

Supporting Information

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Synthesis of 1-Haloethenamides from Ynamide through Halotrimethylsilane-mediated Hydrohalogenation

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a) **General:** All reactions sensitive to air or moisture were carried out under argon atmosphere and anhydrous conditions unless otherwise noted. Dry solvents were purchased from Wako Pure Chemicals., LTD. and used without further purification and dehydration. All reagents were purchased and used without further purification. Column chromatography was carried out with silica gel, Silica Gel 60 N that is purchased from Kanto Chemical Co., Inc. ¹H and ¹³C NMR spectra were recorded on a BRUKER-SPECTRON-400 with a 5 mm QNP probe at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in δ (ppm) with reference to residual solvent signals [¹H NMR: CHCl₃ (7.26); ¹³C NMR: CDCl₃ (77.0)]. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

b) **Preparation of 1 M halotrimethylsilane (TMSX) stock solution in dichloromethane:** 2.6 g of TMSCl (Wako Pure Chemicals, Co., LTD.) was added to 21 mL of dry CH₂Cl₂, and 3.5 of TMSBr (Tokyo Chemical Industry Co., LTD.) was added to 20 mL of dry CH₂Cl₂, and each was used as a 1 M TMSX

solution. As for TMSI, we purchased the seal-tubed version in neat form from Tokyo Chemical Industry Co., LTD, and it included a portion of Al metal inside the tube for inhibiting the decomposition of TMSI. 5 g of TMSI was added to 25 mL of dried CH₂Cl₂ along with the Al metal as a solid, thus providing colorless 1 M stock solution for our experimental usage. The Al metal would not have a crucial role for the reactivity of the TMSI solution: actually, the reactivity of the freshly prepared TMSI solution was not influenced by with or without the metal. The stock solution in the presence of the Al metal was stable for at least two weeks, although it turned to slightly red colored solution. However, in the case of 1 M toluene solution, unfortunately, complete decomposition on ¹H NMR spectra was observed only in 24 h.

c) **General procedure for hydrohalogenation of terminal alkynes in ynamides, and characterization of compound 2-6;**

***N*-(1-bromovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (2):** To a solution of **1** (0.5 mmol) in anhydrous CH₂Cl₂ (4 mL) at -78 °C was added TMSBr (1 M in CH₂Cl₂) dropwise over 5 min, and the mixture was stirred for 10 min. Then, H₂O (10 mmol) was added, and the cooling-bath was removed to warm to room temperature. After additional stirring for 50 min, the reaction was quenched at 0 °C with saturated aqueous sodium thiosulfate, and stirred for 30 min, and allowed to warm to ambient temperature. To the mixture was added CH₂Cl₂, and organic phases were washed with brine, and then dried over Na₂SO₄, and concentrated to give a crude product. Purification by silica gel column chromatography (eluent; hexane/EtOAc = 4/1) afforded **2** in 89% yield (157 mg) as white solid materials. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.38-7.28 (m, 7H), 5.98 (d, *J* = 1.9 Hz, 1H), 5.68 (d, *J* = 1.9 Hz, 1H), 2.44 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 144.8, 138.6, 136.3, 129.9, 129.5, 129.0, 128.62, 128.57, 126.0, 122.8, 21.9. MS (DI) *m/z*: 351 (MH⁺), 272 ([MH-Br]⁺). IR (neat): 3117 (C=C), 3032, 1344 (NSO₂), 1233, 1162 cm⁻¹. HRMS (DI) calcd for C₁₅H₁₄(79)BrNO₂S 350.9929, found 350.9913.

***N*-(1-chlorovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (3):** 92% yield (141 mg); whitish yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.37-7.27 (m, 7H), 5.58 (d, *J* = 1.8 Hz, 1H), 5.46 (d, *J* = 1.8 Hz, 1H), 2.44 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 138.4, 136.3, 136.2, 129.8, 129.5, 129.0, 128.7, 128.5, 117.7, 21.9. MS (DI) *m/z*: 307 (MH⁺), 272 ([MH-Cl]⁺). IR (neat): 3124 (C=C), 3036, 1343 (NSO₂), 1162 cm⁻¹; HRMS (DI) calcd for C₁₅H₁₄ClNO₂S 307.0434, found 307.0425.

***N*-(1-iodovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (4):** 90% yield (180

mg); white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, $J = 8.3$ Hz, 2H), 7.39-7.27 (m, 7H), 6.41 (d, $J = 1.4$ Hz, 1H), 5.96 (d, $J = 1.4$ Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.7, 138.8, 136.4, 131.1, 129.9, 129.5, 128.9, 128.5, 128.2, 100.2, 21.9. IR (neat): 3107 (C=C), 1610, 1590, 1487, 1346 (NSO_2), 1231 (NSO_2), 1162 (NSO_2) cm^{-1} . MS (EI) m/z : 399 (M^+), 272 ($[\text{M}-\text{I}]^+$). HRMS (DI) calcd for $\text{C}_{15}\text{H}_{14}\text{INO}_2\text{S}$: 398.9790, found 398.9807.

***N*-allyl-*N*-(1-iodovinyl)-4-methylbenzenesulfonamide (5):** 95% yield (129 mg); white solid. ^1H NMR (400 MHz, C_6D_6) δ 7.73 (d, $J = 8.4$ Hz, 2H), 6.74 (d, $J = 8.4$ Hz, 2H), 5.60 (dddd, $J = 17.0, 11.8, 6.5, 6.5$ Hz, 1H), 5.40 (d, $J = 1.5$ Hz, 1H), 5.13 (d, $J = 1.5$ Hz, 1H), 5.03 (ddd, $J = 17.0, 2.7, 1.2$ Hz, 1H), 4.93 (dddd, $J = 11.8, 6.5, 2.7, 1.2$ Hz, 1H), 3.8 (ddd, $J = 6.5, 1.2, 1.2$ Hz, 2H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 144.1, 136.2, 134.9, 132.0, 129.8, 128.4, 119.6, 119.4, 50.5, 21.2. IR (neat): 3066, 2923, 1630, 1596, 1354, 1337, 1162, 1081 cm^{-1} . MS (EI) m/z : 271 (M^+). HRMS (DI) calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2\text{S}$: 271.0434, found 271.0447.

