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Triazole-Enabled Ruthenium(II)carboxylate-Catalyzed C–H Arylation with Electron-deficient Aryl Halides

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Abstract:
The triazole-directed direct C–H arylation of arenes with electron-deficient aryl halides and a synthetically-useful pyrimidyl chloride was achieved via ruthenium catalysis. Our novel strategy provides operationally-simple and environmentally-benign access to highly functionalized heteroarenes, avoiding the use strong organometallic bases. Detailed studies revealed a significant effect of the phosphine ligand, thus allowing for the reaction to occur with excellent levels of chemo- and position-selectivity.

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Thieme

Triazole-Enabled Ruthenium(II)carboxylate-Catalyzed C–H Arylation with Electron-deficient Aryl Halides

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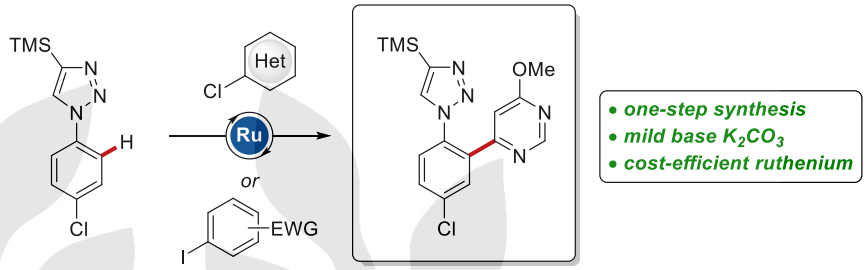

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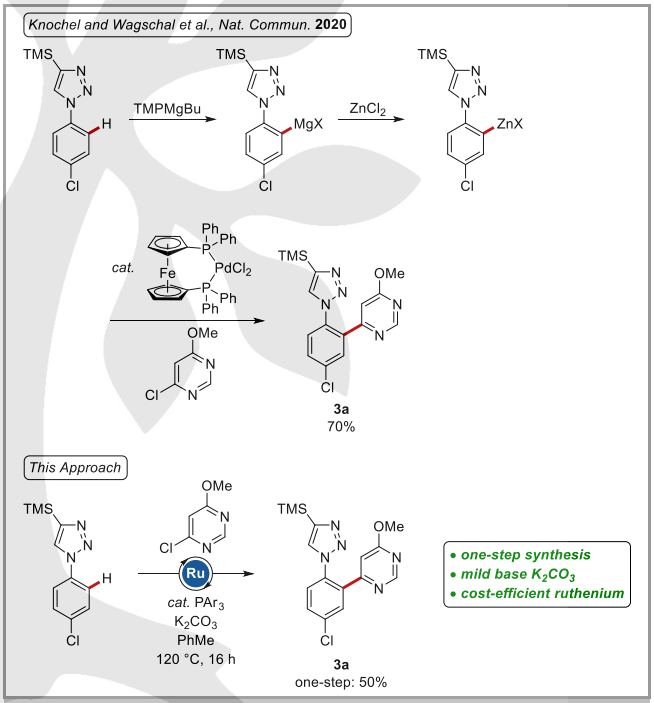
Abstract The triazole-directed direct C–H arylation of arenes with electron-deficient aryl halides and a synthetically-useful pyrimidyl chloride was achieved *via* ruthenium catalysis. Our novel strategy provides operationally-simple and environmentally-benign access to highly functionalized heteroarenes, avoiding the use strong organometallic bases. Detailed studies revealed a significant effect of the phosphine ligand, thus allowing for the reaction to occur with excellent levels of chemo- and position-selectivity.

Key words C–H activation, arylation; ruthenium; heteroarenes

During the last decade, transition metal-catalyzed C–H activation has emerged as an increasingly powerful tool in molecular syntheses,[1] with notable applications to late-stage diversification,[2] drug discovery[3] and material sciences,[4] among others. In contrast to traditional cross-coupling reactions, C–H activation does not require the use of pre-functionalized substrates, thereby reducing the number of synthetic operations and minimizing the generation of potentially toxic chemical waste. Very recently, *Knochel* and *Wagschal* disclosed an elegant approach for the synthesis of aryl triazole **3a**, which was evaluated in the synthesis of a novel Active Pharmaceutical Ingredient (API).[5] Despite this indisputable advance, this strategy relied on highly reactive and costly 2,2,6,6-tetramethylpiperidinyl butyl magnesium (TMPMgBu), $ZnCl_2$ in overstoichiometric amounts and a precious palladium catalyst. Within our continued interest in cost-efficient[6] ruthenium-catalyzed[7] C–H activation,[8] we have now developed a novel strategy to access triazole[9] **3a**, thus providing user-friendly access to a novel drug currently in development. Notable features of our approach include i) cost-efficient ruthenium catalysts, ii) a user-friendly one-step approach, and iii) K_2CO_3 as a mild base (Scheme 1).



Scheme 1 Direct C–H arylation by ruthenium catalysis.

We initiated our studies by probing various phosphine ligands for the direct C–H arylation of TMS-substituted triazole **1a** bearing a sensitive chloro substituent (Figure 1). While electron-rich alkyl phosphines **L1**, **L3** and **L4** as well as methoxy-substituted phosphine **L5** resulted in the formation of significant amounts of de-silylated compounds **1b** and **3b** (entries 1, 3-5), the de-silylation process could be suppressed, when electron-deficient ligands were employed (entries 9-11). The use of ligand **L12** featuring a strongly electron-withdrawing

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trifluoromethyl substituent delivered the desired product **3a** in an improved yield (entry 12).

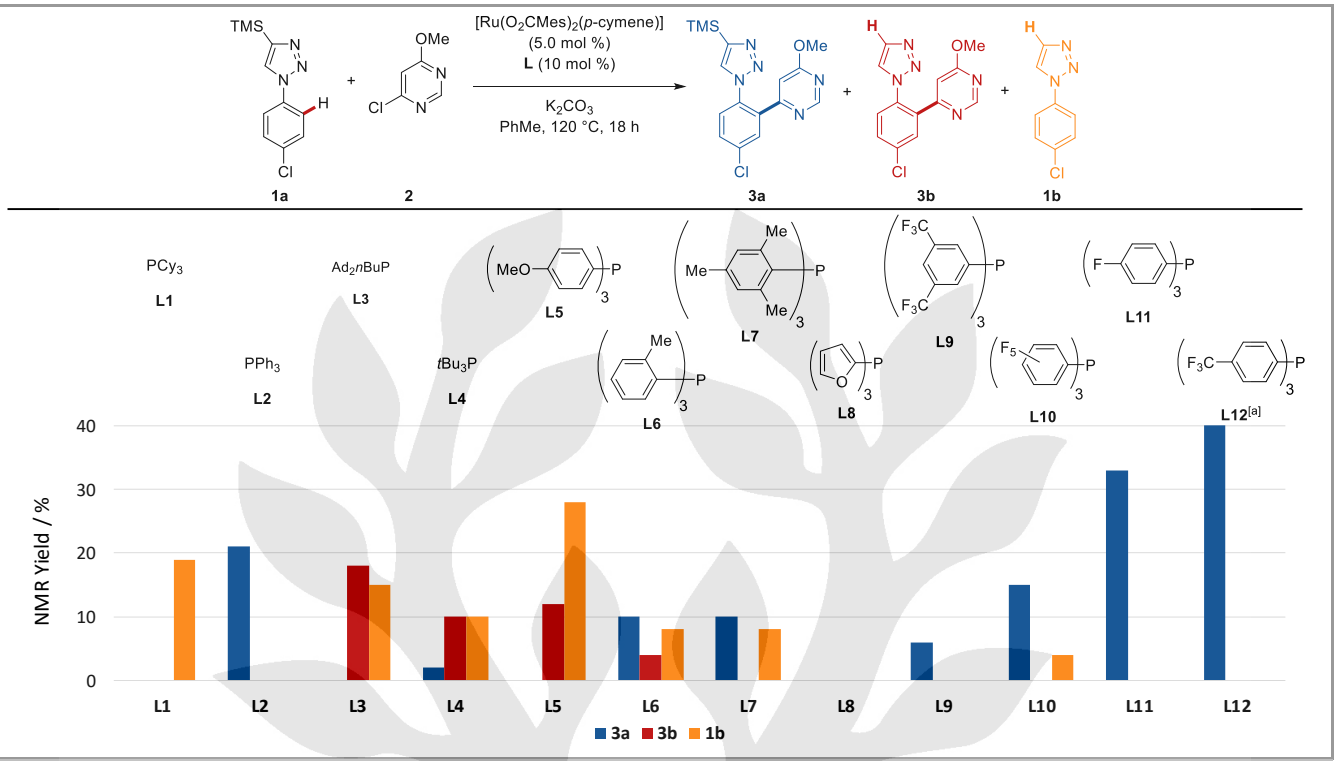
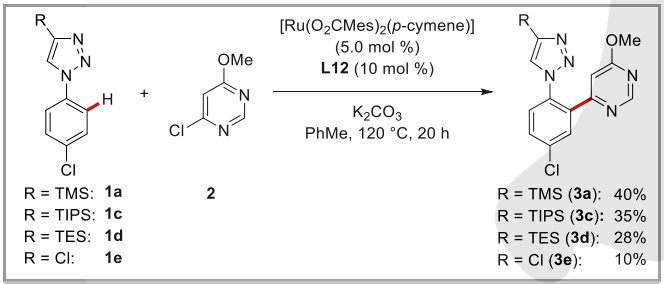


Figure 1 Effect of the phosphine ligand **L**. The conversion was determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as the internal standard. Unreacted **1a** accounts mostly for the remaining mass balance.[10] [a] Isolated yield.

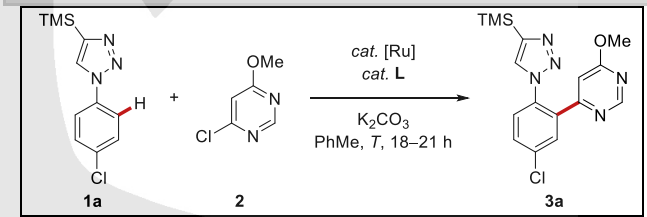
Next, the effect of the triazole C-4 substituent on the reaction outcome was tested (Scheme 2). A comparable efficiency was observed when the TMS group was replaced with a triisopropylsilyl (TIPS) substituent. In contrast, the yield of product **3** dropped significantly when triethylsilyl-substituted (TES) compound **1d** was employed. Replacing the silyl-group with a chloro substituent resulted in an unsatisfactory reaction outcome.



Scheme 2 Influence of the Triazole **1** substitution pattern.

Among a variety of solvents and bases, orienting studies identified toluene and K_2CO_3, respectively, as being optimal. A careful analysis of various reaction parameters revealed [Ru(O$_2$CMes)$_2$(*p*-cymene)] to be the optimal catalyst for this transformation, while cationic [Ru(NCMe)$_6$][BF$_4$]$_2$ as well as cyclometallated complexes **Ru-I** and **Ru-II**[11] fell short in delivering the desired product **3a** (Table 1, entries 8-10).[12] The obtained yield could be further increased by adjusting the [Ru]/phosphine ratio from 1:2 to 1:1 (entry 13).[13] In contrast, varying the reaction temperature and the concentration did not prove beneficial (entries 2-6).

Table 1 Optimization of reaction parameters.[a]



Entry	[Ru] (x mol %)	Ligand (y mol %)	*T* / °C	Yield / %
1	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	120	40
2	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (10)	**L12** (20)	120	37
3[b]	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (15)	**L12** (30)	120	34
4	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	100	33
5[b,c]	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	120	47
6[d]	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	140	33

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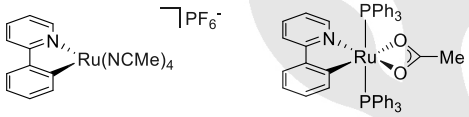
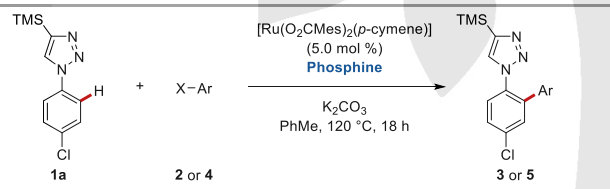
7	[Ru(OAc)$_2$(*p*-cymene)] (5.0)	**L12** (10)	120	40
8	[Ru(NCMe)$_6$][BF$_4$]$_2$ (5.0)	**L11** (10)	120	--
9[e]	**Ru-I**	**L12** (10)	120	--
10[e]	**Ru-II**	**L12** (10)	120	--
11[f]	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	120	41
12[g]	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (10)	120	--
13	**[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)**	**L12 (5.0)**	**120**	**50**
14	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (5.0)	**L12** (2.5)	120	44

[a] **1a** (0.3 mmol), **2a** (0.45 mmol), [Ru] (x–x mol %), **L** (x–x mol %), K_2CO_3 (2.0 equiv.), PhMe (1.2 mL), 120 °C, 18–21 h, yield of isolated product. [b] **2a** (0.6 mmol), PhMe (2.0 mL). [c] for 48 h. [d] in *m*-xylene (1.2 mL). [e] with or without KOAc (10 mol %). [f] in PhMe (0.6 mL). [g] $Pd(OAc)_2$ (5.0 mol %) added.

