SUPPORTING INFORMATION

One-pot two-step radioiodination based on copper-mediated iododeboronation and azide–alkyne cycloaddition reaction

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1. Materials and methods

1.1. General information

All reagents were purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), Nacalai Tesque, Inc. (Kyoto, Japan), Fujifilm Wako Chemical Corp. (Osaka, Japan), Crysdot (Bel Air, MD, USA), and Sigma-Aldrich (St. Louis, MO, USA), and used without purification unless otherwise indicated. Sodium iodide-125 ([^{125}I]NaI) carrier-free solution was acquired from PerkinElmer, Inc. (Waltham, MA, USA).

The ^{1}H NMR and ^{13}C NMR spectra of samples were evaluated using Ascend^{TM} 500 MHz and Bruker Avance III 300 MHz NMR spectrometers (Bruker, Billerica, MA, USA); $CDCl_3$, CD_3OD, and DMSO-d_6 were used as solvents. Chemical shifts are reported as δ in units of parts per million (ppm) relative to an internal standard (tetramethylsilane); multiplicities are symbolized as follows: s (singlet), d (doublet), t (triplet), q (quintet), br. s (broad singlet), dd (doublet of doublet), or m (multiplet); coupling constants are expressed as a *J* value in Hertz (Hz); the number of protons (*n*) for a given resonance is indicated as *n*H, based on spectral integration values.

High-resolution mass spectra were obtained using ion-trap- and time-of-flight-coupled liquid chromatograph mass spectrometer (electrospray ionization spectrometry; Shimadzu, Kyoto, Japan), GC mate II (electron impact spectrometry, JEOL, Tokyo, Japan), or SX-102A (fast atom bombardment spectrometry; JEOL, Tokyo, Japan).

An autoradiograph of the reagents was acquired on a thin-layer chromatography (TLC) sheet (5.0 × 2.0 cm; TLC silica gel 60 F_{254} aluminum plate; Merck, Kenilworth, NJ, USA) using an image analyzer (Typhoon 9410; GE Healthcare, Waukesha, WI, USA). The radioactive signal intensities of each TLC were evaluated by processing the respective images using ImageQuant TL software (GE Healthcare).

An LD-20AD (Shimadzu, Kyoto, Japan) was employed for high-performance liquid chromatography (HPLC), along with a CBM-20A (Shimadzu) communication bus module, a DGU-20A3R (Shimadzu) degassing unit, a CTO-20AC (Shimadzu) column oven, a SPD-20A (Shimadzu) ultraviolet (UV) detector (k = 254 nm), and a γ-survey meter TCS-172 (ALOKA, Mitaka, Japan). Reverse phase (RP)-HPLC was conducted using a Cosmosil 5C_{18}-AR-II column (4.6 ID×150 mm or 10.0 ID×150 mm; Nacalai Tesque, Inc.).

1.2. Synthetic methods

2-[4-(azidomethyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1)

The compounds 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl bromide (118.8 mg, 400.0 μmol) and sodium azide (31.2 mg, 480.0 μmol) were dissolved and stirred in DMF (1 mL) at 25°C for 16 h. The reaction solution was concentrated under reduced pressure, the residue was dissolved in ethyl acetate (EtOAc) and H_2O, and the resultant solution was poured into a separatory funnel. The EtOAc layer was washed with H_2O and dried over magnesium sulfate ($MgSO_4$). This organic layer was concentrated under reduced pressure to yield compound **1** (78.7 mg, 303.7 μmol); yield: 75.9%; ^{1}H NMR [500 MHz, $CDCl_3$] δ: 1.35 (s, 12H), 4.35 (s, 2H), 7.32 (d, J = 7.9 Hz, 2H), 7.83 (d, J = 7.9 Hz, 2H); ^{13}C NMR [126 MHz, $CDCl_3$] δ: 24.89, 54.80, 83.93, 127.44, 135.30, 138.31; high-resolution fast atom bombardment mass spectrometry: calculated for $C_{13}H_{19}O_2N_3B$ $(M+H)^+$ 260.1573 *m/z* and detected to be 260.1582 *m/z*.

1-(Azidomethyl)-4-iodobenzene (2)

The compounds 4-iodobenzyl bromide (148.5 mg, 500.0 μmol) and sodium azide (39.0 mg, 600.0 μmol) were dissolved and stirred in DMF (1 mL) at 25°C for 16 h. The reaction solution was concentrated under reduced pressure, the residue was dissolved in EtOAc and H_2O, and the solution was poured into a separatory funnel. The EtOAc layer was washed with H_2O and dried over $MgSO_4$. This organic layer was concentrated under reduced pressure to yield compound **2** (91.9 mg, 354.8 μmol); yield: 71.0%; ^{1}H NMR [500 MHz, $CDCl_3$] δ: 4.29 (s, 2H), 7.07 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H); ^{13}C NMR [126 MHz, $CDCl_3$] δ: 54.21, 93.92, 129.98, 135.05, 137.98; high-resolution electron ionization mass spectrometry (HREIMS): calculated for $C_7H_6N_3I$ $(M)^+$ 258.9607 *m/z* and detected to be 258.9599 *m/z*.

1-(4-Iodobenzyl)-4-phenethyl-1H-1,2,3-triazole (3)

Compound **2** (25.9 mg, 100 μmol), copper (II) sulfate pentahydrate (12.5 mg, 50 μmol), sodium ascorbate (29.7 mg, 150 μmol), tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA; 26.5 mg, 50 μmol), and 4-phenyl-1-butyne (13.0 mg, 100 μmol) were mixed in a round-bottom flask, and methanol (1 mL) was supplemented to the resultant mixture. The reaction proceeded for 16 h at 25°C. Subsequently, the reaction solution was concentrated under reduced pressure, and the mixture was purified using flash chromatography (SiO_2 column, hexane:EtOAc = 90:10 → 30:70) to yield compound **3** (35.3 mg, 90.7 μmol); yield: 90.7 %; ^{1}H NMR [500 MHz, $CDCl_3$] δ: 2.94−3.05 (m, 4H), 5.40 (s, 2H), 6.93 (d, J = 8.2 Hz, 2H), 7.00 (s, 1H), 7.11−7.15 (m, 2H), 7.16−7.21 (m, 1H), 7.21−7.25

(m, 2H), 7.68 (d, J = 8.1 Hz, 2H); ^{13}C NMR [126 MHz, $CDCl_3$] δ: 27.50, 35.47, 53.32, 94.30, 120.93, 126.08, 128.35, 128.47, 129.62, 134.62, 138.15, 141.03, 147.85; HREIMS: calculated for $C_{17}H_{16}N_3I$ $(M)^+$ 389.0389 *m/z* and detected to be 389.0393 *m/z*.

1-(1-(4-Iodobenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (4)

Compound **2** (25.9 mg, 100 μmol), copper (II) sulfate pentahydrate (12.5 mg, 50 μmol), sodium ascorbate (29.7 mg, 150 μmol), and 4-pentyn-2-ol (9.25 mg, 110 μmol) were mixed in a round-bottom flask, and aqueous methanol (MeOH:H_2O = 4:1; 1.25 mL) was supplemented into the mixture. The reaction proceeded for 5 h at 25°C. Subsequently, the reaction solution was concentrated under reduced pressure, and the mixture was purified using flash chromatography (SiO_2 column, $CHCl_3$:MeOH = 100:0 → 20:80) to yield compound **4** (29.7 mg, 86.5 μmol); yield: 86.5%; ^{1}H NMR [300 MHz, $CDCl_3$] δ: 1.24−1.28 (m, 3H), 2.68−2.91 (m, 3H), 4.07−4.22 (m, 1H), 5.45 (s, 2H), 7.01 (d, J = 8.4 Hz, 2H), 7.29 (s, 1H), 7.71 (d, J = 8.4 Hz, 2H); ^{13}C NMR [75 MHz, $CDCl_3$] δ: 22.91, 34.82, 53.51, 67.09, 94.52, 121.59, 129.81, 134.38, 138.27, 145.93; high-resolution electrospray ionization mass spectrometry (HRESIMS): calculated for $C_{12}H_{15}N_3OI$ $(M+H)^+$ 344.0254 *m/z* and detected to be 344.0257 *m/z*.

1-[(4-Iodophenyl)methyl]-1H-1,2,3-triazole-4-propanoic acid (5)

Compound **2** (25.9 mg, 100 μmol), copper (II) sulfate pentahydrate (12.5 mg, 50 μmol), sodium ascorbate (29.7 mg, 150 μmol), TBTA (26.5 mg, 50 μmol), and 4-pentynoic acid (10.8 mg, 110 μmol) were mixed in a round-bottom flask, and aqueous methanol (MeOH:H_2O = 4:1; 1.25 mL) was supplemented to the mixture. The reaction proceeded for 5 h at 25°C. Subsequently, the reaction solution was concentrated under reduced pressure, and the mixture was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 30% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield compound **5** (13.1 mg, 36.7 μmol); yield: 36.7%; ^{1}H NMR [500 MHz, DMSO-d_6] δ: 2.57 (t, J = 7.4 Hz, 2H), 2.83 (t, J = 7.5 Hz, 2H), 5.51 (s, 2H), 7.09 (d, J = 7.6 Hz, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.89 (s, 1H), 12.17 (br. s, 1H); ^{13}C NMR [126 MHz, DMSO-d_6] δ: 20.53, 32.94, 51.92, 94.23, 122.09, 130.04, 135.88, 137.38, 145.97, 173.48; HRESIMS: calculated for $C_{12}H_{13}N_3O_2I$ $(M+H)^+$ 358.0047 *m/z* and detected to be 358.0060 *m/z*.

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1-(4-iodobenzyl)-1H-1,2,3-triazol-4-yl)propanoic acid (6)

Compound **2** (25.9 mg, 100 μmol), copper (II) sulfate pentahydrate (12.5 mg, 50 μmol), sodium ascorbate (29.7 mg, 150 μmol), TBTA (26.5 mg, 50 μmol), and Fmoc-*L*-propargylglycine (36.9 mg, 110 μmol) were mixed in a round-bottom flask, and aqueous methanol (MeOH:H_2O = 4:1; 1.25 mL) was supplemented to the mixture. The reaction proceeded for 5 h at 25°C. Subsequently, the reaction solution was concentrated under reduced pressure, and the mixture was purified using flash chromatography (SiO_2 column, $CHCl_3$:MeOH = 100:0 → 30:70) to yield crude oily compounds (31.6 mg). The resultant mixture was dissolved in 50% MeCN/H_2O, and 50% MeCN/H_2O (containing 0.1% TFA) was added to form a white precipitate. Next, the precipitate was washed with 50% MeCN/H_2O (containing 0.1% TFA) to yield compound **6** (14.4 mg, 24.2 μmol); yield: 24.2%; ^{1}H NMR [500 MHz, DMSO-d_6] δ: 2.93−3.02 (m, 1H), 3.09−3.15 (m, 1H), 4.13−4.28 (m, 4H), 5.51 (s, 2H), 6.99−7.04 (m, 2H), 7.28−7.34 (m, 2H), 7.39−7.45 (m, 2H), 7.63−7.70 (m, 4H), 7.70−7.76 (m, 1H), 7.87−7.92 (m, 3H), 12.80 (br. s, 1H); ^{13}C NMR [126 MHz, DMSO-d_6] δ: 27.18, 46.44, 51.90, 53.72, 65.57, 94.14, 120.02, 123.09, 125.14, 126.97, 127.54, 129.86, 135.84, 137.31, 140.59, 143.31, 143.62, 143.65, 155.81, 172.80; HRESIMS: calculated for $C_{27}H_{24}N_4O_4I$ $(M+H)^+$ 595.0837 *m/z* and detected to be 595.0836 *m/z*.

(S)-2-((tert-butoxycarbonyl)amino)-3-(1-(4-iodobenzyl)-1H-1,2,3-triazol-4-yl)propanoic acid (7)

Compound **2** (25.9 mg, 100 μmol), copper (II) sulfate pentahydrate (12.5 mg, 50 μmol), sodium ascorbate (29.7 mg, 150 μmol), and Boc-*L*-propargylglycine (23.5 mg, 110 μmol) were mixed in a round-bottom flask, and aqueous methanol (MeOH:H_2O = 4:1; 1.25 mL) was supplemented to the mixture. The reaction proceeded for 5 h at 25°C. Subsequently, the reaction solution was concentrated under reduced pressure, and the mixture was purified using flash chromatography (SiO_2 column, $CHCl_3$:MeOH = 100:0 → 30:70) to yield crude oily compounds (38.5 mg). The resultant mixture was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 45% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield compound **7** (11.2 mg, 23.7 μmol); yield: 23.7%; ^{1}H NMR [500 MHz, DMSO-d_6] δ: 1.31 (s, 9H), 2.86−2.96 (m, 1H), 3.00−3.09 (m, 1H), 4.11−4.19 (m, 1H), 5.53 (s, 2H), 7.03−7.12 (m, 3H), 7.69−7.75 (m, 2H), 7.84 (s, 1H), 12.64 (br. s, 1H); ^{13}C NMR [126 MHz, DMSO-d_6] δ: 27.12, 28.00, 51.90, 53.24, 78.01, 94.21, 122.99, 130.00, 135.86, 137.36, 143.38, 155.20, 173.04; HREIMS: calculated for $C_{17}H_{21}N_4O_4I$ $(M)^+$ 472.0608 *m/z* and detected to be 472.00598 *m/z*.

CCPS-2

(*S*)-Di-*tert*-butyl 2-(3-((*S*)-6-amino-1-(tert-butoxy)-1-oxohexan-2-yl)ureido)pentanedioate (CCPS-1; 48.8 mg, 100.0 μmol), 4-pentynoic acid (11.8 mg, 120.0 μmol), and 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate (HATU; 45.6 mg, 120 μmol) were dissolved in dichloromethane (DCM; 1 mL). Then, *N*,*N*-diisopropylethylamine (DIEA; 20.4 μL, 120.0 μmol) was added into the mixture. The reaction proceeded for 16 h at 25°C. After the reaction solution was concentrated under reduced pressure, the crude solid was dissolved in EtOAc, and the solution was poured into a separatory funnel. The organic layer was washed with H_2O, saturated aqueous $NaHCO_3$, and brine. The obtained solution was dried over $MgSO_4$ and concentrated under reduced pressure to yield an oily compound. Finally, the crude compound was purified using RP-HPLC [column: $5C_{18}$-AR-II (10.0 ID×150 mm), phase: 55% MeCN, flow rate: 4.5 mL/min, temperature: 40°C] to yield CCPS-2 (42.5 mg, 74.9 μmol); yield: 74.9%; ^{1}H NMR [500 MHz, $CDCl_3$] δ: 1.30−1.41 (m, 2H), 1.44 (s, 9H), 1.45 (s, 9H), 1.47 (s, 9H), 1.51−1.63 (m, 3H), 1.73−1.81 (m, 1H), 1.82−1.91 (m, 1H), 2.01 (t, J = 2.4 Hz, 1H), 2.04−2.13 (m, 1H), 2.26−2.39 (m, 2H), 2.42 (t, J = 7.2 Hz, 2H), 2.54 (td, J = 7.0, 2.6 Hz, 2H), 3.17−3.25 (m, 1H), 3.26−3.35 (m, 1H), 4.24−4.37 (m, 2H), 5.21−5.28 (m, 1H), 5.30−5.37 (m, 1H), 6.34 (br. s, 1H); ^{13}C NMR [126 MHz, $CDCl_3$] δ: 14.99, 22.45, 28.02, 28.08, 28.20, 28.69, 31.63, 32.57, 35.28, 39.02, 53.12, 53.27, 69.21, 80.62, 81.77, 82.27, 83.23, 157.02, 171.25, 172.39, 172.65; HRESIMS: calculated for $C_{29}H_{49}N_3O_8Na$ $(M+Na)^+$ 590.3412 *m/z* and detected to be 590.3400 *m/z*.

CCPS-3

CCPS-2 (34.7 mg, 61.1 μmol) was dissolved in TFA (2 mL). The reaction proceeded at 25°C for 2 h. Then, the reaction solution was concentrated under reduced pressure and the residue was dissolved in 7% MeCN (containing 0.1% TFA). The mixture was purified using RP-HPLC [column: $5C_{18}$-AR-II (10.0 ID×150 mm), phase: 7% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCPS-3 (22.6 mg, 56.6 μmol); yield: 92.6 %; ^{1}H NMR [500 MHz, CD_3OD] δ: 1.38−1.48 (m, 2H) 1.48−1.60 (m, 2H) 1.61−1.71 (m, 1H), 1.78−1.95 (m, 2H), 2.09−2.19 (m, 1H), 2.24−2.29 (m, 1H), 2.34−2.48 (m, 6H) 3.15−3.22 (m, 2H), 4.22−4.32 (m, 2H); ^{13}C NMR [126 MHz, CD_3OD] δ: 15.83, 23.99, 29.06, 29.98, 31.22, 33.31, 36.13, 40.23, 53.69, 54.13, 70.39, 83.53, 160.17, 174.06, 176.07, 176.61; HRESIMS: calculated for $C_{17}H_{26}N_3O_8$ $(M+H)^+$ 400.1714 *m/z* and detected to be 400.1725 *m/z*.

Compound 8 (CCPS)

CCPS-3 (16.3 mg, 40.8 μmol), **2** (12.7 mg, 49.0 μmol), copper (II) sulfate pentahydrate (8.2 mg, 32.6 μmol), sodium ascorbate (32.3 mg, 163.2 μmol), and TBTA (17.3 mg, 32.6 μmol) were added into a round-bottom flask, and MeOH/H_2O (= 4:1, 1 mL) was added to the mixture. The reaction proceeded for 3 h at 25°C. Then, the reaction solution was concentrated under reduced pressure, and the residual mixture was dissolved with 25% MeCN (containing 0.1% TFA). After removing the precipitate with a filter, the mixture solution was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 25% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCPS (15.2 mg, 23.1 μmol); yield: 56.6%; ^{1}H NMR [500 MHz, CD_3OD] δ: 1.28−1.38 (m, 2H), 1.39−1.48 (m, 2H), 1.56−1.68 (m, 1H), 1.75−1.84 (m, 1H), 1.84−1.94 (m, 1H), 2.09−2.19 (m, 1H), 2.34−2.47 (m, 2H), 2.51 (t, J = 7.3 Hz, 2H), 2.97 (t, J = 7.3 Hz, 2H), 3.03−3.16 (m, 2H), 4.21−4.34 (m, 2H), 5.51 (s, 2H), 7.04−7.12 (m, 2H), 7.68−7.75 (m, 3H); ^{13}C NMR [126 MHz, CD_3OD] δ: 22.59, 23.86, 28.96, 29.89, 31.20, 33.16, 36.41, 40.06, 53.65, 54.02, 54.24, 94.82, 123.68, 123.73, 131.13, 136.80, 139.29, 160.21, 174.52, 176.50, 176.53; HRESIMS: calculated for $C_{24}H_{32}N_6O_8I$ $(M+H)^+$ 659.1321 *m/z* and detected to be 659.1332 *m/z*.

CCRGD-1

The linear peptide immobilized was manually assembled from 2-chlorotrityl chloride resin following a standard 9-fluorenylmethyloxycarbonyl (Fmoc)-protocol using Fmoc-amino acid derivatives with certain modifications to previous reports.

Coupling of Fmoc-amino acids

2-Chlorotrityl chloride resin (188.7 mg, loading capacity 1.06 mmol/g) was swelled in DCM for 6 h. The resin was washed thoroughly with DMF (1 × 2 mL). Fmoc-Gly-OH (178.4 mg, 0.6 mmol, 3.0 eq.), DMF (1.5 mL), and DIEA (102.0 μL, 0.6 mmol, 3.0 eq.) were mixed and added to a reaction vessel. The reaction mixture was agitated for 16 h at 25°C. After the reaction solution was removed, the resin was washed thoroughly with DMF (5 × 2 mL). Then, DMF (1.5 mL), methanol (0.2 mL), and DIEA (102.0 μL, 0.6 mmol, 3.0 eq.) were added to the reaction vessel. The reaction mixture was agitated for 1 h at 25°C. After the reaction solution was removed, the resin was washed thoroughly with DMF (5 × 2 mL), and 20% piperidine in DMF (1.5 mL) was added to the reaction vessel and agitated for 30 min to remove Fmoc groups. Once completed, the resin was washed thoroughly with DMF (5 × 2 mL). A Kaiser test showed that the resin had deprotected. Fmoc-Arg(Pbf)-OH (389.3 mg, 0.6 mmol, 3.0 eq.), HATU (228.1 mg, 0.6 mmol, 3.0 eq.), DMF (1.5 mL), and DIEA (102.0 μL, 0.6 mmol, 3.0 eq.) were added to the reaction vessel. The reaction mixture was agitated for 6 h at 25°C. After the reaction

solution was removed, the resin was washed thoroughly with DMF (5 × 2 mL). A Kaiser test was performed to confirm the completion of coupling by showing an absence of free amine on the resin. 20% piperidine in DMF (1.5 mL) was added to the reaction vessel and agitated for 30 min to eliminate Fmoc groups. Once completed, the resin was washed thoroughly with DMF (5 × 2 mL). A Kaiser test showed that the resin was deprotected. Cycles of coupling, washing, deprotection, and washing were repeated until the desired peptide sequence was synthesized. Finally, the resin was washed with methanol (5 × 2 mL), and the resin was dried under reduced pressure.

Removal of peptides protected from the resin

The resin was treated with 20% hexafluoro-2-propanol / DCM (2 mL) for 3 h at 25°C to cleave the liner peptide from the solid support. The resin was removed *via* filtration and was washed with DCM. The obtained solution was concentrated under reduced pressure. The crude compound (258.7 mg) was analyzed *via* a mass spectrometric technique to confirm that CCRGD-1 is contained in the crude products. HRESIMS: calculated for $C_{54}H_{79}N_9O_{13}SNa_2$ $(M+2Na)^{2+}$ 569.7651 *m/z* and detected to be 569.7625 *m/z*.

CCRGD-5

The crude CCRGD-1 (258.7 mg) was dissolved in DCM and HATU (89.9 mg, 236.4 μmol), and DIEA (40.2 μL, 236.4 μmol) was added into the reaction solution. After the reaction proceeded for 16 h at 25°C, the reaction solution was concentrated under reduced pressure. Then, the residue was purified using flash chromatography (SiO_2 column, $CHCl_3$:MeOH = 100:0 → 70:30) to yield CCRGD-2 (169.8 mg) as crude products. HRESIMS: calculated for $C_{54}H_{77}N_9O_{12}SNa_2$ $(M+2Na)^{2+}$ 560.7598 *m/z* and detected to be 560.7588 *m/z*.

Subsequently, CCRGD-2 (169.8 mg) was dissolved in 2% hydrazine/DMF (2.0 mL), and the reaction was stirred at 25°C for 2 h. After the reaction mixture was concentrated using a rotary evaporator, the residue was purified using flash chromatography (SiO_2-NH_2 column, $CHCl_3$:MeOH = 95:5 → 70:30) to yield CCRGD-3 (113.0 mg) as crude products. HRESIMS: calculated for $C_{44}H_{65}N_9O_{10}SNa_2$ $(M+2Na)^{2+}$ 478.7180 *m/z* and detected to be 478.7167 *m/z*.

