Supporting Information:

1,2-Dihydropyrimidine Synthesis via Titanium-Mediated Multicomponent Coupling of Alkynes, Nitriles, and Aldehydes

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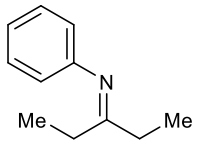
General considerations

All air- and moisture-sensitive compounds were handled in a glovebox under nitrogen atmosphere. Common solvents for inert conditions were degassed and dried with a Pure Process Technology solvent purification system (toluene, CH_2Cl_2, pentane, hexane, MeCN) and stored over 3 Å molecular sieves. NMR solvents were vacuum transferred from Na/Ph_2CO (C_6D_6) or CaH_2 ($CDCl_3$). C_6D_5Br was prepared from the literature procedure,[1] distilled, freeze-pump-thaw degassed, and then dried over alumina and 3 Å molecular sieves. 1-methoxy-4-(prop-1-yn-1-yl)benzene, 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene, 1-(prop-1-yn-1-yl)-4-(trifluoromethyoxy)benzene were prepared according to the literature procedure.[2,3] Liquid alkynes, nitriles, and aldehydes were distilled, freeze-pump-thaw degassed, and passed through alumina in a glovebox. Solid nitriles and all other reagents were dried overnight under vacuum prior to use or used as purchased. $[py_2TiCl_2(NPh)]_2$ and $py_3TiCl_2(NPh)$ were prepared according to the literature procedure.[4] ^1H, ^{13}C, and ^{19}F NMR spectra were collected on Bruker Avance III HD 400 and 500 MHz spectrometers. Chemical shifts were referenced to the proton signals of the solvent ($CHCl_3$, 7.26 ppm, 77.16 ± 0.06 ppm; C_6D_6, 7.16 ppm, 128.06 ± 0.02 ppm). ^1H NMR monitoring of the 1,2-dihydropyrimidine synthesis in C_6D_5Br were referenced to the proton signal of the internal standard 1,3,5-trimethoxybenzene (TMB, $-OCH_3$, s, 3.52 ppm). Qualitative GC-MS chromatographs were collected on an Agilent 8890 GC System with 5977B GC/MSD. GC-FID chromatographs were collected on an Agilent 7890B GC system equipped with an HP-5 ms Ultra Inert column (30 m x 250 μm x 0.25 μm), an oxidation-methanation reactor (Polyarc® System, Activated Research Company), and an FID detector for quantitative carbon detection. High-resolution quadrupole time-of-flight mass spectrometry (QTOF-MS) was performed on isolated samples using a Sciex X500R QTOF-MS.

Synthesis of ADA ligands and titanacycles

_N_-phenylpentan-3-imine



N-phenylpentan-3-imine was synthesized using a general procedure for ketimines adapted from the literature.[5] Dry CH_2Cl_2 (100 mL) was added to a 200 mL Schlenk flask that was placed under N_2. 3-pentanone (1.0 equiv, 6.3 mL, 0.060 mol) was added via syringe, followed by aniline (1.0 equiv, 5.5 mL, 0.060 mol) and triethylamine (2.0 equiv, 17 mL, 0.12 mol). $TiCl_4$ (0.5 equiv, 3.4 mL, 0.03 mmol) was then slowly added dropwise to the orange solution to minimize exotherm. The solution was left to stir overnight and filtered through celite the next day. The filtrate was concentrated to a yellow oil and colorless solid. The oil was diluted with hexanes (150 mL) and then washed with sat. Na_2CO_3 (2 x 20 mL) and brine (50 mL). The organics were dried over Na_2SO4, filtered, and concentrated to a yellow oil (6.268 g, 65% yield). **^{1}H NMR (400 MHz. C_6D_6, δ, ppm):** 7.18 (m, 2H), 6.92 (t, J = 7.4 Hz, 1H), 6.74 (dd, J = 8.4 Hz, 1.2 Hz, 2H), 2.16 (q, J = 7.3 Hz, 2H), 1.88 (q, J = 7.7 Hz, 2H), 1.19 (t, J = 7.3 Hz, 3H), 0.70 (t, J = 7.7 Hz, 3H). **^{13}C{^{1}H} NMR (101 MHz, C_6D_6, δ, ppm):** 175.25, 152.63, 129.18, 122.73, 119.58, 30.97, 26.49, 11.76, 10.46.

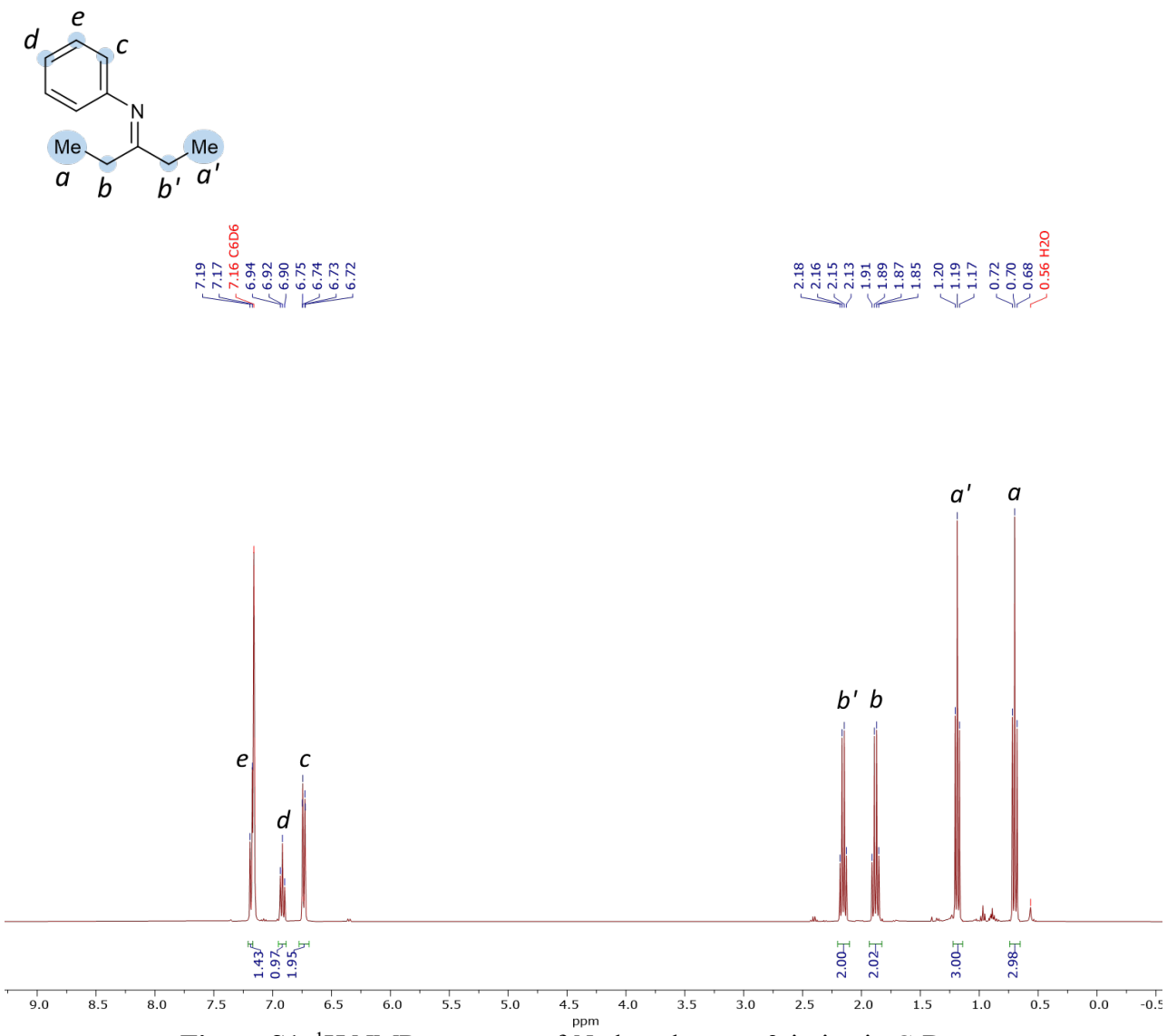


Figure S1. ^{1}H NMR spectrum of *N*-phenylpentan-3-imine in C_6D_6.

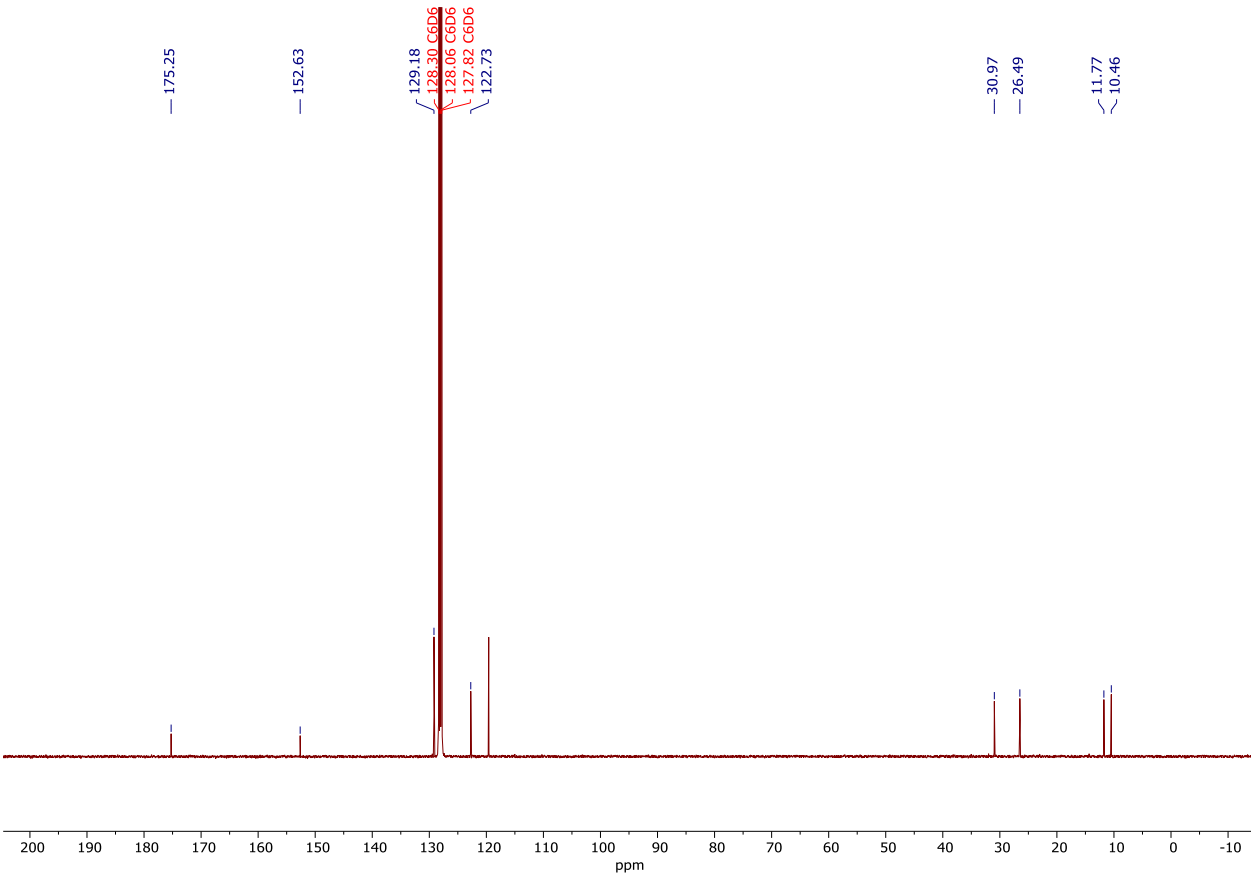
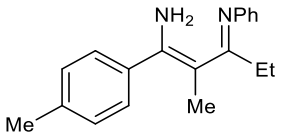


Figure S2. $^{13}C\{^{1}H\}$ NMR spectrum of *N*-phenylpentan-3-imine in C_6D_6.

2-methyl-3-(phenylimino)-1-(p-tolyl)pent-1-en-1-amine



The 4-azadiene-1-amine was prepared using a modified procedure from the literature.[6,7] LDA was first prepared by addition of dry THF (100 mL) and 3.4 mL of $^{i}Pr_2NH$ (1.0 equiv, 24 mmol) that had been stored over CaH_2 to a 250 mL Schlenk flask. The flask was cooled to -78 °C and ^{n}BuLi (10 mL, 1.1 equiv, 2.5M, 25 mmol) was added. The solution was left to stir for 1 h. 100 mL of dry THF and *N*-phenylpentan-3-imine (1.0 equiv, 3.72 g, 23.1 mmol) was added to a second 500 mL Schlenk flask. The flask was cooled to -78 °C and the LDA solution was cannula transferred into the flask with the imine and left to stir for 1 h at -78 °C. Following this, solid anhydrous $ZnCl_2$ was added (2.2 equiv, 6.83 g, 50.1 mmol) under a positive pressure of N_2. The solution was allowed to stir for 10 minutes before the cold bath was removed to ensure that all the $ZnCl_2$ had dissolved. Solid *p*-tolunitrile (1.3 equiv, 3.64 g, 31 mmol) was then added under a stream of N_2 and the yellow solution was then left to stir for 16 h. The reaction was then refluxed for 6 h at 80 °C during which the solution turned a dark orange color. Upon cooling, 60 mL of 2 M NaOH solution was added. The yellow solution was decanted from a white precipitate into a separatory funnel, extracted with ether, dried over Na_2SO_4, and concentrated to a yellow solid. The solid was recrystallized in EtOH to provide yellow needle-like crystals (4.27 g, 67% yield). ^{1}H and ^{13}C NMR data for the title compound is given here in C_6D_6, and has previously reported in $CDCl_3$.[7] **^{1}H NMR (400 MHz. C_6D_6, δ, ppm):** 7.28 – 7.17 (m, 4H), 7.00 – 6.90 (m, 5H), 2.37 (q, J = 7.6 Hz, 2H), 2.09 (s, 3H), 1.87 (s, 3H), 0.98 (t, J = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR (101 MHz, C_6D_6, δ, ppm):** 174.61, 154.55, 152.27, 138.51, 137.85, 129.28, 129.10, 128.52, 122.44, 121.29, 96.53, 25.24, 21.16, 16.67, 13.17.

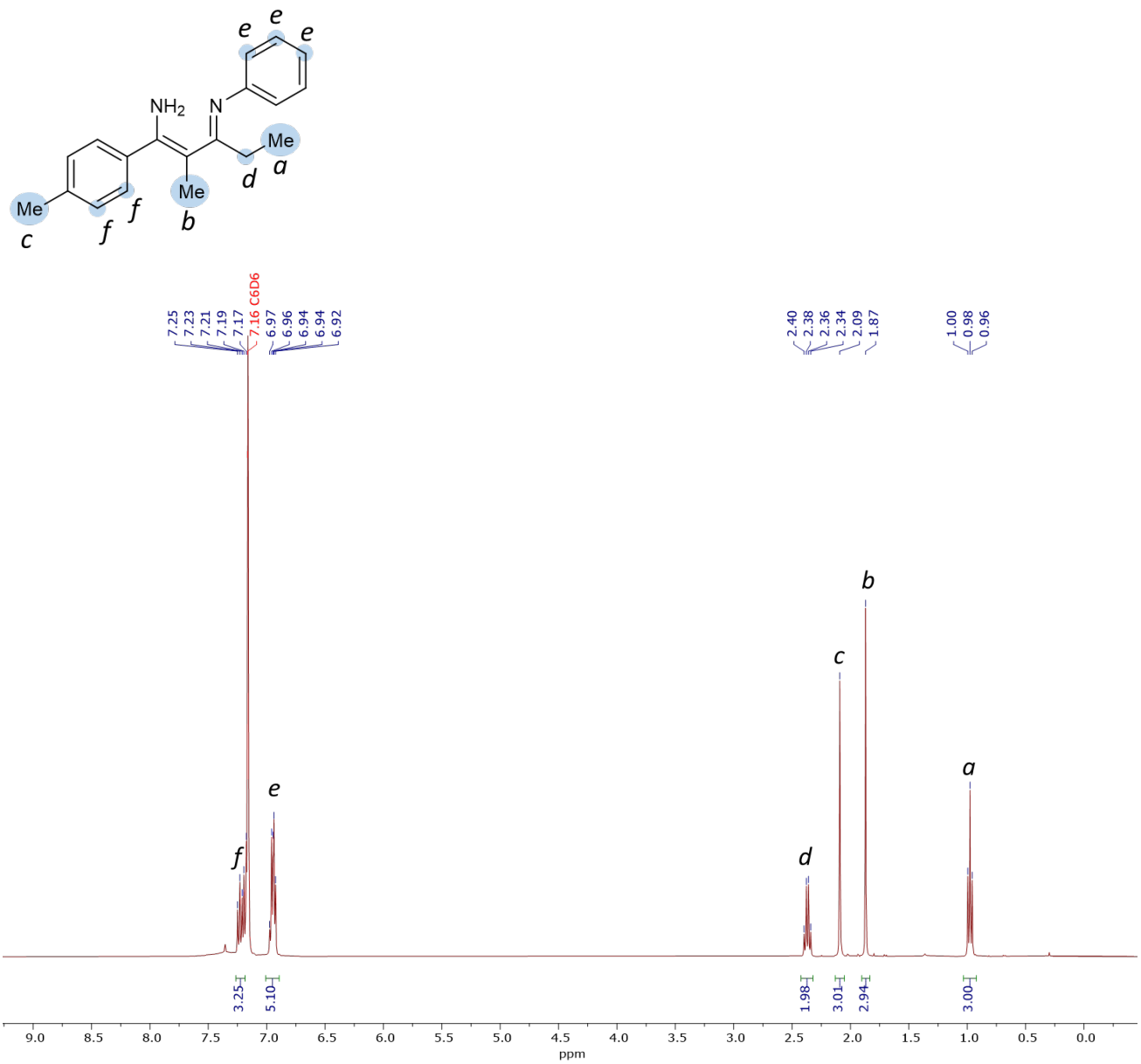


Figure S3. ^{1}H NMR spectrum of 2-methyl-3-(phenylimino)-1-(p-tolyl)pent-1-en-1-amine in C_6D_6.

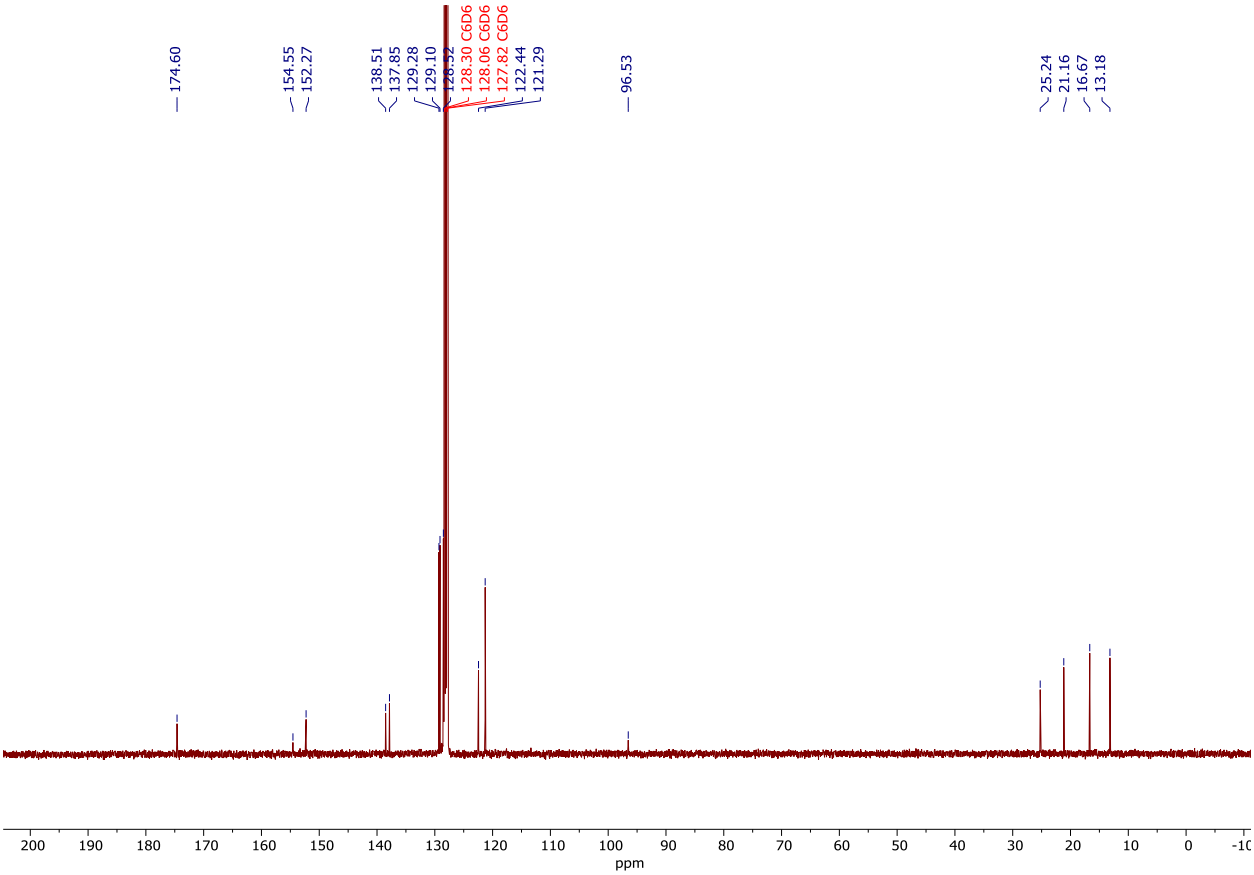
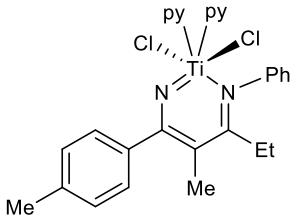


Figure S4. $^{13}C\{^{1}H\}$ NMR spectrum of 2-methyl-3-(phenylimino)-1-(p-tolyl)pent-1-en-1-amine in C_6D_6.

$py_2TiCl_2(ADA)^{ptol,Me,Et}$ (3)



The synthesis of $py_2TiCl_2(ADA)^{ptol,Me,Et}$ was adapted from literature procedures.[7] In the glovebox, $TiCl_4(THF)_2$ (0.1206 g, 0.3612 mmol) and THF (1 mL) were added to a 20 mL scintillation vial with a Teflon stir bar and cooled to -35 °C. A solution of 4-azadiene-1-amine (1.0 equiv, 0.1004 g, 0.3606 mmol) in THF (1 mL) at -35 °C was added to the $TiCl_4(THF)_2$ slurry, resulting in a dark purple solution. In a separate vial, LiHMDS (2.02 equiv, 0.1218 g, 0.7277 mmol) was dissolved in THF (1 mL), cooled to -35 °C, and then added to the stirring solution. The resulting dark brown solution was allowed to stir at room temperature for 2 h before the volatiles were removed to dryness. The residue was taken up in benzene (10 mL) and filtered through celite. The solution was concentrated to ~3 mL, pyridine (0.7 mL) was added, and then set aside to allow for crystal formation. After 72 h, crystals were not observed, so the solution was layered with pentane. A mixture of dark brown crystals and powder was isolated following filtration (102.6 mg, 51% yield). ^{1}H and ^{13}C NMR data for the title compound agrees with those previously reported.[7] **^{1}H NMR (400 MHz, C_6D_6, δ, ppm):** 8.80 (br s, 5H), 7.75 (d, J = 7.4 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 6.1 Hz, 2H), 6.95 – 6.88 (m, 4H), 6.61 (br s, 3 H), 6.27 (br s, 2H), 2.20 (q, J = 7.5 Hz, 2H), 2.05 (s, 3H), 1.93 (s, 3H), 0.84 (t, J = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR (101 MHz, C_6D_6, δ, ppm):** 177.86, 170.17, 150.86, 147.46, 138.28, 134.18, 129.17, 128.62, 128.59, 125.91, 122.54, 26.73, 21.19, 17.62, 12.28.

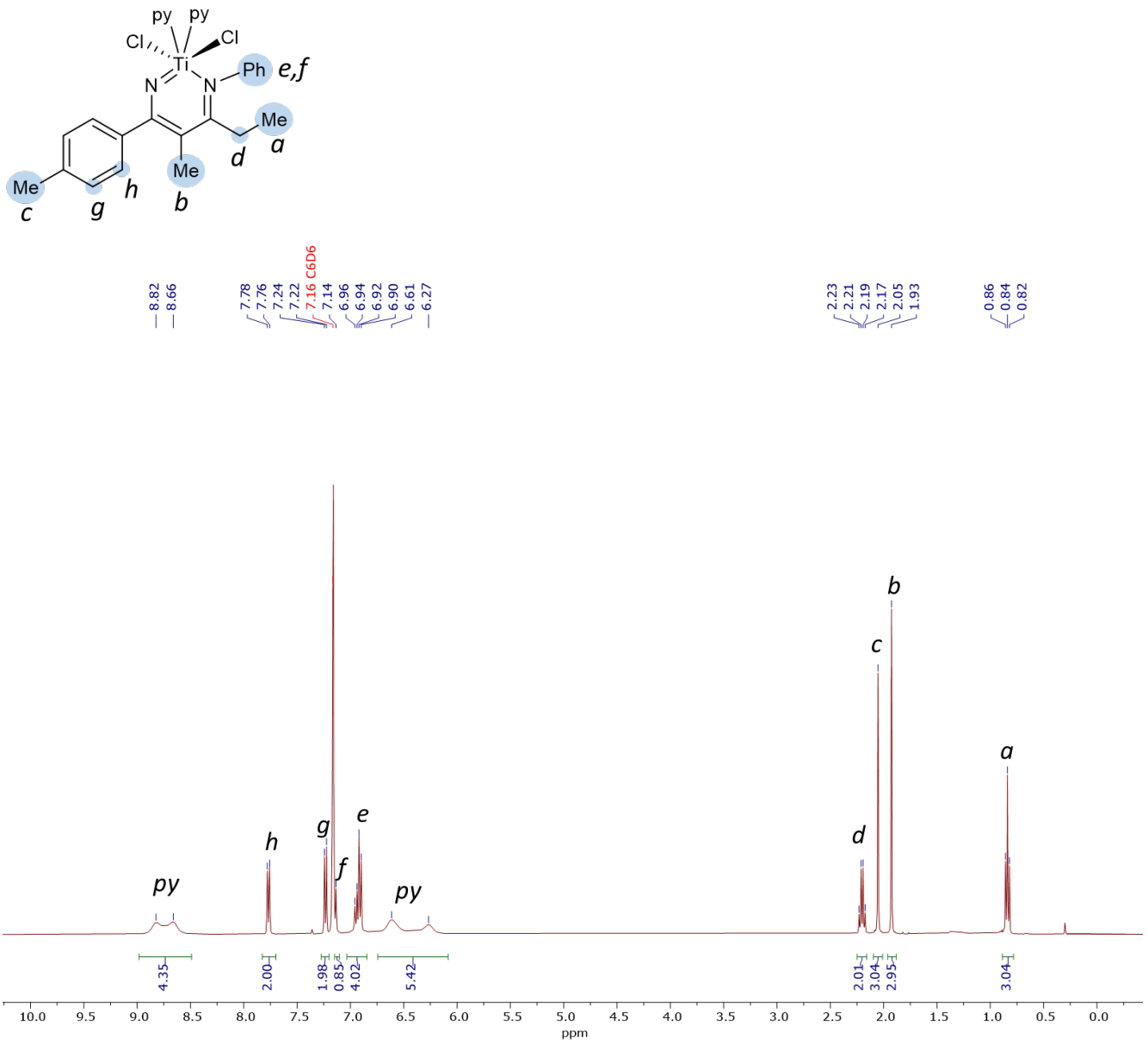


Figure S5. ^{1}H NMR spectrum of $py_2TiCl_2(ADA)^{ptol,Me,Et}$ **3** in C_6D_6.

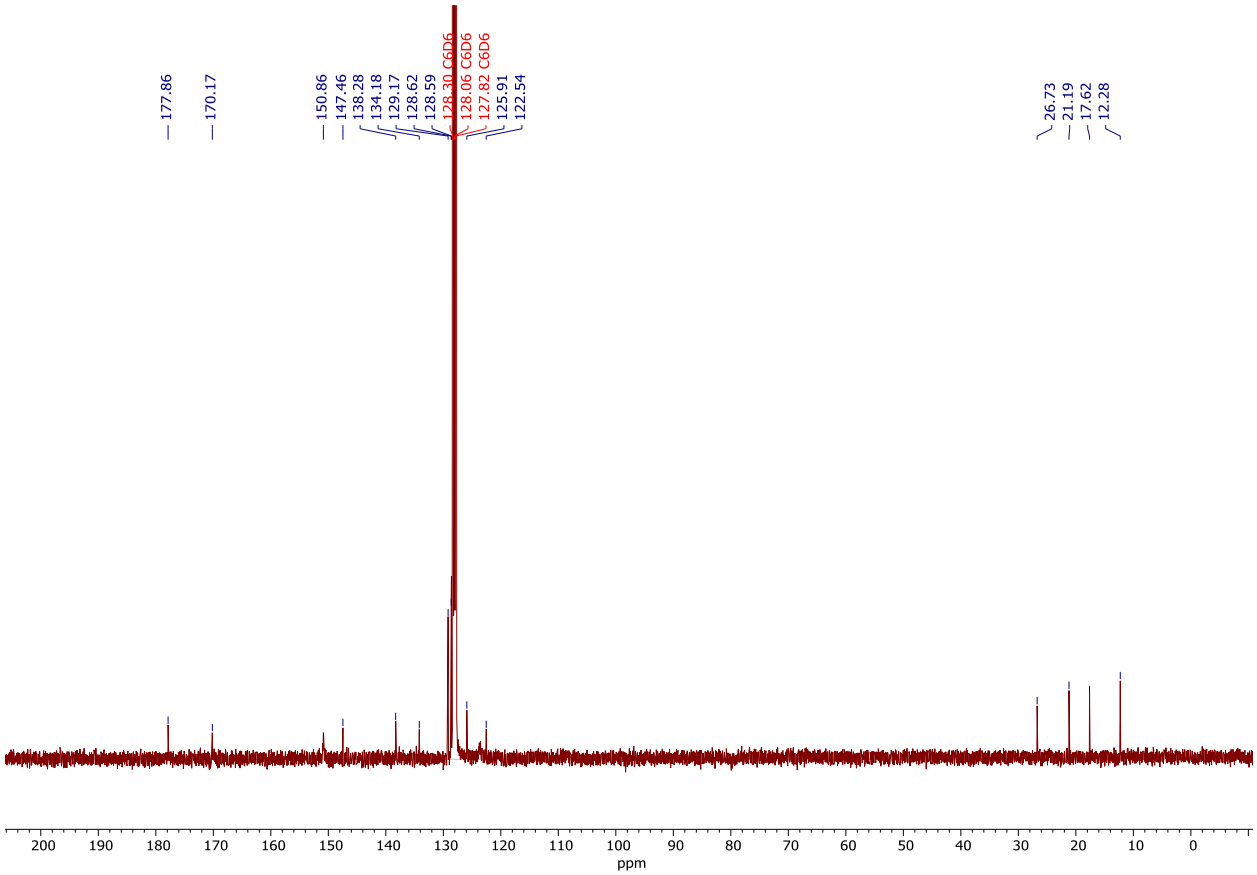
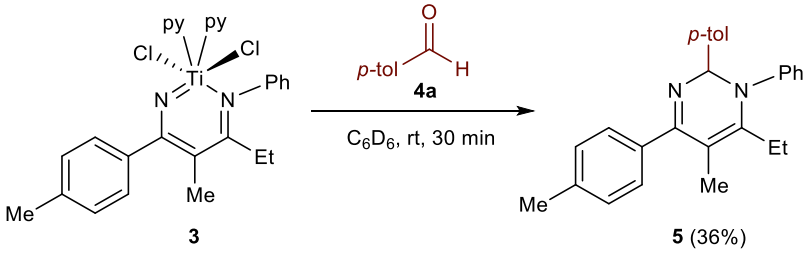


Figure S6. $^{13}C\{^{1}H\}$ NMR spectrum of $py_2TiCl_2(ADA)^{ptol,Me,Et}$ **3** in C_6D_6.

1,2-dihydropyrimidine from titanacycle, isolated



Procedure: In the glovebox, $py_2TiCl_2(ADA)^{ptol,Me,Et}$ **3** (221.4 mg, 0.400 mmol, 1.00 equiv.) was added to a 20 mL scintillation vial with a Teflon stir bar, followed by benzene (6 mL) and *p*-tolualdehyde **4a** (48.0 mg, 0.400 mmol, 1.00 equiv.). The vial was sealed, taken out of the glovebox, and allowed to stir for 30 min at room temperature. The reaction mixture was then quenched with Na_2CO_3, and the aqueous layer was extracted with hexanes. The combined organics were dried with $MgSO_4$, filtered, and then the volatiles were reduced to obtain a yellow oil (54.4 mg. 37% isolated yield). **^{1}H NMR (400 MHz, C_6D_6, δ, ppm):** 7.74 (d, J = 8.0 Hz, 4H), 7.13 – 7.06 (m, 6H), 7.06 – 7.00 (m, 2H), 6.91 (t, J = 6.9 Hz, 1H), 6.72 (s, 1H), 2.27 (m, 1H), 2.15 (m and s, 1H and 6H), 1.71 – 1.67 (s, 3H), 0.79 (t, J = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR (101 MHz, C_6D_6, δ, ppm):** 165.99, 147.36, 146.46, 139.81, 138.65, 137.18, 137.14, 129.49, 129.29, 129.27, 128.93, 128.88, 128.59, 127.44, 124.04, 113.86, 78.22, 22.66, 21.32, 21.15, 14.40, 12.08.

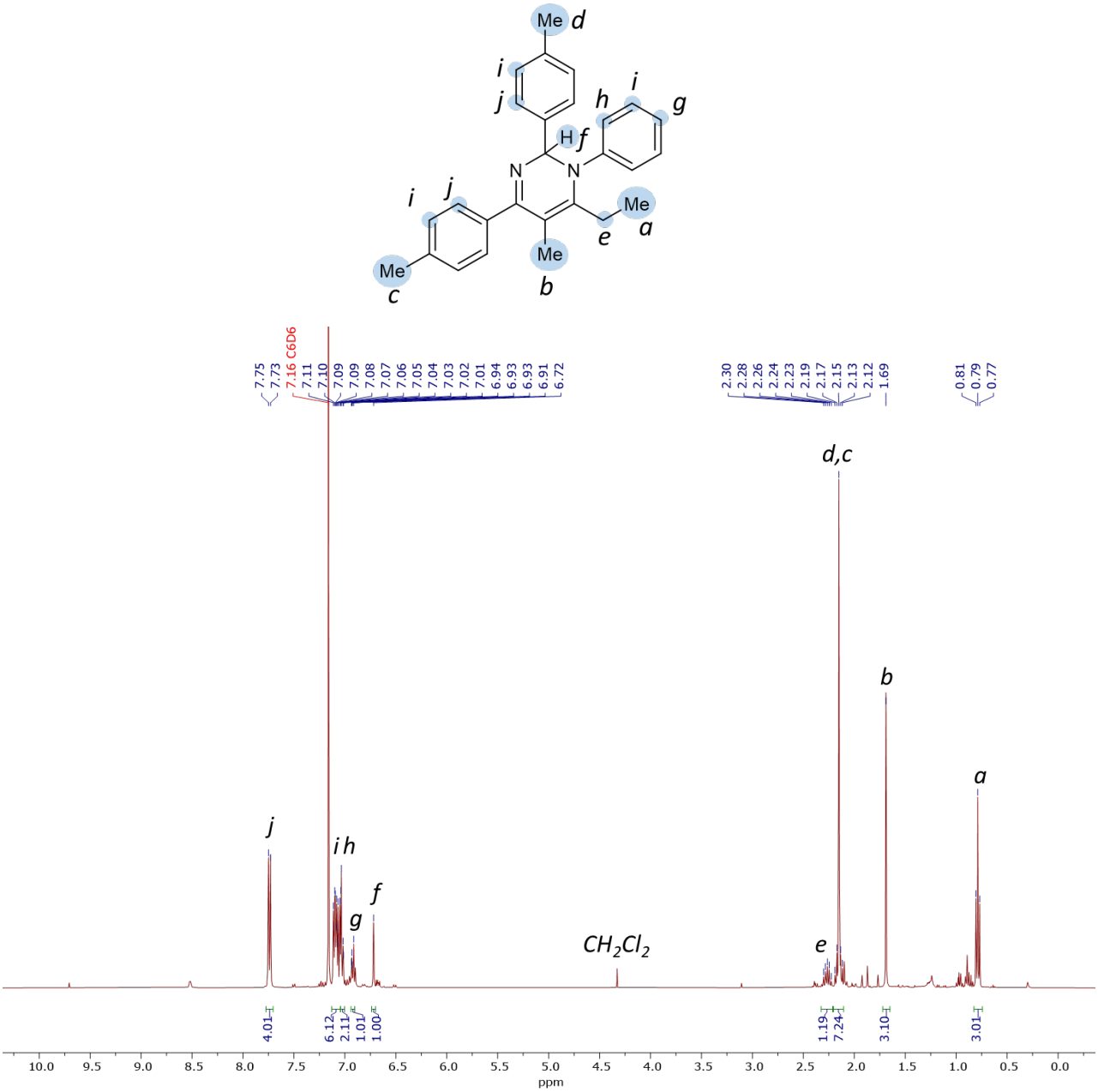


Figure S7. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5** in C_6D_6.

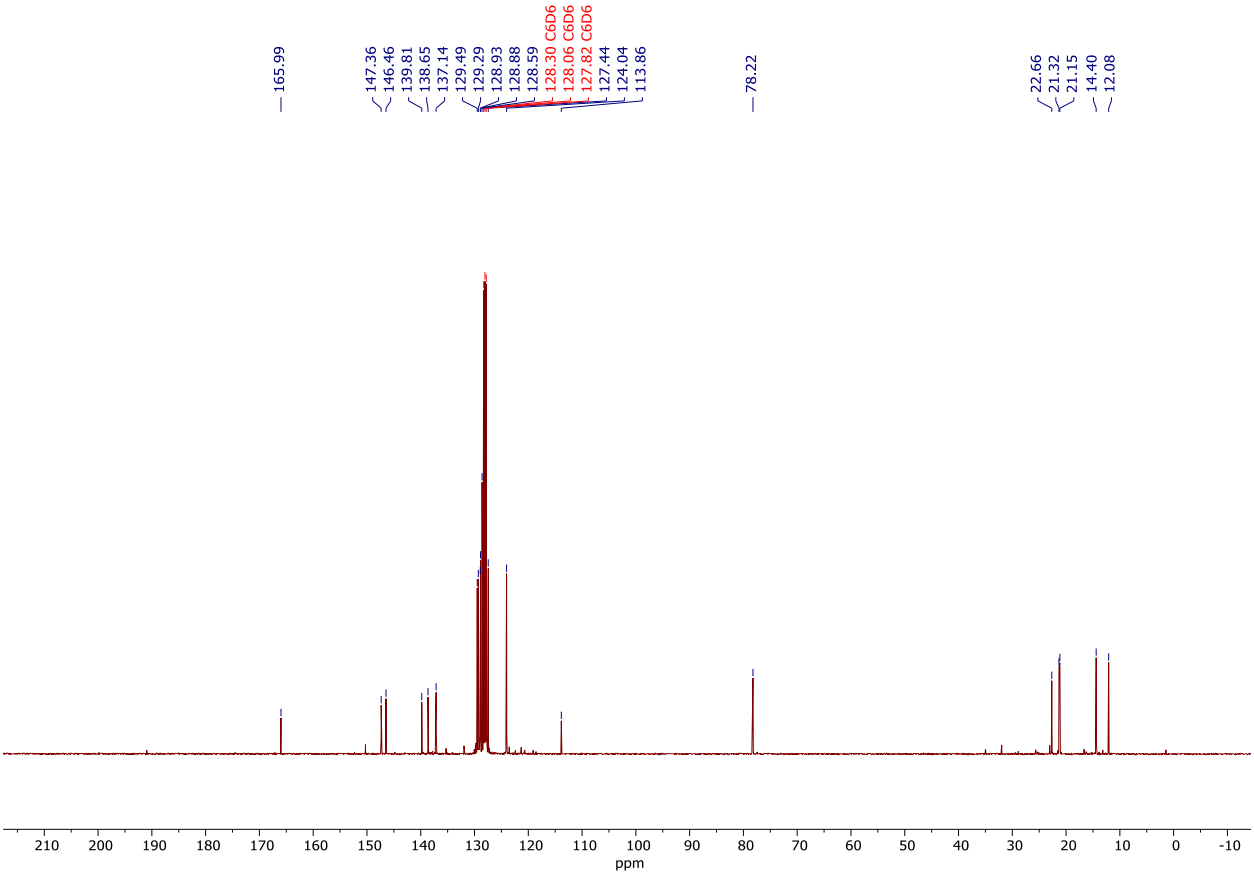
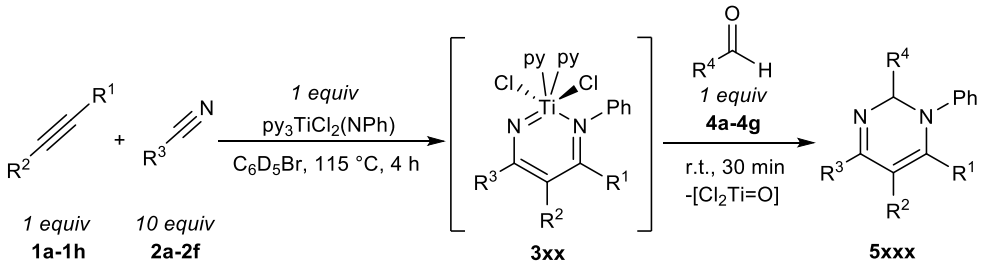
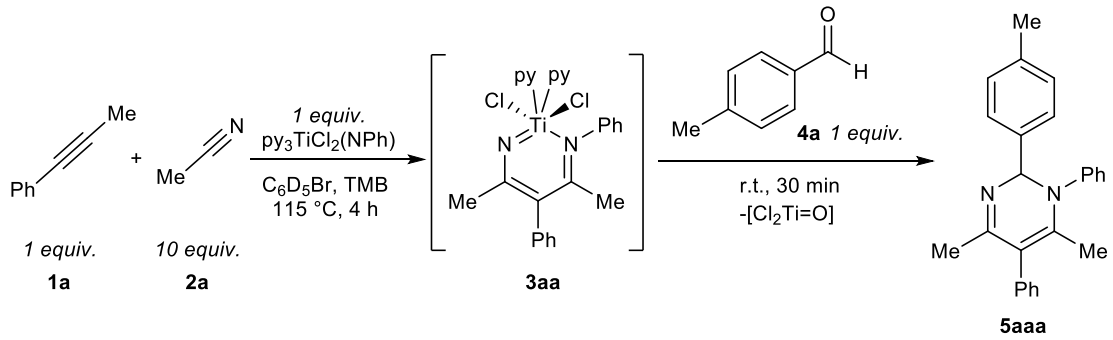


Figure S8. $^{13}C\{^{1}H\}$ NMR spectrum of 1,2-dihydropyrimidine **5** in C_6D_6.

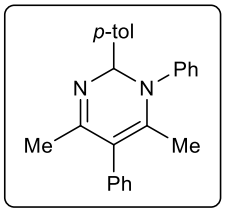
Multicomponent coupling of $py_3TiCl_2(NPh)$, alkynes, nitriles, and aldehydes for synthesis of 1,2-dihydropyrimidines (*in situ,* NMR scale)



General Procedure: In a glovebox, $py_3TiCl_2(NPh)$ (22.0 mg, 0.046 mmol, 1 equiv.) was added to a J Young NMR tube. Separately, the alkyne (0.046 mmol, 1 equiv.), nitrile (0.460 mmol, 10 equiv.), 1,3,5-trimethoxybenzene (2.0 mg), and C_6D_5Br (0.5 mL) were added to a 4 mL vial initially, and then the mixture was added to the J Young tube once mixed. The tube was capped and a t = 0 h ^1H NMR spectrum was taken, after which the tube was heated to 115 °C in a pre-heated oil bath for 4 h, turning the reaction mixture from an opaque orange to a dark brown. After recording a t = 4 h ^1H NMR spectrum, the tube was brought back into the glovebox and the aldehyde (0.046 mmol, 1 equiv.) was added. The tube was recapped, shaken, and left to sit for 30 min at room temperature, followed by obtaining a final ^1H NMR spectrum.



4,6-dimethyl-1,5-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aaa)



43% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.55 (d, *J* = 7.9 Hz, 2H), 7.13 – 7.09 (m, 8H), 7.06 – 7.02 (m, 4H), 6.49 (s, 1H), 2.21 (s, 3H), 1.92 (s, 3H), 1.71 (s, 3H).

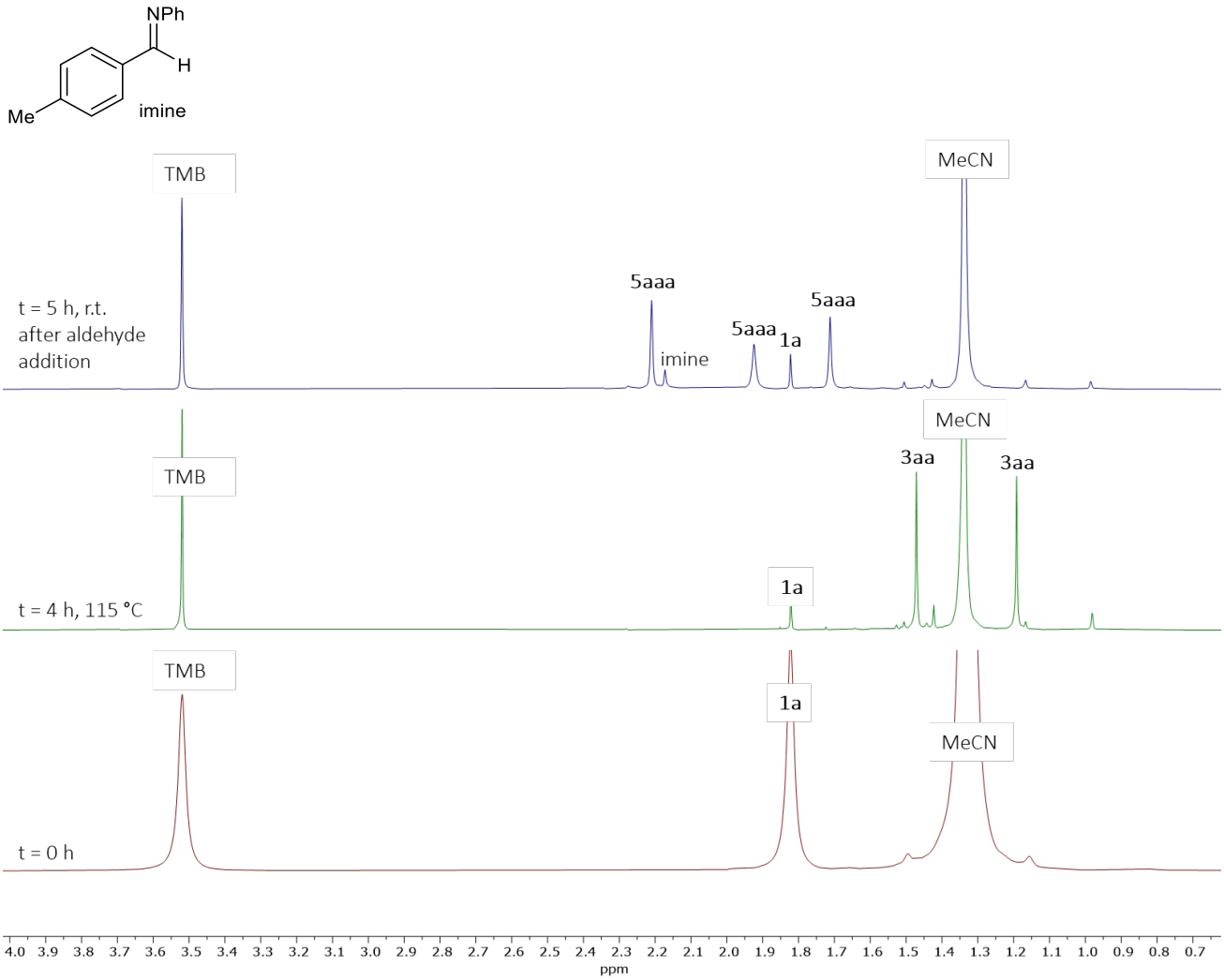


Figure S9. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 61% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aaa** in 43% yield (78% conversion of metallacycle **3aa**).

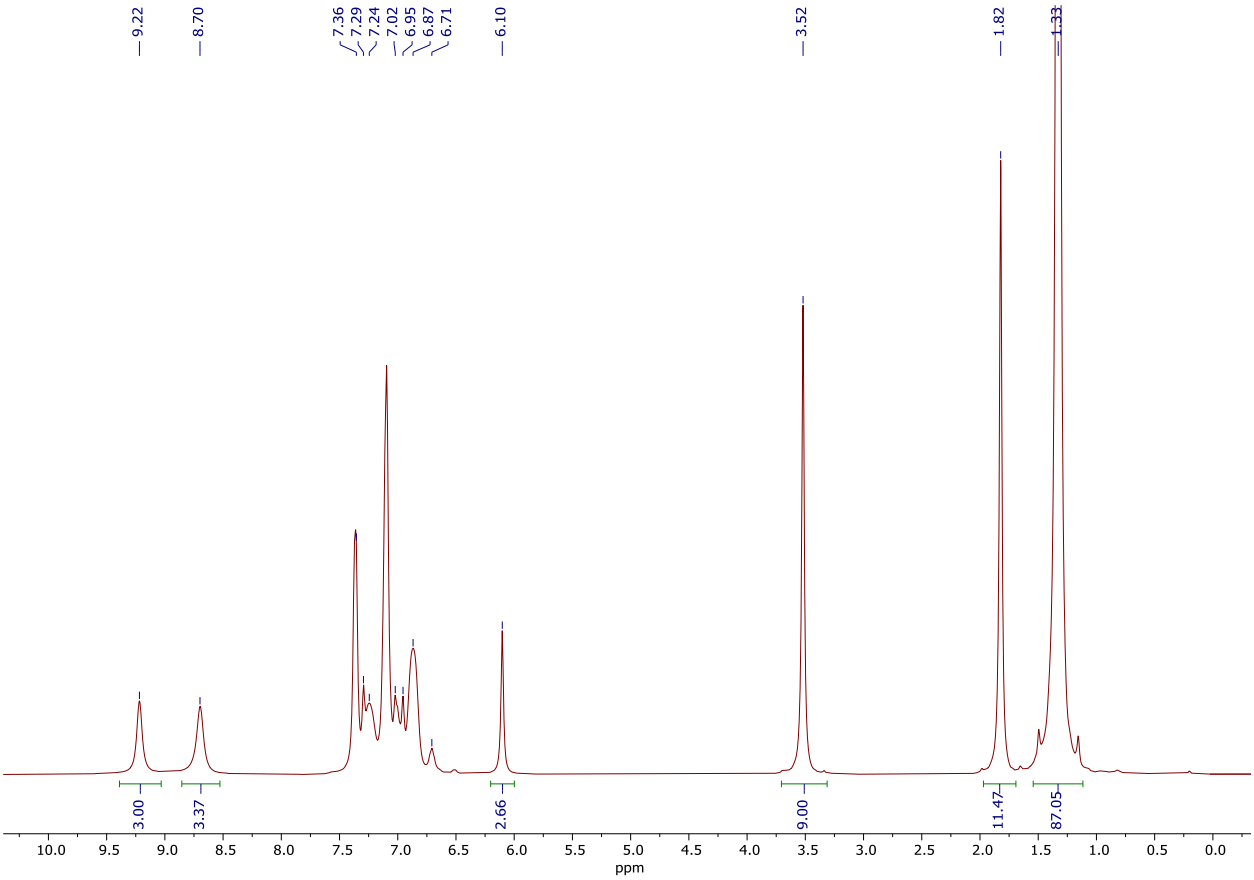


Figure S10. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

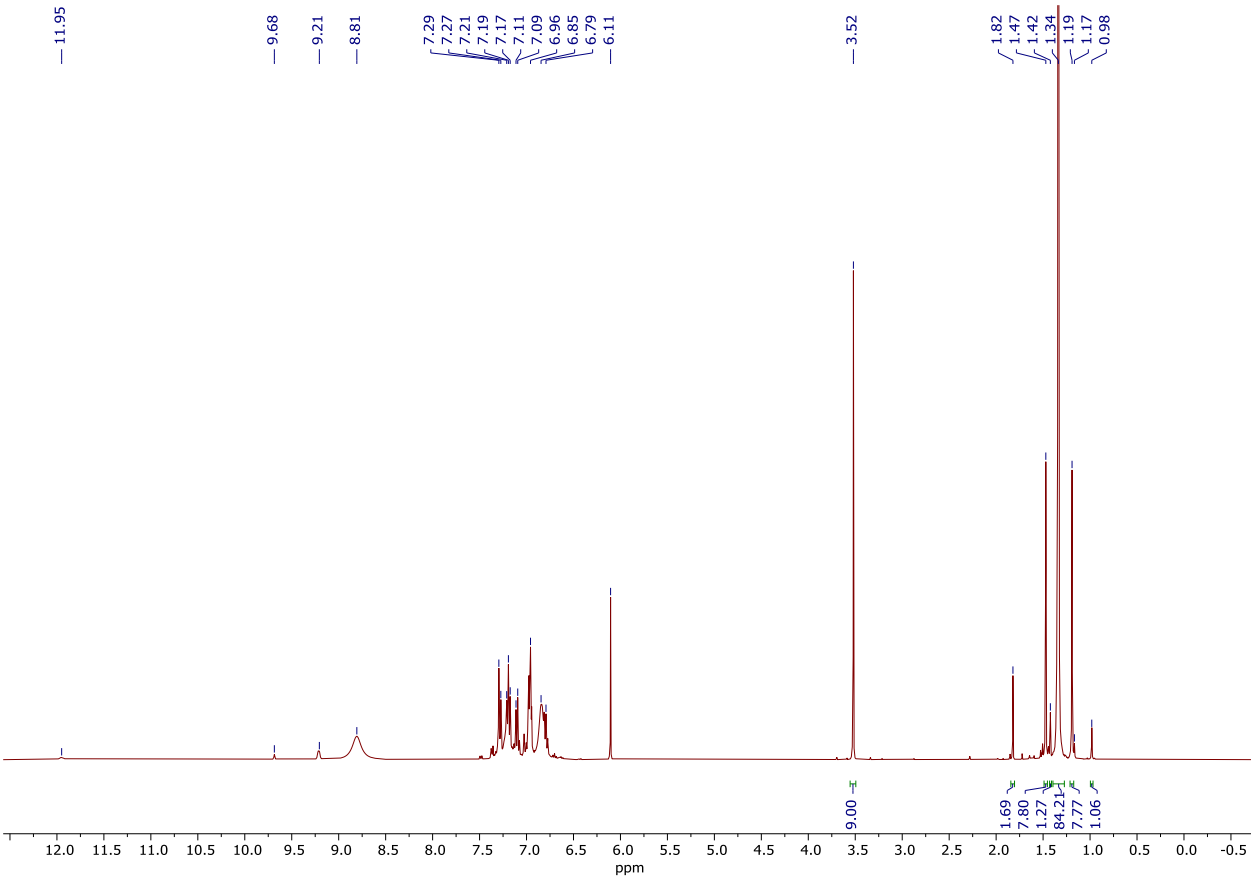


Figure S11. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

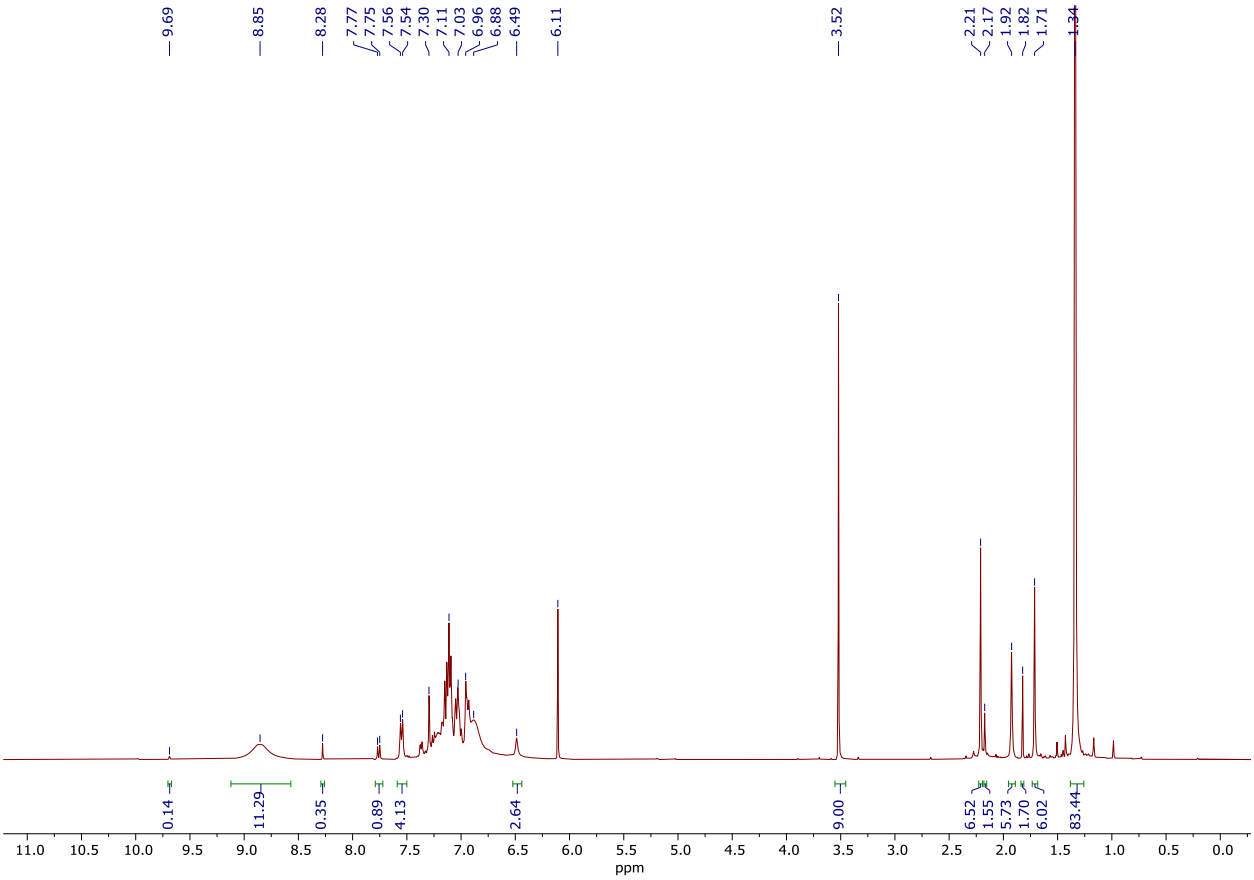
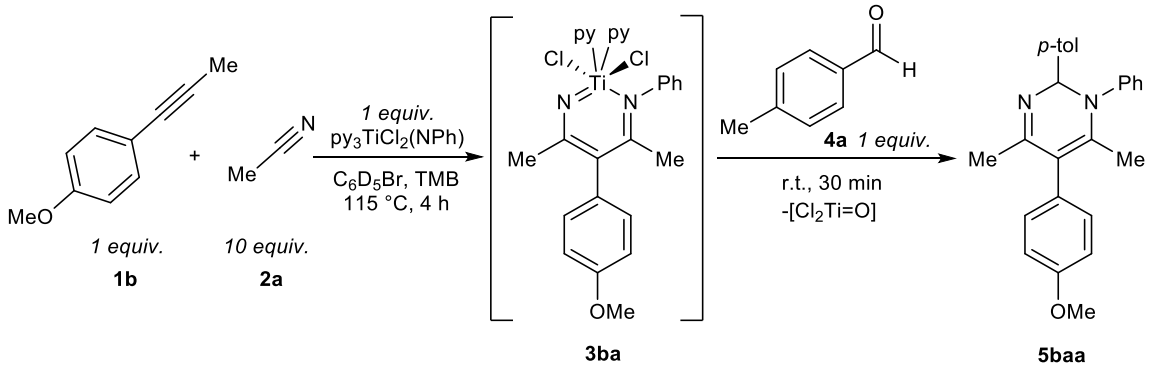
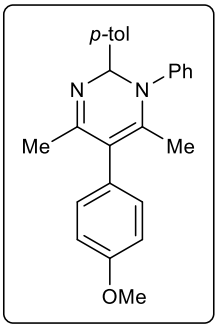


Figure S12. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



5-(4-methoxyphenyl)-4,6-dimethyl-1-phenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5baa)



35% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.59 (d, *J* = 8.1 Hz, 2H), 7.12 – 7.08 (m, 11H), 6.53 (s, 1H), 3.49 (s, 3H), 2.20 (s, 4H), 2.02 (s, 3H), 1.76 (s, 3H).

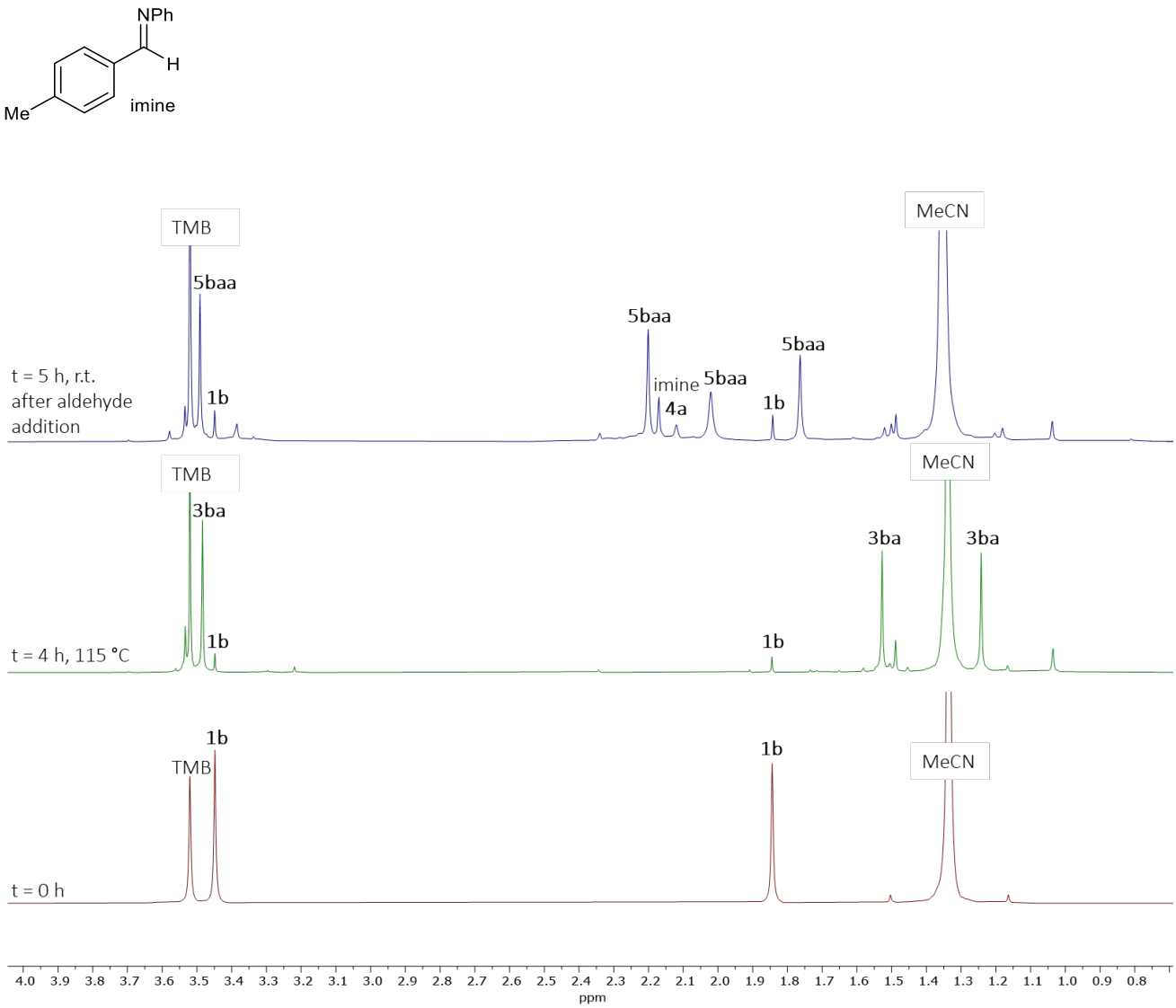


Figure S13. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-methoxy-4-(prop-1-yn-1-yl)benzene (1 equiv., **1b**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ba** in 57% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5baa** in 35% yield (64% conversion from metallacycle **3ba**).

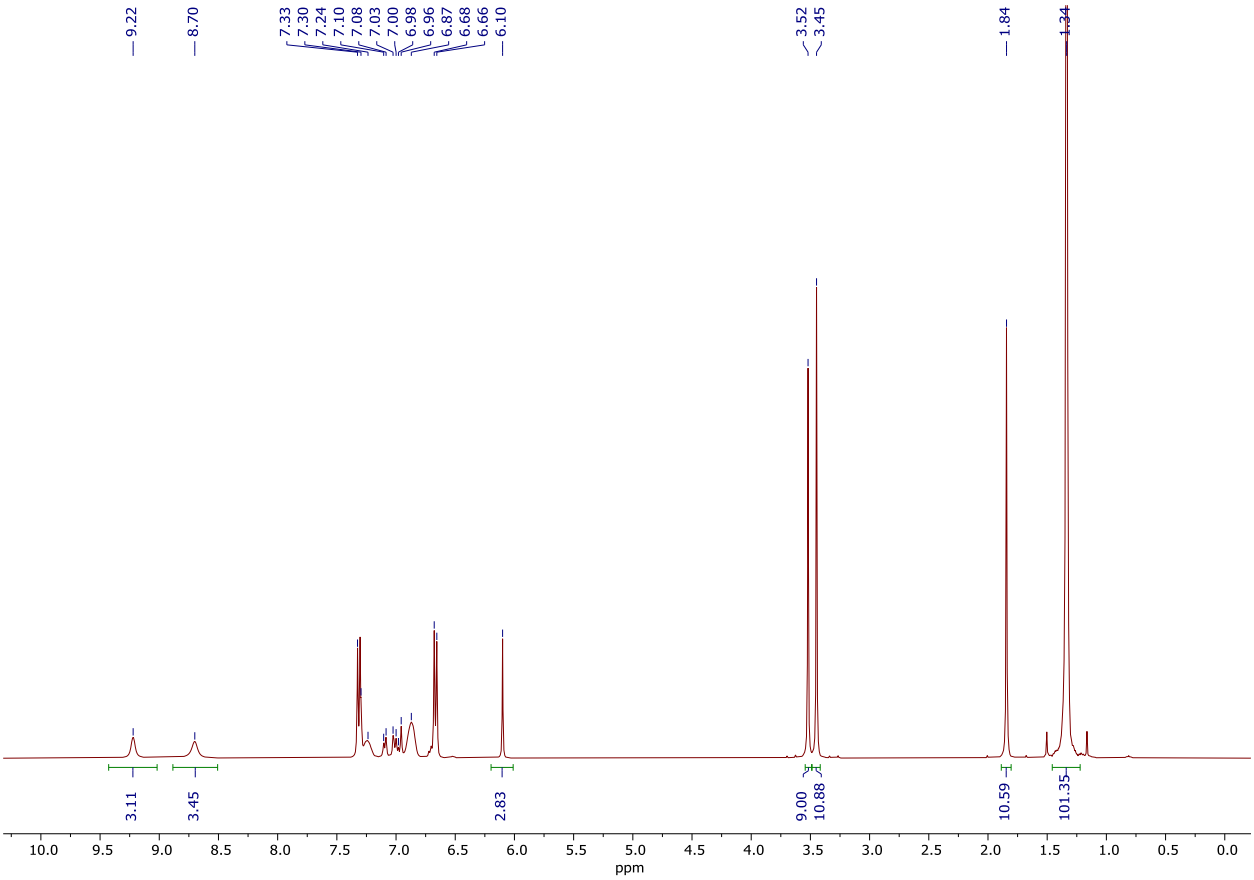


Figure S14. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-methoxy-4-(prop-1-yn-1-yl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

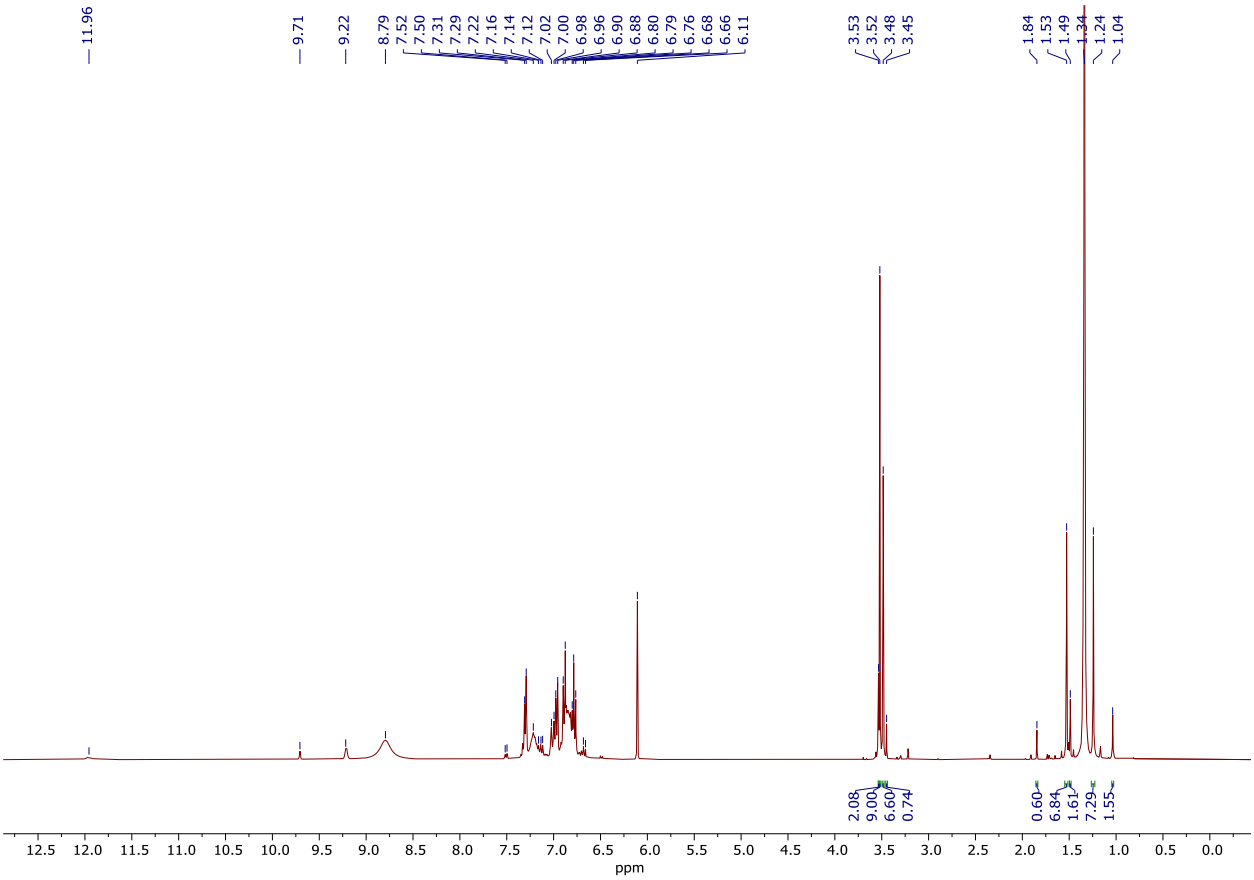


Figure S15. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-methoxy-4-(prop-1-yn-1-yl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

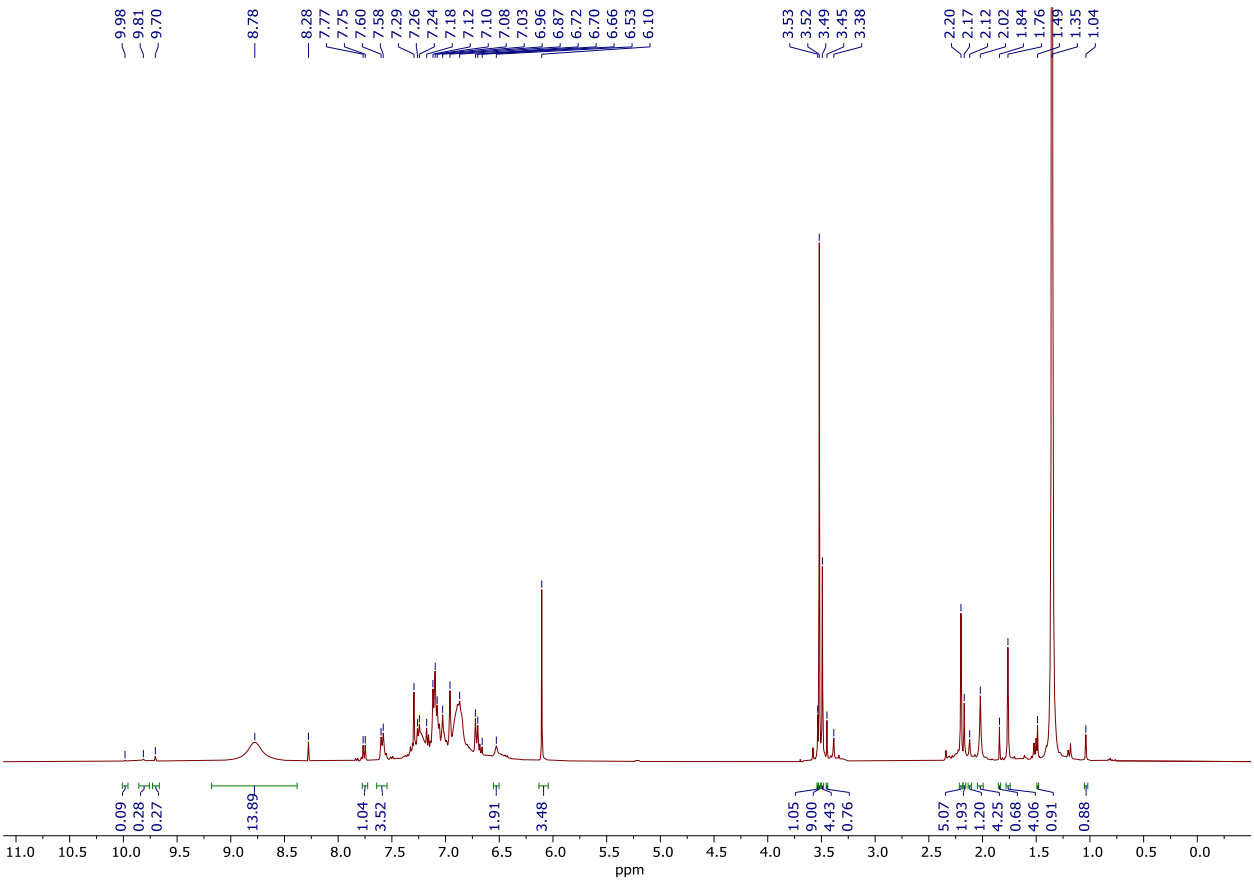
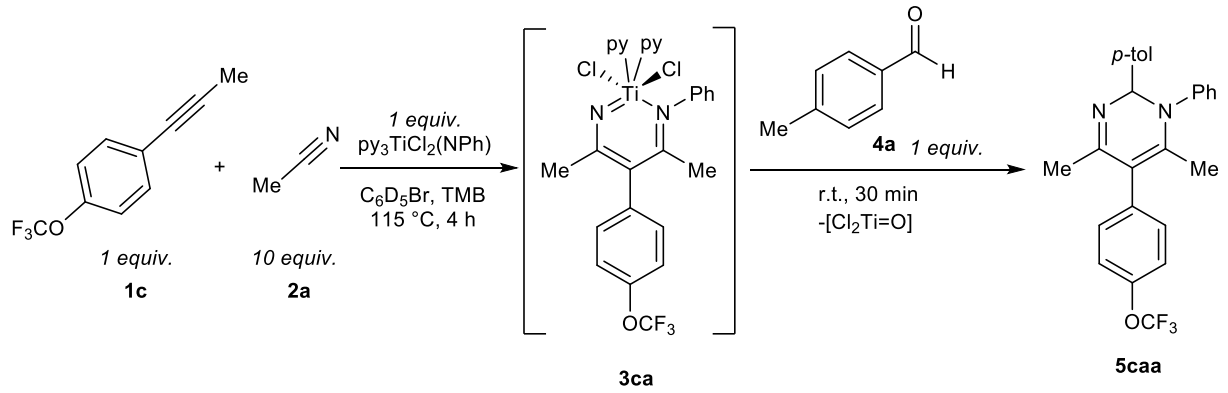
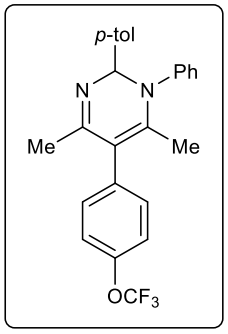


Figure S16. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-methoxy-4-(prop-1-yn-1-yl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



4,6-dimethyl-1-phenyl-2-(p-tolyl)-5-(4-(trifluoromethoxy)phenyl)-1,2-dihydropyrimidine (5caa)



30% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.60 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 7.14 – 7.11 (m, 5H), 7.08 – 7.06 (m, 4H), 6.50 (s, 1H), 2.21 (s, 3H), 1.98 (s, 3H), 1.74 (s, 3H). **^{19}F NMR (376 MHz, C_6D_5Br, δ, ppm):** -57.02.