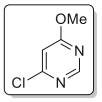


Ru-I **Ru-II**

Intrigued by the considerable influence of the phosphine ligand on the catalyst's efficacy, we became interested in probing the phosphine ligand effect also with the C–H arylations of aryl triazole **1a** with electron-deficient arene **4a**. When the reaction was performed in the absence of an additional ligand, only traces of the arylated compound **5a** could be observed (Scheme 3). In contrast, the use of ligand **L12** led to the formation of 76% of the mono- and diarylated products, thus clearly outperforming PPh_3.

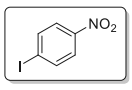


*(a) 2-Chloro-6-methoxy pyrimidine (**2**)*



Phosphine	Yield [%]
no ligand	12
PCy_3 (**L1**, 10 mol %)	n.r.
PPh_3 (**L2**, 10 mol %)	21
P(4-CF$_3$C$_6$H$_4$)$_3$ (L12, 5 mol %)	50

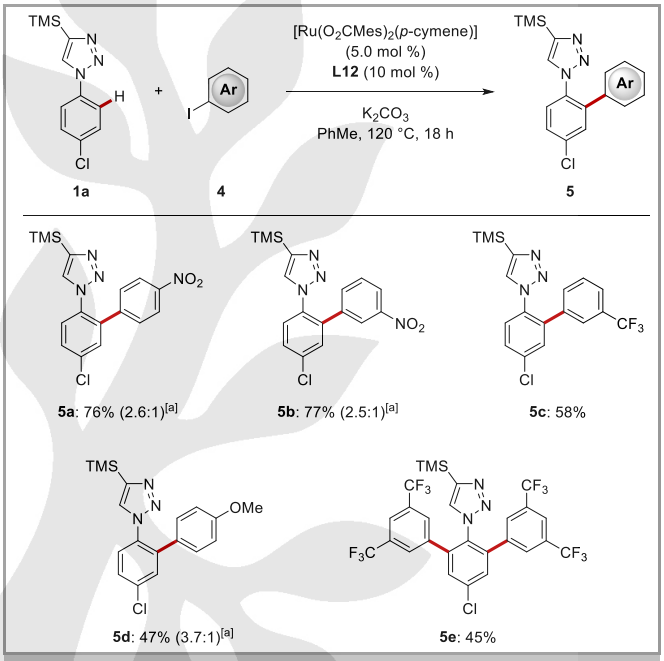
*(b) 4-Iodo nitrobenzene (**4a**)*



Phosphine	Yield [%]
no ligand	traces
PCy_3 (**L1**, 5 mol %)	n.d.
PPh_3 (**L2**, 5 mol %)	65 (2.6:1)[a]
P(4-CF$_3$C$_6$H$_4$)$_3$ (L12, 10 mol %)	76 (2.6:1)[a]

Scheme 3 Performance of phosphine ligands with different electrophiles. [a] The ratio of mono- and diarylated products is given in parenthesis. n.d. = not determined.

Finally, we employed representative aryl iodides **4** bearing various substituents for the C–H arylation of triazole **1a**. Gratifyingly, and in contrast to previously reported approaches,[8g, 14] sensitive nitro substituents were found to be fully tolerated under the reaction conditions. *meta*- or *para*-Nitro-substituted aryl iodides **4a** and **4b** were hence efficiently transformed under the reaction conditions, delivering the arylated products **5a** and **5b** in a similar yield and with an almost identical mono/diarylation ratio, indicating no pronounced influence of the position of the substituent on the reaction outcome (Scheme 4). Interestingly, a notable decrease in yield was observed, when less electron-deficient arene **4c** or electron-rich aryl iodide **4d** was subjected to the C–H arylation, highlighting a preference of the optimized ruthenium catalyst for electron-deficient electrophiles. Compound **4e** bearing two trifluoromethyl substituents exclusively led to the formation of the diarylated product **5e**.



Scheme 4 Ruthenium-catalyzed C–H arylation with aryl iodides **4**. [a] The ratio of mono- and diarylated products is given in parenthesis.

In summary, we have developed a novel approach for the triazole-enabled ruthenium-catalyzed C–H arylations under carboxylate assistance with electron-deficient pyrimidyl and aryl halides, thus representing a user-friendly, concise strategy of interest to drug development. Key to success was the use of a well-defined ruthenium(II)carboxylate complex in combination with an electron-deficient phosphine ligand.

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Supporting Information

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Primary Data

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12. The mass balance largely accounted for unreacted starting material **1**, while only minor amounts of the corresponding desilylated triazole were observed.
13. Under an atmosphere of N_2, a Schlenk-tube was charged with triazole **1a** (0.30 mmol, 1.00 equiv), 2-chloro-6-methoxy pyrimidine (**2**) (0.45 mmol, 1.5 equiv), [Ru(O_2CMes)$_2$(*p*-cymene)] (8.4 mg, 15 µmol, 5.0 mol %), tris(4-trifluoromethylphenyl)phosphine (**L12**) (7.0 mg, 15 µmol, 5.0 mol %) and K_2CO_3 (82.9 mg, 0.60 mmol, 2.00 equiv). PhMe (1.2 mL) was added and the mixture was stirred at 120 °C for 21 h. After cooling to ambient temperature, H_2O (10 mL) was added, the mixture was extracted with EtOAc (3 × 25 mL), washed with brine (25 mL), dried over Na_2SO4 and concentrated *in vacuo*. Purification of the remaining residue by column chromatography on silica gel (*n*-hexane:EtOAc = 5:1) yielded the desired product **3a** (53.6 mg, 50%). **M.p.** = 87–89 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 1.0 Hz, 1H), 7.82 (d, *J* = 2.2 Hz, 1H), 7.58 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 6.19 (d, *J* = 1.1 Hz, 1H), 3.91 (s, 3H), 0.29 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 170.1 (CH), 161.9 (CH), 158.5 (C_q), 147.2 (CH); 136.2 (CH), 135.8 (CH), 133.9 (CH), 131.2 (C_q), 130.9 (C_q), 130.7 (C_q), 128.2 (C_q), 107.3 (C_q), 54.2 (CH_3), -1.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1584, 1500, 1468, 1202, 1032, 838, 823, 758, 632, 417 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 741 [2M+Na]$^+$ (85), 559 (8), 382 [M+Na]$^+$ (49), 360 [M+H]$^+$ (100), 332 (16). **HR-MS** (ESI): *m/z* calcd for $C_{16}H_{19}{}^{35}ClN_5OSi^+$ [M+H]$^+$ 360.1042, found 360.1028.
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Supporting Information

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General Remarks

Reactions involving air- or moisture-sensitive compounds were conducted under an atmosphere of nitrogen using pre-dried glassware and standard Schlenk- or glovebox-techniques. PhMe was dried over Na and distilled under an atmosphere of nitrogen. Ruthenium complexes $[Ru(O_2CMes)_2(p\text{-cymene})]$,[1] $[Ru(OAc)_2(p\text{-cymene})]$,[1] $[Ru(NCMe)_6][BF_4]_2$,[2] **Ru-I**[3] and **Ru-II**[4] were synthesized according to previously described methods. All other compounds were obtained from commercial sources and were used without further purification. If not otherwise noted, yields refer to isolated compounds, estimated to be >95% pure by GC and NMR. Analytical thin layer chromatography (TLC) was performed on TLC Silica gel 60 F_{254} from Merck with detection at 254 nm or 360 nm. Preparative chromatographic separations were carried out on Merck Geduran SI 60 (40–63 μm, 70–230 mesh ASTM) silica gel. Infrared (IR) spectra of pure compounds were measured on Bruker Alpha-P FT-IR spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance III 300, Avance III HD 300 and Avance III HD 500 spectrometers. Chemical shifts (δ) are referenced using the residual proton or carbon solvent signal. ^{19}F spectra were referenced using $CFCl_3$ as external standard. Electron-ionization (EI) mass spectra were recorded on Jeol AccuTOF instrument at 70 eV. Electrospray-ionization (ESI) mass spectra were obtained on Bruker micrOTOF and maXis instruments. All systems are equipped with time-of-flight (TOF) analyzers. The ratios of mass to charge (m/z) are reported and the intensity relative to the base peak (I = 100) is given in parenthesis.

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General Procedure A for the Ruthenium(II)carboxylate-Catalyzed C–H Arylation of Arenes 1 with Pyrimidyl Chloride 2

Under an atmosphere of N_2, a Schlenk-tube was charged with triazole **1** (0.30 mmol, 1.00 equiv), 2-chloro-6-methoxy pyrimidine **2** (0.45 mmol, 1.5 equiv), [Ru(O_2CMes)$_2$(*p*-cymene)] (8.4 mg, 15 μmol, 5.0 mol %), tris(4-trifluoromethylphenyl)phosphine (**L12**) (7.0 mg, 15 μmol, 5.0 mol %) and K_2CO_3 (82.9 mg, 0.60 mmol, 2.00 equiv). PhMe (1.2 mL) was added and the mixture was stirred at 120 °C for 18–21 h. After cooling to ambient temperature, H_2O (10 mL) was added, the mixture was extracted with EtOAc (3 × 25 mL), washed with brine (25 mL), dried over Na_2SO4 and concentrated *in vacuo*. Purification of the remaining residue by column chromatography on silica gel yielded the desired product **3**.

General Procedure B for the Ruthenium(II)carboxylate-Catalyzed C–H Arylation of Arenes 1 with Aryl Iodides 4

Under an atmosphere of N_2, a Schlenk-tube was charged with triazole **1** (0.30 mmol, 1.00 equiv), aryl iodide **4** (0.45 mmol, 1.5 equiv), [Ru(O_2CMes)$_2$(*p*-cymene)] (8.4 mg, 15 μmol, 5.0 mol %), tris(4-trifluoromethylphenyl)phosphine (**L12**) (14.1 mg, 30 μmol, 10.0 mol %) and K_2CO_3 (82.9 mg, 0.60 mmol, 2.00 equiv). PhMe (1.2 mL) was added and the mixture was stirred at 120 °C for 18 h. After cooling to ambient temperature, H_2O (10 mL) was added, the mixture was extracted with EtOAc (3 × 25 mL), washed with brine (25 mL), dried over Na_2SO4 and concentrated *in vacuo*. Purification of the remaining residue by column chromatography on silica gel yielded the desired product **5**.

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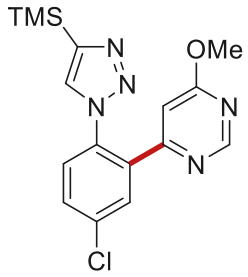
Characterization Data of Products 3 and 5

4-[5-Chloro-2-(4-trimethylsilyl-1*H*-1,2,3-triazol-1-yl)phenyl]-6-methoxypyrimidine (3a)



3a

The General Procedure A was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol) and 4-chloro-6-methoxypyrimidine (**2**) (65.1 mg, 0.45 mmol) for 21 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **3a** (53.6 mg, 50%) as a yellow solid.

M.p. = 87–89 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.70 (d, J = 1.0 Hz, 1H), 7.82 (d, J = 2.2 Hz, 1H), 7.58 (dd, J = 8.5, 2.2 Hz, 1H), 7.51 (d, J = 8.1 Hz, 2H), 6.19 (d, J = 1.1 Hz, 1H), 3.91 (s, 3H), 0.29 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 170.1 (CH), 161.9 (CH), 158.5 (C_q), 147.2 (CH); 136.2 (CH), 135.8 (CH), 133.9 (CH), 131.2 (C_q), 130.9 (C_q), 130.7 (C_q), 128.2 (C_q), 107.3 (C_q), 54.2 (CH_3), -1.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1584, 1500, 1468, 1202, 1032, 838, 823, 758, 632, 417 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 741 $[2M+Na]^+$ (85), 559 (8), 382 $[M+Na]^+$ (49), 360 $[M+H]^+$ (100), 332 (16). **HR-MS** (ESI): *m*/*z* calcd for $C_{16}H_{19}{}^{35}ClN_5OSi^+$ $[M+H]^+$ 360.1042, found 360.1028.

