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A Triazole-Templated Ring-Closing Metathesis for Constructing Novel Fused and Bridged Triazoles.

authored by

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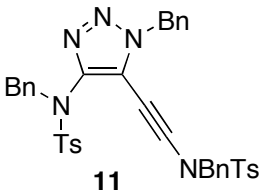
General procedure for the cross coupling of the vinyl-Cu intermediate with ynamides:

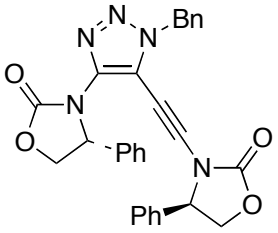


11

Synthesis of triazole 11: To a vial charged with ynamide **9** (85.6 mg, 0.30 mmol) were added CuBr (7.50 mg, 0.060 mmol, 0.20 equiv), BnN_3 (49.0 μL, 0.39 mmol, 1.3 equiv), 83.5 μL Et_3N (0.60 mmol, 60.6 g, 2.0 equiv), and CH_3CN (3 mL). The reaction mixture was vigorously stirred at rt for 2 d under nitrogen. After TLC showed that ynamide **9** was all consumed, the reaction mixture was diluted with H_2O (6 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat aq NaCl and dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave the crude triazole **11**, which was purified via silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure triazole **11** (74.6 mg, 71% yield) as a yellow oil.

11: R_f = 0.36 [33% ethyl acetate in hexane];

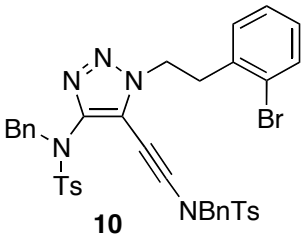
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 6 H), 4.51 (s, 2 H), 4.65(s, 2 H), 5.18(s, 2 H), 6.81-6.83(m, 2 H), 7.01-7.12(m, 5 H), 7.19-7.28(m, 8 H), 7.29-7.32(m, 4 H), 7.69 (dt, 2 H, *J* = 1.6, 8.4 Hz), 7.74 (dt, 2 H, *J* = 1.6, 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.87, 21.94, 53.0, 54.3, 55.8, 92.6, 95.0, 110.0, 121.3, 127.4, 127.7, 128.0, 128.31, 128.35, 128.42, 128.6, 128.79, 128.85, 129.0, 129.1, 129.9, 130.4, 134.0, 134.7, 135.2, 135.5, 144.2, 144.7, 145.3; IR (film) cm^{-1} 3006(w), 2989(w), 2925(w), 2854(w), 2360(w), 2341(w), 2246(w), 1596(w), 1496(w), 1456(w), 1355(m), 1276(s), 1261(s), 1166(m), 1121(w), 1089(m), 1028(w); mass spectrum (APCI): m/e (% relative intensity) 702.1 (100) $(M + H)^+$.



8

8: R_f = 0.10 [33% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = -84.6 (*c* 0.92, $CHCl_3$);

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13(dd, 1 H, *J* = 7.2, 8.8 Hz), 4.42 (dd, 1 H, *J* = 6.8, 8.8 Hz), 4.75(t, 1 H, *J* = 8.8 Hz), 4.84 (t, 1 H, *J* = 8.8 Hz), 5.18 (dd, 1 H, *J* = 6.8, 8.8 Hz), 5.26(s, 2 H), 5.49(dd, 1 H, *J* = 7.2, 8.8 Hz), 6.99-7.02(m, 2 H), 7.10-7.12 (m, 2 H), 7.15-7.26 (m, 6 H), 7.42-7.52 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.5, 58.2, 61.1, 62.2, 70.9, 71.3, 91.7, 115.8, 127.0, 127.5, 128.5, 128.7, 129.0, 129.1, 129.2, 129.8, 130.1, 134.0, 135.9, 137.3, 142.6, 154.7, 154.8; IR (film) cm^{-1} 3006(w), 2924(w), 2854(w), 2360(w), 2341(w), 2263(w), 1764(s), 1592(w), 1493(w), 1457(w), 1435(w), 1392(w), 1319(w), 1276(s), 1261(m), 1210(s), 1169(w), 1118(w), 1079(w), 1055(w); mass spectrum (APCI): m/e (% relative intensity) 506.1 (100) $(M + H)^+$.

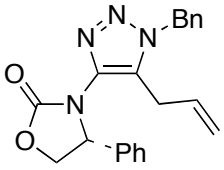


10

10: R_f = 0.22 [20% ethyl acetate in hexane];

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3 H), 2.45 (s, 3 H), 3.00 (t, 2 H, *J* = 7.2 Hz), 4.27(t, 2 H, *J* = 7.2 Hz), 4.57 (s, 2 H), 4.65 (s, 2 H), 6.57 (dd, 1 H, *J* = 1.6, 7.2 Hz), 6.95-7.04 (m, 2 H), 7.10-7.18 (m, 5 H), 7.21-7.32 (m, 7 H), 7.39 (d, 2 H, *J* = 6.8 Hz), 7.46 (dd, 1 H, *J* = 1.6, 8.0 Hz), 7.65 (dt, 2 H, *J* = 1.6, 7.2 Hz), 7.90 (dd, 2 H, *J* = 1.6, 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.0, 35.8, 49.1, 54.2, 55.9, 56.1, 94.8, 120.7, 124.6, 127.80, 127.82, 128.1, 128.4, 128.50, 128.54, 128.8, 128.9, 129.0, 129.2, 129.9, 130.5, 131.2, 133.1, 134.0, 134.8, 135.5, 135.6, 136.3, 144.2, 145.1, 145.5; IR (film) cm^{-1} 3006(w), 2989(w), 2925(w), 2854(w), 2360(w), 2341(w), 1457(w), 1357(w), 1276(s), 1261(s), 1166(w), 1089(m), 1026(w); mass spectrum (APCI): m/e (% relative intensity) 794.0 (100) $(M + H)^+$ 796.0 (100) $(M + H + 2)^+$.

General procedure for tandem cycloaddition-vinyl-Cu trapping reaction:



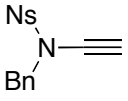
12

Synthesis of Triazole 12: To a round bottom flask charged with ynamide **6** (93.0 mg, 0.50 mmol) were added CuBr (62.0 mg, 0.5 mmol, 1.0 equiv), 2.6-lutidine (0.12 mL, 1.0 mmol, 107.0 mg, 2.0 equiv), and CH_3CN (2.5 mL). After stirring at rt for 2 min, allyl iodide (0.37 mL, 4.0 mmol, 0.672 g, 8.0 equiv) and BnN_3 (82 μL, 86.5 mg, 0.65 mmol, 1.3 equiv) were added to the reaction mixture. The reaction mixture was then vigorously stirred at rt for 2 d under nitrogen, and after which, the reaction mixture was diluted with diluted aq NH_4OH (from 1 mL 30% NH_4OH and 10 mL H_2O) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat aq NaCl and dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave the crude triazole **12**, which was purified via silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure triazole **12** (115.0 mg, 68% yield).

12: R_f = 0.23 [33% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = - 61.7 (*c* 2.56, $CHCl_3$);

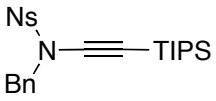
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.11-3.18 (m, 1 H), 3.29-3.35 (m, 1 H), 4.39 (dd, 1 H, *J* = 9.0, 9.0 Hz), 4.77 (dd, 1 H, *J* = 1.5, 7.0 Hz), 4.84 (dd, 1 H, *J* = 9.0, 9.0 Hz), 5.00 (dd, 1 H, *J* = 1.5, 10.0 Hz), 5.30-5.42 (m, 2 H), 5.42-5.51 (m, 1 H), 5.64 (dd, 1 H, *J* = 9.0, 9.0 Hz), 6.95-6.98 (m, 2 H), 7.25-7.33 (m, 8

H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.9, 52.7, 61.6, 70.6, 118.1, 127.2, 127.6, 127.8, 128.6, 129.2, 129.3, 129.8, 132.0, 134.6, 137.7, 139.8, 156.0; IR (film) cm^{-1} 3007(w), 2987(w), 2360(w), 2341(w), 1756(s), 1639(w), 1592(w), 1496(w), 1479(w), 1456(w), 1405(m), 1358(w), 1330(w), 1276(w), 1259(w), 1212(m), 1156(w), 1109(w), 1074(w), 1033(m); mass spectrum (MALDI): m/e (% relative intensity) 361.2 (100) $(M + Na)^+$; HRMS (MALDI) calcd for $C_{21}H_{20}N_4O_2Na$ 361.1659, found 361.1645.



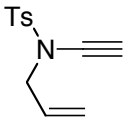
14

14: R_f = 0.56 [20% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (s, 1 H), 4.60 (s, 2 H), 7.27-7.32 (m, 5 H), 7.95 (dt, 2 H, *J* = 2.4, 8.8 Hz), 8.29 (dt, 2 H, *J* = 2.4, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 60.6, 75.7, 124.4, 128.92, 128.97, 129.04, 129.1, 133.8, 143.3, 150.7; IR (film) cm^{-1} 3006(w), 2990(w), 1461(w), 1276(s), 1261(s); mass spectrum (APCI): m/e (% relative intensity) 299.1 (100) $(M + MeOH + H)^+$.



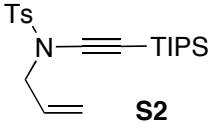
S1

S1: R_f = 0.75 [20% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98-0.99 (m, 21 H), 4.60 (s, 2 H), 7.25-7.30 (m, 5 H), 7.95 (td, 2 H, *J* = 2.4, 8.8 Hz), 8.27 (td, 2 H, *J* = 2.4, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 18.7, 56.4, 71.6, 95.6, 124.2, 128.8, 128.9, 129.0, 129.1, 133.9, 143.3, 150.6; IR (film) cm^{-1} 3006(w), 2990(w), 1462(w), 1276(s), 1261(s); mass spectrum (MALDI): m/e (% relative intensity) 473.2 (100) $(M + H)^+$.



15a

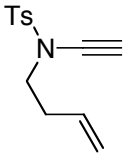
15a: R_f = 0.25 [20% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3 H), 2.72 (s, 1 H), 3.93 (td, 2 H, *J* = 1.2, 6.4 Hz), 5.17-5.26 (m, 2 H), 5.64-5.75 (m, 1 H), 7.33 (d, 2 H, *J* = 8.0 Hz), 7.78 (td, 2 H, *J* = 2.0, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 54.2, 59.5, 76.1, 120.4, 127.9, 130.1, 130.8, 134.8, 145.2; IR (film) cm^{-1} 3271(w), 2926(w), 2866(w), 2139(w), 1647(w), 1594(w), 1490(w), 1463(w), 1429(w), 1352(s), 1295(w), 1276(w), 1160(s), 1118(w), 1087(m), 1033(w), 1013(w); mass spectrum (APCI): m/e (% relative intensity) 268.1 (100) $(M + MeOH + H)^+$.



S2

S2: R_f = 0.62 [20% ethyl acetate in hexane];

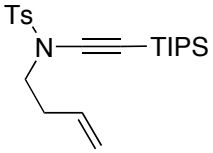
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05-1.10 (m, 21 H), 2.49 (s, 3 H), 4.01 (d, 2 H, *J* = 6.5 Hz), 5.24 (d, 1 H, *J* = 10.5 Hz), 5.28 (d, 1 H, *J* = 17.5 Hz), 5.72-5.82 (m, 1 H), 7.36 (d, 2 H, *J* = 8.5 Hz), 7.84 (d, 2 H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 18.8, 21.9, 54.5, 69.8, 96.5, 120.3, 128.1, 129.9, 131.0, 135.0, 144.9; IR (film) cm^{-1} 2942(w), 2891(w), 2865(w), 2360(w), 2341(w), 2166(w), 1597(w), 1463(w), 1367(m), 1276(m), 1262(m), 1169(s), 1090(w), 1033(w), 1017(w); mass spectrum (MALDI): m/e (% relative intensity) 392.0 (100) $(M + H)^+$.



15b

15b: R_f = 0.50 [20% ethyl acetate in hexane];

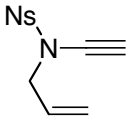
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36-2.43 (m, 2 H), 2.45 (s, 3 H), 2.76 (s, 1 H), 3.37 (t, 2 H, *J* = 7.2 Hz), 5.02-5.12 (m, 2 H), 5.65-5.76 (m, 1 H), 7.35 (d, 2 H, *J* = 8.0 Hz), 7.80 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 21.9, 32.2, 50.8, 59.6, 76.1, 118.1, 127.9, 130.0, 133.7, 134.8, 145.0; IR (film) cm^{-1} 3269(w), 3006(w), 2988(w), 2865(w), 2360(w), 2134(w), 1698(m), 1642(w), 1596(w), 1493(w), 1436(w), 1354(s), 1276(s), 1261(s), 1165(s), 1120(w), 1089(m), 1040(w); mass spectrum (APCI): m/e (% relative intensity) 250.1 (100) $(M + H)^+$.



S3

S3: R_f = 0.68 [20% ethyl acetate in hexane];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04-1.06 (m, 21 H), 2.36-2.43 (m, 2 H), 2.44 (s, 3 H), 3.39 (t, 2 H, *J* = 8.8 Hz), 5.01-5.11 (m, 2 H), 5.67-5.77 (m, 1 H), 7.32 (d, 2 H, *J* = 8.0 Hz), 7.79 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 18.8, 21.9, 32.4, 51.0, 70.0, 96.3, 117.9, 128.0, 129.8, 133.9, 134.9, 144.8; IR (film) cm^{-1} 3006(w), 2989 (w), 2864(w), 2360(w), 2163(w), 1596(w), 1462(w), 1365(w), 1276(s), 1261(s), 1169(m), 1089(w);mass spectrum (MALDI): m/e (% relative intensity) 406.2 (100) $(M + H)^+$.

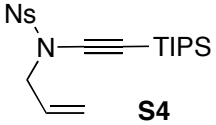


16a

16a: R_f = 0.36 [20% ethyl acetate in hexane];

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (s, 1 H), 4.05 (d, 2 H, *J* = 6.4 Hz), 5.25-5.31 (m, 2 H), 5.73 (ddt, 1 H, *J* = 6.4, 10.0, 16.8 Hz), 8.12 (dt, 2 H, *J* = 2.0, 9.2 Hz), 8.42 (dt, 2 H, *J* = 2.0, 9.2 Hz); ^{13}C NMR (100

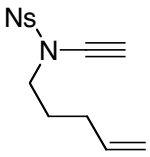
MHz, $CDCl_3$) δ 54.6, 60.3, 75.0, 121.1, 124.7, 129.3, 130.0, 143.2, 150.9; IR (film) cm^{-1} 3302(w), 3006(w), 2989(w), 2360(w), 2137(w), 1607(w), 1539(m), 1476(w), 1403(w), 1376(m), 1350(m), 1310(w), 1276(s), 1261(s), 1173(m), 1113(w), 1084(w), 1031(w), 1010(w); mass spectrum (APCI): m/e (% relative intensity) 267.1 (100) $(M + H)^+$, 299.1 (400) $(M + MeOH + H)^+$.



S4

S4: R_f = 0.60 [20% ethyl acetate in hexane];

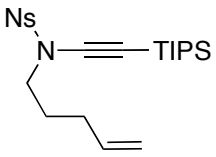
^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 18 H), 1.05 (s, 3 H), 8.04 (td, 2 H, *J* = 1.2, 6.8 Hz), 5.22-5.29 (m, 2 H), 5.72 (ddt, 1 H, *J* = 6.8, 10.4, 16.8 Hz), 8.11 (td, 2 H, *J* = 2.4, 8.8 Hz), 8.38 (td, 2 H, *J* = 2.4, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 17.9, 18.8, 54.9, 95.0, 121.0, 124.5, 129.3, 130.2, 143.3, 150.8; IR (film) cm^{-1} 3006(w), 2943(w), 2866(w), 2172(w), 1529(m), 1463(w), 1403(w), 1370(w), 1349(m), 1310(w), 1276(s), 1261(s), 1170(m), 1087(w), 1012(w); mass spectrum (APCI): m/e (% relative intensity) 423.0 (100) $(M + H)^+$.



16b

16b: R_f = 0.55 [20% ethyl acetate in hexane];

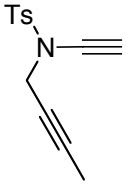
^1H NMR (500 MHz, $CDCl_3$) δ 1.76-1.83 (m, 2 H), 2.08-2.15 (m, 2 H), 2.84 (s, 1 H), 3.40 (t, 2 H, *J* = 7.0 Hz), 4.99-5.07 (m, 2 H), 5.72-5.82 (m, 1 H), 8.14 (d, 2 H, *J* = 8.5 Hz), 8.44 (d, 2 H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.1, 30.3, 51.4, 60.3, 75.1, 116.2, 124.8, 129.2, 136.9, 143.0, 150.9; IR (film) cm^{-1} 3280(w), 3006(w), 2989(w), 2867(w), 2360(w), 1525(w), 1463(w), 1370(w), 1346(w), 1309(w), 1276(s), 1261(s), 1172(w), 1088(w); mass spectrum (APCI): m/e (% relative intensity) 295.1 (100) $(M + H)^+$.



S5

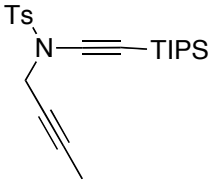
S5: R_f = 0.76 [20% ethyl acetate in hexane];

^1H NMR (500 MHz, $CDCl_3$) δ 1.03-1.08 (m, 21 H), 1.77-1.83 (m, 2 H), 2.09-2.15 (m, 2 H), 3.40 (t, 2 H, *J* = 7.0 Hz), 4.99-5.06 (m, 2 H), 5.71-5.80 (m, 1 H), 8.11 (td, 2 H, *J* = 2.0, 9.0 Hz), 8.39 (td, 2 H, *J* = 2.0, 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 18.8, 27.1, 30.4, 51.4, 71.0, 95.1, 116.1, 124.6, 129.2, 136.9, 143.1, 150.9; IR (film) cm^{-1} 3006(w), 2989(w), 2865(w), 2360(w), 2162(w), 1531(w), 1461(w), 1347(w), 1276(s), 1261(s), 1177(w), 1087(w); mass spectrum (MALDI): m/e (% relative intensity) 451.1 (100) $(M + H)^+$.



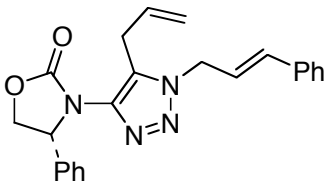
17

17: R_f = 0.49 [33% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (t, 3 H, *J* = 2.4 Hz), 2.43 (s, 3 H), 2.76 (s, 1 H), 4.18 (q, 2 H, *J* = 2.4 Hz), 7.34 (t, 2 H, *J* = 8.4 Hz), 7.83 (t, 2 H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 18.2, 38.8, 56.0, 67.5, 72.4, 79.6, 124.8, 126.1, 130.9, 141.5; IR (film) cm^{-1} 3006(w), 2990(w), 2361(w), 1462(w), 1360(w), 1276(s), 1261(s), 1166(w); mass spectrum (ESI): m/e (% relative intensity) 280.1 00) (M + MeOH + H)$^+$.



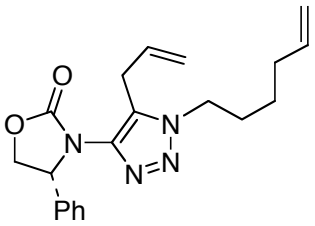
S6

S6: R_f = 0.64 [20% ethyl acetate in hexane]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (s, 21 H), 1.60 (t, 3 H, *J* = 2.3 Hz), 2.42 (s, 3 H), 4.19 (t, 2 H, *J* = 2.3 Hz), 7.31 (d, 2 H, *J* = 8.0 Hz), 7.84 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.0, 8.0, 15.2, 18.3, 39.2, 66.6, 67.8, 79.4, 92.7, 125.0, 126.0, 131.0, 141.3; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1462(w), 1276(s), 1261(s), 1170(w); mass spectrum (MALDI): m/e (% relative intensity) 404.2 (100) (M + H)$^+$.



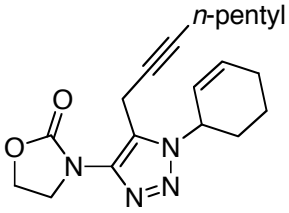
18

18: R_f = 0.17 [33% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = -56.7 (*c* 7.78, $CHCl_3$);
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.41 (dd, 1 H, *J* = 6.0, 17.0 Hz), 3.58 (dd, 1 H, *J* = 6.0, 17.0 Hz), 4.41 (dd, 1 H, *J* = 8.0, 8.0 Hz), 4.85-5.02 (m, 4 H), 5.11 (d, 1 H, *J* = 10.0 Hz),5.59-5.72 (m, 2 H), 6.24 (td, 1 H, *J* = 6.0, 16.0 Hz), 6.40 (d, 1 H, *J* = 16.0 Hz), 7.27-7.40 (m, 10 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.9, 51.2, 61.6, 70.8, 118.1, 122.2, 126.9, 127.6, 128.6, 128.9, 129.31, 129.35, 129.7, 132.3, 134.3, 135.8, 137.8, 139.7, 156.2; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1755(w), 1459(w), 1276(s), 1261(s); mass spectrum (APCI): m/e (% relative intensity) 387.2 (100) (M + H)$^+$.



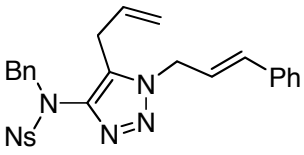
19

19: $\mathbf{R}_f$ = 0.30 [33% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = -83.3 (*c* 5.38, $CHCl_3$);
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31-1.40 (m, 2 H), 1.77-1.86 (m, 2 H), 1.99-2.07 (m, 2 H), 3.30 (tdd, 1 H, *J* = 1.6, 5.6, 10.8 Hz), 3.50 (tdd, 1 H, *J* = 1.6, 5.6, 10.8 Hz), 4.02-4.15 (m, 2 H), 4.39 (tdd, 1 H, *J* = 1.2, 8.8, 8.8 Hz), 4.79-4.88 (m, 2 H), 4.92-5.05 (m, 3 H), 5.51-5.77 (m, 3 H), 7.23-7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 26.9, 29.1, 33.2, 48.7, 61.5, 70.7, 115.4, 117.8, 127.6, 129.1, 129.2, 129.3, 132.4, 137.7, 138.0, 139.3, 156.1; IR (film) cm^{-1} 3006(w), 2989(w), 2924(w), 2360(w), 1758(s), 1639(w), 1592(w), 1478(w), 1458(w), 1406(m), 1358(w), 1276(s), 1260(s), 1212(m), 1114(w), 1082(w), 1037(m); mass spectrum (APCI): m/e (% relative intensity) 353.2 (100) $(M + H)^+$.



20

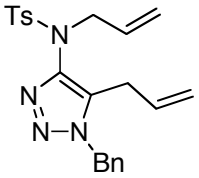
20: R_f = 0.37 [50% ethyl acetate in hexane];
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.76 (t, 3 H, *J* = 7.2 Hz), 1.14-1.26 (m, 4 H), 1.30-1.37 (m, 2 H), 1.57-1.68 (m, 1 H), 1.82-1.88 (m, 1 H), 1.95-2.16 (m, 6 H), 3.62 (dd, 2 H, *J* = 2.0, 4.0 Hz), 4.06 (dt, 2 H, *J* = 2.0, 8.0 Hz), 4.43 (t, 2 H, *J* = 8.0 Hz), 5.10-5.17 (m, 1 H), 5.64 (dd, 1 H, *J* = 1.6, 10.0 Hz), 5.93-5.98 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.2, 18.8, 20.5, 22.4, 24.6, 28.5, 30.1, 31.3, 46.5, 56.1, 63.3, 73.6, 82.8, 125.0, 125.9, 132.4, 140.0, 156.2; IR (film) cm^{-1} 2931(w), 2860(w), 2360(w), 1755(s), 1595(w), 1481(w), 1409(m), 1348(w), 1276(s), 1260(s), 1220(m), 1142(w), 1114(w), 1083(w), 1036(m); mass spectrum (APCI): m/e (% relative intensity) 343.2 (100) $(M + H)^+$.



21

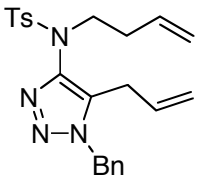
21: R_f = 0.58 [33% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.24 (d, 2 H, *J* = 6.0 Hz), 4.72 (s, 2 H), 4.85 (dd, 1 H, *J* = 0.8, 16.8 Hz), 4.96 (dd, 2 H, *J* = 0.8, 6.0 Hz), 5.00 (dd, 1 H, *J* = 0.8, 10.4 Hz), 5.24-5.35 (m, 1 H), 6.18 (td, 1 H, *J* =

6.0, 16.0 Hz), 6.30 (d, 1 H, *J* = 16.8 Hz), 7.20-7.24 (m, 5 H), 7.26-7.35 (m, 5 H), 8.00 (d, 2 H, *J* = 8.4 Hz), 8.35 (d, 2 H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 51.2, 55.4, 118.4, 121.9, 124.5, 126.9, 128.5, 128.7, 128.8, 128.9, 129.6, 129.7, 131.8, 134.3, 134.5, 134.8, 135.8, 141.0, 144.3, 150.6; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1588(w), 1528(m), 1453(w), 1423(w), 1402(w), 1366(w), 1349(m), 1314(w), 1276(s), 1261(s), 1174(m), 1090(w), 1039(w); mass spectrum (APCI): m/e (% relative intensity) 516.1 (100) $(M + H)^+$.



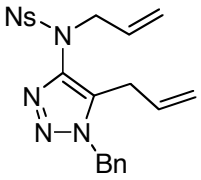
22a

22a: R_f = 0.21 [20% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 3.38 (td, 2 H, *J* = 1.2, 6.4 Hz), 4.15 (d, 2 H, *J* = 6.4 Hz), 4.98-5.03 (m, 2 H), 5.06 (ddd, 1 H, *J* = 1.6, 2.8, 7.2 Hz), 5.13 (ddd, 1 H, *J* = 1.6, 2.8, 7.2 Hz), 5.49 (s, 2 H), 5.65-5.81 (m, 2 H), 7.07 (dd, 2 H, *J* = 2.0, 8.0 Hz), 7.26-7.37 (m, 5 H), 7.63 (td, 2 H, *J* = 2.0, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 26.8, 52.8, 53.7, 118.3, 119.8, 127.1, 128.4, 128.6, 129.2, 129.9, 132.4, 132.5, 134.0, 134.8, 135.2, 142.4, 144.2; IR (film) cm^{-1} 3006(w), 2989(w), 2360(w), 1639(w), 1583(w), 1497(w), 1454(w), 1353(m), 1276(s), 1261(s), 1187(w), 1165(m), 1091(w), 1068(w), 1046(w); mass spectrum (MALDI): m/e (% relative intensity) 409.2 (100) $(M + Na)^+$.



22b

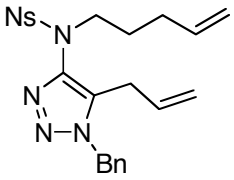
22b: R_f = 0.23 [20% ethyl acetate in hexane];
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.14 (td, 2 H, *J* = 8.0, 8.0 Hz), 2.42 (s, 3 H), 3.39 (d, 2 H, *J* = 6.5 Hz), 3.63 (t, 2 H, *J* = 8.0 Hz), 4.91-4.96 (m, 2 H), 5.07 (dd, 1 H, *J* = 1.5, 13.0 Hz), 5.17 (dd, 1 H, *J* = 1.5, 16.5 Hz), 5.51 (s, 2 H), 5.62-5.70 (m, 1 H), 5.76-5.83 (m, 1 H), 7.12 (d, 2 H, *J* = 7.5 Hz), 7.27-7.40 (m, 5 H), 7.58 (d, 2 H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 27.2, 32.9, 50.0, 52.9, 117.3, 118.4, 127.3, 128.3, 128.7, 129.3, 130.0, 132.5, 134.0, 134.7, 134.8, 135.0, 142.3, 144.2; IR (film) cm^{-1} 3006(w), 2985(w), 2924(w), 2361(w), 2341(w), 1640(w), 1597(w), 1580(w), 1496(w), 1455(w), 1430(w), 1383(w), 1353(s), 1306(w), 1276(m), 1260(m), 1163(s), 1090(m), 1054(w), 1029(w); mass spectrum (MALDI): m/e (% relative intensity) 409.2 (100) $(M + Na)^+$.