CCRGD-3 (46.0 mg) was dissolved in DCM (2.0 mL) followed by the addition of 4-pentynoic acid (5.9 mg, 60.5 μmol), HATU (23.0 mg, 60.5 μmol), and DIEA (10.3 μL, 60.5 μmol). The reaction proceeded for 2 h at 25°C. Then, the reaction solution was concentrated under reduced pressure, and the residue was purified using flash chromatography (SiO_2 column, $CHCl_3$:MeOH = 98:2 → 70:30) to yield CCRGD-4 (15.1 mg) as crude products. HRESIMS: calculated for $C_{49}H_{69}N_9O_{11}SNa$ $(M+Na)^{+}$ 1014.4729 *m/z* and detected to be 1014.4729 *m/z*.

Finally, the CCRGD-4 (11.2 mg) was dissolved in TFA (2.0 mL), and the reaction was stirred for 2 h at 25°C to eliminate protected groups. The reaction solution was concentrated by a rotary evaporator, and the residue was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 20% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCRGD-5 (7.1 mg, 10.4 μmol). HRESIMS: calculated for $C_{32}H_{46}N_9O_8$ $(M+H)^+$ 684.3464 *m/z* and detected to be 684.3461 *m/z*.

Compound 9 (CCRGD)

CCRGD-5 (2.7 mg, 4.0 μmol), **2** (1.2 mg, 4.8 μmol), copper (II) sulfate pentahydrate (0.8 mg, 3.2 μmol), sodium ascorbate (3.2 mg, 16.0 μmol), and TBTA (1.7 mg, 3.2 μmol) were added into a round-bottom flask, and MeOH/H_2O (= 4:1, 1 mL) was added to the mixture. The reaction proceeded for 3 h at 25°C. Then, the reaction solution was concentrated under reduced pressure, and the residual mixture was dissolved with 30% MeCN/H_2O (containing 0.1% TFA). After removing the precipitate with a filter, the mixture solution was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 30% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCRGD (1.4 mg, 1.5 μmol); yield: 37.1%; HRESIMS: calculated for $C_{39}H_{53}N_{12}O_8I$ $(M+2H)^{2+}$ 472.1572 *m/z* and detected to be 472.1558 *m/z*.

CCKA-1

CCKA-1 was synthesized using the same method as that for CCRGD-1. The linear peptide immobilized was manually assembled from 2-chlorotrityl chloride resin (94.3 mg, loading capacity 1.06 mmol/g) following a standard Fmoc-protocol using Fmoc-amino acid derivatives and 4-pentynoic acid.

Removal of peptides protected from the resin

The linear peptide was cleaved from the solid support by the addition of TFA/triisopropylsilane (TIS)/thioanisole/H_2O (94.0:1.0:2.5:2.5, 2.0 mL) for 3 h at 50°C. The resin was removed *via* filtration and was washed with TFA. The obtained solution was concentrated under reduced pressure. The residual oily compound was treated with cold diethyl ether to form a precipitate. The solid was washed with cold diethyl ether thrice. Finally, the mixture was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150mm), phase: 19% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCKA-1 (4Pta-Lys-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg-OH; 10.2 mg, 8.0 μmol). HRESIMS: calculated for $C_{61}H_{92}N_{17}O_{13}$ $(M+3H)^{3+}$ 423.5681 *m/z* and detected to be 423.5700 *m/z*.

Compound 10 (CCKA)

CCKA-1 (2.5 mg, 2.0 μmol), **2** (0.6 mg, 2.4 μmol), copper (II) sulfate pentahydrate (0.4 mg, 1.6 μmol), sodium ascorbate (1.6 mg, 8.0 μmol), and TBTA (0.8 mg, 1.6 μmol) were added into a round-bottom flask, and MeOH/H_2O (= 4:1, 1 mL) were added to the mixture. The reaction proceeded for 3 h at 25°C. Then, the reaction solution was concentrated under reduced pressure, and the residual mixture was dissolved with 26% MeCN (containing 0.1% TFA). After removing the precipitate with a filter, the mixture solution was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 26% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCKA (1.3 mg, 0.9 μmol); yield: 37.5%; HRESIMS: calculated for $C_{68}H_{98}N_{20}O_{13}I$ $(M+3H)^{3+}$ 509.8884 *m/z* and detected to be 509.8892 *m/z*.

CCTA-1 and CCTA-2

CCTA-1 was synthesized using the same method as that for CCRGD-1. The linear peptide immobilized was manually assembled from 2-chlorotrityl chloride resin (188.7 mg, loading capacity 1.06 mmol/g) following a standard Fmoc-protocol using Fmoc-amino acid derivatives and 4-pentynoic acid.

Removal of peptides protected from the resin

The linear peptide was cleaved from the solid support by the addition of TFA/TIS/ 1,2-ethanedithiol/H_2O (94.0:1.0:2.5:2.5, 3 mL) for 3 h at 25°C. The resin was removed by filtration and was washed with TFA. The obtained solution was concentrated using a rotary evaporator. The residual oily compound was treated with cold diethyl ether to form a precipitate. The solid was washed with cold diethyl ether thrice. Finally, the mixture was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150mm), phase: 29% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 25°C] to yield CCTA-1 (4Pta-*β*Ala-*D*Phe-Cys-Tyr-*D*Trp-Lys-Thr-Cys-Thr-OH; 25.0 mg, 20.8 μmol). HRESIMS: calculated for $C_{57}H_{77}N_{11}O_{14}S_2$ $(M+2H)^{2+}$ 601.7541 *m/z* and detected to be 601.7531 *m/z*.

Cyclization by air-oxidation

The purified CCTA-1 (25.0 mg, 20.8 μmol) was dissolved in 2.5 mL of a saturated NH_4HCO_3 / DMF: H_2O (= 1:1). The reaction solution was air-oxidized for 12 h at 25°C. Finally, the mixture was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150mm), phase: 28% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 25°C] to yield CCTA-2 (14.8 mg, 12.3 μmol); yield: 59.3%; HRESIMS: calculated for $C_{57}H_{75}N_{11}O_{14}S_2$ $(M+2H)^{2+}$ 600.7463 *m/z* and detected to be 600.7462 *m/z*.

Compound 11 (CCTA)

CCTA-2 (2.4 mg, 2.0 μmol), **2** (0.6 mg, 2.4 μmol), copper (II) sulfate pentahydrate (0.4 mg, 1.6 μmol), sodium ascorbate (1.6 mg, 8.0 μmol), and TBTA (0.8 mg, 1.6 μmol) were added into a round-bottom flask, and MeOH/H_2O (= 4:1, 1 mL) was added to the mixture. The reaction proceeded for 3 h at 25°C. Then, the reaction solution was concentrated under reduced pressure, and the residual mixture was dissolved with 35% MeCN (containing 0.1% TFA). After removing the precipitate with a filter, the mixture solution was purified using RP-HPLC [column: 5C_{18}-AR-II (10.0 ID×150 mm), phase: 35% MeCN/H_2O (containing 0.1% TFA), flow rate: 4.5 mL/min, temperature: 40°C] to yield CCTA (1.4 mg, 1.0 μmol); yield: 48.0%; HRESIMS: calculated for $C_{64}H_{81}N_{14}O_{14}S_2I$ $(M+2H)^{2+}$ 730.2266 *m/z* and detected to be 730.2276 *m/z*.

1.3. Radiosynthetic methods

Radiosynthesis of [^{125}I] (compound 3)

Compound **1** (100 nmol) in 20 μL of solvent* and the copper catalyst** (80 nmol or 20 nmol) in 20 μL of solvent* were poured into a microtube along with a 10-μM NaOH aqueous solution of ^{125}I (0.3 μL, 1.0−1.4 MBq). The reaction solution was gently vortexed for 10 seconds. The reaction proceeded at 25°C for 3 min. Subsequently, 4-phenyl-1-butyne (200 nmol) in solvent* (20 μL), and sodium ascorbate (400 nmol) and TBTA (80 nmol) in an aqueous solution (solvent*:H_2O = 1:1; 40 μL) were incorporated into the reaction solution, following which the resultant mixture was gently vortexed for 10 seconds. The reaction proceeded at 25°C for 10–60 min. The mixture was analyzed *via* radio-TLC (hexane:EtOAc = 1:1) and radio-HPLC [column: 5C_{18}-AR-II (4.6 ID×150mm), phase: 55% MeCN/H_2O (containing 0.1% TFA), flow rate: 1.0 mL/min, temperature: 40°C]. RCC (%) was determined by radio-TLC analysis.

*Solvent = MeOH, EtOH, MeCN, DMF, or DMSO.

**Copper catalyst = $Cu(py)_4(OTf)_2$, $CuSO_4{\cdot}5H_2O$, $Cu(OTf)_2$, $CuCl_2$, $Cu(OMe)_2$, or $[Cu(CH_3CN)]PF_6$.

Radiosynthetic method-I (Confirmation of synthetic intermediates)

Compound **1** (100 nmol) in 20 μL of MeOH and $Cu(py)_4(OTf)_2$ (80 nmol) in 20 μL of MeOH were added to a microtube along with a 10-μM NaOH aqueous solution of ^{125}I (0.3 μL, 1.3−1.6 MBq). Subsequently, the reaction solution was gently vortexed for 10 seconds. The reaction proceeded at 25°C for 3 min. The resultant mixture was analyzed *via* radio-TLC (hexane:EtOAc = 1:1) and radio-HPLC [column: 5C_{18}-AR-II (4.6 ID×150mm), phase: 55% MeCN/H_2O (containing 0.1% TFA), flow rate: 1.0 mL/min, temperature: 40°C]. RCC (%) was determined by radio-TLC analysis.

Radiosynthetic method-II (Assessment reversing the order of reactions)

Compound **1** (100 nmol) in 20 μL of MeOH, $Cu(py)_4(OTf)_2$ (80 nmol) in 20 μL of MeOH, 4-phenyl-1-butyne (200 nmol) in 20 μL of MeOH, and sodium ascorbate (400 nmol) and TBTA (80 nmol) in aqueous methanol (MeOH:H_2O = 1:1; 40 μL) were collected in a microtube. The reaction solution was gently vortexed for 10 seconds. The reaction was performed at 25°C for 10 min. Subsequently, a 10-μM NaOH aqueous solution of ^{125}I (0.3 μL, 1.2−1.4 MBq) was added to the reaction solution. The reaction solution was gently vortexed for 10 seconds. The reaction was performed at 25°C for 3 min. The mixture was analyzed using radio-TLC (hexane:EtOAc = 1:1) and radio-HPLC [column: 5C_{18}-AR-II (4.6 ID×150mm), phase: 55% MeCN/H_2O (containing 0.1% TFA), flow rate: 1.0 mL/min, temperature: 40°C]. RCC (%) was determined *via* radio-TLC analysis.

Radiosynthesis of ^{125}I-labeled small molecules and peptides

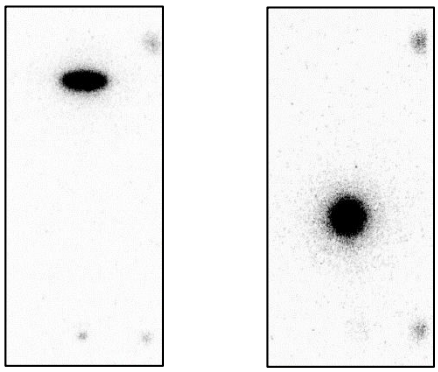
Compound **1** (100 nmol) in 20 μL of MeOH and $Cu(py)_4(OTf)_2$ (80−150 nmol) in 20 μL of MeOH were added into a microtube along with a 10-μM NaOH aqueous solution of ^{125}I (0.3 μL, 1.0−1.3 MBq). The reaction solution was gently vortexed for 10 seconds. The reaction was performed at 25°C for 3 min. Subsequently, corresponding peptides (200 nmol) in MeOH (20 μL), and sodium ascorbate (400−750 nmol) and TBTA (80−150 nmol) in aqueous methanol (MeOH:H_2O = 1:1; 40 μL) were incorporated into the reaction solution, following which the resultant mixture was gently vortexed for 10 seconds. The reaction proceeded at 25°C for 10−20 min. The mixture was analyzed *via* radio-HPLC, and the RCC (%) was determined *via* radio-HPLC analysis.

2. HPLC analysis condition

- **Column:** COSMOSIL 5C_{18}-ARII (4.6 ID×150 mm)
- **Temperature:** 40°C
- **Flow:** 1.0 mL/min
- **Phase A:** H_2O (containing 0.1% TFA)
- **Phase B:** MeCN (containing 0.1% TFA)
- **Condition A:** 55% phase B (0–15 min)
  55% to 100 % phase B (15–16 min)
  100% phase B (16–25 min)
- **Condition B:** 35% phase B (0–15 min)
  35% to 100 % phase B (15–16 min)
  100% phase B (16–25 min)
- **Condition C:** 30% phase B (0–15 min)
  30% to 100 % phase B (15–16 min)
  100% phase B (16–25 min)
- **Condition D:** 25% phase B (0–15 min)
  25% to 100 % phase B (15–16 min)
  100% phase B (16–25 min)
- **Condition E:** 25 to 40% phase B (0–15 min)
  40% to 100 % phase B (15–16 min)
  100% phase B (16–25 min)
- **Condition F:** 30 to 100% phase B (0–15 min)
  100% phase B (15–25 min)
- **Condition G:** 40 to 100% phase B (0–15 min)
  100% phase B (15–25 min)

3. UV- and radio-HPLC chromatograms and radio-TLC traces

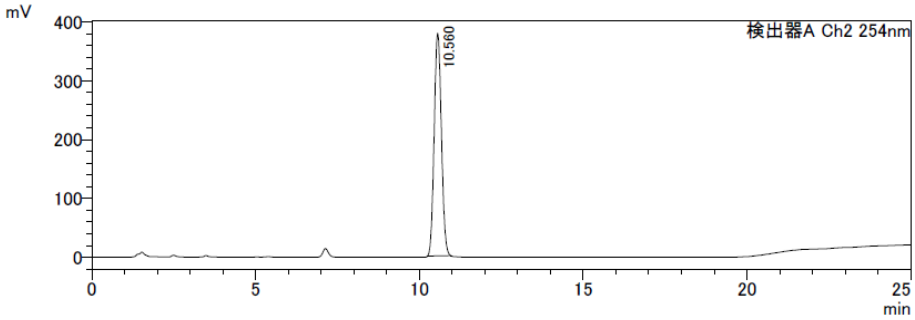
Radio-TLC of **[^{125}I]2** and **[^{125}I]3** [Hexane : Ethyl acetate (= 1:1)]



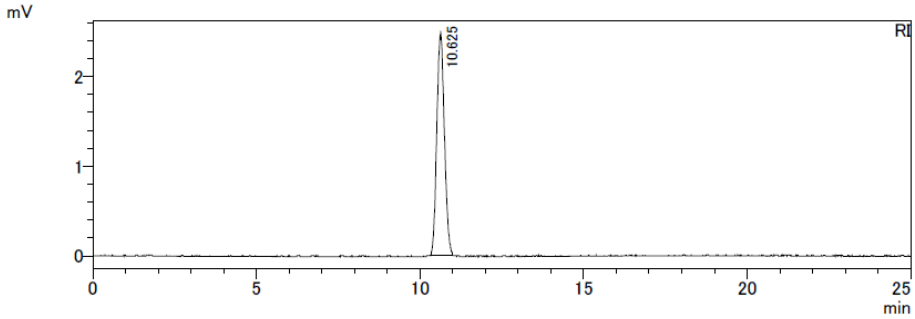
[^{125}I]2 **[^{125}I]3**

UV- and radio-HPLC of **2** and **[^{125}I]2** [HPLC condition A]

UV detector

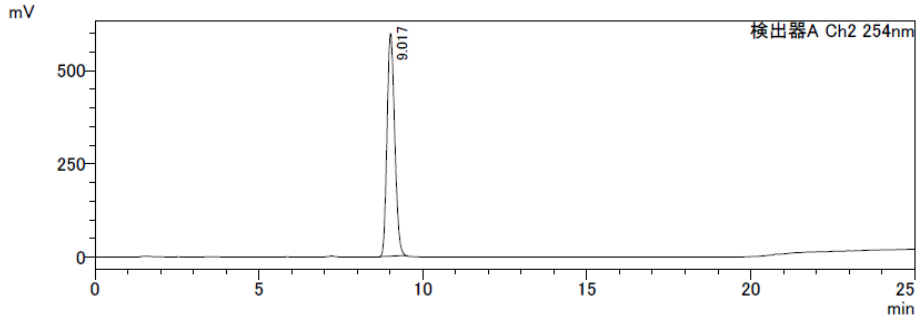


RI detector

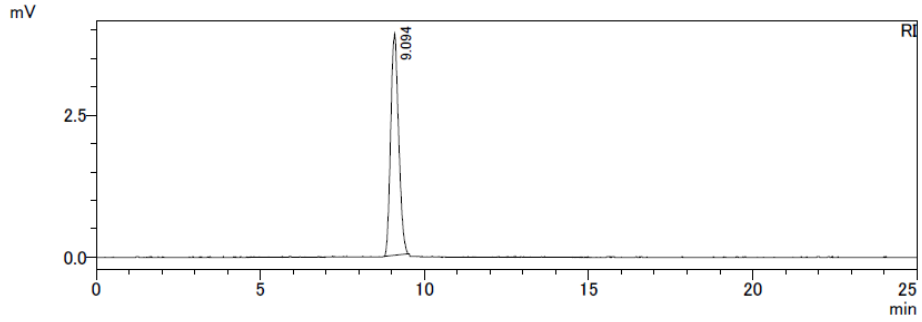


UV- and radio-HPLC of **3** and **[^{125}I]3** [HPLC condition A]

UV detector

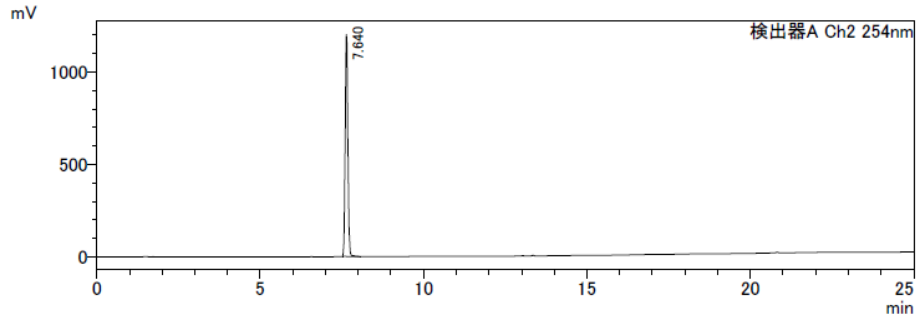


RI detector

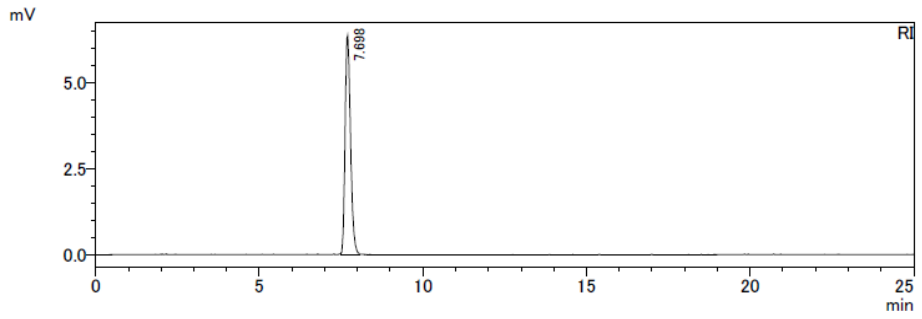


UV- and radio-HPLC of **4** and **[^{125}I]4** [HPLC condition F]

UV detector

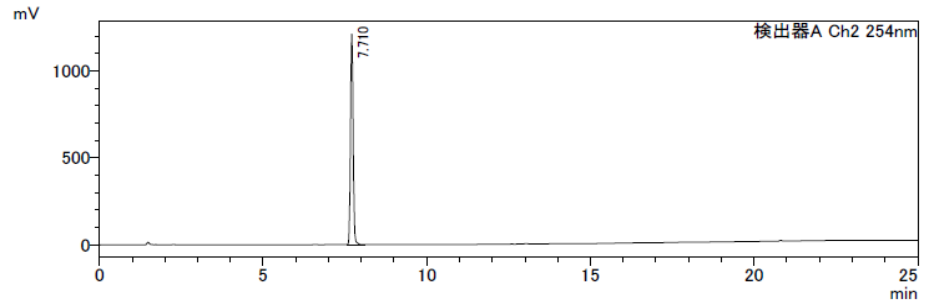


RI detector

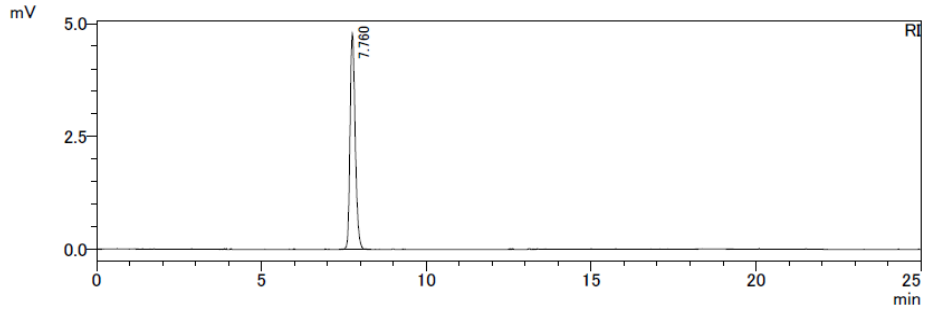


UV- and radio-HPLC of **5** and **[^{125}I]5** [HPLC condition F]

UV detector

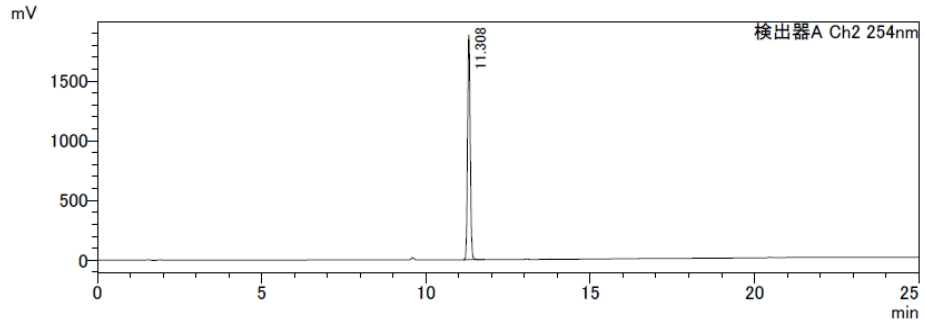


RI detector

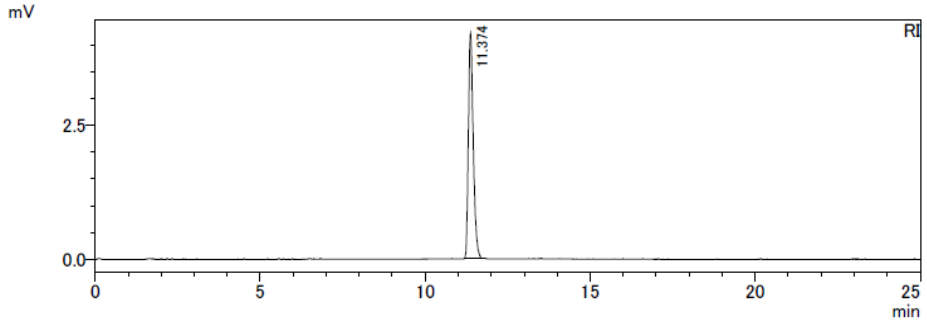


UV- and radio-HPLC of **6** and **[^{125}I]6** [HPLC condition G]