The analytical data are in accordance with those reported in the literature.[5]

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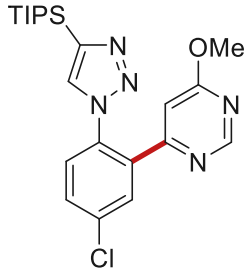
4-[5-Chloro-2-(4-triisopropylsilyl-1*H*-1,2,3-triazol-1-yl)phenyl]-6-methoxypyrimidine (3c)

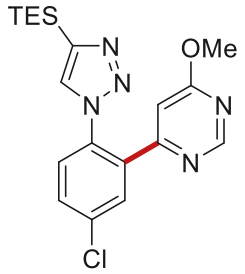


3c

The General Procedure A was followed using 1-(4-chlorophenyl)-4-triisopropylsilyl-1H-1,2,3-triazole (**1c**) (101 mg, 0.30 mmol), 4-chloro-6-methoxypyrimidine (**2**) (65.1 mg, 0.45 mmol) and tris(4-trifluoromethylphenyl)phosphine (**L12**) (14.1 mg, 30 µmol, 10.0 mol %) for 20 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **3c** (46.3 mg, 35%) as a green solid.

M.p. = 113–116 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 7.80 (s, 1H), 7.59 (s, 2H), 7.46 (s, 1H), 6.16 (s, 1H), 3.88 (s, 3H), 1.33 (hept, J = 7.5 Hz, 3H), 1.04 (d, J = 7.5 Hz, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = l69.1 (C_q), 161.9 (C_q), 158.7 (CH), 142.5 (C_q), 136.2 (C_q), 135.8 (C_q), 134.0 (C_q), 132.4 (CH), 130.8 (CH), 130.7 (CH), 128.3 (CH), 107.5 (CH), 54.0 (CH_3), 18.6 (CH_3), 11.1 (CH). **IR** (ATR): $\tilde{\nu}$ = 2941, 2864, 1739, 1584, 1541, 1470, 1390, 1358, 1196, 1031 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 466 $[M+Na]^+$ (4), 444 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{22}H_{31}{}^{35}ClN_5OSi^+$ $[M+H]^+$ 444.1981, found 444.1986.

4-[5-Chloro-2-(4-triethylsilyl-1*H*-1,2,3-triazol-1-yl)phenyl]-6-methoxypyrimidine (3a)



3d

The General Procedure A was followed using 1-(4-chlorophenyl)-4-triethylsilyl-1H-1,2,3-triazole (**1d**) (88.2 mg, 0.30 mmol), 4-chloro-6-methoxypyrimidine (**2**) (65.1 mg, 0.45 mmol)

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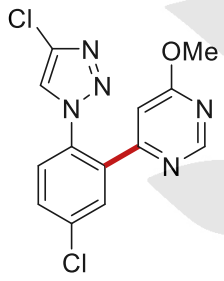
and tris(4-trifluoromethylphenyl)phosphine (**L12**) (14.1 mg, 30 µmol, 10.0 mol %) for 20 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **3d** (34.3 mg, 28%) as a yellow solid.

M.p. = 84–86 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.70 (s, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.61–7.50 (m, 2H), 7.46 (s, 1H), 6.15 (s, 1H), 3.88 (s, 3H), 0.93 (t, J = 7.7 Hz, 9H), 0.78 (q, J = 7.7 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 170.0 (C_q), 161.8 (C_q), 158.5 (CH), 144.2 (C_q), 136.2 (C_q), 135.8 (C_q), 133.9 (C_q), 131.9 (CH), 130.8 (CH), 130.6 (CH), 128.3 (CH), 107.4 (CH), 54.1 (CH_3), 7.29 (CH_3), 3.49 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3099, 2954, 2909, 2874, 1588, 1541, 1469, 1214, 1030, 718 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 424 $[M+Na]^+$ (6), 402 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{19}H_{25}{}^{35}ClN_5OSi^+$ $[M+H]^+$ 402.1511, found 402.1509.

4-[5-Chloro-2-(4-chloro-1*H*-1,2,3-triazol-1-yl)phenyl]-6-methoxypyrimidine (3a)



3e

The General Procedure A was followed using 1-(4-chlorophenyl)-4-chloro-1H-1,2,3-triazole (**1e**) (64.2 mg, 0.30 mmol), 4-chloro-6-methoxypyrimidine (**2**) (65.1 mg, 0.45 mmol) and triscyclohexylphosphine (**L1**) (8.4 mg, 30 µmol, 10.0 mol %) for 20 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **3e** (16 mg, 17%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.69 (s, 1H), 7.75 (d, J = 2.4 Hz, 1H), 7.64–7.57 (m, 2H), 7.49 (d, J = 8.5 Hz, 1H), 6.52 (s, 1H), 3.97 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 170.2 (C_q), 161.8 (C_q), 158.6 (CH), 137.0 (C_q), 135.9 (C_q), 135.8 (C_q), 133.3 (C_q), 131.2 (CH), 130.8 (CH), 128.2 (CH), 123.1 (CH), 107.7 (CH), 54.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3064, 2954, 2925, 2854, 1732, 1585, 1370, 1211, 1024, 815 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 344 $[M+Na]^+$ (100), 322 $[M+H]^+$ (52). **HR-MS** (ESI): *m*/*z* calcd for $C_{13}H_{10}{}^{35}Cl_2N_5O^+$ $[M+H]^+$ 322.0257, found 322.02360.

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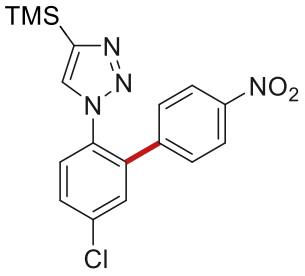
1-(5-Chloro-4'-nitro-[1,1'-biphenyl]-2-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5a)

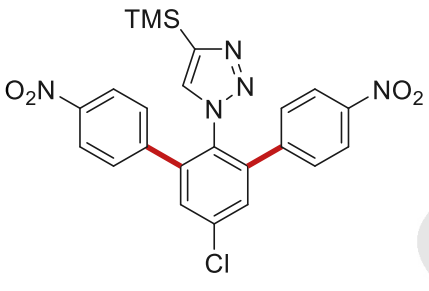


5a

The General Procedure B was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol), 1-iodo-4-nitrobenzene (**4a**) (112 mg, 0.45 mmol) for 19 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **5a** (62 mg, 55%) and **5a'** (31 mg, 21%) as black solids.

M.p. = 129–133°C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.15–8.07 (m, 2H), 7.58–7.50 (m, 3H), 7.28–7.18 (m, 3H), 0.22 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 147.7 (C_q), 147.3 (C_q), 142.9 (C_q), 136.9 (C_q), 136.1 (C_q), 133.7 (C_q), 130.9 (CH), 130.8 (CH), 129.9 (CH), 129.5 (CH), 128.3 (CH), 123.9 (CH), -1.19 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3078, 2960, 2856, 1602, 1516, 1503, 1350, 1029, 840, 830 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 395 $[M+Na]^+$ (5), 373 $[M+H]^+$ (100). **HR-MS** (ESI): *m/z* calcd for $C_{17}H_{18}{}^{35}ClN_4O_2Si^+$ $[M+H]^+$ 373.0882, found 373.0871.

1-(5'-Chloro-4,4''-dinitro-[1,1':3',1''-terphenyl]-2'-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5a')



5a'

M.p. = 208–212°C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.09 (d, J = 8.8 Hz, 4H), 7.60 (s, 2H), 7.27 (d, J = 8.8 Hz, 4H), 7.09 (s, 1H), 0.11 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 147.8 (C_q), 147.6 (C_q), 142.5 (C_q), 140.0 (C_q), 136.7 (C_q), 131.9 (CH), 131.7 (C_q), 130.8 (CH), 129.5 (CH), 123.7 (CH), -1.22 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2958, 1600, 1576, 1492, 1468, 1348, 1247, 1035,

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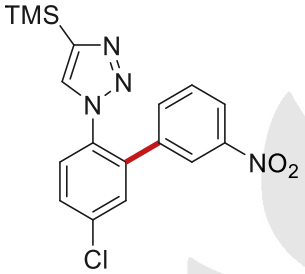
836, 820 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 516 $[M+Na]^+$ (6), 494 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{23}H_{21}{}^{35}ClN_5O_4Si^+$ $[M+H]^+$ 494.1046, found 494.1042.

1-(5-Chloro-3'-nitro-[1,1'-biphenyl]-2-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5b)

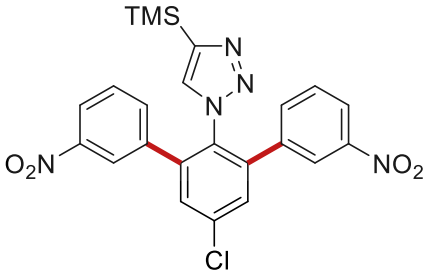


5b

The General Procedure B was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol), 1-iodo-3-nitrobenzene (**4b**) (112 mg, 0.45 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **5b** as a black oil (62 mg, 55%) and **5b'** (32 mg, 22%) as a black solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.11 (m, 1H), 7.95 (d, *J* = 2.0, 2.0 Hz, 1H), 7.56 (s, 3H), 7.46–7.37 (m, 1H), 7.37–7.24 (m, 2H), 0.23 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 148.4 (C_q), 147.3 (C_q), 140.0 (C_q), 136.8 (C_q), 136.3 (C_q), 134.5 (CH), 133.8 (C_q), 130.9 (CH), 130.9 (CH), 129.8 (CH), 129.8 (CH), 128.3 (CH), 123.3 (CH), 123.3 (CH), -1.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3087, 2957, 1528, 1503, 1350, 1249, 1032, 838, 688, 632 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 395 $[M+Na]^+$ (50), 373 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{17}H_{18}{}^{35}ClN_4O_2Si^+$ $[M+H]^+$ 373.0882, found 373.0887.

1-(5'-Chloro-3,3''-dinitro-[1,1':3',1''-terphenyl]-2'-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5b')



5b'

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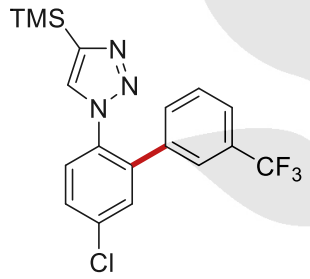
M.p. = 208–212°C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.19–8.11 (m, 2H), 8.01–7.96 (m, 2H), 7.64 (s, 2H), 7.50–7.37 (m, 4H), 7.23 (s, 1H), 0.12 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 140.2 (C_q), 147.6 (C_q), 139.7 (C_q), 137.7 (C_q), 136.9 (C_q), 134.4 (CH), 132.1 (C_q), 131.9 (CH), 130.8 (CH), 129.7 (CH), 123.5 (CH), 123.3 (CH), -1.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2958, 1525, 1494, 1351, 1247, 1034, 842, 809, 740, 686 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 516 $[M+Na]^+$ (45), 494 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{23}H_{21}{}^{35}ClN_5O_4Si^+$ $[M+H]^+$ 494.1046, found 494.1047.

1-(5-Chloro-3'-trifluoromethyl-[1,1'-biphenyl]-2-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5c)



5c

The General Procedure B was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol), 1-iodo-3-trifluoromethylbenzene (**4c**) (122 mg, 0.45 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **5c** (51 mg, 43%) as a colorless oil.

Due to the presence of two rotamers, the ^{1}H and ^{13}C NMR spectra exhibit two partially overlapping sets of resonances.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.50 (m, 4H), 7.45–7.29 (m, 3H), 7.16 (d, J = 3.4 Hz, 1H), 0.25–0.07 (m, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 147.0 (C_q), 140.5 (C_q), 137.4 (C_q), 137.1 (C_q), 136.4 (C_q), 136.0 (C_q), 133.9 (C_q), 132.0 (CH), 131.9 (CH), 131.8 (CH), 131.0 (q, $^2J_{C–F}$ = 32.7 Hz, C_q), 130.9 (CH), 130.8 (CH), 130.4 (CH), 129.4 (CH), 129.2 (CH), 128.2 (CH), 125.2 (q, $^3J_{C–F}$ = 3.9 Hz, CH), 125.0 (q, $^3J_{C–F}$ = 3.9 Hz, CH), 124.0 (q, $^1J_{C–F}$ = 272.6 Hz, C_q), -1.3 (CH_3), -1.4 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -62.8 (s). **IR** (ATR): $\tilde{\nu}$ = 2899, 1576, 1490, 1251, 1121, 1075, 1031, 839, 804, 702 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 396 $[M+H]^+$ (100). **HR-MS** (ESI): *m*/*z* calcd for $C_{18}H_{18}{}^{35}ClN_3SiF_3^+$ $[M+H]^+$ 396.0905, found 396.0901.