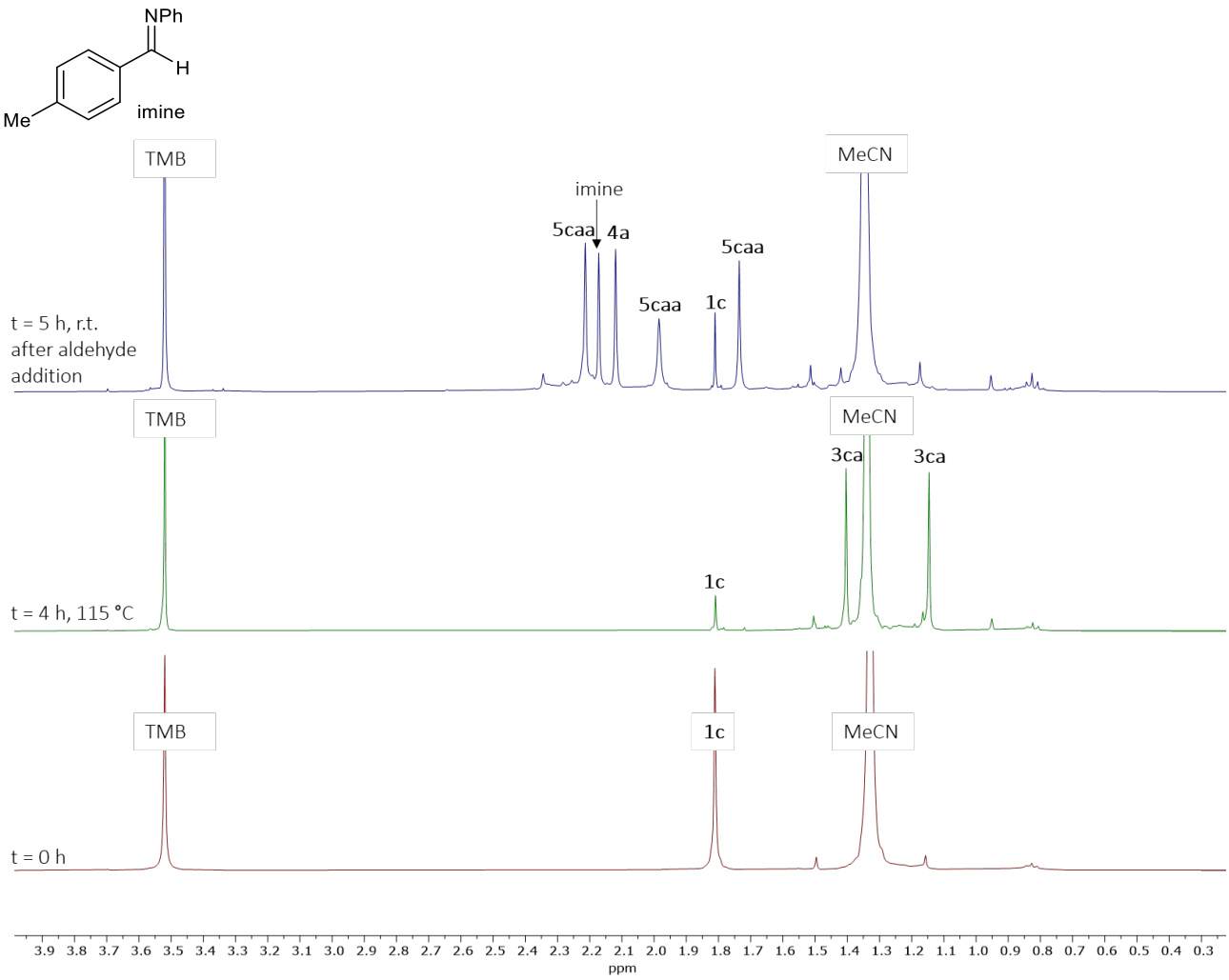


Figure S17. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethoxy)benzene (1 equiv., **1c**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ca** in 50 yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5caa** in 30% yield.

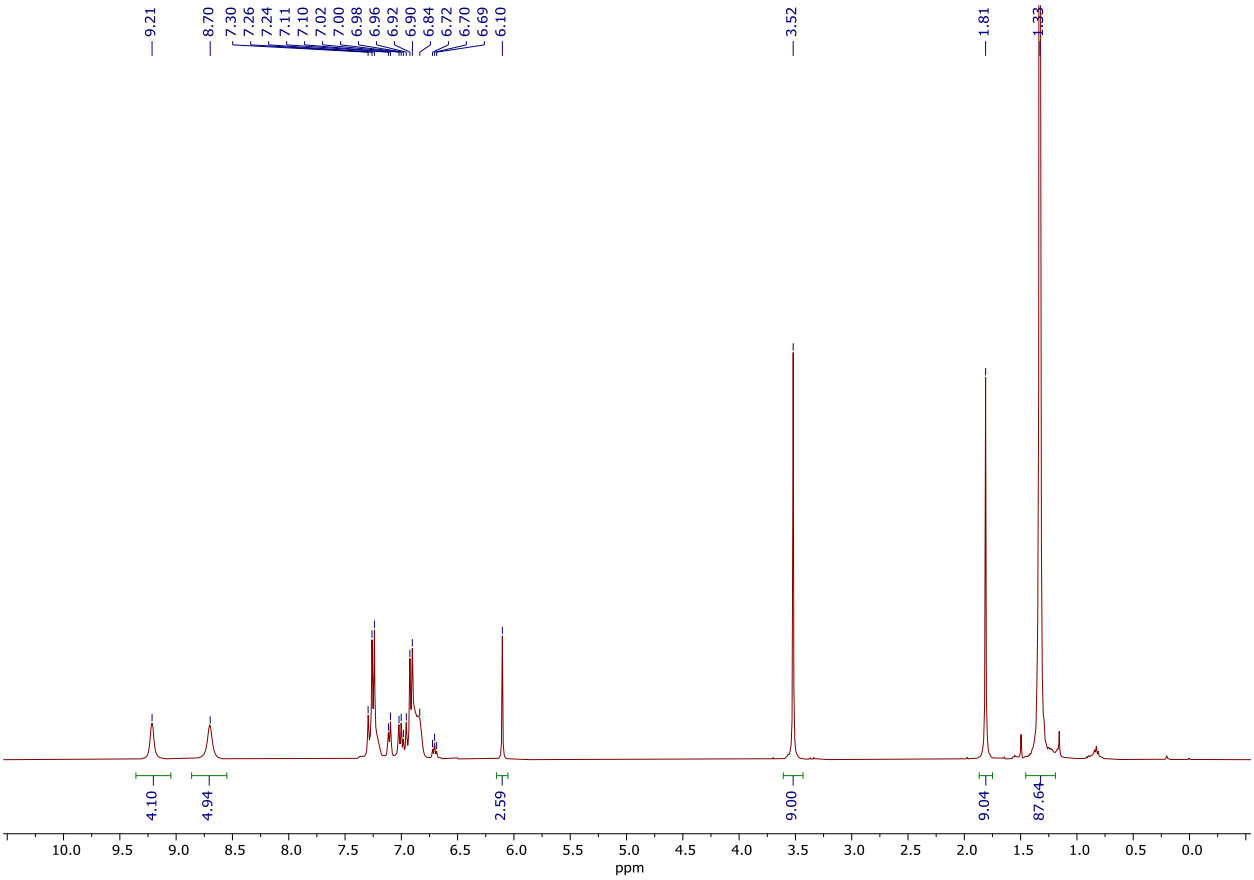


Figure S18. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethoxy)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

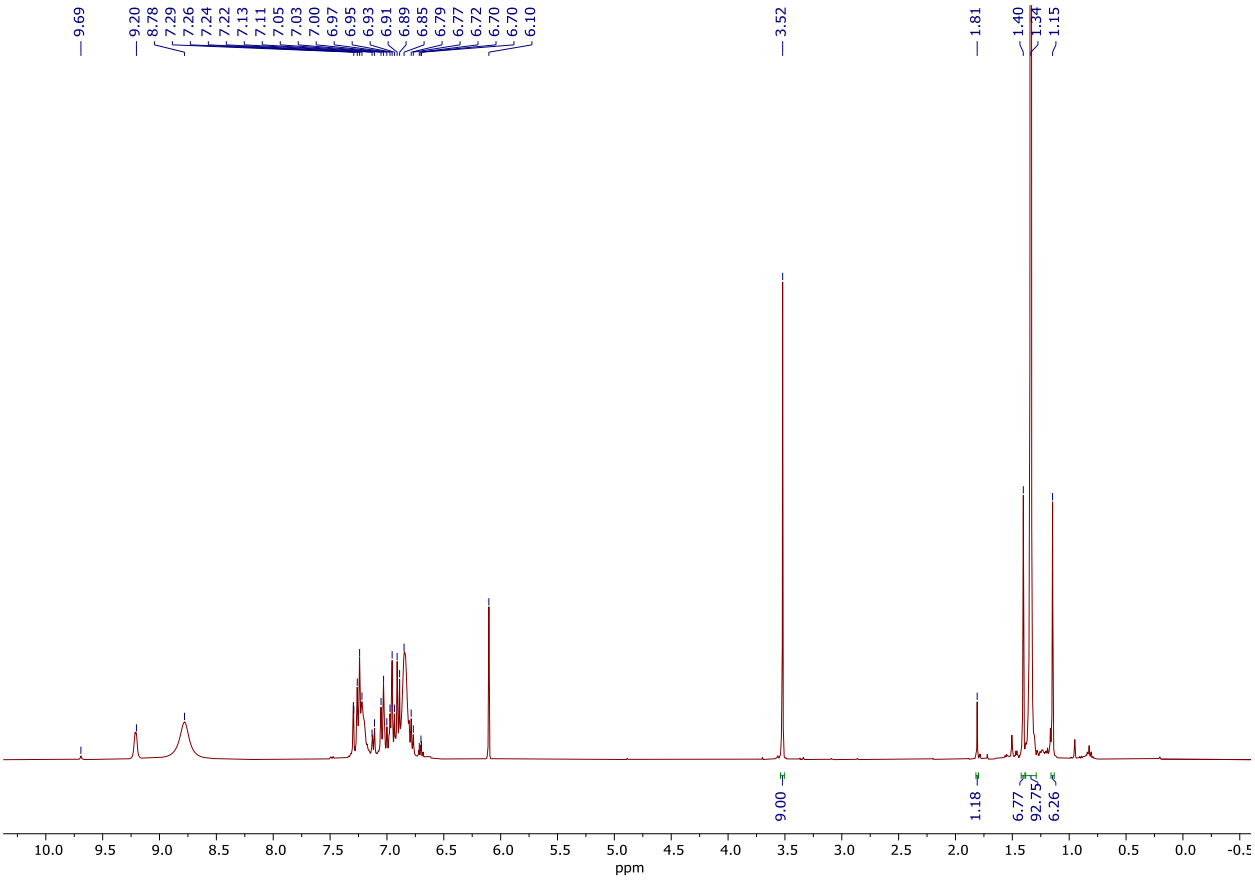


Figure S19. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethoxy)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

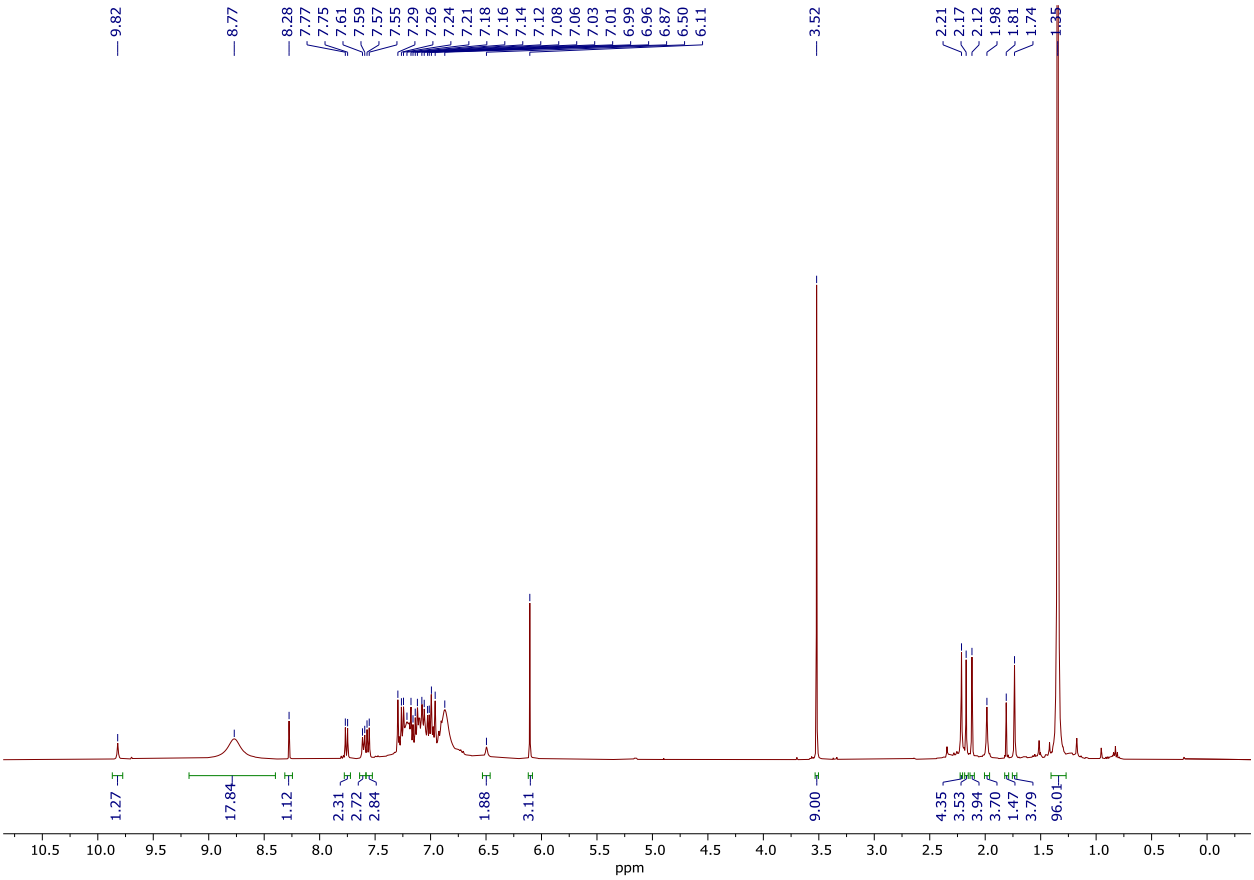


Figure S20. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethoxy)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).

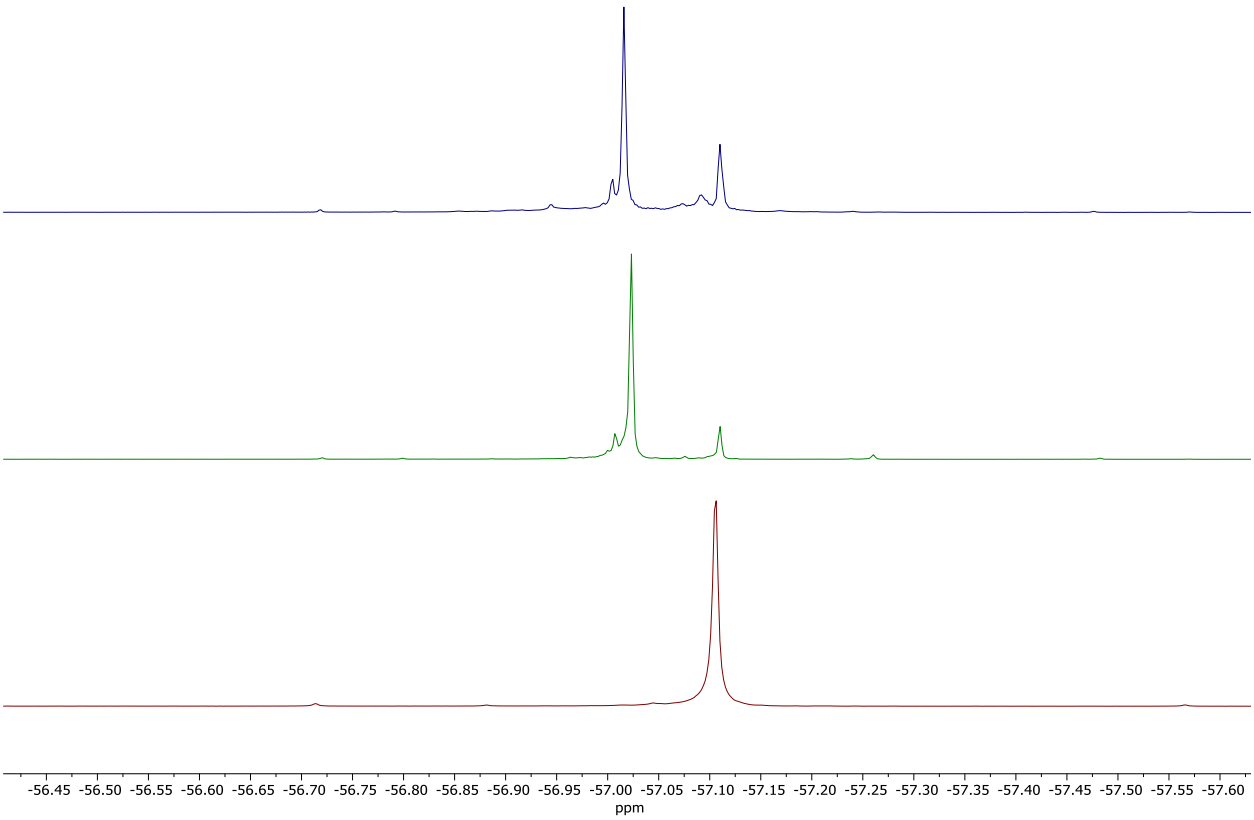
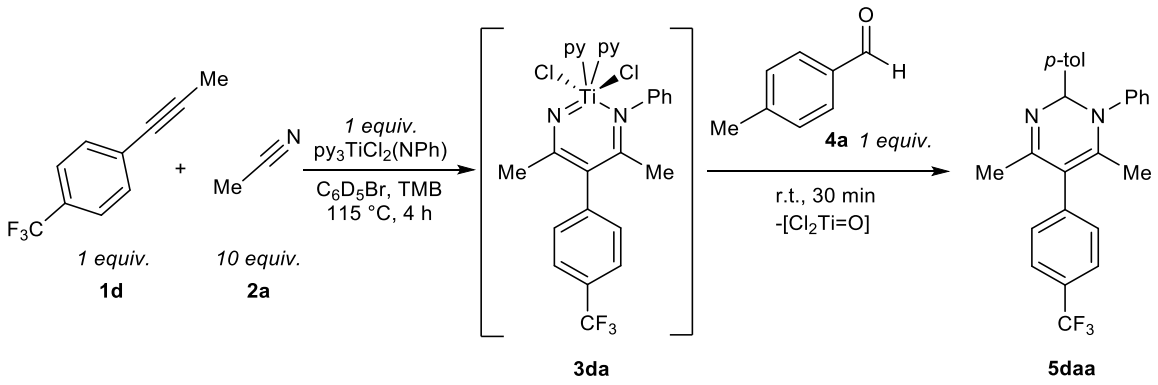
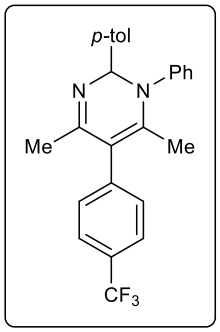


Figure S21. Stacked ^{19}F NMR spectra characterizing the multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethoxy)benzene (1 equiv.), acetonitrile (10 equiv.), *p*-tolualdehyde (1 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C.



4,6-dimethyl-1-phenyl-2-(p-tolyl)-5-(4-(trifluoromethyl)phenyl)-1,2-dihydropyrimidine (5daa)



35% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.53 (d, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.17 – 7.15 (m, 3H), 7.14 – 7.12 (m, 6H), 6.48 (s, 1H), 2.23 (s, 3H), 1.90 (s, 3H), 1.69 (s, 3H). **^{19}F NMR (376 MHz, C_6D_5Br, δ, ppm):** -61.27.

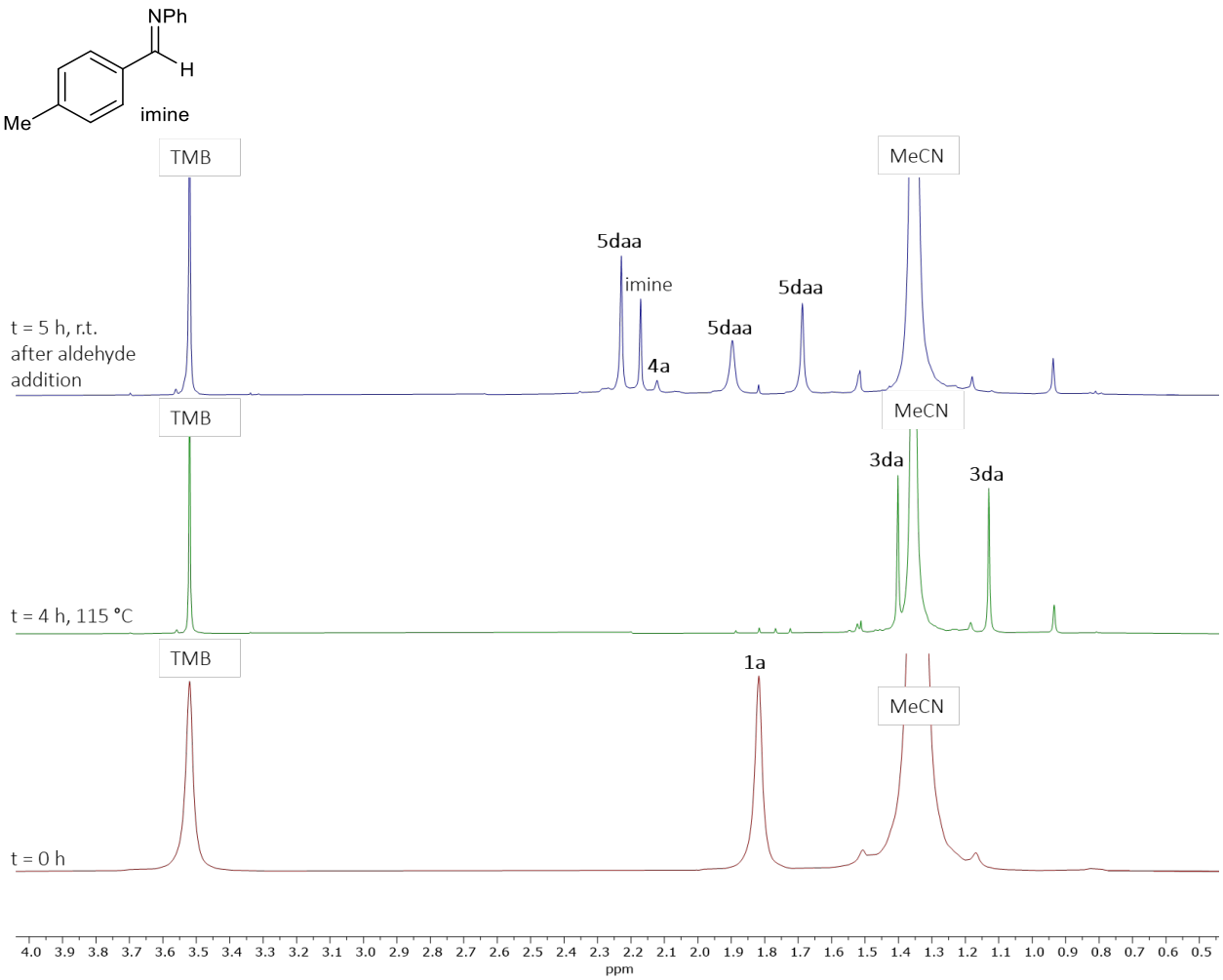


Figure S22. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (1 equiv., **1d**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3da** in 49% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5daa** in 35% yield (68% conversion of metallacycle **3da**).

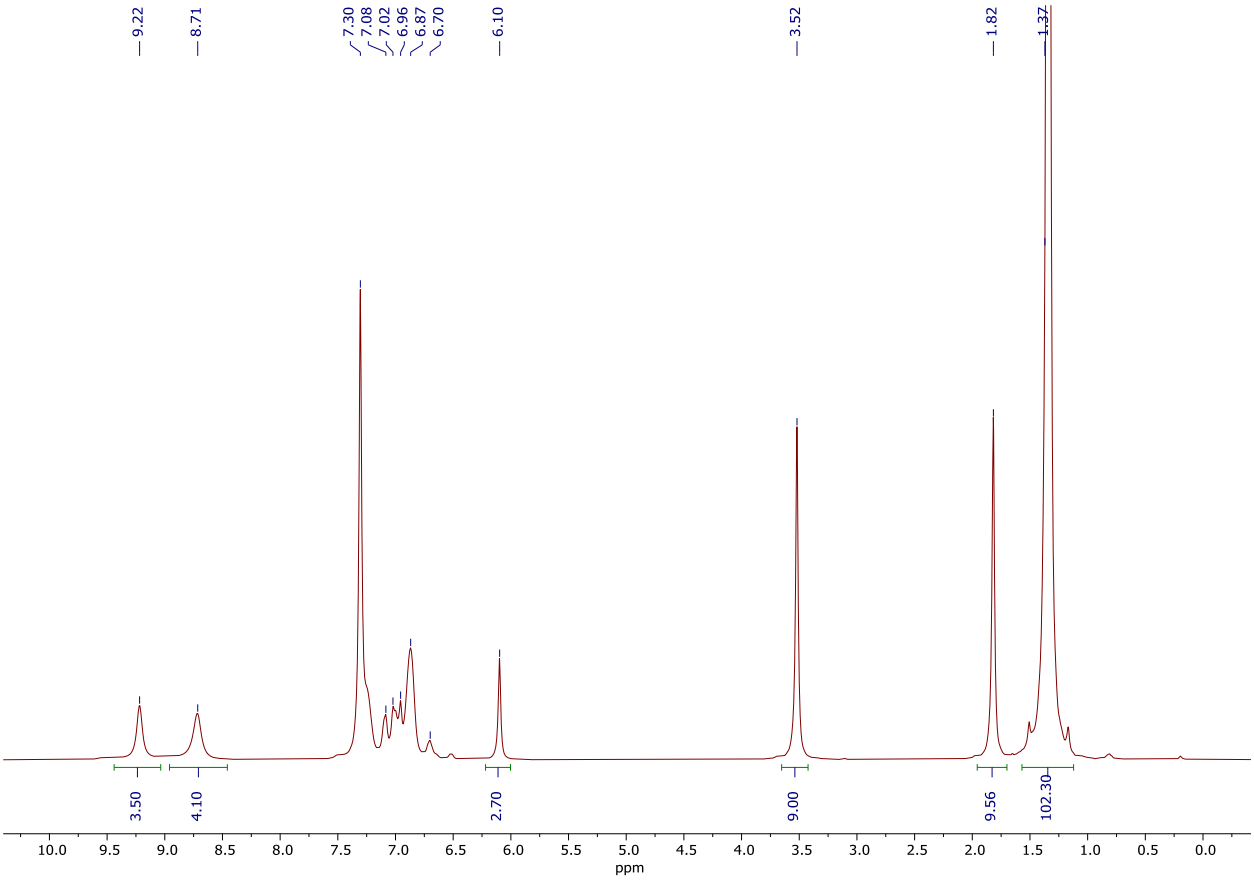


Figure S23. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

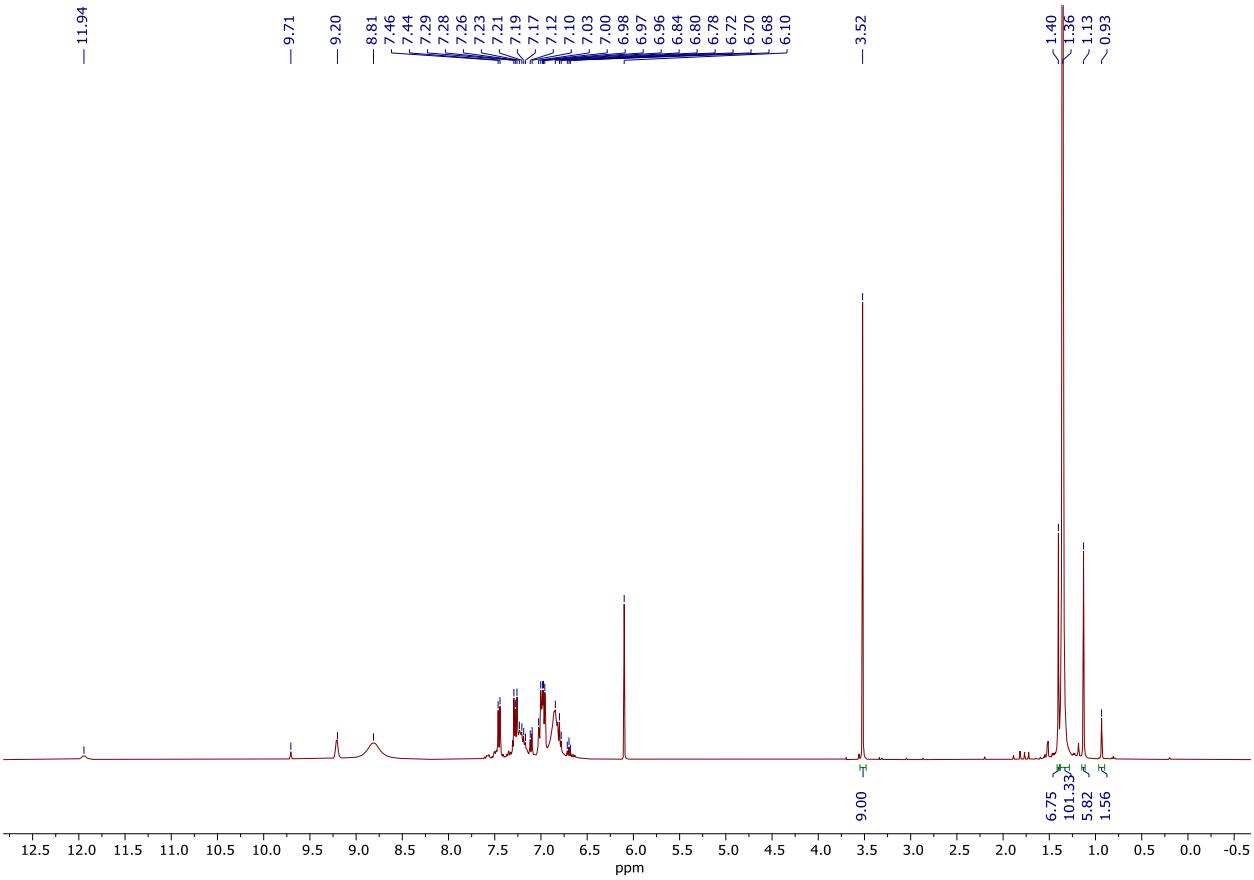


Figure S24. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

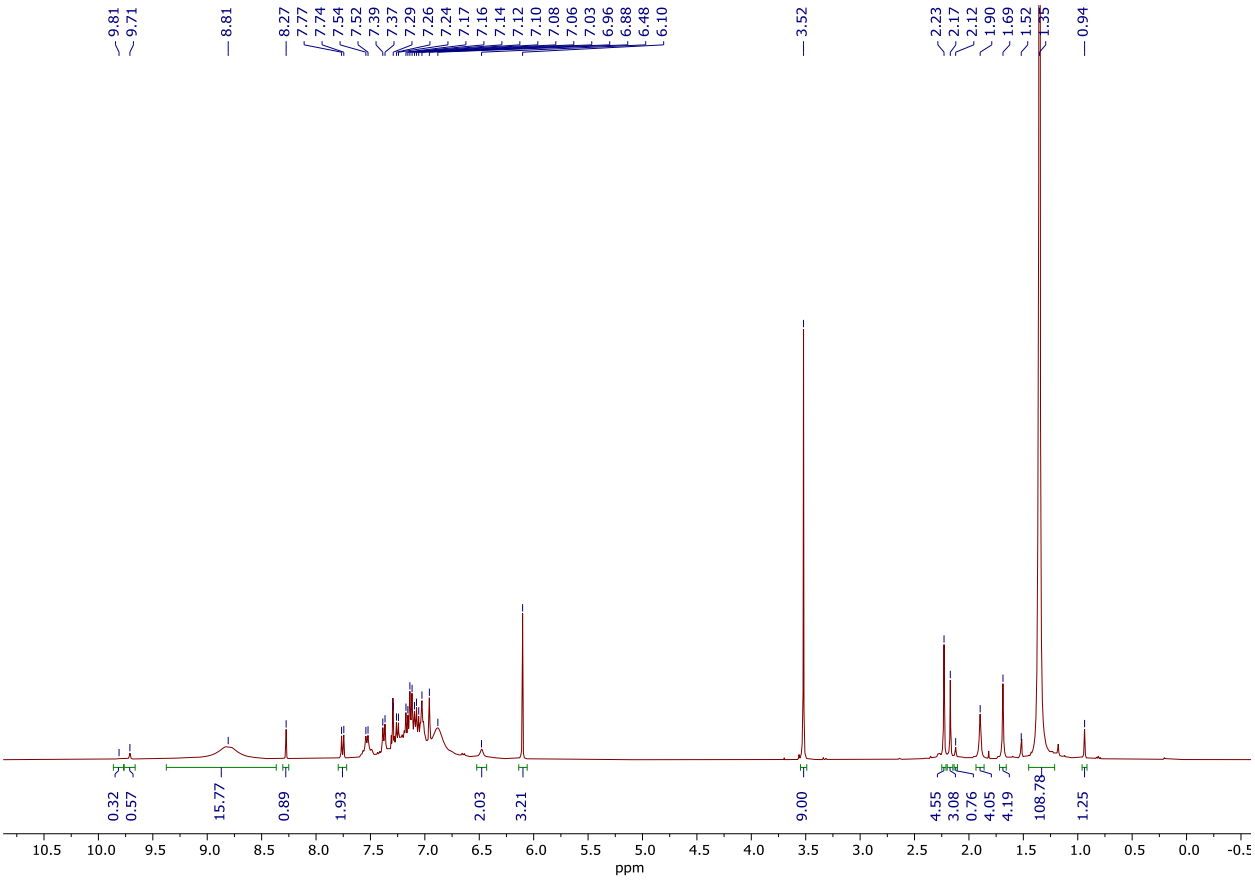


Figure S25. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).

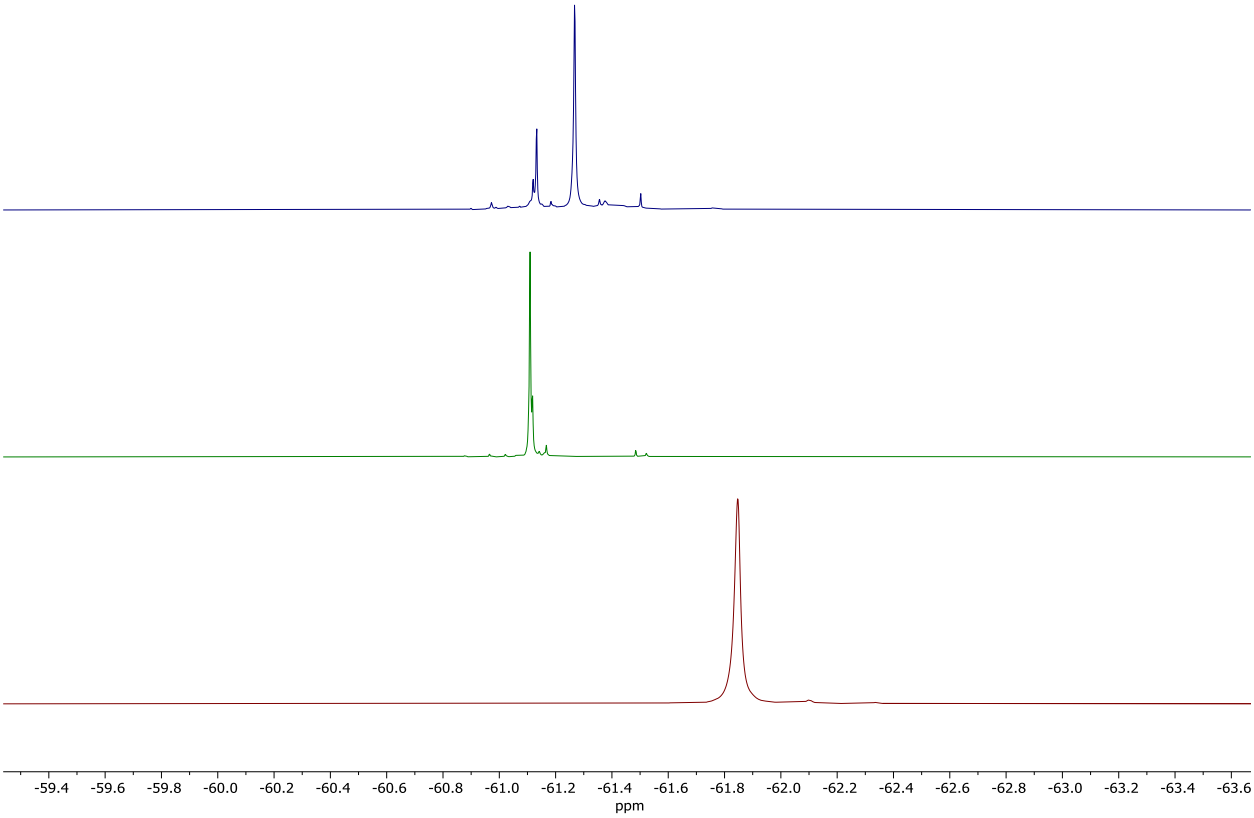
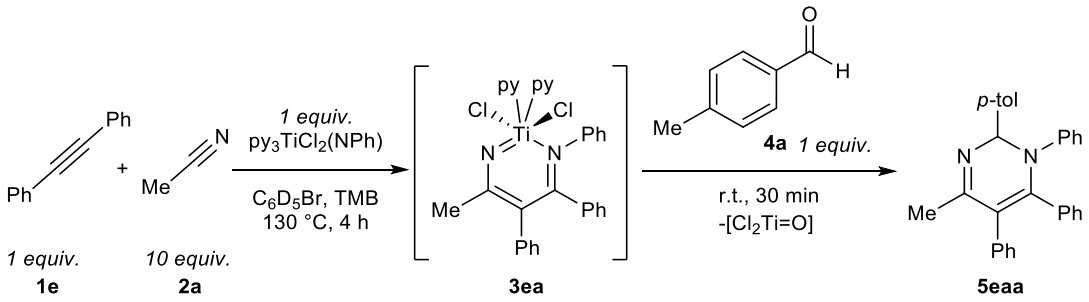
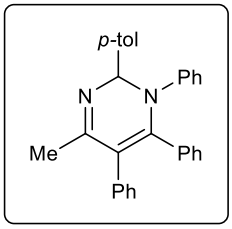


Figure S26. Stacked ^{19}F NMR spectra characterizing the multicomponent coupling of 1-(prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (1 equiv.), acetonitrile (10 equiv.), *p*-tolualdehyde (1 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C.



4-methyl-1,5,6-triphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5eaa)



21% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.20 – 7.11 (m, 19H), 6.65 (s, 1H), 2.33 (s, 3H), 2.22 (s, 3H).

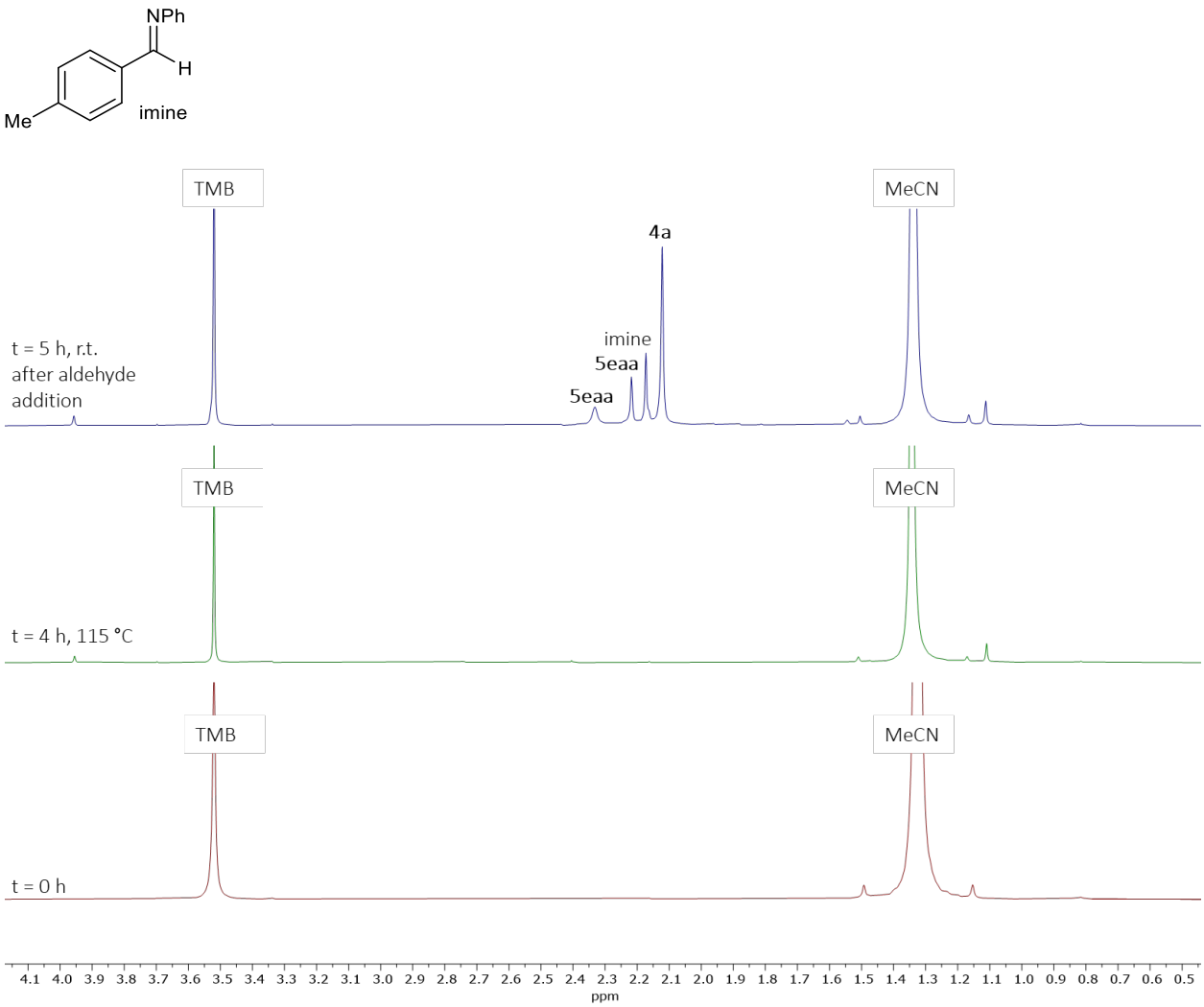


Figure S27. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of diphenylacetylene (1 equiv., **1e**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 130 °C generating metallacycle **3ea**; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5eaa** in 21% yield.

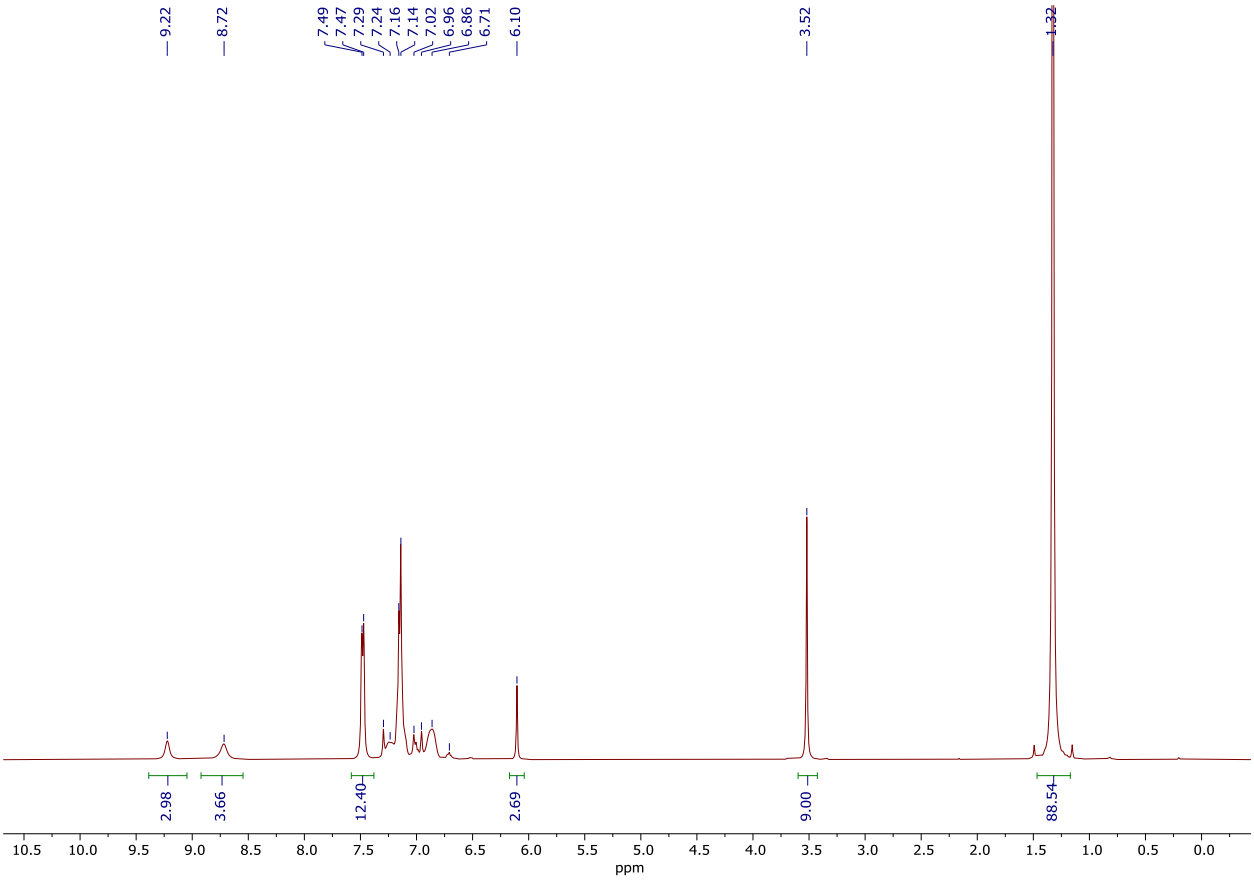


Figure S28. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of diphenylacetylene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

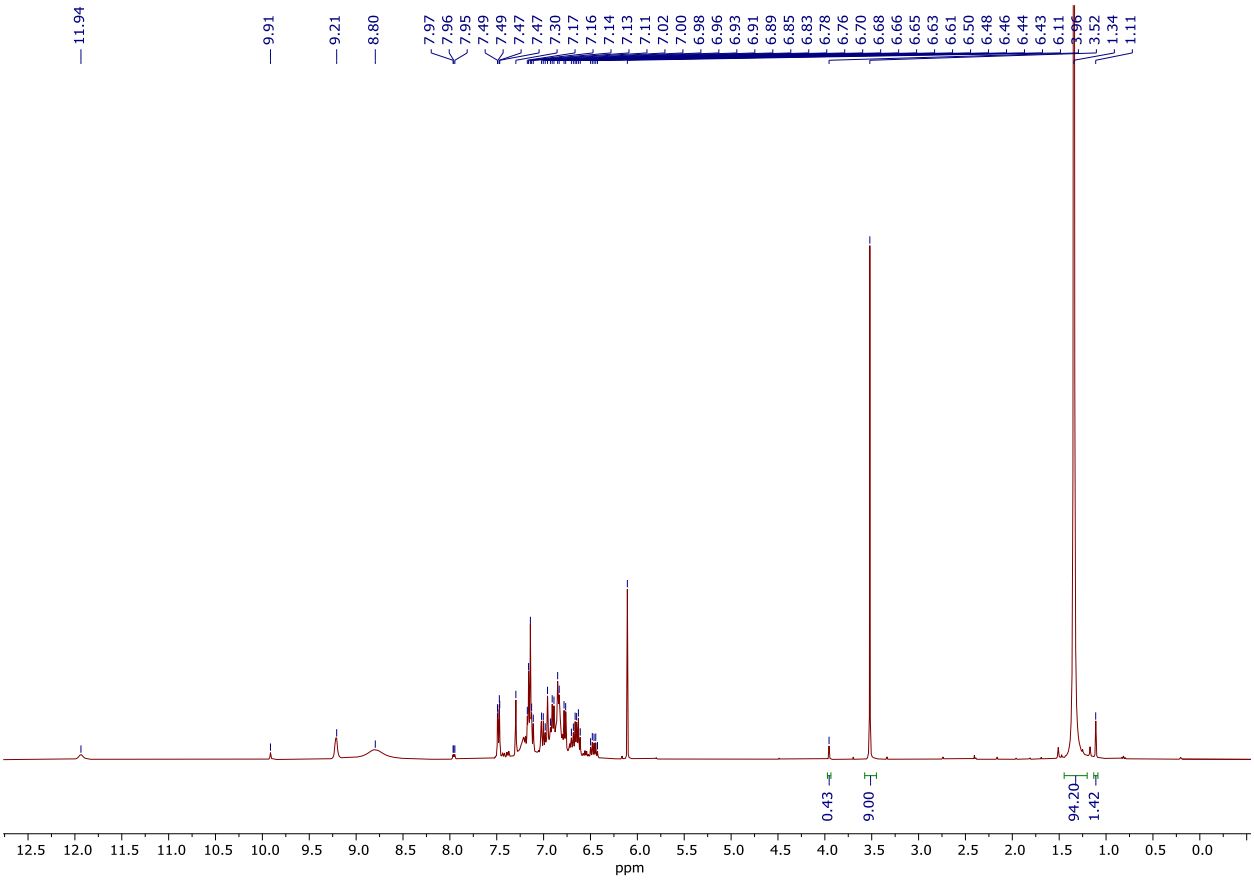


Figure S29. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of diphenylacetylene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

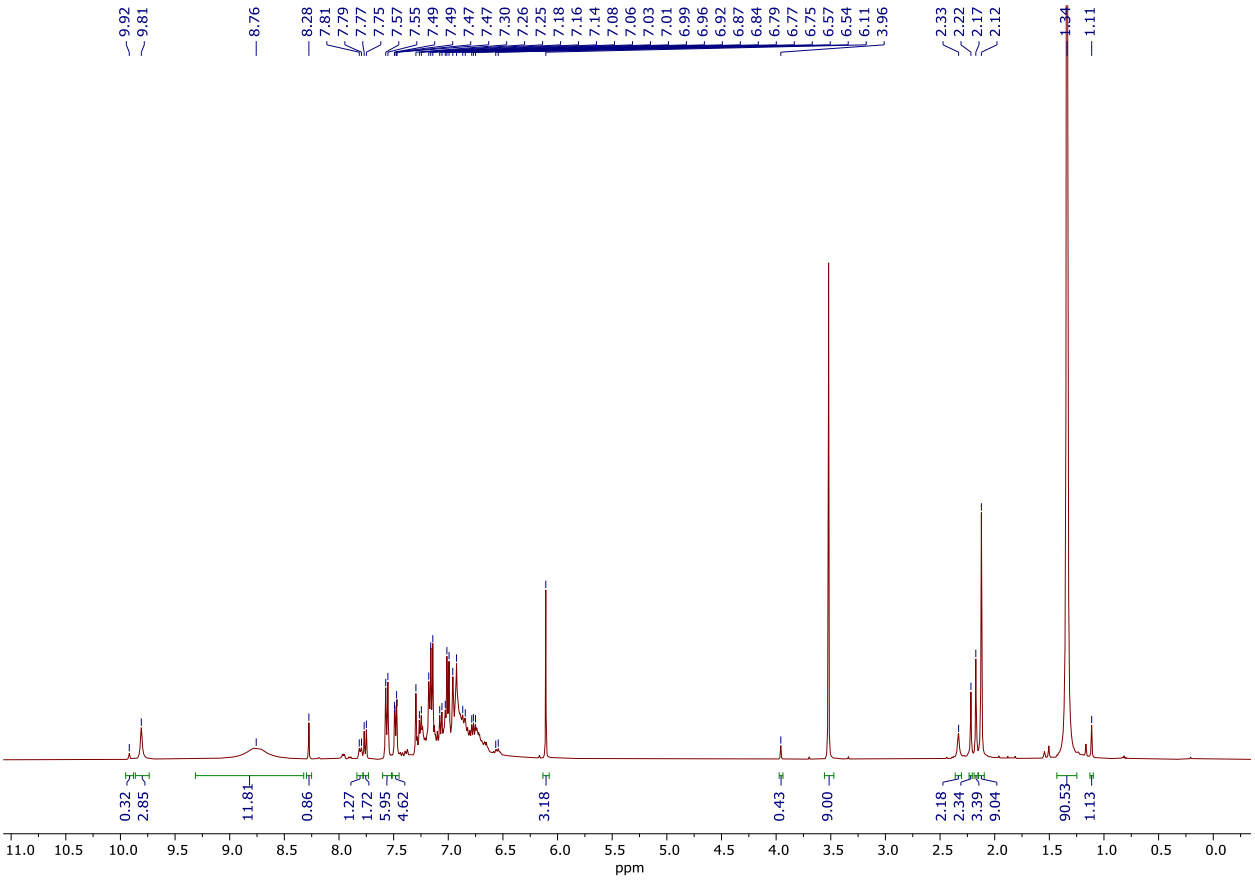
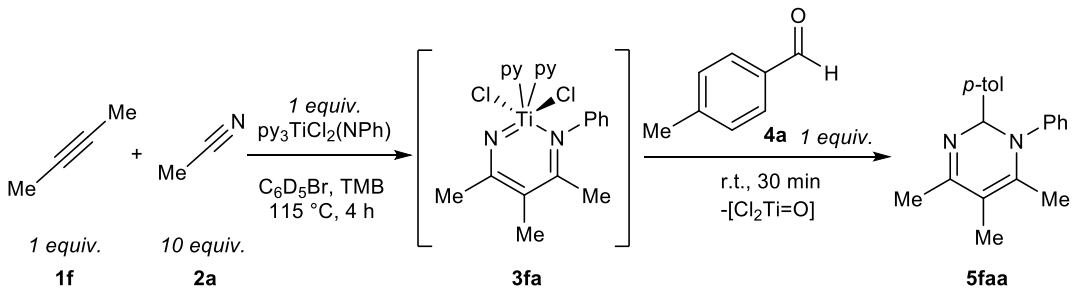
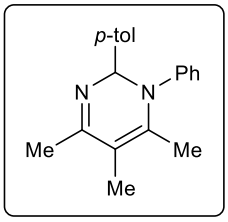


Figure S30. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of diphenylacetylene (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



4,5,6-trimethyl-1-phenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5faa)



17% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.48 (d, *J* = 7.7 Hz, 2H), 7.08 (s, 4H), 6.99 (s, 3H), 6.39 (s, 1H), 2.15 (s, 3H), 2.11 (s, 3H), 1.77 (s, 3H), 1.38 (s, 3H).

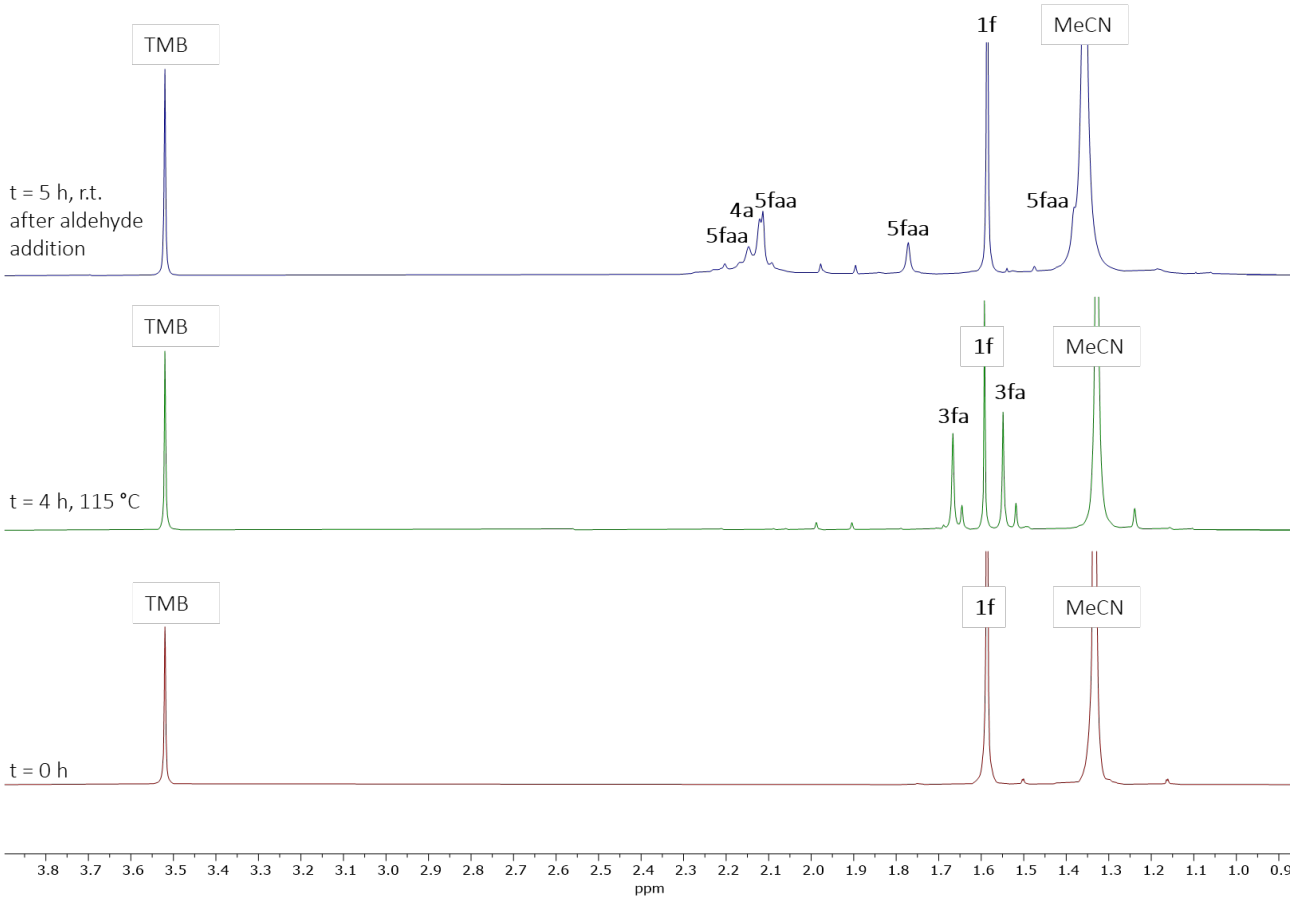


Figure S31. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 2-butyne (1 equiv., **1f**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3fa** in 64% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5faa** in 17% yield (54% conversion from metallacycle **3fa**).

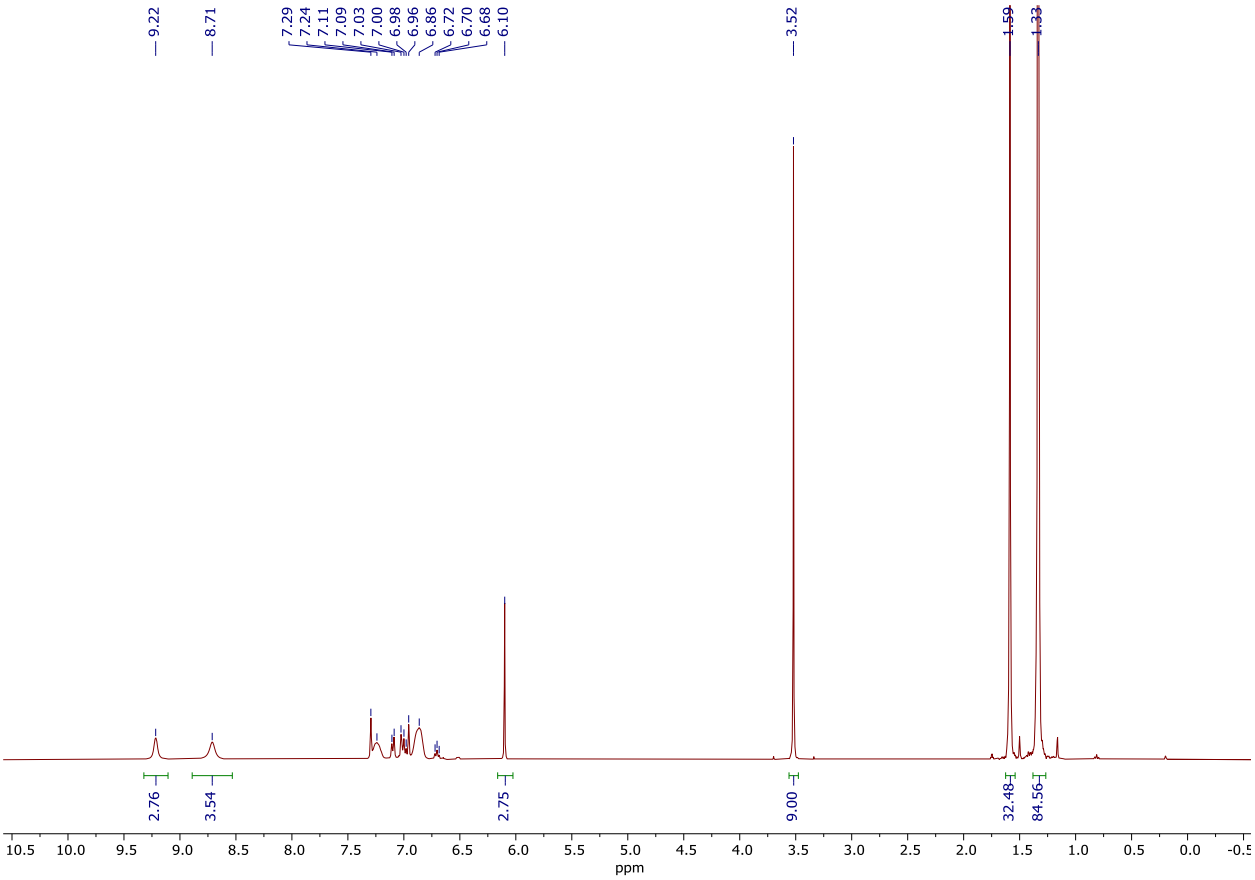


Figure S32. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 2-butyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

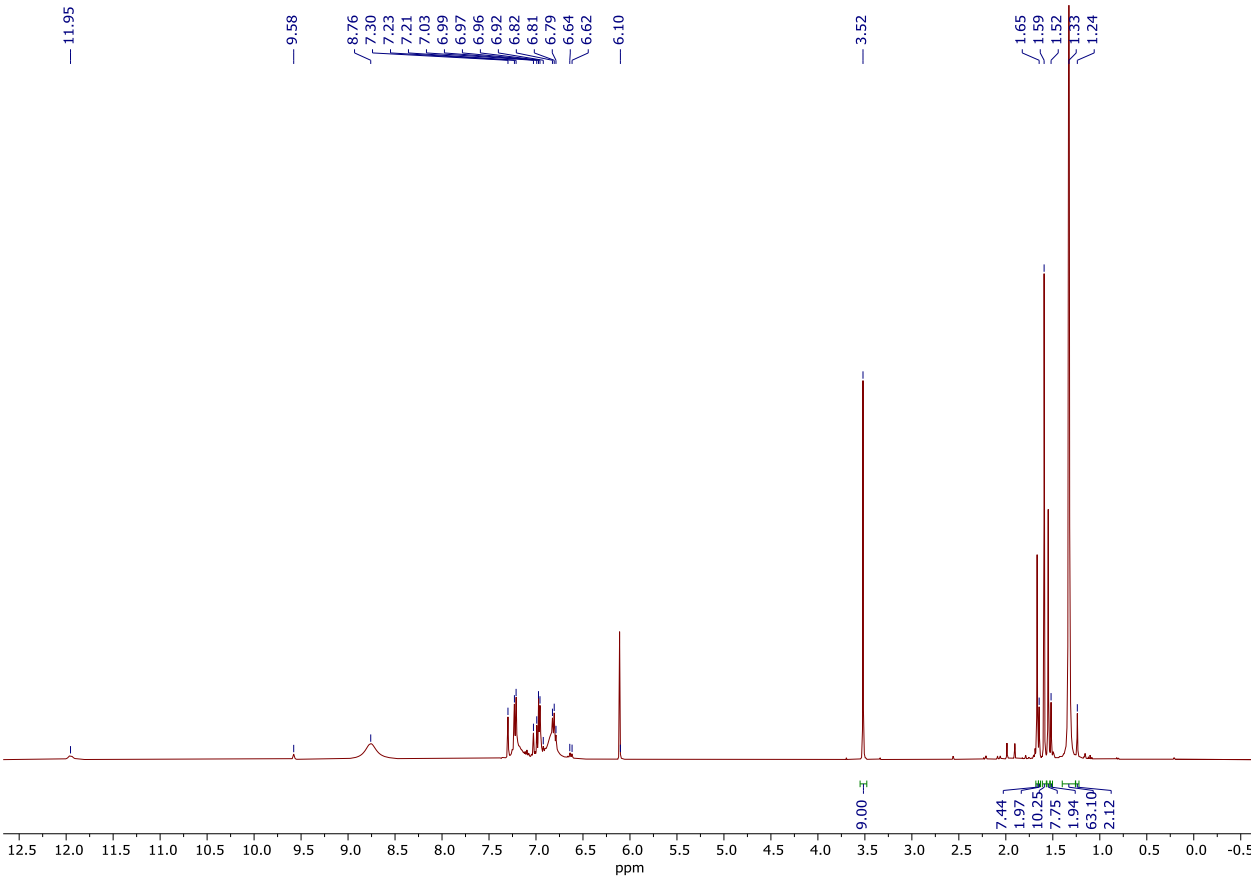


Figure S33. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 2-butyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

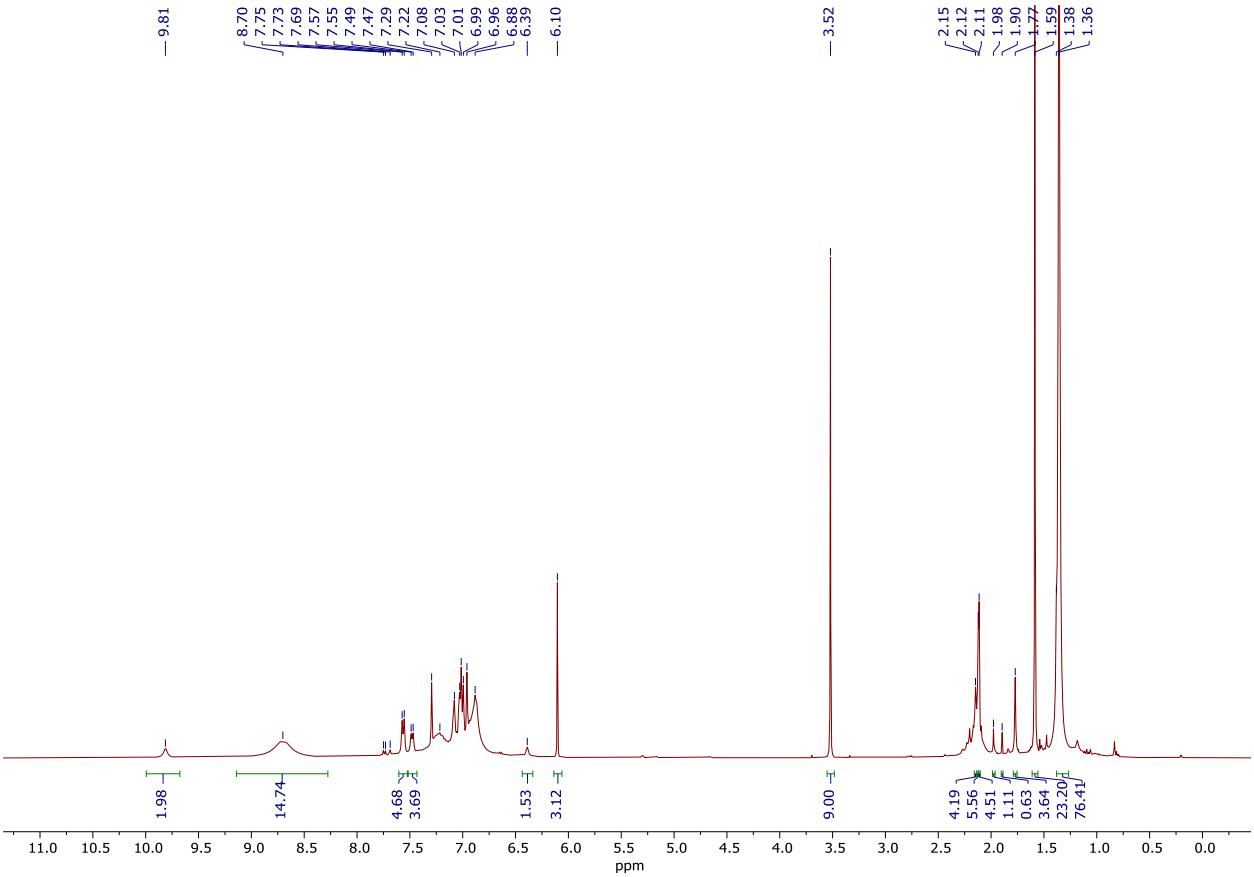
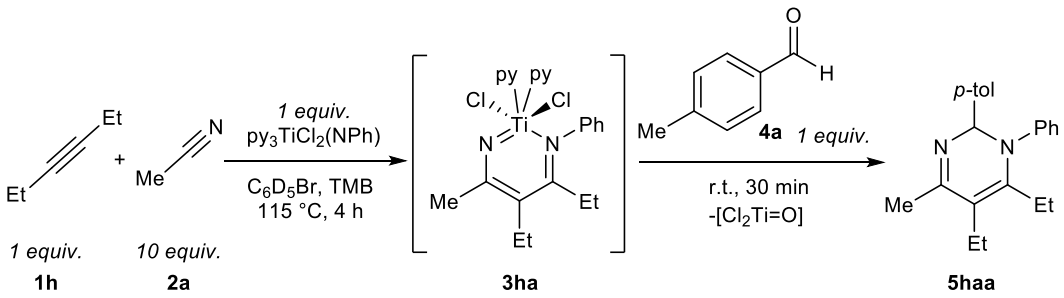
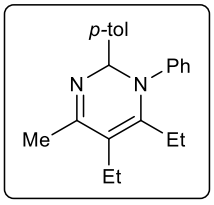


Figure S34. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 2-butyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



5,6-diethyl-4-methyl-1-phenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5haa)



30% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.47 (d, *J* = 8.1 Hz, 2H), 7.11 – 7.06 (m, 7H), 6.31 (s, 1H), 2.25 (s, 2H), 2.13 (s, 3H), 2.10 – 2.06 (m, 2H), 2.02 – 1.96 (m, 2H), 0.74 (t, *J* = 7.5 Hz, 3H), 0.64 (t, *J* = 8.2 Hz, 3H).

