Supporting Information

Enantioselective conjugate addition of an α,α-dithioacetonitrile with nitrostyrenes using chiral bis(imidazoline)-Pd complexes

Shuichi Nakamura,*[a,b] Akari Tokunaga,[a] Hikari Saito,[a] Masaru Kondo[a,b]

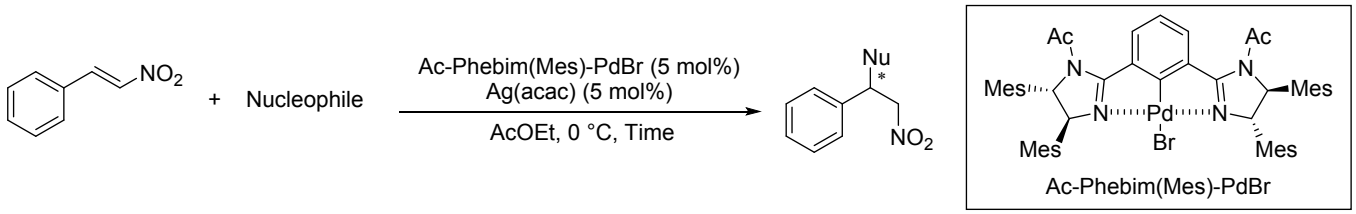
[a]Department of Life Science and Applied Chemistry, Graduate School of Engineering,
Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555 (Japan).
E-mail: snakamur@nitech.ac.jp
[b]Frontier Research Institute for Material Science,
Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555 (Japan)

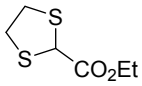
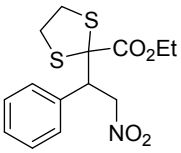
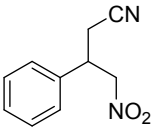
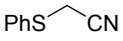
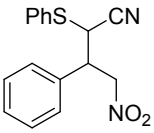
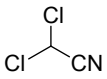
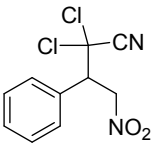
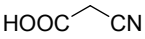
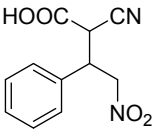
CONTENTS:

General Methods:

All reactions were performed in oven-dried glassware under a positive pressure of argon. Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and Basic $KMnO_4$ aqueous solution/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. Optical rotations were measured on a JASCO P-2200. The ^{1}H NMR (300 MHz), ^{19}F NMR (282 MHz) spectra for solution in $CDCl_3$ were recorded on Varian Mercury 300 or ^{13}C NMR (125 MHz) spectrum for solution in $CDCl_3$ were recorded on Bruker Avance 500. Chemical shifts (δ) are expressed in ppm downfield from internal TMS, $CHCl_3$. Infrared spectra were recorded on a JASCO FT/IR-4600 spectrometer with ZnSe ATR unit. HRMS were recorded on a Waters SYNAPT G2 (ESI). ESI Mass spectra were recorded on a SHIMADZU LCMS-2020 using positive mode. HPLC analyses were performed on a JASCO PU-2089T, UV-2075T, CO-2060Plus using 4.6 x 250 mm DAICEL CHIRALPAK IG®, IF-3®, IH® column. The reagents **2a-d** were synthesized according to previous synthetic methods.[1] Nitroalkenes **1a-p** were synthesized according to previous synthetic methods.[2]

Table S1. Reaction of ethyl 1,3-dithiolane-2-carboxylate 2e or various acetonitrile carbanion equivalents 2f-i with nitrostyrene 1a using 4f-Ag system



Entry	**2**	Nucleophile	product	Time (h)	Yield (%)	Ee (%)
1	**2e**			48	N.R.	-
2	**2f**	CH_3CN		24	N.R.	-
3	**2g**			48	Complex Mixture	-
4	**2h**			24	42	73
5	**2i**			24	N.R.	-

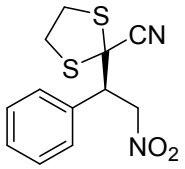
Synthesis of palladium-pincer complex with phebim:

Catalysts **4a-g** were synthesized by using previous method.[3)]

General procedure for the reaction of α,α-dithioacetonitrile with nitroalkenes catalyzed by chiral phebim-Pd(II) complexes:

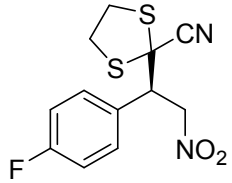
2a (15.1 μL, 0.15 mmol) and *trans*-β-nitrostyrene **1a** (14.9 mg, 0.1 mmol) were added to the mixture of Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ºC. After disappearance of *trans*-β-nitrostyrene **1a** monitored by TLC, the reaction was quenched by saturated NH_4Cl aq. and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (Toluene/Hexane=80/20) giving **3aa** (27.6 mg, 99 %) as a white solid.

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-phenylbutanenitrile (3aa)



$[\alpha]_D^{25}$ +44.8 (*c* 0.603, $CHCl_3$, 98% ee); mp = 108.2-109.0 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41-3.66 (m, 4H), 4.18 (dd, *J* = 9.0, 5.7 Hz, 1H), 5.03-5.15 (m, 2H), 7.37-7.50 (m, 5H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.3, 41.0, 51.6, 59.0, 76.9, 119.3, 128.6, 129.1, 129.7, 134.4; IR (ATR) 2925, 2224, 1551, 1496, 1455, 1423, 1376, 1281, 1198, 1092, 977, 956, 919, 903, 853, 824, 738, 698, 653 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{12}N_2NaO_2S_2$ [M+Na^+]: 303.0238, found 303.0234; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 12.3 min (minor), 13.5 min (major).

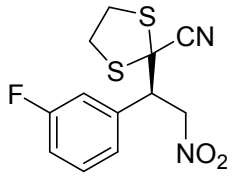
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-fluorophenyl)-4-nitrobutanenitrile (3ba)



Reaction of **1b** (16.7 mg, 0.10 mmol), **2a** (14.5 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 9 h gave (*R*)-**3ba** (29.3 mg, 98%, 95% ee) as a pale yellow solid.

$[\alpha]_D^{25}$ +32.5 (*c* 0.817, $CHCl_3$, 96% ee); mp = 98.3-99.0 ºC;^{1}H NMR (300 MHz, $CDCl_3$) δ 3.43-3.68 (m, 4H), 4.16 (dd, *J* = 10.1, 5.0 Hz, 1H), 4.98-5.13 (m, 2H), 7.05-7.13 (m, 2H), 7.42-7.49 (m, 2H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.4, 41.1, 51.0, 58.8, 76.9, 116.2 (d, $J_{C\text{-}F}$ = 21.7 Hz), 119.1, 130.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 130.5 (d, $J_{C\text{-}F}$ = 8.4 Hz), 163.3 (d, $J_{C\text{-}F}$ = 249.2 Hz); ^{19}F NMR (282.3 MHz, $CDCl_3$) δ −111.1 (s, 1F); IR (ATR) 2924, 2852, 2224, 1604, 1552, 1509, 1423, 1375, 1227, 1163, 1107, 1015, 843, 807, 718, 652 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{11}FN_2NaO_2S_2$ [M+Na^+]: 321.0144, found 321.0135; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 12.4 min (minor), 15.5 min (major).

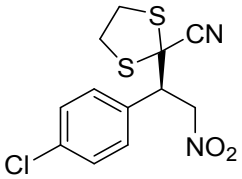
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-fluorophenyl)-4-nitrobutanenitrile (3ca)



Reaction of **1c** (16.7 mg, 0.10 mmol), **2a** (14.7 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 48 h gave (*R*)-**3ca** (23.1 mg, 78%, 97% ee) as a pale yellow solid.

$[\alpha]_D^{25}$ +31.4 (*c* 0.333, $CHCl_3$, 97% ee); mp = 67.1-68.1 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44-3.68 (m, 4H), 4.17 (dd, *J* = 9.9, 4.8 Hz, 1H), 4.99-5.14 (m, 2H), 7.07-7.42 (m, 4H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.5, 41.1, 51.3, 58.5, 76.7, 115.9 (d, $J_{C\text{-}F}$ = 22.6 Hz), 116.8 (d, $J_{C\text{-}F}$ = 20.8 Hz), 119.0, 124.3 (d, $J_{C\text{-}F}$ = 3.1 Hz), 130.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 136.6 (d, $J_{C\text{-}F}$ = 7.3 Hz), 162.7 (d, $J_{C\text{-}F}$ = 247.9 Hz); ^{19}F NMR (282.3 MHz, $CDCl_3$) δ −110.8 (ddd, 1F, *J* = 9.0, 9.0, 5.9 Hz); IR (ATR) 2925, 2854, 2223, 1725, 1612, 1590, 1556, 1546, 1487, 1452, 1434, 1380, 1281, 1260, 1234, 1149, 1096, 1003, 900, 872, 856, 790, 723, 695, 660 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{11}FN_2NaO_2S_2$ [M+Na$^+$]: 321.0144, found 321.0140; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 95:5, 1.0 mL/min, 254 nm) tR = 32.3 min (minor), 33.5 min (major).

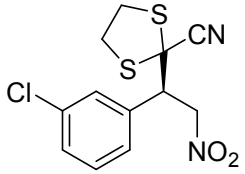
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-chlorophenyl)-4-nitrobutanenitrile (3da)



Reaction of **1d** (18.4 mg, 0.10 mmol), **2a** (14.8 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 24 h gave (*R*)-**3da** (27.5 mg, 87%, 97% ee) as a pale yellow solid.

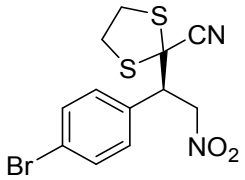
$[\alpha]_D^{25}$ +31.8 (*c* 0.867, $CHCl_3$, 97% ee); mp = 72.9-73.8 ºC ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.43-3.67 (m, 4H), 4.10-4.17 (m, 1H), 4.98-5.13 (m, 2H), 7.36-7.43(m, 4H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.5, 41.1, 51.1, 58.6, 76.7, 119.1, 129.4, 130.0, 132.8, 135.8; IR (ATR) 2925, 2852, 2224, 1718, 1552, 1493, 1415, 1375, 1281, 1198, 1093, 1014, 905, 842, 806, 775, 714, 654 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{11}ClN_2NaO_2S_2$ [M+Na$^+$]: 336.9848, found 336.9840; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 15.6 min (minor), 26.2 min (major).

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-chlorophenyl)-4-nitrobutanenitrile (3ea)



Reaction of **1e** (18.4 mg, 0.10 mmol), **2a** (14.7 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 24 h gave (*R*)-**3ea** (24.1 mg, 77%, 98% ee) as a white solid. $[\alpha]_D^{25}$ +41.7 (*c* 0.503, $CHCl_3$, 98% ee); mp = 77.8-78.4 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44-3.69 (m, 4H), 4.14 (dd, *J* = 9.9, 4.8 Hz, 1H), 4.99-5.14 (m, 2H), 7.30-7.45 (m, 4H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.5, 41.1, 51.3, 58.5, 76.6, 119.0, 126.6, 129.0, 130.0, 130.4, 135.0, 136.3; IR (ATR) 2925, 2855, 2220, 1730, 1545, 1476, 1435, 1381, 1280, 1200, 1089, 841, 785, 696, 657 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{11}ClN_2NaO_2S_2$ [M+Na$^+$]: 336.9848, found 336.9839; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 254 nm) tR = 17.9 min (major), 18.7 min (minor).

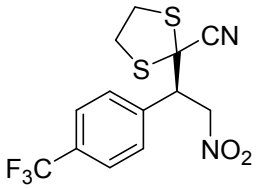
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-bromophenyl)-4-nitrobutanenitrile (3fa)



Reaction of **1f** (22.8 mg, 0.10 mmol), **2a** (14.9 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ºC for 48 h gave (*R*)-**3fa** (28.7 mg, 80%, 98% ee) as a white solid.

$[\alpha]_D^{25}$ +26.1 (*c* 0.853, $CHCl_3$, 96% ee); mp = 98.5-99.4 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.43-3.68 (m, 4H), 4.14 (dd, *J* = 10.2, 4.8 Hz, 1H), 4.98-5.13 (m, 2H), 7.26-7.37 (m, 2H), 7.51-7.55 (m, 2H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.5, 41.2, 51.2, 58.5, 76.6, 119.1, 124.1,130.3, 132.3, 133.3; IR (ATR) 2925, 2853, 2224, 1719, 1552, 1489, 1423, 1374, 1281, 1198, 1075, 1011, 838, 802, 768, 712, 650 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{11}BrN_2NaO_2S_2$, [M+Na$^+$]: 380.9343, found 380.9340; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 17.9 min (minor), 32.4 min (major).

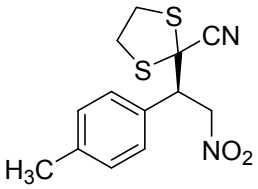
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-(4-trifluoromethyl)phenylbutanenitrile (3ga)



Reaction of **1g** (21.7 mg, 0.10 mmol), **2a** (14.9 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 24 h gave (*R*)-**3ga** (29.9 mg, 86%, 96% ee) as a pale yellow oil.

$[\alpha]_D^{25}$ +27.4 (*c* 0.757, $CHCl_3$, 96% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.45-3.69 (m, 4H), 4.24 (dd, *J* = 9.9, 5.1 Hz, 1H), 5.04-5.18 (m, 2H), 7.59-7.69 (m, 4H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.6, 41.2, 51.4, 58.3, 76.6, 118.9, 122.6, 124.7, 126.1 (q, $J_{C\text{-}F}$ = 3.8 Hz), 129.2, 131.9 (q, $J_{C\text{-}F}$ = 3.3 Hz), 138.2 ; ^{19}F NMR (282.3 MHz, CDCl3) δ −62.9. (s, 3F) IR (ATR) 2923, 2851, 2225, 1722, 1620, 1556, 1422, 1376, 1323, 1166, 1117, 1068, 1017, 849, 815, 737, 657 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{13}H_{11}N_2NaO_2S_2F_3$ [M+Na^+]: 371.0112, found 371.0107; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 9.7 min (minor), 12.3 min (major).

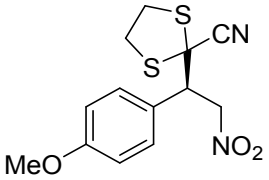
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-methylphenyl)-4-nitrobutanenitrile (3ha)



Reaction of **1h** (16.3 mg, 0.10 mmol), **2a** (15.1 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 50 ºC for 24 h gave (*R*)-**3ha** (13.8 mg, 47%, 94% ee) as a white oil.

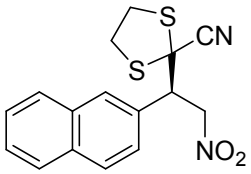
$[\alpha]_D^{25}$ +30.7 (*c* 0.470, $CHCl_3$, 94% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.42-3.67 (m, 4H), 4.11-4.16 (m, 1H), 5.00-5.13 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 21.3, 40.3, 41.0, 51.3, 59.1, 77.0, 119.3, 128.4, 129.8, 131.4, 139.7; IR (ATR) 2924, 2856, 2224, 1721, 1552, 1515, 1425, 1375, 1281, 1261, 1189, 1119, 1022, 978, 955, 907, 796, 716, 642 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{13}H_{14}N_2NaO_2S_2$ [M+Na^+]: 317.0394, found 317.0386; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 12.3 min (minor), 15.4 min (major).

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-methoxyphenyl)-4-nitrobutanenitrile (3ia)



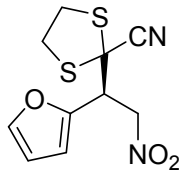
Reaction of **1i** (17.9 mg, 0.10 mmol), **2a** (14.9 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ºC for 72 h gave (*R*)-**3ia** (18.4 mg, 59%, 98% ee) as a yellow oil. $[\alpha]_D^{25}$ +31.1 (*c* 0.307, $CHCl_3$, 98% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41-3.67 (m, 4H), 3.80 (s, 3H), 4.10 (dd, *J* = 9.8, 5.3 Hz, 1H), 4.98-5.12 (m, 2H), 6.88-6.93 (m 2H), 7.32-7.41 (m, 2H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.3, 41.1, 51.1, 55.3, 59.3, 77.0, 114.4, 119.4, 126.2, 129.8, 160.4; IR (ATR) 2932, 2839, 2224, 1715, 1609, 1552, 1513, 1462, 1426, 1376, 1251, 1182, 1120, 1030, 908, 840, 802, 729, 650 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{13}H_{14}N_2NaO_3S_2$ [M+Na^+]: 333.0344, found 333.0335; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 18.7 min (minor), 24.9 min (major).

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(2-naphthyl)-4-nitrobutanenitrile (3ja)



Reaction of **1j** (19.9 mg, 0.10 mmol), **2a** (15.1 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 48 h gave (*R*)-**3ja** (25.3 mg, 77%, 98% ee) as a white solid. $[\alpha]_D^{25}$ +45.3 (*c* 0.623, $CHCl_3$, 98% ee); mp = 140.8-141.0 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44-3.66 (m, 4H), 4.40 (dd, *J* = 8.9, 6.2 Hz, 1H), 5.16-5.26 (m, 2H), 7.50-7.60 (m, 3H), 7.82-7.94 (m, 4H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.4, 41.1, 51.8, 59.0, 77.0, 119.3, 125.4, 126.8, 127.1, 127.8, 128.4, 128.5, 129.1, 131.8, 133.0, 133.6; IR (ATR) 2925, 2853, 2228, 1733, 1555, 1425, 1376, 1345, 1278, 1260, 1243, 1128, 1091, 1048, 1017, 966, 902, 869, 814, 754, 693, 672, 629 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{16}H_{14}N_2NaO_2S_2$ [M+Na^+]:353.0394, found 353.0400; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 17.2 min (major), 18.2 min (minor).

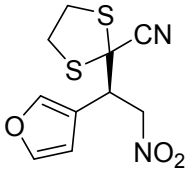
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(2-furyl)-4-nitrobutanenitrile (3ka)



Reaction of **1k** (13.9 mg, 0.10 mmol), **2a** (14.9 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ºC for 96 h gave (*R*)-**3ka** (19.1 mg, 71%, 95% ee) as a brown oil.

$[\alpha]_D^{25}$ +30.0 (*c* 0.497, $CHCl_3$, 95% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.46-3.64 (m, 4H), 4.37 (dd, *J* = 6.4, 5.4 Hz, 1H), 4.99-5.09 (m, 2H), 6.38-6.40 (m, 1H), 6.51 (d, *J* = 3.3 Hz, 1H), 7.45 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.6, 41.0, 45.6, 57.9, 110.9, 111.0, 118.9, 143.8, 147.4; IR (ATR) 3122, 2926, 2225, 1721, 1553, 1500, 1423, 1375, 1281, 1241, 1180, 1146, 1082, 1016, 976, 916, 812, 744, 677, 633 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{10}H_{10}N_2NaO_3S_2$ [M+Na^+]: 293.0031, found 293.0025; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 13.1 min (minor), 23.2 min (major).

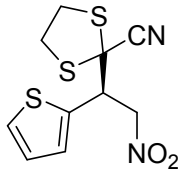
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-furyl)-4-nitrobutanenitrile (3la)



Reaction of **1l** (13.9 mg, 0.10 mmol), **2a** (15.1 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at r.t. for 48 h gave (*R*)-**3la** (20.5 mg, 76%, 94% ee) as a white solid.

$[\alpha]_D^{25}$ +36.3 (*c* 0.577, $CHCl_3$, 94% ee); mp = 53.8-54.5 ºC;^{1}H NMR (300 MHz, $CDCl_3$) δ 3.43-3.68 (m, 4H), 4.15 (dd, *J* = 10.5, 4.2 Hz, 1H), 4.80-4.88 (m, 1H), 5.00-5.06 (m, 1H), 6.58 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 2.1, 2.1 Hz, 1H), 7.56 (s, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.6, 41.2, 44.0, 58.7, 77.1, 109.1, 119.3, 119.4, 141.9, 144.1; IR (ATR) 2925, 2854, 2227, 1736, 1549, 1504, 1435, 1420, 1379, 1339, 1281, 1192, 1165, 1095, 1075, 1024, 940, 908, 873, 827, 792, 735, 672, 605 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{10}H_{10}N_2NaO_3S_2$ [M+Na^+]: 293.0031, found 293.0023; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 15.2 min (minor), 21.0 min (major).

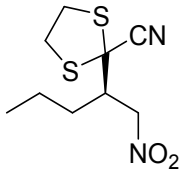
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-(2-thienyl)butanenitrile (3ma)



Reaction of **1m** (15.5 mg, 0.10 mmol), **2a** (14.9 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ℃ for 72 h gave (*R*)-**3ma** (26.0 mg, 91%, 97% ee) as a white solid.

$[\alpha]_D^{25}$ +44.4 (*c* 0.517, $CHCl_3$, 97% ee); mp = 120.8-121.5 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.47-3.66 (m, 4H), 4.50 (dd, *J* = 10.2, 4.2 Hz, 1H), 4.93-5.01 (m, 1H), 5.12 (dd, *J* = 13.2, 4.2 Hz, 1H), 7.01-7.04 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.22-7.26 (m, 1H), 7.35 (dd, *J* = 5.1, 1.2 Hz, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.8, 41.3, 47.8, 59.2, 78.0, 119.1, 127.0, 127.3, 128.7, 135.9; IR (ATR) 2965, 2925, 2231, 1741, 1551, 1438, 1415, 1383, 1281, 1241, 1197, 1168, 1090, 950, 910, 849, 810, 712, 676, 656 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{10}H_{10}N_2NaO_2S_3$ [M+Na^+]: 308.9802, found 308.9808; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 15.7 min (minor), 25.1 min (major).

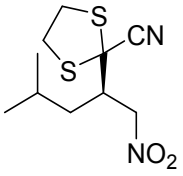
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-propylbutanenitrile (3na)



Reaction of **1n** (11.6 μl, 0.10 mmol), **2a** (14.7 μL, 0.15 mmol) using Ag(acac) (1.0 mg, 5 μmol) and **4f** (4.8 mg, 5 μmol) in AcOEt (0.65 mL) at 0 ℃ for 48 h. The residue was purified by silica gel column chromatography (eluent: hexane/diethyl ether, 80:20) to afford (*R*)-**3na** (17.6 mg, 72%, 95% ee) as a white oil.

$[\alpha]_D^{25}$ −5.5 (*c* 0.457, $CHCl_3$, 95% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.2 Hz, 3H), 1.40-1.64 (m, 3H), 1.88-1.99 (m, 1H), 3.11-3.19 (m, 1H), 3.45-3.61 (m, 4H), 4.40 (dd, *J* = 14.4, 5.4 Hz, 1H), 4.77 (dd, *J* = 14.4, 4.8 Hz, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 13.8, 20.4, 35.2, 40.1, 40.2, 44.0, 59.9, 75.9, 119.9; IR (ATR) 2961, 2927, 2873, 2224, 1551, 1465, 1422, 1377, 1281, 1243, 1212, 1148, 1106, 1039, 977, 903, 852, 802, 741, 677, 643 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_9H_{14}N_2NaO_2S_2$ [M+Na^+]: 269.0394, found 269.0403; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 13.0 min (major), 15.6 min (minor).

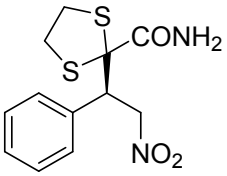
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(2-methylpropyl)-4-nitrobutanenitrile (3oa)



Reaction of **1o** (14.3 µl, 0.10 mmol), **2a** (29.8 µL, 0.30 mmol) using Ag(acac) (1.0 mg, 5 µmol) and **4f** (4.8 mg, 5 µmol) in AcOEt (0.65 mL) at r.t. for 24 h. The residue was purified by silica gel column chromatography (eluent: hexane/diethyl ether, 80:20) to afford (*R*)-**3oa** (20.9 mg, 80%, 96% ee) as a white oil.

$[\alpha]_D^{25}$ −11.9 (*c* 0.293, $CHCl_3$, 96% ee); mp = 42.6-43.0 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97-1.02 (m, 6H), 1.46-1.60 (m, 1H), 1.62-1.76 (m, 2H), 3.18-3.26 (m, 1H), 3.45-3.61 (m, 4H), 4.33 (dd, *J* = 14.7, 4.8 Hz, 1H), 4.77 (dd, *J* = 14.6, 5.6 Hz, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 21.2, 23.5, 26.1, 39.9, 40.2, 42.3, 60.5, 76.1, 119.9; IR (ATR) 2960, 2928, 2871, 2220, 1728, 1550, 1467, 1415, 1375, 1279, 1239, 1170, 1011, 954, 910, 852, 831, 772, 711, 675, 636 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{10}H_{16}N_2NaO_2S_2$ [M+Na^+]: 283.0551, found 283.0558; HPLC (DAICEL CHIRALPAK IF-3®, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 254 nm) tR = 11.3 min (major), 12.9 min (minor).

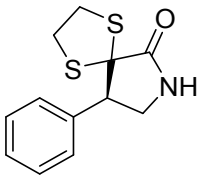
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-phenylbutanamide (5)



A mixture of **3aa** (83.0 mg, 0.296 mmol), acetaldoxime (54.0 µL, 0.882 mmol), $InCl_3{\cdot}4H_2O$ (35.0 mg, 0.119 mmol) in toluene/THF(0.8 mL, v:v=4:1) was heated to 50 ºC overnight under argon atmosphere. The reaction was quenched by water and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc =50:50) to give compound (*R*)-**5** as a white solid (76.8 mg, 87%, 97% ee).

$[\alpha]_D^{25}$ +22.5 (*c* 0.687, $CHCl_3$, 99% ee); mp = 166.3-167.0 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.22-3.36 (m, 4H), 4.47-4.52 (m, 1H), 5.10-5.29 (m, 2H), 6.27 (s, 1H), 7.00 (s, 1H), 7.26-7.37 (m, 5H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 40.3, 51.2, 75.0, 78.1, 128.5, 128.6, 129.0, 135.5, 172.9; IR (ATR) 3403, 3119, 1670, 1547, 1456, 1418, 1375, 1282, 1200, 1094, 1026, 981, 848, 815, 768, 742, 697 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{14}N_2NaO_3S_2$ [M+Na^+]: 321.0344, found 321.0344; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 26.0 min (minor), 27.4 min (major).

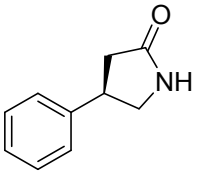
(9*R*)-1,4-Dithia-9-phenyl-7-azaspiro[4.4]nonane (6)



Fe (139.6 mg, 2.50 mmol) was added to the solution of **5** (76.4 mg, 0.255 mmol) in EtOH (3.6 mL) at 90 °C, then aqueous ammonium chloride (133.7 mg in 1.0 mL H_2O, 2.50 mmol) was added. After 2 h, the reaction mixture was passed through celite with AcOEt and removal solvent under reduced pressure. Then, residue was dissolved in AcOEt/water, and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (benzene/AcOEt = 50:50) to give compound (*R*)-**6** as a white solid (48.9 mg, 76%, 96% ee).

$[\alpha]_D^{25}$ −26.3 (*c* 0.477, $CHCl_3$, 98% ee); mp = 205.1-205.3 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.72-2.82 (m, 1H), 3.15-3.27 (m, 1H), 3.34-3.51 (m, 1H), 3.62-3.72 (m, 1H), 3.84 (t, *J* = 7.5 Hz, 1H), 7.28-7.43 (m, 5H), 7.89 (s, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 39.0, 39.6, 45.3, 51.8, 71.1, 128.0, 128.1, 129.0, 136.6, 177.0; IR (ATR) 3195, 3093, 1693, 1479, 1454, 1423, 1352, 1279, 1254, 1279, 1254, 1087, 833, 763, 695, 636 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{12}H_{13}NNaOS_2$ [M+Na$^+$]: 274.0336, found 274.0338; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 14.0 min (major), 15.3 min (minor).

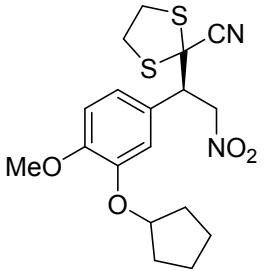
(4*R*)-4-Phenyl-2-pyrrolidinone (7)



$NaBH_4$ (64.3 mg, 1.70 mmol) was added to the solution of **6** (42.7 mg, 0.170 mmol) and $NiCl_2 \cdot 6H_2O$ (204 mg, 0.858 mmol) in MeOH/THF (2.0 mL, v:v=4:1) at 0 ℃, and the reaction mixture was stirred at room temperature. After 1 h, the reaction mixture was passed through celite with AcOEt and removal solvent under reduced pressure. Then, residue was dissolved in AcOEt/water, and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (AcOEt only) to give compound **7** as a white solid (21.9 mg, 80%, 97% ee).

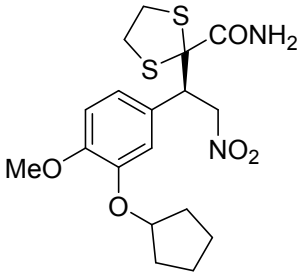
$[\alpha]_D^{25}$ −69.3 (*c* 0.39, MeOH, 97% ee) [lit. [4] value $[\alpha]_D^{20}$ −30.0 (c 0.3, MeOH)]; mp = 94.5-95.1ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.47-2.56 (m, 1H), 2.70-2.79 (m, 1H), 3.43 (dd, *J* = 9.0, 6.9 Hz, 1H), 3.64-3.82 (m, 2H), 6.63 (s, 1H), 7.25-7.37 (m, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 37.9, 40.3, 49.5, 126.8, 127.1, 128.9, 142.1, 177.7; IR (ATR) 3237, 2924, 2860, 1668, 1494, 1444, 1362, 1259, 1121, 1052, 744, 694, 630 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{10}H_{11}NNaO$ [M+Na$^+$]: 184.0738, found 184.0743; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 13.2 min (minor), 14.6 min (major).

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-[3-(cyclopentyloxy)-4-methoxyphenyl]butanenitrile (8)



Reaction of **1p** (105.3 mg, 0.40 mmol), **2a** (60.6 μL, 0.60 mmol) using Ag(acac) (4.1 mg, 20 μmol) and **4f** (19.1 mg, 20 μmol) in AcOEt (2.6 mL) at r.t. for 48 h gave (*R*)-**8** (138.8 mg, 88%, 95% ee) as a yellow oil. $[\alpha]_D^{25}$ +31.4 (*c* 0.290, $CHCl_3$, 95% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60-1.64 (m, 2H), 1.77-1.99 (m, 6H), 3.47-3.67 (m, 4H), 3.85 (s, 1H), 4.08 (dd, *J* = 4.2, 3.0 Hz, 1H), 4.12-4.81 (m, 1H), 4.98-5.09 (m, 2H), 6.82-6.86 (m, 1H), 6.94-6.98 (m, 2H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 24.2, 32.8, 40.2, 41.1, 51.4, 55.9, 59.3, 80.4, 111.7, 114.4, 119.5, 120.9, 126.4, 147.7, 150.8; IR (ATR) 2958, 2871, 2224, 1717, 1590, 1555, 1514, 1429, 1375, 1257, 1238, 1164, 1142, 1020, 983, 909, 856, 802, 778, 729, 672, 648 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{18}H_{22}N_2NaO_4S_2$ [M+Na$^+$]: 417.0919, found 417.0909; HPLC (DAICEL CHIRALPAK IG®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 12.1 min (major), 13.2 min (minor).

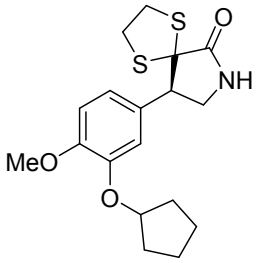
(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-[3-(cyclopentyloxy)-4-metoxyphenyl]butanamide (9)



A mixture of **8** (125.6 mg, 0.318 mmol), acetaldoxime (58.4 μL, 0.954 mmol), $InCl_3 \cdot 4H_2O$ (28.0 mg, 0.0954 mmol) in toluene/THF(1.6 mL, v:v=4:1) was heated to 100 ℃ overnight under argon atmosphere. The reaction was quenched by water and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (hexane/EtOAc =50:50) to give compound (*R*)-**9** as a white solid (120.5 mg, 92%, 97% ee).

$[\alpha]_D^{25}$ +12.0 (*c* 0.203, $CHCl_3$, 97% ee); mp = 144.3-144.9 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58-1.65 (m, 2H), 1.76-1.98 (m, 6H), 3.24-3.34 (m, 4H), 3.79 (s 3H), 4.42 (dd, *J* = 10.8, 4.2 Hz, 1H), 4.69-4.75 (m,1H), 5.06-5.24 (m, 2H), 5.94 (s, 1H), 6.74 (d, *J* = 8.7 Hz, 1H), 6.84–6.86 (m, 2H), 7.01 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 24.2, 32.8, 40.4, 51.0, 55.9, 75.3, 78.2, 80.3, 111.4, 115.4, 121.1, 127.5, 147.3, 150.0, 172.6; IR (ATR) 3432, 2955, 1676, 1548, 1512, 1427, 1375, 1260, 1234, 1163, 1141, 1022, 980, 846, 802, 777, 741, 687, 620 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{18}H_{24}N_2NaO_5S_2$ [M+Na$^+$]: 435.1024, found 435.1020; HPLC (DAICEL CHIRALPAK IH®, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 254 nm) tR = 28.4 min (minor), 30.7 min (major).

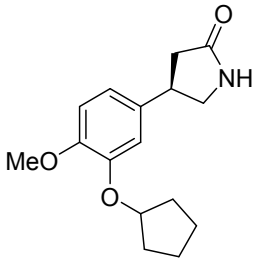
(9*R*)-1,4-Dithia-9-[3-(cyclopentyloxy)-4-methoxyphenyl]-7-azaspiro[4.4]nonane (10)



Fe (48.9 mg, 0.875 mmol) was added to the solution of **9** (36.1 mg, 0.0875 mmol) in EtOH (1.3 mL) at 100 ℃, then aqueous ammonium chloride (46.8 mg in 0.37 mL H_2O, 0.875 mmol) was added. After 2.5 h, the reaction mixture was passed through celite with AcOEt and removal solvent under reduced pressure. Then, residue was dissolved in AcOEt/water, and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (benzene/AcOEt = 60:40) to give compound (*R*)-**10** as a white solid (27.2 mg, 85%, 96% ee).

$[\alpha]_D^{25}$ −20.0 (*c* 0.710, $CHCl_3$, 96% ee); mp = 191.0-191.2 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51-1.67 (m, 2H), 1.74-2.04 (m, 6H), 2.75-2.83 (m, 1H), 3.18-3.25 (m, 1H), 3.34-3.51 (m, 2H), 3.63 (d, *J* = 7.5 Hz, 2H), 3.72-3.79 (m, 1H), 3.84 (s, 1H), 4.75-4.81 (m, 1H), 6.80-6.90 (m, 1H), 6.98 (d, *J* = 2.1 Hz, 1H), 7.53 (s, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 24.2, 32.9, 38.9, 39.7, 45.2, 51.3, 55.9, 71.1, 80.4, 111.0, 115.8, 121.0, 128.8, 147.0, 149.7, 176.4; IR (ATR) 3189, 3088, 2927, 2869, 1699, 1589, 1515, 1444, 1425, 1358, 1326, 1244, 1164, 1140, 1031, 1005, 982, 848, 796, 774, 737, 702, 635, 614 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{18}H_{23}NNaO_3S_2$ [M+Na^+]: 388.1017, found 388.1020; HPLC (DAICEL CHIRALPAK IH®, Hexane:*i*PrOH = 70:30, 1.0 mL/min, 254 nm) tR = 16.2 min (major), 19.1 min (minor).