22c

22c: R_f = 0.43 [25% ethyl acetate in hexane];

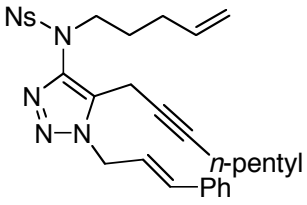
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.38 (td, 2 H, *J* = 1.6, 6.4 Hz), 4.18 (d, 2 H, *J* = 6.4 Hz), 5.03-5.09 (m, 3 H), 5.18 (dd, 1 H, *J* = 1.6, 8.8 Hz), 5.50 (s, 2 H), 5.66-5.81 (m, 2 H), 7.07-7.10 (m, 2 H), 7.32-7.39 (m, 3 H), 7.97 (td, 2 H, *J* = 2.4, 8.8 Hz), 8.36 (td, 2 H, *J* = 2.4, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 53.0, 54.3, 118.7, 120.7, 124.4, 127.2, 128.8, 129.3, 129.7, 131.7, 131.9, 134.2, 134.5, 141.5, 144.2, 150.6; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1530(w), 1460(w), 1350(w), 1276(s), 1261(s), 1177(w); mass spectrum (APCI): m/e (% relative intensity) 440.1 (100) $(M + H)^+$.



22d

22d: R_f = 0.29 [20% ethyl acetate in hexane];

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44-1.53 (m, 2 H), 1.99-2.06 (m, 2 H), 3.43 (td, 2 H, *J* = 1.6, 6.0 Hz), 3.59 (t, 2 H, *J* = 7.6 Hz), 4.91-4.97 (m, 2 H), 5.05-5.11 (m, 1 H), 5.18-5.22 (m, 1 H), 5.52 (s, 2 H), 5.63-5.84 (m, 2 H), 7.14 (dd, 2 H, *J* = 1.6, 7.6 Hz), 7.33-7.40 (m, 3 H), 7.92 (td, 2 H, *J* = 2.2, 8.8 Hz), 8.35 (td, 2 H, *J* = 2.2, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 27.5, 30.5, 50.8, 53.1, 115.8, 118.7, 124.4, 127.3, 128.8, 129.4, 129.6, 131.9, 134.1, 134.5, 137.1, 141.6, 143.9, 150.5; IR (film) cm^{-1} 3006(w), 2923(w), 2852(w), 2360(w), 2341(w), 1706(w), 1640(w), 1587(w), 1530(s), 1497(w), 1456(w), 1402(w), 1349(s), 1313(m), 1276(s), 1261(s), 1168(s), 1089(m), 1030(w), 1013(w); mass spectrum (APCI): m/e (% relative intensity) 468.1 (100) $(M + H)^+$.

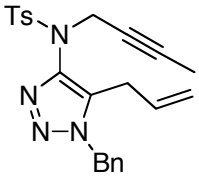


23

23: R_f = 0.22 [20% ethyl acetate in hexane];

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3 H, *J* = 7.2 Hz), 1.24-1.36 (m, 4 H), 1.43-1.51 (m, 2 H), 1.53-1.61 (m, 2 H), 2.05-2.16 (m, 4 H), 3.60 (t, 2 H, *J* = 7.2 Hz), 3.76 (t, 2 H, *J* = 7.2 Hz), 4.93-5.13 (m, 2 H), 5.27 (dd, 2 H, *J* = 1.2, 6.4 Hz), 5.67-5.78 (m, 1 H), 6.38 (td, 1 H, *J* = 6.4, 16.0 Hz), 6.64 (d, 1 H, *J* = 16.0

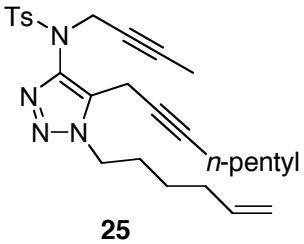
Hz), 7.24-7.40 (m, 5 H), 7.91 (td, 2 H, J = 2.2, 8.8 Hz), 8.31 (td, 2 H, J = 2.2, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 14.2, 18.9, 22.4, 27.6, 28.6, 30.6, 31.3, 50.8, 51.8, 72.7, 83.8, 115.8, 121.5, 124.4, 127.0, 128.8, 129.0, 129.5, 132.5, 135.1, 135.8, 137.3, 140.7, 144.0, 150.5; IR (film) cm^{-1} 3005(w), 2932(w), 2861(w), 2360(w), 1640(w), 1587(w), 1530(s), 1496(w), 1450(w), 1401(w), 1348(s), 1313(m), 1276(s), 1261(s), 1168(s), 1089(m), 1013(w); mass spectrum (MALDI): m/e (% relative intensity) 562.2 (100) $(M + H)^+$.



24

24: R_f = 0.17 [20% ethyl acetate in hexane];

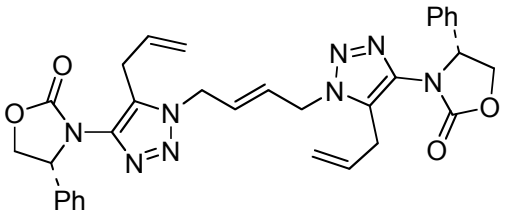
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59(t, 3 H, J = 2.4 Hz), 2.41 (s, 3 H), 3.41 (td, 2 H, J = 1.6, 6.0 Hz), 4.29 (q, 2 H, J = 2.4 Hz), 5.07(tdd, 1 H, J = 1.6, 3.2, 17.2 Hz), 5.14(tdd, 1 H, J = 1.6, 3.2, 9.6 Hz), 5.51(s, 2 H), 5.76-5.86 (m, 1 H), 7.10 (dd, 2 H, J = 2.4, 7.6 Hz), 7.26-7.37 (m, 5 H), 7.65 (td, 2 H, J = 1.8, 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.0, 18.2, 23.2, 38.1, 49.2, 69.2, 78.1, 114.5, 123.5, 124.7, 124.9, 125.6, 126.2, 128.8, 130.7, 131.2, 131.5, 138.4, 140.6; IR (film) cm^{-1} 3006(w), 2988(w), 2920(w), 2360(w), 2341(w), 2243(w), 2097(w), 1640(w), 1596(w), 1497(w), 1455(w), 1381(w), 1351(s), 1306(w), 1276(m), 1261(m), 1185(w), 1164(s), 1092(m), 1057(w); mass spectrum (APCI): m/e (% relative intensity) 421.1 (100) $(M + H)^+$.



25

25: R_f = 0.33 [20% ethyl acetate in hexane];

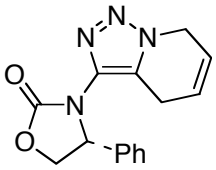
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 7.0 Hz), 1.24-1.36 (m, 6 H), 1.45-1.52 (m, 2 H), 1.68 (t, 3 H, J = 2.2 Hz), 1.93-2.04 (m, 2 H), 2.10-2.17 (m, 4 H), 2.41 (s, 3 H), 3.74 (t, 2 H, J = 2.2 Hz), 4.28 (q, 2 H, J = 2.2 Hz), 4.45 (t, 2 H, J = 7.5 Hz), 4.97-5.06 (m, 2 H), 5.74-5.83 (m, 1 H), 7.28 (d, 2 H, J = 8.0 Hz), 7.62 (d, 2 H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.0, 9.7, 10.4, 15.1, 18.0, 18.6, 22.2, 24.8, 25.3, 27.5, 29.5, 37.9, 45.5, 69.0, 69.4, 78.0, 79.0, 111.6, 124.5, 126.0, 128.2, 131.7, 134.3, 137.0, 140.4; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1461(w), 1276(s), 1261(s); mass spectrum (MALDI): m/e (% relative intensity) 503.2 (100) $(M + Na)^+$.



26

26: R_f = 0.53 [67% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = -89.4 (*c* 1.78, $CHCl_3$);
IR (film) cm^{-1} 2924(w), 2360(w), 1754(s), 1640(w), 1591(w), 1479(w), 1458(w), 1406(m), 1213(m), 1111(w), 1035(w); ^1H NMR (400 MHz, $CDCl_3$) δ 3.25 (ddt, 2 H, *J* = 1.6, 6.0, 16.8 Hz), 3.44 (ddt, 2 H, *J* = 1.6, 6.0, 16.8 Hz), 4.38 (dd, 2 H, *J* = 7.6, 8.0 Hz), 4.65-4.73 (m, 6 H), 4.86 (t, 2 H, *J* = 8.8 Hz), 4.98 (dd, 2 H, *J* = 1.6, 10.4 Hz), 5.45-5.55 (m, 4 H), 5.62 (dd, 2 H, *J* = 7.6, 8.8 Hz), 7.27-7.35 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 49.8, 61.5, 70.7, 118.2, 127.5, 127.8, 129.31, 129.34, 129.6, 132.0, 137.6, 139.6, 156.1; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1461(w), 1276(s), 1261(s); mass spectrum (APCI): m/e (% relative intensity) 593.2 (100) $(M + H)^+$.

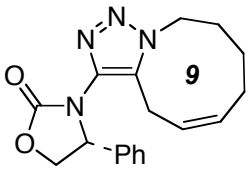
General procedures for ring-closing metathesis reaction:



27

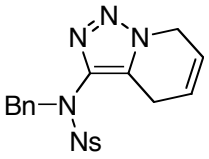
Synthesis of the fuse triazole 27: To a solution of triazole **18** (53.5 mg, 0.14 mmol) in CH_2Cl_2 (10 mL, *c* = 0.014 M) was added 2nd Generation Grubbs catalyst (11.8 mg). The reaction mixture was heated on an oil bath and refluxed for 6 h. After TLC showed that all of triazole **18** was consumed, the reaction mixture was concentrated under reduce pressure to give the crude product, which was purified via silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure fused triazole **27** (38.0 mg, 95% yield).

27: R_f = 0.20 [50% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = - 65.6 (*c* 1.96, $CHCl_3$);
^1H NMR (400 MHz, $CDCl_3$) δ 3.06-3.11 (m, 1 H), 3.12-3.16 (m, 1 H), 4.39 (dd, 1 H, *J* = 6.4, 8.8 Hz), 4.79-4.84 (m, 2 H), 4.89 (dd, 1 H, *J* = 8.8, 8.8 Hz), 5.69 (dd, 1 H, *J* = 6.4, 8.8 Hz), 5.83-5.89 (m, 1 H), 5.92-5.98 (m, 1 H), 7.27-7.36 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5, 46.1, 61.0, 71.0, 119.1, 121.7, 125.4, 127.1, 129.2, 129.4, 137.5, 138.3, 155.8; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1461(w), 1276(s), 1261(s); mass spectrum (APCI): m/e (% relative intensity) 283.2 (100) $(M + H)^+$.



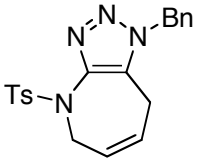
28

28: R_f = 0.60 [50% ethyl acetate in hexane]; $[\alpha]_D^{20}$ = - 120.4 (*c* 0.37, $CHCl_3$);
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48-1.57 (m, 2 H), 1.85-1.92 (m, 2 H), 2.07-2.25 (m, 2 H), 3.32-3.44 (m, 2 H), 4.25-4.37 (m, 2 H), 4.40 (dd, 1 H, *J* = 7.2, 8.8 Hz), 4.88 (dd, 1 H, *J* = 8.8, 8.8 Hz), 5.40-5.50 (m, 2 H), 5.62 (dd, 1 H, *J* = 7.2, 8.8 Hz), 7.29-7.35 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.2, 25.0, 25.7, 46.6, 61.6, 70.7, 125.9, 127.4, 129.2, 129.3, 130.4, 130.6, 138.0, 139.0, 156.3; IR (film) cm^{-1} 3006(w), 2360(w), 1750(w), 1459(w), 1410(w), 1276(s), 1261(s), 1030(w); mass spectrum (APCI): m/e (% relative intensity) 325.2 (100) $(M + H)^+$.



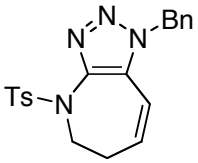
29

29: R_f = 0.32 [33% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.14-3.19 (m, 2 H), 4.74 (s, 2 H), 4.82-4.87(m, 2 H), 5.83-5.93 (m, 2 H), 7.23-7.28 (m, 5 H), 7.99 (td, 2 H, *J* = 2.2, 8.8 Hz), 8.37 (td, 2 H, *J* = 2.2, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 46.3, 55.2, 119.1, 121.7, 124.5, 128.5, 128.8, 129.1, 129.5, 130.8, 135.3, 138.8, 144.4, 150.5; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1531(w), 1461(w), 1347(w), 1276(s), 1261(s), 1169(w); mass spectrum (APCI): m/e (% relative intensity) 412.1 (100) $(M + H)^+$.



30

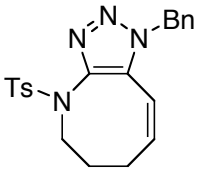
30: R_f = 0.10 [33% ethyl acetate in hexane];
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 2.76 (dd, 2 H, *J* = 2.0, 4.5 Hz), 4.25 (dd, 2 H, *J* = 2.0, 4.5 Hz), 5.29-5.34 (m, 1 H), 5.40 (s, 2 H), 5.59-5.65 (m, 1 H), 7.05 (d, 2 H, *J* = 8.0 Hz), 7.13 (dd, 2 H, *J* = 2.0, 7.0 Hz), 7.34-7.38 (m, 3 H), 7.56 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 24.1, 47.5, 52.8, 122.9, 127.2, 127.5, 128.3, 128.8, 129.4, 129.5, 129.8, 134.5, 136.4, 144.0, 144.1; IR (film) cm^{-1} 3006(w), 2990(w), 2361(w), 1461(w), 1349(w), 1276(s), 1261(s), 1162(w), 1089(w); mass spectrum (MALDI): m/e (% relative intensity) 381.3 (100) $(M + Na)^+$.



31

31: R_f = 0.20 [33% ethyl acetate in hexane];

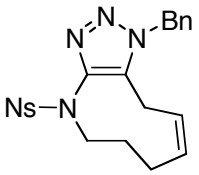
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 2.73-2.79 (m, 2 H), 3.60 (t, 2 H, *J* = 4.8 Hz), 5.50 (s, 2 H), 5.98 (td, 1 H, *J* = 4.8, 11.6 Hz), 6.21 (td, 1 H, *J* = 4.8, 11.6 Hz), 7.14-7.18 (m, 2 H), 7.27-7.37 (m, 5 H), 8.00 (d, 2 H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 34.1, 45.6, 52.7, 112.3, 127.3, 128.1, 128.2, 128.7, 129.3, 129.4, 129.8, 129.9, 133.7, 134.8, 144.0; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 1458(w), 1276(s), 1261(s), 1162(w); mass spectrum (MALDI): m/e (% relative intensity) 381.3 (100) $(M + Na)^+$.



32

32: R_f = 0.32 [33% ethyl acetate in hexane];

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.76-1.81 (m, 2 H), 2.28-2.32 (m, 2 H), 2.42 (s, 3 H), 3.53 (t, 2 H, *J* = 6.5 Hz), 5.44 (s, 2 H), 5.97-6.05 (m, 2 H), 7.16 (d, 2 H, *J* = 8.0 Hz), 7.28-7.34 (m, 5 H), 7.99 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 25.7, 27.2, 49.0, 53.1, 112.9, 127.5, 128.3, 128.4, 128.7, 129.3, 129.7, 134.7, 137.57, 137.59, 142.9, 143.8; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 2341(w), 1458(w), 1276(s), 1261(s); mass spectrum (MALDI): m/e (% relative intensity) 381.1 (100) $(M + Na)^+$.

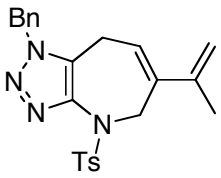


33

33: R_f = 0.40 [33% ethyl acetate in hexane];

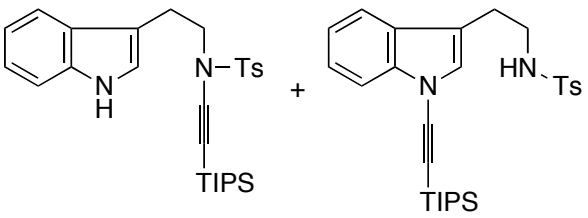
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87-1.95 (m, 2 H), 2.51-2.57 (m, 2 H), 3.31-3.35 (m, 2 H), 3.41-3.46 (m, 2 H), 4.90-4.98 (m, 1 H), 5.44-5.50 (m, 1 H), 5.51 (s, 2 H), 7.19 (dd, 2 H, *J* = 2.4, 7.6 Hz), 7.35-7.40 (m, 3 H), 8.28 (td, 2 H, *J* = 2.0, 8.8 Hz), 8.39 (td, 2 H, *J* = 2.0, 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 22.8, 28.6, 29.9, 52.6, 124.2, 124.3, 127.6, 129.0, 129.5, 130.3, 133.2, 133.3, 134.3, 134.7, 144.1, 144.8; IR (film) cm^{-1} 3006(w), 2962(w), 2922(w), 2852(w), 2360(m), 2341(w), 1575(w), 1528(w), 1499(w),

1458(w), 1350(m), 1312(w), 1276(s), 1261(s), 1165(m), 1089(m), 1025(w); mass spectrum (APCI): m/e (% relative intensity) 440.1 (100) $(M + H)^+$.



34

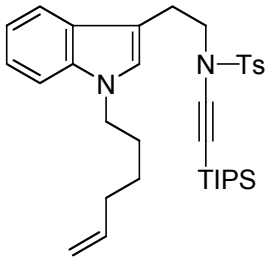
34: R_f = 0.46 [25% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81 (s, 3 H), 2.34 (s, 3 H), 2.98 (d, 2 H, *J* = 5.2 Hz), 4.50 (s, 2 H), 5.05 (s, 1 H), 5.24 (s, 1 H), 5.41 (s, 2 H), 5.45 (t, 1 H, *J* = 5.2 Hz), 7.07 (d, 2 H, *J* = 8.4 Hz), 7.10-7.14 (m, 2 H), 7.34-7.38 (m, 3 H), 7.57 (d, 2 H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.75, 21.78, 23.6, 48.3, 52.7, 114.1, 120.3, 126.7, 127.4, 128.2, 128.8, 129.2, 129.3, 134.4, 136.4, 138.8, 142.9, 143.8, 144.7; IR (film) cm^{-1} 3006(w), 2990(w), 2360(w), 2341(w), 1458(w), 1276(s), 1261(s); mass spectrum (APCI): m/e (% relative intensity) 421.1 (100) $(M + H)^+$.



(6 : 1 inseperable regioisomers)

S7

S7: R_f = 0.57 [33% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.09 (m, 21 H), 2.41 (s, 3 H), 3.13 (t, 2 H, *J* = 7.8 Hz), 3.63 (t, 2 H, *J* = 7.8 Hz), 7.01 (d, 1 H, *J* = 2.8 Hz), 7.07-7.11 (m, 1 H), 7.16-7.20 (m, 1 H), 7.23 (d, 2 H, *J* = 8.0 Hz), 7.33 (td, 1 H, *J* = 0.8, 8.0 Hz), 7.54 (d, 1 H, *J* = 8.0 Hz), 7.71 (d, 2 H, *J* = 8.0 Hz), 7.99 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.7, 18.9, 21.9, 24.2, 52.1, 70.1, 96.6, 111.6, 111.7, 118.7, 119.7, 122.3, 122.8, 127.4, 127.9, 129.8, 134.9, 136.5, 144.7; IR (film) cm^{-1} 3006(w), 2864(w), 2360(w), 2171(w), 1458(w), 1350(w), 1276(s), 1261(s), 1167(w), 1088(w); mass spectrum (MALDI): m/e (% relative intensity) 495.3 (100) $(M + H)^+$.

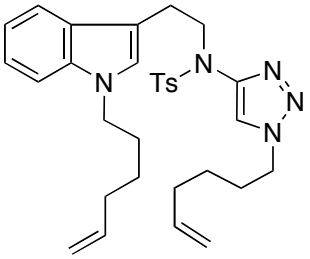


S8

Synthesis of Ynamide S8: To a solution of ynamide **S7** (500.0 mg, 1.00 mmol) in THF (5 mL) was added NaH (60% dispersion in mineral oil, 120.0 mg, 3.0 mol, 3.0 equiv). After stirring at rt for 2 h, 6-bromo-1-hexene (0.174 mL, 0.212g, 1.3 mmol, 1.3 equiv) was added dropwise. The reaction mixture was stirred at rt for 24 h, and after which, it was quenched with H_2O (0.5 mL) at 0 ^oC and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat aq NaCl and dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave the crude alkylated product **S8**, which was purified via silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure ynamide **S8** (368.0 mg, 65% yield) as a yellow oil.

S8: R_f = 0.64 [20% ethyl acetate in hexane];
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07-1.09 (m, 21 H), 1.36-1.45(m, 2 H), 1.76-1.84(m, 2 H), 2.04-2.10(m, 2 H), 2.41 (s, 3 H), 3.11 (t, 2 H, *J* = 8.0 Hz), 3.62 (t, 2 H, *J* = 8.0 Hz), 4.01 (t, 2 H, *J* = 7.2 Hz), 4.93-5.02 (m, 2 H), 5.70-5.81 (m, 1 H), 6.90 (s, 1 H), 7.07 (dd, 1 H, *J* = 7.2, 8.0 Hz), 7.16-7.29 (m, 4 H), 7.52 (d, 1 H, *J* = 8.0 Hz), 7.70 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 19.0, 21.9, 24.2, 26.5,

30.0, 33.6, 46.3, 52.2, 70.1, 96.7, 109.7, 110.3, 115.3, 118.9, 119.2, 121.8, 126.4, 127.9, 128.0, 129.8, 135.1, 136.6, 138.5, 144.6; IR (film) cm^{-1} 2940(w), 2864(w), 2360(w), 2162(w), 1597(w), 1467(m), 1369(m), 1276(s), 1261(s), 1168(s), 1091(w), 1015(w); mass spectrum (MALDI): m/e (% relative intensity) 599.3 (100) $(M + Na)^+$.

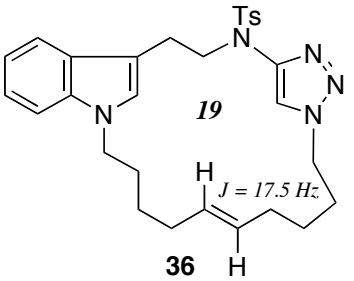


35

Synthesis of triazole 35: To a solution of ynamide **S8** (100.0 mg, 0.173 mmol) in THF (2 mL) was added TBAF (0.26 mL, 1.0 *M* in THF) dropwise at 0 ^oC. After stirring at 0 ^oC for 1 h, to this reaction mixture were added $CuSO_4$-$5H_2O$ (8.80 mg, 0.035 mmol, 0.10 equiv), sodium ascorbate (7.00 mg, 0.035 mmol, 0.1 equiv), and H_2O (0.5 mL) were added. The reaction mixture was then stirred at rt for 24 h before it was diluted with H_2O (6 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat aq NaCl and dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave the crude triazole **37**, which was purified via silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure triazole **35** (61.5 mg, 65% yield) as a yellow oil.

35: R_f = 0.78 [25% ethyl acetate in hexane];

^1H NMR (400 MHz, $CDCl_3$) δ 1.38-1.48 (m, 4 H), 1.78-1.85 (m, 2 H), 1.89-1.97 (m, 2 H), 2.05-2.16 (m, 4 H), 2.37 (s, 3 H), 3.07 (t, 2 H, *J* = 8.0 Hz), 4.01-4.08 (m, 4 H), 4.32 (t, 2 H, *J* = 7.2 Hz), 4.95-5.09 (m, 4 H), 5.73-5.85 (m, 2 H), 6.98 (s, 1 H), 7.10 (dd, 1 H, *J* = 7.2, 7.2 Hz), 7.17-7.23 (m, 3 H), 7.29 (d, 1 H, *J* = 8.0 Hz), 7.54 (d, 2 H, *J* = 8.0 Hz), 7.61-7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 25.0, 25.8, 26.5, 29.6, 29.9, 33.2, 33.6, 46.3, 49.8, 50.9, 109.5, 111.0, 115.2, 115.6, 119.1, 119.4, 119.5, 121.7, 126.2, 127.5, 128.2, 129.9, 135.5, 136.4, 138.0, 138.5, 144.1, 144.6; IR (film) cm^{-1} 3005(w), 2989(w), 2930(w), 2860(w), 2360(w), 2341(w), 1639(w), 1614(w), 1597(w), 1550(w), 1468(w), 1352(m), 1305(w), 1276(s), 1261(s), 1221(w), 1163(s), 1127(w), 1091(w), 1073(w), 1014(w); mass spectrum (APCI): m/e (% relative intensity) 546.7 (100) $(M + H)^+$.



36: R_f = 0.41 [25% ethyl acetate in hexane];
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31-1.38 (m, 2 H), 1.41-1.47 (m, 2 H), 1.57-1.64 (m, 2 H), 1.71-1.77 (m, 2 H), 2.04-2.07 (m, 2 H), 2.09-2.13 (m, 2 H), 2.39 (s, 3 H), 3.07 (t, 2 H, *J* = 4.8 Hz), 3.98-4.03 (m, 4 H), 4.05 (t, 2 H, *J* = 6.0 Hz), 5.30(td, 2 H, *J* = 6.5, 17.5 Hz), 6.88 (d, 2 H, *J* = 4.8 Hz), 7.02-7.06 (m, 1 H), 7.15 (dd, 1 H, *J* = 6.0, 6.0 Hz), 7.20-7.25 (m, 3H), 7.51-7.57 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 25.1, 25.3, 26.2, 28.4, 29.4, 31.5, 32.0, 46.0, 50.28, 50.3, 109.3, 111.2, 119.0, 119.4, 120.7, 121.5, 126.3, 127.9, 128.5, 129.9, 130.6, 131.8, 135.6, 136.2, 144.0, 144.7; IR (film) cm^{-1} 3006(w), 2360(w), 1459(w), 1276(s), 1261(s), 1164(w); mass spectrum (MALDI): m/e (% relative intensity) 518.2 (100) $(M + Na)^+$.

SUPPORTING INFORMATION

PROTON NMR AND SELECTED CARBON NMR SPECTRA

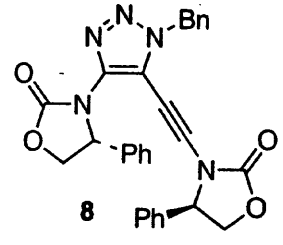
for the
communication
entitled

A Triazole-Templated Ring-Closing Metathesis for Constructing Novel Fused and Bridged Triazoles.

