Supporting Information

Lacosamide Isothiocyanate-based Agents: Novel Agents to Target and Identify Lacosamide Receptors

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Table of Contents

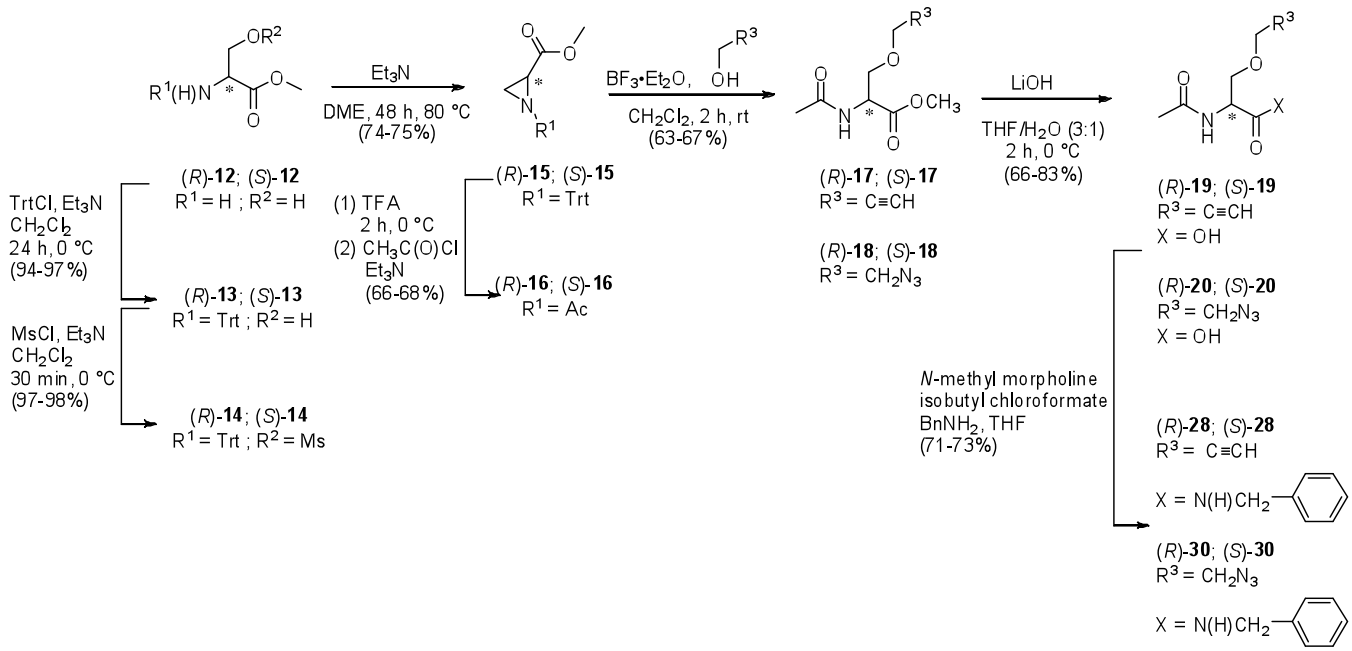
Purification of Probe-labeled Proteins. Mouse brain lysate (500 μL of 2.0 mg/mL protein in 50 mM HEPES buffer (pH 7.4)) was passed through a NAP-5 column to exchange buffer to an aqueous 50 mM HEPES buffer (pH 8.0). Lysate aliquots (200 μL) were treated with (*R*)-**9** (30 μM) at room temperature (30 min). To the modified lysate was sequentially added **35** (200 μM), TCEP (500 μM), TBTA (200 μM) and $CuSO_4$ (1 mM). The samples was shaken and then allowed to rotate using Roto-shake (8 rpm, Scientific Industries Inc., Model No. SI-1100, Bohemia, NY) at room temperature (1 h). After passage through a NAP-5 column, the sample was added to an immobilized streptavidin slurry (0.3 mL) (High Capacity Streptavidin Agarose Resin, Pierce, Rockford, IL) and rotated (15 rpm) at 4 °C (90 min). The streptavidin beads were sequentially washed with aqueous 0.1% Triton X-100/15 mM HEPES buffer (pH 7.4) (3 × 0.8 mL), an aqueous 6 M urea solution (3 × 0.8 mL), and an aqueous 15 mM HEPES buffer (pH 7.4) (4 × 0.8 mL). The beads were centrifuged (1000 rpm, 1 min), and the supernatant removed. The beads were treated with loading buffer (aqueous 2% SDS, 10% glycerol, 1% mercaptoethanol, 0.01% bromophenol blue [final concentration]) (95 °C, 5 min). The samples were loaded on a 10% SDS-PAGE gel and the proteins visualized by silver staining.

Western Blot. The SDS-PAGE gel was transferred to a nitrocellulose membrane (RPN203D, Amersham) and the membrane was washed (10 min) with TBST (aqueous 25 mM Tris buffer, 150 mM NaCl, 0.1% Tween-20 (pH 7.6)). The membrane was incubated in aqueous 5% NFDM (Non-Fat Dried Milk)/TBST solution (50 mL) at room temperature (1 h) and then incubated with either a polyclonal antibody (0.15 μg/mL) specific for CRMP2 (C2993, Sigma) or a monoclonal antibody (0.5 μg/mL) specific for GST (sc-138, Santa Cruz Biotech.) in aqueous 5% NFDM/TBST solution (1.5 mL) at room temperature (2 h). After washing (× 4, 5 min each) with TBST, the membrane was incubated with either ECLTM anti-rabbit IgG (NA934, GE Healthcare) or anti-mouse IgG (31430, Pierce Biotech.) in an aqueous 5% NFDM/TBST solution (1.5 mL) at room temperature (1 h) and washed (× 5, 5 min each) with TBST. Chemiluminescent reagent (RPN2132, GE Healthcare) was added to the blot and the signal developed in the darkroom.

In-gel tryptic digestion. All gel pieces were dehydrated and then rehydrated with an aqueous trypsin solution in 50 mM triethyl ammonium bicarbonate buffer (TEAB) (100 μL, 0.02 mg/mL), and incubated overnight (37 ºC). An equal volume (100 μL) of acetonitrile was added to the gel pieces and shaken for 20 min. The supernatant was collected and acetonitrile removed. To each digested sample tubes were added iTRAQ reagents in ethanol and the reaction solutions were incubated at room temperature (1 h). The iTRAQ labeled samples were combined into one tube, evaporated to dryness and analyzed as described below.

Mass spectrometry analysis. The iTRAQ labelled peptides were separated using an Ultimate 3000 capillary LC system (Dionex, Surrey, UK). The HPLC eluent was infused directly into nano-electrospray source of QToF Global (Waters, Manchester, UK). The mass spectrometry data was searched using the Mascot search algorithm to get protein identification and iTRAQ quantification. The search was done against swiss-Prot database, miss cleavages were set to 1 and peptide and tandem MS tolerances were set at 100ppm.

Scheme S1. Synthesis of (*R*)- and (*S*)-**28** and **30**



(*R*)-Methyl 3-Hydroxy-2-(*N*-tritylamino)propionate ((*R*)-13).[1] To a solution of D-serine methyl ester hydrochloride ((*R*)-**12**) (20.00 g, 0.13 mol) and Et_3N (35.82 mL, 0.26 mol) in CH_2Cl_2 (80 mL) at 0 °C, was added in one portion a solution of TrtCl (36.53 g, 0.13 mol) in CH_2Cl_2 (80 mL). The mixture was allowed to stir at 0 °C (24 h) under Ar and then successively washed with 10% aqueous citric acid (120 mL) and brine (120 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo to yield 45.20 g (97%) of crude (*R*)-**13** as a pale yellow crystalline solid. The product was used for next step without further purification: R_f = 0.50 (1/1 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 2.29 (br s, 1 H), 2.98 (br s, 1 H), 3.29 (s, OC**H$_3$**), 3.51–3.60 (m, C**H**H'OH, C**H**), 3.64–3.74 (m, CH**H'**OH), 7.16–7.30 (m, 9 Ar**H**), 7.47–7.50 (m, 6 Ar**H**).

(*S*)-Methyl 3-Hydroxy-2-(*N*-tritylamino)propionate ((*S*)-13).[2,3] Utilizing the procedure and work up procedure for (*R*)-**13**, and using L-serine methyl ester hydrochloride ((*S*)-12 (20.00 g, 0.13 mol), Et_3N (35.82 mL, 0.26 mol) and TrtCl (36.53 g, 0.13 mol) gave 43.80 g (94%) of crude (*S*)-**13** as a pale yellow crystalline solid: R_f = 0.50 (1/1 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 2.31 (br s, 1 H), 2.84-3.02 (br m, 1 H), 3.29 (s, OC**H$_3$**), 3.50–3.59 (m, C**H**H'OH, C**H**), 3.63–3.74 (m, CH**H'**OH), 7.18–7.29 (m, 9 Ar**H**), 7.48–7.50 (m, 6 Ar**H**).

(*R*)-Methyl 1-Tritylaziridine-2-carboxylate ((*R*)-15).[4,5] Crude (*R*)-**13** (45.20 g, 0.13 mol) was dissolved in CH_2Cl_2 (300 mL) and cooled to 0 °C under Ar. Methanesulfonyl chloride (10.64 mL, 0.14

mol) was added to the cooled solution, followed by the dropwise addition of Et_3N (26.14 mL, 0.19 mol). The resulting solution was allowed to stir at 0 °C (30 min) and then successively washed with 10% aqueous citric acid (200 mL) and brine (200 mL). After drying (Na_2SO_4) and evaporation of the solvent, the crude mesylate ((*R*)-**14**) (53.30 g, 0.12 mol) was dissolved in DME (300 mL) and Et_3N (33.73 mL, 0.24 mol) was added. The reaction mixture was stirred at 80 °C (48 h) and then evaporated in vacuo. The residue was dissolved in EtOAc (300 mL) and washed with 10% aqueous citric acid (200 mL) and brine (200 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo. The crude product was recrystallized (EtOH) to yield 30.81 g (74%) of (*R*)-**15** as a transparent crystal: mp 127–128 °C (lit.[3a] mp 129–131 °C); $[\alpha]^{25}_D$ +94.7° (*c* 1.5, $CHCl_3$) (lit.[3b] $[\alpha]^{20}_D$ +95° (*c* 1.0, $CHCl_3$)); R_f = 0.45 (1/5 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 1.41 (dd, *J* = 1.7, 6.4 Hz, NC**H**H'CH), 1.89 (dd, *J* = 2.8, 6.4 Hz, CHH'C**H**N), 2.26 (dd, *J* = 1.7, 2.8 Hz, NCH**H'**CH), 3.76 (s, OC**H$_3$**), 7.20–7.31 (m, 9 Ar**H**), 7.48–7.52 (m, 6 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 28.8 (N**C**H_2CH), 31.8 (CH_2**C**HN), 52.2 (O**C**H_3), 74.5 (N**C**Ph_3), 127.1, 127.8, 129.4, 143.7 (3 **C$_6$**H_5), 172.0 (**C**(O)).

(*S*)-Methyl 1-Tritylaziridine-2-carboxylate ((*S*)-15).[2,4,5] Utilizing the preceding procedure and work-up for (*R*)-**15**, and using crude (*S*)-**2** (43.80 g, 0.12 mol), methanesulfonyl chloride (10.30 mL, 0.13 mol) and Et_3N (25.30 mL, 0.18 mol) gave crude mesylate ((*S*)-**14**) (53.90 g, 0.12 mol), which was treated with Et_3N (34.29 mL, 0.25 mol) to yield 31.58 g (75%) of (*S*)-**15** as a transparent crystal: mp 127–128 °C (lit.[3a] mp 130–131 °C); $[\alpha]^{20}_D$ –95.1 (*c* 1.5, $CHCl_3$) (lit.[3b] $[\alpha]^{20}_D$ –94.2° (*c* 1.0, $CHCl_3$)); R_f = 0.45 (1/5 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 1.41 (dd, *J* = 1.7, 6.4 Hz, NC**H**H'CH), 1.89 (dd, *J* = 2.8, 6.4 Hz, CHH'C**H**N), 2.26 (dd, *J* = 1.7, 2.8 Hz, NCH**H'**CH), 3.75 (s, OC**H$_3$**), 7.18–7.30 (m, 9 Ar**H**), 7.48–7.52 (m, 6 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 28.9 (N**C**H_2CH), 31.9 (CH_2**C**HN), 52.3 (O**C**H_3), 74.6 (N**C**Ph_3), 127.1, 127.8, 129.5, 143.8 (3 **C$_6$**H_5), 172.1 (**C**(O)).

(*R*)-Methyl 1-Acetylaziridine-2-carboxylate ((*R*)-16).[6] (*R*)-Methyl 1-tritylaziridine-2-carboxylate ((*R*)-**15**) (9.00 g, 26.24 mmol) was dissolved in MeOH/$CHCl_3$ (1:1, 90 mL) and cooled to 0 °C under Ar and TFA (15.15 mL, 196.80 mmol) was added dropwise. After the reaction mixture was allowed to stir at 0 °C (2 h), the solvent was evaporated in vacuo. The product was dissolved in CH_2Cl_2 (120 mL), cooled to 0 °C, and Et_3N (18.29 mL, 131.20 mmol) and AcCl (2.04 mL, 28.86 mmol) were added in two portions over 5 min. The solution was stirred at 0 °C (1 h) and then washed with saturated aqueous $NaHCO_3$ (100 mL) and saturated aqueous brine (100 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo, and then the crude product was purified by silica gel column chromatography (1/1 EtOAc/hexanes) and crystallized (cold hexanes) to yield 2.46 g (66%) of (*R*)-**16** as a clear crystal: mp 39–40 °C; $[\alpha]^{25}_D$ +84.3° (*c* 1.2, $CHCl_3$); R_f = 0.30 (1/2 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 2.16 (s, C**H$_3$**C(O)), 2.51 (dd, *J* = 1.8, 5.5 Hz, NC**H**H'CH), 2.58 (dd, *J* = 1.8, 3.0 Hz, NCH**H'**CH), 3.16 (dd, *J* = 3.0, 5.5 Hz, CHH'C**H**N), 3.80 (s, OC**H$_3$**); ^{13}C NMR ($CDCl_3$) δ 23.7 (**C**H_3C(O)),

30.9 (N**C**H_2CH), 34.4 (CH_2**C**HN), 52.9 (O**C**H_3), 168.9 (**C**(O)O), 180.6 (**C**(O)N); M_r (+ESI) 166.0474 $[M+Na]^+$ (calcd for $C_6H_9NO_3Na^+$ 166.0480 $[M+Na]^+$).

(*S*)-Methyl 1-Acetylaziridine-2-carboxylate ((*S*)-16).[6] Utilizing the preceding procedure and work-up for (*R*)-**16**, and using (*S*)-**15** (9.00 g, 26.24 mmol), TFA (15.15 mL, 196.80 mmol), Et_3N (18.29 mL, 131.20 mmol) and AcCl (2.04 mL, 28.86 mmol) gave 2.56 g (68%) of (*S*)-**16** as a clear crystal: mp 39–40 °C; $[\alpha]^{25}_D$ –83.9° (*c* 1.2, $CHCl_3$); R_f = 0.30 (1/2 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 2.17 (s, C**H$_3$**C(O)), 2.51 (dd, *J* = 1.8, 5.4 Hz, NC**H**H'CH), 2.58 (dd, *J* = 1.8, 2.9 Hz, NCH**H'**CH), 3.16 (dd, *J* = 2.9, 5.4 Hz, CHH'C**H**N), 3.80 (s, OC**H$_3$**); ^{13}C NMR ($CDCl_3$) δ 23.7 (**C**H_3C(O)), 30.8 (N**C**H_2CH), 34.4 (CH_2**C**HN), 52.8 (O**C**H_3), 168.8 (**C**(O)O), 180.5 (**C**(O)N); M_r (+ESI) 166.0474 $[M+Na]^+$ (calcd for $C_6H_9NO_3Na^+$ 166.0480 $[M+Na]^+$).

(*R*)-*N*-Benzyl 2-Acetamido-3-(prop-2-ynyloxy)propionamide ((*R*)-28). Utilizing Method C, (*R*)-**19** (1.28 g, 6.92 mmol), NMM (1.14 mL, 10.38 mmol), IBCF (1.14 mL, 8.72 mmol), and benzylamine (0.90 mL, 8.30 mmol) gave 1.15 g (61%) of (*R*)-**28** as a white solid: mp 149.0–149.5 °C; $[\alpha]^{25}_D$ –26.8° (*c* 1.5, $CHCl_3$); R_f = 0.45 (1/9 MeOH/$CHCl_3$); IR (nujol mull) 3263, 2925, 2111, 1639, 1553, 1459 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.04 (s, C**H$_3$**C(O)), 2.45 (t, *J* = 2.4 Hz, CH_2C**C**H), 3.64 (dd, *J* = 7.4, 9.3 Hz, C**H**H'OCH_2), 3.94 (dd, *J* = 3.9, 9.3 Hz, CH**H'**OCH_2), 4.15 (1/2**H**H'$_q$, *J* = 2.4, 15.9 Hz, OC**H**H'C), 4.23 (1/2H**H'**$_q$, *J* = 2.4, 15.9 Hz, OCH**H'**C), 4.45 (1/2**H**H'$_q$, *J* = 6.0, 15.0 Hz, C**H**H'Ph), 4.51 (1/2H**H'**$_q$, *J* = 6.0, 15.0 Hz, CH**H'**Ph), 4.57–4.63 (m, C**H**), 6.43–6.45 (br d, *J* = 6.6 Hz, N**H**CH), 6.65-6.73 (br m, N**H**CH_2), 7.25–7.37 (m, C_6**H$_5$**), addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*R*)-**28** gave only a single signal for the acetyl methyl protons and the alkyne proton, addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*R*)-**28** and (*S*)-**28** (3:5 ratio) gave two signals for the acetyl methyl protons (δ 2.005 (*R*) and 2.020 (*S*) (Δppm = 0.015)), and two signals for the alkyne proton (δ 2.391 (*S*) and 2.432 (*R*) (Δppm = 0.041)); ^{13}C NMR ($CDCl_3$) δ 23.3 (**C**H_3C(O)), 43.8 (**C**H_2Ph), 52.7 (**C**H), 58.8 (**C**H_2CCH), 69.3 (**C**H_2OCH_2), 75.5 (CH_2C**C**H), 79.0 (CH_2**C**CH), 127.7, 128.9, 138.0 (**C$_6$**H_5), 169.8, 170.5 (2 **C**(O)), the remaining aromatic signal was not detected; M_r (+ESI) 275.1389 $[M+H]^+$ (calcd for $C_{15}H_{18}N_2O_3H^+$ 275.1396 $[M+H]^+$). Anal. ($C_{15}H_{18}N_2O_3$): C, H, N.

(*S*)-*N*-Benzyl 2-Acetamido-3-(prop-2-ynyloxy)propionamide ((*S*)-28). Utilizing the procedure and work up procedure for (*R*)-**28**, and using (*S*)-**19** (1.30 g, 7.03 mmol), NMM (1.16 mL, 10.55 mmol), IBCF (1.16 mL, 8.86 mmol), and benzylamine (0.92 mL, 8.44 mmol) gave 1.21 g (63%) of (*S*)-**28** as a white solid: mp 148.5–149.0 °C; $[\alpha]^{25}_D$ +27.3° (*c* 1.7, $CHCl_3$); R_f = 0.45 (1/9 MeOH/$CHCl_3$); IR (nujol mull) 3132, 2924, 2111, 1640, 1552, 1459 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.04 (s, C**H$_3$**C(O)), 2.45 (t, *J* = 2.4 Hz, CH_2C**C**H), 3.64 (dd, *J* = 7.5, 9.1 Hz, C**H**H'OCH_2), 3.94 (dd, *J* = 4.1, 9.1 Hz, CH**H'**OCH_2), 4.15 (1/2**H**H'$_q$, *J* = 2.4, 15.9 Hz, OC**H**H'C), 4.23 (1/2H**H'**$_q$, *J* = 2.4, 15.9 Hz, OCH**H'**C), 4.45 (1/2**H**H'$_q$, *J* = 6.0,

15.0 Hz, C**H**H'Ph), 4.51 (1/2H**H'**$_q$, J = 6.0, 15.0 Hz, CH**H'**Ph), 4.57–4.63 (m, C**H**), 6.43–6.45 (br d, J = 6.3 Hz, N**H**CH), 6.65–6.74 (br m, N**H**CH_2), 7.25–7.36 (m, C_6**H**$_5$), addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*S*)-**28** gave only a single signal for the acetyl methyl protons and the alkyne proton, addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*R*)-**28** and (*S*)-**28** (3:5 ratio) gave two signals for the acetyl methyl protons (δ 2.005 (*R*) and 2.020 (*S*) (Δppm = 0.015)), and two signals for the alkyne proton (δ 2.391 (*S*) and 2.432 (*R*) (Δppm = 0.041)); ^{13}C NMR ($CDCl_3$) δ 23.3 (**C**H_3C(O)), 43.7 (**C**H_2Ph), 52.7 (**C**H), 58.8 (**C**H_2CCH), 69.4 (**C**H_2OCH_2), 75.4 (CH_2C**C**H), 79.1 (CH_2**C**CH), 127.6, 127.7, 128.8, 138.0 (**C$_6$**H$_5$), 169.9, 170.6 (2 **C**(O)); M_r (+ESI) 275.1390 $[M+H]^+$ (calcd for $C_{15}H_{18}N_2O_3H^+$ 275.1396 $[M+H]^+$). Anal. ($C_{15}H_{18}N_2O_3$): C, H, N.

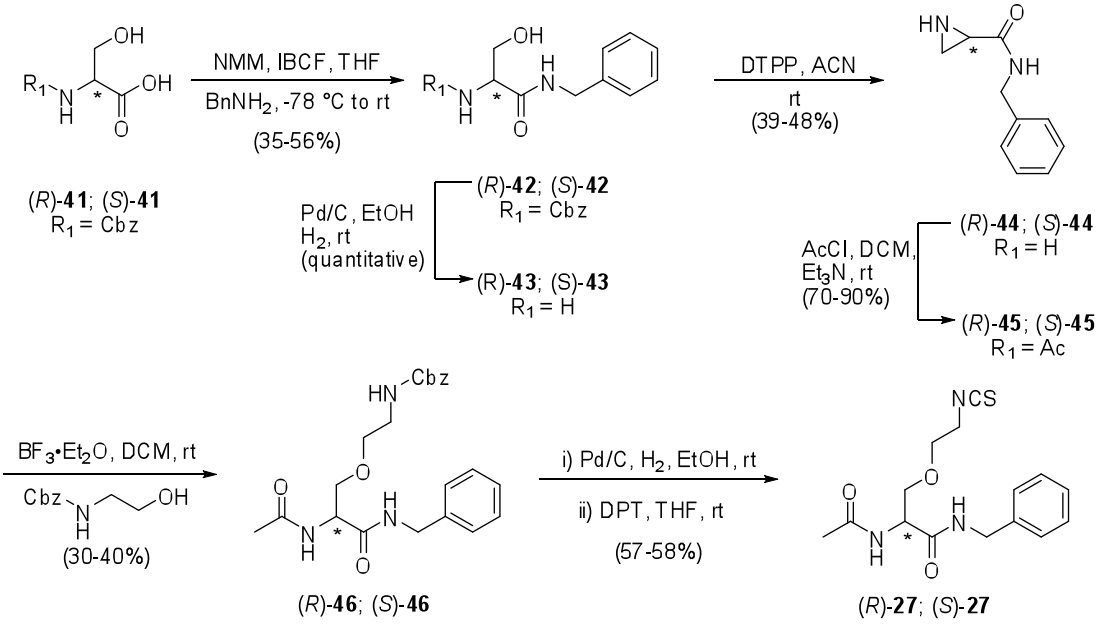
2-Azidoethanol.[7] NaN_3 (70.00 g, 1.08 mol) was dissolved in H_2O (200 mL) and 2-chloroethanol (55.6 mL, 0.829 mol) was added all at once. The reaction was stirred at 80 °C (24 h) behind a safety shield. After 24 h, the reaction was cooled to room temperature, saturated with NaCl, and extracted with CH_2Cl_2 (8 x 150 mL). The organic layers were dried (Na_2SO_4) and evaporated at room temperature to obtain 58.42 g (81%) of a colorless liquid that was used without further purification: R_f = 0.47 (1/2 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 2.62 (t, J = 6.7 Hz, CH_2O**H**), 3.45 (t, J = 5.1 Hz, C**H$_2$**N_3), 3.78 (app. q, J = 5.1 Hz, C**H$_2$**OH); ^{13}C NMR ($CDCl_3$) δ 53.6 (**C**H_2N_3), 61.4 (**C**H_2OH).

(*R*)-*N*-Benzyl 2-Acetamido-3-(2-azidoethoxy)propionamide ((*R*)-30). Utilizing Method D, (*R*)-**20** (950 mg, 4.4 mmol), benzylamine (622 μL, 5.7 mmol), and DMTMM (1.58 g, 5.7 mmol) in THF (50 mL) gave 715 mg (53%) of (*R*)-**30** as a white solid after purification by flash chromatography (4/96 MeOH/$CHCl_3$) followed by recrystallization from EtOAc: mp 111–112.5 °C; $[\alpha]^{25}_D$ +12.0° (*c* 1.0; MeOH); R_f = 0.51 (5/95 MeOH/$CHCl_3$); IR (nujol mull) 3139, 2107, 1635, 1547 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.98 (s, C**H$_3$**C(O)NH), 3.32–3.43 (m, OCH_2C**H$_2$**N_3), 3.50–3.56 (m, CHC**H**H'OCH_2), 3.58–3.75 (m, OC**H$_2$**CH_2N_3), 3.88–3.96 (m, CHCH**H'**OCH_2), 4.39–4.51 (m, NHC**H$_2$**Ph), 4.52–4.58 (m, C**H**CH_2OCH_2), 6.55–6.65 (br d, N**H**$CHCH_2O$), 6.76–6.86 (m, N**H**CH_2Ph), 7.21-7.35 (C_6**H$_5$**), addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*R*)-**30** gave only one signal for the acetyl protons, addition of excess (*R*)-(–)-mandelic acid to a $CDCl_3$ solution of (*S*)-**30** and (*R*)-**30** (1:2 ratio) gave two signals for the acetyl protons (δ 2.006 (*S*) and 1.993 (*R*) (Δppm = 0.013)); ^{13}C NMR ($CDCl_3$) δ 23.4 (**C**H_3C(O)), 43.9 (NH**C**H_2Ph), 50.9 (**C**H_2N_3), 52.7 (**C**HCH_2O), 70.3 (O**C**$H_2CH_2N_3$ or CH**C**H_2O), 70.4 (CH**C**H_2O or O**C**$H_2CH_2N_3$), 127.7, 128.9, 138.0 (**C**$_6$H$_5$), 169.8, 170.9 (CH_3**C**(O)NH, **C**(O)NHCH_2), the remaining aromatic resonance was not detected and is believed to overlap with nearby signals; M_r (+ESI) 328.1380 $[M+Na]^+$ (calcd for $C_{14}H_{19}N_5O_3Na^+$ 328.1386 $[M+Na]^+$). Anal. ($C_{14}H_{19}N_5O_3$):C, H, N.

(*S*)-*N*-Benzyl 2-Acetamido-3-(2-azidoethoxy)propionamide ((*S*)-30). Utilizing the preceding procedure, and using (*S*)-**20** (1.08 g, 5 mmol), benzylamine (600 μL, 5.5 mmol) and DMTMM (1.52 g,

5.5 mmol) in THF (50 mL) gave 854 mg (56%) of (*S*)-**30** as a white solid after purification by flash chromatography (4/96 MeOH/$CHCl_3$) followed by recrystallization from EtOAc and hexanes: mp 111–112.5 °C; $[\alpha]^{25}_D$ -12.1° (*c* 1.0; MeOH); R_f = 0.51 (5/95 MeOH/$CHCl_3$); IR (nujol mull) 3139, 2107, 1635, 1547 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.98 (s, C**H$_3$**C(O)NH), 3.32–3.43 (m, OCH_2C**H$_2$**N_3), 3.50–3.56 (m, CHC**H**H'OCH_2), 3.58–3.75 (m, OC**H$_2$**CH_2N_3), 3.88–3.96 (m, CHCH**H'**OCH_2), 4.39–4.51 (m, NHC**H$_2$**Ph), 4.52–4.58 (m, C**H**CH_2OCH_2), 6.42–6.52 (br d, N**H**$CHCH_2O$), 6.74–6.84 (br t, N**H**CH_2Ph), 7.21–7.35 (C_6**H$_5$**), addition of excess (*R*)-(−)-mandelic acid to a $CDCl_3$ solution of (*S*)-**30** gave only one signal for the acetyl protons, addition of excess (*R*)-(−)-mandelic acid to a $CDCl_3$ solution of (*S*)-**30** and (*R*)-**30** (1:2 ratio) gave two signals for the acetyl protons (δ 2.006 (*S*) and 1.993 (*R*) (Δppm = 0.013)); ^{13}C NMR ($CDCl_3$) δ 23.4 (**C**H_3C(O)), 43.9 (NH**C**H_2Ph), 50.9 (**C**H_2N_3), 52.7 (**C**HCH_2O), 70.3 (O**C**$H_2CH_2N_3$ or CH**C**H_2O), 70.4 (CH**C**H_2O or O**C**$H_2CH_2N_3$), 127.7, 128.9, 138.0 (**C**$_6H_5$), 169.8, 170.9 (CH_3**C**(O)NH, **C**(O)$NHCH_2$), the remaining aromatic resonance was not detected and is believed to overlap with nearby signals; M_r (+ESI) 328.1380 $[M+Na]^+$ (calcd for $C_{14}H_{19}N_5O_3Na^+$ 328.1386 $[M+Na]^+$). Anal. ($C_{14}H_{19}N_5O_3$): C, H, N.

Scheme S2. Synthesis of (*R*)- and (*S*)-**27**



(*R*)-*N*-Benzyl 2-*N*-(Benzyloxycarbonyl)amino-3-hydroxypropionamide ((*R*)-42).[8] Using Method C, Cbz-D-serine ((*R*)-**41**) (15.00 g, 62.7 mmol), NMM (8.3 mL, 75.2 mmol), IBCF (9.8 mL, 75.2 mmol), and benzylamine (7.60 mL, 69.0 mmol) gave (*R*)-**42** (7.55 g, 35%) as a white solid: mp 147–149 °C (lit.[8] mp 147–149); $[\alpha]^{25}_{D}$ +4.5° (*c* 1.0, MeOH); ^{1}H NMR (DMSO-d_6) δ 3.61 (d, J = 5.4 Hz, C**H**$_2$), 4.06–4.13 (br m, C**H**CH$_2$), 4.29 (d, J = 5.4 Hz, C**H**$_2$N), 4.86–4.93 (br t, O**H**), 5.04 (s, C**H**$_2$O), 7.23–7.36 (m, 10 Ar**H**), 8.40-8.45 (br m, N**H**).

(*S*)-*N*-Benzyl 2-*N*-(Benzyloxycarbonyl)amino-3-hydroxypropionamide ((*S*)-42).[9] Utilizing the preceding procedure, and using Cbz-L-serine ((*S*)-**41**) (15.00 g, 62.7 mmol), NMM (8.3 mL, 75.2 mmol), IBCF (9.8 mL, 75.2 mmol), and benzylamine (7.60 mL, 69.0 mmol) gave (*S*)-**42** (7.55 g, 35%) as a white solid: mp 139–141 °C (lit.[10] mp 148–149.5 °C); ^{1}H NMR (DMSO-d_6) δ 3.56–3.66 (m, C**H**$_2$), 4.07–4.13 (m, C**H**CH$_2$), 4.29 (d, J = 5.7 Hz, C**H**$_2$N), 4.91 (t, J = 5.4 Hz, O**H**), 5.04 (s, C**H**$_2$O), 7.23–7.38 (m, 10 Ar**H**), 8.40-8.45 (br t, N**H**).

(*R*)-*N*-Benzyl Aziridine-2-carboxamide ((*R*)-44). Pd/C (10%, 2.00 g, 20% w/w) was added to a hot ethanolic solution (215 mL) of (*R*)-*N*-benzyl 2-*N*-(benzyloxycarbonyl)amino-3-hydroxypropionamide ((*R*))-**42**) (10.00 g, 30.5 mmol). The solution was stirred at room temperature under H_2 (1 atm) overnight. The mixture was filtered through a bed of Celite® and the filtrate was evaporated in vacuo. Acetonitrile (60 mL) was added to the residue followed by DTPP (11.80 g, 33.6 mmol). The mixture was stirred at room temperature (3 h). The reaction was concentrated, aqueous 1

M H_2SO_4 (100 mL) added, and then washed with toluene (3 x 100 mL). A saturated aqueous solution of Na_2CO_3 was added to the aqueous layer until pH ~ 8 and then washed with CH_2Cl_2 (5 x 100 mL). The organic layers were combined and concentrated in vacuum. The solid was purified by silica gel column chromatography (7/3 EtOAc/acetone) to obtain 1.83 g of a white solid (48%): R_f = 0.30 (EtOAc); mp 71-72 °C; $[\alpha]^{25}_D$ +18.8° (*c* 1.0, DMSO); IR (nujol mull) 3219, 1662, 1556, 1458, 1377, 1245, 1157, 1024, 912, 833, 729 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-1.25 (br m, N**H**), 1.82 (d, *J* = 2.6 Hz, **H$_1$**), 1.94 (d, *J* = 5.7 Hz, **H$_1$'**), 2.50 (dd, *J* = 2.6, 5.7 Hz, **H$_2$**), 4.44 (d, *J* = 5.7 Hz, NC**H$_2$**), 6.50–6.70 (br m, N**H**), 7.25–7.37 (m, C_6**H$_5$**); ^{13}C NMR ($CDCl_3$) δ 26.5 (N**C**H_2), 30.5 (**C$_1$**), 43.1 (br, **C$_2$**), 127.6, 127.8, 128.7, 137.9 (4 Ar**C**), 170.8 (C(O)); M_r (+ESI) 177.1023 $[M+H]^+$ (calcd for $C_{10}H_{12}N_2OH^+$ 177.1028 $[M+H]^+$). Anal. ($C_{10}H_{12}N_2O$•0.1H_2O): C, H, N.

(*S*)-*N*-Benzyl Aziridine-2-carboxamide ((*S*)-44).[9] Utilizing the preceding procedure, and using (*S*)-*N*-benzyl 2-*N*-*(*benzyloxycarbonyl)amino-3-hydroxypropionamide ((*S*)-**42**) (7.00 g, 21.3 mmol), Pd/C 10% (1.40 g, 20% w/w), DTPP (8.30 g, 23.46 mmol), EtOH (150 mL), and acetonitrile (42 mL) gave 1.83 g (48%) of a white solid: R_f = 0.30 (EtOAc); mp 72–73 °C (lit.[9] mp 68 °C); $[\alpha]^{25}_D$ –18.4° (*c* 1.0, DMSO); IR (nujol mull) 3215, 1662, 1557, 1458, 1392, 1245, 1157, 1093, 1023, 912, 832, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9–1.4 (m, N**H**), 1.77–1.82 (br, **H$_1$**), 1.84 (d, *J* = 5.4 Hz, **H$_1$'**), 2.40–2.45 (br m, **H$_2$**), 4.39 (d, *J* = 5.7 Hz, NC**H$_2$**), 6.90–7.10 (br m, CON**H**), 7.22–7.37 (m, 5 Ar**H**); M_r (+ESI) 177.1023 $[M+H]^+$ (calcd for $C_{10}H_{12}N_2OH^+$ 177.1028 $[M+H]^+$). Anal. ($C_{10}H_{12}N_2O$): C, H, N.

(*R*)-*N*-Benzyl 1-Acetylaziridine-2-carboxamide ((*R*)-45). To a CH_2Cl_2 solution (50 mL) of (*R*)-*N*-benzyl aziridine-2-carboxamide ((*R*)-**44**) (2.00 g, 11.4 mmol) maintained at 0 °C was successively added Et_3N (3.19 mL, 22.7 mmol) and AcCl (886 μL, 12.5 mmol). The mixture was stirred at room temperature (1 h), then aqueous 10% citric acid (75 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 75 mL). The organic layers were combined, and successively washed with aqueous saturated $NaHCO_3$ (75 mL) and H_2O (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The solid was dissolved in minimal amount of EtOAc and then precipitated by addition of cold hexanes to obtain (*R*)-**45** (2.00 g, 71%) as a white solid: R_f = 0.78 (1/1 acetone/EtOAc); mp 82–83 °C; $[\alpha]^{25}_D$ = –2.6° (*c* 1.0, DMSO); IR (nujol mull) 3270, 1692, 1649, 1564, 1458, 1373, 1331, 1249, 1186, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.17 (s, C**H$_3$**C(O)), 2.37 (dd, *J* = 0.9, 3.0 Hz, C**H**H'), 2.55 (dd, *J* = 0.9, 6.3 Hz, CH**H'**), 3.08 (dd, *J* = 3.0, 6.3 Hz, C**H**), 4.38–4.45 (m, C**H$_2$**N), 6.49–6.58 (br m, NC**H**CO), 7.23–7.38 (m, C_6**H$_5$**); ^{13}C NMR ($CDCl_3$) δ 23.5 (**C**H_3C(O)), 32.2 (**C**1), 36.6 (**C**2), 43.3 (**C**H_2N), 127.6, 127.7, 128.8, 137.5 (Ar**C**), 167.2, 181.3 (2 **C**(O)); M_r (+ESI) 241.0948 $[M+Na]^+$ (calcd for $C_{12}H_{13}N_2O_2Na^+$ 241.0953 $[M+Na]^+$). Anal. ($C_{12}H_{13}N_2O_2$): C, H, N.

(*S*)-*N*-Benzyl 1-Acetylaziridine-2-carboxamide ((*S*)-45).[9] Utilizing the preceding procedure, and using (*S*)-**44** (1.37 g, 7.8 mmol), Et_3N (2.18 mL, 15.6 mmol) and AcCl (606 μL, 8.6 mmol) gave 1.69 g (90%) of (*S*)-**45** as a white solid after precipitation with cold hexanes from ethyl acetate: R_f = 0.78 (1/1 acetone/EtOAc); mp 83–84 °C (lit.[9] mp 72 °C); $[\alpha]^{25}_D$ = +3.0° (*c* 1.0, DMSO); IR (nujol mull) 3267, 1693, 1650, 1562, 1457, 1374, 1331, 1249, 1185, 1050, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (s, C**H**$_3$C(O)), 2.37 (dd, *J* = 1.2, 3.0 Hz, C**H**H'), 2.50 (dd, *J* = 1.2, 6.3 Hz, CH**H'**), 3.07 (dd, *J* = 3.0, 6.3 Hz, C**H**), 4.42 (d, *J* = 5.7 Hz, C**H**$_2$N), 6.78–6.85 (m, N**H**CO), 7.23–7.36 (m, Ar**H**); M_r (+ESI) 241.0948 $[M+Na]^+$ (calcd for $C_{12}H_{13}N_2O_2Na^+$ 241.0953 $[M+Na]^+$). Anal. ($C_{12}H_{13}N_2O_2$): C, H, N.