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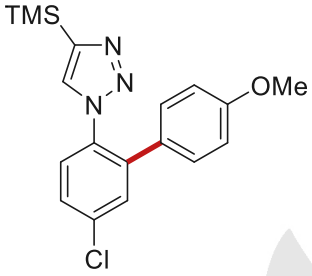
1-(5-Chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5d)



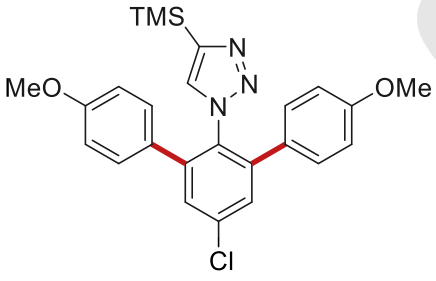
5d

The General Procedure B was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol), 4-iodoanisole (**4d**) (105 mg, 0.45 mmol) for 17 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **5d** as a colorless oil (40 mg, 37%) and **5d'** (14 mg, 10%) as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.44 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.09 (d, *J* = 1.1 Hz, 1H), 6.95–6.89 (m, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 3H), 0.22 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.8 (C_q), 146.6 (C_q), 138.5 (C_q), 135.5 (C_q), 133.8 (C_q), 131.2 (CH), 130.8 (CH), 129.7 (CH), 128.5 (C_q), 128.2 (CH), 127.9 (CH), 114.2 (CH), 55.4 (CH_3), -1.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3118, 2956, 2899, 2838, 1609, 1516, 1495, 1247, 1033, 982 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 380 $[M+Na]^+$ (29), 358 $[M+H]^+$ (100). **HR-MS** (ESI): *m/z* calcd for $C_{18}H_{21}{}^{35}ClN_3OSi^+$ $[M+H]^+$ 358.1137, found 358.1141.

The analytical data are in accordance with those reported in the literature.[5]

1-(5'-Chloro-4,4''-dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (5d')



5d'

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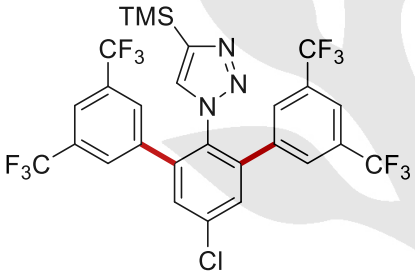
M.p. = 158–163°C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.45 (s, 2H), 7.09 (s, 1H), 6.98 (d, J = 8.8 Hz, 4H), 6.73 (d, J = 8.8 Hz, 4H), 3.74 (s, 6H), 0.15 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.5 (C_q), 146.1 (C_q), 141.6 (C_q), 135.6 (C_q), 132.4 (C_q), 131.8 (C_q), 129.6 (CH), 129.4 (CH), 129.0 (CH), 113.8 (CH), 55.3 (CH_3), -1.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3111, 3006, 2957, 2901, 2838, 1608, 1247, 1033, 826, 564 cm^{-1}. **MS** (ESI) m/z (relative intensity): 486 $[M+Na]^+$ (24), 464 $[M+H]^+$ (100). **HR-MS** (ESI): m/z calcd for $C_{25}H_{27}{}^{35}ClN_3O_2Si^+$ $[M+H]^+$ 464.1556, found 464.1559.

1-[5'-Chloro-3,3'',5,5''-tetrakis(trifluoromethyl)-[1,1':3',1''-terphenyl]-2'-yl]-4-trimethylsilyl-1*H*-1,2,3-triazole (5e)



5e

The General Procedure B was followed using 1-(4-chlorophenyl)-4-trimethylsilyl-1H-1,2,3-triazole (**1a**) (75.5 mg, 0.30 mmol), 1-iodo-3,5-bis(trifluoromethyl)benzene (**4e**) (153 mg, 0.45 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded **5e** (91 mg, 45%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (s, 1H), 7.58 (d, J = 2.9 Hz, 3H), 7.45 (s, 2H), 7.34 (s, 1H), 0.25 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 147.6 (C_q), 138.5 (C_q), 136.5 (C_q), 136.3 (C_q), 133.9 (C_q), 132.3 (q, $^{2}J_{C-F}$ = 33.8 Hz, C_q), 130.8 (C_q), 130.7 (C_q), 130.1 (CH), 128.5 (q, $^{3}J_{C-F}$ = 2.5 Hz, CH), 128.4 (CH), 122.9 (q, $^{1}J_{C-F}$ = 273.0 Hz, C_q), 122.2 (hept, $^{3}J_{C-F}$ = 3.1 Hz, CH), -1.3 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -63.0 (s). **IR** (ATR): $\tilde{\nu}$ = 1503, 1367, 1275, 1182, 1131, 1059, 1034, 834, 707, 681 cm^{-1}. **MS** (ESI) m/z (relative intensity): 395 $[M+Na]^+$ (50), 464 $[M+H]^+$ (100). **HR-MS** (ESI): m/z calcd for $C_{19}H_{19}{}^{35}ClN_3SiF_6^+$ $[M+H]^+$ 464.0779, found 464.0780.

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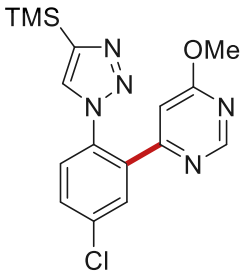
NMR Spectra



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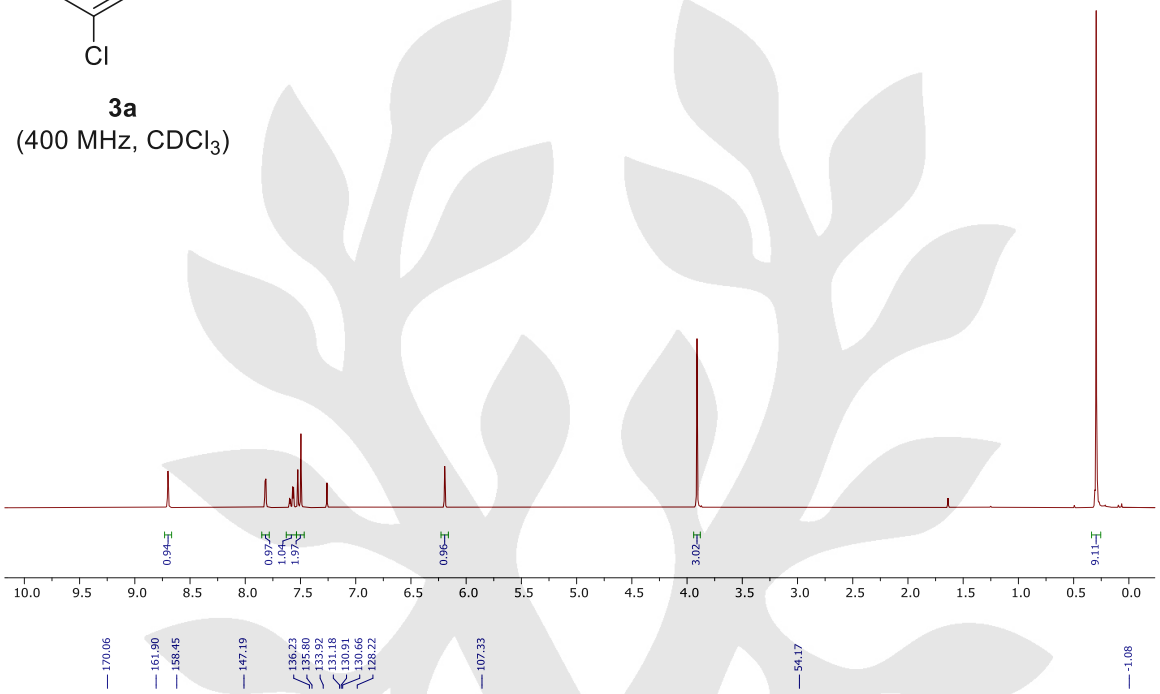
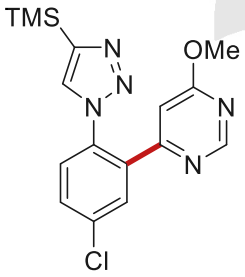
(400 MHz, $CDCl_3$)





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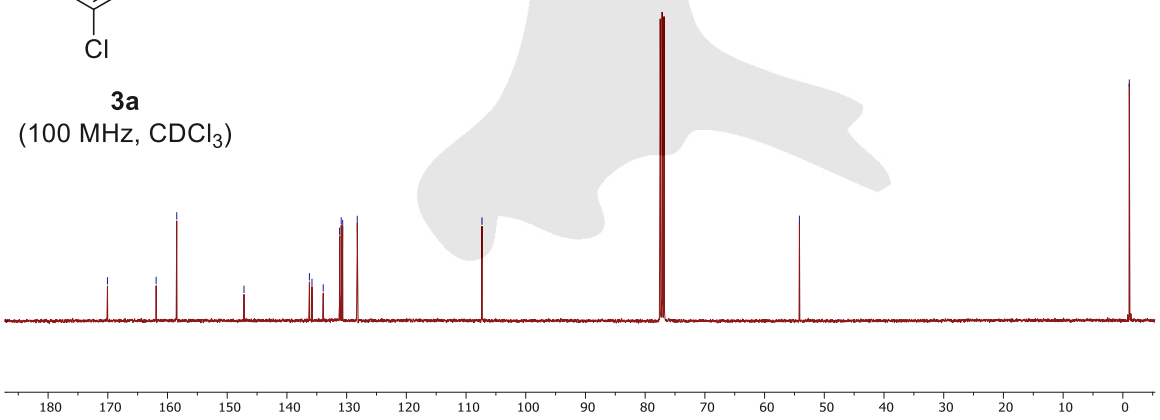

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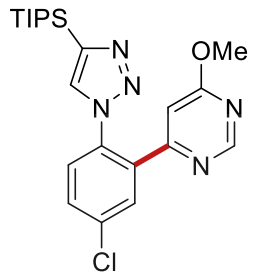

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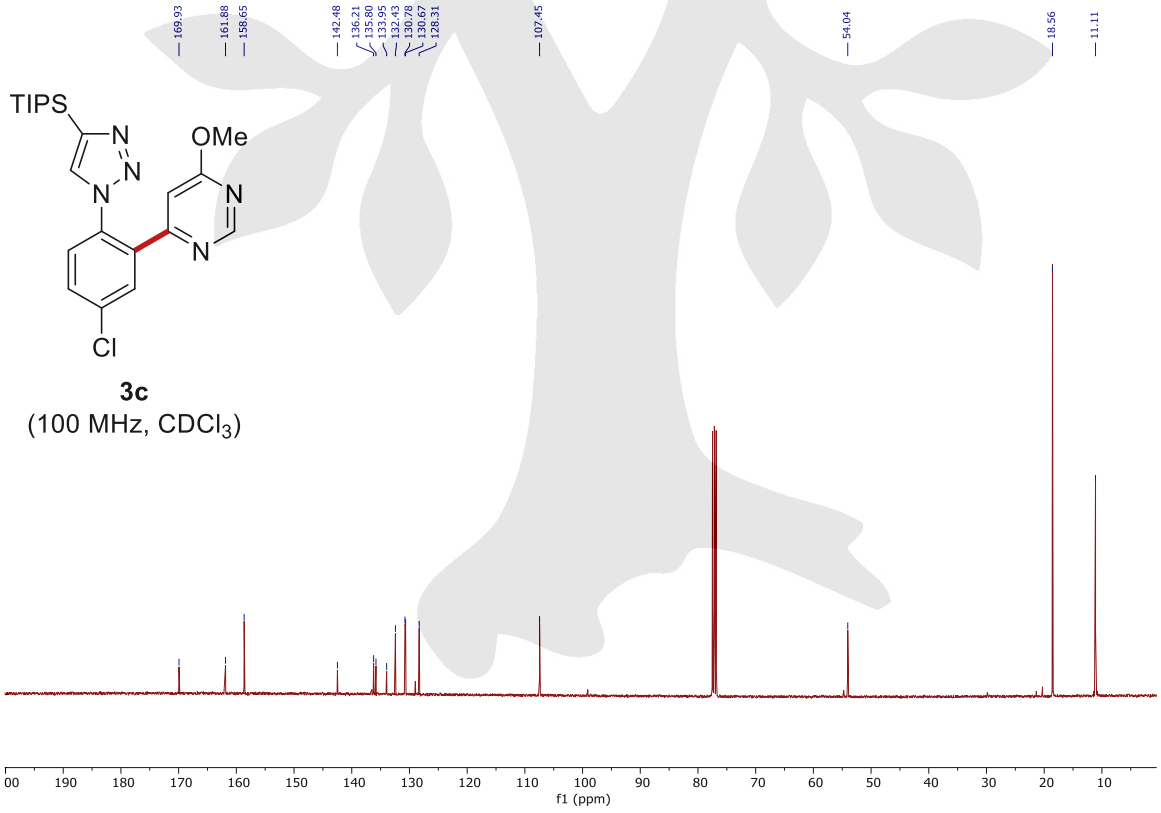