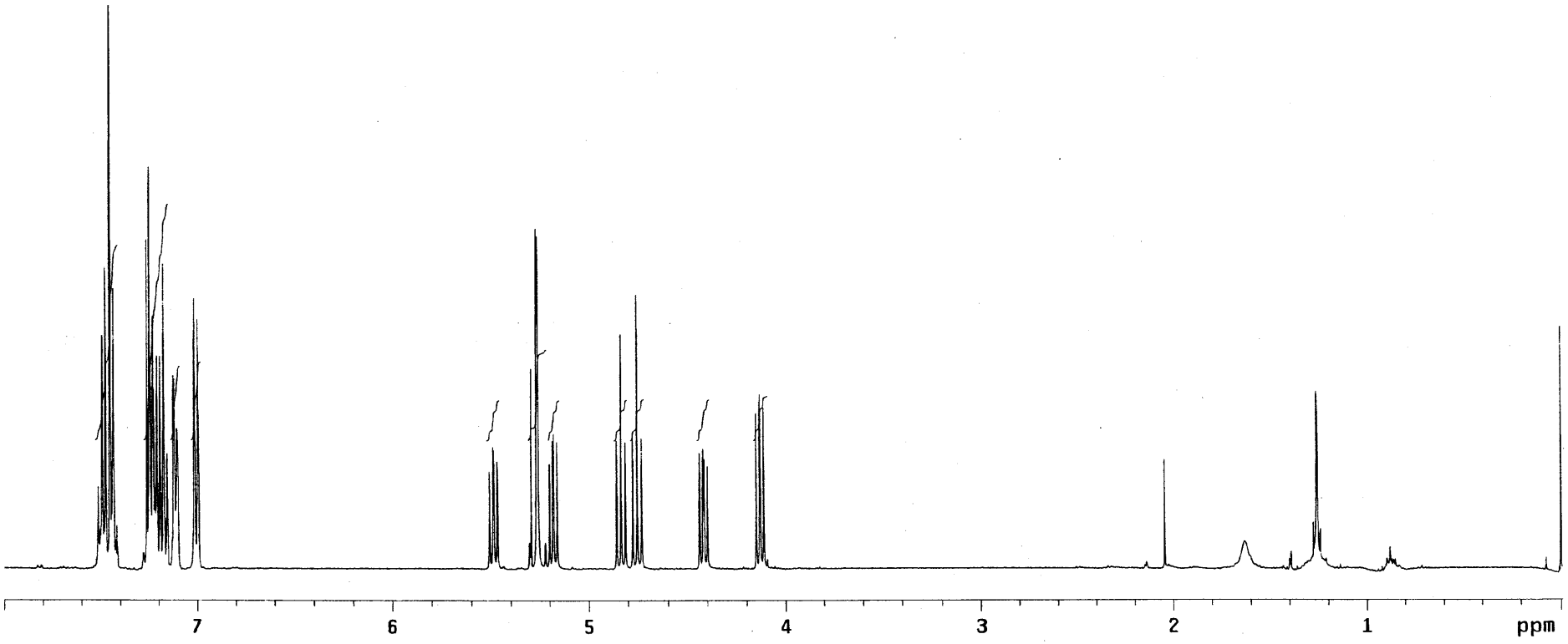
authored by

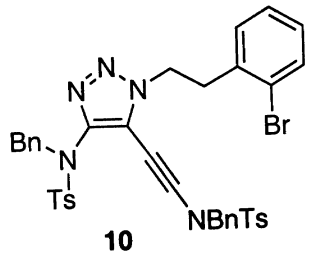
Xuejun Zhang, Richard P. Hsung*, and Hongyan Li

Division of Pharmaceutical Sciences and Department of Chemistry, 7111 Rennebohm Hall, 777 Highland Avenue
University of Wisconsin at Madison, Madison, WI 53705-2222



8





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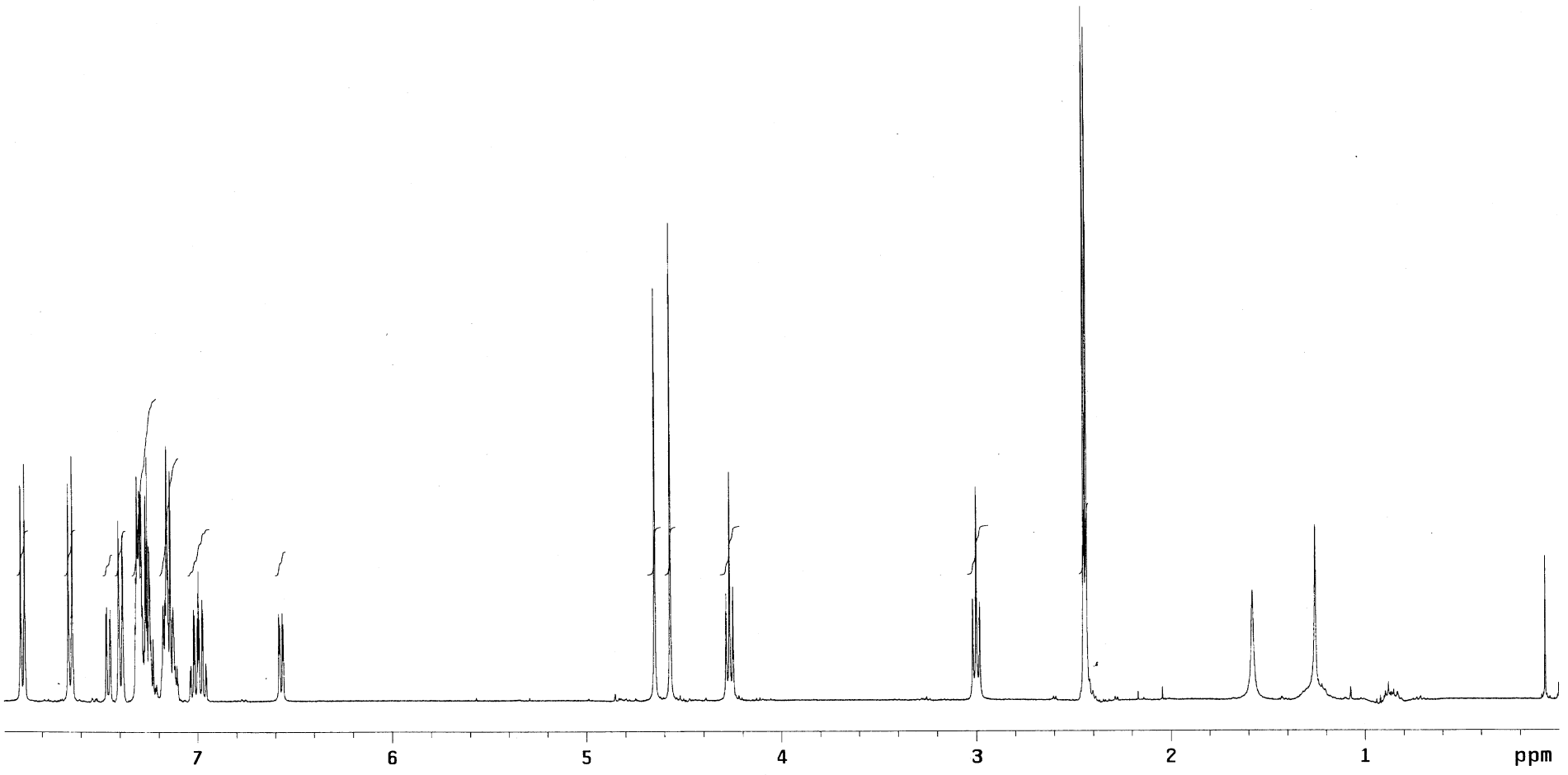

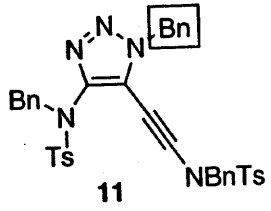

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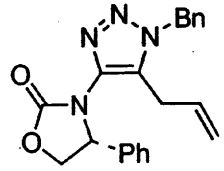

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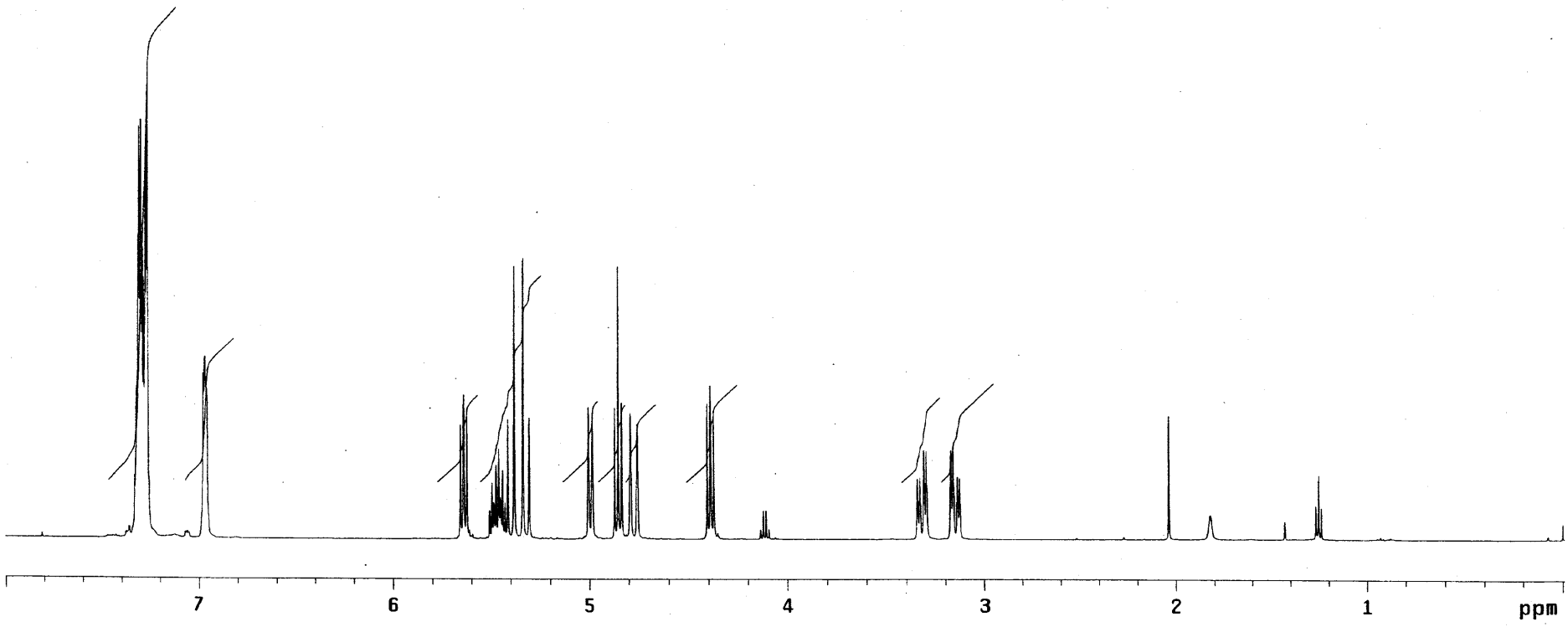

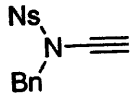

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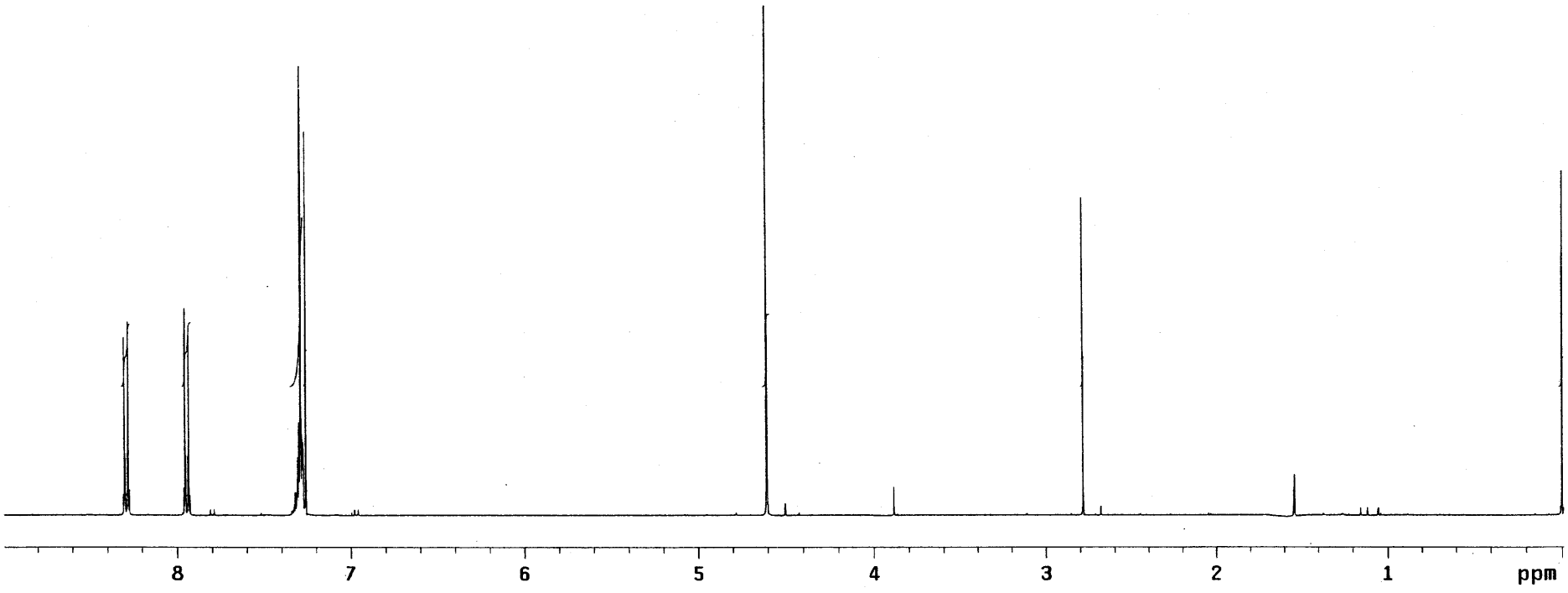
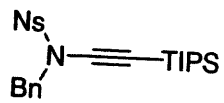
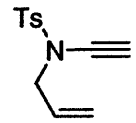
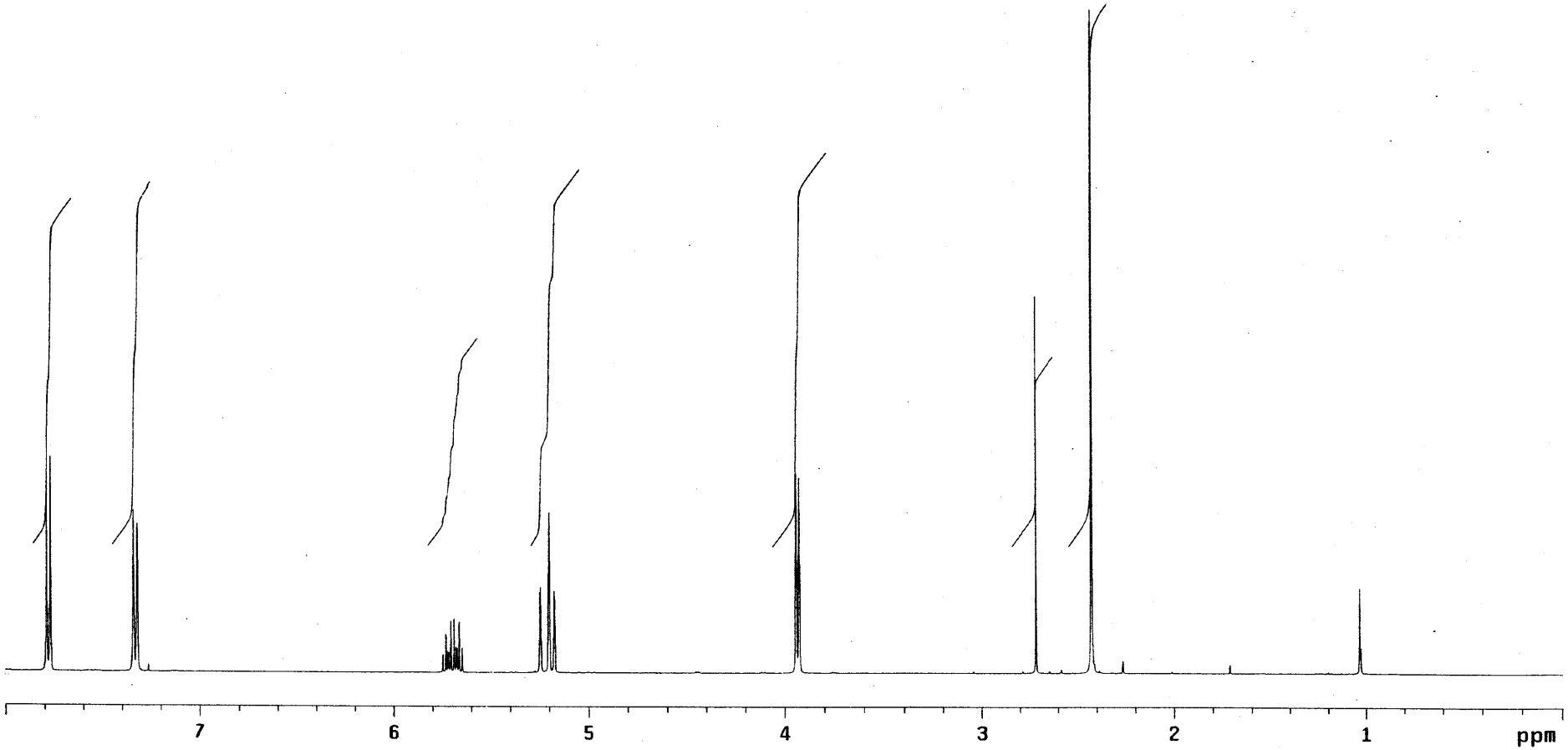


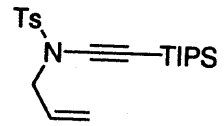


S1

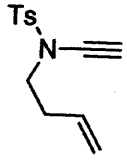


15a

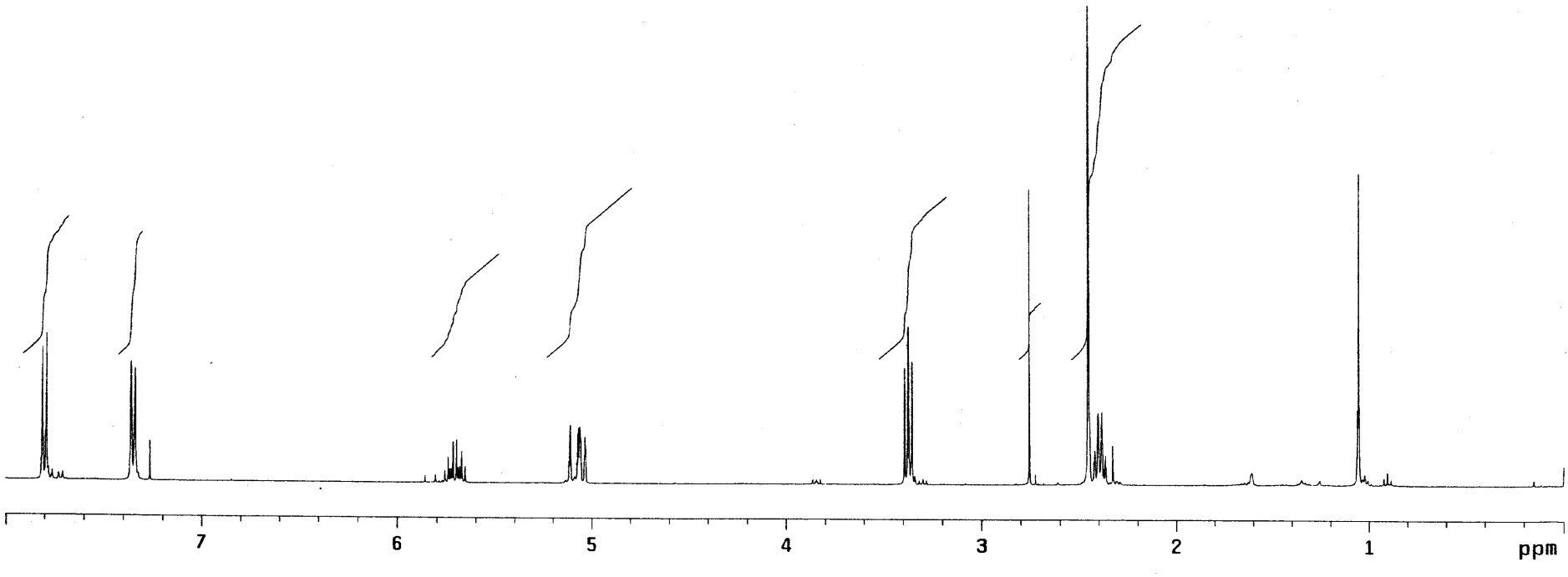


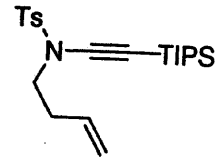


S2



15b





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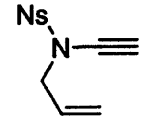

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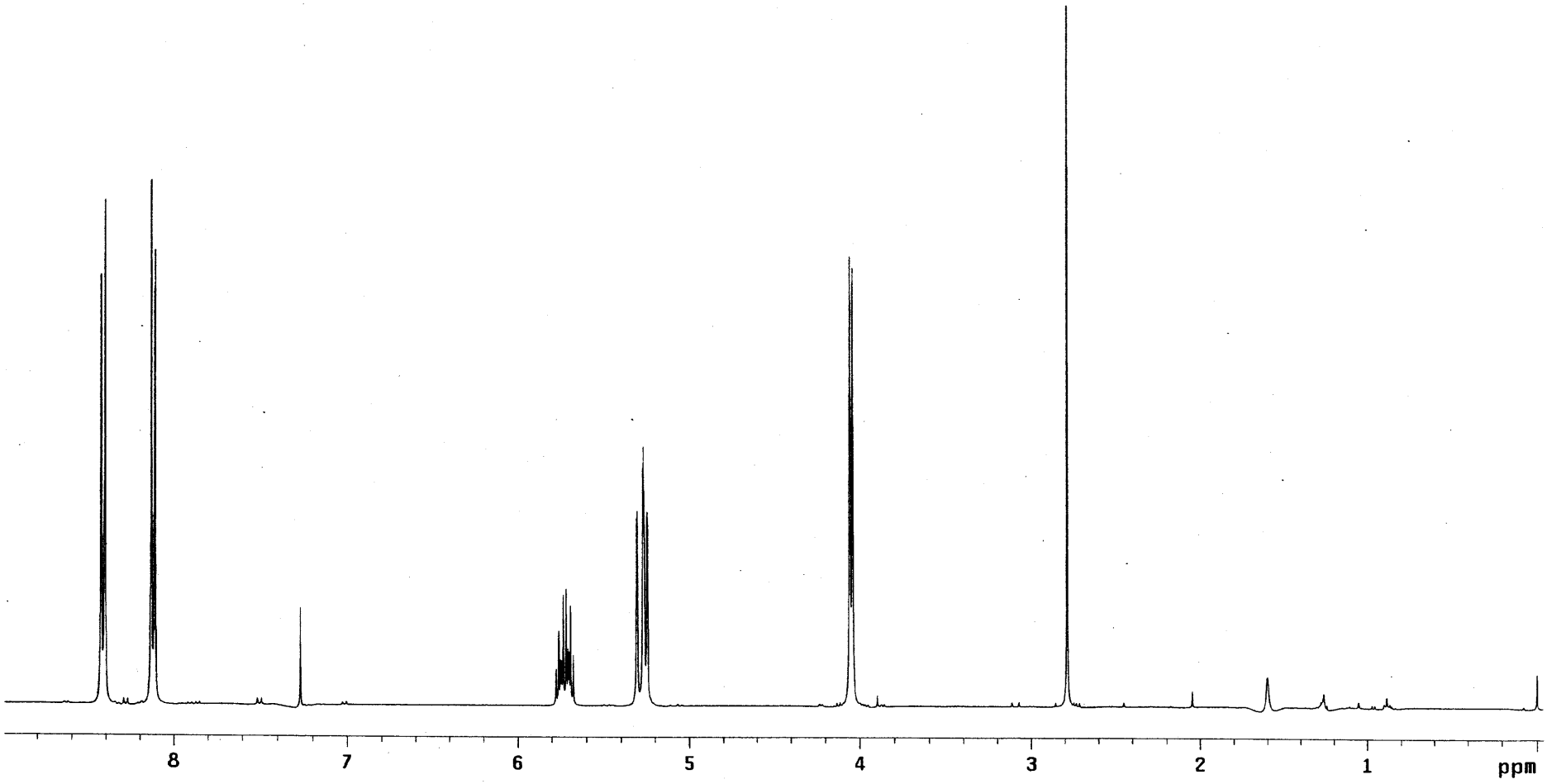

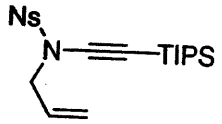

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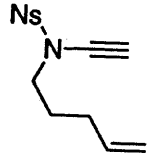

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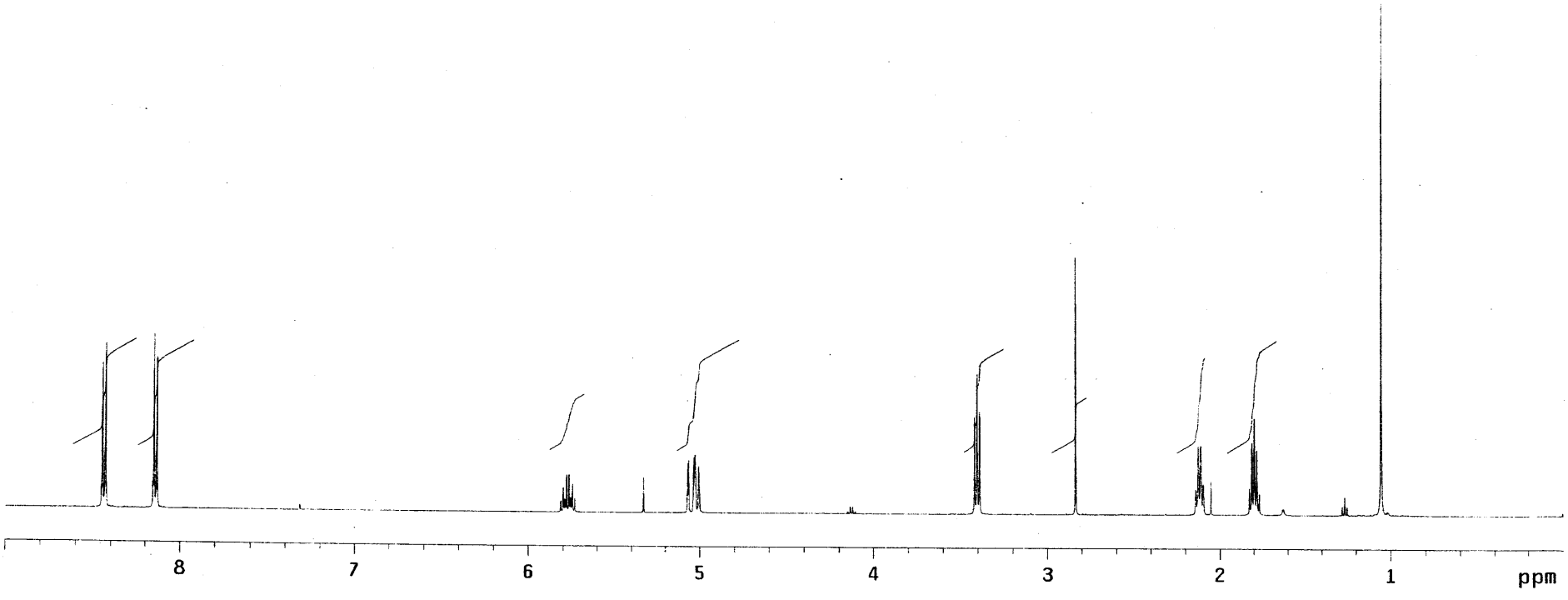

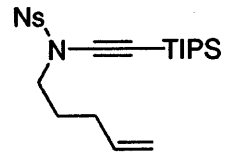

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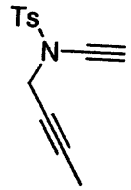

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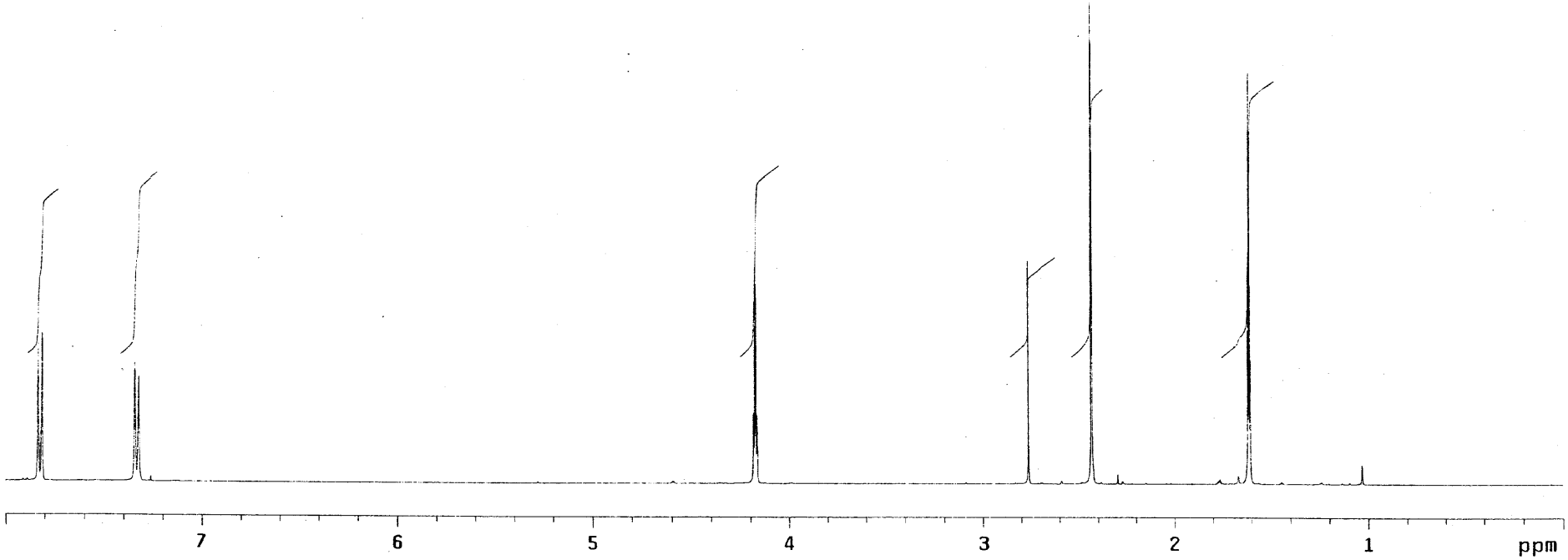

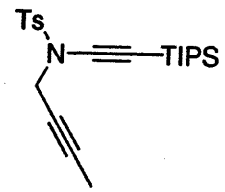

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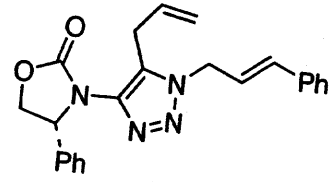