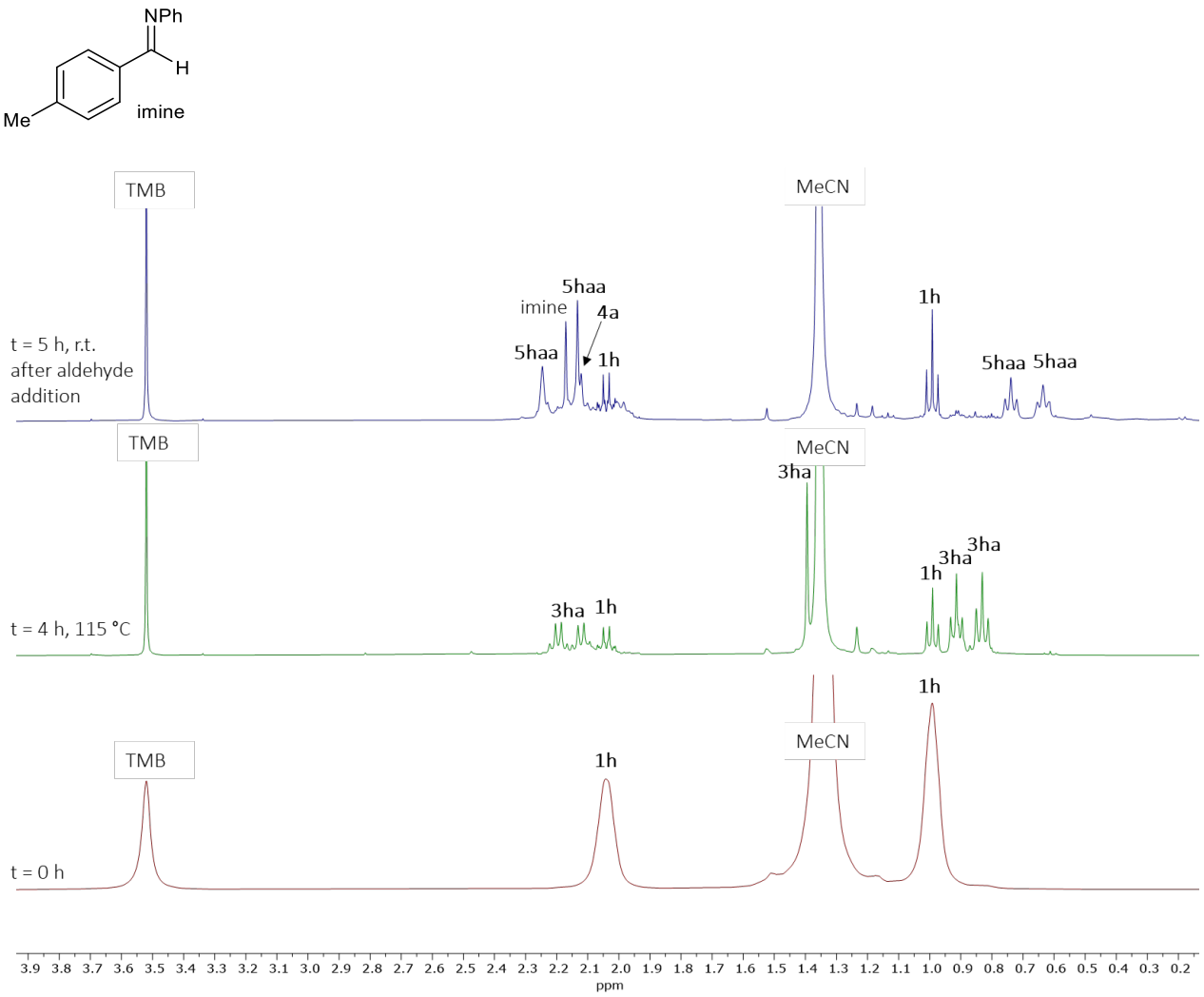


Figure S35. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 3-hexyne (1 equiv., **1h**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ha** in 56% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5haa** in 30% yield (62% conversion from metallacycle **3ha**).

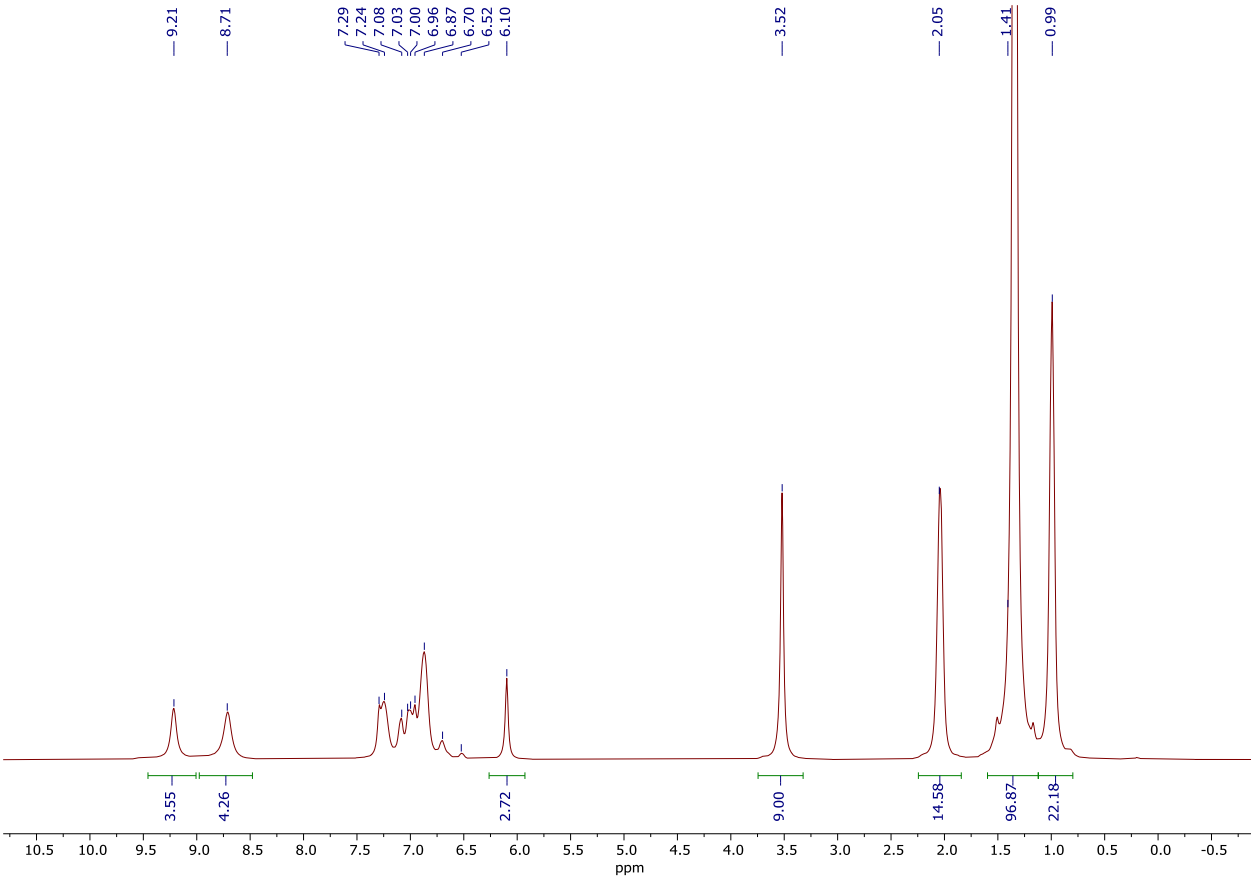


Figure S36. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 3-hexyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

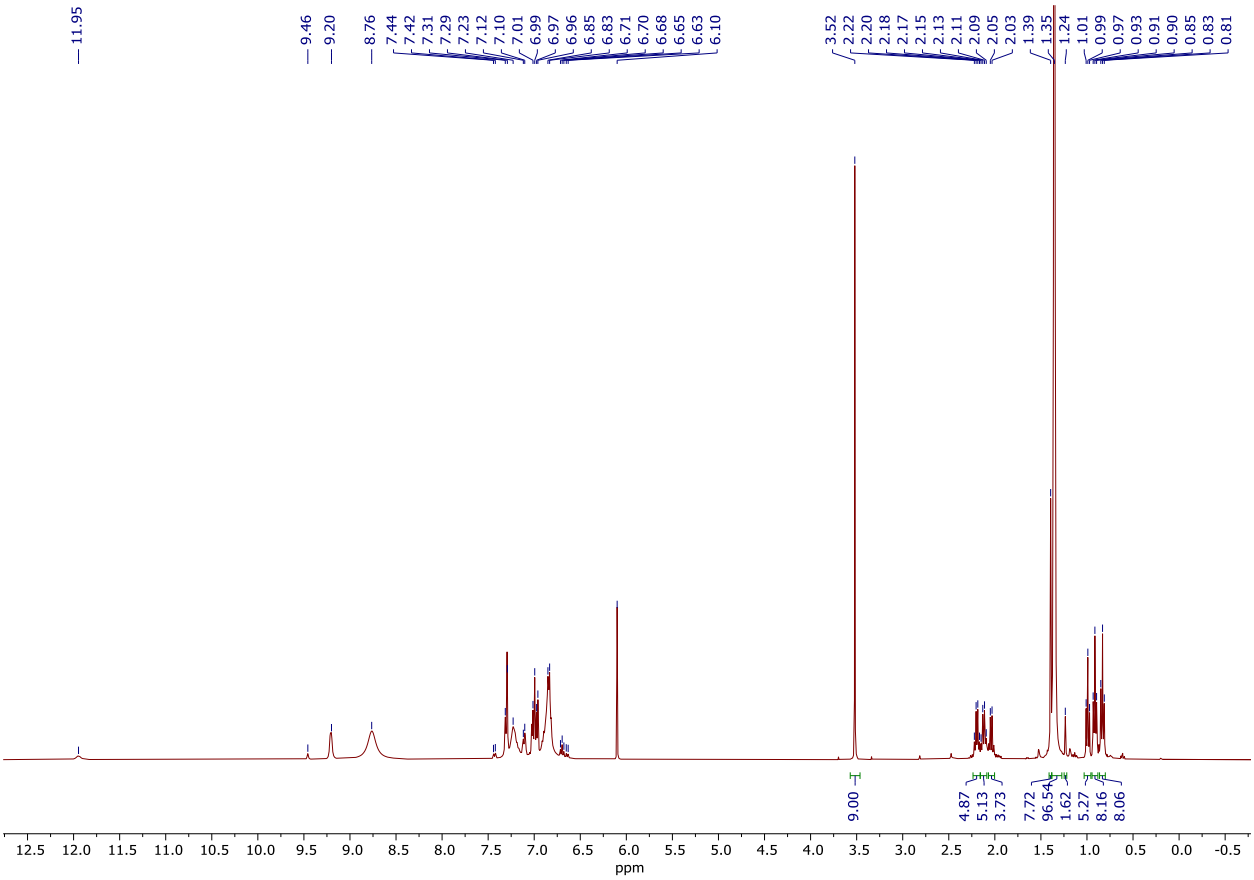


Figure S37. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 3-hexyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

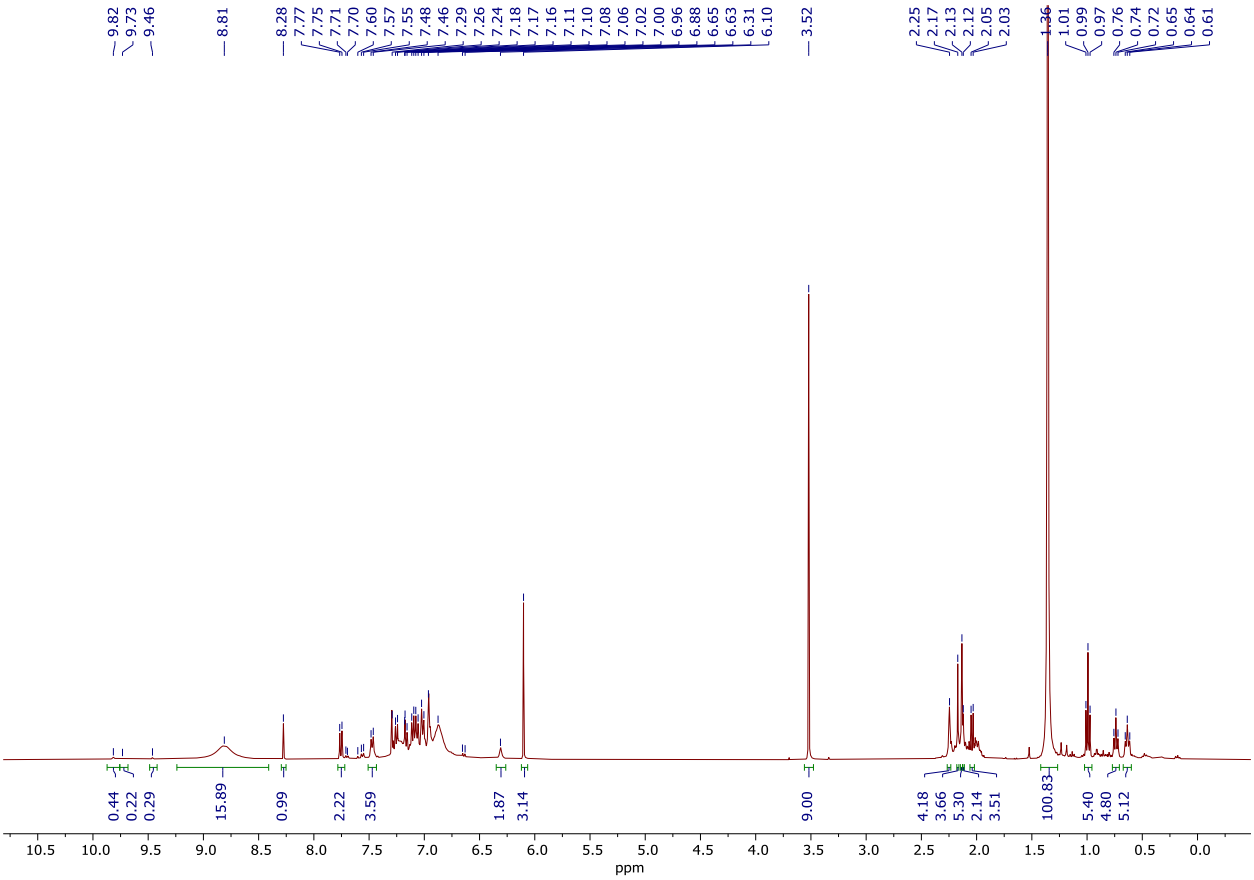
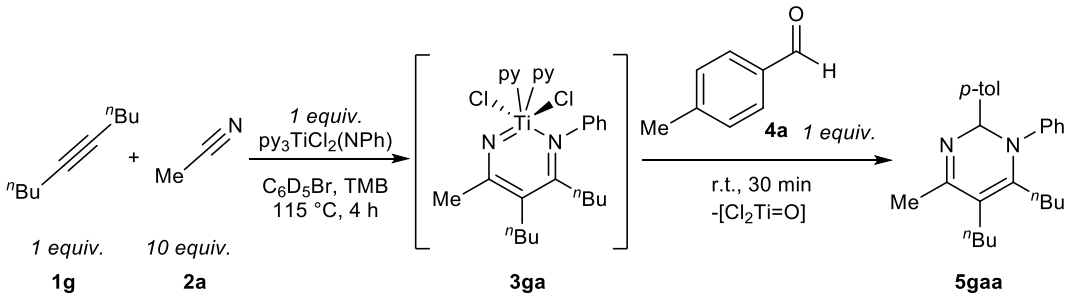
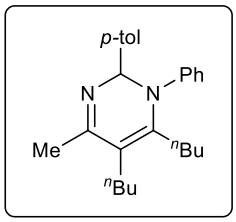


Figure S38. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 3-hexyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



5,6-dibutyl-4-methyl-1-phenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5gaa)



32% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.50 (d, *J* = 7.8 Hz, 2H), 7.14 – 7.09 (m, 4H), 7.08 – 7.06 (m, 4H), 6.36 (s, 1H), 2.32 (s, 3H), 2.15 (s, 3H), 1.22 – 1.13 (m, 2H), 1.07 – 0.83 (m, 10H), 0.64 (t, *J* = 7.2 Hz, 3H), 0.59 (t, *J* = 7.3 Hz, 3H).

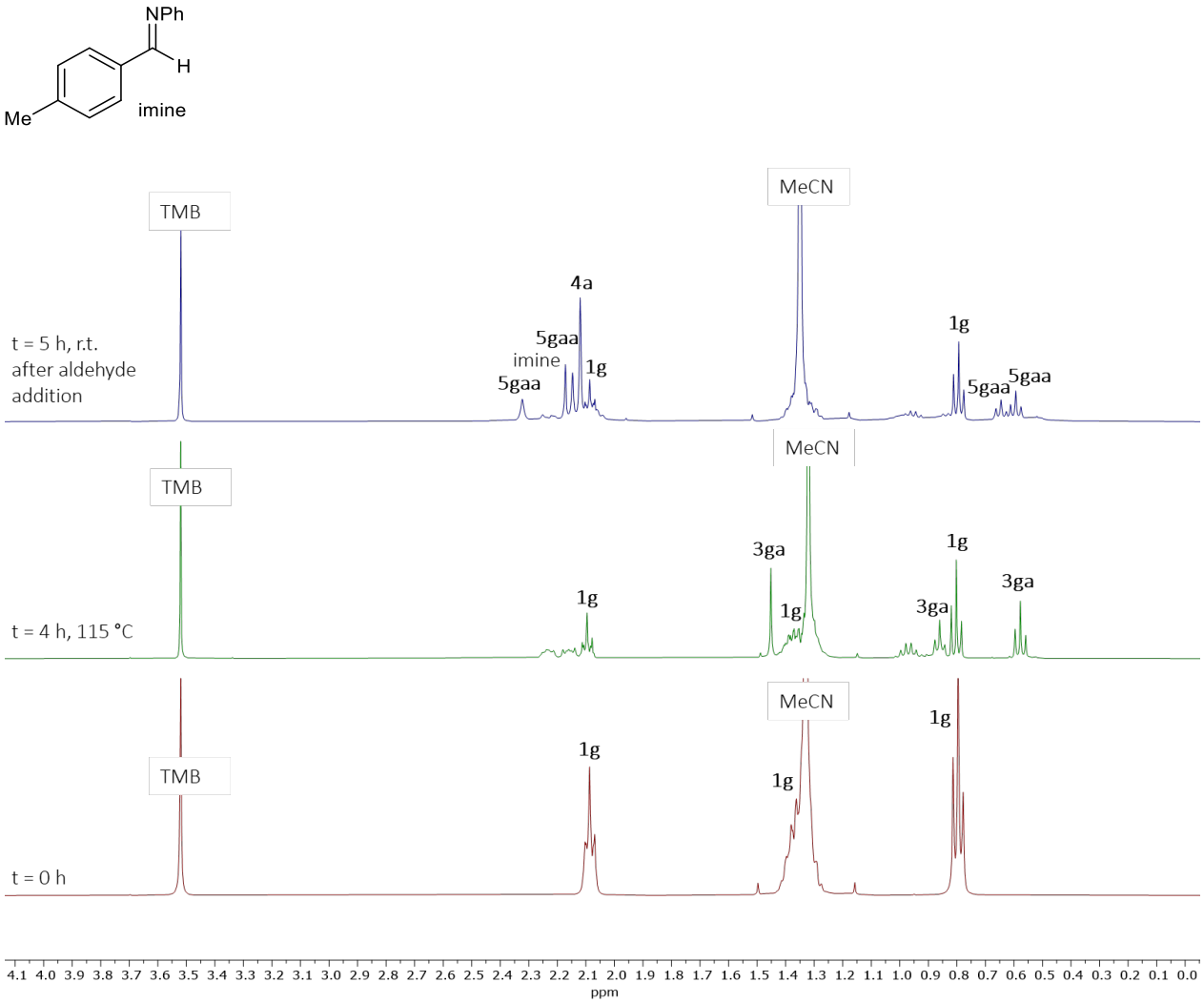


Figure S39. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 5-decyne (1 equiv., **1g**), acetonitrile (10 equiv., **2a**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ga** in 50% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5gaa** in 32% yield (79% conversion from metallacycle **3ga**).

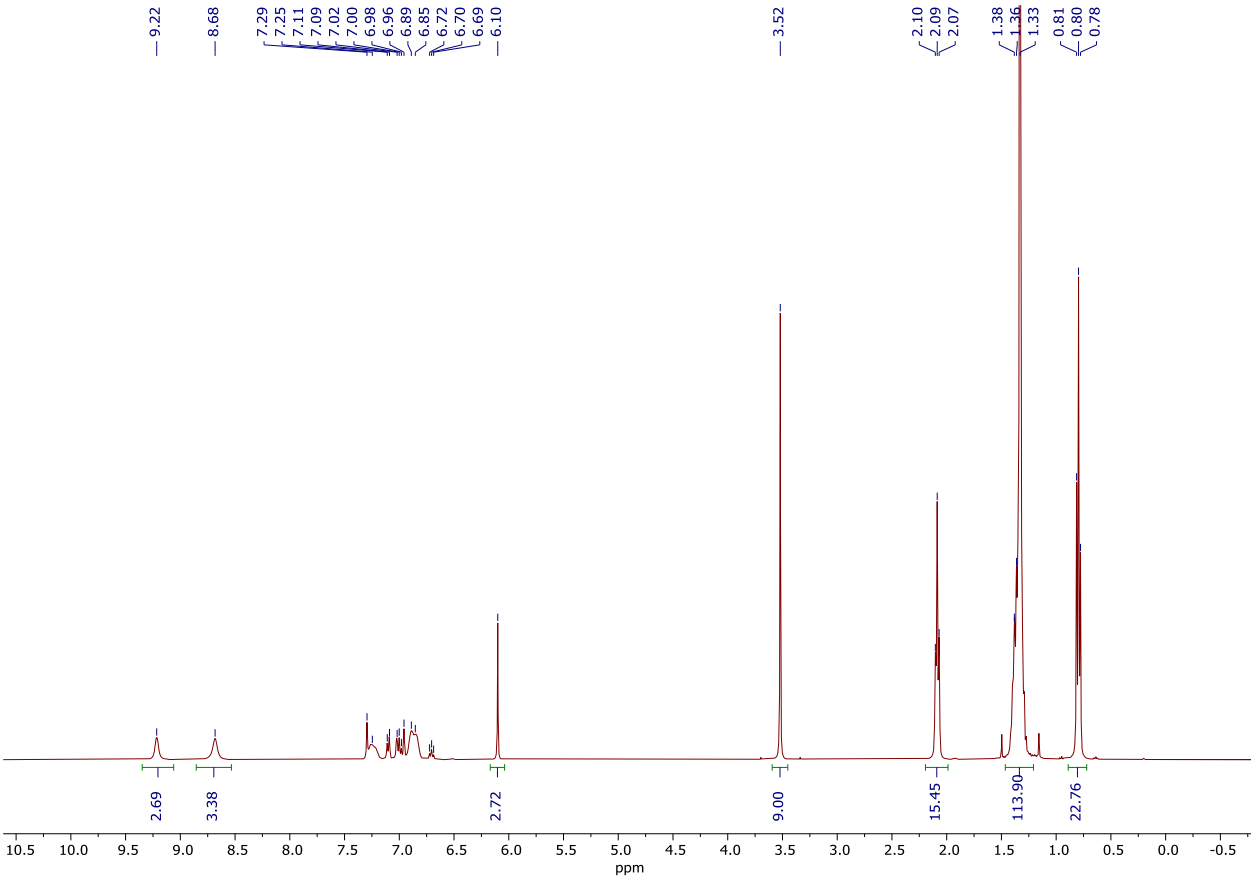


Figure S40. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 5-decyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

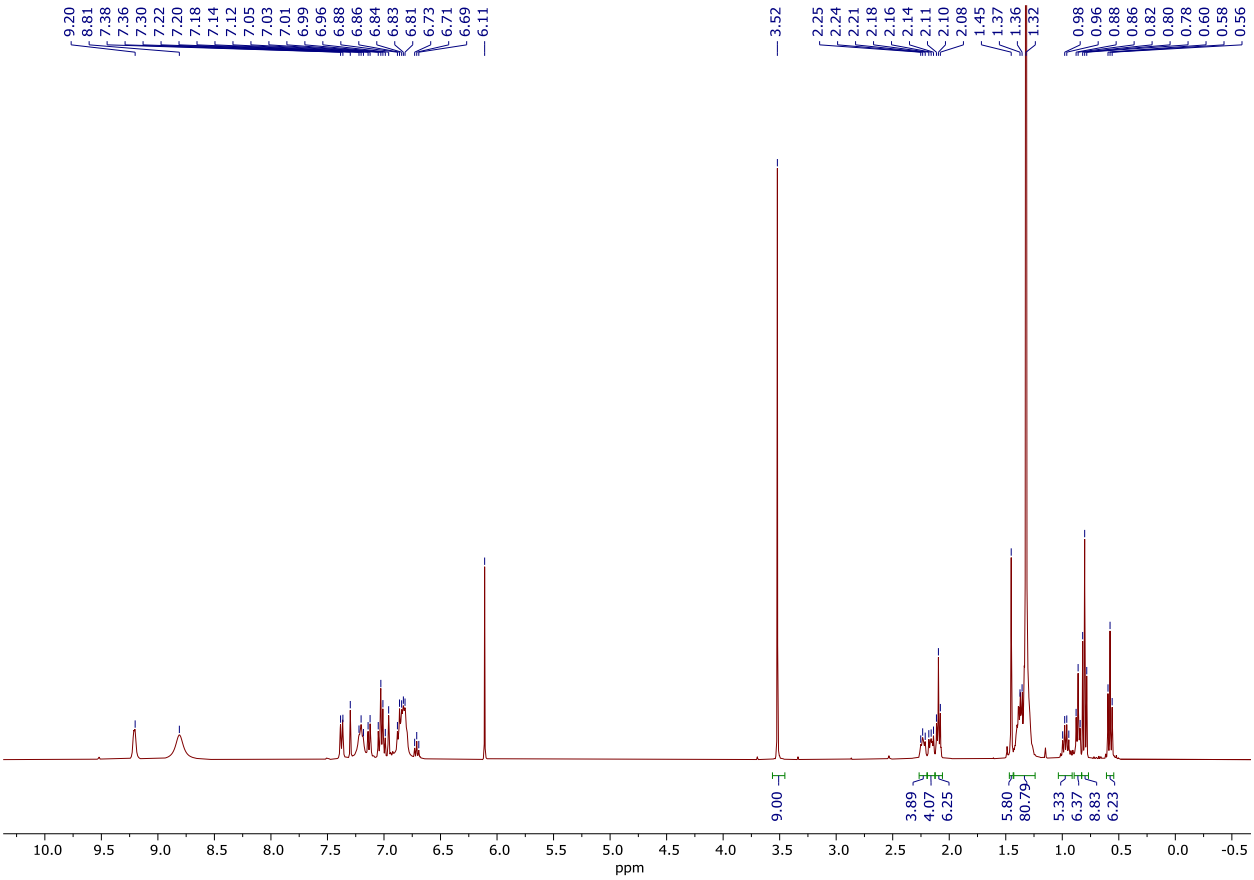


Figure S41. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 5-decyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

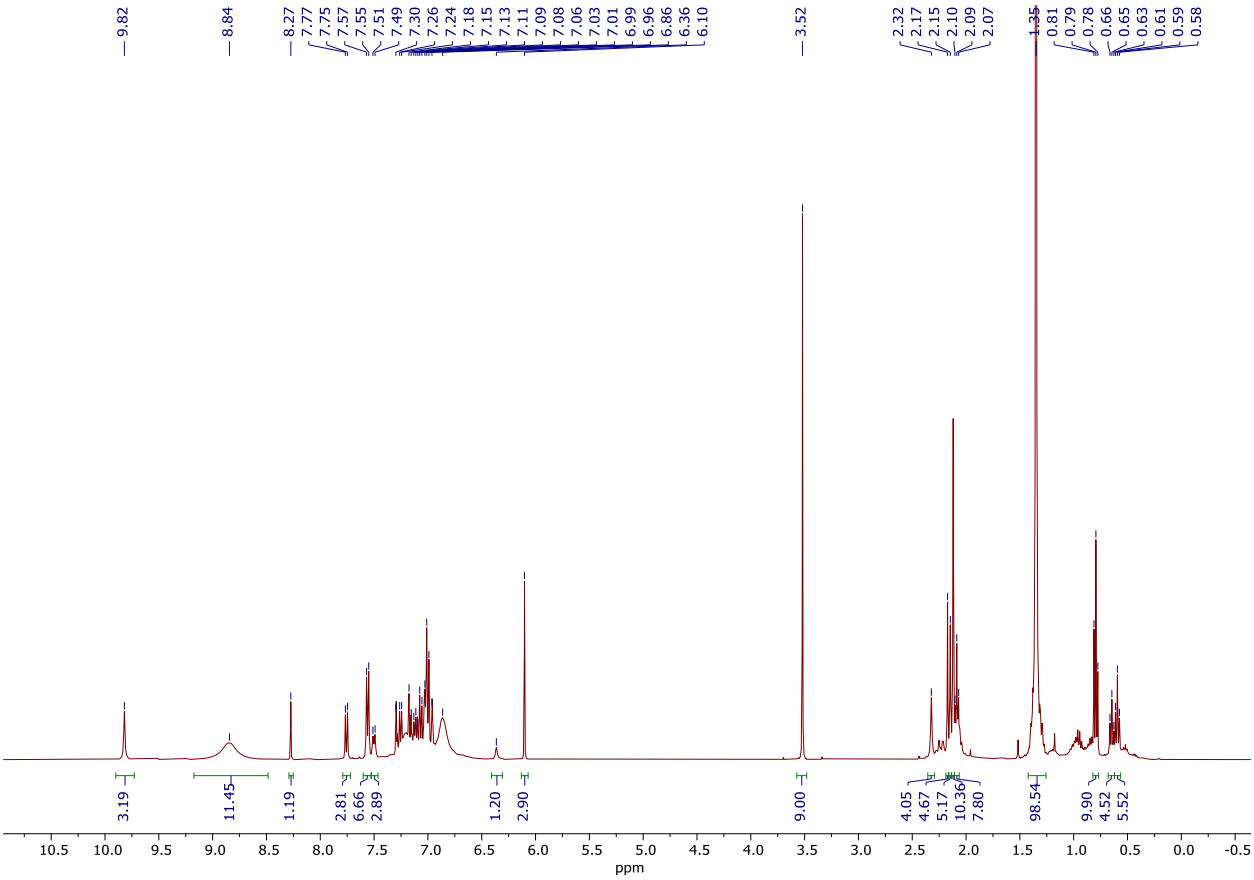
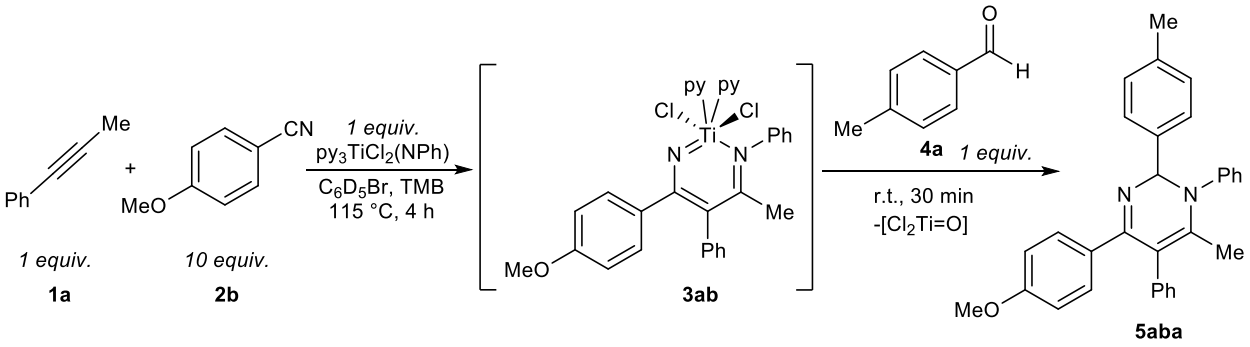
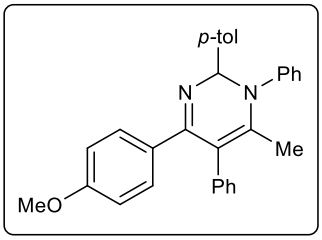


Figure S42. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 5-decyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



4-(4-methoxyphenyl)-6-methyl-1,5-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aba)



42% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.62 (d, *J* = 7.6 Hz, 2H), 7.18 – 7.16 (m, 3H), 7.14 – 7.06 (m, 8H), 7.02 – 6.97 (m, 5H), 6.53 (s, 1H), 3.31 (s, 3H), 2.20 (s, 3H), 1.99 (s, 3H).

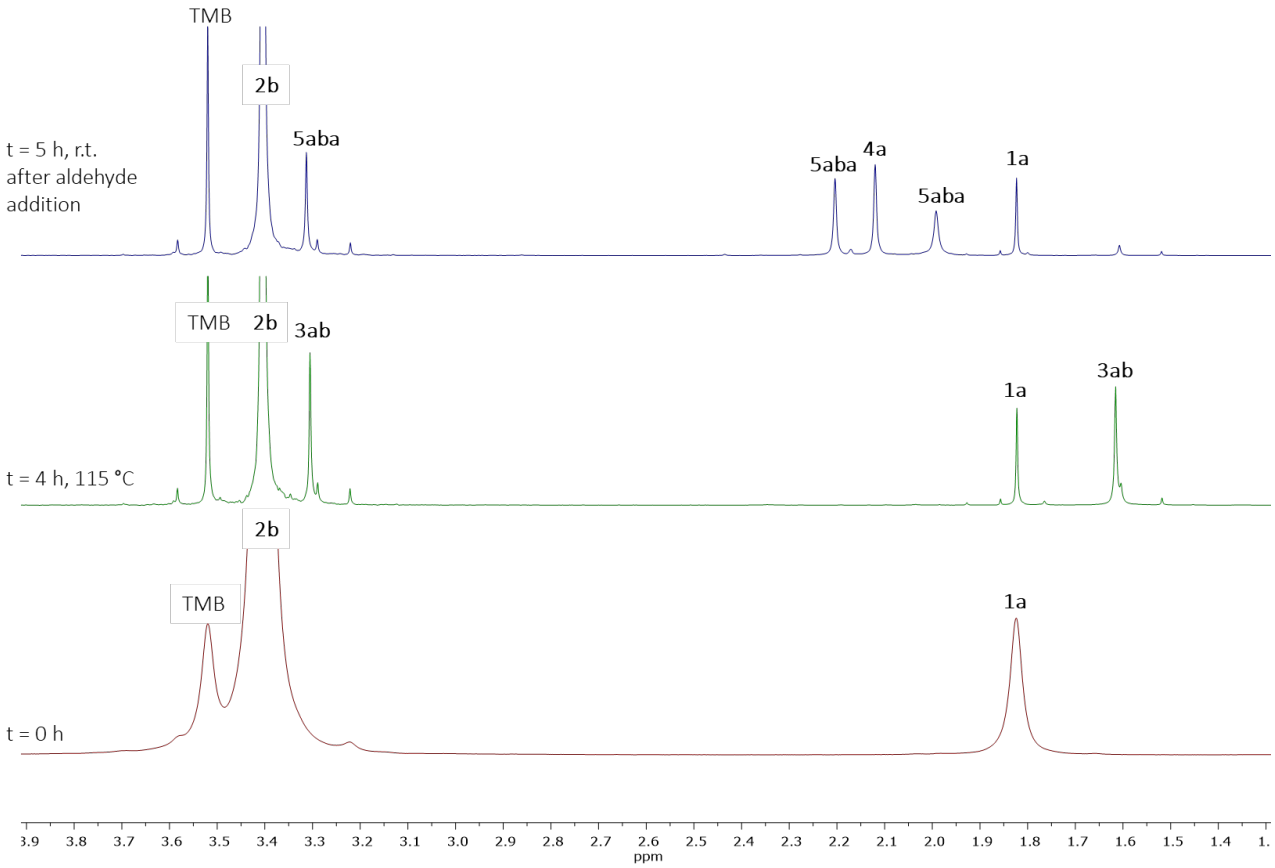


Figure S43. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), 4-methoxybenzonitrile (10 equiv., **2b**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ab** in 68% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aba** in 42% yield (64% conversion from metallacycle **3ab**).

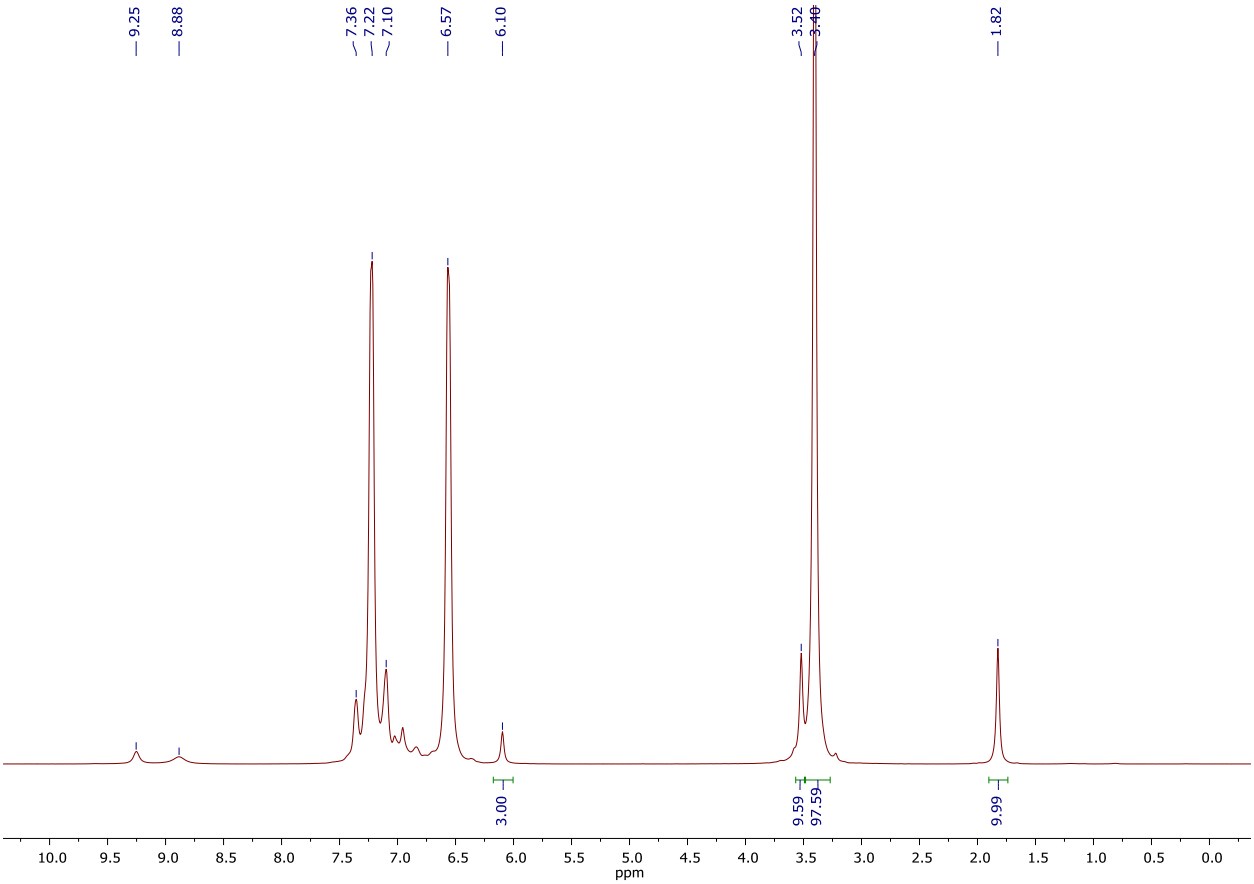


Figure S44. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-methoxybenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

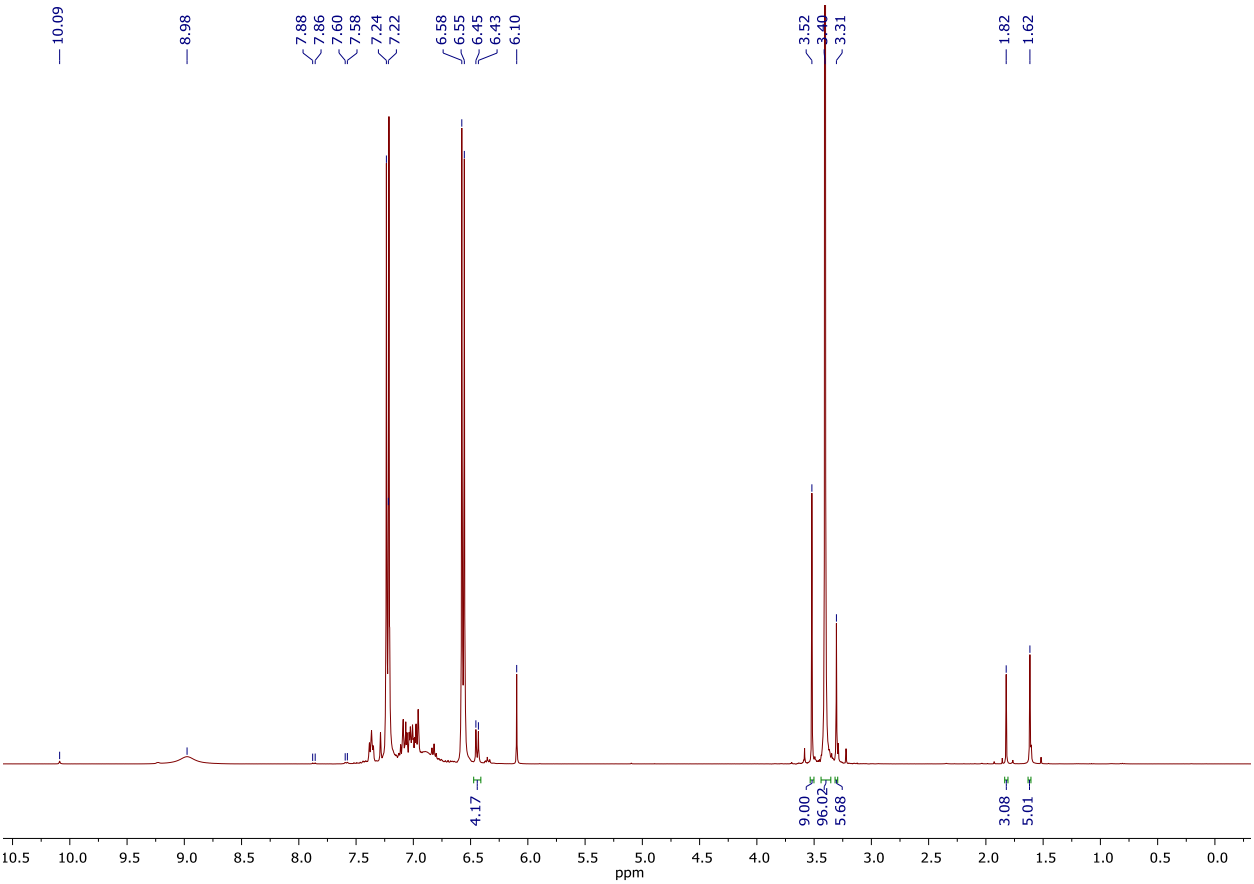


Figure S45. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-methoxybenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

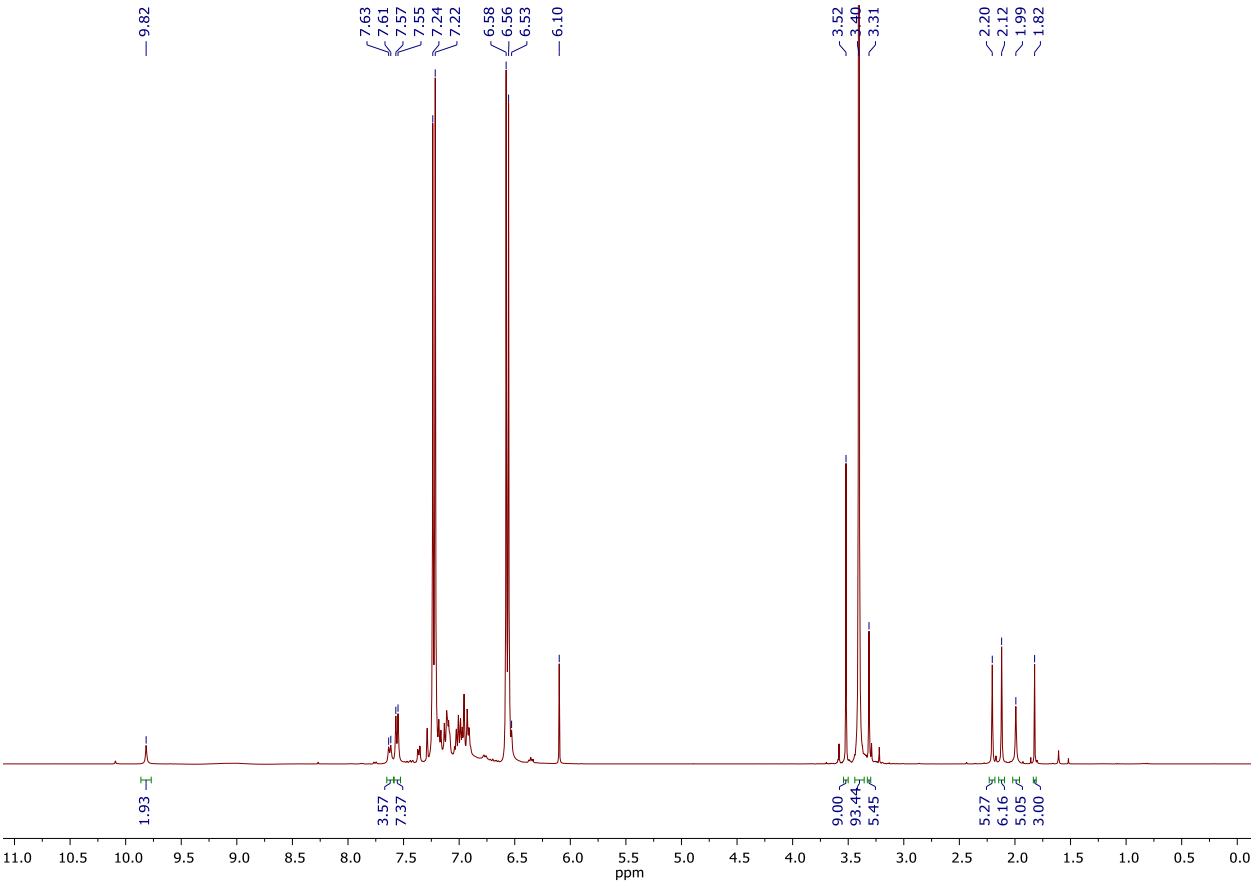
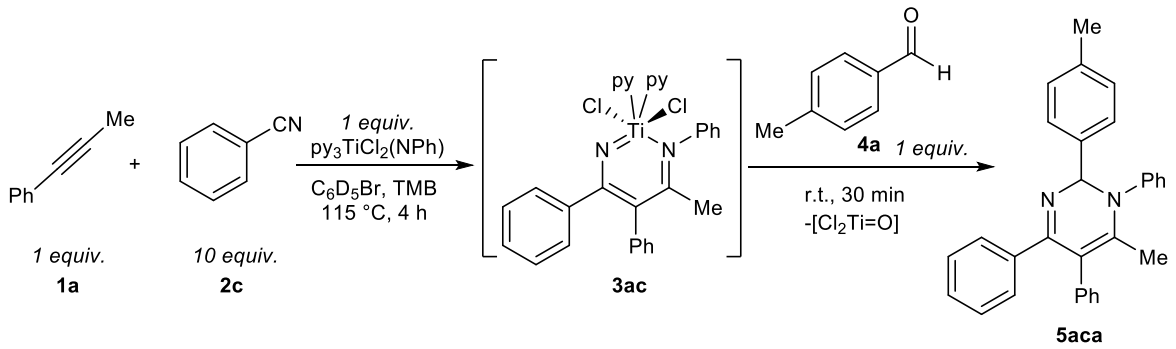
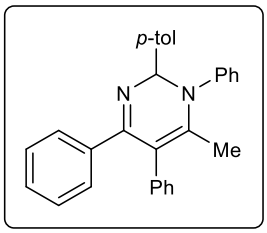


Figure S46. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-methoxybenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



6-methyl-1,4,5-triphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aca)



37% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.62 (d, *J* = 8.1 Hz, 2H), 7.12 – 7.07 (m, 7H), 6.94 – 6.85 (m, 10H), 6.76 (s, 1H), 2.21 (s, 3H), 1.97 (s, 3H).

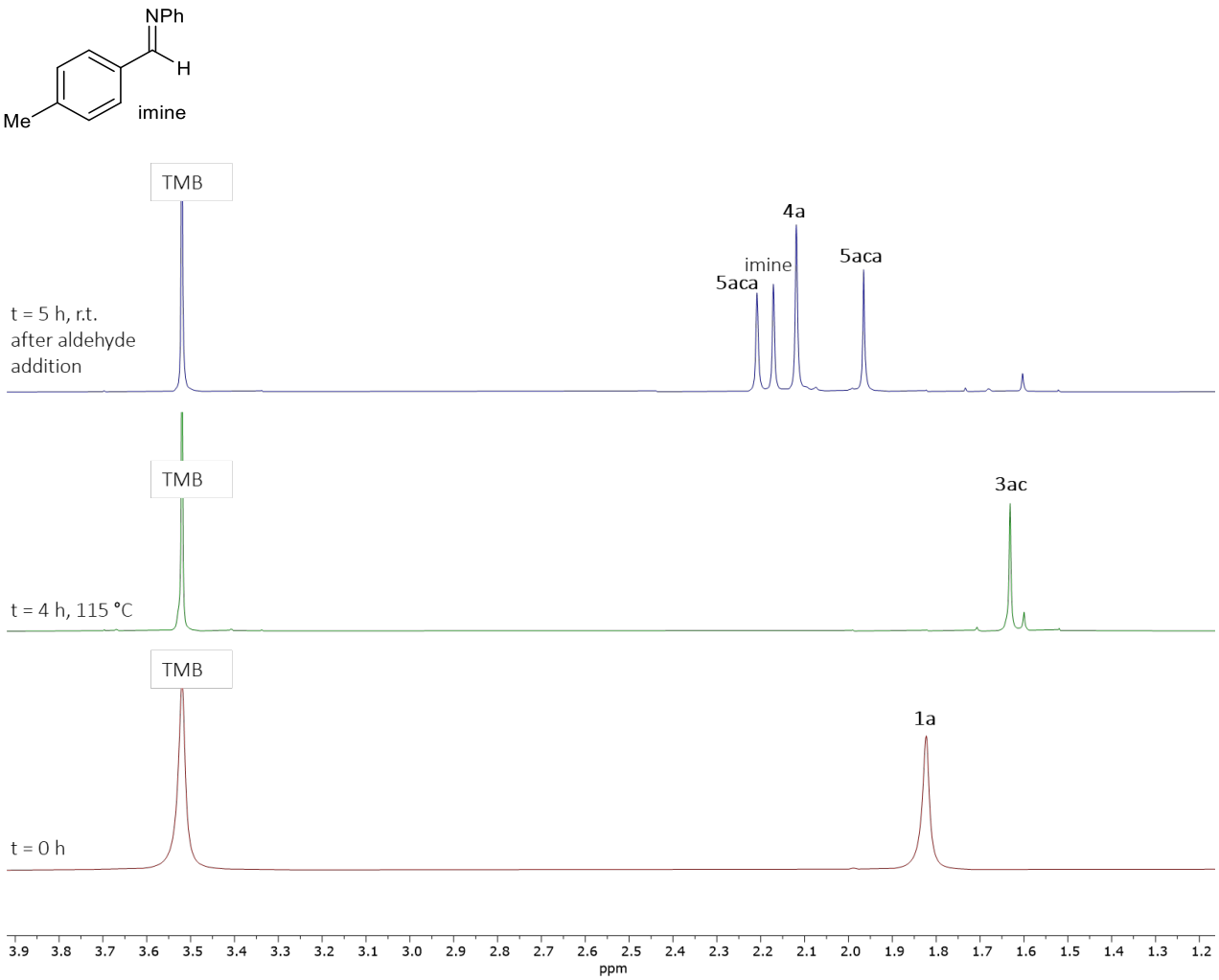


Figure S47. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), benzonitrile (10 equiv., **2c**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ac** in 39% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aca** in 37% yield (93% conversion from metallacycle **3ac**).

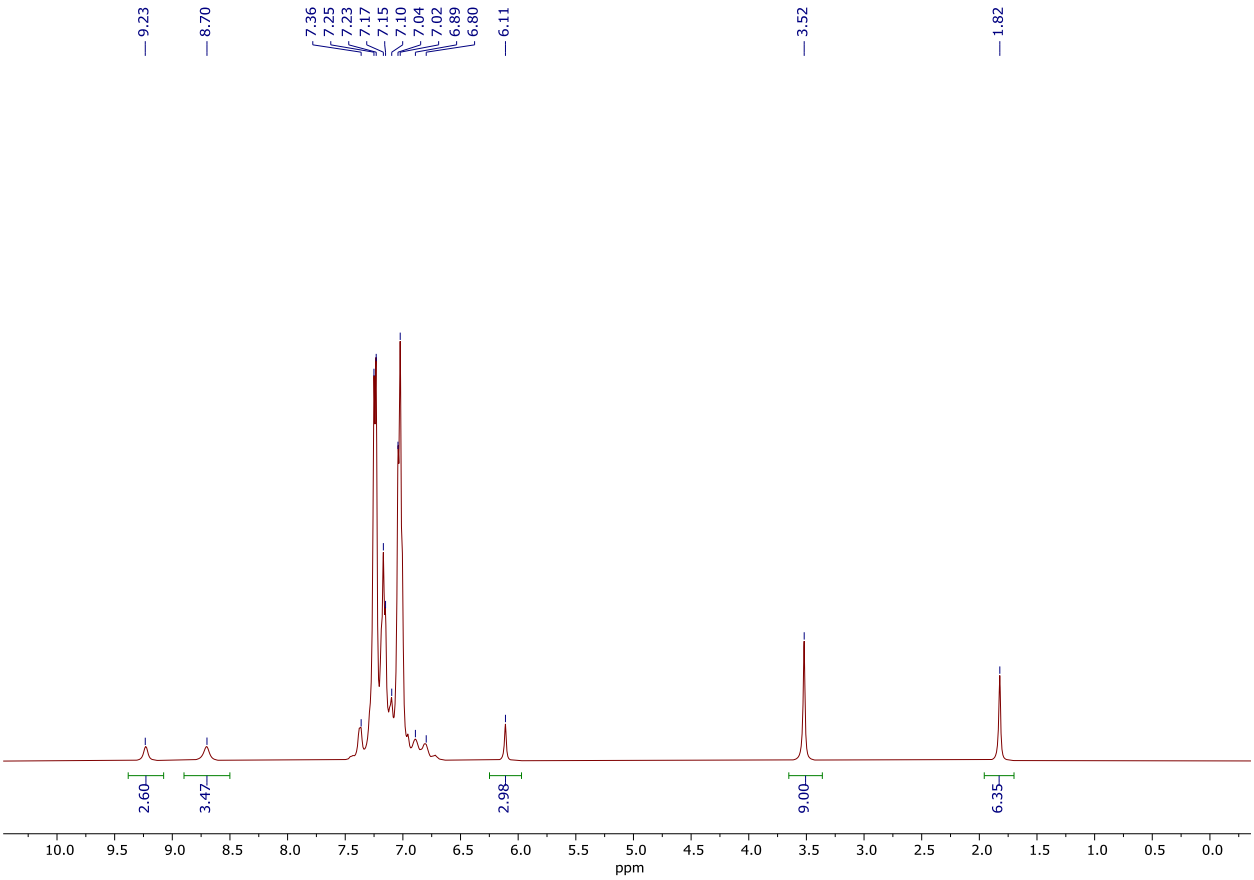


Figure S48. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), benzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

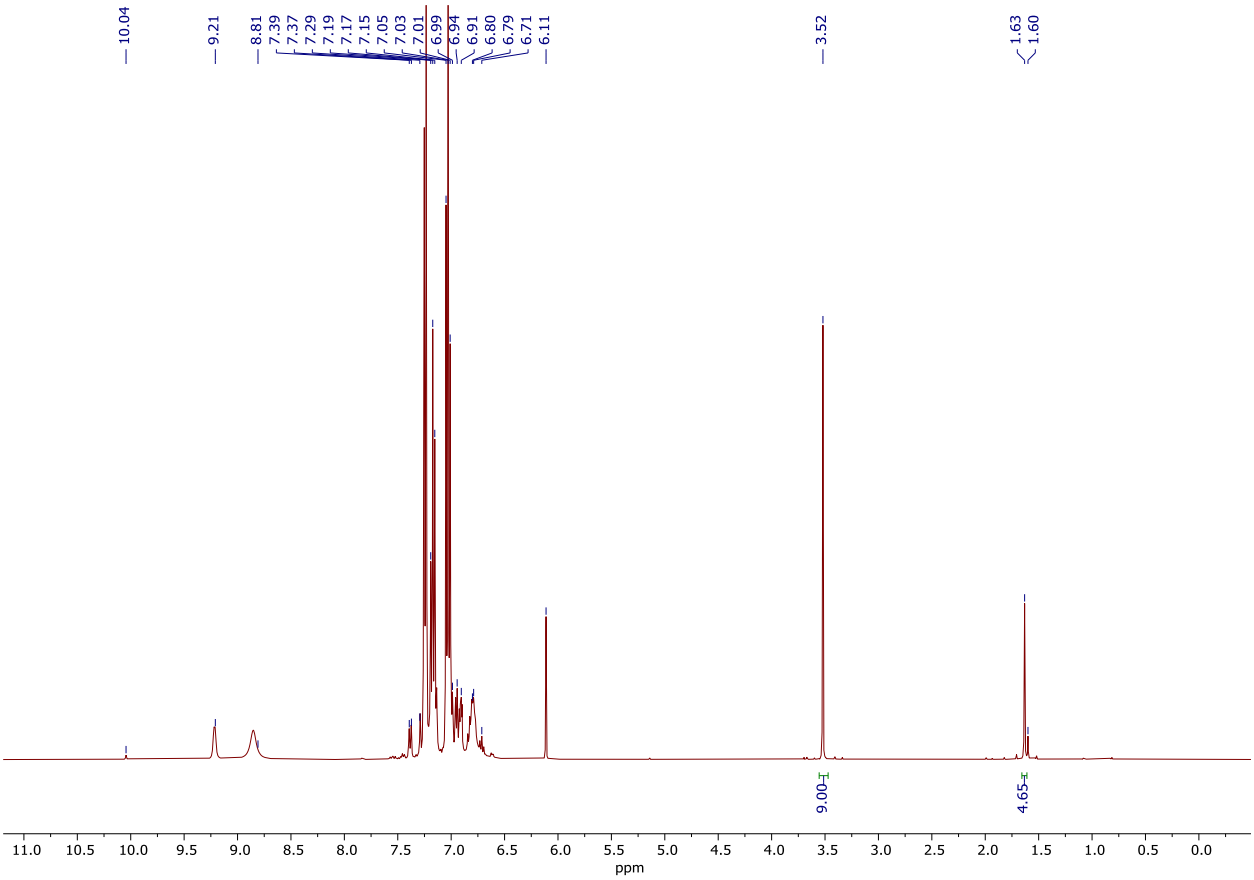


Figure S49. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), benzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

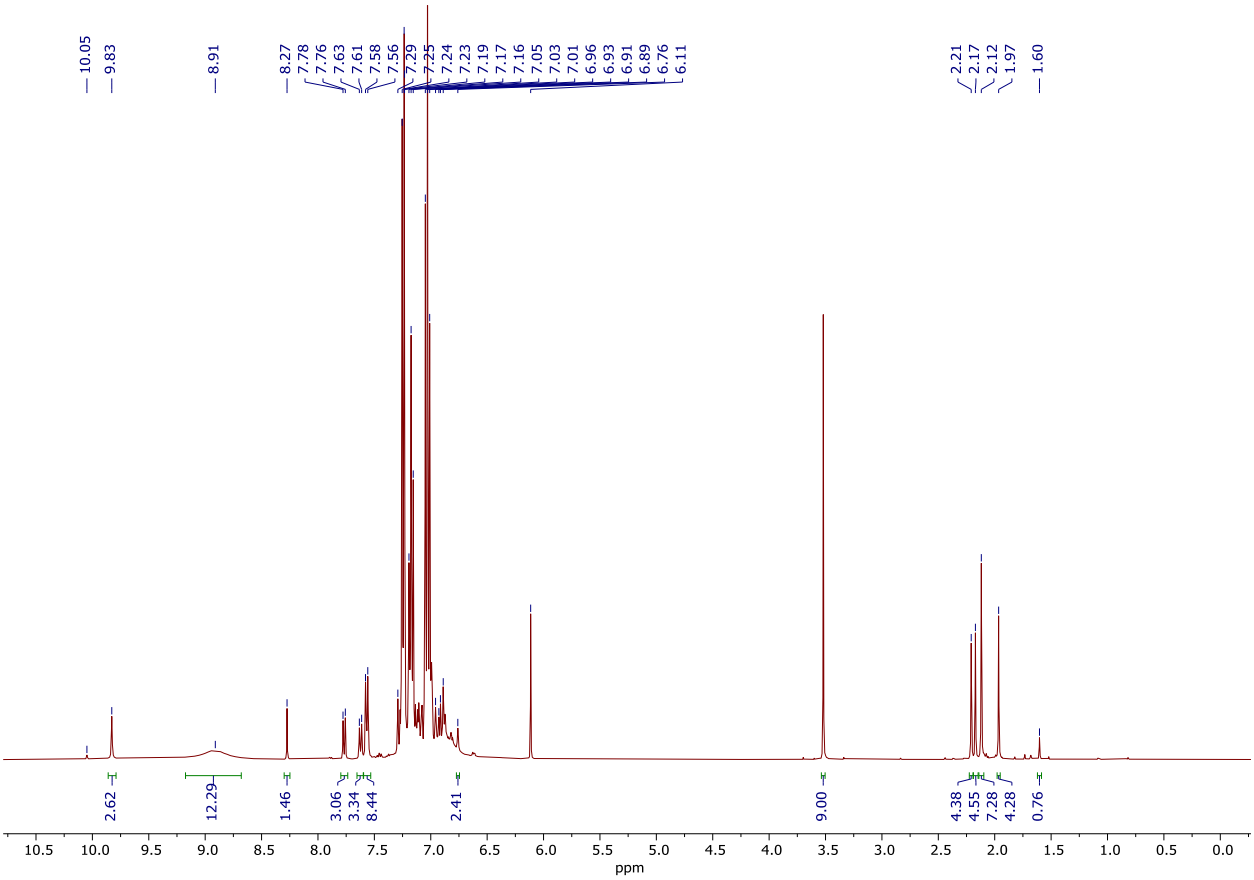
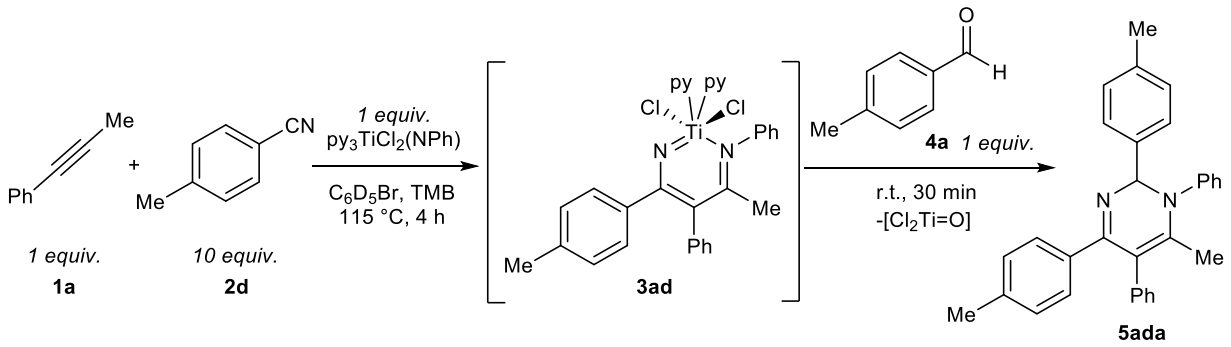
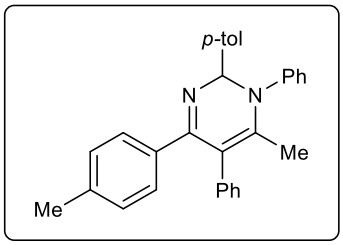


Figure S50. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), benzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



6-methyl-1,5-diphenyl-2,4-di-p-tolyl-1,2-dihydropyrimidine (5ada)



62% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.62 (d, *J* = 7.9 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.14 – 7.05 (m, 8H), 6.91 (td, *J* = 6.9, 5.1 Hz, 6H), 6.75 (s, 1H), 2.20 (s, 3H), 1.97 (s, 6H).

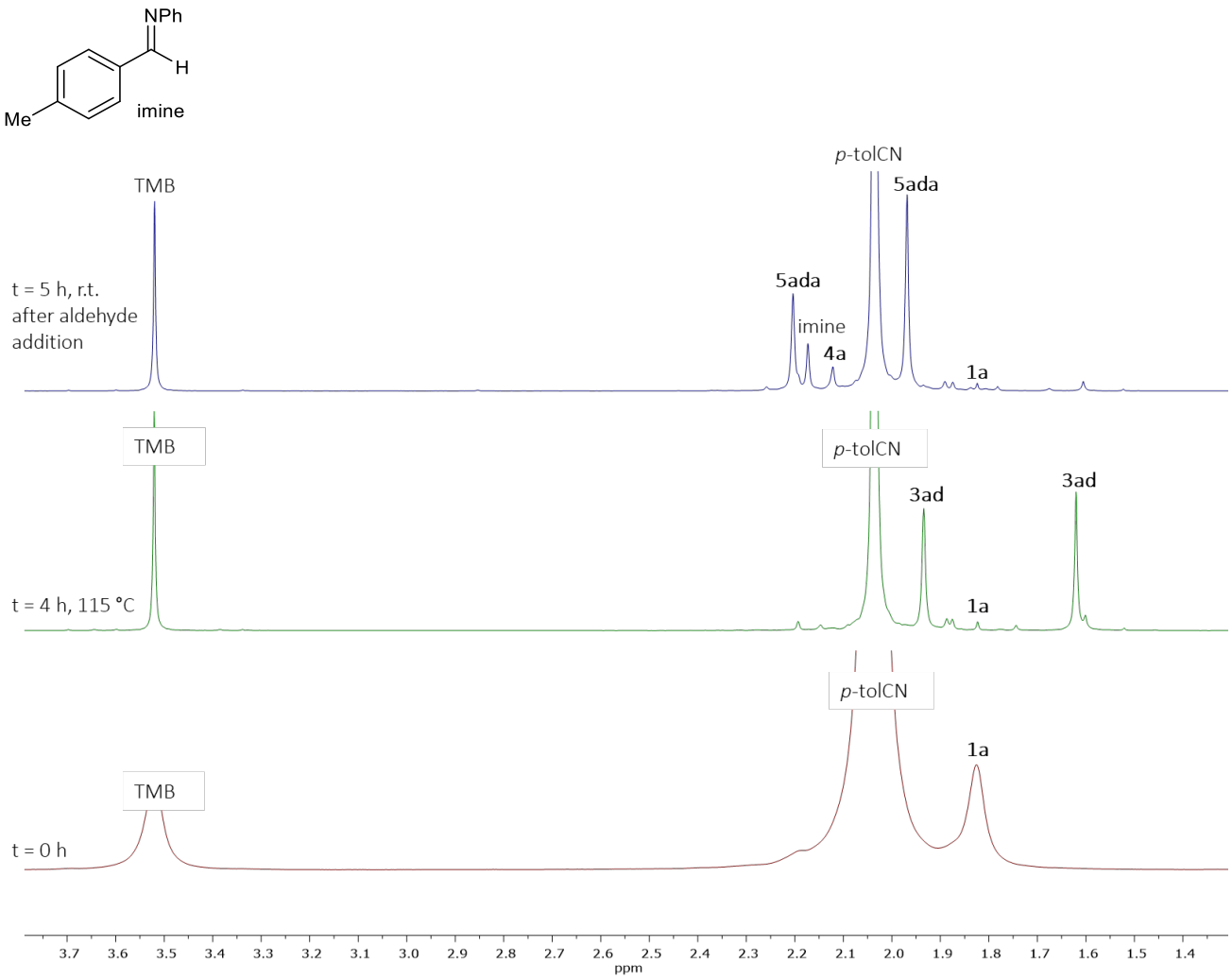


Figure S51. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), *p*-tolunitrile (10 equiv., **2d**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ad** in 59% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5ada** in 62% yield (94% conversion from the metallacycle **3ad**).

