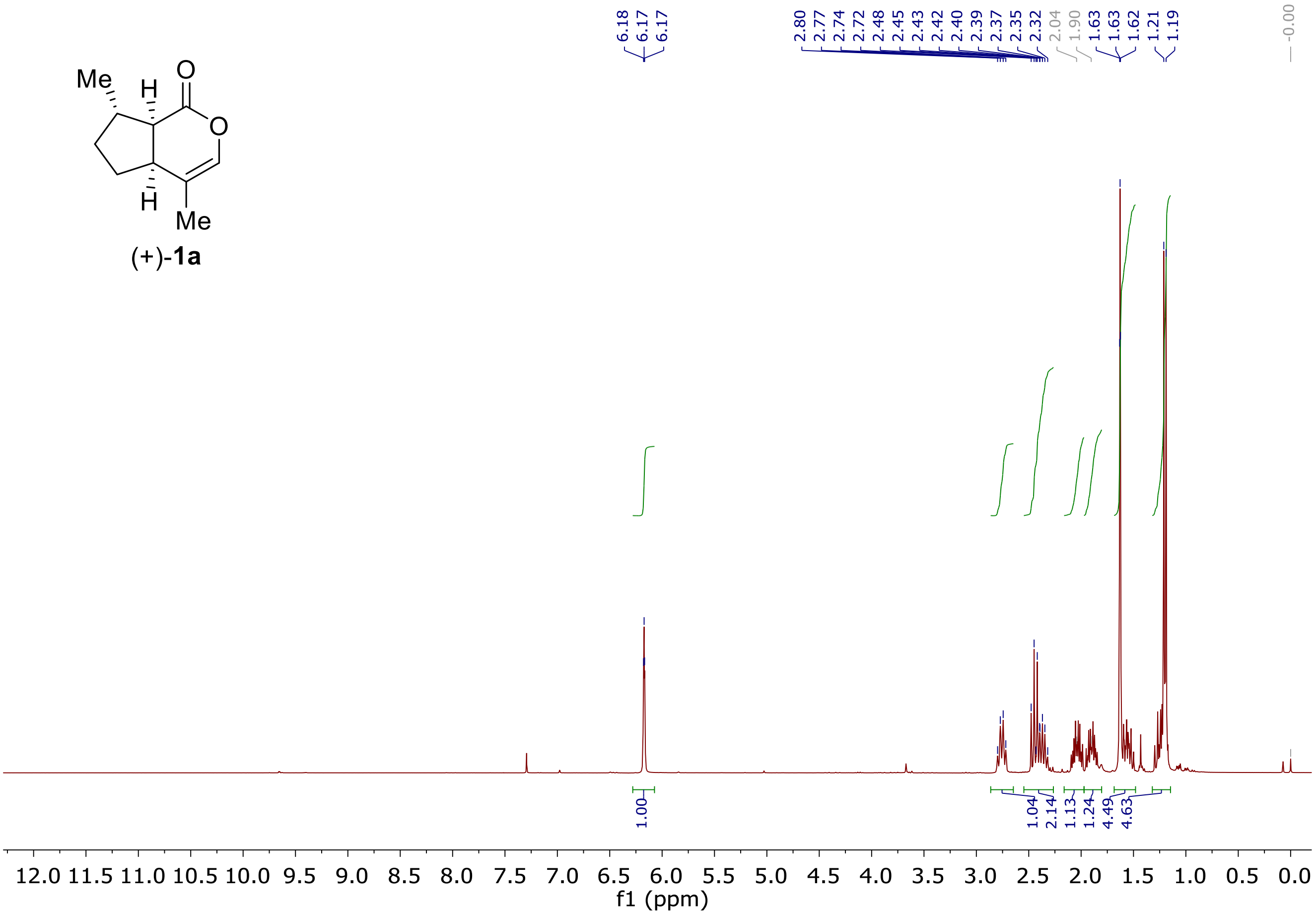


Figure S43. ^{1}H NMR (300 MHz, CDCl$_3$) of (+)-**1a**

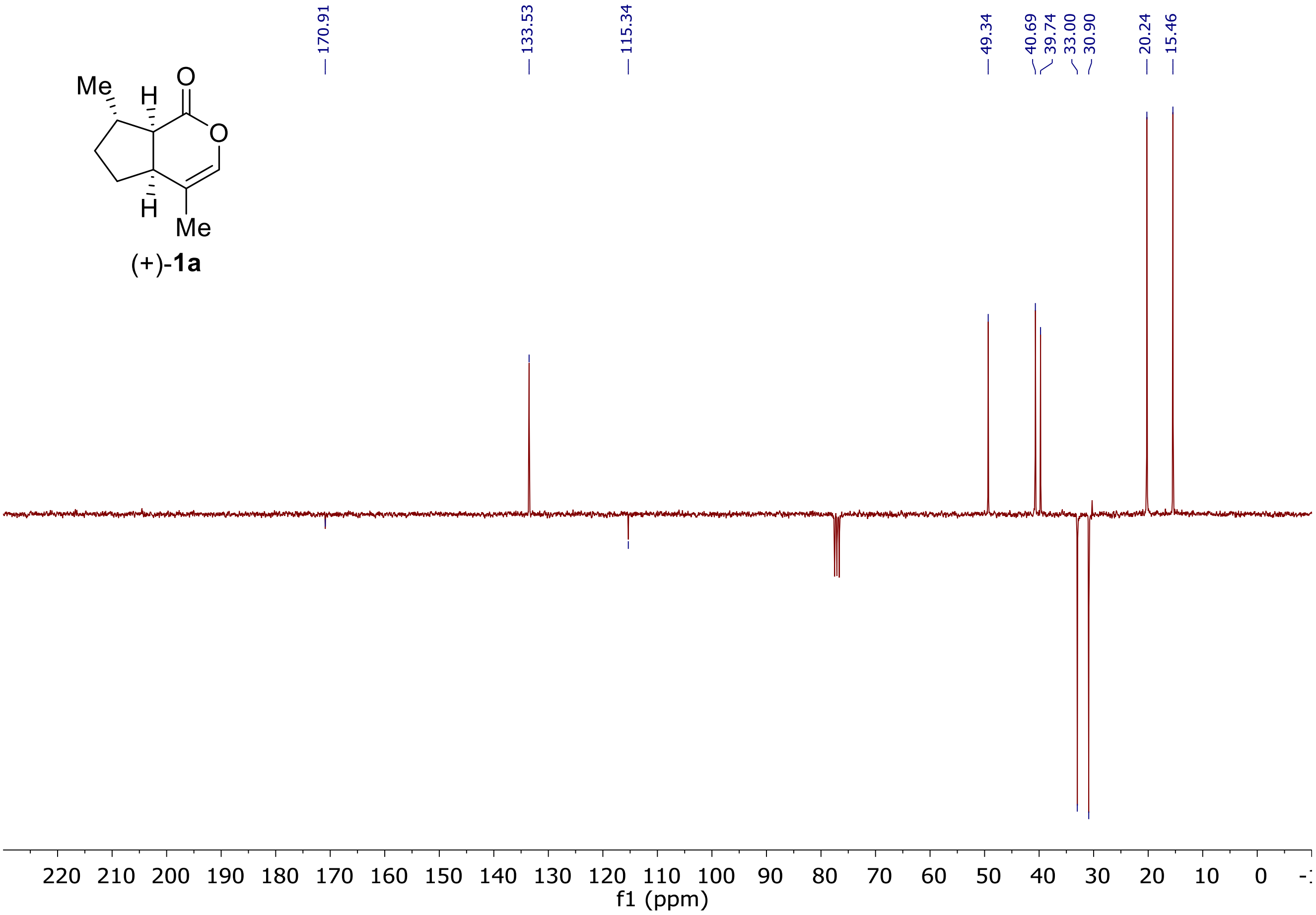


Figure S44. ^{13}C NMR (75 MHz, APT, CDCl$_3$) of (+)-**1a**

9. X-ray data

9.1 X-ray data of **14**

Table S1. Crystal data and structure refinement for **14** (CCDC 1961414)