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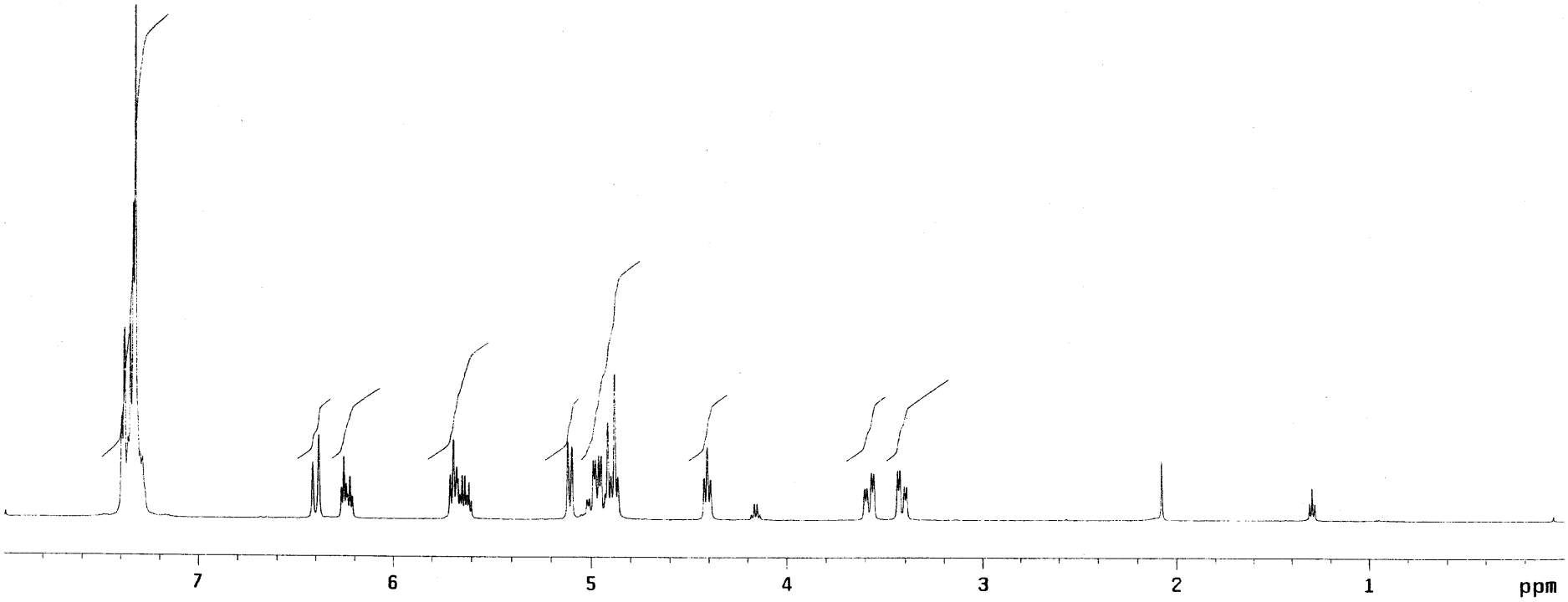

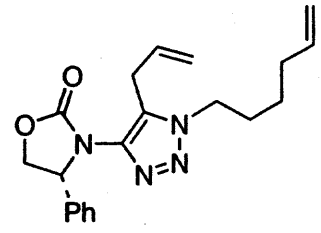

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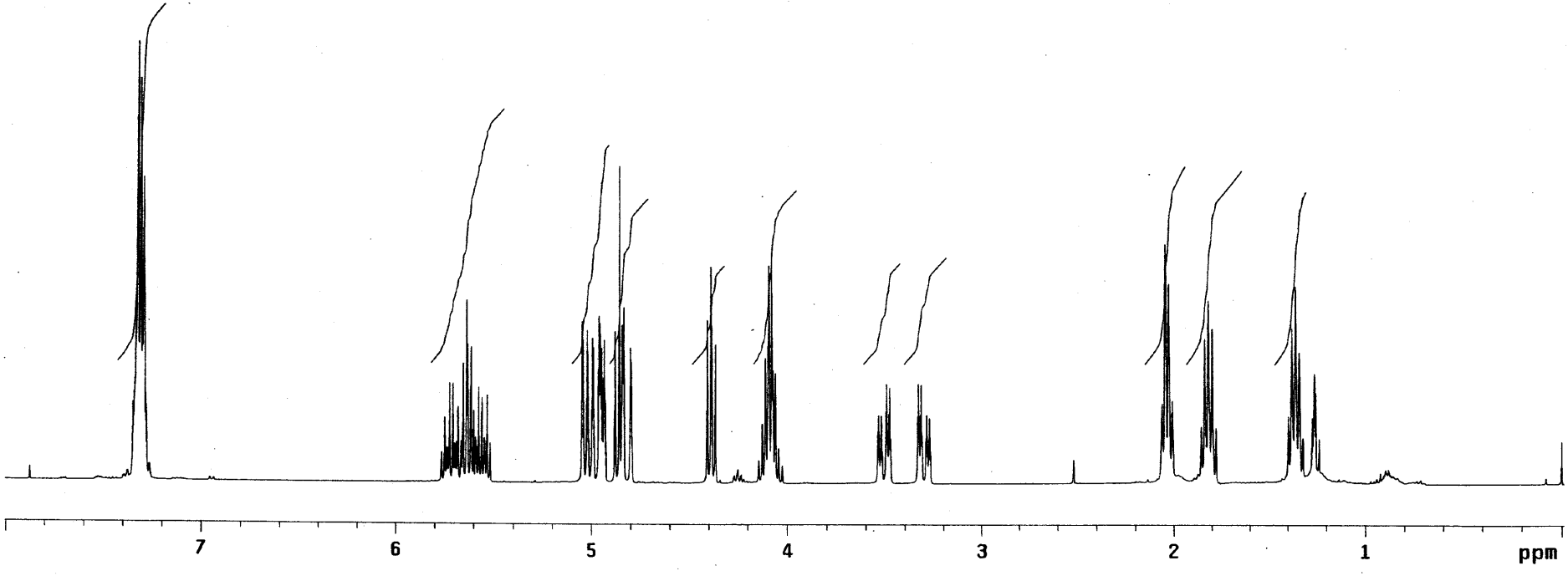

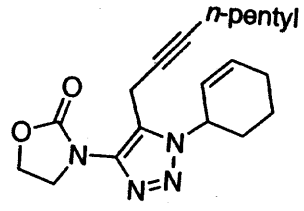

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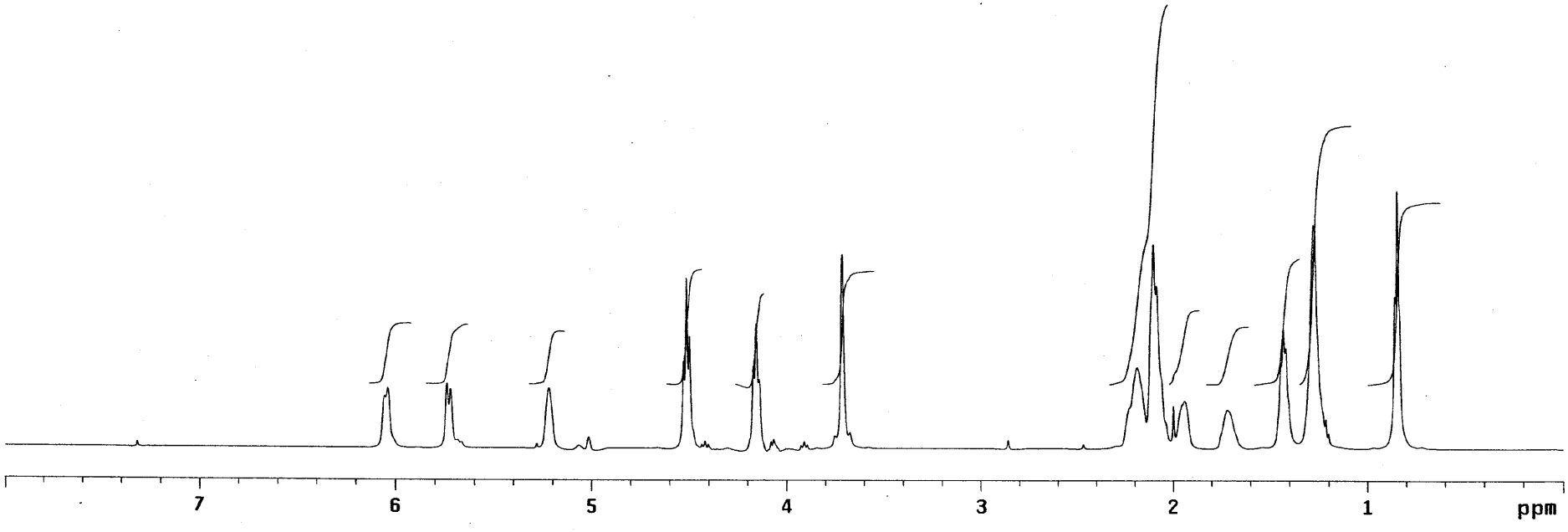

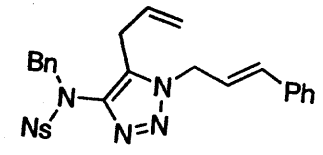

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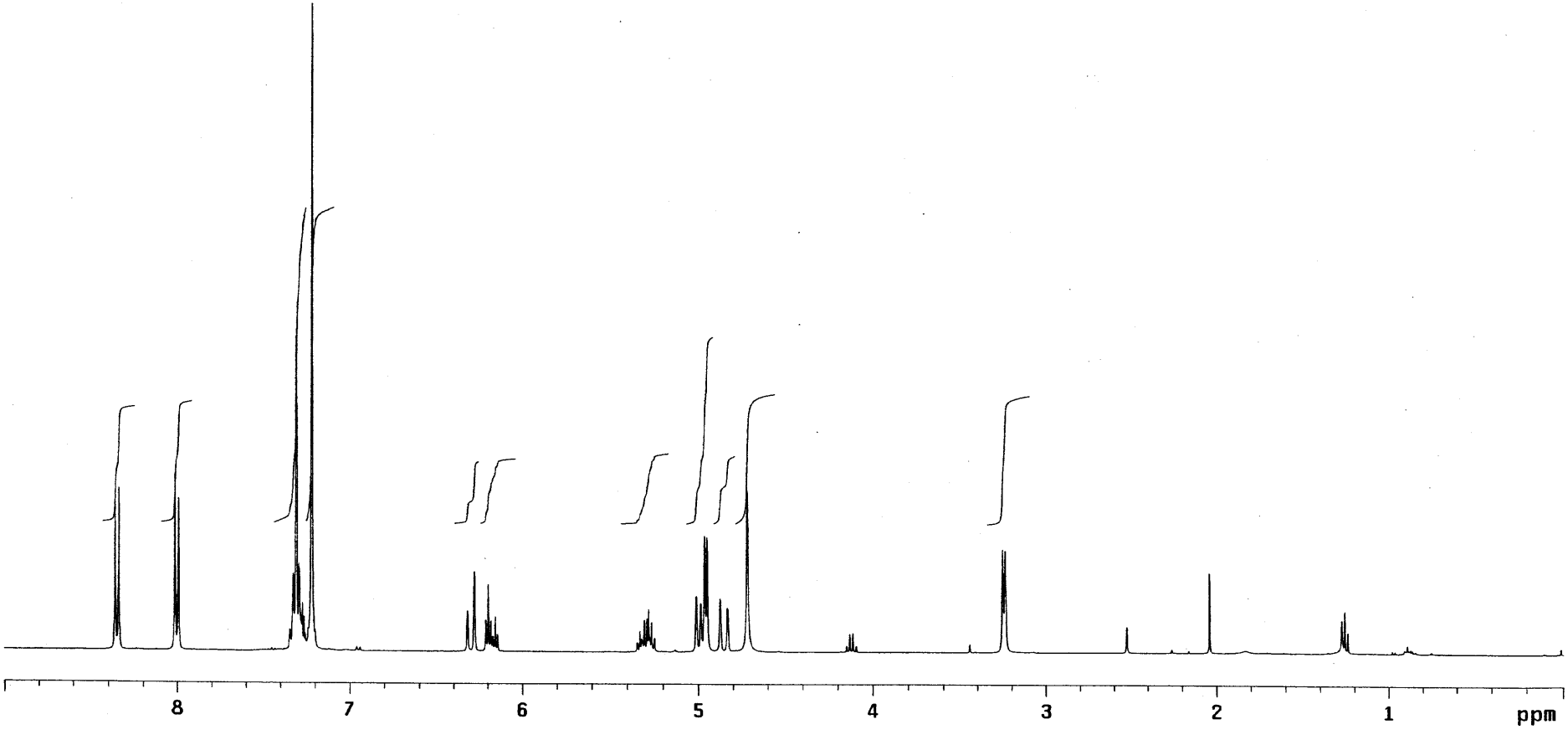

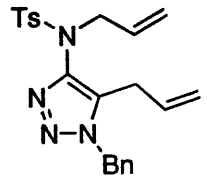

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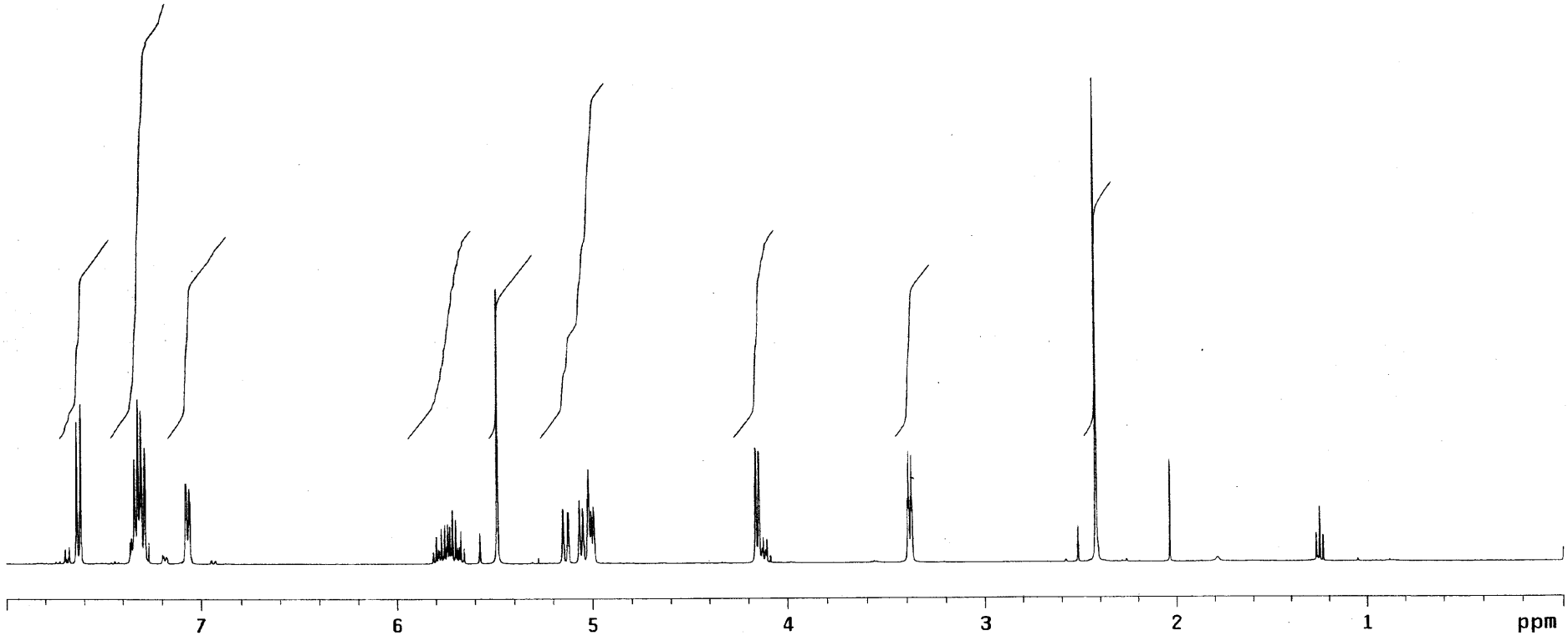

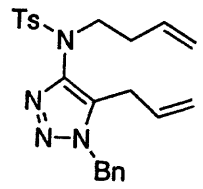

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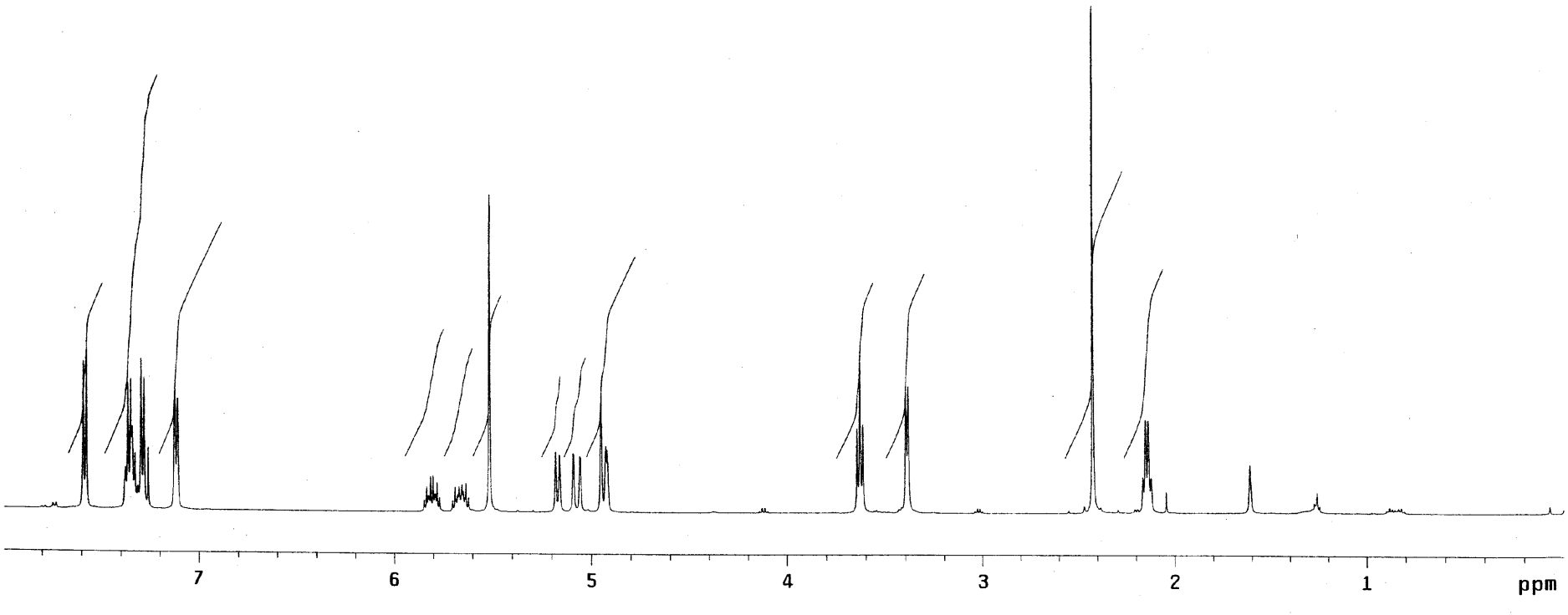

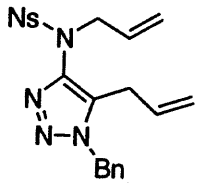

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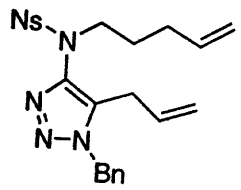

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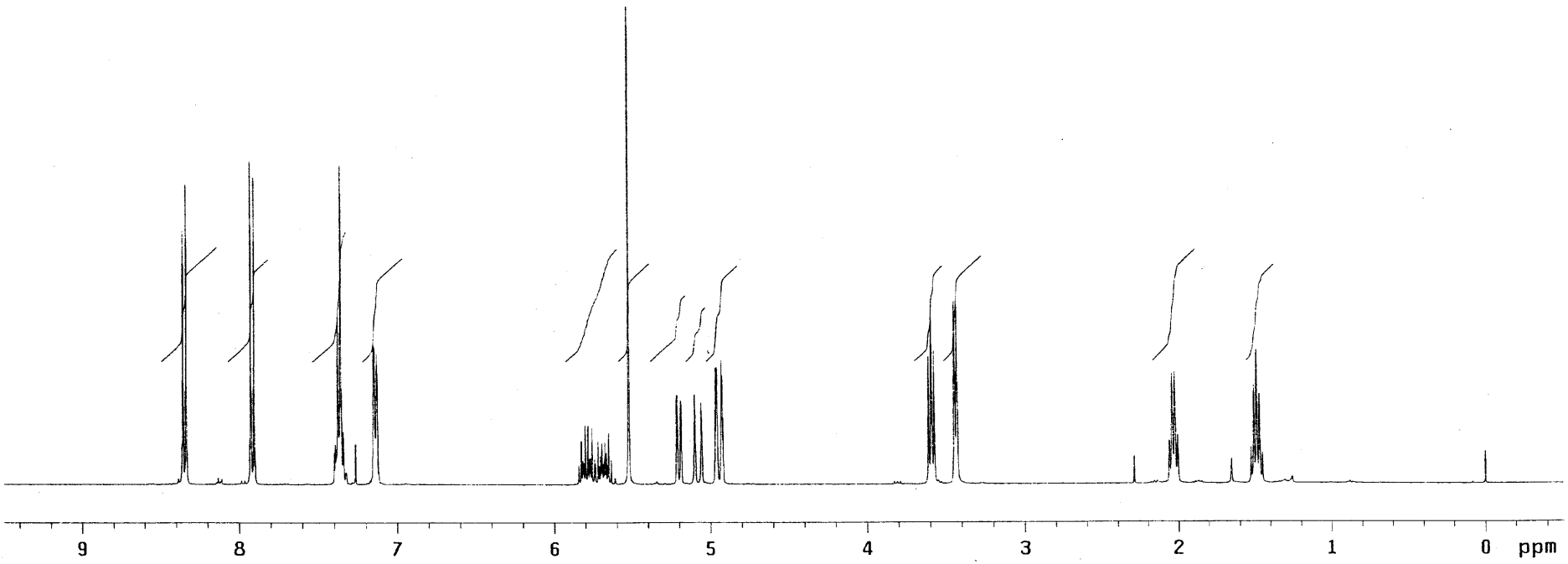

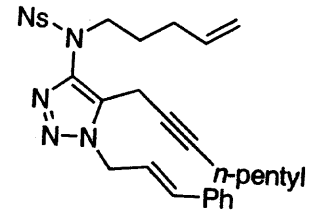

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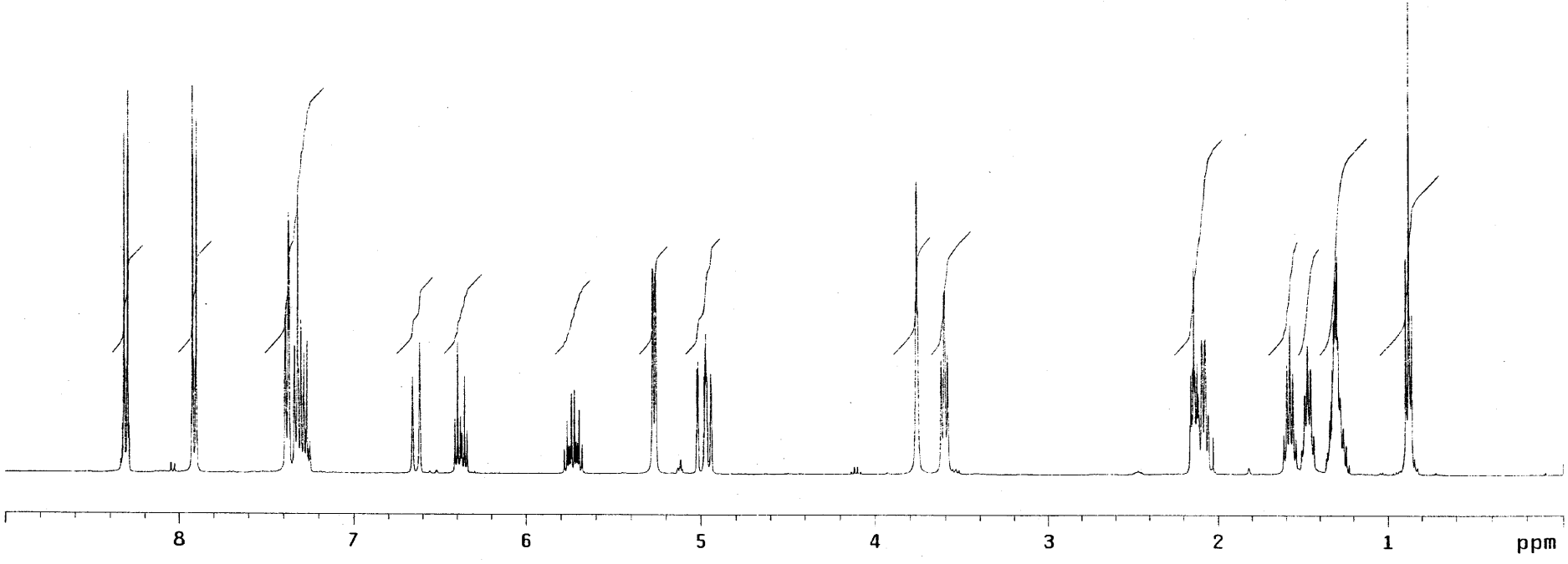

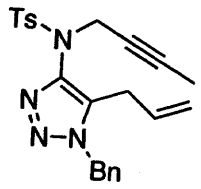

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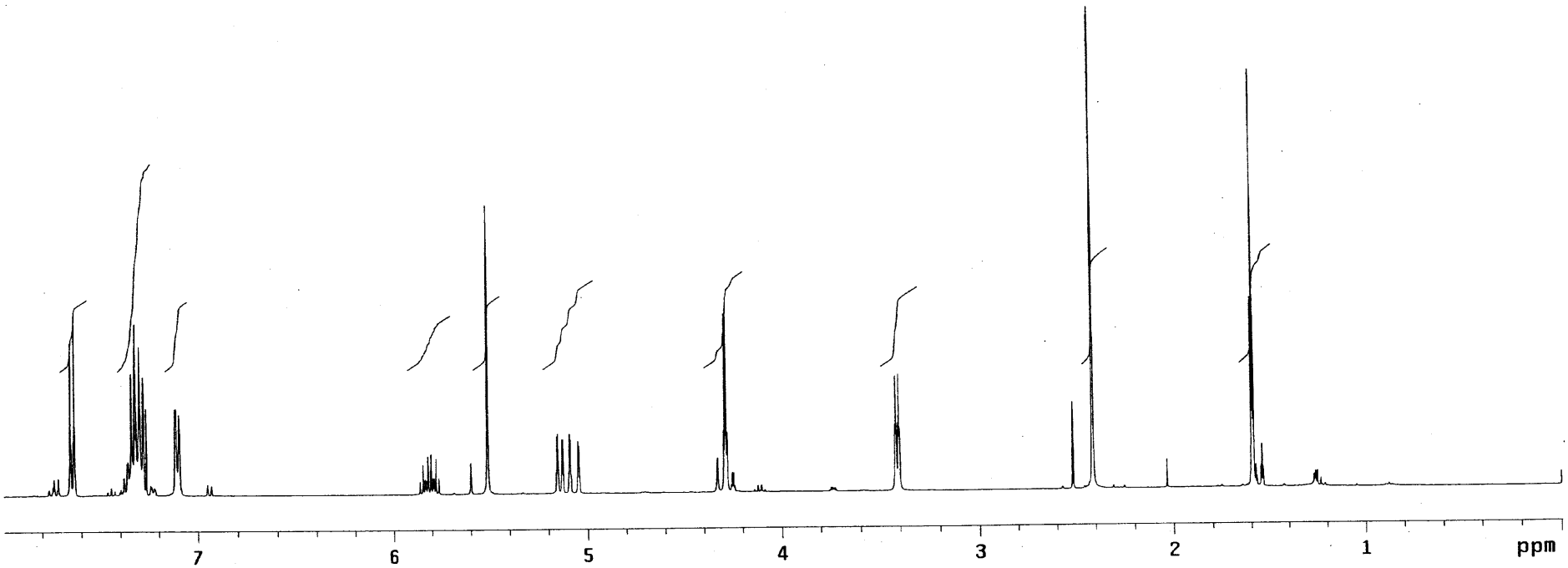