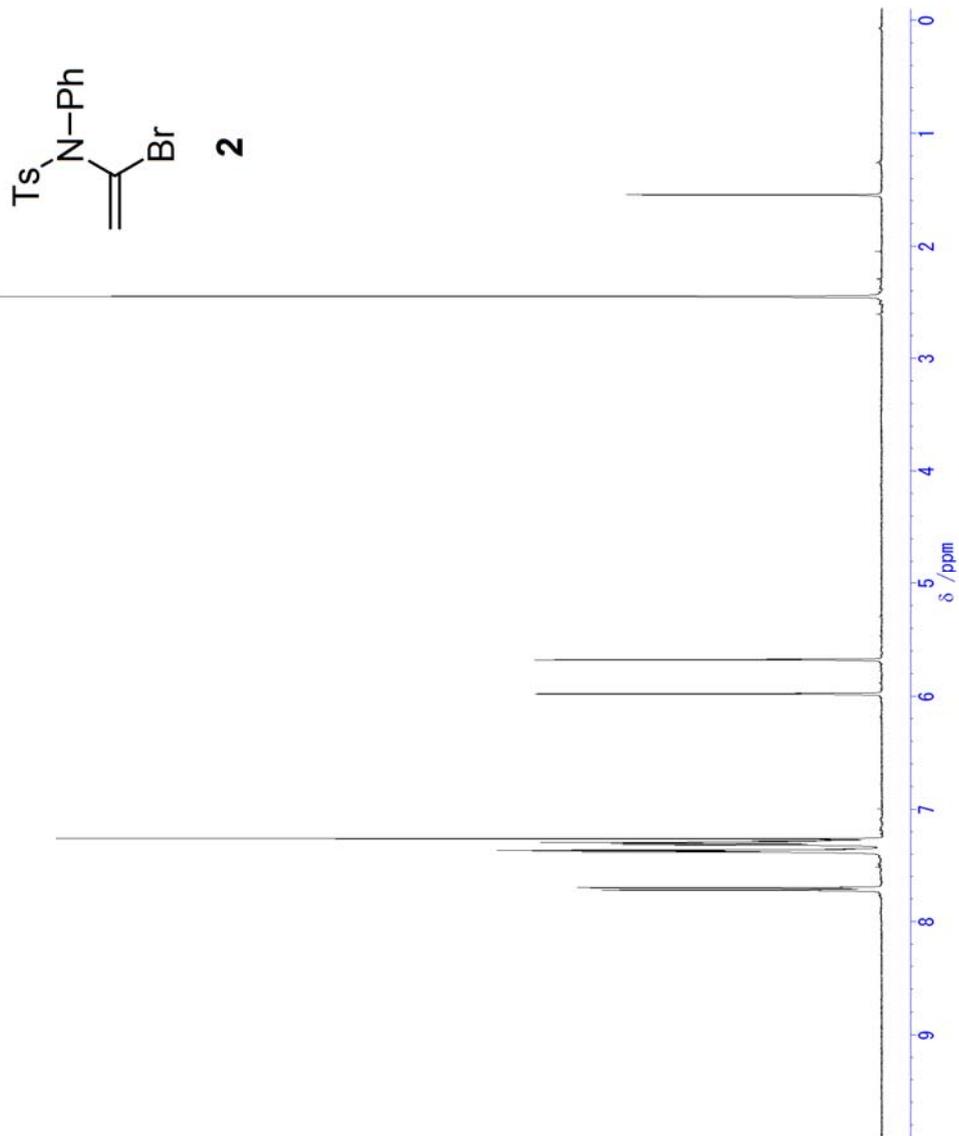
***N*-(1-iodovinyl)-4-methyl-*N*-*p*-tolylbenzenesulfonamide (6):** 98% yield (157 mg); white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, $J = 8.4$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 2H), 7.15 (s, 4H), 5.56 (d, $J = 1.8$ Hz, 1H), 5.43 (d, $J = 1.8$ Hz, 1H), 2.44 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.6, 139.2, 136.42, 136.40, 135.7, 130.2, 129.8, 128.7, 128.5, 117.3, 21.9, 21.4. This compound was too fragile to obtain accurate data of HRMS and IR: as described in the manuscript, compound **6** totally decomposed in *ca.* 4 h.

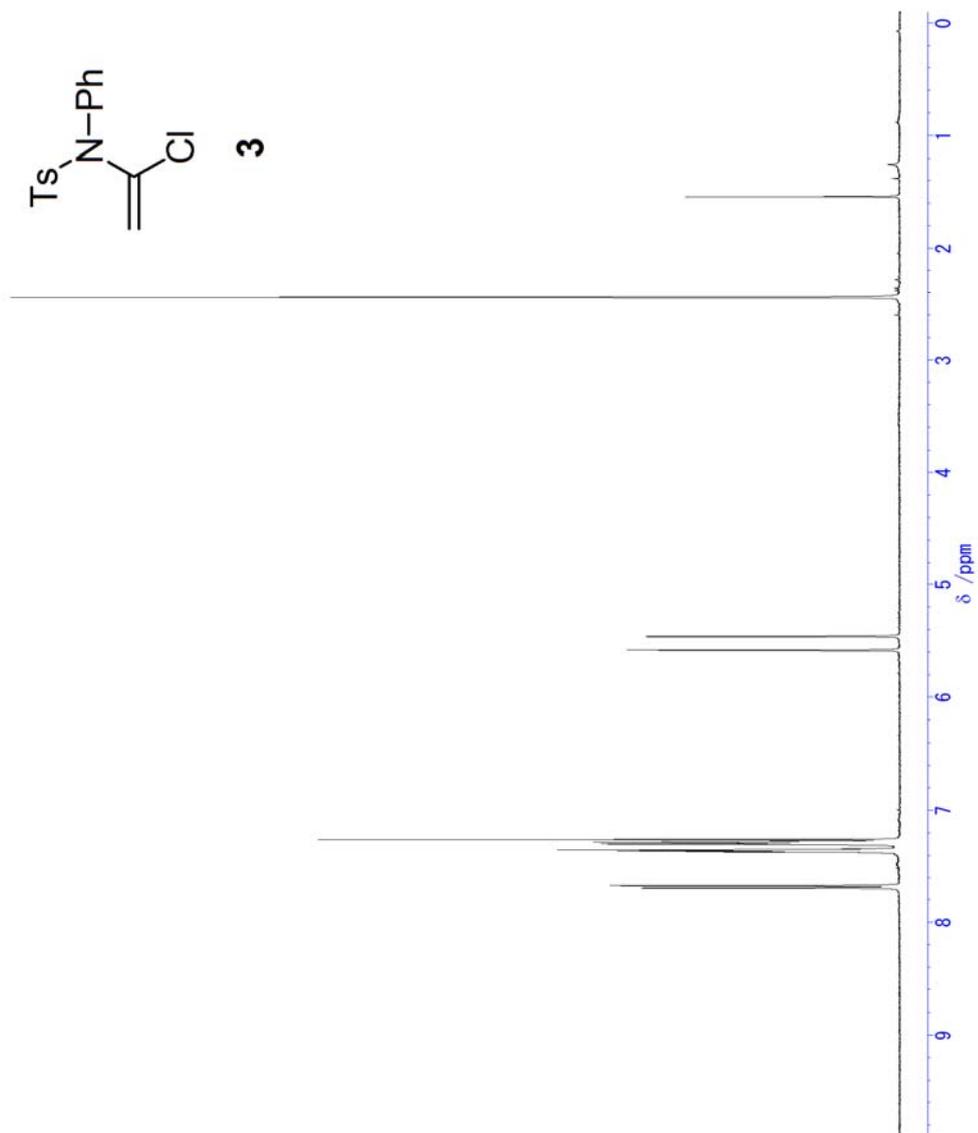
d) **General procedure for Sonogashira cross-coupling reaction in Table 5, entry 1, and characterization of compound 7-9; 4-methyl-N-phenyl-N-(4-(trimethylsilyl)but-1-en-3-yn-2-yl)benzenesulfonamide (7):** To a mixture of diisopropylamine (2.2 mL) and toluene (2.2 mL) were added **2** (224 mg, 0.56 mmol), Pd(PPh₃)₄ (69 mg, 0.06 mmol), CuI (21 mg, 0.11 mmol), and trimethylsilylacetylene (82 mg, 0.84 mmol), and the mixture was stirred at 0 °C for 15 min. After the reaction was conducted at room temperature for 18 h, the solvent was evaporated. To the residue was added ethylacetate, and the insoluble materials were filtered out. The solution was concentrated *in vacuo* to give a crude, and the purification by silica gel column chromatography was performed to afford the desired molecule **7** in 66% yield (137 mg) as brown needles. ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.33-7.25 (m, 7H), 5.68 (s, 1H), 5.54 (s, 1H), 2.43 (s, 3H), 0.06 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 143.9, 139.8, 137.0, 129.5, 129.23, 129.18, 129.1, 128.44, 128.38, 122.3, 100.7, 96.8, 21.8, -0.4. IR (neat): 3074 (C=C), 2960, 2151, 2138, 1590, 1488, 1350 (NSO₂), 1167 (NSO₂) cm⁻¹. MS (EI) *m/z*: 369 (M⁺), 214 ([M-Ts]⁺), 220 ([MH-Ph-CH₃Ph]⁺). HRMS (DI) calcd for C₂₀H₂₄NO₂SSi ([MH]⁺): 370.1298, found 370.1306.