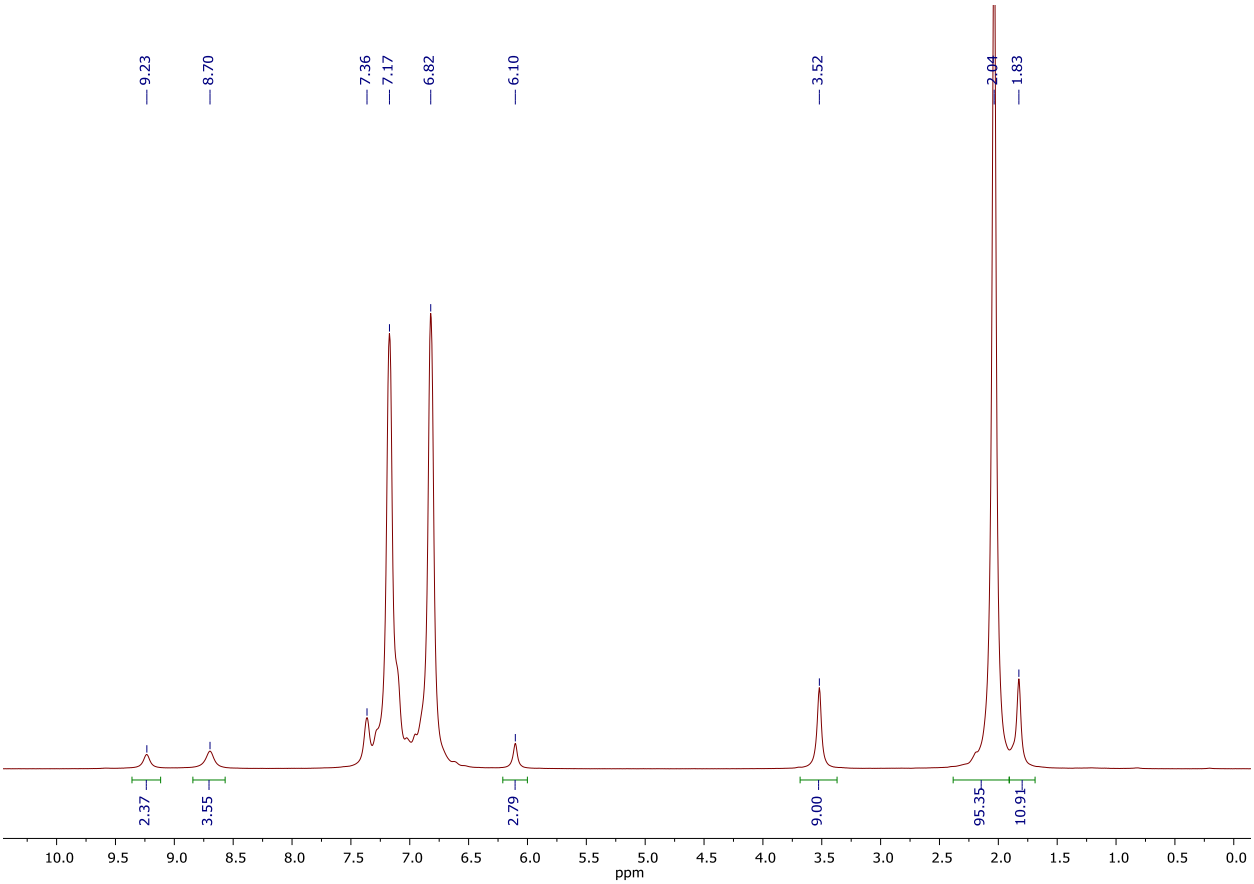


Figure S52. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), *p*-tolunitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

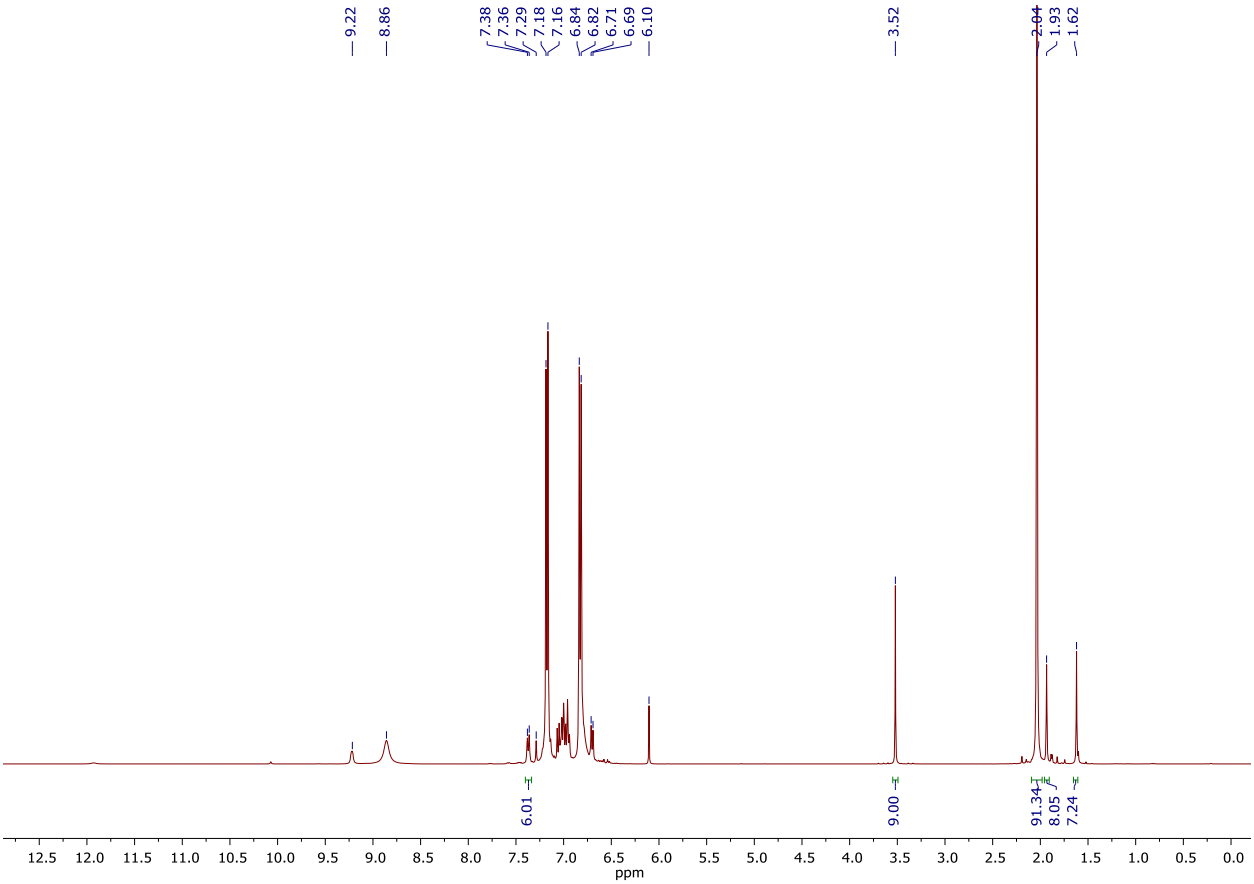


Figure S53. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), *p*-tolunitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

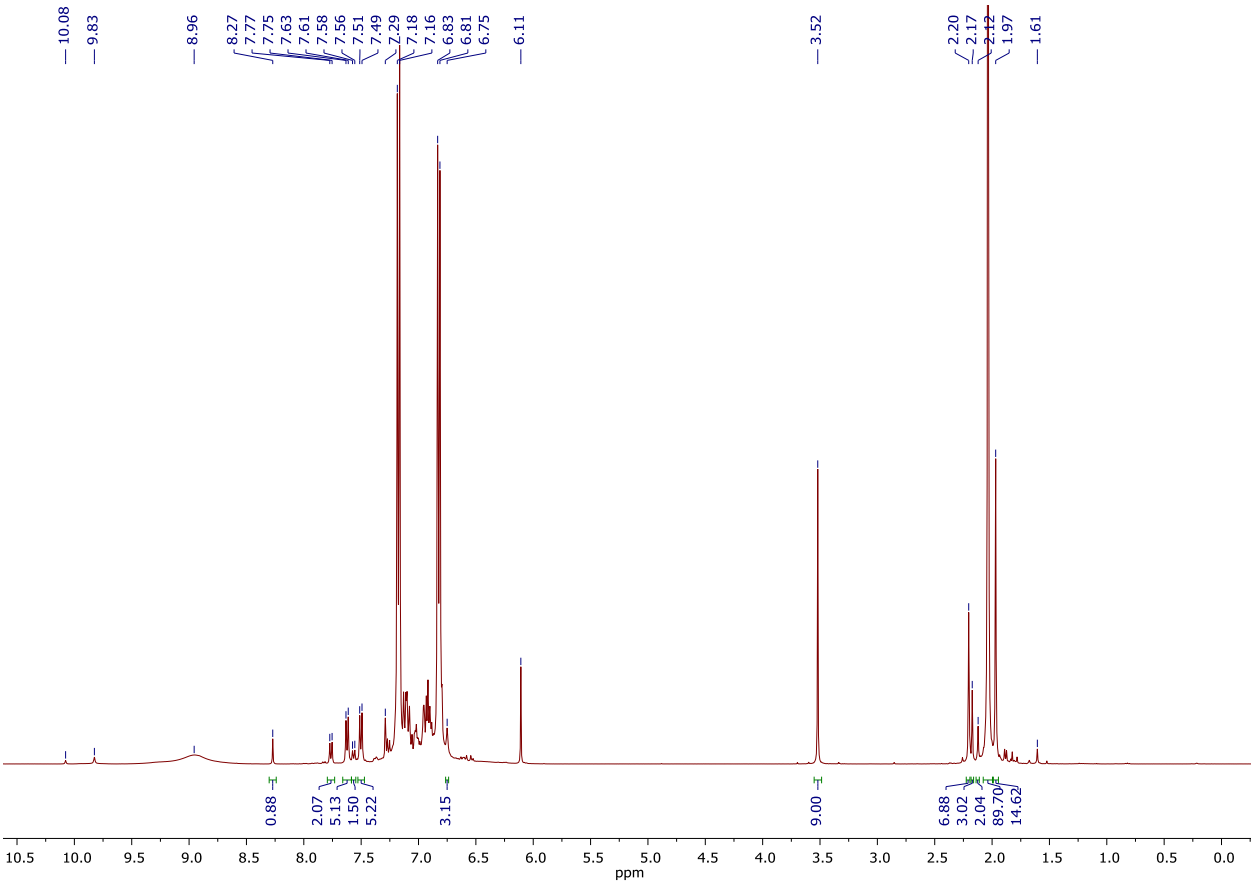
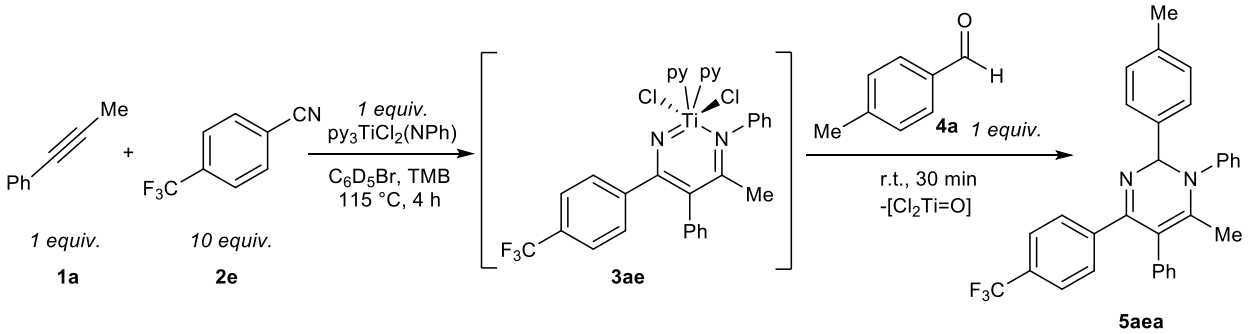
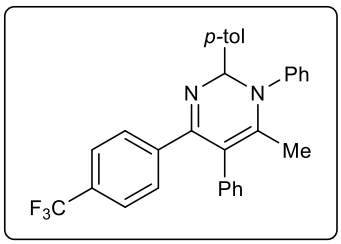


Figure S54. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), *p*-tolunitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



6-methyl-1,5-diphenyl-2-(p-tolyl)-4-(4-(trifluoromethyl)phenyl)-1,2-dihydropyrimidine (5aea)



37% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.58 (t, *J* = 8.0 Hz, 5H), 7.18 – 7.16 (m, 6H), 7.14 – 7.12 (m, 4H), 7.07 – 7.04 (m, 3H), 6.74 (s, 1H), 2.22 (s, 3H), 1.96 (s, 3H). **^{19}F NMR (376 MHz, C_6D_5Br, δ, ppm):** -62.83.

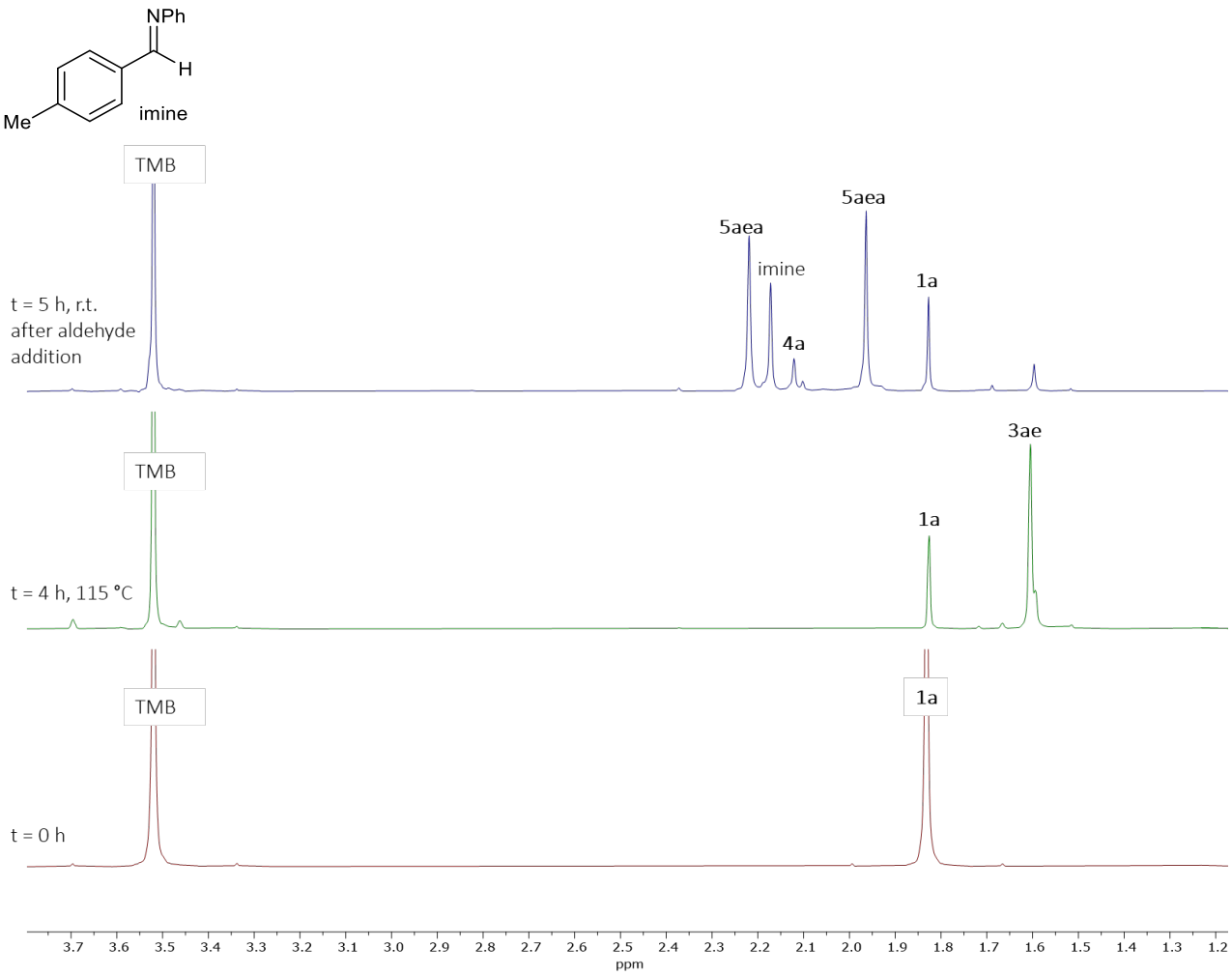


Figure S55. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), 4-trifluoromethylbenzonitrile (10 equiv., **2e**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3ae** in 35% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aea** in 37% yield.

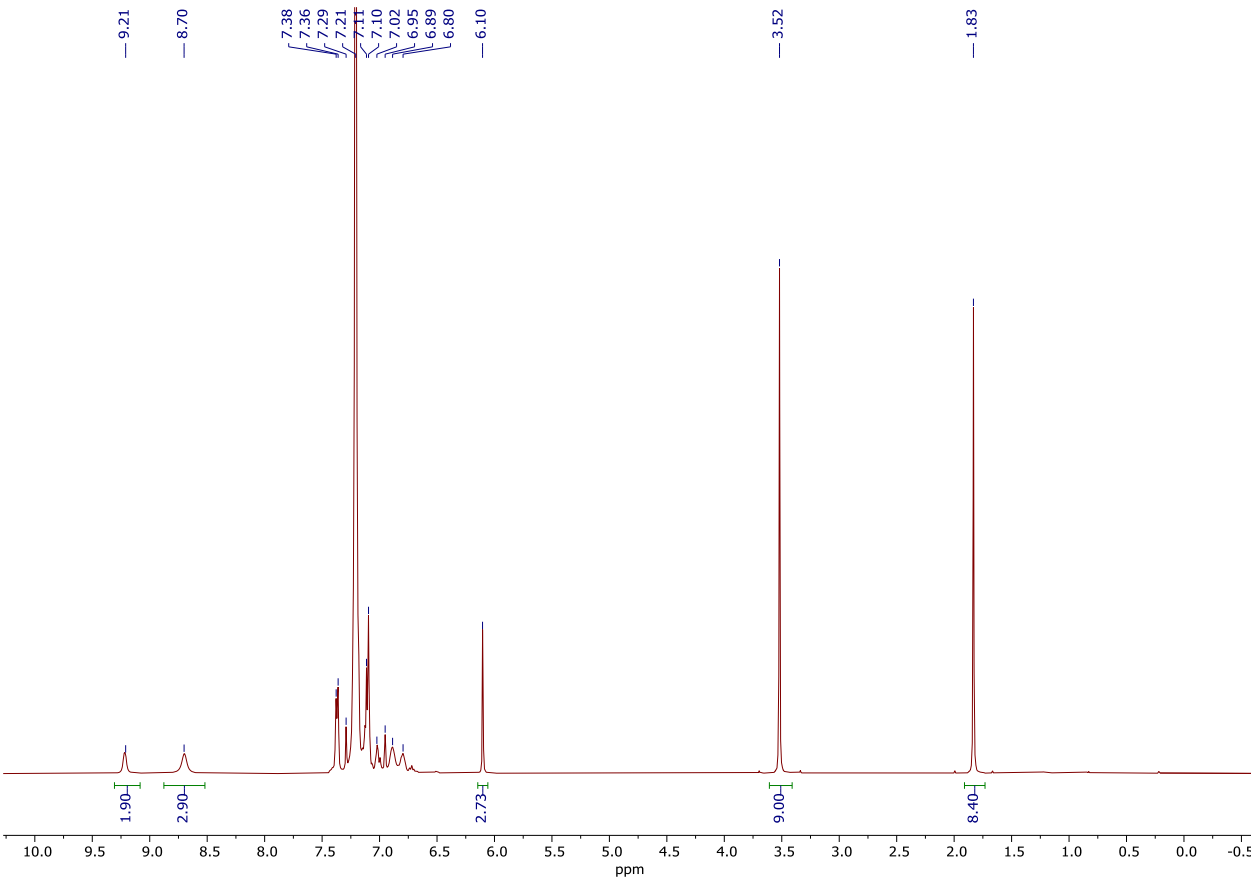


Figure S56. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-trifluoromethylbenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

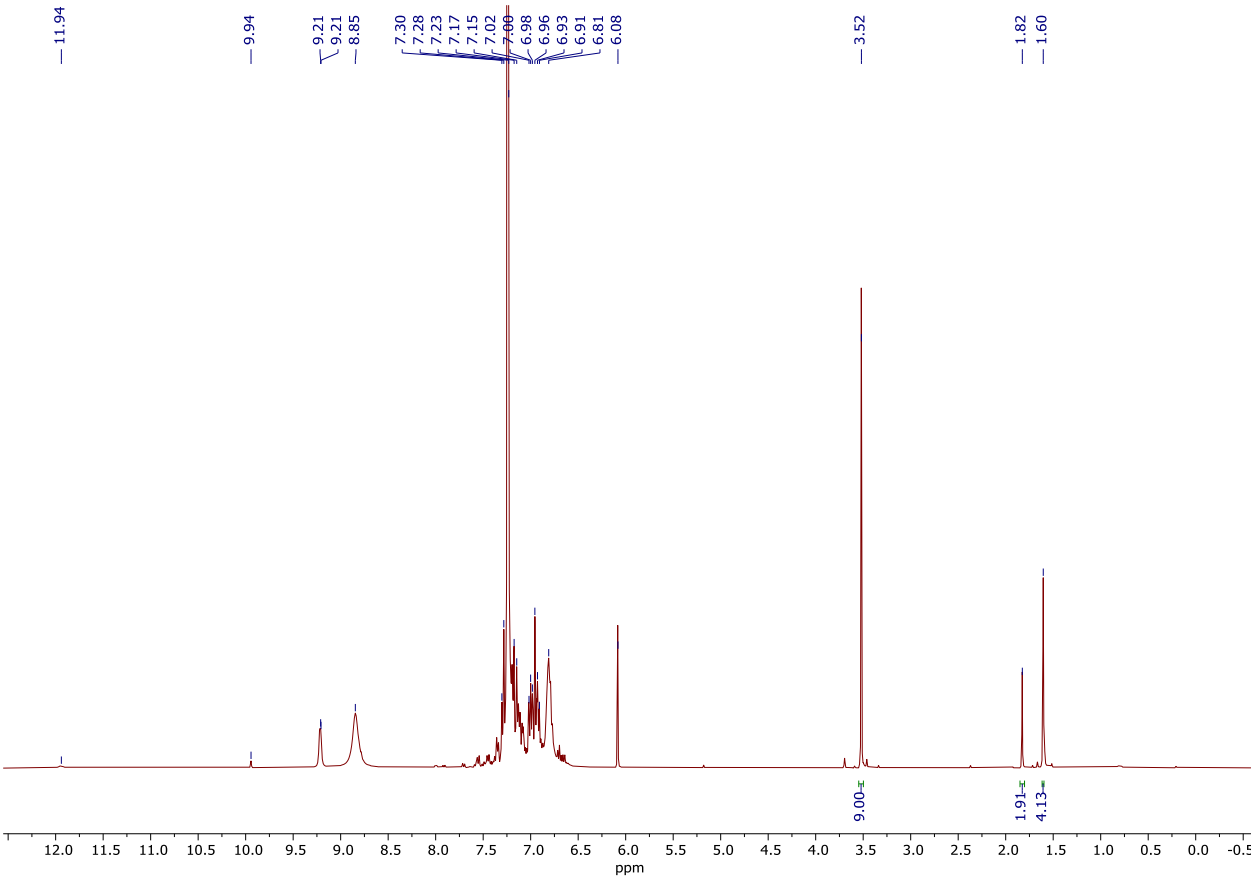


Figure S57. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-trifluoromethylbenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

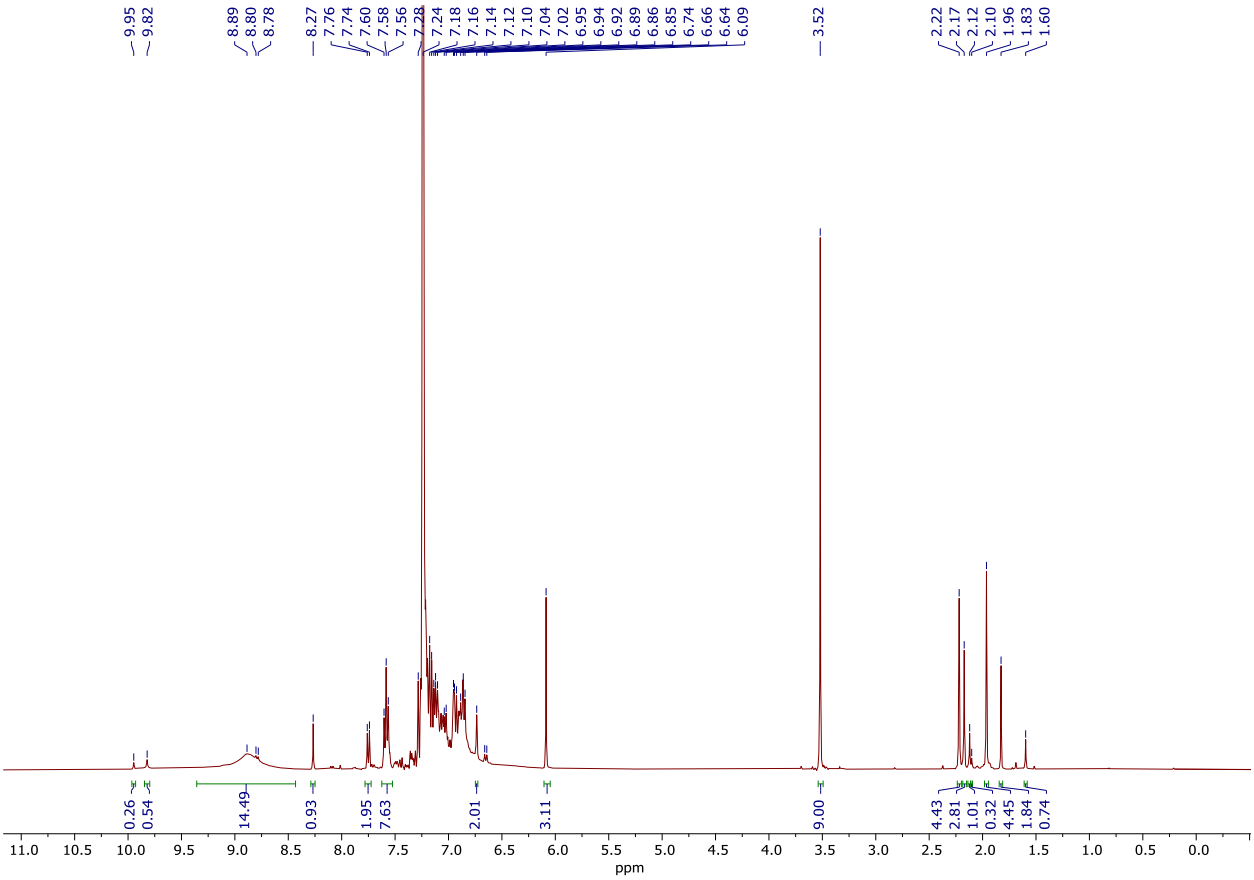


Figure S58. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-trifluoromethylbenzonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).

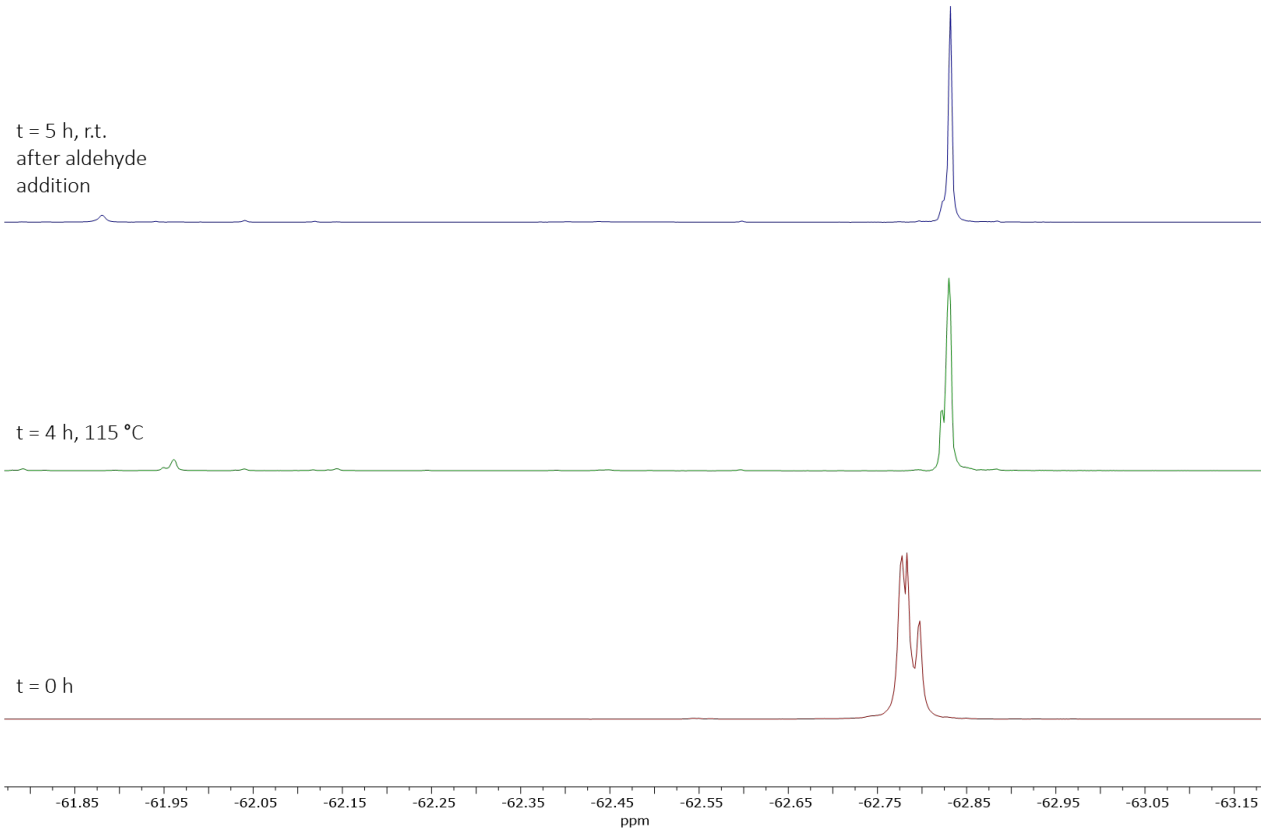
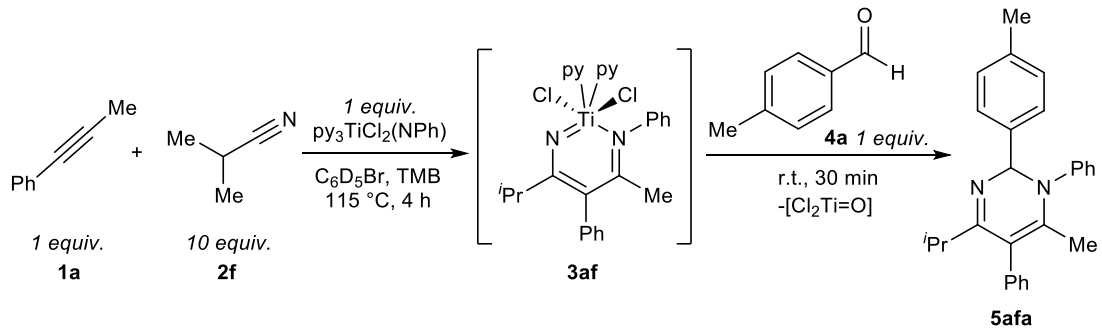
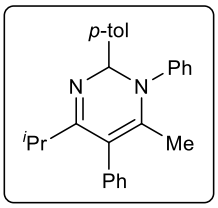


Figure S59. Stacked ^{19}F NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), 4-trifluoromethylbenzonitrile (10 equiv.), *p*-tolualdehyde (1 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C.



4-isopropyl-6-methyl-1,5-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5afa)



48% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.53 (d, *J* = 8.2 Hz, 2H), 7. 19 – 7.12 (m, 9H), 7.00 – 6.99 (m, 4H), 6.48 (s, 1H), 2.51 (p, *J* = 6.7 Hz, 1H), 2.21 (s, 3H), 1.70 (s, 3H), 1.09 (d, *J* = 6.7 Hz, 6H).

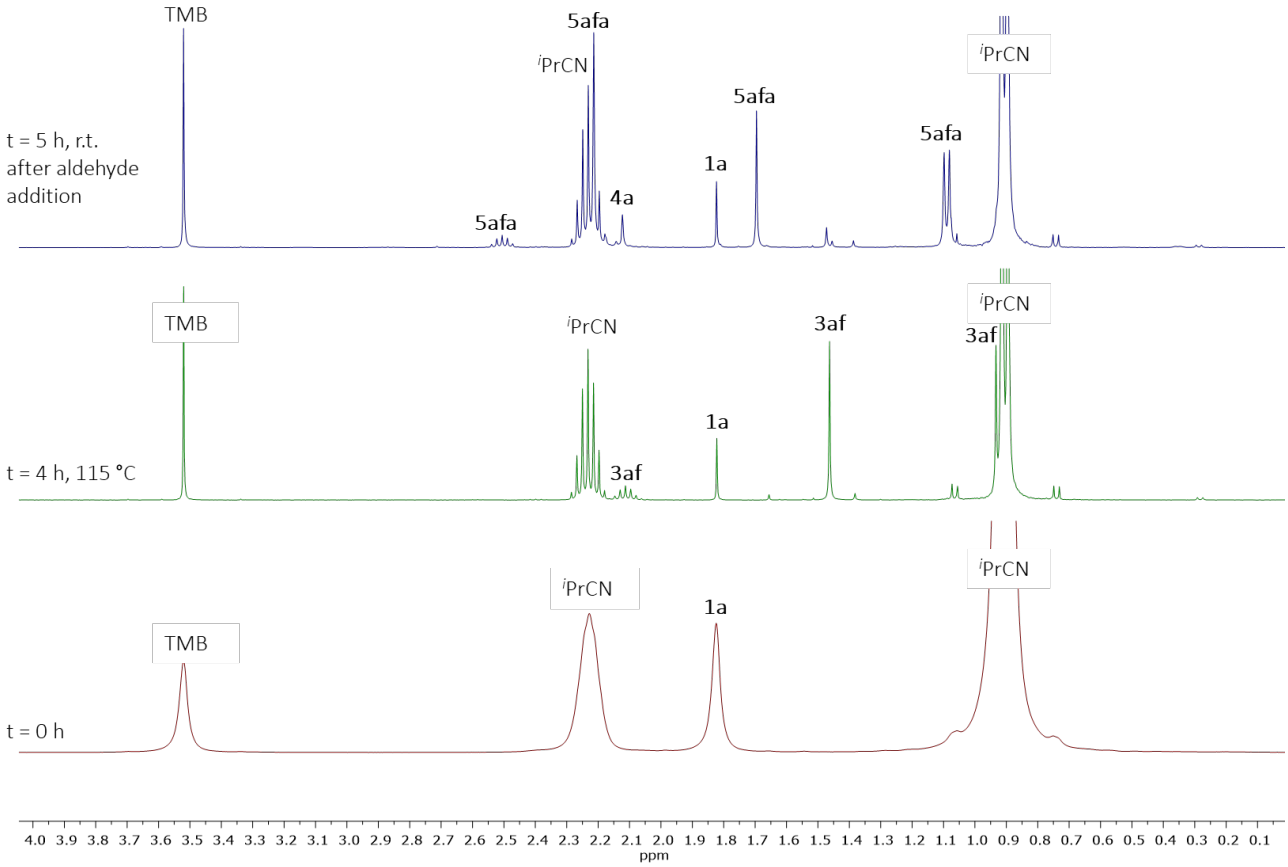


Figure S60. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), isobutyronitrile (10 equiv., **2f**), *p*-tolualdehyde (1 equiv., **4a**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3af** in 61% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5afa** in 48% yield (74% conversion of metallacycle **3af**).

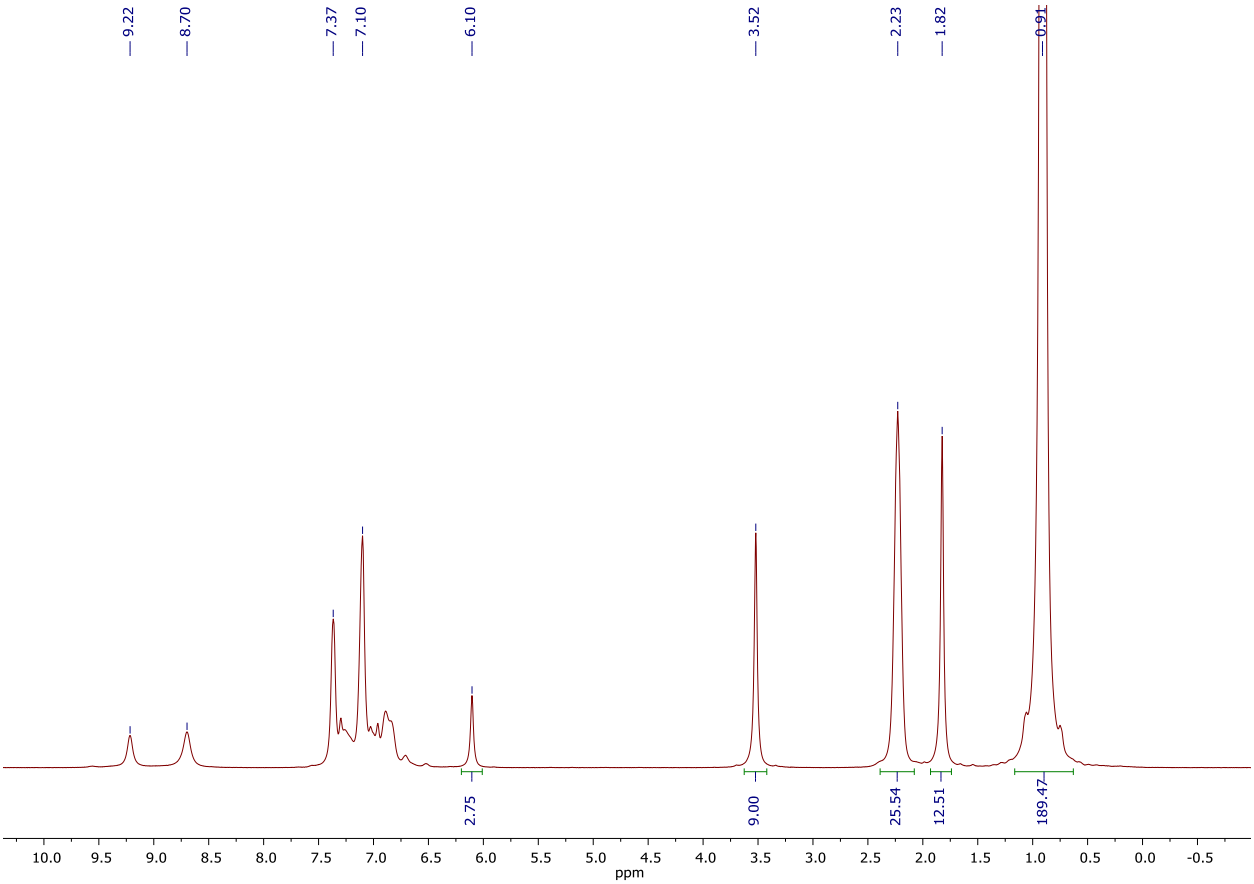


Figure S61. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), isobutyronitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

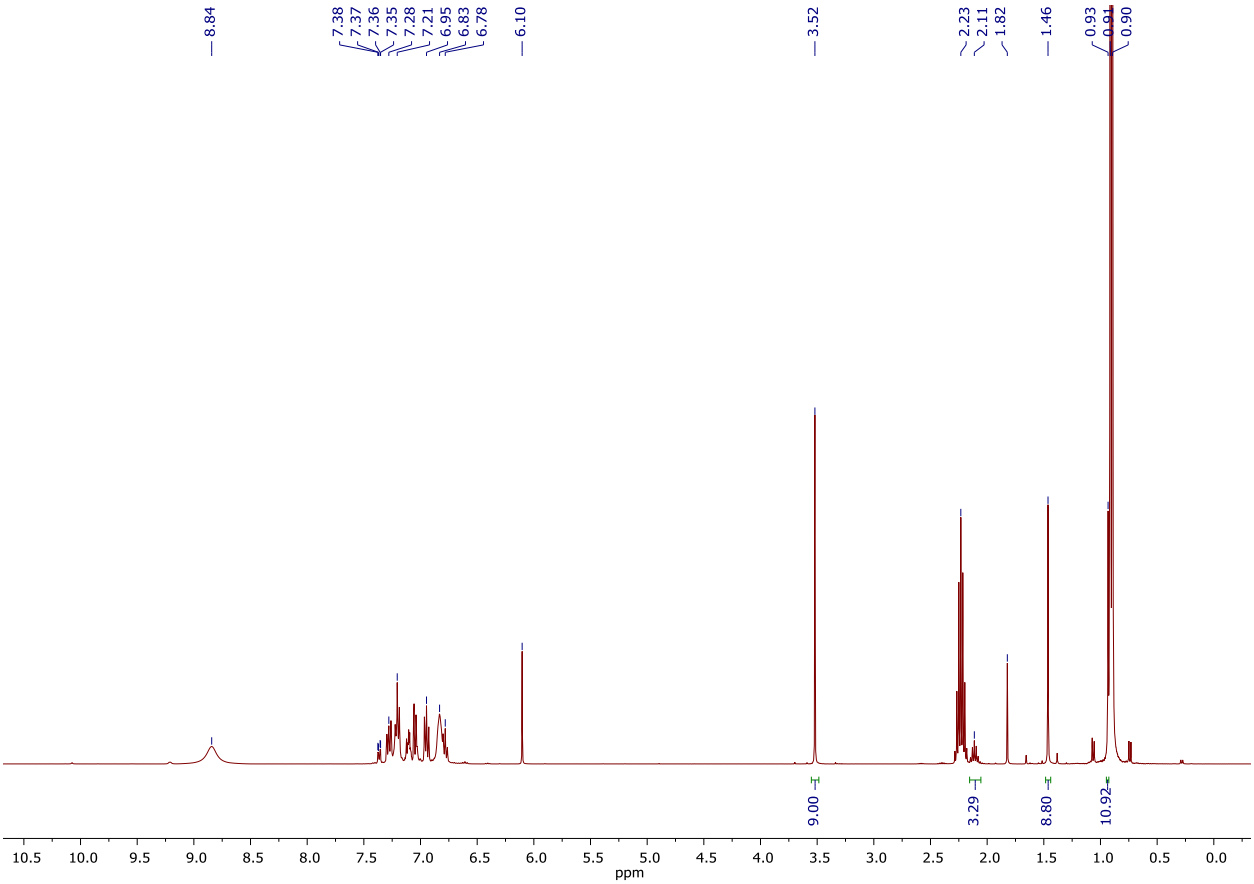


Figure S62. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), isobutyronitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

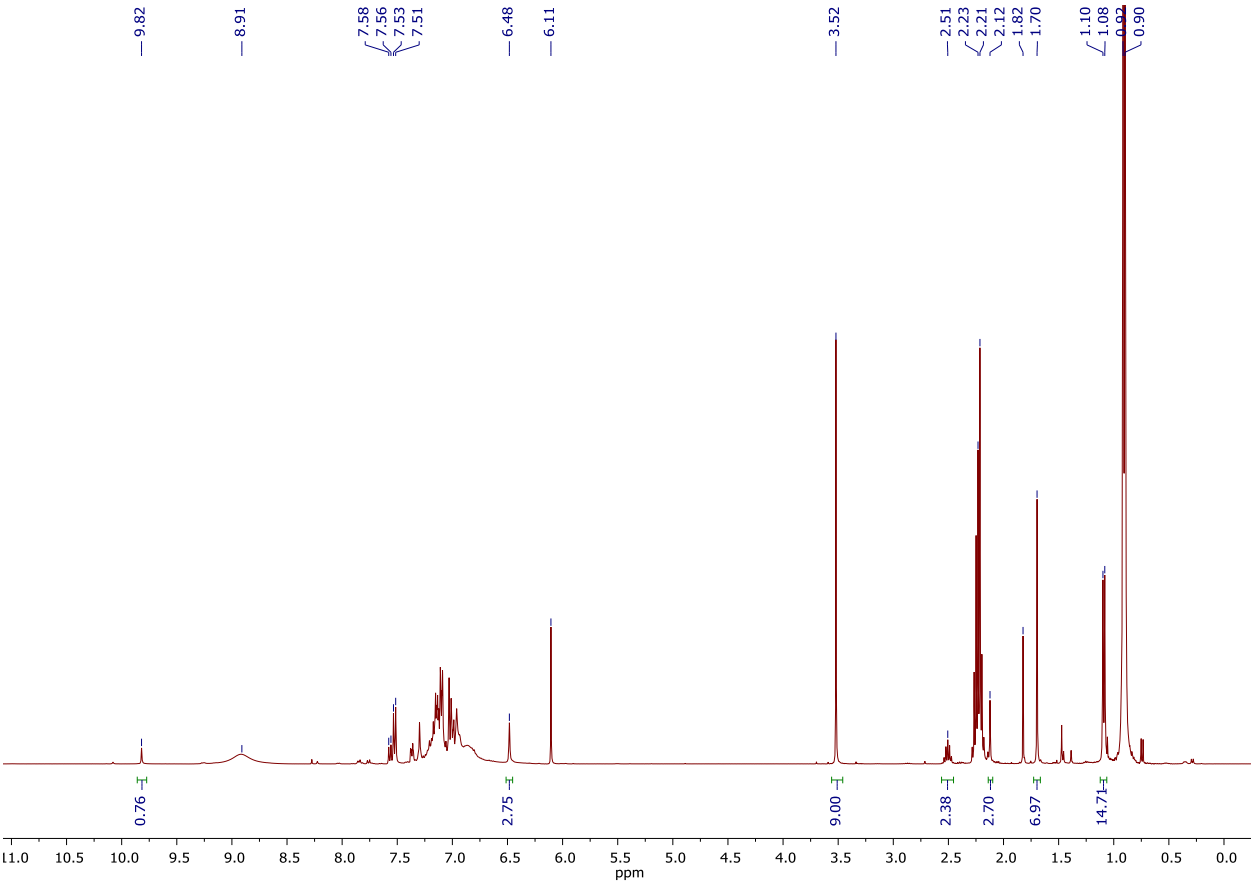
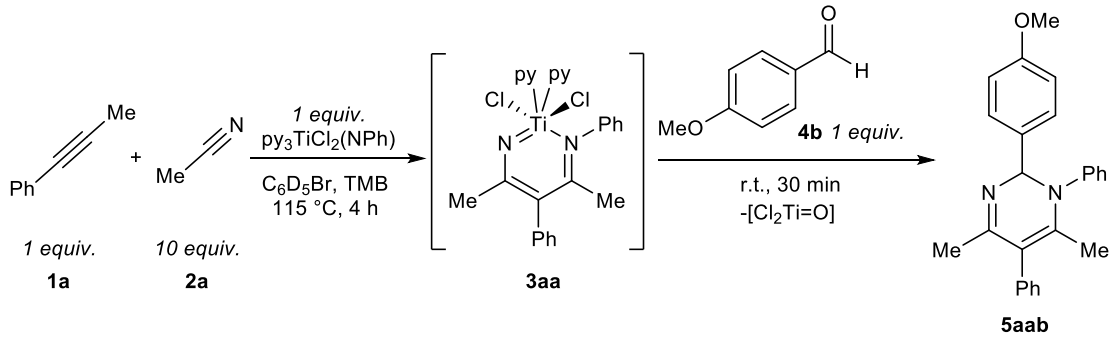
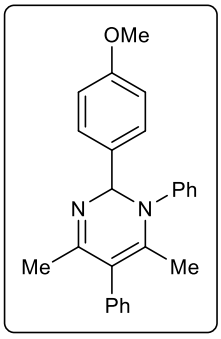


Figure S63. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), isobutyronitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of *p*-tolualdehyde (1 equiv.).



2-(4-methoxyphenyl)-4,6-dimethyl-1,5-diphenyl-1,2-dihydropyrimidine (5aab)



40% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.58 (d, *J* = 8.5 Hz, 2H), 7.19 – 7.11 (m, 7H), 6.86 – 6.84 (m, 5H), 6.48 (s, 1H), 3.47 (s, 3H), 1.95 (s, 3H), 1.71 (s, 3H).

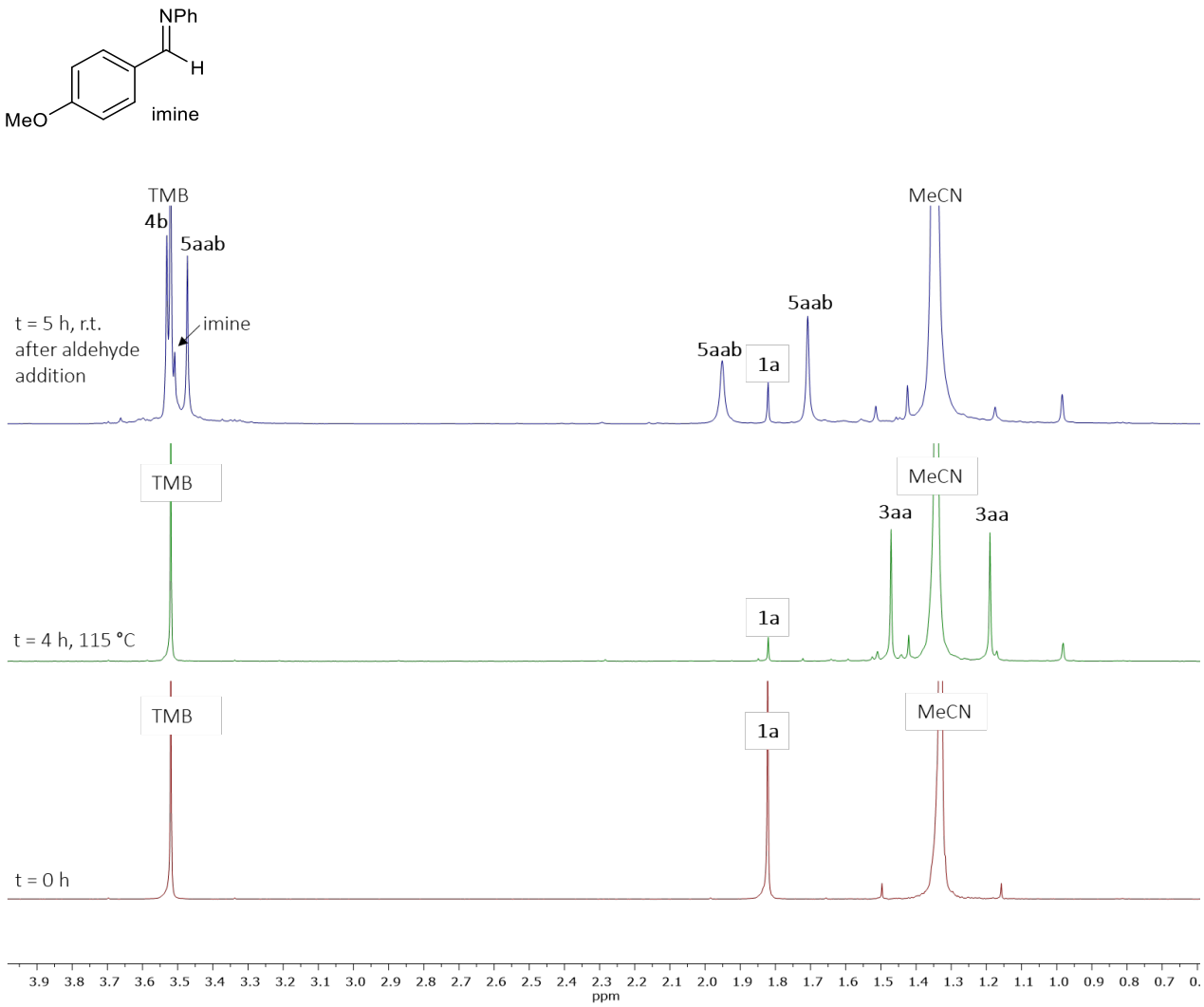


Figure S64. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), 4-methoxybenzaldehyde (1 equiv., **4b**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 55% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine (**5aab**) in 40% yield (73% conversion of the metallacycle **3aa**).

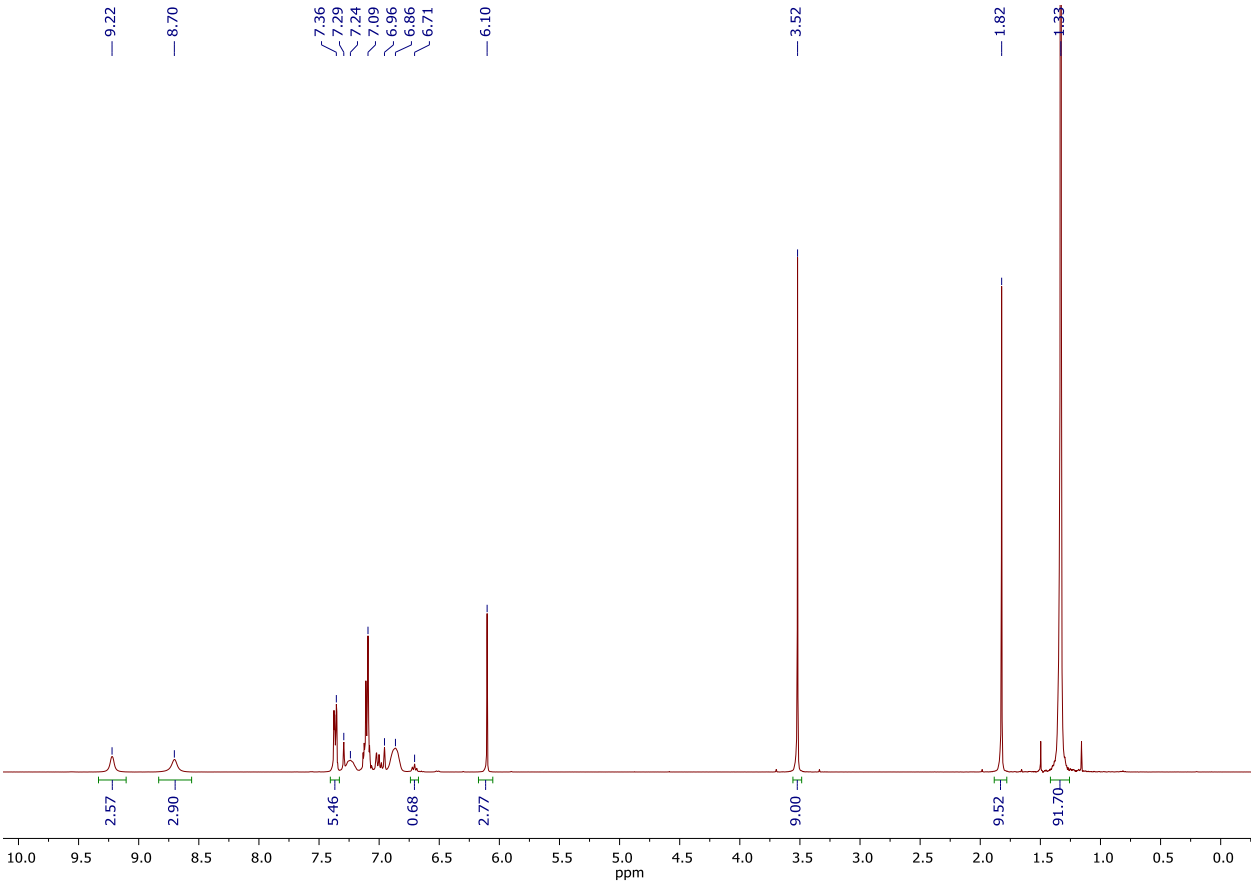


Figure S65. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

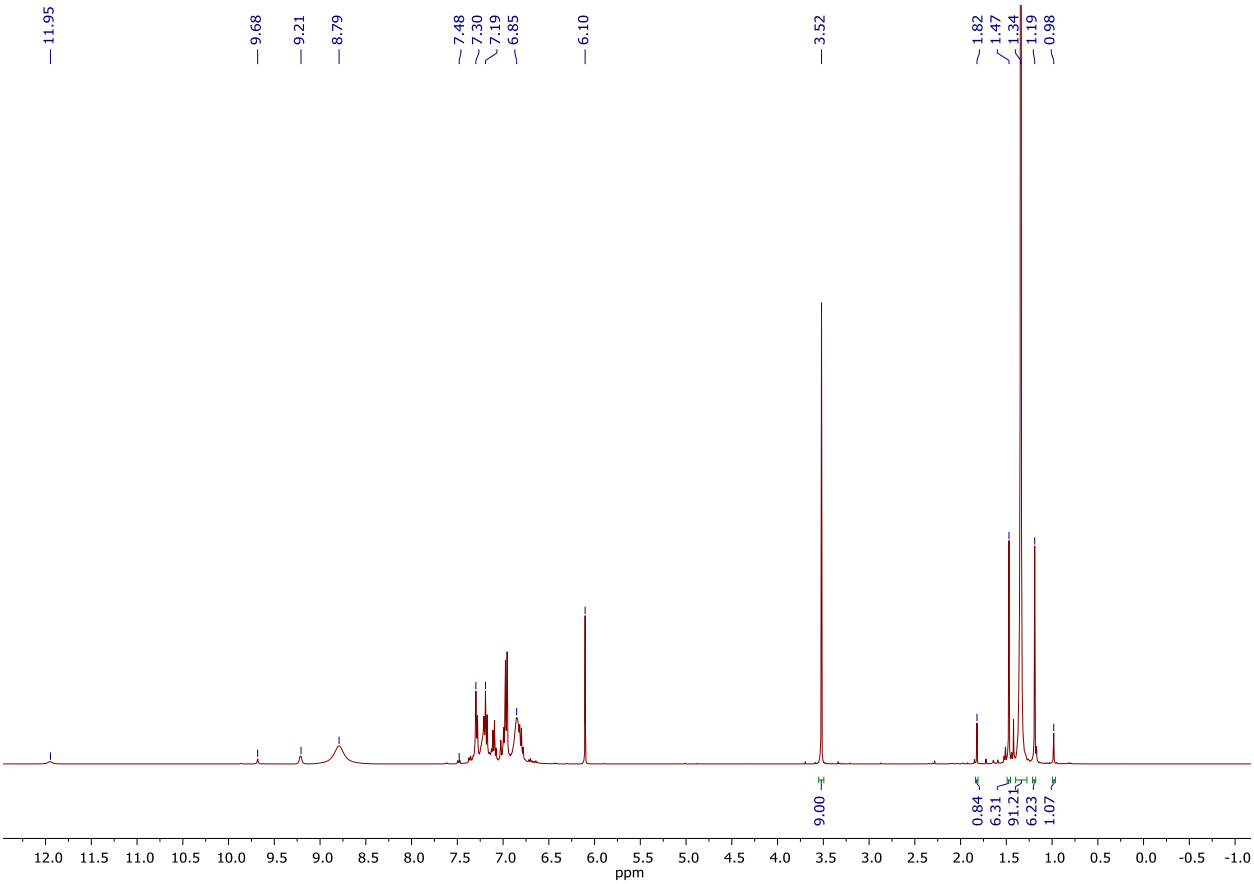


Figure S66. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

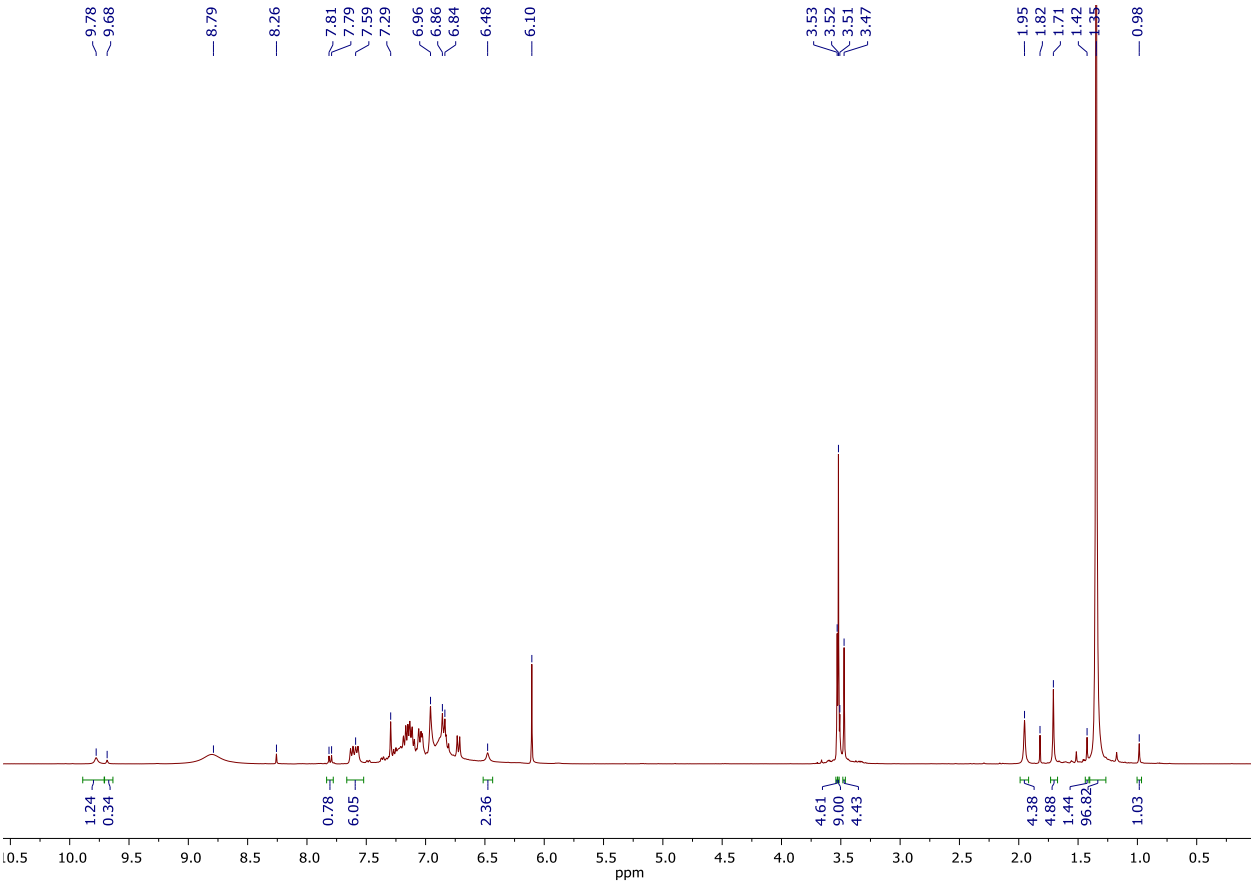
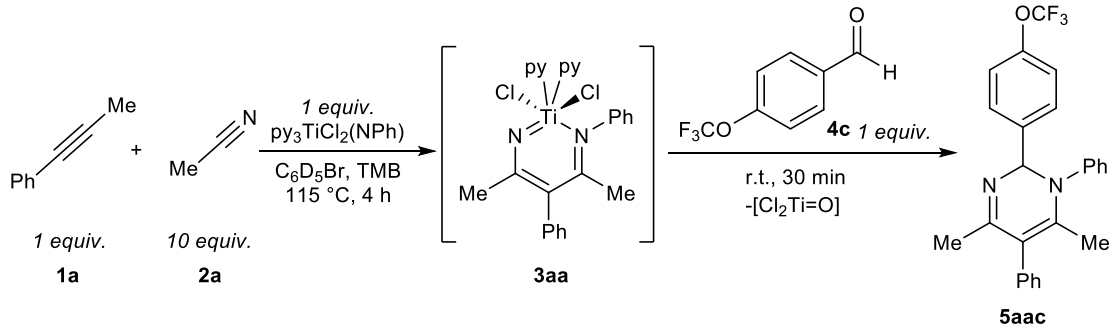
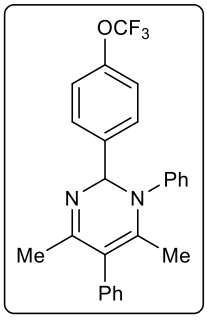


Figure S67. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 4-methoxybenzaldehyde (1 equiv.).



4,6-dimethyl-1,5-diphenyl-2-(4-(trifluoromethoxy)phenyl)-1,2-dihydropyrimidine (5aac)



35% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.60 (d, J = 8.7 Hz, 2H), 7.18 – 7.11 (m, 12H), 6.38 (s, 1H), 1.87 (s, 3H), 1.69 (s, 3H). **^{19}F NMR (376 MHz, C_6D_5Br, δ, ppm):** -56.96.

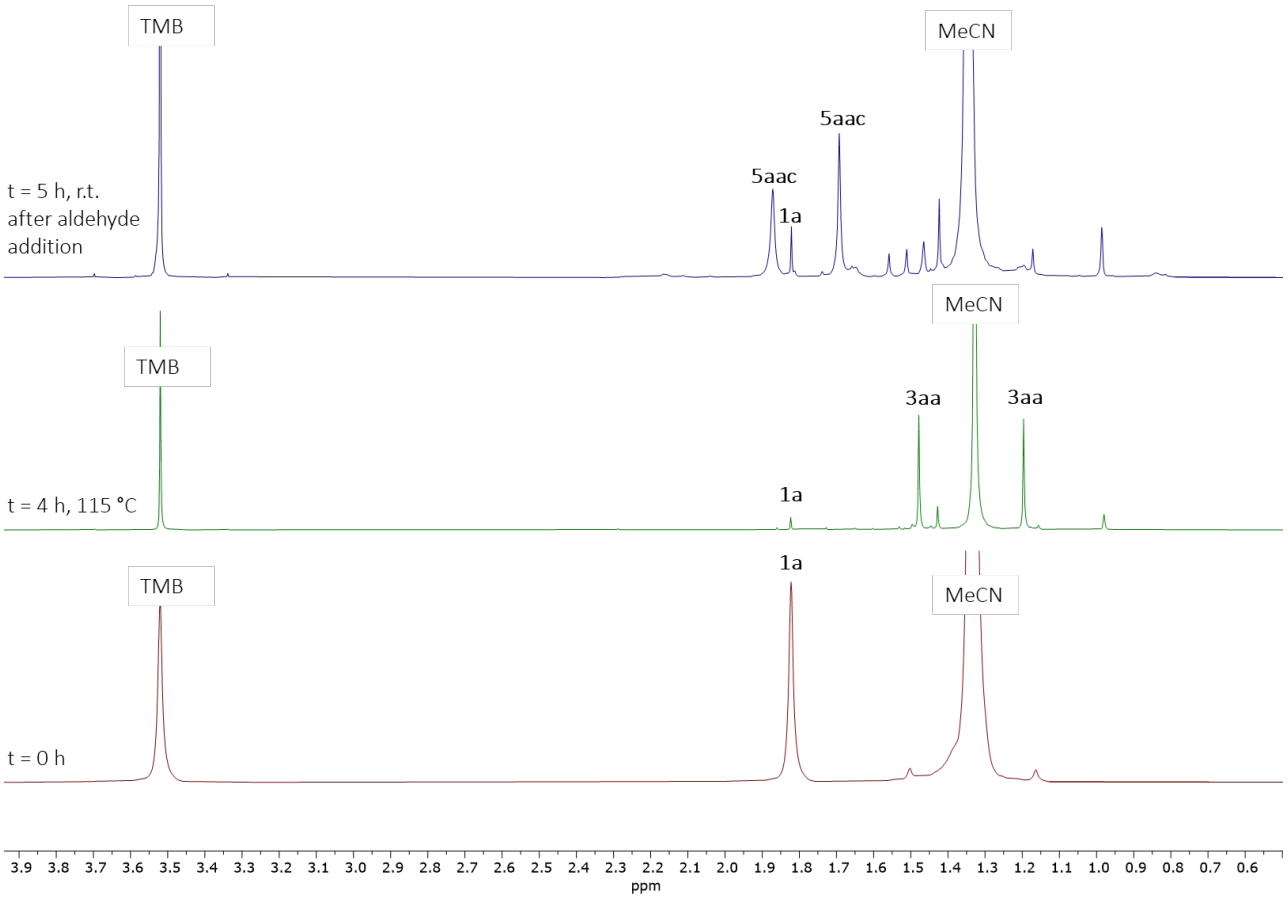


Figure S68. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), 4-trifluromethoxybenzaldehyde (1 equiv., **4c**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 58% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aac** in 35% yield (62% conversion from metallacycle **3aa**).

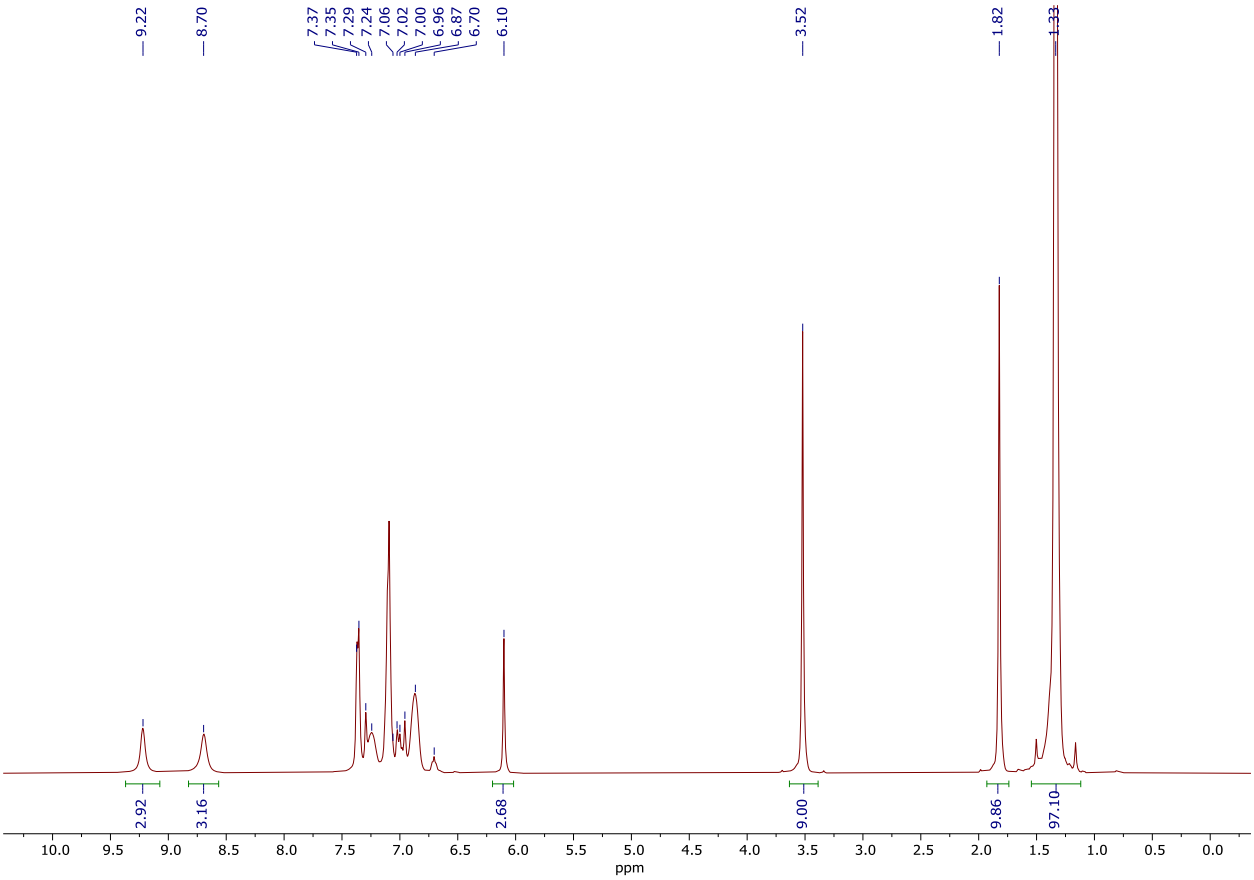


Figure S69. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

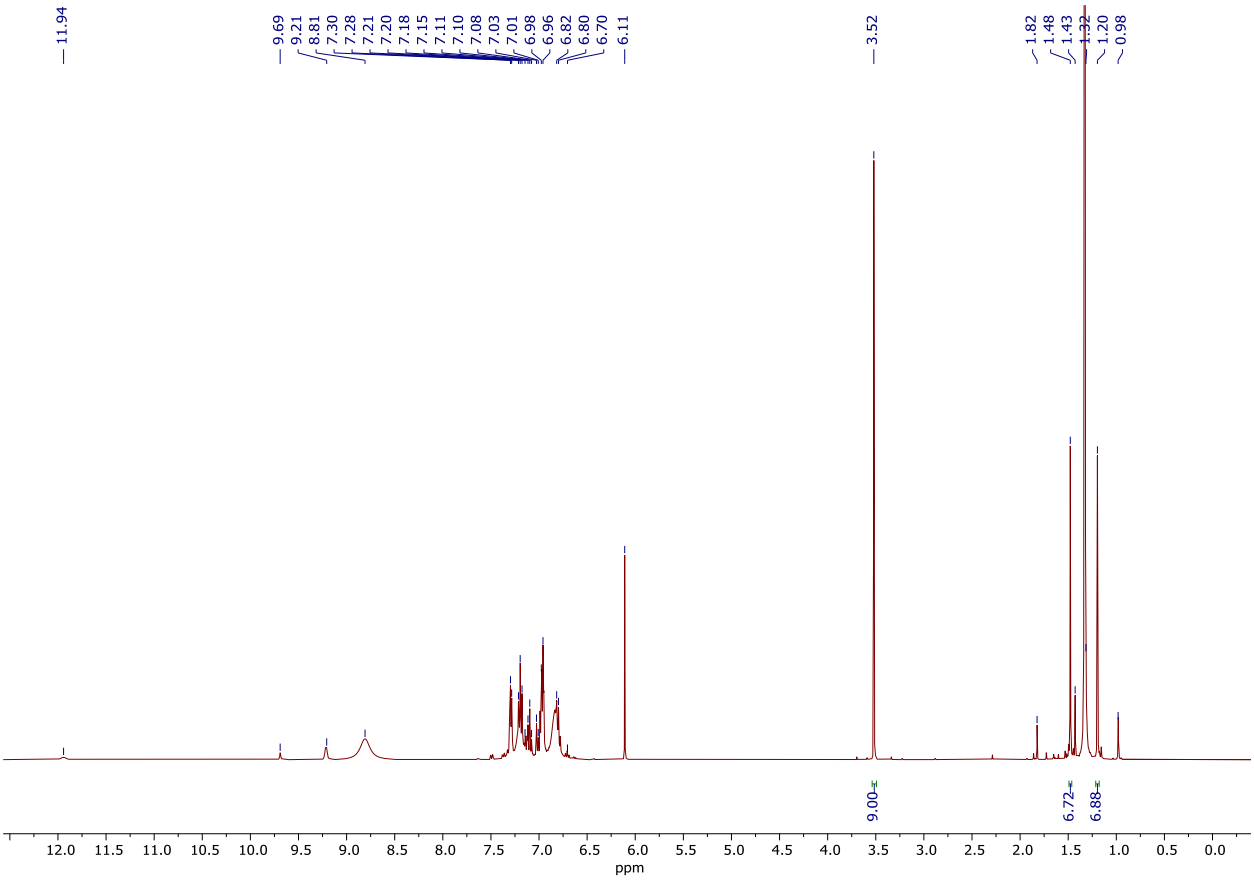


Figure S70. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

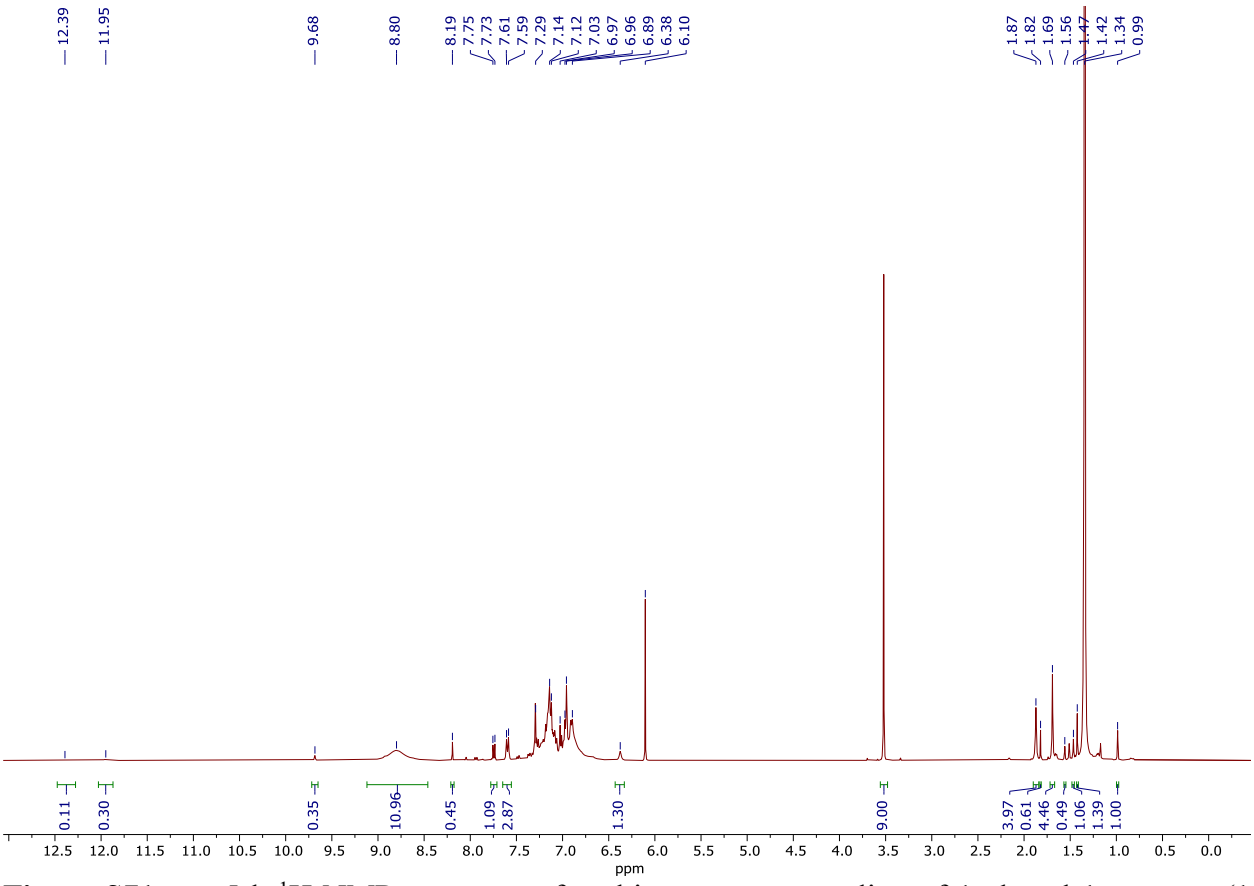


Figure S71. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 4-trifluromethoxybenzaldehyde (1 equiv.).