UV detector

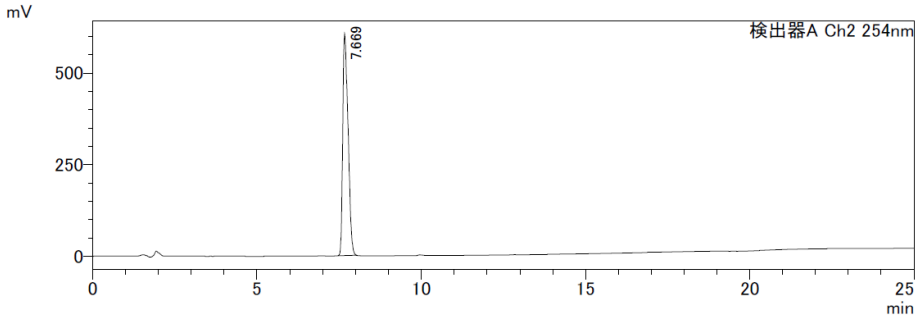


RI detector

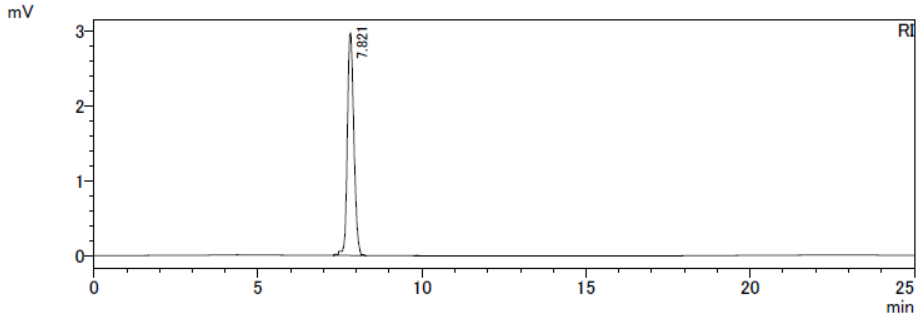


UV- and radio-HPLC of **7** and **[^{125}I]7** [HPLC condition G]

UV detector

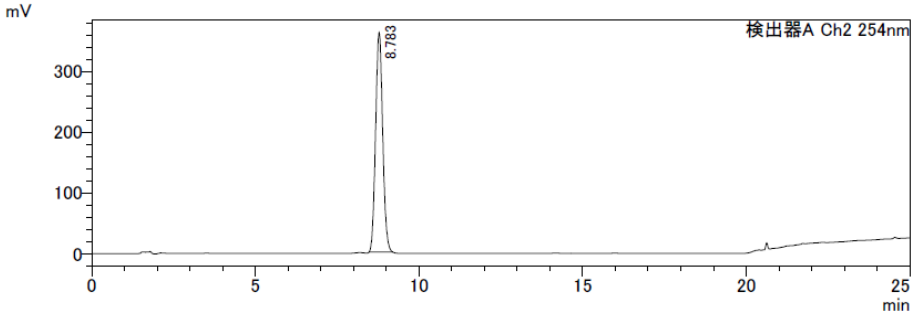


RI detector

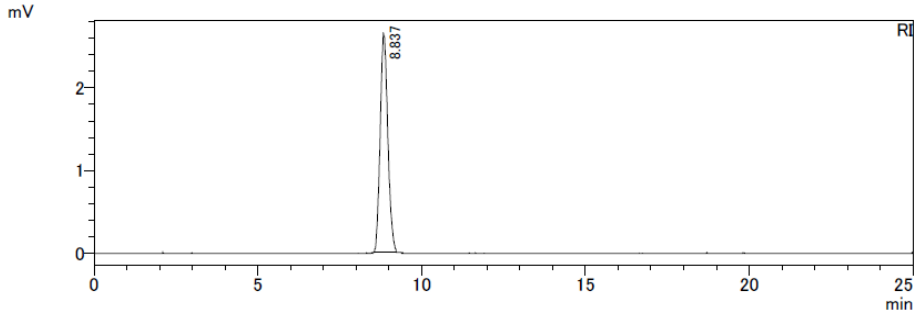


UV- and radio-HPLC of **CCPS** and **[^{125}I]CCPS** [HPLC condition D]

UV detector

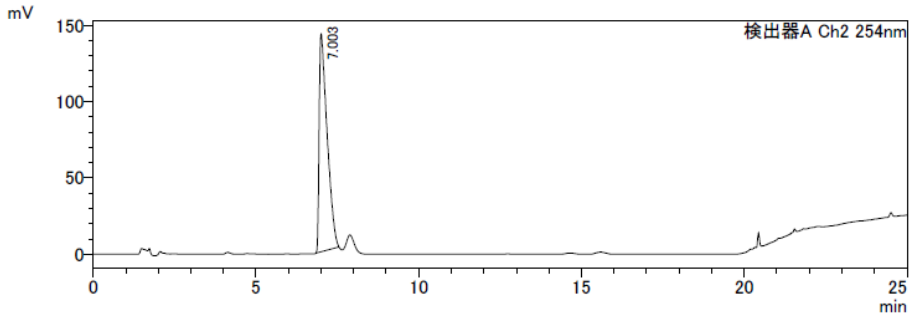


RI detector

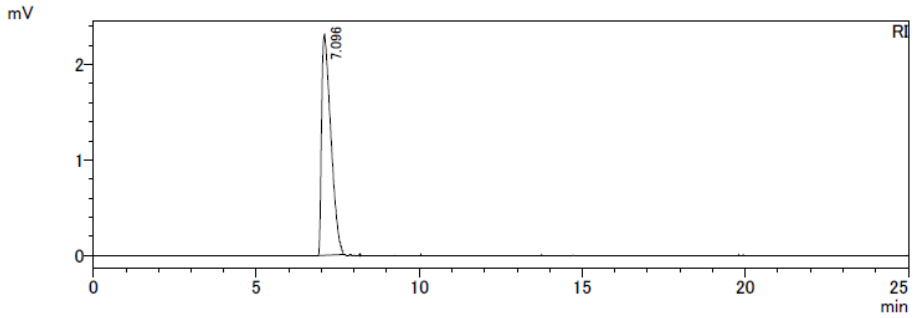


UV- and radio-HPLC of **CCRGD** and **[^{125}I]CCRGD** [HPLC condition C]

UV detector

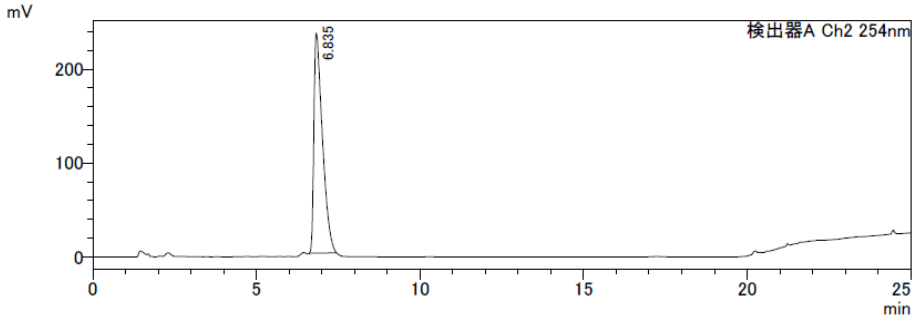


RI detector

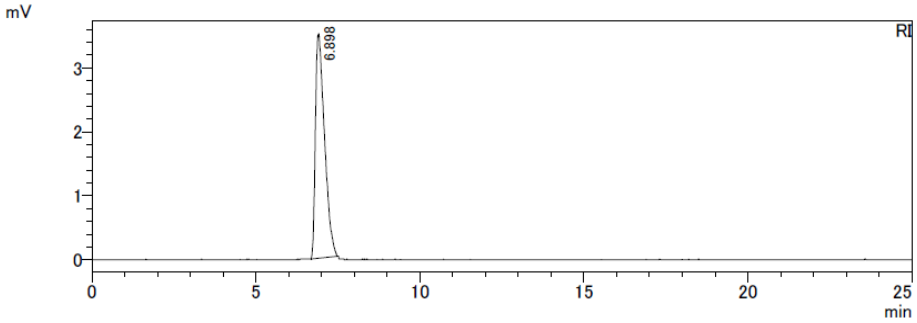


UV- and radio-HPLC of **CCTA** and **[^{125}I]CCTA** [HPLC condition B]

UV detector

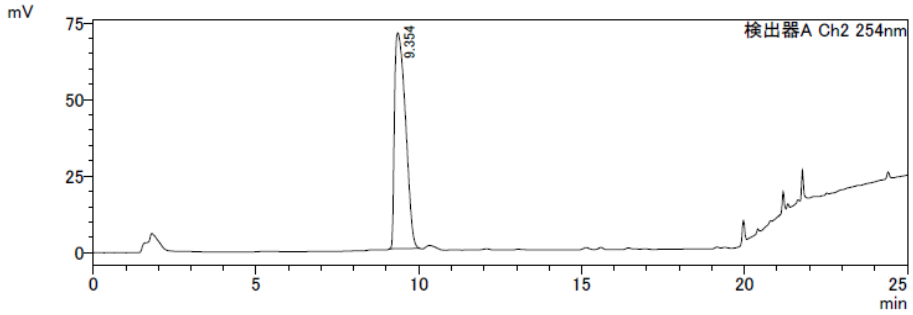


RI detector

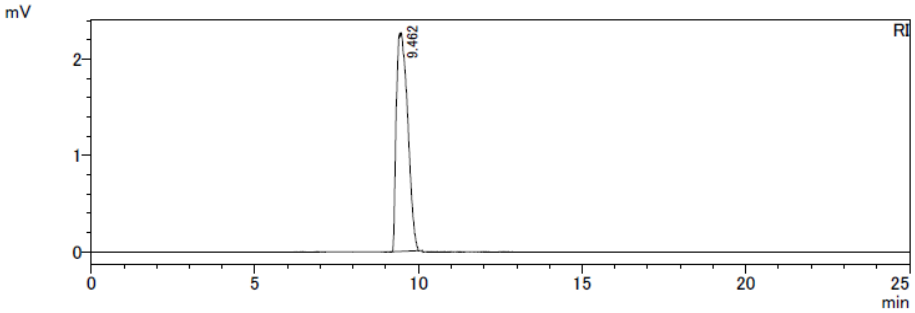


UV- and radio-HPLC of **CCKA** and **[^{125}I]CCKA** [HPLC condition E]

UV detector

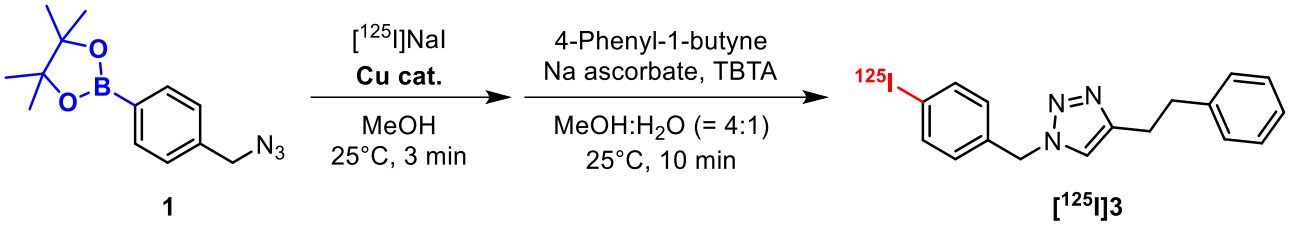


RI detector



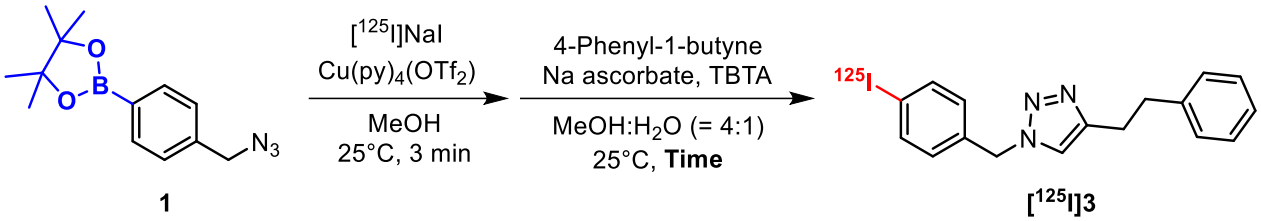
4. Optimization of reaction condition

4.1. Optimization of copper catalyst on the one-pot two-step radioiodination



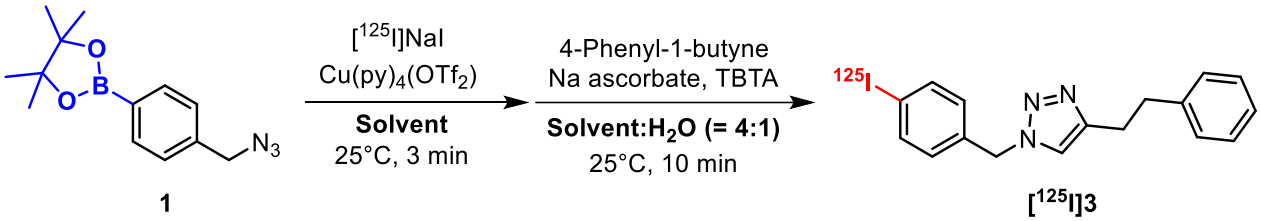
Reaction condition: **1** (100 nmol), 4-phenyl-1-butyne (200 nmol), sodium ascorbate (400 nmol), TBTA (80 nmol), **Cu cat. = $Cu(py)_4(OTf)_2$ [py = pyridine, OTf = trifluoromethanesulfonate], $CuSO_4·5H_2O$, $Cu(OTf)_2$, $CuCl_2$, $Cu(OMe)_2$, or $[Cu(CH_3CN)]PF_6$.**

4.2. Effect of CuAAC reaction time on RCCs of [^{125}I]3



Reaction condition: **1** (100 nmol), 4-phenyl-1-butyne (200 nmol), $Cu(py)_4(OTf)_2$ (20 nmol), sodium ascorbate (400 nmol), TBTA (80 nmol), **time = 10, 20, 30, or 60 min.**

4.3. Effect of solvent on the radiosynthesis of [^{125}I]3

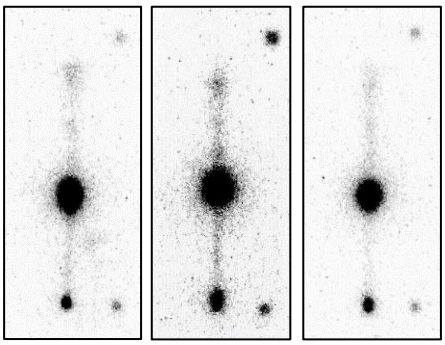


Reaction condition: **1** (100 nmol), $Cu(py)_4(OTf)_2$ (80 nmol), 4-phenyl-1-butyne (200 nmol), sodium ascorbate (400 nmol), TBTA (80 nmol), **solvent = methanol (MeOH), acetonitrile (CH_3CN), *N,N*-dimethylformamide (DMF), or dimethyl sulfoxide (DMSO)**.

4.1. Optimization of copper catalyst on the one-pot two-step radioiodination

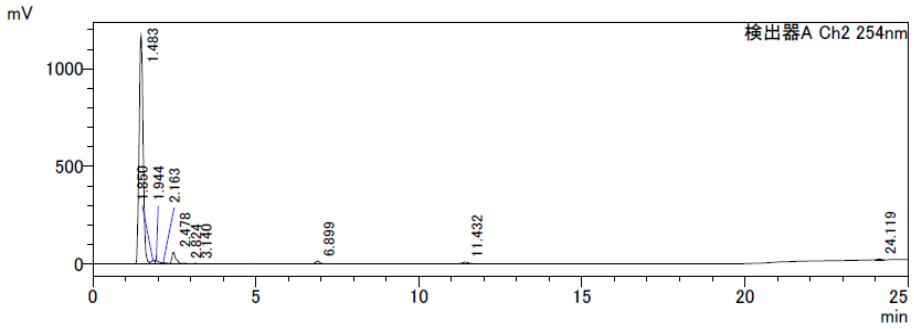
Cu catalyst: $Cu(py)_4(OTf)_2$ (0.8 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

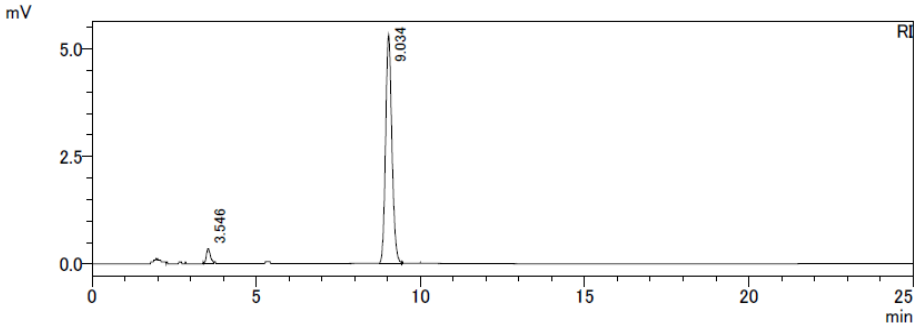


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

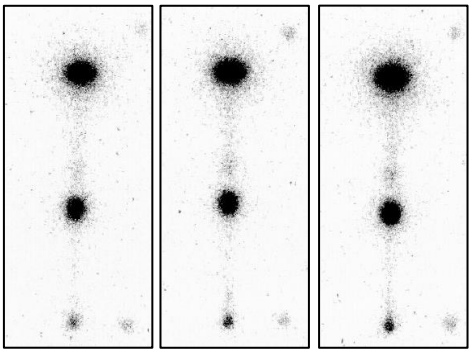


RI detector



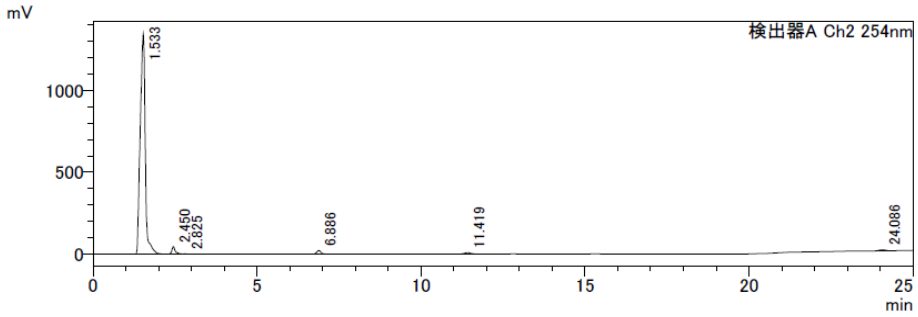
Cu catalyst: $Cu(py)_4(OTf)_2$ (0.2 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

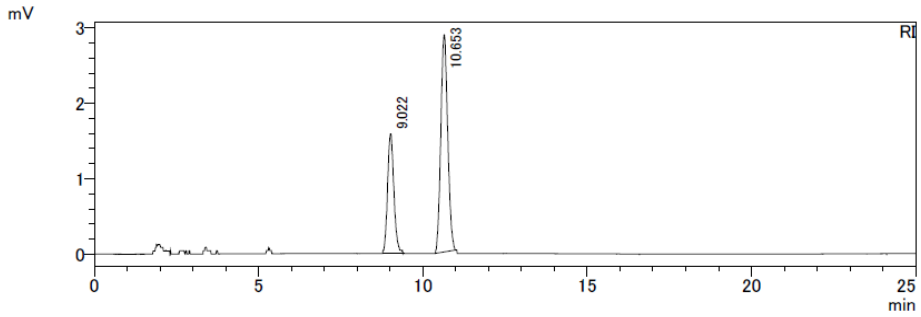


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

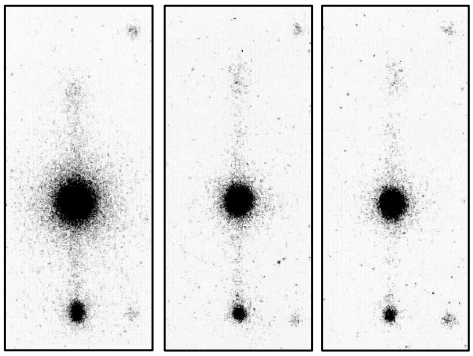


RI detector



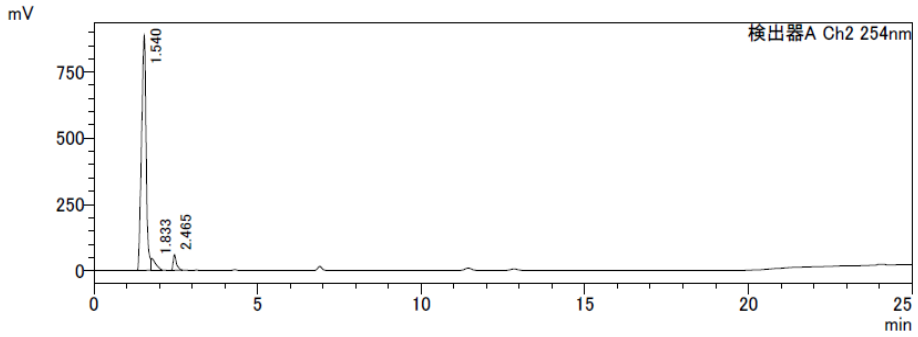
Cu catalyst: $CuSO_4$ (0.8 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

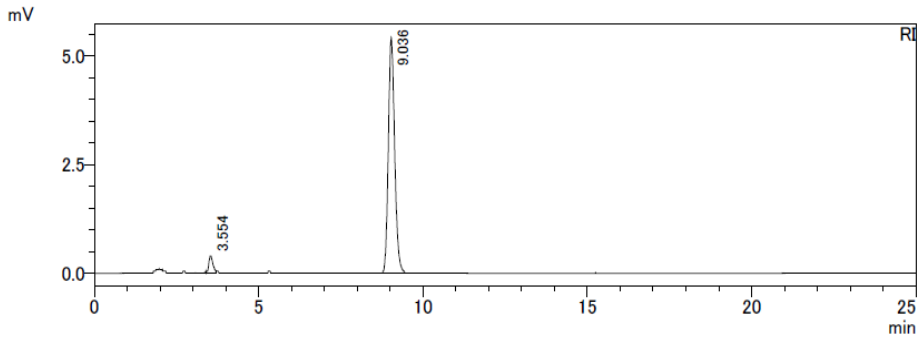


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

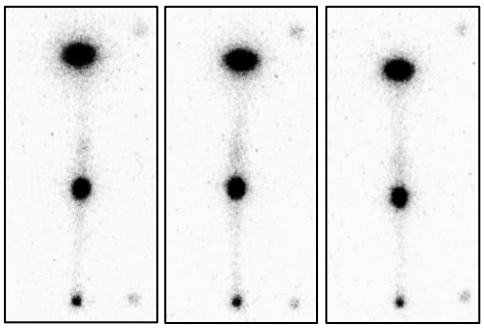


RI detector



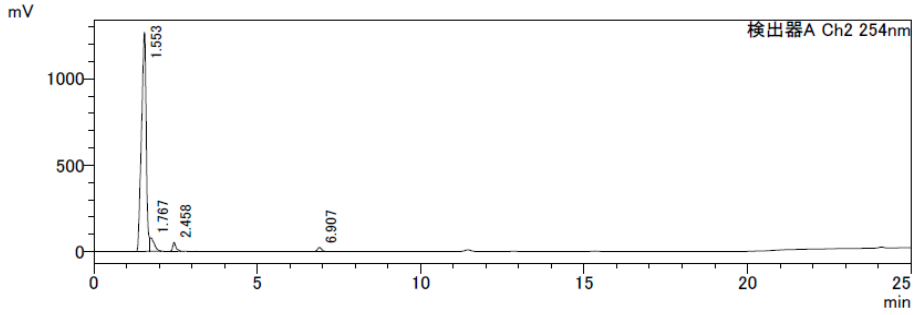
Cu catalyst: $CuSO_4$ (0.2 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