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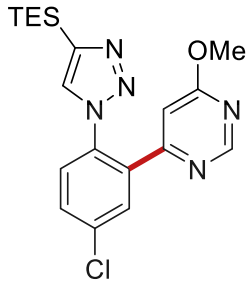

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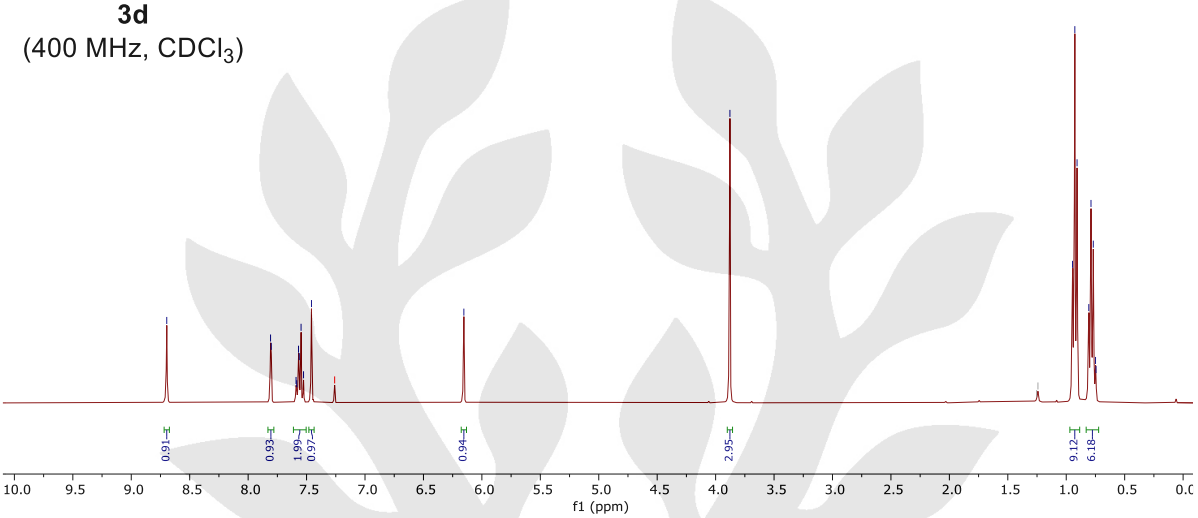

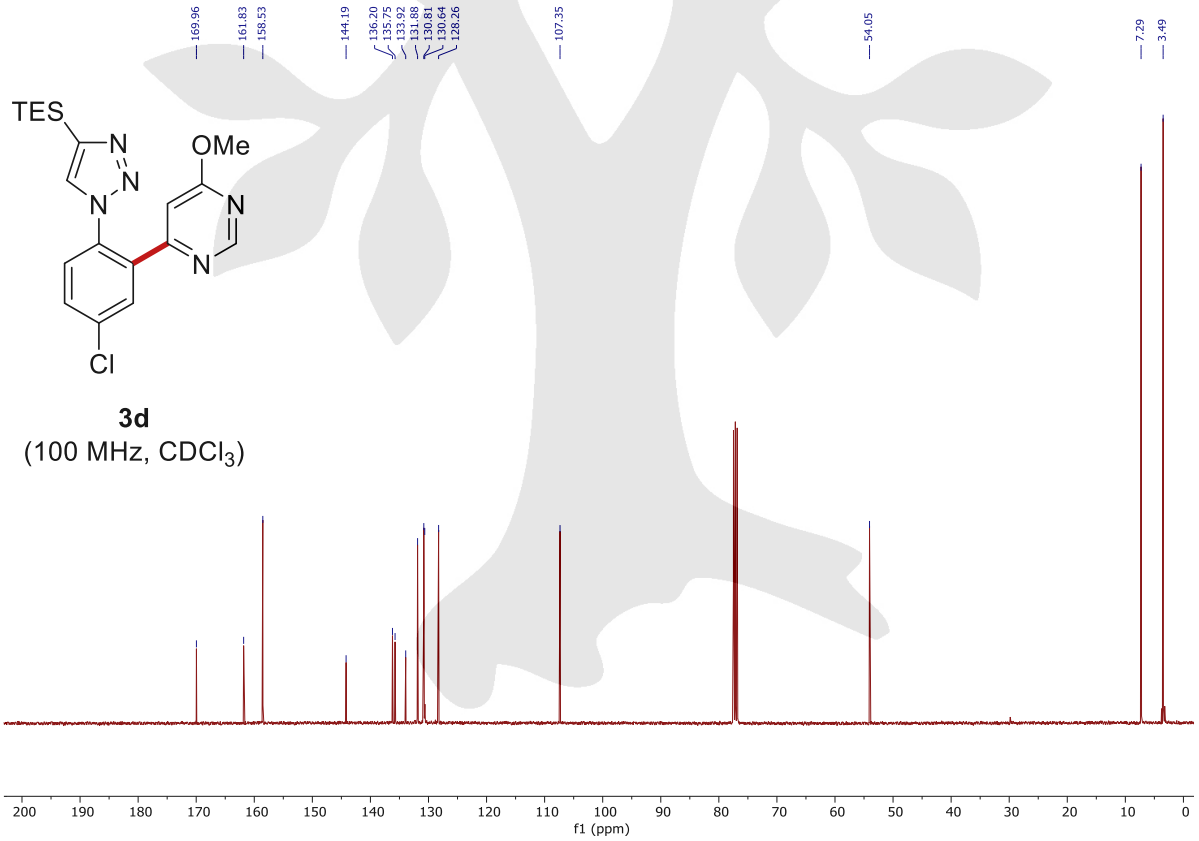

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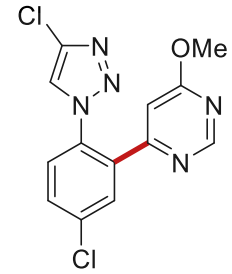

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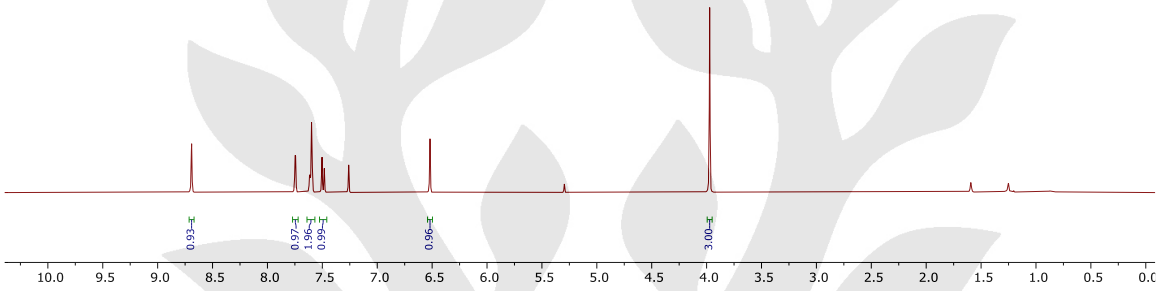

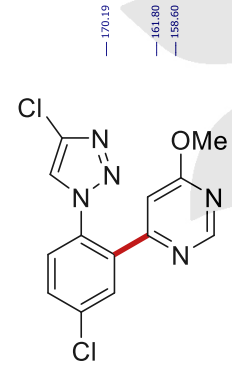

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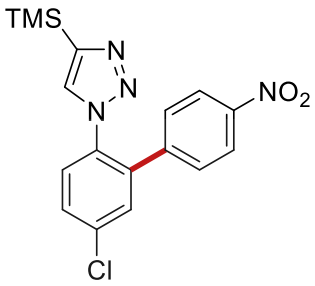

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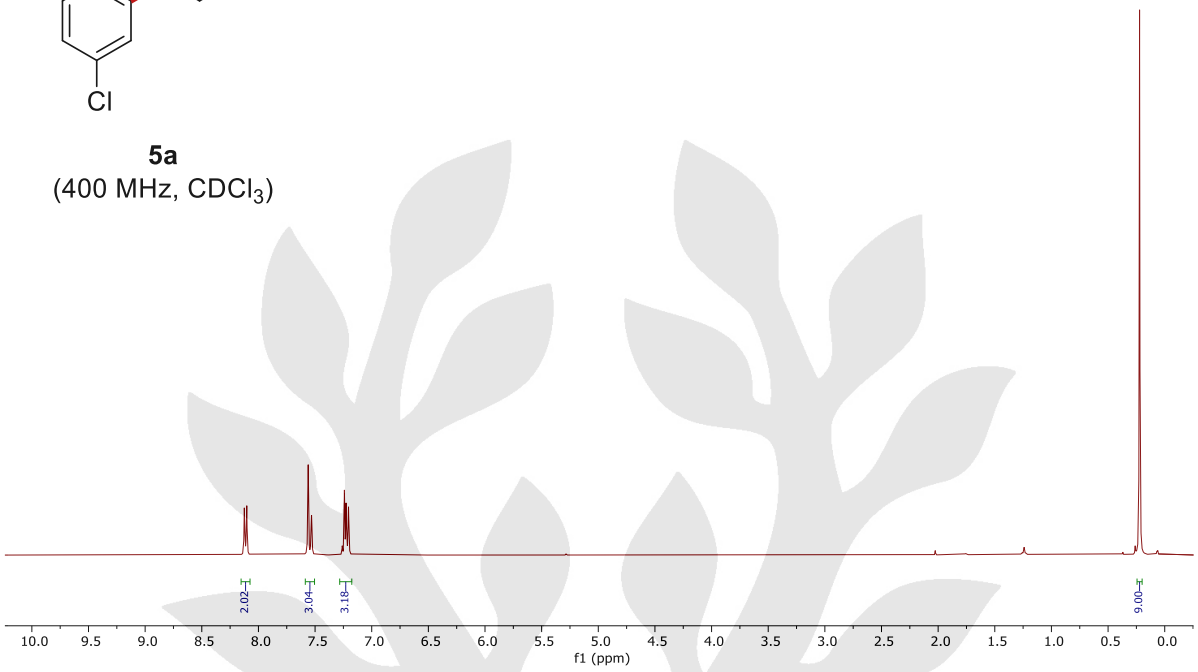

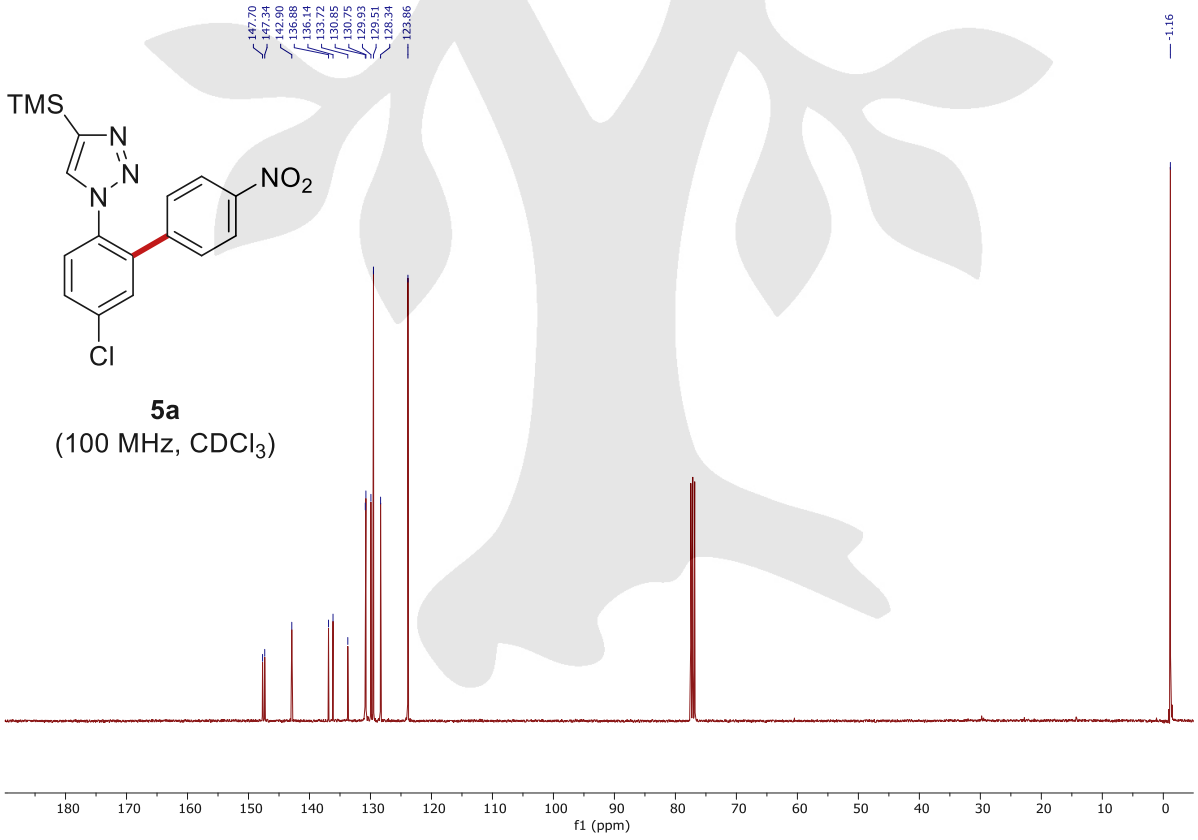

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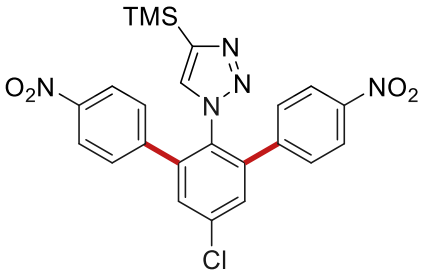