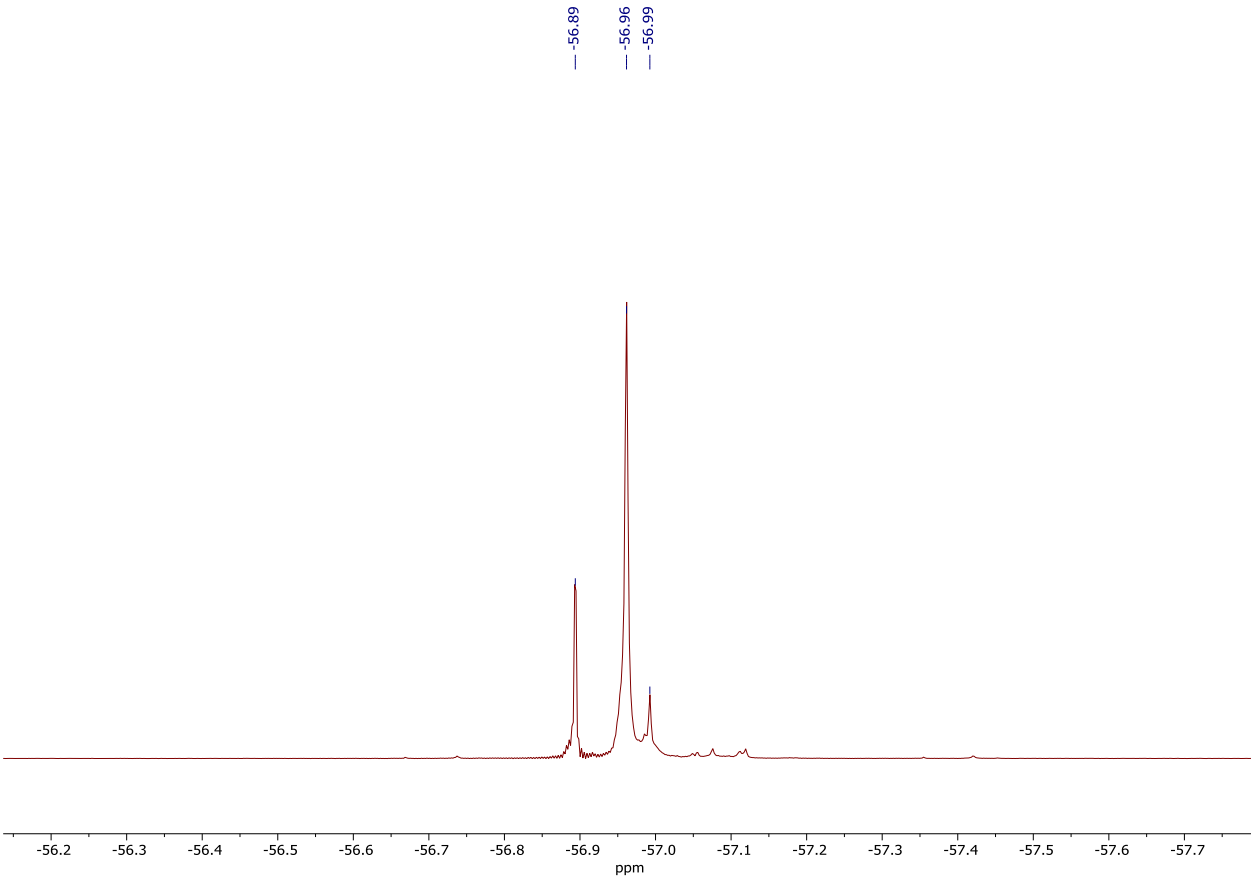
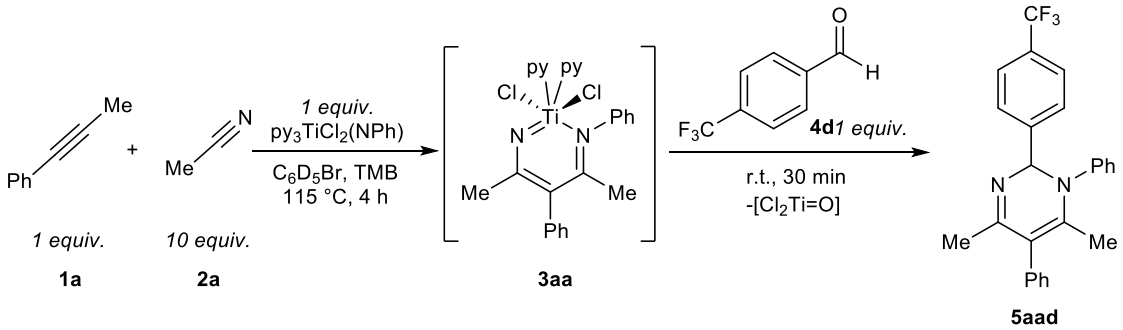
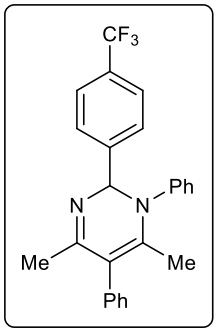


Figure S72. t = 5 h ^{19}F NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 4-trifluromethoxybenzaldehyde (1 equiv.).



4,6-dimethyl-1,5-diphenyl-2-(4-(trifluoromethyl)phenyl)-1,2-dihydropyrimidine (5aad)



32% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.81 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.16 – 7.11 (m, 10H), 6.66 (s, 1H), 2.05 (s, 3H), 1.77 (s, 3H). **^{19}F NMR (376 MHz, C_6D_5Br, δ, ppm):** -61.88.

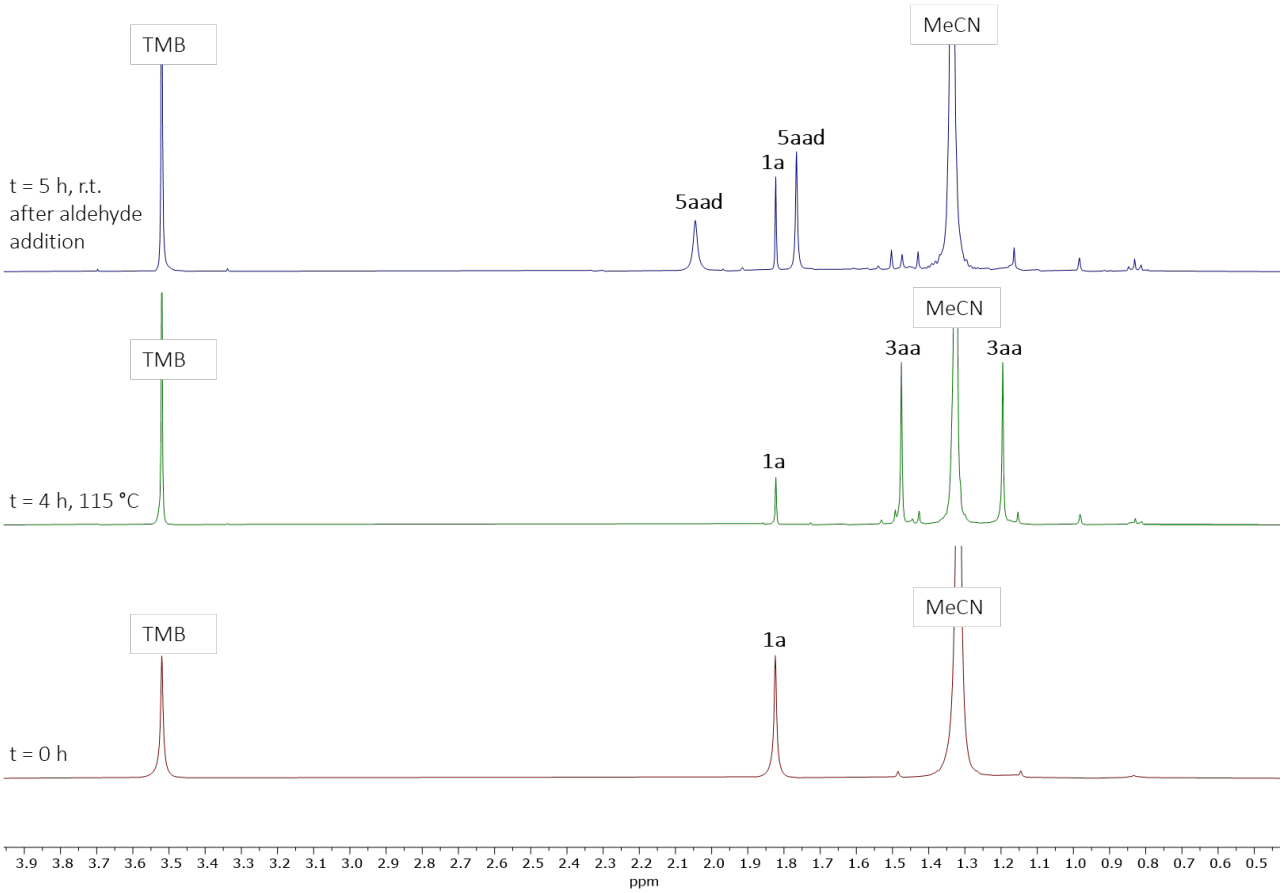


Figure S73. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), 4-trifluromethylbenzaldehyde (1 equiv., **4d**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 56% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aad** in 32% yield.

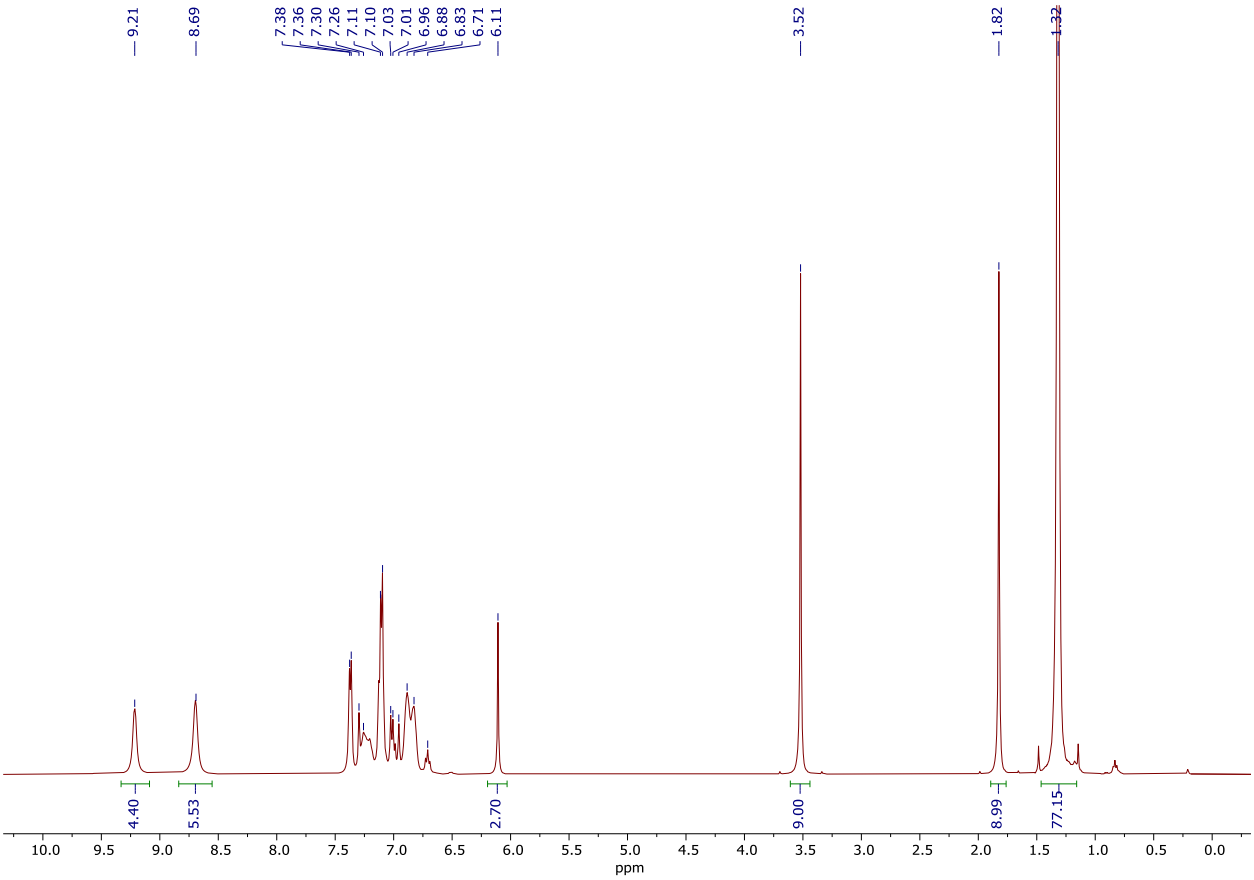


Figure S74. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

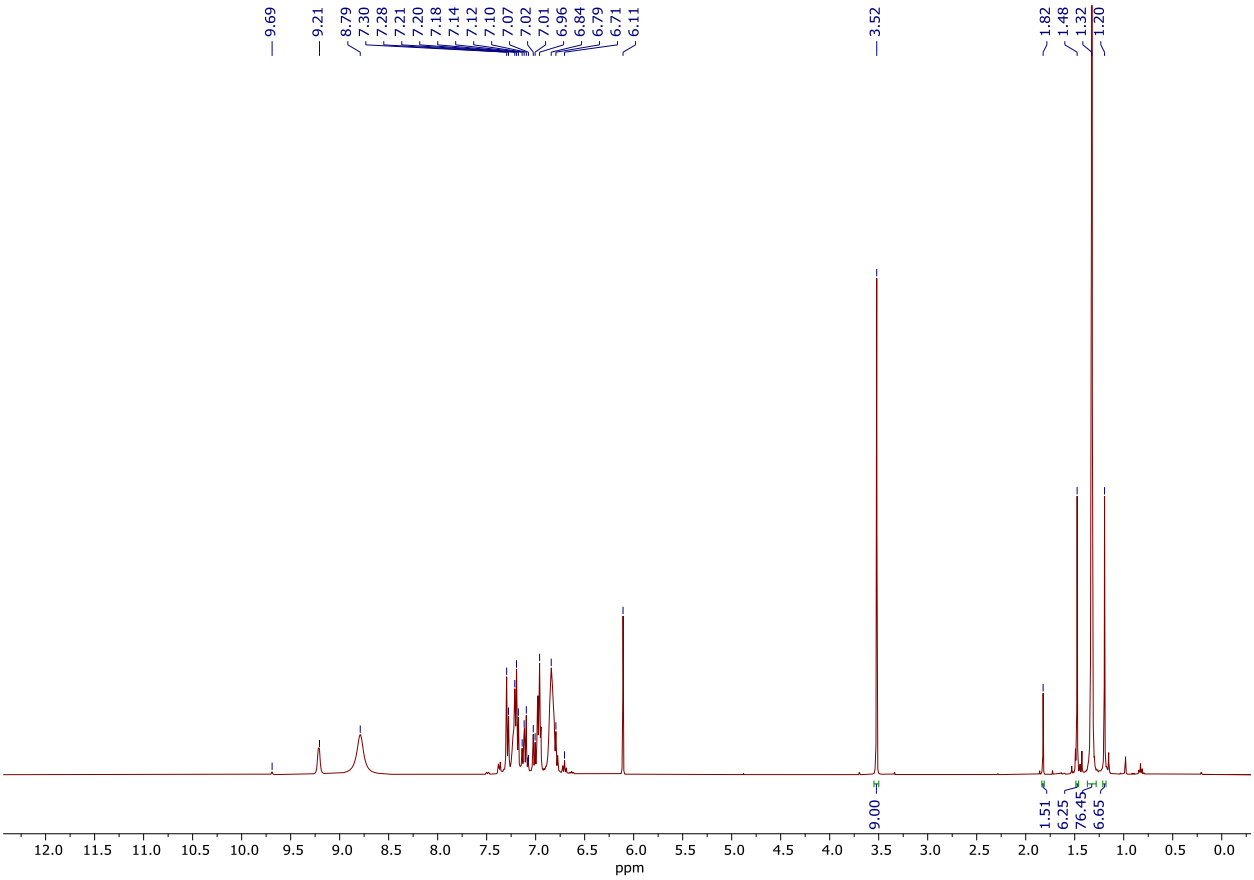


Figure S75. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

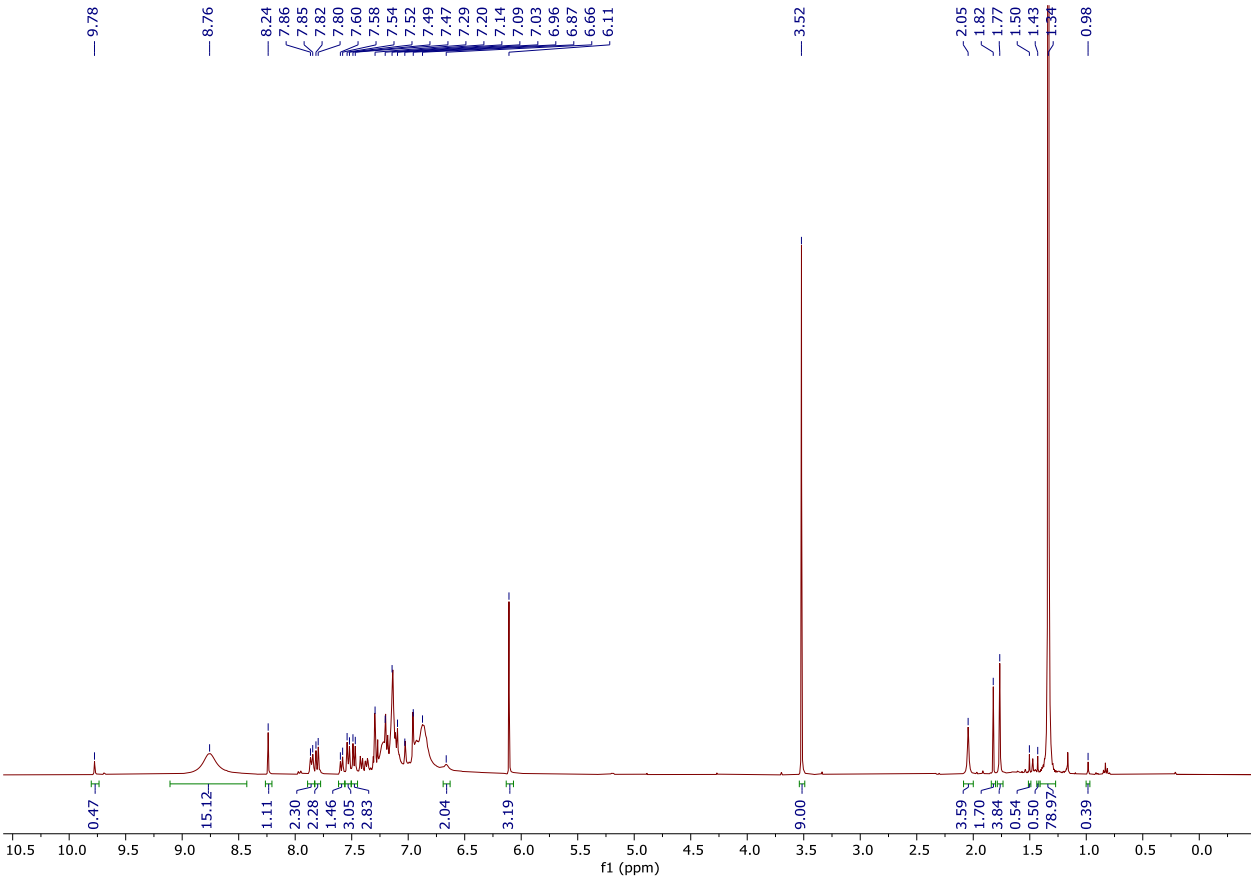


Figure S76. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 4-trifluromethylbenzaldehyde (1 equiv.).

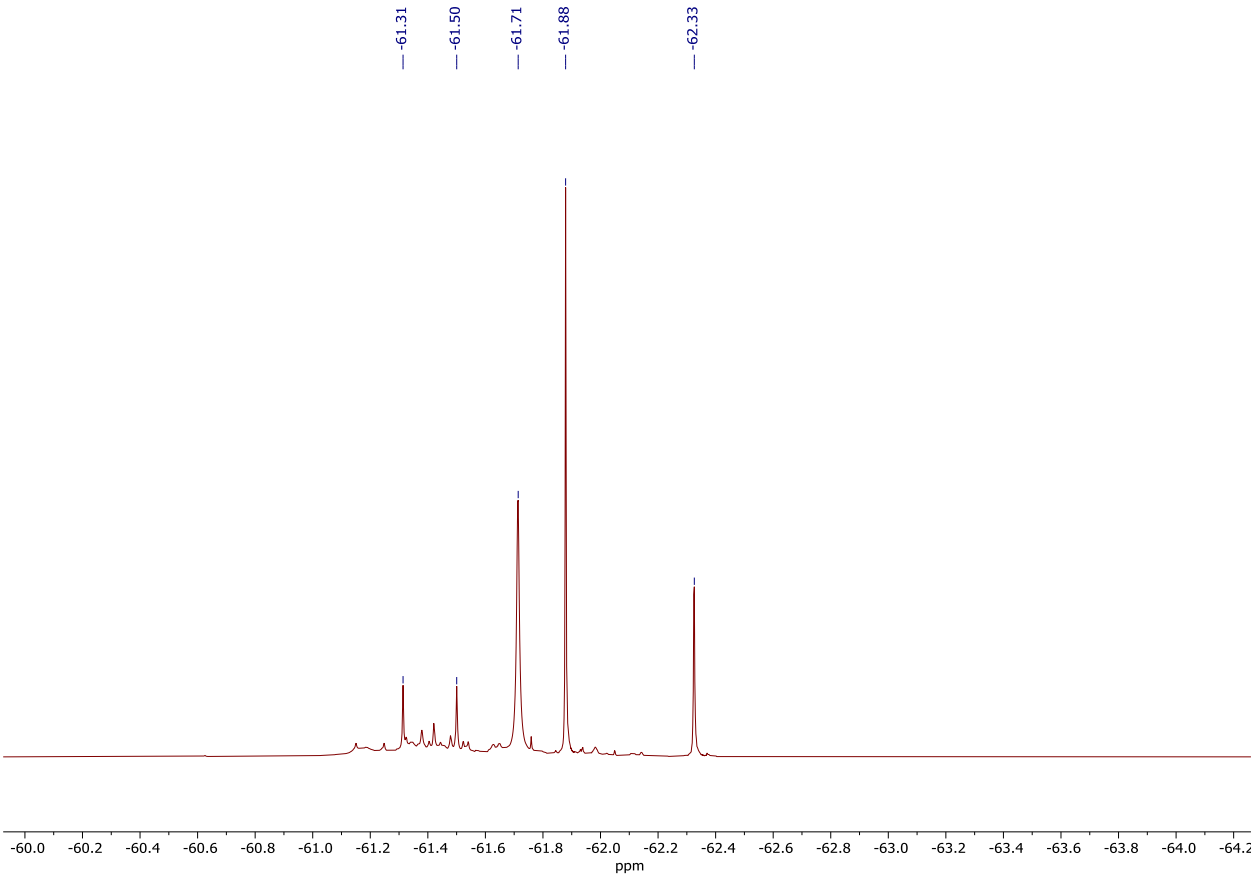
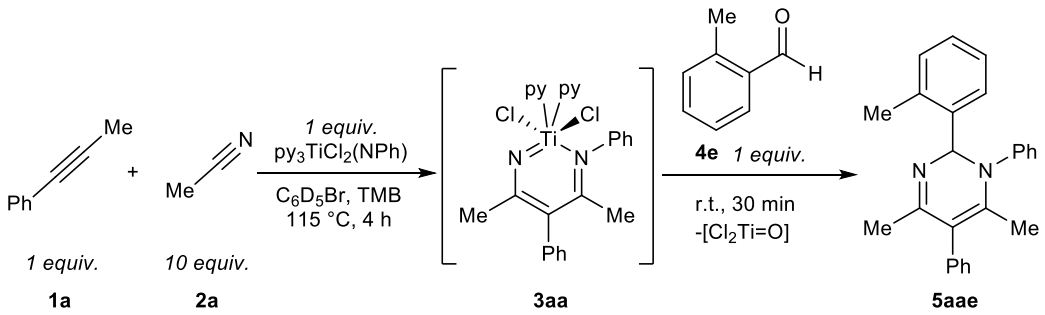
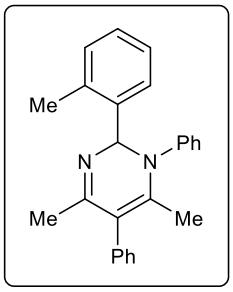


Figure S77. t = 5 h ^{19}F NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 4-trifluromethylbenzaldehyde (1 equiv.).



4,6-dimethyl-1,5-diphenyl-2-(o-tolyl)-1,2-dihydropyrimidine (5aae)



47% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.21 – 7.06 (m, 14H), 6.54 (s, 1H), 2.65 (s, 3H), 1.79 (s, 3H), 1.77 (s, 3H).

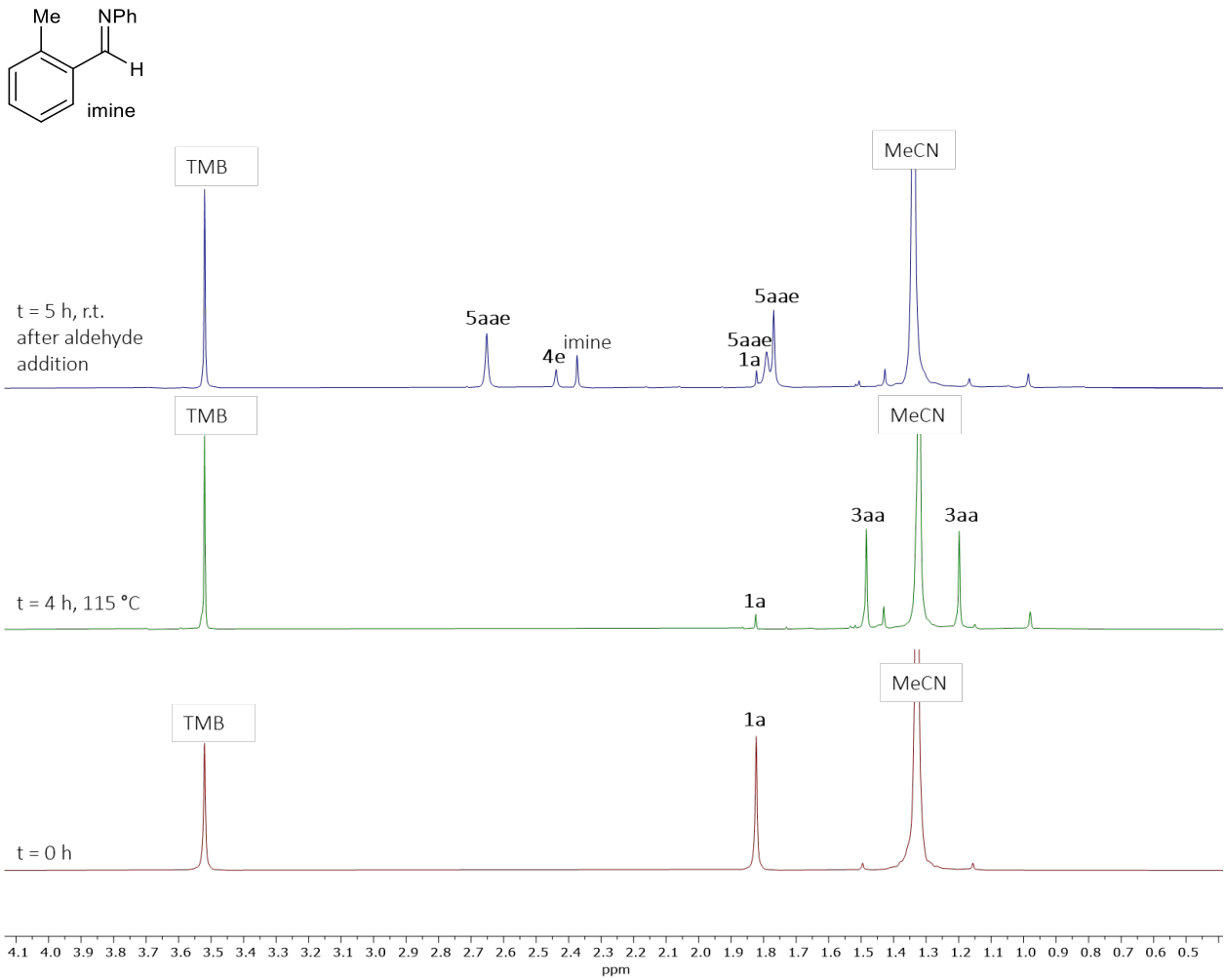


Figure S78. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), 2-methylbenzaldehyde (1 equiv., **4e**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 58% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aae** in 47% yield (82% conversion from metallacycle **3aa**).

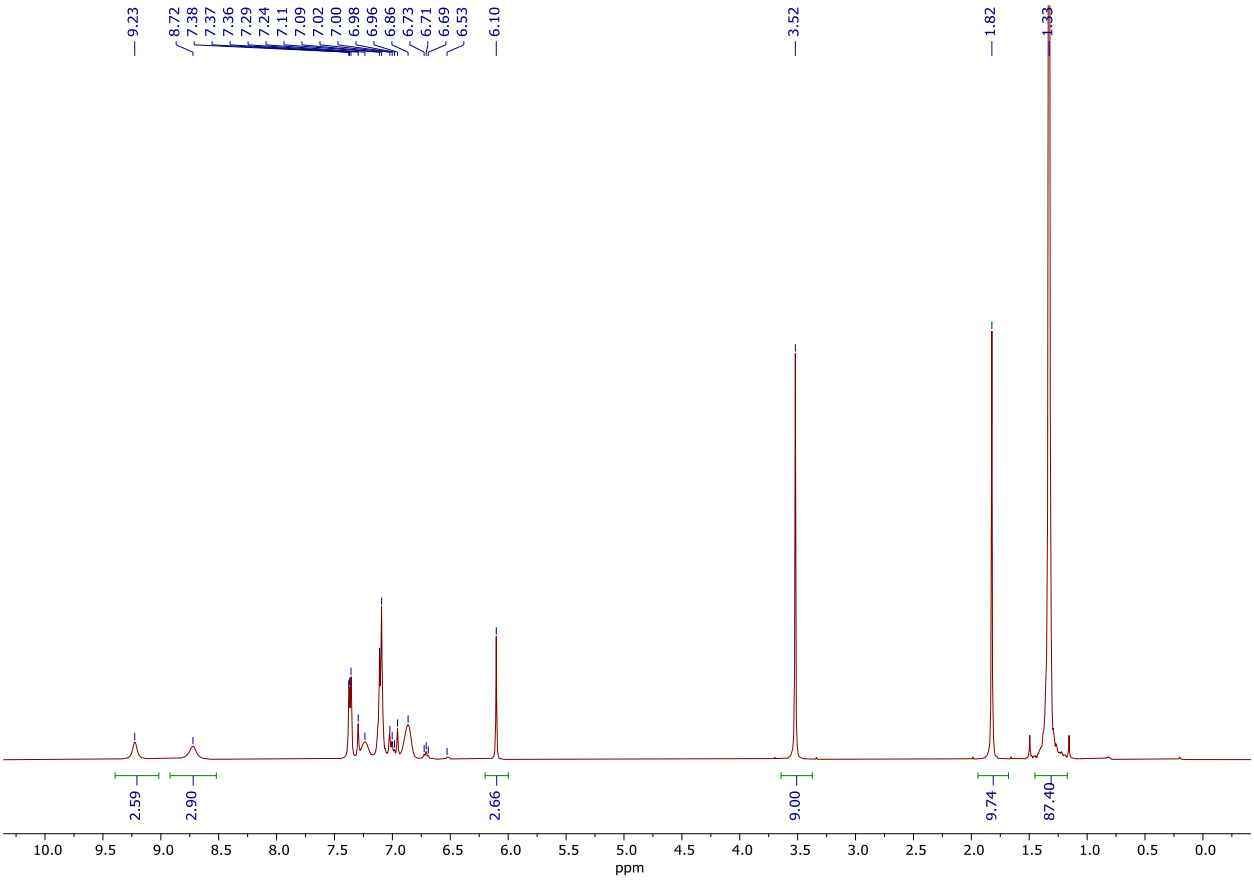


Figure S79. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

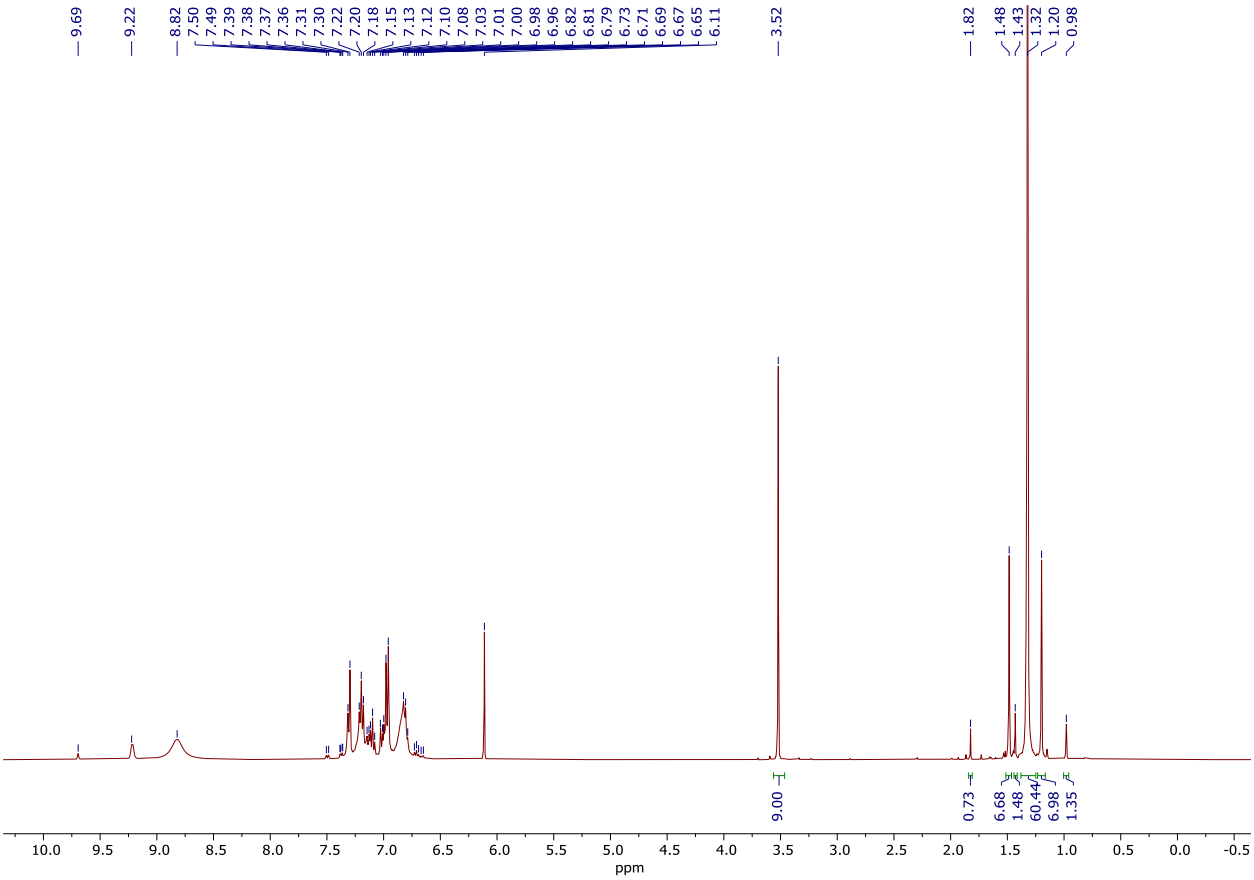


Figure S80. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

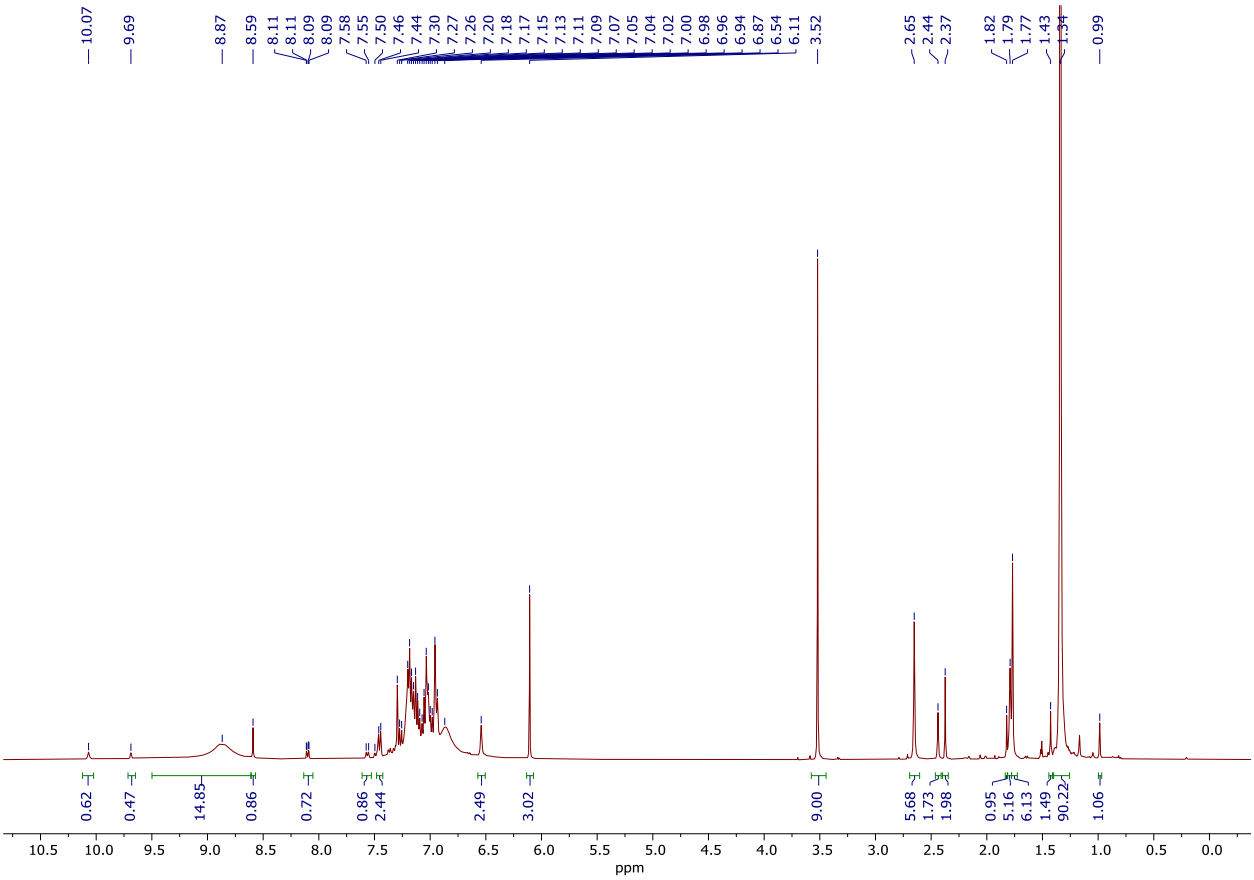
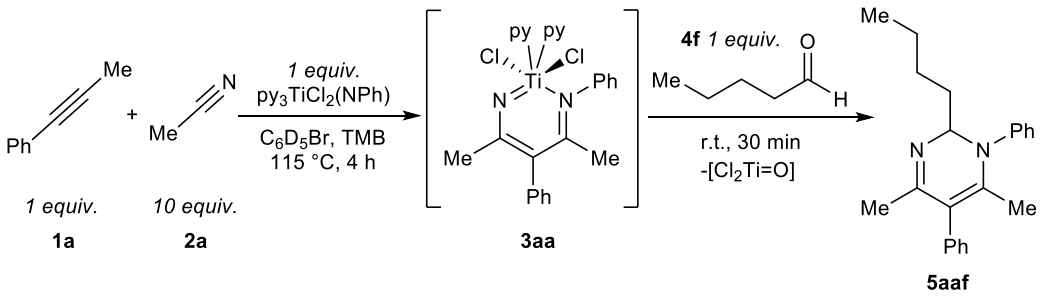
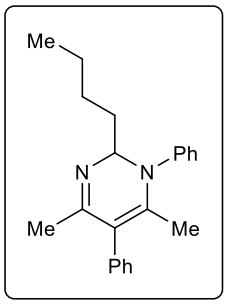


Figure S81. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of 2-methylbenzaldehyde (1 equiv.).



2-butyl-4,6-dimethyl-1,5-diphenyl-1,2-dihydropyrimidine (5aaf)



67% yield by ^{1}H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.25 (t, *J* = 7.1 Hz, 6H), 7.22 – 7.17 (m, 4H), 5.35 (d, *J* = 5.1 Hz, 1H), 2.35 – 2.21 (m, 1H), 2.17 (s, 3H), 1.71 – 1.57 (m, 2H), 1.50 (s, 3H), 1.31 – 1.21 (m, 4H), 0.82 (t, *J* = 7.3 Hz, 3H).

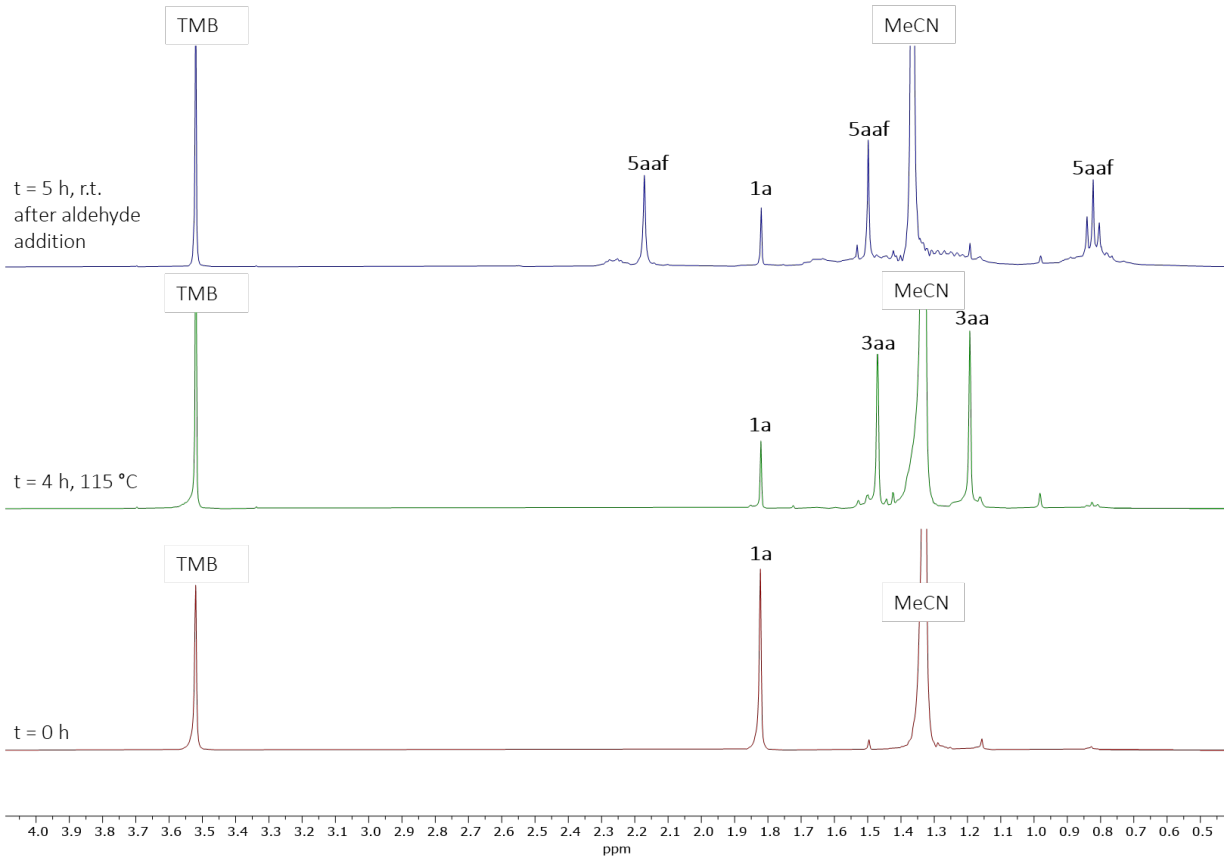


Figure S82. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), valeraldehyde (1 equiv., **4f**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 55% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aaf** in 67% yield.

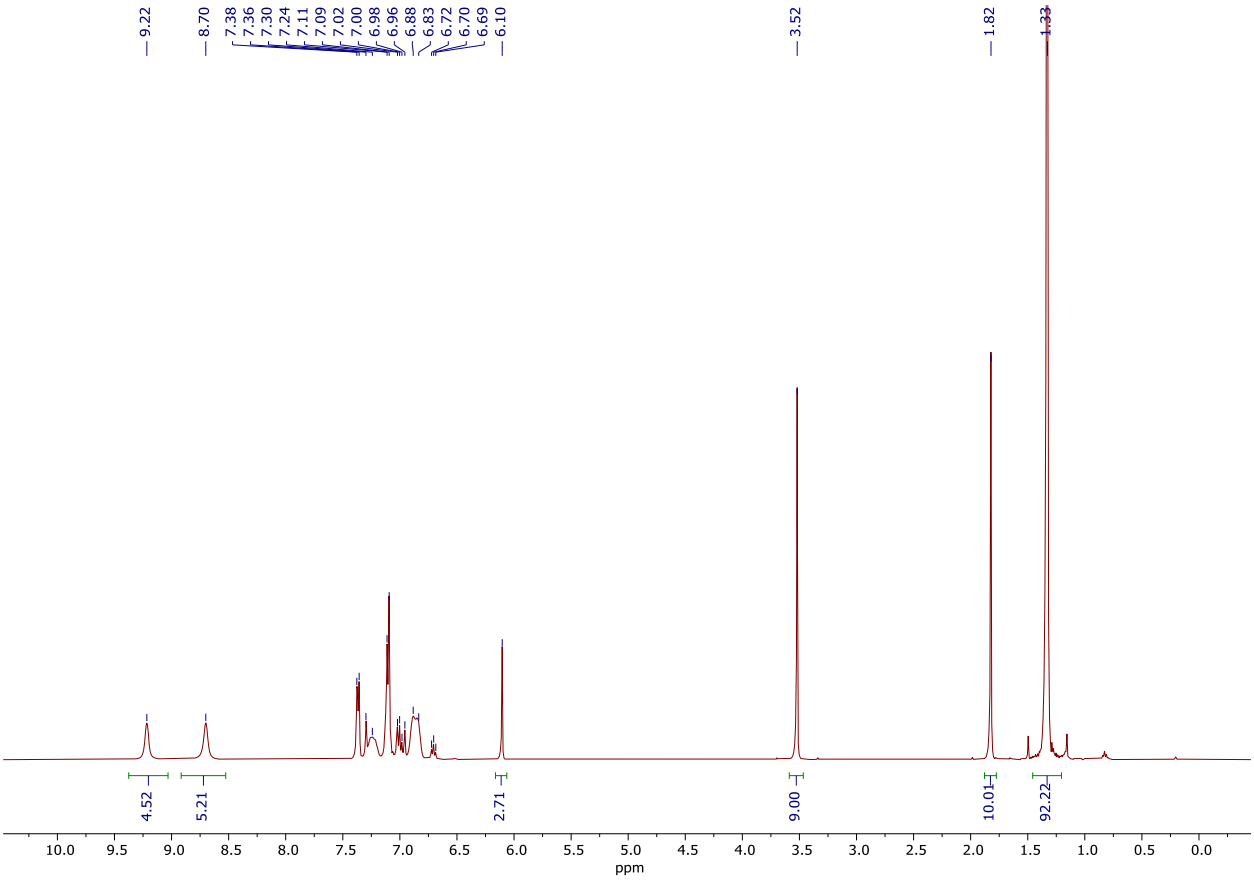


Figure S83. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

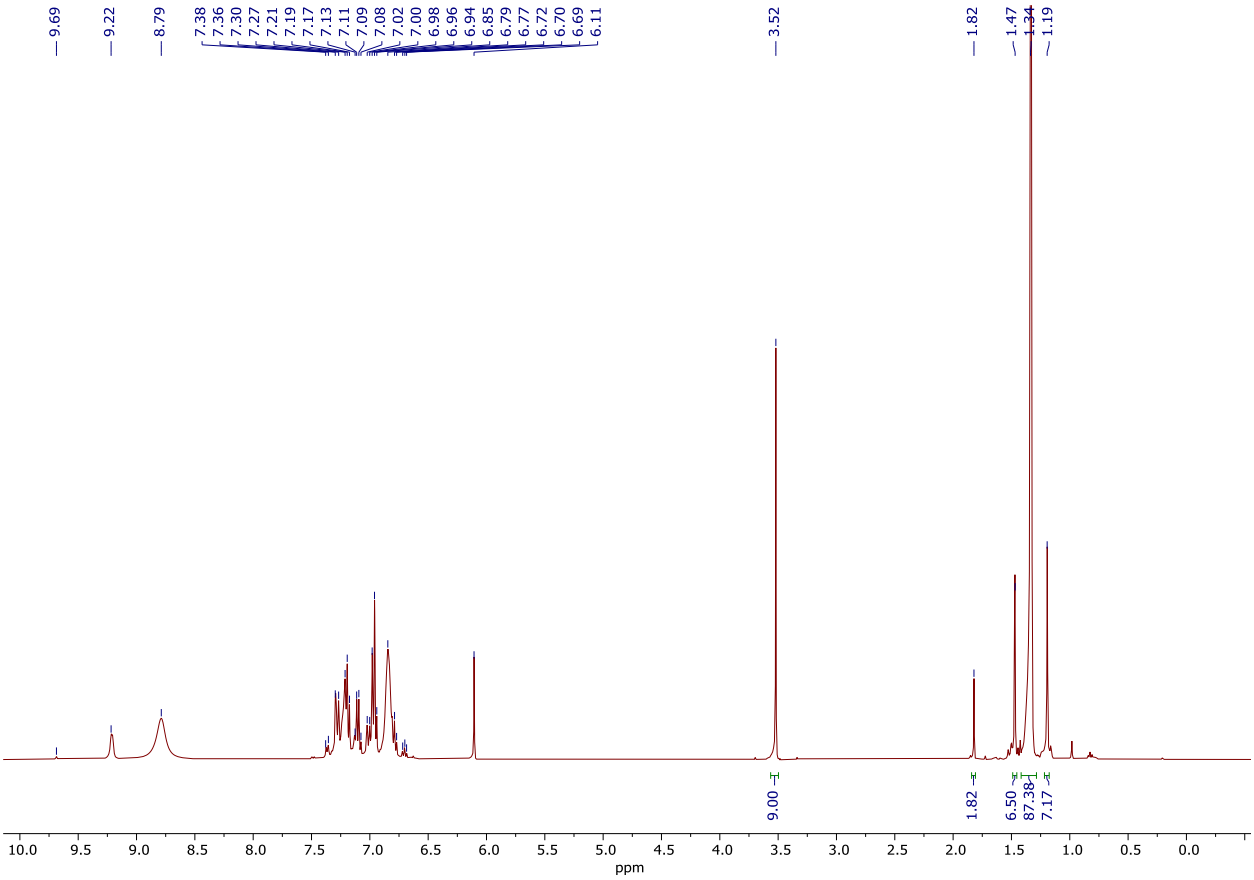


Figure S84. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

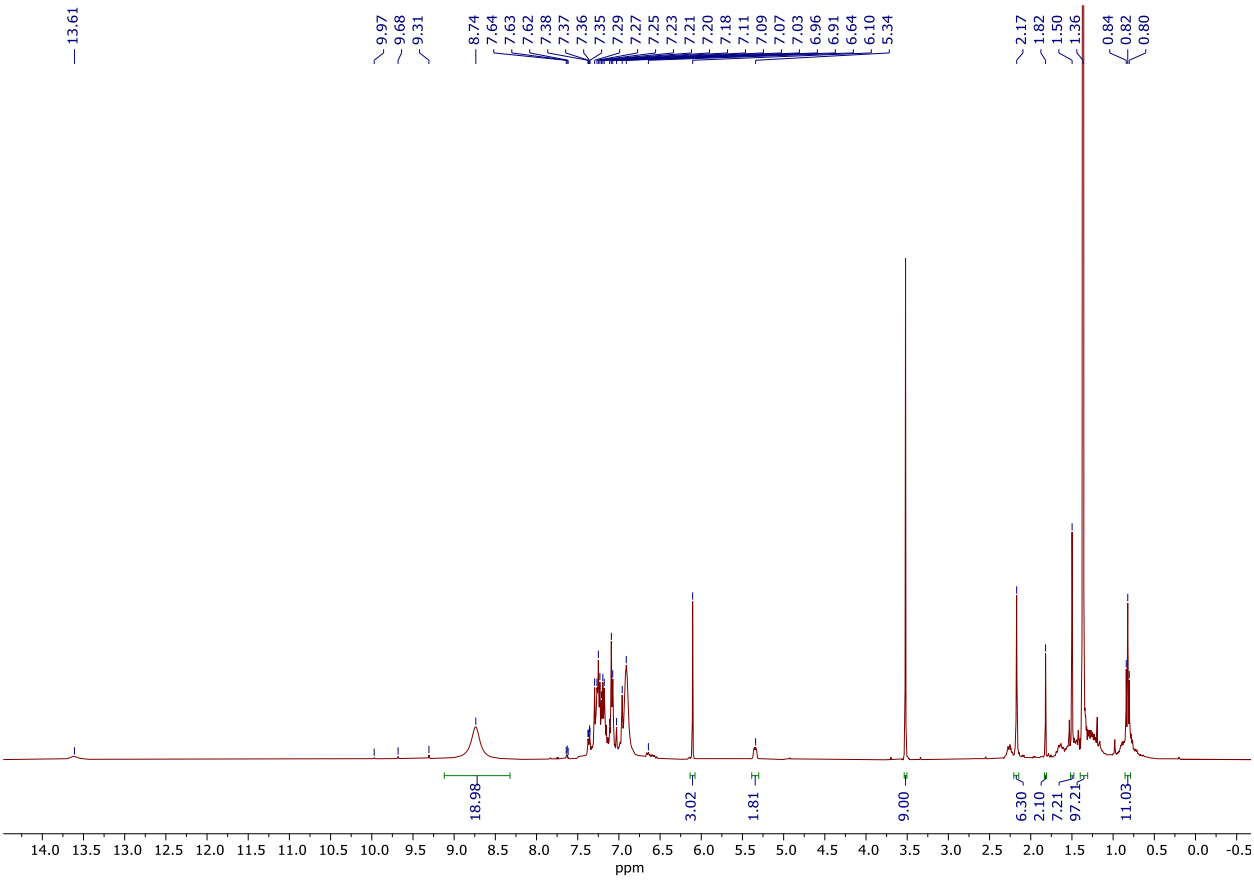
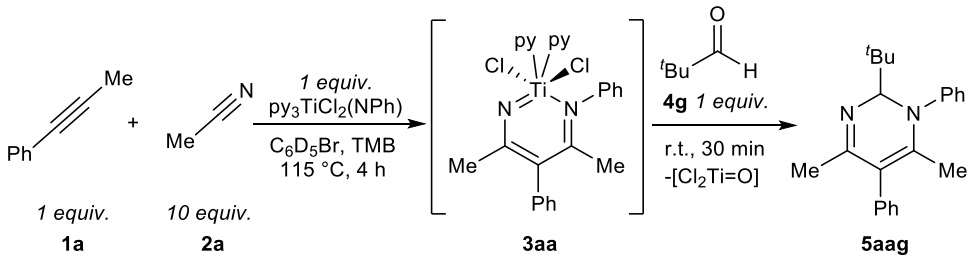
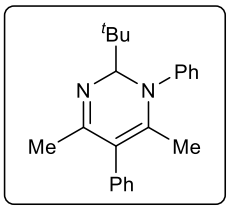


Figure S85. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of valeraldehyde (1 equiv.).



2-(tert-butyl)-4,6-dimethyl-1,5-diphenyl-1,2-dihydropyrimidine (5aag)



38% yield by 1H NMR. **^{1}H NMR (400 MHz, C_6D_5Br, δ, ppm):** 7.30 – 7.26 (m, 3H), 7.21 – 7.16 (m, 7H), 5.07 (s, 1H), 1.94 (s, 3H), 1.53 (s, 3H), 1.09 (s, 9H).

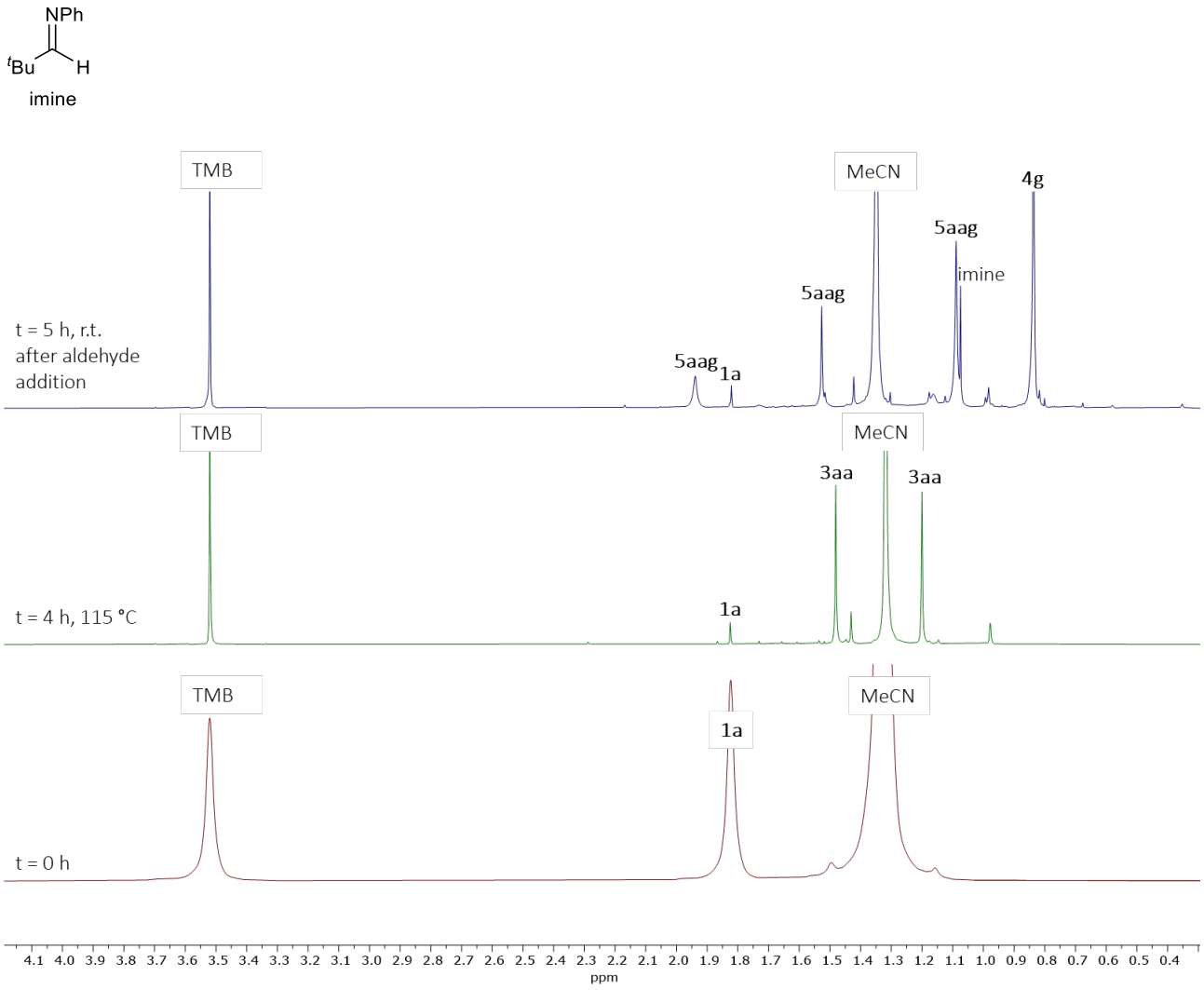


Figure S86. Stacked ^{1}H NMR spectra characterizing the multicomponent coupling of 1-phenyl-1-propyne (1 equiv., **1a**), acetonitrile (10 equiv., **2a**), pivaldehyde (1 equiv., **4g**), and $py_3TiCl_2(NPh)$ in C_6D_5Br; Bottom (red trace): t=0; Middle (green trace): t = 4 h at 115 °C generating metallacycle **3aa** in 62% yield; Top (blue trace): t= 0.5 h after aldehyde addition to give 1,2-dihyropyrimidine **5aaf** in 38% yield (70% conversion from metallacycle **3aa**).

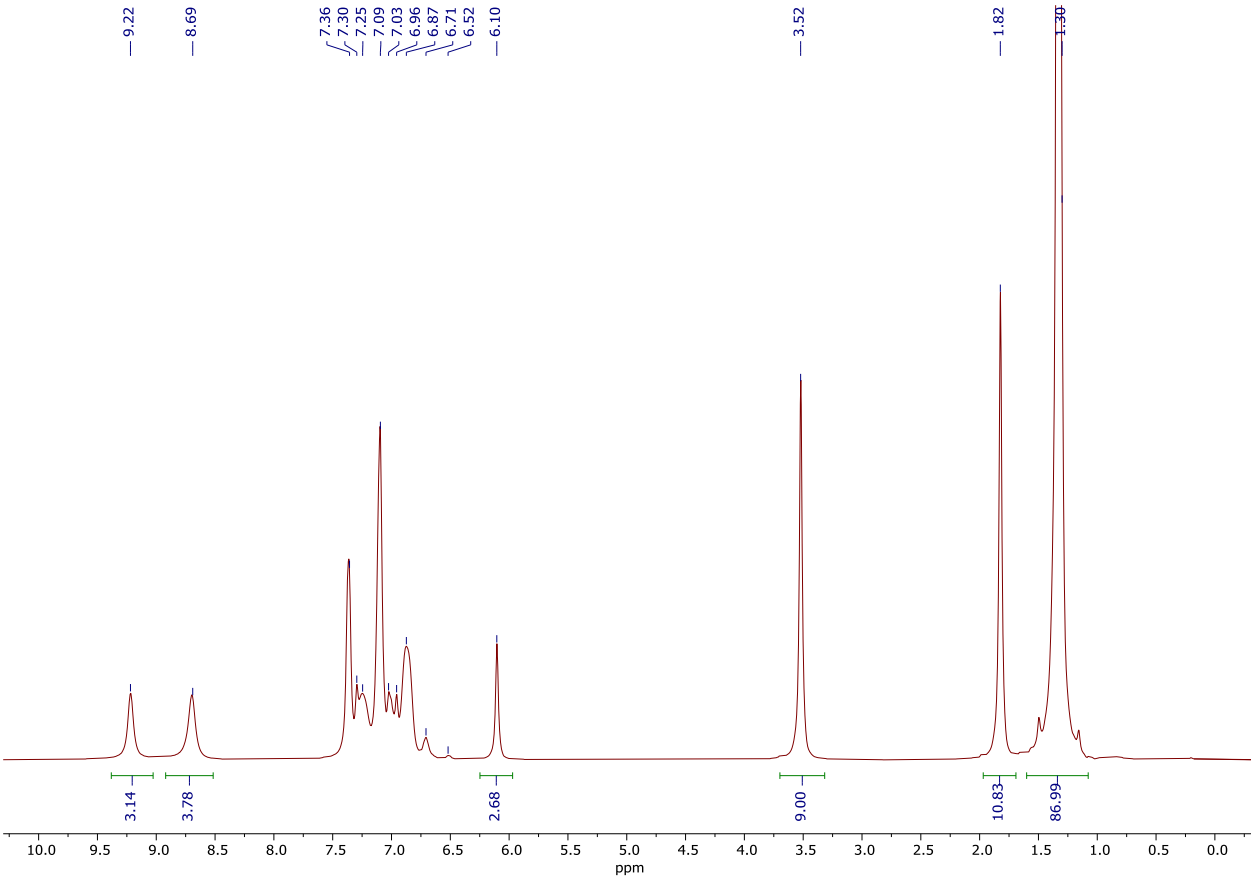


Figure S87. t = 0 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

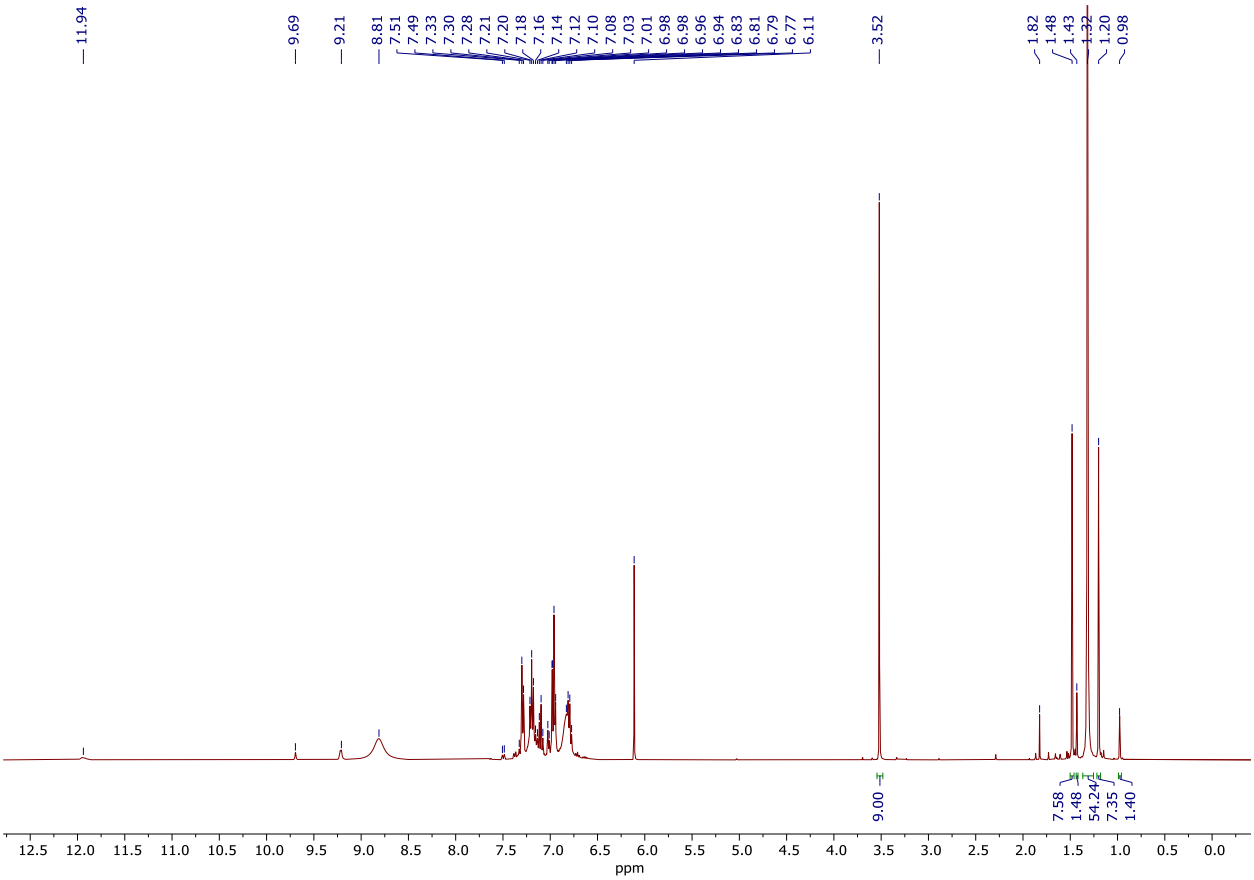


Figure S88. t = 4 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br.

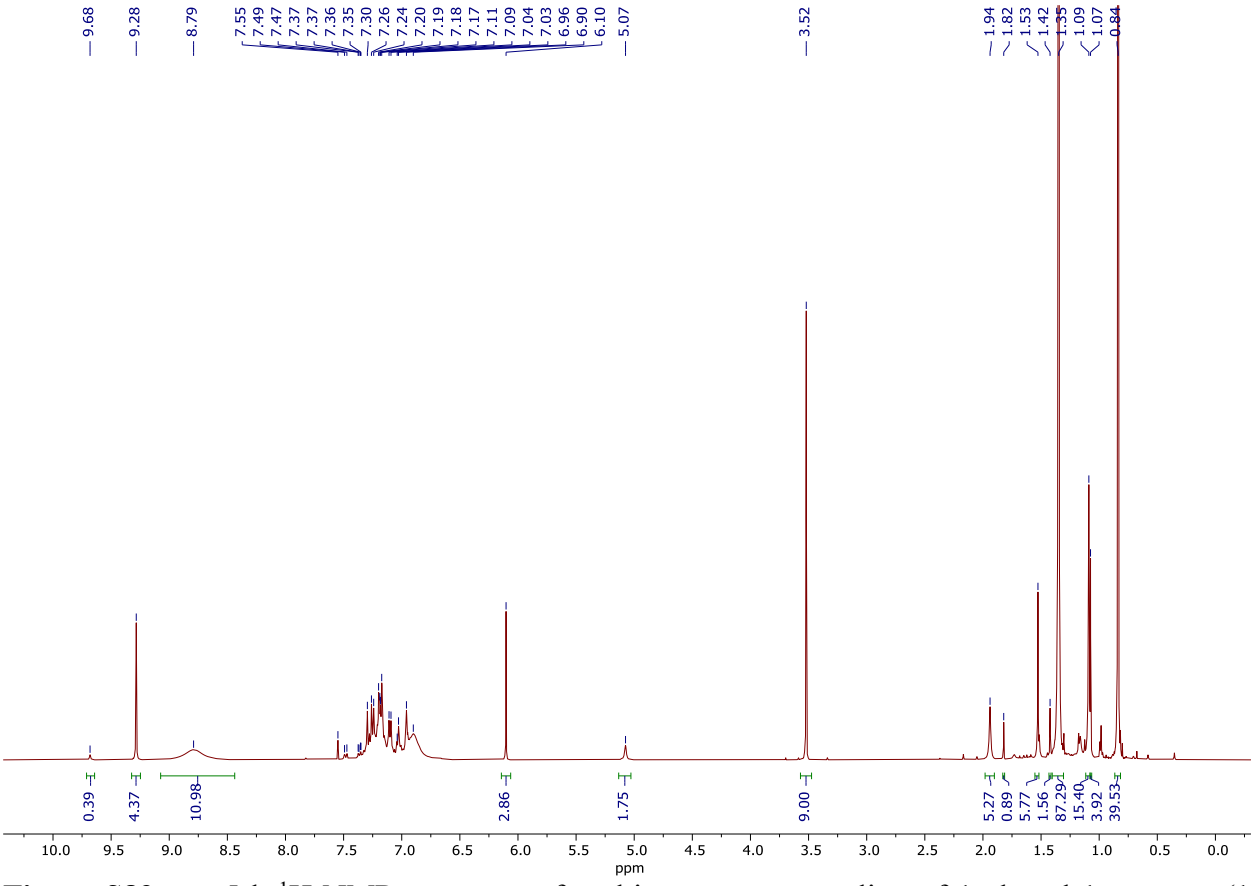
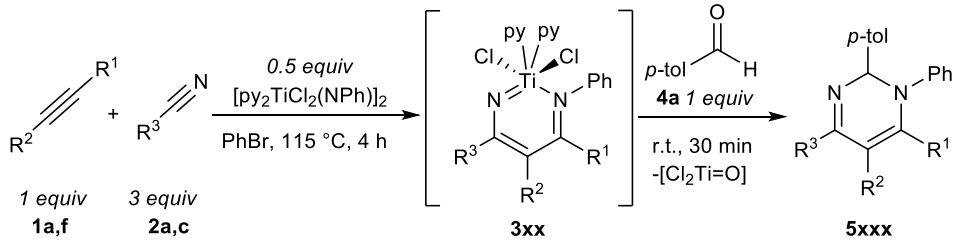
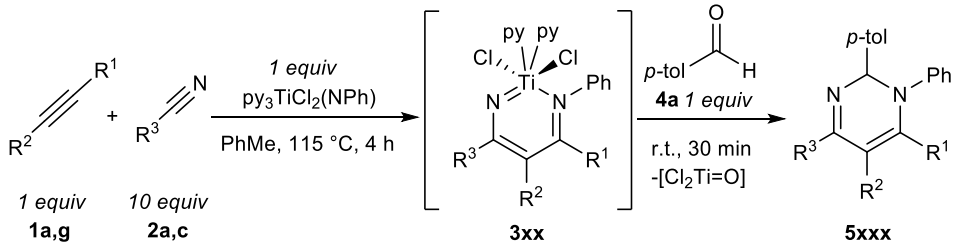


Figure S89. t = 5 h ^{1}H NMR spectrum of multicomponent coupling of 1-phenyl-1-propyne (1 equiv.), acetonitrile (10 equiv.), and $py_3TiCl_2(NPh)$ in C_6D_5Br after addition of pivaldehyde (1 equiv.).

Multicomponent coupling of $[py_2TiCl_2(NPh)]_2$, alkynes, nitriles, and aldehydes for synthesis of 1,2-dihydropyrimidines (isolation conditions)



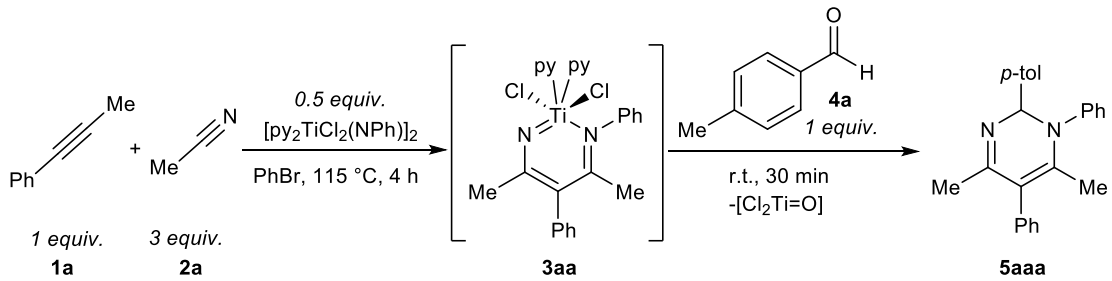
General procedure for 5aaa and 5fca: 4 mL of bromobenzene was added to a 20 mL scintillation vial containing $[py_2TiCl_2(NPh)]_2$ (0.400 mmol, 1.00 equiv) along with a stir bar, followed by the alkyne **1** (0.400 mmol, 1.00 equiv) and nitrile **2** (1.20 mmol, 3 equiv). The vial was sealed with a Teflon cap and electrical tape and placed in a pre-heated oil bath at 115 °C to stir for 4 h. After bringing the vial back into the glovebox, *p*-tolualdehyde **4a** (0.400 mmol, 1 equiv) was added to the reaction mixture and allowed to stir for an additional 30 min at room temperature. The vial was then removed from the glovebox and the reaction mixture was passed through a pipette with glass wool to remove the Ti oxo byproduct. The reaction mixture was then washed with 2 M HCl solution followed by sat. Na_2CO_3 with extractions of Et_2O and the organic layer was then dried over Na_2SO_4. The volatiles were removed *in vacuo* and residual aldehyde was removed by heating at 80 °C under vacuum to afford the 1,2-dihydropyrimidine **5xxx**. Alternatively, the HCl salt can be isolated by not performing the Na_2CO_3 wash. In this case, the Et_2O layer is collected after the 2 M HCl wash and dried over Na_2SO_4. The volatiles are then removed under reduced pressure to yield the 1,2-dihydropyrimidine salt **5xxx•HCl**.