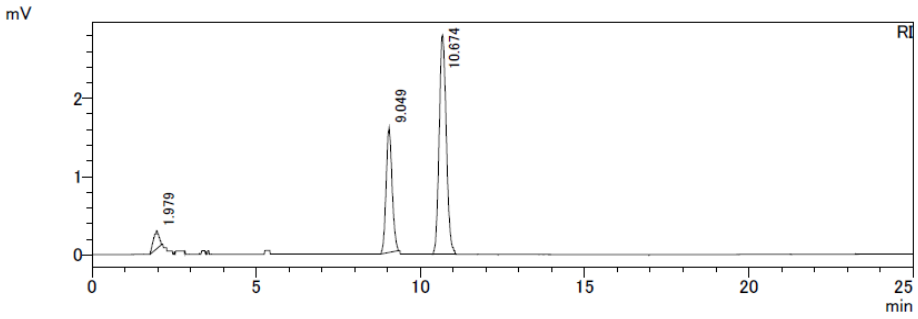


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

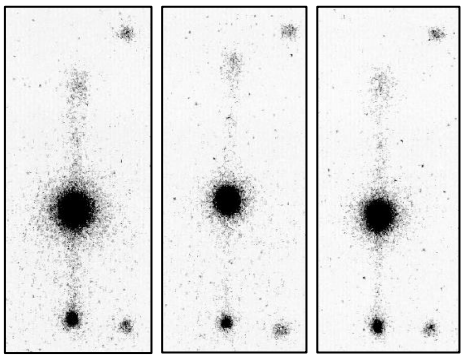


RI detector



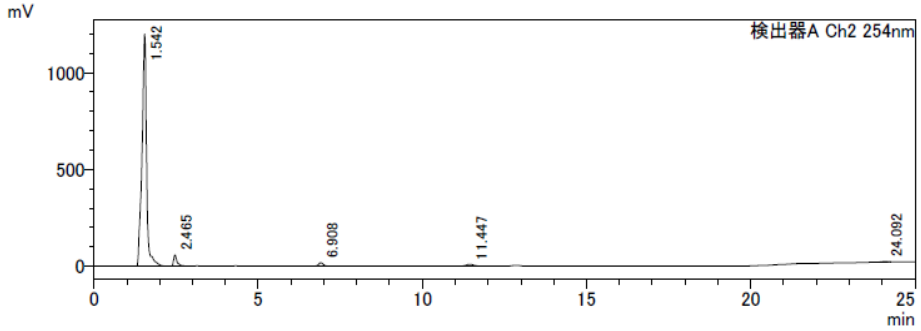
Cu catalyst: $Cu(OTf)_2$ (0.8 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

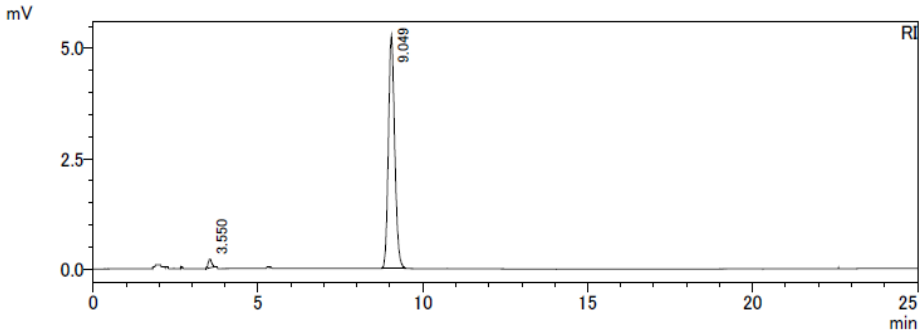


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

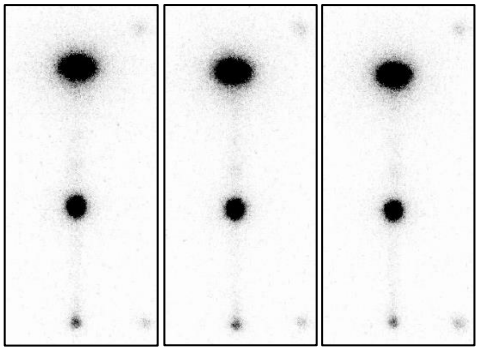


RI detector



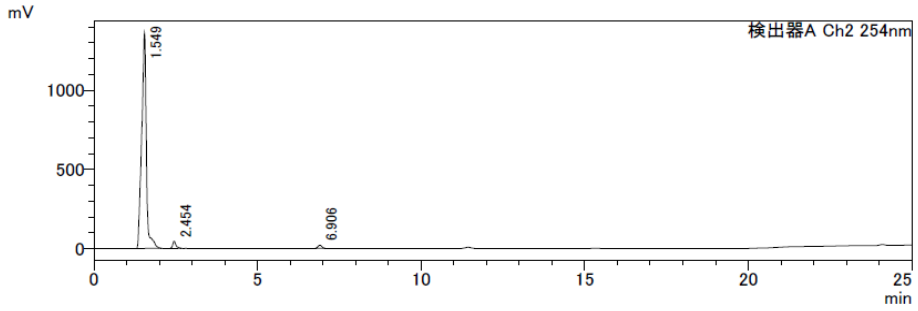
Cu catalyst: $Cu(OTf)_2$ (0.2 eq.)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

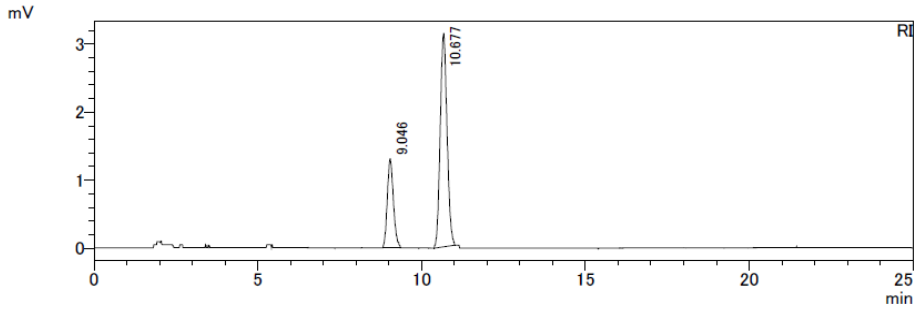


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

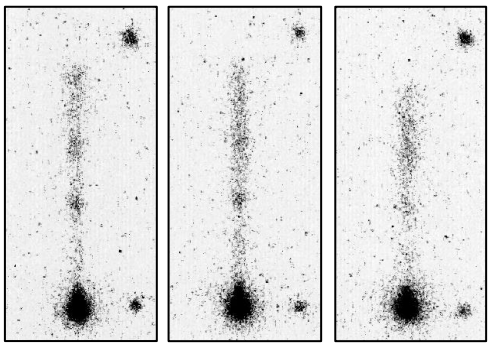


RI detector



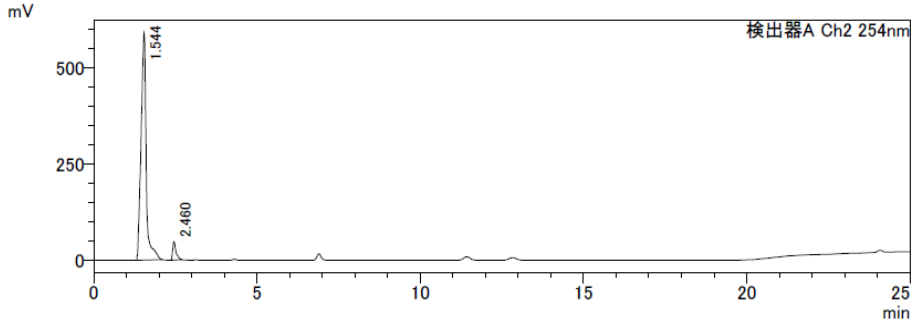
Cu catalyst: $CuCl_2$

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

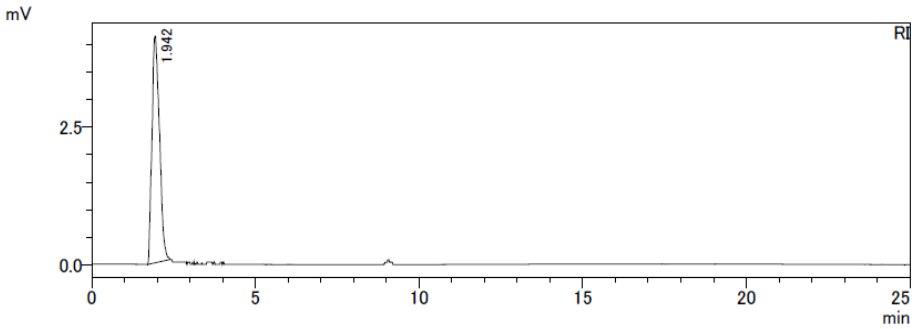


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

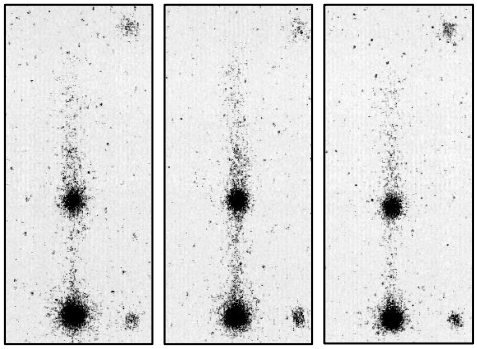


RI detector



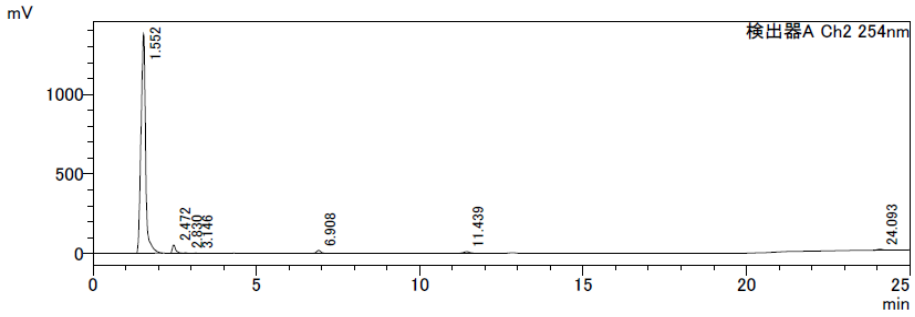
Cu catalyst: $Cu(OMe)_2$

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

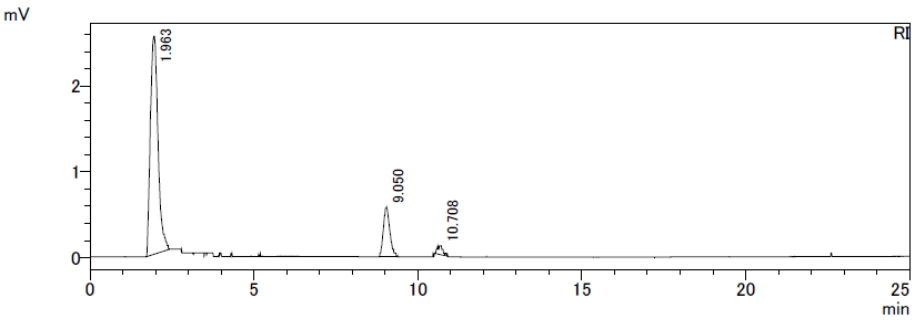


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

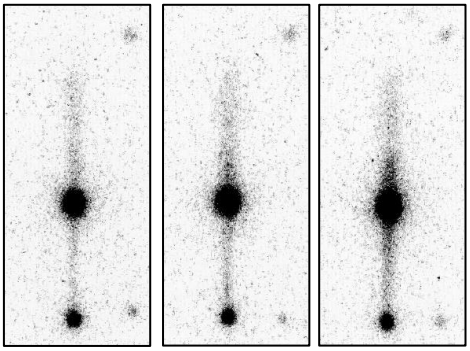


RI detector



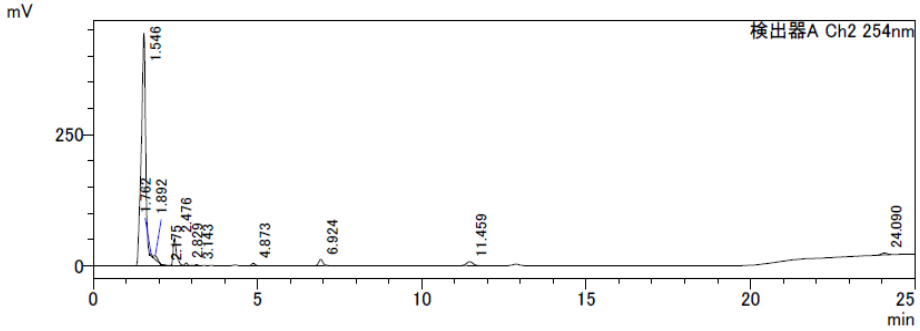
Cu catalyst: $[Cu(CH_3CN)_4]PF_6$

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

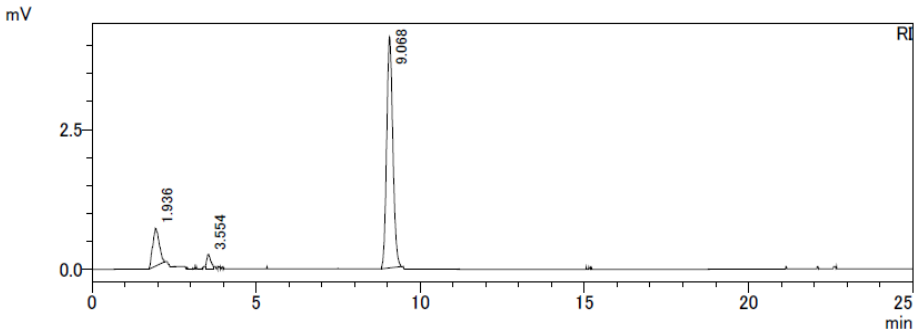


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector



RI detector



4.2. Effect of CuAAC reaction time on RCCs of [^{125}I]3

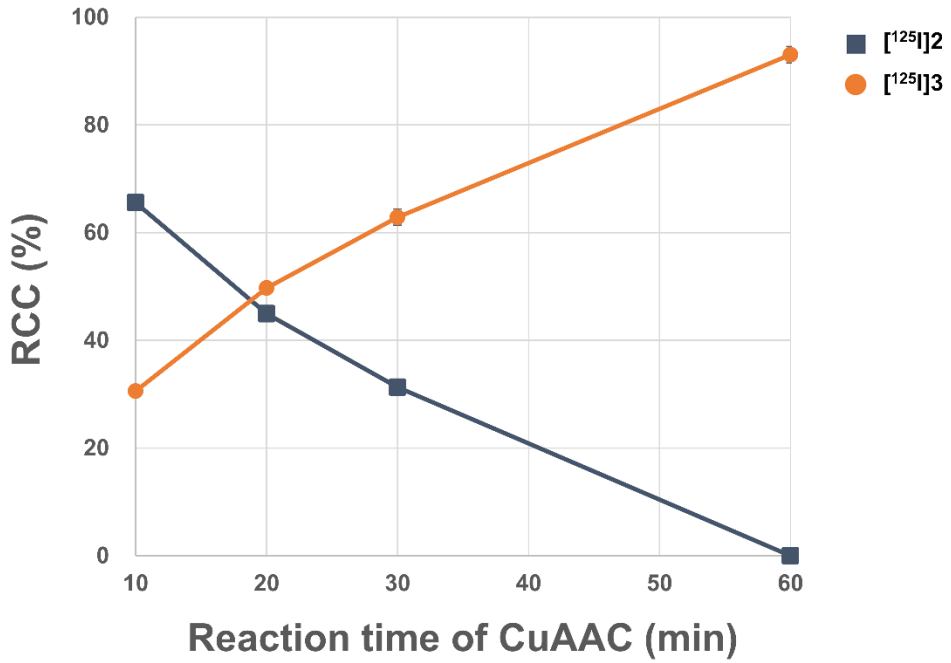
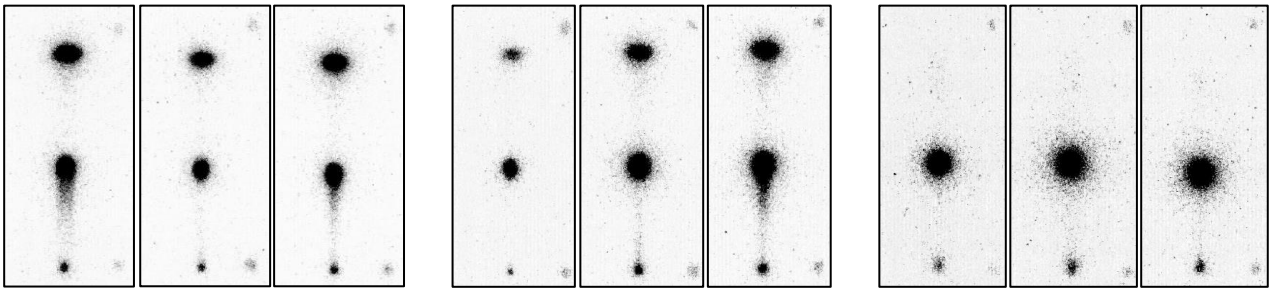


Fig. S1 Effect of CuAAC reaction time on the RCCs of [^{125}I]**3**.
Reaction conditions: **1** (100 nmol), 4-phenyl-1-butyne (200 nmol), $Cu(py)_4(OTf)_2$ (20 nmol), sodium ascorbate (400 nmol), TBTA (80 nmol), MeOH (final volume: 100 μL), 25°C. (N = 3)

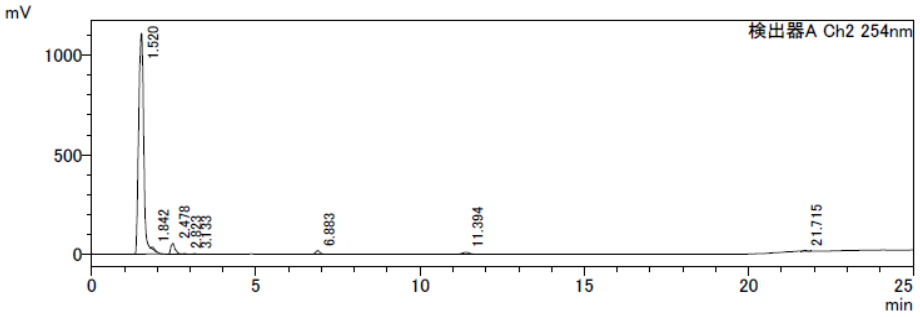
Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

Time: 20 **Time: 30** **Time: 60**

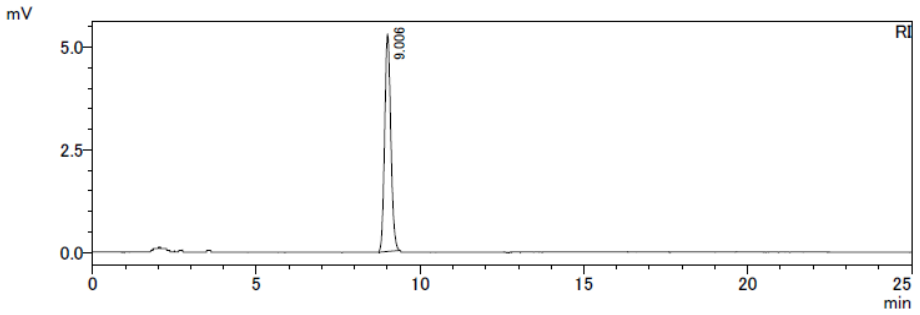


UV- and radio-HPLC of the reaction mixture after 60 min [HPLC condition A]