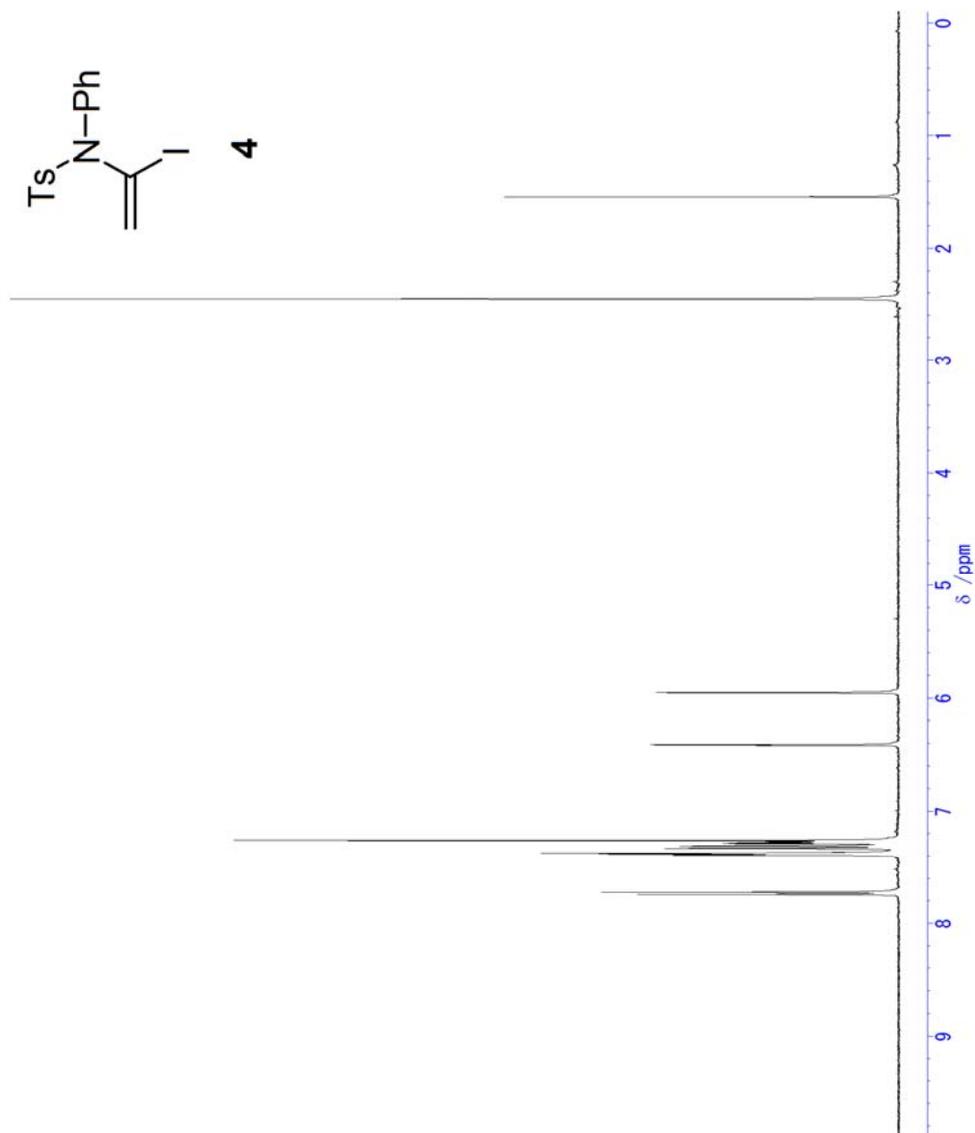
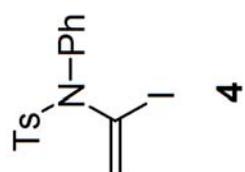
4-methyl-N-phenyl-N-(4-phenylbut-1-en-3-yn-2-yl)benzenesulfonamide (8): 74% yield (183 mg); yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.37-7.18 (m, 12H), 5.69 (s, 1H), 5.59 (s, 1H), 2.40 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 144.0, 140.1, 137.1, 131.8, 129.6, 129.43, 129.41, 129.18, 129.17, 128.6, 128.52, 128.50, 122.2, 121.8, 91.0, 86.0, 21.9. IR (neat): 3060, 2923, 2204, 1594, 1488, 1352, 1157, 1089 cm⁻¹. MS (EI) *m/z*: 373 (M⁺). HRMS (DI) calcd for C₂₃H₁₉NO₂S: 373.1136, found 373.1156.