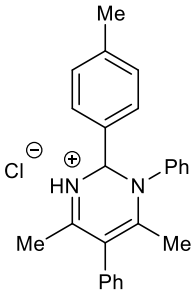
*This optimized procedure uses toluene as the solvent instead of bromobenzene, a 10-fold excess of nitrile rather than 3 equivalents of nitrile to promote full conversion to diazatitanacycle **3xx**, and $py_3TiCl_2(NPh)$ instead of $[py_2TiCl_2(NPh)]$ for greater consistency of between batches of the Ti imido species.*

General procedure for 5aca and 5gaa: 4 mL of toluene was added to a 20 mL scintillation vial containing $py_3TiCl_2(NPh)$ (0.400 mmol, 1.00 equiv) along with a stir bar, followed by the alkyne **1** (0.400 mmol, 1.00 equiv) and nitrile **2** (4.00 mmol, 10 equiv). The vial was sealed with a Teflon cap and electrical tape and placed in a pre-heated oil bath at 115 °C to stir for 4 h. After bringing the vial back into the glovebox, *p*-tolualdehyde **4a** (0.400 mmol, 1 equiv) was added to the reaction

mixture and allowed to stir for an additional 30 minutes at room temperature. The vial was then removed from the glovebox and the reaction mixture was passed through a pipette with glass wool to remove the Ti oxo byproduct. The reaction mixture was then washed with 2 M HCl solution followed by sat. Na_2CO_3 with extractions of Et_2O and the organic layer was then dried over Na_2SO_4. The volatiles were removed *in vacuo* and residual aldehyde was removed by heating at 80 °C under vacuum to afford the 1,2-dihydropyrimidine **5xxx**. Alternatively, the HCl salt can be isolated by not performing the Na_2CO_3 wash. In this case, the Et_2O layer is collected after the 2 M HCl wash and dried over Na_2SO_4. The volatiles are then removed under reduced pressure to yield the 1,2-dihydropyrimidine salt **5xxx•HCl**.



4,6-dimethyl-1,5-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aaa•HCl)



Red crystalline solid, 101.3 mg. 65% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 13.33 (br s, 1H, NH), 7.46 (d, J = 7.8 Hz, 2H), 7.40 – 7.27 (m, 6H), 7.21 (d, J = 7.8 Hz, 2H), 7.19 – 7.11 (m, 2H), 7.00 – 6.90 (m, 2H), 6.51 (s, 1H, CH), 2.34 (s, 3H), 2.12 (s, 3H), 1.97 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 162.19, 157.50, 140.84, 139.63, 133.32, 132.76, 130.90, 130.02, 129.62, 129.23, 129.19, 128.57, 126.20, 126.00, 114.02, 71.21, 21.20, 19.52, 19.10.

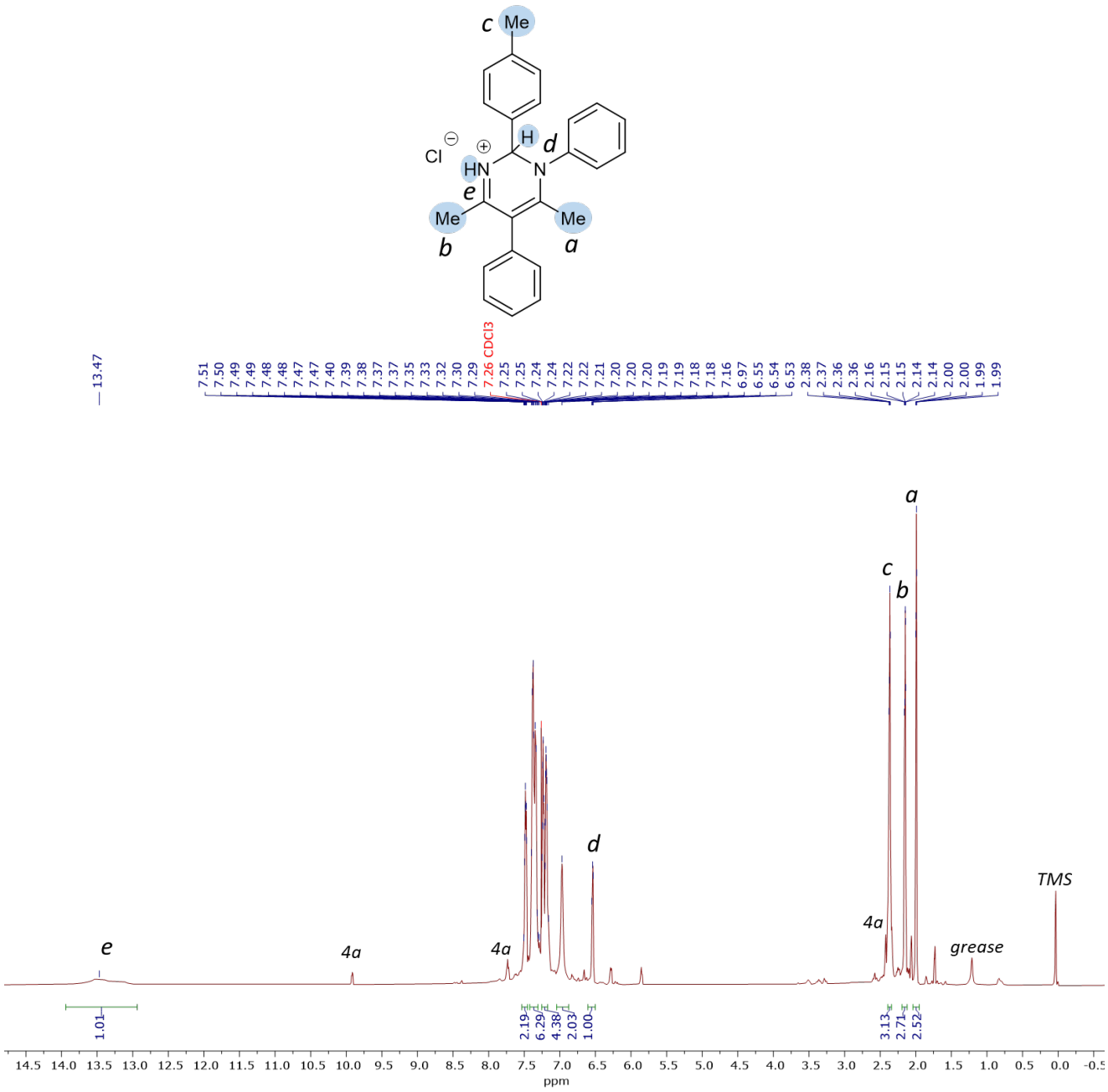


Figure S90. ^{1}H NMR spectrum of **5aaa•HCl** in $CDCl_3$.

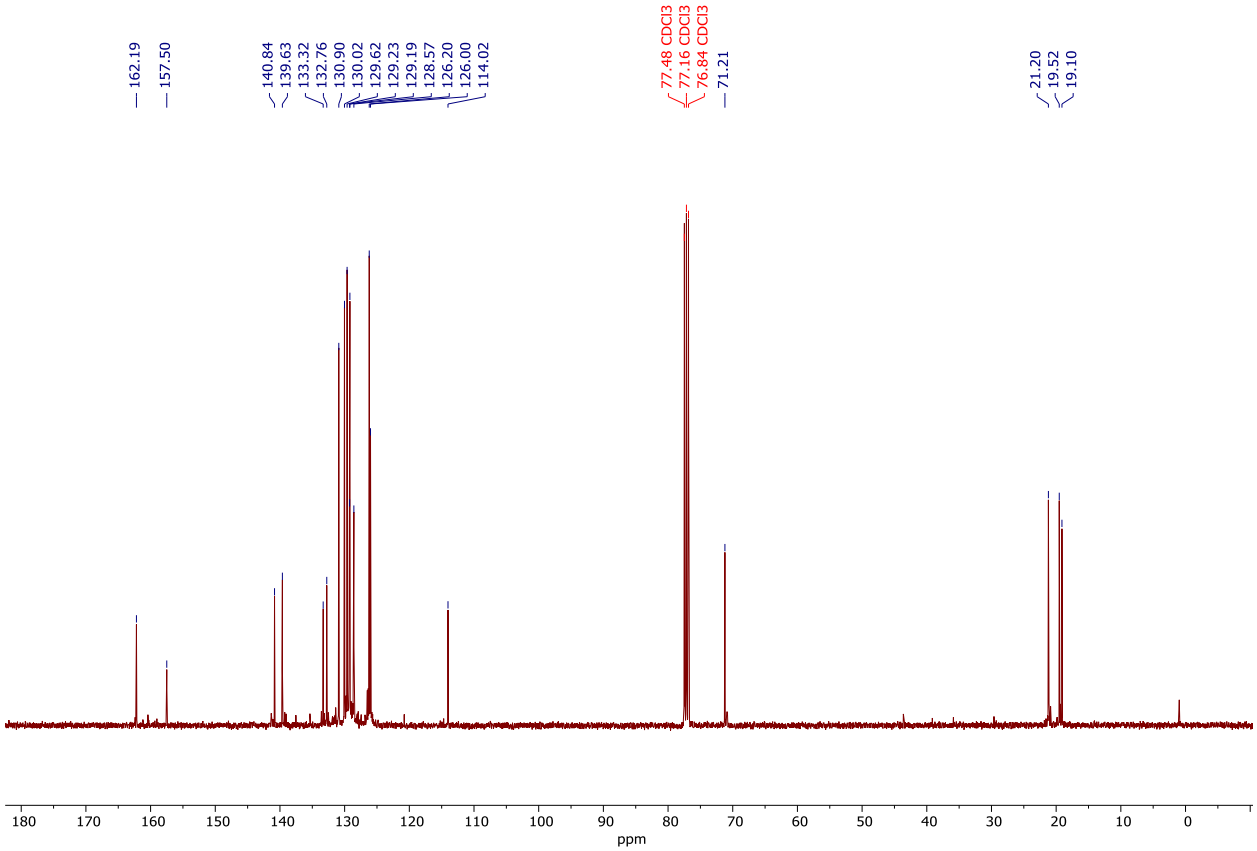


Figure S91. $^{13}C\{^{1}H\}$ NMR spectrum of **5aaa•HCl** in $CDCl_3$.

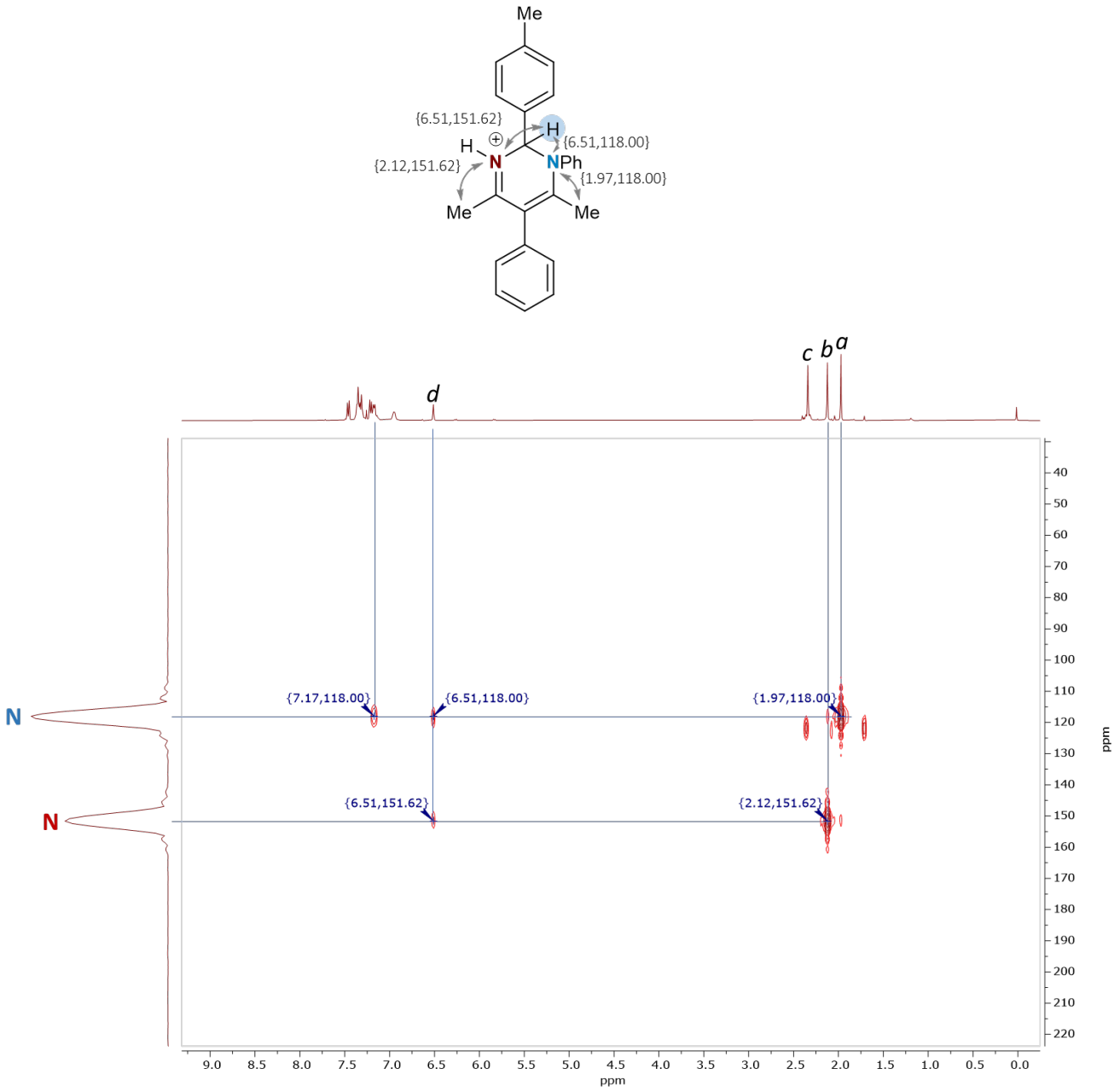
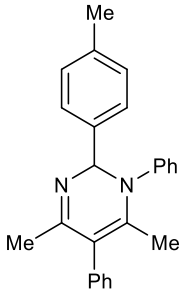


Figure S92. ^{1}H-^{15}N HMBC NMR spectrum of **5aaa•HCl** in $CDCl_3$.

4,6-dimethyl-1,5-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aaa)



Yellow solid, 107.9 mg. 77% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 7.45 (d, *J* = 8.1 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 4H), 7.27 – 7.11 (m, 7H), 7.00 (d, *J* = 7.0 Hz, 2H), 6.33 (s, 1H), 2.38 (s, 3H), 1.86 (s, 3H), 1.83 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 161.79, 144.51, 137.13, 131.55, 130.87, 130.04, 128.94, 128.81, 128.27, 126.88, 126.81, 126.30, 124.87, 124.59, 122.52, 23.38, 21.17, 18.17. **ESI-HRMS (m/z) $[M+H]^+$:** calcd. for $C_{25}H_{24}N_2^+$, 353.20121; found, 353.2001.

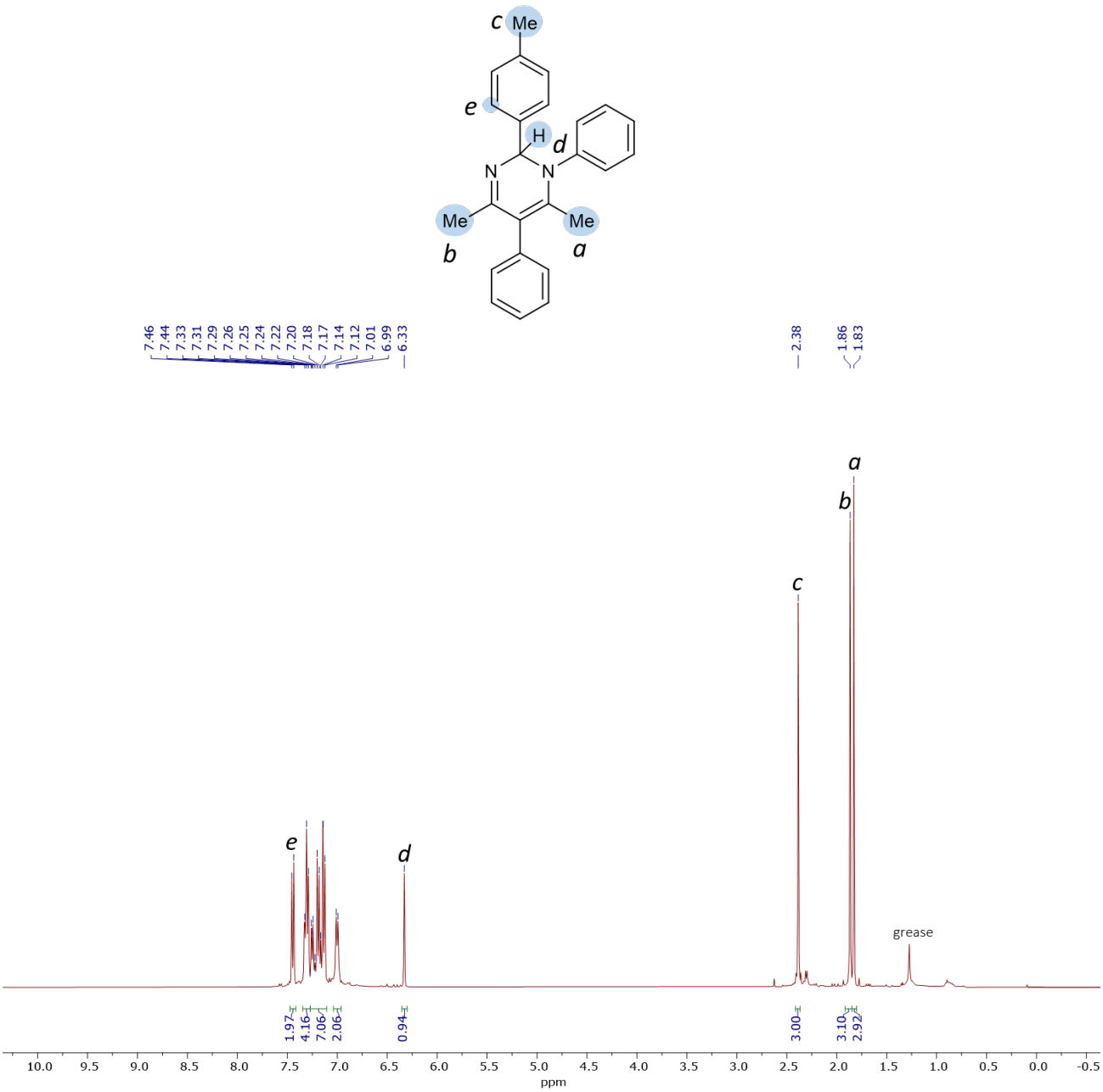


Figure S93. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$.

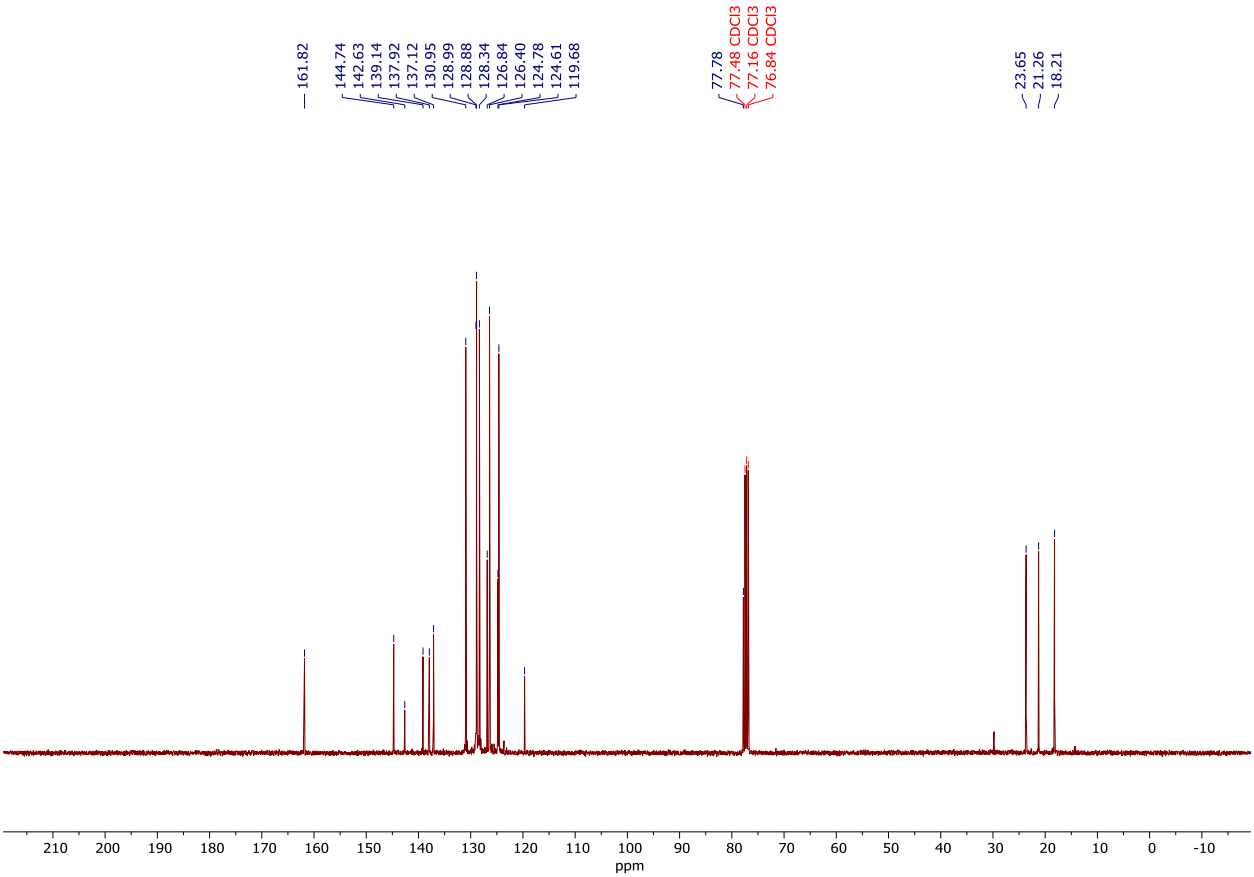


Figure S94. $^{13}C\{^{1}H\}$ NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$**.**

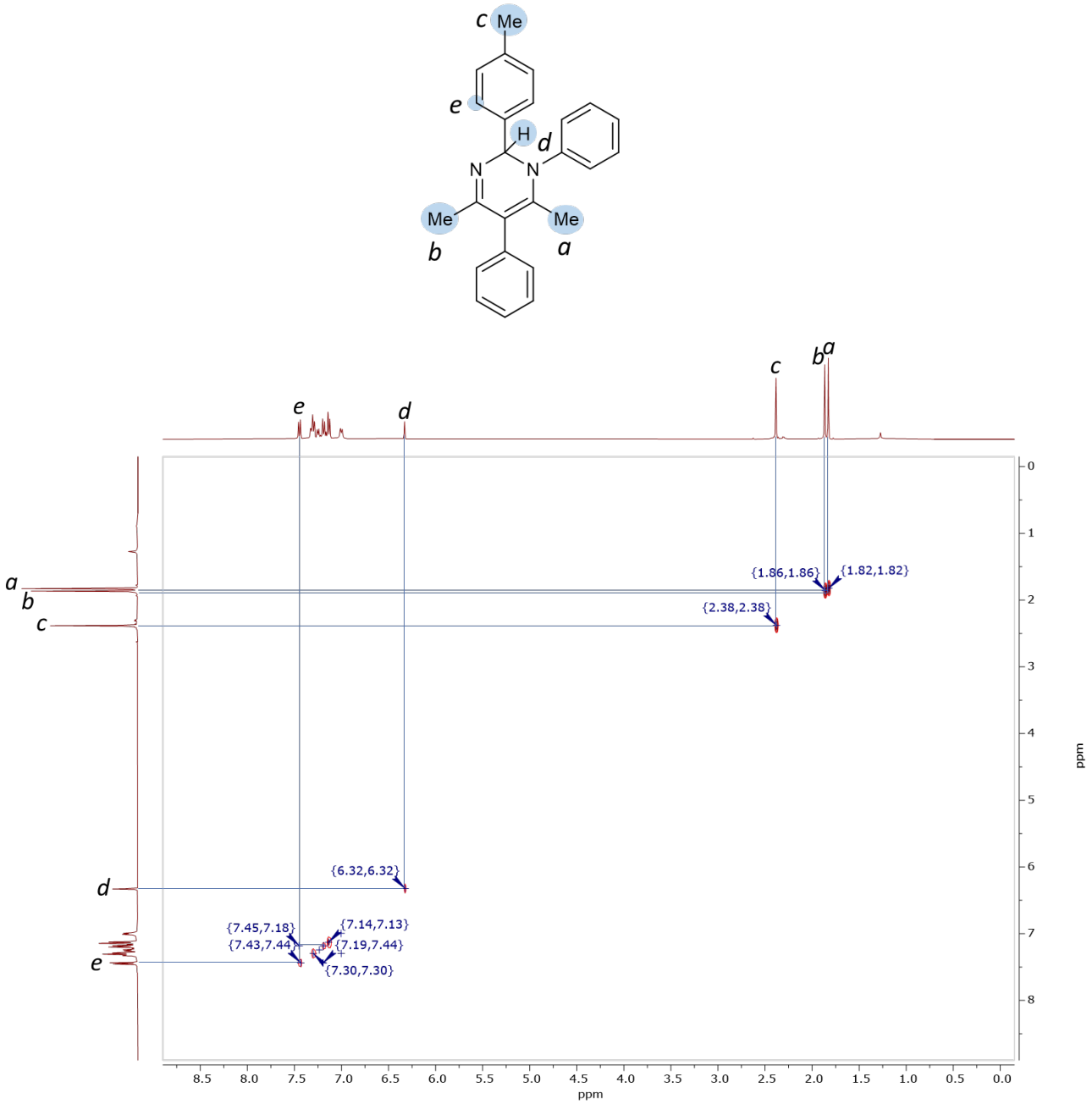


Figure S95. ^{1}H-^{1}H COSY NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$.

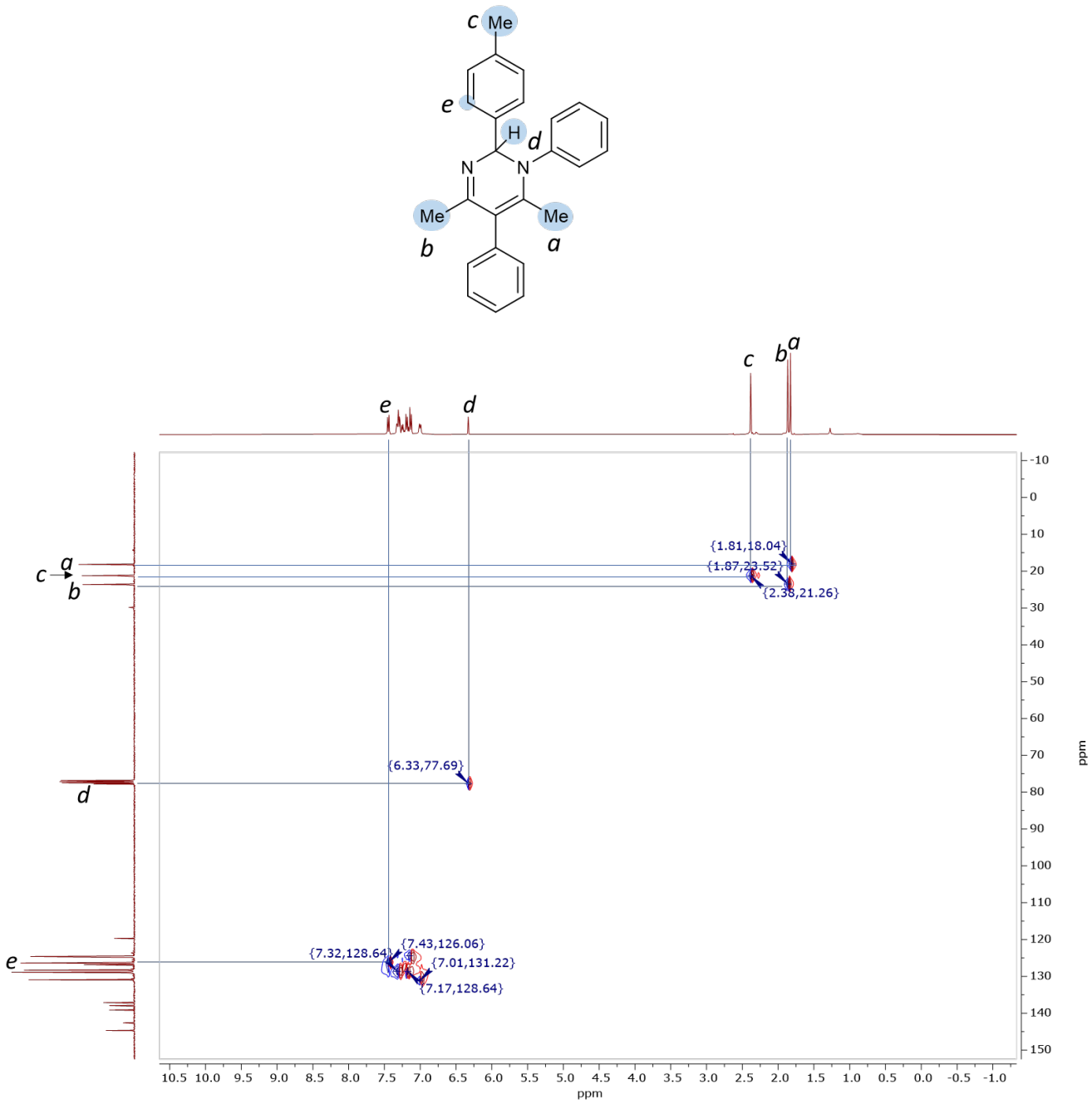


Figure S96. ^{1}H-^{13}C HSQC NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$.

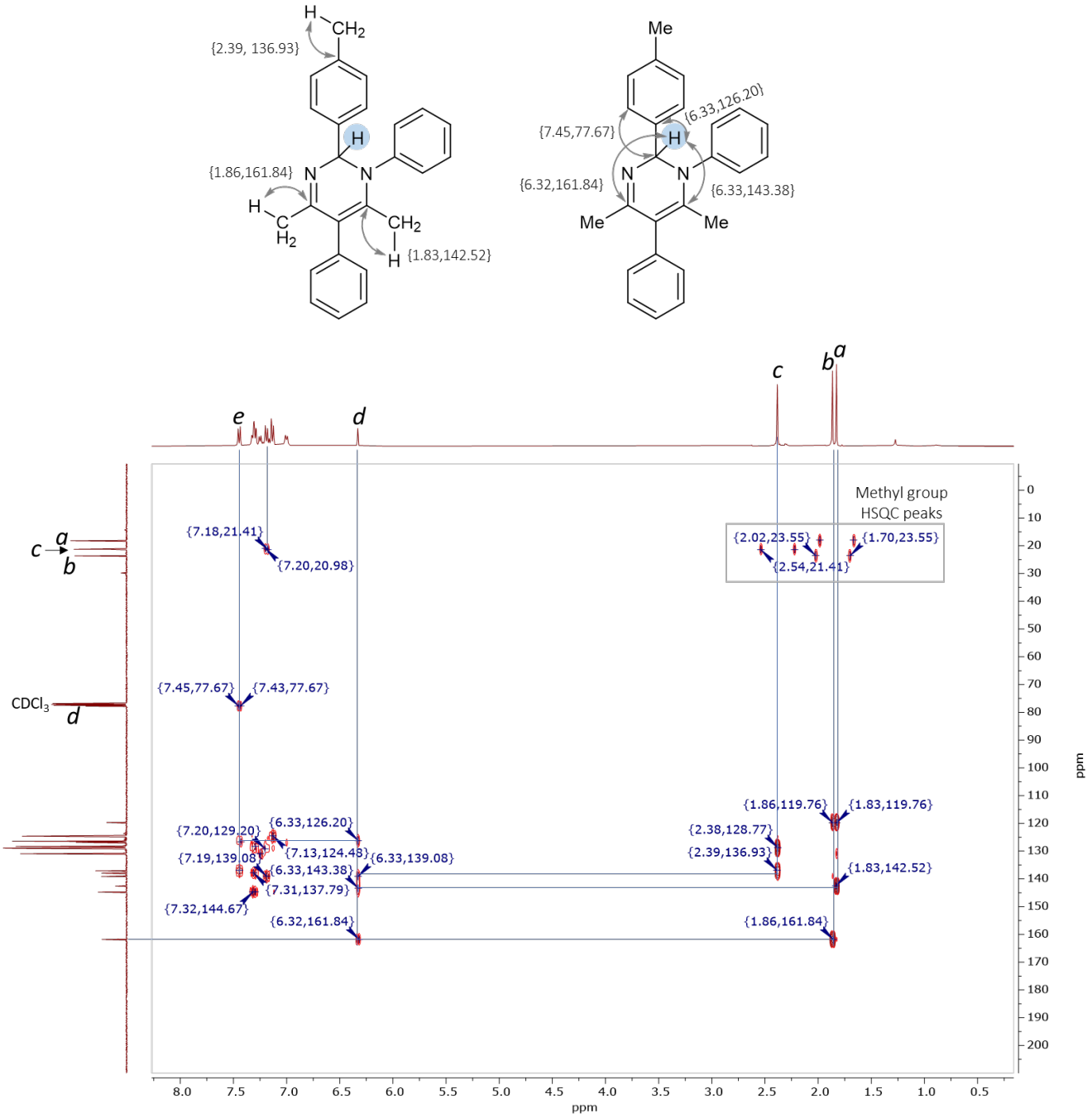


Figure S97. ^{1}H-^{13}C HMBC NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$.

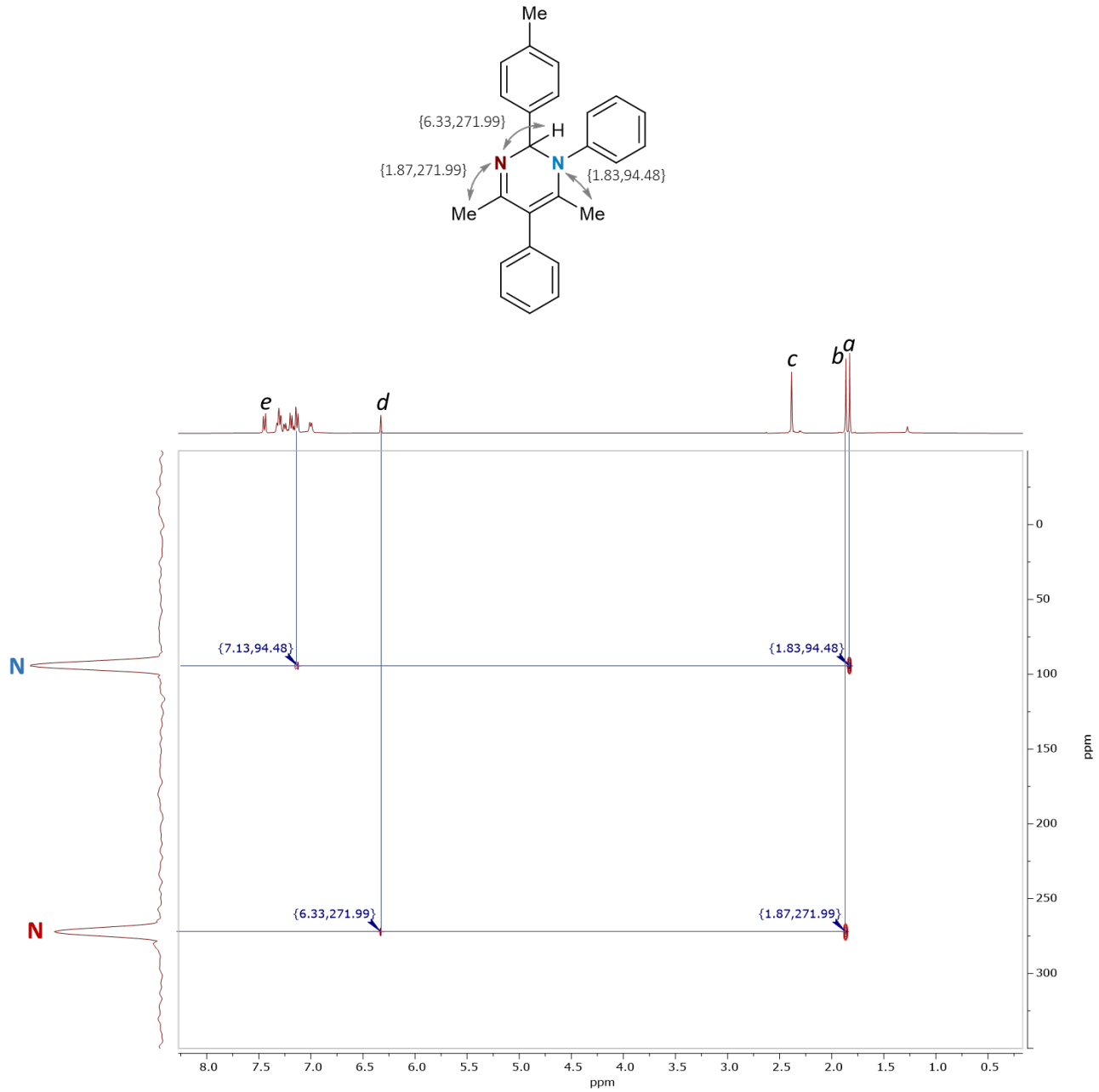
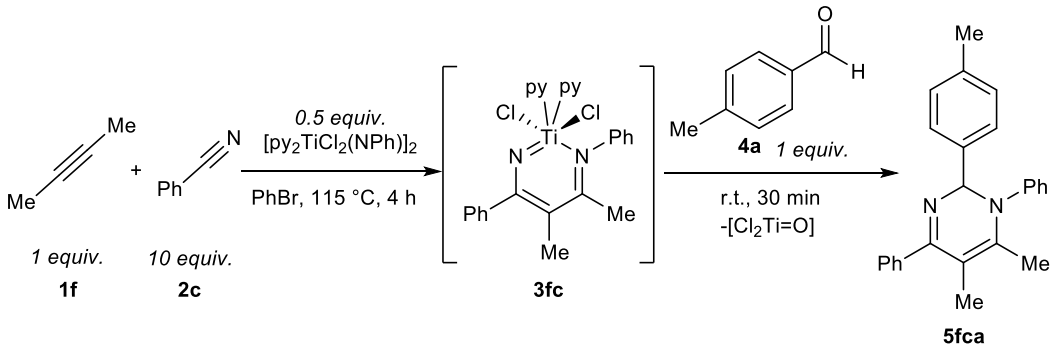
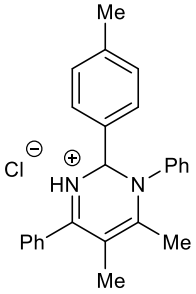


Figure S98. ^{1}H-^{15}N HMBC NMR spectrum of 1,2-dihydropyrimidine **5aaa** in $CDCl_3$.



5,6-dimethyl-1,4-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5fca•HCl)



Yellow crystalline solid, 121.1 mg. 78% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 12.62 (br s, 1H, NH), 7.64 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.52 – 7.40 (m, 3H), 7.36 (d, J = 7.5 Hz, 3H), 7.23 – 7.15 (m, 4H), 6.80 (s, 1H), 2.36 (s, 3H), 2.32 (s, 3H), 1.86 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 159.57, 141.04, 139.27, 132.97, 132.74, 130.73, 130.00, 129.95, 129.52, 129.02, 128.92, 126.17, 125.71, 105.82, 70.62, 21.20, 18.95, 14.41.

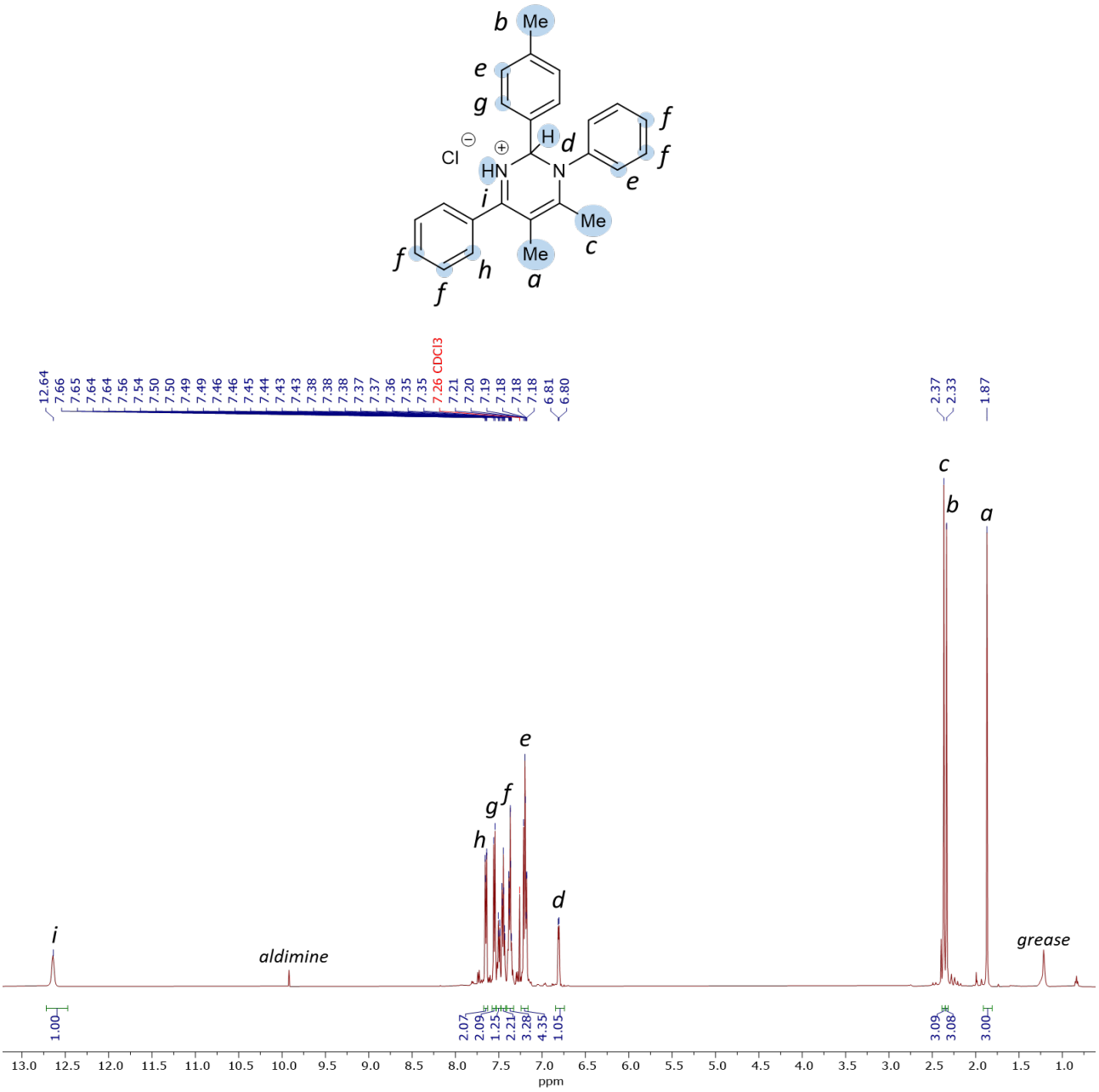


Figure S99. ^{1}H NMR spectrum of **5fca•HCl** in $CDCl_3$.

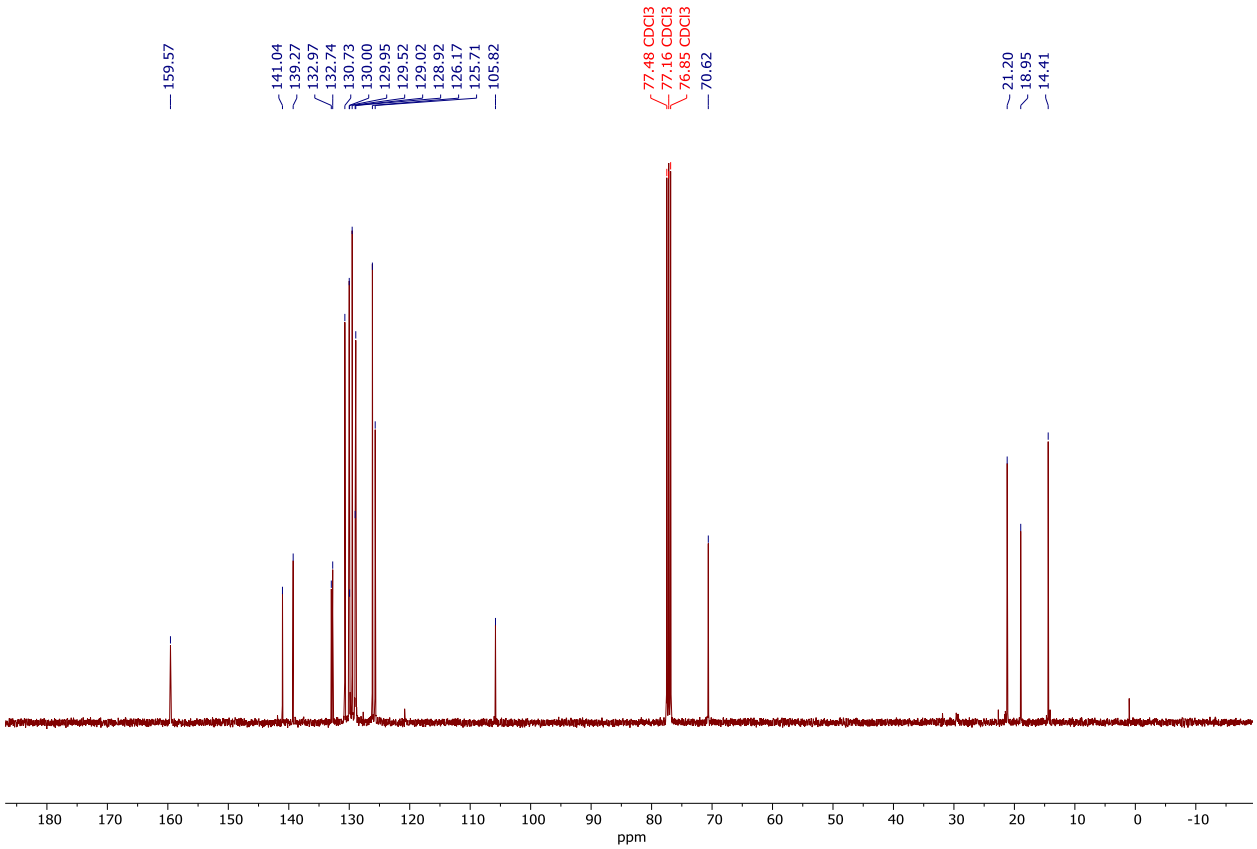


Figure S100. $^{13}C\{^{1}H\}$ NMR spectrum of **5fca•HCl** in $CDCl_3$**.**

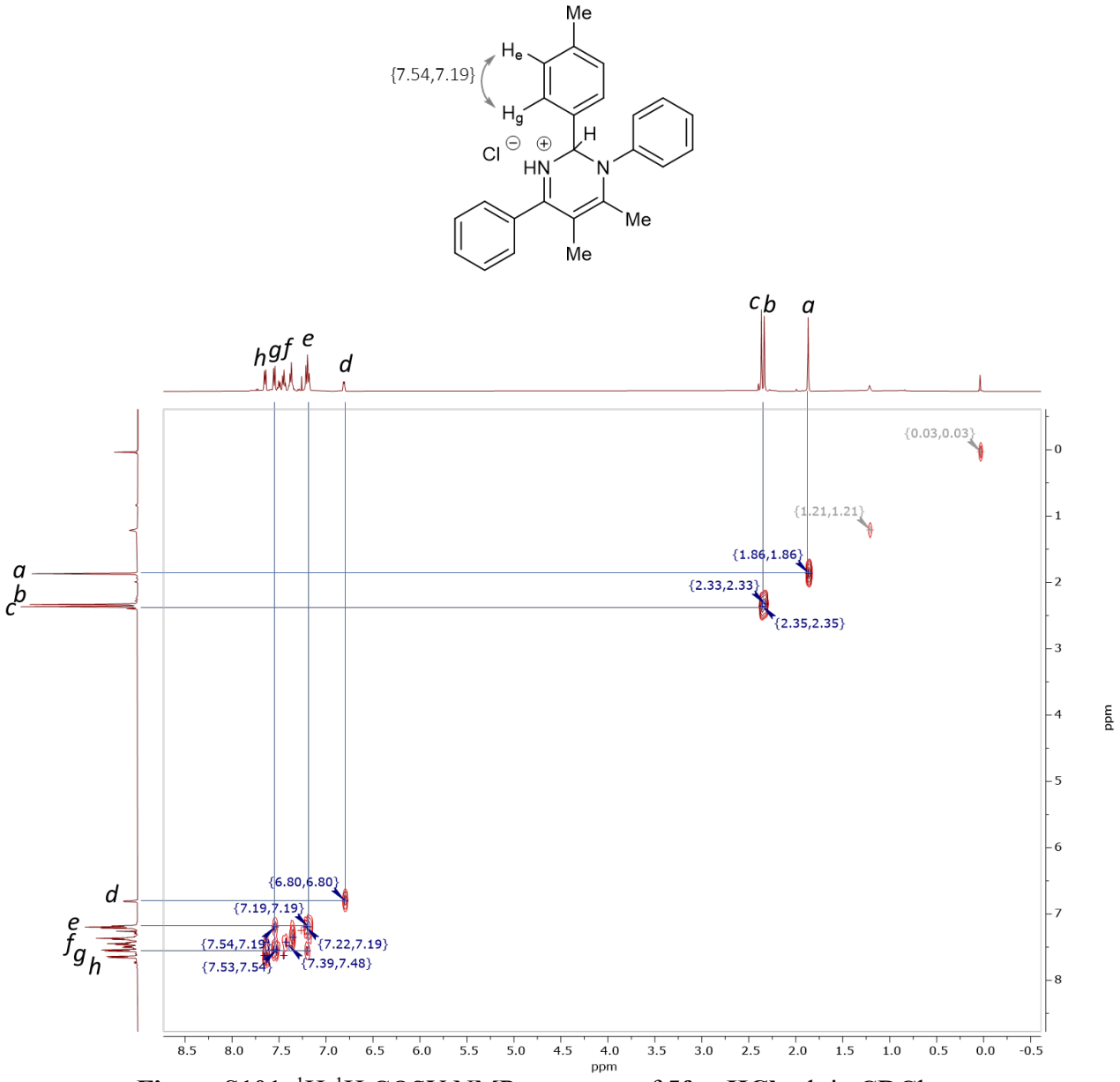


Figure S101. ^{1}H-^{1}H COSY NMR spectrum of **5fca•HCl** salt in $CDCl_3$.

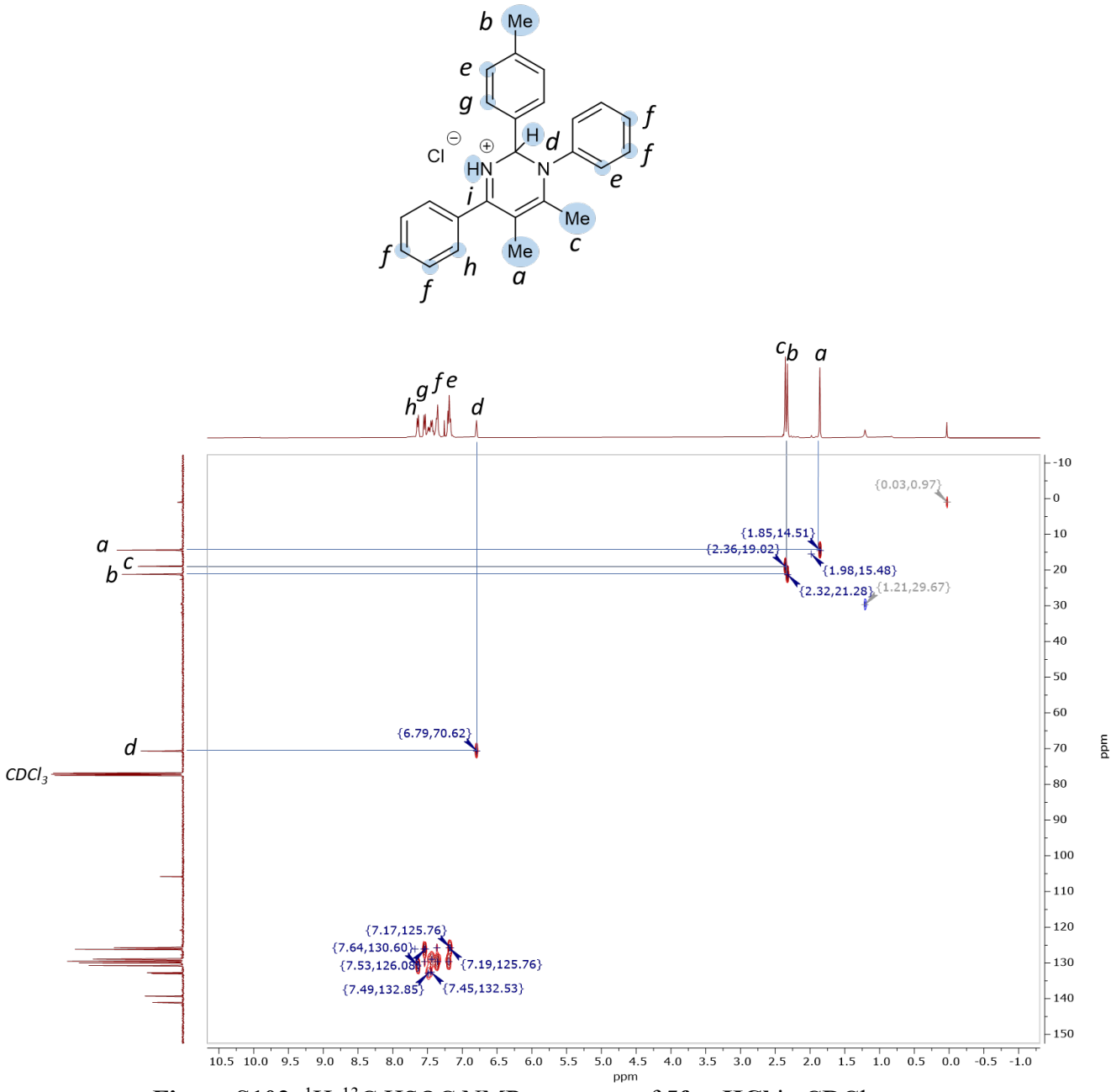


Figure S102. ^{1}H-^{13}C HSQC NMR spectrum of **5fca•HCl** in $CDCl_3$.

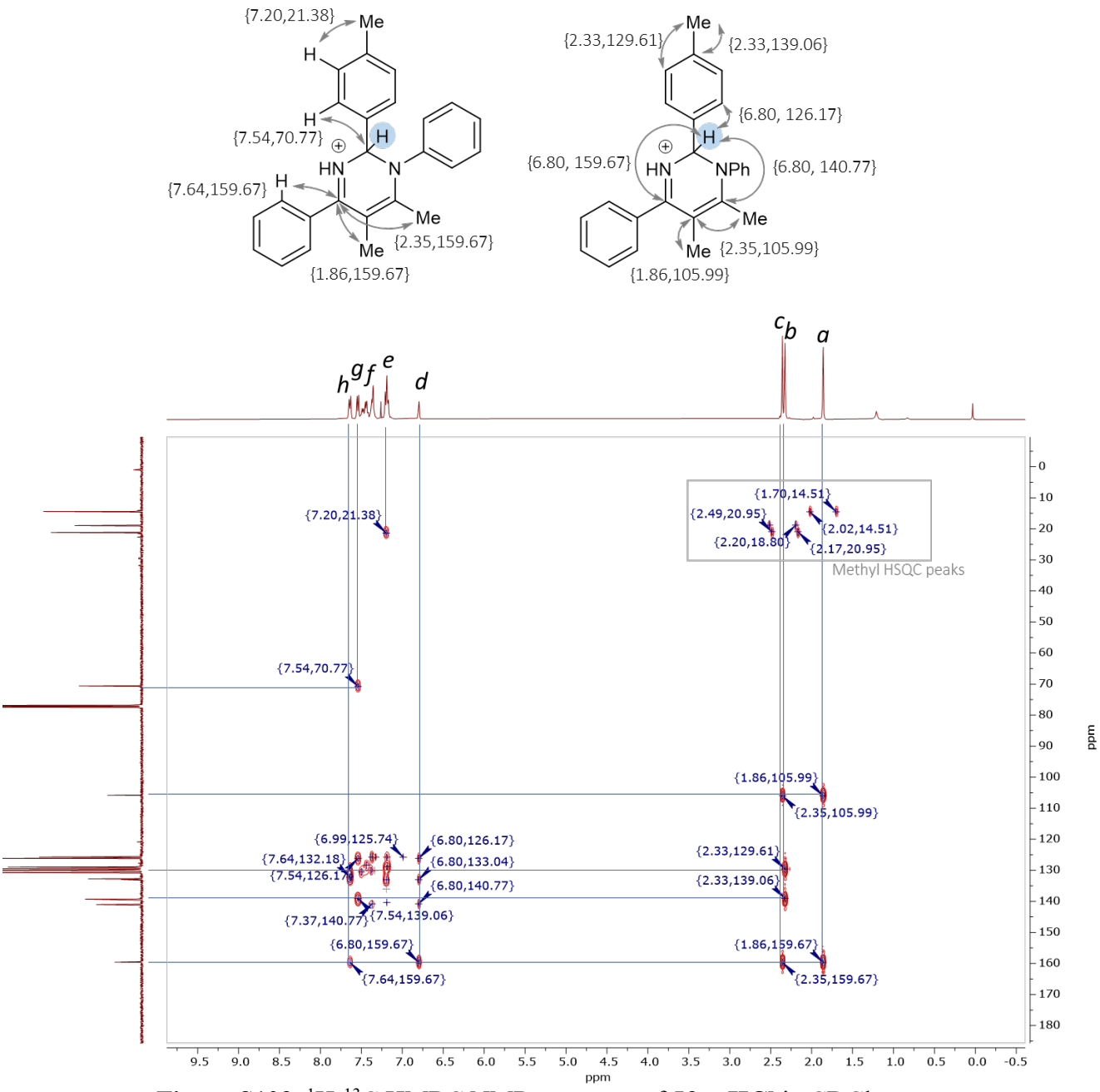


Figure S103. ^{1}H-^{13}C HMBC NMR spectrum of **5fca•HCl** in $CDCl_3$.

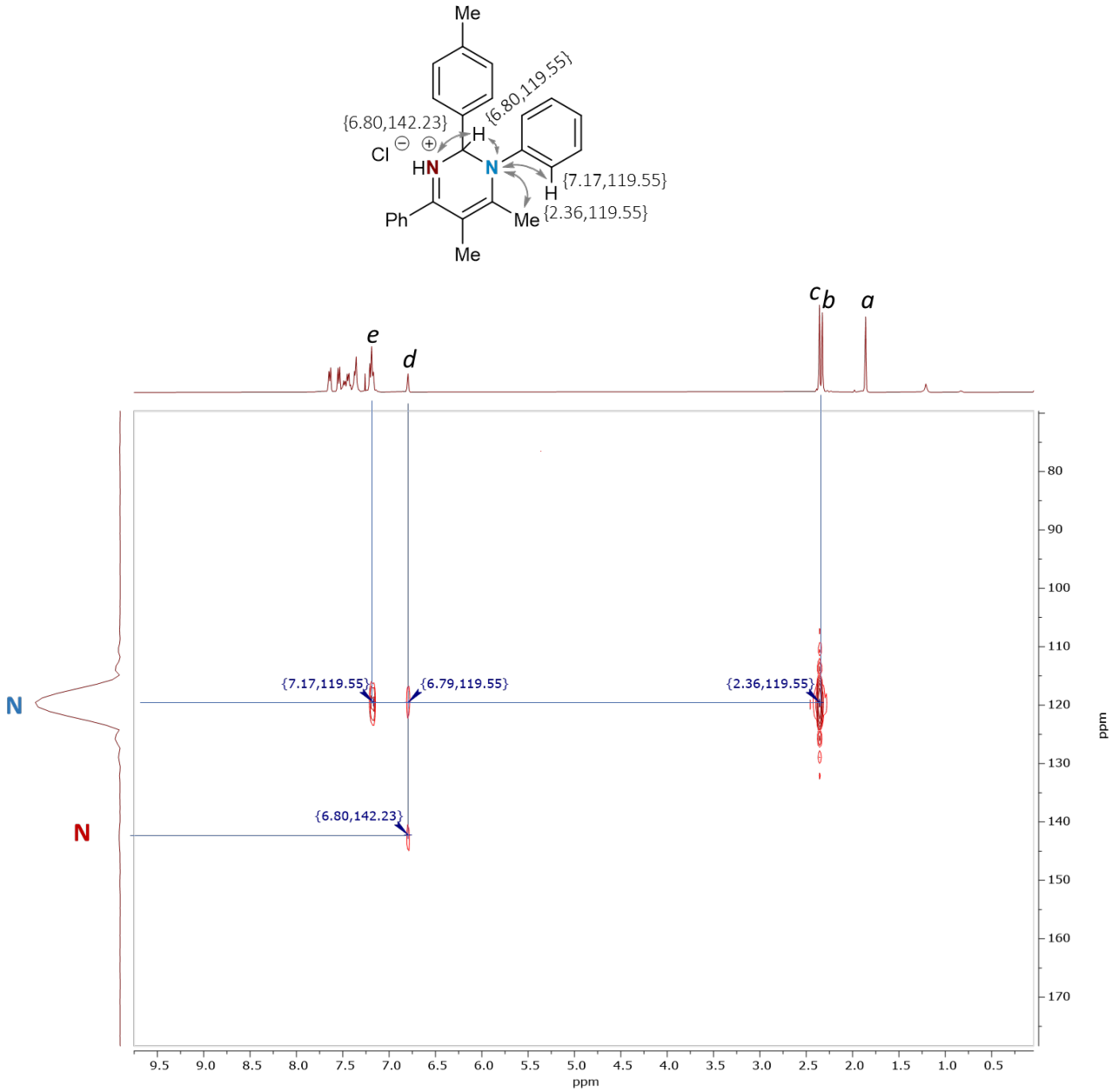
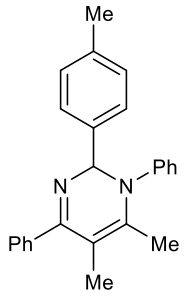


Figure S104. ^{1}H-^{15}N HMBC NMR spectrum of **5fca•HCl** in $CDCl_3$.

5,6-dimethyl-1,4-diphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5fca)



Red oil, 121.1 mg. 73% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 7.63 – 7.56 (m, 2H), 7.56 – 7.50 (m, 2H), 7.46 – 7.38 (m, 3H), 7.36 – 7.29 (m, 2H), 7.25 – 7.19 (m, 2H), 7.16 – 7.08 (m, 3H), 6.59 (s, 1H), 2.40 (s, 3H), 2.10 (s, 3H), 1.75 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 165.34, 145.24, 142.82, 139.23, 139.10, 137.02, 128.94, 128.85, 128.80, 128.78, 127.99, 126.21, 123.89, 123.34, 111.86, 77.16, 21.21, 17.10, 14.66.

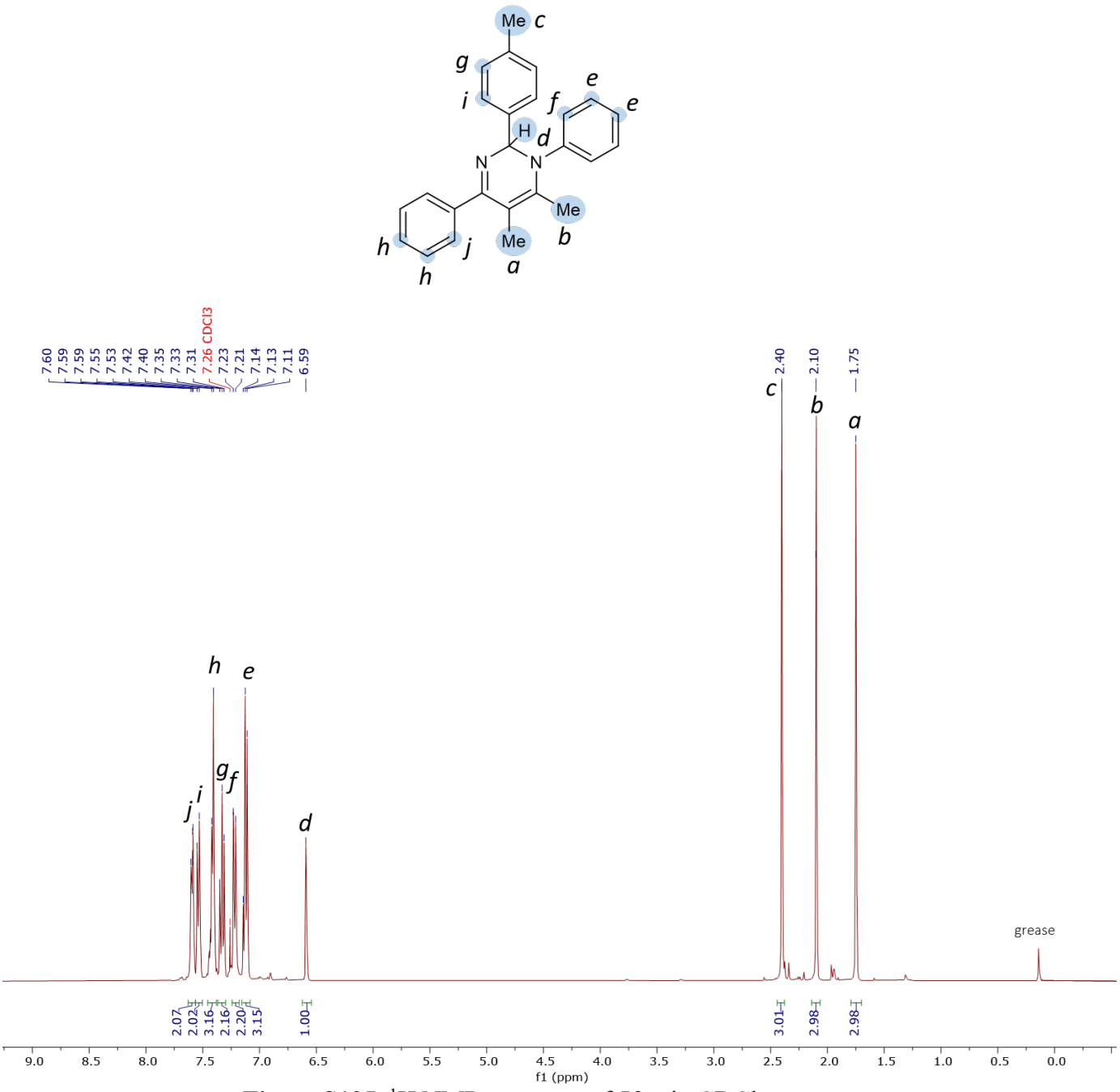


Figure S105. ^{1}H NMR spectrum of **5fca** in $CDCl_3$.

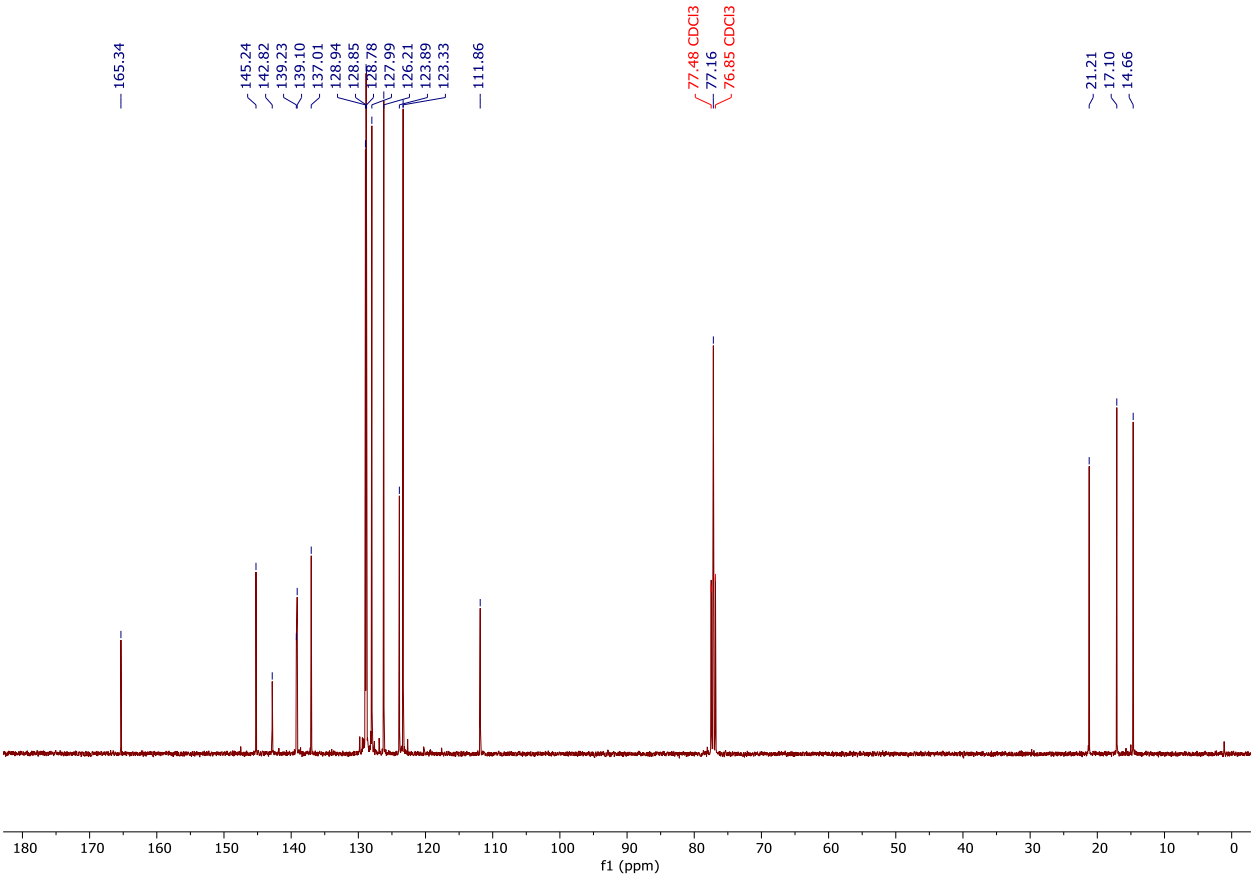


Figure S106. $^{13}C\{^{1}H\}$ NMR spectrum of **5fca** in $CDCl_3$.

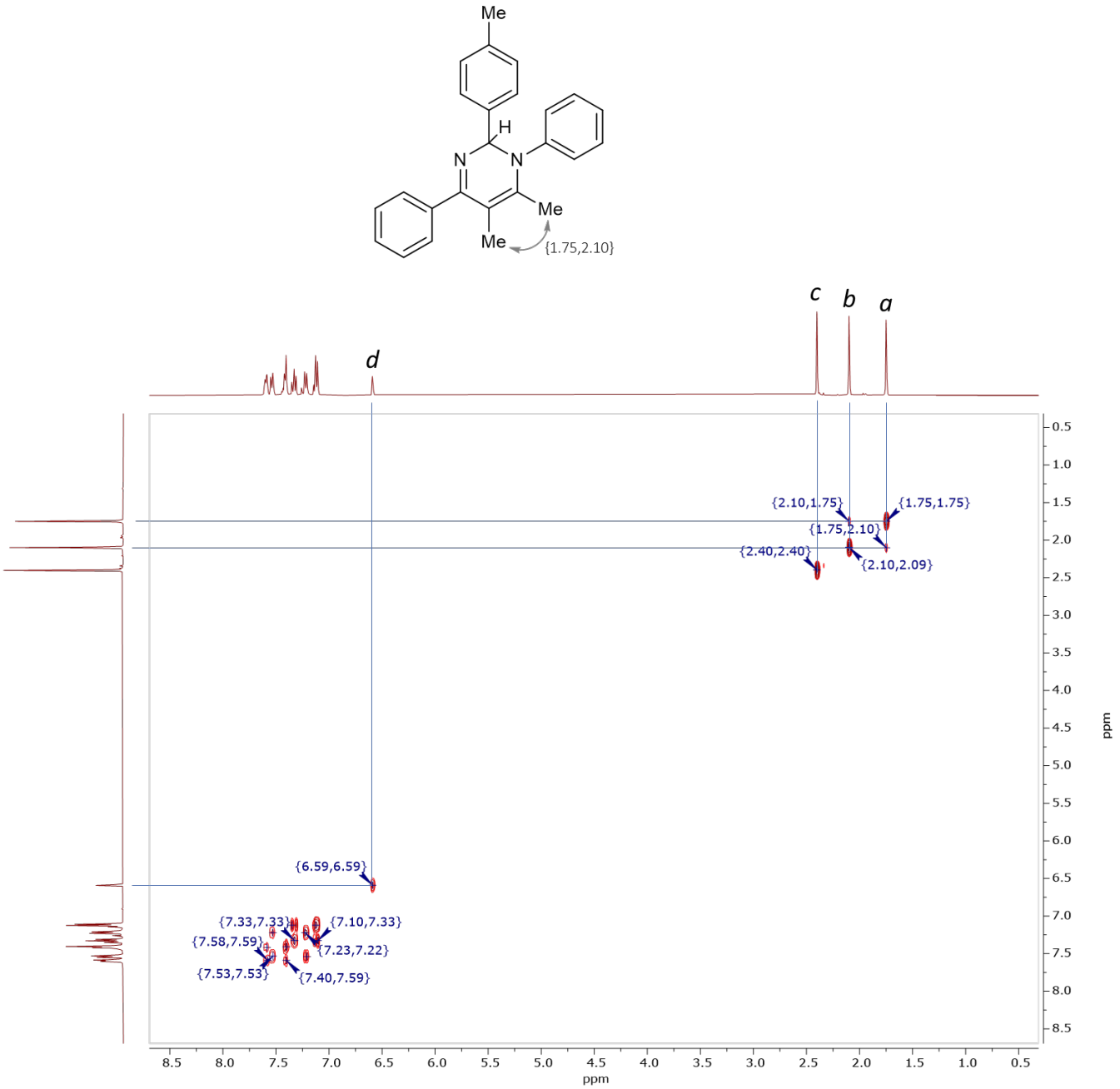


Figure S107. ^{1}H-^{1}H COSY NMR spectrum of **5fca** in $CDCl_3$.