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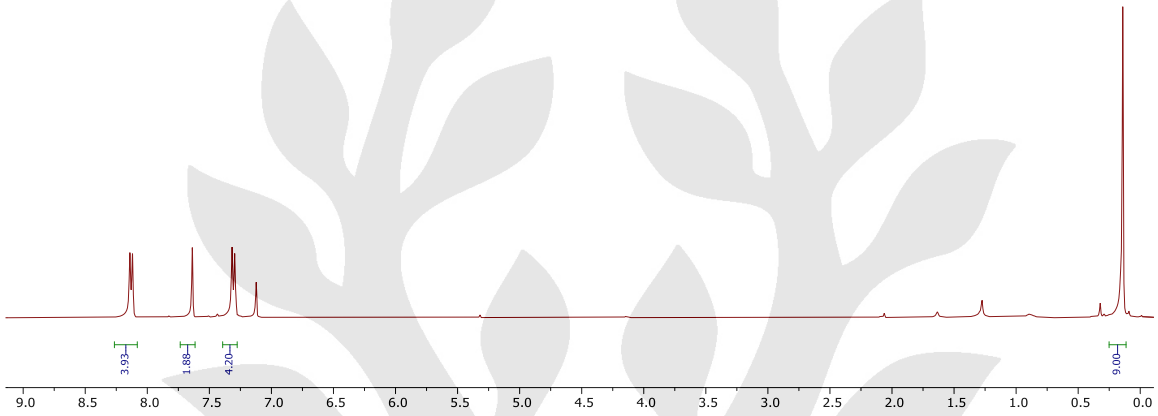

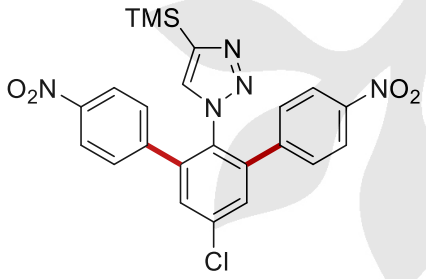

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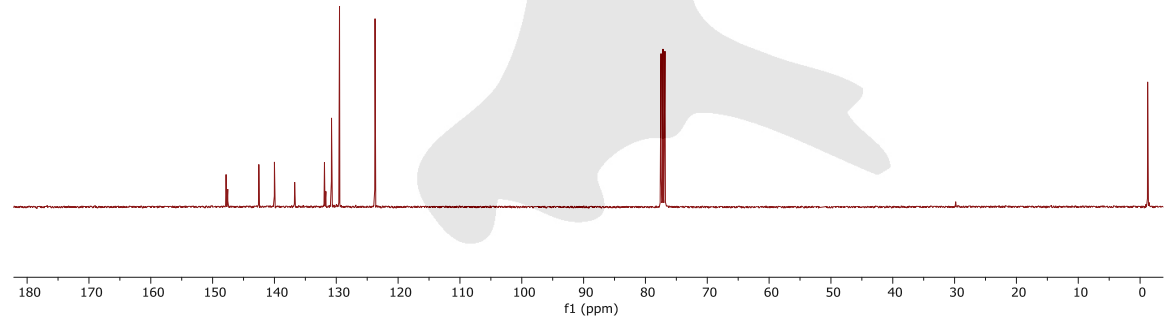

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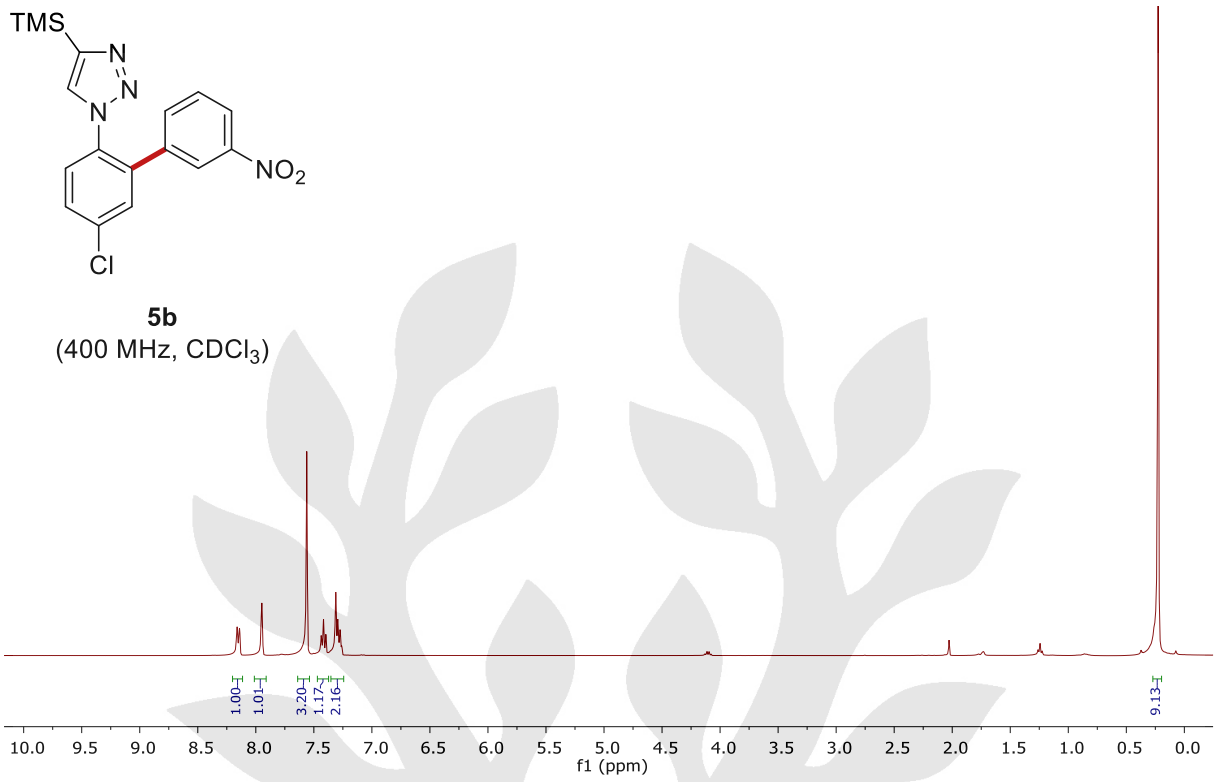

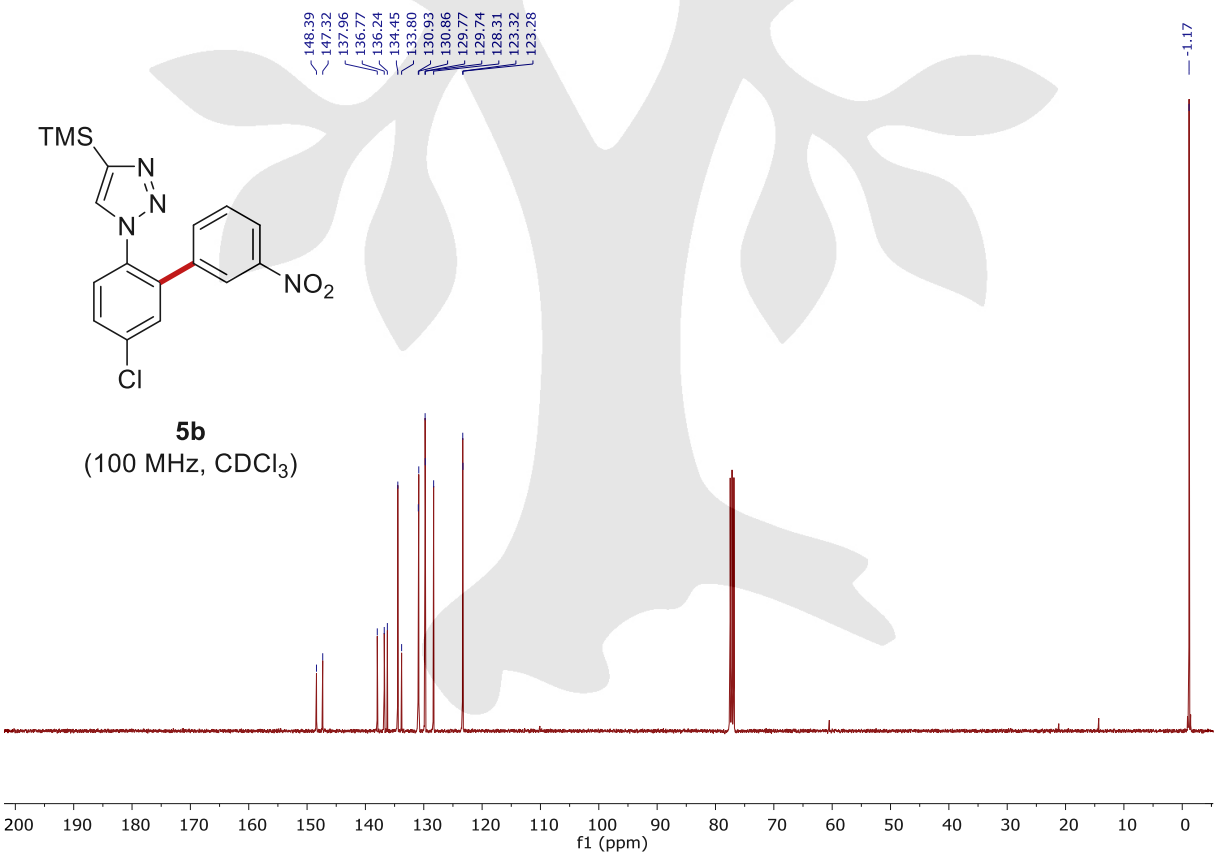

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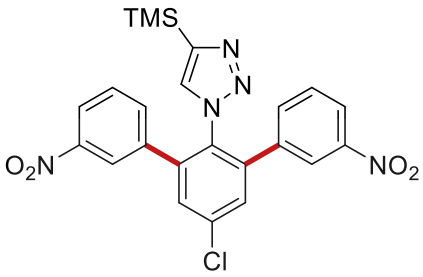

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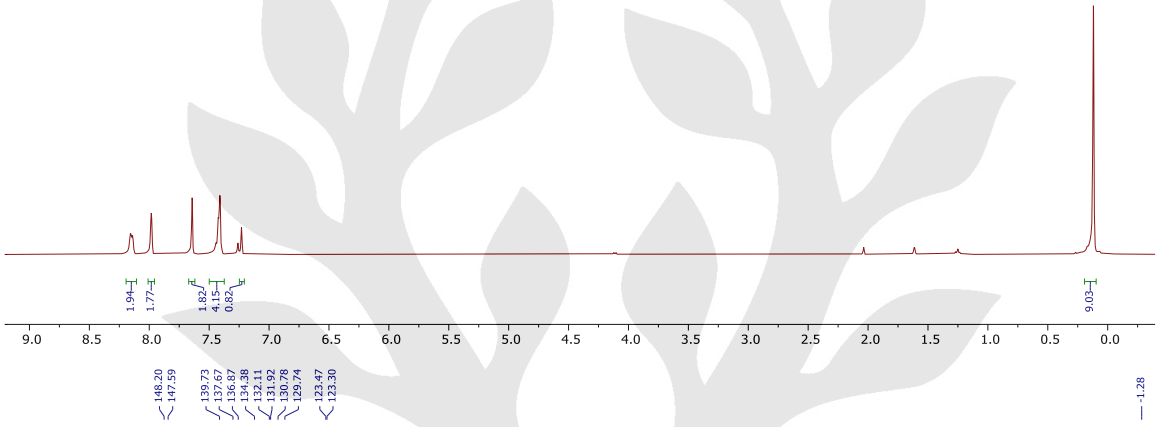