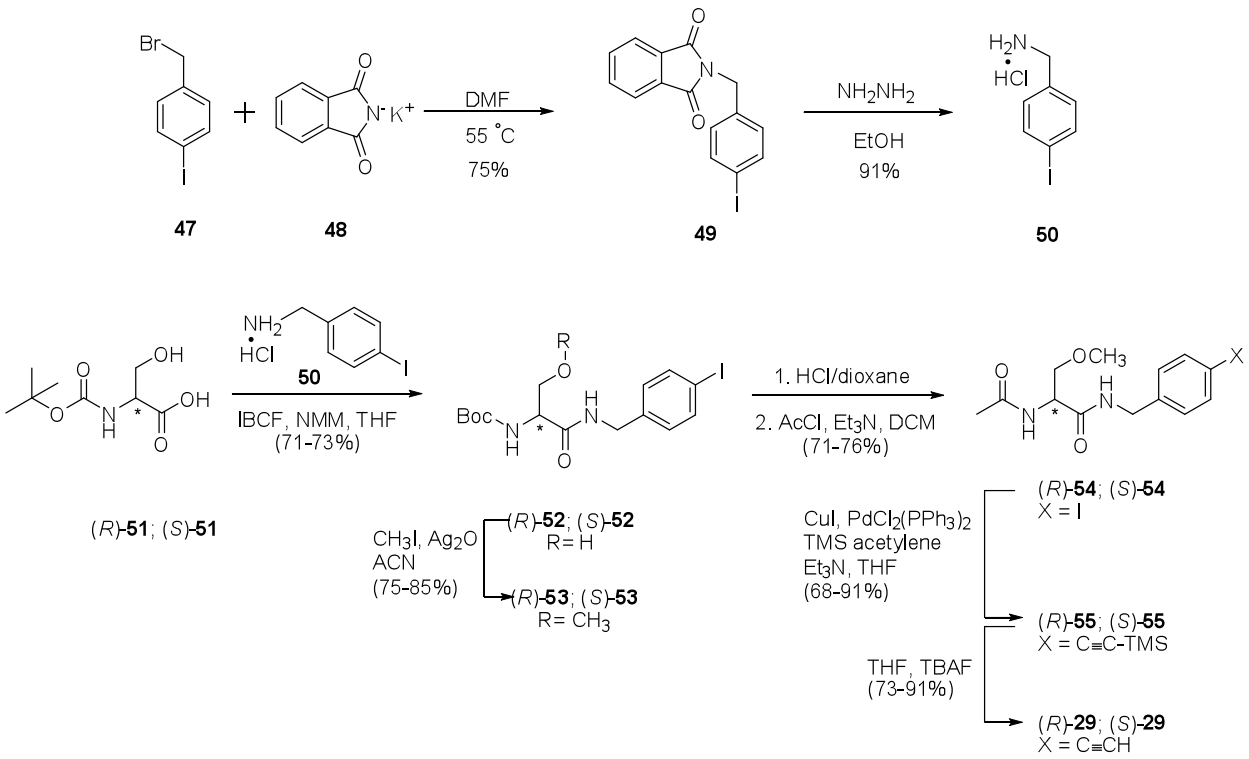
(*R*)-*N*-Benzyl 2-Acetamido-3-(2-amino-*N*-(benzyloxycarbonyl)ethoxy)propionamide ((*R*)-46). Using Method A, (*R*)-**45** (3.10 g, 14.2 mmol), BF_3•Et_2O (1.96 mL, 15.6 mmol), and *N*-benzyl 2-hydroxyethylcarbamate (8.33 g, 42.7 mmol) gave 2.40 g (41%) of (*R*)-**46** as a white solid after silica gel column chromatography (5/95 MeOH/EtOac): R_f = 0.33 (EtOAc); mp 125–126 °C; $[\alpha]^{25}_D$ +3.8° (*c* 1.0, DMSO); IR (nujol mull) 3292, 2726, 1691, 1635, 1540, 1457, 1375, 1263, 1096, 1017, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00 (s, C**H**$_3$C(O)), 3.31–3.40 (m, C**H**$_2$N-Cbz), 3.48–3.57 (m, CH_2C**H**$_2$O, OC**H**H'), 3.87 (dd, *J* = 4.2, 9.3 Hz, OCH**H'**), 4.41–4.47 (m, NC**H**$_2$Ph), 4.50–4.57 (m, C**H**), 5.05 (s, C**H**$_2$O), 5.12–5.20 (br t, N**H**), 6.60 (d, *J* = 5.7 Hz, N**H**C(O)CH_3), 6.81–6.93 (br t, N**H**), 7.21-7.35 (m, 2 C_6**H**$_5$); ^{13}C NMR ($CDCl_3$) δ 22.7 (**C**H_3C(O)), 40.5 (CH_2**C**H_2NH), 43.2 (C(O)N(H)**C**H_2), 52.7 (OCH_2**C**H), 66.5, 70.1, 70.2 (3 O**C**H_2), 127.2, 127.3, 127.9, 128.0, 128.3, 128.4, 136.4, 137.8 (8 Ar**C**), 156.6 (OC(O)), 170.0, 170.7 (2 N**C**(O)); M_r (+ESI) 414.2025 $[M+H]^+$ (calcd for $C_{22}H_{27}N_3O_5H^+$ 414.2029 $[M+H]^+$). Anal. ($C_{22}H_{27}N_3O_5$•$0.33H_2O$): C, H, N.

(*S*)-*N*-Benzyl 2-Acetamido-3-(2-amino-*N*-(benzyloxycarbonyl)ethoxy)propionamide ((*S*)-46). Utilizing the preceding procedure, and using BF_3•Et_2O (2.43 mL, 17.2 mmol), (*S*)-*N*-benzyl 1-acetylaziridine-2-carboxamide ((*S*)-**45**) (3.40 g, 15.6 mmol), and *N*-benzyl 2-hydroxyethylcarbamate (9.00 g, 46.8 mmol) gave 1.81 g (30%) of a white solid: R_f = 0.33 (EtOAc); mp 126.0–126.5 °C; $[\alpha]^{25}_D$ −3.3° (*c* 1.0, DMSO); IR (nujol mull) 3288, 1691, 1635, 1538, 1458, 1375, 1260, 1097, 1017, 908, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00 (s, C**H**$_3$C(O)), 3.32–3.40 (m, C**H**$_2$N-Cbz), 3.51–3.56 (m, CH_2C**H**$_2$O, OC**H**H'), 3.86 (dd, *J* = 4.2, 8.7 Hz, OCH**H'**), 4.38–4.55 (m, NC**H**$_2$Ph, C**H**), 5.05 (s, C**H**$_2$O), 5.15–5.20 (br m, N**H**), 6.58–6.62 (br m, N**H**C(O)CH_3), 6.82–6.93 (br m, N**H**), 7.21–7.35 (m, 2 C_6**H**$_5$); ^{13}C NMR ($CDCl_3$) δ 23.0 (**C**H_3C(O)), 40.6 (CH_2**C**H_2NH), 43.5 (C(O)N(H)**C**H_2), 52.7 (OCH_2**C**H), 66.8, 70.0, 70.5 (3 O**C**H_2), 127.5, 127.6, 128.0, 128.1, 128.5, 128.7, 136.4, 137.9 (8 Ar**C**), 156.7 (OC(O)), 169.9, 170.6 (2 N**C**(O)); M_r (+ESI) 436.1842 $[M+Na]^+$ (calcd for $C_{22}H_{27}N_3O_5Na^+$ 436.1848 $[M+Na]^+$). Anal. ($C_{22}H_{27}N_3O_5$•$0.25H_2O$): C, H, N.

(*R*)-*N*-Benzyl 2-Acetamido-3-(2-isothiocyanatoethoxy)propionamide ((*R*)-27). Pd/C (10%, 0.20 g, 10% w/w) was added to an ethanolic solution (20 mL) of (*R*)-*N*-benzyl 2-acetamido-3-(2-amino-*N*-(benzyloxycarbonyl)ethoxy)propionamide ((*R*)-**46**) (2.00 g, 4.9 mmol) and the mixture was stirred at room temperature (12 h) under H_2 (1 atm). The mixture was filtered through a bed of Celite® and the filtrate was evaporated in vacuum to obtain a colorless oil. THF (20 mL) was added to the residue followed by di(2-pyridyl) thionocarbonate (DPT) (0.12 g, 4.9 mmol). The solution was stirred at room temperature (12 h), and then the THF was removed. The residue was purified by silica gel column chromatography (1/9 acetone/EtOAc) to obtain 0.76 g of a white solid (57%): R_f = 0.49 (1/9 acetone/EtOAc); mp 131–132 °C; $[\alpha]^{25}_D$ +8.1° (*c* 1.0, DMSO); IR (nujol mull) 3284, 2207, 2105, 1635, 1547, 1458, 1376, 1230, 1128, 1044, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (s, C**H**$_3$C(O)), 3.51–3.76 (m, C**H**$_2$NCS, CH_2C**H**$_2$O, OC**H**H'), 3.99 (dd, *J* = 3.6, 9.3 Hz, CH**H'**), 4.41–4.58 (m, NC**H**$_2$Ph), 4.58–4.64 (m, C**H**), 6.55 (d, *J* = 6.3 Hz, N**H**C(O)CH_3), 6.77–6.82 (br t, N**H**), 7.26–7.37 (m, C_6**H**$_5$), addition of excess (*R*)-(-)-mandelic acid to a $CDCl_3$ solution of (*R*)-**27** gave only on signal for the acetyl protons; ^{13}C NMR ($CDCl_3$) δ 23.2 (**C**H_3C(O)), 43.6 (CH_2**C**H_2NH), 45.3 (C(O)N(H)**C**H_2), 52.7 (OCH_2**C**H), 69.3, 70.2 (2 O**C**H_2), 127.5, 127.6, 128.7 (3 Ar**C**), 134.5 (N**C**S), 137.9 (Ar**C**), 169.6, 170.6 (2 N**C**(O)); M_r (+ESI) 344.1040 $[M+Na]^+$ (calcd for $C_{15}H_{19}N_3O_3SNa^+$ 344.1045 $[M+Na]^+$). Anal. ($C_{15}H_{19}N_3O_3S$•0.2EtOAc): C, H, N, S.

(*S*)-*N*-Benzyl 2-Acetamido-3-(2-isothiocyanatoethoxy)propionamide ((*S*)-27). Utilizing the preceding procedure, and using Pd/C (10%, 0.17 g, 10% w/w), ethanol (17 mL), (*S*)-*N*-benzyl 2-acetamido-3-(2-amino-*N*-(benzyloxycarbonyl)ethoxy)propionamide ((*S*)-**46**) (1.70 g, 4.1 mmol), THF (17 mL) and di(2-pyridyl) thionocarbonate (DPT) (0.95 g, 4.1 mmol) gave 0.76 g of a white solid (57%): R_f = 0.49 (1/9 acetone/EtOAc); mp 131–132 °C; $[\alpha]^{25}_D$ –8.6° (*c* 1.0, DMSO); IR (nujol mull) 3283, 2206, 2105, 1725, 1635, 1546, 1458, 1375, 1231, 1127, 724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (s, C**H**$_3$C(O)), 3.51–3.74 (m, C**H**$_2$NCS, CH_2C**H**$_2$O, OC**H**H'), 3.99 (dd, *J* = 3.6, 9.3 Hz, CH**H'**), 4.46–4.52 (m, NC**H**$_2$Ph), 4.58–4.63 (m, C**H**), 6.55 (d, *J* = 6.9 Hz, N**H**C(O)CH_3), 6.75–6.85 (br t, N**H**), 7.26–7.36 (m, C_6**H**$_5$), addition of excess (*R*)-(-)-mandelic acid to a $CDCl_3$ solution of (*S*)-**27** gave only on signal for the acetyl protons; ^{13}C NMR ($CDCl_3$) δ 23.2 (**C**H_3C(O)), 43.6 (CH_2**C**H_2NH), 45.3 (C(O)N(H)**C**H_2), 52.7 (OCH_2**C**H), 69.3, 70.1 (2 O**C**H_2), 127.5, 127.6, 128.7 (3 Ar**C**), 134.6 (N**C**S), 137.9 (Ar**C**), 169.6, 170.6 (2 N**C**(O)); M_r (+ESI) 344.1039 $[M+Na]^+$ (calcd for $C_{15}H_{19}N_3O_3SNa^+$ 344.1045 $[M+Na]^+$). Anal. ($C_{15}H_{19}N_3O_3S$•0.1EtOAc): C, H, N, S.

Scheme S3. Synthesis of (*R*)- and (*S*)-**29**



***N*-(4-Iodobenzyl)phthalimide (49).**[11] A mixture of 4-iodobenzylbromide (**47**) (40.00 g, 134.7 mmol), potassium phthalimide (**48**) (26.20 g, 141.5 mmol) and dry DMF (150 mL) was heated overnight at 55 °C under Ar, and then the solvent was removed at reduced pressure. The solid residue was triturated with $CHCl_3$ (200 mL), filtered, and washed with $CHCl_3$ (3 x 200 mL). The combined organic extracts were successively washed with aqueous 0.2 M NaOH (200 mL) and H_2O (400 mL), and then dried ($MgSO_4$). The solvent was removed at reduced pressure to afford a crude solid, which was triturated with Et_2O to obtain a white solid (37.00 g, 75%): R_f = 0.75 (1/1 EtOAc/hexanes); mp 138–139 °C; ^{1}H NMR ($CDCl_3$) δ 4.77 (s, C**H**$_2$), 7.17 (d, J = 8.6 Hz, 2 Ar**H**), 7.63 (d, J = 8.6 Hz, 2 Ar**H**), 7.78 (dd, J = 3.0, 5.7 Hz, 2 Pht**H**), 7.83 (dd, J = 3.0, 5.7 Hz, 2 Pht**H**); ^{13}C NMR ($CDCl_3$) δ 41.0 (**C**H$_2$), 93.5 (**C**I), 123.4, 130.6, 131.9, 134.1, 135.9, 137.7 (6 Ar**C**), 167.2 (2 **C**(O)); M_r (+ESI) 363.9831 $[M+H]^+$ (calcd for $C_{17}H_{13}NO_2H^+$ 363.9835 $[M+H]^+$).

4-Iodobenzylamine Hydrochloride (50). An EtOH solution (50 mL) of hydrazine hydrate (7.28 mL, 152.9 mmol) was added to an EtOH solution (800 mL) of *N*-(4-iodobenzyl)phthalimide (**49**) (37.00 g, 101.9 mmol) maintained at reflux under Ar. The solution was stirred at reflux (2.5 h), and then the solvent was removed at reduced pressure. The solid residue was dissolved in CH_2Cl_2 (200 mL) and treated with aqueous 20% NaOH (200 mL). The aqueous phase was separated, extracted with $CHCl_3$

(3 x 300 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to afford the free base as an oil.

The free base was converted to the corresponding hydrochloride salt **50** by addition of a 4 M HCl solution in dioxane. The white precipitate was filtered and dried to obtain 25.00 g of **2** (91%): R_f = 0.1 (EtOAc); mp > 250 °C (lit.[12] mp 299–303 °C); ^{1}H NMR (DMSO-d_6) δ 3.97 (d, J = 5.4 Hz, C**H**$_2$), 7.34 (d, J = 8.1 Hz, 2 Ar**H**), 7.76 (d, J = 8.1 Hz, 2 Ar**H**), 8.50–8.85 (br s, NH_3^+); M_r (+ESI) 233.9780 $[M+H]^+$ (calcd for $C_{17}H_{13}NO_2H^+$ 233.9775 $[M+H]^+$).

(*R*)-*N*-(4-Iodo)benzyl 2-*N*-(*tert*-Butoxycarbonyl)amino-3-hydroxypropionamide ((*R*)-52). Using Method C, Boc-D-serine ((*R*)-**51**) (6.00 g, 29.2 mmol), NMM (3.80 mL, 35.04 mmol), IBCF (4.6 mL, 35.04 mmol) and 4-iodobenzylamine hydrochloride (**50**) (8.65 g, 32.60 mmol) in THF (400 mL) gave 8.97 g (73%) as a white solid: R_f = 0.60 (EtOAc); mp 129–130 °C; $[\alpha]^{25}_D$ +0.97° (*c* 2.8, DMSO); IR (nujol mull) 3327, 1656, 1521, 1458, 1375, 1302, 1244, 1164, 1009 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.39 (s, (C**H**$_3$)$_3$C), 3.49–3.60 (br m, C**H**$_2$OH), 3.95–4.01 (br m, C**H**CH$_2$), 4.18–4.31 (m, C**H**$_2$N), 4.86 (br s, O**H**), 6.68 (d, J = 7.8 Hz, BocN**H**), 7.08 (d, J = 8.1 Hz, 2 Ar**H**), 7.64 (d, J = 8.1 Hz, 2 Ar**H**), 8.37 (br s, CH$_2$N**H**); ^{13}C NMR ($CDCl_3$) δ 28.2 ((**C**H$_3$)$_3$C), 42.8 (N**C**H$_2$), 54.7 (OCH$_2$**C**H), 62.7 (O**C**H$_2$CH), 80.8 ((CH$_3$)$_3$**C**), 92.8 (**C**I), 129.3, 137.5, 137.7 (3 Ar**C**), 156.4 (C(O)), 171.5 (C(O)); M_r (+ESI) 443.0435 $[M+Na]^+$ (calcd for $C_{15}H_{21}IN_2O_4Na^+$ 443.0444 $[M+Na]^+$). Anal. ($C_{15}H_{21}IN_2O_4$): C, H, N, I.

(*S*)-*N*-(4-Iodo)benzyl 2-*N*-(*tert*-Butoxycarbonyl)amino-3-hydroxypropionamide ((*S*)-52). Utilizing the preceding procedure, and using Boc-L-serine ((*S*)-**51**) (1.72 g, 8.42 mmol), NMM (1.1 mL, 10.10 mmol), IBCF (1.3 mL, 10.10 mmol) and 4-iodobenzylamine hydrochloride (**50**) (2.50 g, 9.26 mmol) gave the desired product that was recrystallized with EtOAc to obtain (*S*)-**52** (2.51 g, 71%) as a white solid: R_f = 0.60 (EtOAc); mp 129–130 °C; $[\alpha]^{25}_D$ –0.93° (*c* 2.8, DMSO); IR (nujol mull) 3324, 1652, 1520, 1373, 1301, 1246, 1163, 1008, 850, 779 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.39 (s, (C**H**$_3$)$_3$C), 3.50–3.60 (br m, C**H**$_2$OH), 3.94–4.02 (br m, C**H**CH$_2$), 4.16–4.30 (m, C**H**$_2$N), 4.83–4.87 (br s, O**H**), 6.68 (d, J = 8.1 Hz, BocN**H**), 7.07 (d, J = 8.4 Hz, 2 Ar**H**), 7.64 (d, J = 8.4 Hz, 2 Ar**H**), 8.37 (t, J = 5.7 Hz, CH$_2$N**H**); ^{13}C NMR (DMSO-d_6) δ 28.1 ((**C**H$_3$)$_3$C), 41.4 (N**C**H$_2$), 56.9 (OCH$_2$**C**H), 61.7 (O**C**H$_2$CH), 78.1 ((CH$_3$)$_3$**C**), 92.1 (**C**I), 129.3, 136.7, 139.3 (**C**$_6$H$_4$), 155.1 (C(O)), 170.5 (C(O)); M_r (+ESI) 443.0445 $[M+Na]^+$ (calcd for $C_{15}H_{21}IN_2O_4Na^+$ 443.0444 $[M+Na]^+$). Anal. ($C_{15}H_{21}IN_2O_4$): C, H, N, I.

(*R*)-*N*-(4-Iodo)benzyl 2-*N*-(*tert*-Butoxycarbonyl)amino-3-methoxypropionamide ((*R*)-53). Ag_2O (20.63 g, 89.29 mmol) was added to a CH_3CN solution (300 mL) of (*R*)-*N*-(4-iodo)benzyl 2-*N*-(*tert*-butoxycarbonyl)amino-3-hydroxypropionamide ((*R*)-**52**) (7.50 g, 17.86 mmol) and then CH_3I (11.12 mL, 178.57 mmol) was added at room temperature under Ar. The reaction mixture was stirred at room temperature (3 d), filtered, and the filtrate concentrated in vacuo. The residue was purified by

silica gel column chromatography (2/3 EtOAc/hexanes) to obtain 5.80 g (75%) of (*R*)-**53** as a white solid after trituration with Et_2O: R_f = 0.53 (1/1 EtOAc/hexanes); mp 86–87 °C; $[\alpha]^{25}_D$ −3.4° (*c* 1.0, DMSO); IR (nujol mull) 3334, 1659, 1528, 1461, 1376, 1303, 1245, 1165, 1110, 1049, 954, 870, 788, 619 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, $(CH_3)_3C$), 3.37 (s, OCH_3), 3.48 (dd, *J* = 6.3, 9.3 Hz, $CHH'OCH_3$), 3.84 (dd, *J* = 3.9, 9.3 Hz, $CHH'OCH_3$), 4.20–4.28 (br m, $CHCH_2$), 4.41 (d, *J* = 5.4 Hz, CH_2N), 5.37–7.41 (br s, BocN**H**), 6.75–6.80 (br t, CH_2NH), 7.01 (d, *J* = 8.2 Hz, 2 Ar**H**), 7.64 (d, *J* = 8.2 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 28.2 ($(CH_3)_3C$), 42.8 (NCH_2), 54.0 (OCH_2CH), 59.1 (OCH_3), 71.9 (OCH_2CH), 80.5 ($(CH_3)_3C$), 92.7 (**C**I), 129.3, 137.7, 137.8 (3 Ar**C**), 155.5 (C(O)), 170.4 (C(O)); M_r (+ESI) 435.0777 $[M+H]^+$ (calcd for $C_{16}H_{23}IN_2O_4H^+$ 435.0781 $[M+H]^+$). Anal. ($C_{16}H_{23}IN_2O_4$): C, H, N, I.

(*S*)-*N*-(4-Iodo)benzyl 2-*N*-(*tert*-Butoxycarbonyl)amino-3-methoxypropionamide ((*S*)-53). Utilizing the preceding procedure, and using Ag_2O (23.40 g, 101.20 mmol), (*S*)-*N*-(4-iodo)benzyl 2-*N*-(*tert*-butoxycarbonyl)amino-3-hydroxypropionamide ((*S*)-**52**) (8.50 g, 20.24 mmol) and CH_3I (12.60 mL, 202.4 mmol) gave 7.56 g (85%) of a white solid: R_f = 0.53 (1/1 EtOAc/hexanes); mp 87.0–87.5 °C; $[\alpha]^{25}_D$ +3.3° (*c* 1.0, DMSO); IR (nujol mull) 3337, 2728, 1657, 1527, 1461, 1376, 1303, 1244, 1164, 1109, 1048, 953, 869, 787, 617 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.39 (s, $(CH_3)_3C$), 3.24 (s, OCH_3), 3.47 (d, *J* = 6.0 Hz, CH_2OCH_3), 4.14–4.18 (br m, $CHCH_2$), 4.20–4.25 (m, CH_2N), 6.88 (d, *J* = 7.5 Hz, BocN**H**), 7.05 (d, *J* = 8.2 Hz, 2 Ar**H**), 7.64 (d, *J* = 8.2 Hz, 2 Ar**H**), 8.45 (t, *J* = 6.0 Hz, CH_2NH); ^{13}C NMR (DMSO-d_6) δ 28.0 ($(CH_3)_3C$), 41.4 (NCH_2), 54.2 (OCH_2CH), 58.0 (OCH_3), 71.8 (OCH_2CH), 78.1 ($(CH_3)_3C$), 92.2 (**C**I), 129.3, 136.7, 139.2 (3 Ar**C**), 155.1 (C(O)), 170.0 (C(O)); M_r (+ESI) 435.0775 $[M+H]^+$ (calcd for $C_{16}H_{23}IN_2O_4H^+$ 435.0781 $[M+H]^+$). Anal. ($C_{16}H_{23}IN_2O_4$): C, H, N, I.

(*R*)-*N*-(4-Iodo)benzyl 2-Acetamido-3-methoxypropionamide ((*R*)-54). A saturated HCl solution in dioxane (0.5 M, 25.00 mL) was added to (*R*)-*N*-(4-iodo)benzyl 2-*N*-(*tert*-butoxycarbonyl)amino-3-methoxypropionamide ((*R*)-**53**) (5.50 g, 12.67 mmol) at 0 °C and the solution was stirred at room temperature (2 h). The reaction solution was concentrated in vacuo and dried (30 min). CH_2Cl_2 (30 mL) was added to the residue followed by the successive additions of Et_3N (10.66 mL, 76.02 mmol) and AcCl (2.70 mL, 38.01 mmol) at 0 °C. The mixture was stirred at room temperature (2 h), aqueous 10% citric acid was added and then the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, washed with aqueous saturated $NaHCO_3$ (30 mL) and H_2O (30 mL), dried ($MgSO_4$), and concentrated in vacuo. The solid was recrystallized with EtOAc to obtain (*R*)-**54** as a white solid: R_f = 0.76 (1/1 acetone/EtOAc); mp 159–160 °C; $[\alpha]^{25}_D$ = +3.3° (*c* 1.0, DMSO); IR (nujol mull) 3279, 1636, 1552, 1457, 1375, 1305, 1139, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (s, CH_3CO), 3.38 (s, OCH_3), 3.44 (dd, *J* = 7.2, 9.0 Hz, C**H**H'), 3.79 (dd, *J* = 4.2, 9.0 Hz, CH**H'**), 4.38–4.41 (m, CH_2N), 4.52–4.59 (m, NC(**H**)CO), 6.46 (br d, *J* = 6.6 Hz, N**H**C(O)CH_3), 6.85–6.93 (br t, CH_2NH), 7.00 (d, *J* = 8.4 Hz, 2 Ar**H**), 7.64 (d, *J* = 8.4 Hz, 2 Ar**H**); ^{13}C

NMR ($CDCl_3$) δ 23.1 (**C**H_3CO), 42.9 (**C**H_2N), 52.4 (**C**HCH_2), 59.1 (O**C**H_3), 71.6 (**C**H_2OCH_3), 92.7 (**C**I), 129.3, 137.7, 139.1 (3 Ar**C**), 170.1, 170.3 (2 **C**(O)); M_r (+ESI) 399.0177 $[M+Na]^+$ (calcd for $C_{13}H_{17}IN_2O_3Na^+$ 399.0182 $[M+Na]^+$). Anal. ($C_{13}H_{17}IN_2O_3$): C, H, N, I.

(*S*)-*N*-(4-Iodo)benzyl 2-Acetamido-3-methoxypropionamide ((*S*)-54). Utilizing the preceding procedure and, using a saturated HCl solution in dioxane (0.5 M, 17 mL), (*S*)-*N*-(4-iodo)benzyl 2-*N*-(*tert*-butoxycarbonyl)amino-3-methoxypropionamide ((*S*)-**53**) (3.70 g, 8.52 mmol), Et_3N (3.6 mL, 25.60 mmol) and AcCl (906 μL, 12.30 mmol) gave (*S*)-**54** (2.43 g, 76%) as a white solid: R_f = 0.76 (1/1 acetone/EtOAc); mp 159–160 °C; $[\alpha]^{25}_D$ = –3.2° (*c* 1.0, DMSO); IR (nujol mull) 3278, 1636, 1552, 1458, 1375, 1305, 1138, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (s, C**H**$_3$CO), 3.38 (s, OC**H**$_3$), 3.43 (dd, *J* = 7.2, 9.0 Hz, C**H**H'), 3.79 (dd, *J* = 4.2, 9.0 Hz, CH**H'**), 4.38–4.42 (m, C**H**$_2$N), 4.53–4.59 (m, NC(**H**)CO), 6.47 (br d, *J* = 6.0 Hz, N**H**C(O)CH_3), 6.85–6.93 (br t, CH_2N**H**), 7.00 (d, *J* = 8.4 Hz, 2 Ar**H**), 7.64 (d, *J* = 8.4 Hz, 2 Ar**H**); ^{13}C NMR (DMSO-d_6) δ 22.4 (**C**H_3CO), 41.4 (**C**H_2N), 52.5 (**C**HCH_2), 58.1 (O**C**H_3), 71.9 (**C**H_2OCH_3), 92.2 (**C**I), 129.3, 136.8, 139.1 (3 Ar**C**), 169.3, 169.7 (2 **C**(O)); M_r (+ESI) 399.0177 $[M+Na]^+$ (calcd for $C_{13}H_{17}IN_2O_3Na^+$ 399.0182 $[M+Na]^+$). Anal. ($C_{13}H_{17}IN_2O_3$): C, H, N, I.

(*R*)-*N*-(4-(Trimethylsilyl)ethynyl)benzyl 2-Acetamido-3-methoxypropionamide ((*R*)-55). To an anhydrous THF (70 mL) solution of (*R*)-*N*-(4-iodo)benzyl 2-acetamido-3-methoxypropionamide ((*R*)-**54**) (2.40 g, 6.38 mmol), were sequentially added under Ar, triethylamine (1.79 mL, 12.76 mmol), trimethylsilylacetylene (1.35 ml, 9.57 mmol), dichlorobis(triphenylphosphine)palladium (II) (224 mg, 0.319 mmol), and CuI (121 mg, 0.638 mmol). The mixture was stirred at room temperature (4 h), and then Et_2O added and the precipitate filtered through a Celite pad. The filtrate was concentrated in vacuo and the residue was purified by flash chromatography on silica gel with EtOAc/MeOH (9/1) as the eluant to obtain (*R*)-**55** (1.50 g, 68%) as a brown solid. To remove the traces of palladium, the solid was treated with 14.00 g of resin scavenger (SPM32, PhosPhonics) in CH_2Cl_2. The mixture was stirred at room temperature (2 h) and filtered. The filtrate evaporated under vacuum to give (R)-**55**: R_f = 0.41 (EtOAc); mp 126–127 °C; $[\alpha]^{25}_D$ = +6.1° (*c* 1.0, DMSO); IR (nujol mull) 3285, 2157, 1641, 1546, 1457, 1375, 1302, 1248, 1130, 975, 862, 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (s, $(CH_3)_3$Si), 1.99 (s, C**H**$_3$CO), 3.35 (s, OC**H**$_3$), 3.45 (dd, *J* = 7.2, 9.0 Hz, C**H**H'), 3.75 (dd, *J* = 4.2, 9.0 Hz, CH**H'**), 4.33–4.47 (m, C**H**$_2$N), 4.57–4.62 (m, NC(**H**)CO), 6.66 (br d, *J* = 6.9 Hz, N**H**C(O)CH_3), 7.07–7.13 (br t, CH_2N**H**), 7.17 (d, *J* = 7.9 Hz, 2 Ar**H**), 7.40 (d, *J* = 7.9 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ -0.1 (TMS), 23.2 (**C**H_3CO), 43.2 (**C**H_2N), 52.4 (**C**HCH_2), 59.1 (O**C**H_3), 71.6 (**C**H_2OCH_3), 94.4 (**C**≡C), 104.7 (C≡**C**), 122.4, 127.2, 132.3, 138.3 (4 Ar**C**), 170.0, 170.3 (2 **C**(O)); M_r (+ESI) 369.1605 $[M+Na]^+$ (calcd for $C_{18}H_{26}N_2O_3SiNa^+$ 369.1610 $[M+Na]^+$). Anal. ($C_{18}H_{26}N_2O_3Si$): C, H, N.

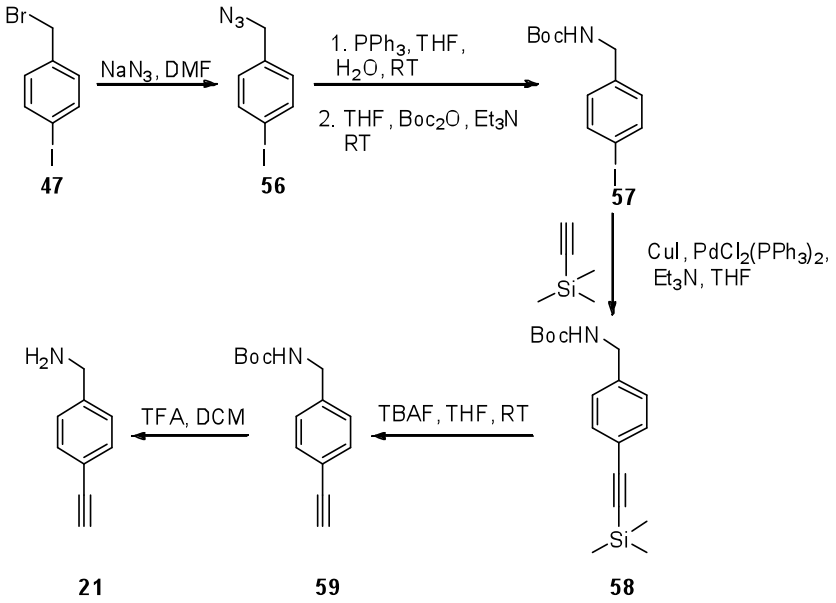
(*S*)-*N*-(4-(Trimethylsilyl)ethynyl)benzyl 2-Acetamido-3-methoxypropionamide ((*S*)-55). Utilizing the preceding procedure, and using (*S*)-**54** (2.40 g, 6.38 mmol), triethylamine (1.79 mL, 12.76 mmol), CuI (121 mg, 0.638 mmol), dichlorobis(triphenylphosphine)palladium (II) (224 mg, 0.319 mmol), and trimethylsilylacetylene (1.35 mL, 9.57 mmol) gave 1.97 g (91%) of (*S*)-**55** as a brown solid: R_f = 0.41 (EtOAc); mp 126–127 °C; $[\alpha]^{25}_D$ = –6.2° (*c* 1.0, DMSO); IR (nujol mull) 3285, 2727, 2157, 1641, 1546, 1457, 1374, 1304, 1250, 1137, 862, 725 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.22 (s, (C**H$_3$**)$_3$Si), 1.87 (s, C**H$_3$**CO), 3.25 (s, OC**H$_3$**), 3.44–3.55 (m, C**H$_2$**), 4.29 (d, *J* = 5.7 Hz, C**H$_2$**N), 4.43–4.51 (m, NC(**H**)CO), 7.24 (d, *J* = 8.2 Hz, 2 Ar**H**), 7.40 (d, *J* = 8.2 Hz, 2 Ar**H**), 8.10 (br d, *J* = 8.1 Hz, N**H**C(O)CH$_3$), 8.53 (br t, *J* = 6.0 Hz, CH$_2$N**H**); ^{13}C NMR (DMSO-d_6) δ -0.2 (TMS), 22.4 (**C**H$_3$CO), 41.7 (**C**H$_2$N), 52.6 (**C**HCH$_2$), 58.1 (O**C**H$_3$), 71.9 (**C**H$_2$OCH$_3$), 93.6 (**C**≡C), 105.1(C≡**C**), 120.0, 127.1, 131.4, 140.4 (4 Ar**C**), 169.3, 169.8 (2 **C**(O)); M_r (+ESI) 369.1603 $[M+Na]^+$ (calcd for $C_{18}H_{26}N_2O_3SiNa^+$ 369.1610 $[M+Na]^+$). Anal. ($C_{18}H_{26}N_2O_3Si$): C, H, N.

(*R*)-*N*-(4-Ethynyl)benzyl 2-Acetamido-3-methoxypropionamide ((*R*)-29). A 1 M THF solution of TBAF (8.66 mL, 8.66 mmol) was added to a THF (60 mL) solution of (*R*)-*N*-(4-(trimethylsilyl)ethynyl)benzyl 2-acetamido-3-methoxypropionamide ((*R*)-**55**) (1.50 g, 4.33 mmol) and then the solution was stirred at room temperature (4 h). CH_2Cl_2 (30 mL) and an aqueous 10% citric acid solution (30 mL) were added and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography on silica gel with EtOAc as the eluant to obtain (*R*)-**56** (0.81 g, 68%) as a white solid: R_f = 0.41 (EtOAc); mp 161–162 °C; $[\alpha]^{25}_D$ = +4.2° (*c* 0.5, DMSO); IR (nujol mull) 3290, 1634, 1544, 1458, 1375, 1311, 1240, 1197, 1104, 1041, 714 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.02 (s, C**H$_3$**CO), 3.07 (s, C≡C**H**), 3.37 (s, OC**H$_3$**), 3.45 (dd, *J* = 7.2 Hz, 9.3 Hz, C**H**H'), 3.77 (dd, *J* = 4.5 Hz, 9.3 Hz, CH**H'**), 4.36–4.49 (m, C**H$_2$**N), 4.56–4.63 (m, NC(**H**)CO), 6.60 (br d, *J* = 6.9 Hz, N**H**C(O)CH$_3$), 7.01–7.10 (br t, CH$_2$N**H**), 7.20 (d, *J* = 8.2 Hz, 2 Ar**H**), 7.44 (d, *J* = 8.2 Hz, 2 Ar**H**), addition of excess (*R*)-(-)-mandelic acid to a $CDCl_3$ solution of (*R*)-**56** gave only on signal for the acetyl protons and the methyl protons; ^{13}C NMR ($CDCl_3$) δ 23.1 (**C**H$_3$CO), 43.1 (**C**H$_2$N), 52.5 (**C**HCH$_2$), 59.0 (O**C**H$_3$), 71.7 (**C**H$_2$OCH$_3$), 77.3 (**C**≡C), 82.2(C≡**C**), 121.2, 127.3, 132.4, 138.7 (4 Ar**C**), 170.1, 170.4 (2 **C**(O)); M_r (+ESI) 297.1210 $[M+Na]^+$ (calcd for $C_{15}H_{18}N_2O_3Na^+$ 297.1215 $[M+Na]^+$). Anal. ($C_{15}H_{18}N_2O_3$•0.5H_2O): C, H, N.

(*S*)-*N*-(4-Ethynyl)benzyl 2-Acetamido-3-methoxypropionamide ((*S*)-29). Utilizing the preceding procedure, and using (*S*)-**55** (50 mg, 0.145 mmol), and TBAF (290 μL, 8.66 mmol) gave 0.75 g (91%) of (*S*)-**56** as a white solid (39 mg, 91%): R_f = 0.41 (EtOAc); mp 159–160 °C; $[\alpha]^{25}_D$ = –4.4° (*c* 0.5, DMSO); IR (nujol mull) 3289, 2728, 1635, 1544, 1458, 1375, 1304, 1234, 975, 724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.03 (s, C**H$_3$**CO), 3.07 (s, C≡C**H**), 3.38 (s, OC**H$_3$**), 3.44 (dd, *J* = 7.5, 9.0 Hz, C**H**H'),

3.80 (dd, *J* = 4.2, 9.0 Hz, CH**H'**), 4.41–4.51 (m, C**H$_2$**N), 4.52–4.57 (m, NC(**H**)CO), 6.46 (br d, *J* = 5.4 Hz, N**H**C(O)CH$_3$), 6.80–6.92 (br t, CH$_2$N**H**), 7.21 (d, *J* = 8.4 Hz, 2 Ar**H**), 7.45 (d, *J* = 8.4 Hz, 2 Ar**H**), addition of excess (*R*)-(-)-mandelic acid to a $CDCl_3$ solution of (*S*)-**56** gave only on signal for the acetyl protons and the methyl protons; ^{1}H NMR (DMSO-d_6) δ 1.87 (s, C**H$_3$**CO), 3.25 (s, OC**H$_3$**), 3.44–3.55 (m, C**H$_2$**), 4.14 (s, C≡C**H**), 4.29 (d, *J* = 6.0 Hz, C**H$_2$**N), 4.43–4.48 (m, NC(**H**)CO), 7.25 (d, *J* = 8.4 Hz, 2 Ph**H**), 7.42 (d, *J* = 8.4 Hz, 2 Ph**H**), 8.11 (br d, *J* = 7.8 Hz, N**H**C(O)CH$_3$), 8.52 (br t, *J* = 6.0 Hz CH$_2$N**H**); ^{13}C NMR ($CDCl_3$) 23.2 (**C**H$_3$C(O)), 43.2 (**C**H$_2$N), 52.5 (**C**HCH$_2$), 59.1 (O**C**H$_3$), 71.7 (**C**H$_2$OCH$_3$), 77.3 (**C**≡C), 83.3 (C≡**C**), 121.2, 127.3, 132.4, 138.8 (4 Ar**C**), 170.1, 170.4 (2 **C**(O)); ^{13}C NMR (DMSO-d_6) 22.3 (**C**H$_3$C(O)), 41.6 (**C**H$_2$N), 52.4 (**C**HCH$_2$), 58.0 (O**C**H$_3$), 71.8 (**C**H$_2$OCH$_3$), 80.2 (**C**≡C), 83.2 (C≡**C**), 119.8, 126.9, 131.3, 140.2 (4 Ar**C**), 169.2, 169.6 (2 **C**(O)); the HMQC experiment showed a correlation between the δ = 3.07 ppm in the ^{1}H NMR ($CDCl_3$) and δ = 77.3 in the ^{13}C NMR ($CDCl_3$) and a correlation between δ = 4.14 ppm in the ^{1}H NMR (DMSO-d_6) and δ = 80.2 in the ^{13}C NMR (DMSO-d_6); M_r (+ESI) 297.1212 $[M+Na]^+$ (calcd for $C_{15}H_{18}N_2O_3Na^+$ 297.1215 $[M+Na]^+$). Anal. ($C_{15}H_{18}N_2O_3$•0.25H_2O): C, H, N.