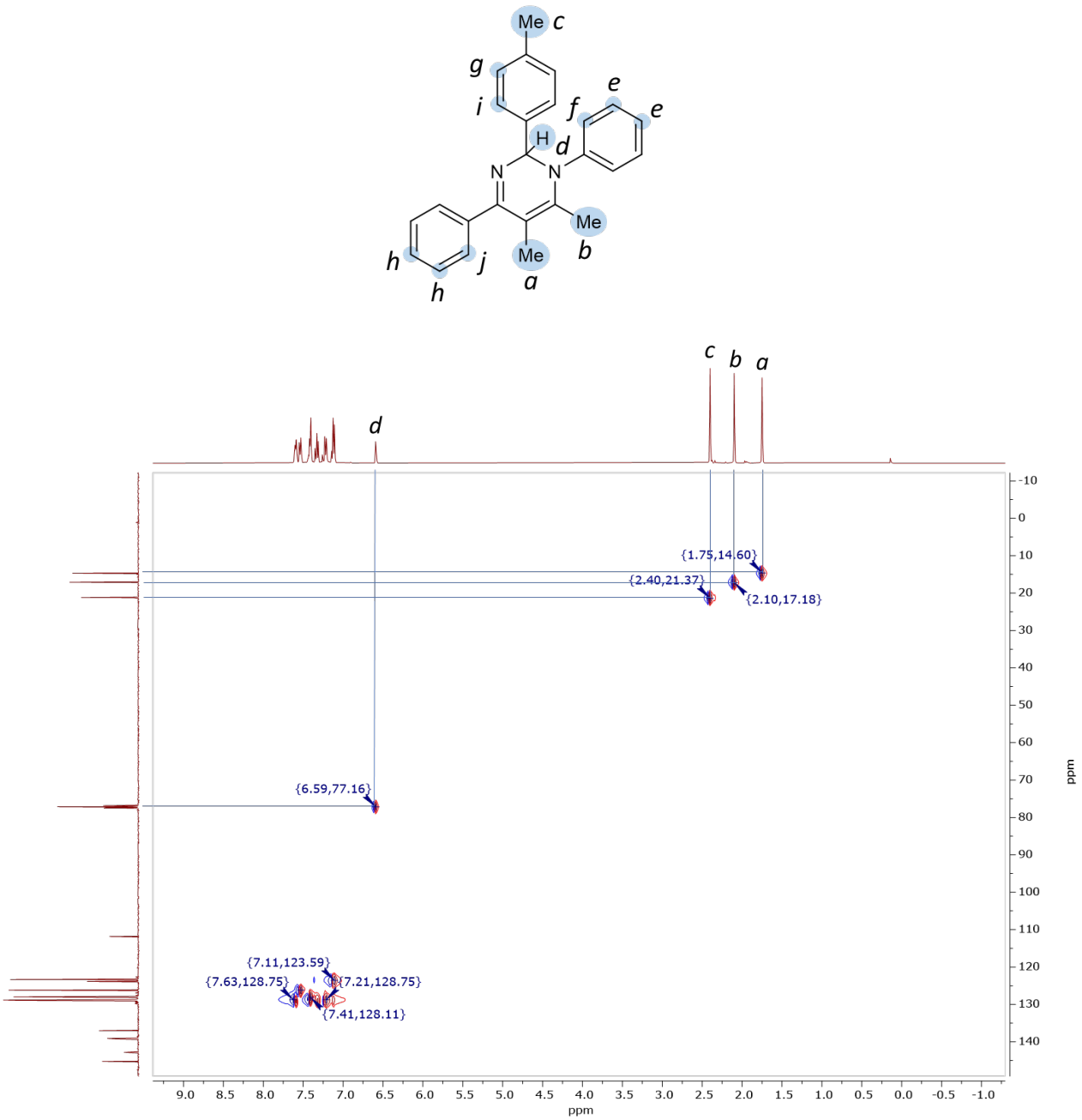


Figure S108. ^{1}H-^{13}C HSQC NMR spectrum of **5fca** in $CDCl_3$.

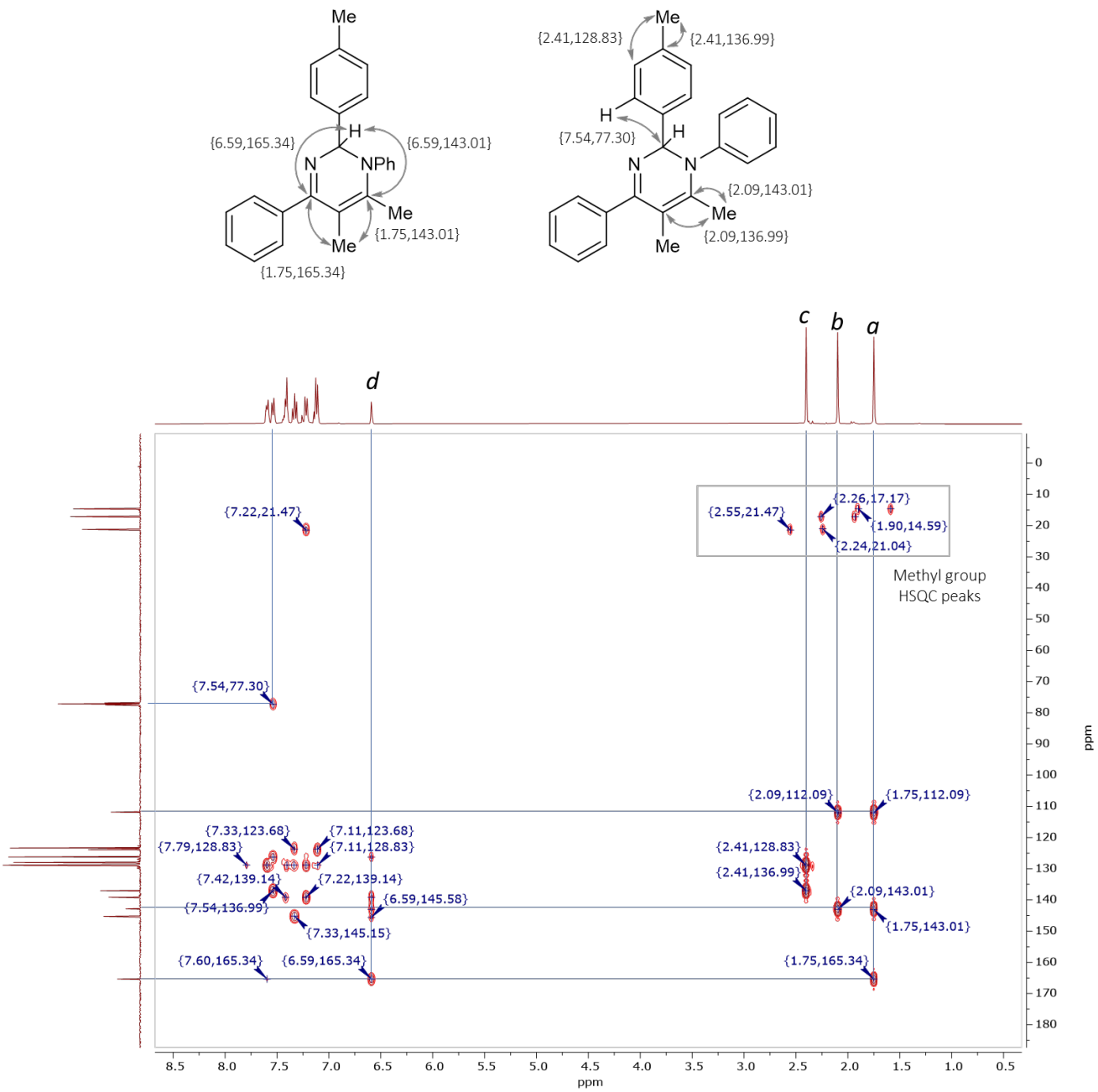


Figure S109. ^{1}H-^{13}C HMBC NMR spectrum of **5fca** in $CDCl_3$.

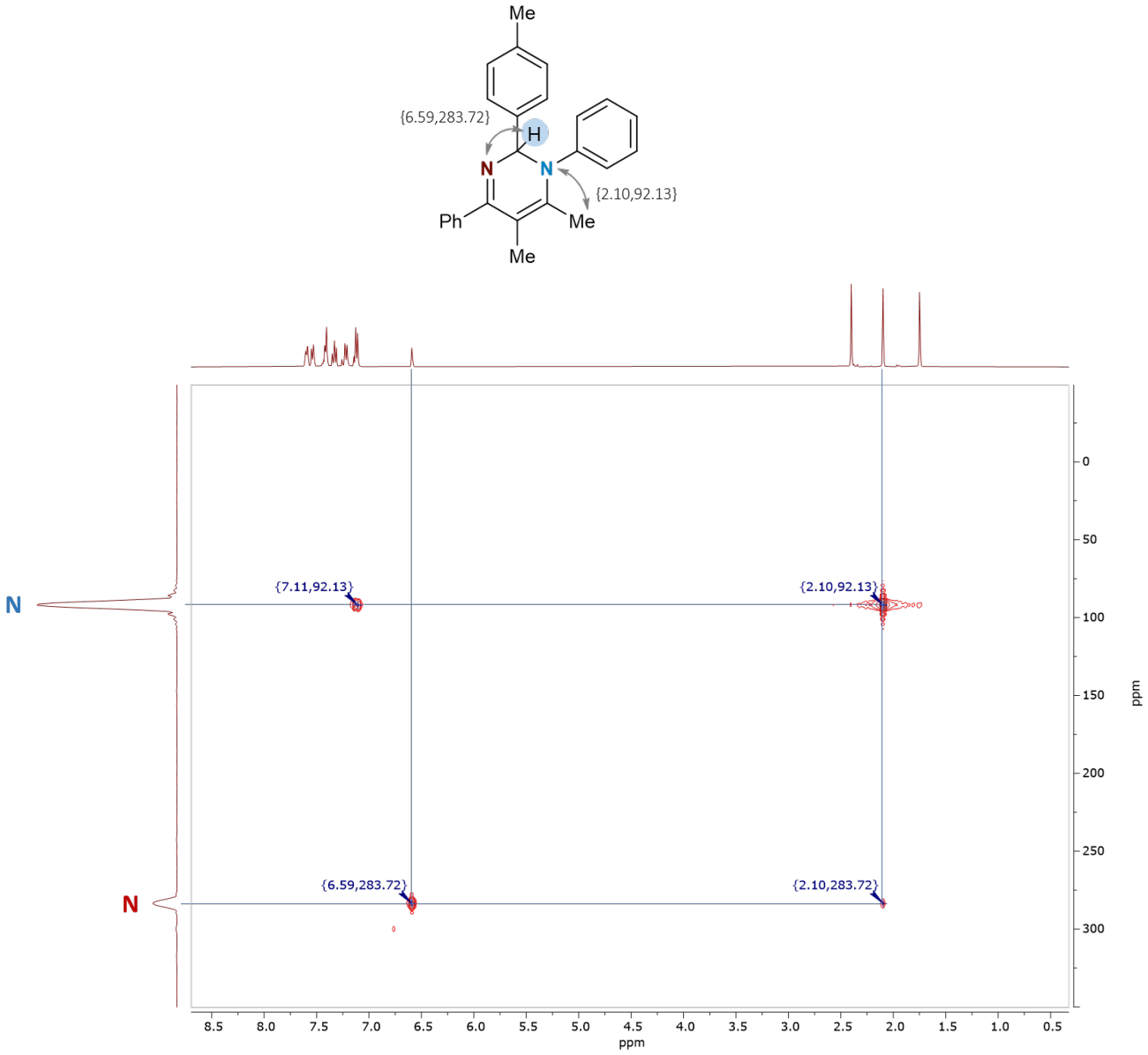
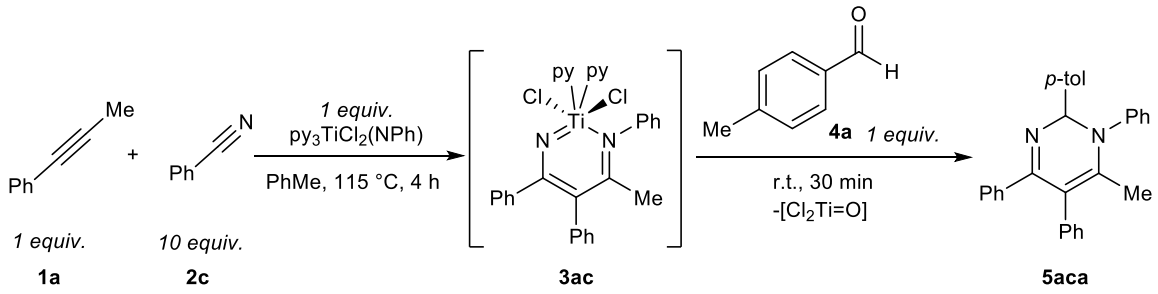
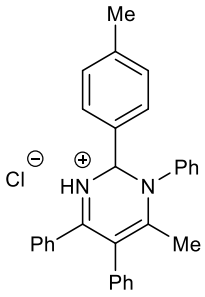


Figure S110. ^{1}H-^{15}N HMBC NMR spectrum of **5fca** in $CDCl_3$.



4-methyl-3,5,6-triphenyl-2-(p-tolyl)-2,3-dihydropyrimidin-1-ium chloride (5aca•HCl)



Yellow solid precipitated out of the toluene solution rather than isolated by removing the volatiles *in vacuo*. 108.2 mg, 29% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 13.23 (s, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 7.2 Hz, 5H), 7.32 (dt, J = 17.7, 7.8 Hz, 5H), 7.26 – 7.18 (m, 5H), 6.96 (d, J = 5.7 Hz, 1H), 6.88 (d, J = 3.7 Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 159.73, 141.17, 139.73, 133.24, 132.52, 132.01, 131.14, 130.23, 129.83, 129.47, 128.71, 128.61, 128.09, 126.52, 125.87, 70.97, 21.41, 20.96. **HRMS (m/z):** calcd. for $C_{30}H_{27}N_2^+$, 415.2168; found, 415.2165.

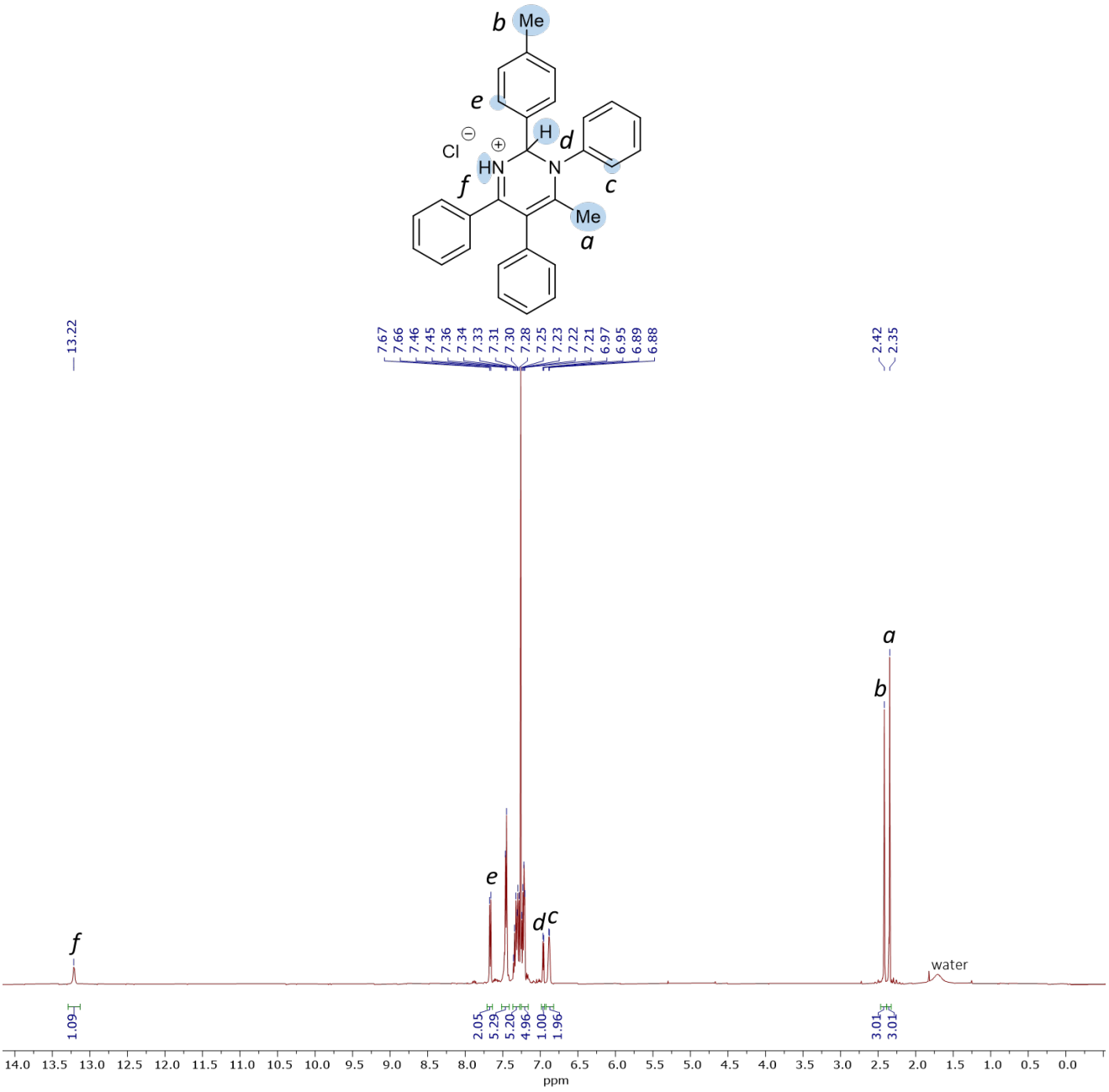


Figure S111. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5aca•HCl** in $CDCl_3$**.**

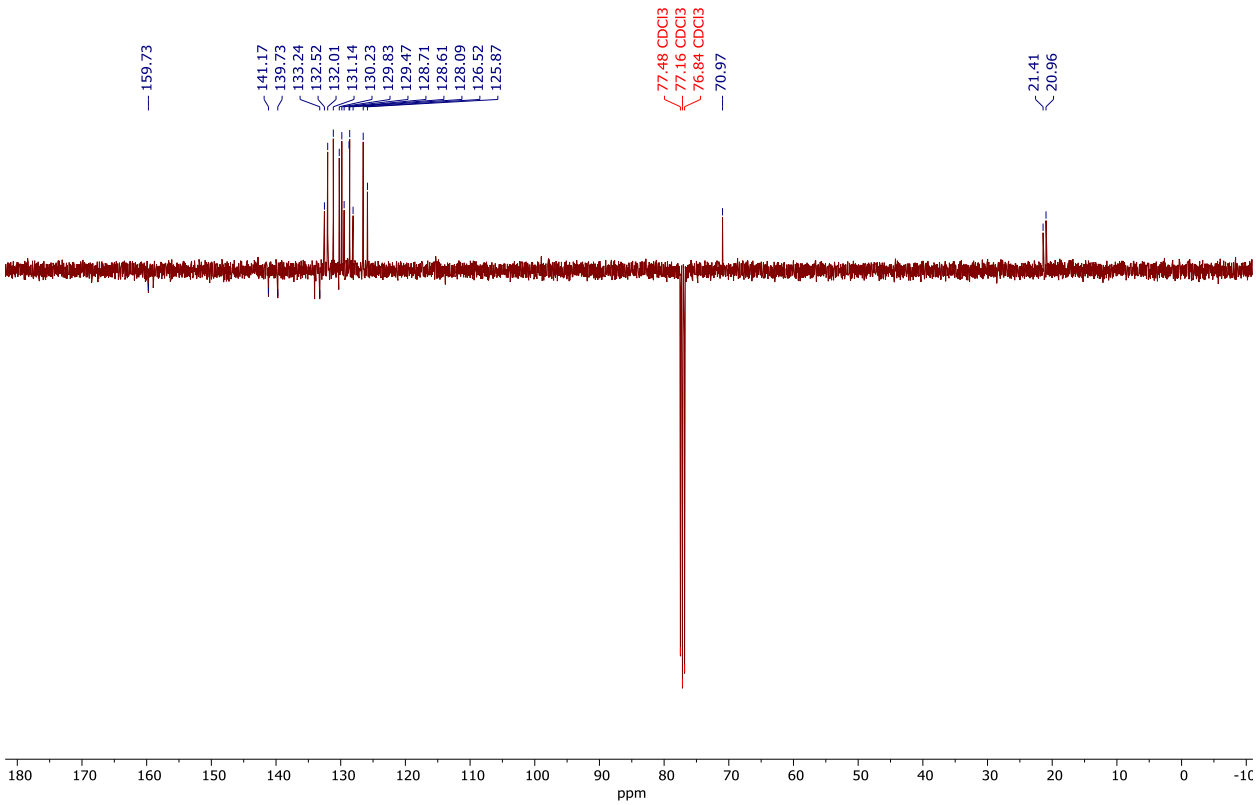


Figure S112. $^{13}C\{^{1}H\}$ APT NMR spectrum of 1,2-dihydropyrimidine (**5aca•HCl**) in $CDCl_3$.

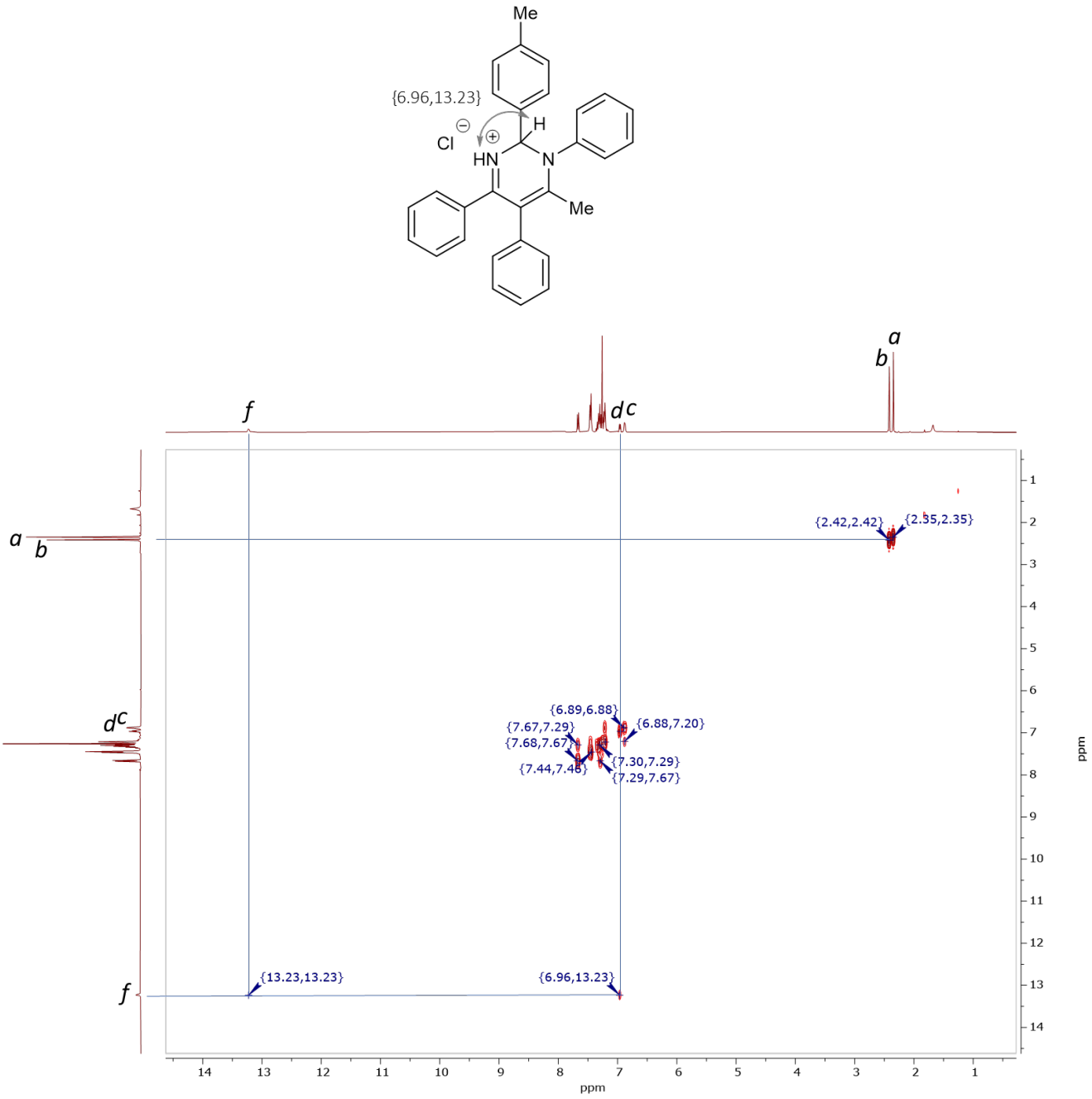


Figure S113. ^{1}H-^{1}H COSY NMR spectrum of 1,2-dihydropyrimidine **5aca•HCl** in $CDCl_3$.

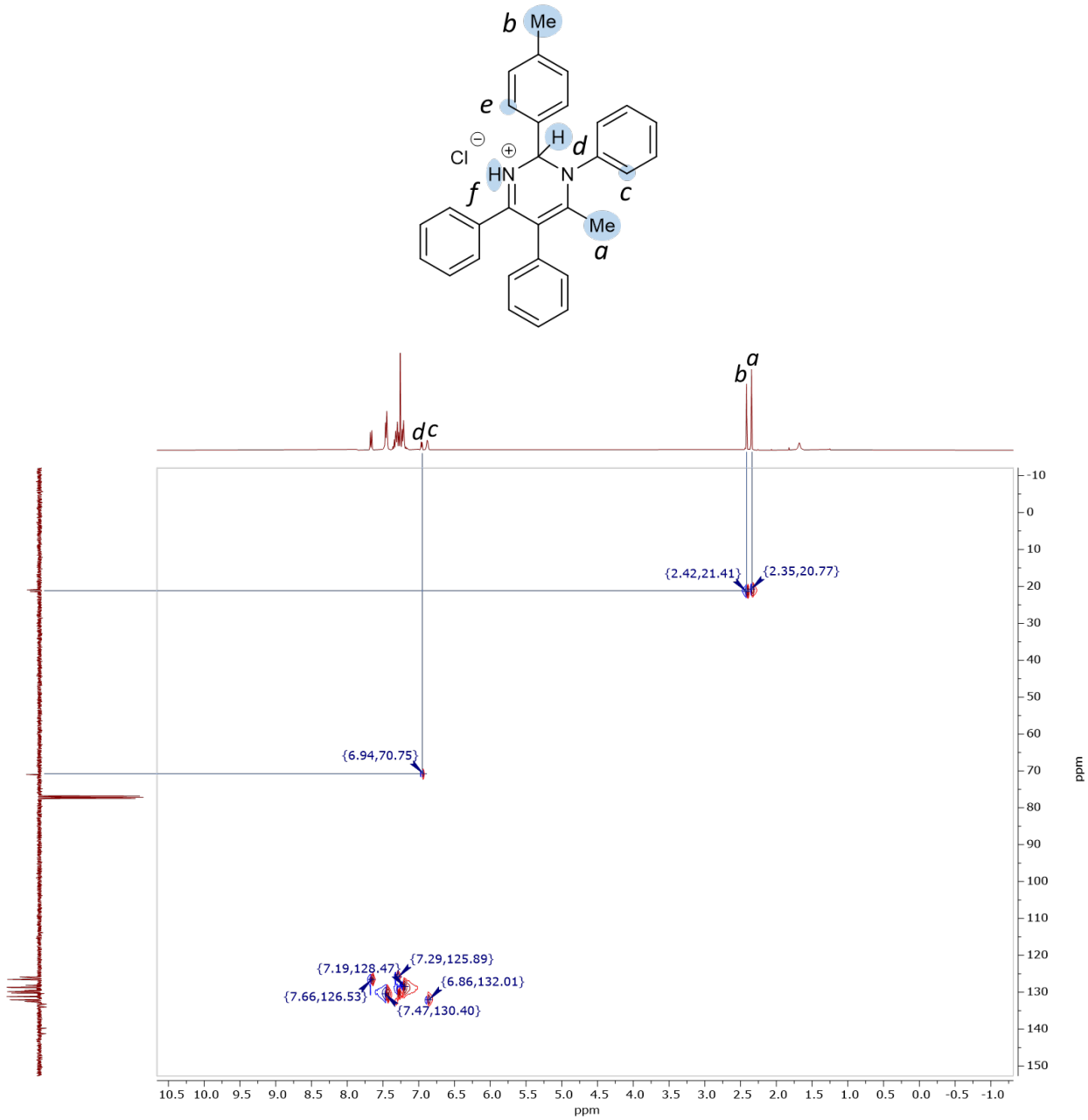


Figure S114. ^{1}H-^{13}C HSQC NMR spectrum of 1,2-dihydropyrimidine **5aca•HCl** in $CDCl_3$.

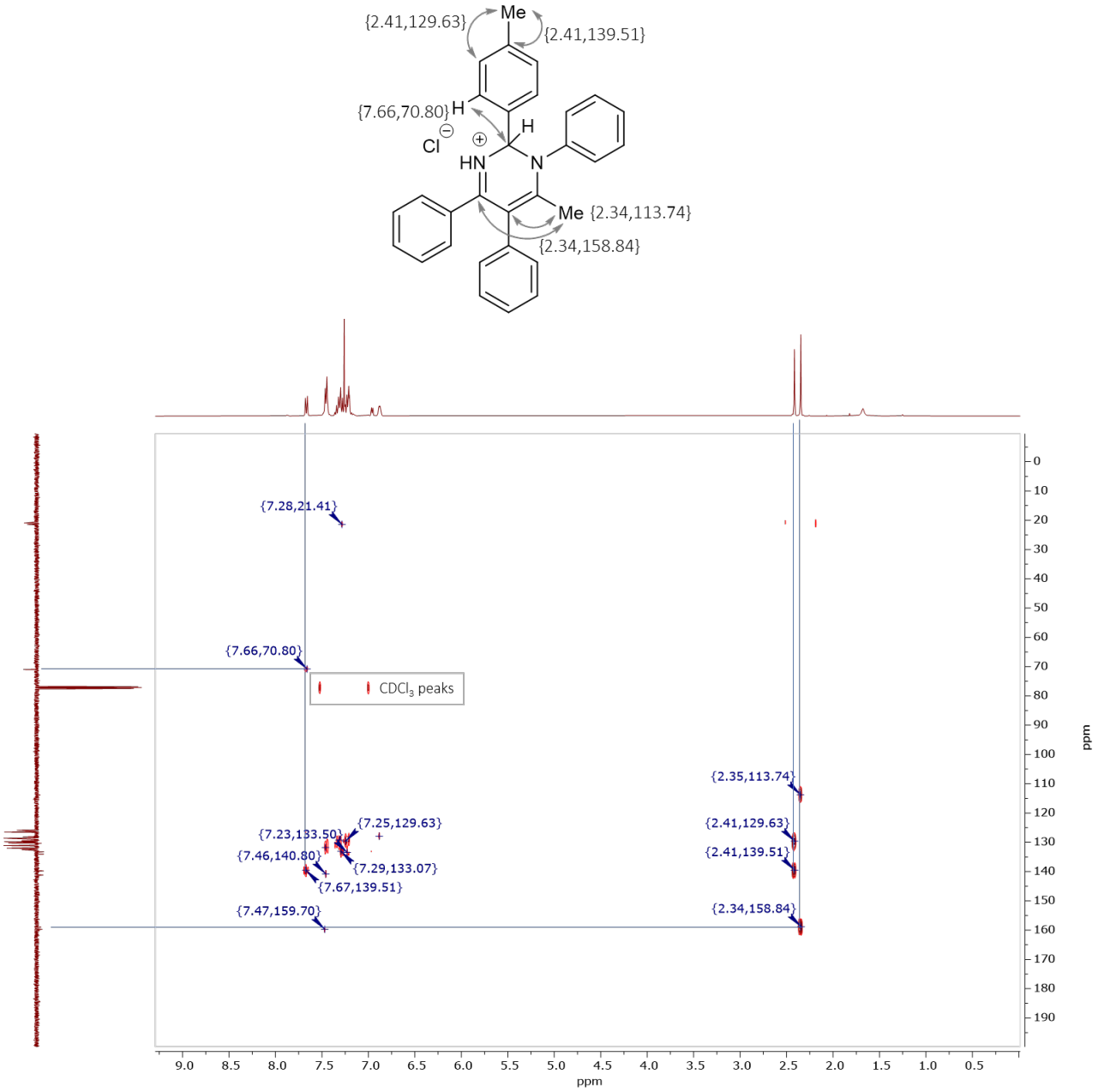


Figure S115. ^{1}H-^{13}C HMBC NMR spectrum of 1,2-dihydropyrimidine **5aca•HCl** in $CDCl_3$.

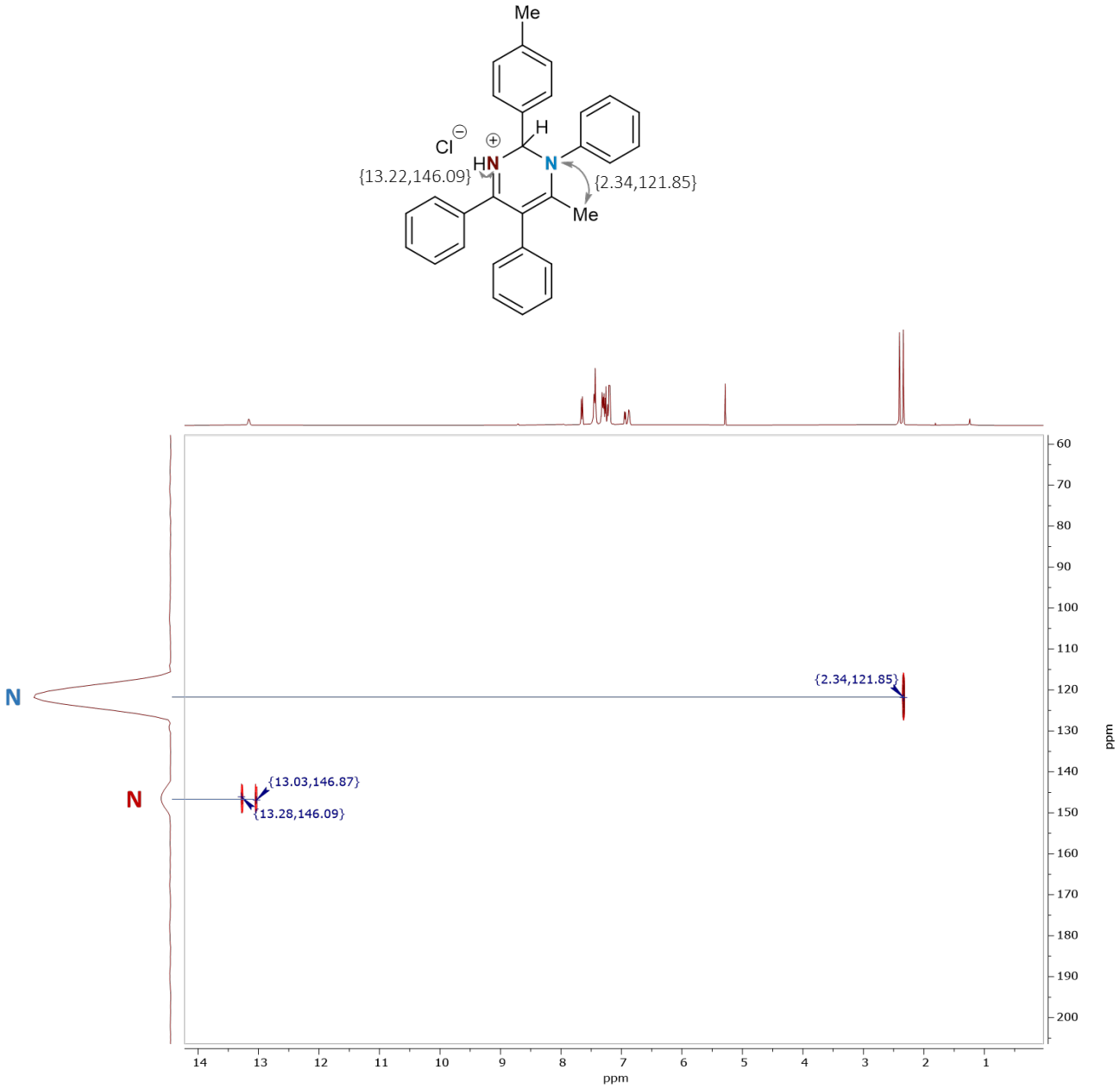
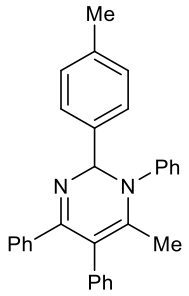


Figure S116. ^{1}H-^{15}N HMBC NMR spectrum of 1,2-dihydropyrimidine **5aca•HCl** in $CDCl_3$.

6-methyl-1,4,5-triphenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5aca)



Orange solid, 60.6 mg. 27% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 7.54 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 6.2 Hz, 5H), 7.24 – 7.19 (m, 5H), 7.12 (dd, *J* = 11.0, 7.6 Hz, 5H), 6.86 (d, J = 6.7 Hz, 2H), 6.64 (s, 1H), 2.39 (s, 3H), 2.11 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ, ppm):** 163.62, 144.63, 137.56, 137.32, 131.39, 129.45, 129.13, 128.98, 127.81, 127.52, 126.32, 126.26, 124.14, 21.29, 19.48. **ESI-HRMS (m/z) [M+H]$^{+}$:** calcd. for $C_{30}H_{26}N_2^{+}$, 415.21686; found 415.2164.

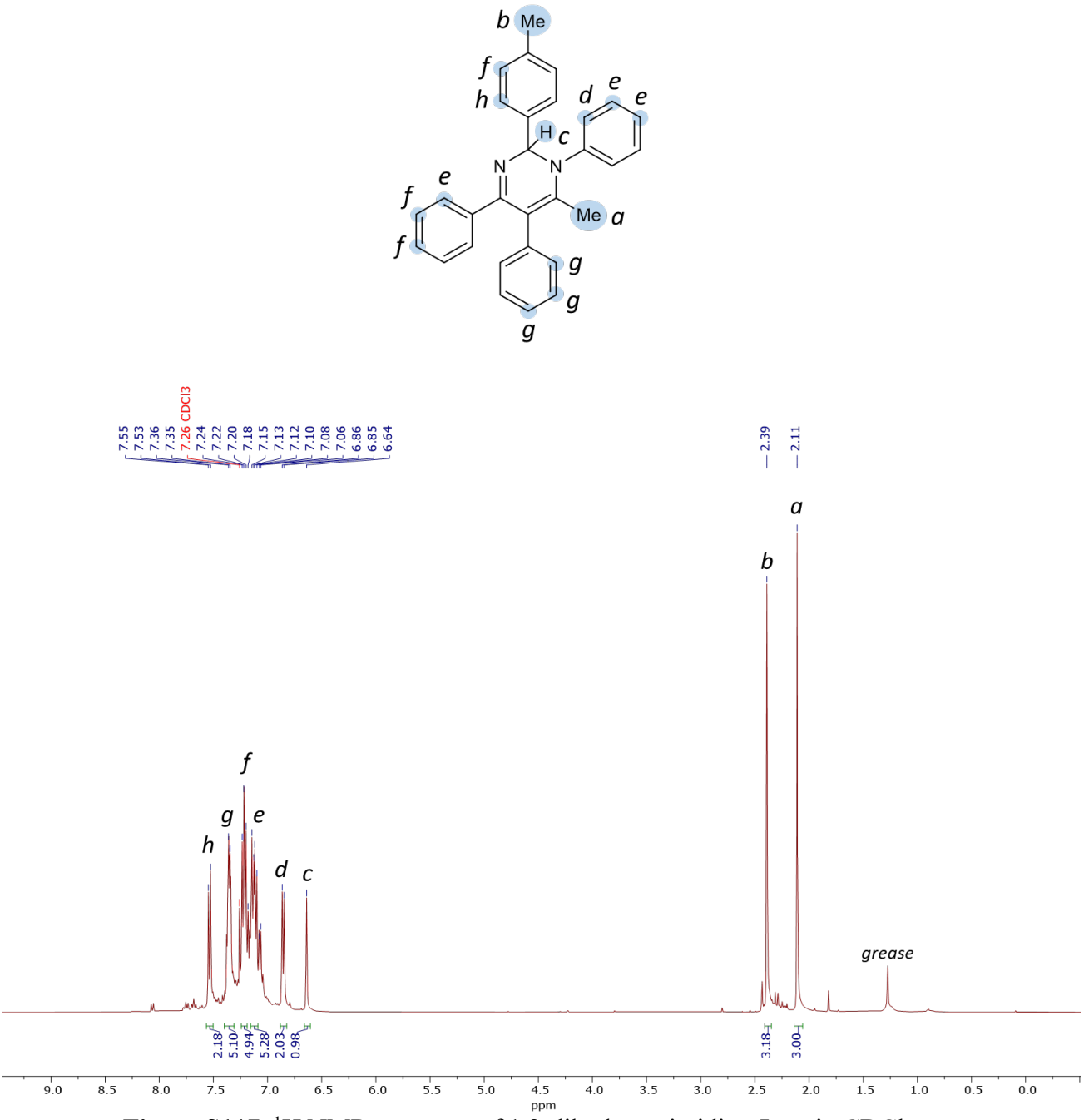


Figure S117. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.

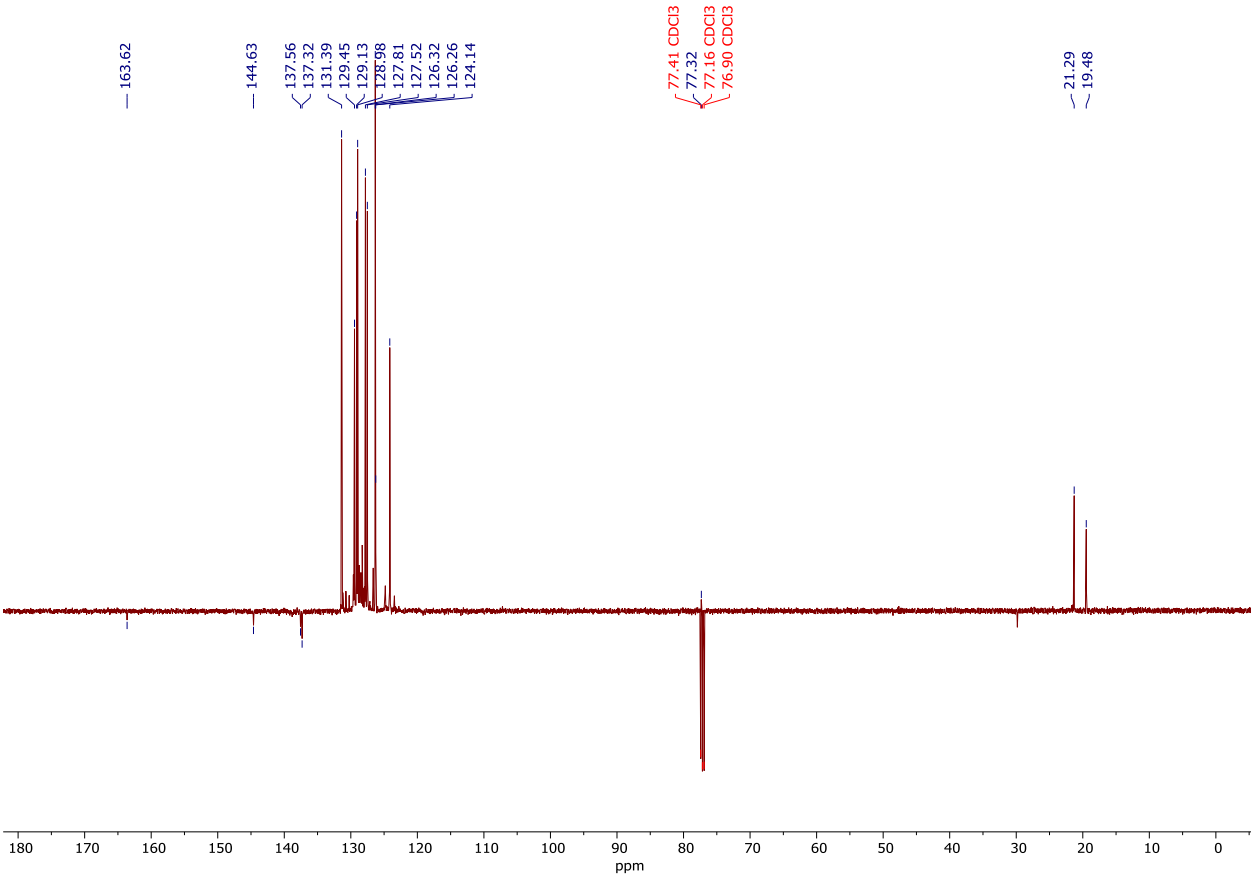


Figure S118. $^{13}C\{^{1}H\}$ APT NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.

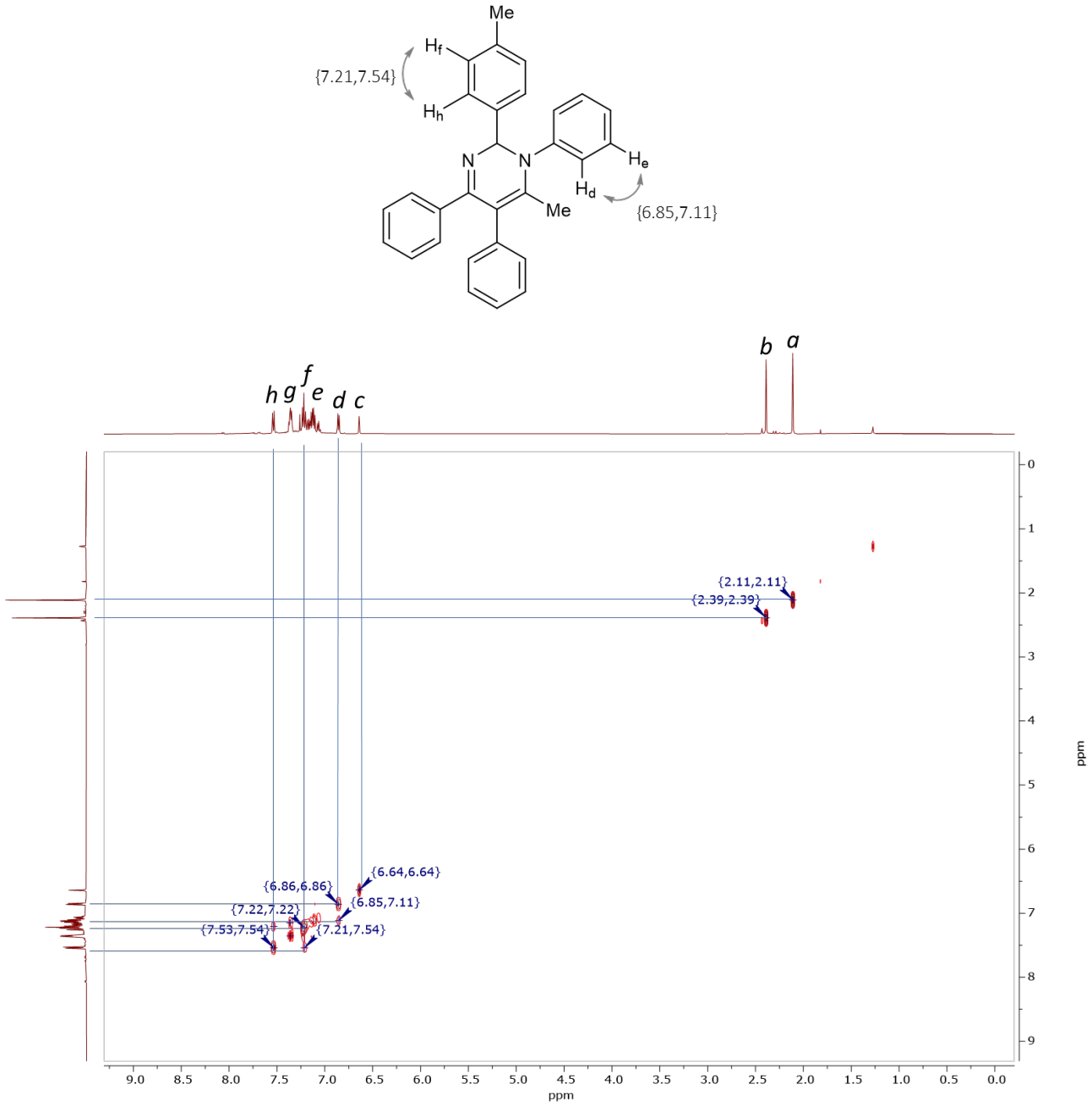


Figure S119. ^{1}H-^{1}H COSY NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.

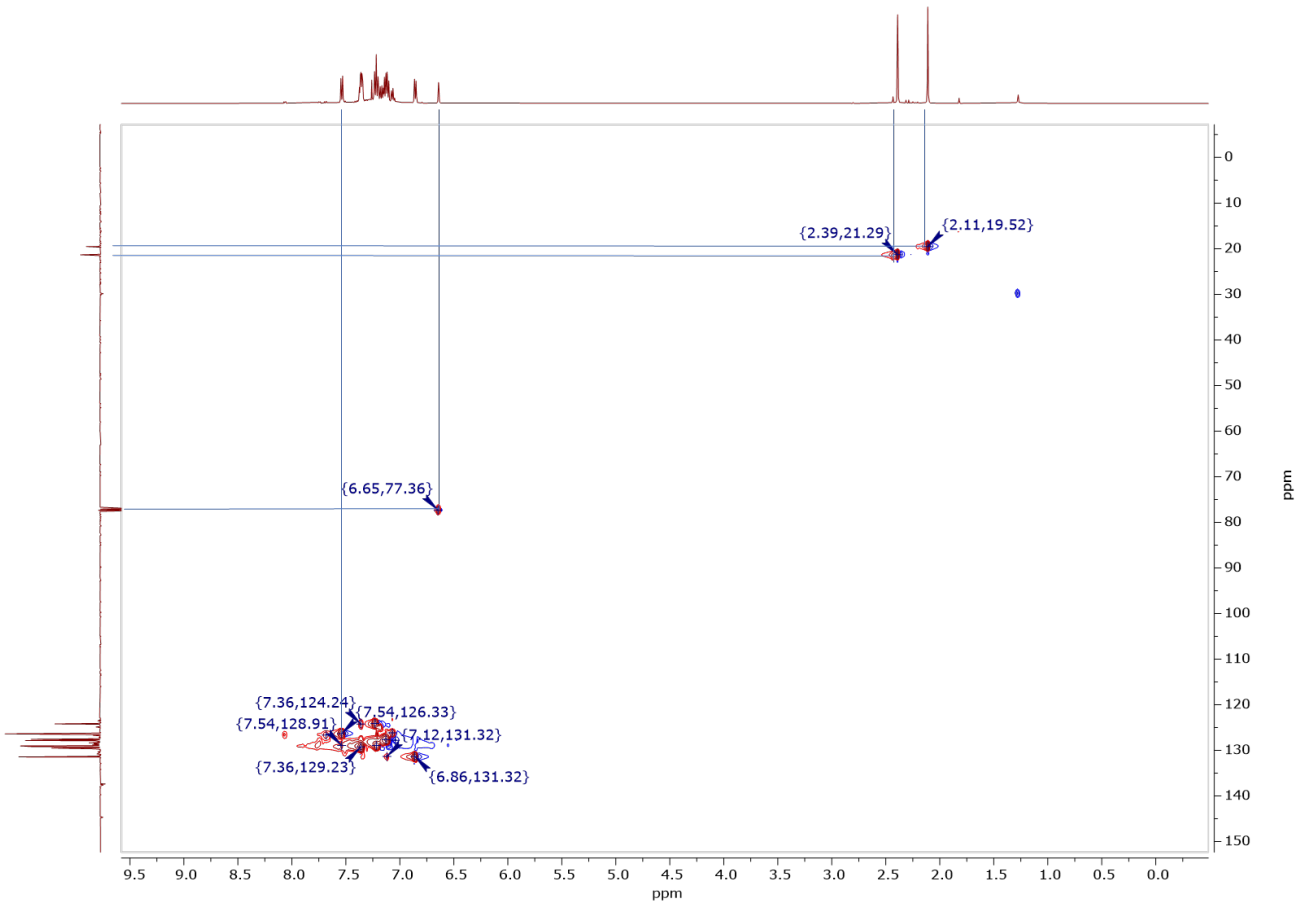


Figure S120. ^{1}H -^{13}C HSQC NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.

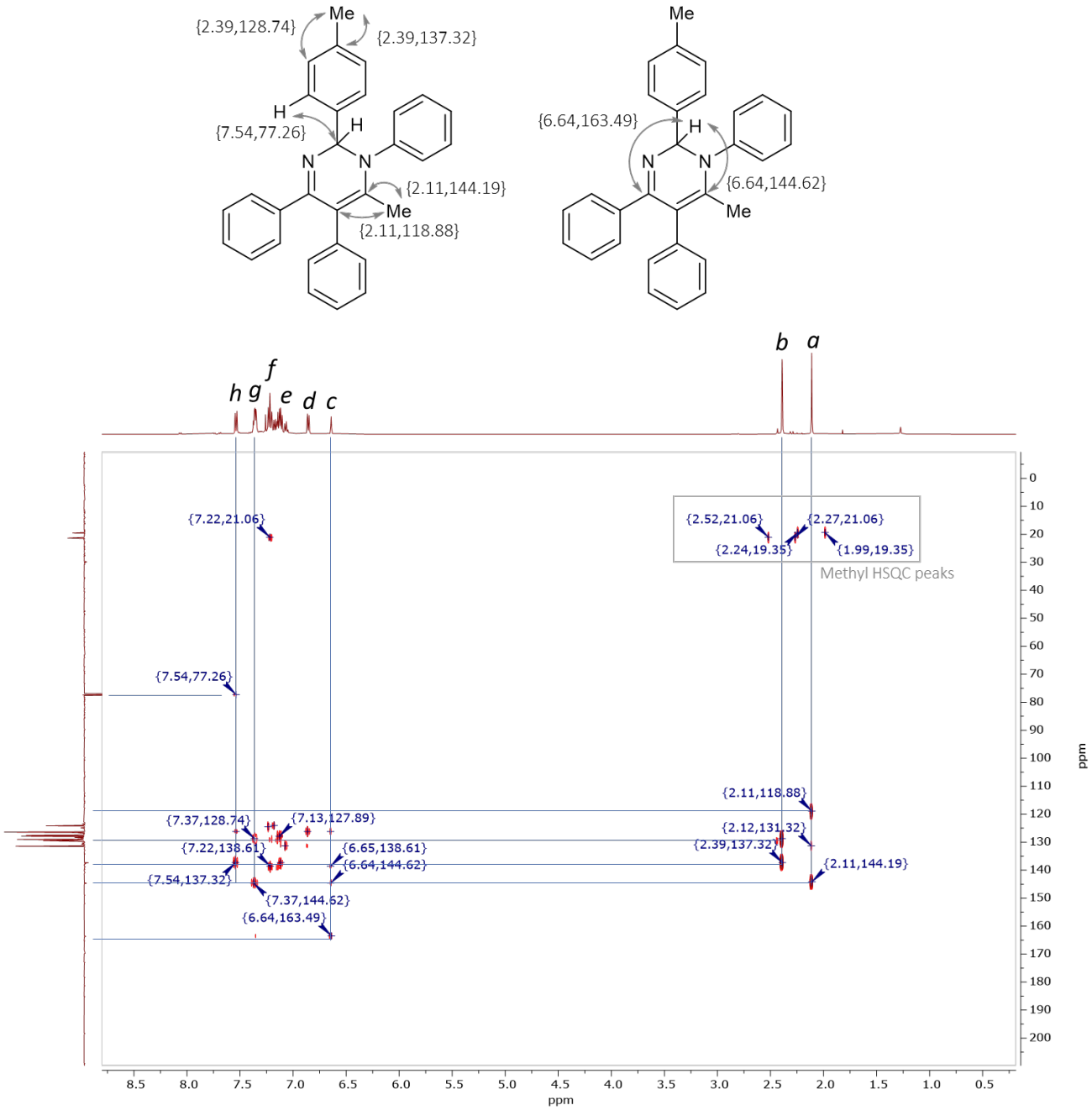


Figure S121. ^{1}H-^{13}C HMBC NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.

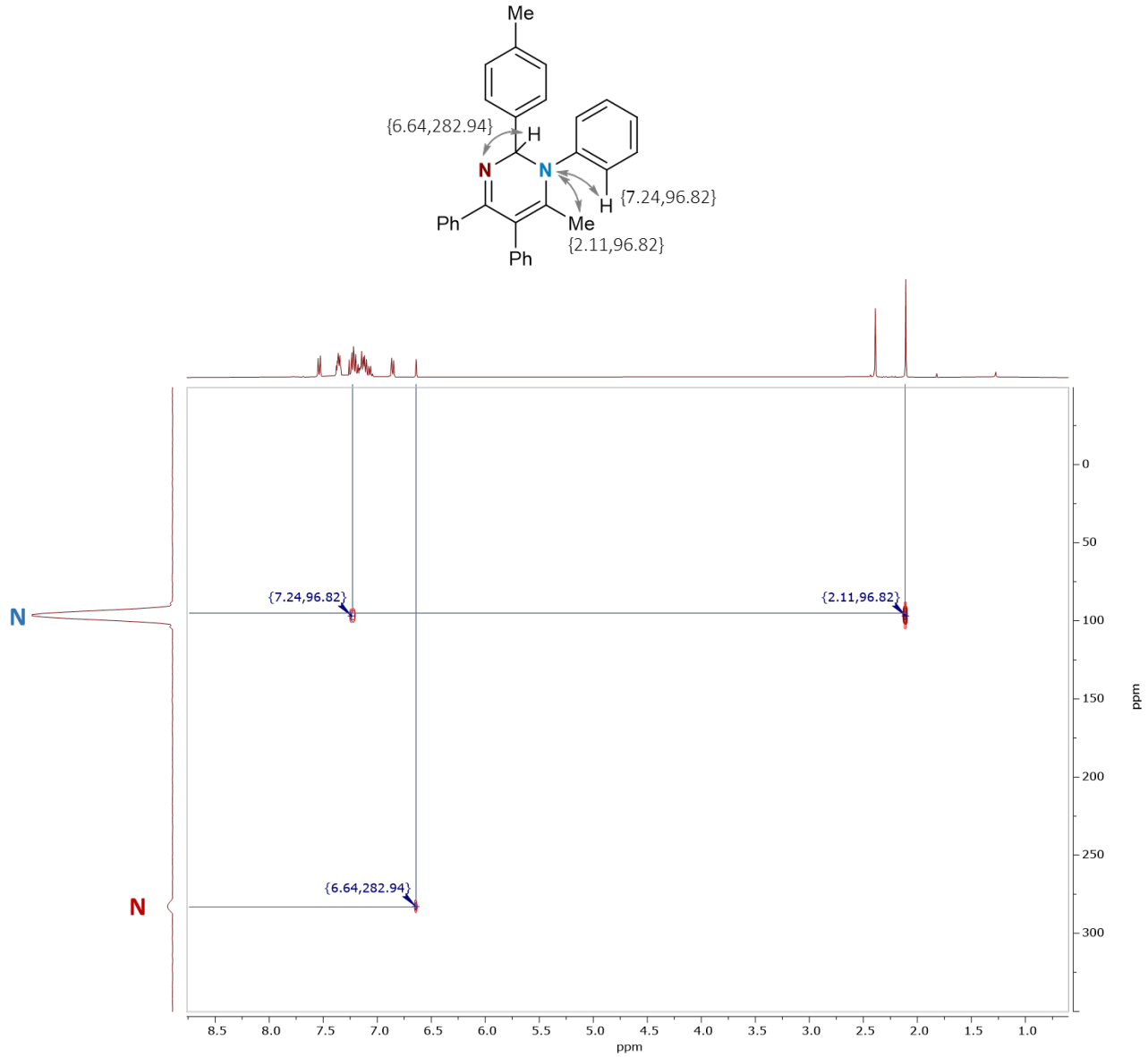
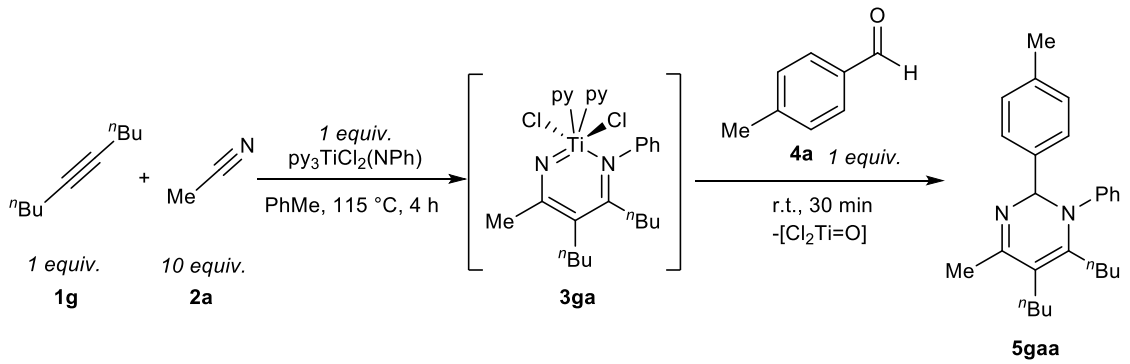
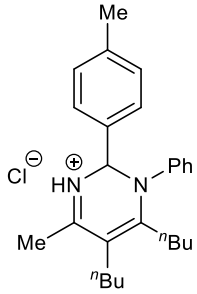


Figure S122. ^{1}H-^{15}N HMBC NMR spectrum of 1,2-dihydropyrimidine **5aca** in $CDCl_3$.



4,5-dibutyl-6-methyl-3-phenyl-2-(p-tolyl)-2,3-dihydropyrimidin-1-ium chloride (5gaa•HCl)



Red solid, 69% yield (254.3 mg). **^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm):** 13.12 (s, 1H), 7.49 – 7.40 (m, 5H), 7.24 (s, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.42 (d, *J* = 5.3 Hz, 1H), 2.51 (s, 3H), 2.37 (s, 3H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.63 – 1.36 (m, 3H), 1.26 (q, *J* = 7.3 Hz, 3H), 1.16 (t, *J* = 7.6 Hz, 2H), 1.01 (dt, *J* = 15.3, 7.6 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 1H), 0.78 (dt, *J* = 17.1, 7.2 Hz, 6H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 162.75, 159.82, 141.24, 139.25, 132.73, 129.93, 129.19, 129.12, 126.69, 126.02, 112.19, 71.07, 32.74, 30.34, 29.52, 25.82, 22.61, 21.80, 21.02, 18.01, 13.59, 13.15. **ESI-HRMS (m/z) $[M+H]^+$:** calcd. for $C_{26}H_{34}N_2^+$, 375.27946; found 375.2789.

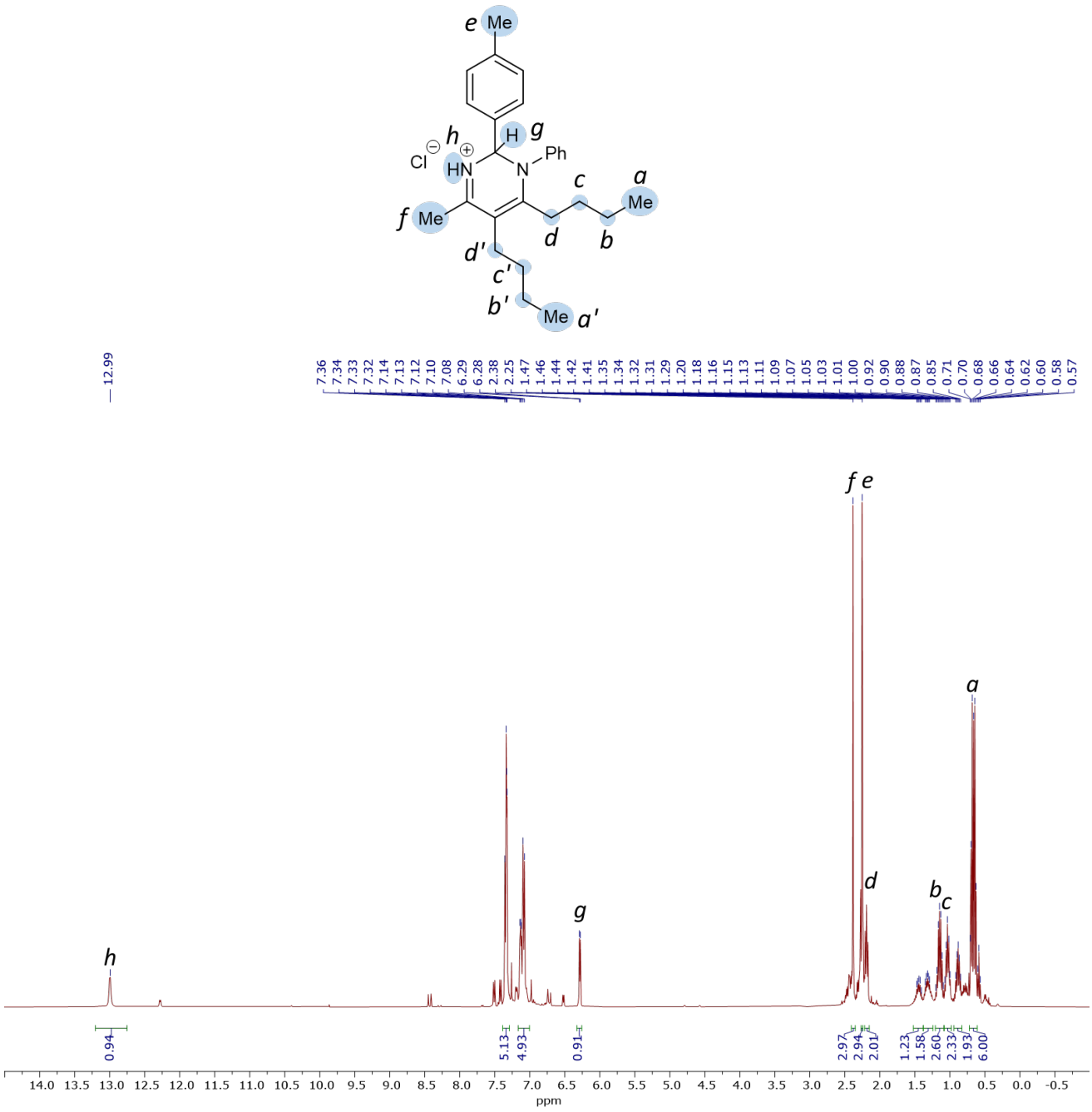


Figure S123. ^{1}H NMR spectrum of **5gaa•HCl** in $CDCl_3$.

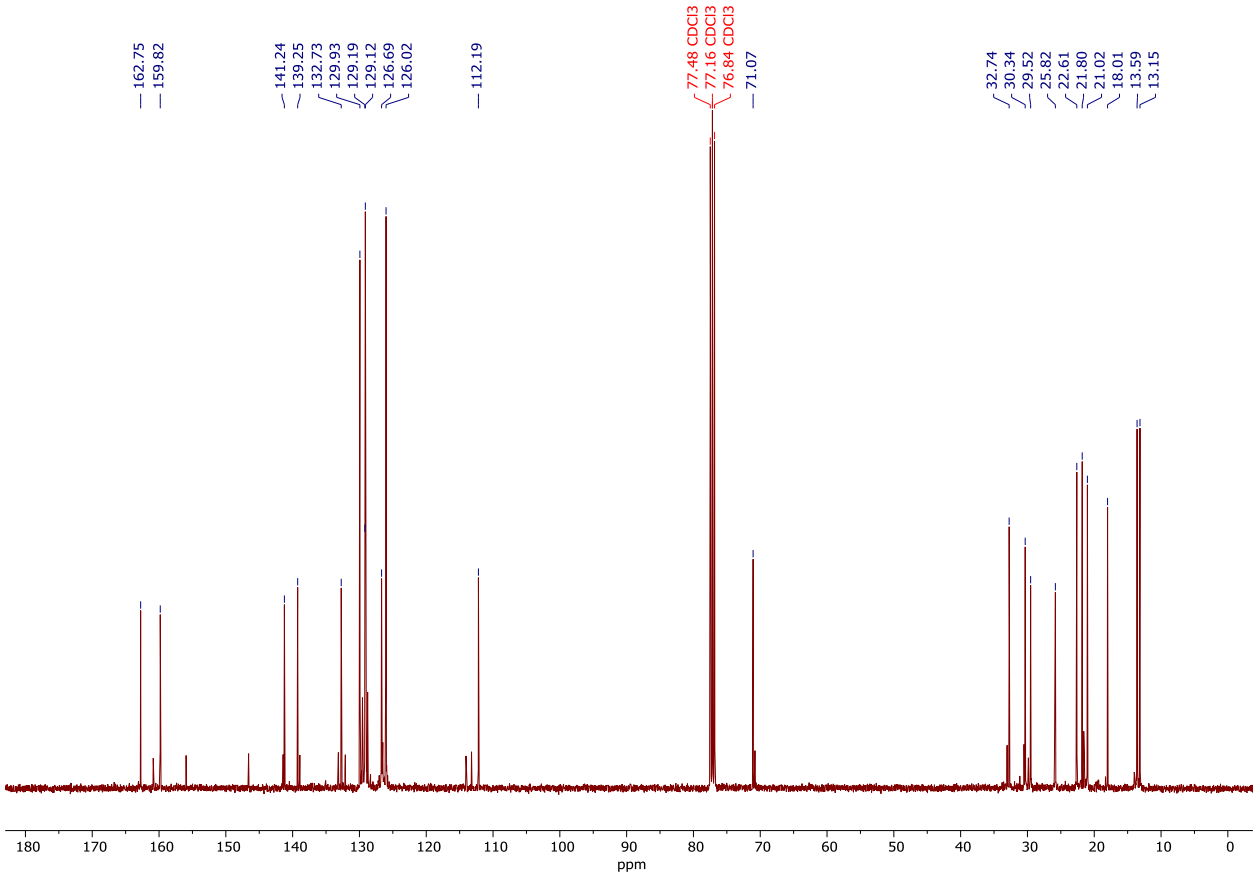


Figure S124. $^{13}C\{^{1}H\}$ NMR spectrum of **5gaa•HCl** in $CDCl_3$.

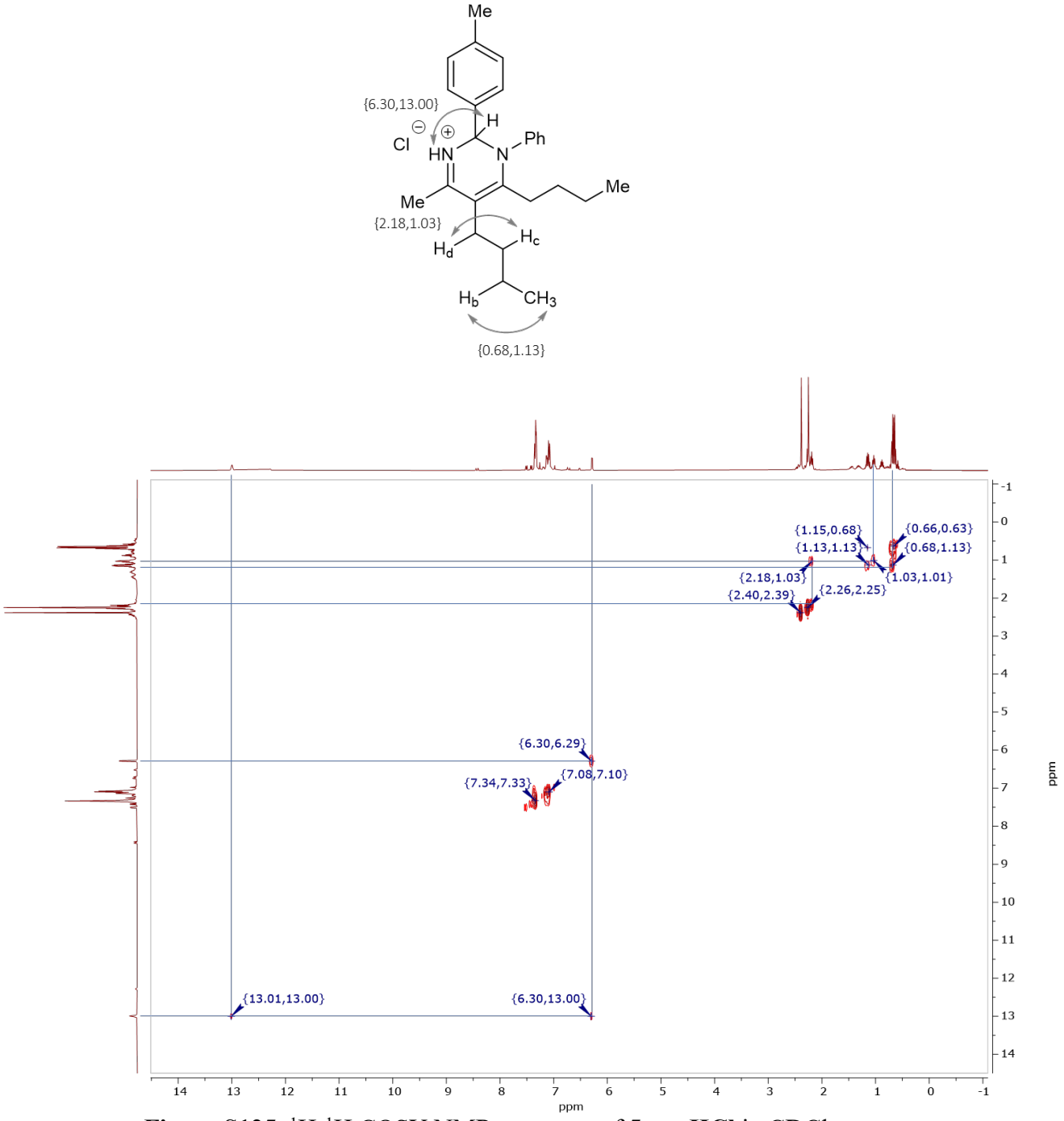


Figure S125. ^{1}H-^{1}H COSY NMR spectrum of **5gaa•HCl** in $CDCl_3$.