(4*R*)-4-[3-(Cyclopentyloxy)-4-methoxyphenyl]-2-pyrrolidinone (11)

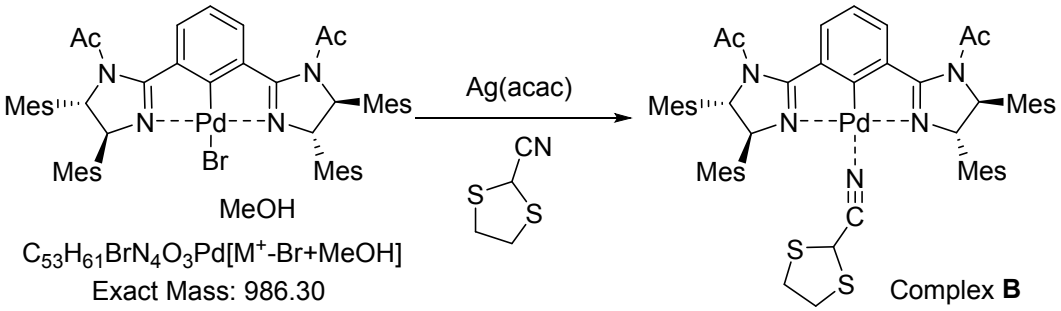


$NaBH_4$ (34.3 mg, 0.908 mmol) was added to the solution of **10** (22.1 mg, 0.0605 mmol) and $NiCl_2 \cdot 6H_2O$ (72.0 mg, 0.303 mmol) in MeOH/THF (0.75 mL, v:v=4:1) at 0 ºC, and the reaction mixture was stirred at room temperature. After 6 h, the reaction mixture was passed through celite with MeOH and removal solvent under reduced pressure. Then, residue was dissolved in AcOEt/water, and extracted with AcOEt, and combined organic layer was dried over Na_2SO_4. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography (benzene/AcOEt = 10:90) to give compound **11** as a white solid (8.8 mg, 53%, 95% ee).

$[\alpha]_D^{25}$ −28.1 (*c* 0.177, $CHCl_3$, 96% ee); mp = 132.4-133.1 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58-1.64 (m, 2H), 1.77-1.94 (m, 6H), 2.42-2.52 (m, 1H), 2.66-2.76 (m, 1H), 3.35-3.40 (m, 2H), 3.57-3.78 (m, 1H), 3.83

(s, 3H), 4.73-4.79 (m, 1H), 6.03 (s, 1H), 6.75-6.85 (m, 1H); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 24.1, 32.8, 38.1, 40.0, 49.8, 56.1, 80.6, 112.1, 113.7, 118.8, 134.5, 147.9, 149.1, 177.7; IR (ATR) 3199, 3097, 2941, 1697, 1685, 1593, 1513, 1493, 1439, 1327, 1271, 1249, 1235, 1144, 1025, 1002, 876, 815, 771, 686, 641, 619 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{16}H_{21}NNaO_3$ [$M+Na^+$]: 298.1419, found 298.1414; HPLC (DAICEL CHIRALPAK IH®, Hexane:*i*PrOH = 70:30, 1.0 mL/min, 254 nm) tR = 19.1 min (major), 34.2 min (minor).

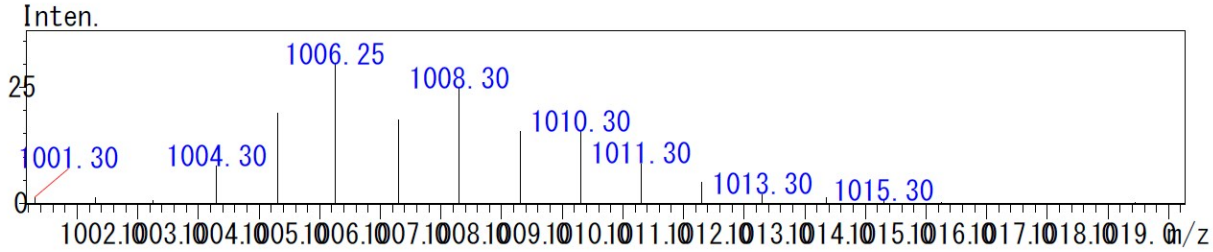
ESI-Mass spectroscopic analysis for complex between 4f and Ag(acac)



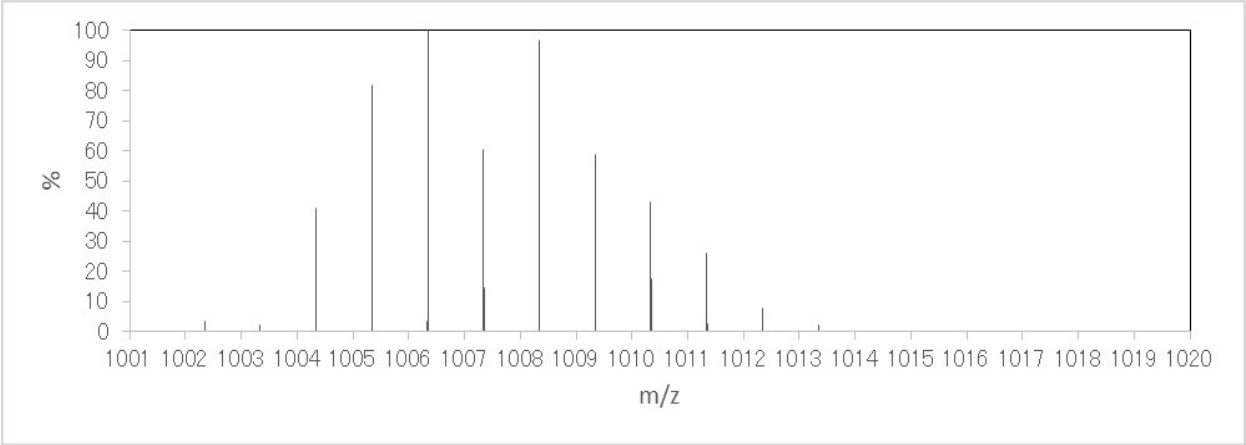
$C_{53}H_{61}BrN_4O_3Pd[M^+-Br+MeOH]$
Exact Mass: 986.30

$C_{56}H_{62}N_5O_2PdS_2$
Exact Mass: 1006.3380

ESI Mass spectrum of 4f, Ag(acac), and 2a



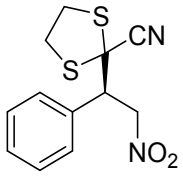
Theoretical peaks about complex B



References

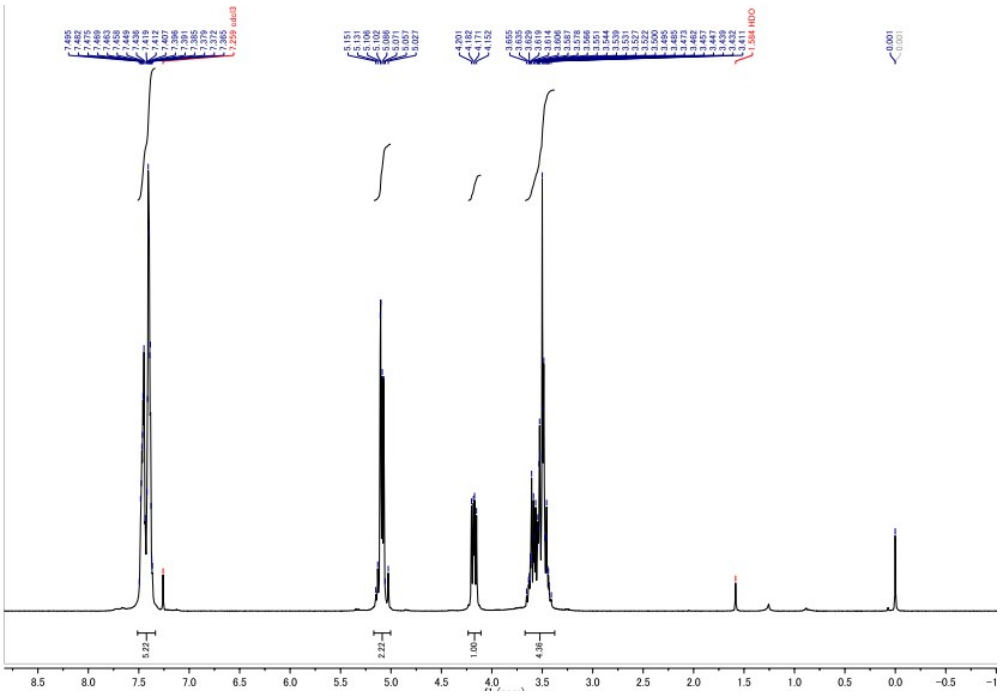
1) J. Gonzalez, F. Sanchez, T. Torres, *Synthesis* **1983**, *11*, 911.
2) a) A. J. Simpson and Hon Wai Lam, *Org. Lett.* **2013**, *15*, 2586; b) Qiaozhi Yan, Man Liu, Duanyang Kong, Guofu Zi, Guohua Hou, *Chem. Commun*. **2014**, *50*, 12870.
3) a) K. Hyodo, S. Nakamura, K. Tsuji, T. Ogawa, Y. Funahashi, N. Shibata, *Adv. Synth. Catal.* **2011**, *353*, 3385; b) K. Hyodo, S. Nakamura, N. Shibata, *Angew. Chem. Int. Ed.* **2012**, *51*, 10337.
4) H. Jin, S. T. Kim, G.-S. Hwang, D. H. Ryu, *J. Org. Chem*. **2016**, *81*, 3263.

^{1}H and ^{13}C NMR

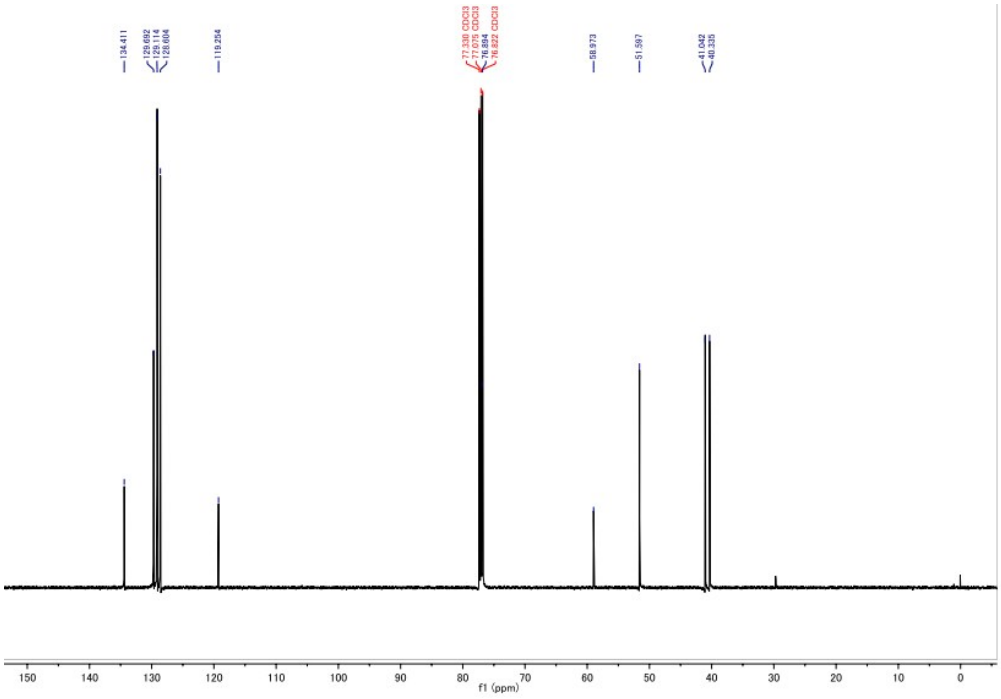


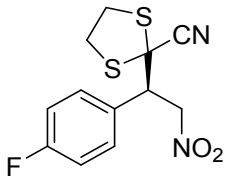
3aa

^{1}H NMR



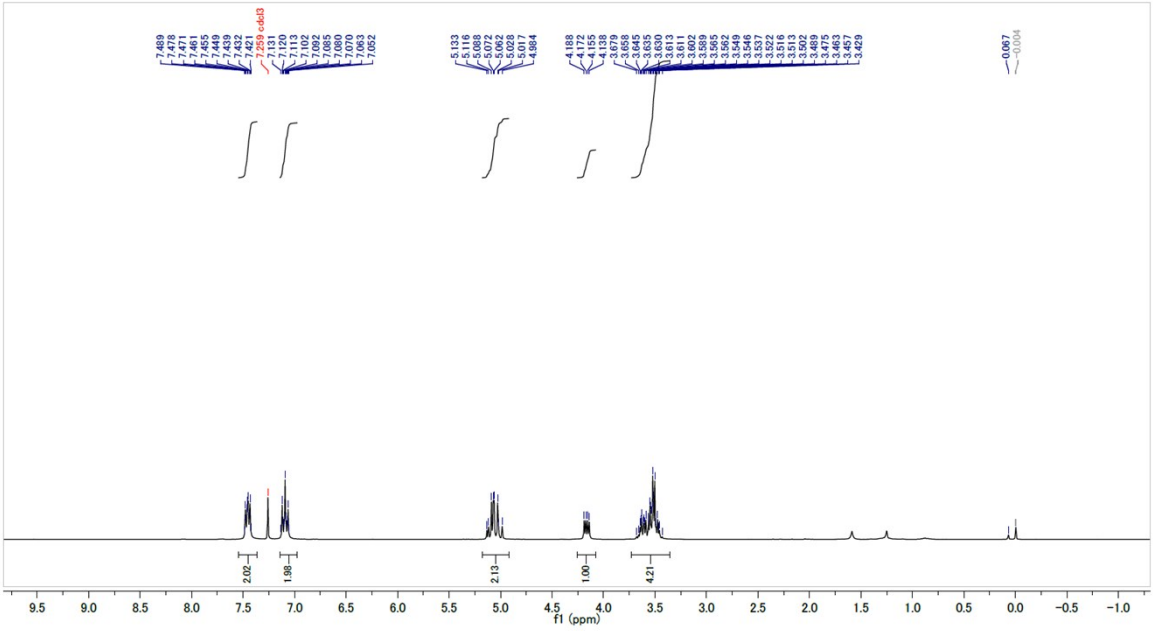
^{13}C NMR



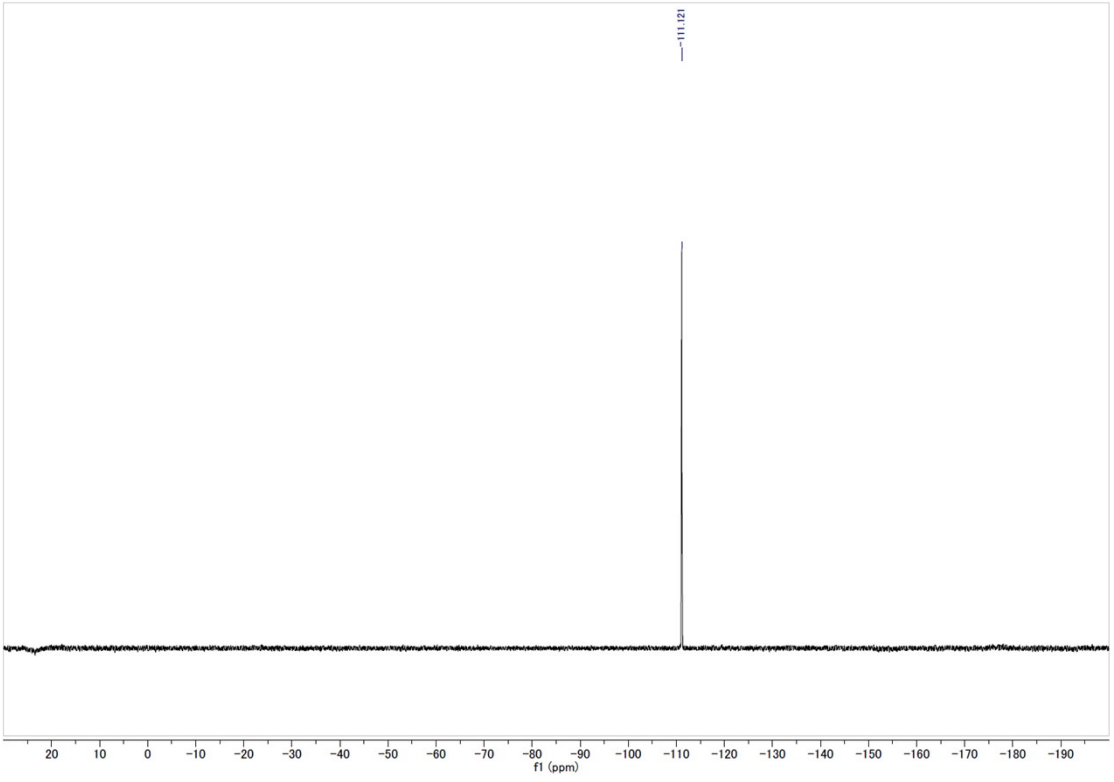


3ba

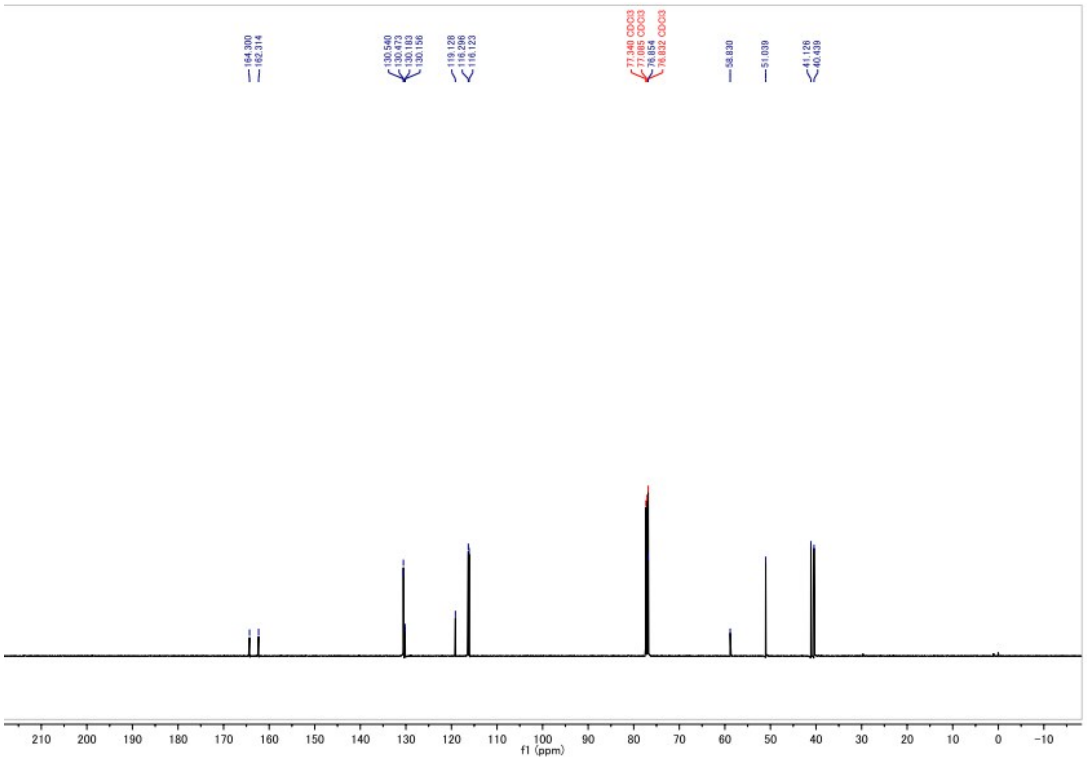
^{1}H NMR

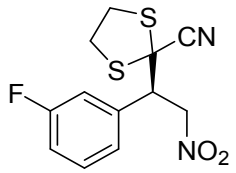


^{19}F NMR



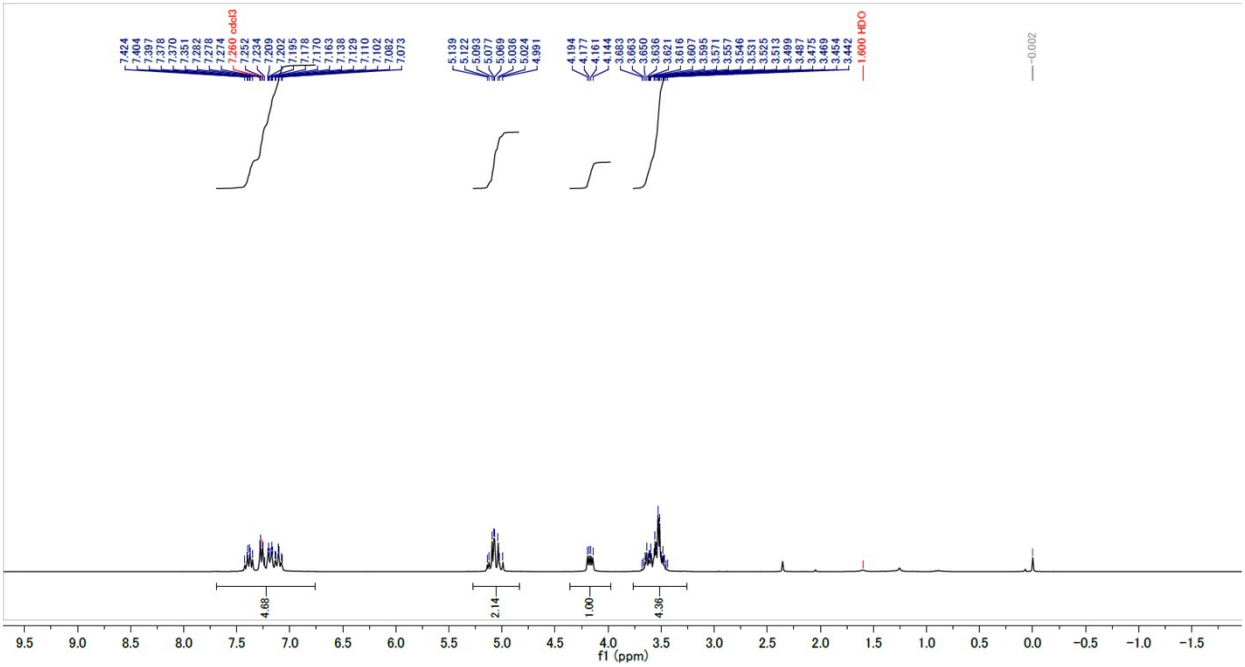
^{13}C NMR


164.300
162.314
130.540
130.473
130.183
130.156
119.128
116.296
116.123
77.340 CDCl3
77.015
76.854
76.832 CDCl3
58.830
51.039
41.126
40.439
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

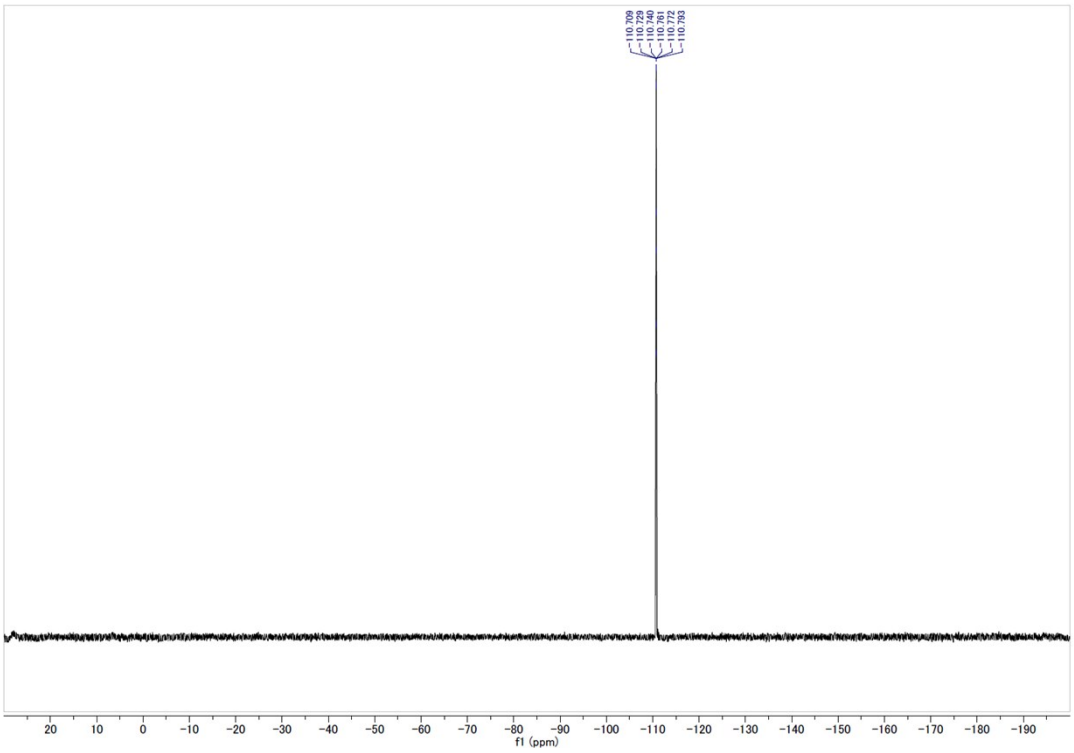


3ca

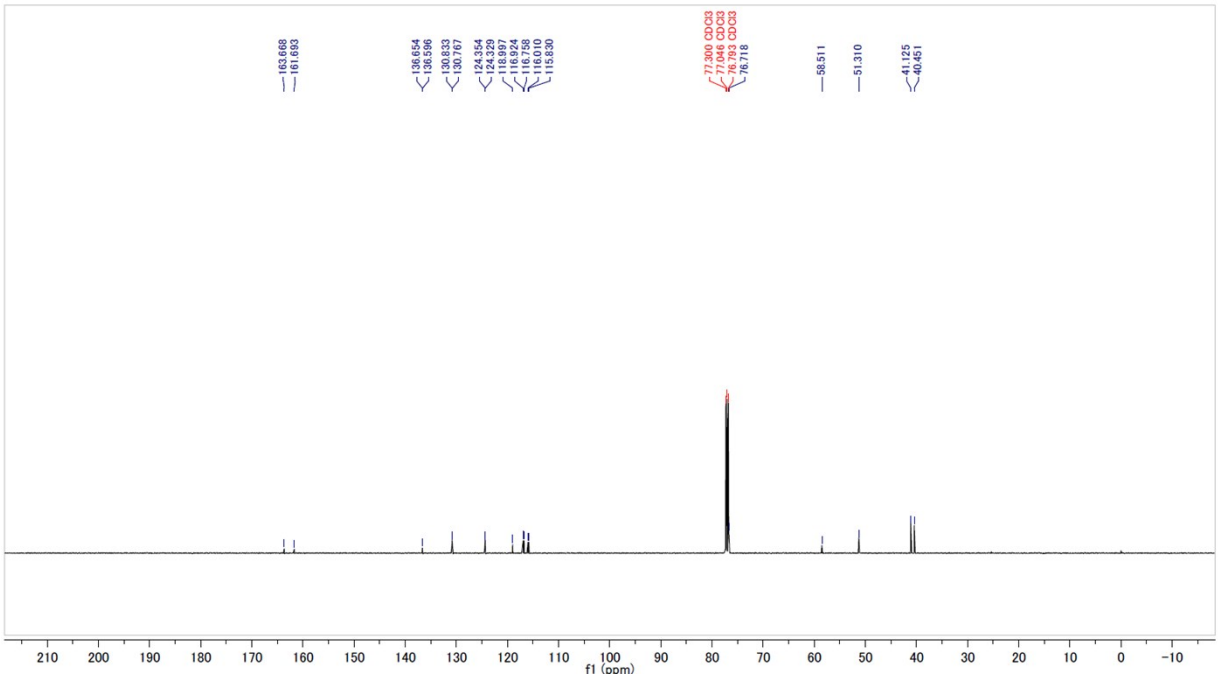
^{1}H NMR

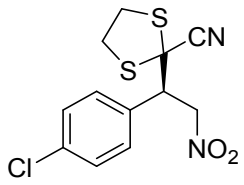


^{19}F NMR



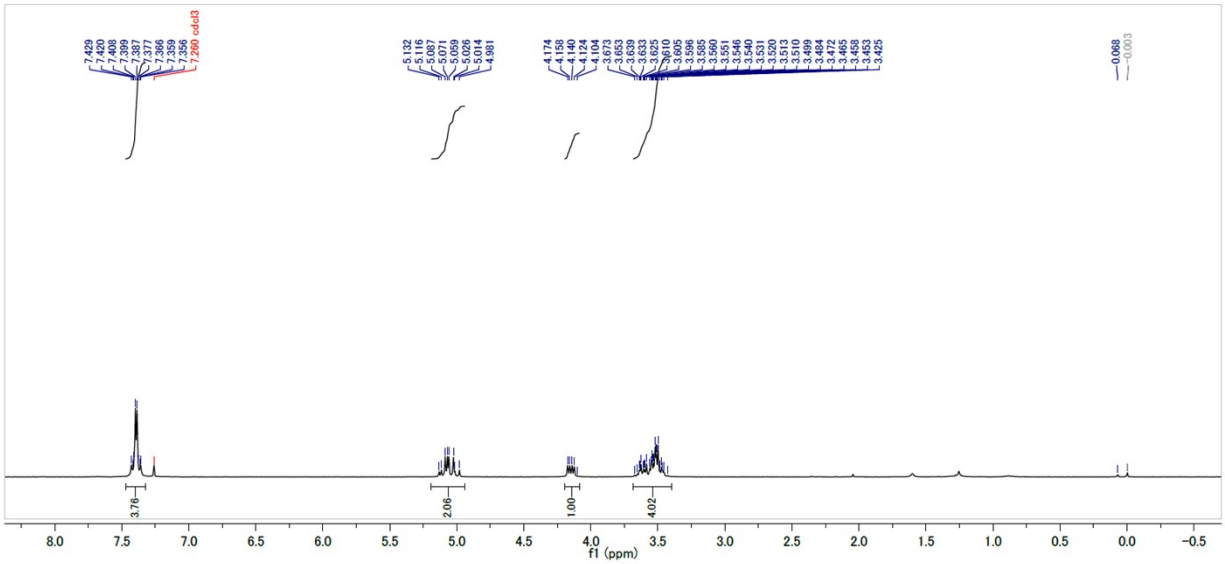
^{13}C NMR


163.668
161.693
136.654
136.596
130.833
130.767
124.354
124.299
118.997
116.924
116.758
116.010
115.830
77.300 CDCl3
77.046 CDCl3
76.793 CDCl3
76.718
58.511
51.310
41.125
40.451
f1 (ppm)