Scheme S4. Synthesis of **21**



4-Iodobenzyl Azide (56).[13] NaN_3 (0.98 g, 15.09 mmol) was added to a solution of 4-iodobenzyl bromide (**47**) (1.49 g, 5.03 mmol) in DMF (5 mL) and then the mixture was stirred at room temperature (2 h). The reaction was diluted with H_2O and extracted with EtOAc (5 x 30 mL). The combined organic layers were washed with H_2O and saturated aqueous brine (30 mL), dried ($MgSO_4$), filtered, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (1/9 EtOAc/hexanes) to obtain a white solid (1.18 g, 92%): R_f = 0.72 (1/9 EtOAc/hexanes); mp 36 °C (lit.[13] mp 36 °C); ^{1}H NMR ($CDCl_3$) δ 4.29 (s, C**H**$_2$), 7.06 (d, J = 8.3 Hz, 2 Ar**H**), 7.70 (d, J = 8.3 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 54.1 (**C**H$_2$), 93.9 (**C**-I), 129.9, 135.0 , 137.9 (3 Ar**C**).

***tert*-Butyl *N*-(4-Iodo)benzyl Carbamate (57).**[13] A THF solution (25 mL) of **56** (1.04 g, 4 mmol) was treated with PPh_3 (1.50 g, 4 mmol) and H_2O (0.36 g, 20 mmol). The reaction mixture was stirred overnight (room temperature), and then concentrated in vacuo. The residue was dissolved in THF (40 mL) and treated with Et_3N (1.12 mL, 8 mmol) and di-*tert*-butyl dicarbonate (1.75 mL, 8 mmol). The reaction was stirred at room temperature (3 h), and then H_2O (25 mL) was added, and the reaction mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with H_2O (30 mL) and saturated aqueous brine (30 mL), dried ($MgSO_4$), filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (3/7 EtOAc/hexanes) to obtain a white solid (0.99 g, 75%): R_f = 0.85 (1/1 EtOAc /hexanes); mp 90 °C (lit.[7] mp 91 °C); ^{1}H NMR ($CDCl_3$) δ 1.45 (s, C(C**H**$_3$)$_3$), 4.22 (d, J = 6.0 Hz, C**H**$_2$), 5.02 (br s, N**H**), 7.02 (d, J

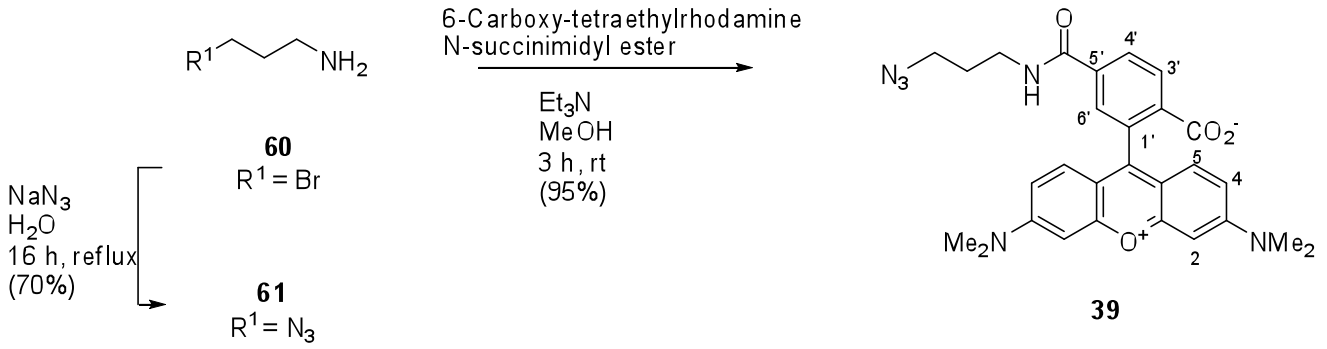
= 8.1 Hz, 2 Ar**H**), 7.63 (d, J = 8.1 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 28.4 (C$\mathbf{H}_3$), 44.0 (C$\mathbf{H}_2$), 79.6 (**C**$(CH_3)_3$), 92.5 (**C**-I), 129.3, 137.6, 138.8 (3 Ar**C**), 155.8 (**C**(O)).

***tert*-Butyl *N*-(4-(Trimethylsilyl)ethynyl)benzyl Carbamate (58).**[13] A THF solution (20 mL) of **57** (666 mg, 2.0 mmol) was treated with (trimethylsilyl)acetylene (0.34 mL, 2.4 mmol), Et_3N (0.56 mL, 4 mmol), CuI (38 mg, 0.2 mmol) and dichlorobis(triphenylphosphine)palladium (II) (70 mg, 0.1 mmol) and stirred at room temperature (3 h). The reaction mixture was diluted with Et_2O, filtered through Celite, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (1/9 EtOAc/hexanes) to yield **58** (721 mg, 99%) as a yellow solid: R_f = 0.48 (1/9 EtOAc/hexanes); mp 94–95 °C (lit.[7] mp 95 °C); ^{1}H NMR ($CDCl_3$) δ 0.23 (s, Si(C$\mathbf{H}_3)_3$), 1.44 (s, C(C$\mathbf{H}_3)_3$), 4.26 (d, J = 5.7 Hz, C$\mathbf{H}_2$), 4.99 (br s, N**H**), 7.18 (d, J = 8.1 Hz, 2 Ar**H**), 7.40 (d, J = 8.1 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 0.00 (Si(**C**$H_3)_3$), 28.4 (C(**C**$H_3)_3$), 44.4 (**C**H_2), 79.8 (**C**$(CH_3)_3$), 94.1 (C≡**C**), 104.9 (C≡**C**), 122.1, 127.2, 132.2, 139.5 (4 Ar**C**), 155.9 (**C**(O)).

***tert*-Butyl *N*-(4-Ethynylbenzyl)carbamate (59).**[13] A THF solution (10 mL) of **58** (530 mg, 1.75 mmol) was treated with a 1.0 M solution of TBAF in THF (3.5 mL, 3.50 mmol) and stirred at room temperature (1 h). After evaporation, the residue was purified by flash chromatography (15/85 EtOAc/hexanes) to yield **59** (344 mg, 80%) as a white solid: mp 83 °C (lit.[1] mp 82 °C); R_f = 0.49 (15/85 EtOAc /hexanes); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, C(**C**$H_3)_3$), 3.06 (s, C≡C**H**), 4.30 (d, J = 6.0 Hz, C$\mathbf{H}_2$), 4.91 (br s, N**H**), 7.23 (d, J = 8.1 Hz, 2 Ar**H**), 7.45 (d, J = 8.1 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 28.8 (C(**C**$H_3)_3$), 44.8 (C$\mathbf{H}_2$), 80.1 (**C**$(CH_3)_3$), 83.9 (**C**≡C), 98.3 (**C**≡C), 121.5, 127.7, 132.8, 140.3 (4 Ar**C**), 156.3 (**C**(O)).

***N*-(4-Ethynylbenzyl)amine (21).**[13] A CH_2Cl_2 solution (60 mL) of **59** (2.80 g, 12.1 mmol) at 0 °C was treated with trifluoroacetic acid (12 mL), and then stirred at room temperature (1 h). The solution was evaporated, and aqueous saturated Na_2CO_3 (100 mL) added, and extracted with $CHCl_3$ (3 x 150 mL). The organics layers were combined, dried ($MgSO_4$), filtered, and concentrated in vacuum to obtain **21** as a brown oil (1.40 g, 88%): ^{1}H NMR ($CDCl_3$) δ 3.05 (s, C≡C**H**), 3.89 (s, C$\mathbf{H}_2$), 7.28 (d, J = 7.6 Hz, 2 Ar**H**), 7.47 (d, J = 7.6 Hz, 2 Ar**H**); ^{13}C NMR ($CDCl_3$) δ 46.2 (**C**H_2), 83.6 (**C**≡C), 120.5 (**C**≡C), 127.0, 127.8, 132.3, 144.1 (Ar**C**).

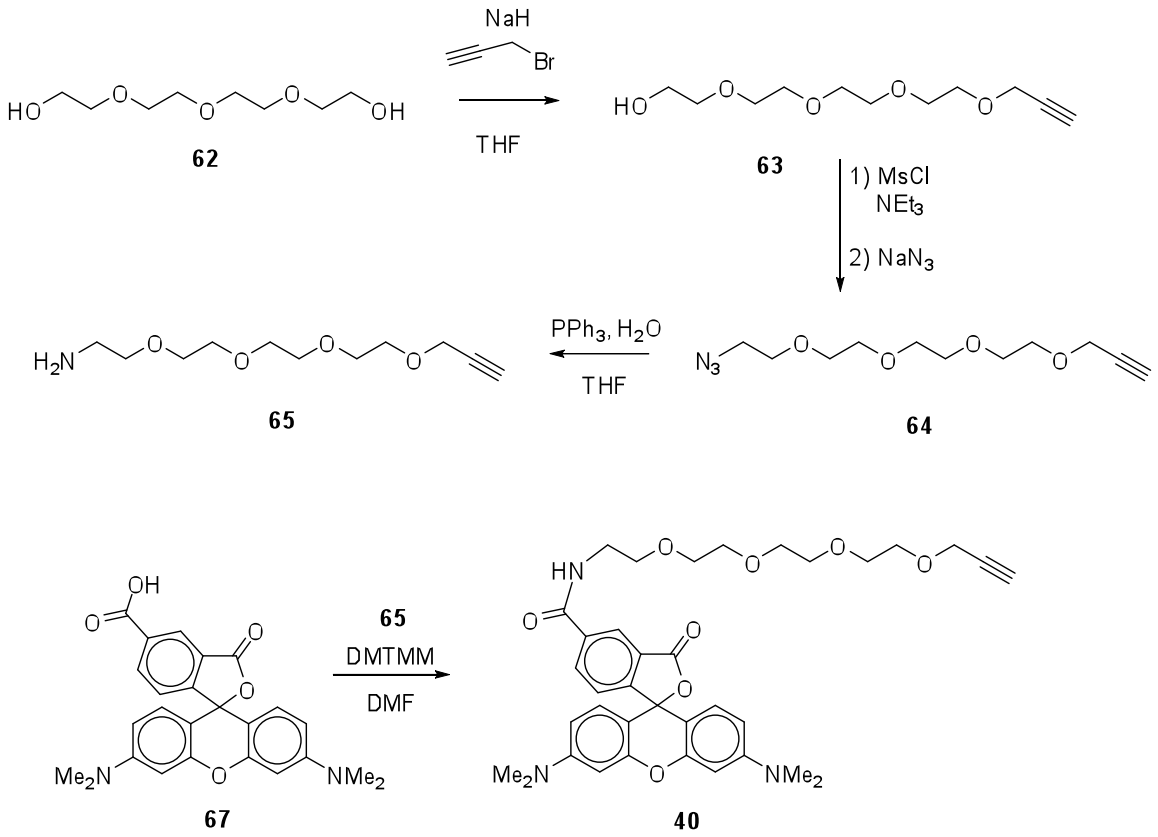
Scheme S5. Synthesis of **39**



3-Azido Propylamine (61).[14] 1-Bromo-3-aminopropane hydrochloride (**60**) (5.00 g, 22.84 mmol) was suspended in H_2O (16 mL) followed by the addition of an aqueous NaN_3 (4.45 g, 68.5 mmol) solution (23 mL). The mixture was heated to reflux (16 h) and then concentrated to ~1/3 volume in vacuo. The resulting mixture was cooled in an ice bath and Et_2O (50 mL) and KOH pellets (6.24 g) were added while keeping the temperature below 10 °C. The organic layer was separated and the aqueous phase extracted with Et_2O (2 × 50 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo, and then purified by bulb-to-bulb distillation to give 1.60 g (70%) of **61** as an yellow oil: R_f = 0.60 (3/97 NH_4OH/EtOH); IR (nujol mull) 2933, 2864, 2098, 1595, 1459 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.54–1.63 (m, $CH_2C\mathbf{H_2}CH_2$), 2.59 (t, J = 6.6 Hz, $C\mathbf{H_2}NH_2$), 3.37 (t, J = 6.8 Hz, $N_3C\mathbf{H_2}$); ^{13}C NMR (DMSO-d_6) δ 32.2 ($CH_2\mathbf{C}H_2CH_2$), 38.7 ($\mathbf{C}H_2NH_2$), 48.5 ($N_3\mathbf{C}H_2$).

Rhodamine-azide (39).[15] 6-Carboxytetramethylrhodamine succinimidyl ester (Berry & Associate. Cat. No. FT 6230, 10.0 mg, 18.96 μmol) was dissolved in MeOH (1 mL), and 3-azido propylamine (**61**) (11.4 mg, 113.74 μmol), and triethylamine (13.3 μL, 94.78 μmol) were added to the stirred solution at room temperature. After 3 h, the solvent was evaporated in vacuo, and the crude product purified by silica gel column chromatography (1/4 MeOH/$CHCl_3$) to give the desired product along with some starting amine. The product was dissolved in aqueous 1% citric acid (15 mL) and extracted with $CHCl_2$ (3 × 20 mL). The organic extracts were combined, washed with saturated aqueous brine (15 mL), and dried (Na_2SO_4) to yield 9.2 mg (95%) of **39** as a dark red solid: R_f = 0.40 (1/4 MeOH/$CHCl_3$); ^1H NMR (CD_3OD) δ 1.82–1.91 (m, $CH_2C\mathbf{H_2}CH_2$), 3.40 (t, J = 6.6 Hz, $C\mathbf{H_2}NH_2$), 3.46 (t, J = 6.9 Hz, $N_3C\mathbf{H_2}$), 6.93 (d, J = 2.6 Hz, 2 C(2)**H**), 7.02 (dd, J = 2.6, 9.6 Hz, 2 C(4)**H**), 7.26 (d, J = 9.6 Hz, 2 C(5)**H**), 7.71 (d, J = 1.8 Hz, C(6')**H**). 8.08 (dd, J = 1.8, 8.2 Hz, C(4')**H**), 8.14 (d, J = 8.2 Hz, C(3')**H**).

Scheme S6. Synthesis of **40**



3,6,9,12-Tetraoxapentadec-14-yn-1-ol (63).[16] Tetraethylene glycol (**62**) (2.00 g, 10.3 mmol) was dissolved in THF (50 mL) and cooled at 0 °C (ice bath). NaH (60% suspension in oil, 272 mg, 11.34 mmol) was added and the suspension was stirred at 0 °C (15 min). Propargyl bromide (80% wt in toluene, 1.68 mL, 11.34 mmol) was then added dropwise at 0 °C. The suspension was warmed to room temperature and stirred at room temperature (1 h). The salts were removed by filtration, the filtrate concentrated in vacuo, and purified by flash chromatography to yield **63** as a colorless oil (642 mg, 27%): R_f = 0.58 (1/9 MeOH/$CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.44 (t, J = 2.2 Hz, $OCH_2CC\mathbf{H}$), 2.68 (t, J = 6.3 Hz, $CH_2O\mathbf{H}$), 3.58–3.64 (m, $C\mathbf{H_2}OH$), 3.64–3.76 (m, 3 $C\mathbf{H_2}OC\mathbf{H_2}$, $C\mathbf{H_2}OCH_2CCH$), 4.21 (d, J = 2.2 Hz, $C\mathbf{H_2}CCH$); ^{13}C NMR ($CDCl_3$) δ 58.6 ($\mathbf{C}H_2CCH$), 61.9 ($\mathbf{C}H_2OH$), 69.3, 70.5, 70.6, 70.7, 70.8, 70.9, 72.7 (7 $O\mathbf{C}H_2$), 74.7 ($CH_2C\mathbf{C}H$), 79.8 ($CH_2\mathbf{C}CH$).

1-Azido-3,6,9,12-tetraoxapentadec-14-yne (64). Compound **63** (624 mg, 2.69 mmol) was dissolved in THF (25 mL) and NEt_3 (450 μL, 3.22 mmol) was added and then mesyl chloride (250 μL, 3.22 mmol) was added dropwise, while stirring at room temperature (water bath). The reaction was stirred (45 min), the salts filtered, and the filtrate concentrated in vacuo. The residue was dissolved in

CH_2Cl_2 (25 mL), successively washed with aqueous 10% citric acid (25 mL) and brine (25 mL), dried (Na_2SO_4) and evaporated to dryness. The crude mesylated product was obtained as an oil (788 mg, 2.54 mol, 94%) and directly dissolved in DMF (10 mL). NaN_3 was added (214 mg, 3.3 mmol) and the reaction was heated at 60 °C (18 h). After cooling to room temperature, H_2O (90 mL) was added, and then the reaction mixture was extracted with Et_2O (3 x 100 mL). The combined organic layers were successively washed with H_2O (2 x 50 mL), brine (50 mL), and dried (Na_2SO_4). The solvents were removed under vacuum to yield **64** as pale yellow oil (400 mg, 61%) that was used without further purification: R_f = 0.46 (5/95 MeOH/CH_2Cl_2); IR (neat) 3251, 2869, 2106, 1454, 1531, 1293, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.44 (t, J = 2.2 Hz, $OCH_2CC\mathbf{H}$), 3.41 (t, J = 5.1 Hz, CH_2N_3), 3.62–3.74 (m, 3 $C\mathbf{H_2}OC\mathbf{H_2}$, $C\mathbf{H_2}OCH_2CCH$), 4.21 (d, J = 2.2 Hz, $C\mathbf{H_2}CCH$); ^{13}C NMR ($CDCl_3$) δ 50.9 ($\mathbf{C}H_2N_3$), 58.6 ($\mathbf{C}H_2CCH$), 69.3, 70.2, 70.5, 70.6, 70.7, 70.8, 70.9 (7 $O\mathbf{C}H_2$), 74.7 ($CH_2C\mathbf{C}H$), 79.8 ($CH_2\mathbf{C}CH$); M_r (+ESI) 296.1012 $[M+K]^+$ (calcd for $C_{11}H_{19}N_3O_4K^+$ 296.1013 $[M+K]^+$).

3,6,9,12-Tetraoxapentadec-14-yn-1-amine (65). Azide **64** (355 mg, 1.38 mmol) was dissolved in THF (20 mL) and PPh_3 (724 mg, 2.74 mmol) was added. Upon dissolution, H_2O (1 mL) was added to the reaction and the solution was stirred at room temperature (12 h). The solvents were removed in vacuo, the residue was dissolved in aqueous 0.1 M HCl (20 mL), and washed with CH_2Cl_2 (6 x 80 mL) and EtOAc (2 x 100 mL). The aqueous layer was evaporated to dryness and the remaining salts were suspended in CH_2Cl_2 (25 mL), vigorously stirred (5 min), and filtered. The cake was extensively rinsed with CH_2Cl_2, and the combined organic fractions were evaporated to yield **65** (247 mg, 77%) as a hygroscopic pale yellow oil that was used without further purification: R_f = 0-0.10 (1/9 MeOH/CH_2Cl_2); IR (neat) 3367, 2870, 2112, 1661, 1596, 1457, 1353, 1294, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38–1.56 (br s, $CH_2N\mathbf{H_2}$), 2.44 (t, J = 2.2 Hz, $OCH_2CC\mathbf{H}$), 2.87 (t, J = 5.4 Hz, $C\mathbf{H_2}NH_2$), 3.51 (t, J = 5.4 Hz, $C\mathbf{H_2}CH_2NH_2$), 3.60–3.75 (m, 2 $C\mathbf{H_2}OC\mathbf{H_2}$, $C\mathbf{H_2}OCH_2CCH$, $C\mathbf{H_2}OCH_2CH_2NH_2$), 4.21 (d, J = 2.2 Hz, $C\mathbf{H_2}CCH$); ^{13}C NMR ($CDCl_3$) δ 42.0 ($\mathbf{C}H_2NH_2$), 58.6 ($\mathbf{C}H_2CCH$), 69.3, 70.5, 70.6, 70.7, 70.8, 73.7 (6 $O\mathbf{C}H_2$), 74.7 ($CH_2C\mathbf{C}H$), 79.8 ($CH_2\mathbf{C}CH$), the remaining signal was not detected and is believed to overlap with nearby peaks; M_r (+ESI) 232.1547 $[M+K]^+$ (calcd for $C_{11}H_{21}NO_4H^+$ 232.1549 $[M+K]^+$). Anal. ($C_{11}H_{21}NO_4$•0.35H_2O): C, H, N.

Tetramethylrhodamine-PEG-alkyne (40). Using Method D, 5-carboxytetramethylrhodamine (20 mg, 47 μmol), compound **65** (14 mg, 61 μmol), and DMTMM (17 mg, 61 μmol) in DMF (500 μL) gave **40** as a dark pink residue (10 mg, 33%) after purification by preparative TLC (5/95 to 15/85 MeOH/CH_2Cl_2): R_f = 0.25 (1/9 MeOH/CH_2Cl_2); ^1H NMR (CD_3OD) δ 2.85 (t, J = 2.4 Hz, $OCH_2CC\mathbf{H}$), 3.30 (s, 2 $N(C\mathbf{H_3})_2$), 3.60–3.80 (m, 3 $C\mathbf{H_2}OC\mathbf{H_2}$, $NHC\mathbf{H_2}$), 4.17 (d, J = 2.4 Hz, $C\mathbf{H_2}CCH$), 6.92–7.08 (m, 2 C(4)**H**, 2 C(2)**H**), 7.13–7.28 (m, 2 C(5)**H**), 7.41 (d, J = 8.7 Hz, C(9)**H**), 8.09 (d, J = 8.7 Hz, C(10)**H**),

8.60–8.75 (br s, C(12)**H**); ^{13}C NMR (CD_3OD) δ 41.0 (2 N(**C**H_3)$_2$), 41.3 (C(O)NH**C**H_2), 59.2 (**C**H_2CCH), 70.2, 70.7, 71.4, 71.5, 71.6, 71.7, 71.8 (7 O**C**H_2), 76.1 (CH_2C**C**H), 80.8 (CH_2**C**CH), 97.5, 115.0, 115.2, 129.9, 131.0, 132.7, 137.3, 158.9, 159.2, 162.3, 169.4 (tetramethylrhodamine), the remaining signals were not detected; M_r (+ESI) 644.2968 $[M+H]^+$ (calcd for $C_{36}H_{41}N_3O_8H^+$ 644.2972).

Table S1. Quantification of the (*R*)-**9**, (*S*)-**9** of the 62kDa using iTRAQ.

Identified Protein	Observed	Miss	Score	Peptide	Protein	R	S	Average	S.D.
Dihydropyrimidinase-related protein 2	580.2753	0	54	K.SAAEVIAQAR.K	CRMP2	1.14	1.00	-	-
	719.8425	0	53	R.MVIPGGIDVHTR.F	CRMP2	1.60	1.00	-	-
	609.6126	0	33	K.IVLEDGTLHVTEGSGR.Y	CRMP2	1.46	1.00	-	-
	1102.4961	0	82	R.ISVGSDADLVIWDPDSVK.T	CRMP2	1.27	1.00	-	-
	1219.9767	0	59	R.FQMPDQGMTSADDFFQGTK.A	CRMP2	1.35	1.00	-	-
	905.0775	1	47	K.AVVTGKMDENQFVAVTSTNAAK.V	CRMP2	1.20	1.00	-	-
	1015.4612	0	77	R.ILDLGITGPEGHVLSRPEEVEAEAVNR.S	CRMP2	1.43	1.00	1.35	0.16
	583.7814	0	40	R.MSVIWDK.A	CRMP2,3	1.40	1.00	-	-
	1319.056	0	62	K.IVNDDQSFYADIYMEDGLIK.Q	CRMP2,3	1.37	1.00	1.36	0.14
	806.4076	0	72	K.QIGENLIVPGGVK.T	CRMP1,2	1.88	1.00	-	-
	671.9577	0	35	K.MDENQFVAVTSTNAAK.V	CRMP1,2,3	1.21	1.00	1.39	0.21
Dihydropyrimidinase-related protein 1	572.8043	0	46	K.SAADIIALAR.K	CRMP1	1.33	1.00	-	-
	583.7839	0	40	R.MTVVWDK.A	CRMP1	1.43	1.00	1.38	-
	806.4076	0	72	K.QIGENLIVPGGVK.T	CRMP1,2	1.88	1.00	-	-
	671.9577	0	35	K.MDENQFVAVTSTNAAK.I	CRMP1,2,3	1.21	1.00	1.46	0.29
Tubulin alpha chain	923.4354	0	72	R.AVFVDLEPTVIDEVR.T	TBA	0.92	1.00	-	-

Table S2. Elemental Analysis of the Synthesized Compounds.

Compound No.	Formula	Calcd.					Found				
		C	H	N	S	I	C	H	N	S	I
(*R*)-**9**	$C_{16}H_{17}N_3O_3S$	57.99	5.17	12.68	9.68		58.04	5.18	12.47	9.61	
(*S*)-**9**	$C_{16}H_{17}N_3O_3S$	57.99	5.17	12.68	9.68		57.77	5.14	12.44	9.55	
(*R*)-**10**	$C_{17}H_{19}N_3O_3S{\cdot}0.2H_2O$	58.50	5.60	12.04	9.19		58.53	5.49	12.03	8.97	
(*S*)-**10**	$C_{17}H_{19}N_3O_3S{\cdot}0.16CH_3OH$	58.74	5.67	11.95	9.12		59.01	5.67	12.24	8.73	
(*R*)-**11**	$C_{15}H_{18}N_6O_3S$	49.71	5.01	23.19	8.85		49.55	4.91	23.13	8.63	
(*S*)-**11**	$C_{15}H_{18}N_6O_3S$	49.71	5.01	23.19	8.85		49.86	5.07	23.10	8.75	
(*R*)-**17**	$C_9H_{13}NO_4$	54.26	6.58	7.03			54.30	6.66	6.89		
(*S*)-**17**	$C_9H_{13}NO_4$	54.26	6.58	7.03			54.05	6.55	6.95		
(*R*)-**19**	$C_8H_{11}NO_4{\cdot}0.14H_2O$	51.18	6.06	7.46			51.15	6.13	7.27		
(*S*)-**19**	$C_8H_{11}NO_4{\cdot}0.25H_2O$	50.66	6.11	7.38			50.76	6.29	7.10		
(*R*)-**20**	$C_7H_{12}N_4O_4{\cdot}0.07EtOAc$	39.30	5.69	25.23			39.30	5.73	25.33		
(*S*)-**20**	$C_7H_{12}N_4O_4{\cdot}0.07EtOAc$	39.30	5.69	25.23			39.28	5.71	25.37		
(*R*)-**23**	$C_{15}H_{19}N_3O_3$	62.27	6.62	14.52			62.07	6.62	14.30		
(*S*)-**23**	$C_{15}H_{19}N_3O_3$	62.27	6.62	14.52			62.06	6.70	14.30		
(*R*)-**27**	$C_{15}H_{19}N_3O_3S{\cdot}0.2EtOAc$	55.99	6.10	12.50	9.54		55.68	5.96	12.72	9.26	
(*S*)-**27**	$C_{15}H_{19}N_3O_3S{\cdot}0.1EtOAc$	56.02	6.04	12.73	9.71		55.96	5.81	12.73	9.51	
(*R*)-**28**	$C_{15}H_{18}N_2O_3$	65.68	6.61	10.21			65.72	6.62	10.06		
(*S*)-**28**	$C_{15}H_{18}N_2O_3$	65.68	6.61	10.21			65.55	6.61	10.07		
(*R*)-**29**	$C_{15}H_{18}N_2O_3{\cdot}0.5H_2O$	65.68	6.61	10.21			65.39	6.58	10.08		
(*S*)-**29**	$C_{15}H_{18}N_2O_3{\cdot}0.25H_2O$	64.62	6.69	10.05			64.60	6.57	9.99		
(*R*)-**30**	$C_{14}H_{19}N_5O_3$	55.07	6.27	22.94			54.85	6.27	22.94		
(*S*)-**30**	$C_{14}H_{19}N_5O_3$	55.07	6.27	22.94			55.16	6.28	22.91		
(*R*)-**38**	$C_{18}H_{25}N_5O_4$	57.59	6.71	18.65			57.34	6.72	18.49		
(*R*)-**44**	$C_{10}H_{12}N_2O{\cdot}0.1H_2O$	67.47	6.91	15.74			67.74	6.92	15.63		
(*S*)-**44**	$C_{10}H_{12}N_2O$	68.16	6.86	15.90			68.40	7.03	16.05		
(*R*)-**45**	$C_{12}H_{13}N_2O_2$	66.04	6.47	12.84			65.91	6.45	12.75		
(*S*)-**45**	$C_{12}H_{13}N_2O_2$	66.04	6.47	12.84			66.15	6.56	12.72		
(*R*)-**46**	$C_{22}H_{27}N_3O_5{\cdot}0.33H_2O$	62.99	6.65	10.02			62.74	6.55	10.01		
(*S*)-**46**	$C_{22}H_{27}N_3O_5{\cdot}0.25H_2O$	63.22	6.63	10.05			63.16	6.56	10.21		
(*R*)-**52**	$C_{15}H_{21}IN_2O_4$	42.87	5.04	6.67		30.20	43.13	5.14	6.71		29.96
(*S*)-**52**	$C_{15}H_{21}IN_2O_4$	42.87	5.04	6.67		30.20	43.08	5.10	6.62		29.94
(*R*)-**53**	$C_{16}H_{23}IN_2O_4$	44.25	5.34	6.45		29.22	44.51	5.34	6.41		28.99
(*S*)-**53**	$C_{16}H_{23}IN_2O_4$	44.25	5.34	6.45		29.22	44.54	5.38	6.35		28.92
(*R*)-**54**	$C_{13}H_{17}IN_2O_3$	41.51	4.55	7.45		33.73	41.70	4.49	7.39		33.69
(*S*)-**54**	$C_{13}H_{17}IN_2O_3$	41.51	4.55	7.45		33.73	41.37	4.52	7.37		33.47
(*R*)-**55**	$C_{18}H_{26}N_2O_3Si$	62.39	7.56	8.08			62.41	7.56	7.99		
(*S*)-**55**	$C_{18}H_{26}N_2O_3Si$	62.39	7.56	8.08			62.10	7.67	7.93		
65	$C_{11}H_{21}NO_4{\cdot}0.35H_2O$	55.60	9.21	5.89			55.34	8.95	6.26		

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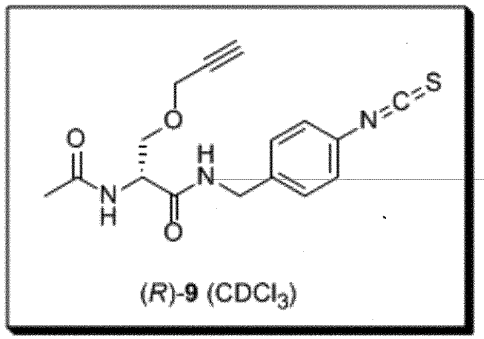
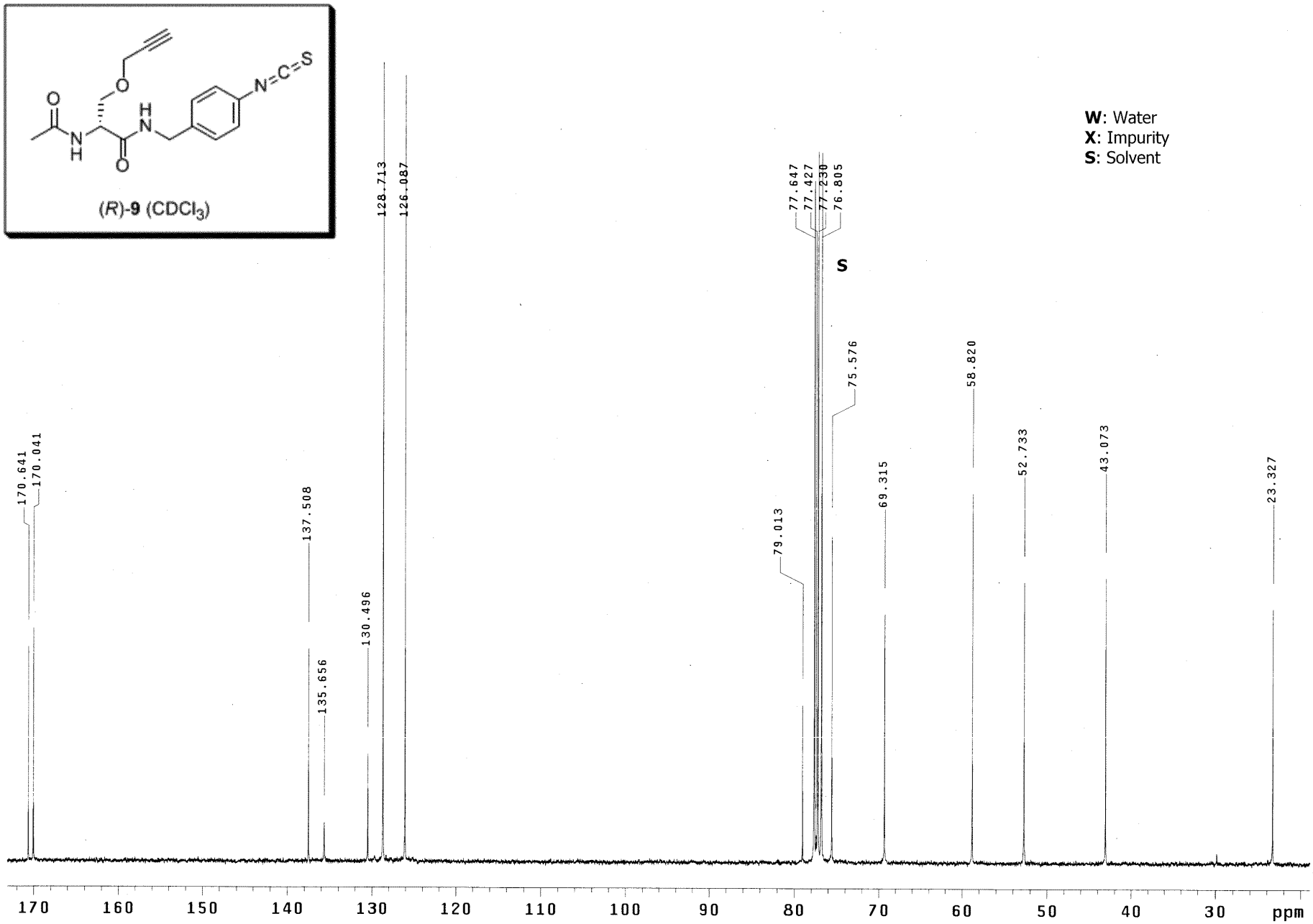
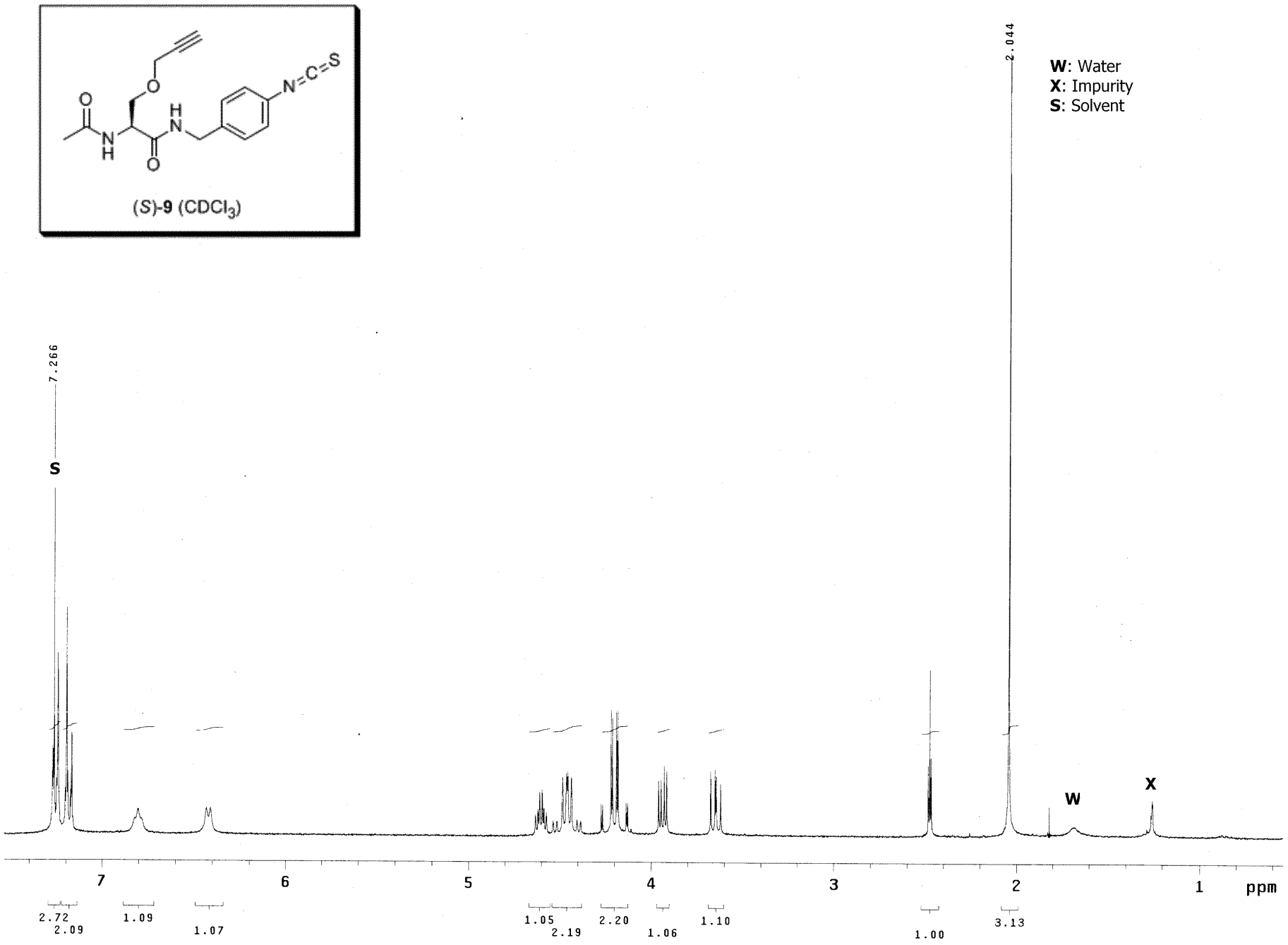
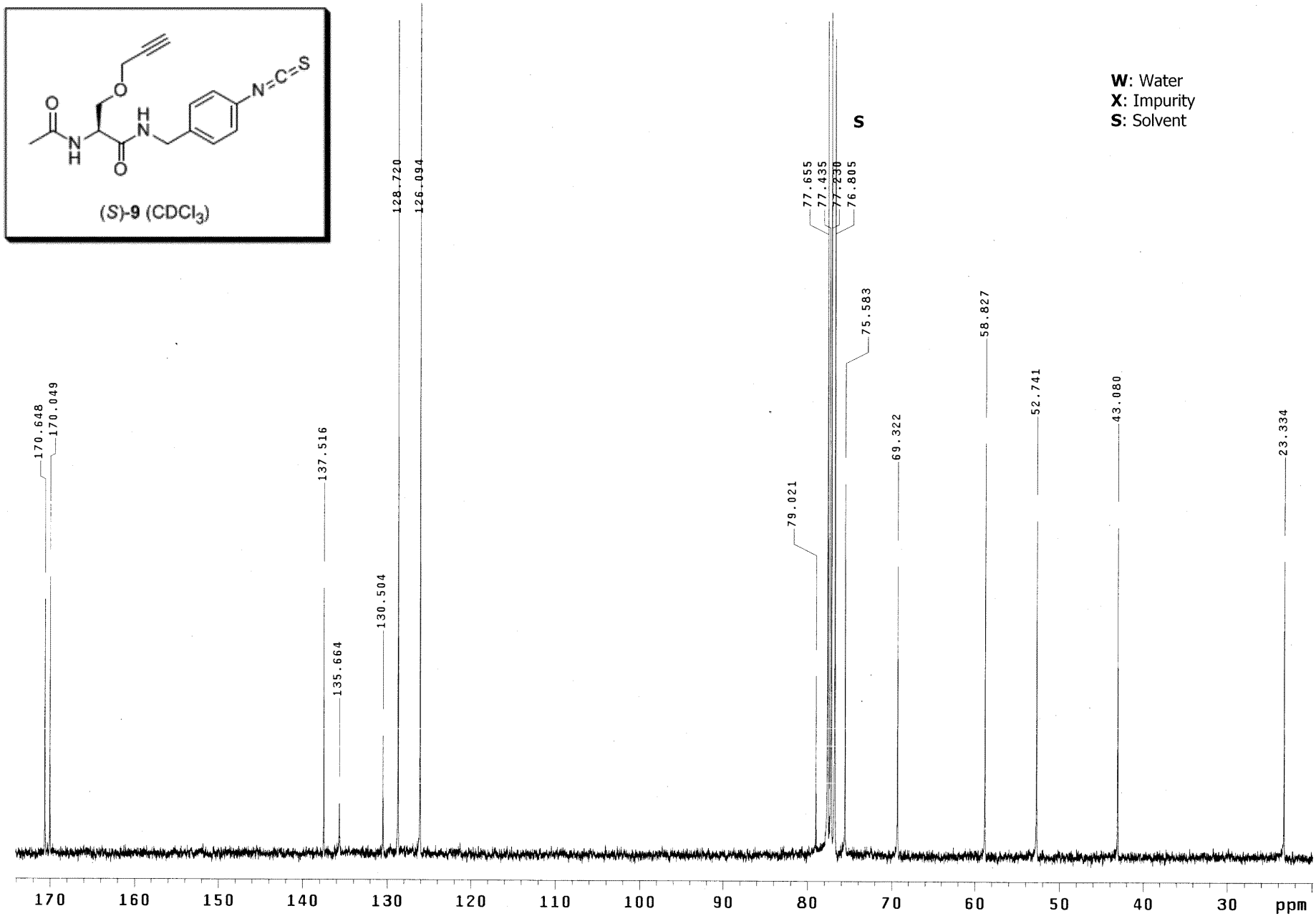
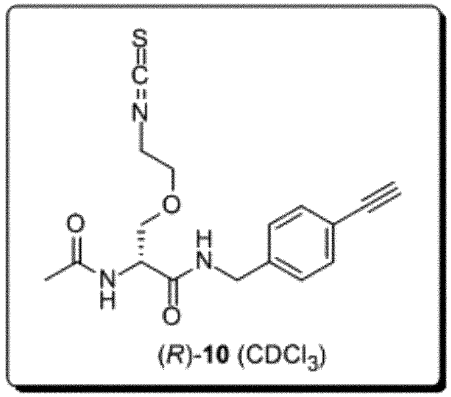