UV detector



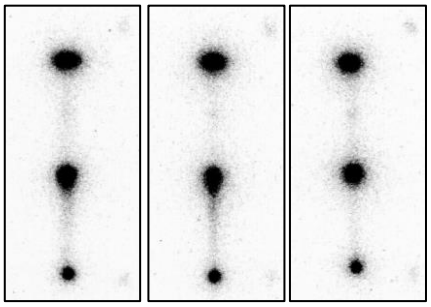
RI detector



4.3. Effect of solvent on the radiosynthesis of [^{125}I]3

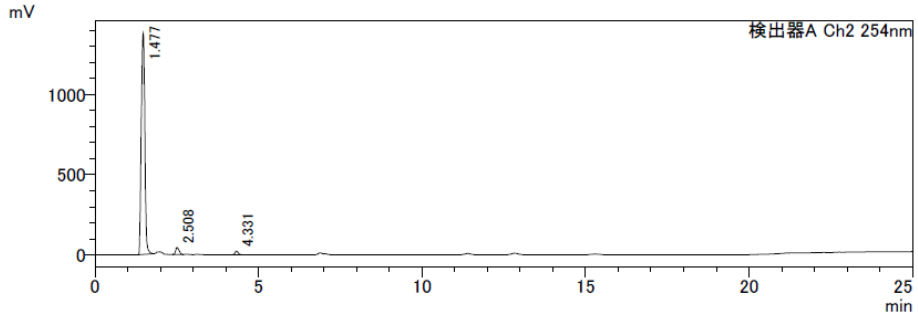
Solvent: EtOH

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

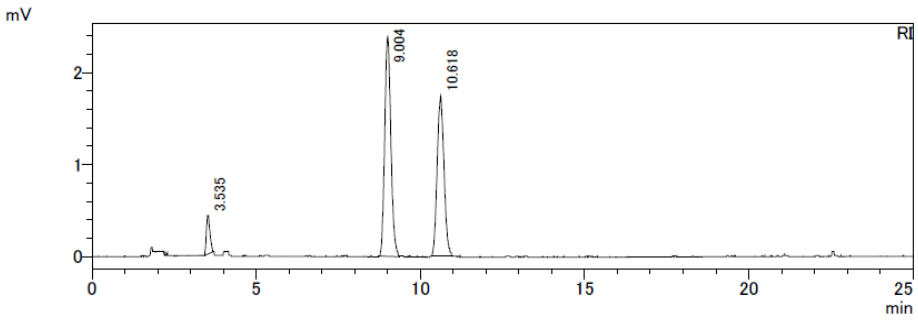


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

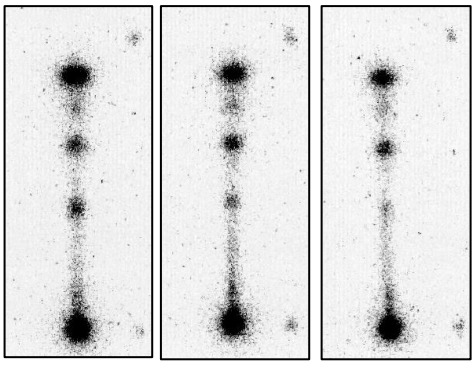


RI detector



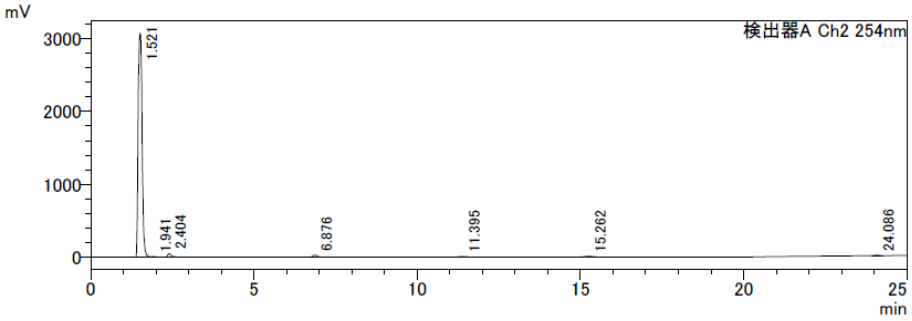
Solvent: CH_3CN

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

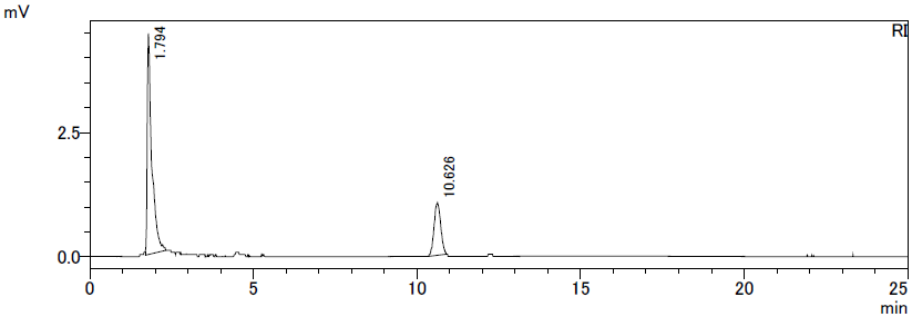


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

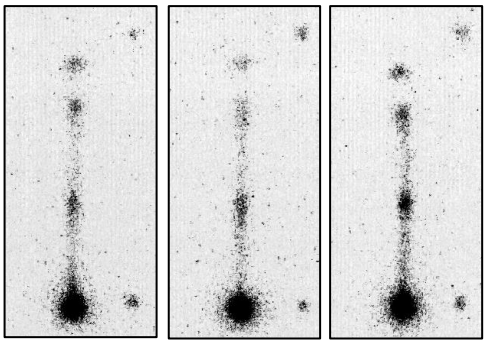


RI detector



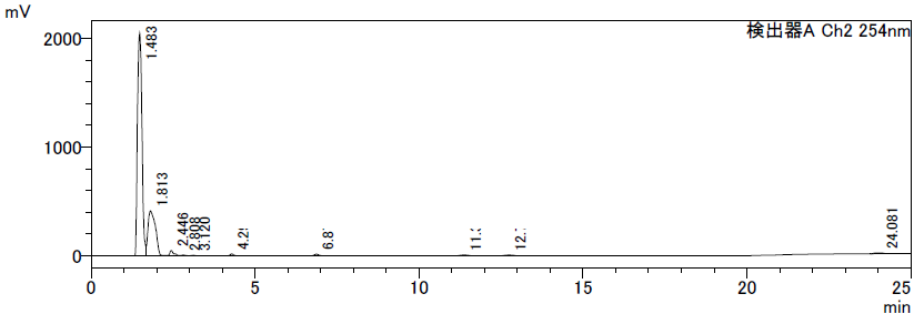
Solvent: DMF

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

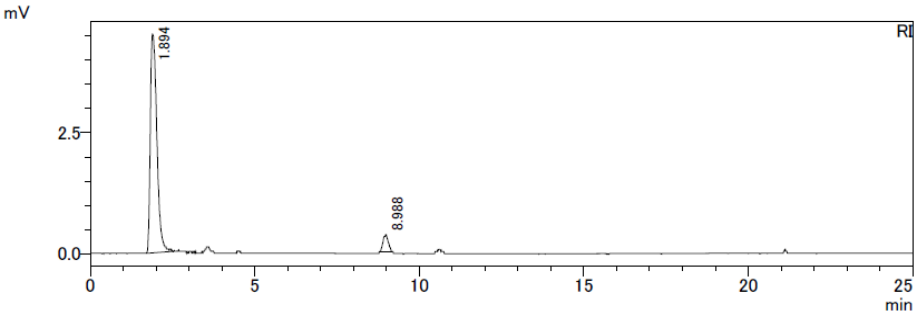


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector

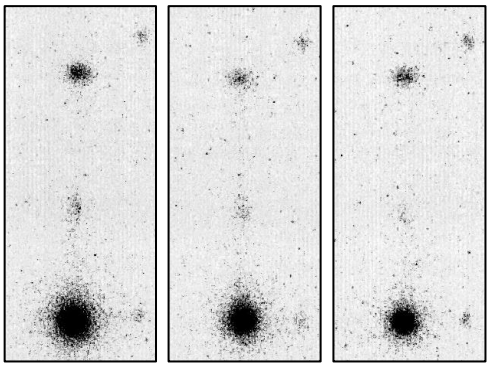


RI detector



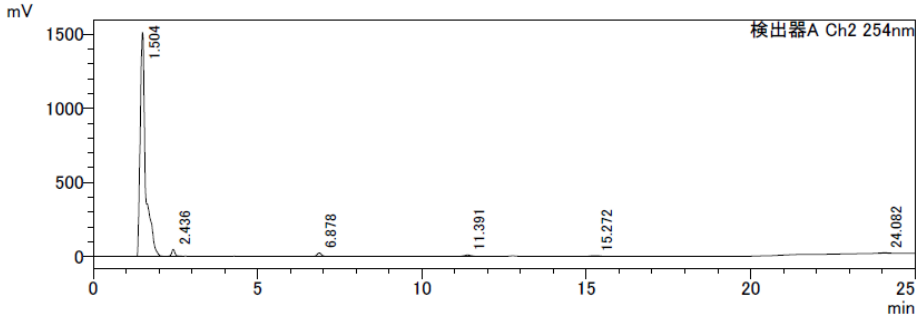
Solvent: DMSO

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

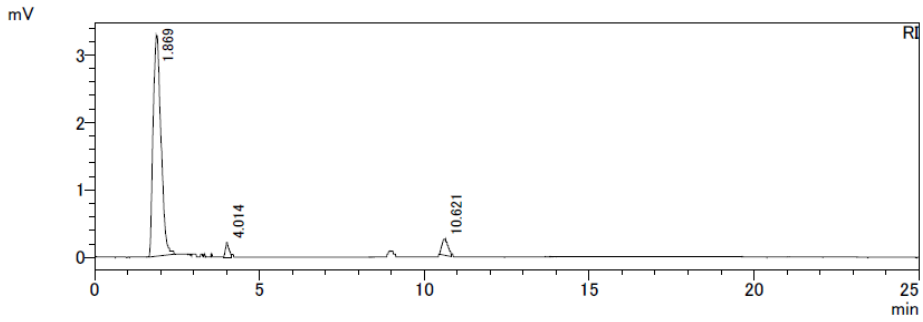


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector



RI detector



5. Mechanistic investigation

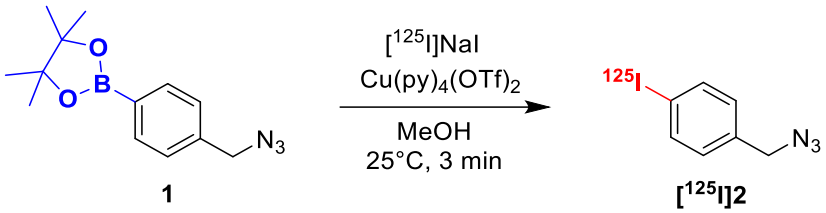
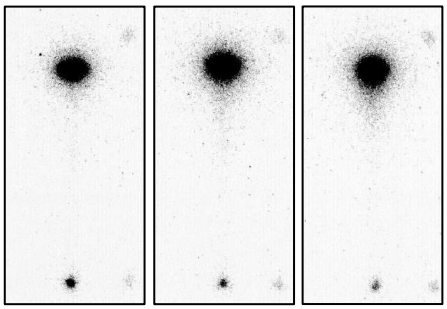


Fig. S2 Confirmation of synthetic intermediates.

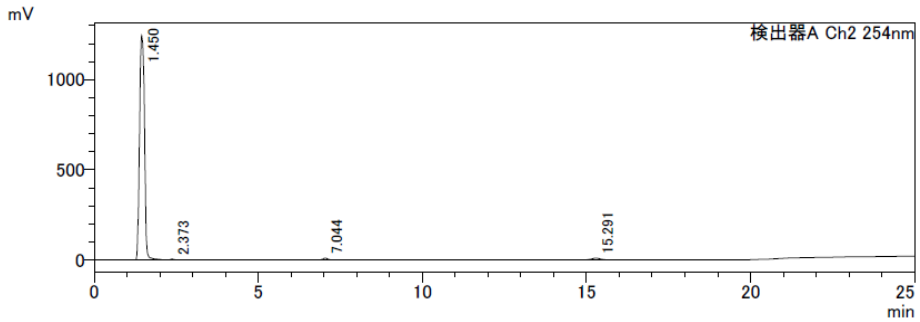
Reaction condition: **1** (100 nmol), $Cu(py)_4(OTf)_2$ (80 nmol), MeOH (40 µL)

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

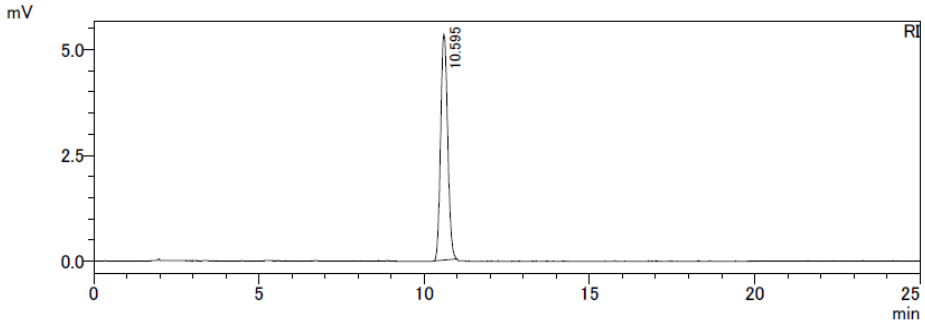


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector



RI detector



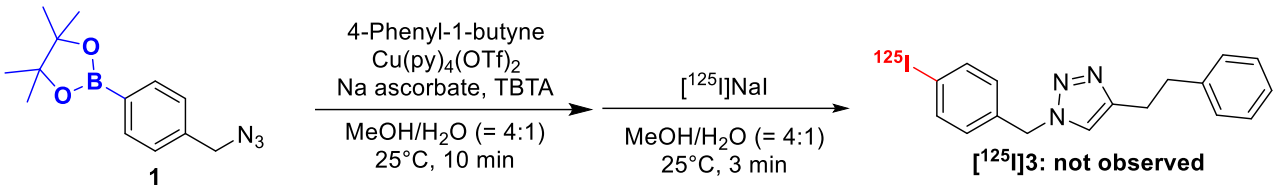
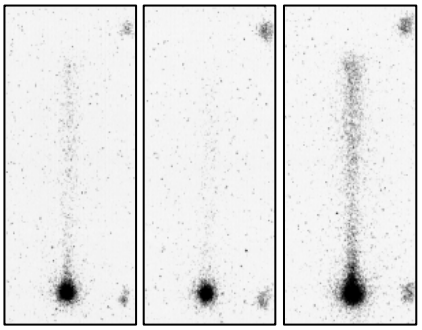


Fig. S3 Assessment reversing the order of reactions.

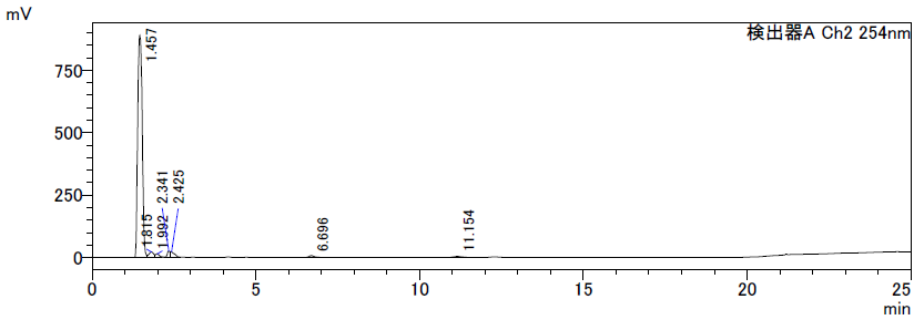
Reaction condition: **1** (100 nmol), $Cu(py)_4(OTf)_2$ (80 nmol), 4-phenyl-1-butyne (200 nmol), sodium ascorbate (400 nmol), TBTA (80 nmol), MeOH:H_2O (= 4:1, 100 μL).

Radio-TLC of reaction mixture [hexane : EtOAc (= 1:1)]

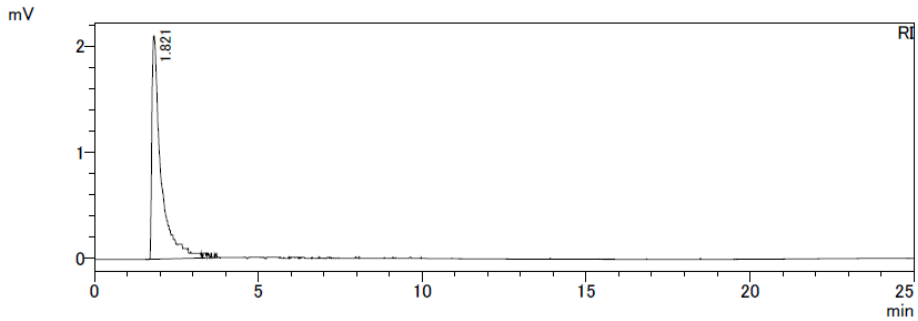


UV- and radio-HPLC of reaction mixture [HPLC condition A]

UV detector



RI detector



6. Radiosynthesis of [^{125}I]4–7

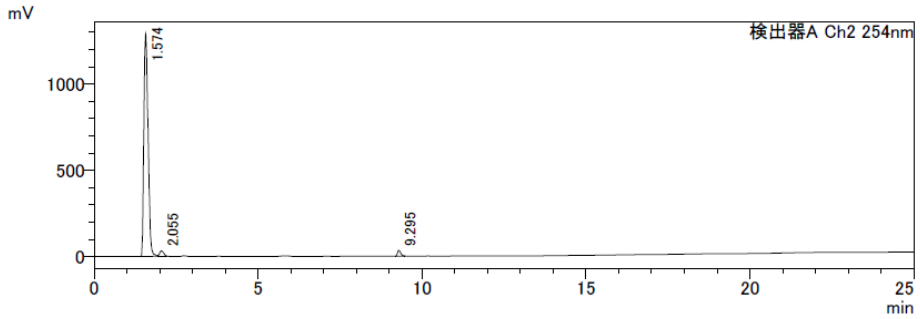
6.1. Synthesis of [^{125}I]4

Entry	$Cu(py)_4OTf_2$ (nmol)	Time (min)	RCC (%) [^{125}I]2	RCC (%) [^{125}I]4
1	80	10	19.2	79.0
2	80	20	0.6 ± 1.0*	96.4 ± 1.5*

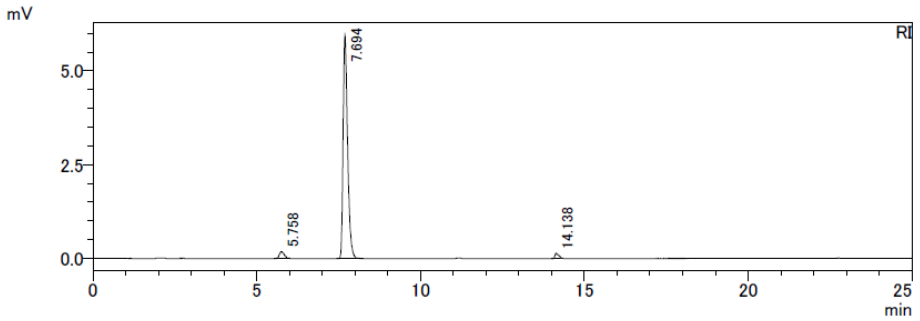
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 2) [HPLC condition F]

UV detector



RI detector



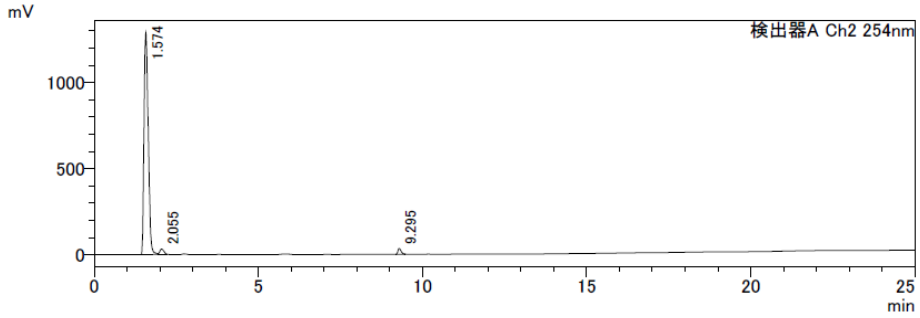
6.2. Synthesis of [^{125}I]5

Entry	$Cu(py)_4OTf_2$ (nmol)	Time (min)	RCC (%) [^{125}I]2	RCC (%) [^{125}I]5
1	80	10	12.8	87.2
2	150	10	3.5 ± 0.6*	96.5 ± 0.6*

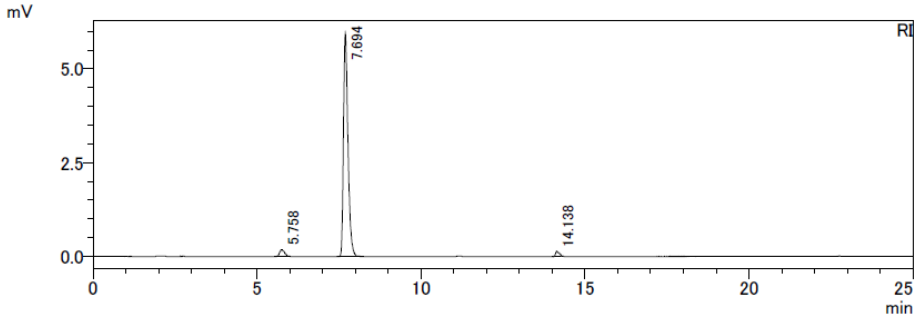
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 2) [HPLC condition F]

UV detector



RI detector



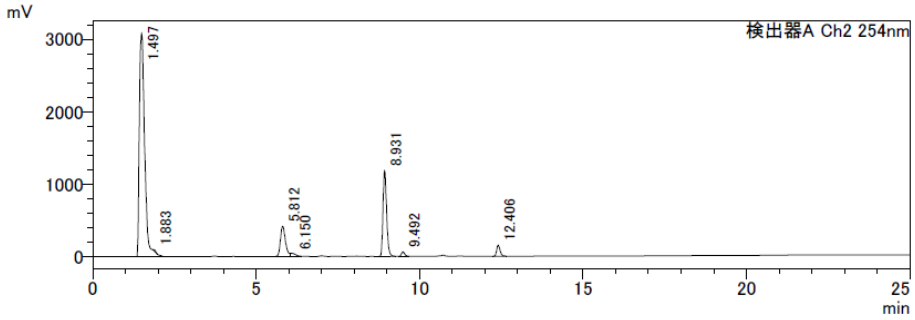
6.3. Synthesis of [^{125}I]6

Entry	$Cu(py)_4OTf_2$ (nmol)	Time (min)	RCC (%) [^{125}I]2	RCC (%) [^{125}I]6
1	80	10	32.6	67.4
2	80	15	4.9	95.1
3	80	20	2.4 ± 1.0*	97.6 ± 1.0*

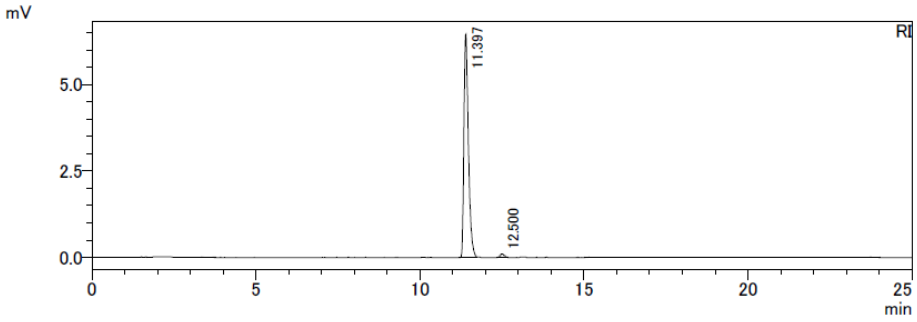
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 3) [HPLC condition G]

UV detector



RI detector



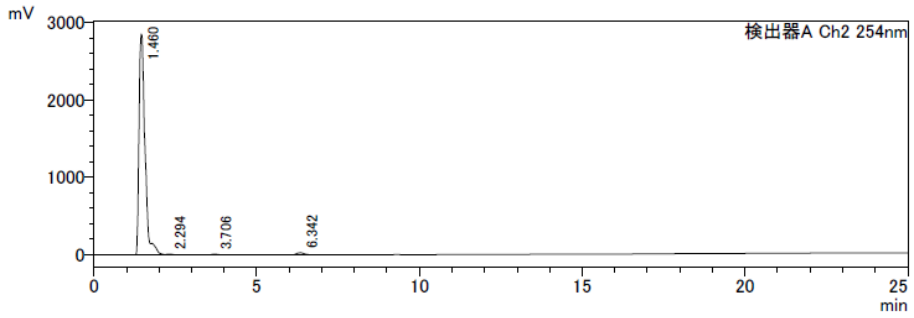
6.4. Synthesis of [^{125}I]7

Entry	$Cu(py)_4OTf_2$ (nmol)	Time (min)	[^{125}I]2	RCC (%) [^{125}I]7
1	150	20	1.7 ± 0.8*	97.6 ± 0.6*

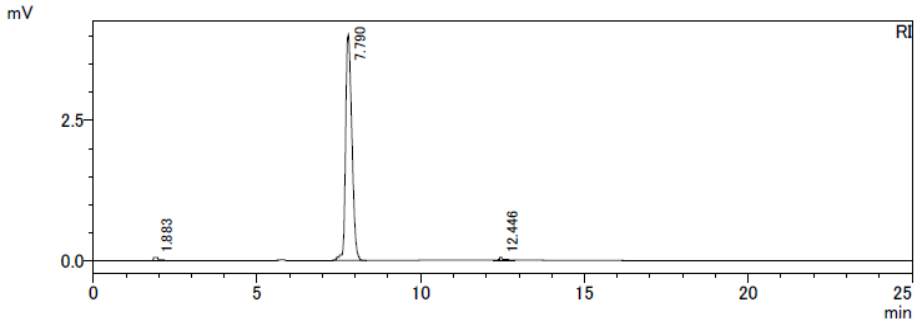
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 1) [HPLC condition G]