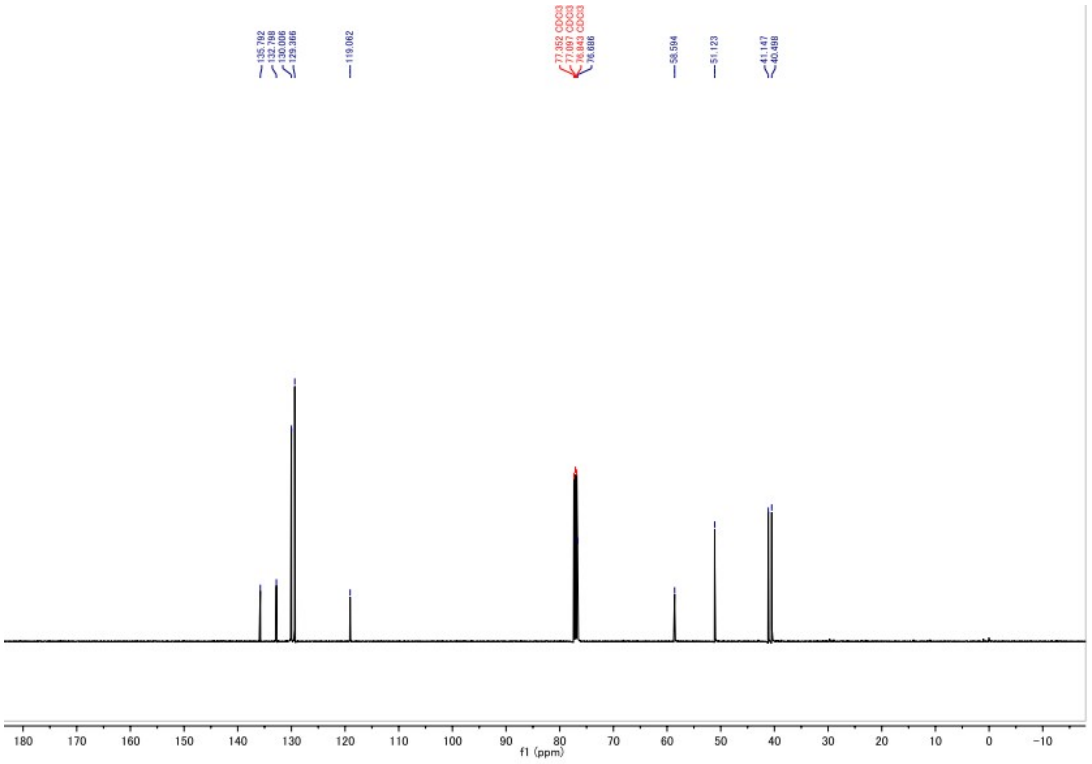


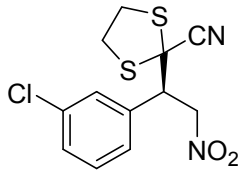
3da

^{1}H NMR



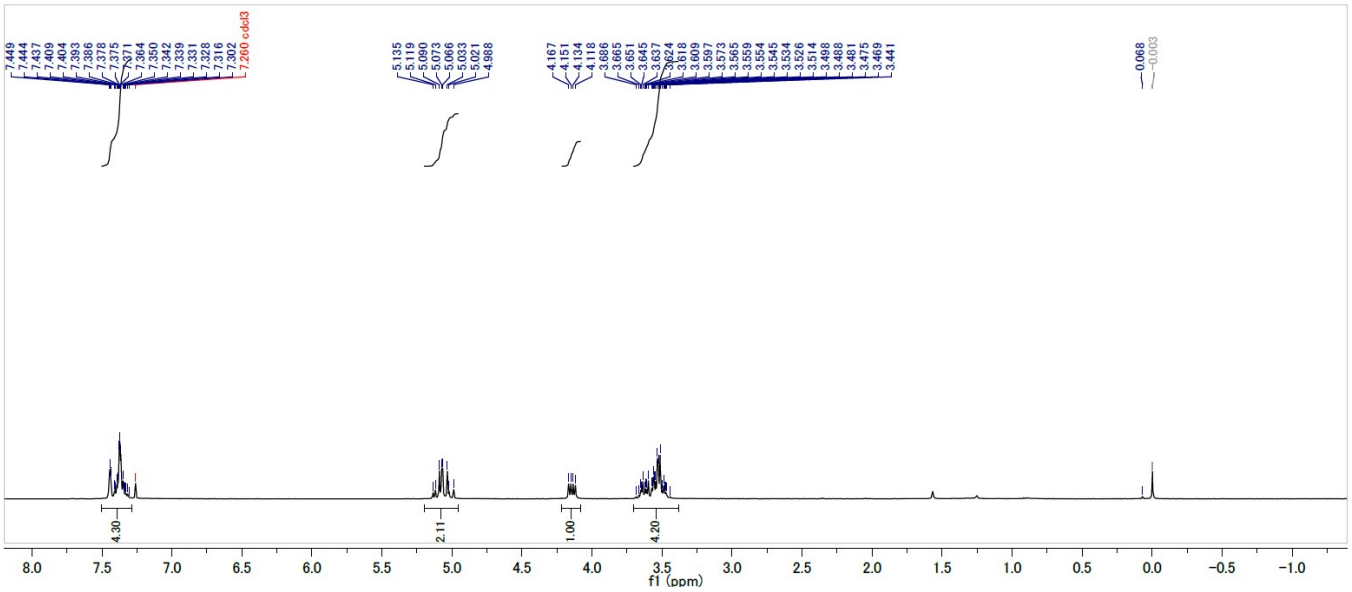
^{13}C NMR



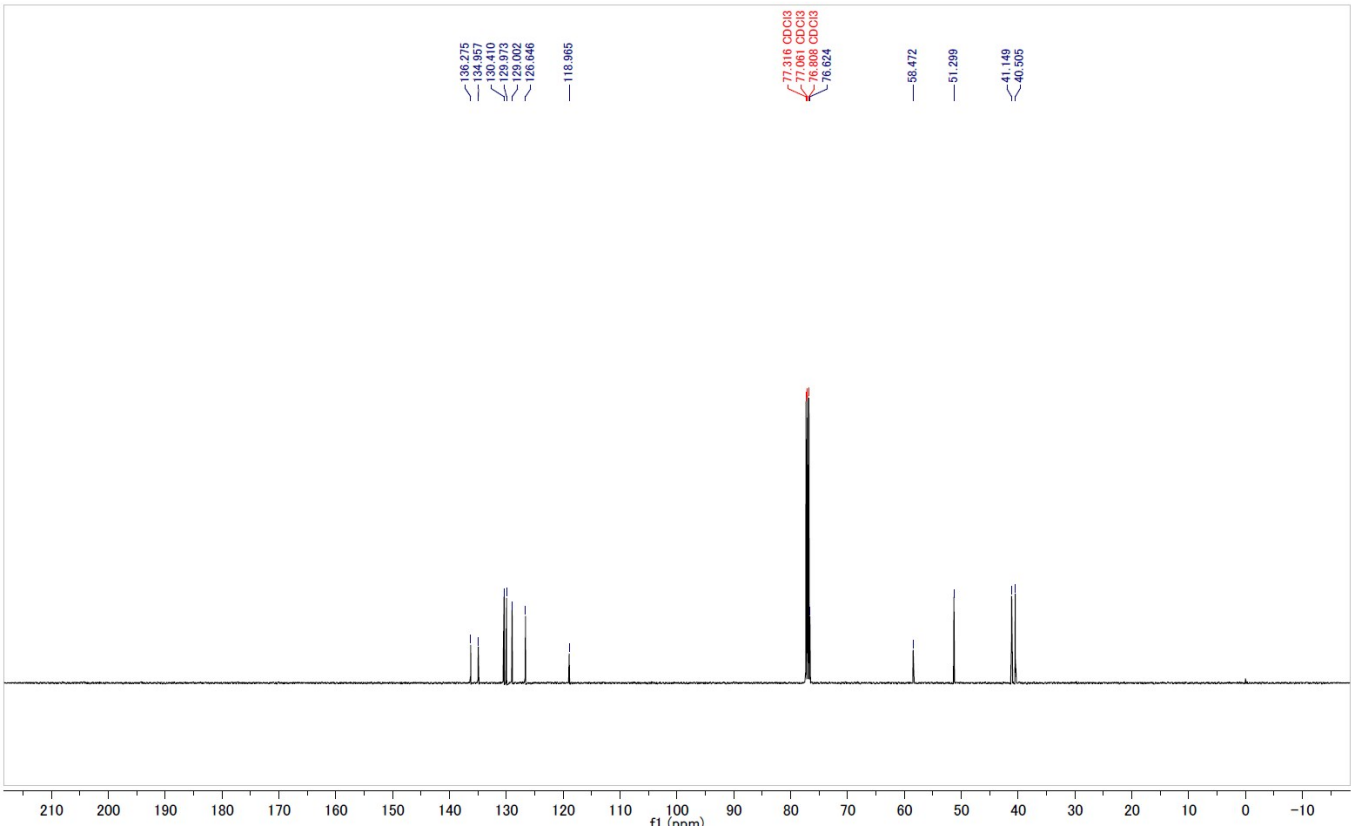


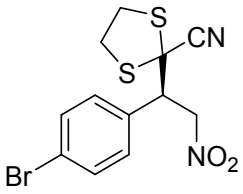
3ea

^{1}H NMR



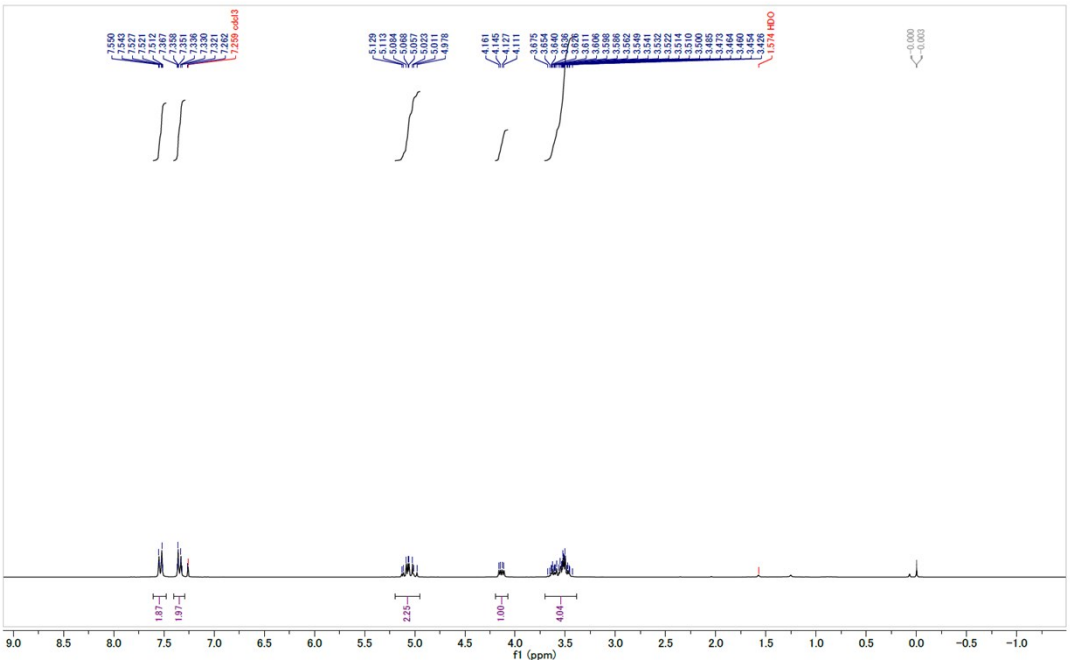
^{13}C NMR



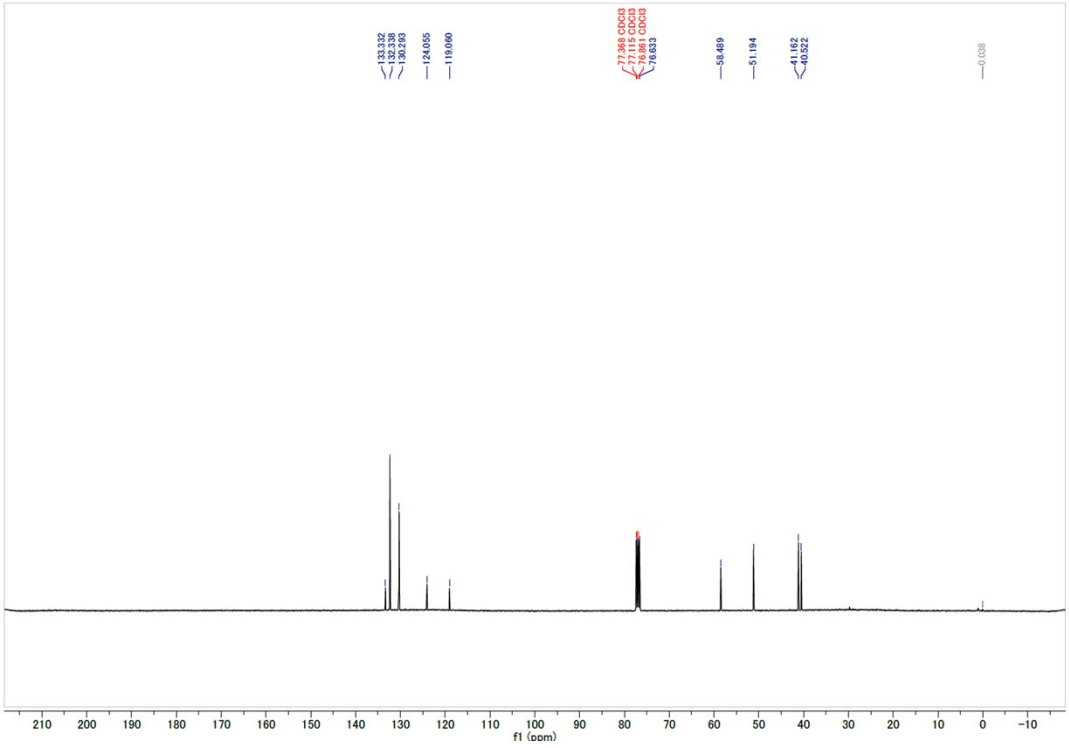


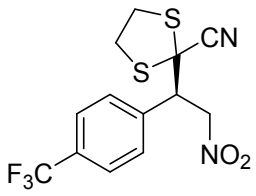
3fa

^{1}H NMR



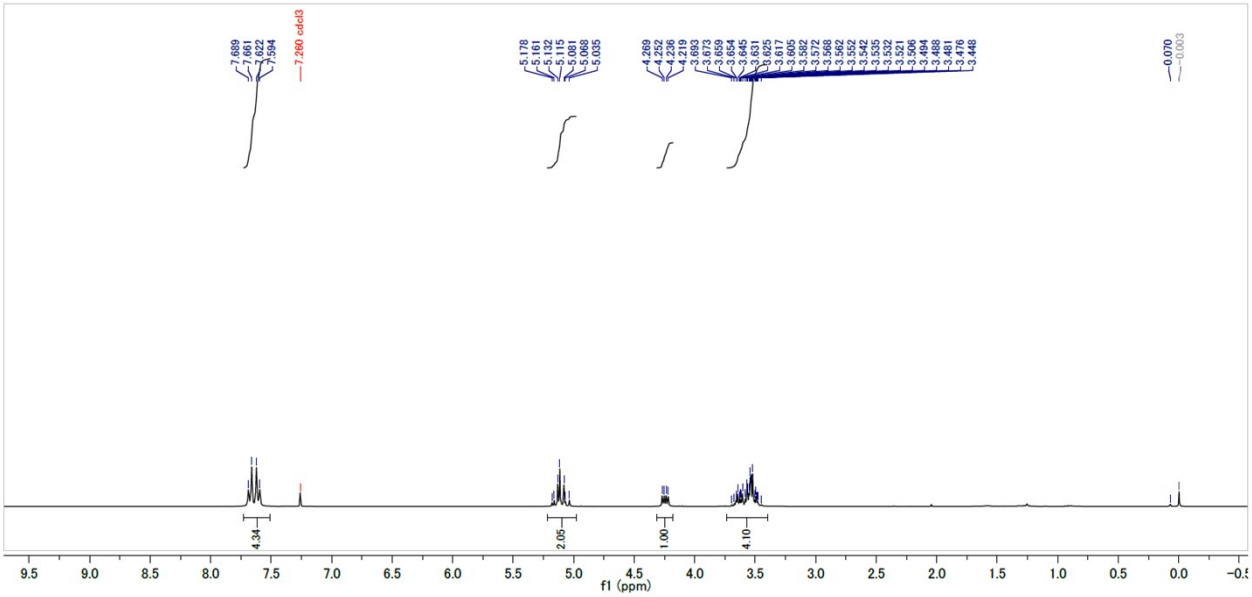
^{13}C NMR



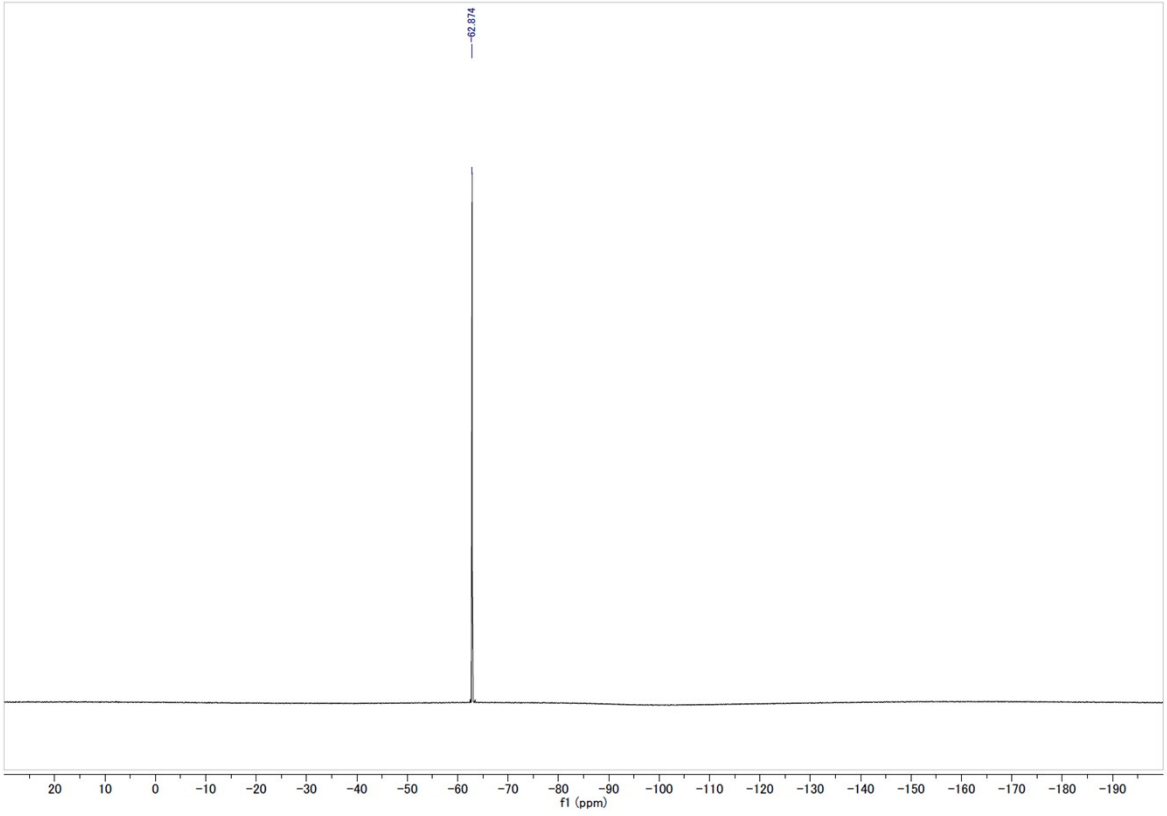


3ga

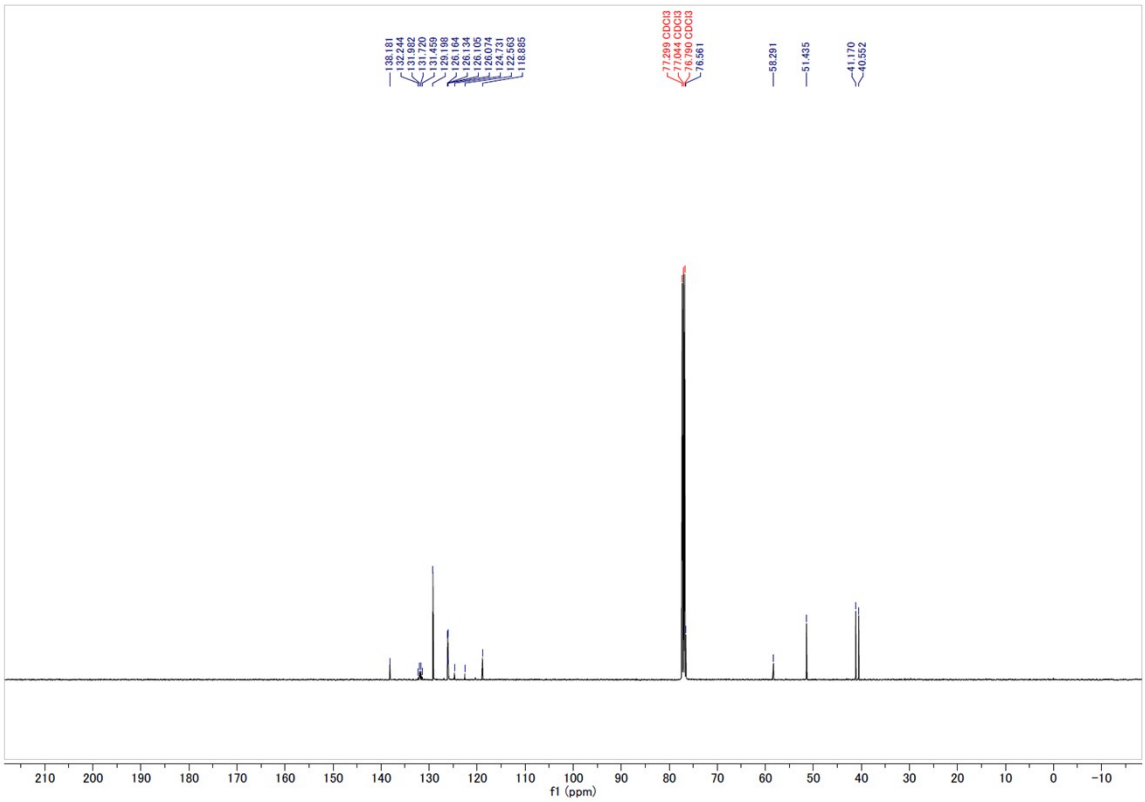
^{1}H NMR

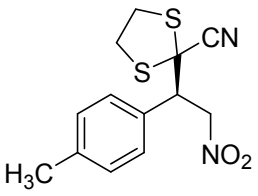


^{19}F NMR



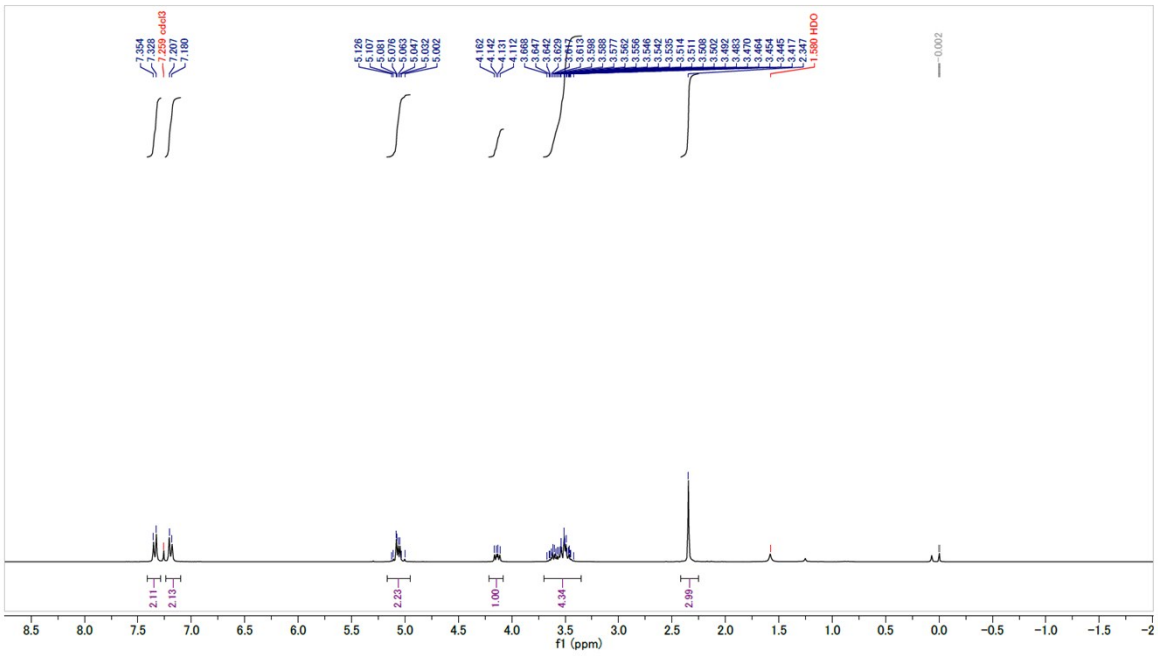
^{13}C NMR


138.181
132.244
131.982
131.720
131.468
130.168
126.164
126.134
126.105
126.074
124.731
122.563
118.885
77.299 CDCl3
77.044 CDCl3
76.790 CDCl3
76.561
58.291
51.435
41.170
40.552
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