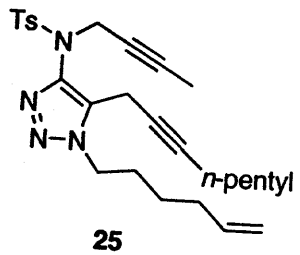

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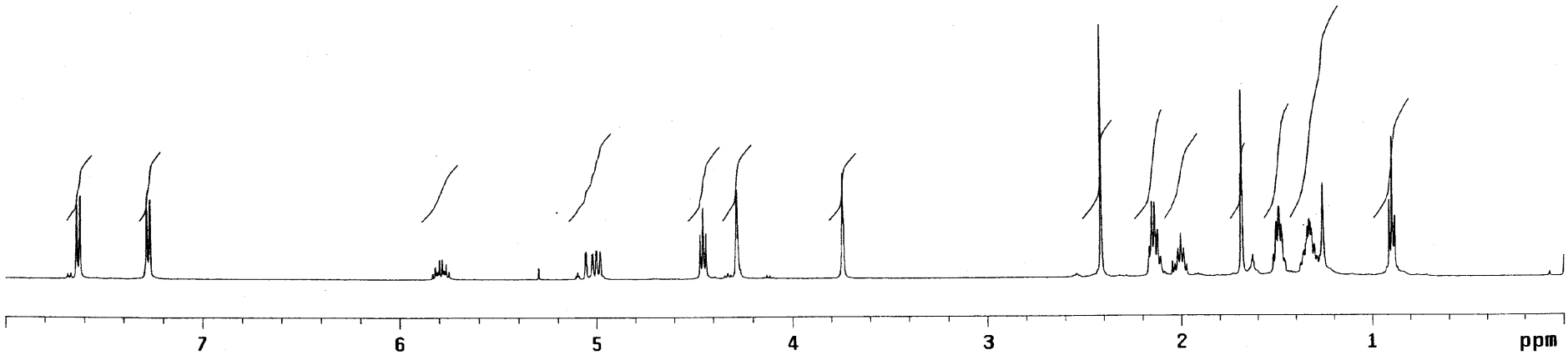

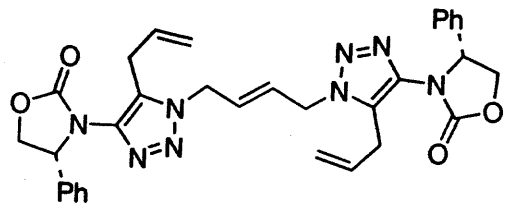

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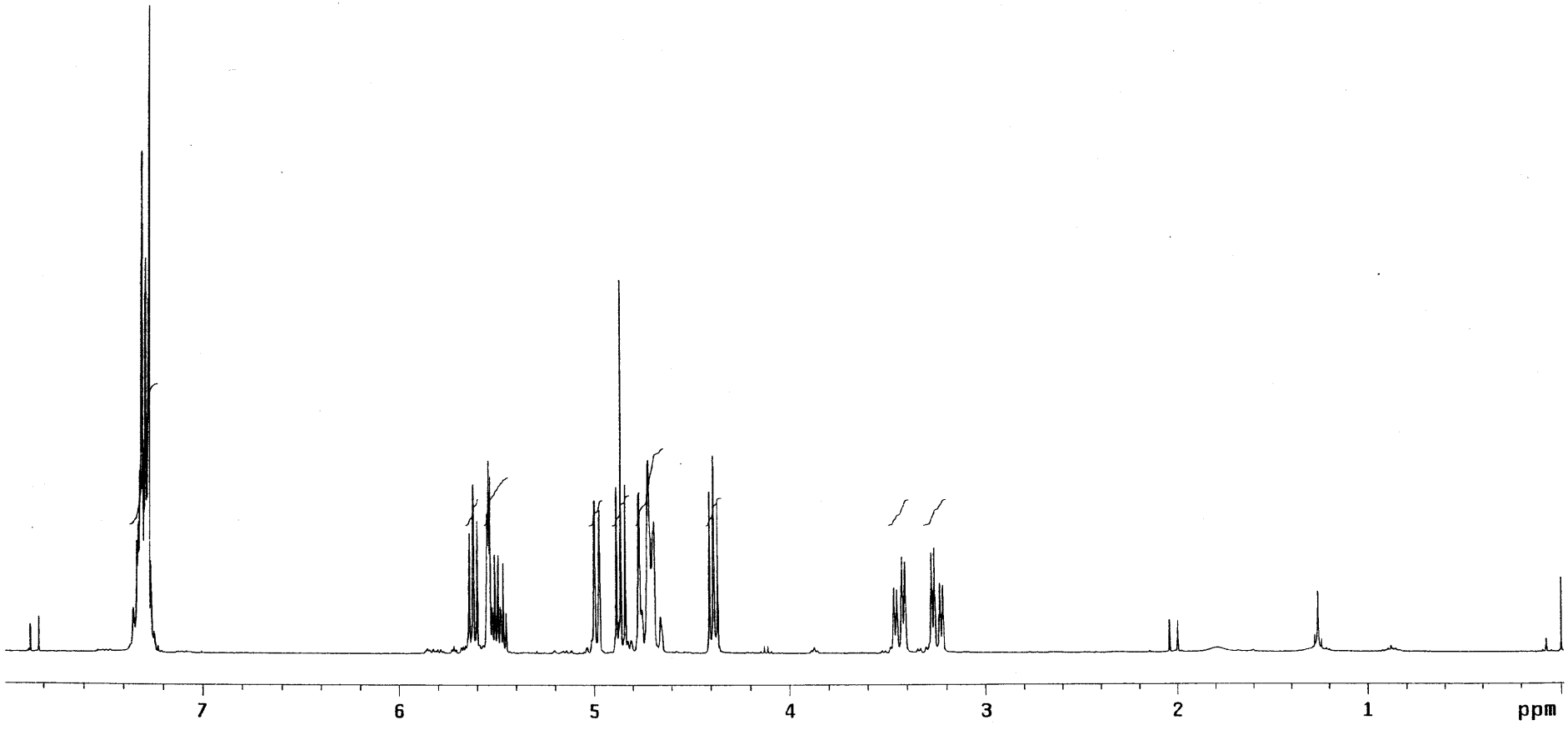

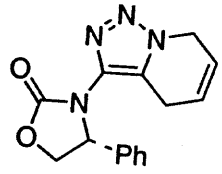

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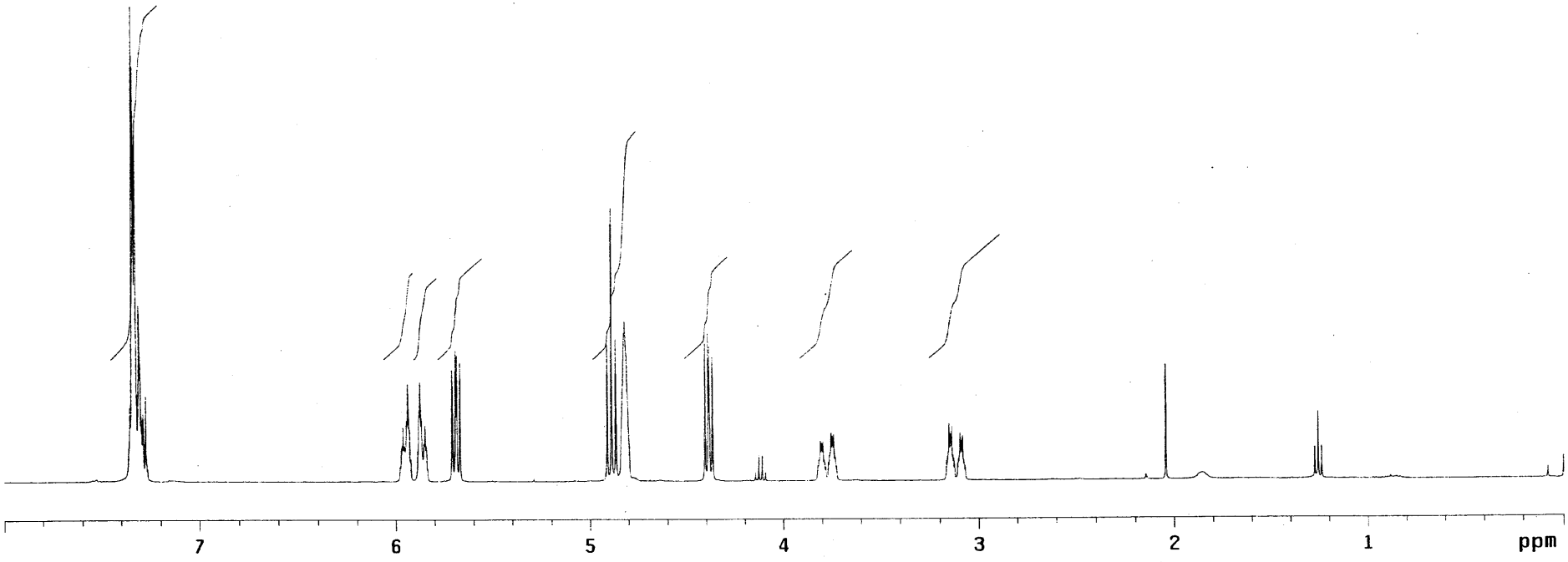

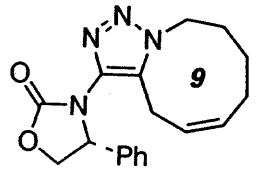

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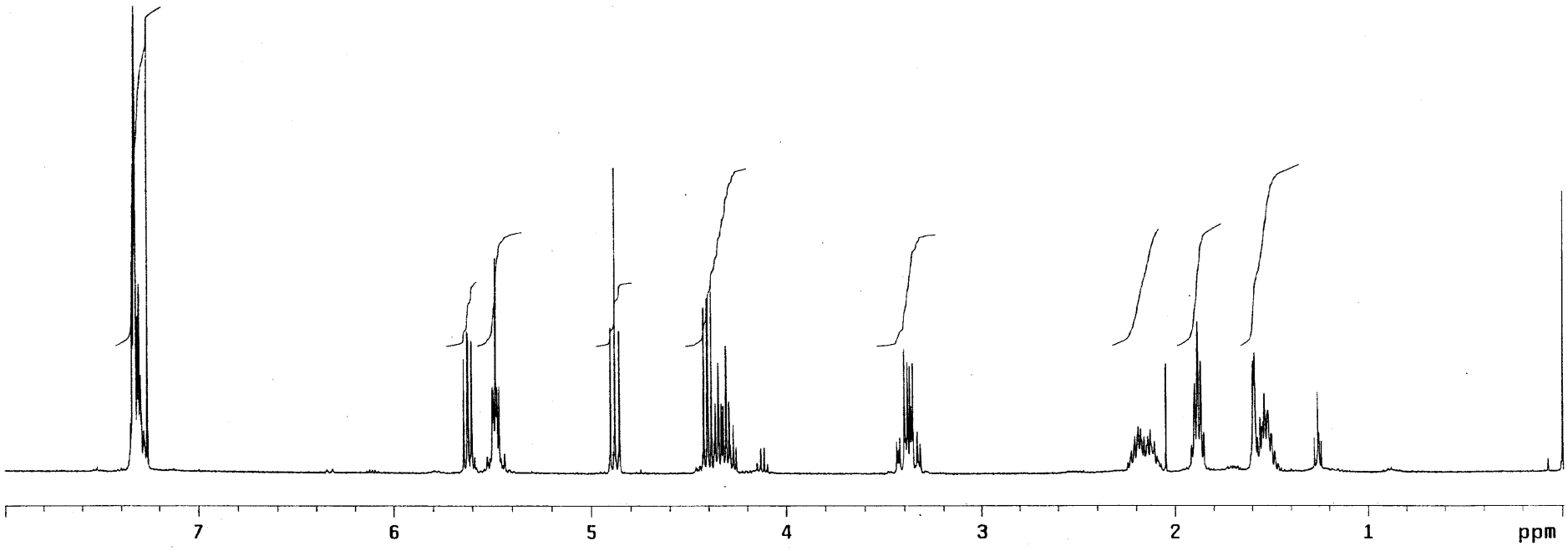

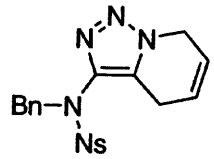

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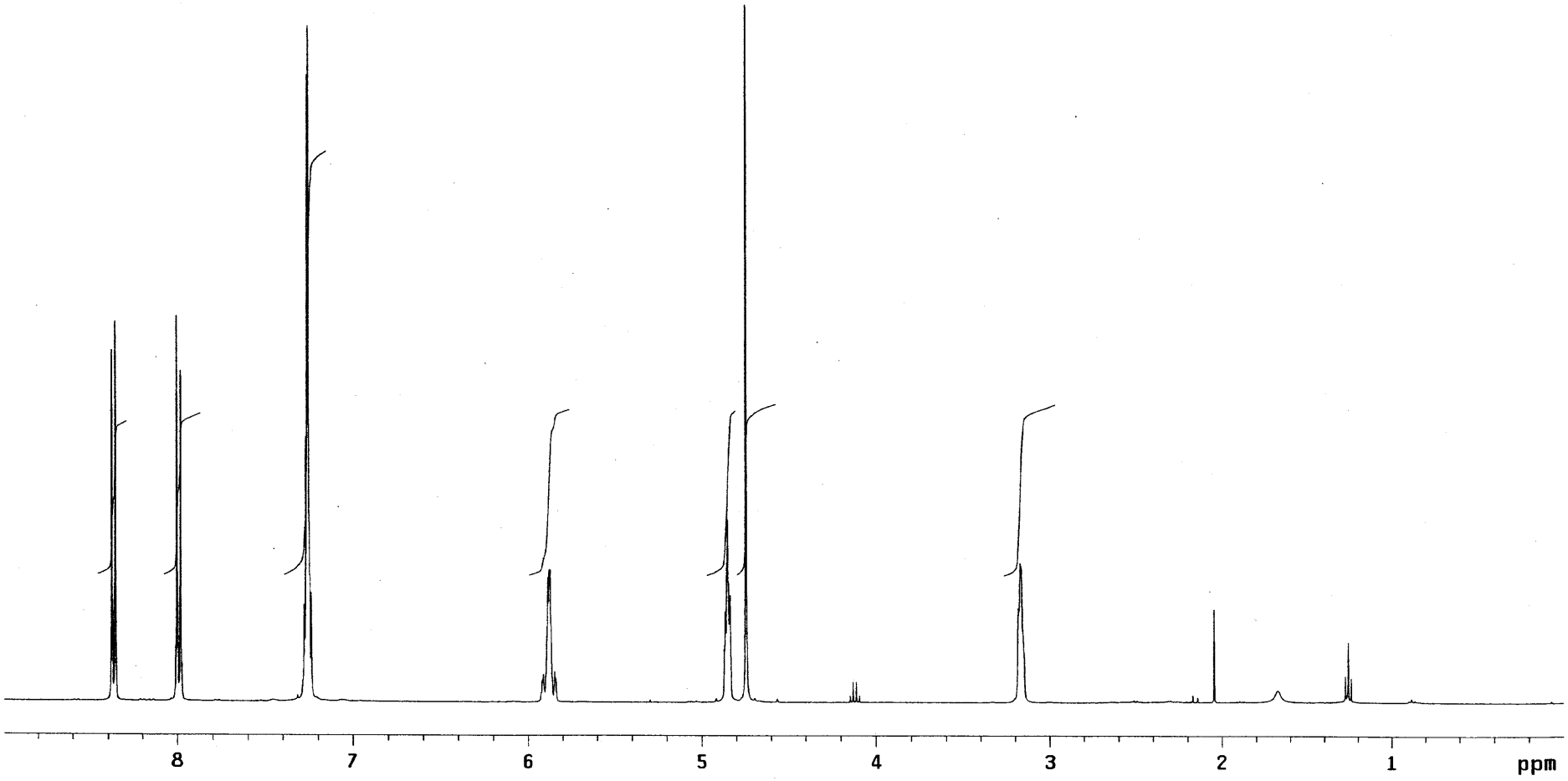

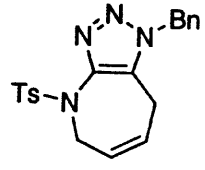

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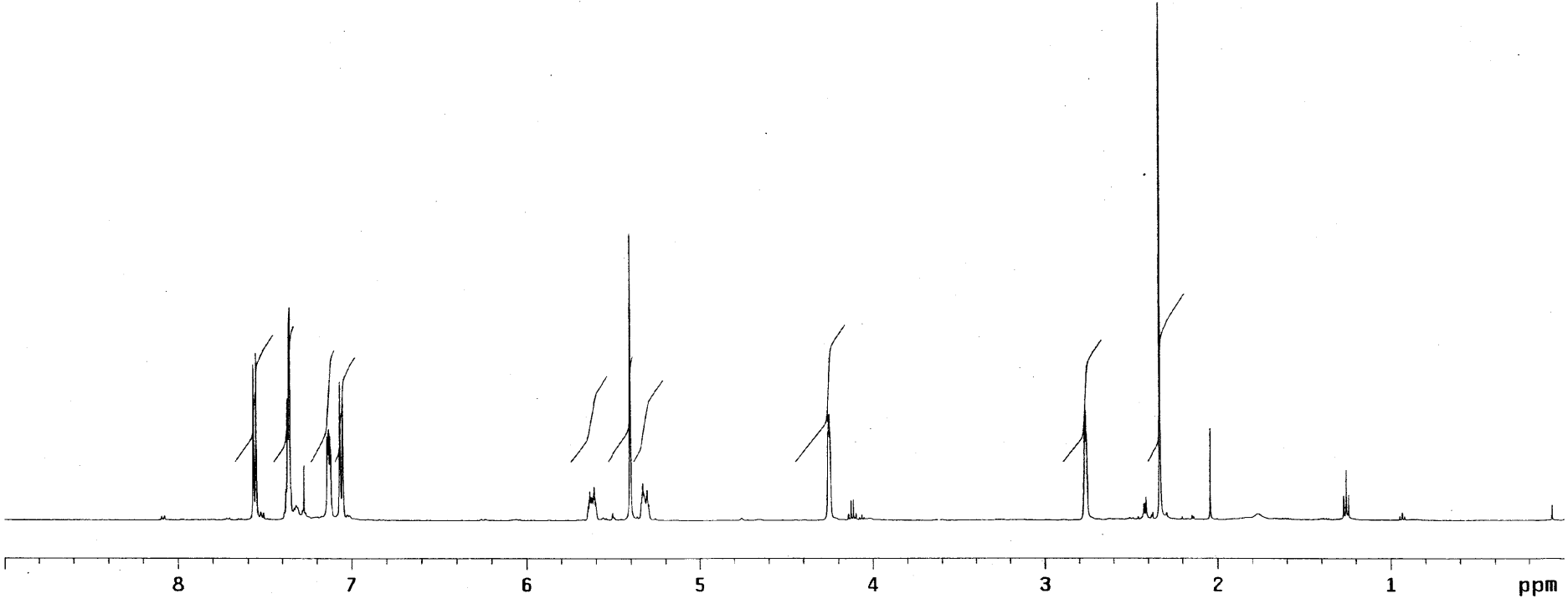

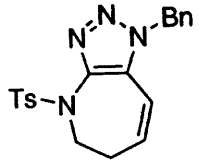

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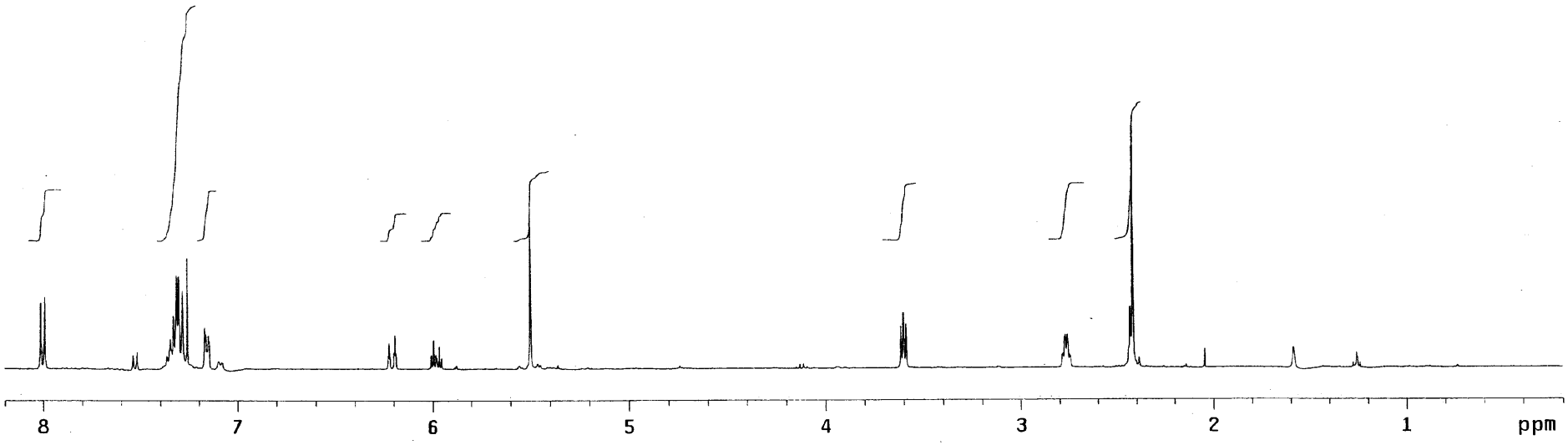

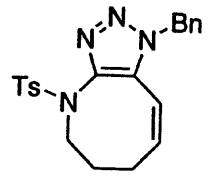

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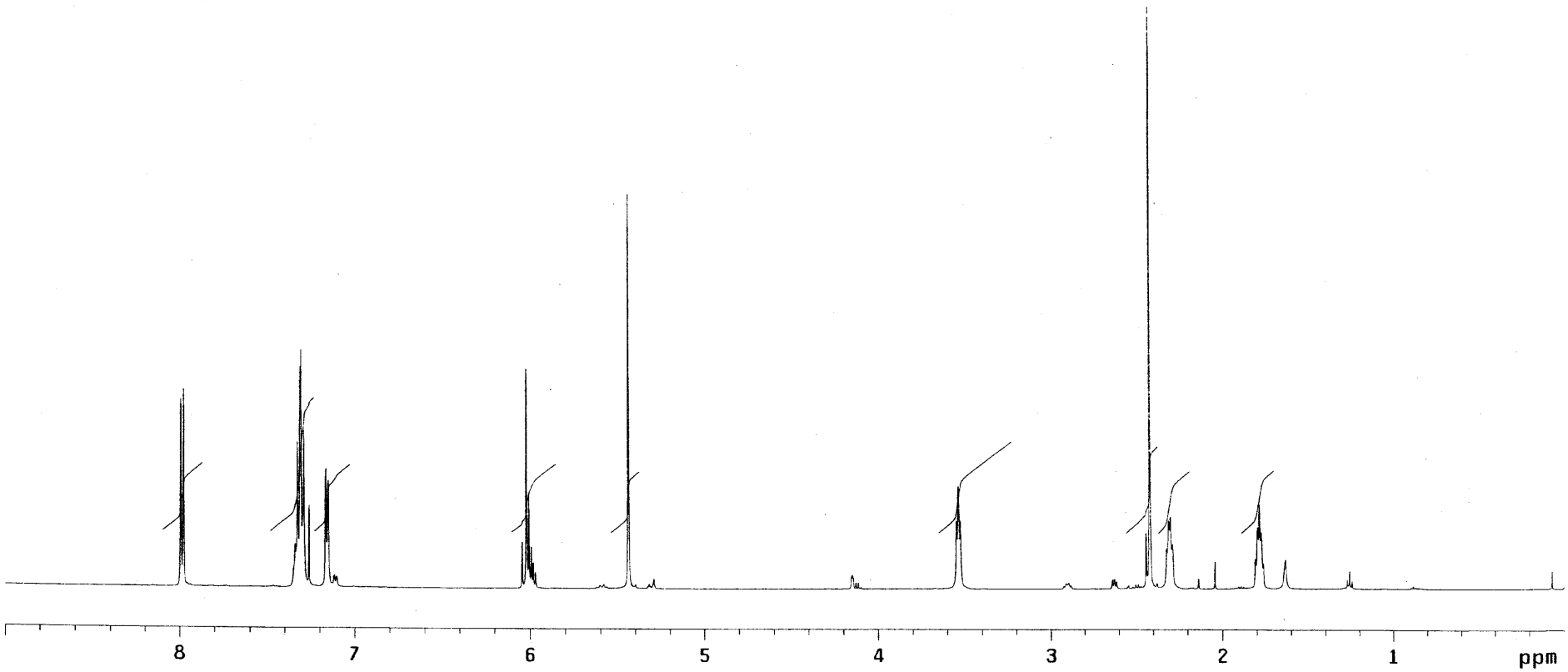

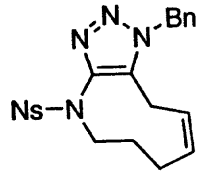

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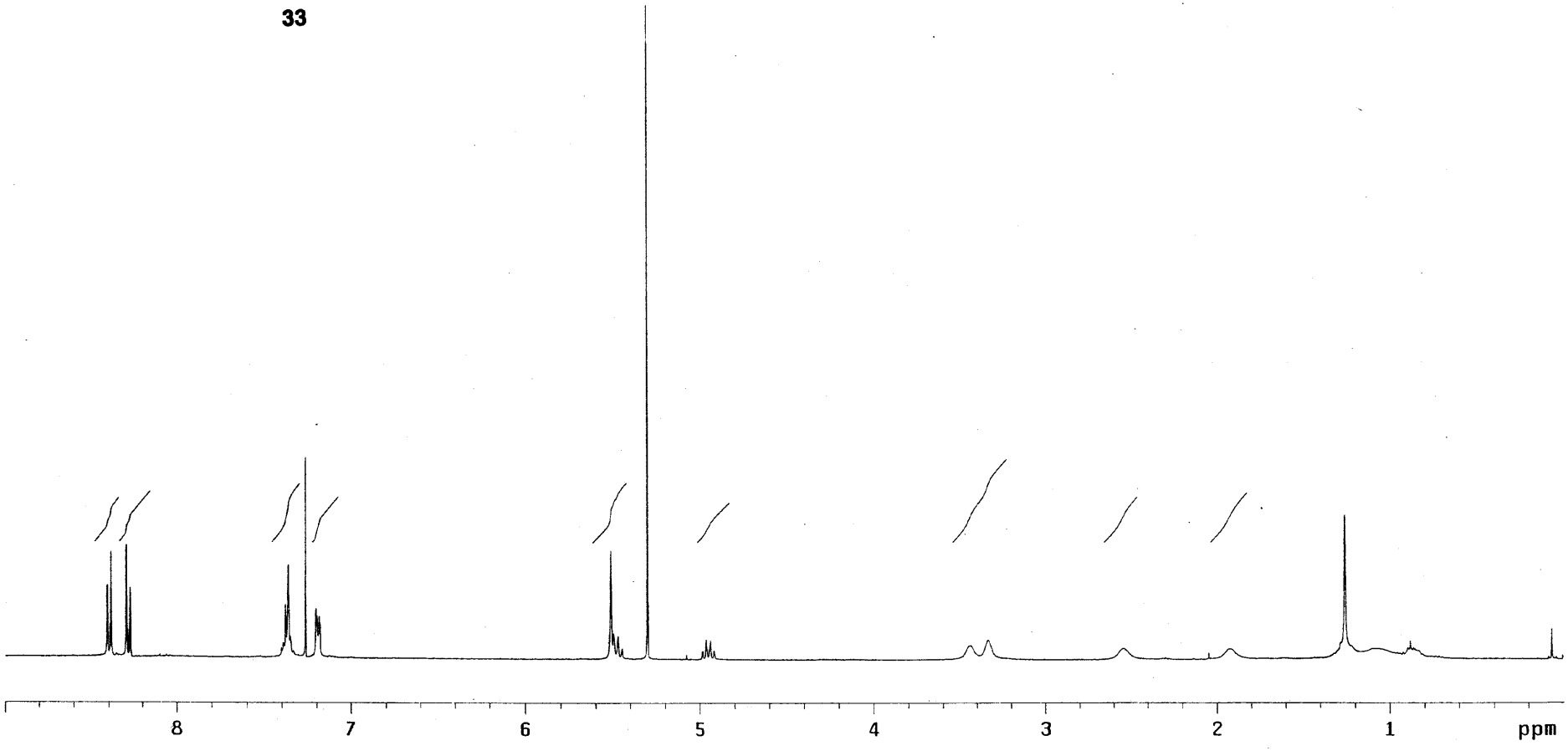