Identification code	nok423_1	
Empirical formula	C26 H27 Cl N4 O2	
Moiety formula	C26 H27 N4 O2; Cl	
Formula weight	462.96	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions	a = 22.5200(9) Å	α= 90°.
	b = 7.8346(3) Å	β= 90°.
	c = 13.7697(5) Å	γ = 90°.
Volume	2429.46(16) Å^3	
Z	4	
Density (calculated)	1.266 Mg/m^3	
Absorption coefficient	1.629 mm^{-1}	
F(000)	976	
Crystal size	0.250 x 0.250 x 0.050 mm^3	
Theta range for data collection	3.926 to 72.115°.	
Index ranges	-27<=h<=27, -9<=k<=8, -17<=l<=16	
Reflections collected	48295	
Independent reflections	4673 [R(int) = 0.0508]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7536 and 0.4957	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4673 / 1 / 308	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0245, wR2 = 0.0634	
R indices (all data)	R1 = 0.0260, wR2 = 0.0638	
Absolute structure parameter	0.052(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.184 and -0.217 e.Å^{-3}	

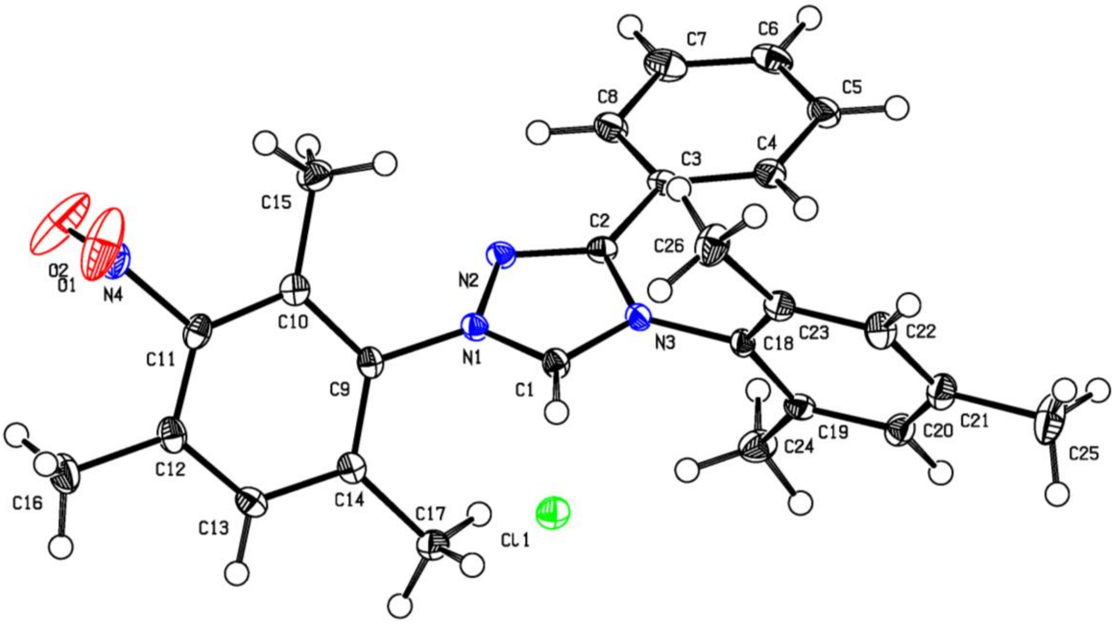


Figure S45. ORTEP of the X-ray crystal structure of **14**. Thermal ellipsoids are drawn at 50 % probability level.