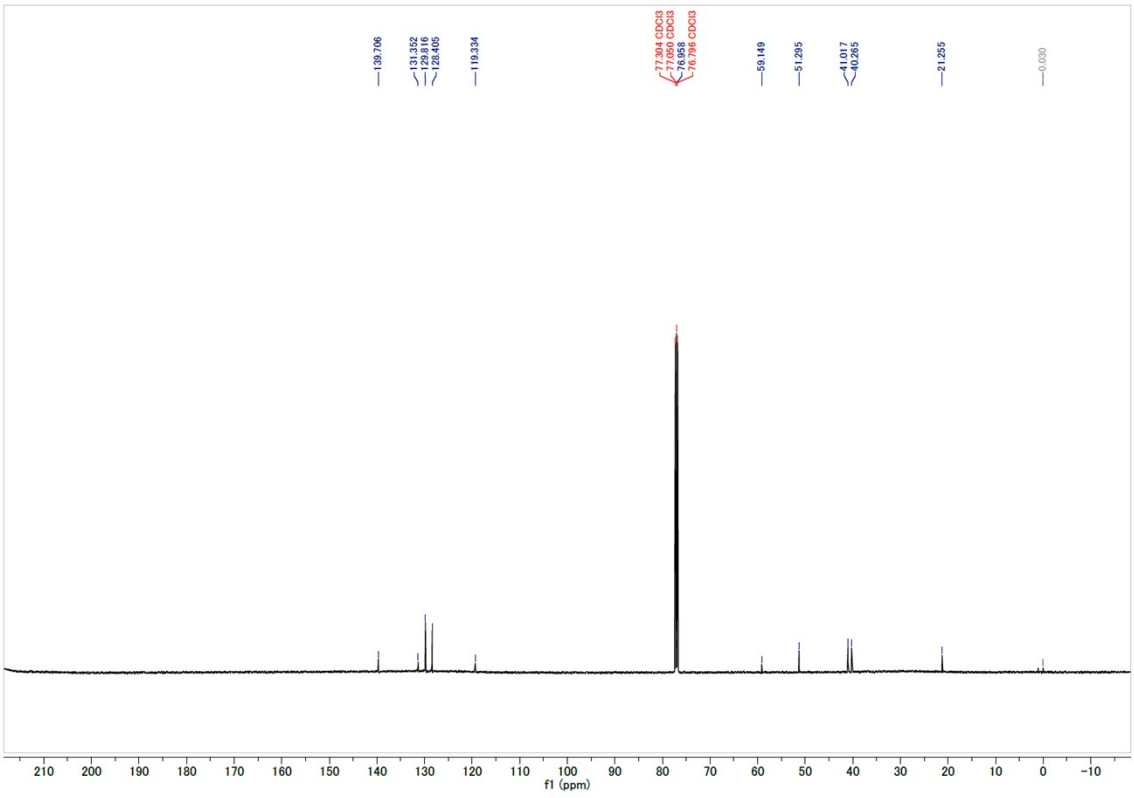


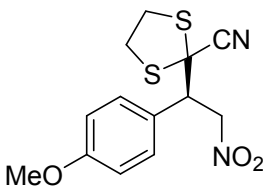
3ha

^{1}H NMR



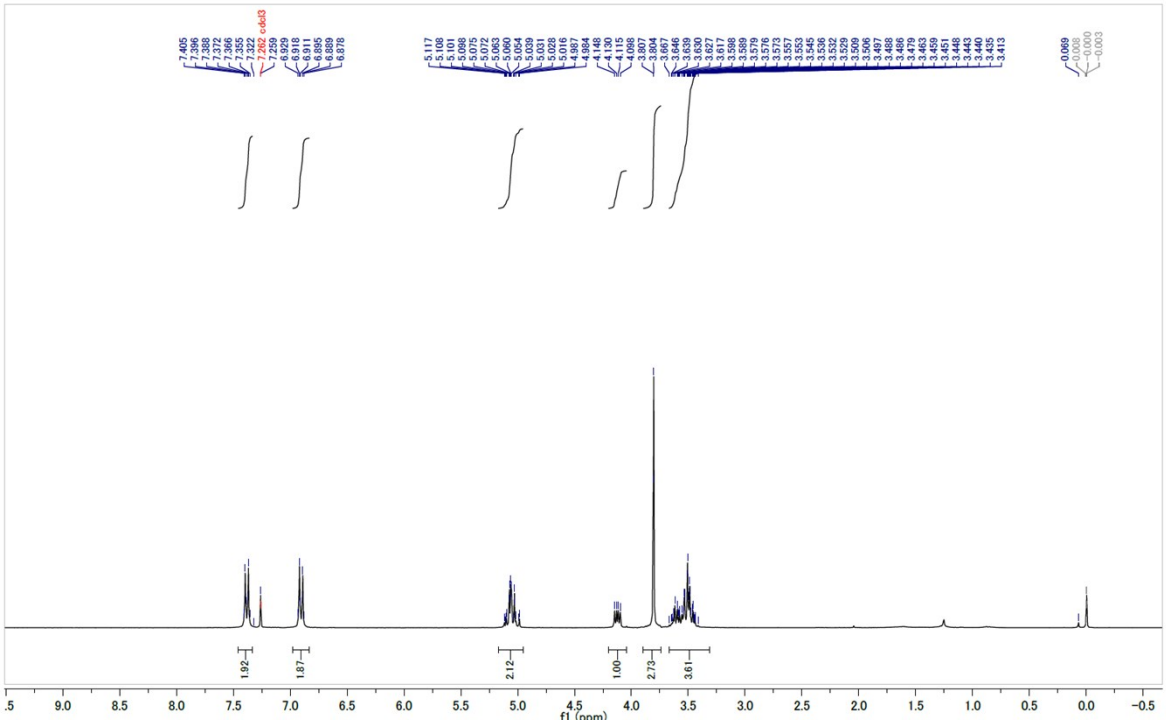
^{13}C NMR



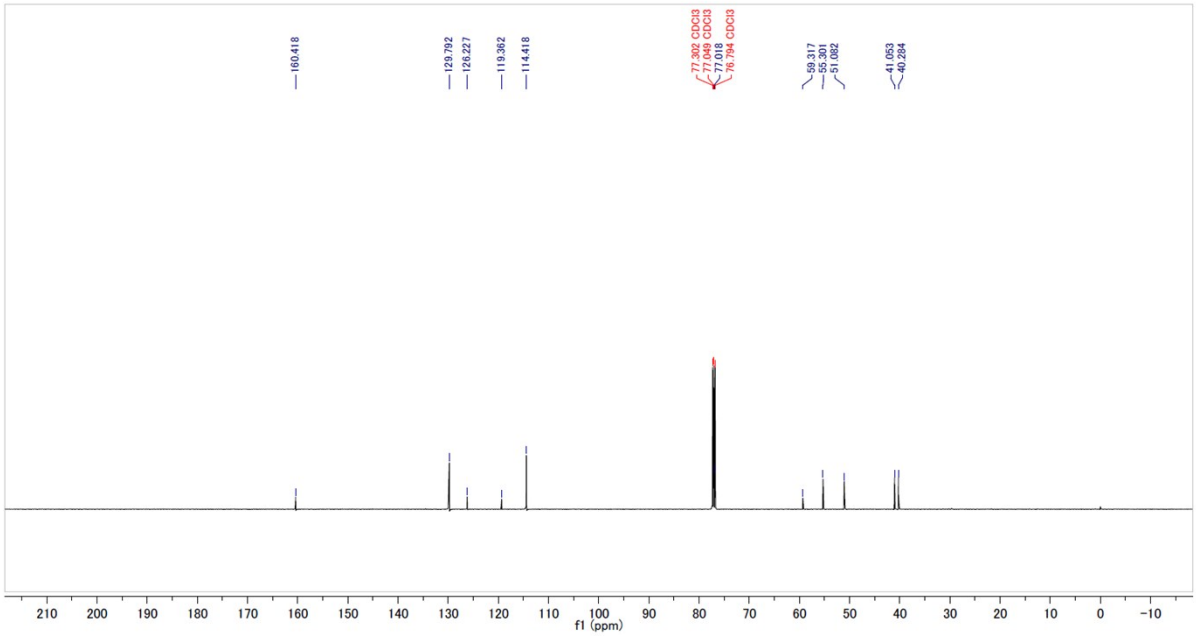


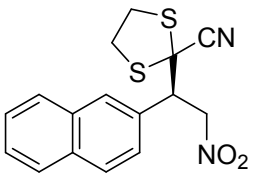
3ia

^{1}H NMR



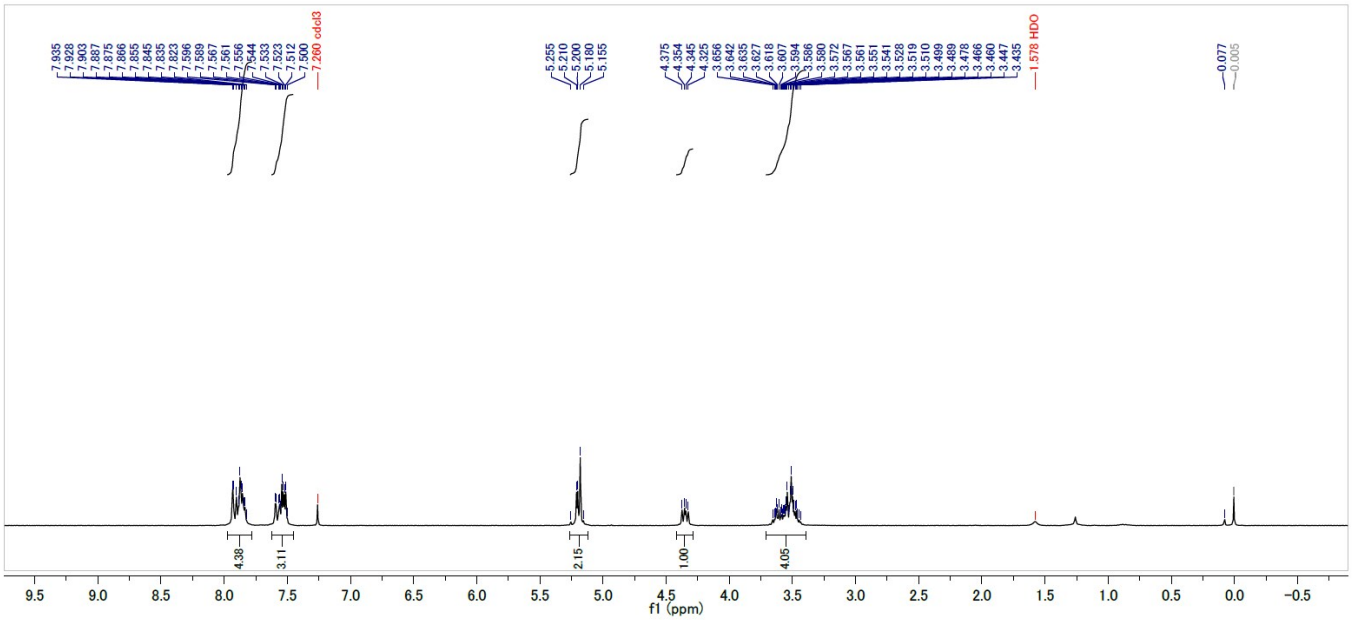
^{13}C NMR



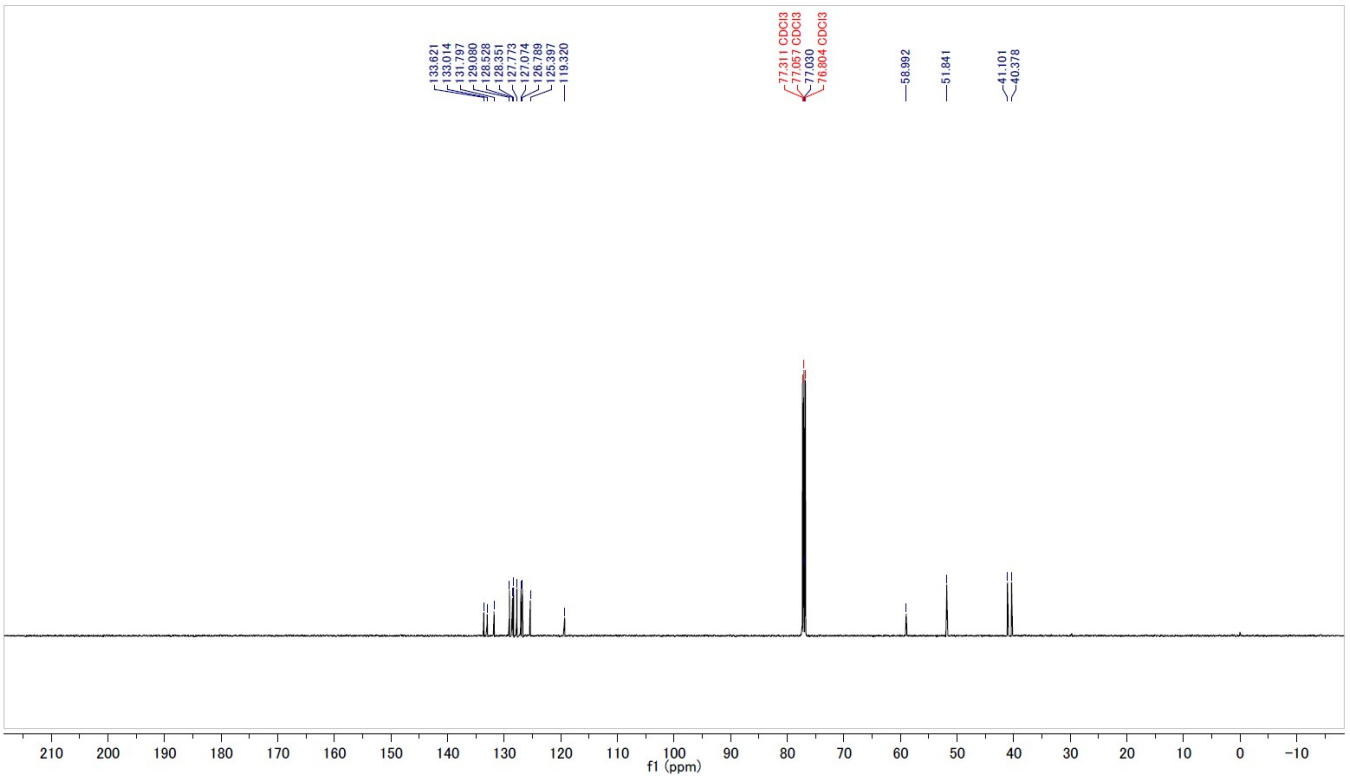


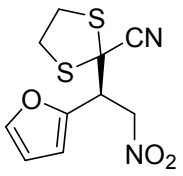
3ja

^{1}H NMR



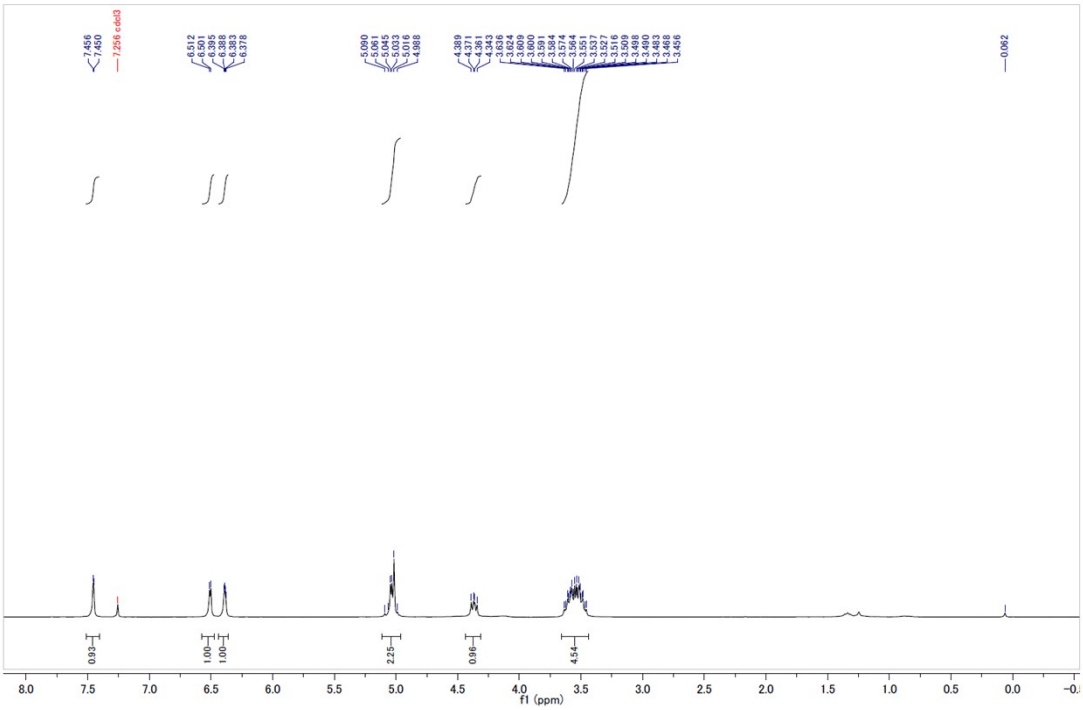
^{13}C NMR



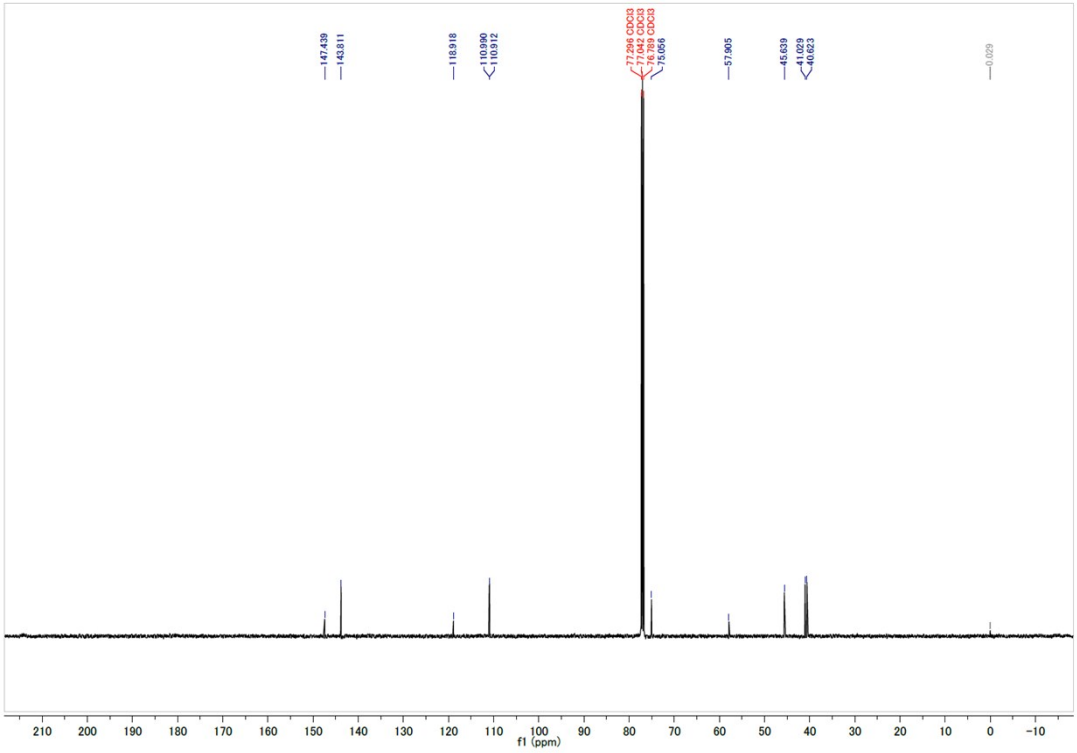


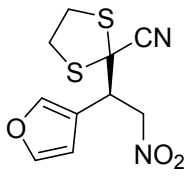
3ka

^{1}H NMR



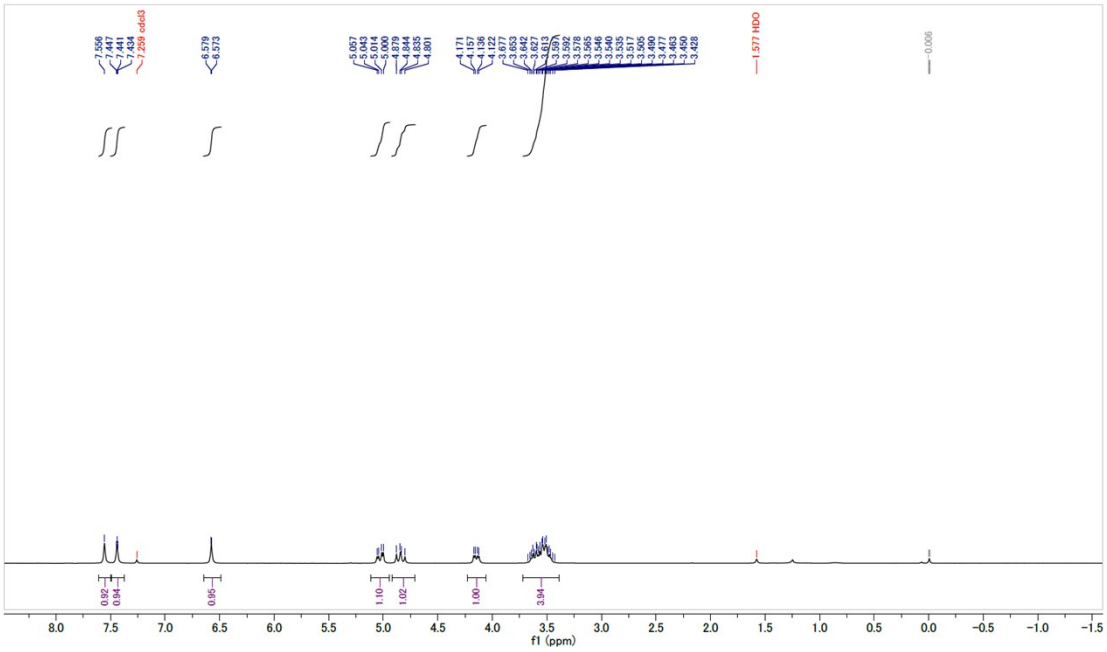
^{13}C NMR



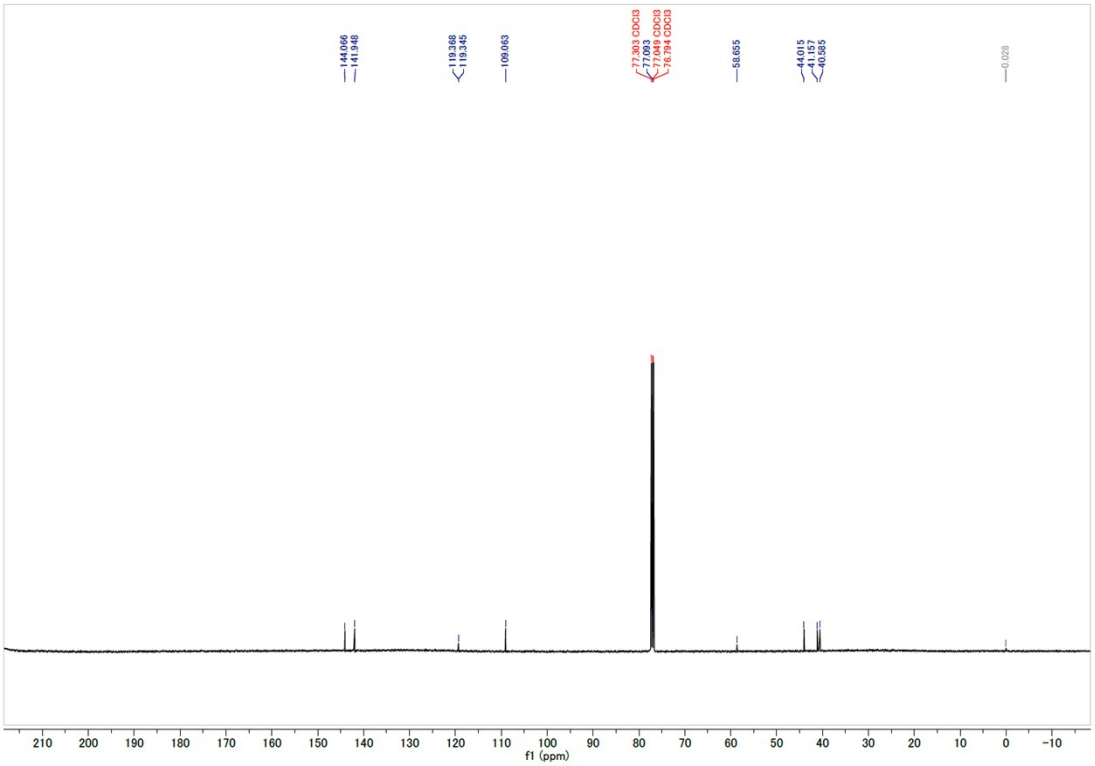


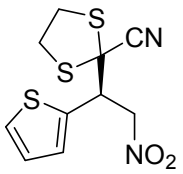
3la

^{1}H NMR



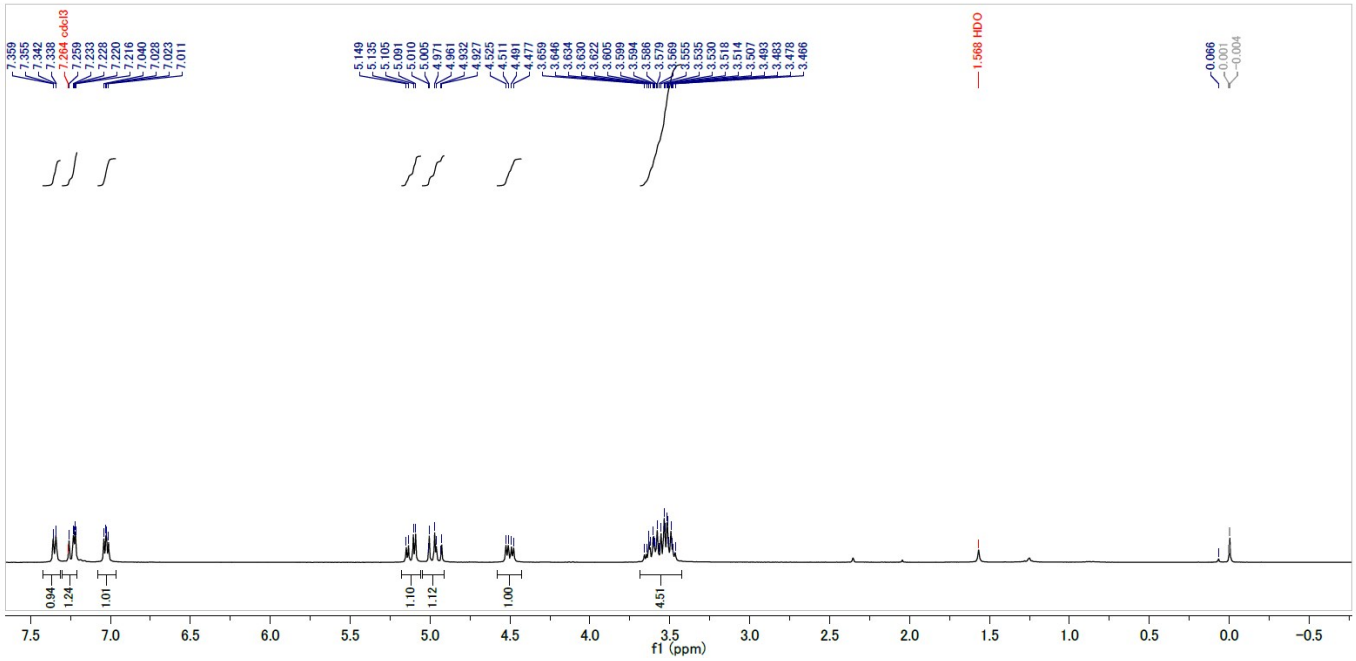
^{13}C NMR



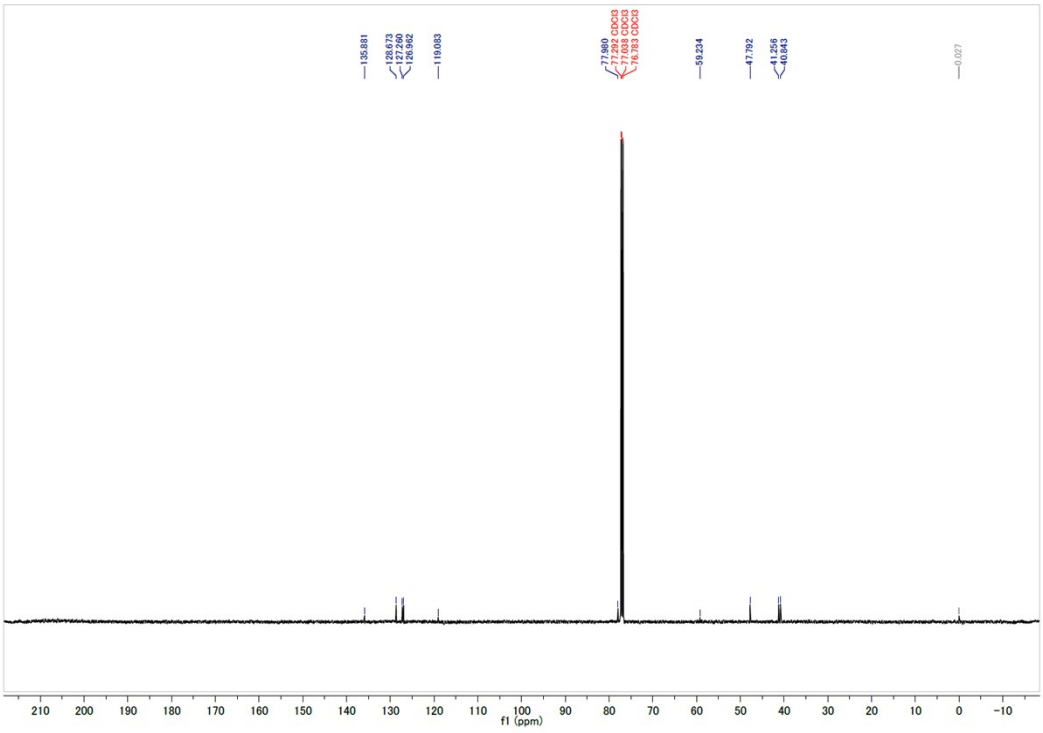


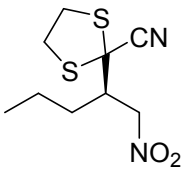
3ma

^{1}H NMR



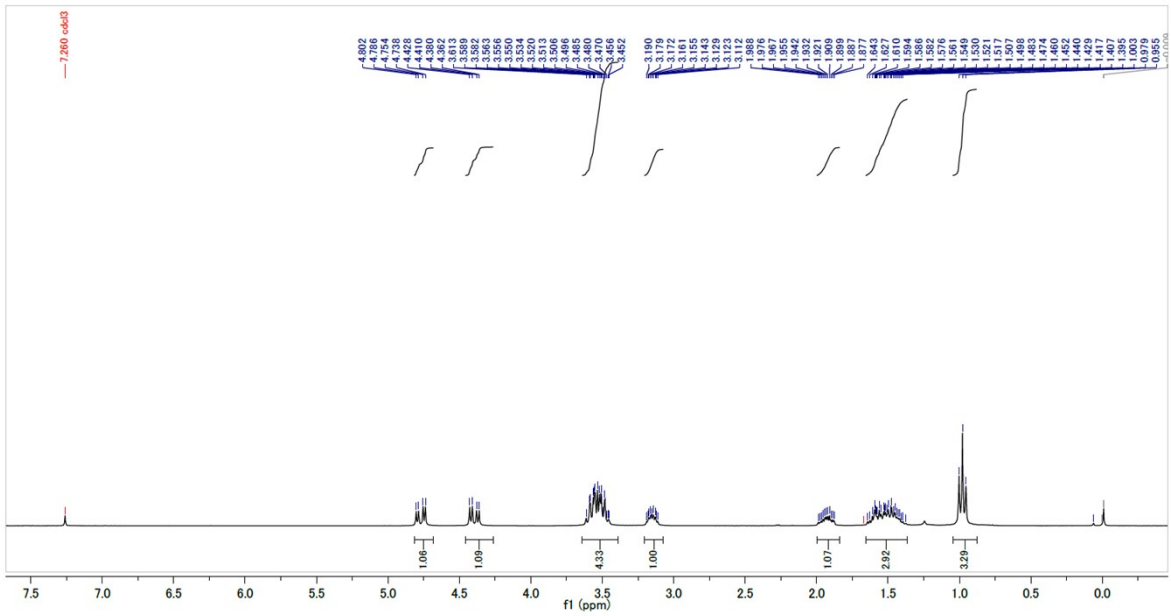
^{13}C NMR



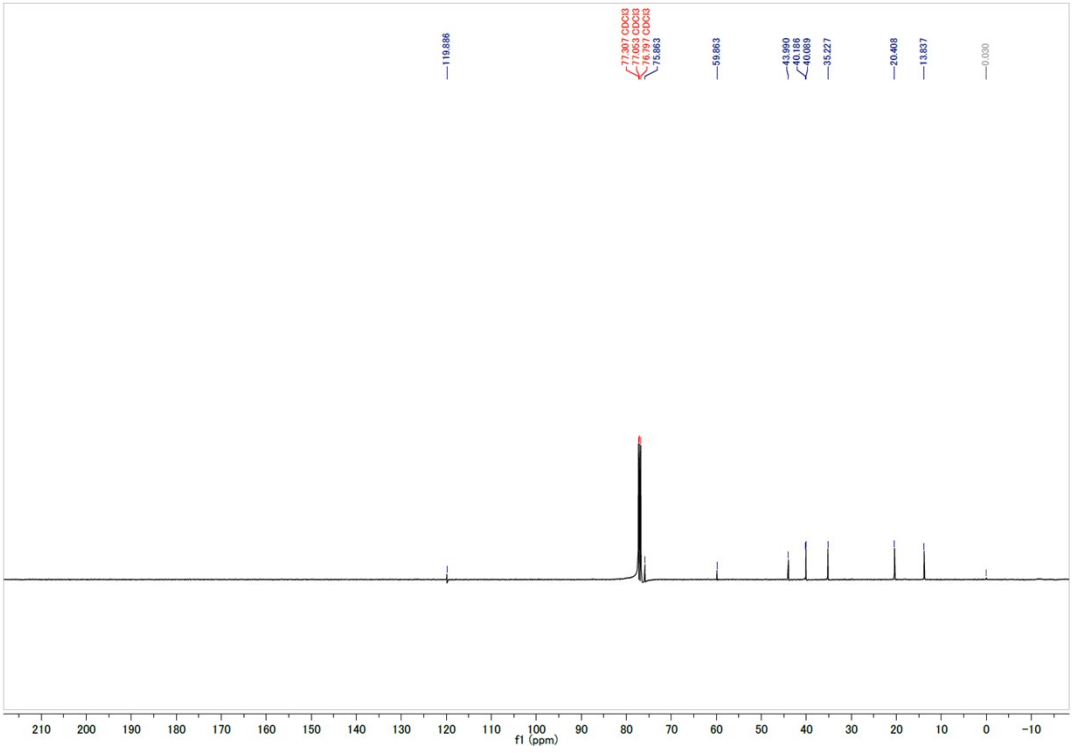


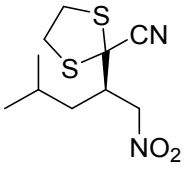
3na

^{1}H NMR



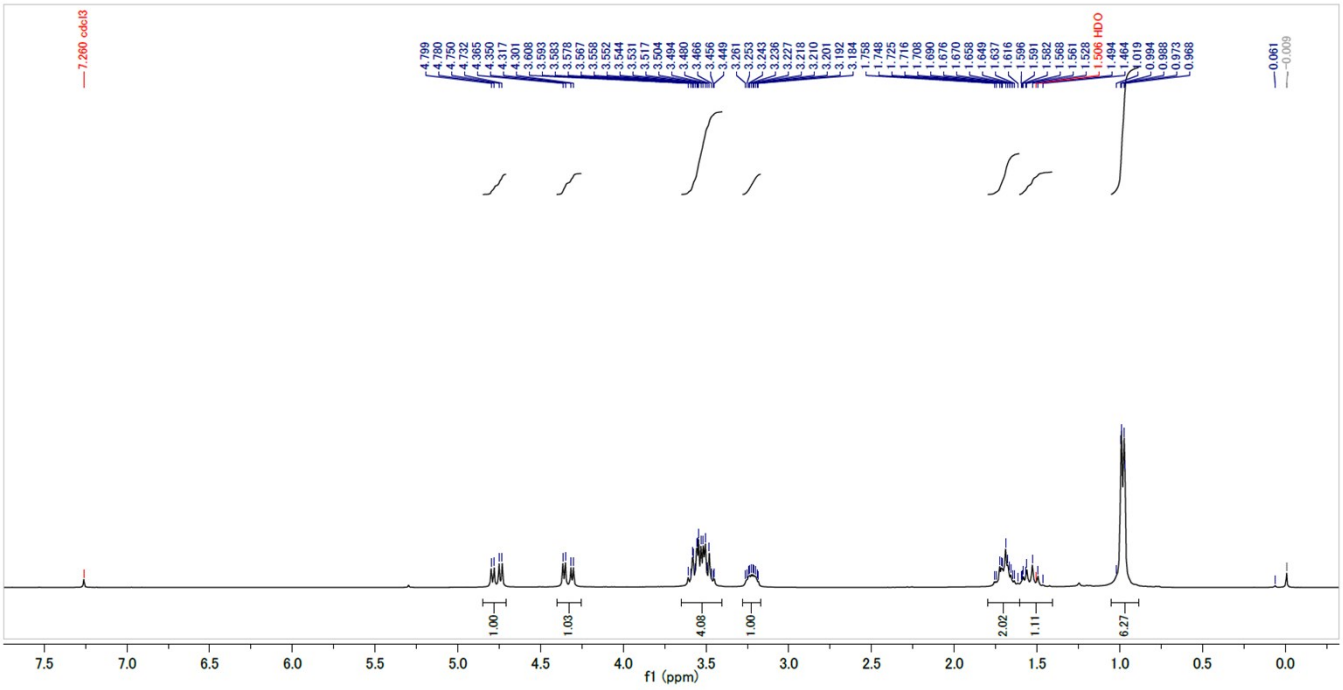
^{13}C NMR



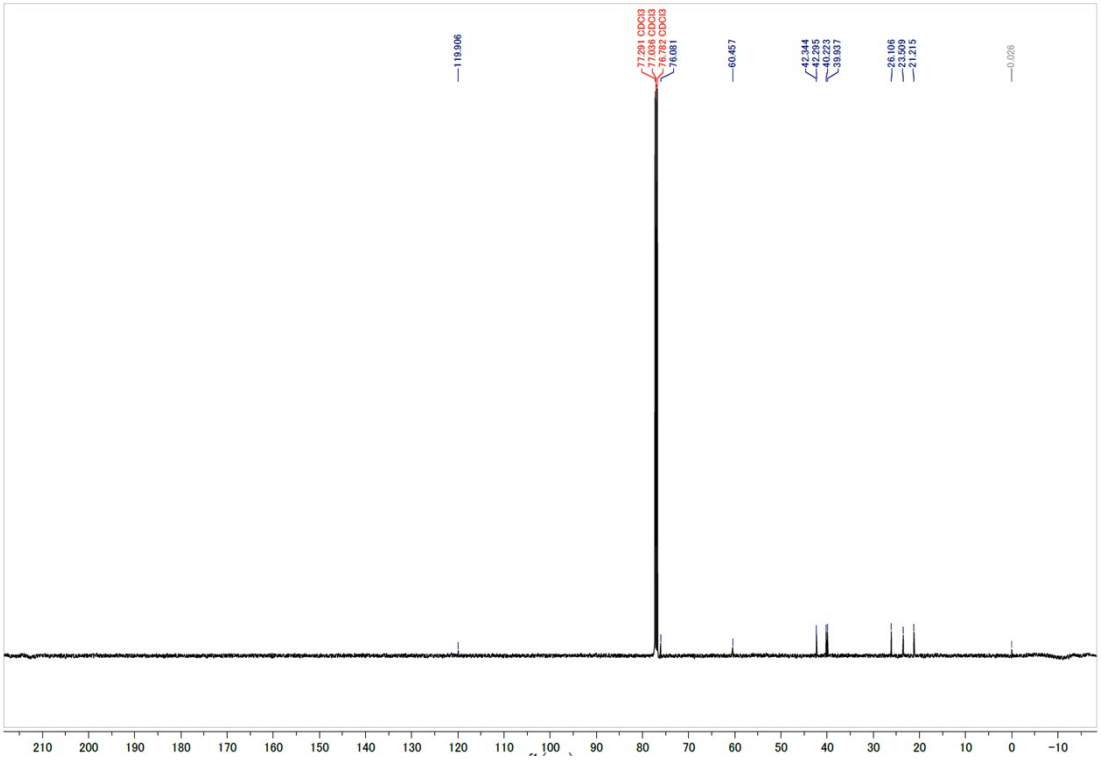


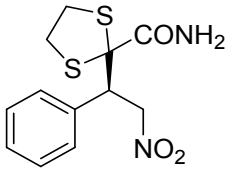
3oa

^{1}H NMR



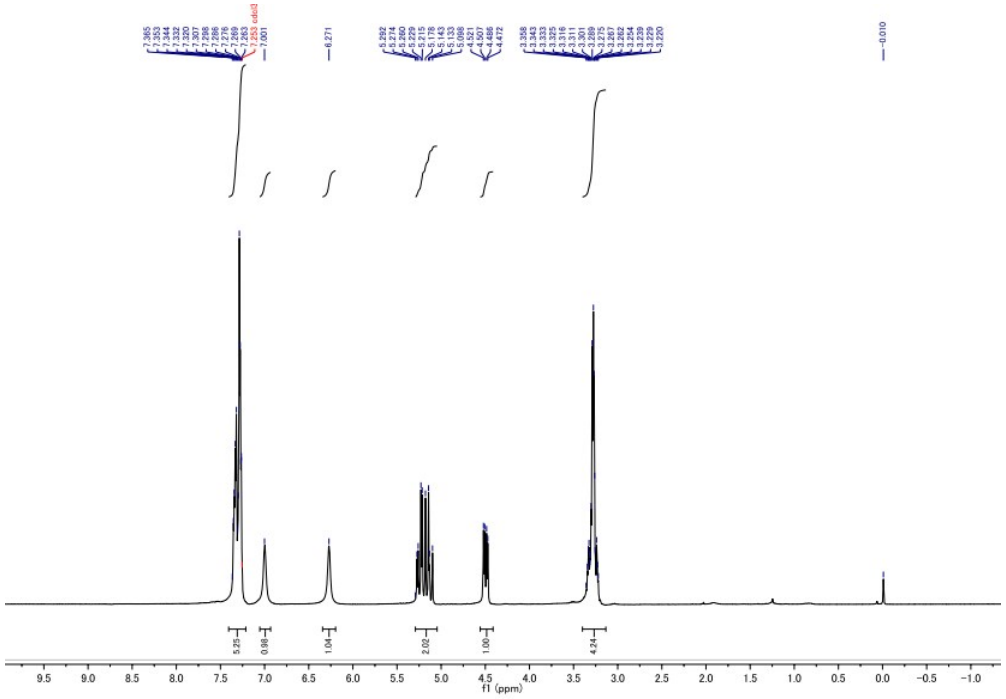
^{13}C NMR



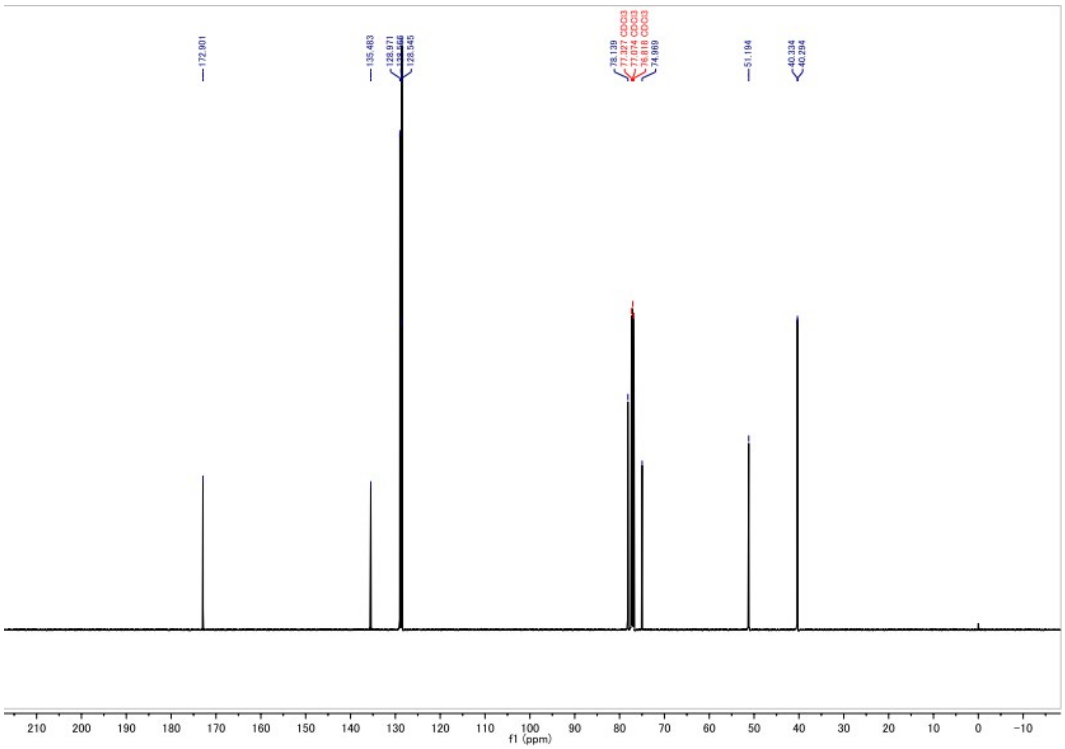


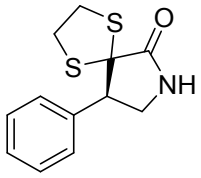
5

^{1}H NMR



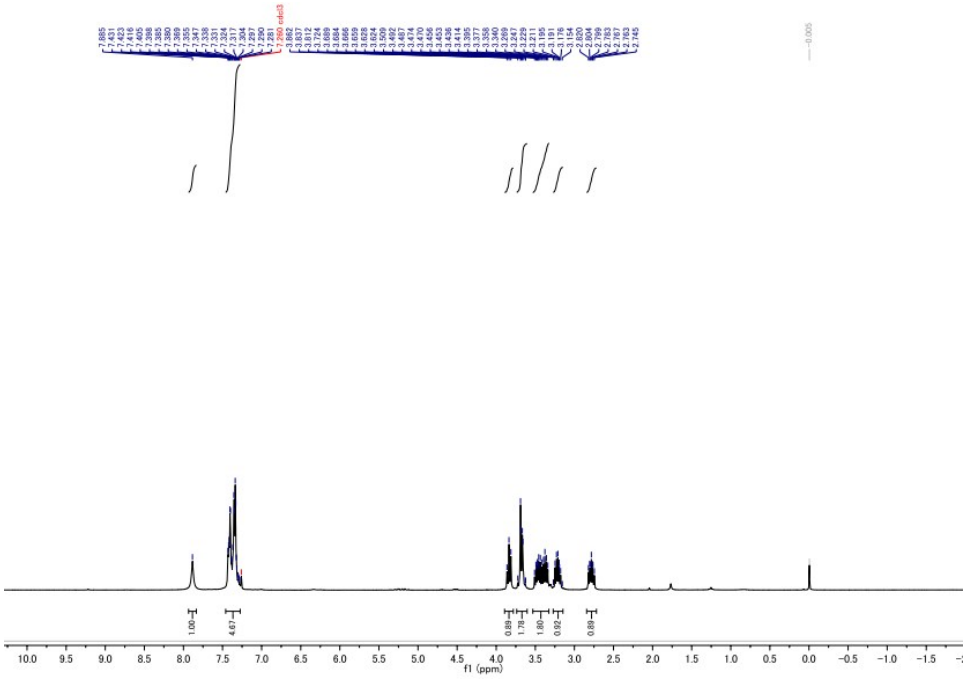
^{13}C NMR