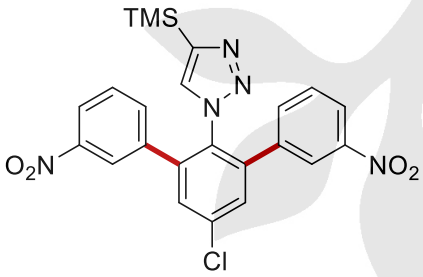

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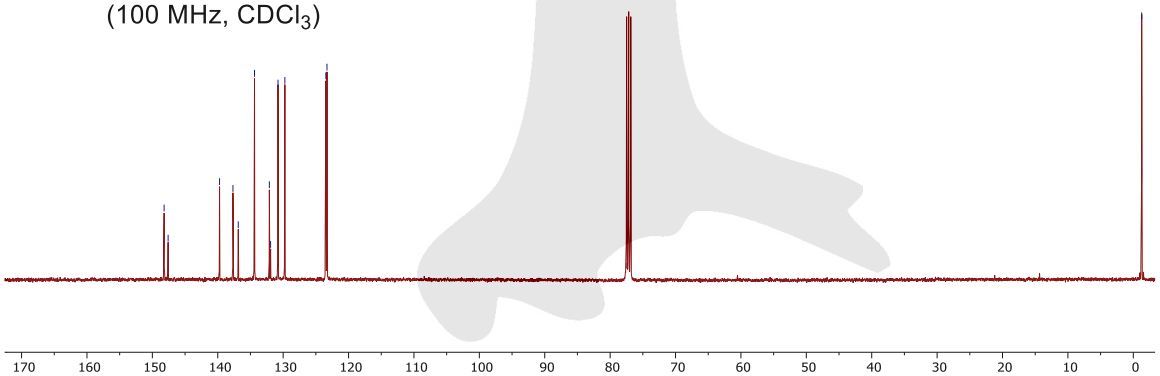

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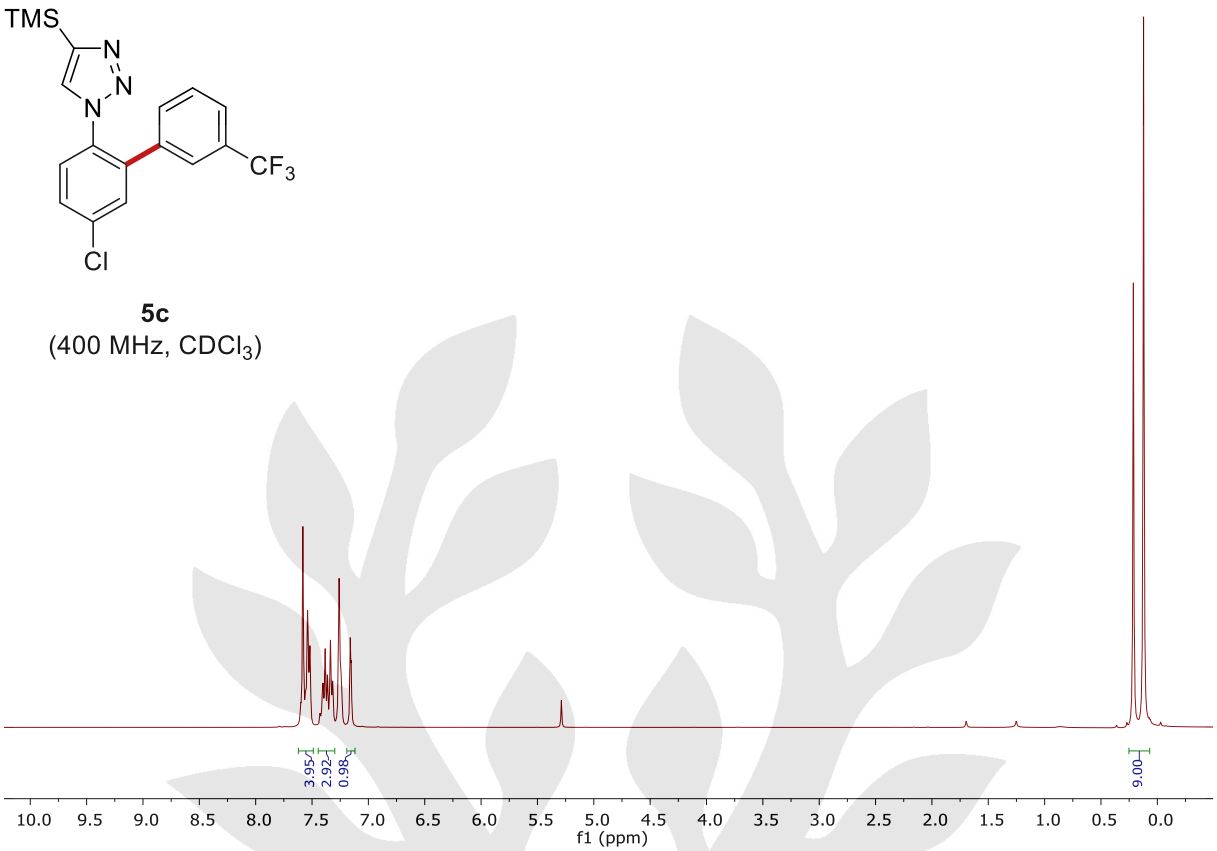

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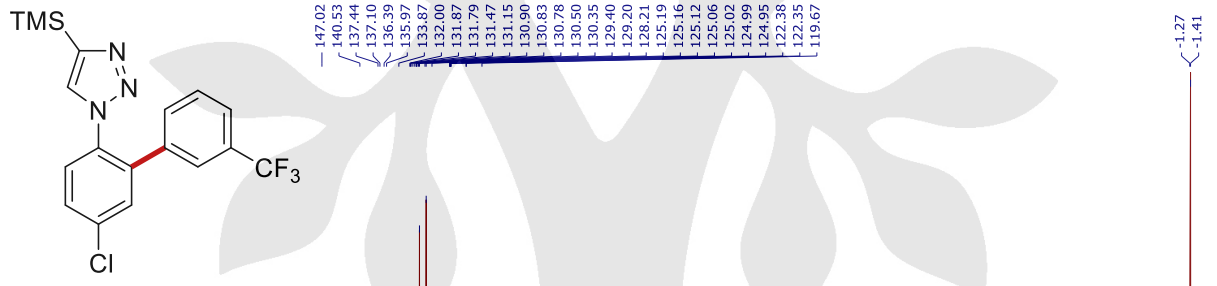

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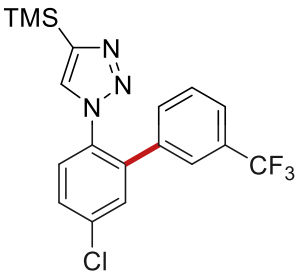

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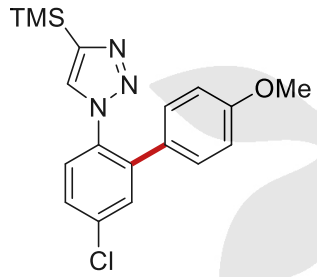

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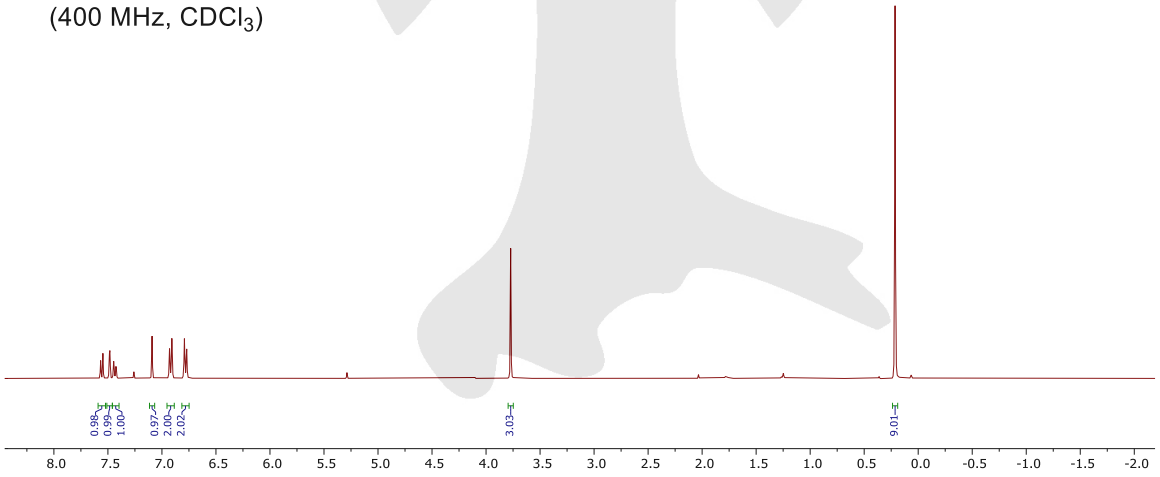

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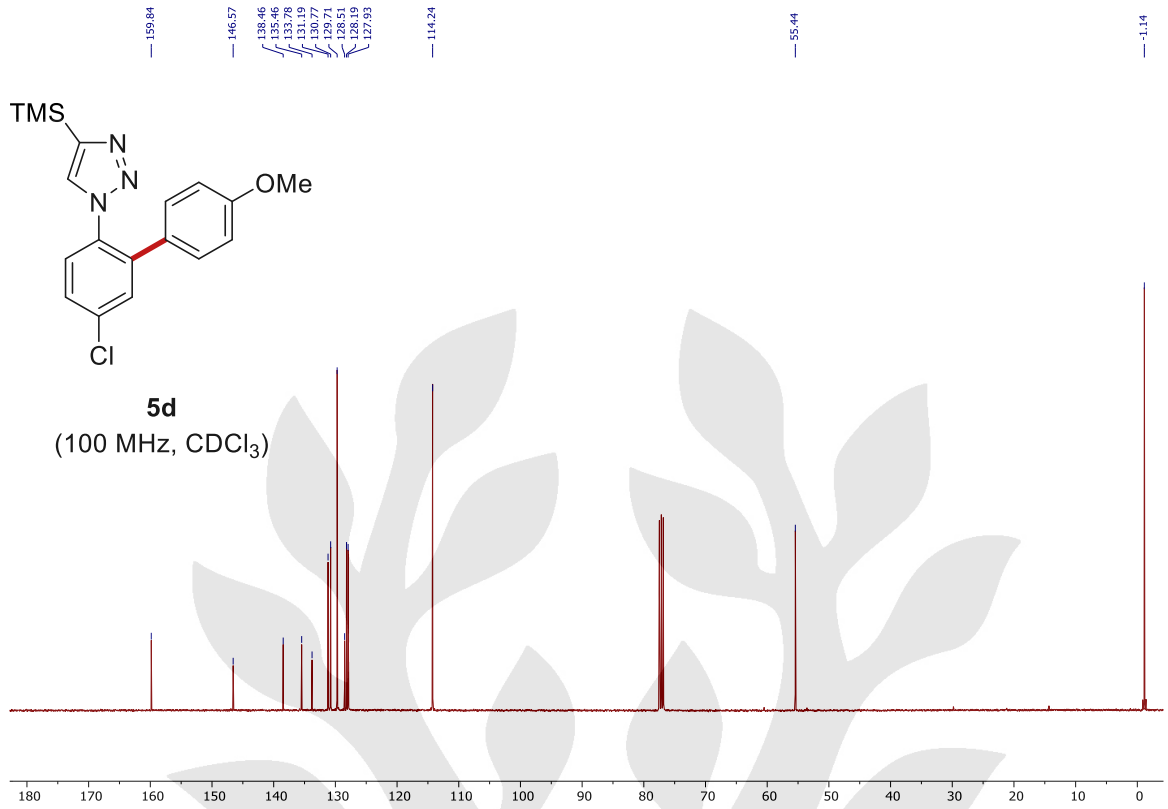