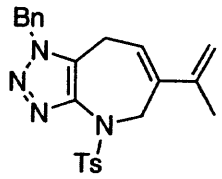

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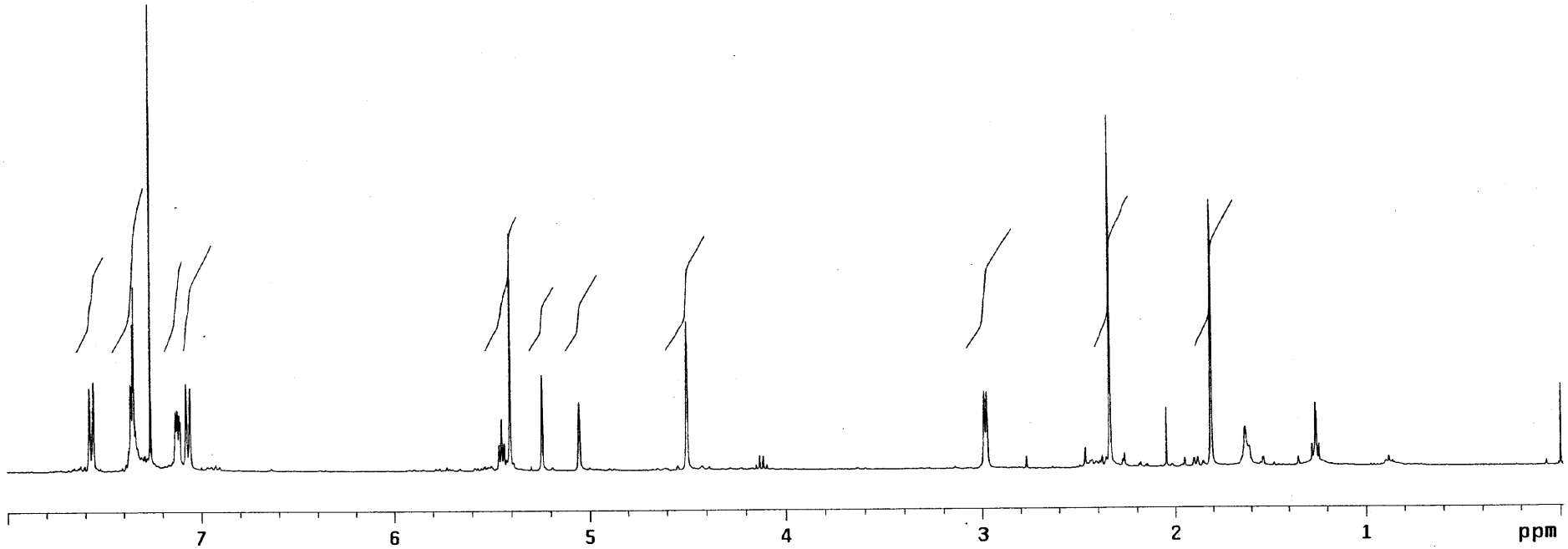

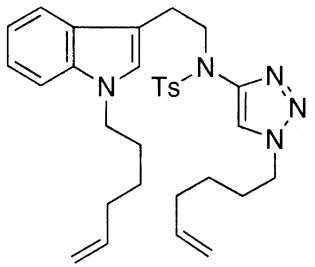

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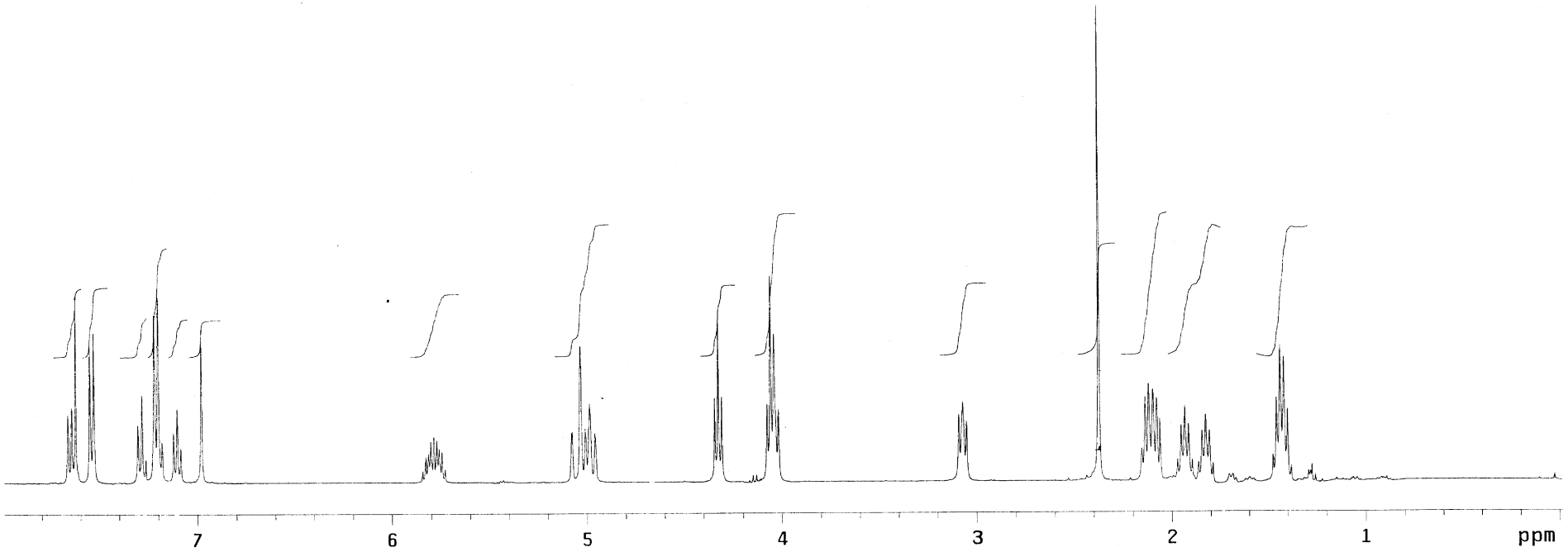

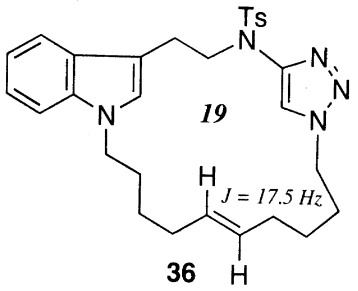

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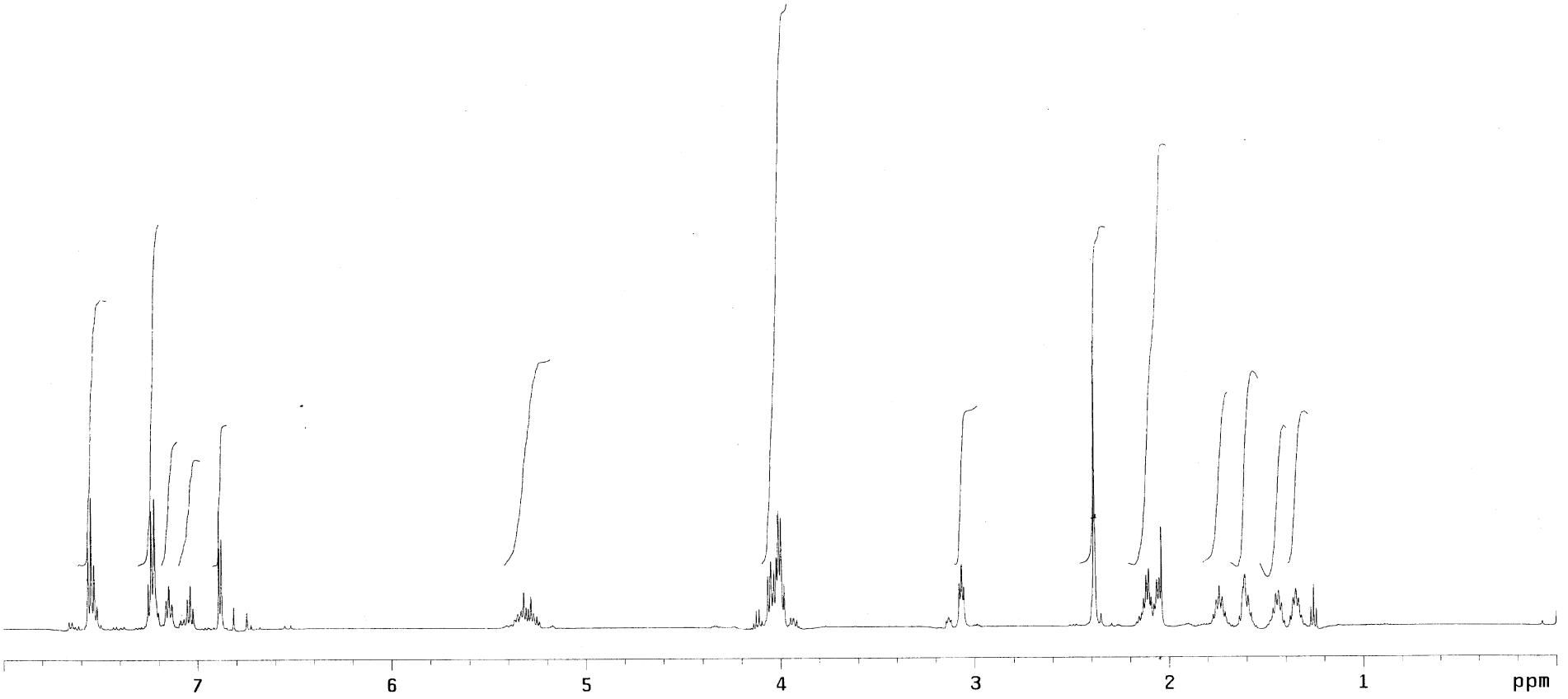
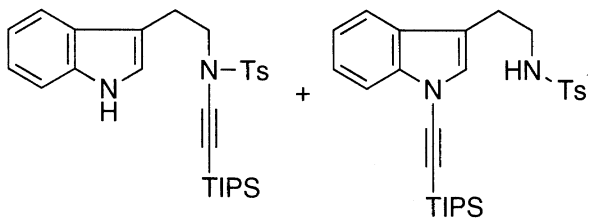
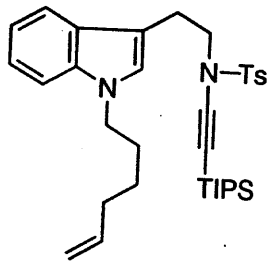


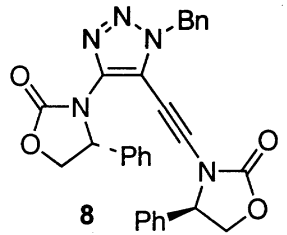


(6 : 1 inseperable regioisomers)

S7



S8



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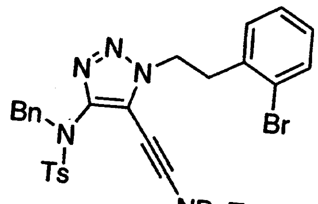

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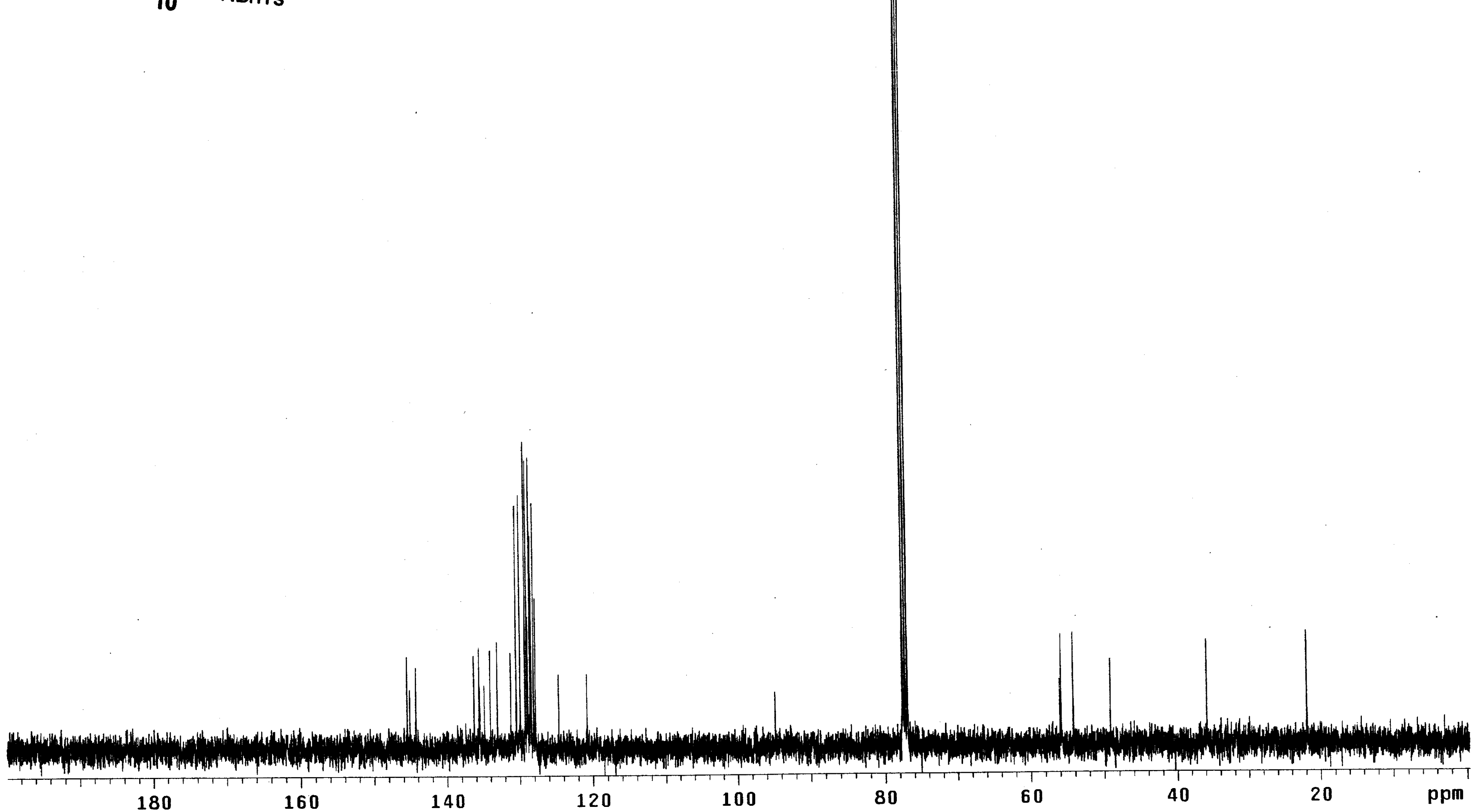

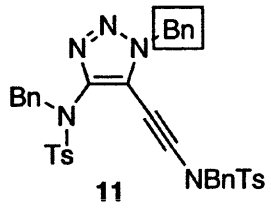

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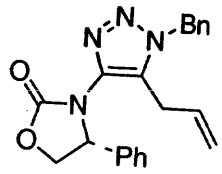

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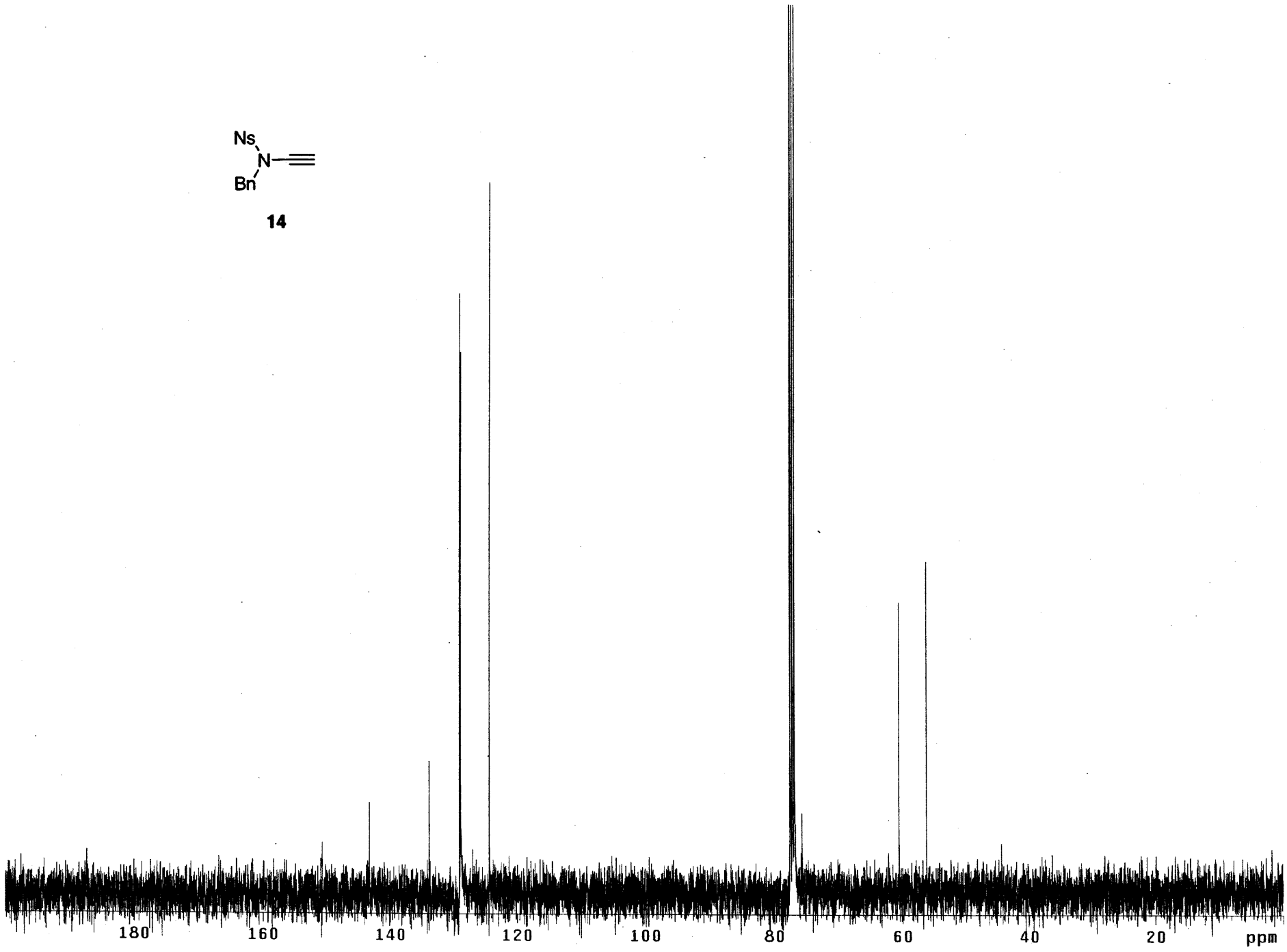

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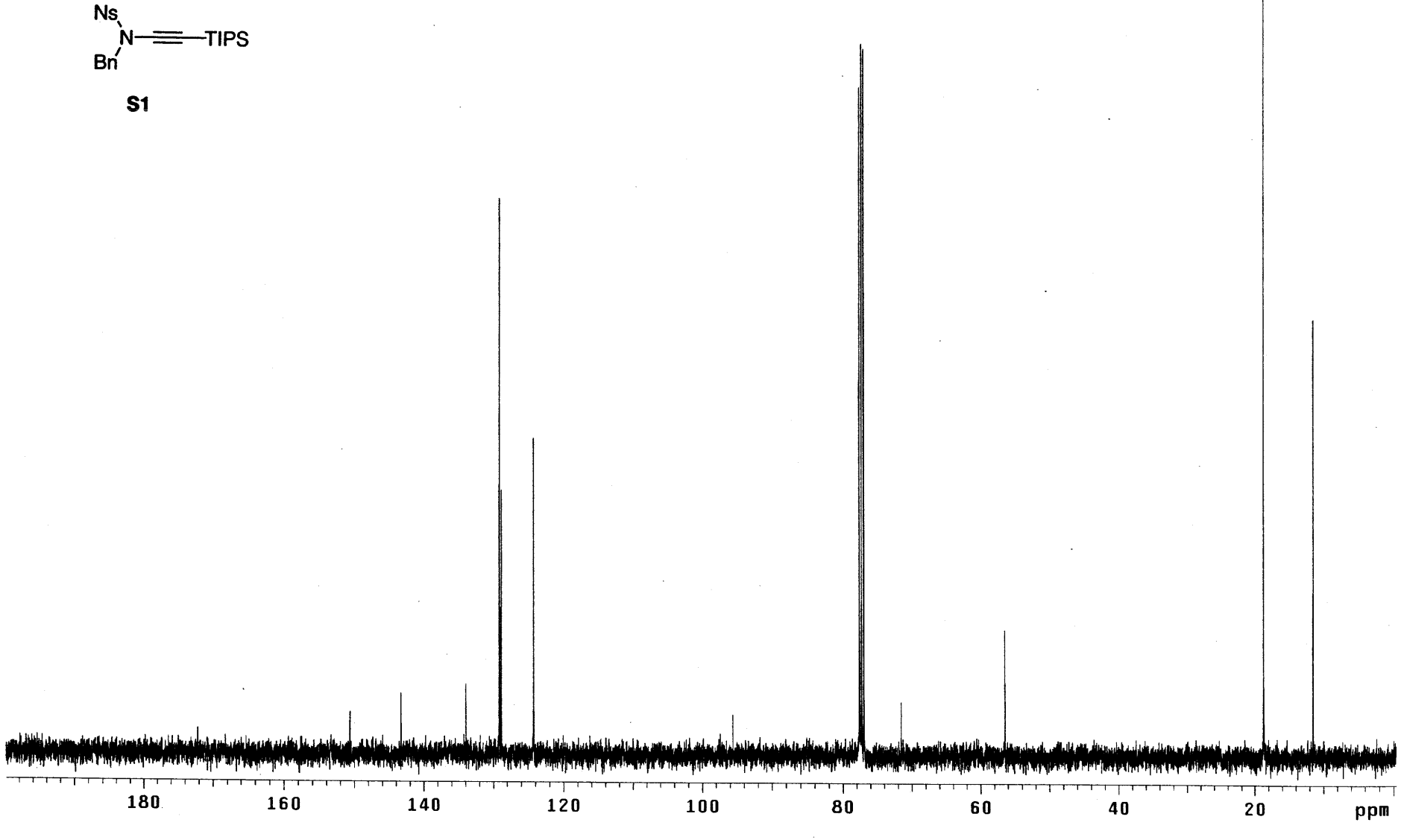

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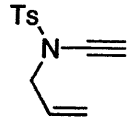

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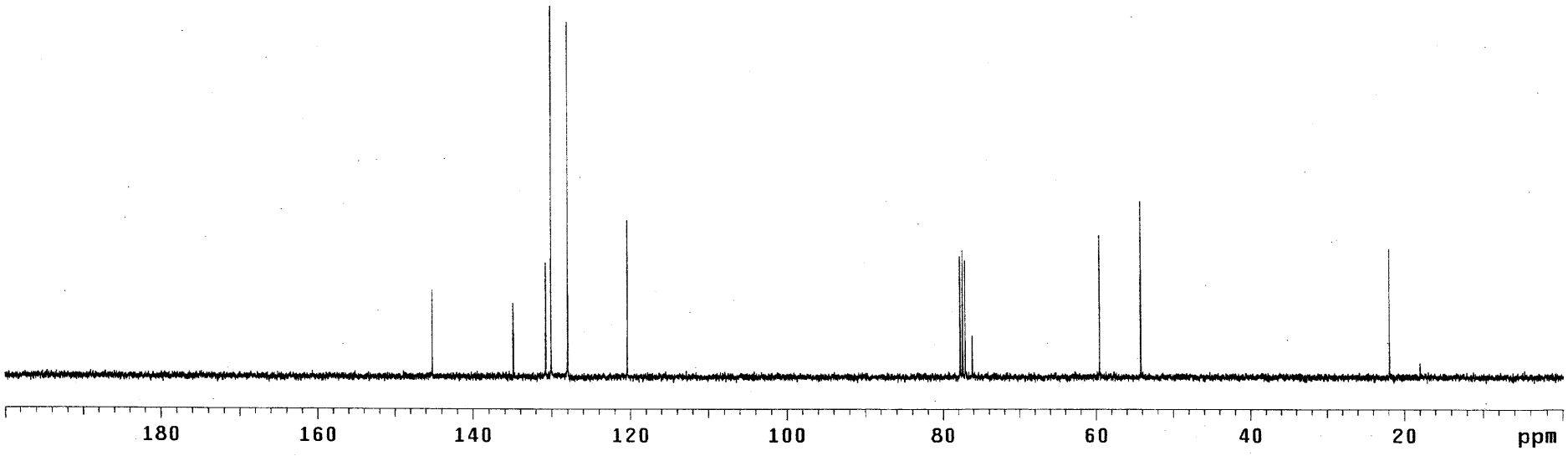

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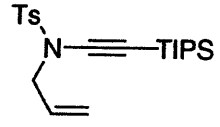

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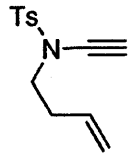

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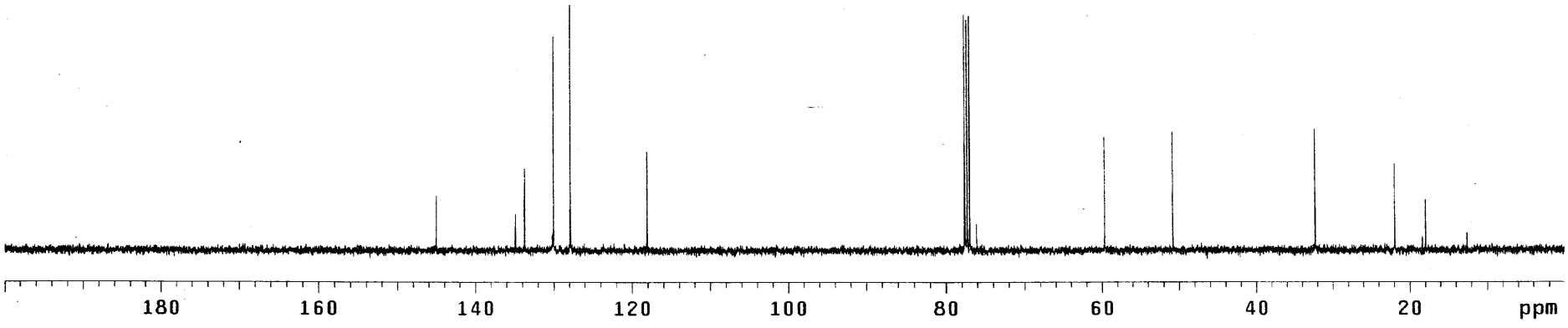

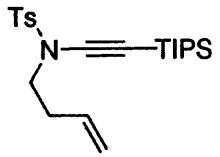

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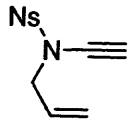

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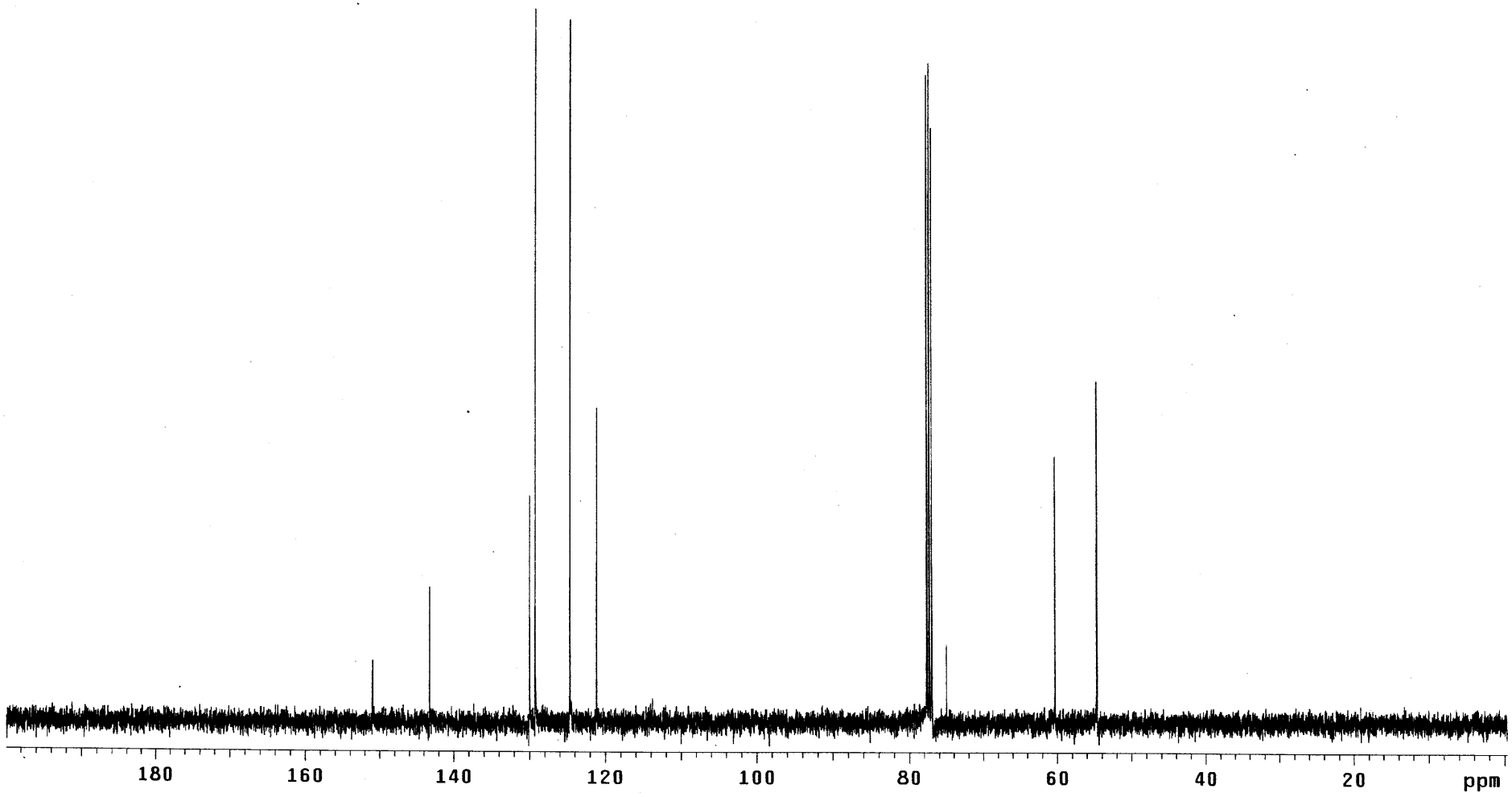