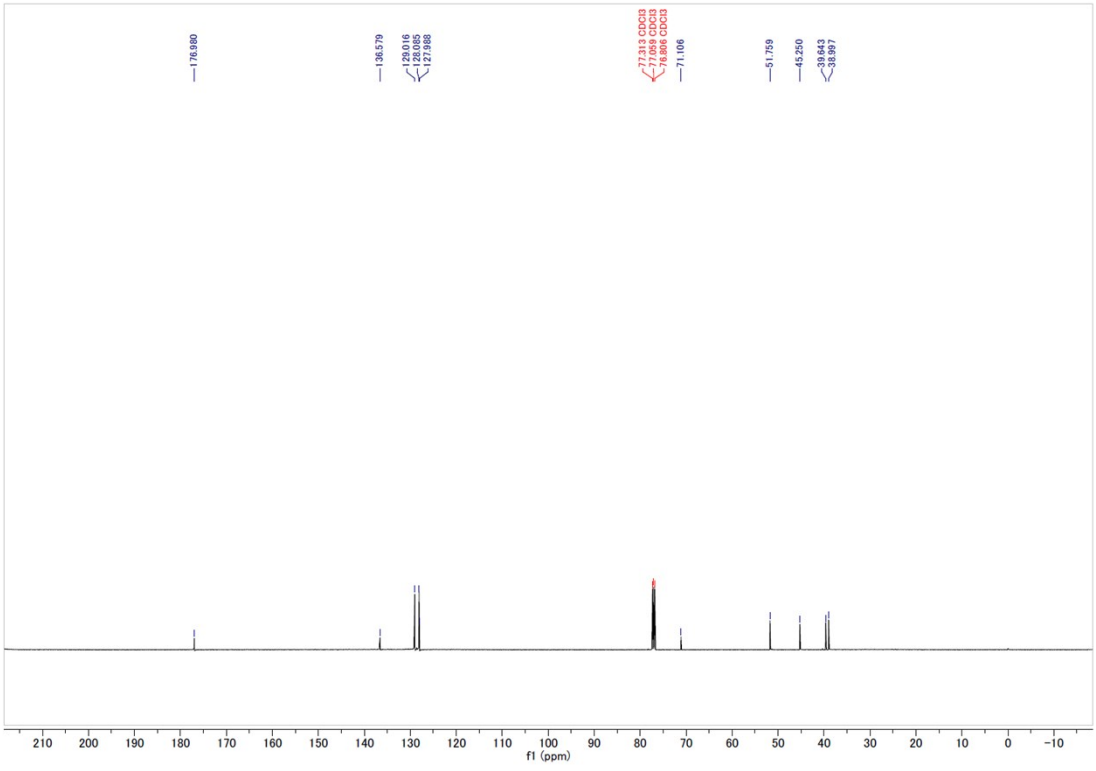


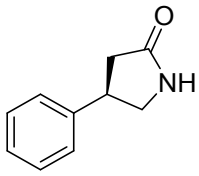
6

^{1}H NMR



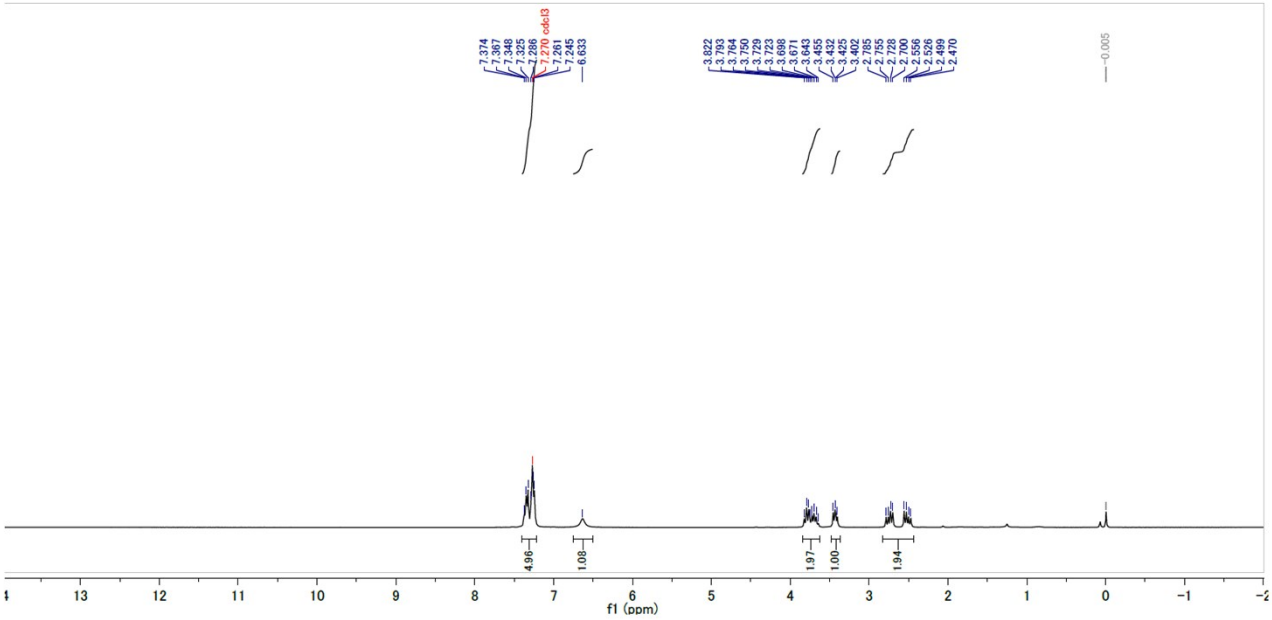
^{13}C NMR



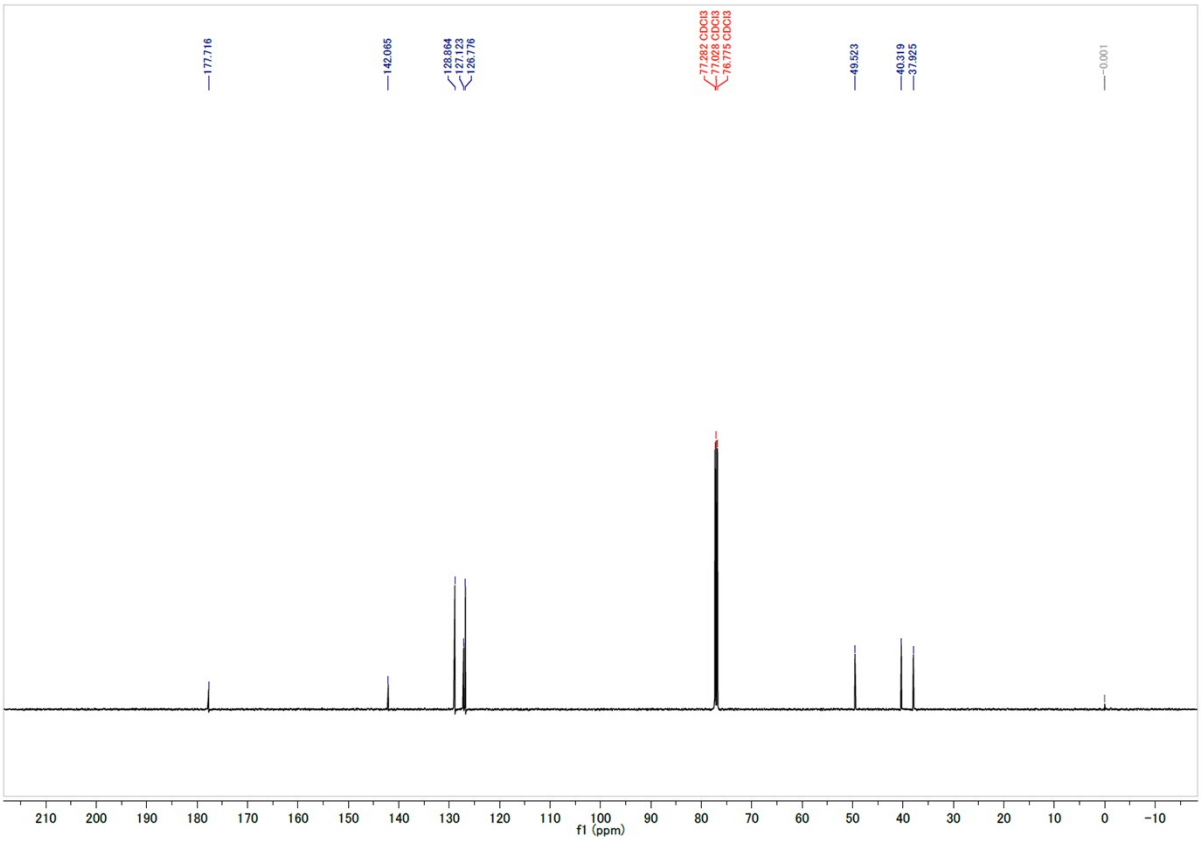


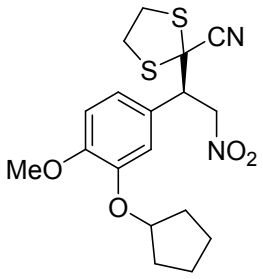
7

^{1}H NMR



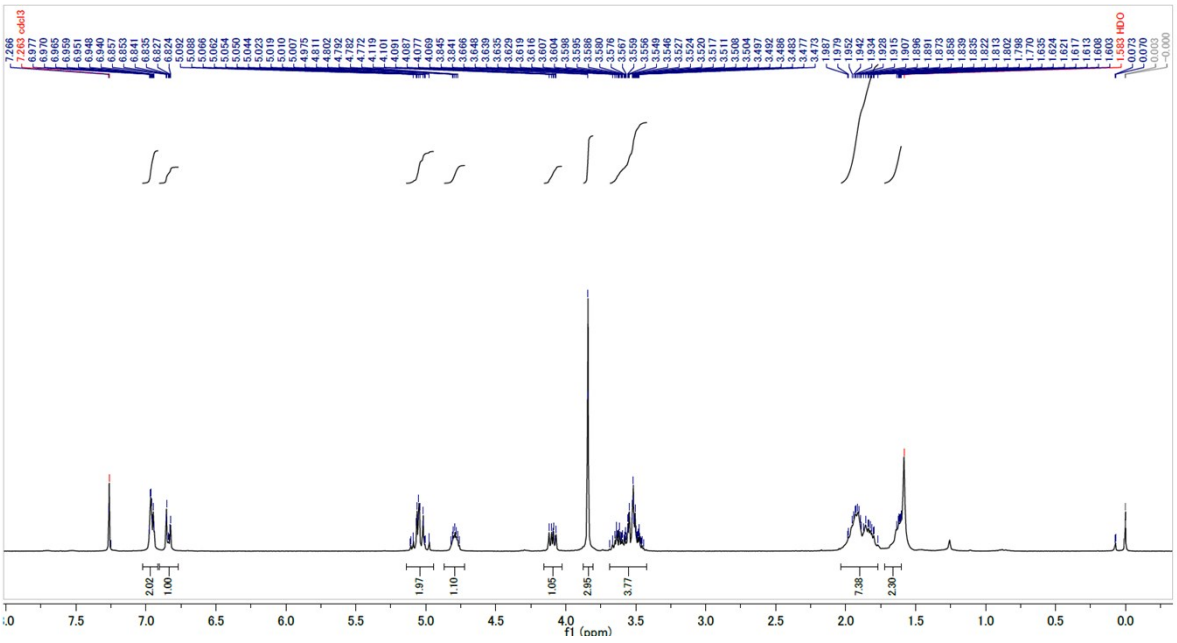
^{13}C NMR



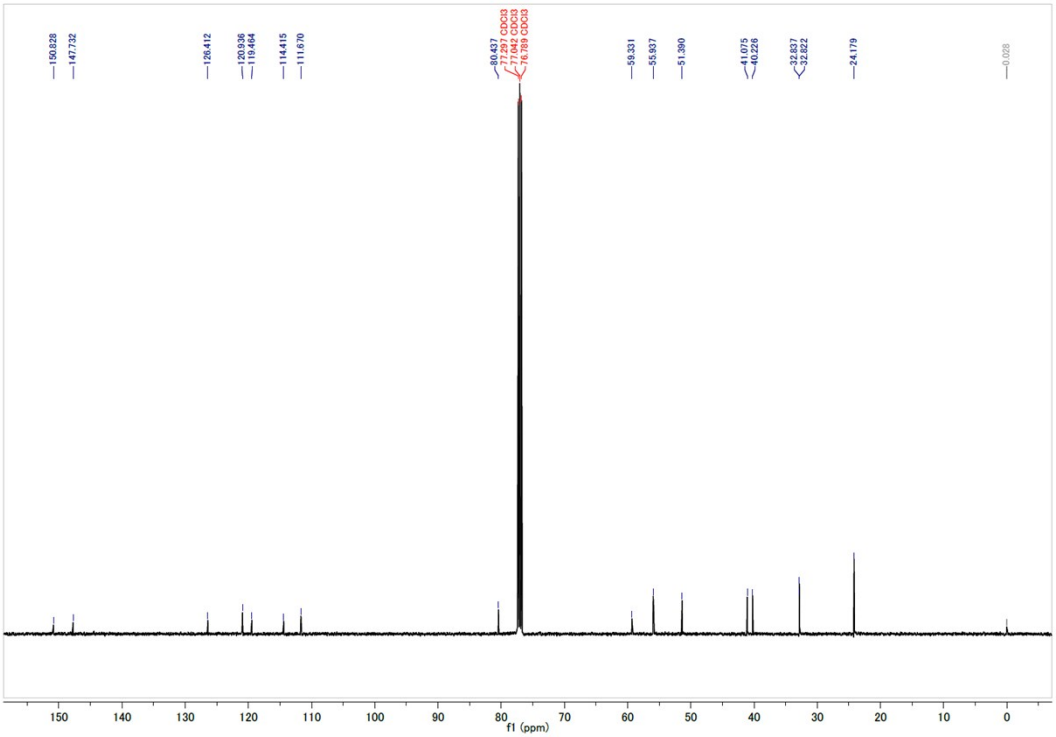


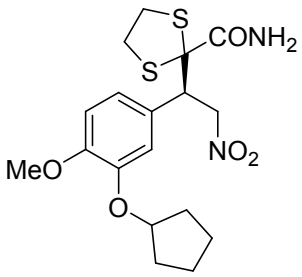
8

^{1}H NMR



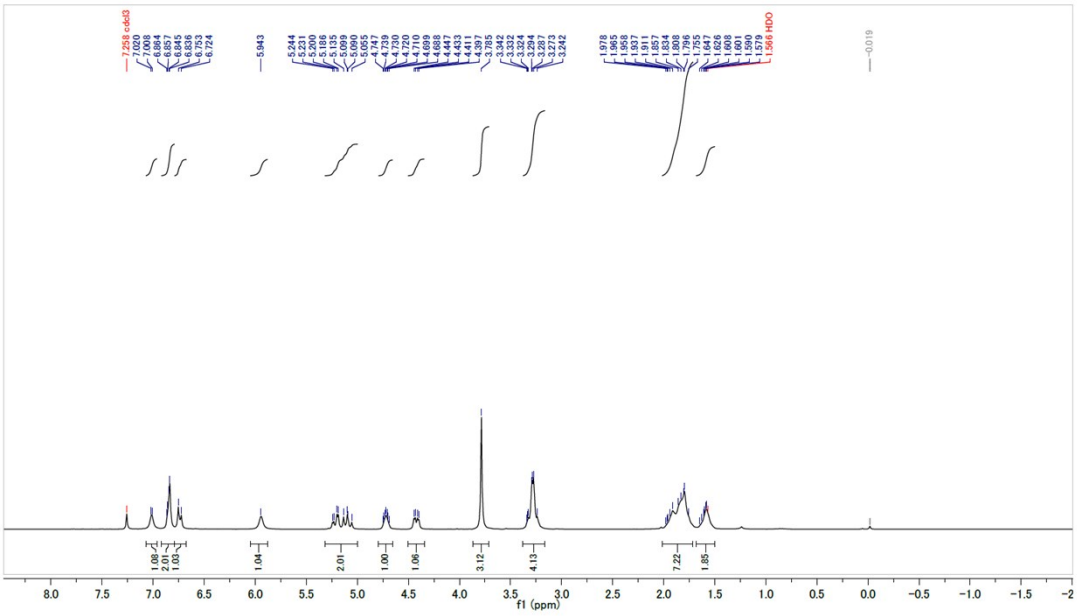
^{13}C NMR



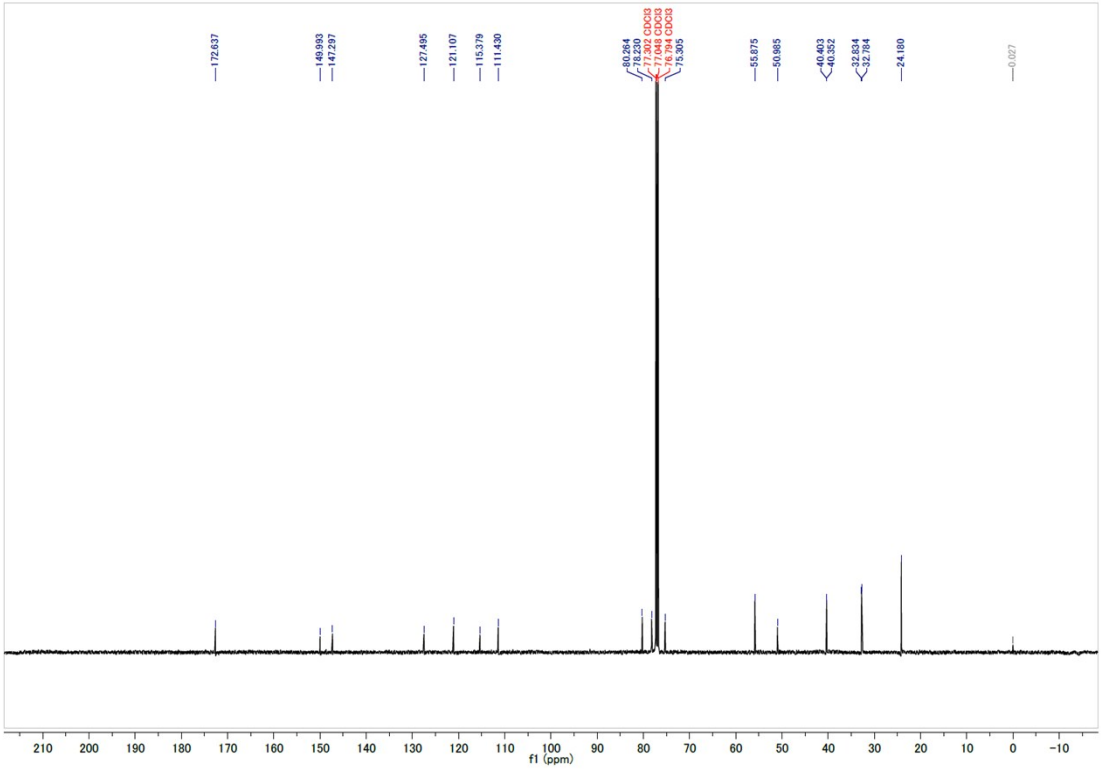


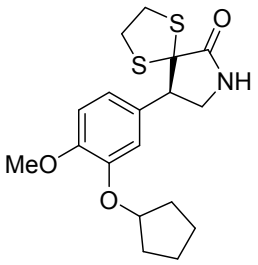
9

^{1}H NMR



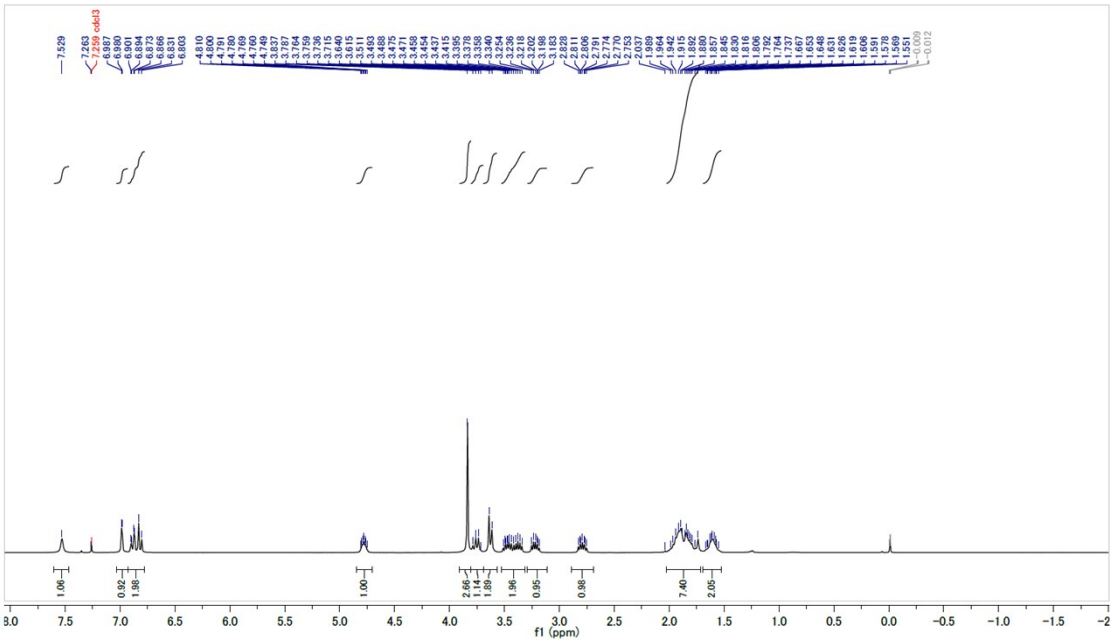
^{13}C NMR



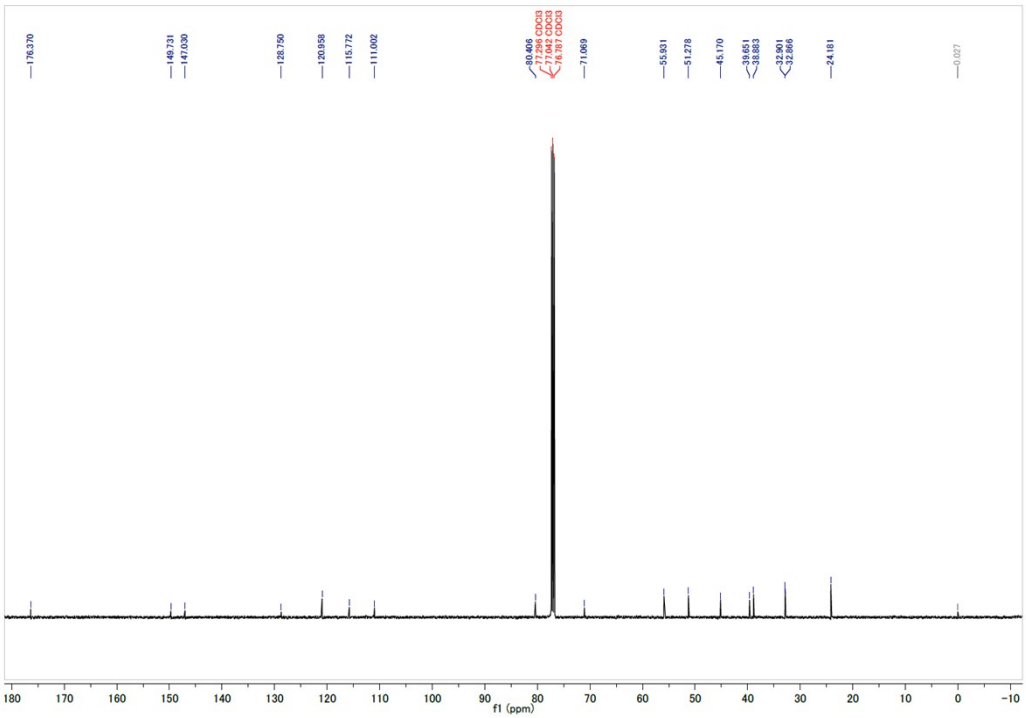


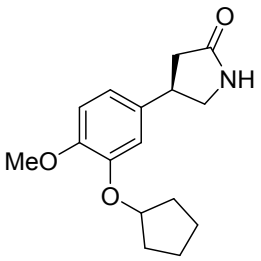
10

^{1}H NMR



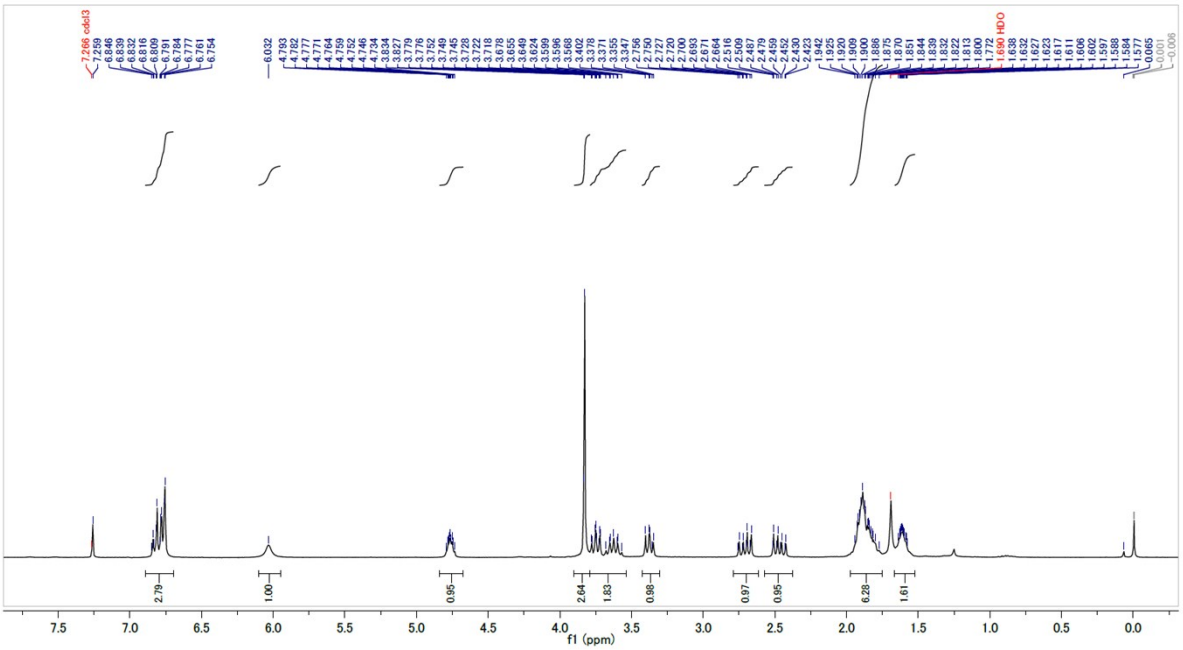
^{13}C NMR



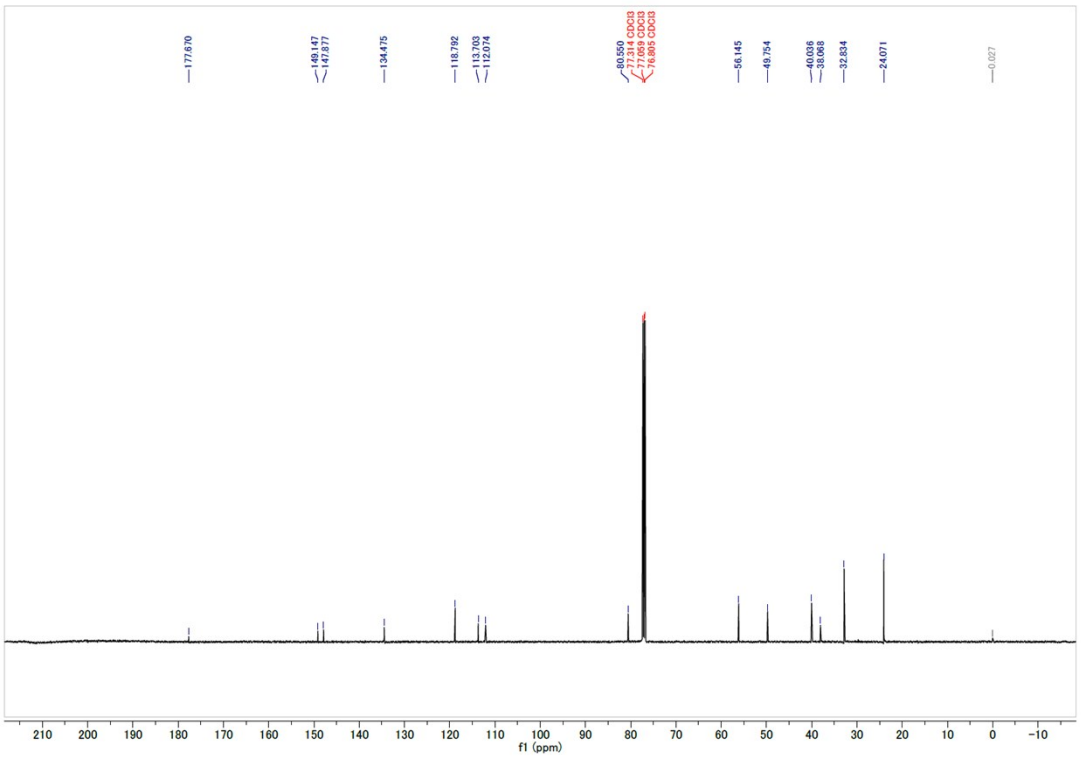


11

^{1}H NMR

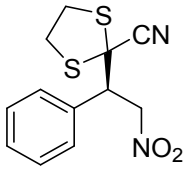


^{13}C NMR



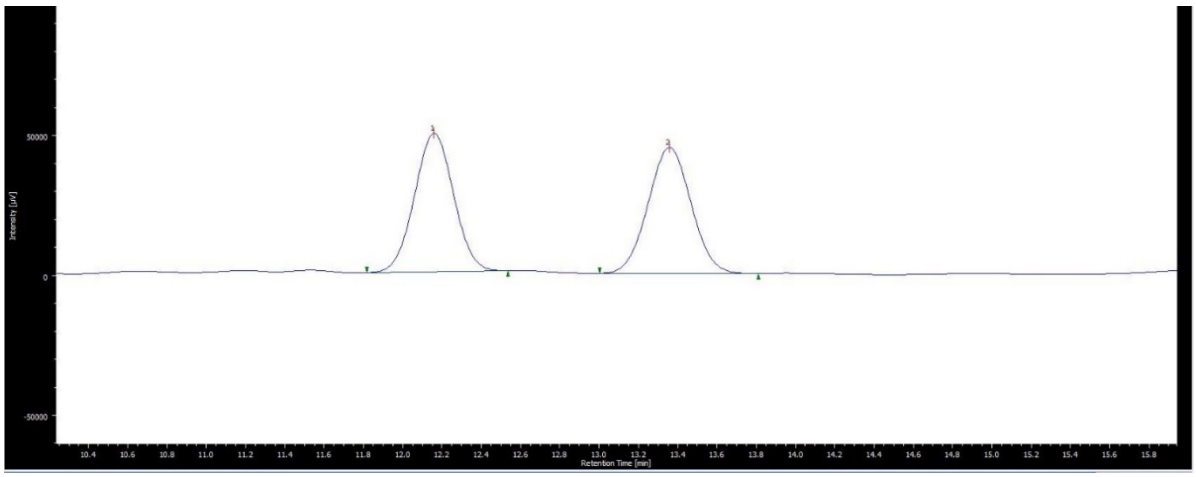
HPLC Chart

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-phenylbutanenitrile (3aa)

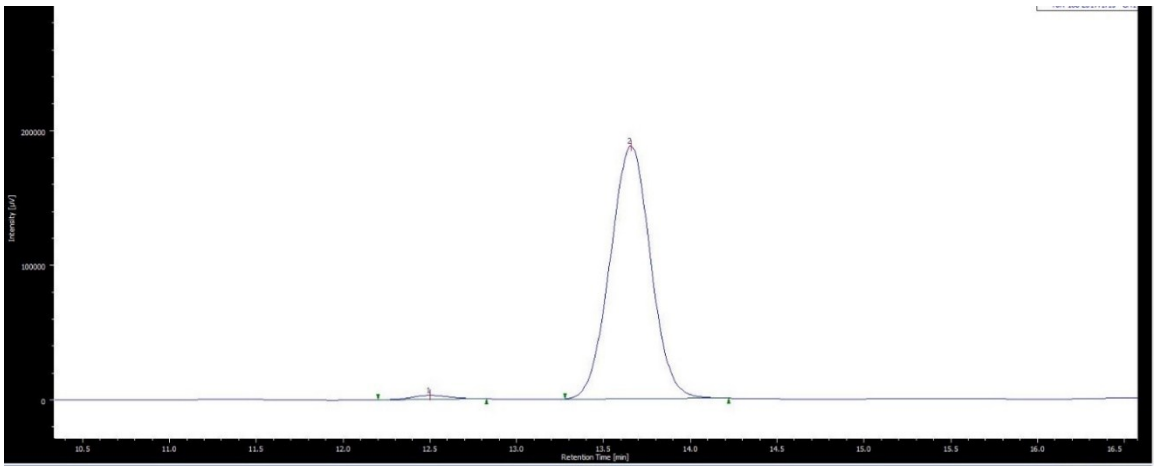


3aa

racemic-**3aa**



(*R*)-**3aa**



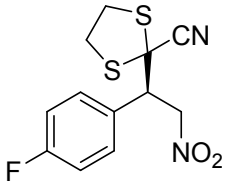
racemic-**3aa**

Peak	tR (min)	Area (%)
1	12.5	50.0
2	13.4	50.0

(*R*)-**3aa**

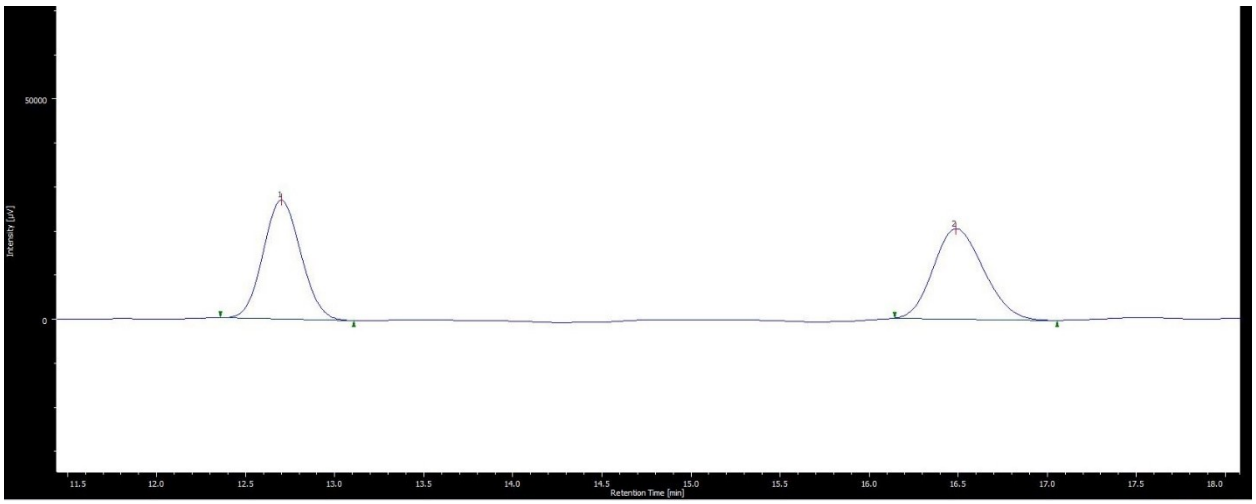
Peak	tR (min)	Area (%)
1	12.3	1.2
2	13.5	98.8

(3*R*)-2-[(1,3-dithiolane)-2-yl]-3-(4-fluorophenyl)-4-nitrobutanenitrile (3ba)