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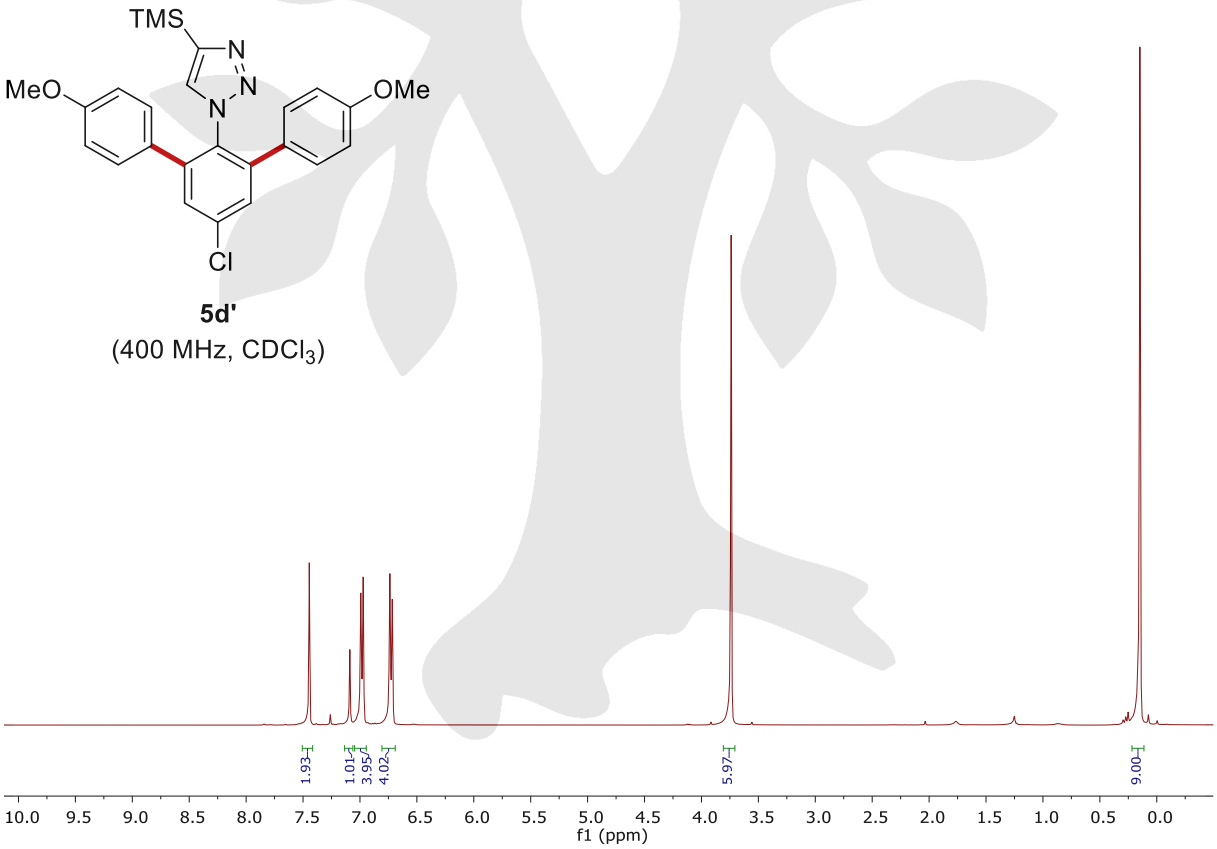

5d'

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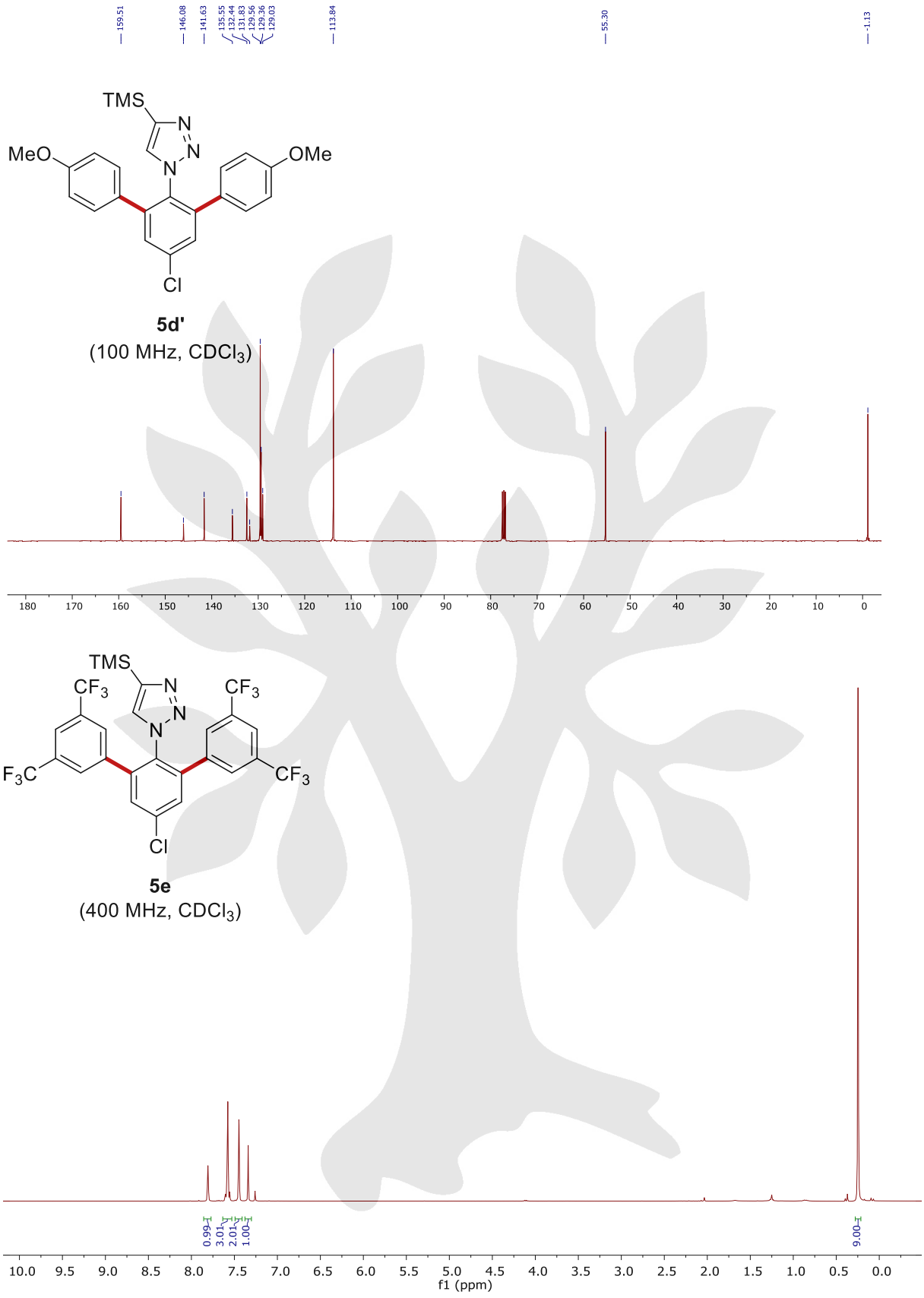

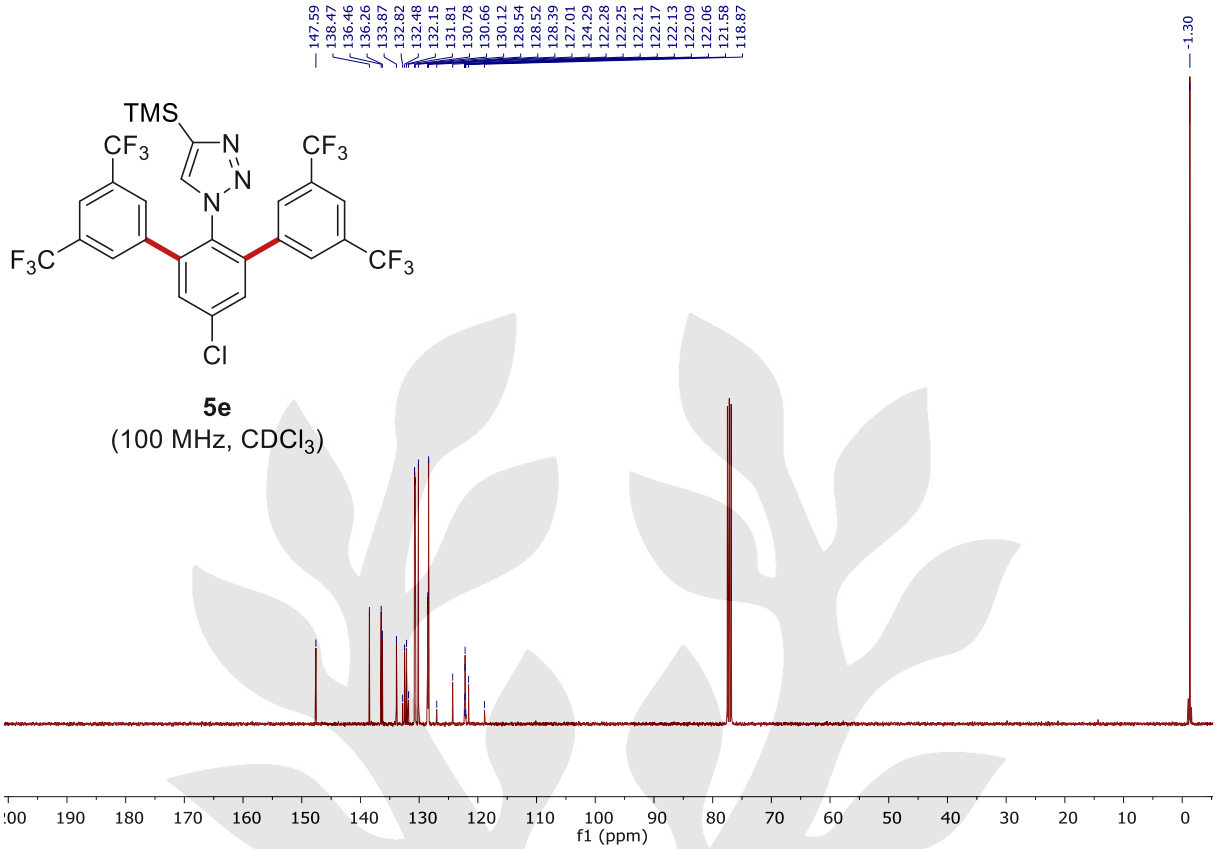

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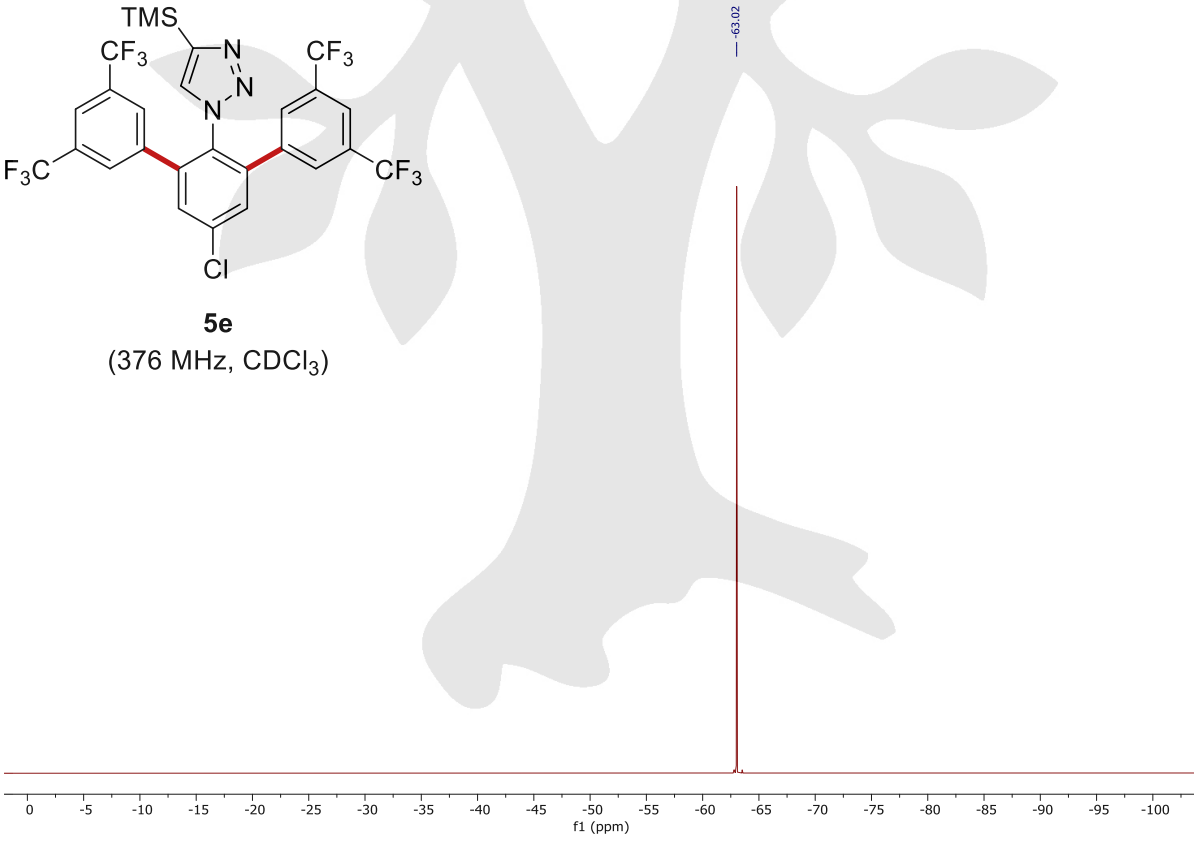

5e

(376 MHz, $CDCl_3$)

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