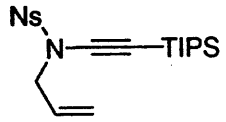

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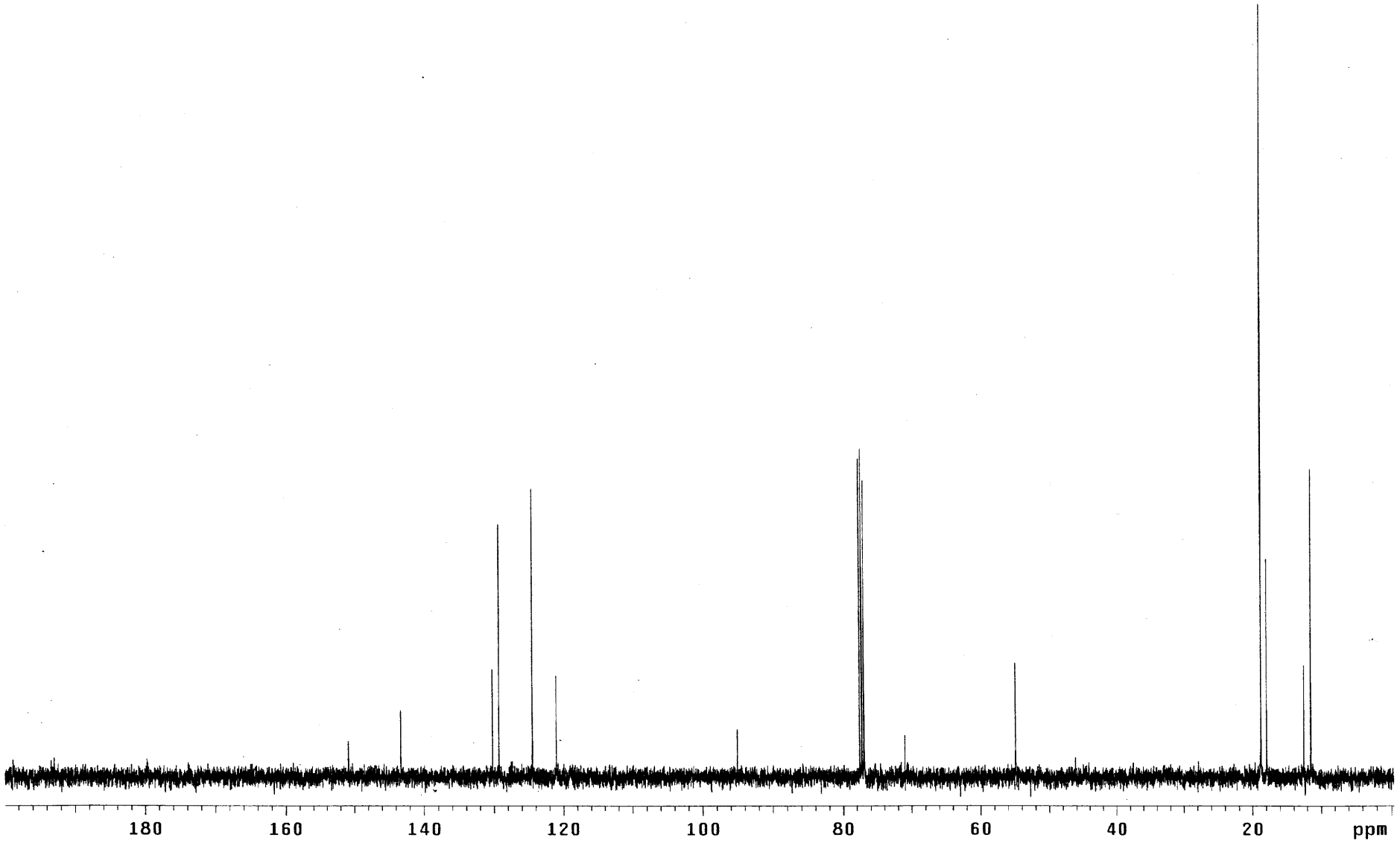

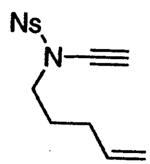

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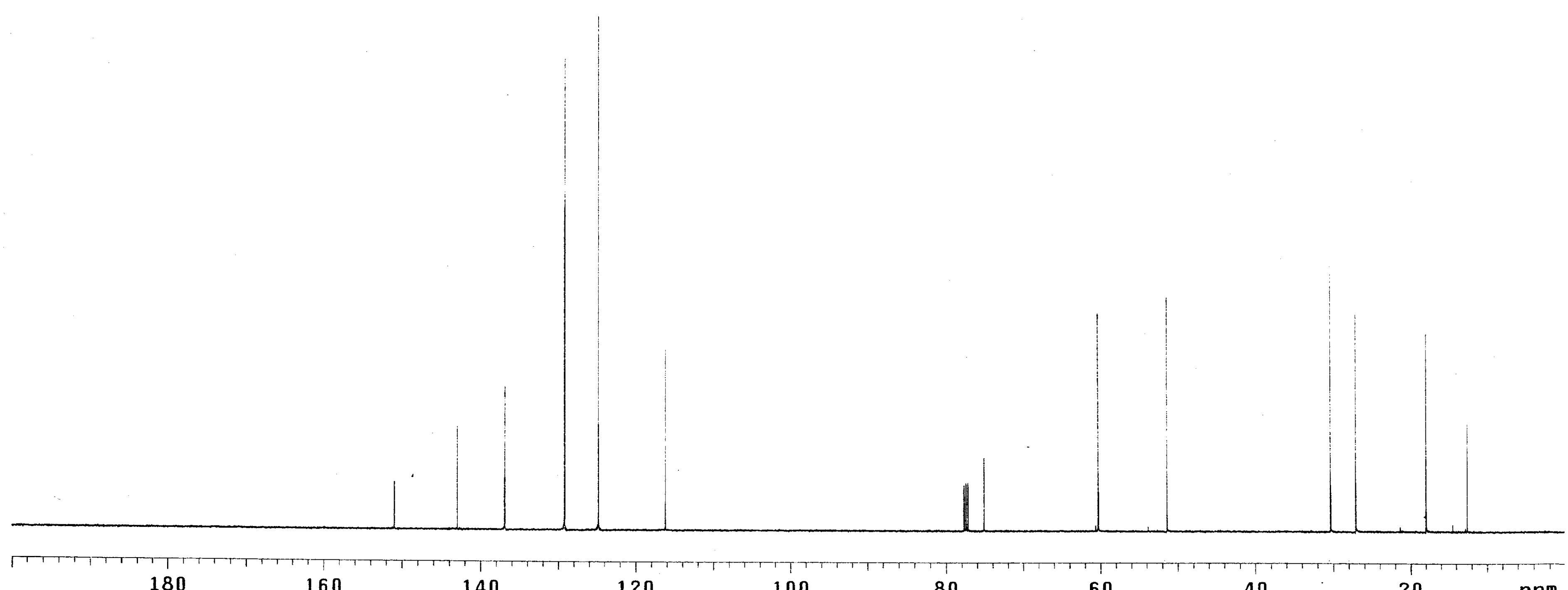

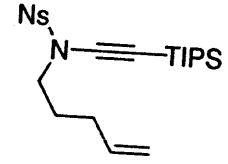

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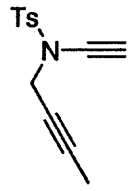

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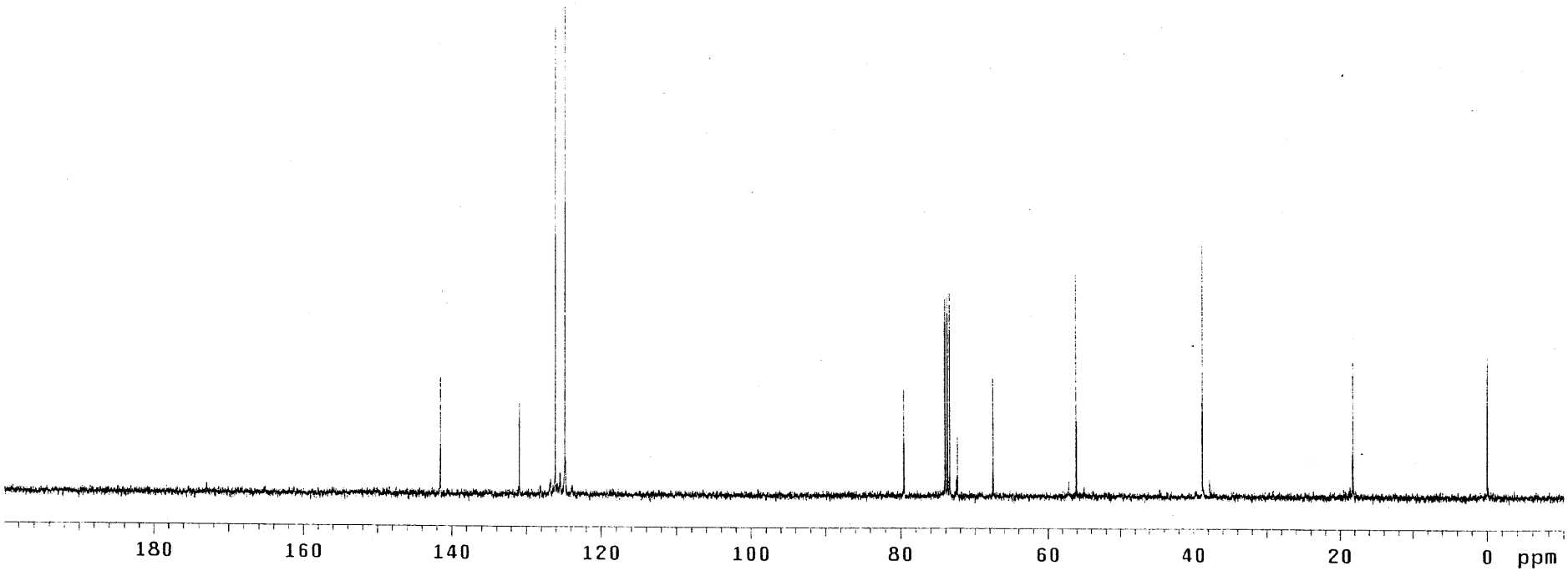

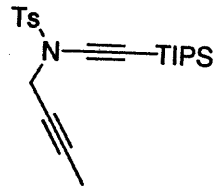

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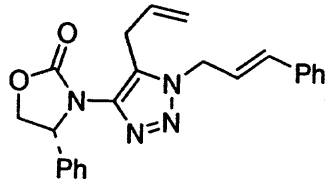

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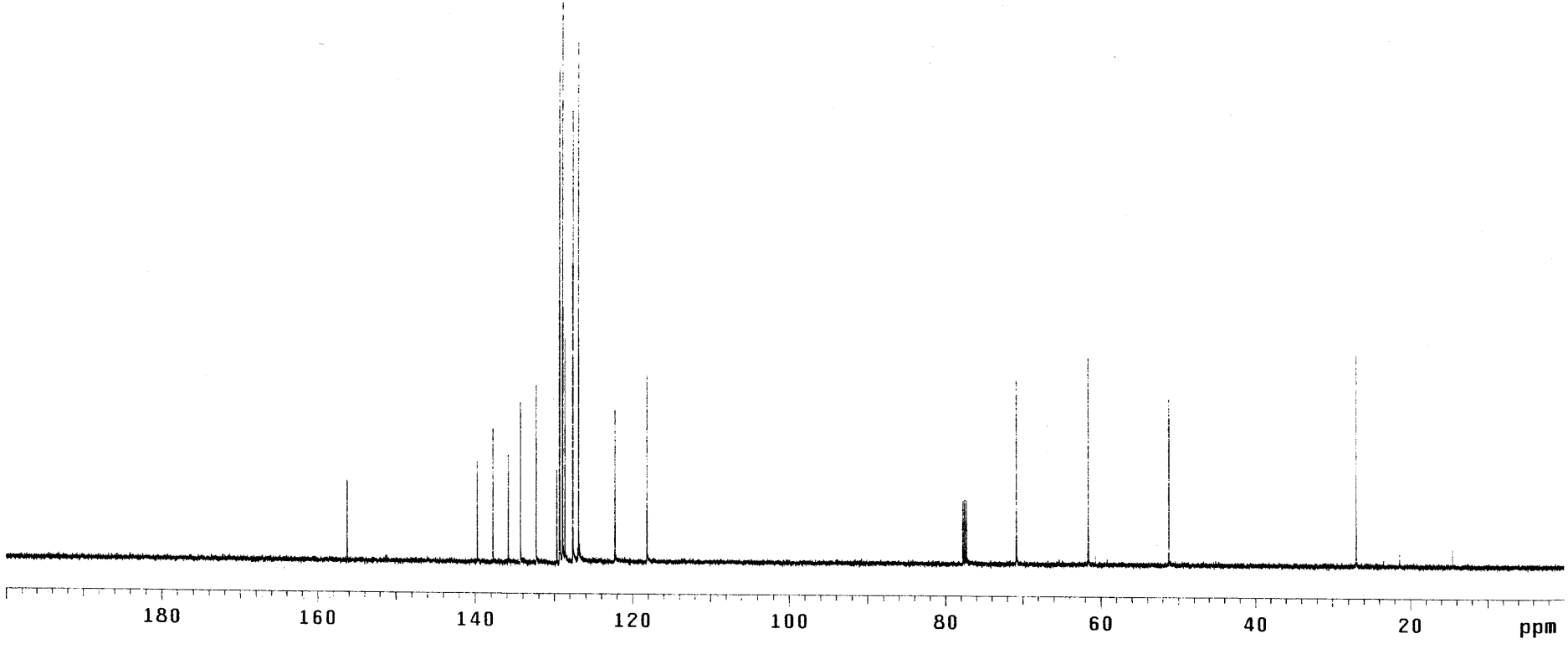

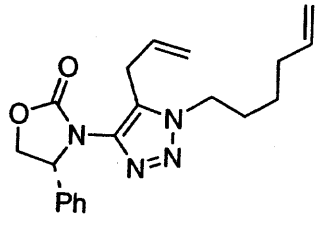

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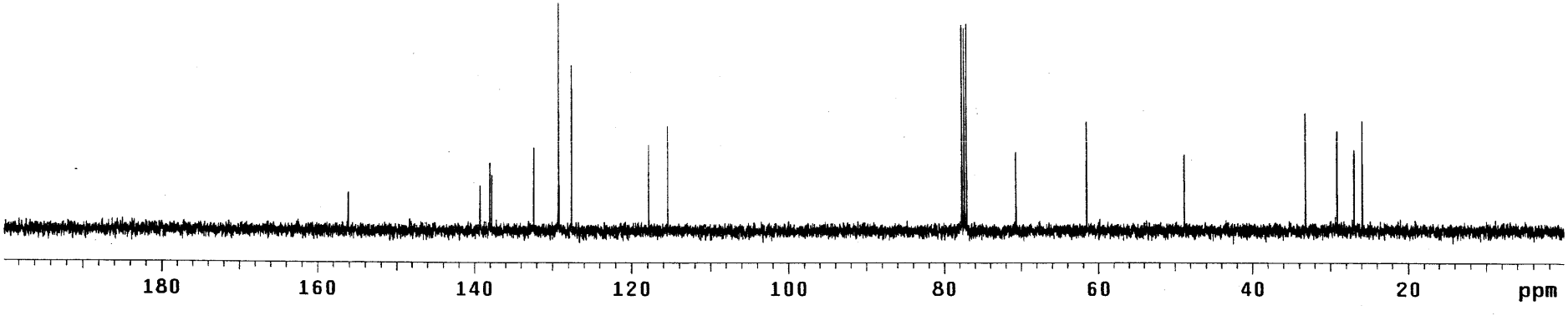

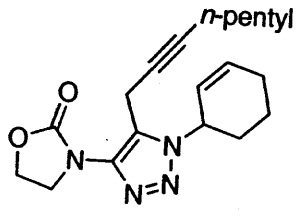

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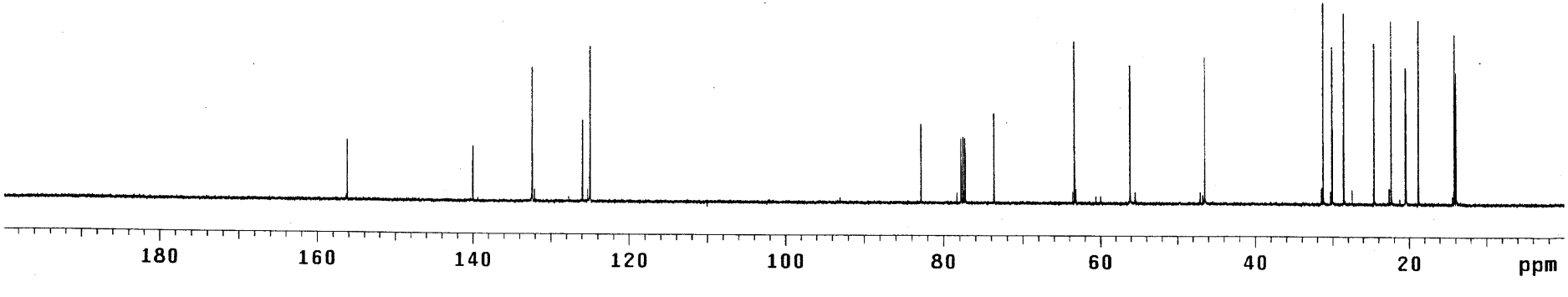

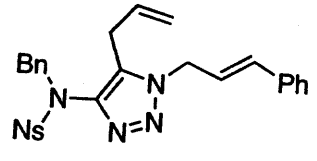

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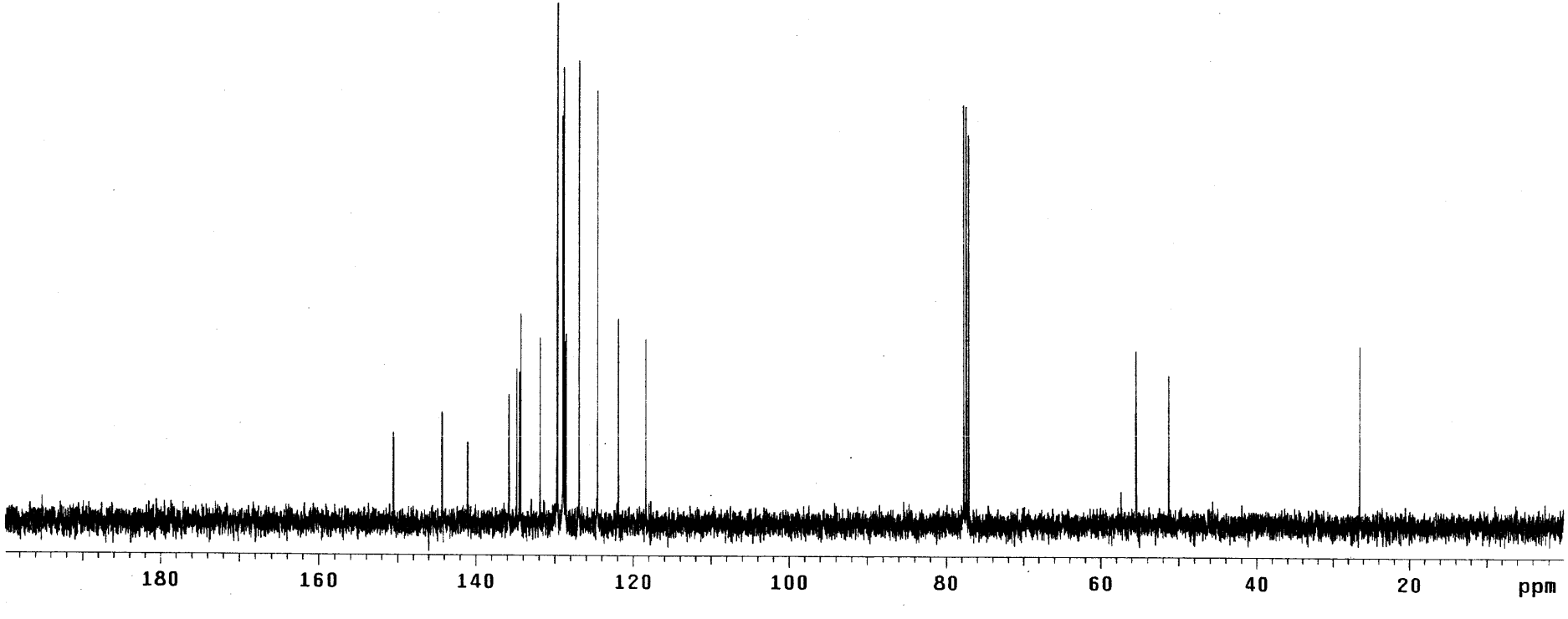

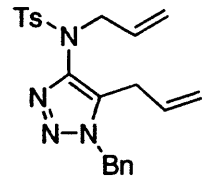

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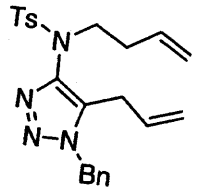

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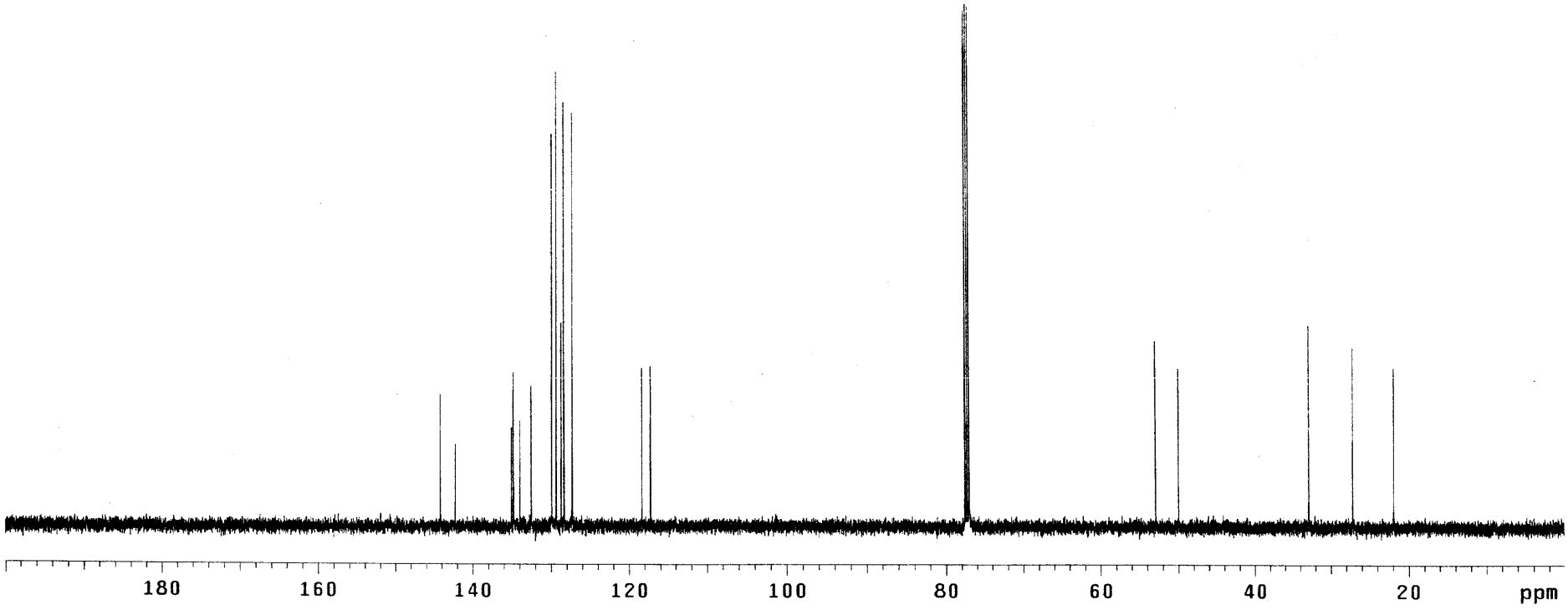

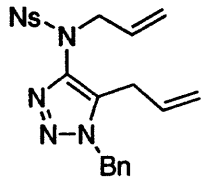

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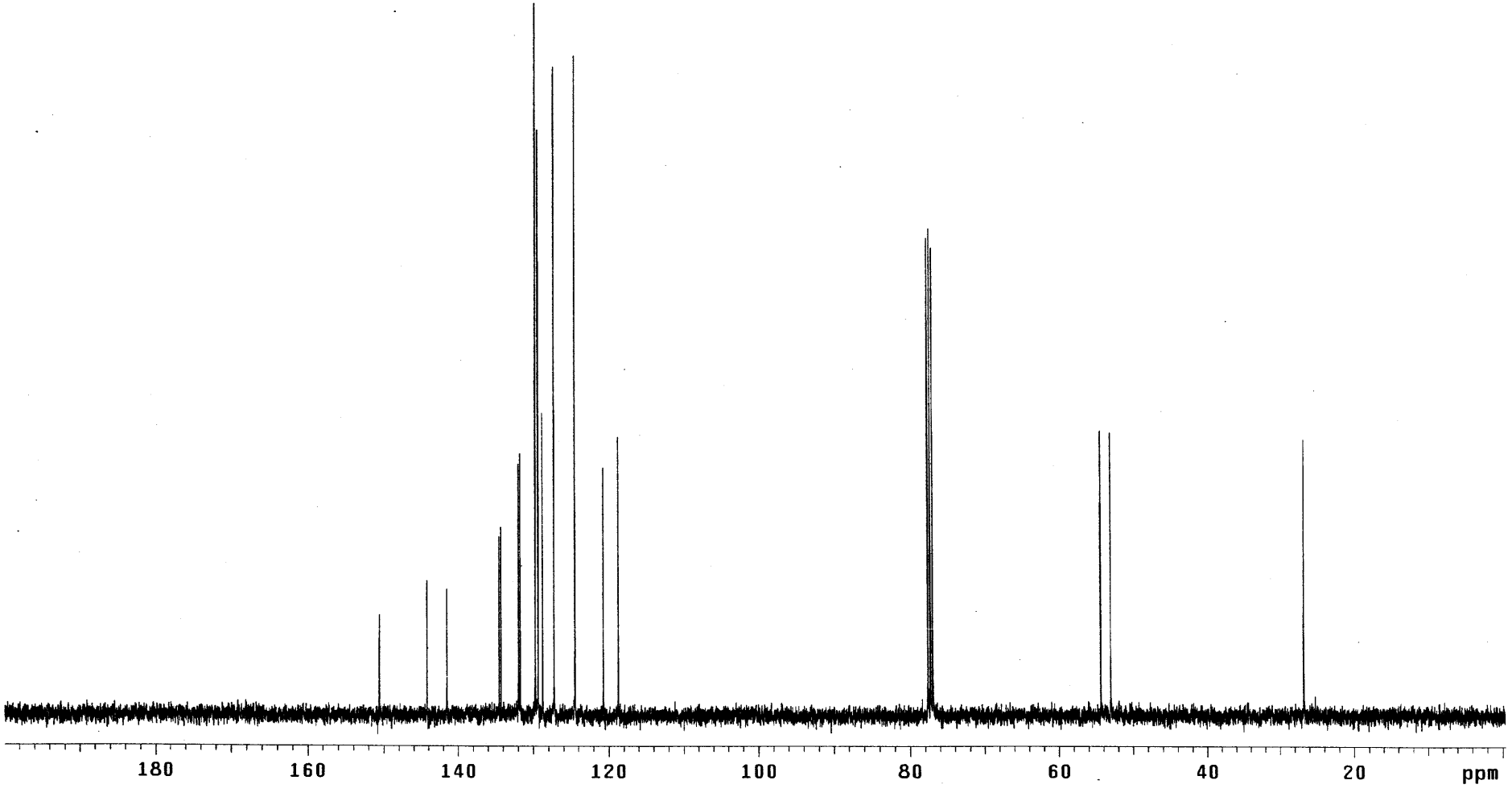