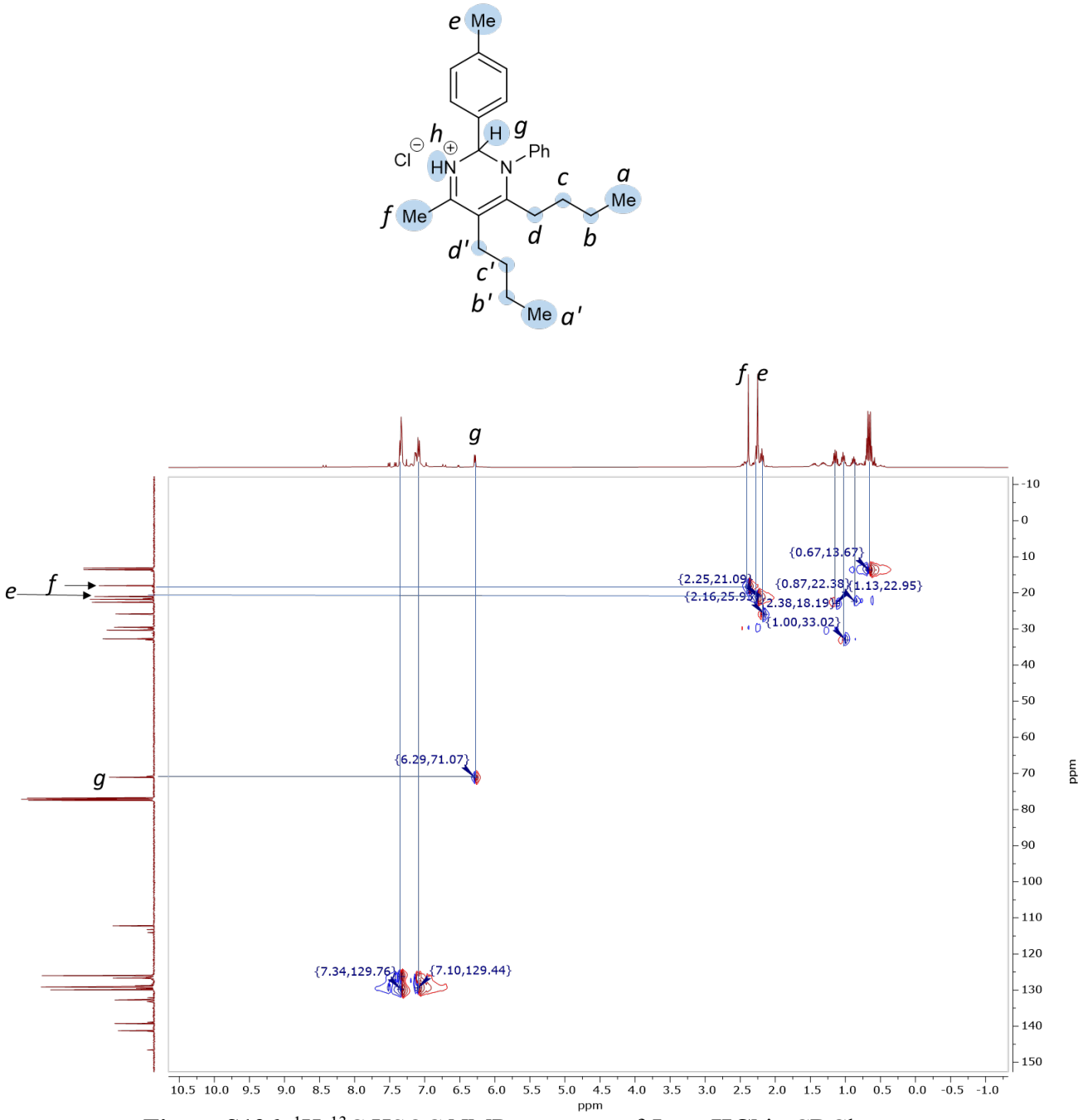


Figure S126. ^{1}H-^{13}C HSQC NMR spectrum of **5gaa•HCl** in $CDCl_3$.

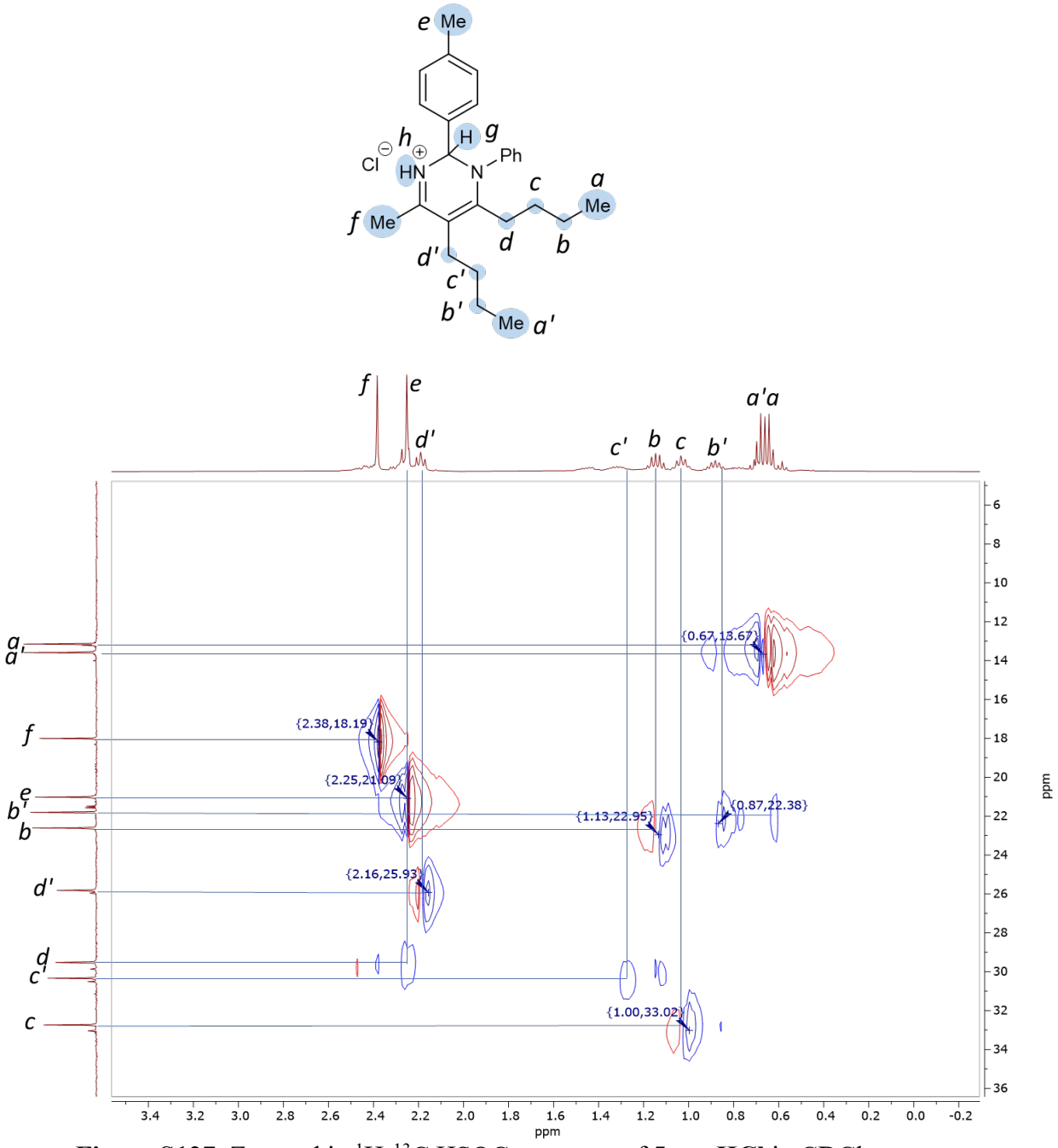


Figure S127. Zoomed in ^{1}H-^{13}C HSQC spectrum of **5gaa•HCl** in $CDCl_3$.

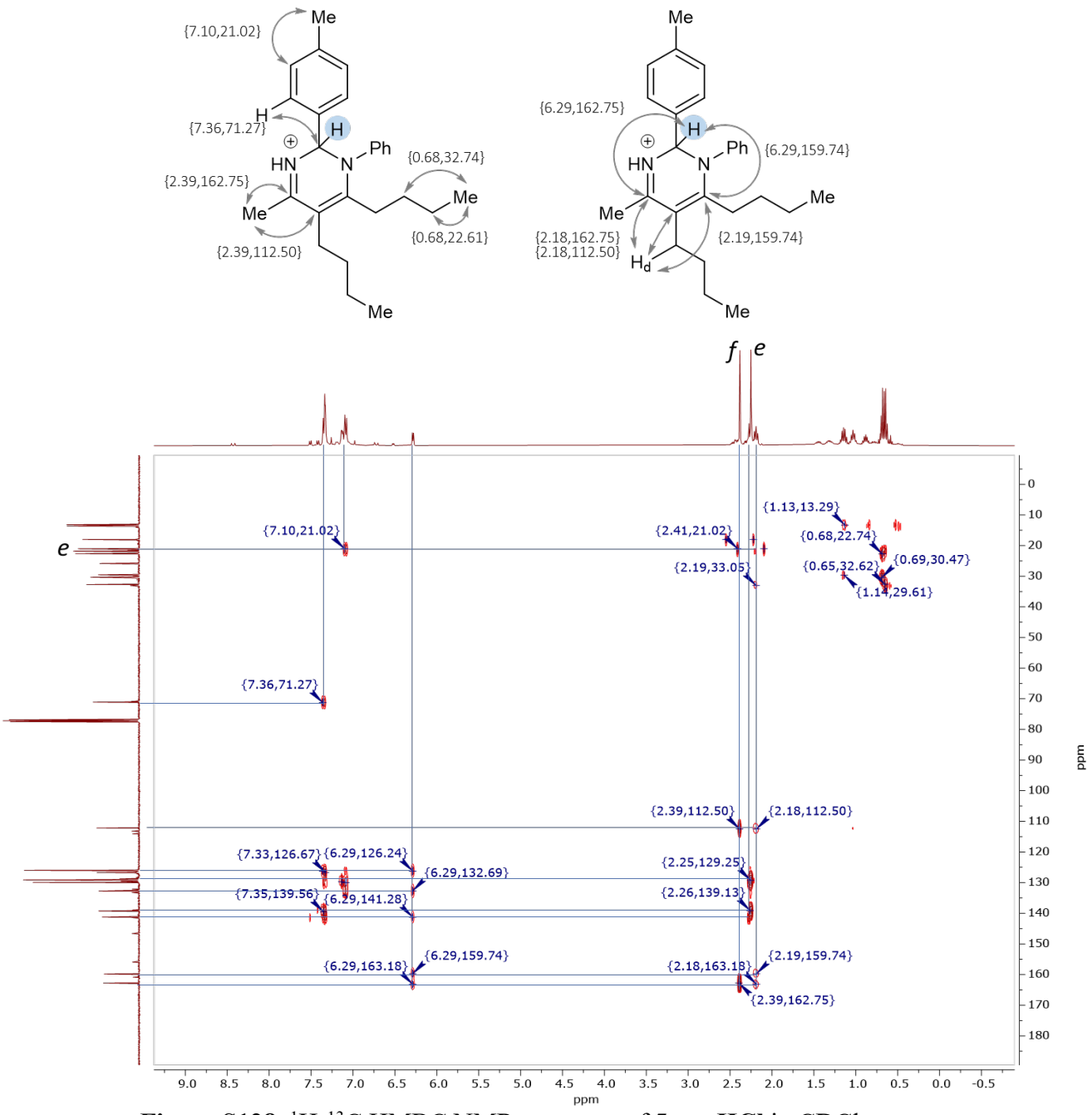


Figure S128. ^{1}H-^{13}C HMBC NMR spectrum of **5gaa•HCl** in $CDCl_3$.

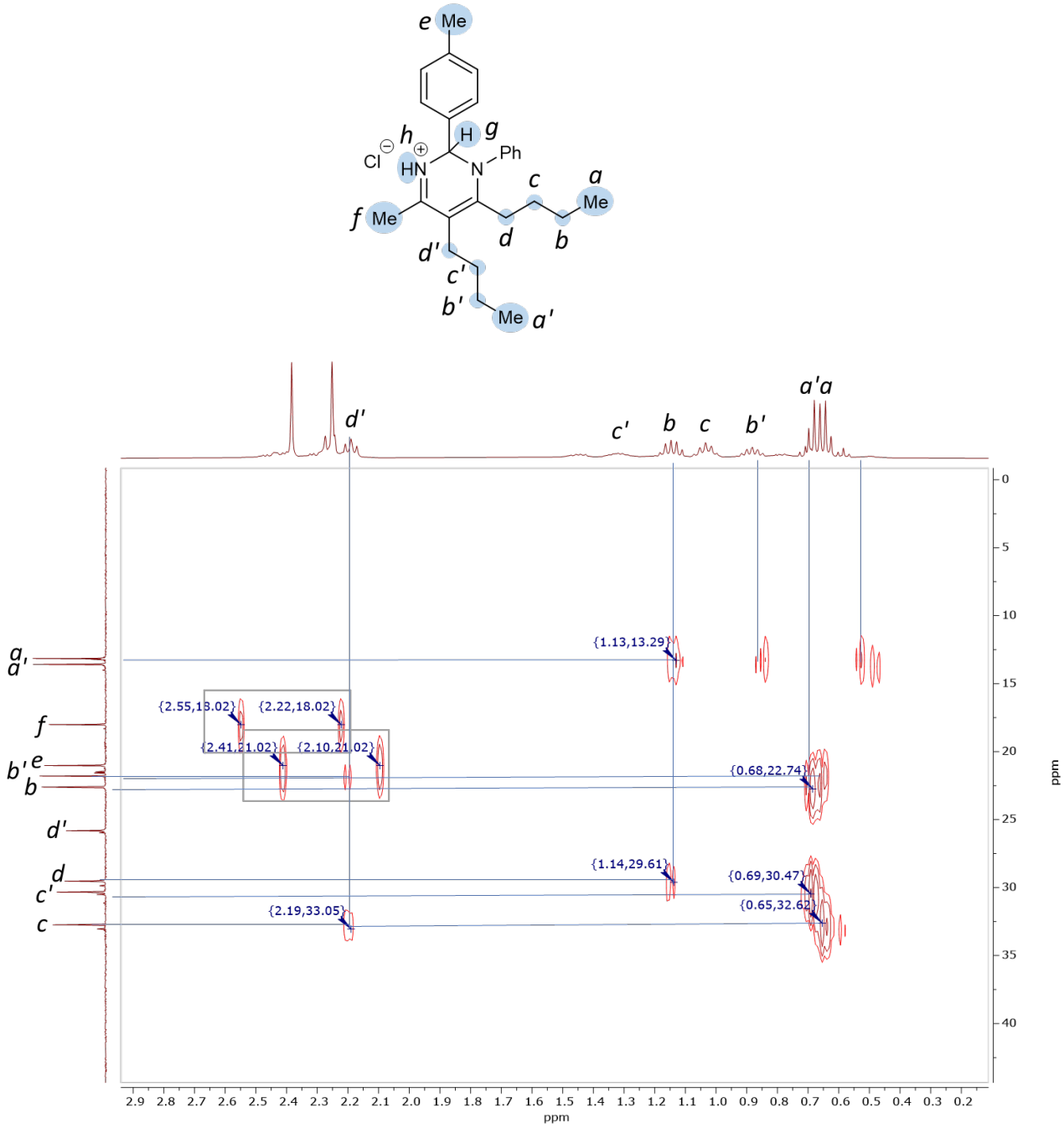


Figure S129. Zoomed in ^{1}H-^{13}C HMBC NMR spectrum of **5gaa•HCl** in $CDCl_3$.

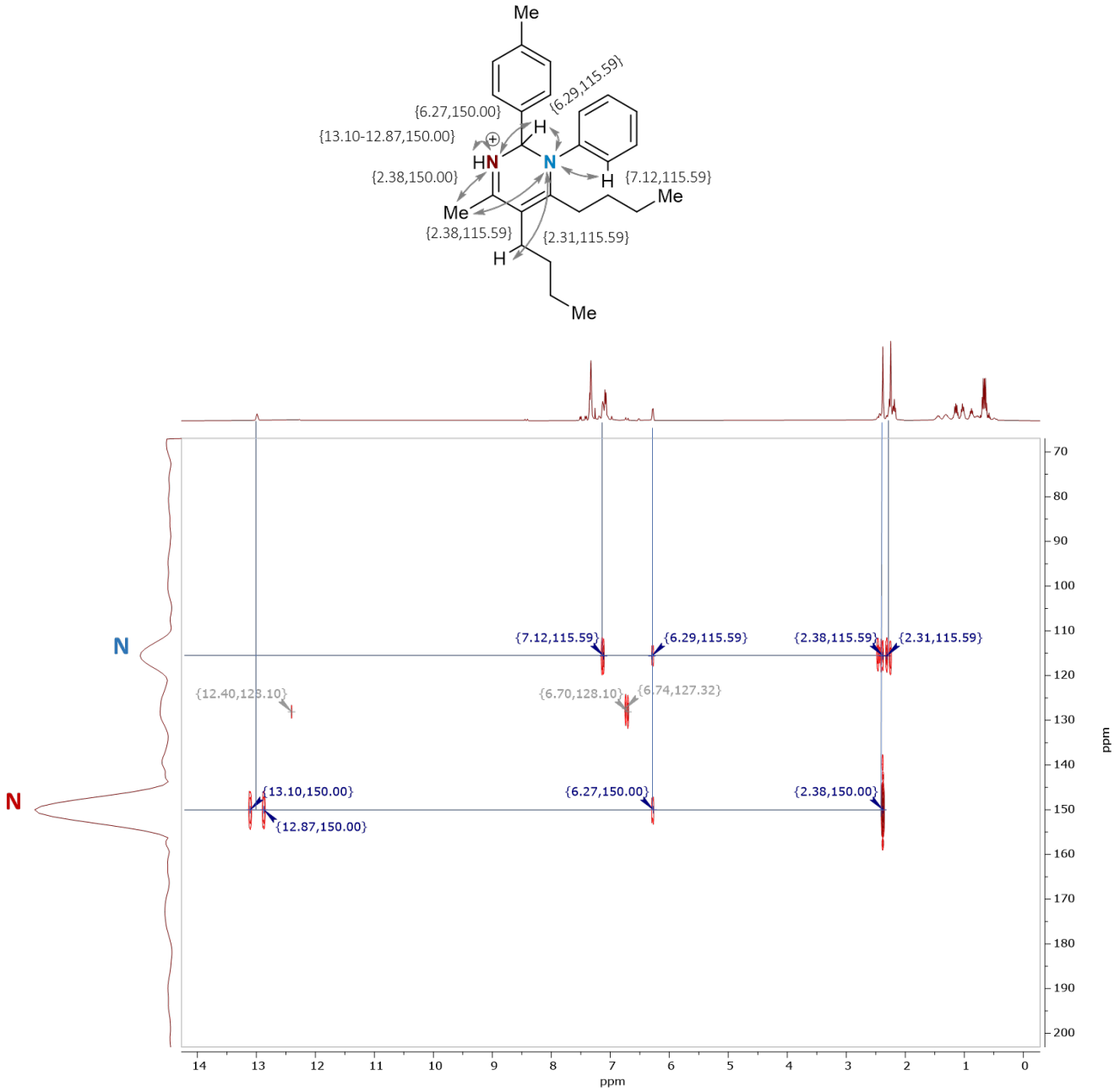
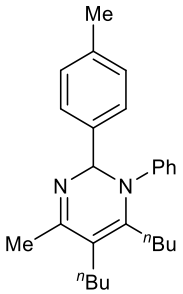


Figure S130. ^{1}H-^{15}N HMBC NMR spectrum of **5gaa•HCl** in $CDCl_3$.

5,6-dibutyl-4-methyl-1-phenyl-2-(p-tolyl)-1,2-dihydropyrimidine (5gaa)



Yellow solid, 130.8 mg (39% isolated yield). **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 7.41 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.26 (m, 2H), 7.11 (d, *J* = 8.2 Hz, 5H), 6.23 (s, 1H), 2.34 (s, 3H), 2.27 (t, *J* = 9.3 Hz, 2H), 2.23 (s, 3H), 1.28 (s, 10H), 0.80 (t, *J* = 7.1 Hz, 3H), 0.72 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 164.00, 145.96, 138.79, 137.01, 128.99, 128.89, 128.31, 128.16, 127.02, 126.96, 124.59, 124.42, 119.84, 77.40, 32.97, 30.50, 28.34, 27.08, 22.76, 22.71, 22.50, 22.30, 22.19, 21.25, 21.20, 14.00, 13.96, 13.91, 13.86, 13.75, 13.70. **ESI-HRMS (m/z) $[M+H]^+$:** calcd for $C_{26}H_{34}N_2^+$, 375.27946; found 375.2786.

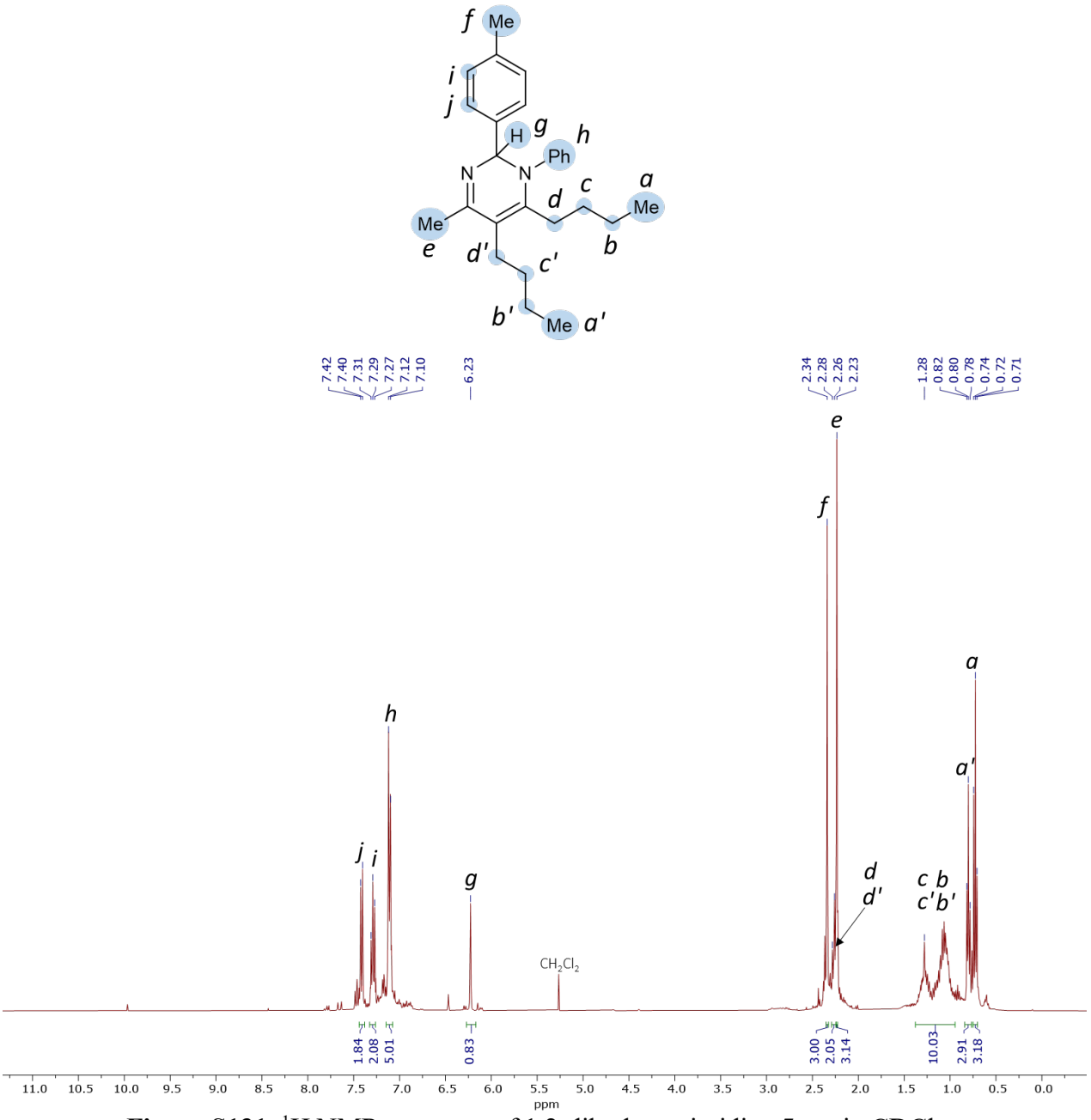


Figure S131. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$**.**

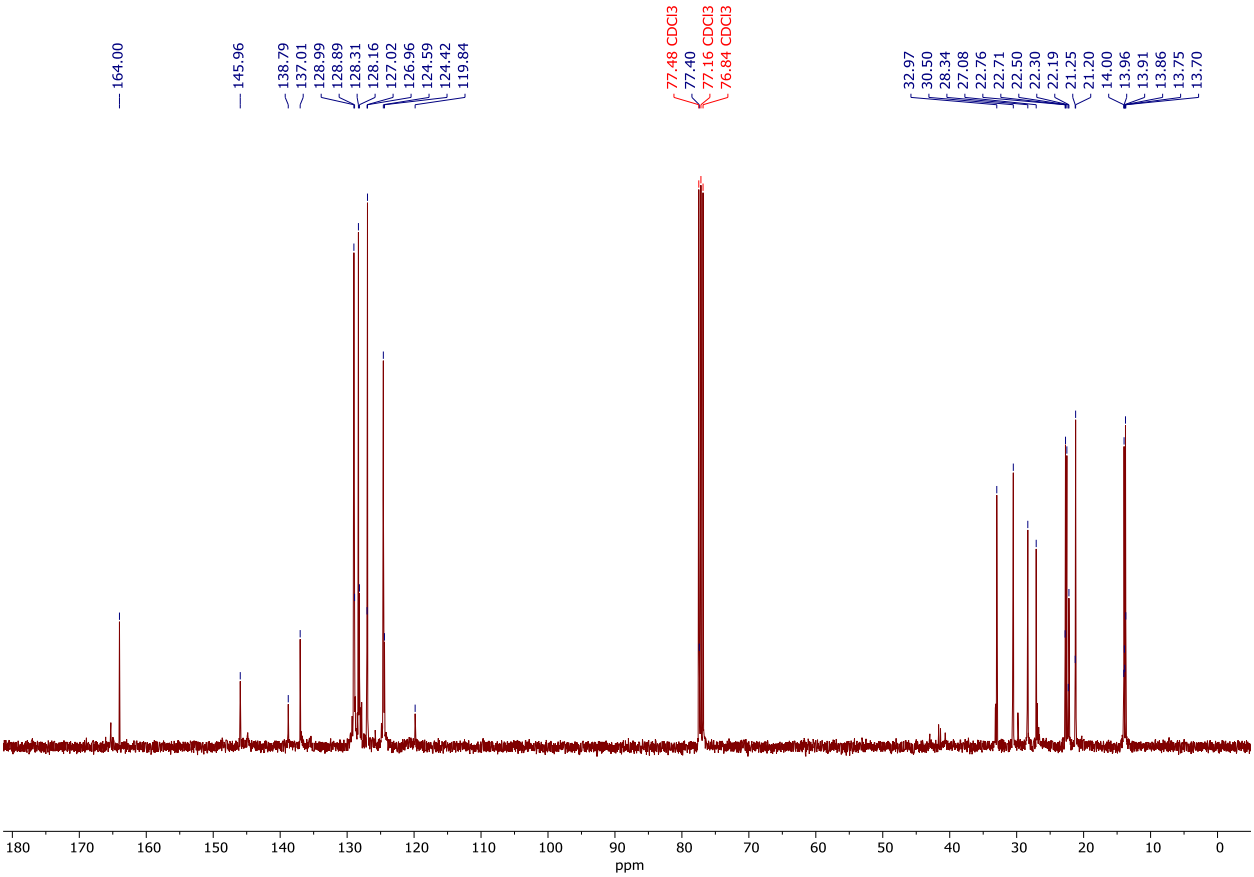


Figure S132. $^{13}C\{^{1}H\}$ NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$**.**

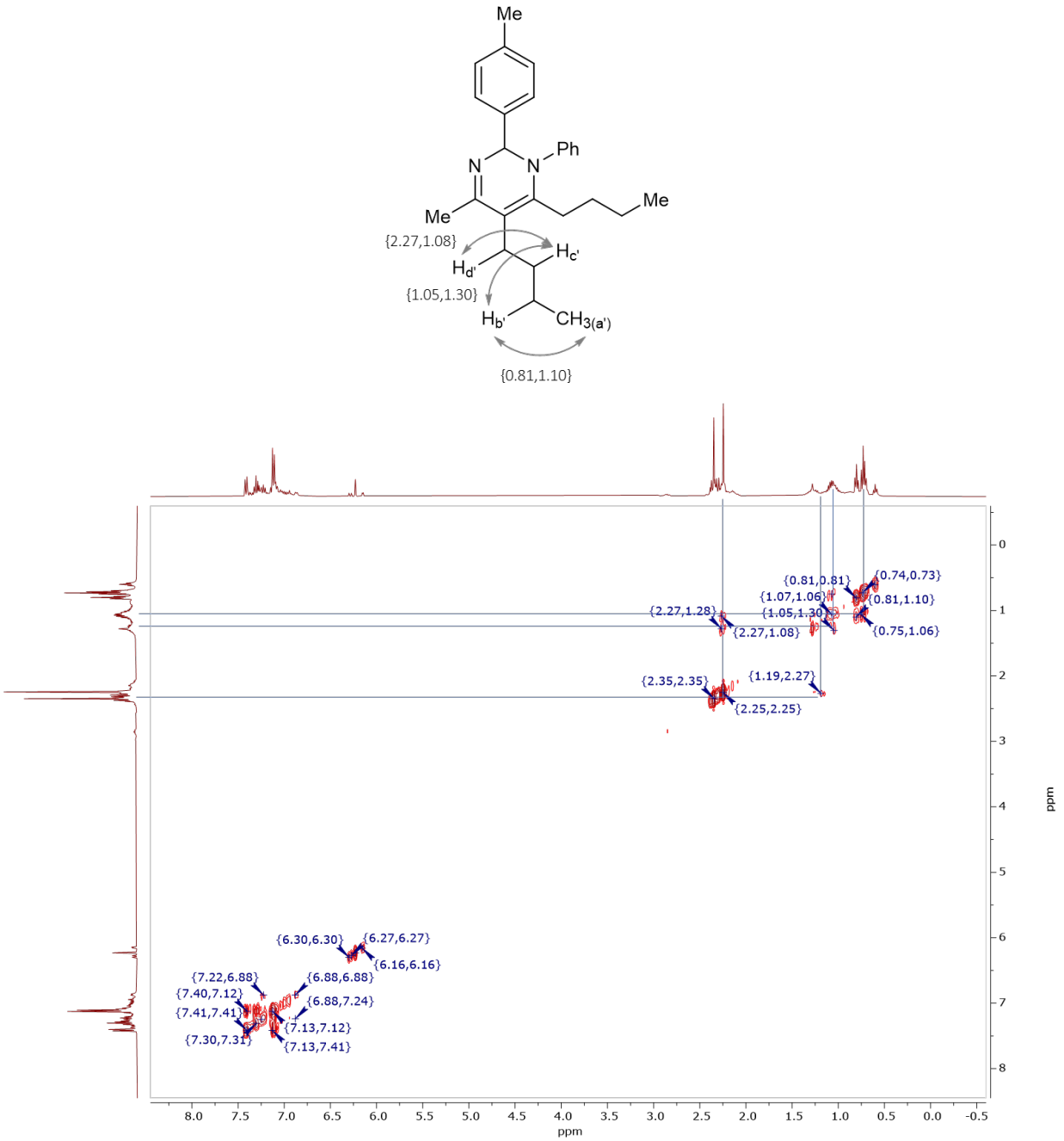


Figure S133. ^{1}H-^{1}H COSY NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$.

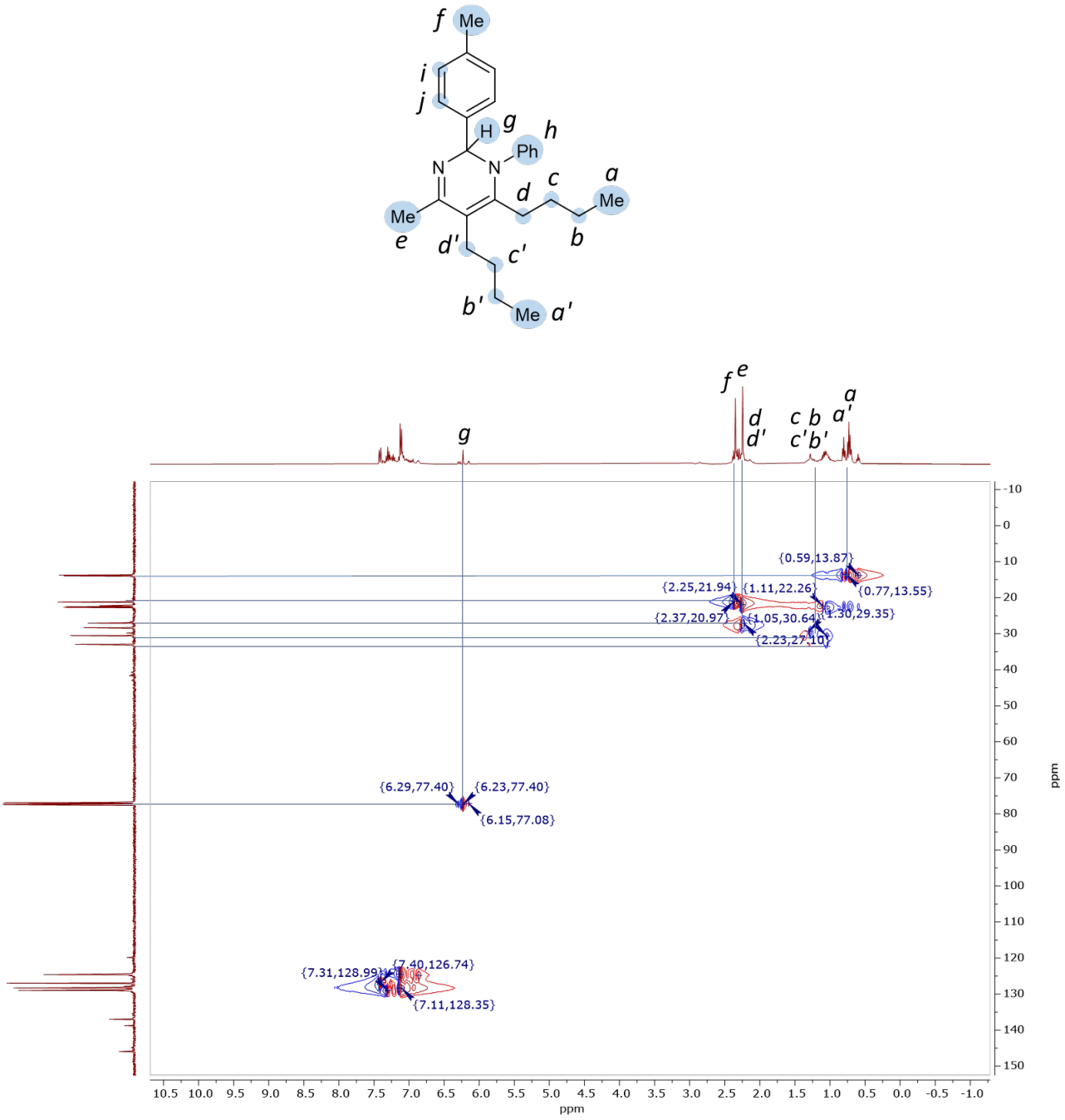


Figure S134. ^{1}H-^{13}C HSQC NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$.

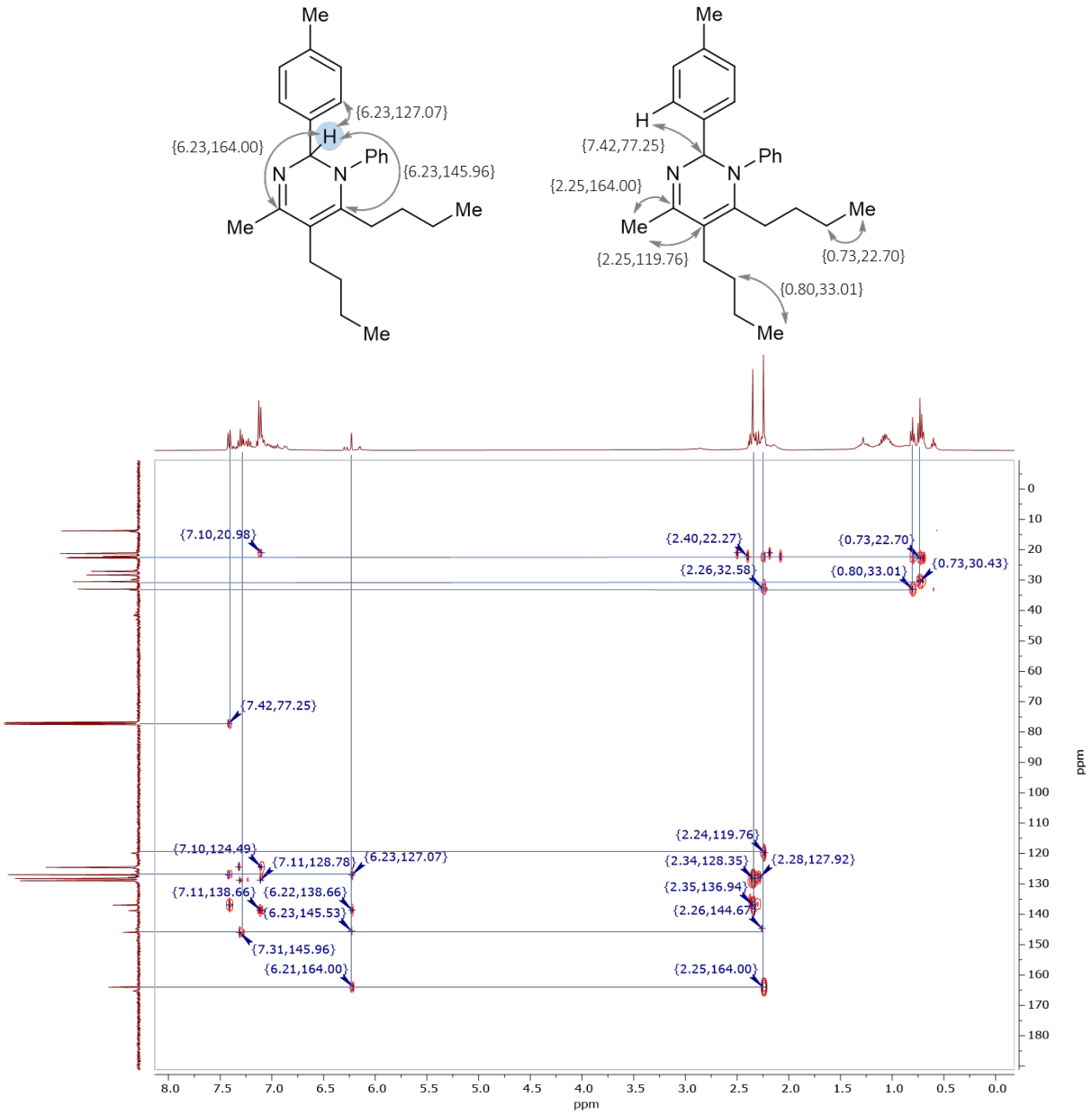


Figure S135. ^{1}H-^{13}C HMBC NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$.

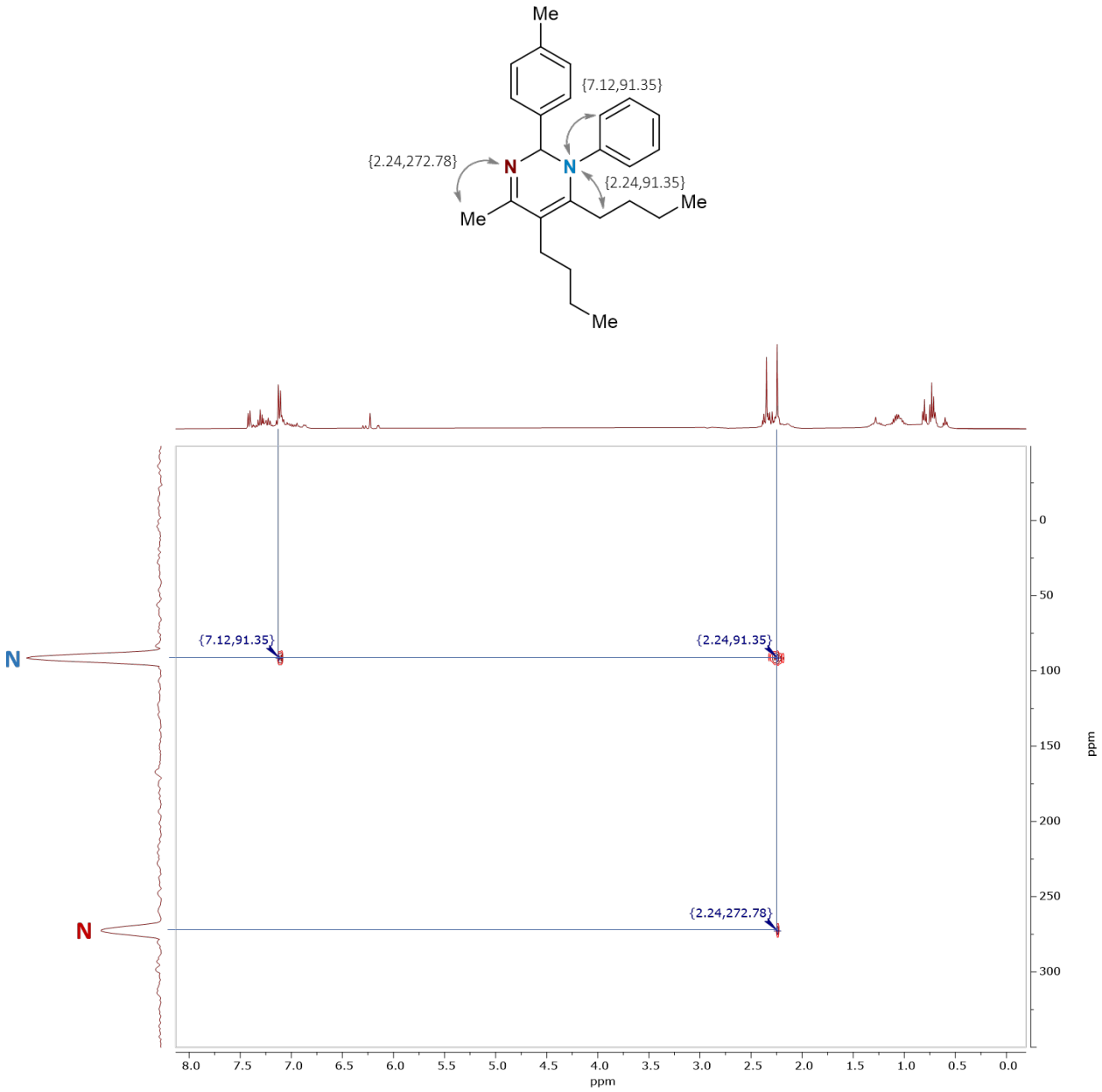
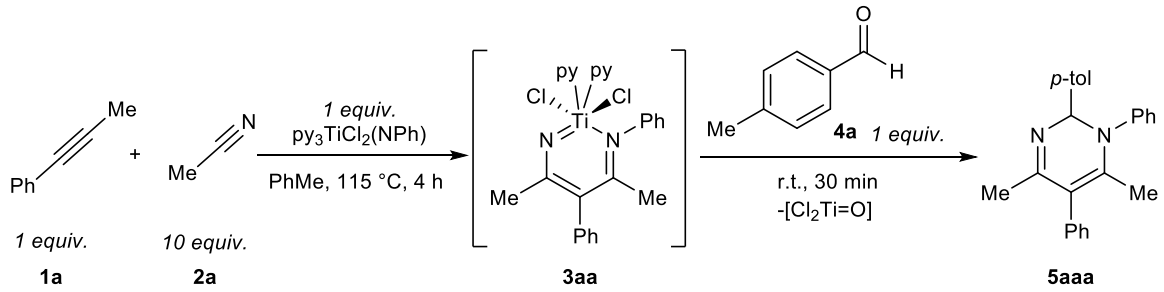


Figure S136. ^{1}H-^{15}N HMBC NMR spectrum of 1,2-dihydropyrimidine **5gaa** in $CDCl_3$**.**

Scale up reaction



General Procedure: 28 mL of toluene was added to a 250 mL Schlenk flask containing $py_3TiCl_2(NPh)$ (1.27 g, 2.90 mmol, 1.00 equiv) along with a stir bar in a N_2-filled glovebox, followed by 1-phenyl-1-propyne **1a** (0.33 mL, 2.90 mmol, 1.00 equiv) and acetonitrile **2a** (1.5 mL, 28.7 mmol, 10 equiv). The flask was sealed with a greased glass stopper and then removed from the glovebox, equipped with a reflux condenser while under a stream of nitrogen, and placed in a pre-heated oil bath at 115 °C to stir for 4 h. After bringing the Schlenk flask back into the glovebox, *p*-tolualdehyde **4a** (0.4 mL, 2.90 mmol, 1 equiv) was added to the reaction mixture and allowed to stir for an additional 30 min at room temperature. The flask was then removed from the glovebox and the reaction mixture was filtered through a plug of Celite to remove the Ti oxo byproduct. The reaction mixture was then washed with 2 M aqueous HCl solution followed by aqueous sat. Na_2CO_3 and the organic layer was then dried over $MgSO_4$. The volatiles were removed in vacuo and the resulting solid purified by column chromatography on silica gel (7:3 hexanes : EtOAc) as the eluent to afford the 1,2-dihydropyrimidine **5aaa** in 33% yield (330 mg). **^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):** 7.44 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.17 – 7.10 (m, 3H), 7.00 (d, *J* = 7.0 Hz, 2H), 6.33 (s, 1H), 2.39 (s, 3H), 1.86 (s, 3H), 1.83 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, δ, ppm):** 161.87, 144.71, 142.85, 139.07, 137.89, 137.18, 130.97, 129.03, 128.91, 128.37, 126.88, 126.42, 124.86, 124.66, 119.63, 77.71, 23.61, 21.28, 18.25.

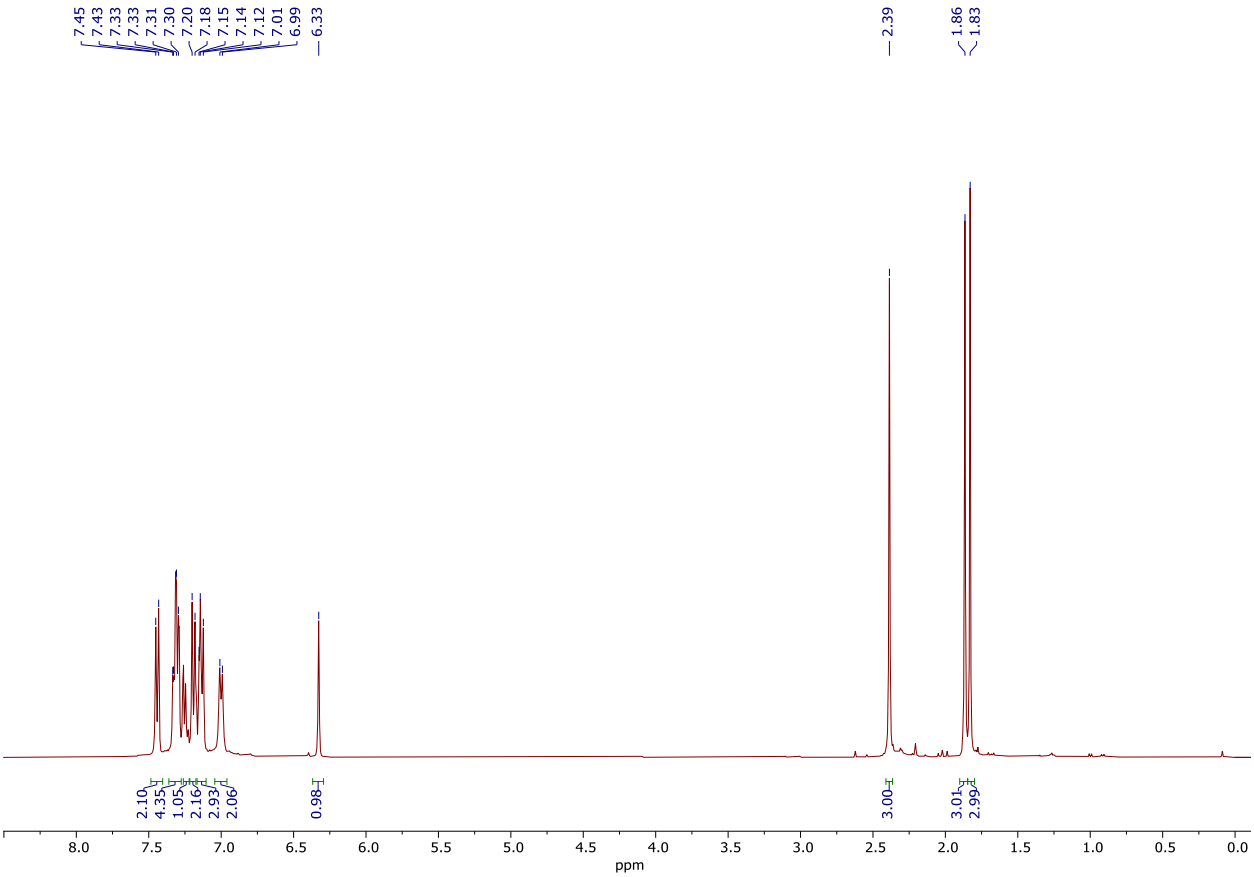


Figure S137. ^{1}H NMR spectrum of 1,2-dihydropyrimidine **5aaa**.

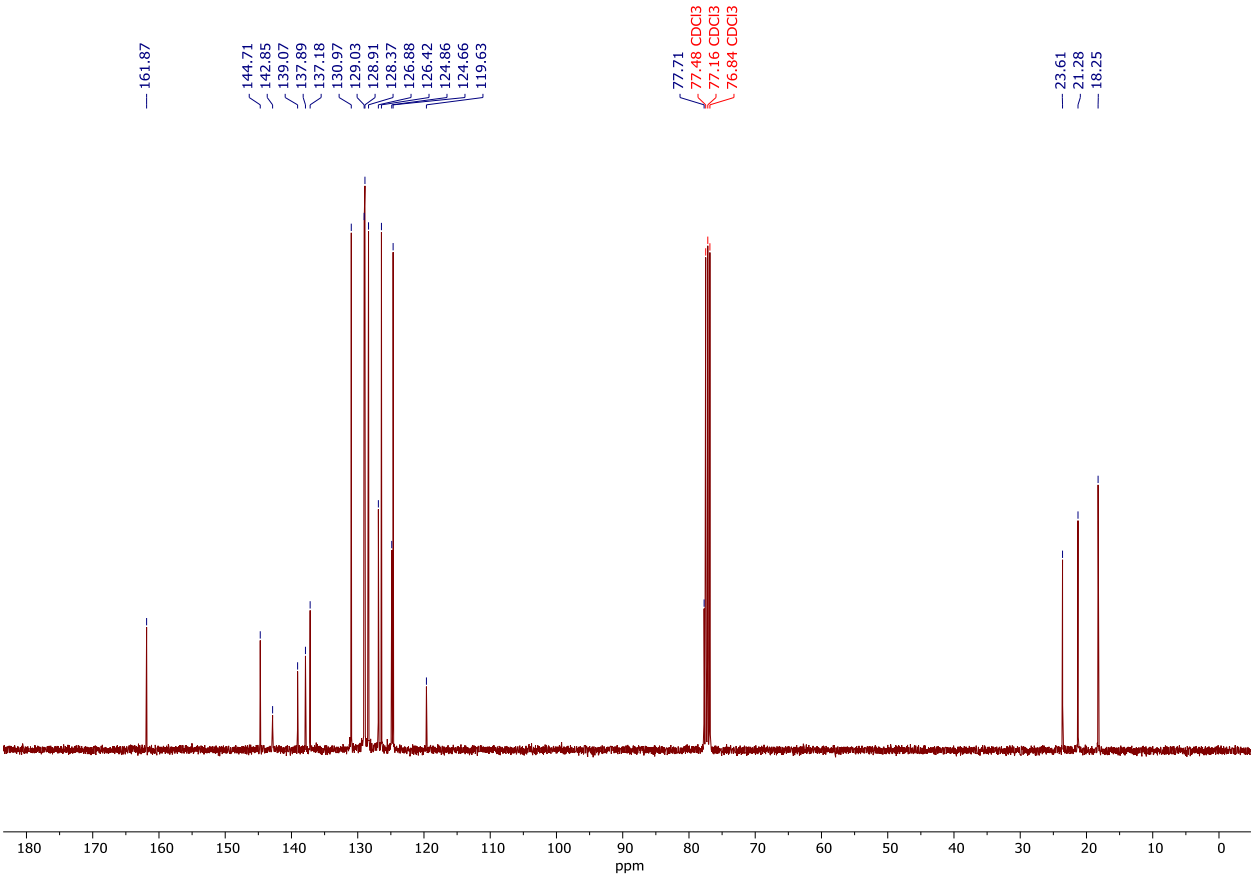
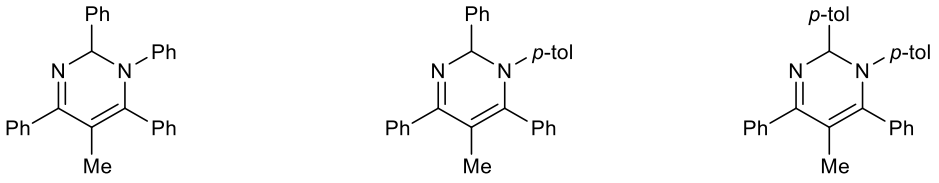


Figure S138. $^{13}C\{^{1}H\}$ NMR spectrum of 1,2-dihydropyrimidine **5aaa**.

Comparison of Condensation Routes to 1,2-Dihydropyrimidines



last step 91% yield, 12 h
cumulative 25 - 48% yield, 157 - 180 h
3 total steps

last step 87% yield, 12 h
cumulative 31 - 65% yield, 39 - 61 h
3 total steps

last step 90% yield, 12 h
cumulative 32 - 68% yield, 39 - 61 h
3 total steps

Figure S139. Comparison of the final step's yields and reaction time with the cumulative yields and reaction times for three 1,2-dihydropyrimidines in the literature

Barluenga has previously reported the Lewis-acid catalyzed synthesis of 1,2-dihydropyrimidines from 4-azadiene-1-amines and aldehydes with $AlCl_3$ in 72-93% yields (Figure SX) in contrast to this Ti-mediated synthesis which range from 30-78% yield. However, the synthetic route via 4-azadiene-1-amines requires three steps to achieve the desired 1,2-dihydropyrimidine with cumulative yields ranging from 25 - 68% yield and requiring between 39 and 157 h to prepare. Below are three examples of reported 1,2-dihydropyrimidines and their syntheses.

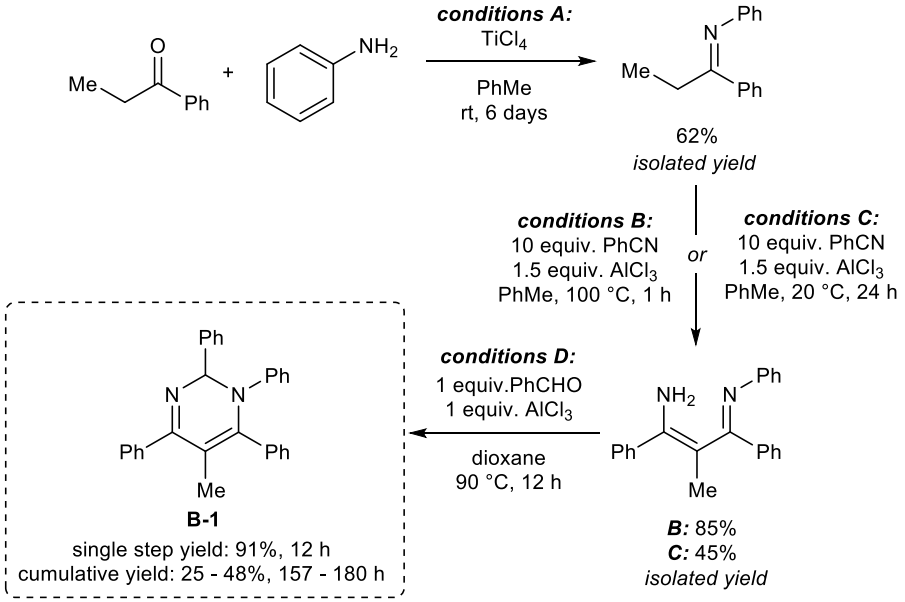


Figure S140. Reported synthesis of 1,2-dihydropyrimidine **B-1** from propiophenone and aniline over three steps.

The initial step in the synthesis of the 1,2-dihydropyrimidine **B-1** is the preparation of the imine. The condensation of propiophenone and aniline yields the (*Z*)-*N*,1-diphenylpropan-1-imine in 62% yield over 6 days (conditions A).[8] Following this, the 4-azadiene-1-amine can be prepared

through a Blaise-like reaction with $AlCl_3$ in either 85 or 45% yield depending on the temperature and time used in the reaction (conditions B and C).[9] The 4-azadiene-1-amine is then converted to **B-1** through a Lewis-acid catalyzed condensation and cyclization with $AlCl_3$ in 91% yield over 12 h (conditions D).[10] Overall this leads to a cumulative yield ranging between 25 – 48 % yield and requiring between 157 – 180 h.

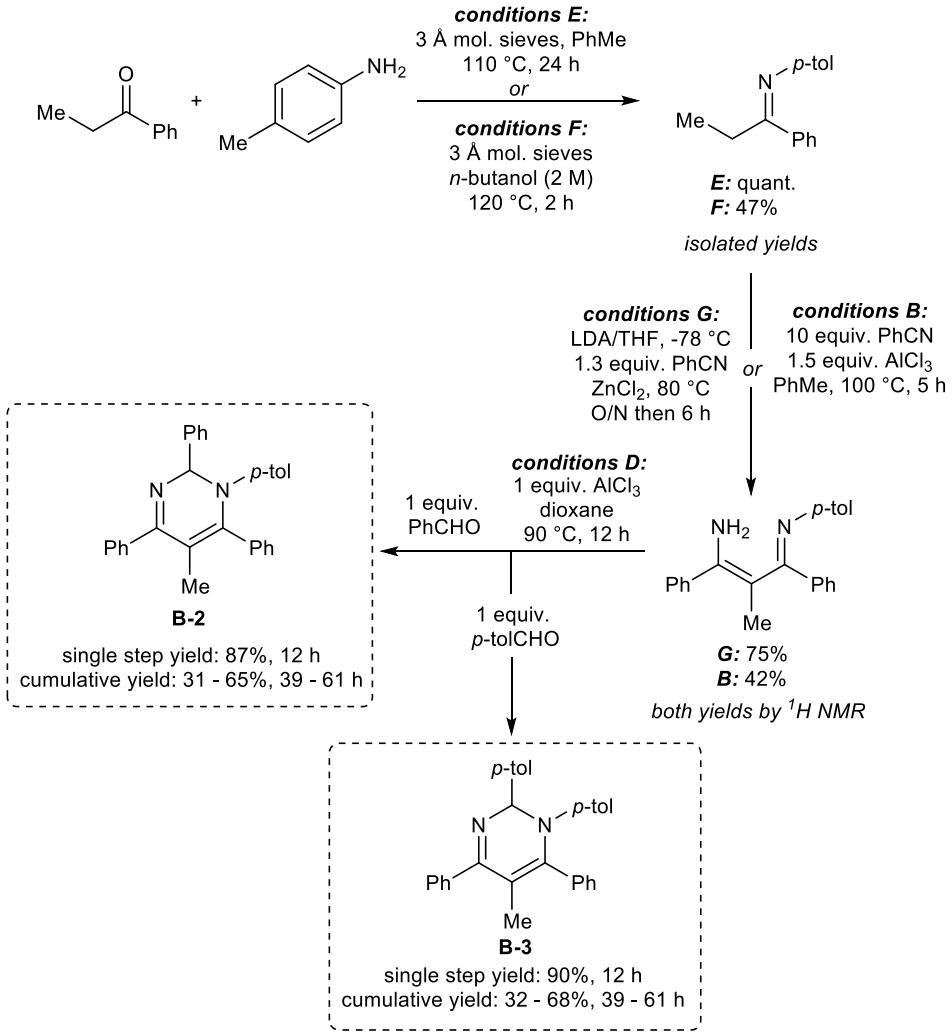


Figure S141. Synthetic route of 1,2-dihydropyrimidines (**B-2** and **B-3**) from propiophenone and 4-methylaniline over three steps.

1,2-dihydropyrimidines **B-2** and **B-3** derived from 4-methylaniline follows a similar pathway to **B-1**. (*Z*)-1-phenyl-*N*-(*p*-tolyl)propan-1-imine is prepared from the condensation of propiophenone and 4-methylaniline with two potential sets of conditions, either quantitatively with 3 Å molecular sieves in toluene at 110 °C (conditions E)[11] or 3 Å molecular sieves in *n*-butanol at 120 °C yielding the imine in 47% (conditions F).[12] The 4-azadiene-1-amine is formed through a Blaise-like reaction with LDA, benzonitrile, and $ZnCl_2$ in 75% by ^{1}H NMR over approximately 22 - 30 h (conditions G).[6] Alternatively, it can be prepared with $AlCl_3$ and benzonitrile over 5 h in toluene in 42% yield by ^{1}H NMR (conditions B).[9] From here, the 1,2-dihydropyrimidine is prepared through the $AlCl_3$-catalyzed condensation/cyclization with the desired aldehyde, either

benzaldehyde or *p*-tolualdehyde (conditions D).[10] Overall the preparation of 1,2-dihydropyrimidine **B-2** yields 31 – 65% over the course of three steps and 39 – 61 h while **B-3** can be made in 32 – 68 % yield over the same time period.

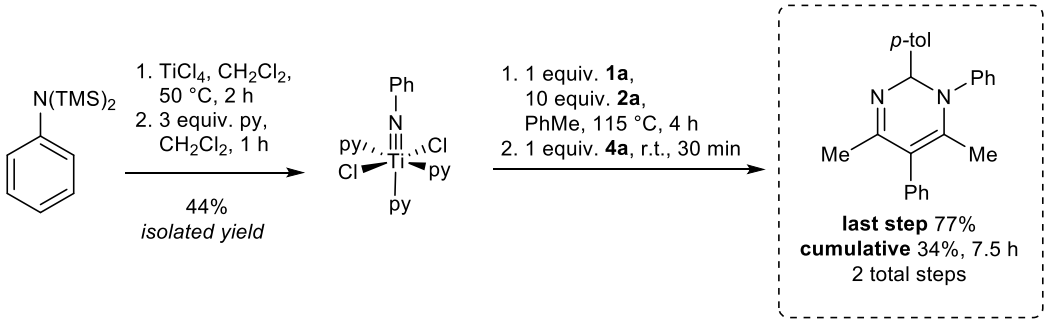


Figure S142. Synthetic route to 1,2-dihydropyrimidine (**5aaa**) over three steps beginning with the synthesis of the $py_3TiCl_2(NPh)$

In comparison, the Ti-mediated route prepares 1,2-dihydropyrimidine **5aaa** in two steps. The reaction of *N,N*-bis(trimethylsilyl)aniline with $TiCl_4$ followed by 3 equivalents of pyridine yield $py_3TiCl_2(NPh)$ in 44%. From this, 1,2-dihydropyrimidine **5aaa** is prepared in 77% yield as reported by first preparing the diazatitanacycle **3aa** from **1a**, **2a**, and $py_3TiCl_2(NPh)$ followed by addition of **4a**. Thus, cumulatively this route prepares **5aaa** in 34% cumulative yield over 7.5 h and two overall steps where the second step is a two-step one-pot process.

XRD Data

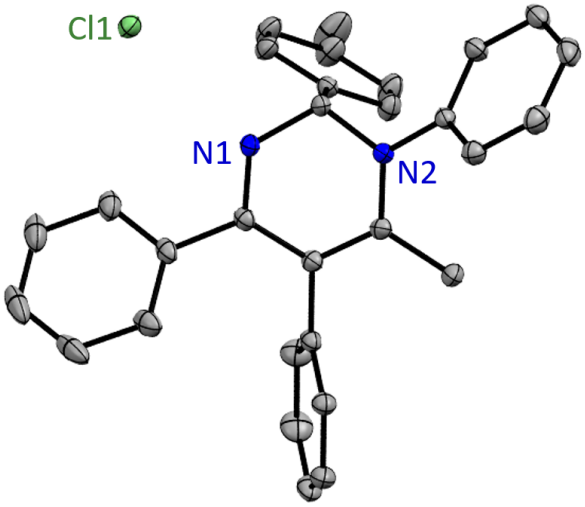


Figure S143. Crystal structure of **5aca•HCl**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms and solvent molecules are omitted for clarity. A disordered hexane molecule was removed from the unit cell using Platon SQUEEZE.

Table 1. Refined data and cell parameters for crystal structure of **5aca•HCl**

CCDC number	2440576
Empirical formula	$C_{30.50}H_{28}Cl_2N_2$
Formula weight	493.45
Temperature (K)	100(2)
a (Å)	21.8221(12)
b (Å)	10.4425(5)
c (Å)	23.4492(12)
α (°)	90
β (°)	95.9890(10)
γ (°)	90
Volume (Å^3)	5314.4(5)
Z	8
Crystal system	monoclinic
Space group	C2/c
d_{calc} (g/cm^{-3})	1.233
2θ range (°)	4.33 to 61.02 (0.70 Å)
μ (mm^{-1})	0.265
Abs. correction	Multi-scan
GooF	1.063
R_1[a]	0.0466
wR_2[b] [$I \geq 2\sigma(I)$]	0.1181
[a] $R1 = \sum\|\|F_o\|-\|F_c\|\|/\sum\|F_o\|$. [b] $wR2 = [\sum[w(F_o^2-F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$.	

Computational Results

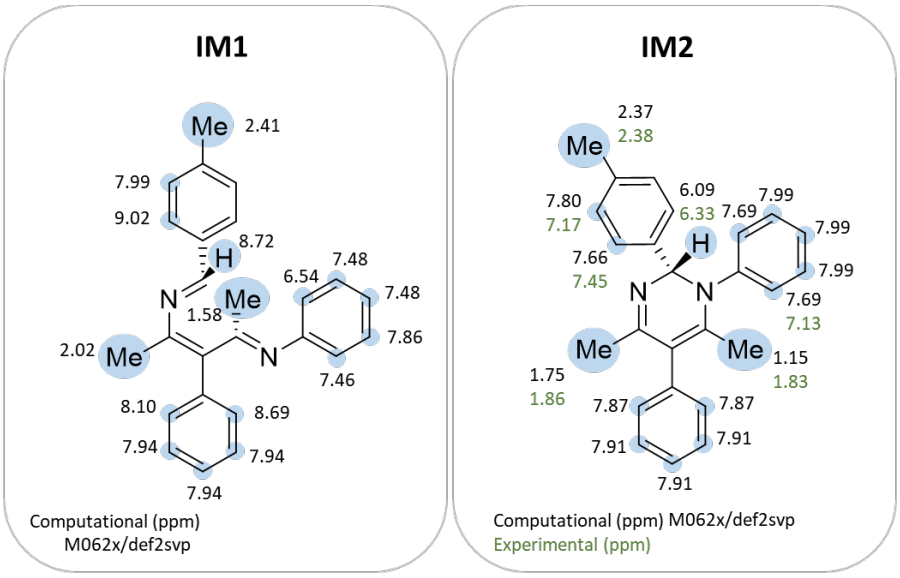
These computational methods were adapted from previous work on similar systems. [7,14–16] All geometry optimizations and frequency calculations were performed with Gaussian 16 package (Rev C.01).[17] Structures were optimized with the M06-2x functional[18–20] and def2svp basis set.[21–23] A SMD continuum solvation model[24] for toluene was used to approximate experimental conditions. The ultrafine grid setting was used for all calculations. Thermal energies were calculated at 388.15 K (115 °C) and 1 atm. Frequency calculations were performed on the optimized geometries with the same functional and basis set (M062x/def2svp) to obtain free energies and verify minima with no imaginary frequencies or a transition state which would have a single imaginary frequency. All frequencies below 50 cm^{-1} were scaled to 50 cm^{-1} for the thermal energy calculation.

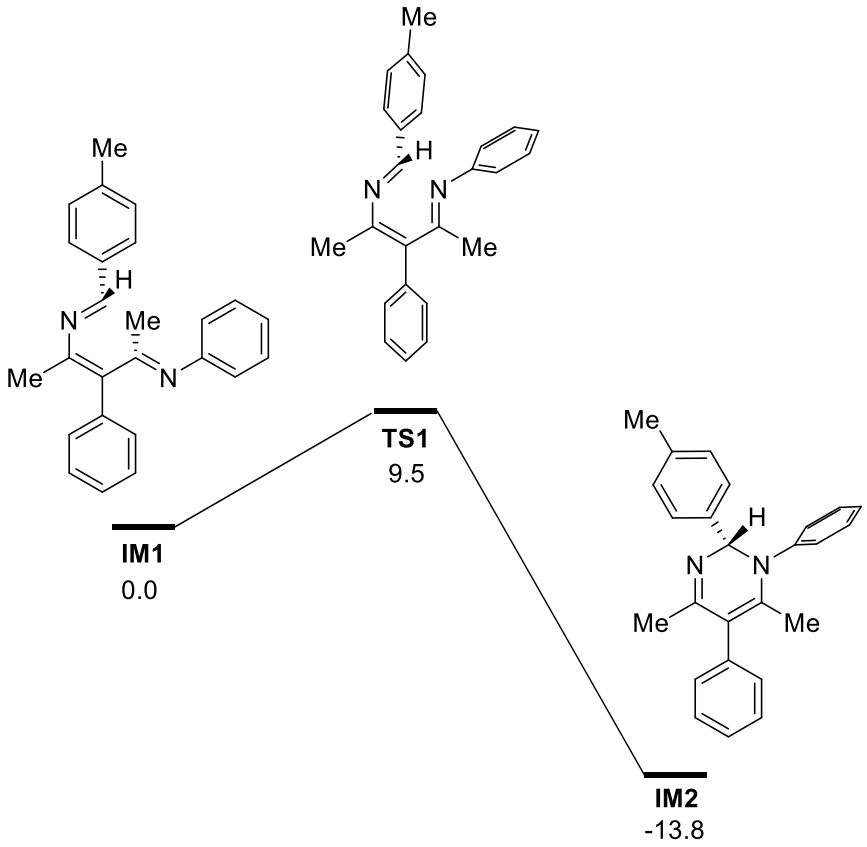
Additionally, NMR shielding constants of IM1 and IM2 were calculated using the Gauge Independent Atomic Orbital (GIAO) method with the M06-2x functional and def2svp basis set.[25] The structures were reoptimized in chloroform at 298.15 K. NMR chemical shifts were obtained by referencing the shielding constants of IM1 and IM2 to tetramethylsilane (TMS, σ_{TMS}) using the equation below.[26]

$$\delta = \frac{(\sigma_{TMS} - \sigma)}{(1 - (10^{-6} \times \sigma_{TMS}))} \quad \text{(Equation 1)}$$

Table S2. Calculated ^{1}H NMR chemical shifts

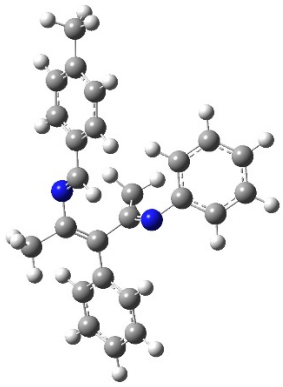
IM1 Calculated chemical shift (ppm)	**IM2** Calculated chemical shift (ppm)	**5aaa** Experimental chemical shift (ppm)
1.58	1.15	1.83
2.02	1.75	1.86
2.41	2.37	2.38
8.72	6.09	6.33
7.00	7.69	7.00
7.61	7.99	7.27 -7.11
7.94	7.91	
7.99	7.80	7.31
8.40	7.87	
9.02	7.66	7.45



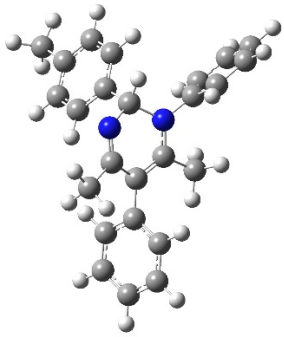


All corrected free energies (kcal/mol)
298.15 K

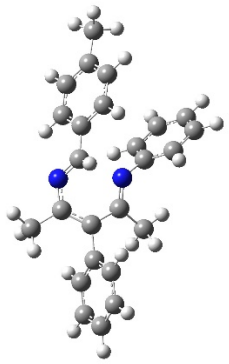
Cartesian XYZ coordinates (Å) of optimized structures with electronic, free, and frequency corrected free energies (a.u.) at 298.15 K and 1 atm using M06-2x/def2svp/ultrafine in toluene



IM1
The electronic energy (Hartrees): -1075.369739
The Thermal Free Energy (Hartrees): -1075.002788
The Corrected Thermal Free Energy (Hartrees): -1075.000486



IM2
The electronic energy (Hartrees): -1075.39601
The Thermal Free Energy (Hartrees): -1075.025723
The Corrected Thermal Free Energy (Hartrees): -1075.022445



TS1
The electronic energy (Hartrees): -1075.355462
The Thermal Free Energy (Hartrees): -1074.987850
The Corrected Thermal Free Energy (Hartrees): -1074.985295

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