9.2 X-ray data of **16**

Table S2. Crystal data and structure refinement for **16** (CCDC 1961413)

Identification code	nok_ask18n	
Empirical formula	C23 H21 Cl N4 O2	
Moiety formula	C23 H21 N4 O2; Cl	
Formula weight	420.89	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.0476(3) Å	α= 99.0720(10)°.
	b = 11.0348(4) Å	β= 111.3790(10)°.
	c = 12.0848(4) Å	γ = 103.8250(10)°.
Volume	1050.22(6) Å^3	
Z	2	
Density (calculated)	1.331 Mg/m^3	
Absorption coefficient	1.832 mm^{-1}	
F(000)	440	
Crystal size	0.200 x 0.100 x 0.100 mm^3	
Theta range for data collection	4.081 to 72.263°.	
Index ranges	-11<=h<=11, -13<=k<=13, -14<=l<=14	
Reflections collected	23402	
Independent reflections	4116 [R(int) = 0.0372]	
Completeness to theta = 67.679°	99.7 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7536 and 0.5916
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4116 / 0 / 278
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0337, wR2 = 0.0895
R indices (all data)	R1 = 0.0366, wR2 = 0.0921
Extinction coefficient	n/a
Largest diff. peak and hole	0.224 and -0.323 e.Å^{-3}

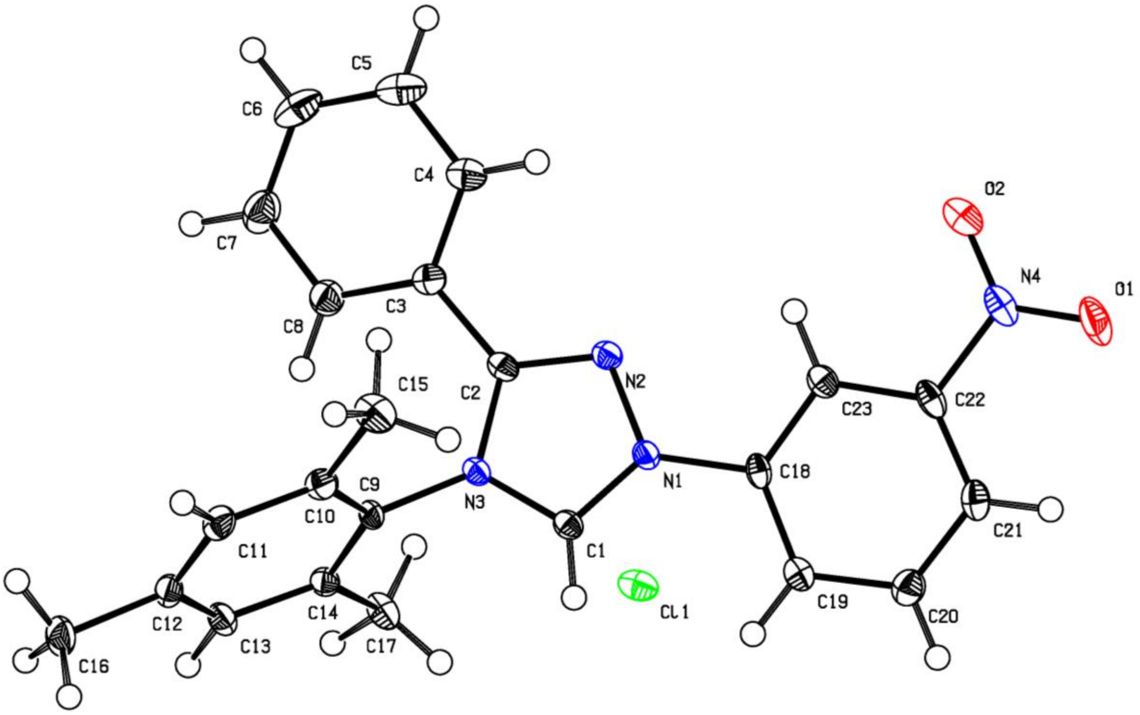


Figure S46. ORTEP of the X-ray crystal structure of **16**. Thermal ellipsoids are drawn at 50 % probability level.