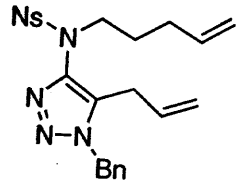

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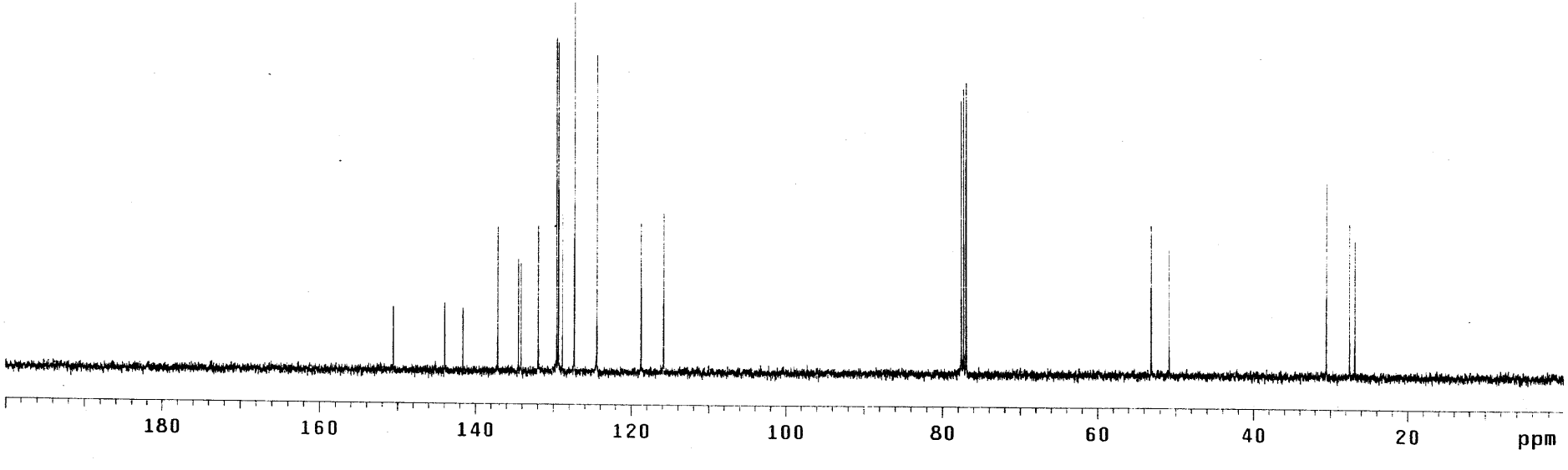

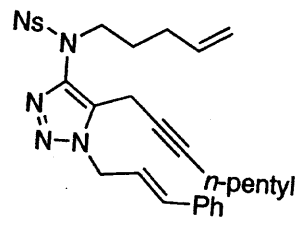

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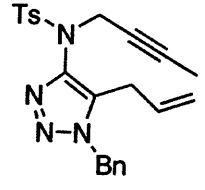

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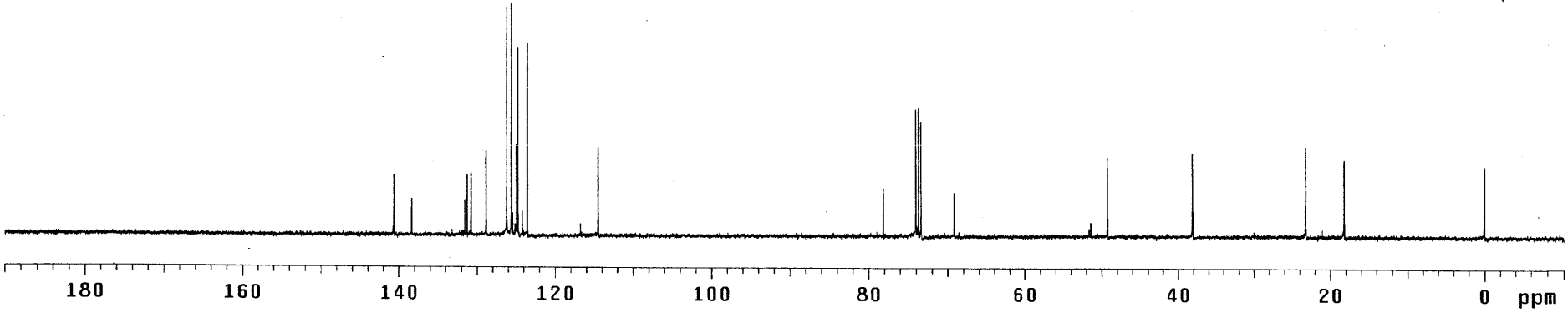

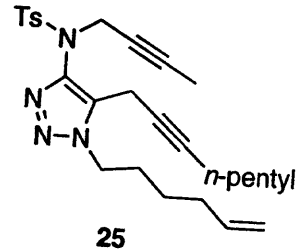

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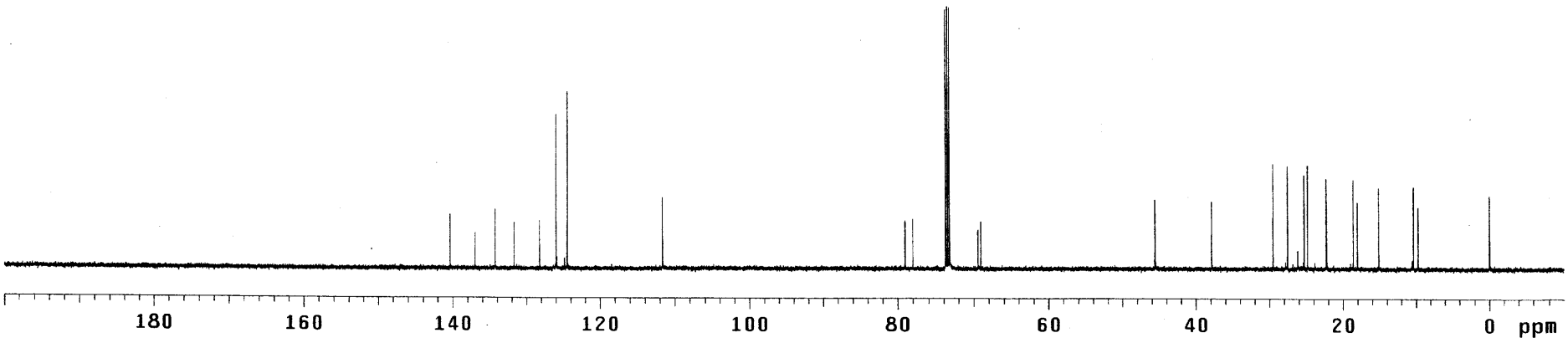

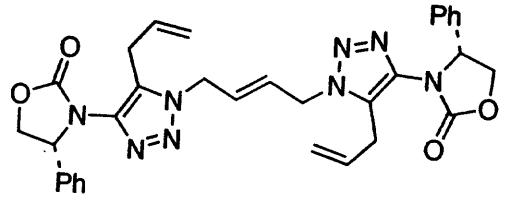

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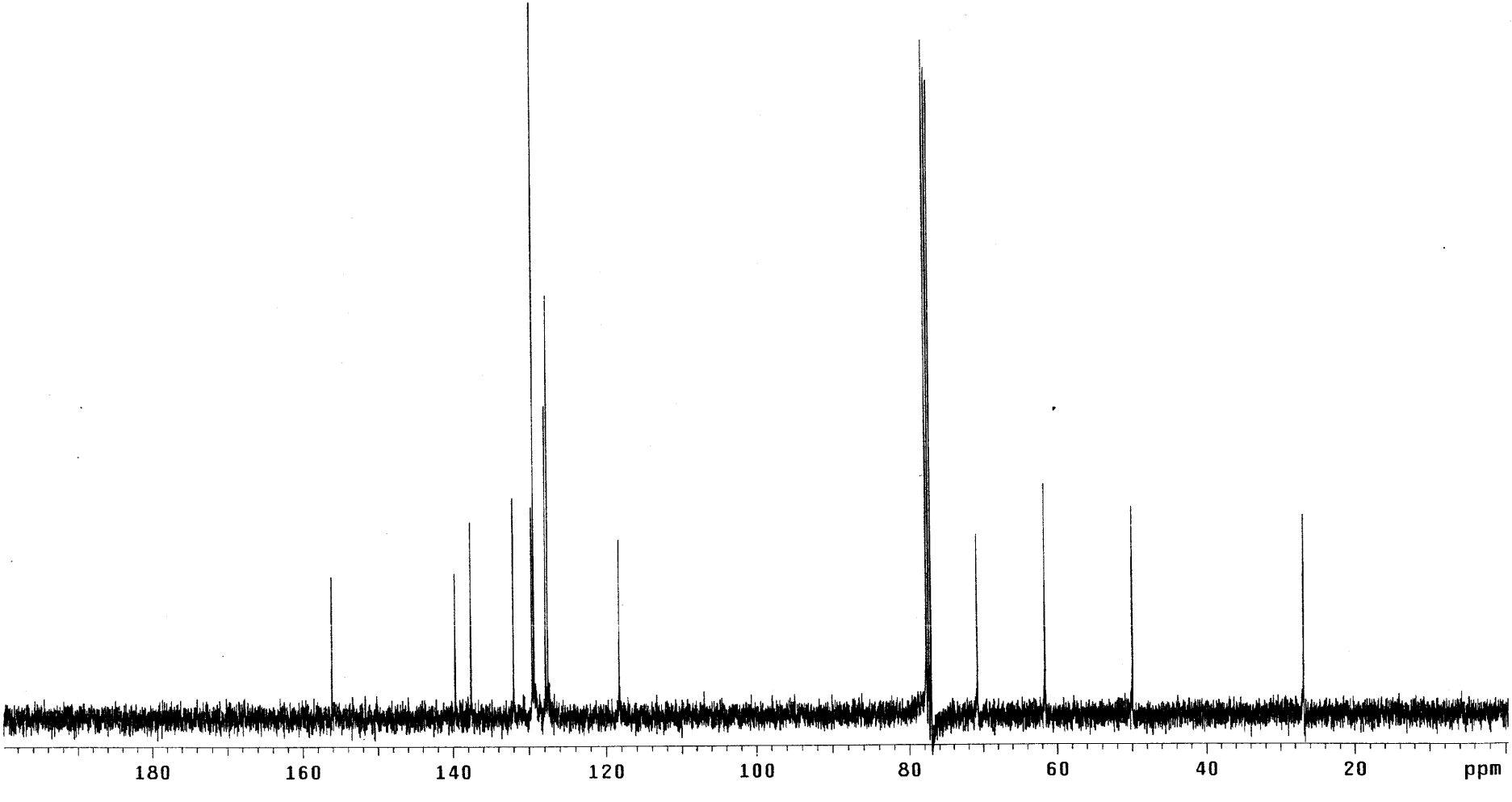

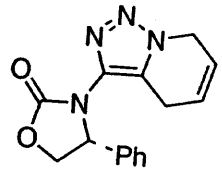

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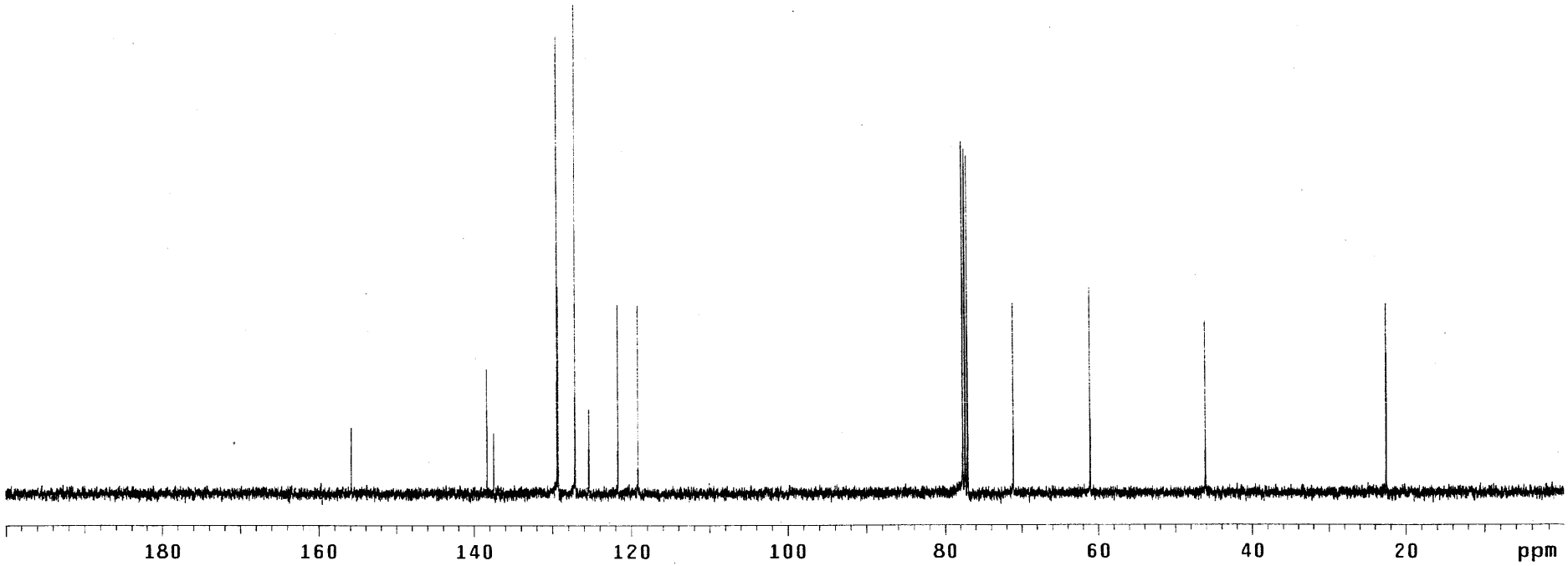

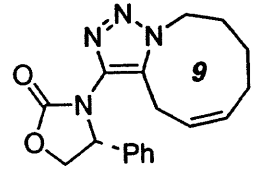

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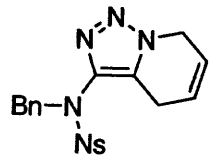

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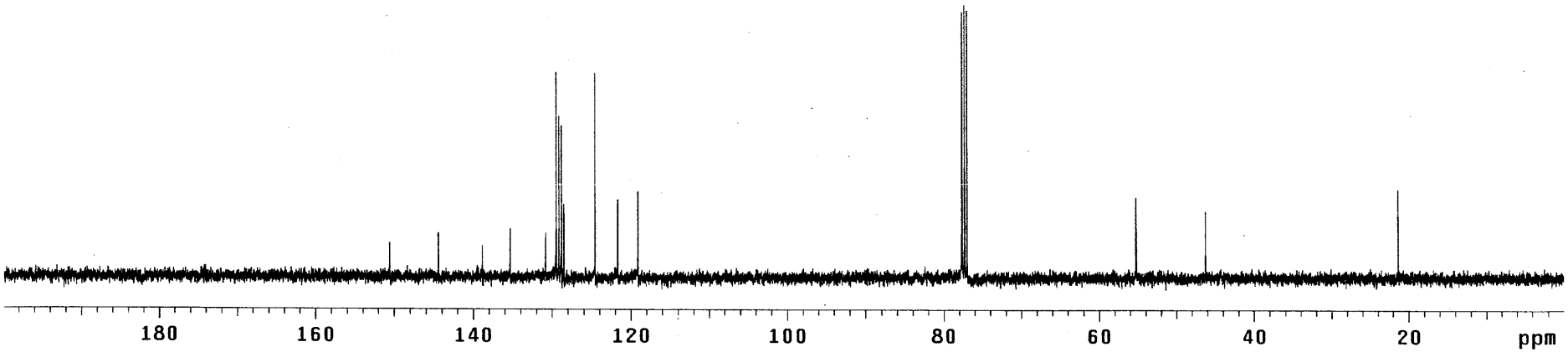

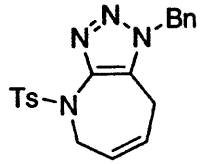

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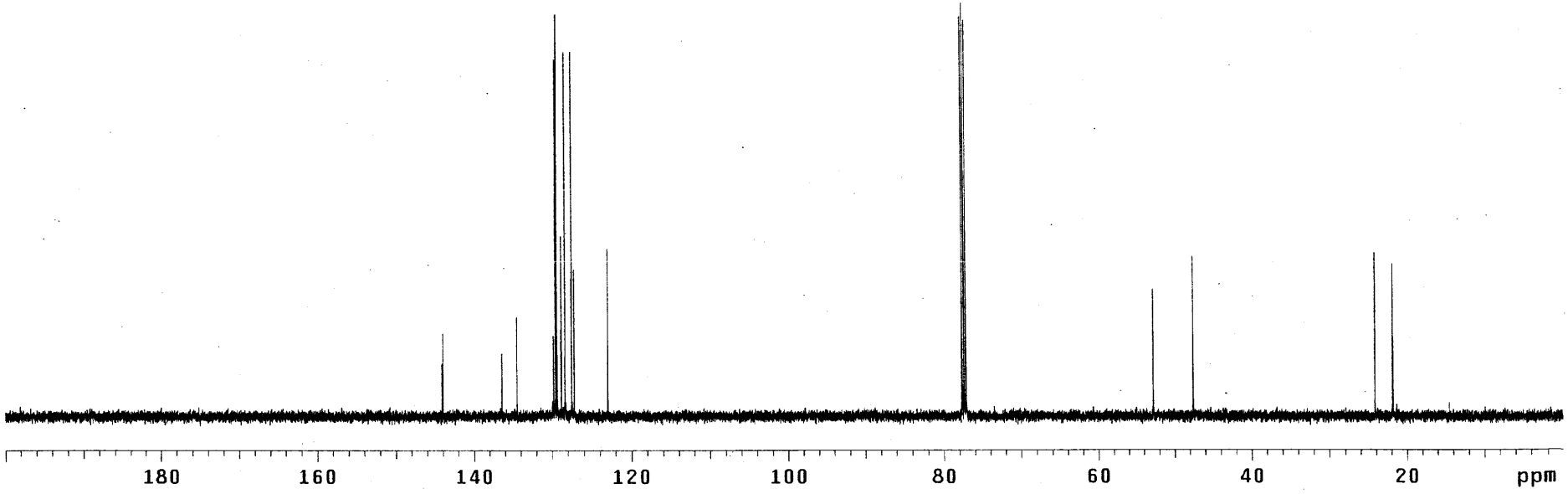

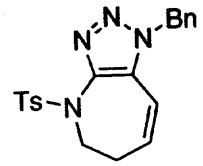

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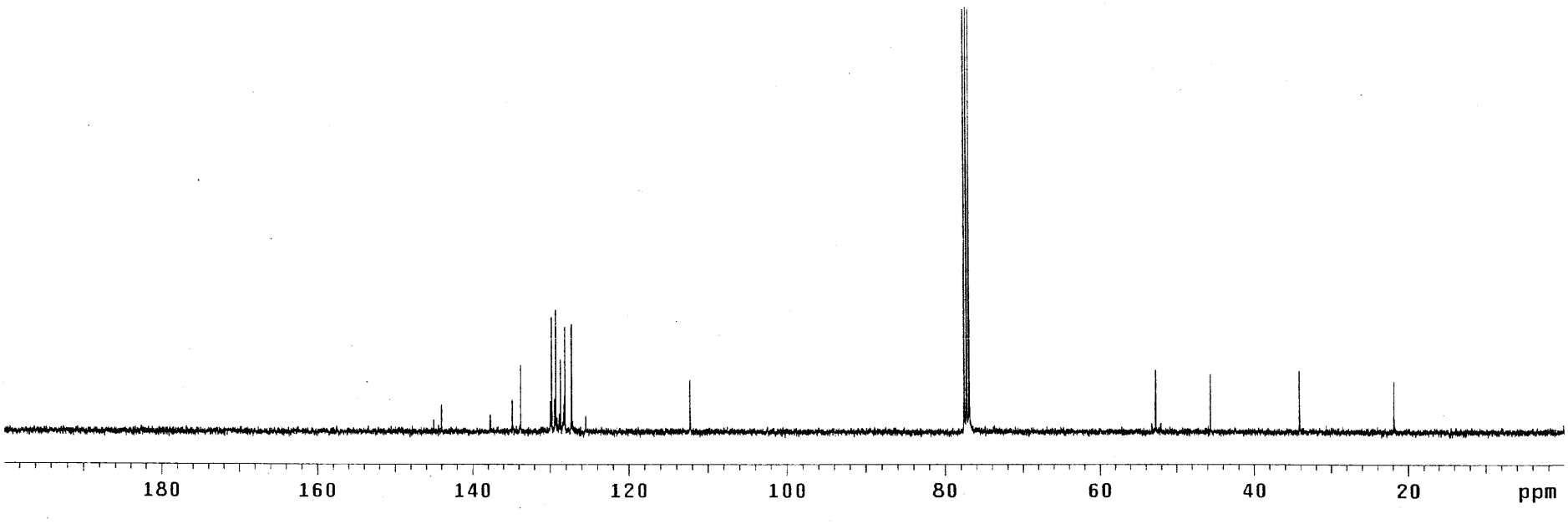

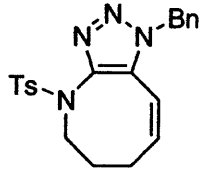

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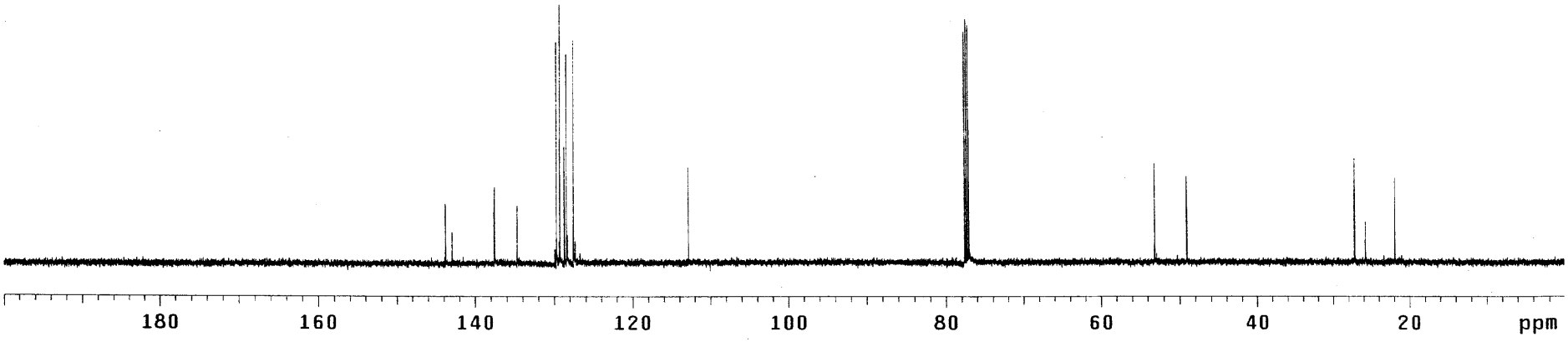

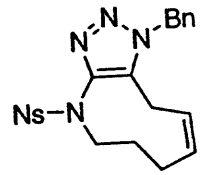

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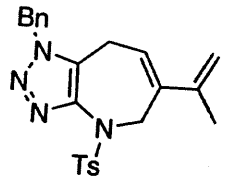

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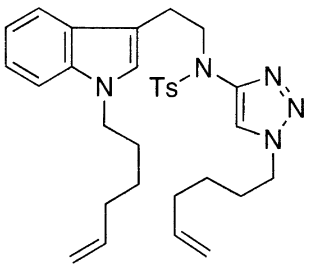

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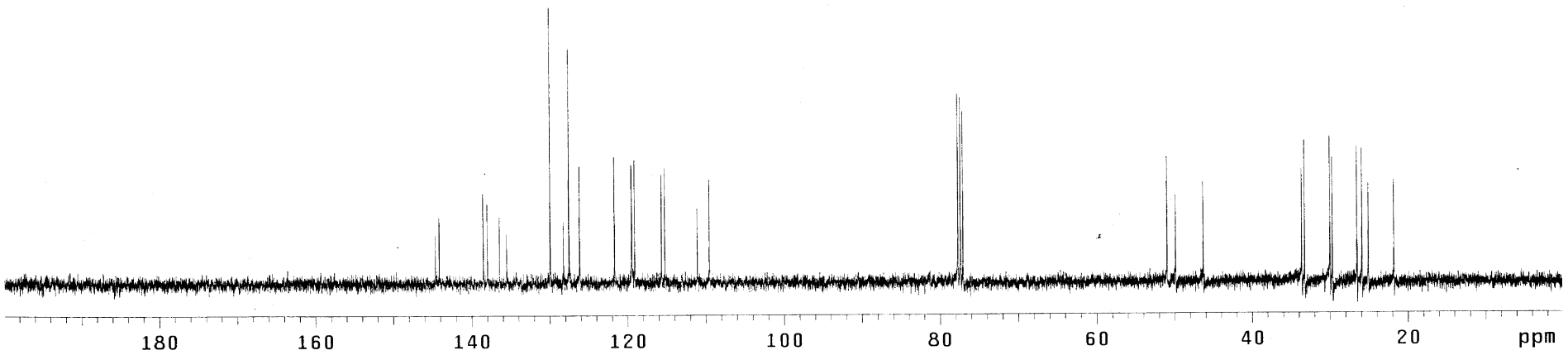

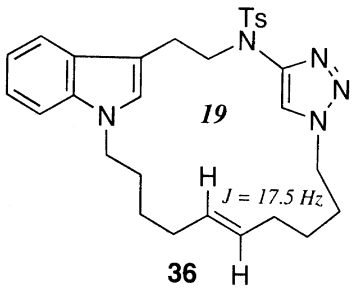

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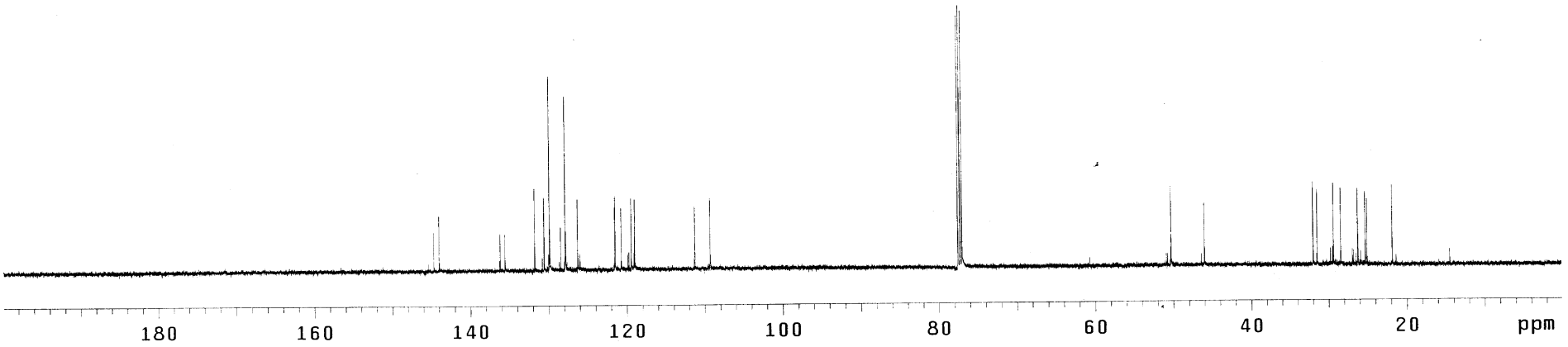
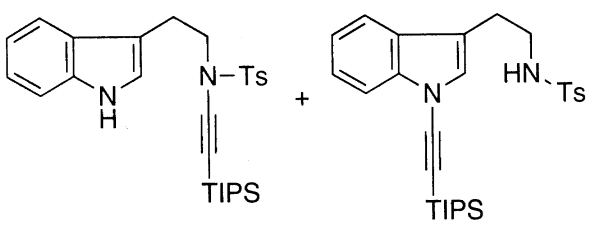
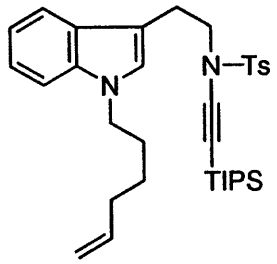




(6 : 1 inseperable regioisomers)

S7



S8