W: Water
X: Impurity
S: Solvent

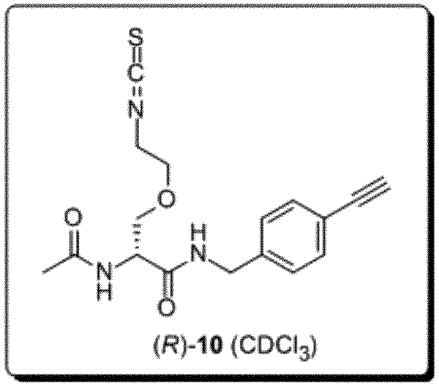

(R)-9 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
170.641
170.041
137.508
135.656
130.496
128.713
126.087
79.013
77.647
77.427
77.230
76.805
75.576
69.315
58.820
52.733
43.073
23.327
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm


(S)-9 (CDCl3)
W: Water
X: Impurity
S: Solvent
7.266
2.044
S
W
X
7
6
5
4
3
2
1
ppm
2.72
2.09
1.09
1.07
1.05
2.19
2.20
1.06
1.10
1.00
3.13

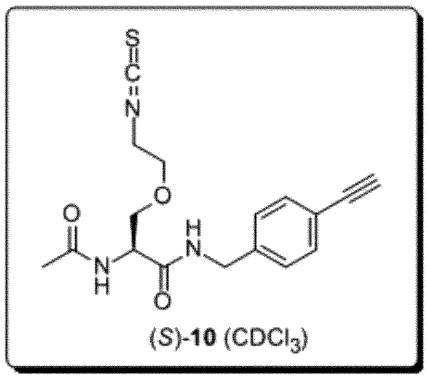

(S)-9 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
170.648
170.049
137.516
135.664
130.504
128.720
126.094
79.021
77.655
77.435
77.230
76.805
75.583
69.322
58.827
52.741
43.080
23.334
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm



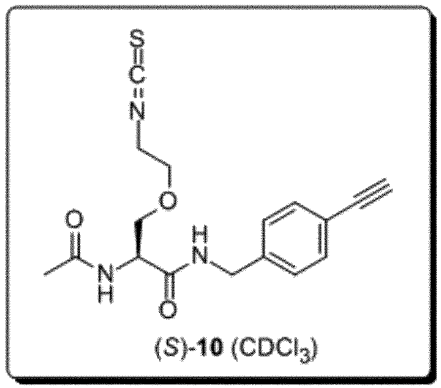
W: Water
X: Impurity
S: Solvent


(R)-10 (CDCl3)

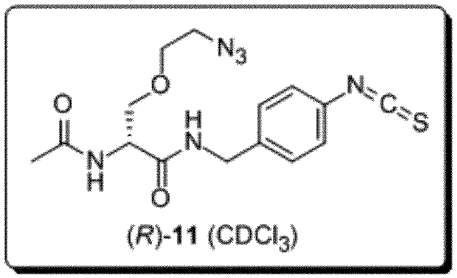
S
W: Water
X: Impurity
S: Solvent
170.627
169.717
138.769
132.433
127.500
121.300
83.333
77.444
77.361
77.019
76.594
70.015
69.316
52.735
45.412
43.332
23.260
0.000
160
140
120
100
80
60
40
20
ppm


(S)-10 (CDCl3)

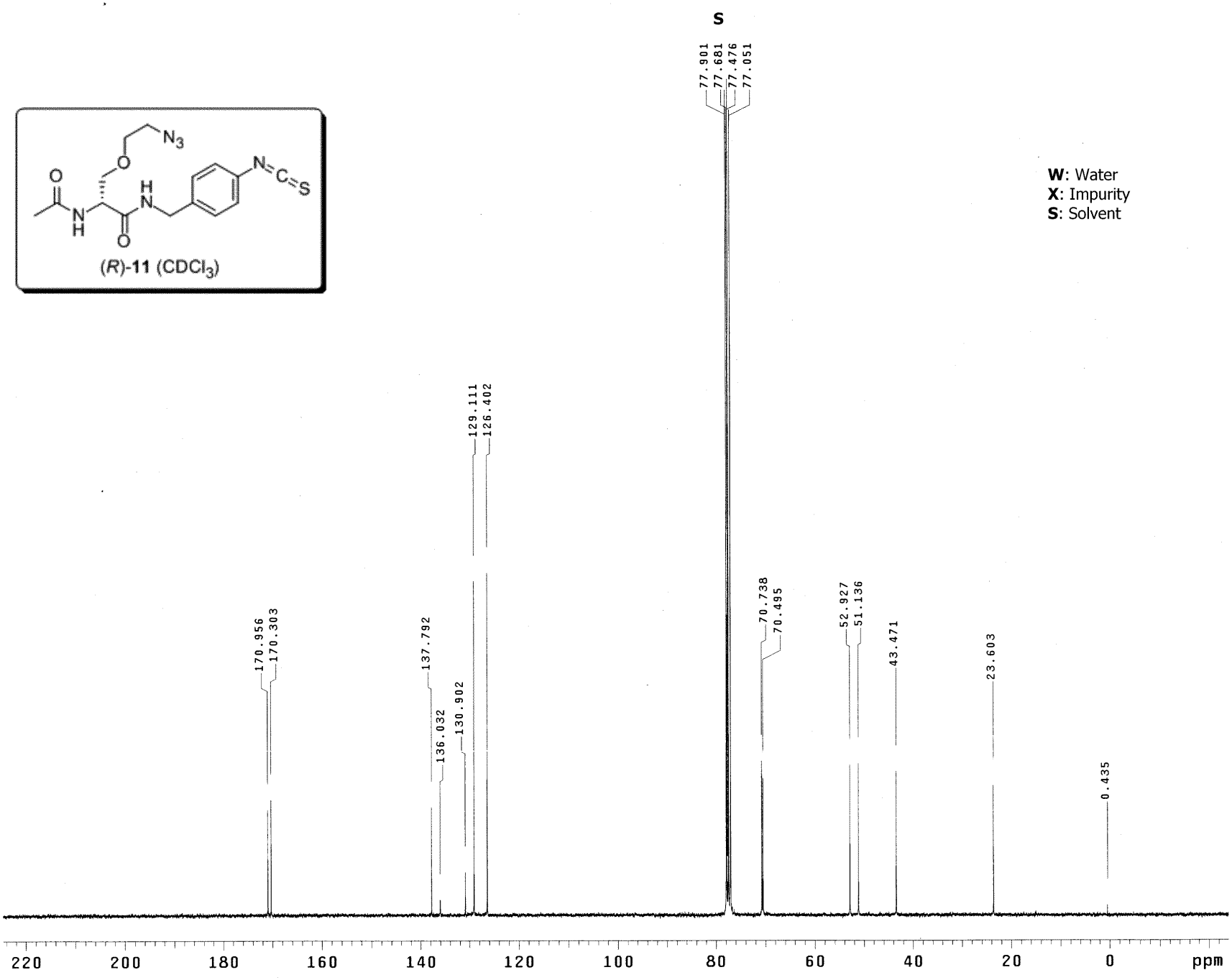
W: Water
X: Impurity
S: Solvent
S
S
X
S
7.472
7.445
7.267
7.260
7.231
6.863
6.562
6.539
4.639
4.627
4.616
4.604
4.594
4.581
4.510
4.498
4.490
4.478
4.024
4.011
3.992
3.981
3.761
3.742
3.714
3.708
3.691
3.659
3.629
3.608
3.599
3.591
3.577
3.571
3.553
3.539
3.073
2.072
2.038
1.055
0.002
0.000
2.02
2.05
0.91
0.96
1.00
1.98
0.98
5.27
0.87
3.02
8
7
6
5
4
3
2
1
ppm

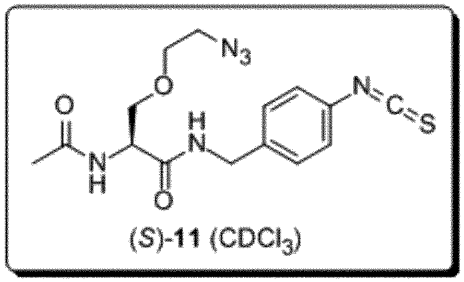


W: Water
X: Impurity
S: Solvent



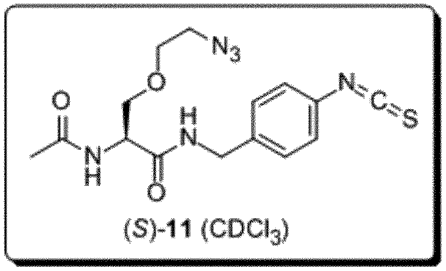
W: Water
X: Impurity
S: Solvent


(R)-11 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
77.901
77.681
77.476
77.051
170.956
170.303
137.792
136.032
130.902
129.111
126.402
70.738
70.495
52.927
51.136
43.471
23.603
0.435
220
200
180
160
140
120
100
80
60
40
20
0
ppm

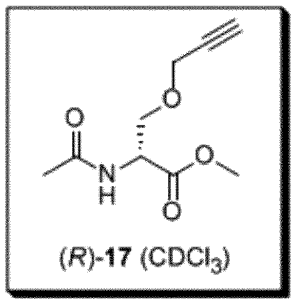


(*S*)-**11** ($CDCl_3$)

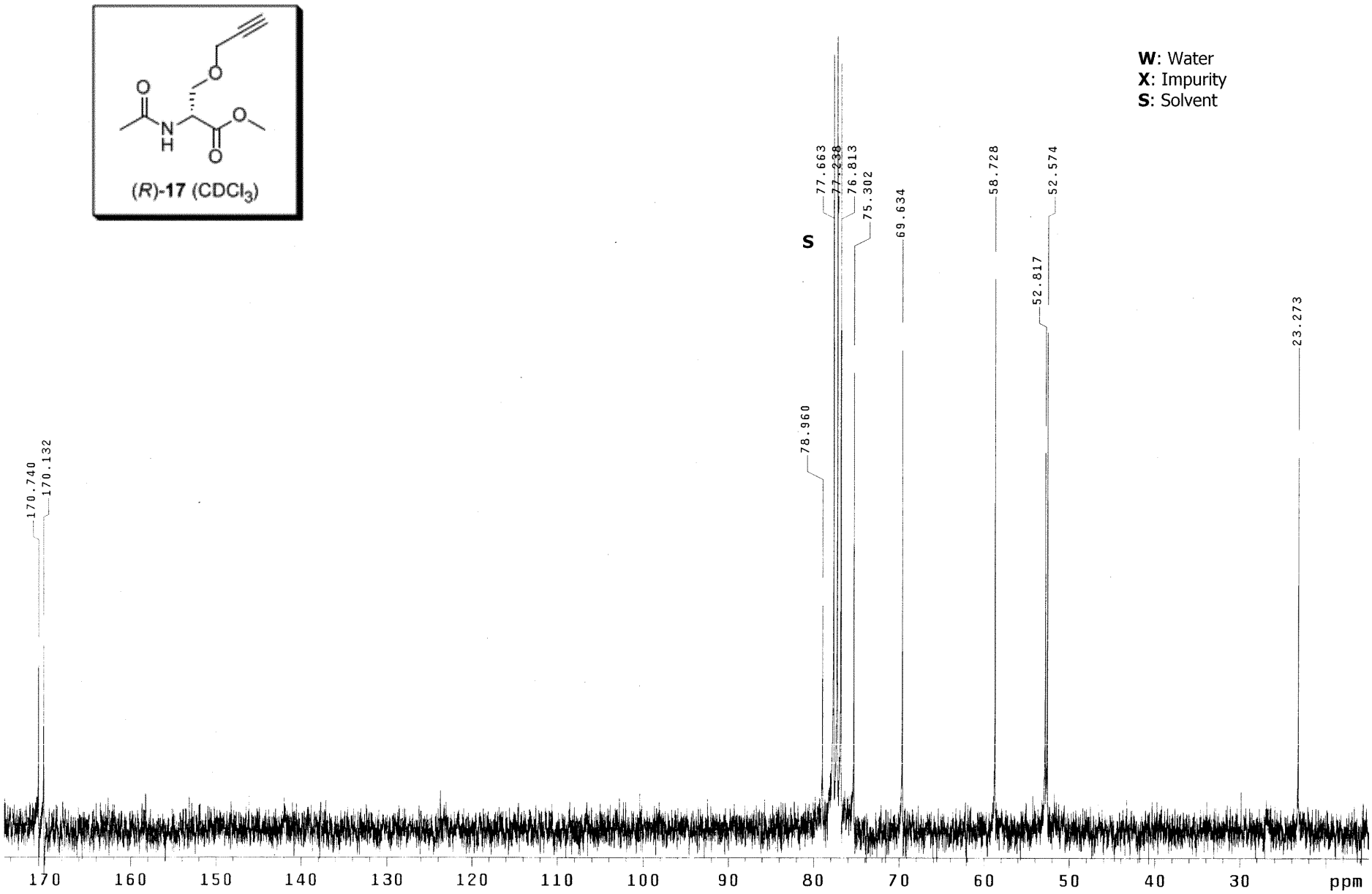
W: Water
X: Impurity
S: Solvent

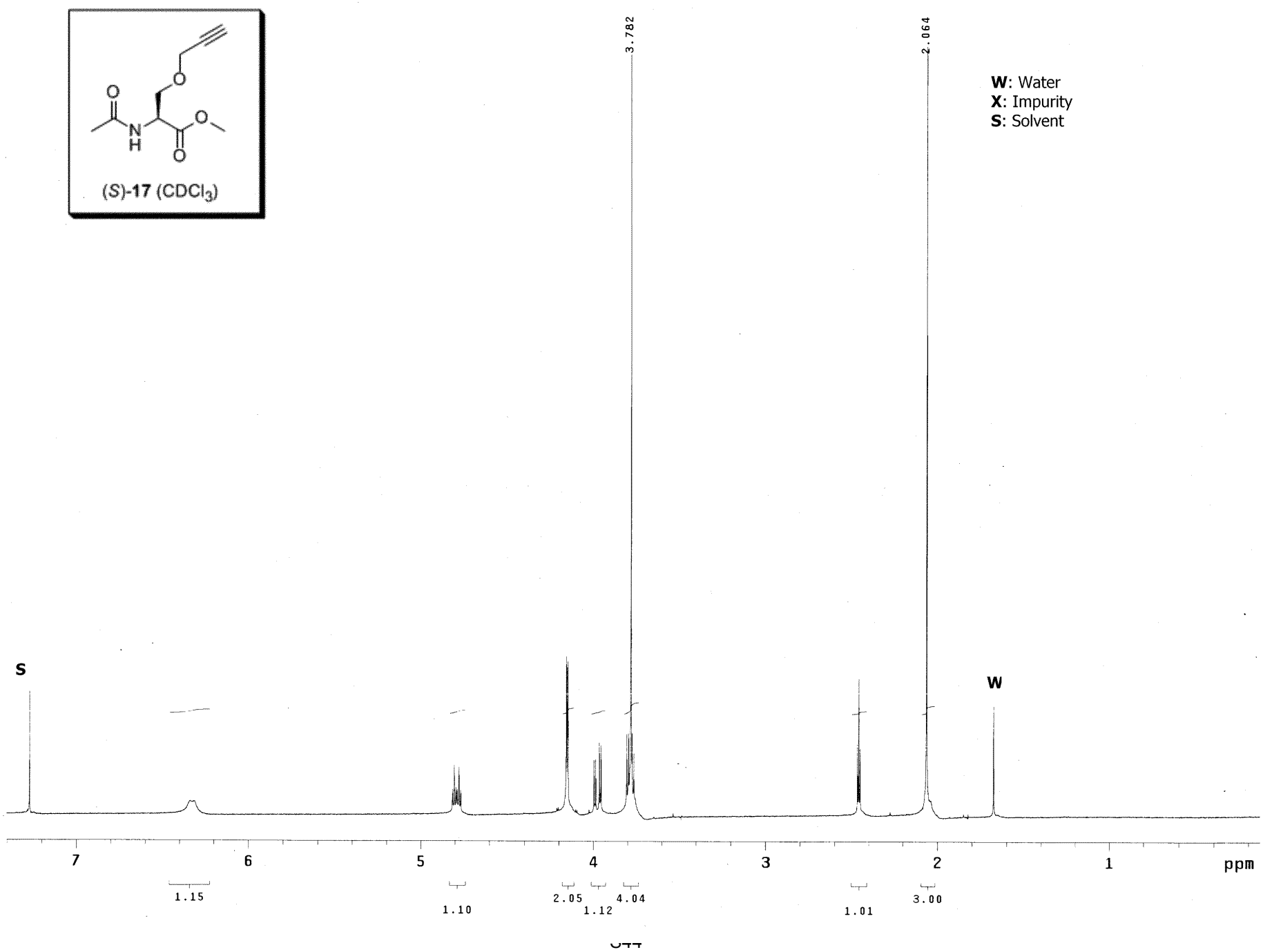

(S)-11 (CDCl3)

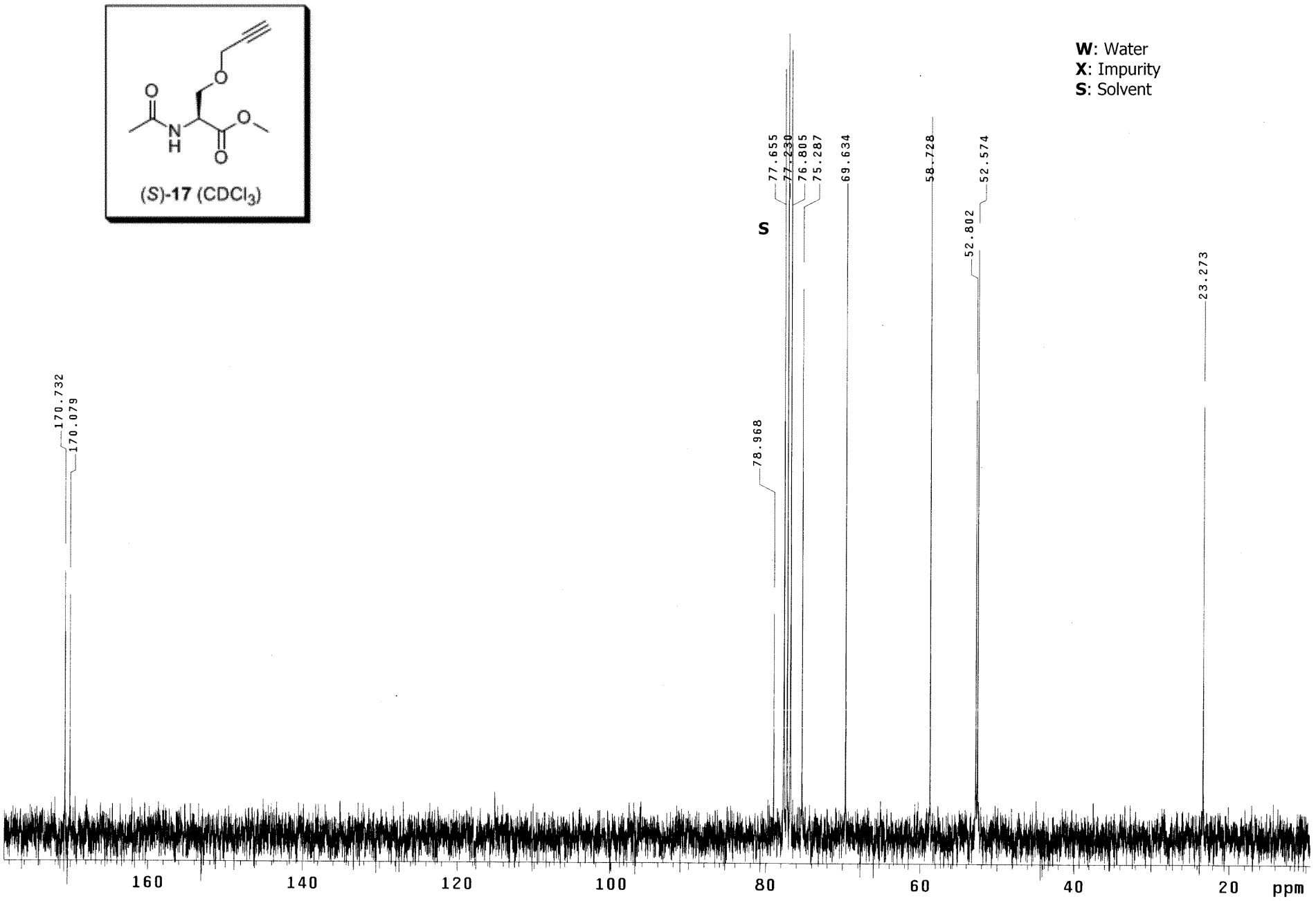
S
128.842
126.125
77.655
77.230
76.805
70.476
70.301
52.688
50.859
43.187
23.327
170.694
170.041
137.554
135.763
130.610
W: Water
X: Impurity
S: Solvent
200
180
160
140
120
100
80
60
40
20
ppm

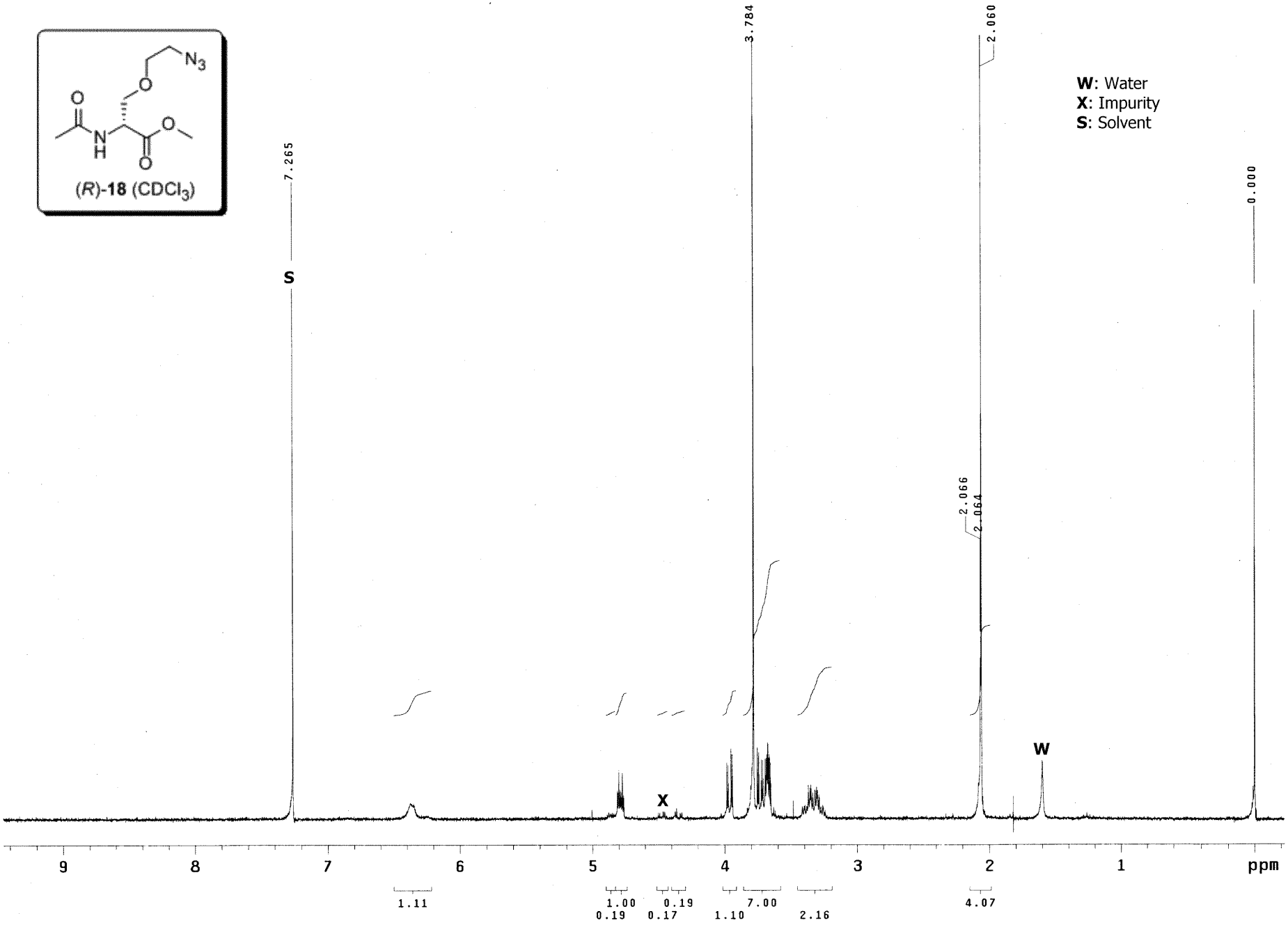

(R)-17 (CDCl3)

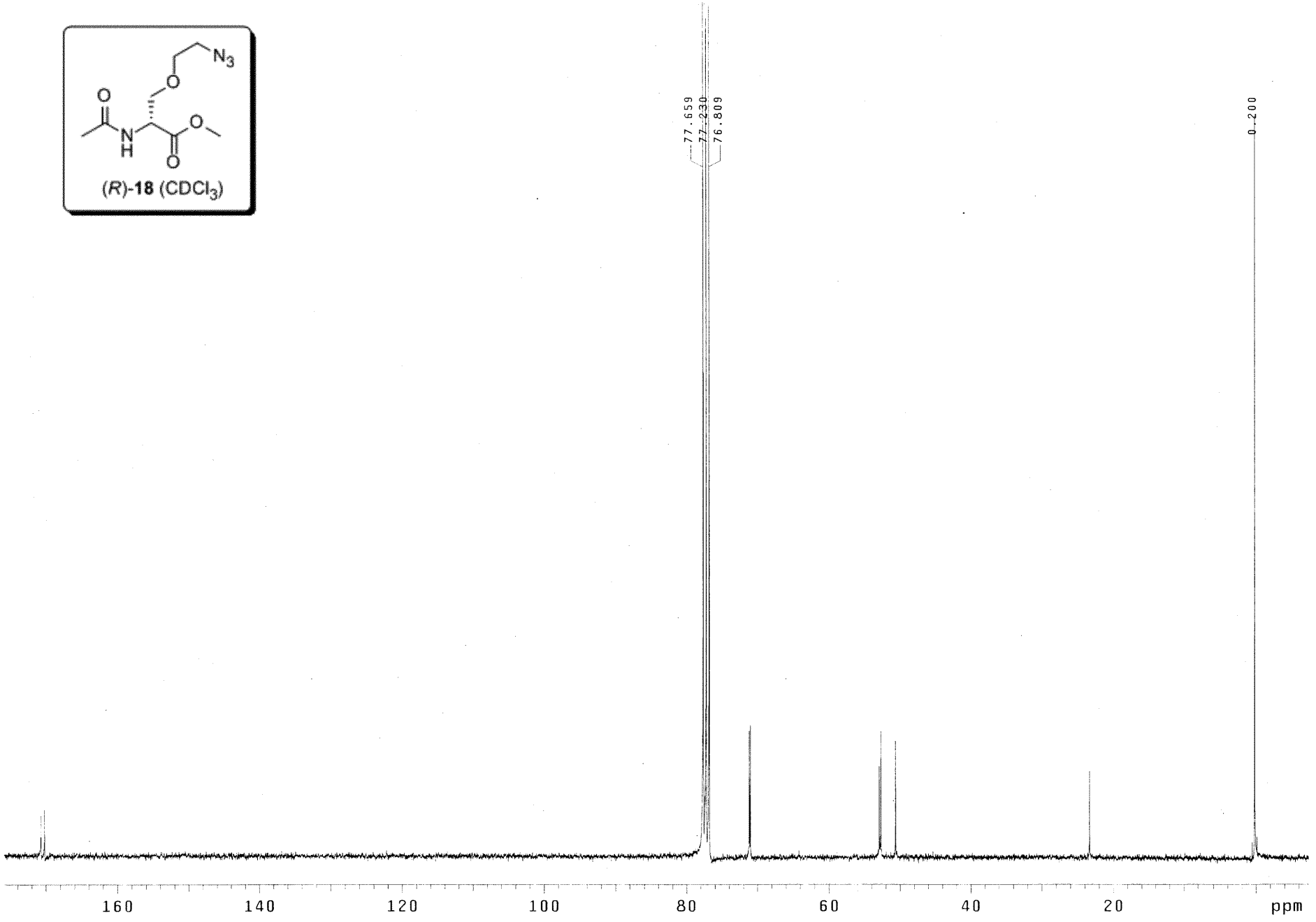
3.782
2.064
W: Water
X: Impurity
S: Solvent
S
W
7
6
5
4
3
2
1
ppm
0.89
0.93
1.95
1.13
4.08
0.92
3.00

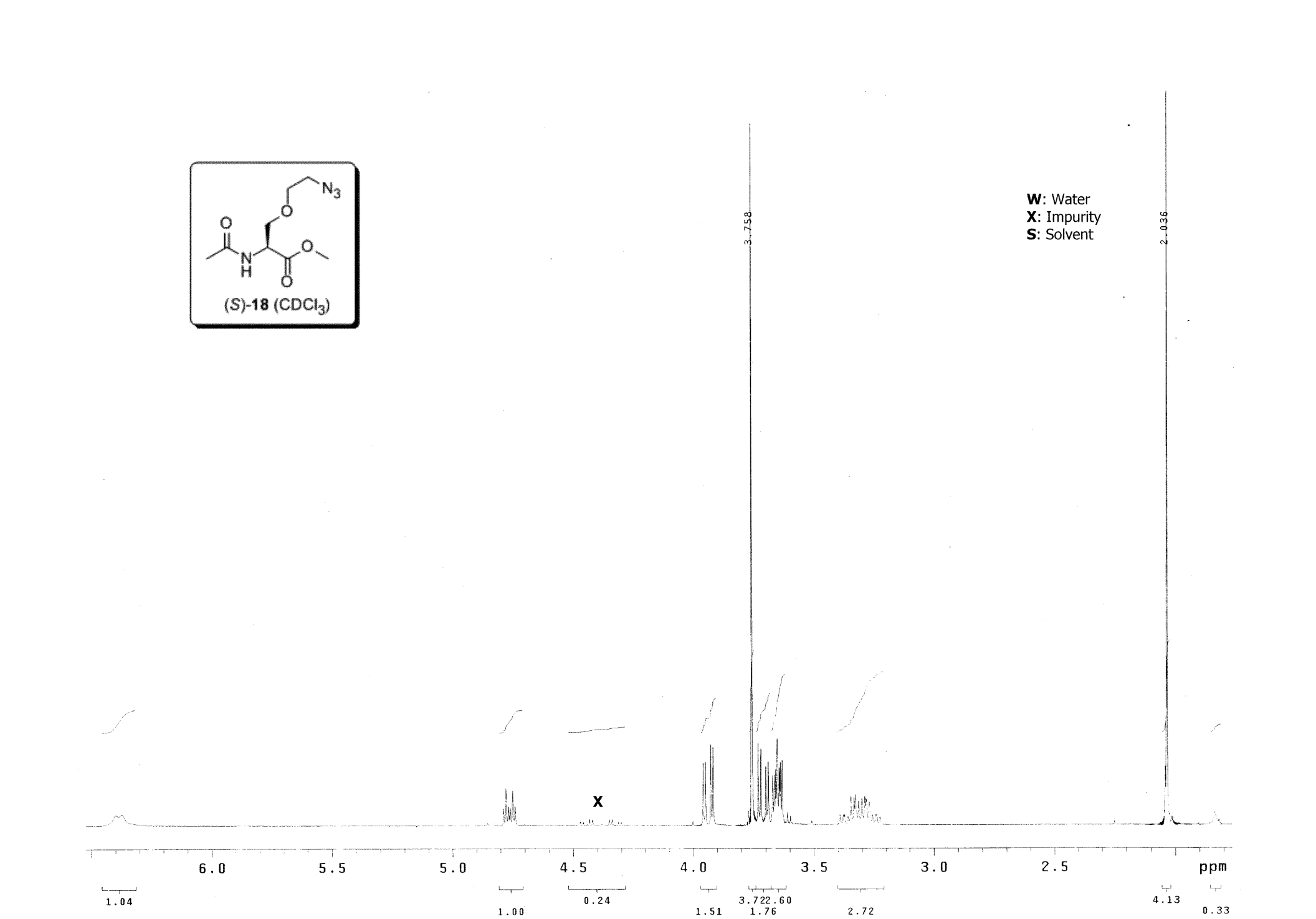

(R)-17 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
170.740
170.132
78.960
77.663
77.238
76.813
75.302
69.634
58.728
52.817
52.574
23.273
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

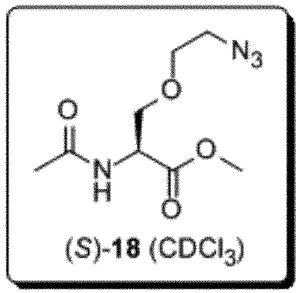

(S)-17 (CDCl3)
3.782
2.064
W: Water
X: Impurity
S: Solvent
S
W
7
6
5
4
3
2
1
ppm
1.15
1.10
2.05
1.12
4.04
1.01
3.00


(S)-17 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
170.732
170.079
78.968
77.655
77.230
76.805
75.287
69.634
58.728
52.802
52.574
23.273
160
140
120
100
80
60
40
20
ppm


(R)-18 (CDCl3)
W: Water
X: Impurity
S: Solvent
7.265
3.784
2.060
2.066
2.064
0.000
S
X
W
9
8
7
6
5
4
3
2
1
ppm
1.11
1.00
0.19
0.19
0.17
7.00
1.10
2.16
4.07


(R)-18 (CDCl3)
77.659
77.230
76.809
0.200
160
140
120
100
80
60
40
20
ppm

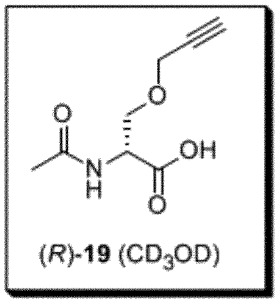

(S)-18 (CDCl3)
W: Water
X: Impurity
S: Solvent
3.758
2.036
X
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.04
1.00
0.24
1.51
3.72
2.60
1.76
2.72
4.13
0.33



W: Water
X: Impurity
S: Solvent

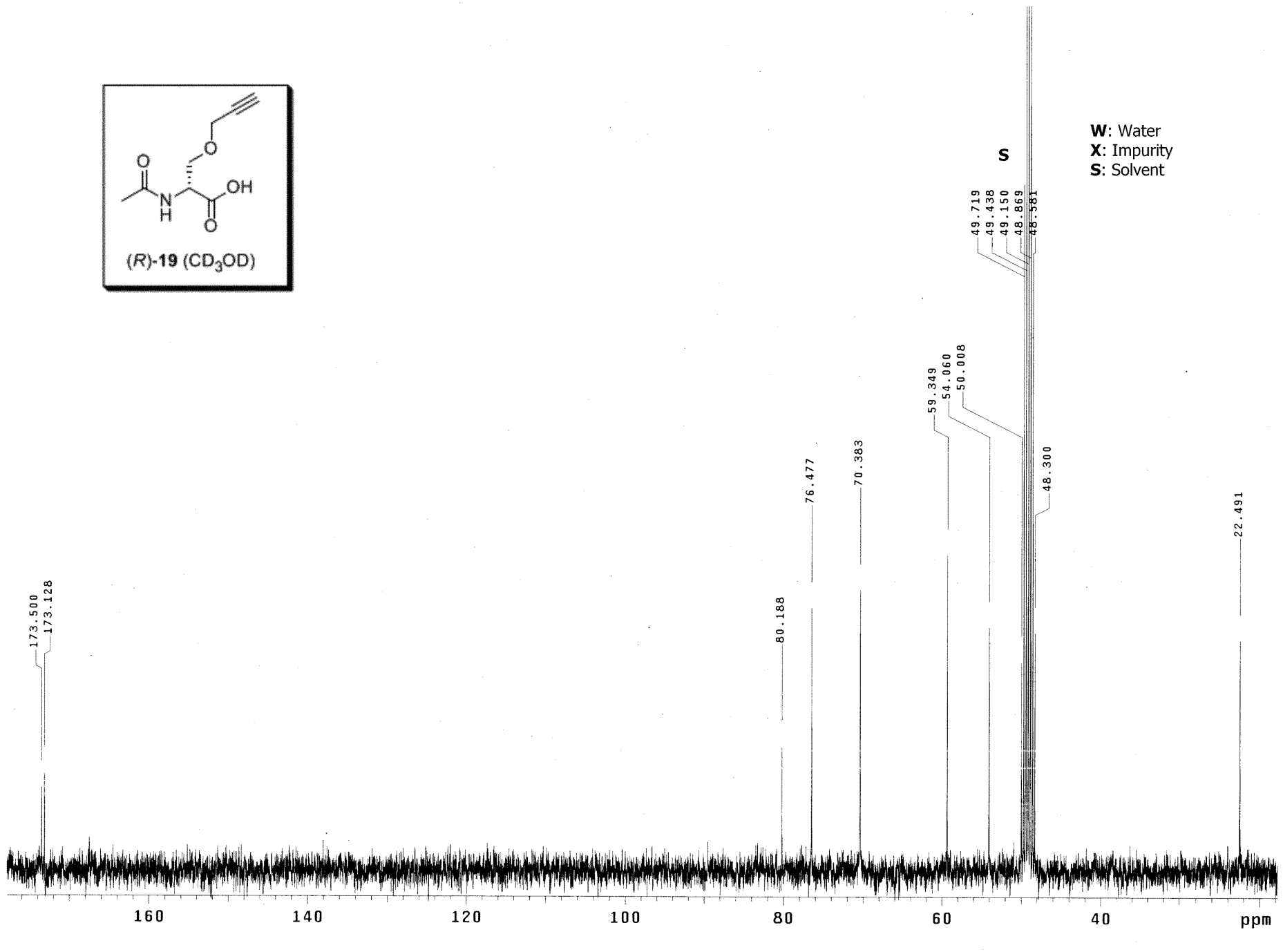
77.655
77.230
76.805
71.007
70.825
52.771
52.574
50.502
23.144
170.580
170.148