9.3 X-ray data of **17**

Table S3. Crystal data and structure refinement for **17** (CCDC 1961415)

Identification code	nok427ggn1_CHCl3	
Empirical formula	C30 H34 Cl4 N4 O2	
Moiety formula	C29 H33 N4 O2; Cl; C H Cl3	
Formula weight	624.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 11.3217(7) Å	α= 112.3446(18)°.
	b = 11.5130(7) Å	β= 97.9298(18)°.

	c = 13.6237(8) Å γ = 103.7307(19)°.
Volume	1543.21(16) Å^3
Z	2
Density (calculated)	1.344 Mg/m^3
Absorption coefficient	3.756 mm^{-1}
F(000)	652
Crystal size	0.400 x 0.400 x 0.200 mm^3
Theta range for data collection	3.627 to 72.173°.
Index ranges	-13<=h<=13, -13<=k<=14, -16<=l<=16
Reflections collected	28124
Independent reflections	6005 [R(int) = 0.0671]
Completeness to theta = 67.679°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7536 and 0.4808
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6005 / 0 / 369
Goodness-of-fit on F^2	1.054
Final R indices [I>2sigma(I)]	R1 = 0.0401, wR2 = 0.1040
R indices (all data)	R1 = 0.0539, wR2 = 0.1080
Extinction coefficient	0.0069(4)
Largest diff. peak and hole	0.424 and -0.492 e.Å^{-3}

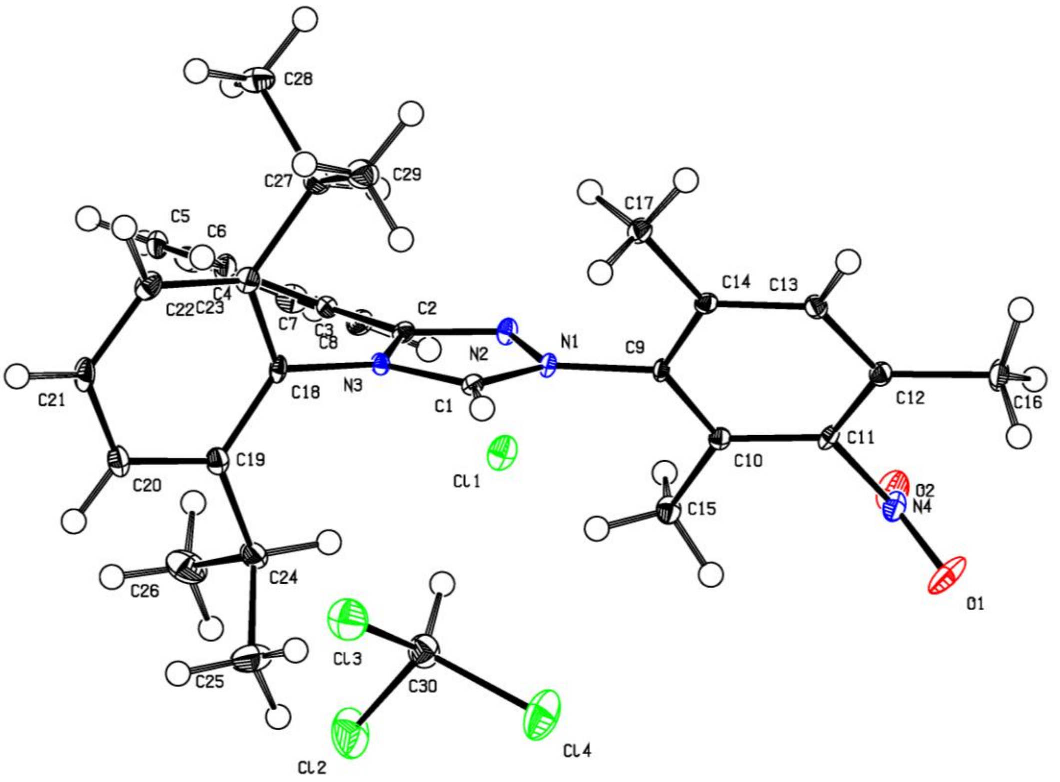


Figure S47. ORTEP of the X-ray crystal structure of **17•**CHCl$_3$. Thermal ellipsoids are drawn at 50 % probability level.