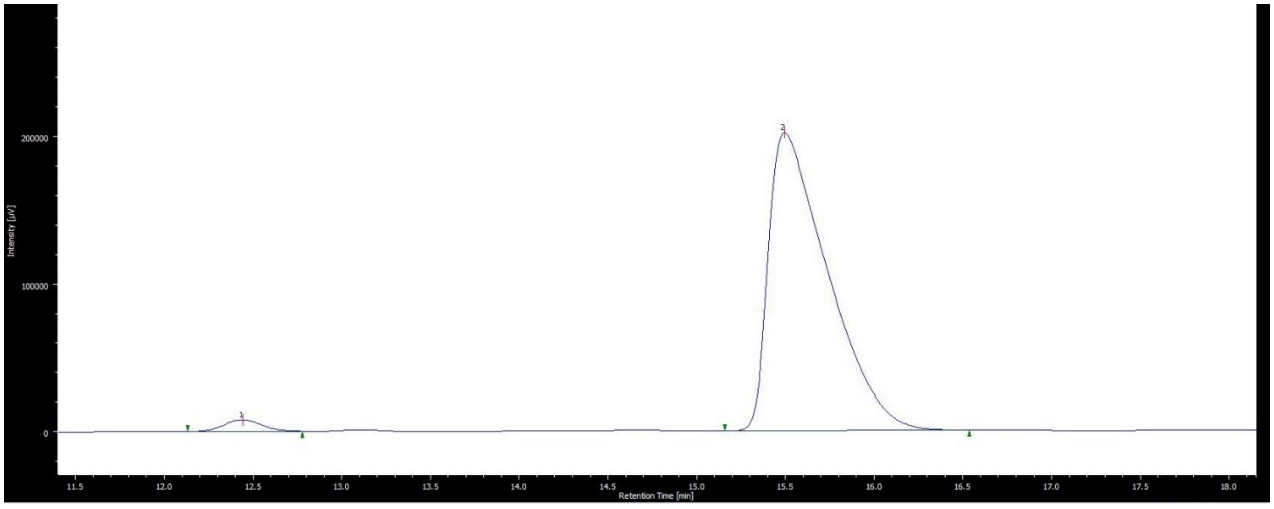


3ba

racemic-**3ba**



(*R*)-**3ba**



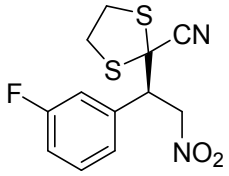
racemic-**3ba**

Peak	tR (min)	Area (%)
1	12.7	49.8
2	16.5	50.3

(*R*)-**3ba**

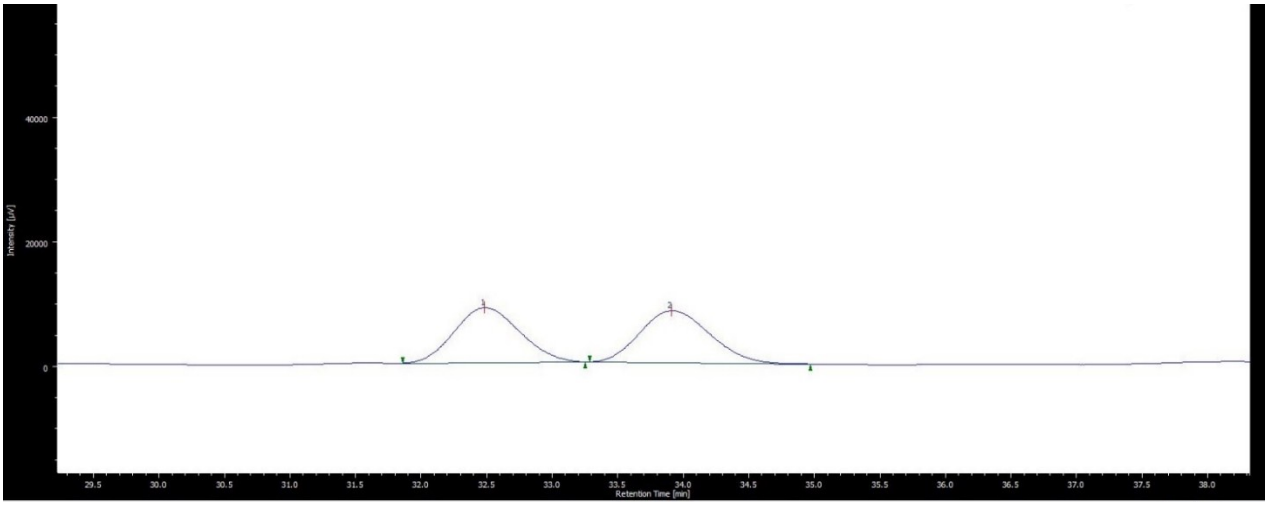
Peak	tR (min)	Area (%)
1	12.4	2.4
2	15.5	97.6

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-fluorophenyl)-4-nitrobutanenitrile (3ca)

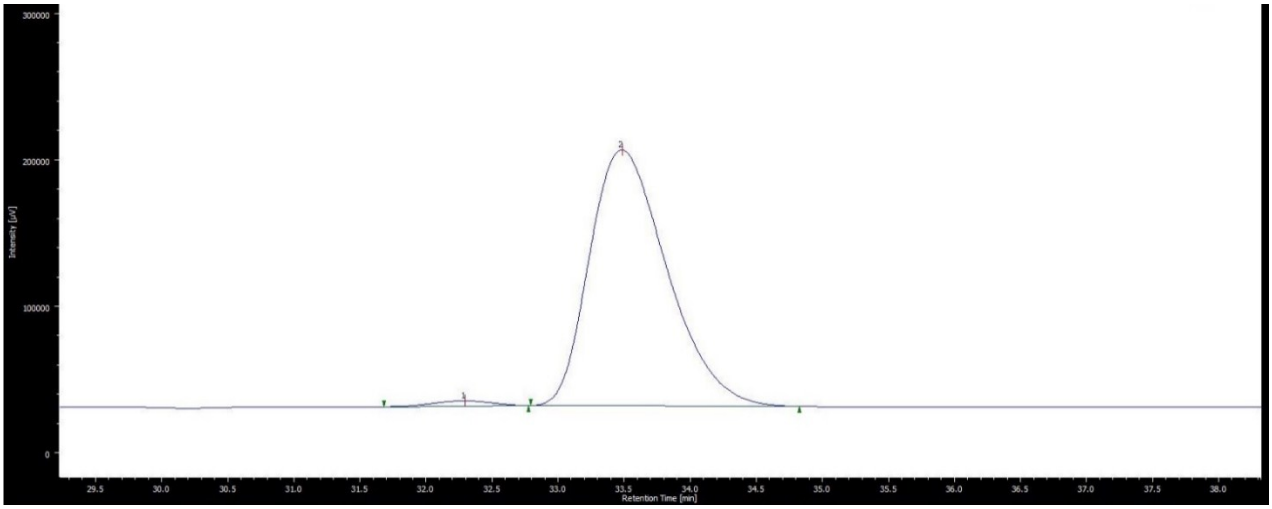


3ca

racemic-**3ca**



(*R*)-**3ca**



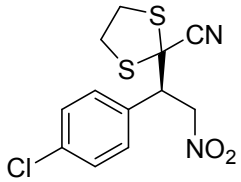
racemic-**3ca**

Peak	tR (min)	Area (%)
1	32.5	49.7
2	33.9	50.3

(*R*)-**3ca**

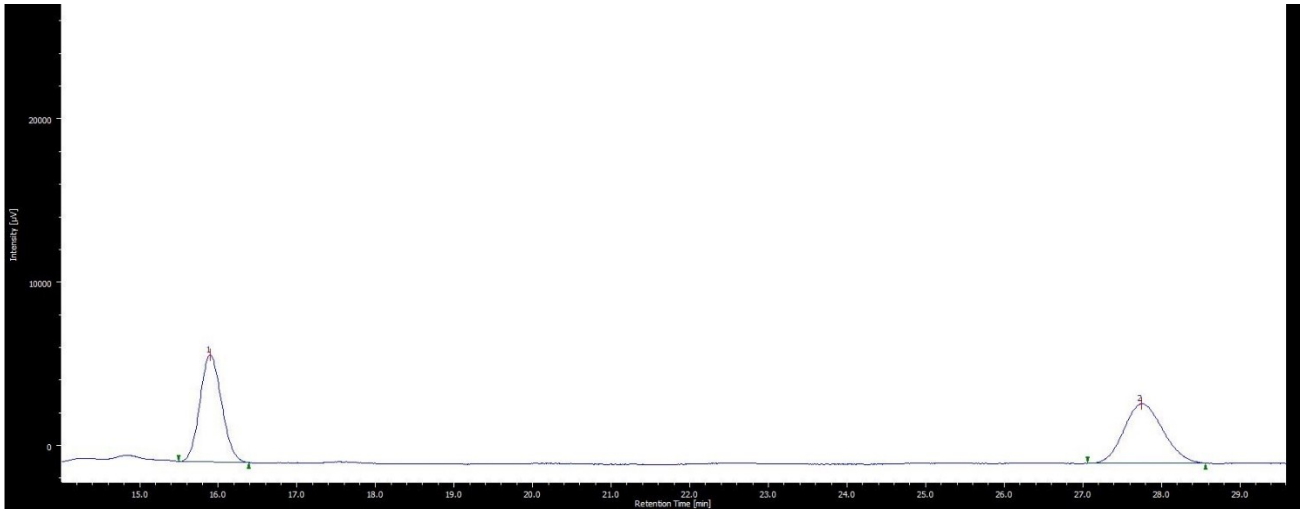
Peak	tR (min)	Area (%)
1	32.3	1.5
2	33.5	98.5

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-chlorophenyl)-4-nitrobutanenitrile (3da)

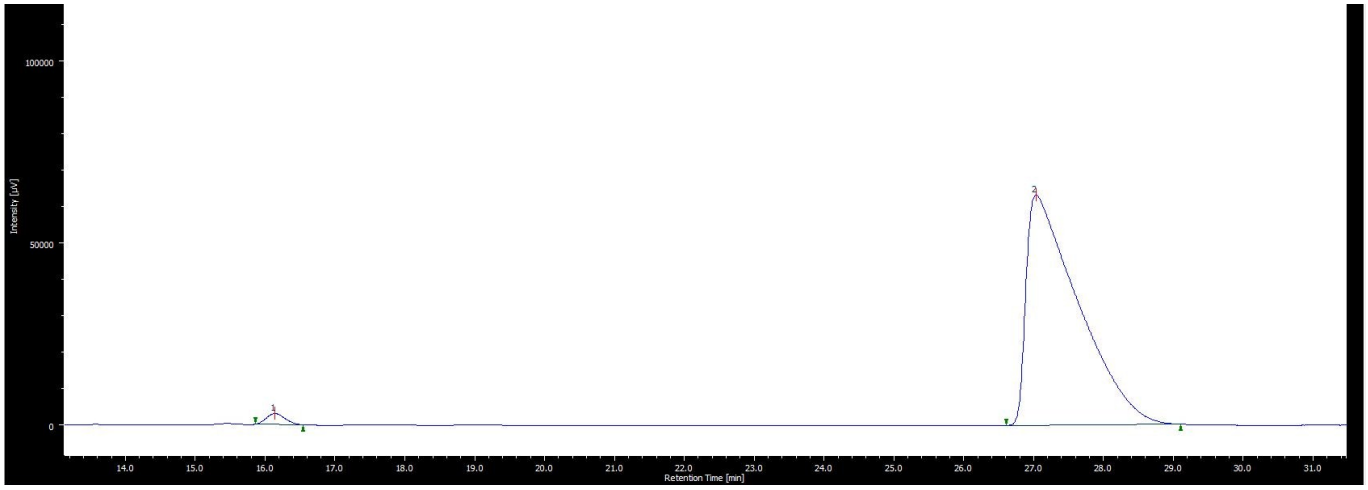


3da

racemic-**3da**



(*R*)-**3da**



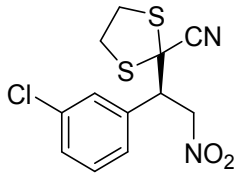
racemic-**3da**

Peak	tR (min)	Area (%)
1	15.9	50.0
2	27.7	50.0

(*R*)-**3da**

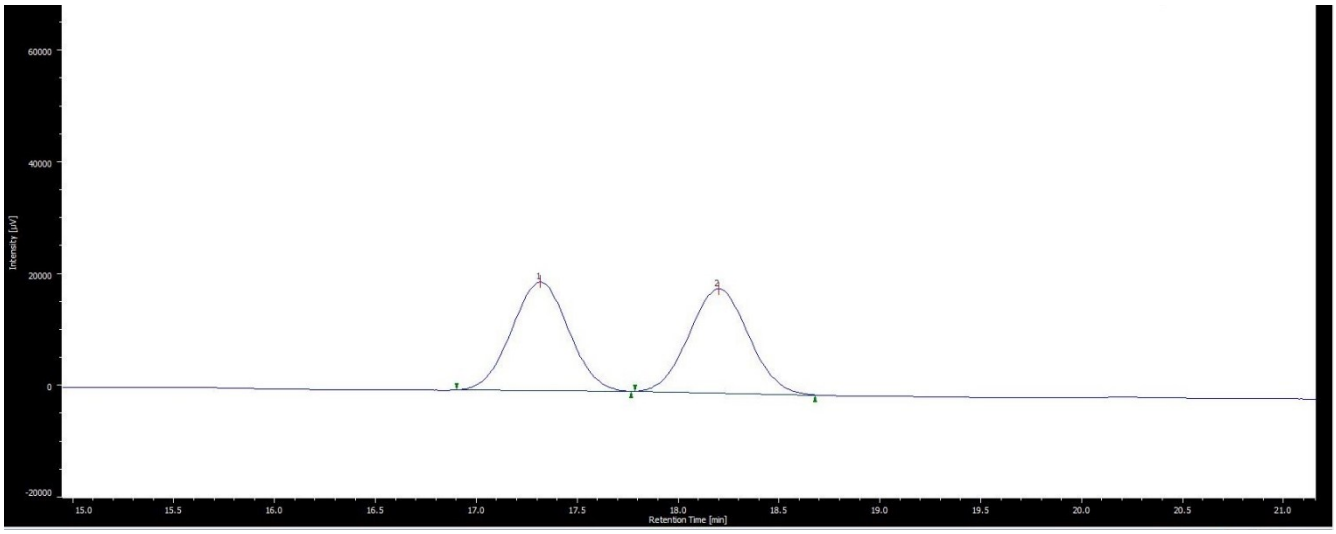
Peak	tR (min)	Area (%)
1	16.1	1.7
2	27.0	98.3

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-chlorophenyl)-4-nitrobutanenitrile (3ea)

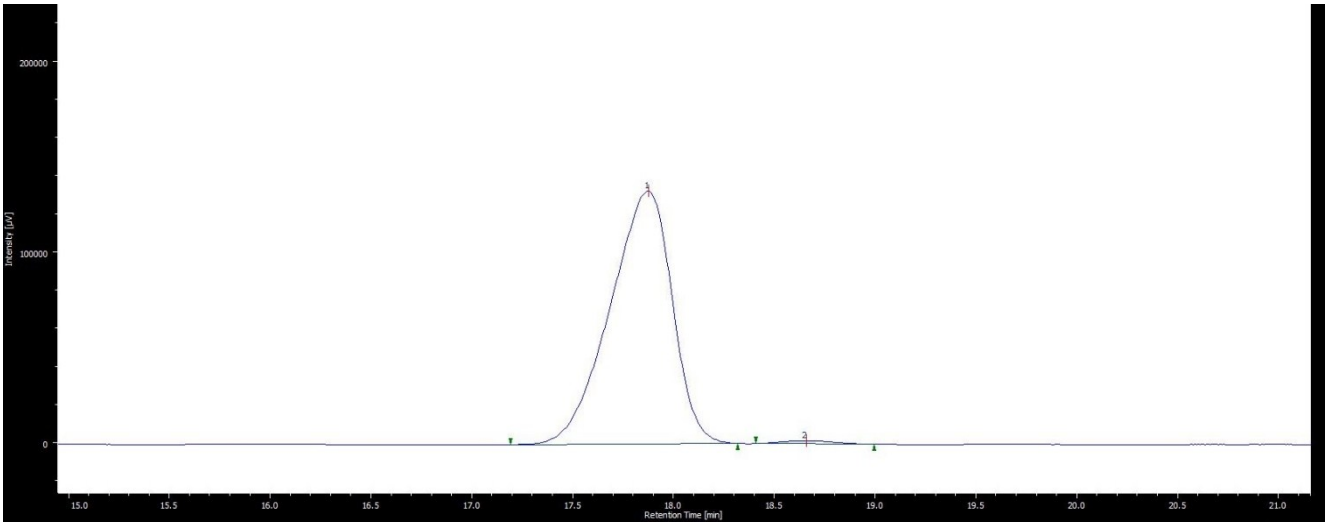


3ea

racemic-**3ea**



(*R*)-**3ea**



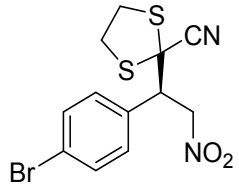
racemic-**3ea**

Peak	tR (min)	Area (%)
1	17.3	50.0
2	18.2	50.0

(*R*)-**3ea**

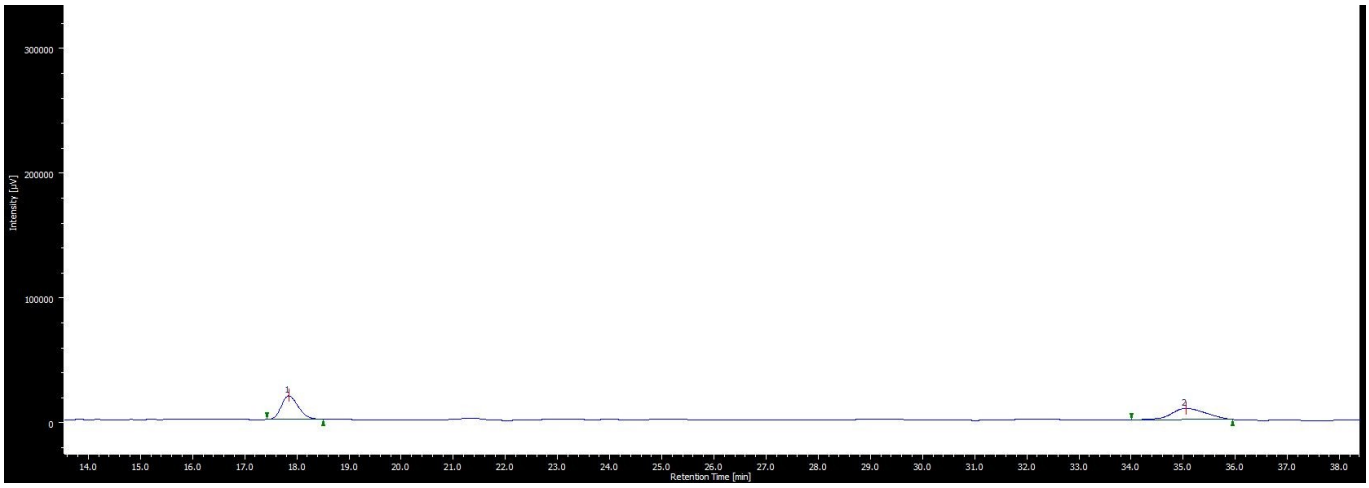
Peak	tR (min)	Area (%)
1	17.9	99.0
2	18.7	1.0

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-bromophenyl)-4-nitrobutanenitrile (3fa)

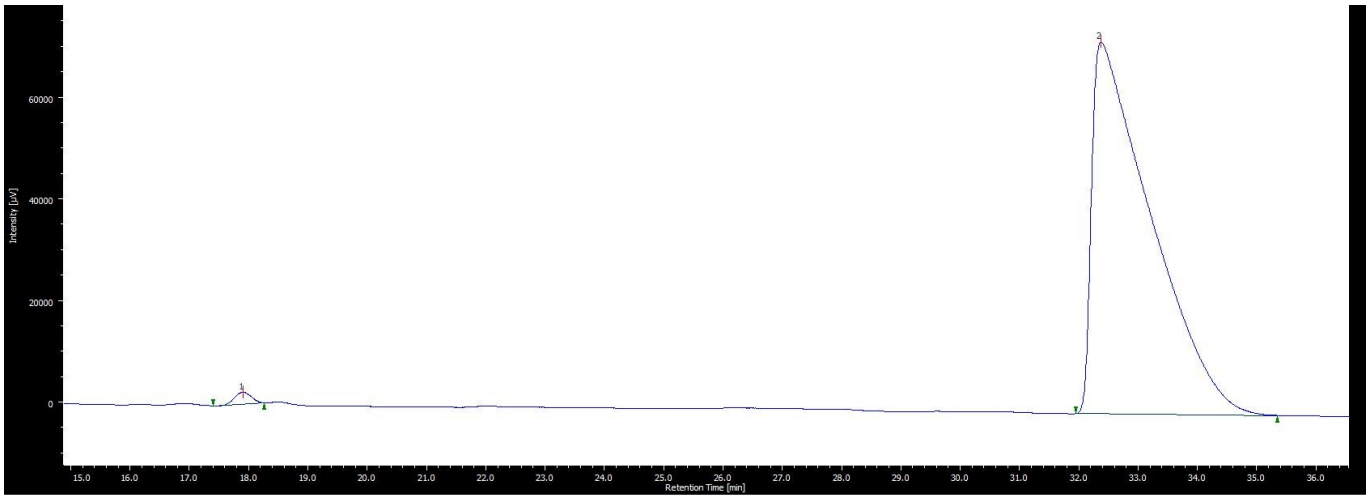


3fa

racemic-**3fa**



(*R*)-**3fa**



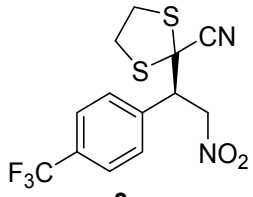
racemic-**3fa**

Peak	tR (min)	Area (%)
1	17.8	50.0
2	35.0	50.0

(*R*)-**3fa**

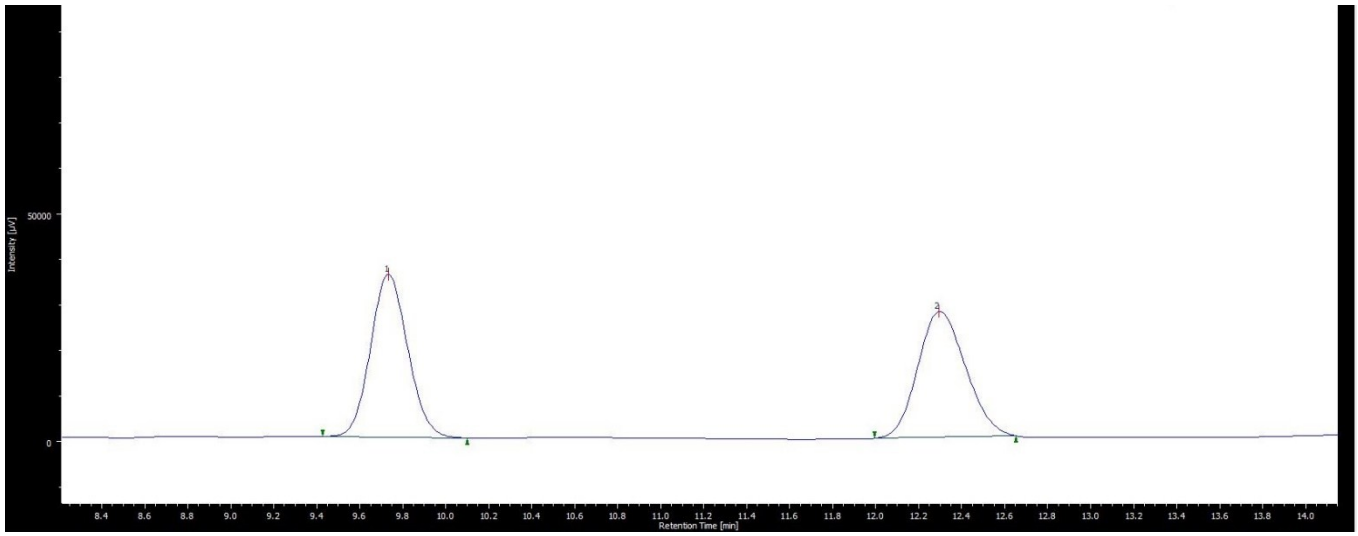
Peak	tR (min)	Area (%)
1	17.9	0.9
2	12.3	99.1

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-(4-trifluoromethyl)phenylbutanenitrile (3ga)

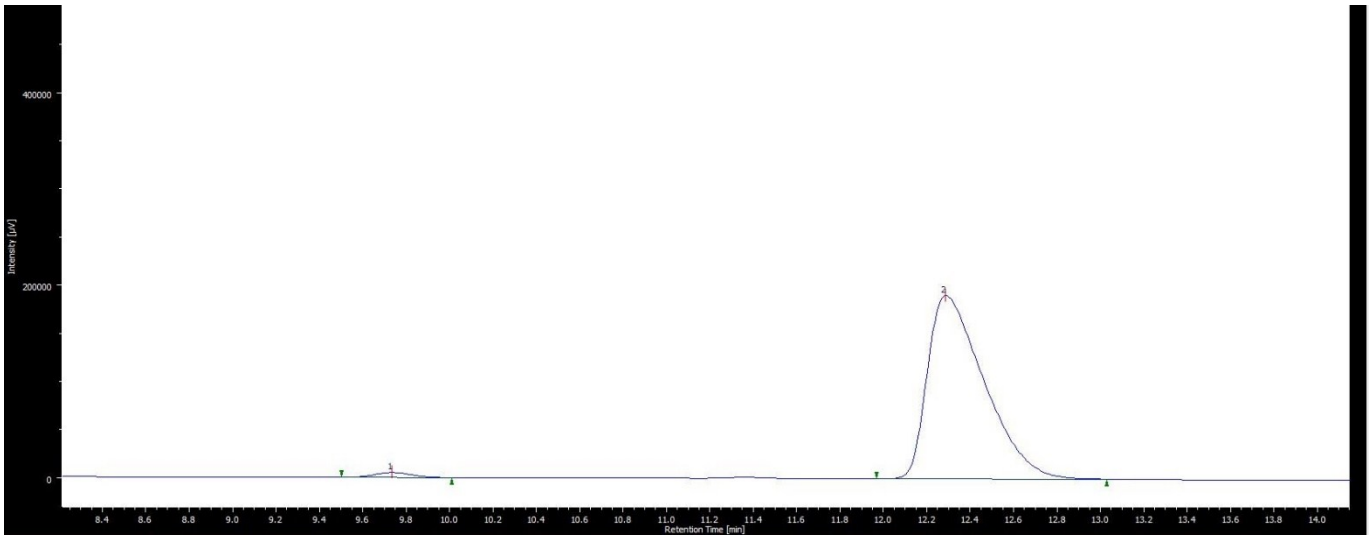


3ga

racemic-**3ga**



(*R*)-**3ga**



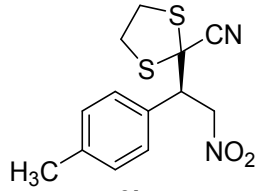
racemic-**3ga**

Peak	tR (min)	Area (%)
1	9.7	50.2
2	12.3	49.8

(*R*)-**3ga**

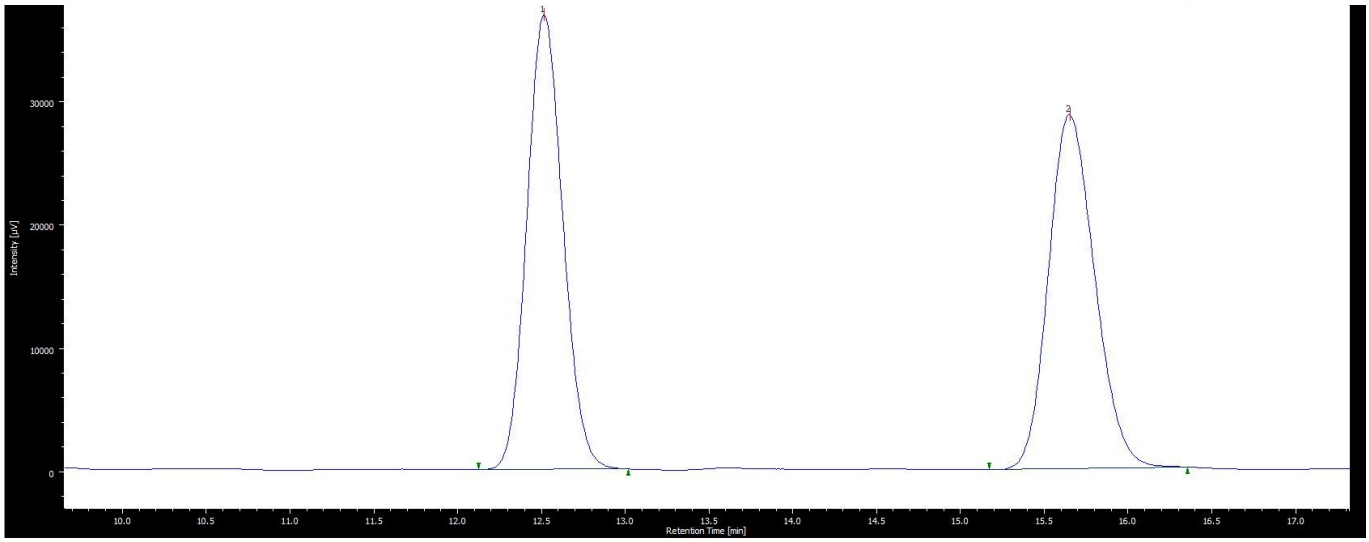
Peak	tR (min)	Area (%)
1	9.7	1.8
2	12.3	98.2

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-methylphenyl)-4-nitrobutanenitrile (3ha)

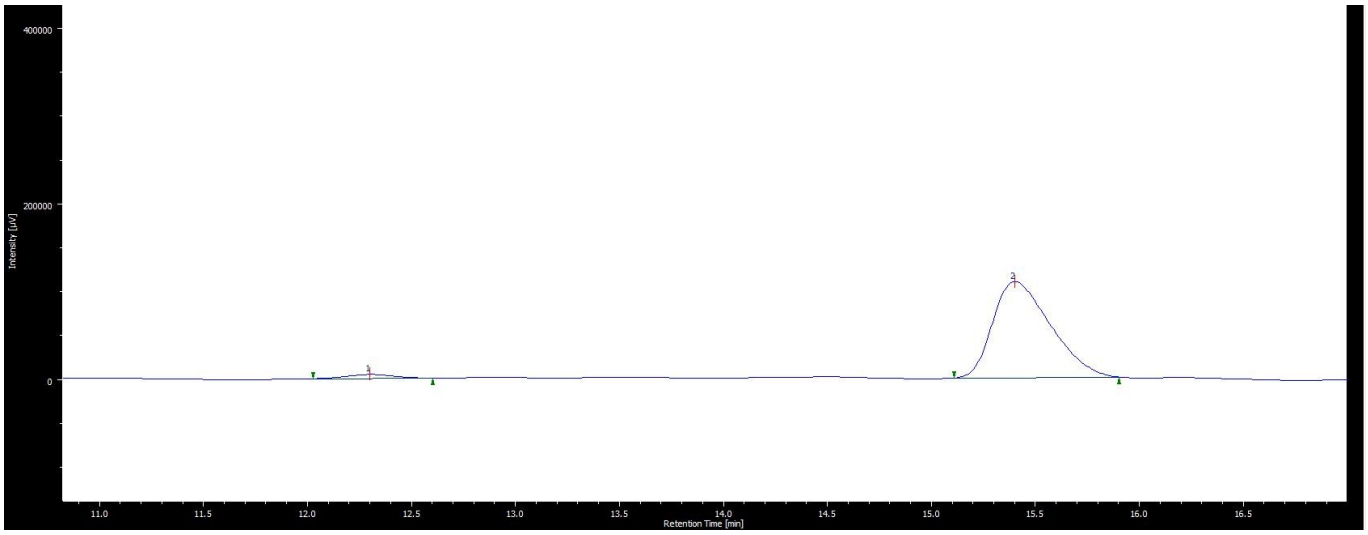


3ha

racemic-**3ha**



(*R*)-**3ha**



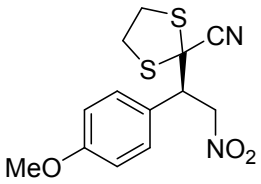
racemic-**3ha**

Peak	tR (min)	Area (%)
1	12.5	50.0
2	15.7	50.0

(*R*)-**3ha**

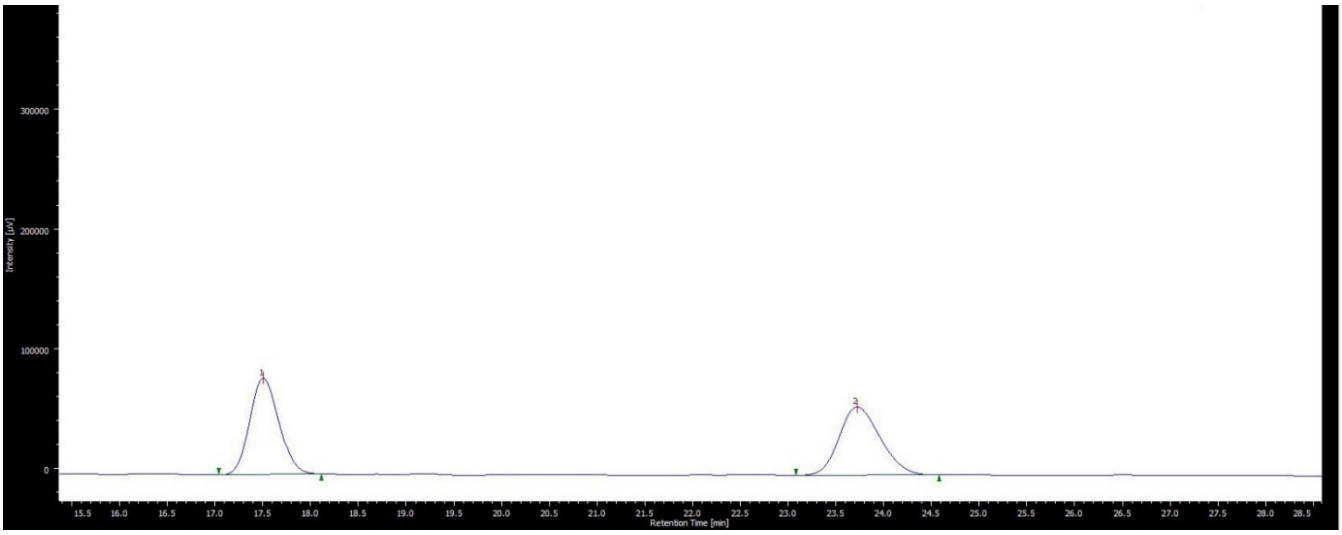
Peak	tR (min)	Area (%)
1	12.3	2.8
2	15.4	97.2

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(4-methoxyphenyl)-4-nitrobutanenitrile (3ia)