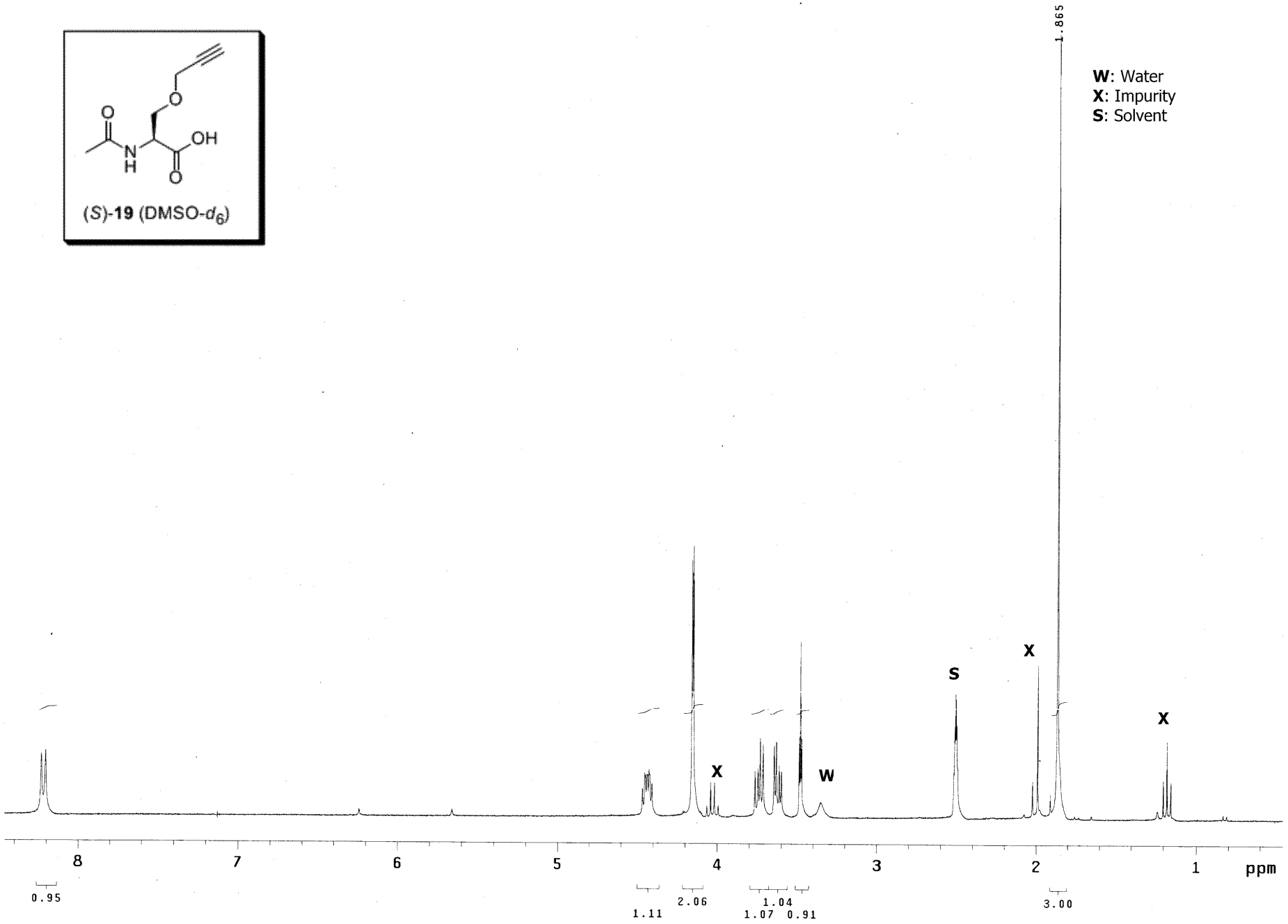
200 180 160 140 120 100 80 60 40 20 ppm

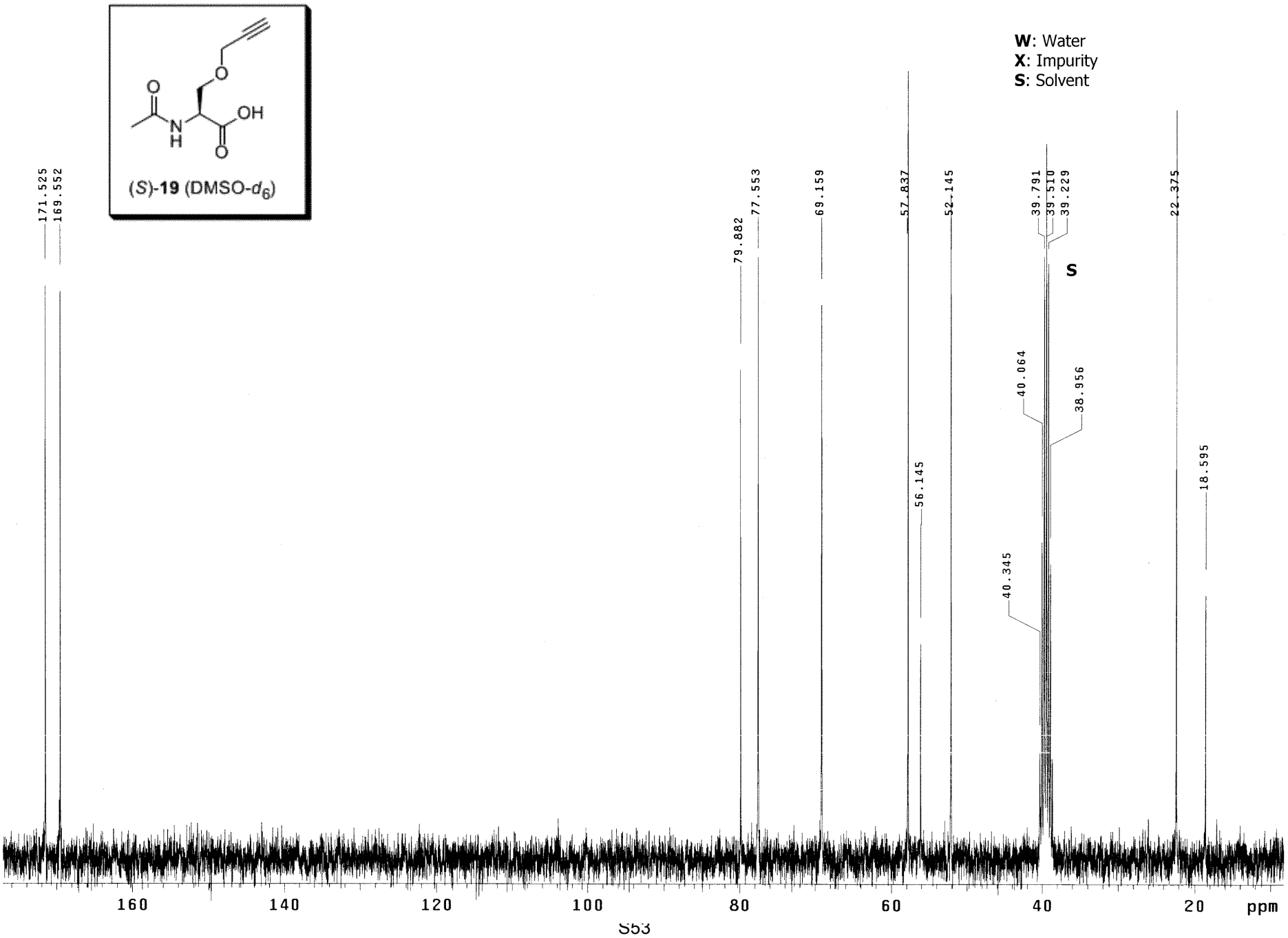


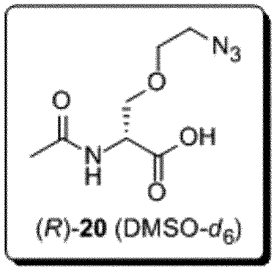
(*R*)-**19** (CD_3OD)

W: Water
X: Impurity
S: Solvent


(R)-19 (CD3OD)
W: Water
X: Impurity
S: Solvent
S
49.719
49.438
49.150
48.869
48.581
59.349
54.060
50.008
48.300
76.477
70.383
80.188
22.491
173.500
173.128
160
140
120
100
80
60
40
ppm


(S)-19 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
1.865
X
S
X
X
W
8
7
6
5
4
3
2
1
ppm
0.95
1.11
2.06
1.04
1.07
0.91
3.00

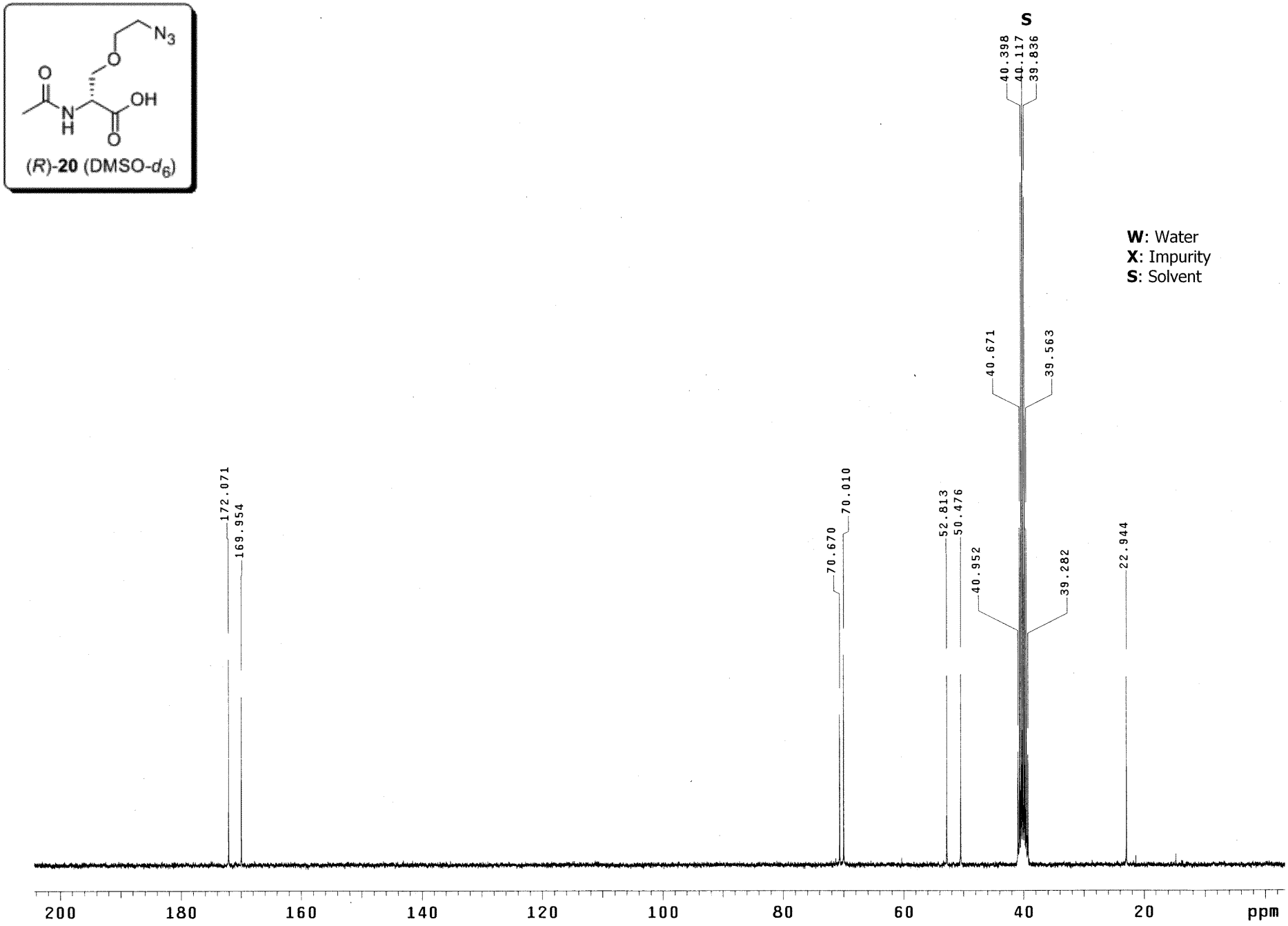

(S)-19 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
171.525
169.552
79.882
77.553
69.159
57.837
56.145
52.145
40.345
40.064
39.791
39.510
39.229
38.956
22.375
18.595
S
160
140
120
100
80
60
40
20
ppm

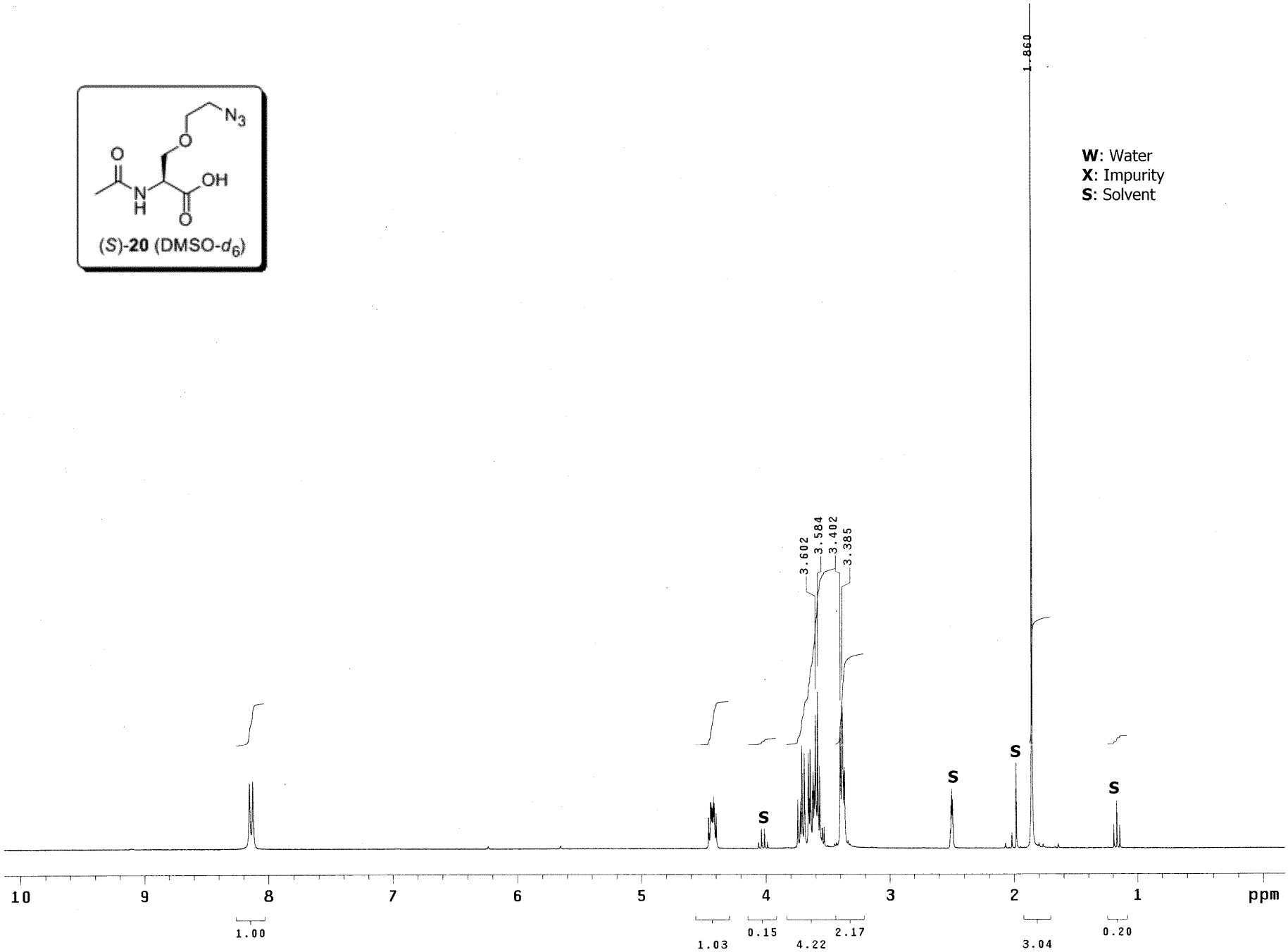


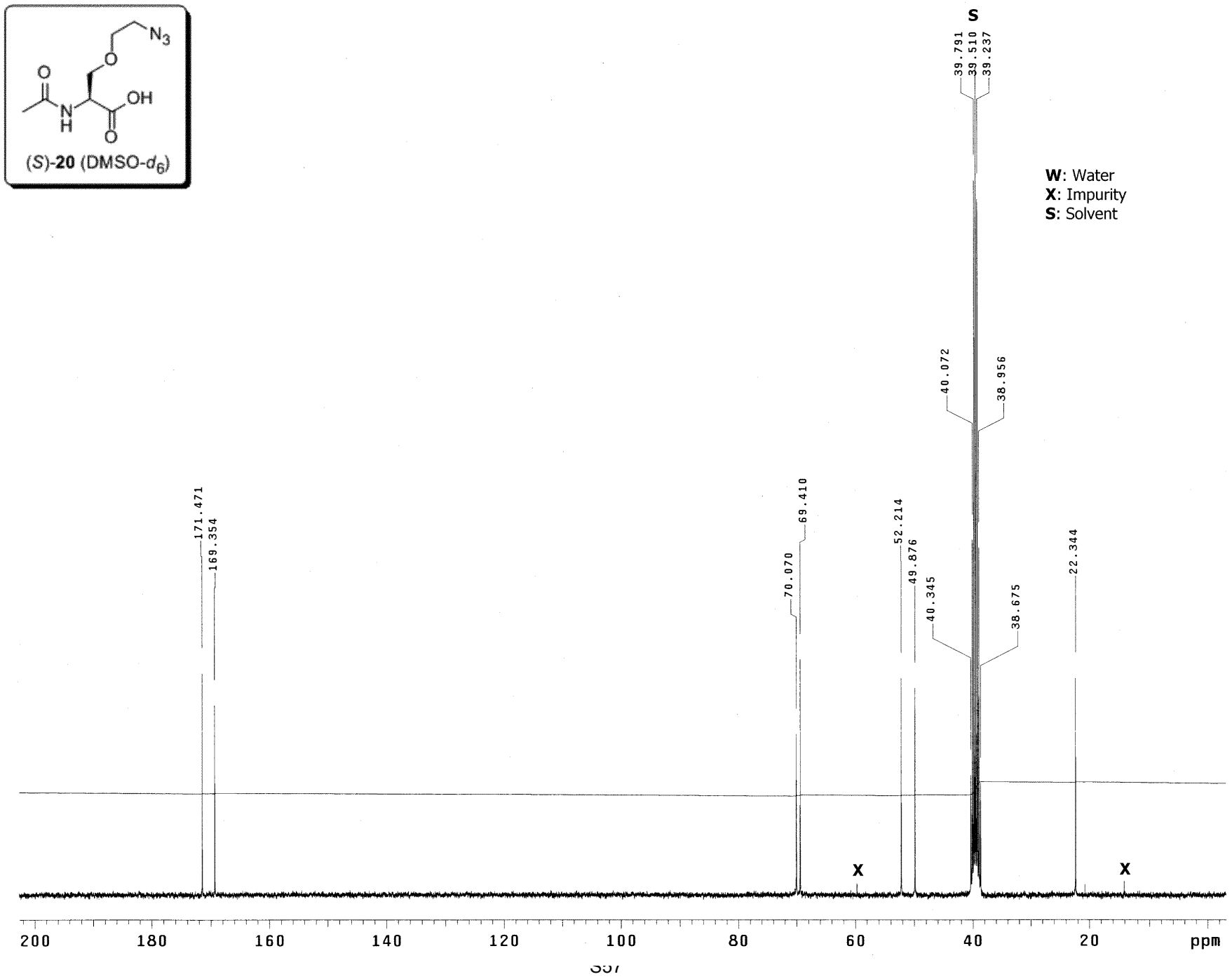
(*R*)-**20** (DMSO-d_6)

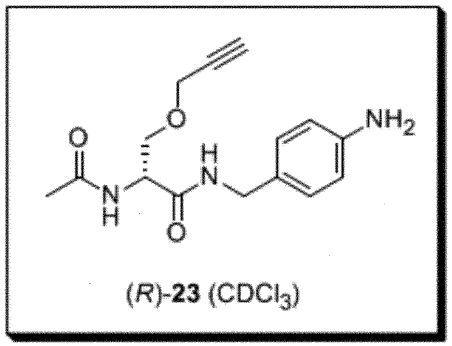
W: Water
X: Impurity
S: Solvent

1.860
3.602
3.584
3.402
3.386
S
S
S
S
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.03
0.15
4.12
2.14
0.21
2.97
0.21

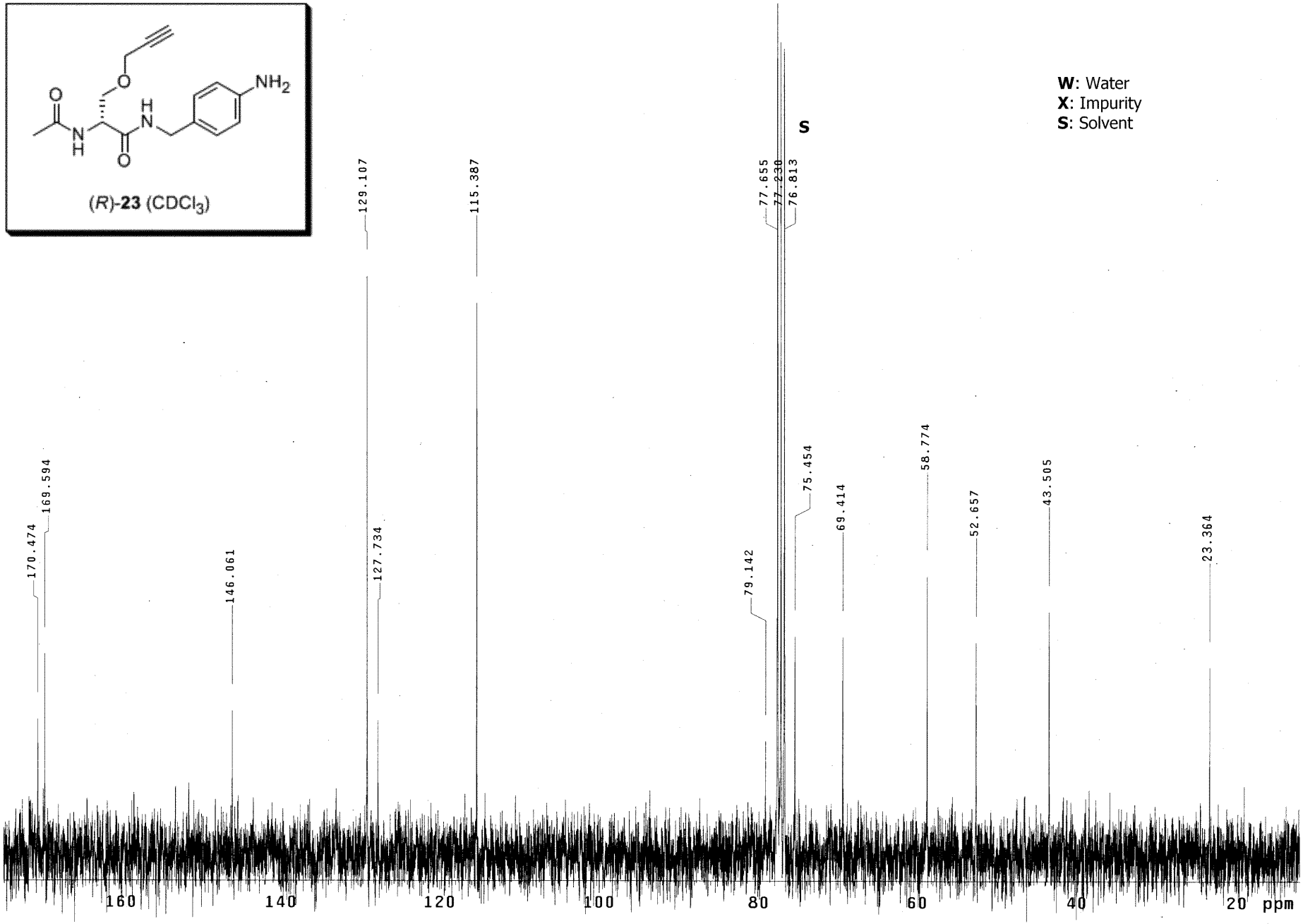

(R)-20 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
S
40.398
40.117
39.836
40.671
39.563
172.071
169.954
70.670
70.010
52.813
50.476
40.952
39.282
22.944
200
180
160
140
120
100
80
60
40
20
ppm

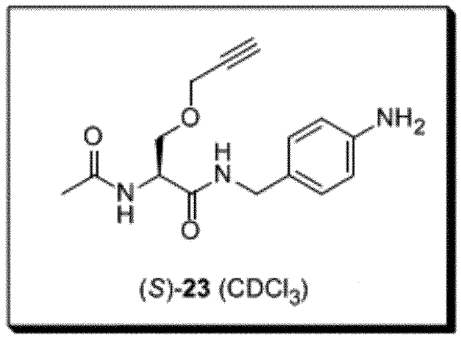

(S)-20 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
1.860
3.602
3.584
3.402
3.385
S
S
S
S
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.03
0.15
4.22
2.17
3.04
0.20


(S)-20 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
S
39.791
39.510
39.237
40.072
38.956
171.471
169.354
70.070
69.410
52.214
49.876
40.345
38.675
22.344
X
X
200
180
160
140
120
100
80
60
40
20
ppm



W: Water
X: Impurity
S: Solvent


(R)-23 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
170.474
169.594
146.061
129.107
127.734
115.387
79.142
77.655
77.230
76.813
75.454
69.414
58.774
52.657
43.505
23.364
160
140
120
100
80
60
40
20
ppm



(*S*)-**23** ($CDCl_3$)

W: Water
X: Impurity
S: Solvent

7.264

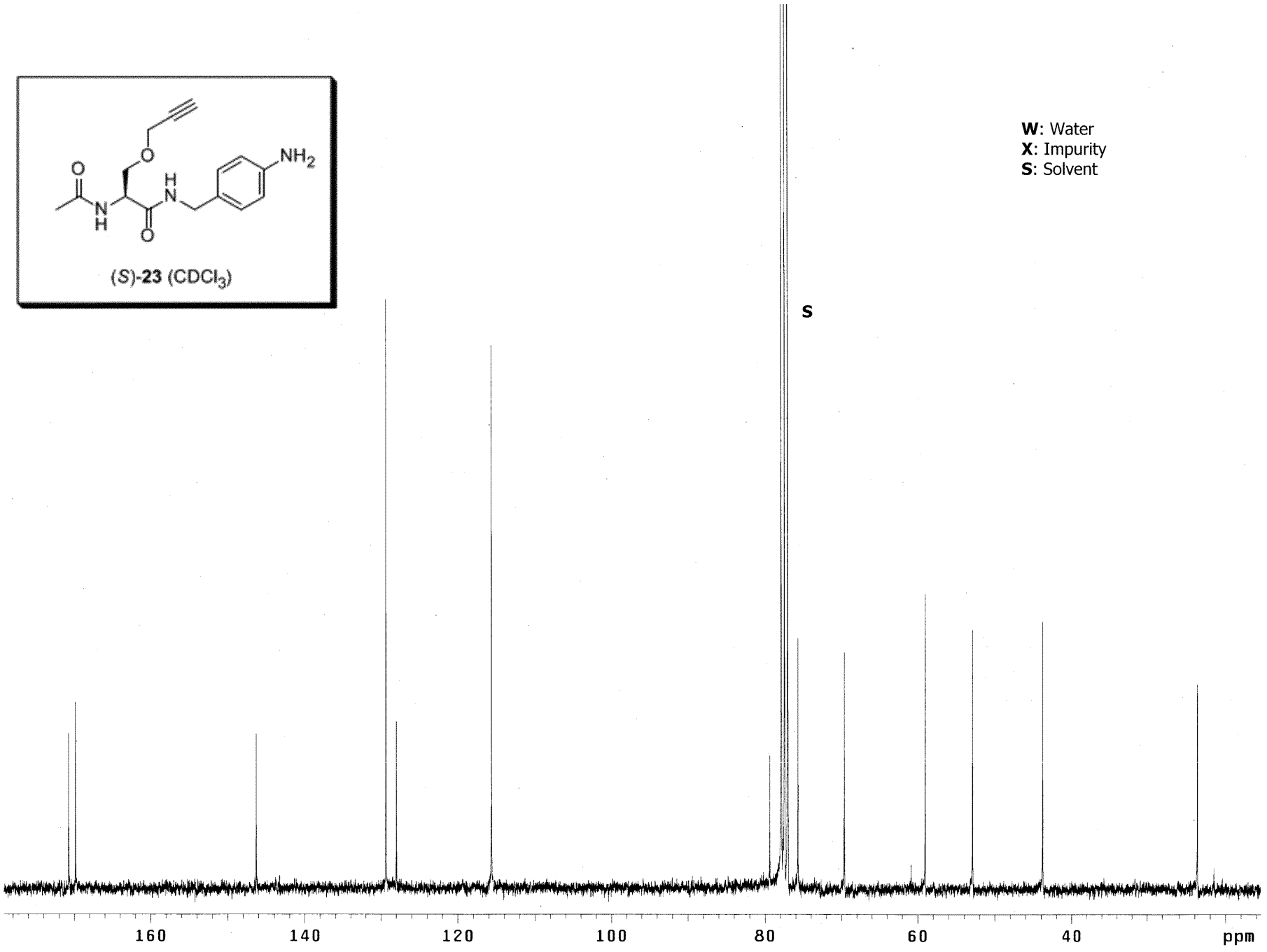
2.032

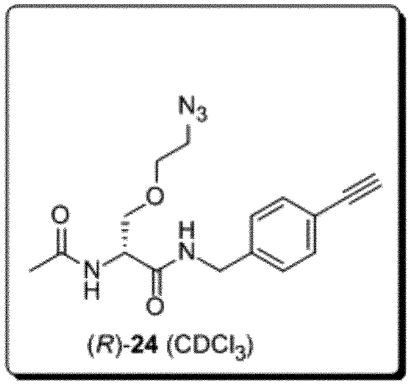
S

X

7 6 5 4 3 2 1 ppm

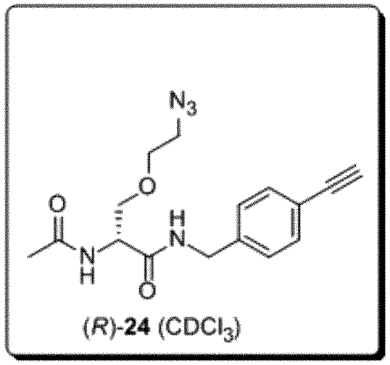
2.03 0.86 2.16 0.79 1.18 2.10 2.14 1.09 2.86 1.00 2.98


(S)-23 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
160
140
120
100
80
60
40
ppm



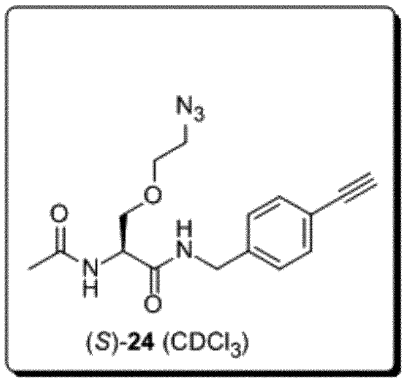
(*R*)-**24** ($CDCl_3$)

W: Water
X: Impurity
S: Solvent

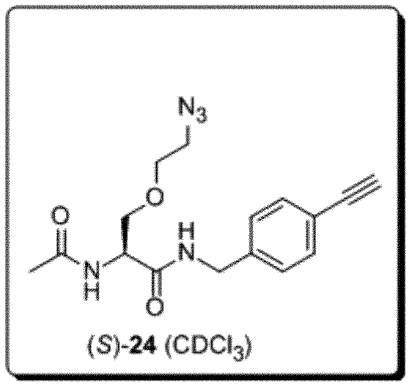


(*R*)-**24** ($CDCl_3$)

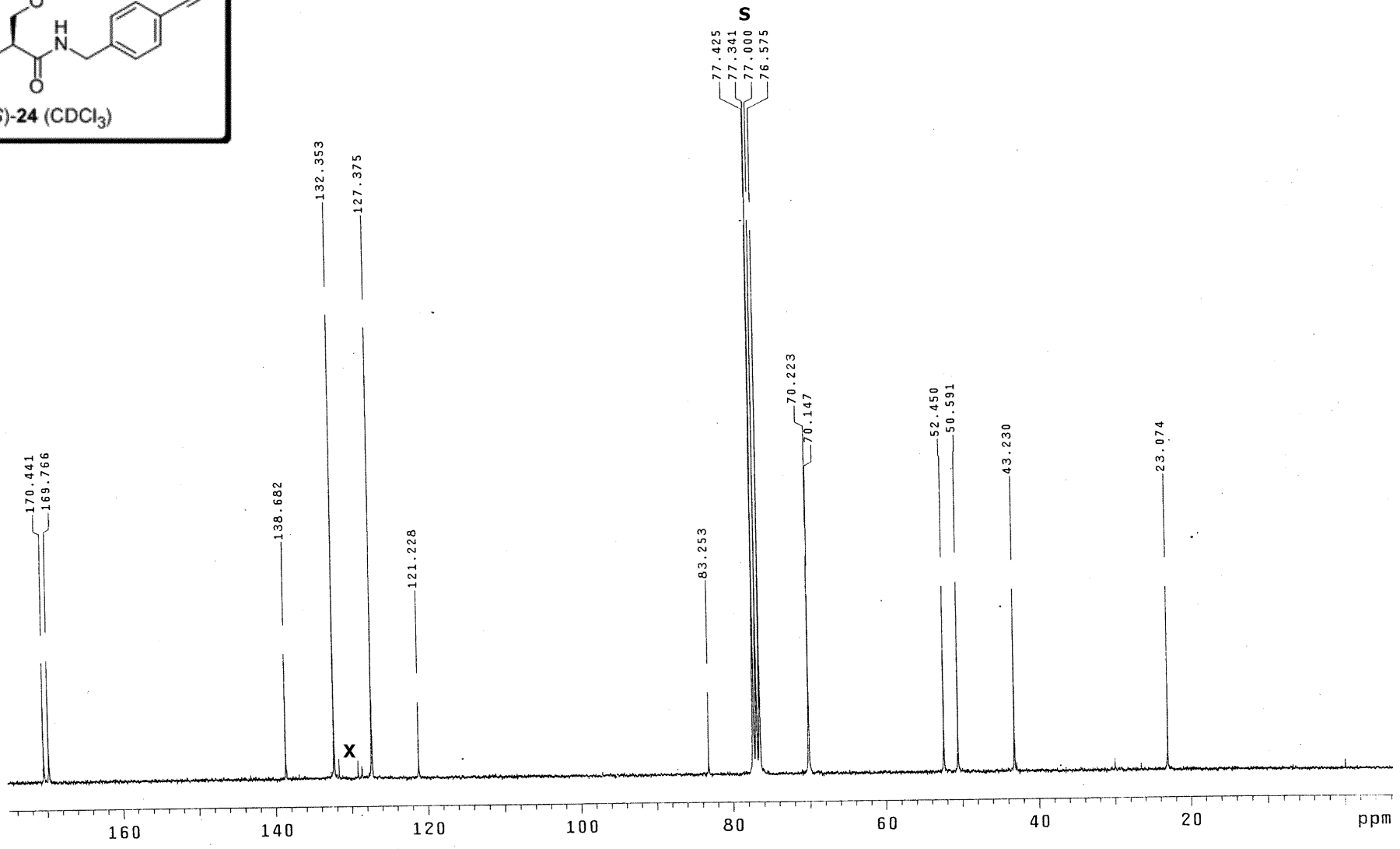
W: Water
X: Impurity
S: Solvent

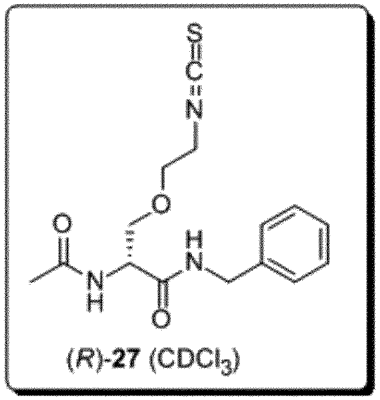

N3
O
O
H
N
N
H
O
(S)-24 (CDCl3)

W: Water
X: Impurity
S: Solvent
7.464
7.437
7.273
7.234
7.208
6.978
6.551
6.531
4.629
4.616
4.606
4.593
4.583
4.569
4.463
4.443
3.937
3.924
3.905
3.893
3.763
3.752
3.743
3.732
3.729
3.717
3.709
3.698
3.680
3.669
3.657
3.646
3.634
3.623
3.613
3.592
3.569
3.562
3.537
3.454
3.443
3.431
3.420
3.410
3.399
3.387
3.376
3.348
3.337
3.328
3.317
3.303
3.293
3.283
3.273
3.077
2.585
2.042
2.019
1.051
0.000
-0.002
X
X
1.95
2.00
0.87
0.94
1.00
2.06
1.02
2.10
0.98
2.06
0.89
2.99
7
6
5
4
3
2
1
ppm