UV detector



RI detector



7. Radiosynthesis of ^{125}I-labeled peptides

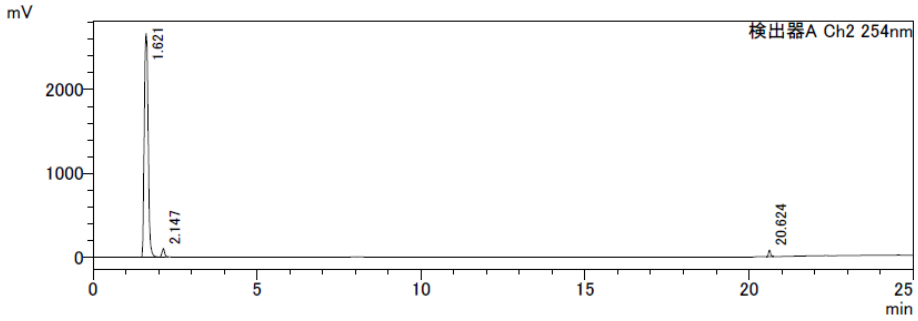
7.1. Synthesis of [^{125}I]CCPS

Entry	$Cu(py)_4(OTf)_2$ (nmol)	Time (min)	RCC (%) [^{125}I]2	RCC (%) [^{125}I]CCPS
1	80	10	34.7	60.2
2	80	20	7.6	82.2
3	150	20	1.0 ± 0.6*	87.8 ± 2.0*

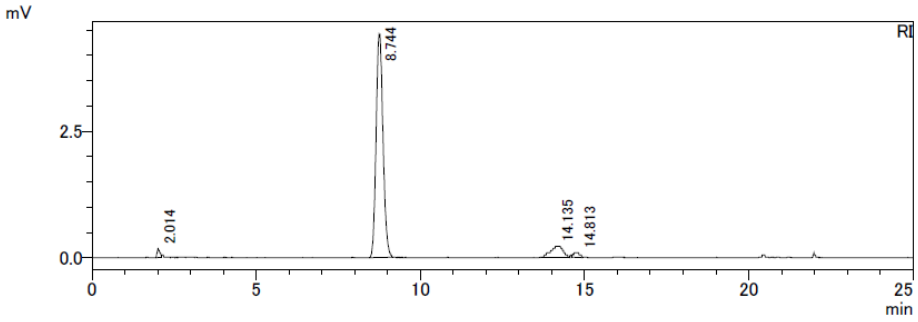
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 3) [HPLC condition D]

UV detector



RI detector



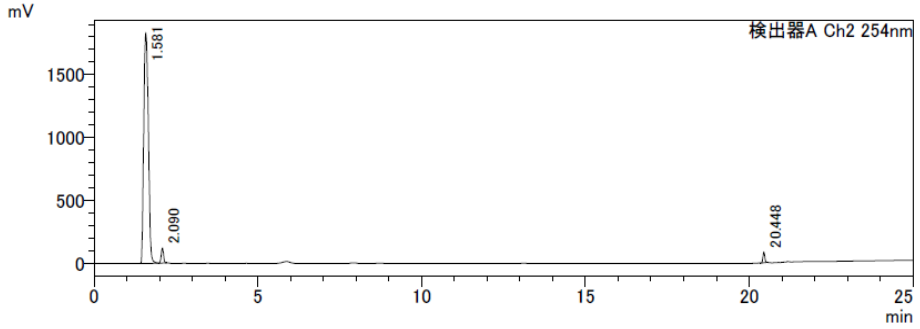
7.2. Synthesis of [^{125}I]CCRGD

Entry	$Cu(py)_4(OTf)_2$ (nmol)	Time (min)	RCC (%)	
			[^{125}I]2	[^{125}I]CCRGD
1	80	10	28.6	71.4
2	80	20	27.9	72.1
3	150	20	5.1 ± 2.7*	93.3 ± 2.1*

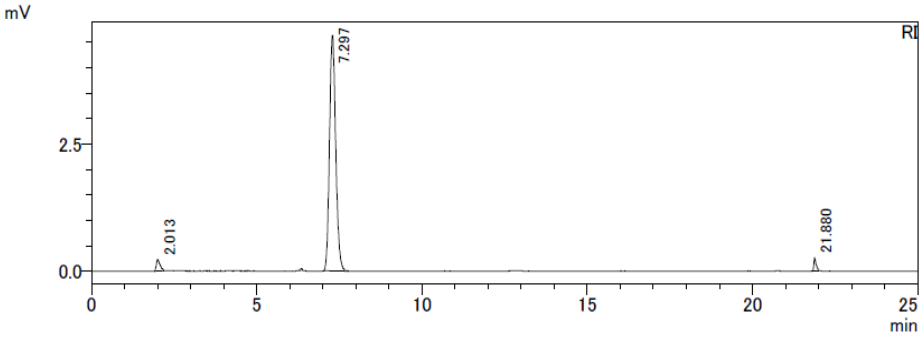
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 3) [HPLC condition C]

UV detector



RI detector



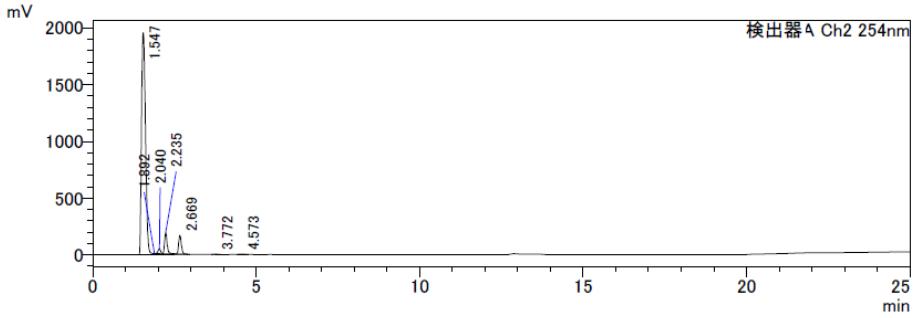
7.3. Synthesis of [^{125}I]CCTA

Entry	$Cu(py)_4(OTf)_2$ (nmol)	Time (min)	RCC (%)	
			[^{125}I]2	[^{125}I]CCTA
1	80	10	16.1	80.6
2	80	15	7.9	89.6
3	80	20	4.6 ± 0.3*	92.7 ± 0.3*
4	100	10	23.1	75.0
5	150	10	11.9	85.4

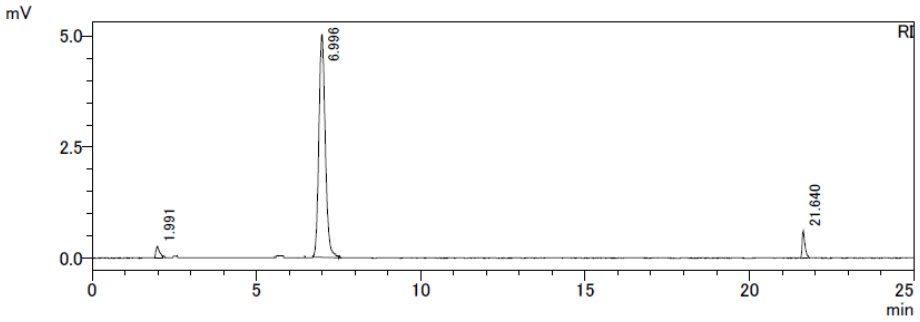
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 3) [HPLC condition B]

UV detector



RI detector



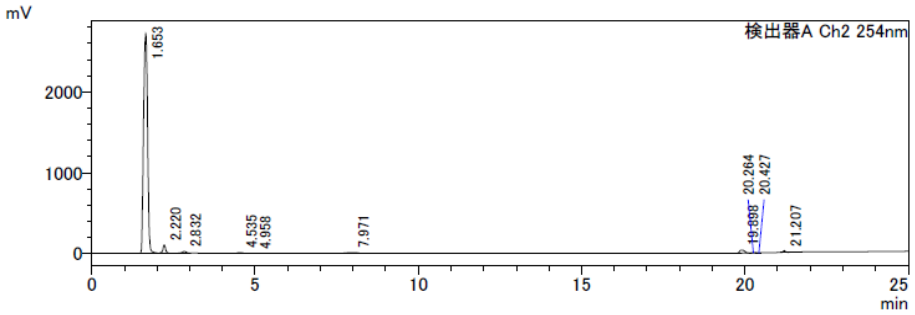
7.4. Synthesis of [^{125}I]CCKA

Entry	$Cu(py)_4(OTf)_2$ (nmol)	Time (min)	RCC (%)	
			[^{125}I]2	[^{125}I]CCKA
1	80	10	27.9	69.5
2	80	20	15.5	81.4
3	150	20	6.6 ± 1.6*	90.9 ± 1.2*

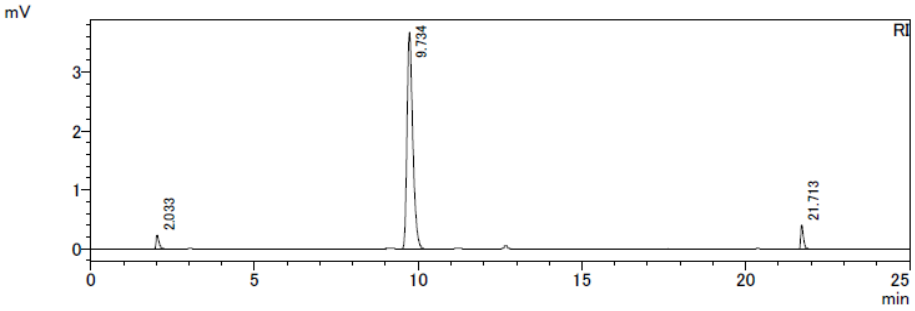
*Data are presented as the mean ± standard deviation (N = 3).

UV- and radio-HPLC of the reaction mixture (Entry 3) [HPLC condition E]

UV detector



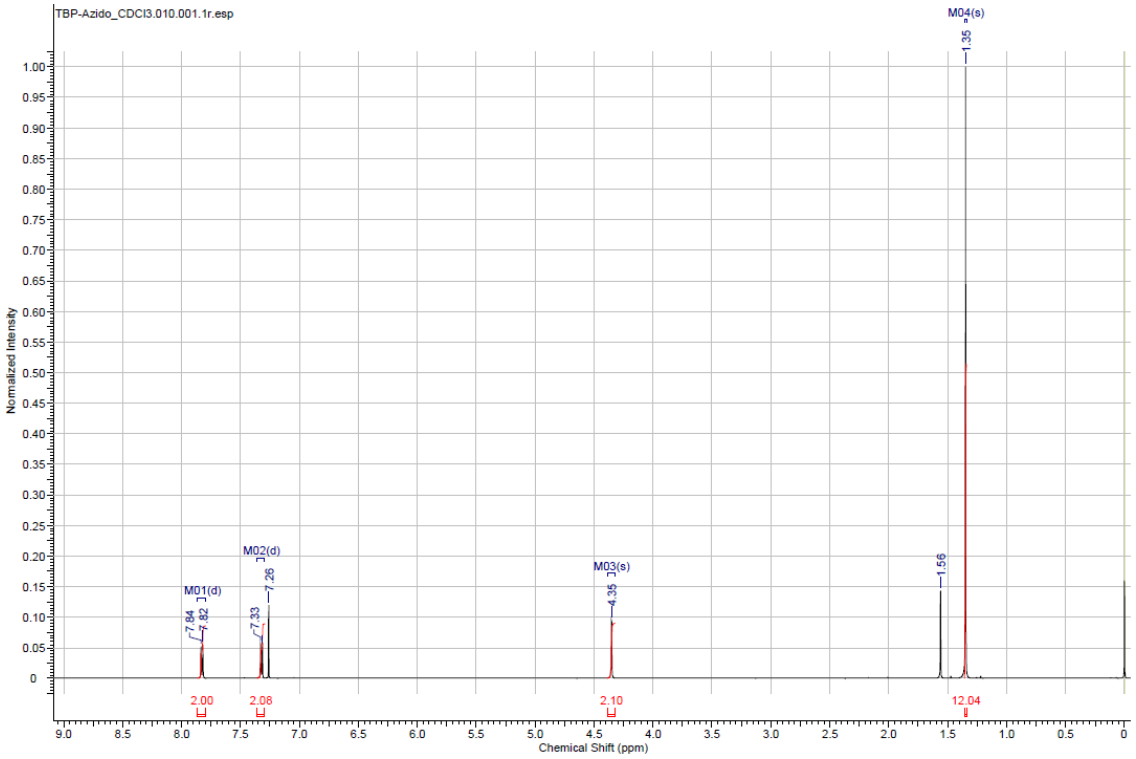
RI detector



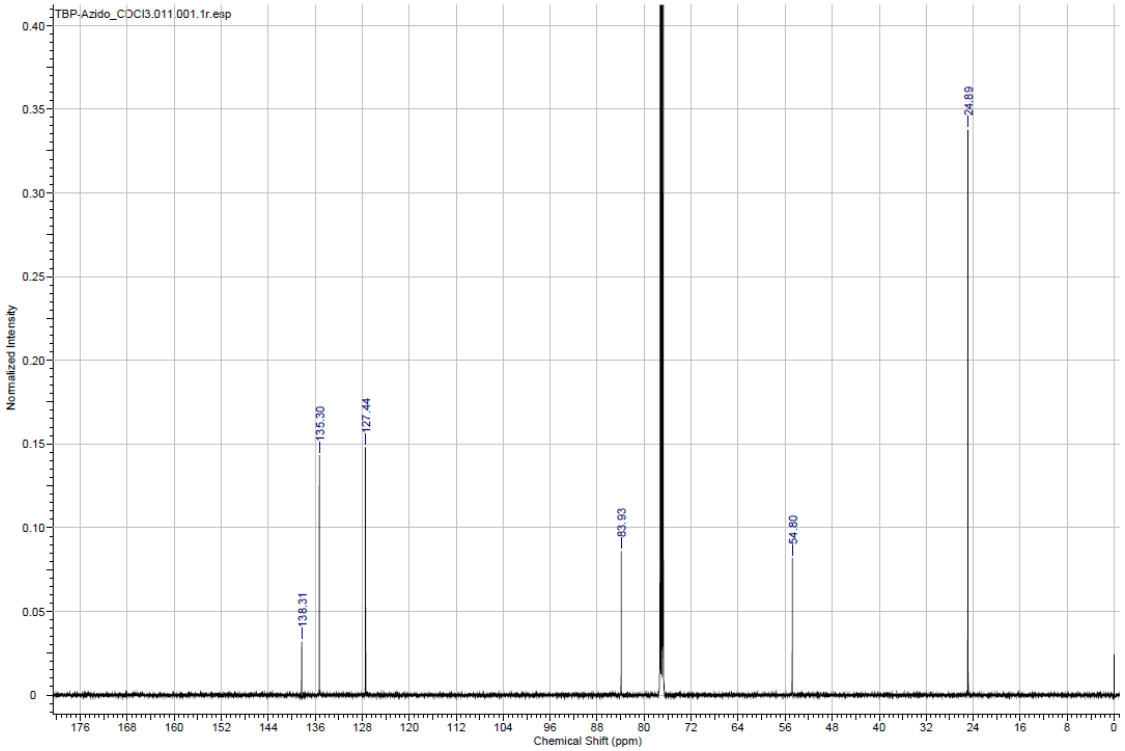
8. ^{1}H and ^{13}C NMR spectra

NMR spectra of **1**

^{1}H NMR (500MHz, $CDCl_3$)

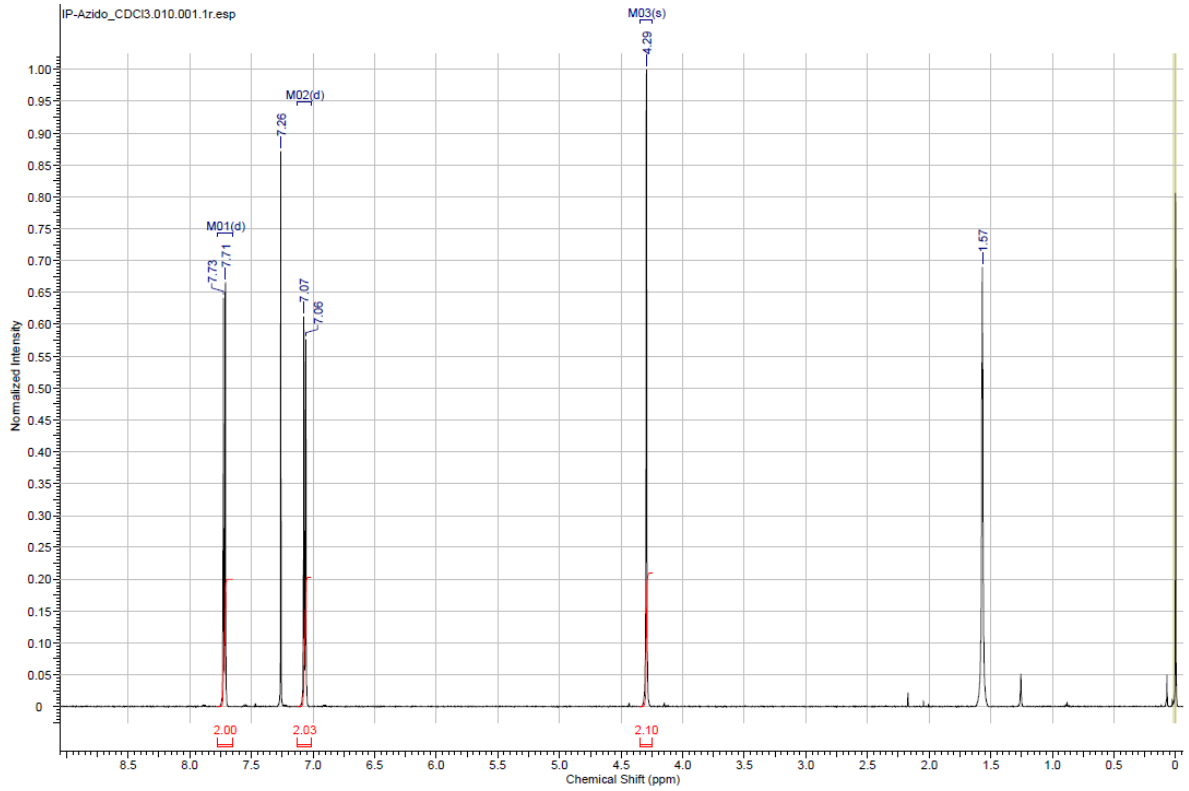


^{13}C NMR (126MHz, $CDCl_3$)

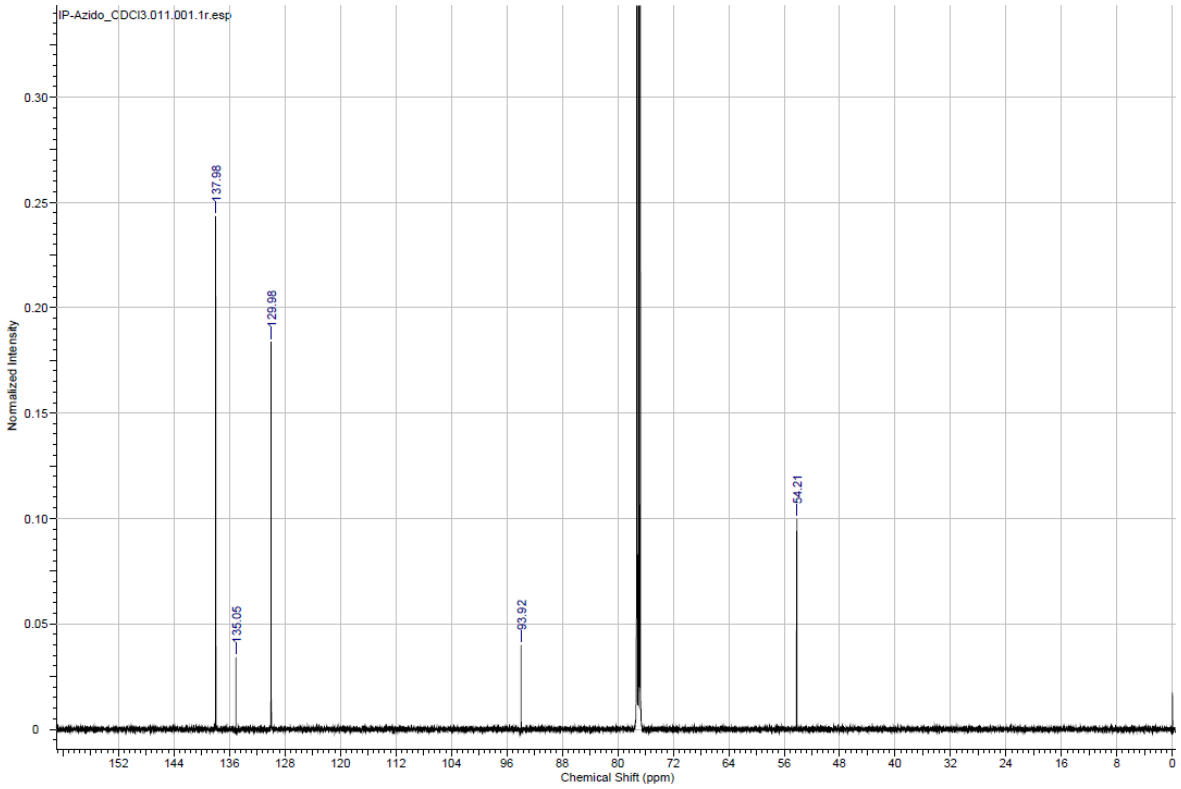


NMR spectra of **2**

^{1}H NMR (500MHz, $CDCl_3$)

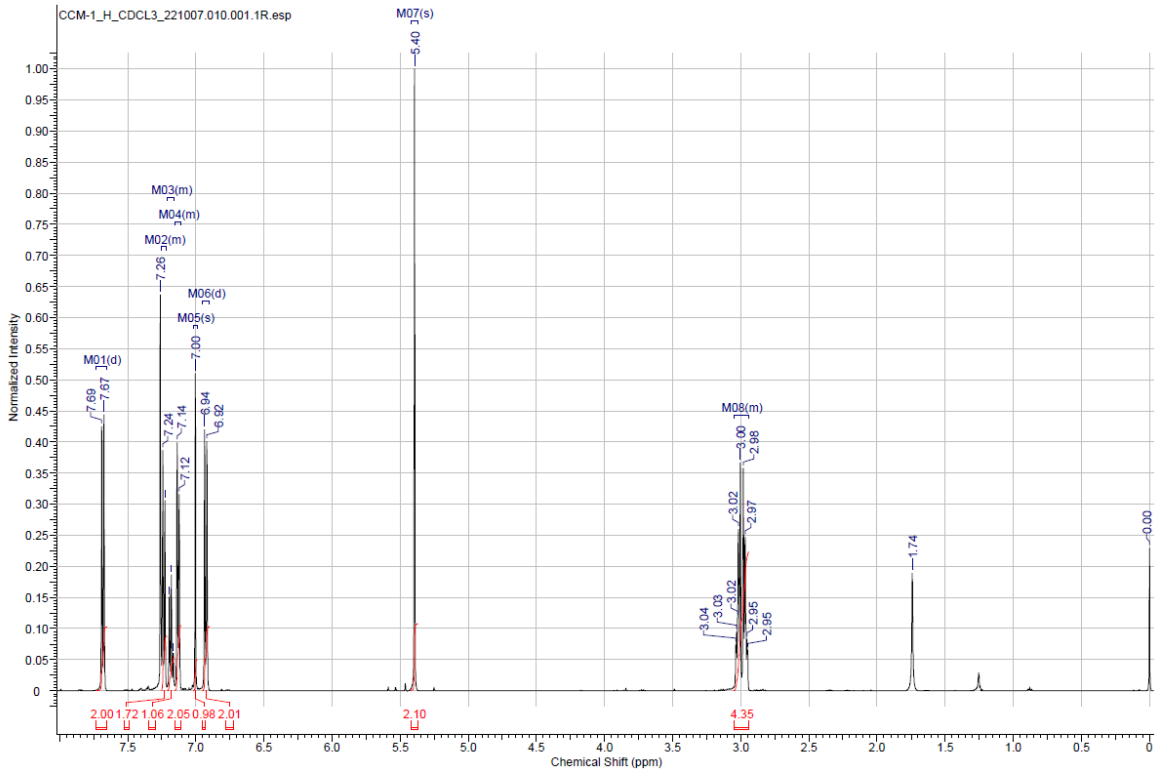


^{13}C NMR (126MHz, $CDCl_3$)