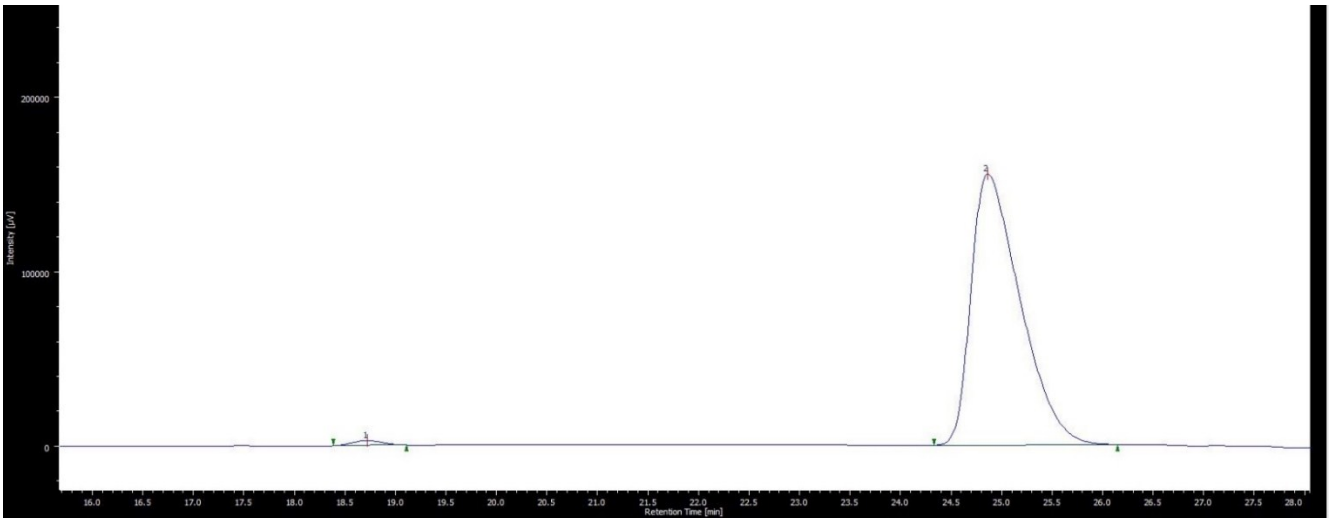


3ia

racemic-**3ia**



(*R*)-**3ia**



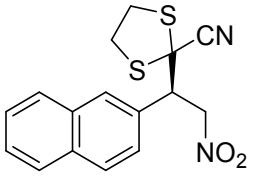
racemic-**3ia**

Peak	tR (min)	Area (%)
1	17.5	49.9
2	23.7	50.1

(*R*)-**3ia**

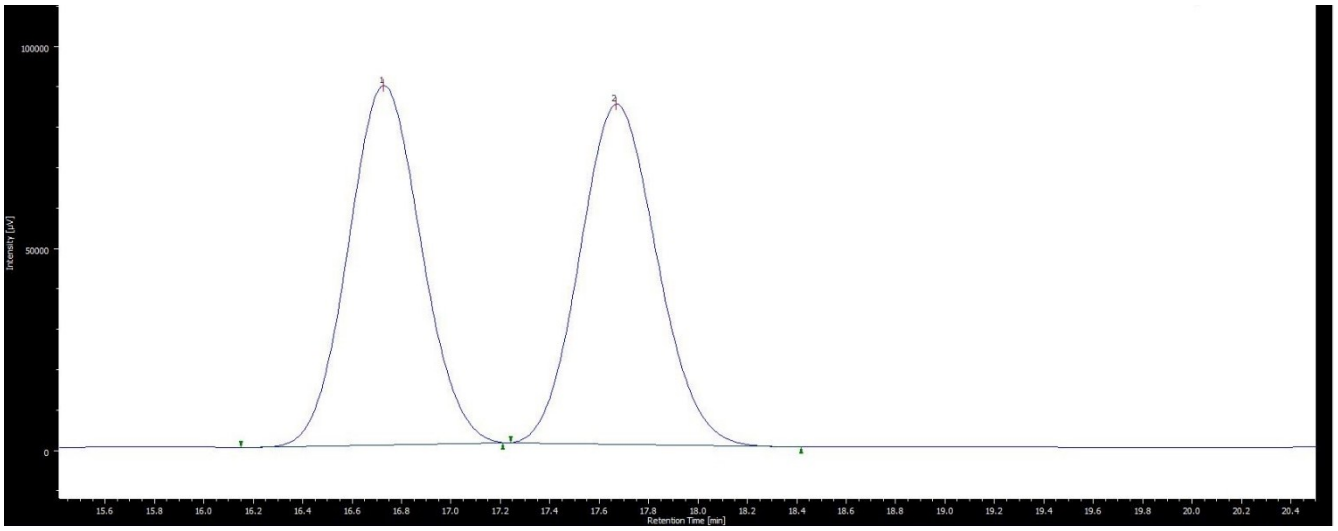
Peak	tR (min)	Area (%)
1	18.7	1.1
2	24.8	98.9

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(2-naphthyl)-4-nitrobutanenitrile (3ja)

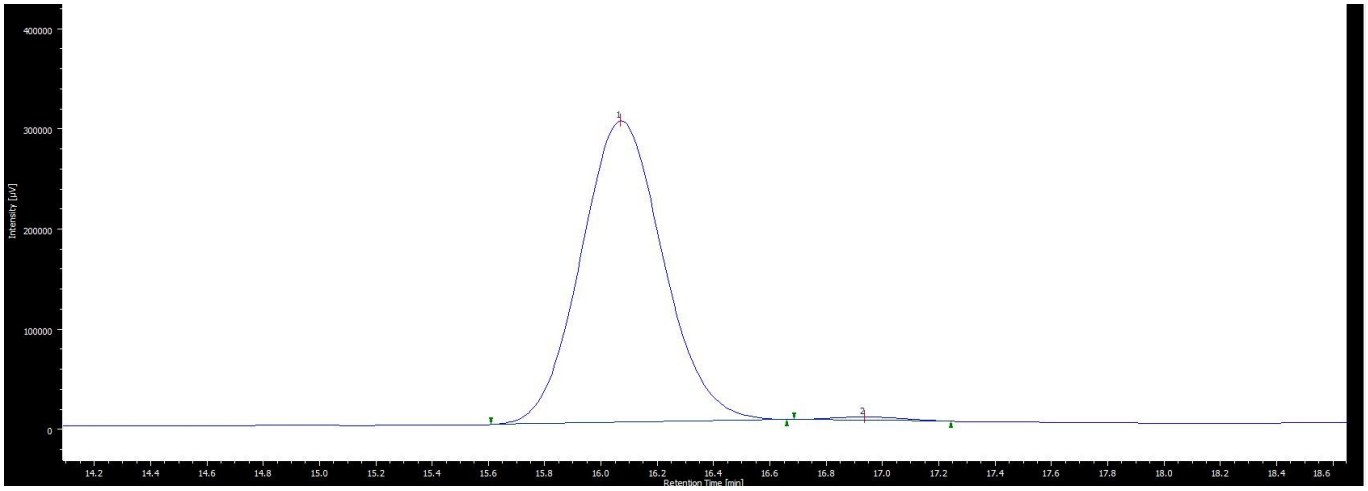


3ja

racemic-**3ja**



(*R*)-**3ja**



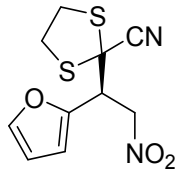
racemic-**3ja**

Peak	tR (min)	Area (%)
1	16.7	49.9
2	17.7	50.1

(*R*)-**3ja**

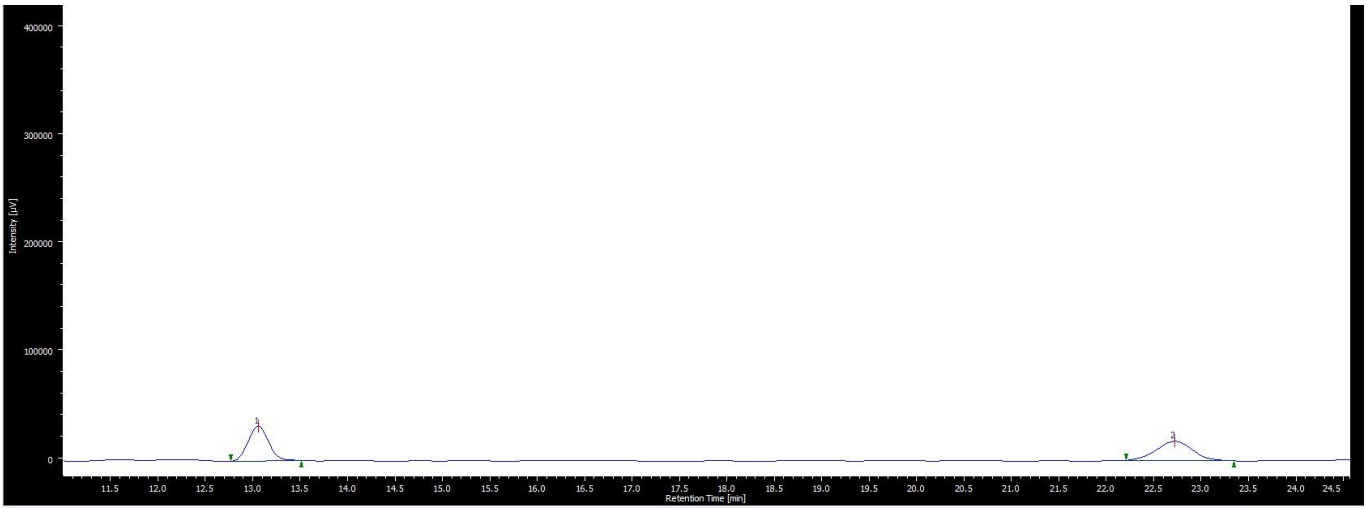
Peak	tR (min)	Area (%)
1	16.1	99.0
2	16.9	1.0

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(2-furyl)-4-nitrobutanenitrile (3ka)

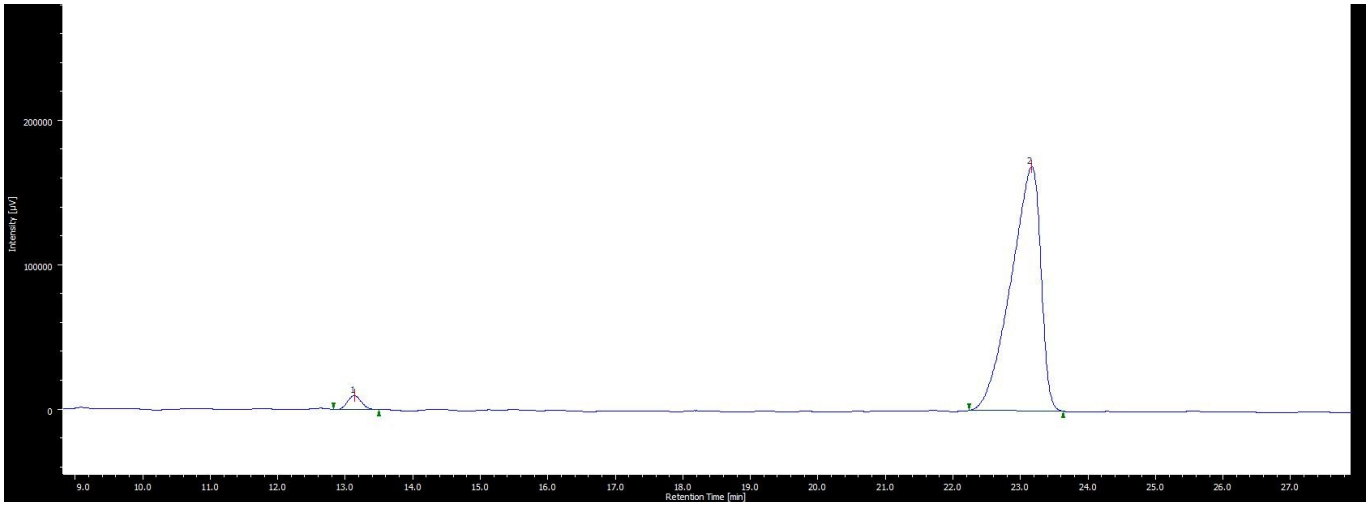


3ka

racemic-**3ka**



(*R*)-**3ka**



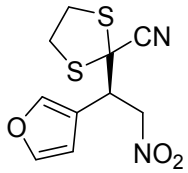
racemic-**3ka**

Peak	tR (min)	Area (%)
1	13.1	50.2
2	22.7	49.8

(*R*)-**3ka**

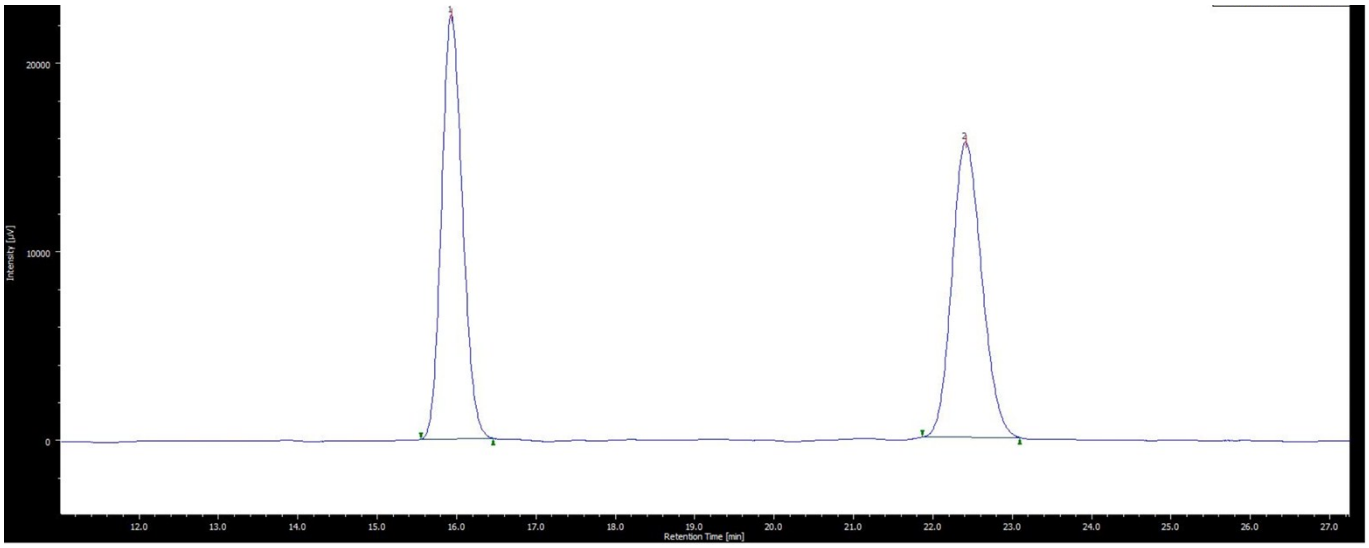
Peak	tR (min)	Area (%)
1	13.1	2.5
2	23.2	97.5

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-3-(3-furyl)-4-nitrobutanenitrile (3la)

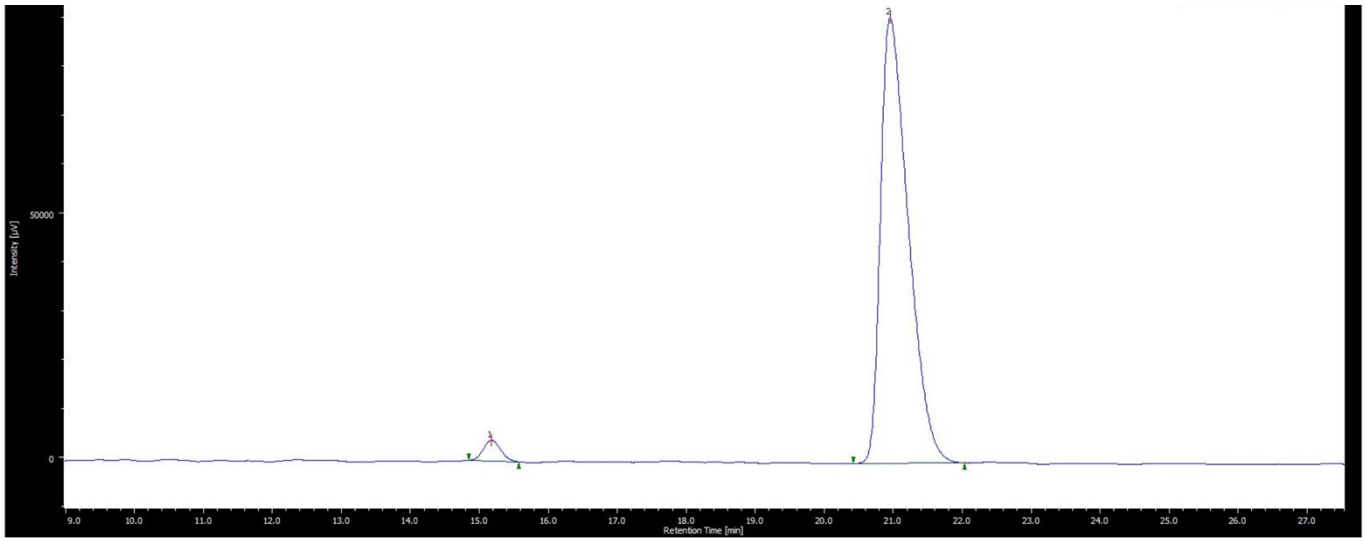


3la

racemic-**3la**



(*R*)-**3la**



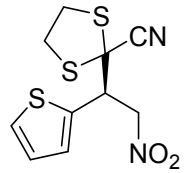
racemic-**3la**

Peak	tR (min)	Area (%)
1	15.9	50.1
2	22.4	49.9

(*R*)-**3la**

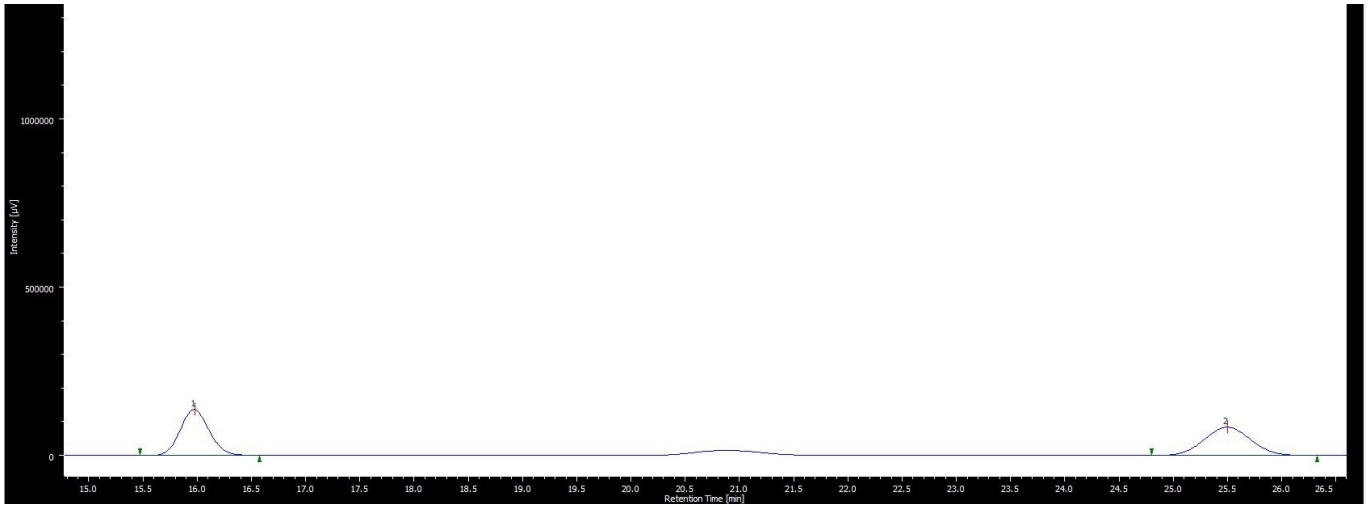
Peak	tR (min)	Area (%)
1	15.2	2.8
2	21.0	97.2

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-(2-thienyl)butanenitrile (3ma)

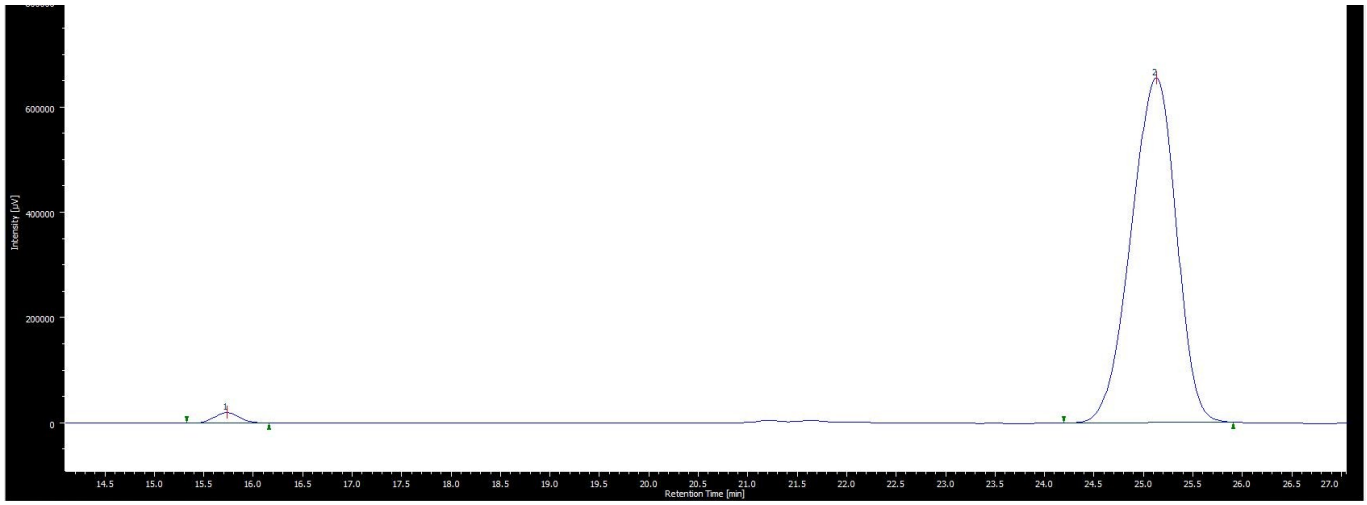


3ma

racemic-**3ma**



(*R*)-**3ma**



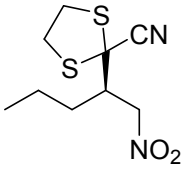
racemic-**3ma**

Peak	tR (min)	Area (%)
1	16.0	50.2
2	25.5	49.8

(*R*)-**3ma**

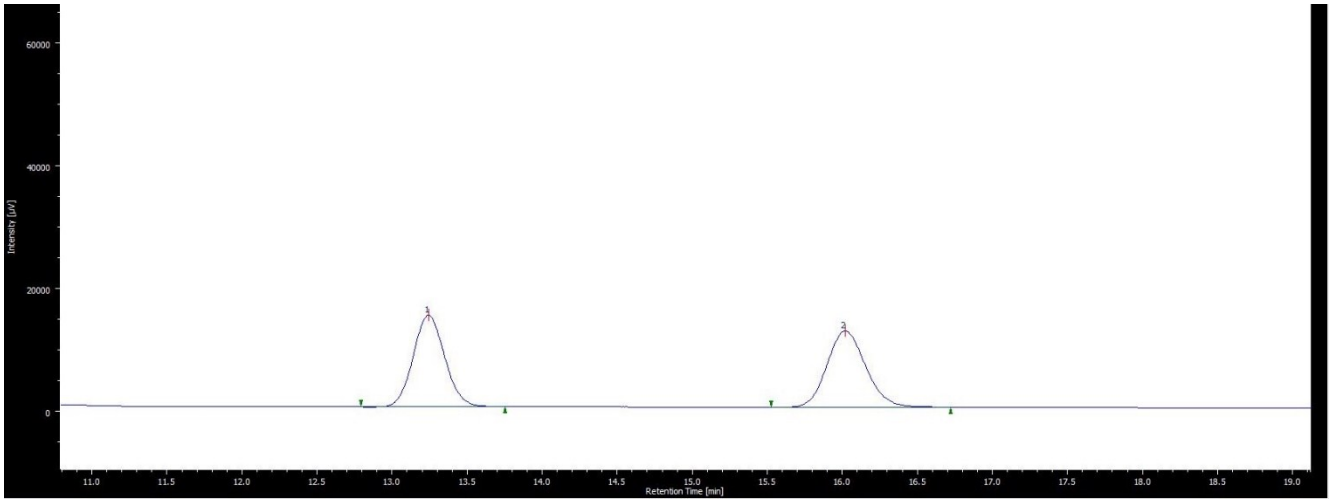
Peak	tR (min)	Area (%)
1	15.7	1.7
2	25.1	98.3

(3*R*)-3-(Nitromethyl)-2-[(1,3-dithiolane)-2-yl]-hexanenitrile (3na)

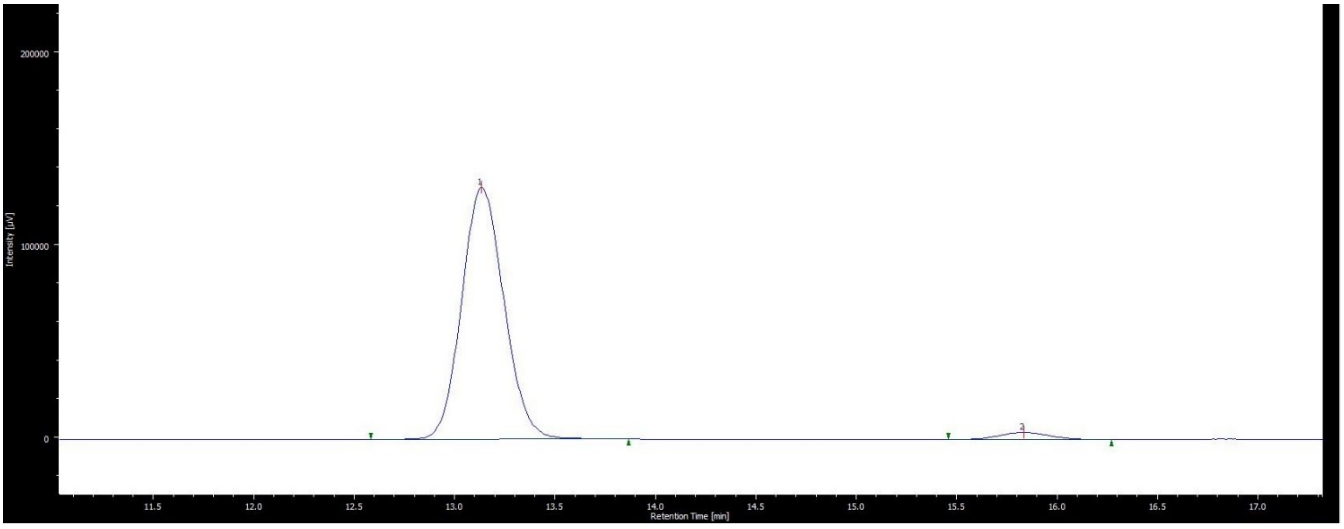


3na

racemic-**3na**



(*R*)-**3na**



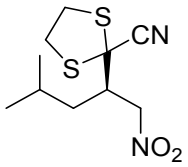
racemic-**3na**

Peak	tR (min)	Area (%)
1	13.2	49.5
2	16.0	50.5

(*R*)-**3na**

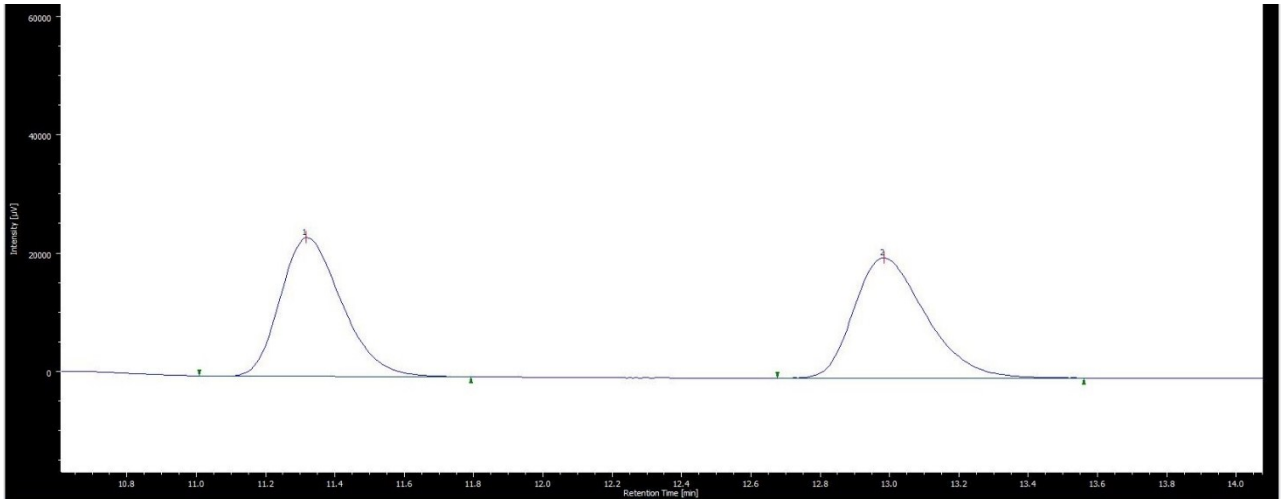
Peak	tR (min)	Area (%)
1	13.1	96.8
2	15.8	3.2

(3*R*)-3-(Nitromethyl)-5-methyl-2-[(1,3-dithiolane)-2-yl]-hexanenitrile (3oa)

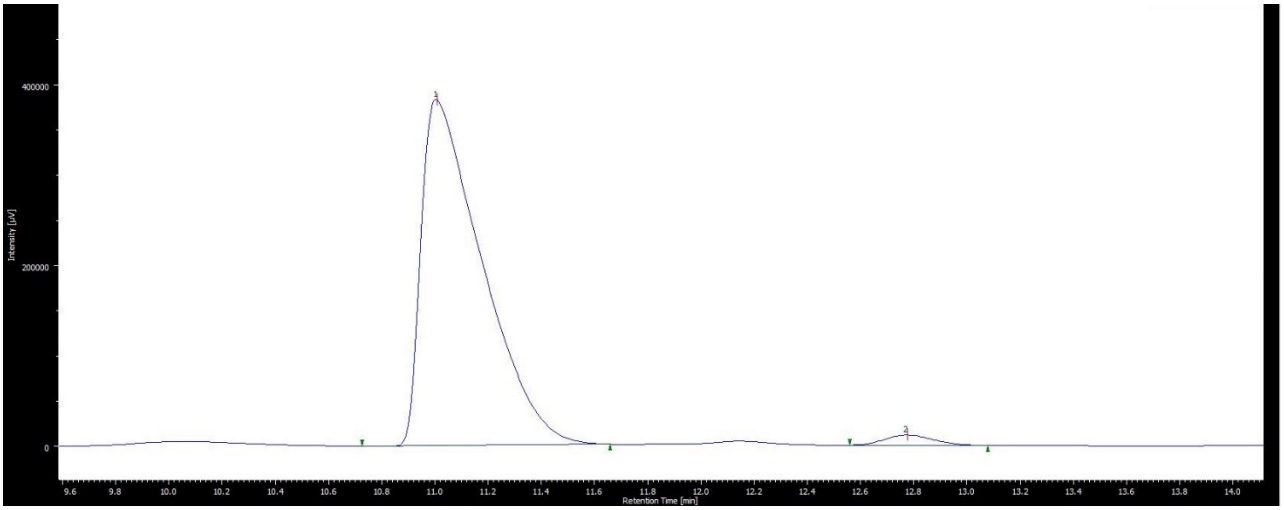


3oa

racemic-**3oa**



(*R*)-**3oa**



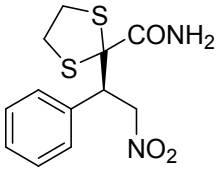
racemic-**3oa**

Peak	tR (min)	Area (%)
1	11.3	49.7
2	13.0	50.3

(*R*)-**3oa**

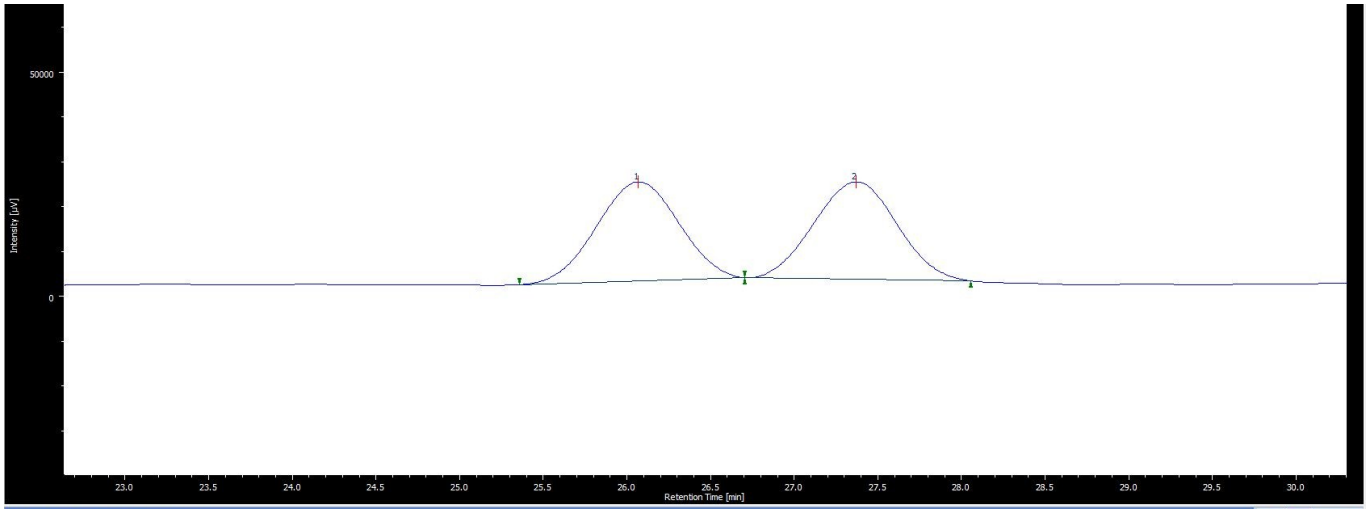
Peak	tR (min)	Area (%)
1	11.0	97.7
2	12.8	2.3

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-phenylbutanamide (5)

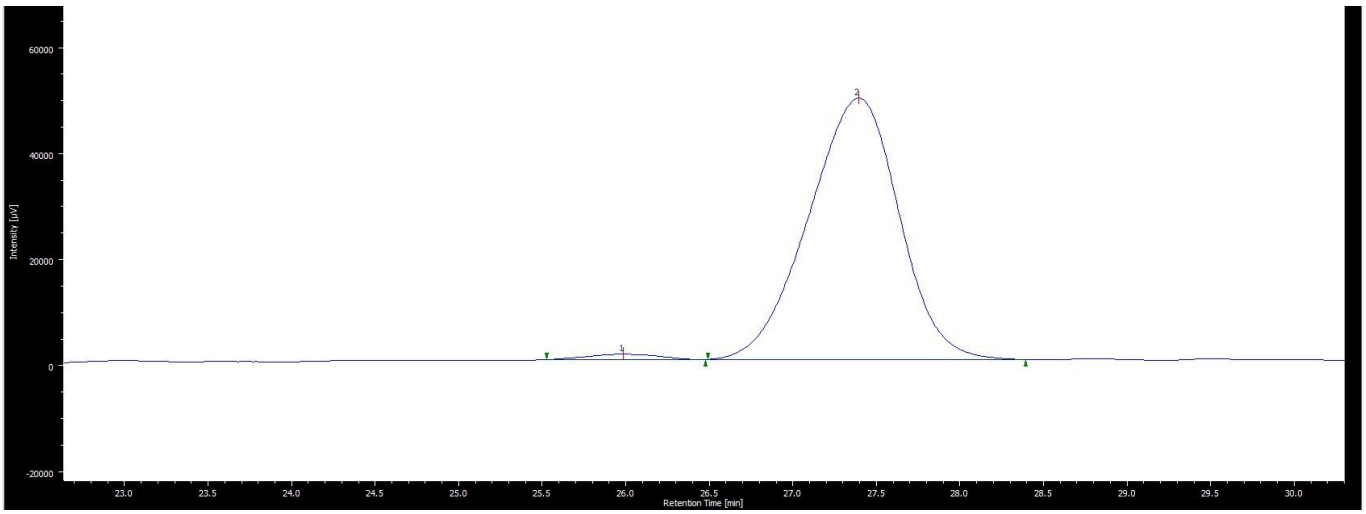


5

racemic-**5**



(*R*)-**5**



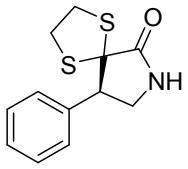
racemic-**5**

Peak	tR (min)	Area (%)
1	26.1	50.2
2	27.4	49.8

(*R*)-**5**

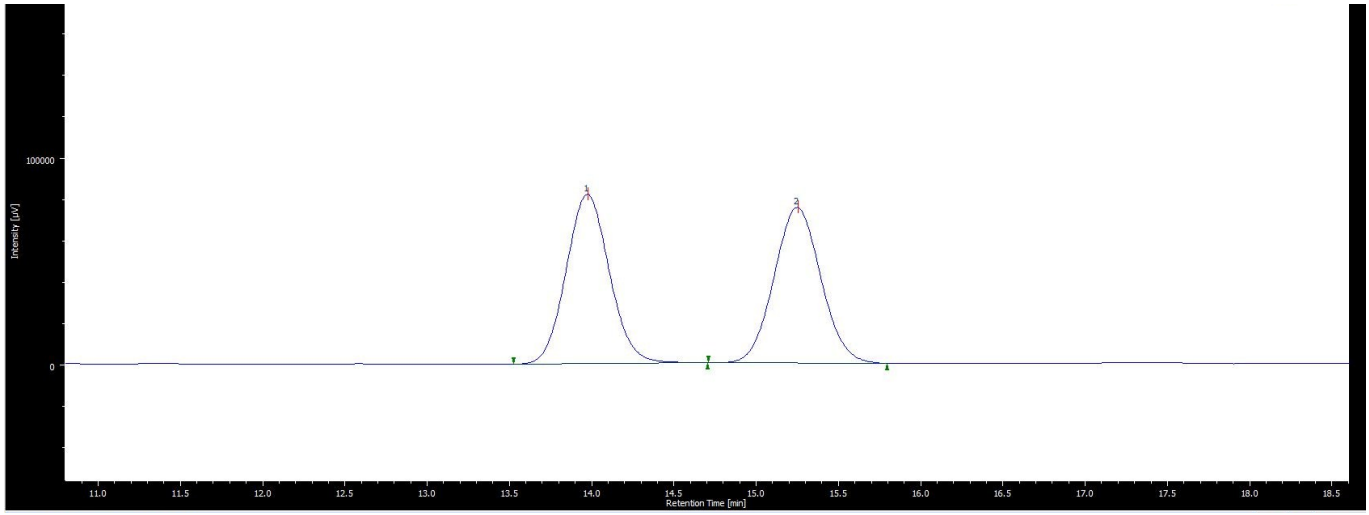
Peak	tR (min)	Area (%)
1	26.0	1.6
2	27.4	98.4