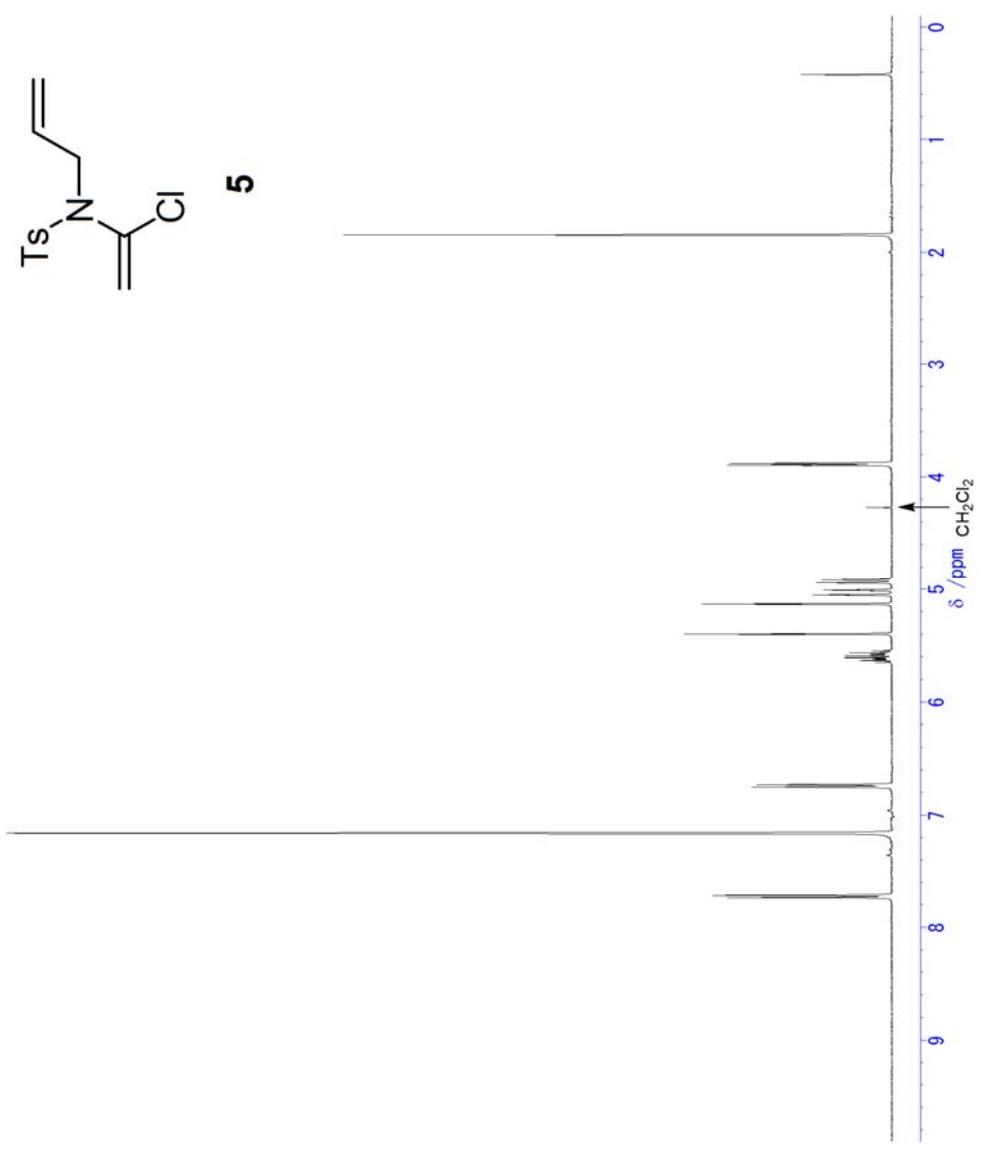
N-(4-(3-chlorophenyl)but-1-en-3-yn-2-yl)-4-methyl-N-phenylbenzenesulfonamide (9): 75% yield (199 mg); orange viscous materials. ¹H NMR (400 MHz, C₆D₆) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.46-7.44 (m, 2H), 7.06-6.96 (m, 4H), 6.87-6.84 (m, 2H), 6.67 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 8.0 Hz, 1H), 5.65 (s, 1H), 5.41 (s, 1H), 1.84 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 143.7, 140.7, 137.8, 134.3, 131.6, 129.89, 129.86, 129.7, 129.6, 129.4, 129.3, 129.2, 128.6, 128.5, 124.1, 121.9, 89.4, 87.6, 21.2. IR (neat) 3061, 2922, 2201, 1591, 1488, 1354, 1159, 1090 cm⁻¹. MS (EI) *m/z*: 407 (M⁺). HRMS (DI) calcd for C₂₃H₁₈ClNO₂S (M⁺): 407.0747, found 407.0751.

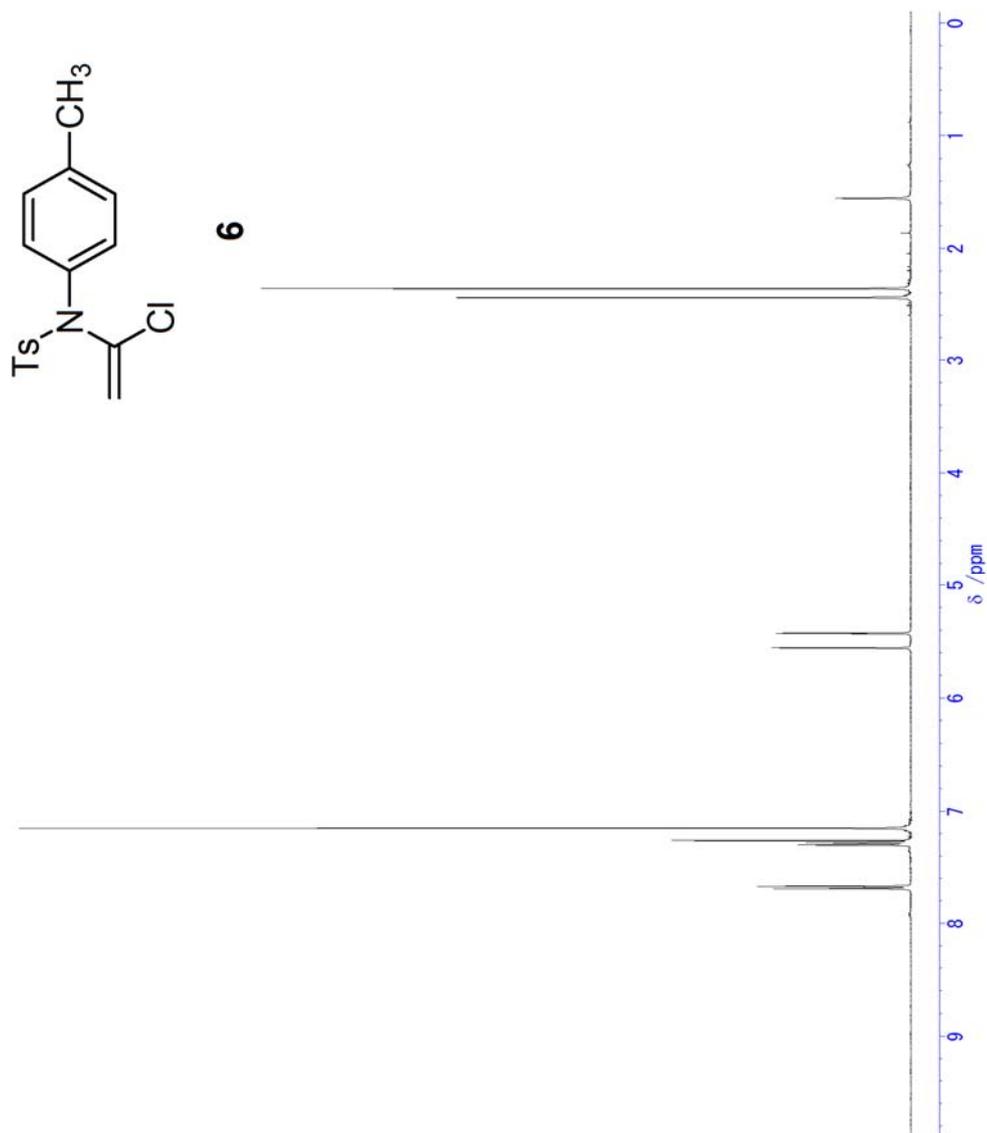
e) ^1H & ^{13}C NMR spectra of newly synthesized compounds 2-9.