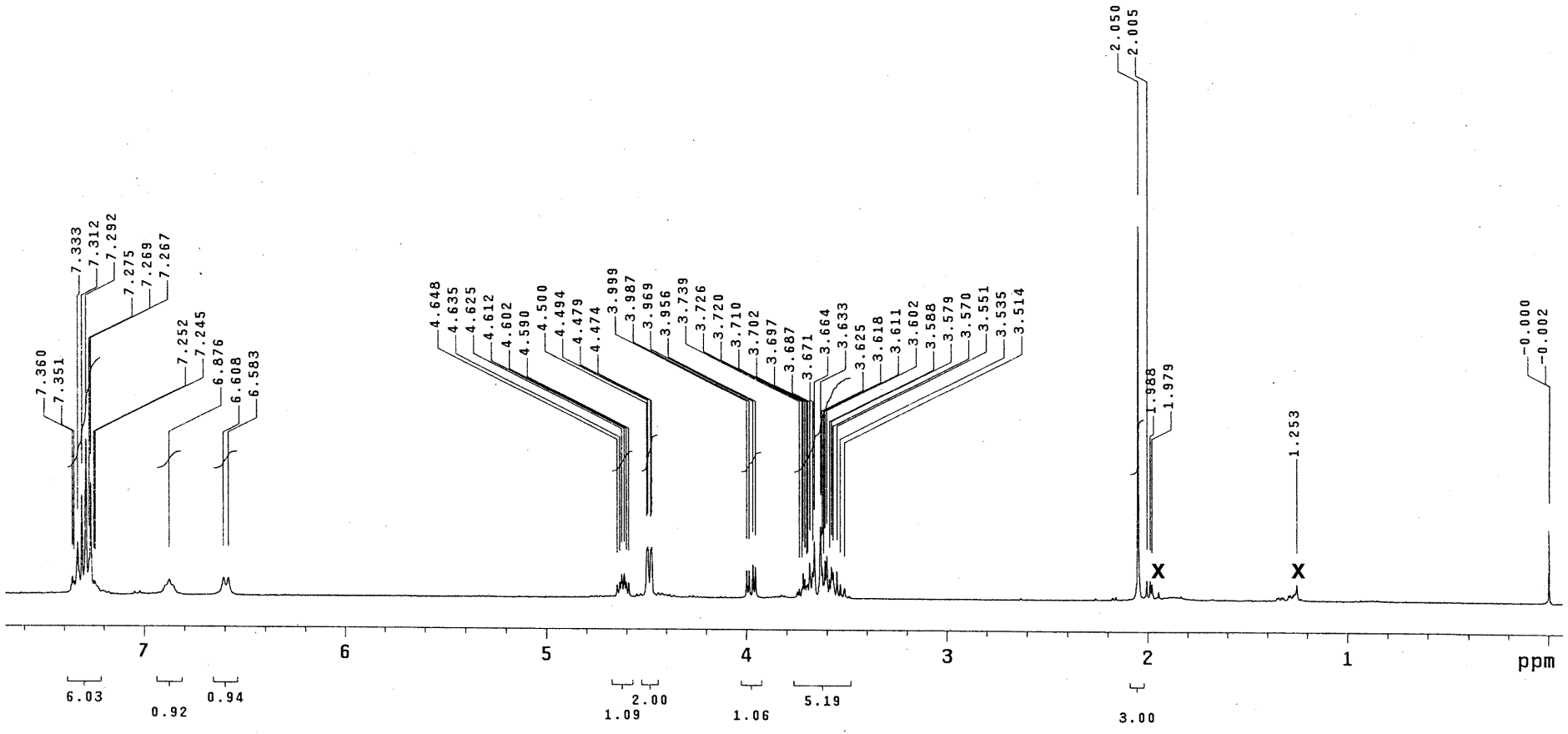


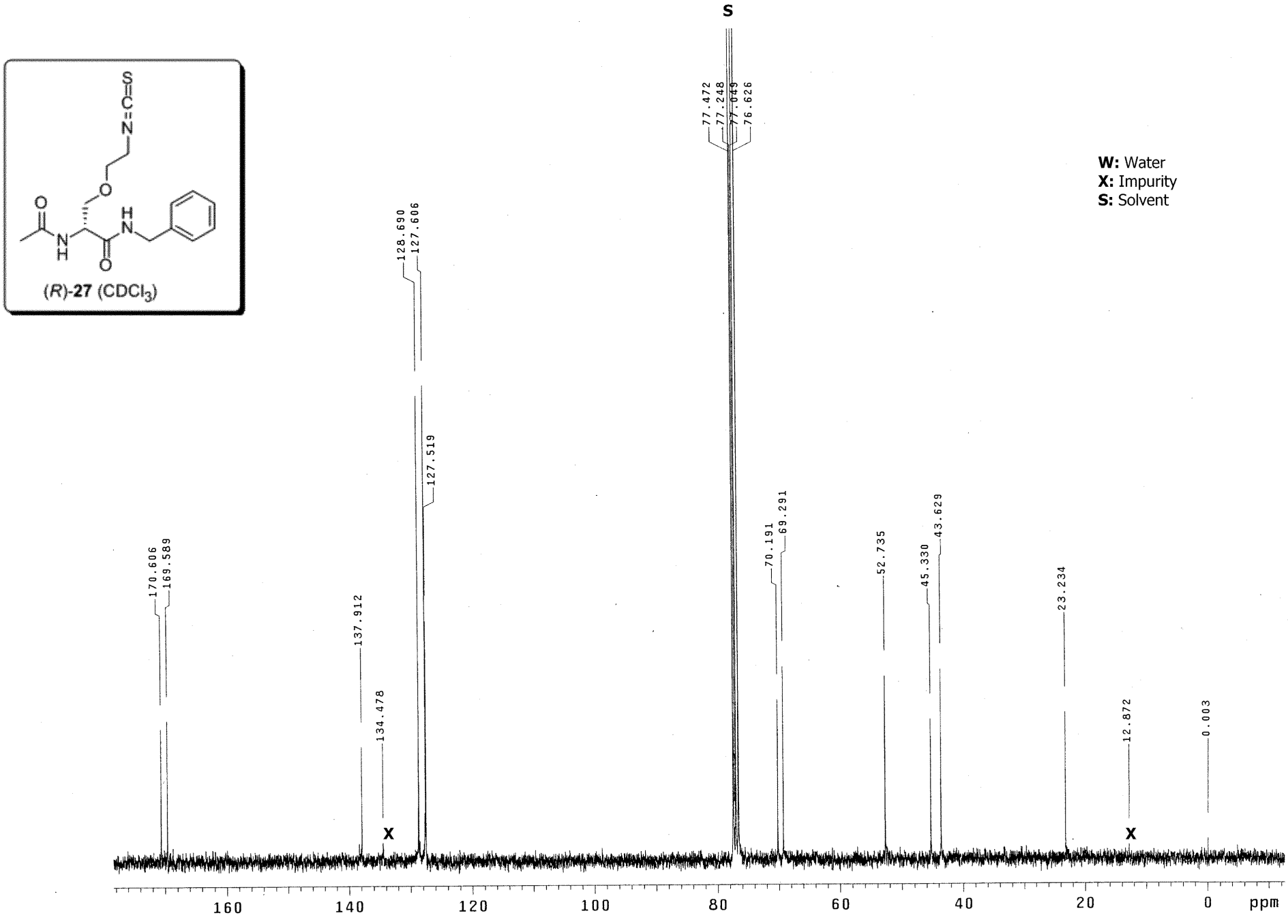
W: Water
X: Impurity
S: Solvent

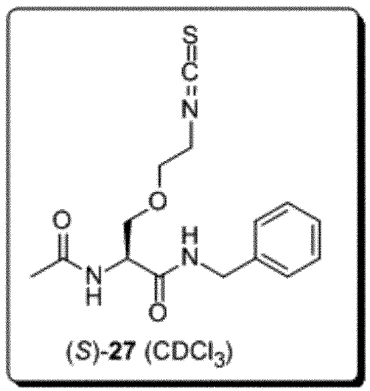




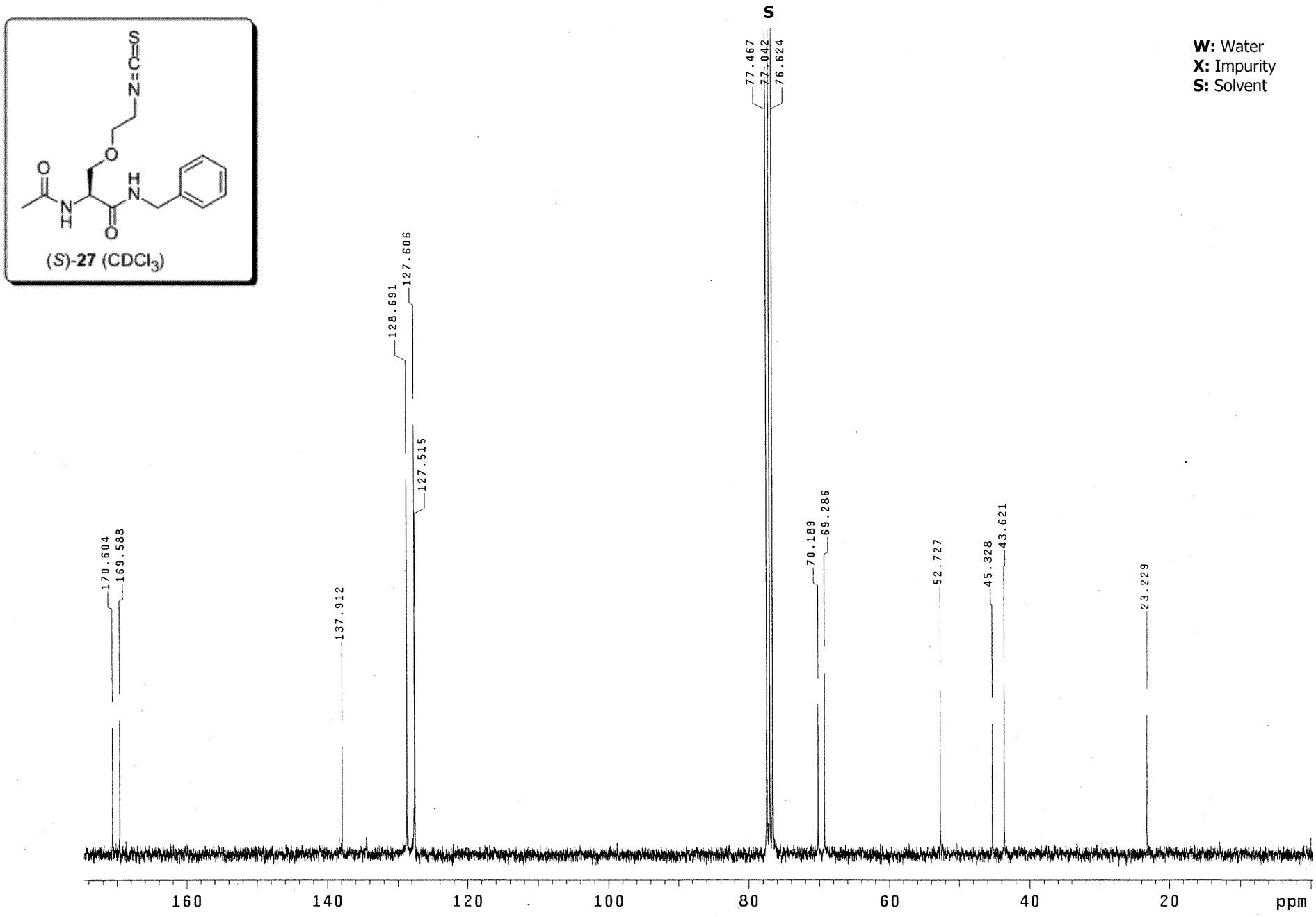
W: Water
X: Impurity
S: Solvent

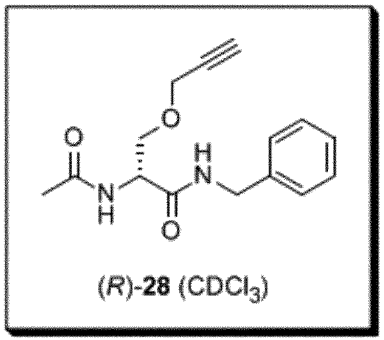



(R)-27 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
X
X
170.606
169.589
137.912
134.478
128.690
127.606
127.519
77.472
77.248
77.049
76.626
70.191
69.291
52.735
45.330
43.629
23.234
12.872
0.003
160
140
120
100
80
60
40
20
0
ppm



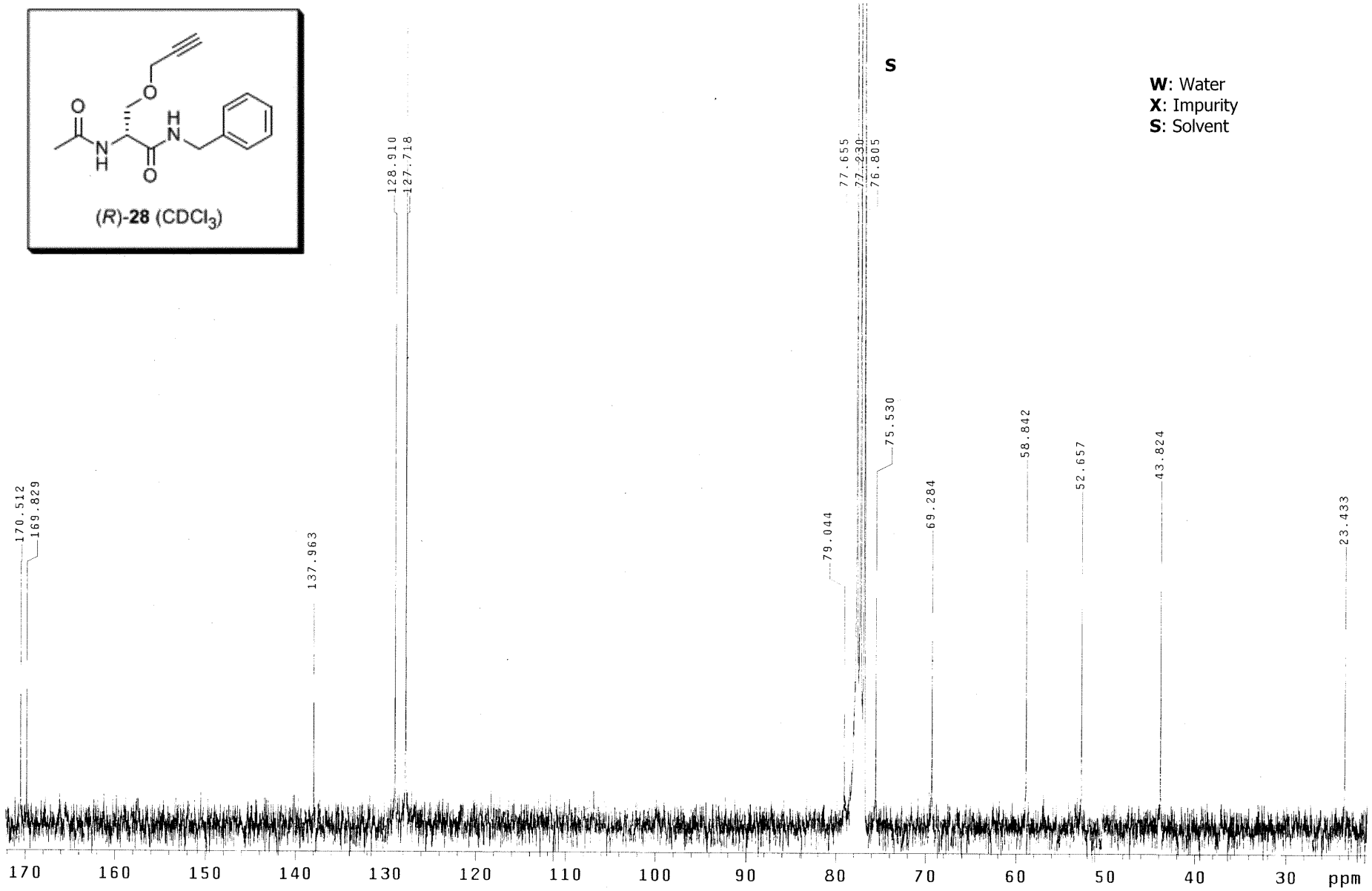
W: Water
X: Impurity
S: Solvent

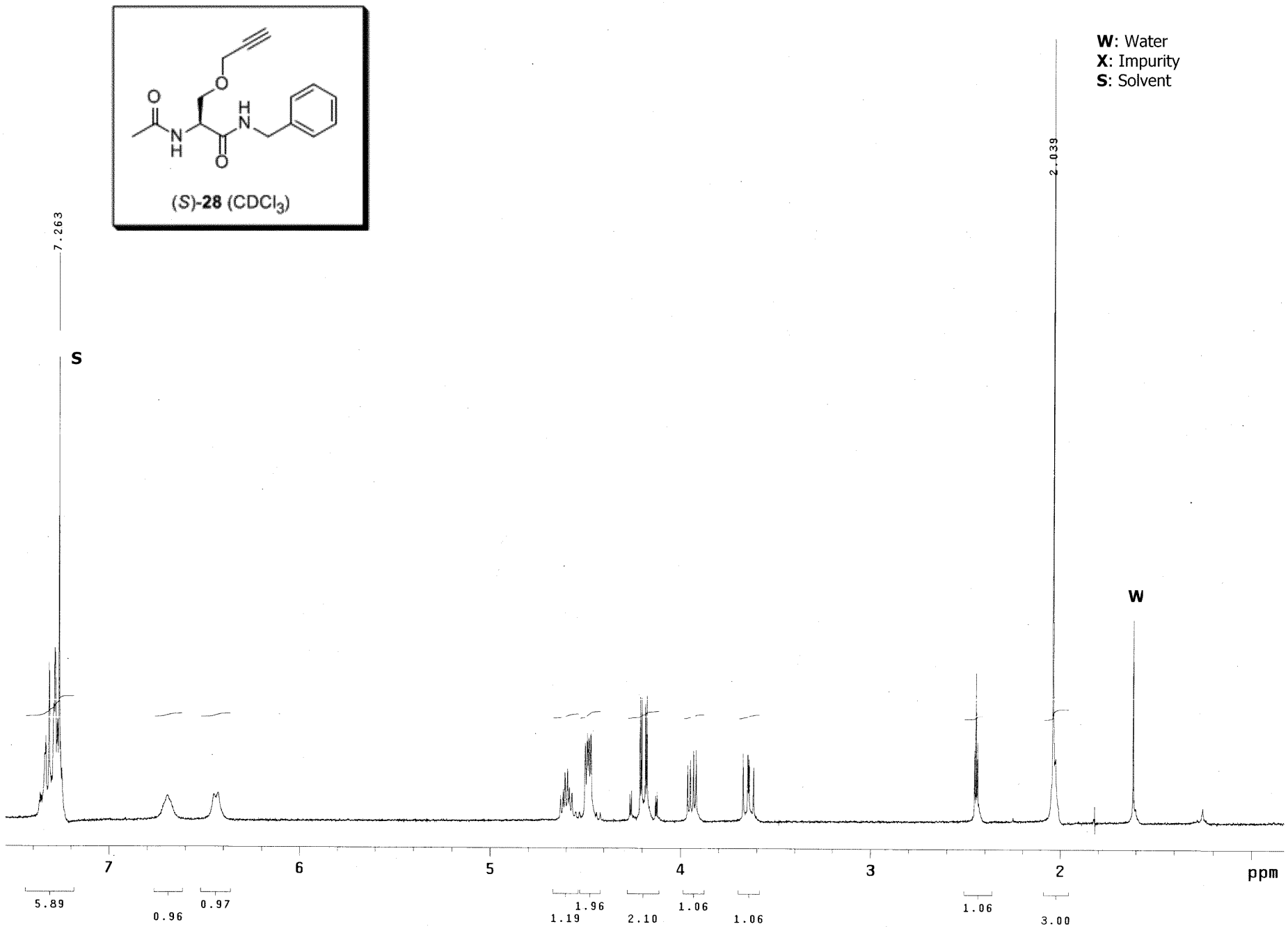

(S)-27 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
77.467
77.042
76.624
128.691
127.606
127.515
170.604
169.588
137.912
70.189
69.286
52.727
45.328
43.621
23.229
160
140
120
100
80
60
40
20
ppm

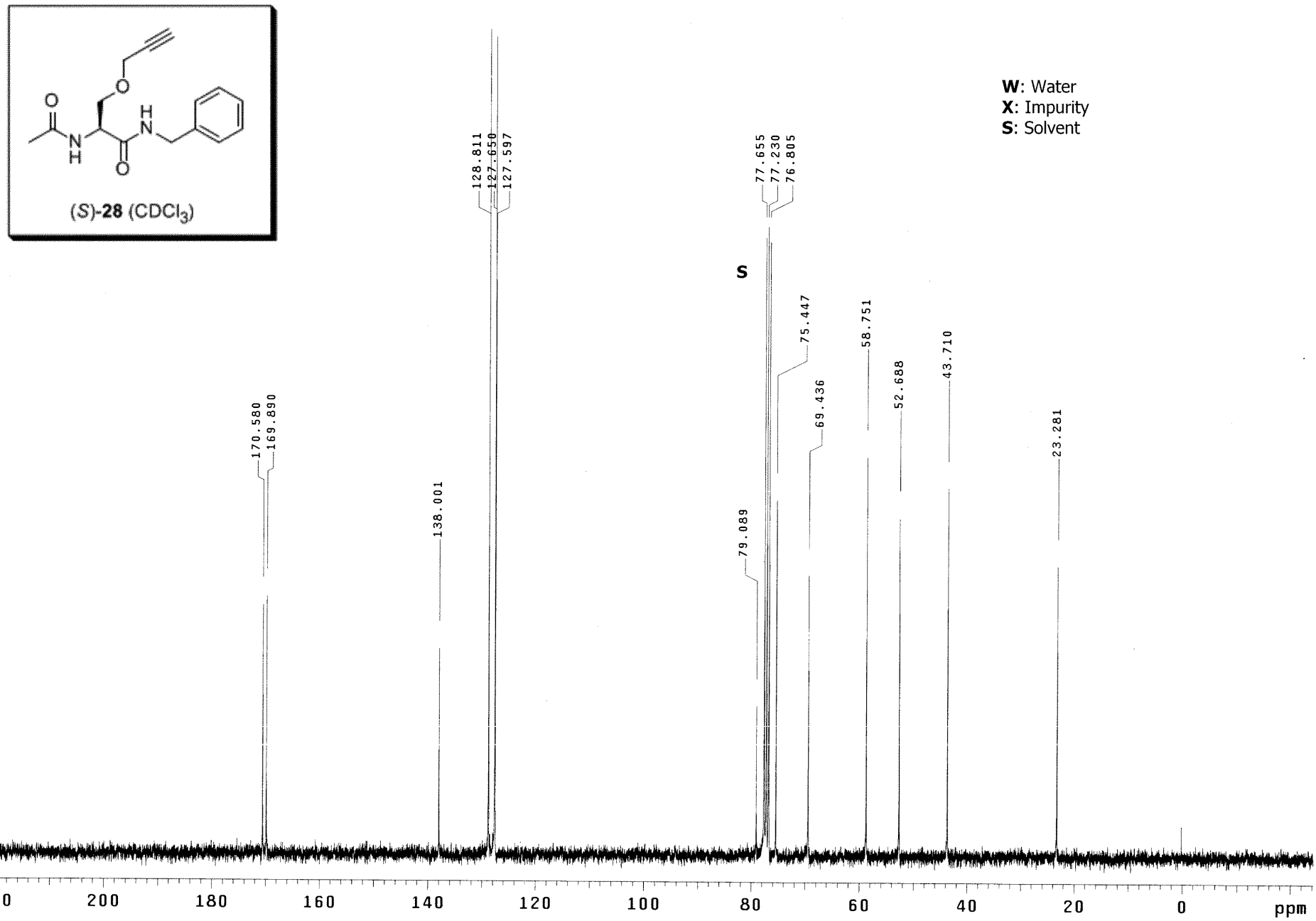

O
O
N
H
H
N
O

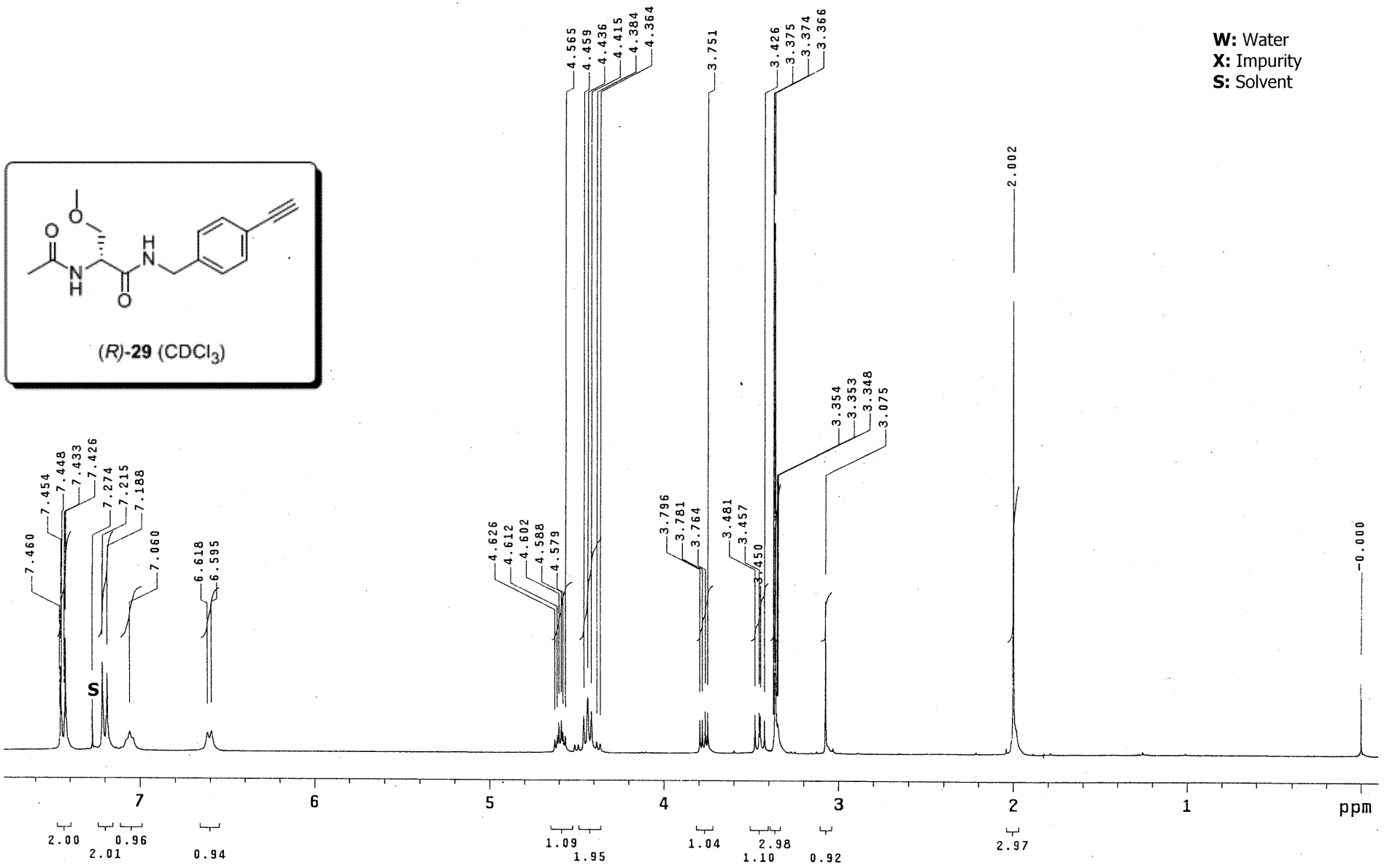
(*R*)-**28** ($CDCl_3$)

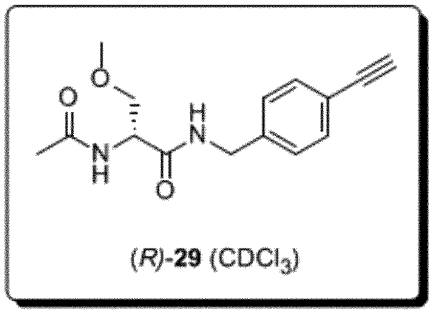
7.263
2.040
W: Water
X: Impurity
S: Solvent
S
W
7
6
5
4
3
2
1
ppm
5.96
0.98
0.97
1.01
2.10
2.18
1.12
1.09
0.98
3.00


(R)-28 (CDCl3)
S
W: Water
X: Impurity
S: Solvent
170.512
169.829
137.963
128.910
127.718
79.044
77.655
77.230
76.805
75.530
69.284
58.842
52.657
43.824
23.433
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm


(S)-28 (CDCl3)
W: Water
X: Impurity
S: Solvent
7.263
2.039
S
W
7
6
5
4
3
2
ppm
5.89
0.96
0.97
1.19
1.96
2.10
1.06
1.06
1.06
3.00

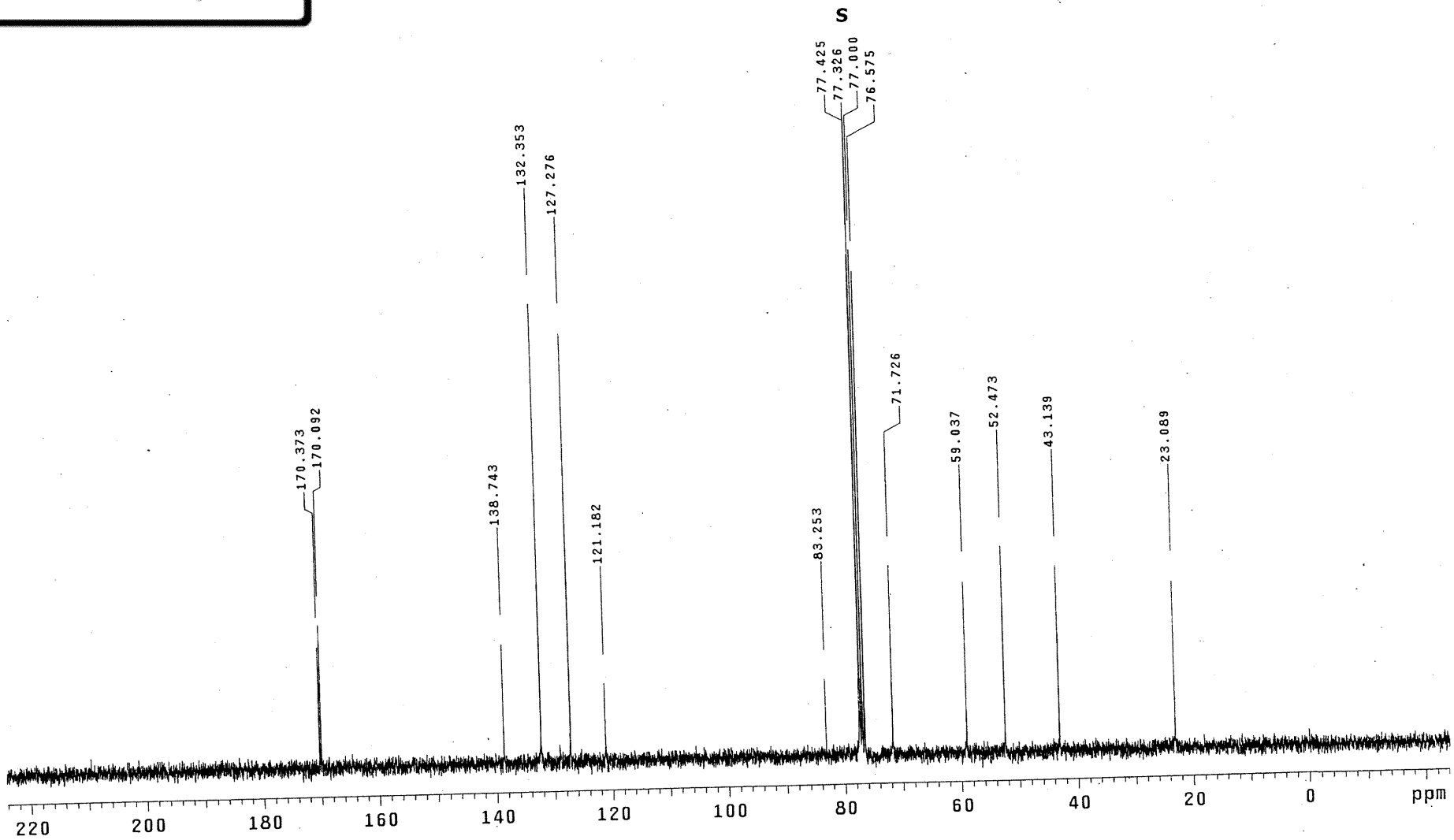

(S)-28 (CDCl3)
W: Water
X: Impurity
S: Solvent
170.580
169.890
138.001
128.811
127.650
127.597
79.089
77.655
77.230
76.805
S
75.447
69.436
58.751
52.688
43.710
23.281
220
200
180
160
140
120
100
80
60
40
20
0
ppm

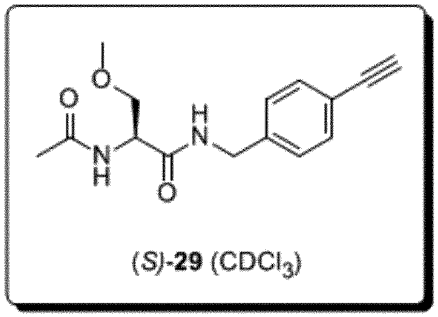

(R)-29 (CDCl3)
W: Water
X: Impurity
S: Solvent
7.460
7.454
7.448
7.433
7.426
7.274
7.215
7.188
7.060
6.618
6.595
S
4.626
4.612
4.602
4.588
4.579
4.565
4.459
4.436
4.415
4.384
4.364
3.796
3.781
3.764
3.751
3.481
3.457
3.450
3.426
3.375
3.374
3.366
3.354
3.353
3.348
3.075
2.002
-0.000
7
6
5
4
3
2
1
ppm
2.00
2.01
0.96
0.94
1.09
1.95
1.04
2.98
1.10
0.92
2.97



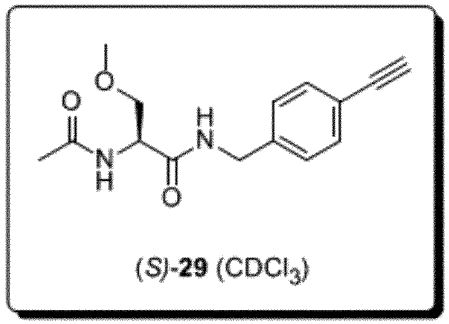
(*R*)-**29** ($CDCl_3$)

W: Water
X: Impurity
S: Solvent

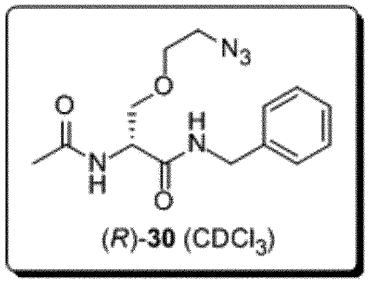




W: Water
X: Impurity
S: Solvent

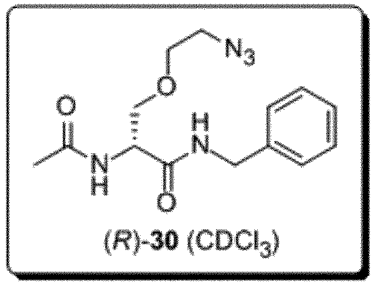


W: Water
X: Impurity
S: Solvent



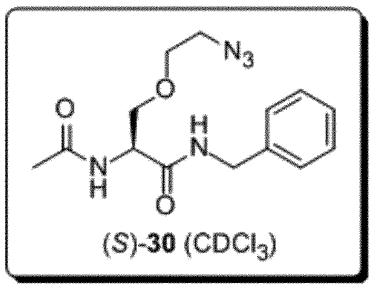
(*R*)-**30** ($CDCl_3$)

W: Water
X: Impurity
S: Solvent



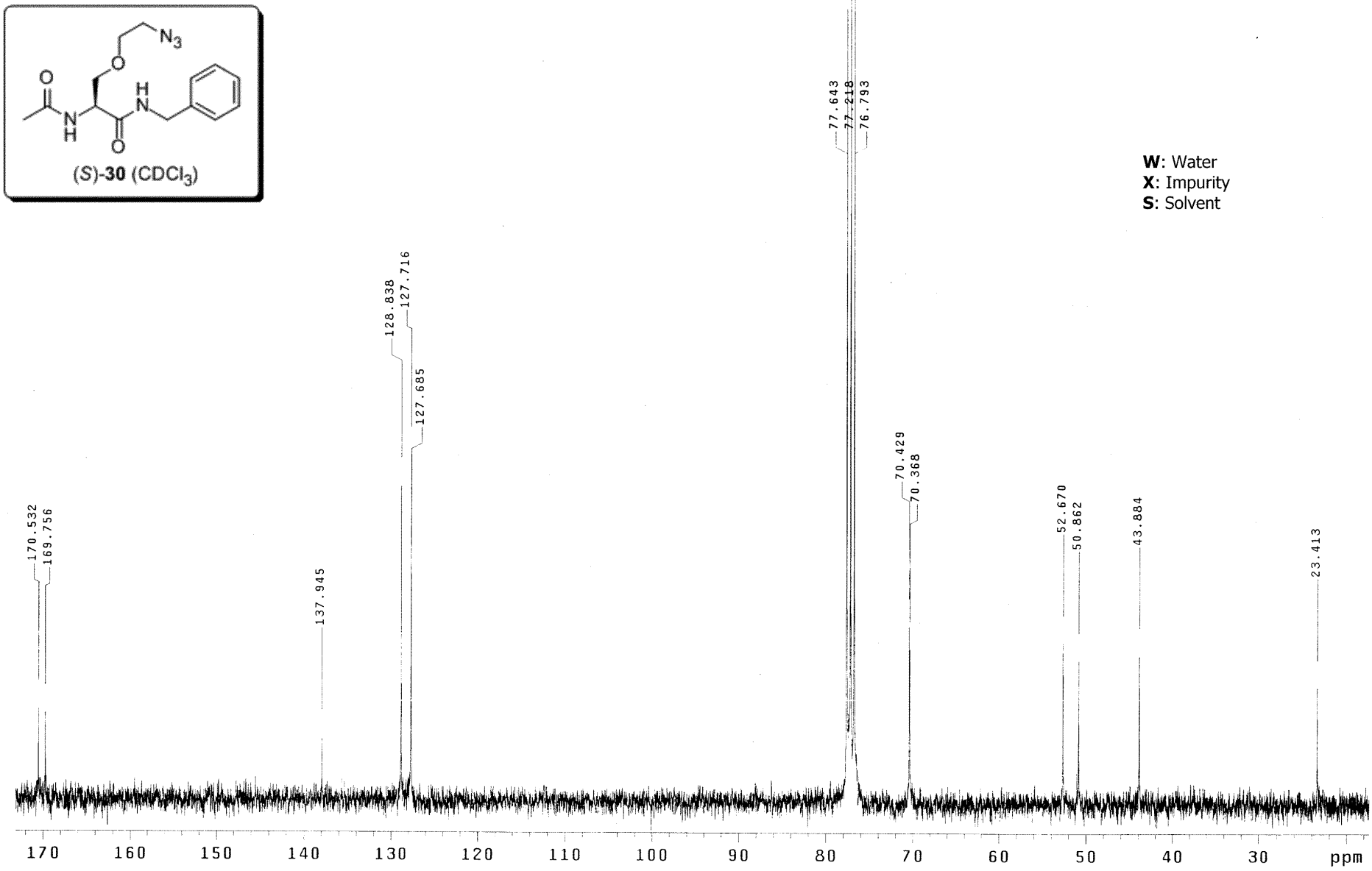
(*R*)-**30** ($CDCl_3$)