(9*R*)-1,4-Dithia-9-phenyl-7-azaspiro[4.4]nonane (6)

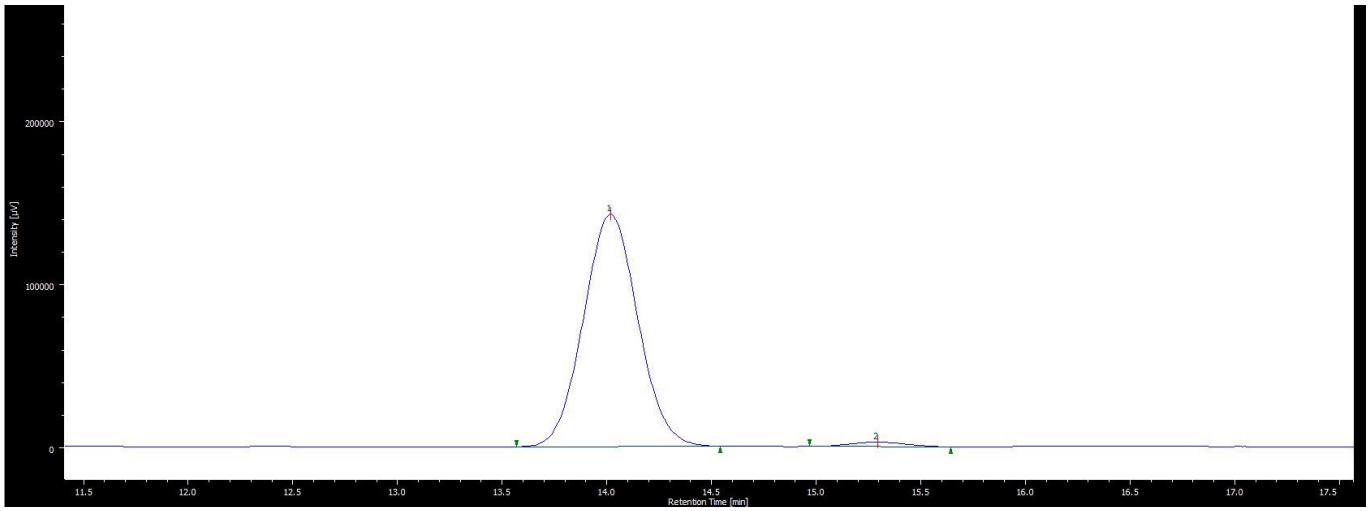


6

racemic-**6**



(*R*)-**6**



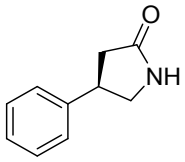
racemic-**6**

Peak	tR (min)	Area (%)
1	14.0	50.1
2	15.3	49.9

(*R*)-**6**

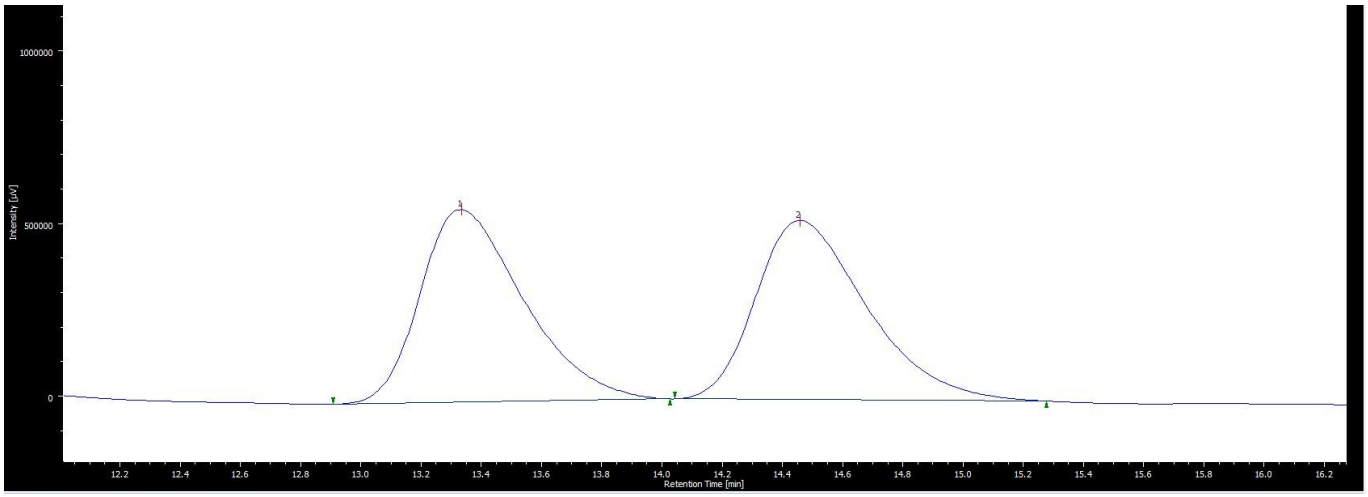
Peak	tR (min)	Area (%)
1	14.0	98.1
2	15.3	1.9

(4*R*)-4-Phenyl-2-pyrrolidinone (7)

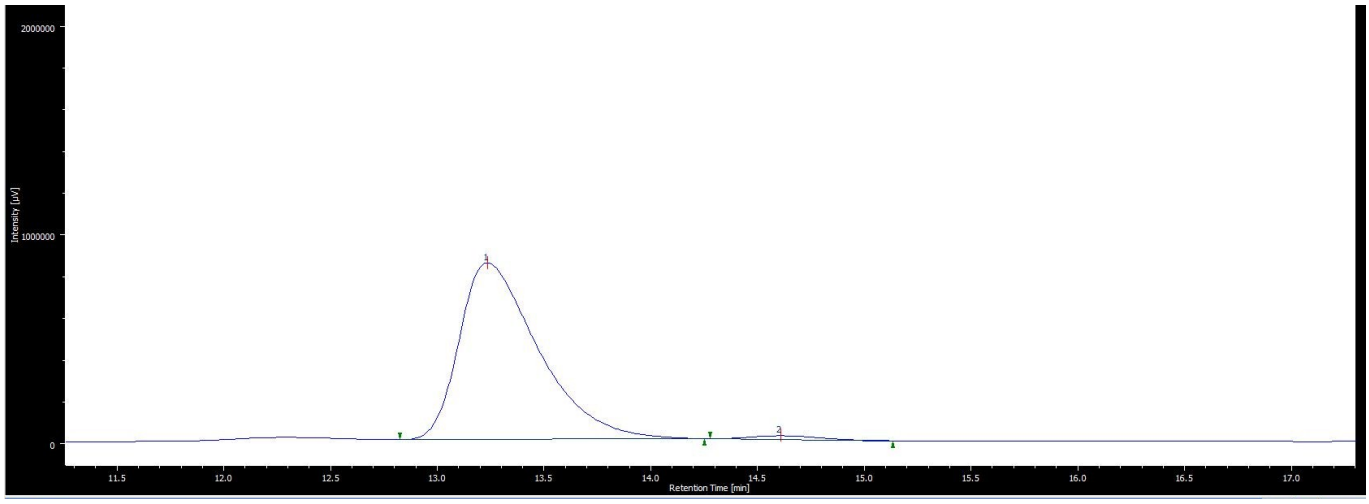


7

racemic-**7**



(*R*)-**7**



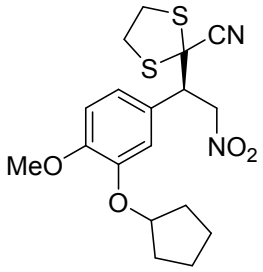
racemic-**7**

Peak	tR (min)	Area (%)
1	13.3	50.0
2	14.5	50.0

(*R*)-**7**

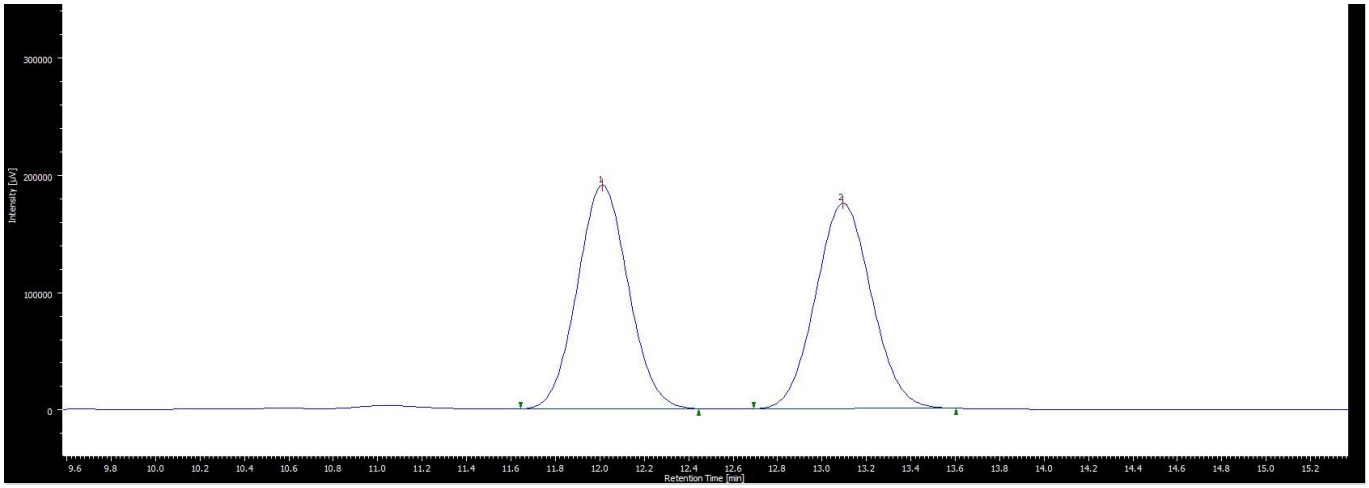
Peak	tR (min)	Area (%)
1	13.2	98.3
2	14.6	1.7

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-[3-(cyclopentyloxy)-4-methoxyphenyl]butanenitrile (8)

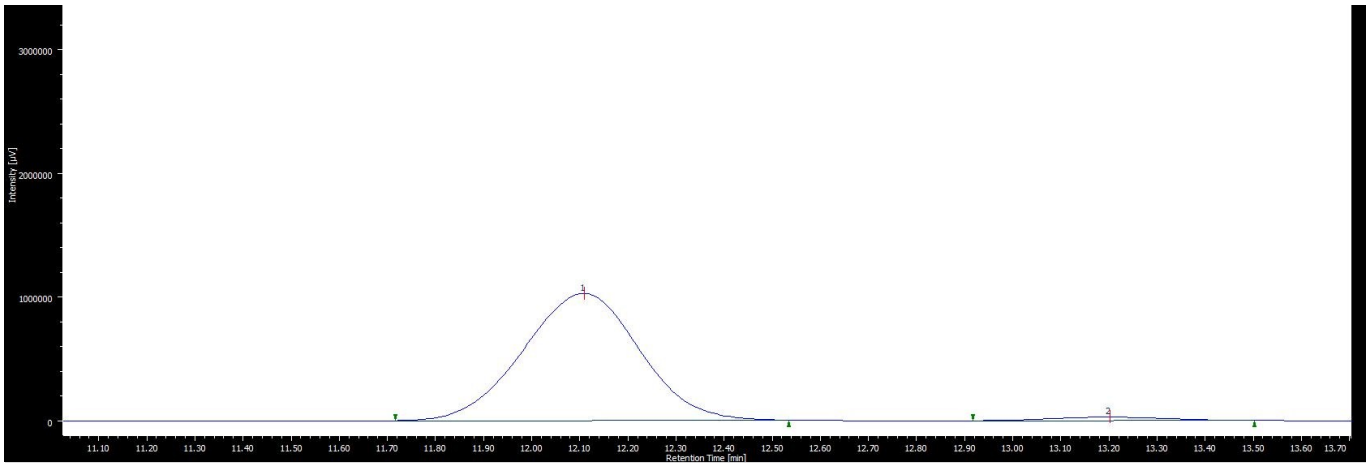


8

racemic-**8**



(*R*)-**8**



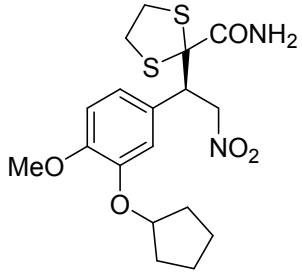
racemic-**8**

Peak	tR (min)	Area (%)
1	12.0	49.9
2	13.1	50.1

(*R*)-**8**

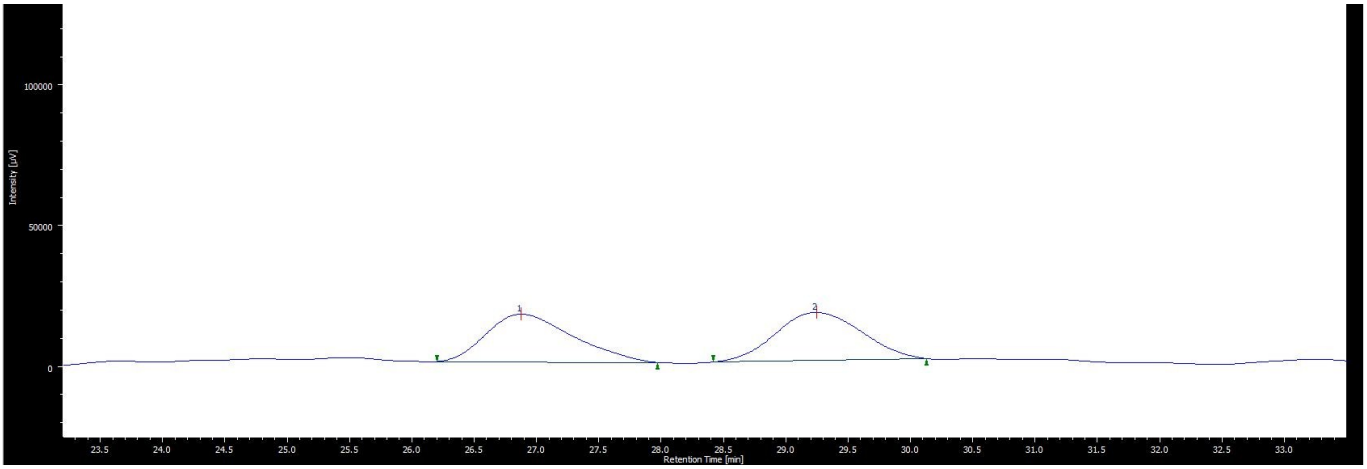
Peak	tR (min)	Area (%)
1	12.0	97.3
2	13.1	2.7

(3*R*)-2-[(1,3-Dithiolane)-2-yl]-4-nitro-3-[3-(cyclopentyloxy)-4-metoxyphenyl]butanamide (9)

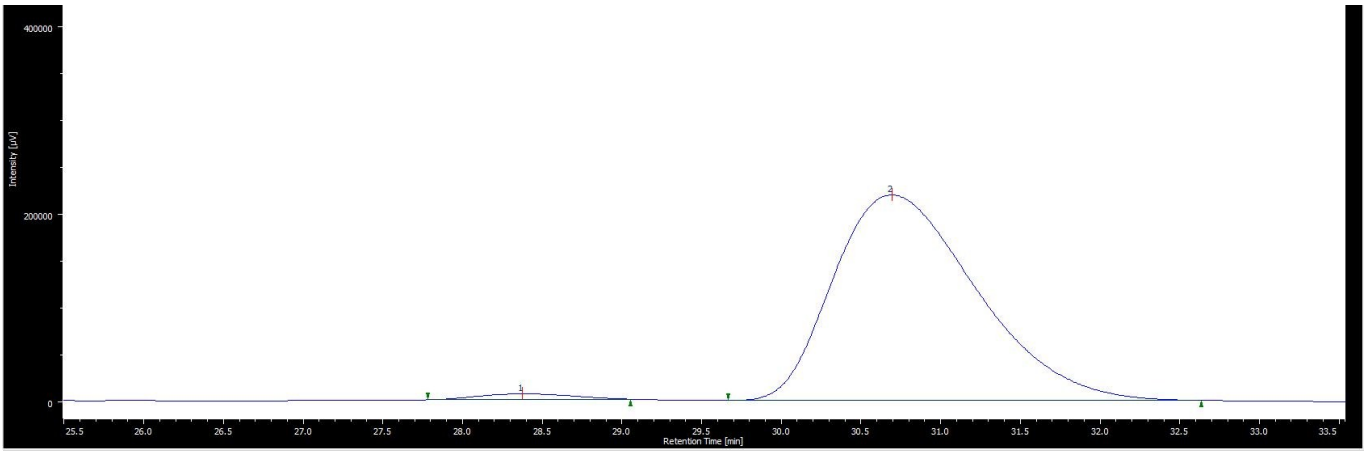


9

racemic-**9**



(*R*)-**9**



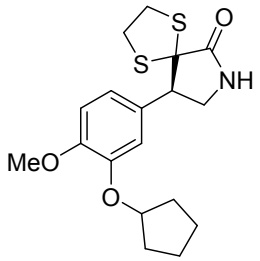
racemic-**9**

Peak	tR (min)	Area (%)
1	26.9	50.1
2	29.2	49.9

(*R*)-**9**

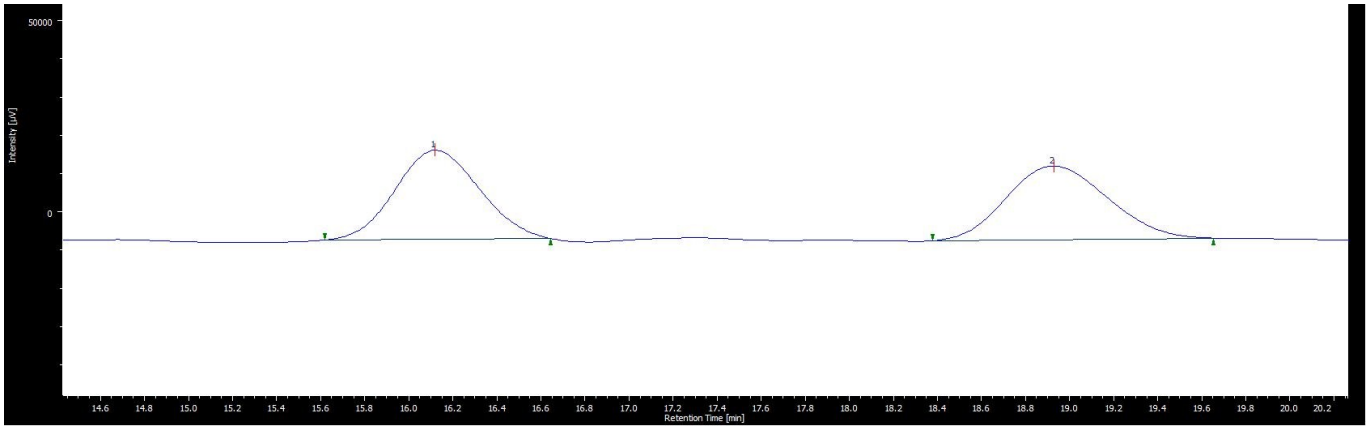
Peak	tR (min)	Area (%)
1	28.4	1.7
2	30.7	98.3

(9*R*)-1,4-Dithia-9-[3-(cyclopentyloxy)-4-methoxyphenyl]-7-azaspiro[4.4]nonane (10)

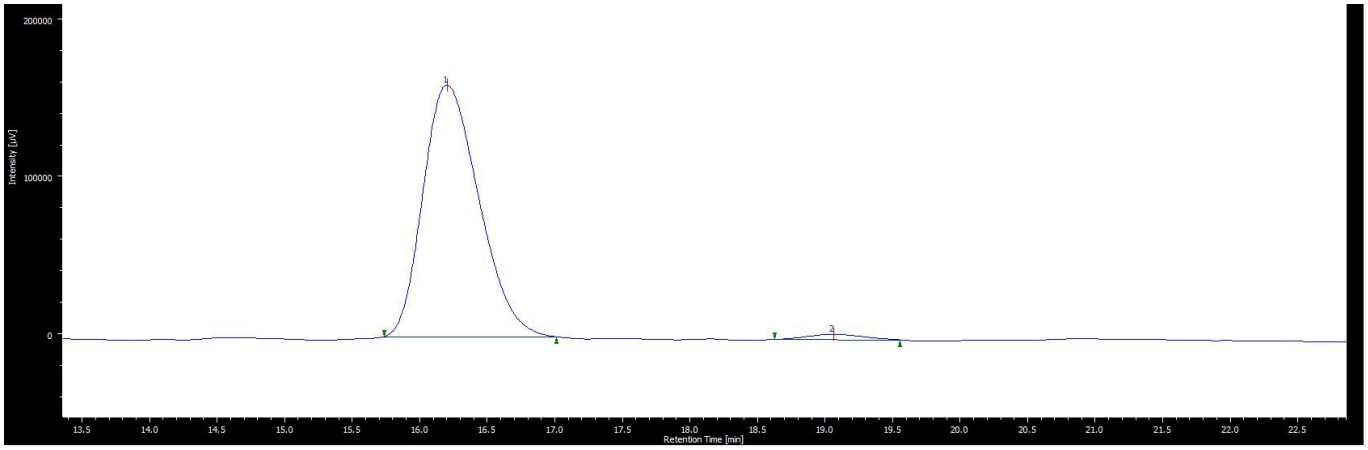


10

racemic-**10**



(*R*)-**10**



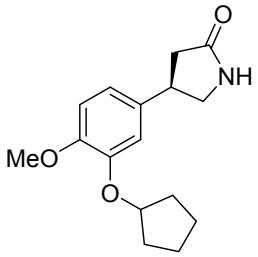
racemic-**10**

Peak	tR (min)	Area (%)
1	16.1	50.2
2	18.9	49.8

(*R*)-**10**

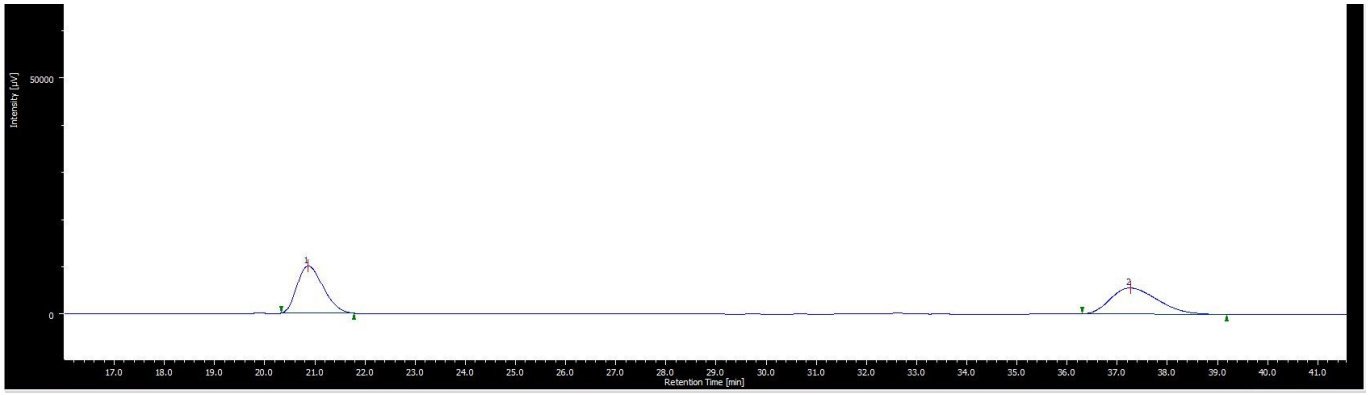
Peak	tR (min)	Area (%)
1	16.2	97.9
2	19.1	2.1

(4*R*)-4-[3-(Cyclopentyloxy)-4-methoxyphenyl]-2-pyrrolidinone (11)

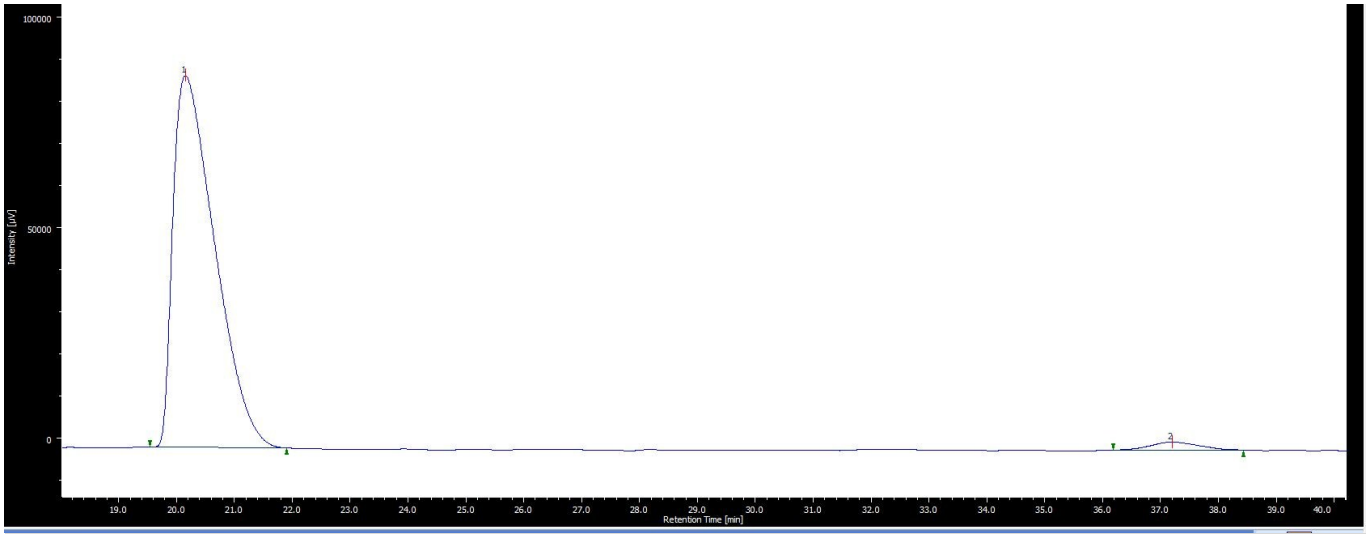


11

racemic-**11**



(*R*)-**11**



racemic-**11**

Peak	tR (min)	Area (%)
1	20.9	50.0
2	37.3	50.0

(*R*)-**11**

Peak	tR (min)	Area (%)
1	20.2	97.6
2	37.2	2.4

MO Calculations:

The Cartesian Coordination of **4f** and **2a** using Gaussian 16 B3LYP/6-31G*, LANL2DZ(Pd) was shown in Table S2.

Table S2

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-0.041523	-0.492089	-0.002411
2	7	0	0.100939	1.583189	0.229805
3	8	0	-5.563823	-3.087775	-1.949662
4	7	0	-2.070167	-0.851463	-0.392259
5	7	0	-3.718500	-2.318068	-0.890061
6	6	0	-3.375036	1.223483	-1.114958
7	6	0	-0.086409	-5.188584	-0.496156
8	6	0	-3.108952	1.228741	-2.503308
9	6	0	-0.066492	-2.433801	-0.179439
10	6	0	-4.352232	-3.146592	-1.836906
11	6	0	-3.294707	-0.039184	-0.265632
12	6	0	-2.361359	-2.099332	-0.658991
13	6	0	-1.267175	-3.075181	-0.529280
14	6	0	-6.792691	-0.755723	0.388595
15	6	0	-5.467900	-1.206308	0.616443
16	6	0	-3.797774	2.418973	-0.486517
17	6	0	-5.126263	-1.726202	1.887108
18	6	0	-7.729731	-0.827255	1.421853
19	6	0	-3.944525	3.579660	-1.252810
20	6	0	-6.104580	-1.780981	2.887089
21	6	0	-4.461554	-1.065977	-0.516470
22	6	0	-7.410927	-1.334007	2.683195
23	6	0	-3.254488	2.421836	-3.221948
24	6	0	-3.665273	3.611268	-2.619741
25	6	0	-1.283206	-4.476374	-0.623036
26	8	0	5.353059	-3.566195	1.561269
27	7	0	1.992118	-0.972292	0.302604
28	7	0	3.579851	-2.555223	0.588955
29	6	0	3.301483	0.879152	1.487720
30	6	0	3.849069	2.140154	1.147373

31	6	0	4.147660	-3.571001	1.381037
32	6	0	3.237556	-0.186326	0.397470
33	6	0	2.239946	-2.255223	0.345155
34	6	0	1.124670	-3.154928	0.010425
35	6	0	5.136826	-1.486408	-1.958094
36	6	0	5.429115	-1.238152	-0.596123
37	6	0	2.897381	0.639634	2.821590
38	6	0	6.753623	-0.898787	-0.224880
39	6	0	6.164108	-1.387517	-2.905742
40	6	0	3.018955	1.663102	3.765022
41	6	0	7.741386	-0.806764	-1.210904
42	6	0	4.368755	-1.280285	0.496750
43	6	0	7.471349	-1.043688	-2.559629
44	6	0	3.958194	3.127881	2.129333
45	6	0	3.537272	2.920613	3.444238
46	6	0	1.120588	-4.539894	-0.214169
47	1	0	-0.091696	-6.265832	-0.623636
48	1	0	-3.323377	0.264804	0.781681
49	1	0	-5.830617	-2.192107	3.857836
50	1	0	-5.001369	-0.772682	-1.411673
51	1	0	-3.034804	2.418201	-4.285716
52	1	0	-2.202881	-5.020627	-0.801863
53	1	0	5.927734	-1.583151	-3.949421
54	1	0	2.698997	1.467254	4.788288
55	1	0	2.035077	-5.120338	-0.171193
56	1	0	3.327288	0.324690	-0.561700
57	1	0	4.869900	-1.179851	1.454444
58	6	0	0.023703	2.708017	-0.151727
59	6	0	-0.077739	3.983882	-0.623645
60	1	0	4.382937	4.091565	1.856512
61	1	0	8.752501	-0.542760	-0.914360
62	1	0	-4.262083	4.493229	-0.751748
63	1	0	-8.743755	-0.482899	1.230912
64	16	0	1.306179	4.794288	-1.386528
65	16	0	-1.130340	5.174992	0.145496
66	6	0	0.324018	6.014094	0.946946
67	1	0	0.006603	6.999474	1.305759
68	1	0	0.634161	5.409531	1.805386
69	6	0	1.474604	6.128973	-0.070541

70	1	0	1.450078	7.088600	-0.591292
71	1	0	2.437804	6.025957	0.439291
72	6	0	-3.538365	-4.022393	-2.773292
73	1	0	-2.482725	-3.759210	-2.844283
74	1	0	-3.628756	-5.074498	-2.485058
75	1	0	-4.002935	-3.923696	-3.758512
76	6	0	3.275953	-4.603335	2.072219
77	1	0	2.225777	-4.328965	2.158429
78	1	0	3.352133	-5.568973	1.557077
79	1	0	3.703366	-4.742280	3.067703
80	6	0	-4.087859	2.503962	1.000617
81	1	0	-3.184464	2.315922	1.596780
82	1	0	-4.434450	3.506189	1.260311
83	1	0	-4.857696	1.793028	1.324290
84	6	0	-2.664966	0.002618	-3.274083
85	1	0	-1.674904	-0.345412	-2.958739
86	1	0	-3.361818	-0.836785	-3.165932
87	1	0	-2.609472	0.232362	-4.342839
88	6	0	-3.761864	4.898002	-3.401496
89	1	0	-4.643329	5.480638	-3.104302
90	1	0	-2.880822	5.524646	-3.214152
91	1	0	-3.820566	4.710738	-4.476062
92	6	0	-7.247306	-0.207909	-0.949104
93	1	0	-6.675717	0.677419	-1.256714
94	1	0	-7.149522	-0.963456	-1.737430
95	1	0	-8.300325	0.082614	-0.894467
96	6	0	-8.435657	-1.375916	3.791034
97	1	0	-8.551037	-0.393150	4.262748
98	1	0	-9.420272	-1.672650	3.414715
99	1	0	-8.147916	-2.084818	4.576485
100	6	0	-3.750196	-2.259537	2.232046
101	1	0	-3.506047	-3.162700	1.658059
102	1	0	-2.947828	-1.537819	2.047808
103	1	0	-3.705301	-2.528491	3.291322
104	6	0	2.328087	-0.681997	3.298122
105	1	0	1.346273	-0.884893	2.858028
106	1	0	2.979898	-1.530579	3.058762
107	1	0	2.208885	-0.669252	4.385448
108	6	0	4.321596	2.475207	-0.254376

109	1	0	3.478391	2.558404	-0.950158
110	1	0	4.823453	3.447718	-0.255760
111	1	0	5.029100	1.740508	-0.650850
112	6	0	3.623443	4.019131	4.476633
113	1	0	4.504443	4.649613	4.319753
114	1	0	2.742010	4.672850	4.432652
115	1	0	3.673974	3.611258	5.493832
116	6	0	3.763561	-1.883062	-2.461868
117	1	0	3.459459	-2.866332	-2.084834
118	1	0	2.978945	-1.169872	-2.181927
119	1	0	3.771152	-1.939226	-3.554298
120	6	0	7.157107	-0.638977	1.213952
121	1	0	6.991536	-1.525936	1.833905
122	1	0	8.220630	-0.386012	1.268281
123	1	0	6.601268	0.193767	1.661008
124	6	0	8.550711	-0.907944	-3.608996
125	1	0	8.328826	-1.510129	-4.493571
126	1	0	8.647797	0.136706	-3.941620
127	1	0	9.526187	-1.212964	-3.220779