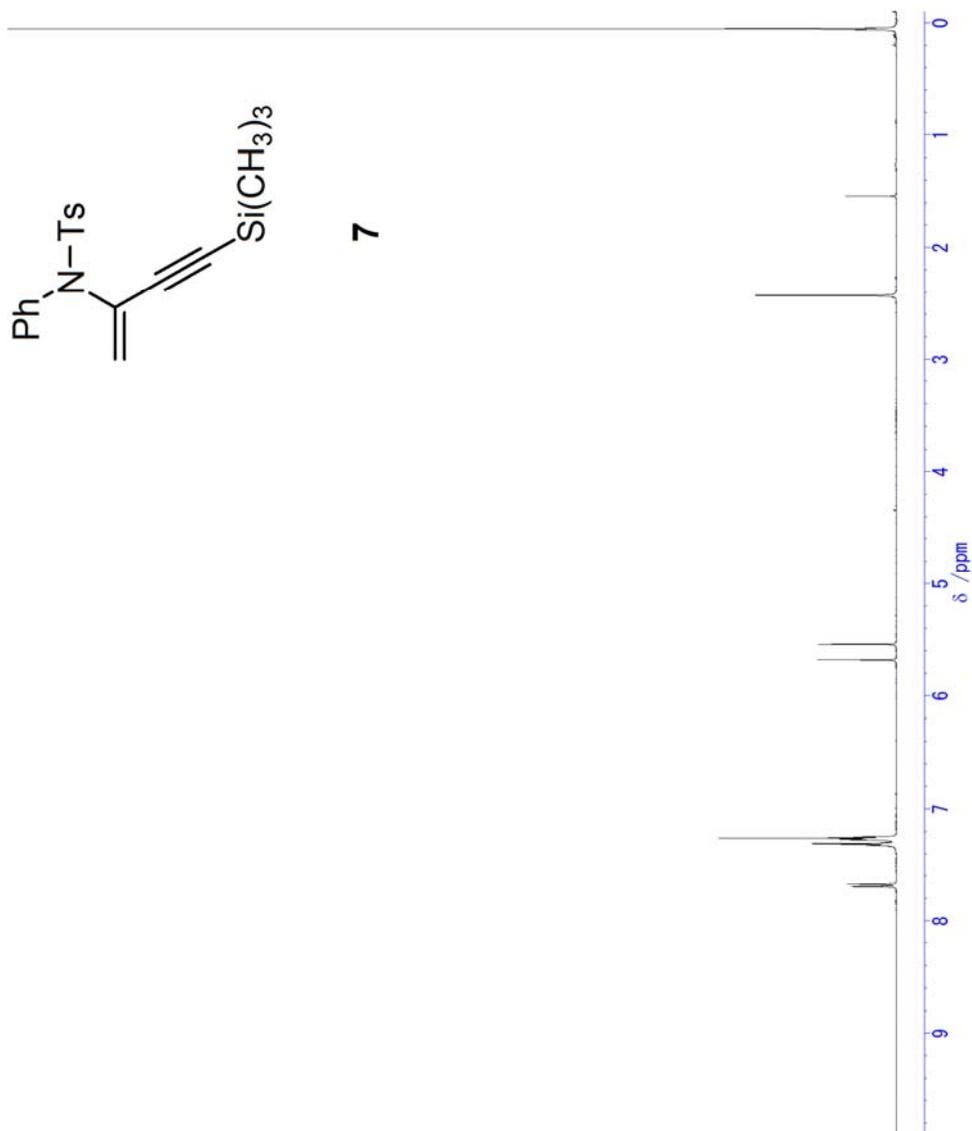


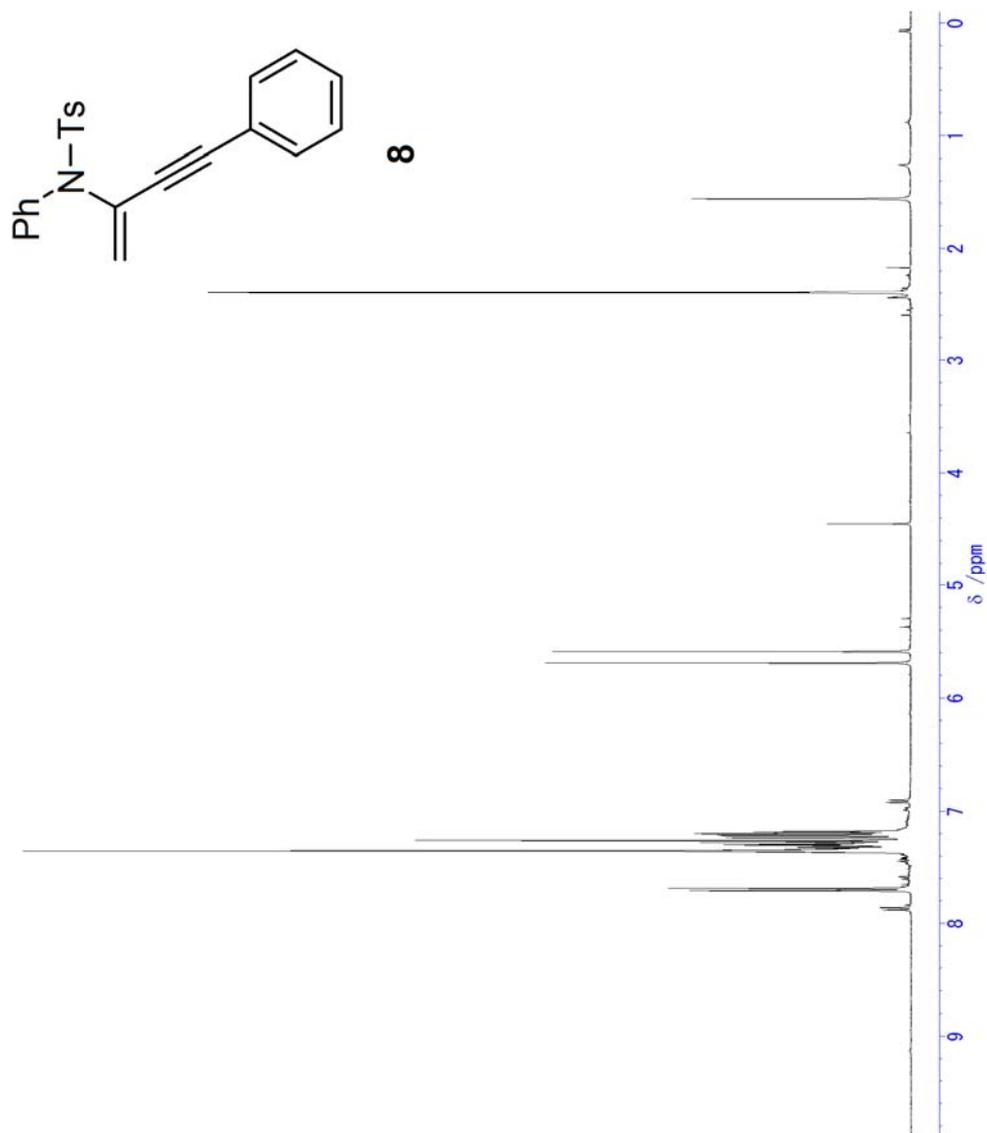


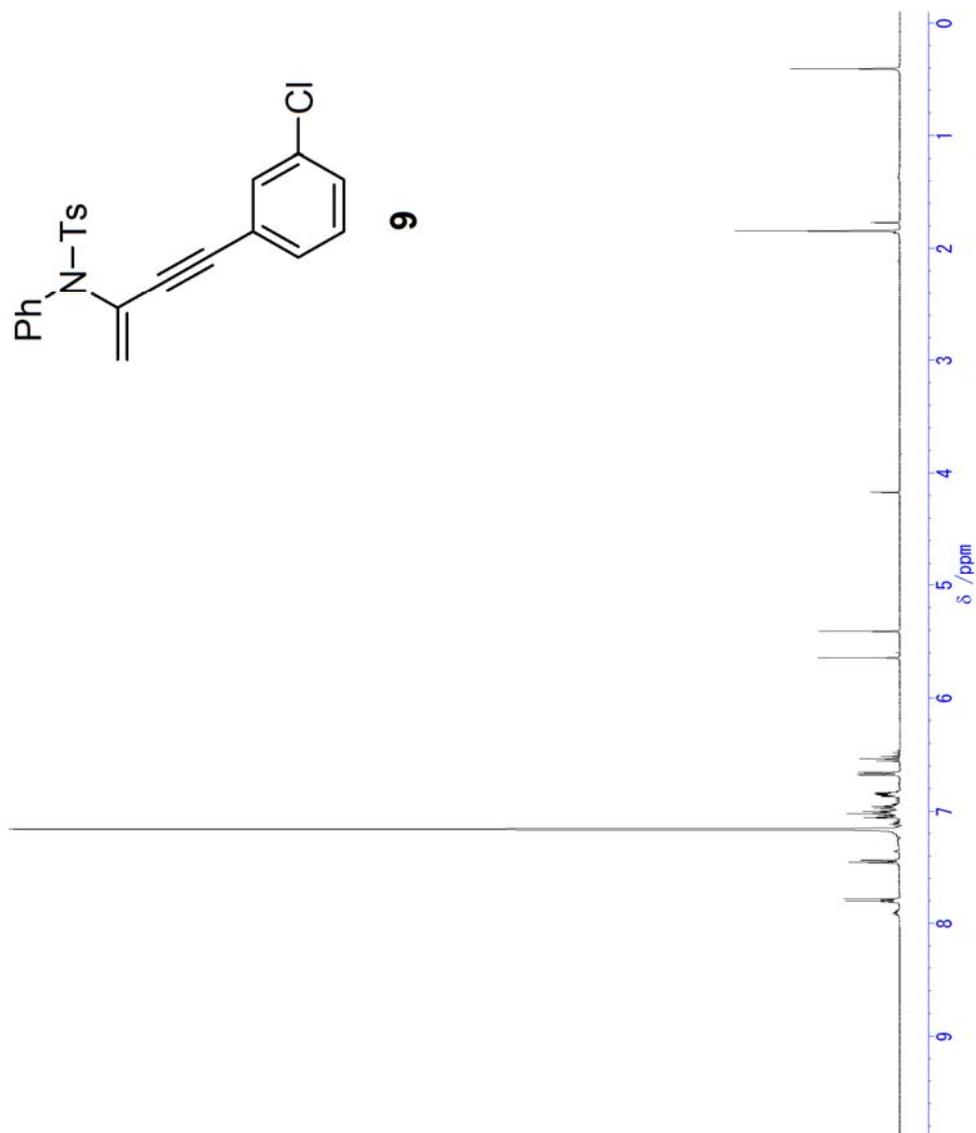