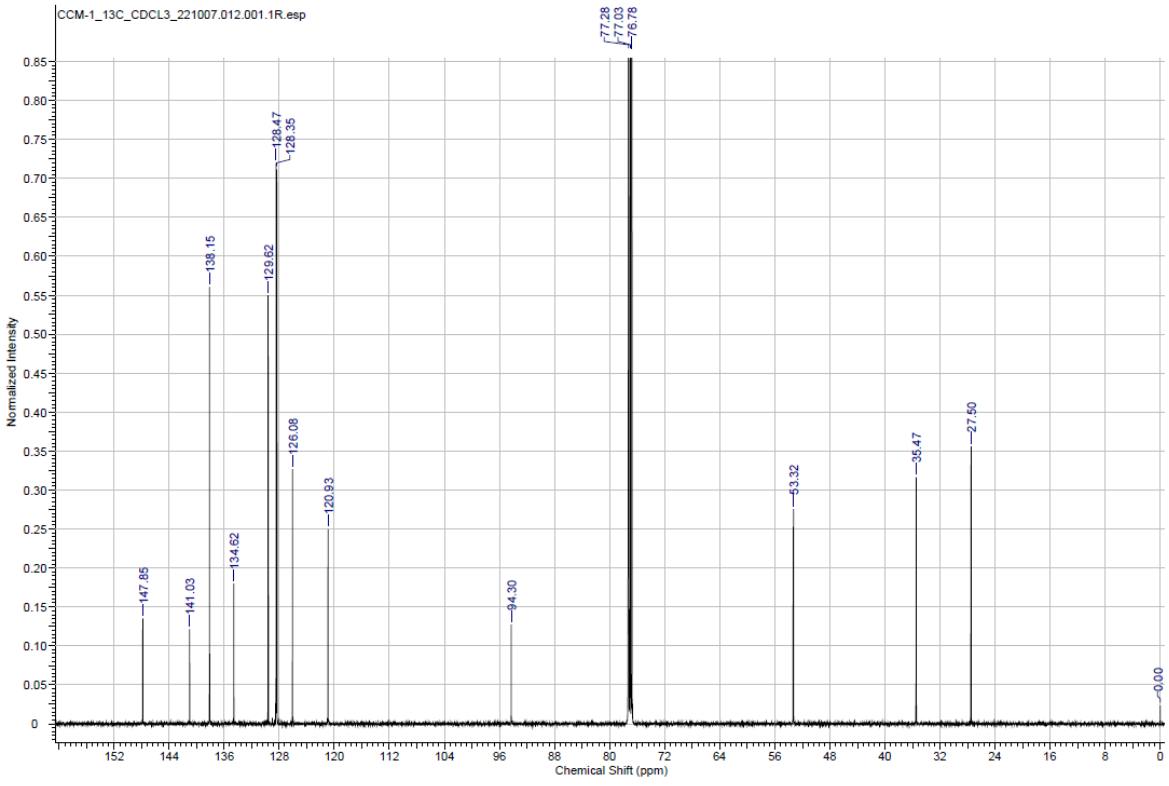


NMR spectra of **3**

^{1}H NMR (500MHz, $CDCl_3$)

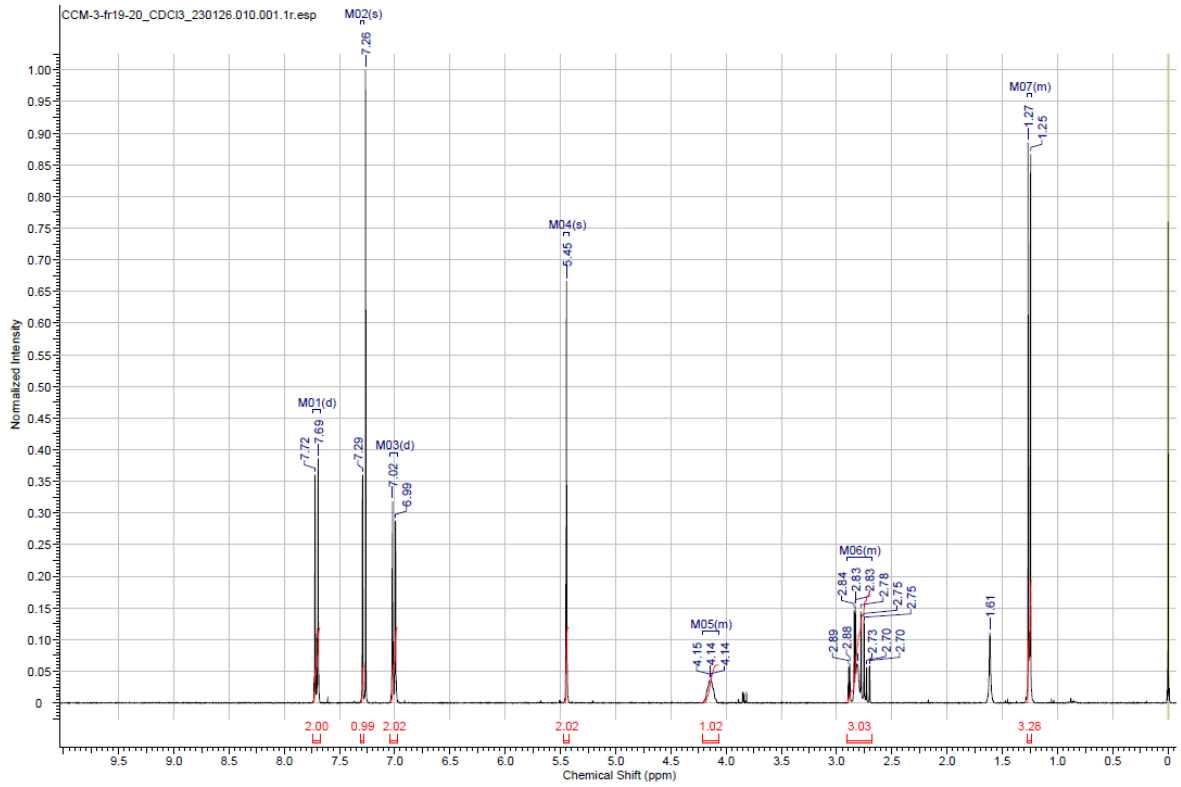


^{13}C NMR (126MHz, $CDCl_3$)

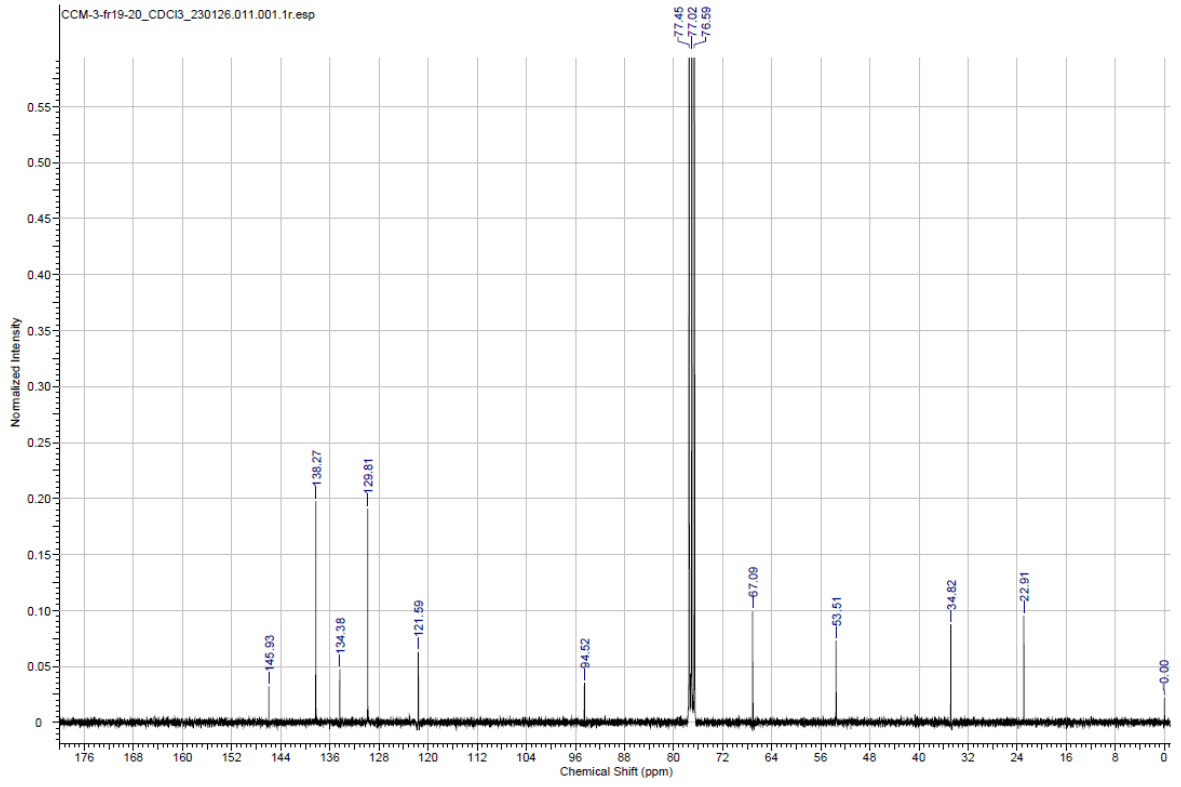


NMR spectra of **4**

^{1}H NMR (300MHz, $CDCl_3$)

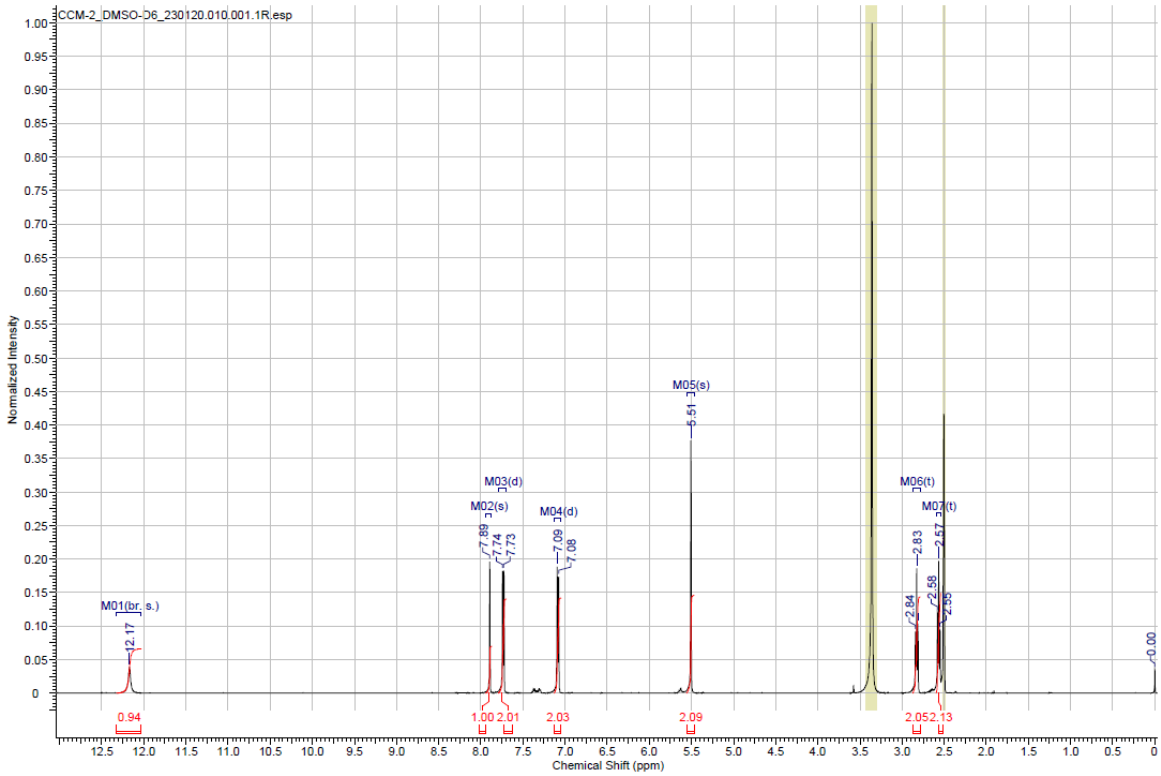


^{13}C NMR (75MHz, $CDCl_3$)

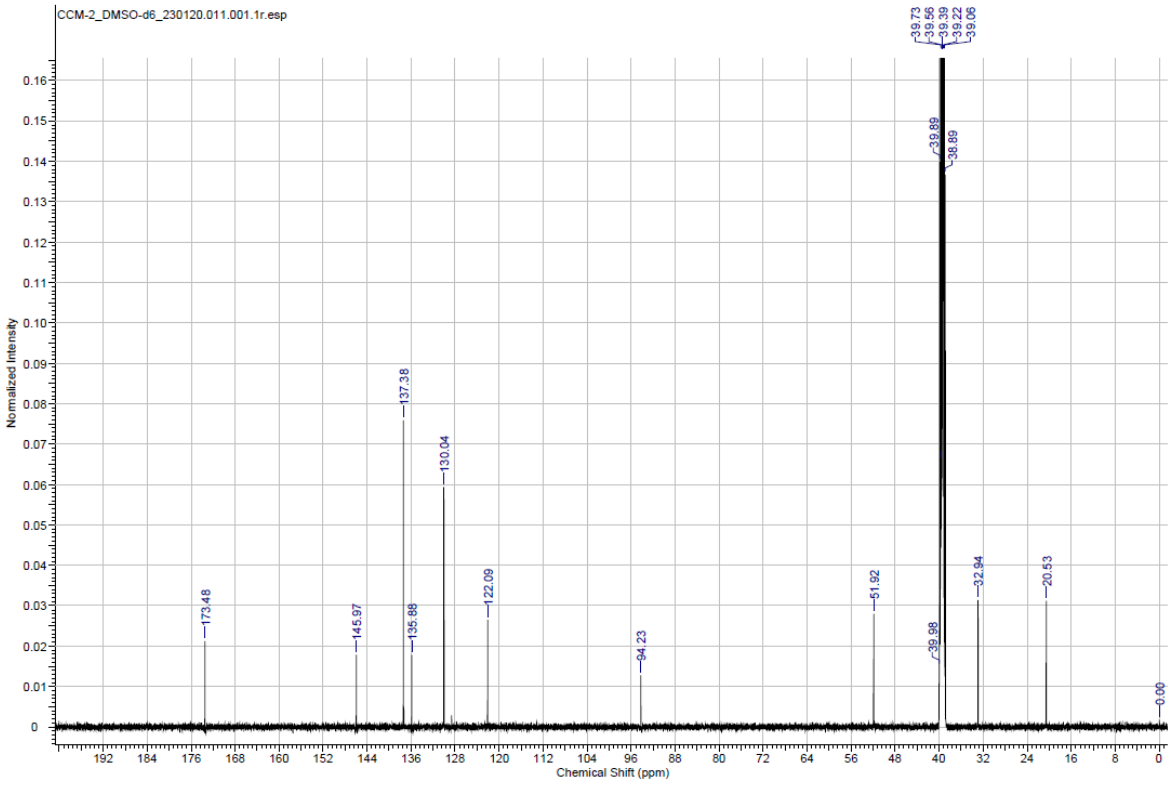


NMR spectra of **5**

^{1}H NMR (500MHz, DMSO-d_6)

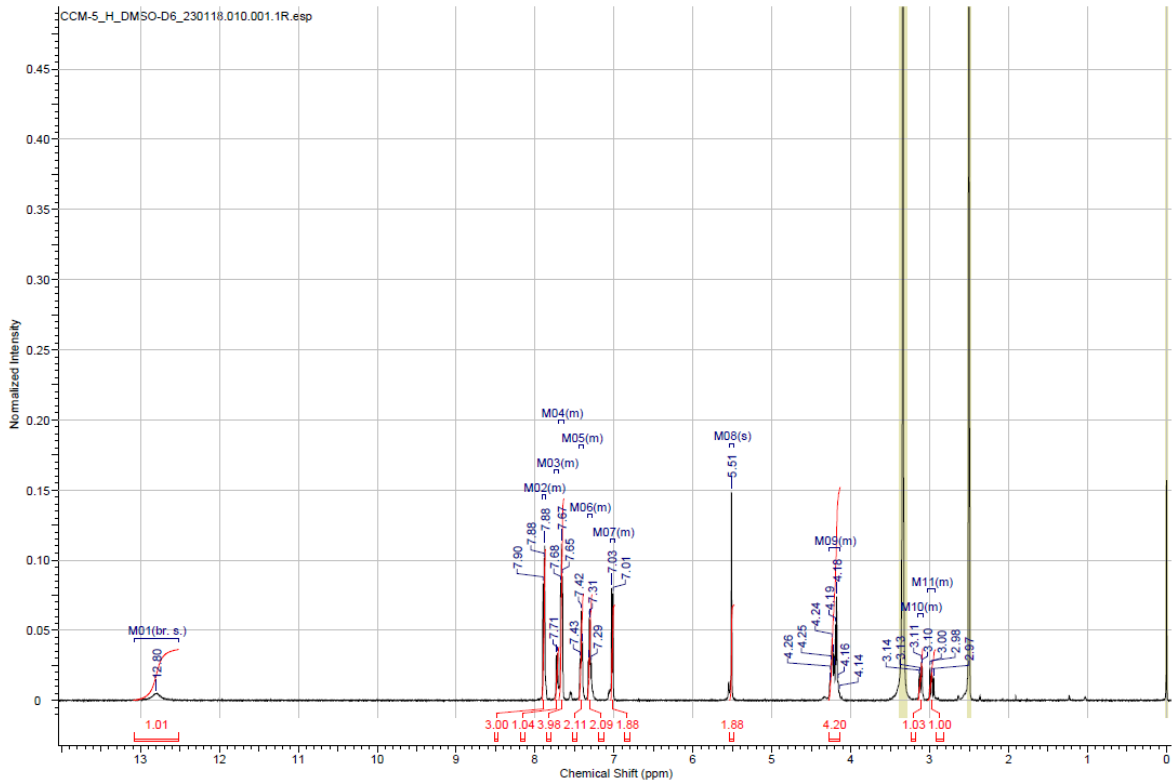


^{13}C NMR (126MHz, DMSO-d_6)

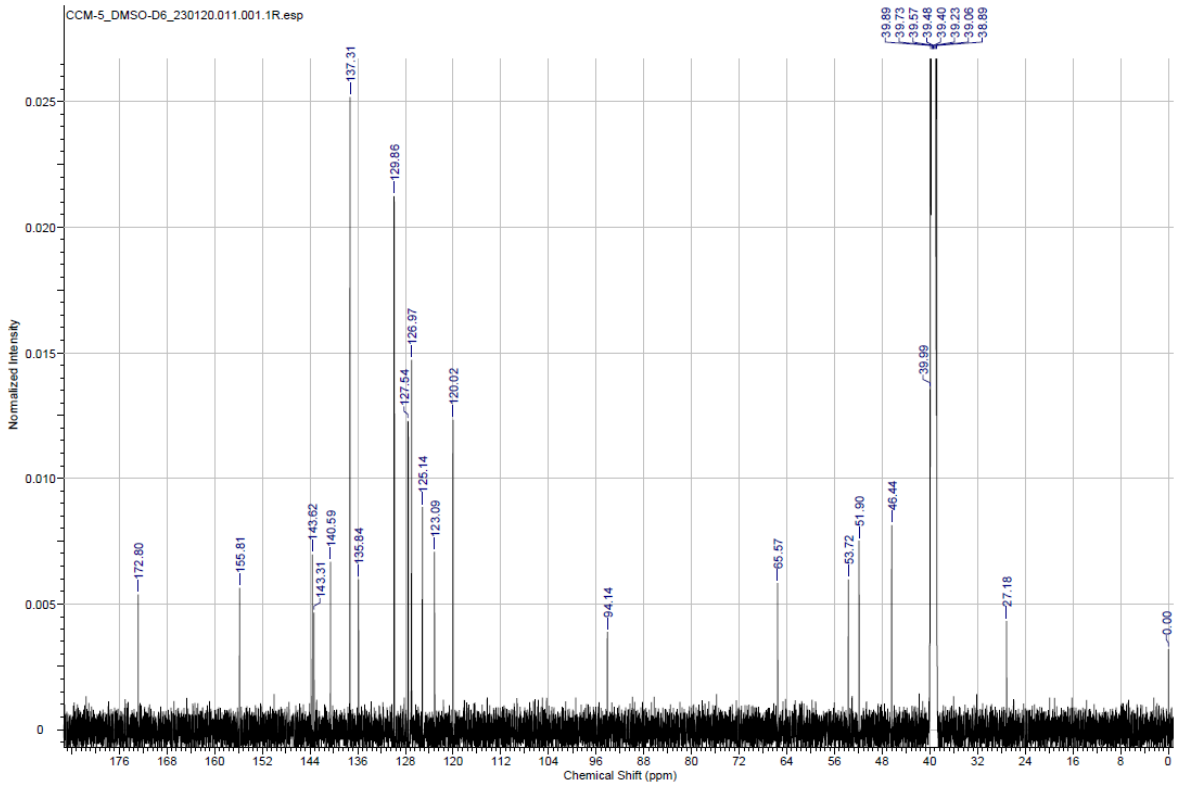


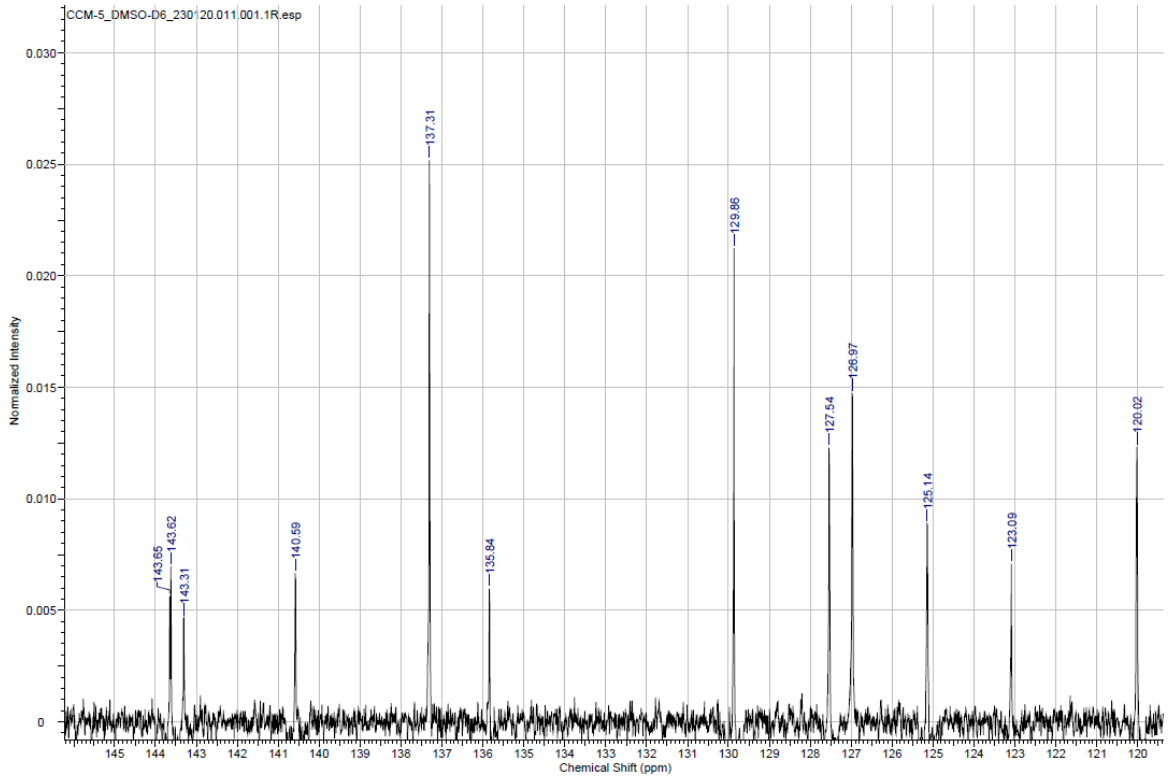
NMR spectra of **6**

^{1}H NMR (500MHz, DMSO-d_6)