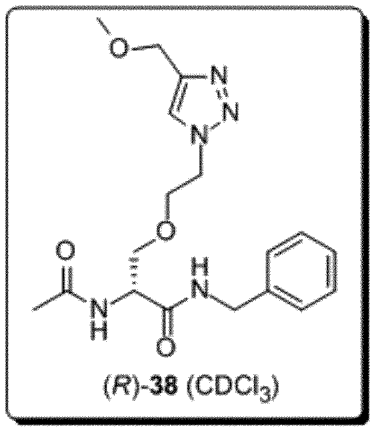
W: Water
X: Impurity
S: Solvent



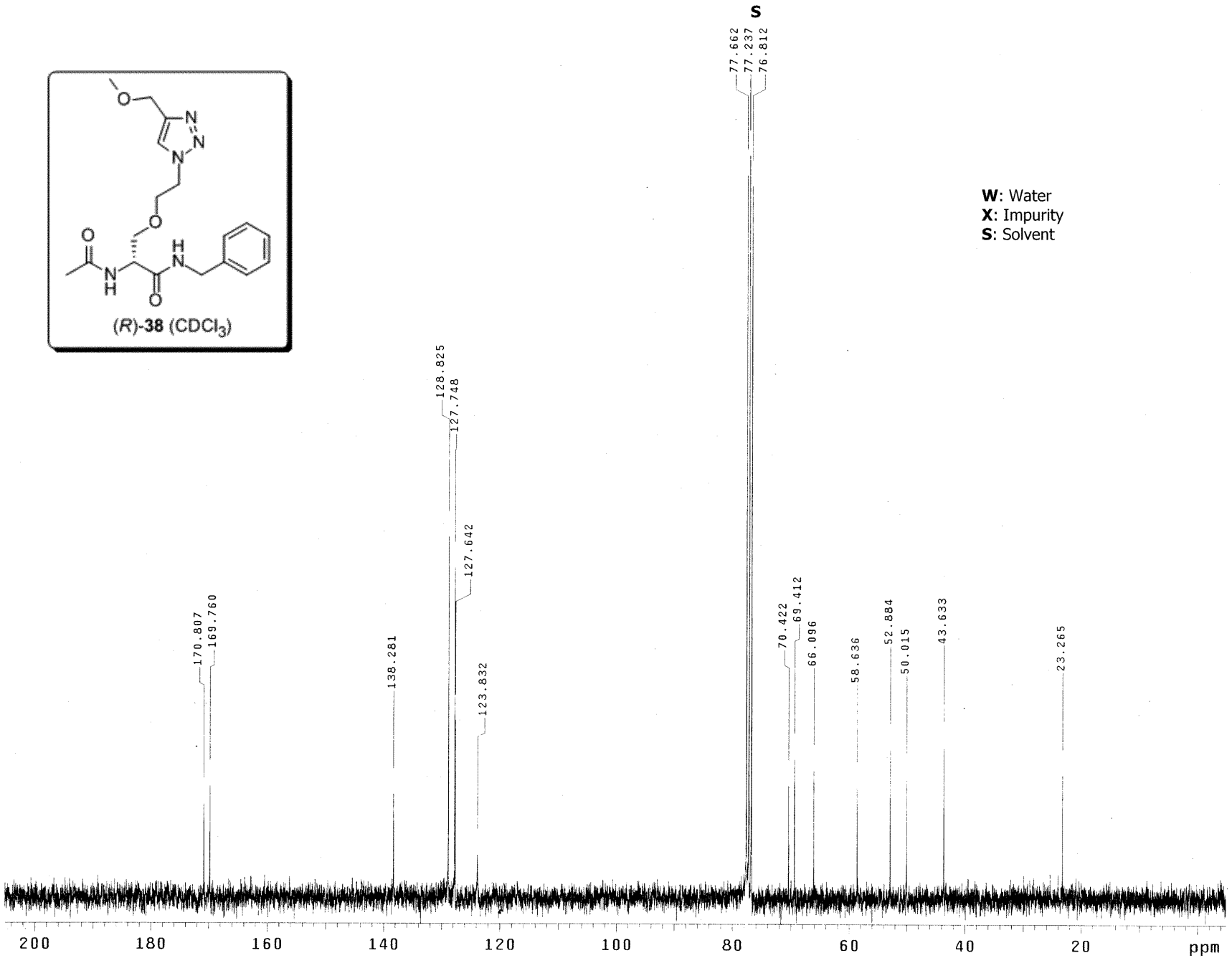
(*S*)-**30** ($CDCl_3$)

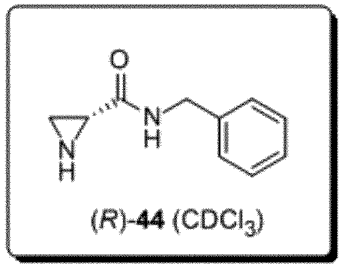
W: Water
X: Impurity
S: Solvent


(S)-30 (CDCl3)
S
W: Water
X: Impurity
S: Solvent
170.532
169.756
137.945
128.838
127.716
127.685
77.643
77.218
76.793
70.429
70.368
52.670
50.862
43.884
23.413
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm


(R)-38 (CDCl3)

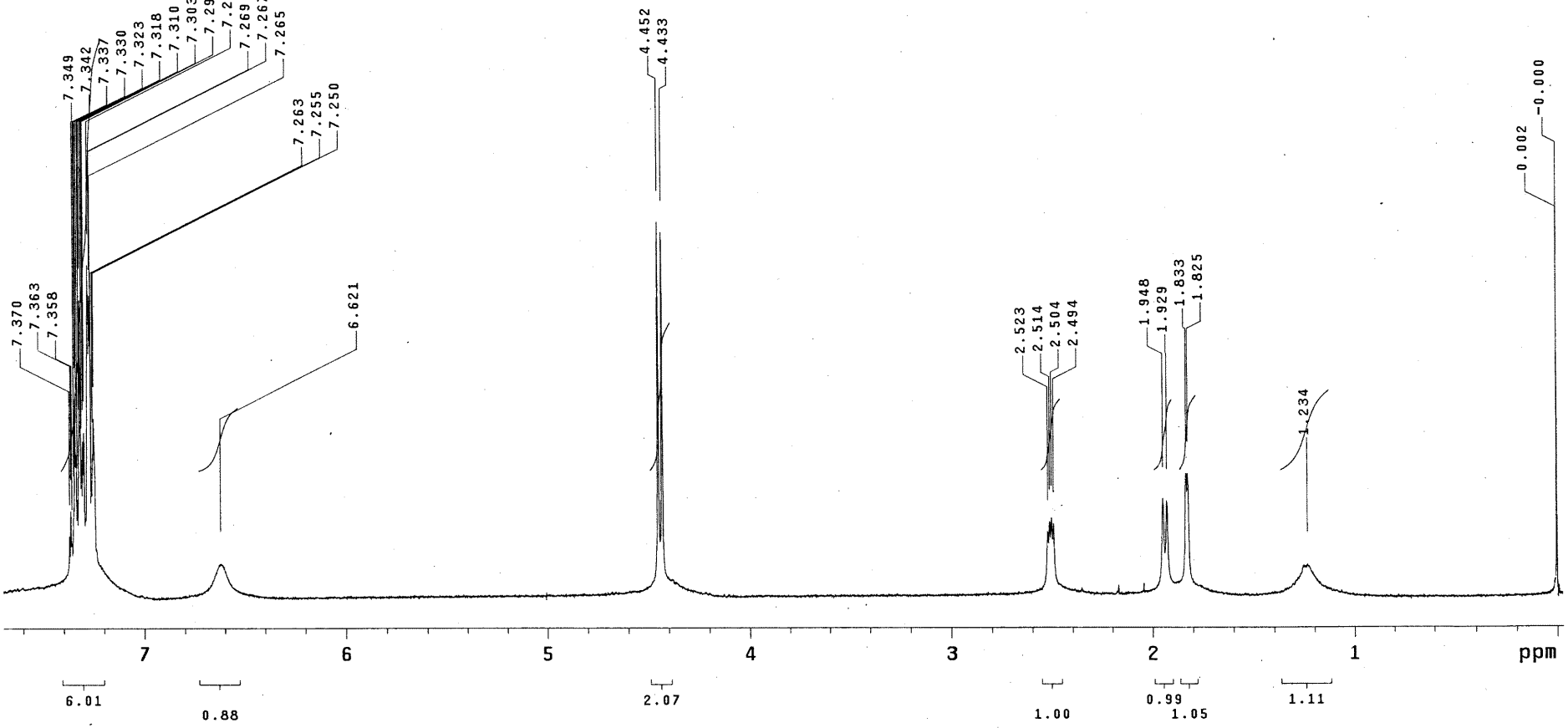
W: Water
X: Impurity
S: Solvent
S
W
3.382
2.009
4.497
4.473
4.420
7.516
7.289
7.274
7.253
10
9
8
7
6
5
4
3
2
1
ppm
0.98
5.55
1.01
0.99
7.44
3.34
1.10
3.00
3.38

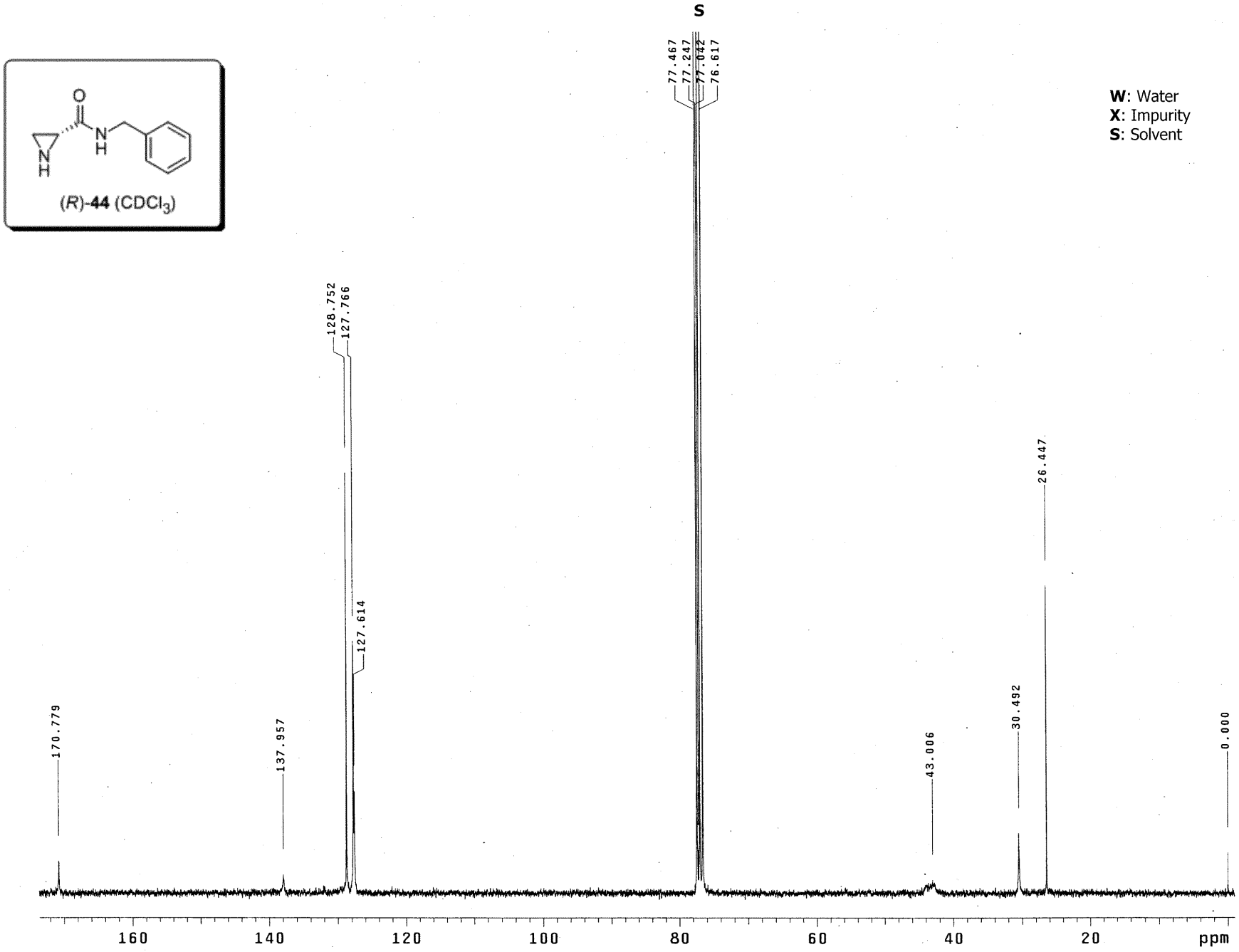

(R)-38 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
77.662
77.237
76.812
128.825
127.748
127.642
123.832
170.807
169.760
138.281
70.422
69.412
66.096
58.636
52.884
50.015
43.633
23.265
200
180
160
140
120
100
80
60
40
20
ppm

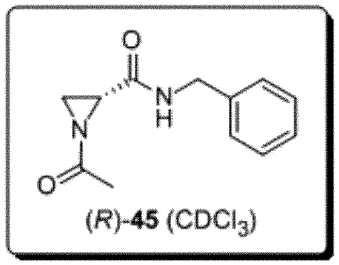


(*R*)-**44** ($CDCl_3$)

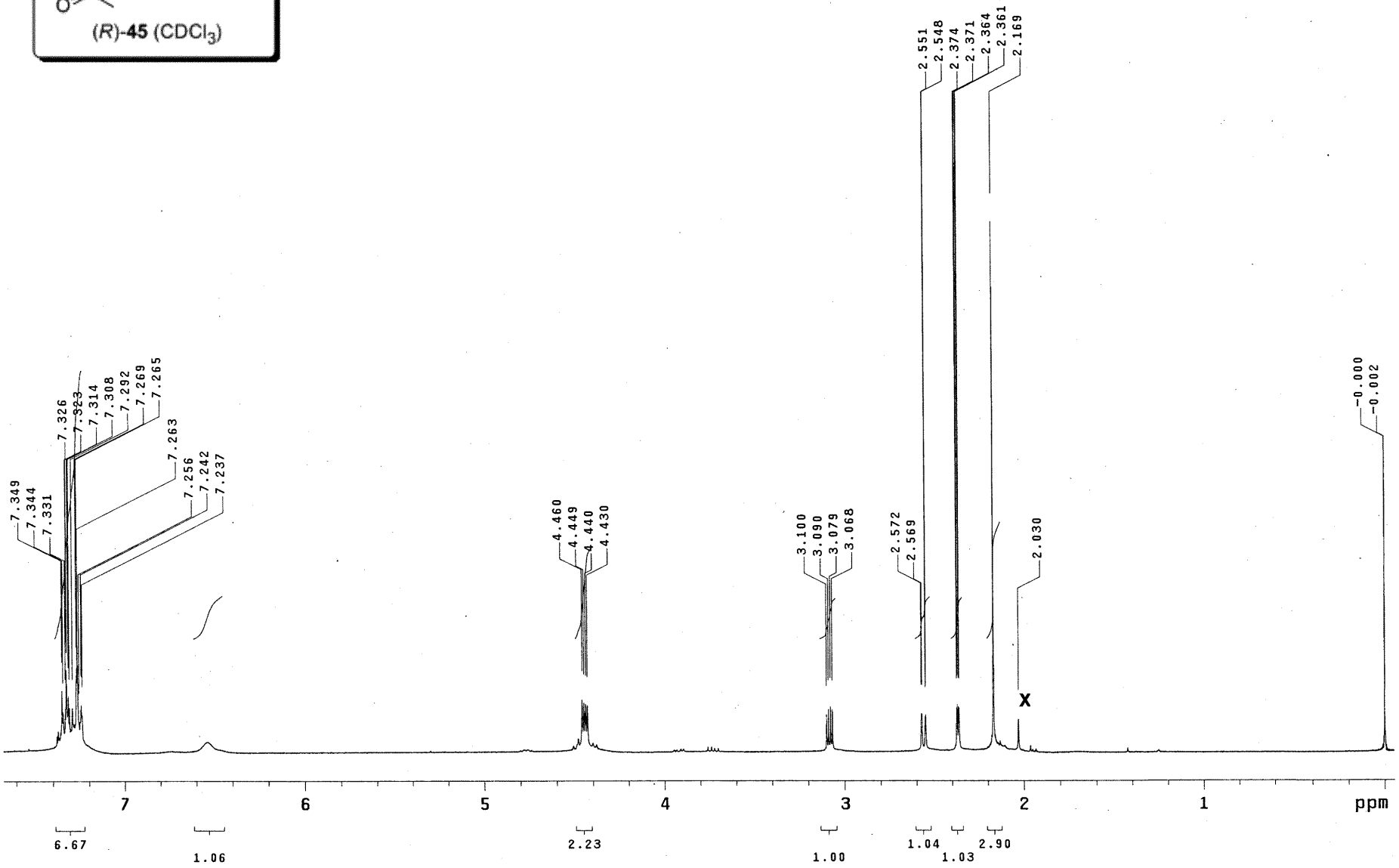
W: Water
X: Impurity
S: Solvent

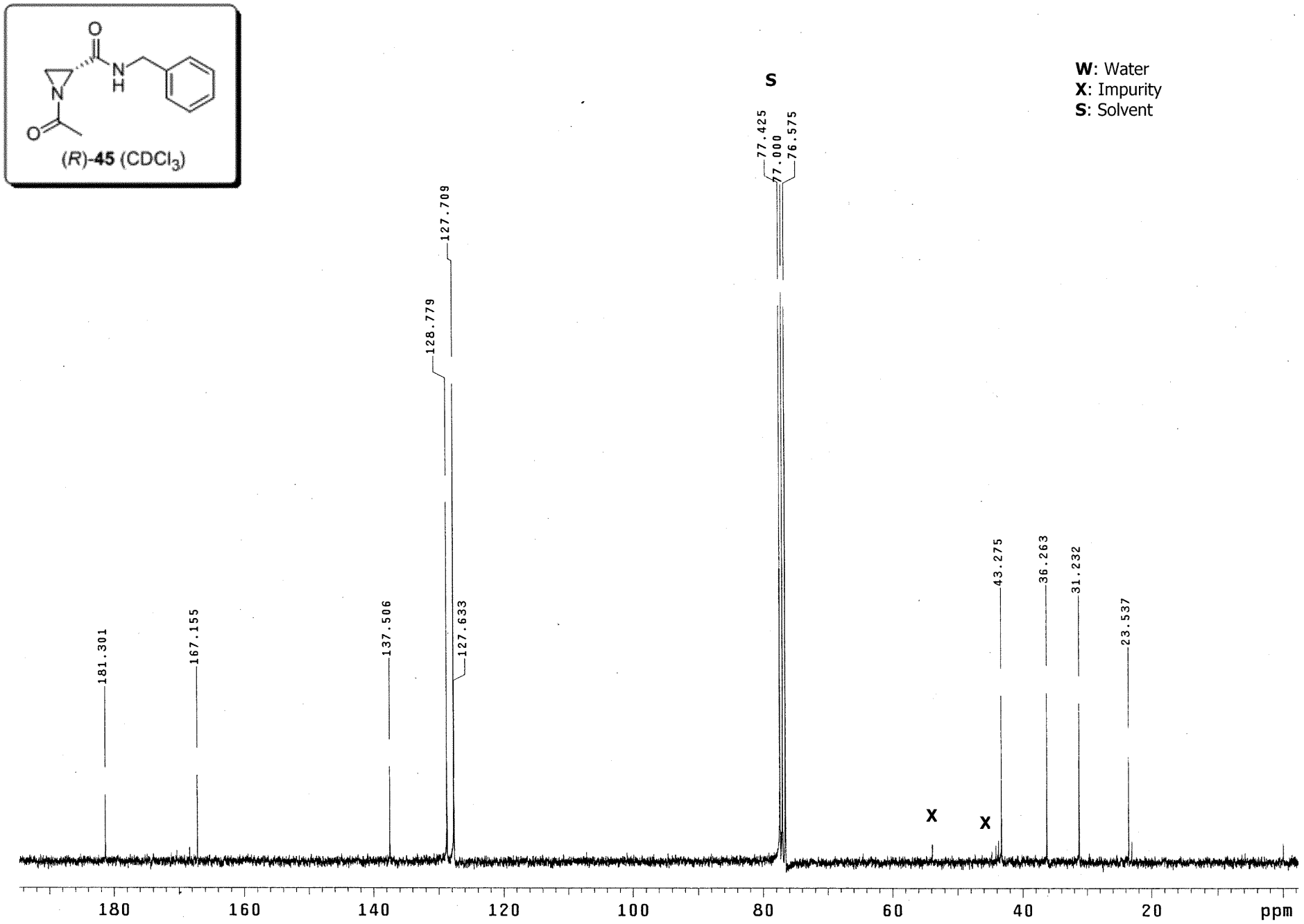


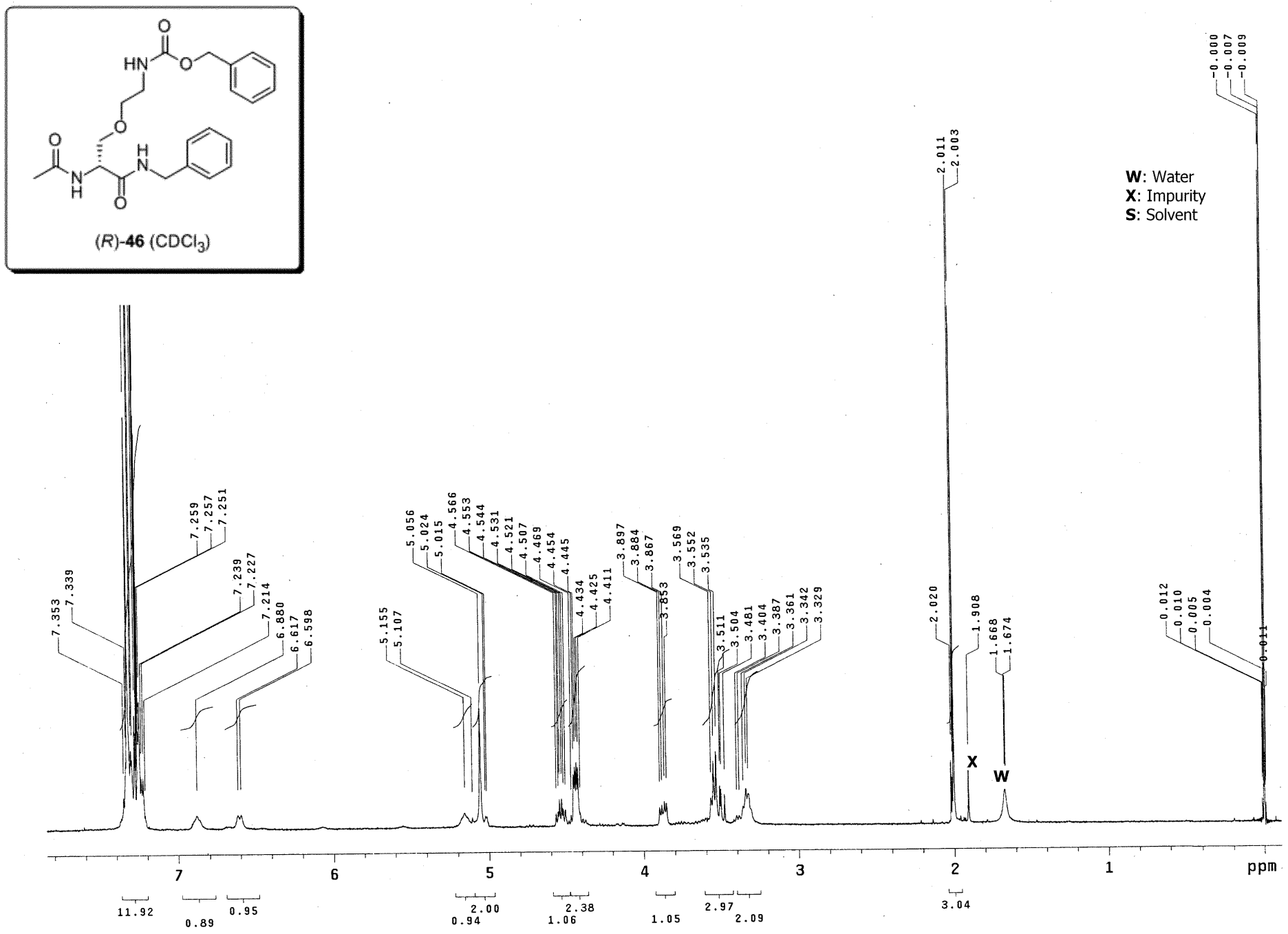

(R)-44 (CDCl3)
S
W: Water
X: Impurity
S: Solvent
77.467
77.242
77.042
76.617
128.752
127.766
127.614
170.779
137.957
43.006
30.492
26.447
0.000
160
140
120
100
80
60
40
20
ppm

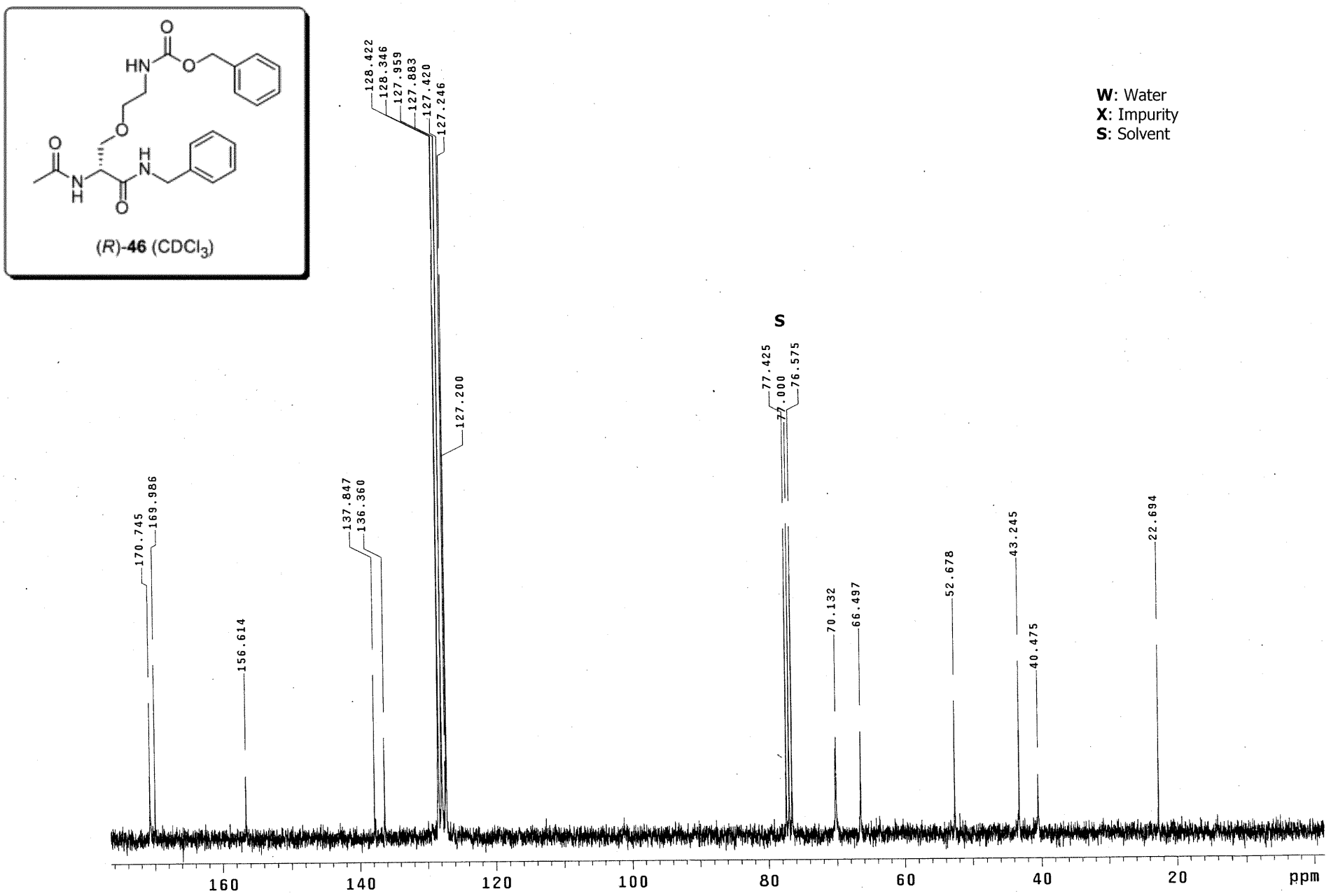


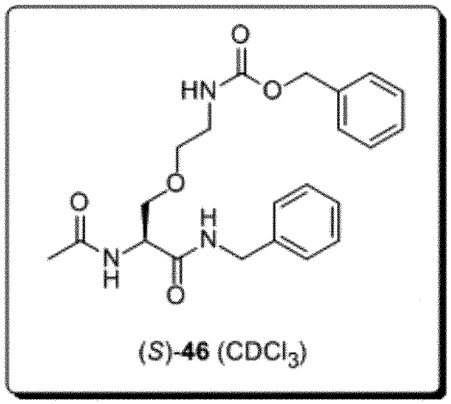
W: Water
X: Impurity
S: Solvent



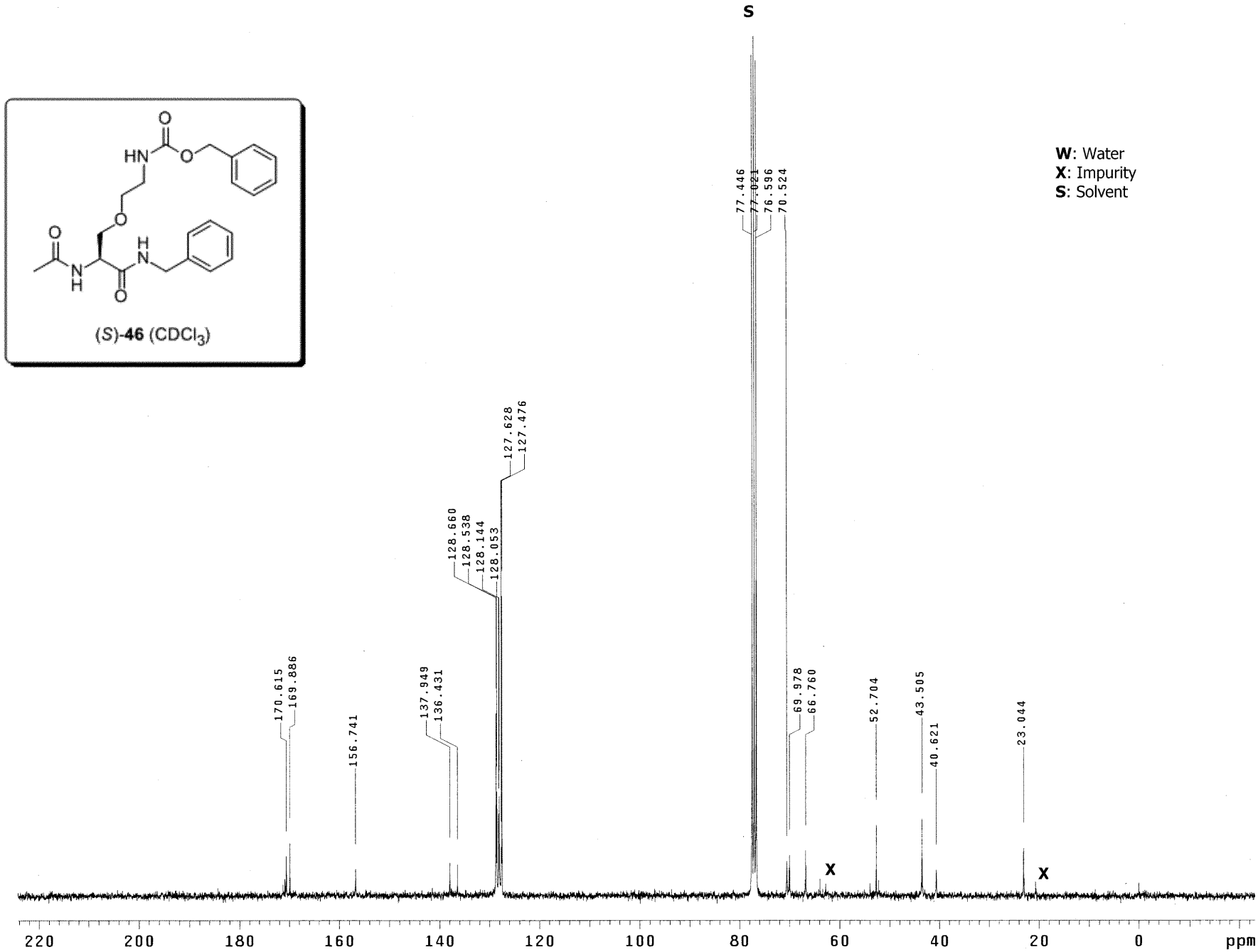

(R)-45 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
77.425
77.000
76.575
127.709
128.779
127.633
137.506
167.155
181.301
43.275
36.263
31.232
23.537
X
X
180
160
140
120
100
80
60
40
20
ppm

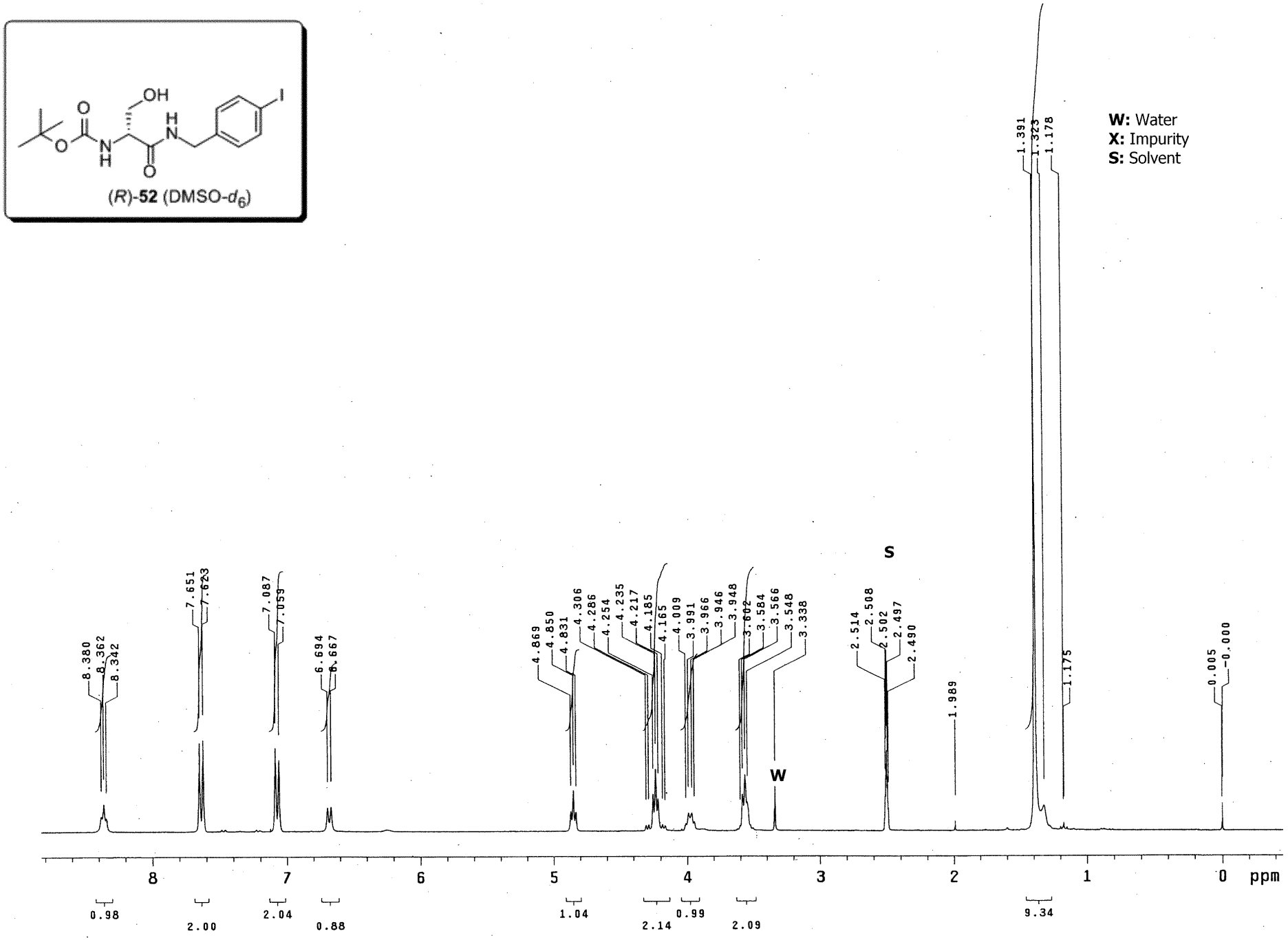

(R)-46 (CDCl3)
W: Water
X: Impurity
S: Solvent
7.353
7.339
7.259
7.257
7.251
7.239
7.227
7.214
6.880
6.617
6.598
5.155
5.107
5.056
5.024
5.015
4.566
4.553
4.544
4.531
4.521
4.507
4.469
4.454
4.445
4.434
4.425
4.411
3.897
3.884
3.867
3.853
3.569
3.552
3.535
3.511
3.504
3.481
3.404
3.387
3.361
3.342
3.329
2.020
2.011
2.003
1.908
1.668
1.674
0.012
0.010
0.005
0.004
-0.000
-0.007
-0.009
X
W
ppm
11.92
0.89
0.95
2.00
0.94
2.38
1.06
1.05
2.97
2.09
3.04


(R)-46 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
128.422
128.346
127.959
127.883
127.420
127.246
127.200
77.425
77.000
76.575
170.745
169.986
156.614
137.847
136.360
70.132
66.497
52.678
43.245
40.475
22.694
160
140
120
100
80
60
40
20
ppm

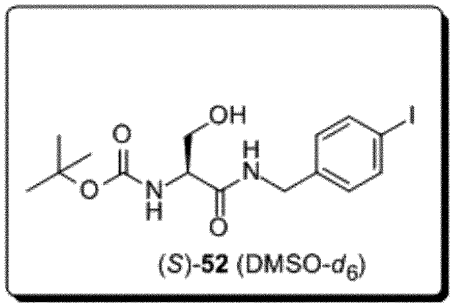

(S)-46 (CDCl3)

W: Water
X: Impurity
S: Solvent
2.003
1.993
0.000
0.011
7.257
7.255
7.247
7.237
7.224
7.211
7.349
7.336
6.897
6.602
5.053
5.019
5.169
4.555
4.546
4.532
4.525
4.510
4.497
4.490
4.477
4.470
4.448
4.439
4.429
4.420
4.387
3.887
3.873
3.858
3.844
3.563
3.547
3.532
3.510
3.503
3.480
3.338
3.321
2.045
2.008
1.903
1.690
0.010
0.005
0.004
X
W
7
6
5
4
3
2
1
ppm
11.82
0.95
0.84
0.94
1.97
1.08
1.99
0.95
2.96
1.98
3.00

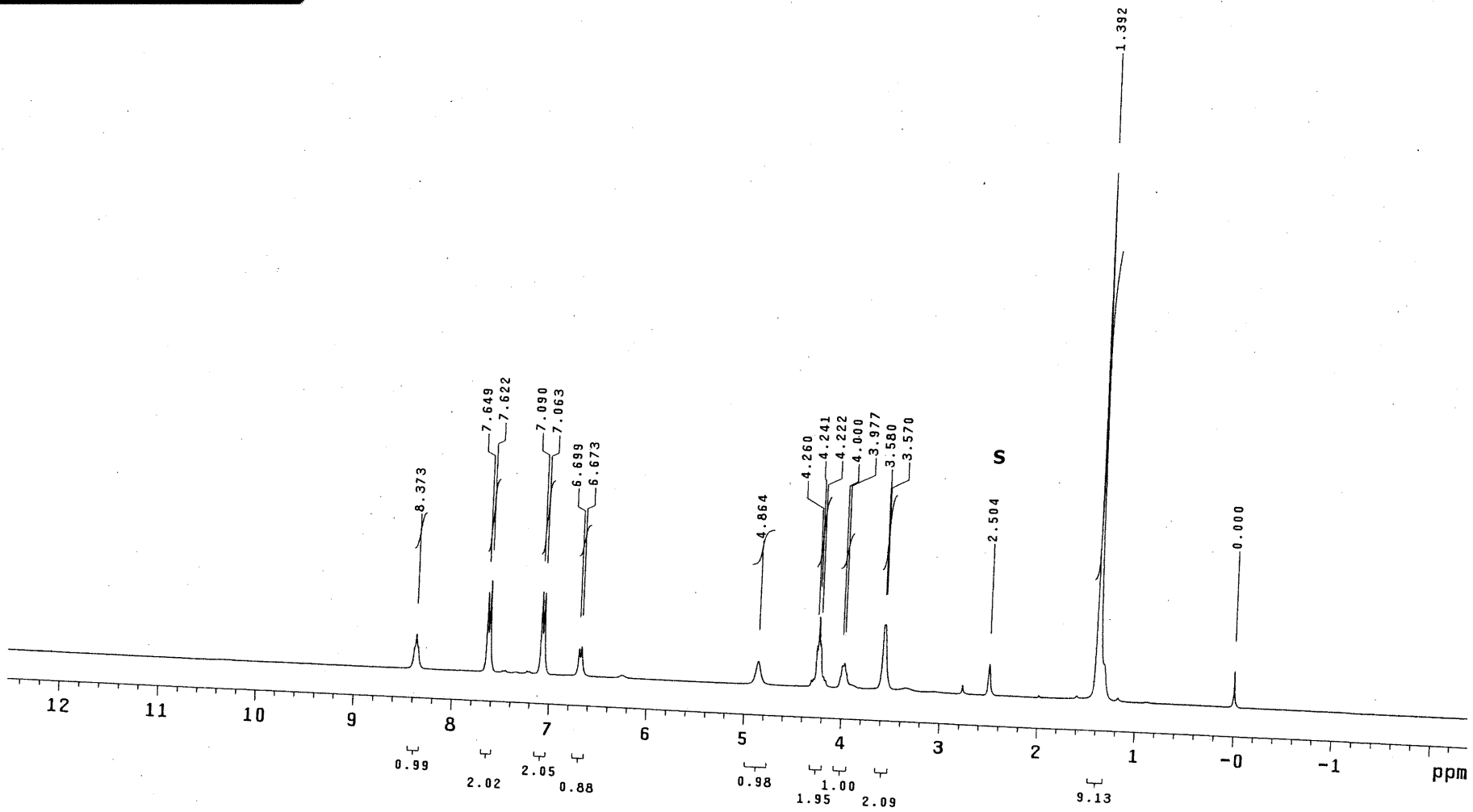

(S)-46 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
77.446
77.021
76.596
70.524
170.615
169.886
156.741
137.949
136.431
128.660
128.538
128.144
128.053
127.628
127.476
69.978
66.760
52.704
43.505
40.621
23.044
X
X
220
200
180
160
140
120
100
80
60
40
20
0
ppm