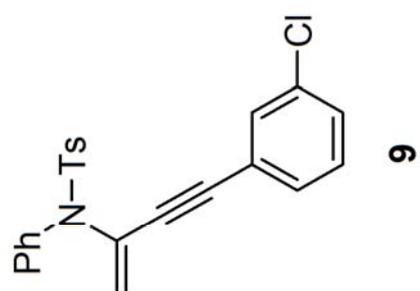


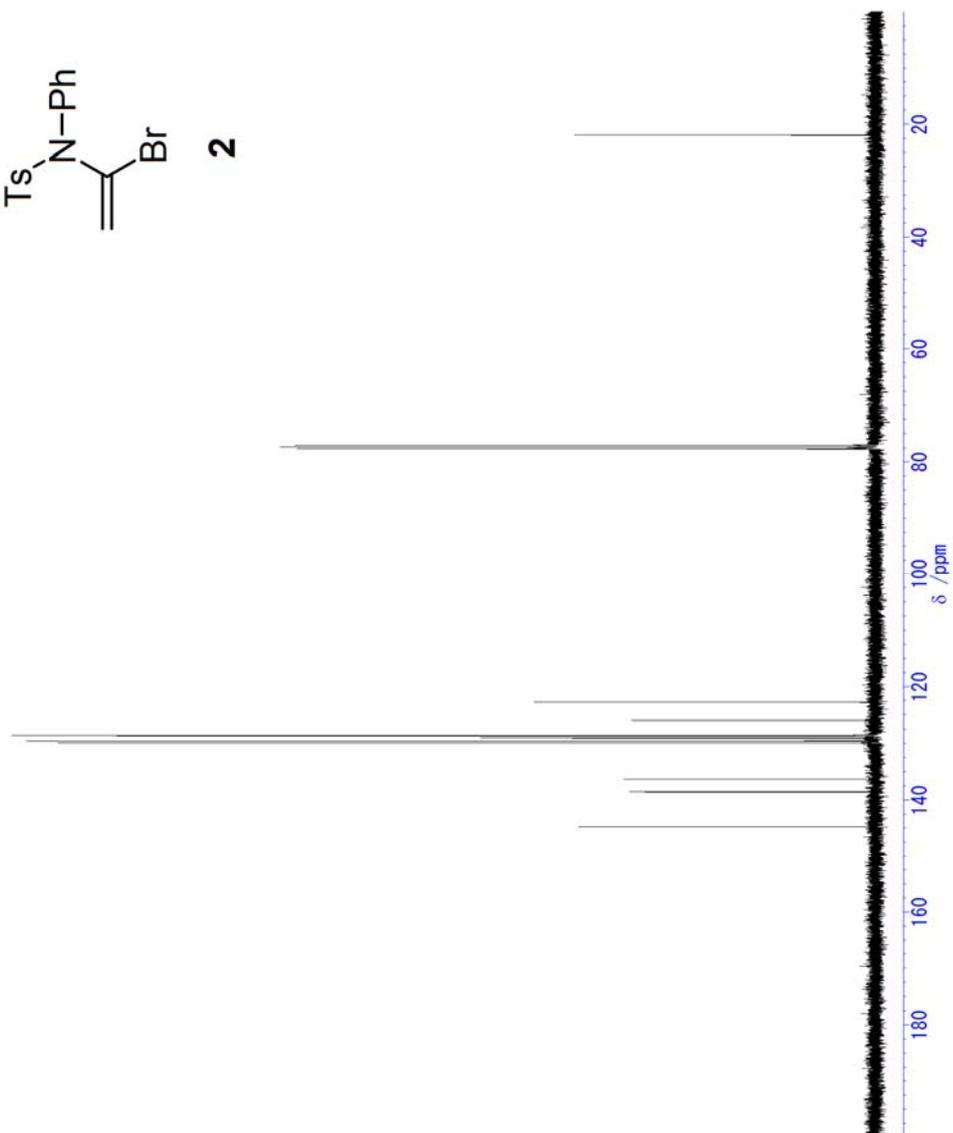
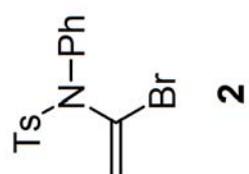