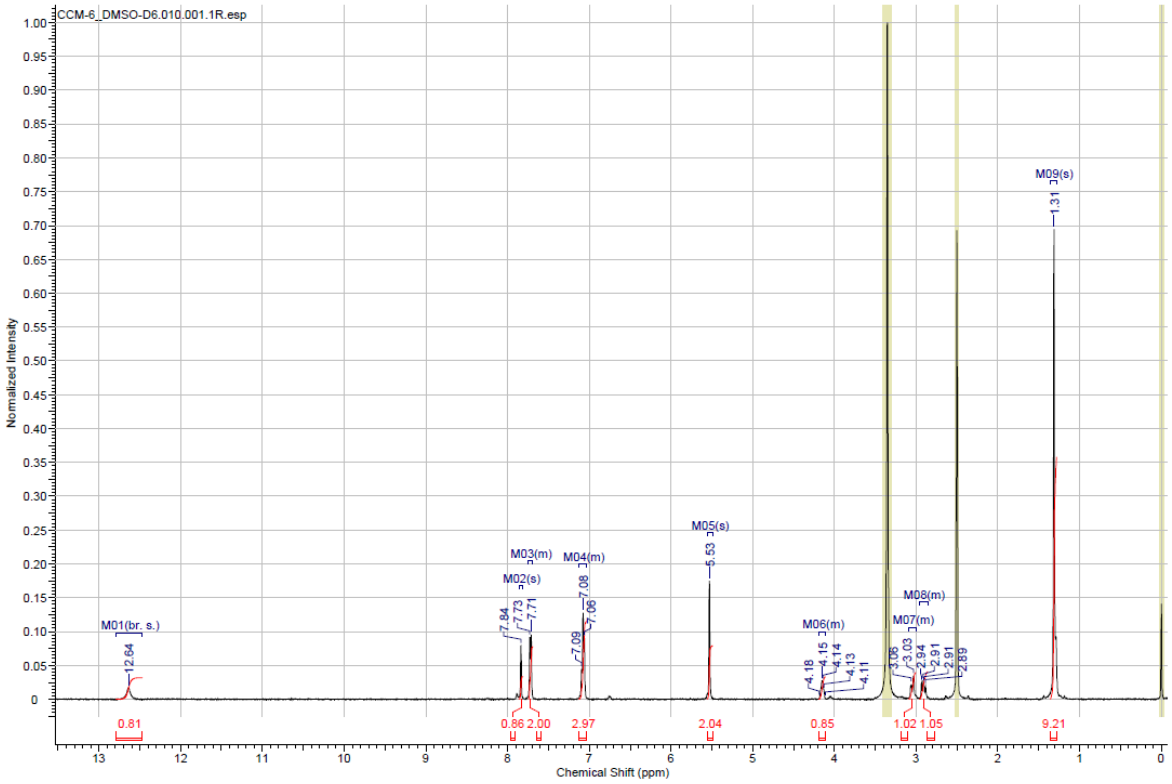
^{13}C NMR (126MHz, DMSO-d_6)



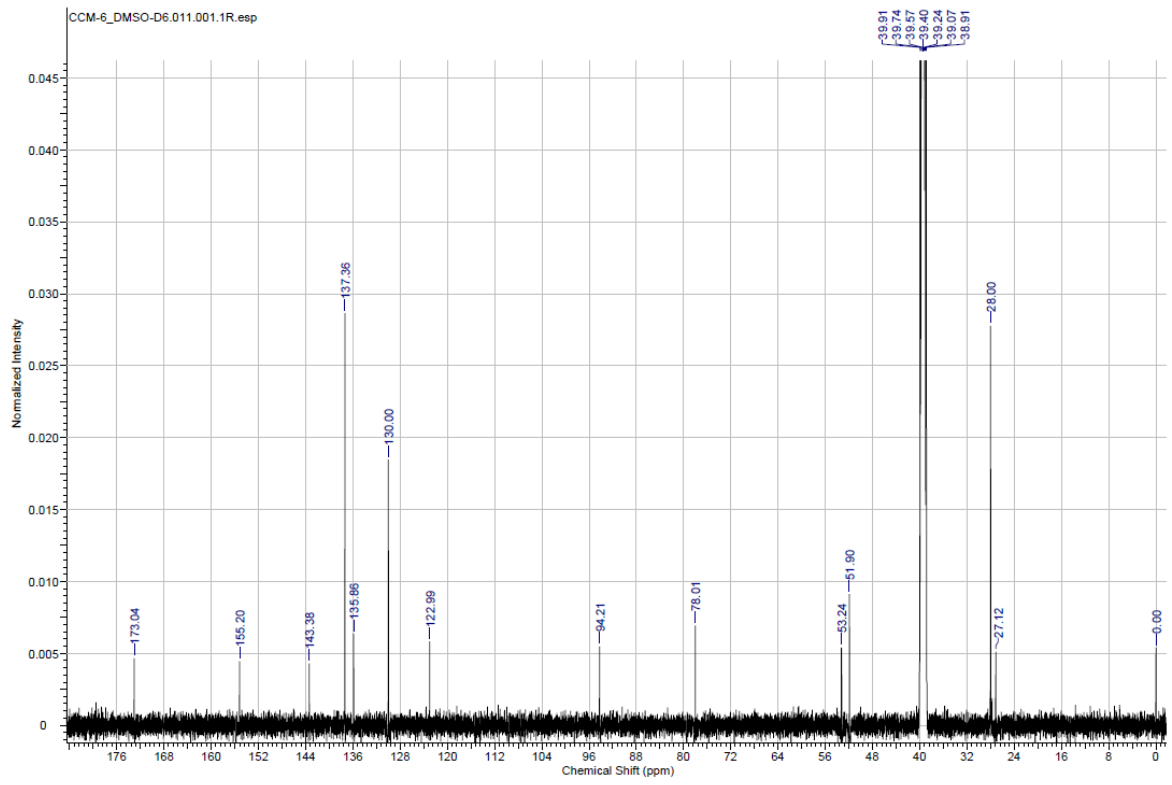

CCM-5_DMSO-D6_230 20.011.001.1R.esp
Normalized Intensity
Chemical Shift (ppm)
143.65
143.62
143.31
140.59
137.31
135.84
129.86
127.54
126.97
125.14
123.09
120.02

NMR spectra of **7**

^{1}H NMR (500MHz, DMSO-d_6)

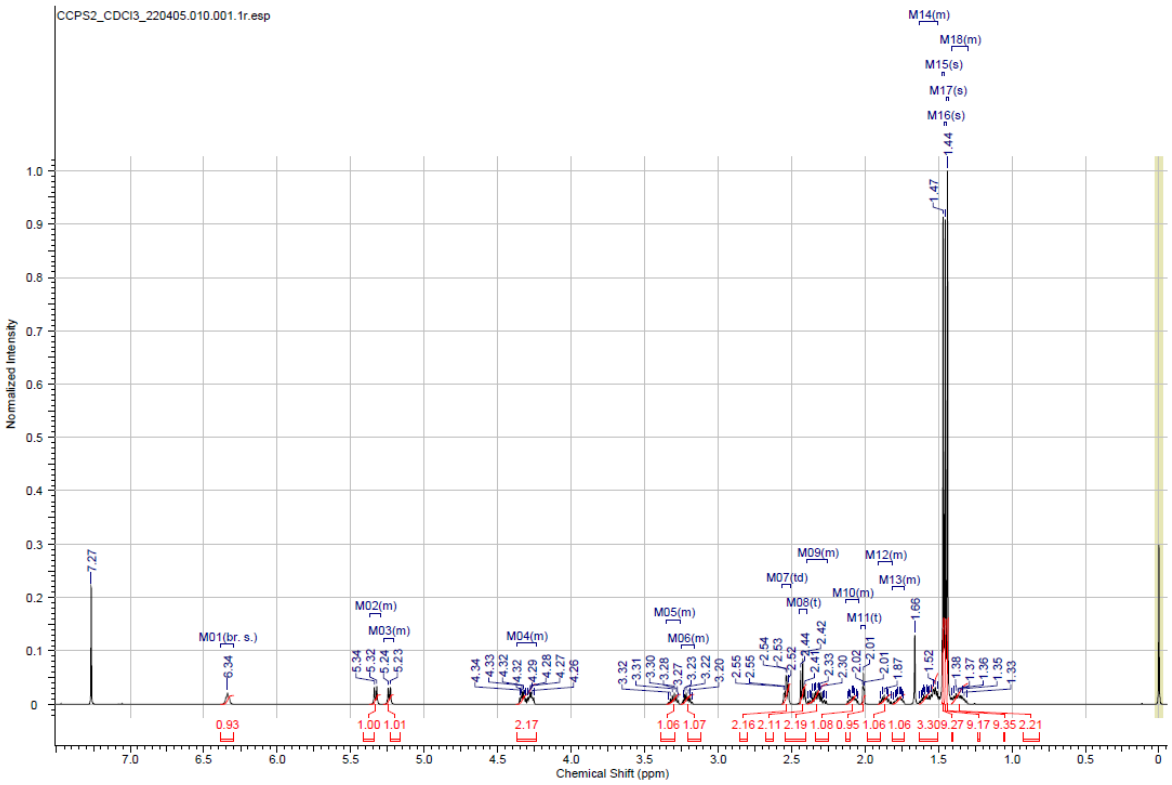


^{13}C NMR (126MHz, DMSO-d_6)

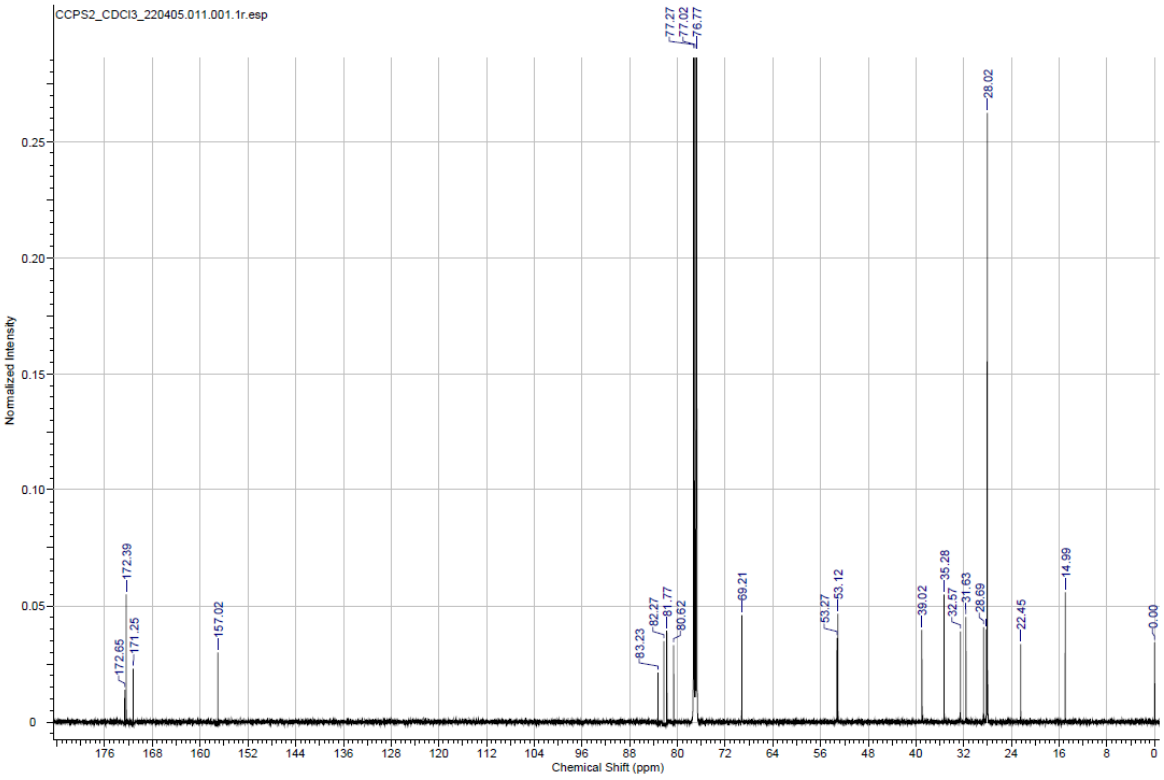


NMR spectra of **CCPS-2**

^{1}H NMR (500MHz, $CDCl_3$)

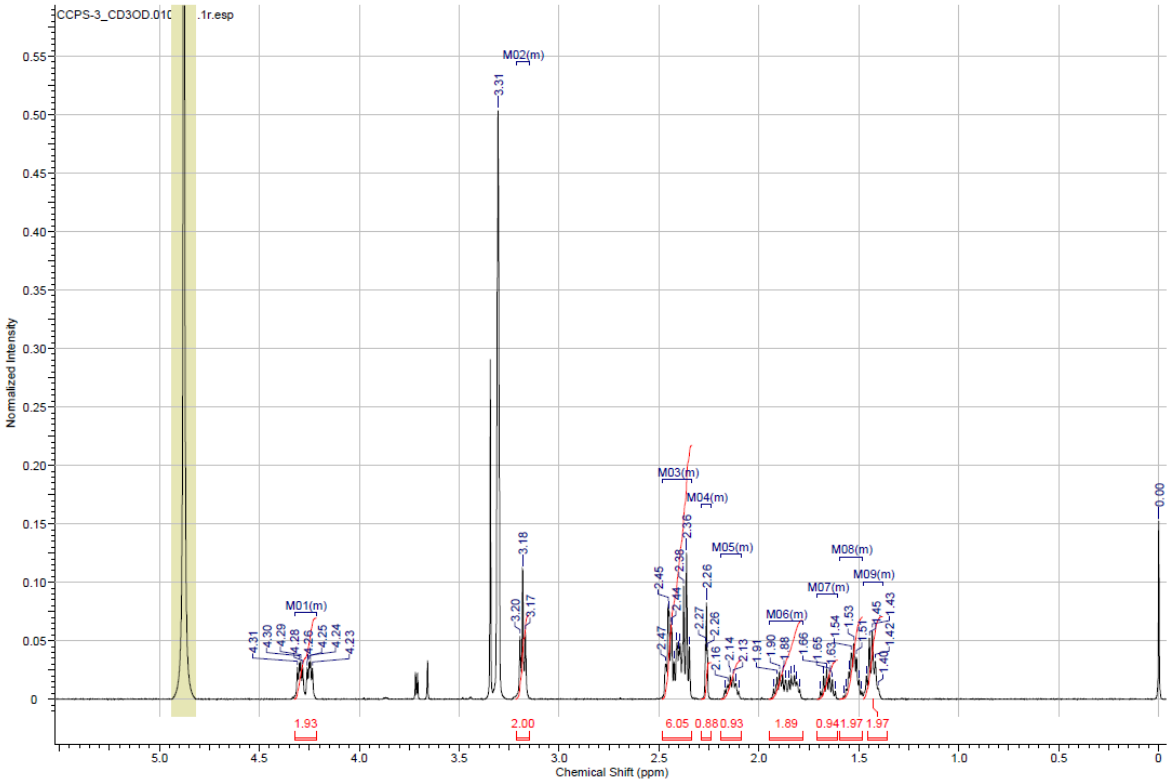


^{13}C NMR (126MHz, $CDCl_3$)

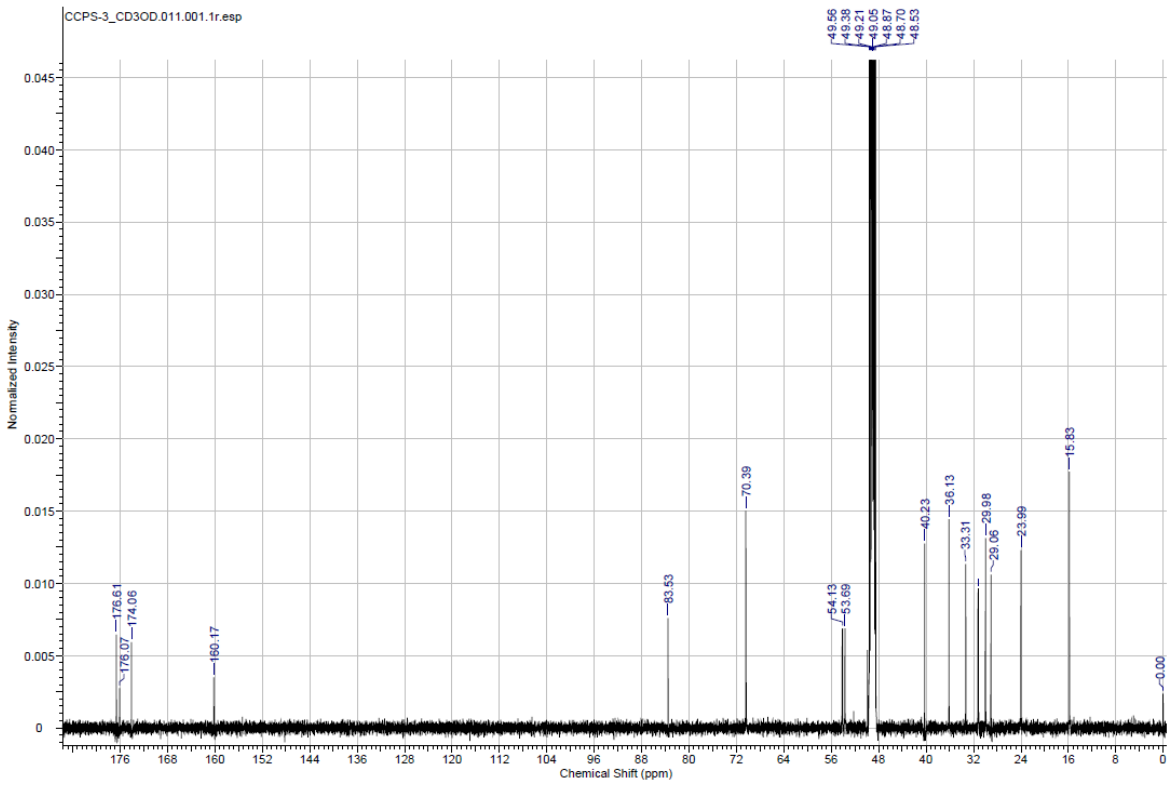


NMR spectra of **CCPS-3**

^{1}H NMR (500MHz, CD_3OD)

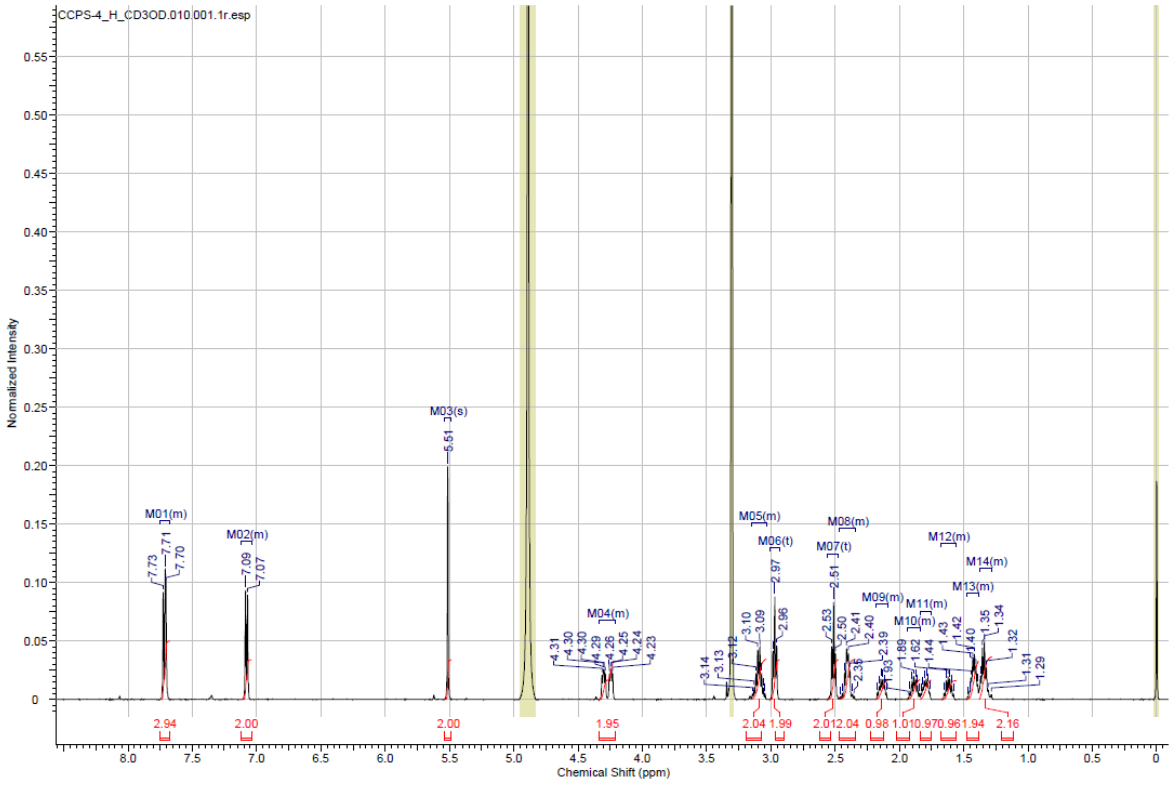


^{13}C NMR (126MHz, CD_3OD)



NMR spectra of **CCPS**

^{1}H NMR (500MHz, CD_3OD)



^{13}C NMR (126MHz, CD_3OD)