9.4 X-ray data of **18**

Table S4. Crystal data and structure refinement for **18** (CCDC 1961416)

Identification code	nok380nn	
Empirical formula	C30 H33 Cl7 N4 O2	
Moiety formula	C28 H31 Cl N4 O2; "(C H Cl3)	
Formula weight	729.75	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.6459(8) Å	α= 83.456(3)°.
	b = 12.5634(8) Å	β= 76.905(3)°.
	c = 14.9967(14) Å	γ = 83.434(2)°.
Volume	1751.2(2) Å^{3}	
Z	2	
Density (calculated)	1.384 Mg/m^{3}	
Absorption coefficient	5.447 mm^{-1}	
F(000)	752	
Crystal size	0.300 x 0.200 x 0.050 mm^{3}	
Theta range for data collection	3.038 to 72.338°.	
Index ranges	-10<=h<=11, -15<=k<=15, -18<=l<=18	
Reflections collected	78799	
Independent reflections	6917 [R(int) = 0.0506]	
Completeness to theta = 67.679°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7536 and 0.4551	
Refinement method	Full-matrix least-squares on F^{2}	
Data / restraints / parameters	6917 / 0 / 398	
Goodness-of-fit on F^{2}	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0417, wR2 = 0.1022	
R indices (all data)	R1 = 0.0451, wR2 = 0.1048	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.729 and -0.880 e.Å^{-3}	

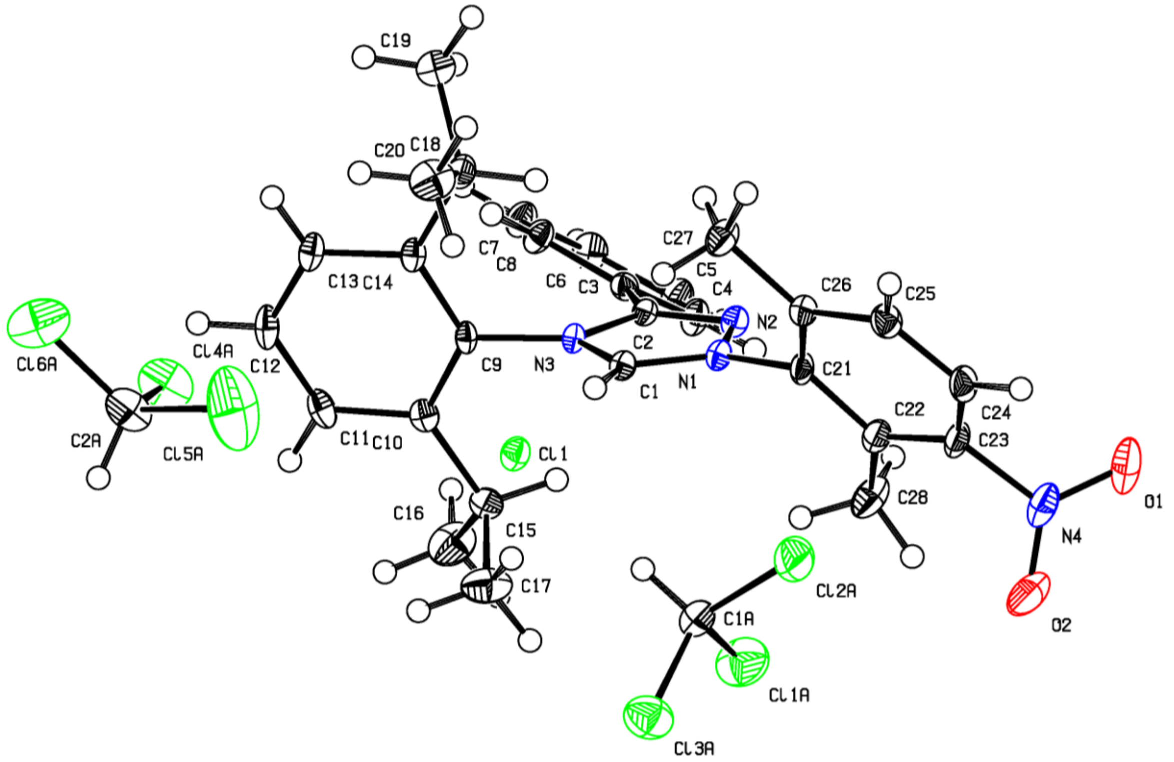


Figure S48. ORTEP of the X-ray crystal structure of **18•**2CHCl$_3$. Thermal ellipsoids are drawn at 50 % probability level.