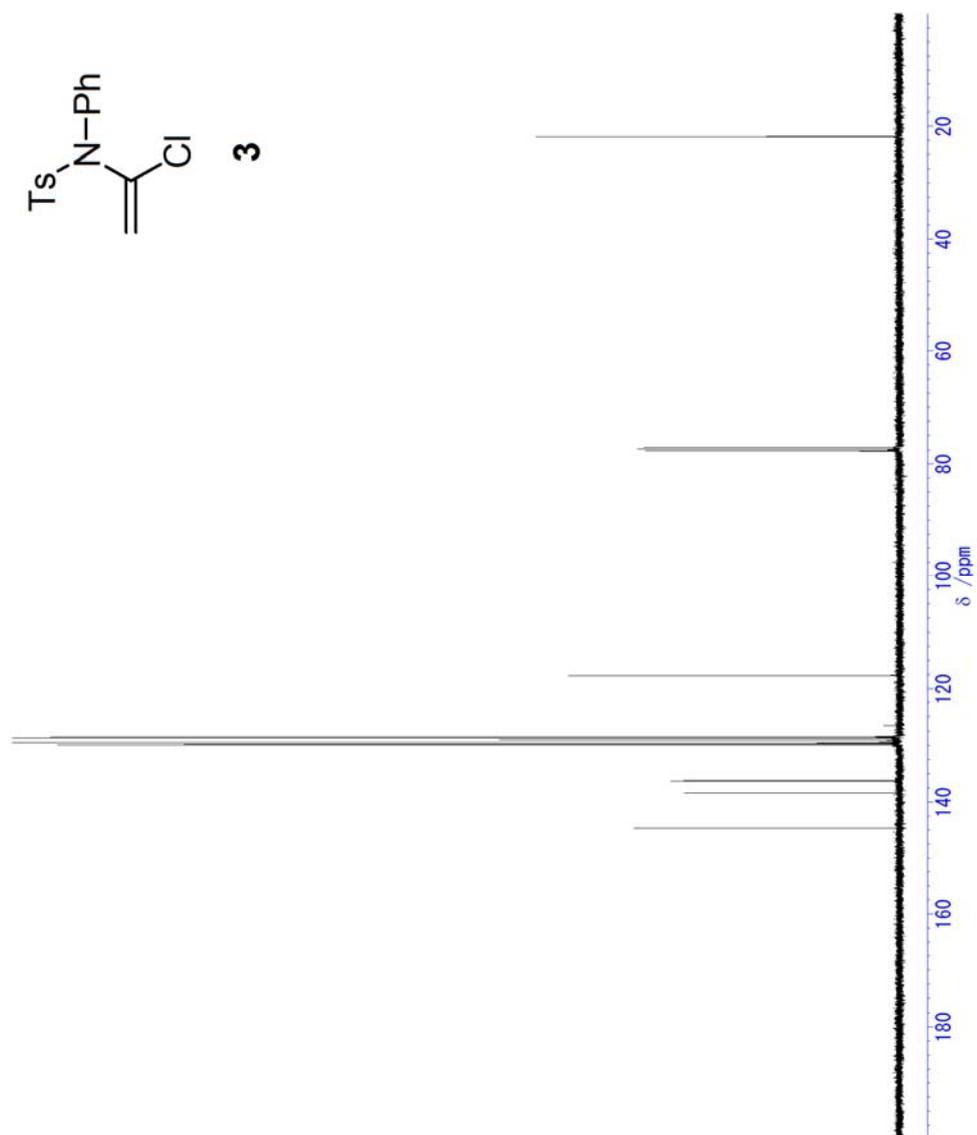
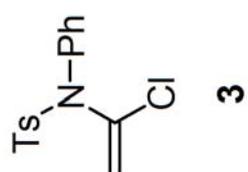


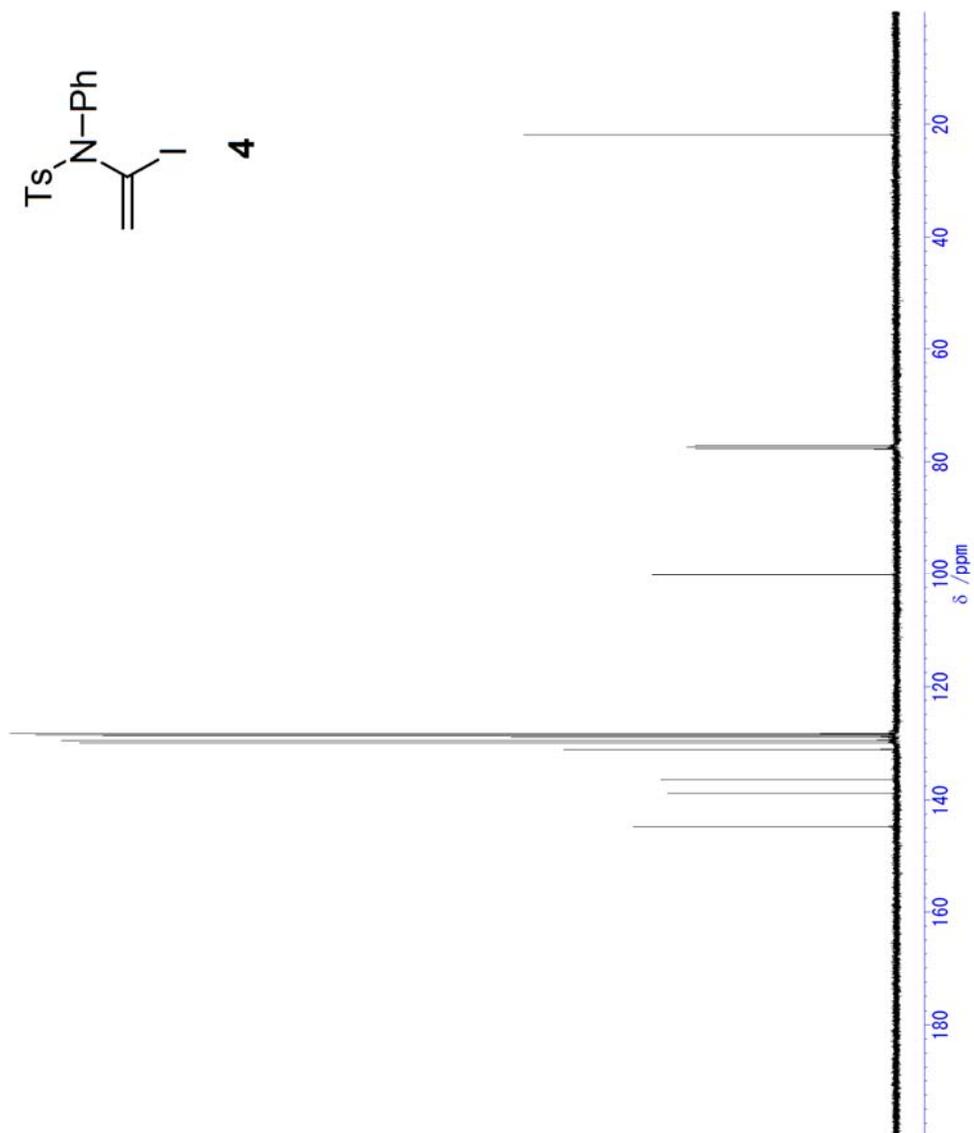
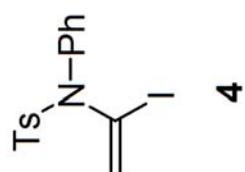