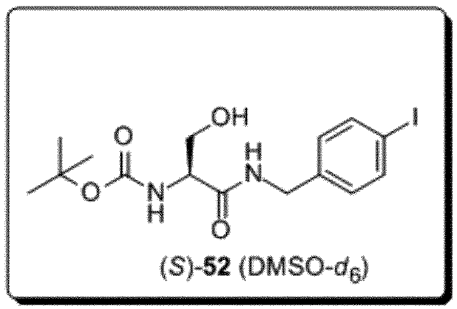

(R)-52 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
8.380
8.362
8.342
7.651
7.623
7.087
7.059
6.694
6.667
4.869
4.850
4.831
4.306
4.286
4.254
4.235
4.217
4.185
4.165
4.009
3.991
3.966
3.946
3.948
3.602
3.584
3.566
3.548
3.338
2.514
2.508
2.502
2.497
2.490
1.989
1.391
1.323
1.178
1.175
0.005
-0.000
S
W
8
7
6
5
4
3
2
1
0
ppm
0.98
2.00
2.04
0.88
1.04
2.14
0.99
2.09
9.34

171.512
156.374
137.757
129.369
92.848
80.779
62.717
54.780
42.803
28.261
0.000
R-52 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
X X

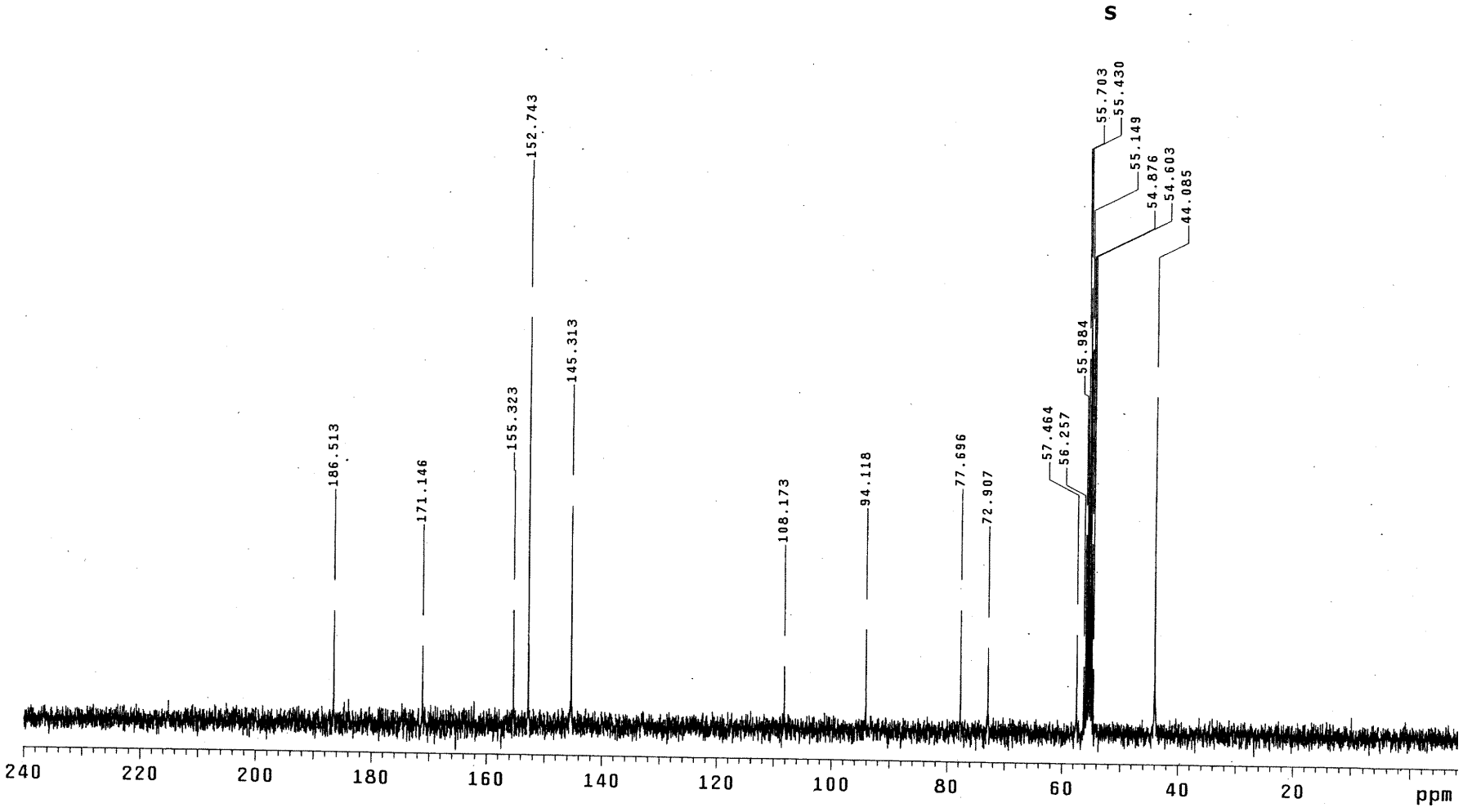


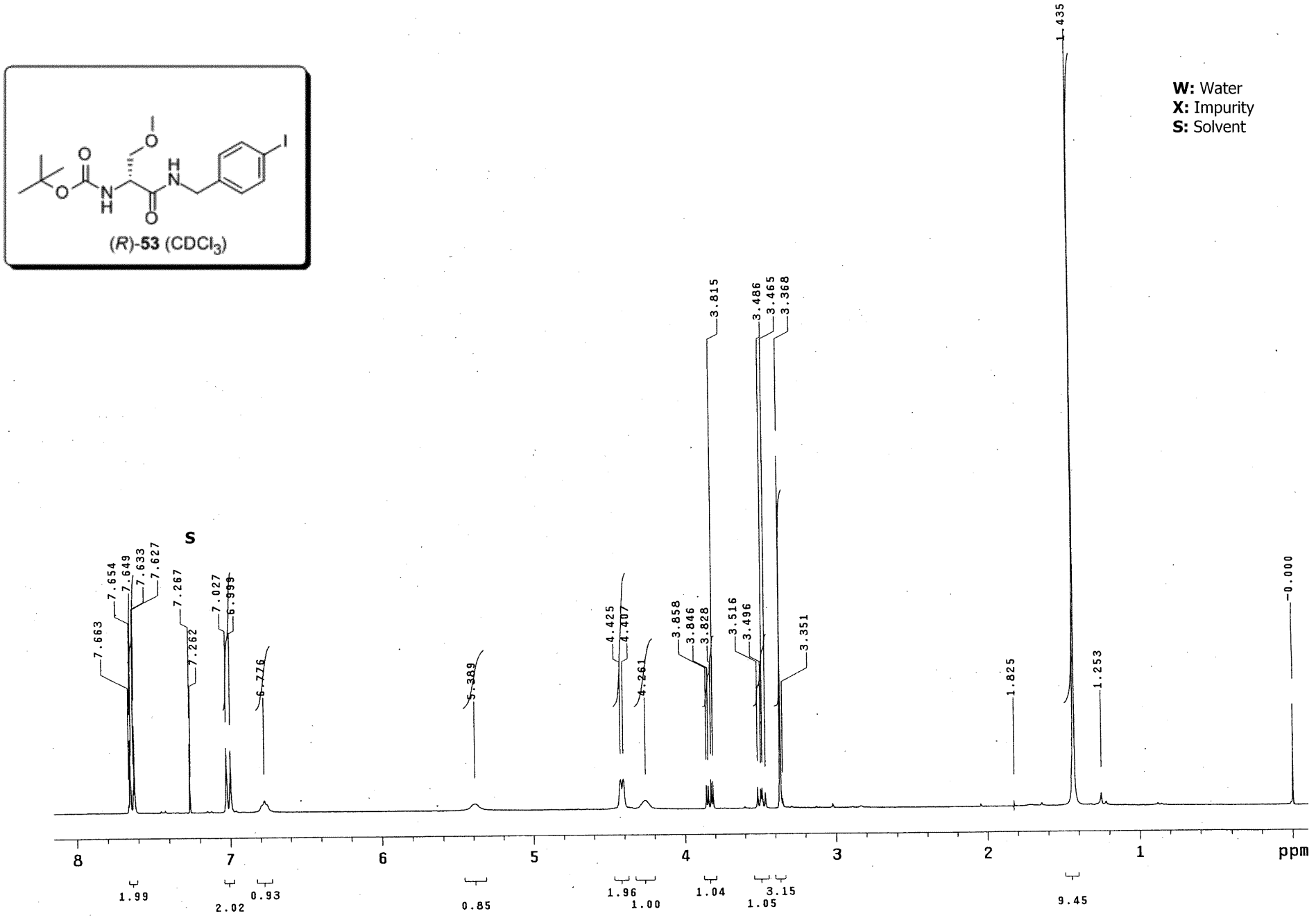
W: Water
X: Impurity
S: Solvent

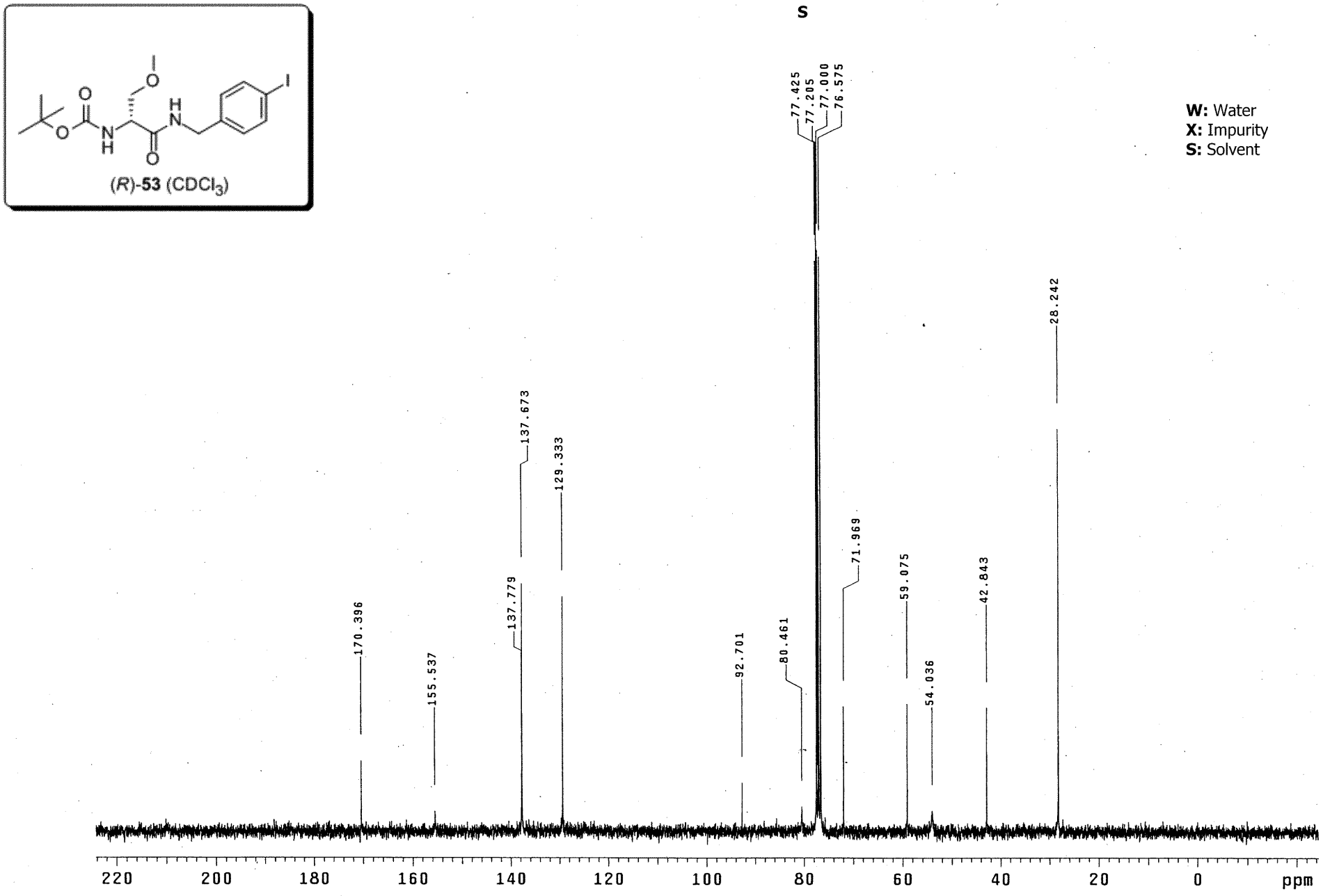


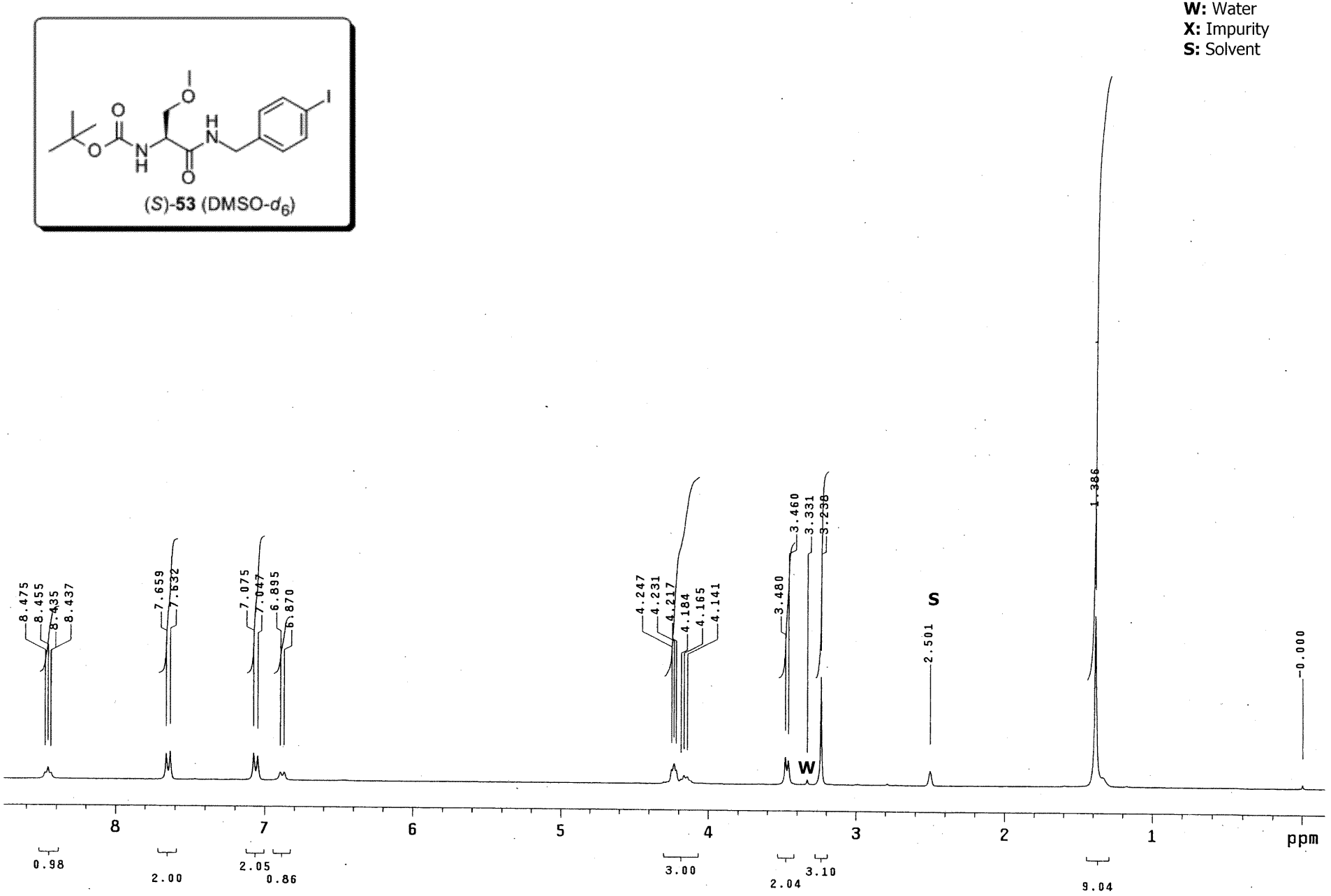


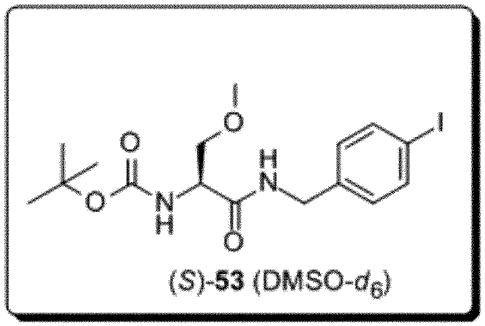
W: Water
X: Impurity
S: Solvent



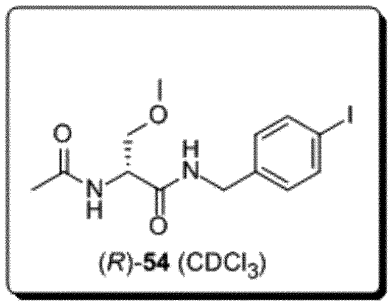

(R)-53 (CDCl3)
W: Water
X: Impurity
S: Solvent
S
7.663
7.654
7.649
7.633
7.627
7.267
7.262
7.027
6.999
6.776
5.389
4.425
4.407
4.261
3.858
3.846
3.828
3.815
3.516
3.496
3.486
3.465
3.368
3.351
1.825
1.435
1.253
0.000
8
7
6
5
4
3
2
1
ppm
1.99
2.02
0.93
0.85
1.96
1.00
1.04
1.05
3.15
9.45


(R)-53 (CDCl3)
S
W: Water
X: Impurity
S: Solvent
77.425
77.205
77.000
76.575
170.396
155.537
137.779
137.673
129.333
92.701
80.461
71.969
59.075
54.036
42.843
28.242
220
200
180
160
140
120
100
80
60
40
20
0
ppm

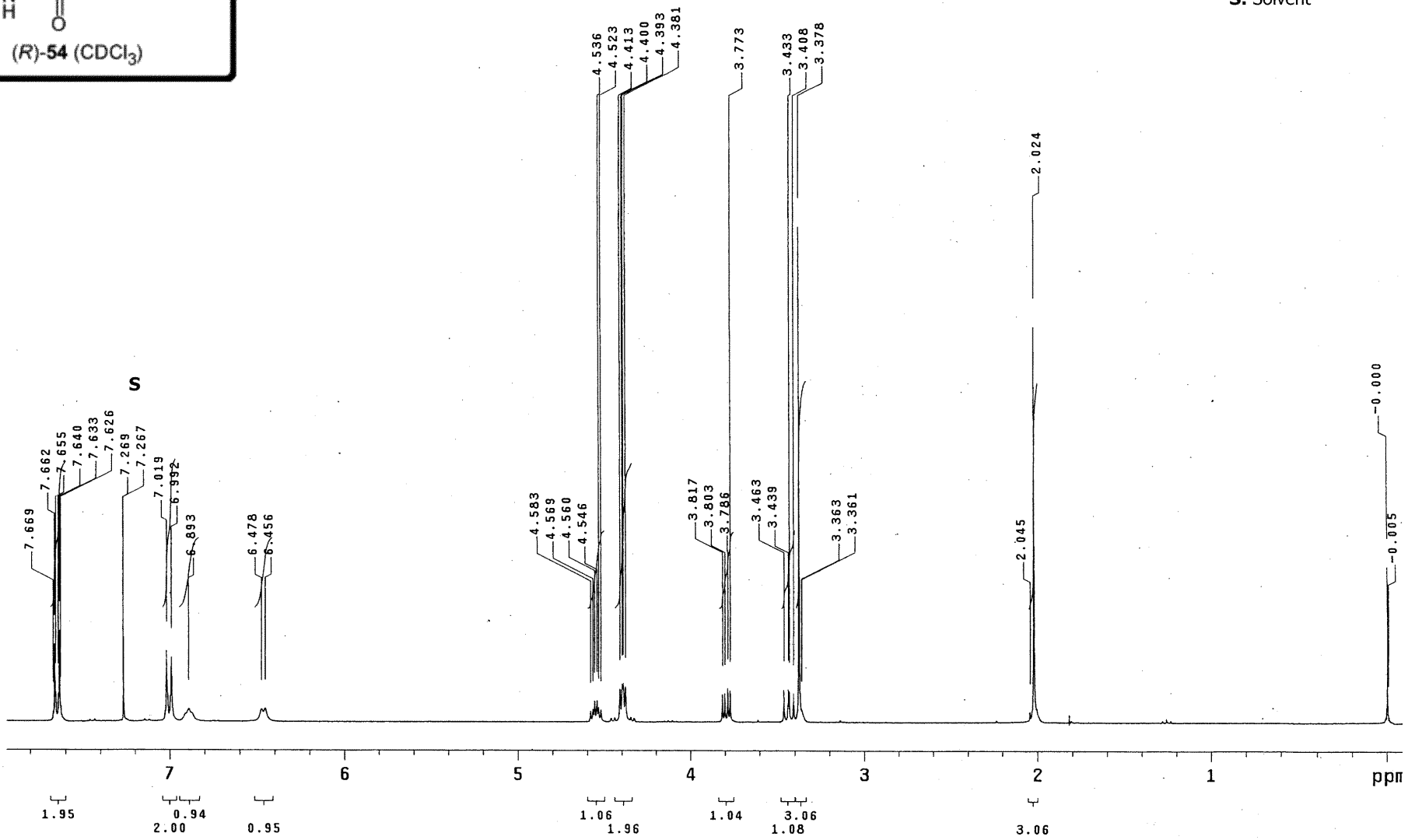

(S)-53 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
8.475
8.455
8.435
8.437
7.659
7.632
7.075
7.047
6.895
6.870
4.247
4.231
4.217
4.184
4.165
4.141
3.480
3.460
3.331
3.238
2.501
1.386
-0.000
W
S
8
7
6
5
4
3
2
1
ppm
0.98
2.00
2.05
0.86
3.00
2.04
3.10
9.04

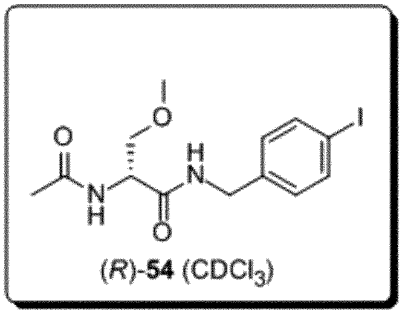

(S)-53 (DMSO-d6)

S
39.703
39.430
39.149
W: Water
X: Impurity
S: Solvent
38.868
39.984
38.595
28.047
136.741
170.003
155.098
139.177
129.251
92.180
78.140
71.796
58.030
54.205
41.441
40.265
220
200
180
160
140
120
100
80
60
40
20
0
ppm

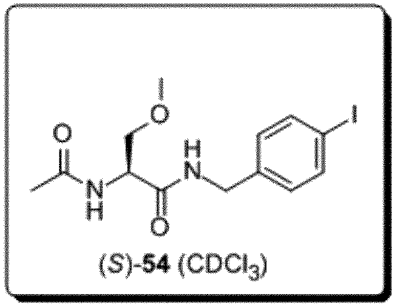


W: Water
X: Impurity
S: Solvent

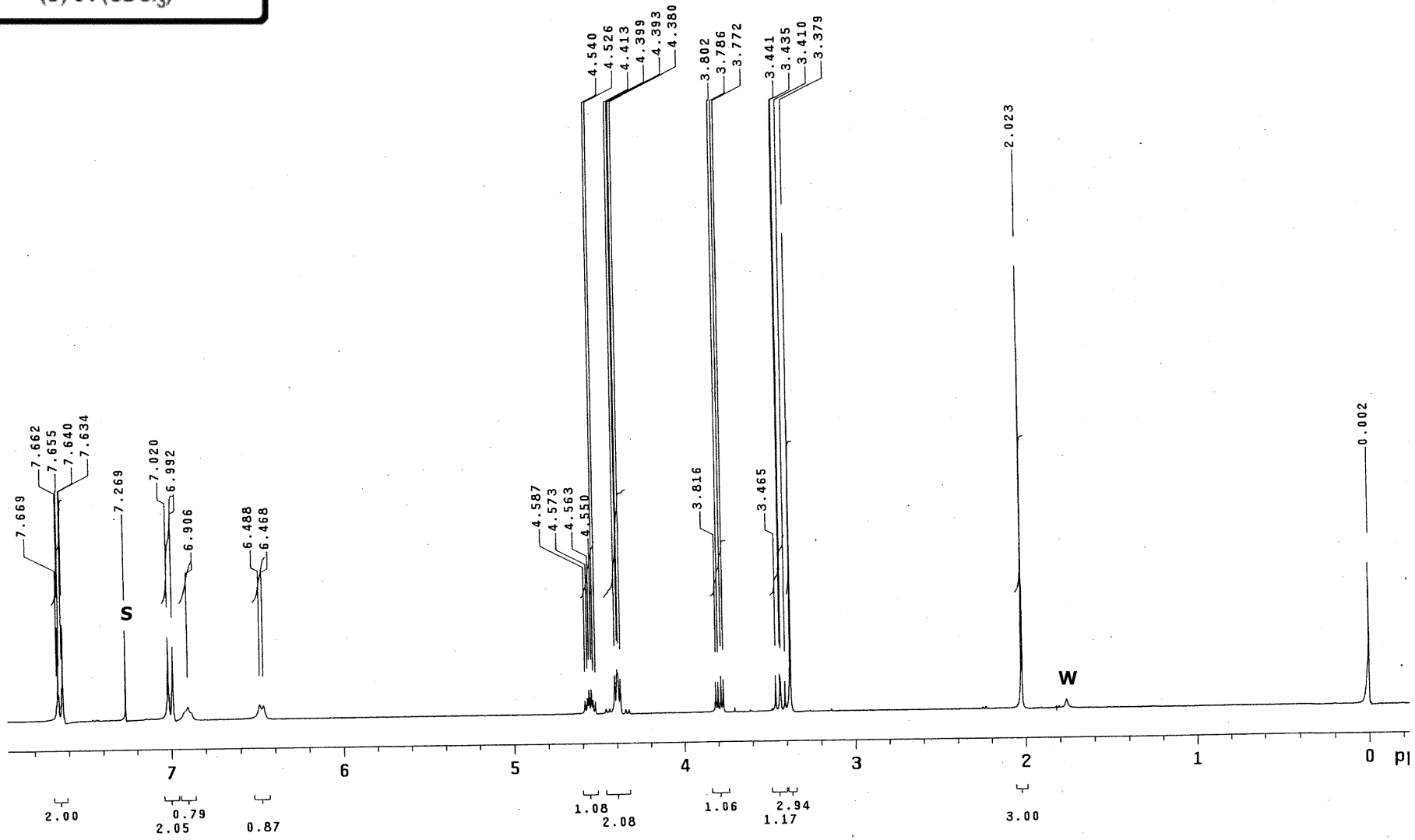


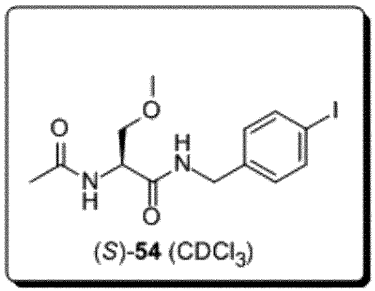

(R)-54 (CDCl3)

S
W: Water
X: Impurity
S: Solvent
137.688
129.333
77.417
77.000
76.575
71.627
59.068
52.443
42.934
23.135
170.343
170.069
92.754
220
200
180
160
140
120
100
80
60
40
20
0
ppm

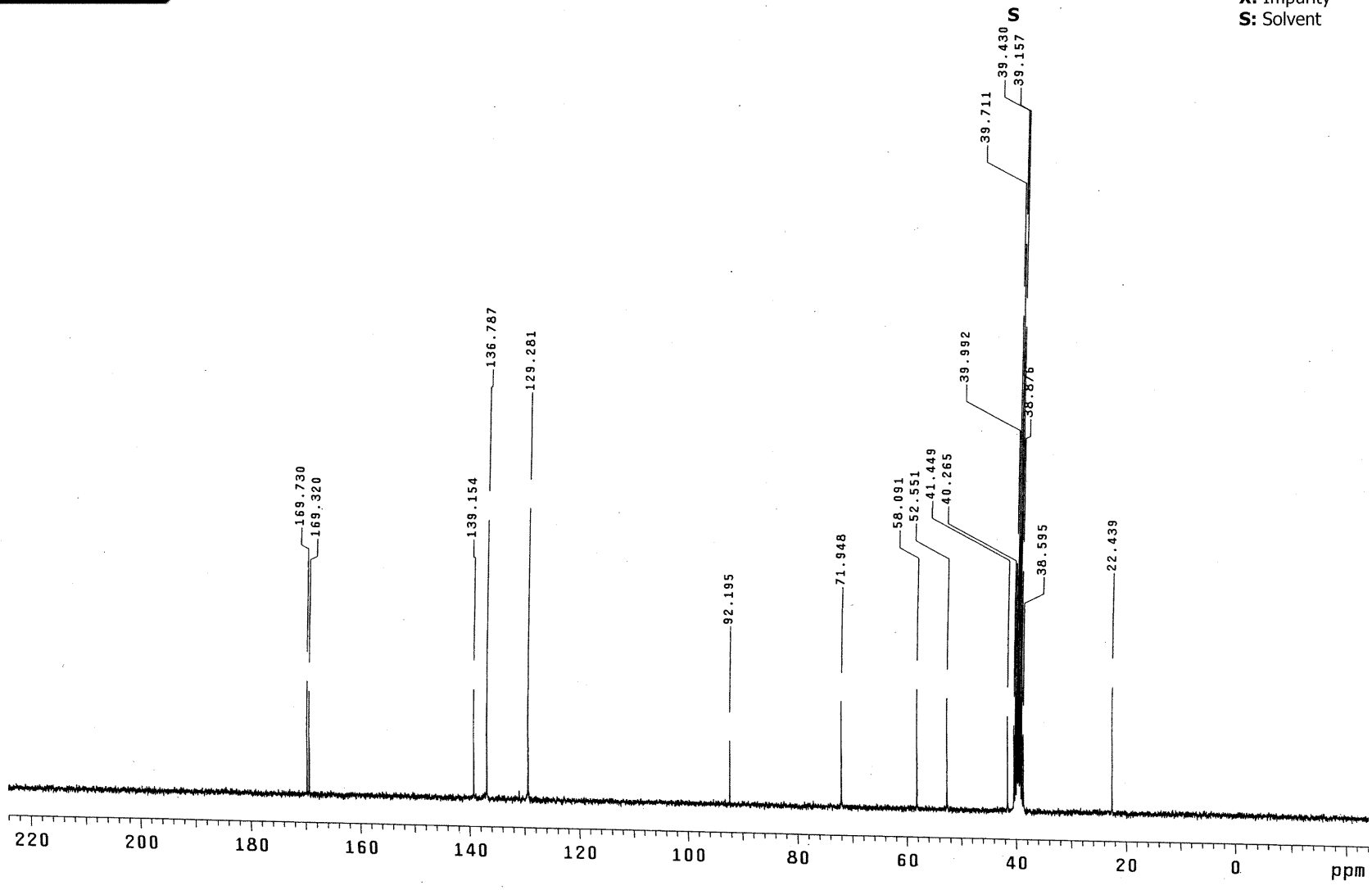


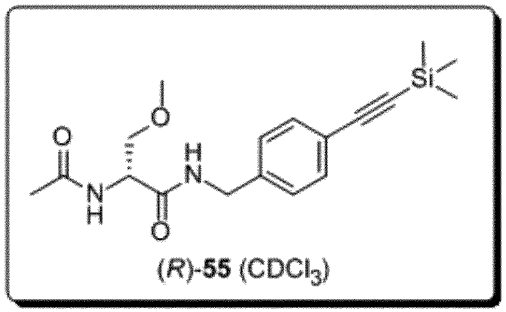
W: Water
X: Impurity
S: Solvent



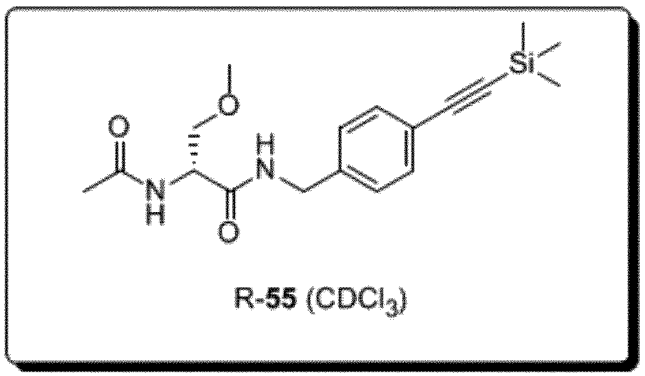


W: Water
X: Impurity
S: Solvent



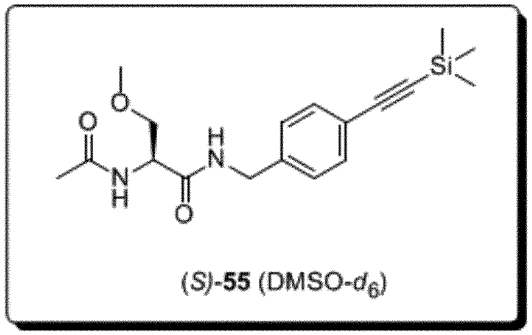


W: Water
X: Impurity
S: Solvent

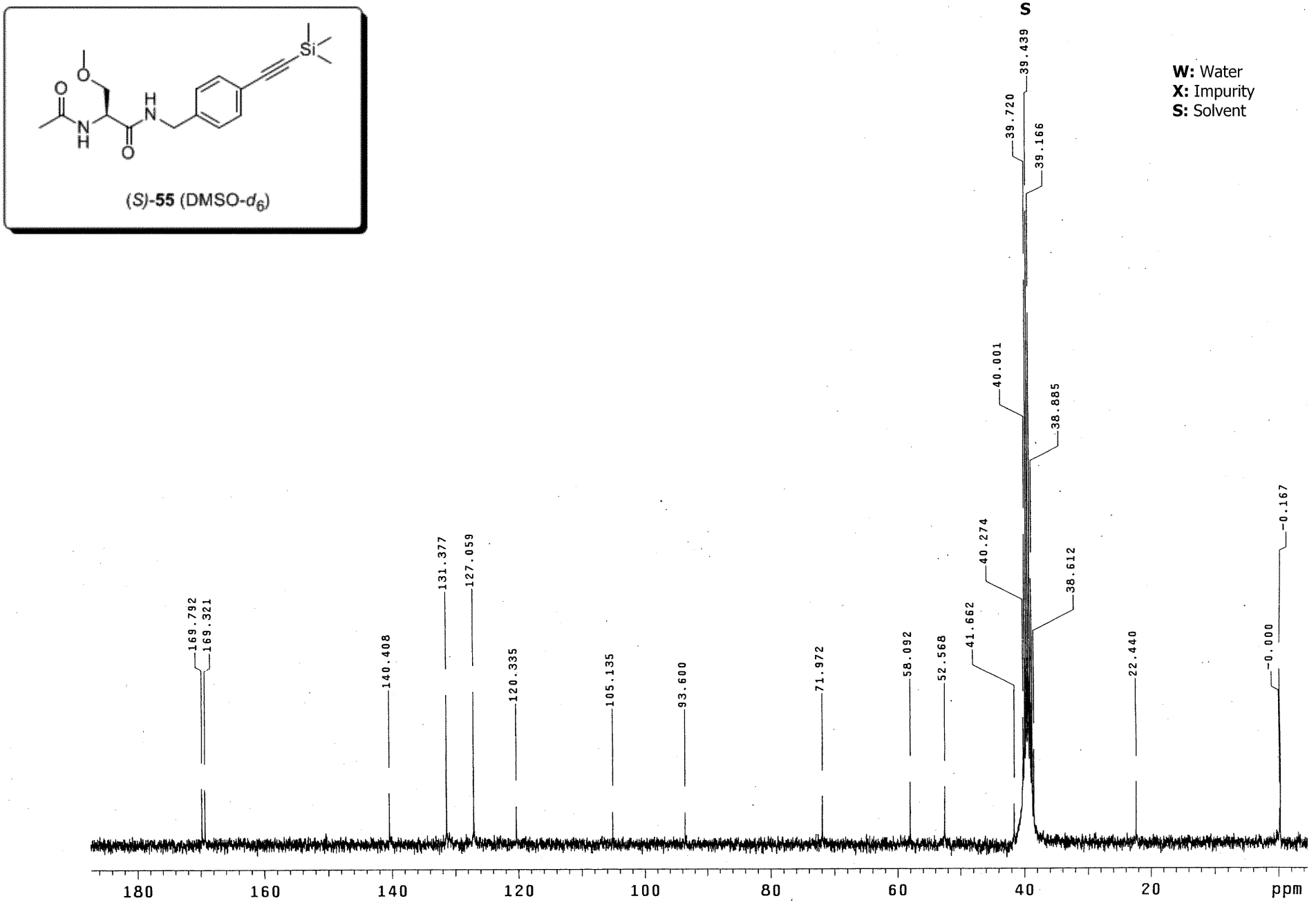


R-**55** ($CDCl_3$)

W: Water
X: Impurity
S: Solvent


(S)-55 (DMSO-d6)

W: Water
X: Impurity
S: Solvent
8.547
8.527
8.506
8.508
8.124
8.097
7.412
7.384
7.251
7.224
4.502
4.483
4.457
4.437
4.302
4.283
3.552
3.531
3.520
3.496
3.477
3.463
3.445
3.335
3.254
2.508
2.503
2.497
1.869
0.233
0.211
0.000
0.222
W
S
9
8
7
6
5
4
3
2
1
ppm
1.03
1.04
2.06
2.09
1.08
2.00
2.10
2.98
2.98
9.10


(S)-55 (DMSO-d6)
W: Water
X: Impurity
S: Solvent
S
169.792
169.321
140.408
131.377
127.059
120.335
105.135
93.600
71.972
58.092
52.568
41.662
40.274
40.001
39.720
39.439
39.166
38.885
38.612
22.440
0.000
-0.167
180
160
140
120
100
80
60
40
20
ppm