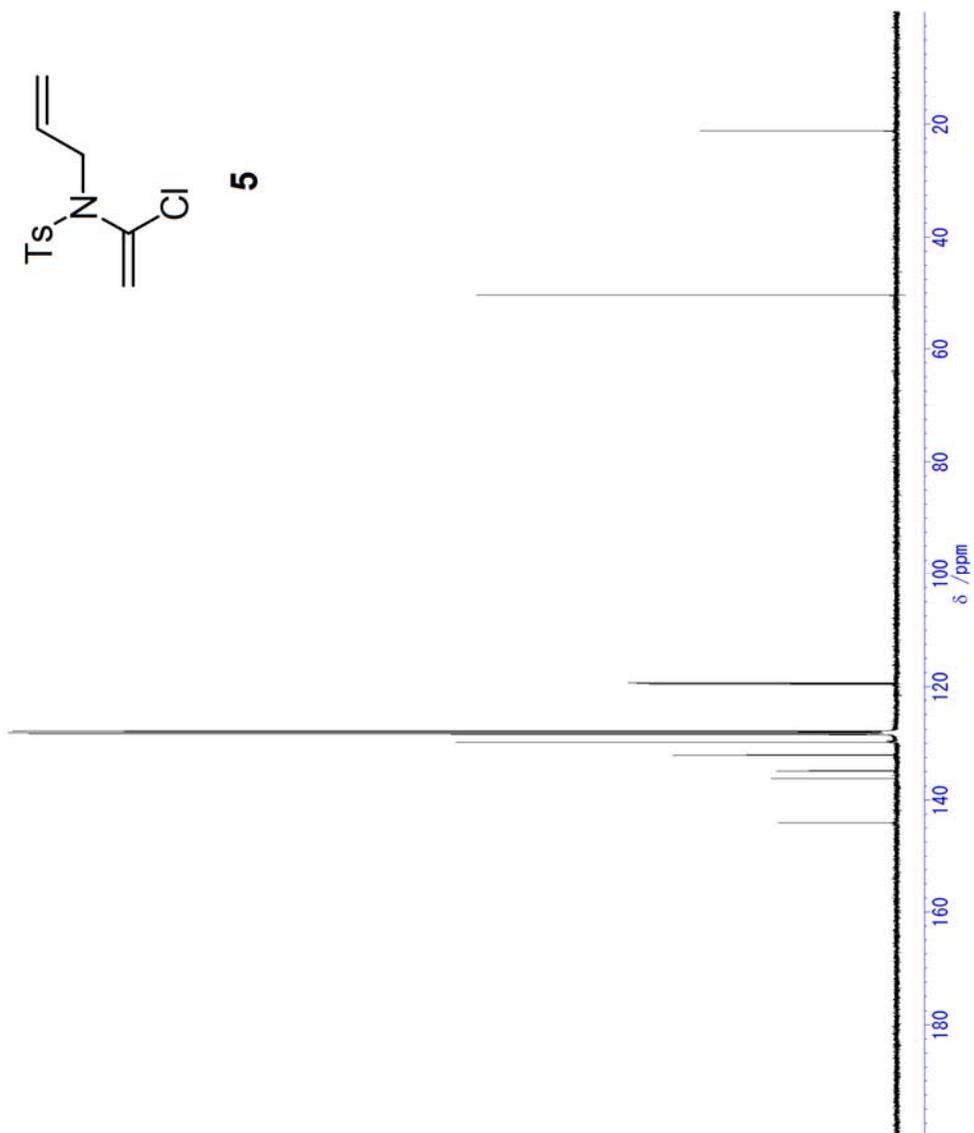
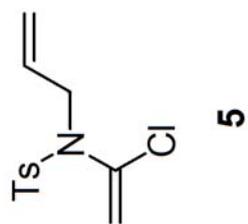


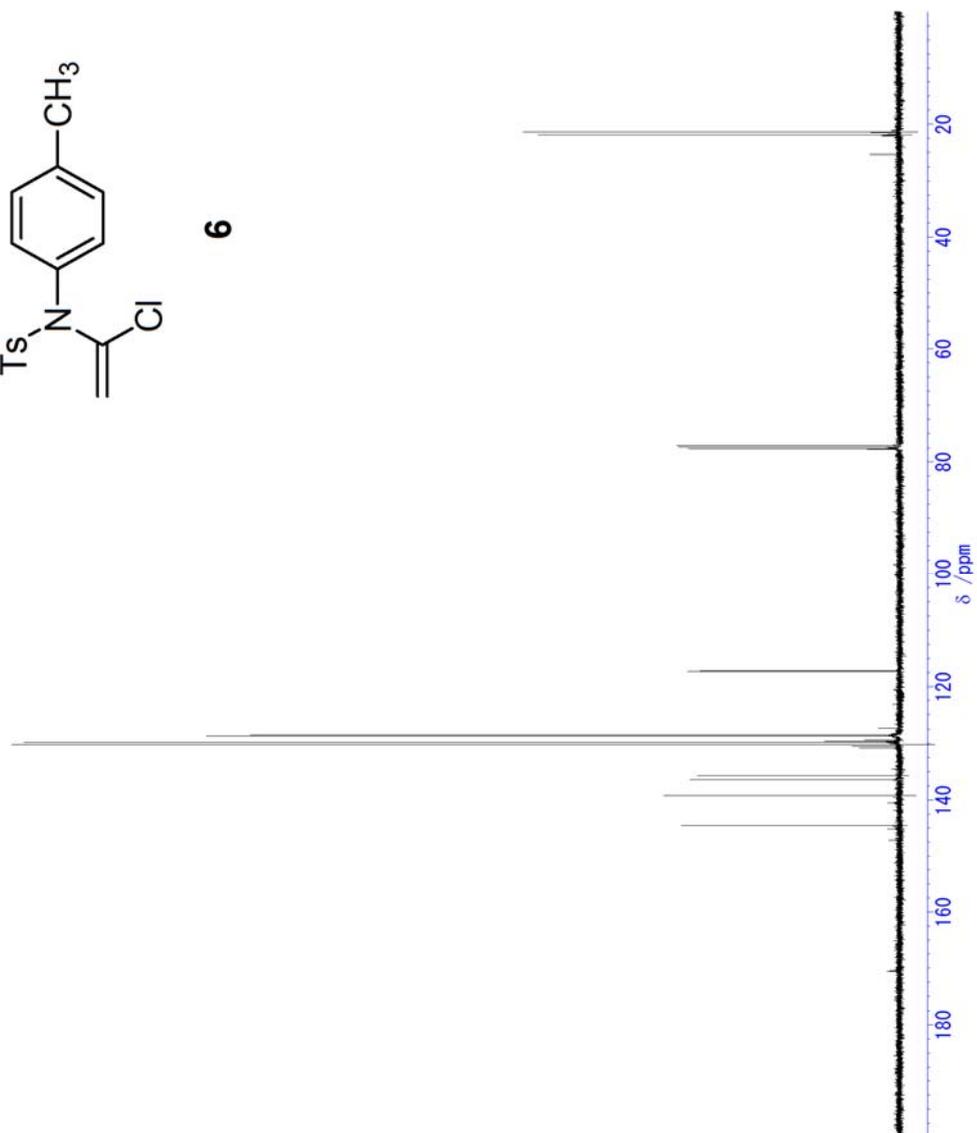
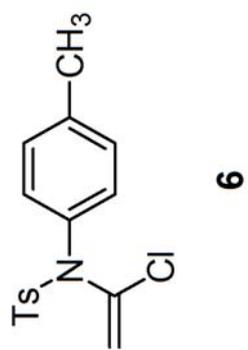


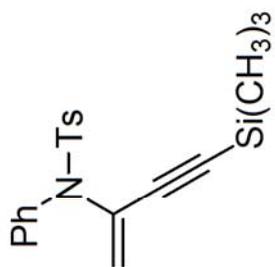












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