Catalytic conversion of lactide to optically pure heterocycles

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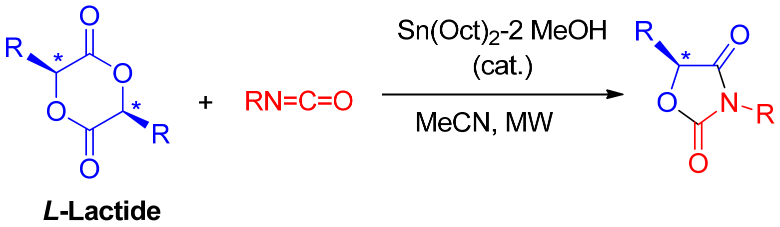


Supporting Information

General

Analysis. IR spectra were recorded as thin film on a Nocolet Magna-750 spectrometer. All ^{1}H and ^{13}C NMR spectra were recorded with a JEOL JMTC-400/54/SS (400 and 100 MHz, respectively) in deuteriochloroform ($CDCl_3$) containing 0.03% (w/v) of tetramethylsilane as internal standard. Mass spectra were recorded on a JEOL JMS-DS-303 spectrometer. Specific rotation was measured with DIP-181 made by JASCO in $CHCl_3$. PLC was performed TOSOH CCPS-UV8020 system using Daicel CHIRALPAK IA (0.46 cmD x 25cmL) detected at 254 nm eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50. Flash column chromatography was performed by Yamazen YFLC-AI-580 using Hi-Flash Silica gel 2L Hi-Flash Column 20-3-mL/min eluted by Hexane/EtOAc with gradation mode changing from 9/1 to 3/7. Purification of products by recycle GPC system was performed by Japan Analytical Industry Co., Ltd. LC-908 eluted by $CHCl_3$.

Materials. Di-*n*-butyltin dimethoxide [$^{n}Bu_2Sn(OMe)_2$] was prepared according to the reported method using $^{n}Bu_2SnO$ and dimethyl carbonate (A. G. Davies, D. C. Kleinschmidt, P. R. Palan, S. C. Vasishtha, *J. Chem. Soc. (C)* **1971**, 3972-3975.). $Sn(OCOC_7H_{17})_2$ was purchased from Nakarai Tesque Co., Ltd. Substrates such as methyl glycolate **1a** (Tokyo Kasei), glycolide **1b** (Sigma), lactide **1c** (Aldrich) are commercially available. Phenyl lactide **1d** was prepared as an optically pure form by dimerization of phenyl lactic acid (Bacem Co., Ltd.) according to the known method (T. L. Simmons, G. L. Baker, *Biomacromolecules* **2001**, *2*, 658-663.). All reactions were carried out under dry nitrogen.

Representative procedure

Representative procedure for the preparation of 2-oxazolidinone under microwave irradiation.

Microwave assisted reactions were carried out using a focused microwave unit (CEM Discover microwave). The instrument consists of a continuous focused microwave power delivery system with operator selectable power output from 0-300 W. In all experiments, a constant power was applied to ensure reproducibility. Reactions were performed in glass vessels (10 mL) sealed with a septum. Pressure experiment is accomplished by a non-invasive sensor integrated into the cavity lid, which measures the deformation of the Teflon seal of the vessels (maximal 20 bar). Temperature controlled is achieved by means of an IR sensor and the indicated temperature corresponds to the maximal temperature reached during each experiment. The specified reaction time corresponds to the total irradiation time. Efficient cooling is accomplished by means of a pressurized air during the entire experiment.

Reaction of methyl glycolate (1a) with isocyanate catalyzed by $Bu_2Sn(OMe)_2$ (Table 1, entry 5).

A 5 mL of vial was dried by flame under reduced pressure. After nitrogen was filled, $Bu_2Sn(OMe)_2$ (0.0295 g, 0.1 mmol), MeCN (1.0 mL), methyl glycolate (**1a**) (0.09g, 1.0 mmol) and butyl isocyanate (0.099g, 1.0 mmol) were added. The mixture was stirred at rt for 3 h. After the reaction, the mixture was quenched by H_2O (0.5 mL), and the layers were quickly separated. The aqueous phase was further extracted with ether, and the combined extracts were dried over sodium sulfate and concentrated. The yield and product ratio **2a**/**2a'**was determined by ^{1}H NMR. The crude product was then purified by flash column chromatography eluted by Hexane/EtOAc with gradation mode changing from 9/1 to 3/7. The desired product was obtained at Hexane/EtOAc=7:3.

Reaction of glycolide (1b) with isocyanate catalyzed by $Bu_2Sn(OMe)_2$ (Table 2, entry 4).

A 5 mL of vial was dried by flame under reduced pressure. After nitrogen was filled, $Bu_2Sn(OMe)_2$ (0.0295 g, 0.1 mmol), MeCN (1.0 mL), glycolide (**1b**) (0.058g, 0.5 mmol) and the isocyanate (1.0 mmol) were added. The vial was sealed with a septum and was set in microwave reactor. The mixture was stirred under microwave irradiation at 100W for 20 min. The reaction temperature was measured by an IR sensor (120 ^{o}C). After the reaction, the mixture was quenched by H_2O (0.5 mL), and the layers were quickly separated. The aqueous phase was further extracted with ether, and the combined extracts were dried over sodium sulfate and concentrated. The yield was determined by ^{1}H NMR. The crude product was then purified by flash column chromatography eluted by Hexane/EtOAc with gradation mode changing from 9/1 to 3/7. The desired product was obtained at Hexane/EtOAc=7:3.

Reaction of lactide (1c) with isocyanate catalyzed by $Sn(OCOC_7H_{17})_2$ system (Table 4).

A 5 mL of vial was dried by flame under reduced pressure. After nitrogen was filled, Tin catalyst $Sn(OCOC_7H_{17})_2$ (0.0405 g, 0.1 mmol), MeOH (0.0064 g, 0.2 mmol), MeCN (1.0 mL), lactide (**1c**) (0.072g, 0.5 mmol) and isocyanate (1.0 mmol) were added. The vial was sealed with a septum and was set in microwave reactor. The mixture was stirred under microwave irradiation at 150W for 30 min. The reaction temperature was measured by an IR sensor (155-160 ^{o}C). After the reaction, the mixture was quenched by H_2O (0.5 mL), and the layers were quickly separated. The aqueous phase was further extracted with ether, and the combined extracts were dried over sodium sulfate and concentrated. The yield was determined by ^{1}H NMR. The crude product was then purified by flash column chromatography eluted by Hexane/EtOAc with gradation mode changing from 9/1 to 3/7. The desired product was obtained at Hexane/EtOAc=7:3.

MW Profiles

Table 2, entry 1

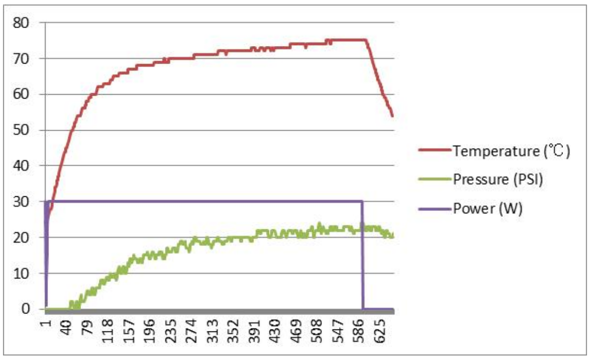


Table 2, entry 2

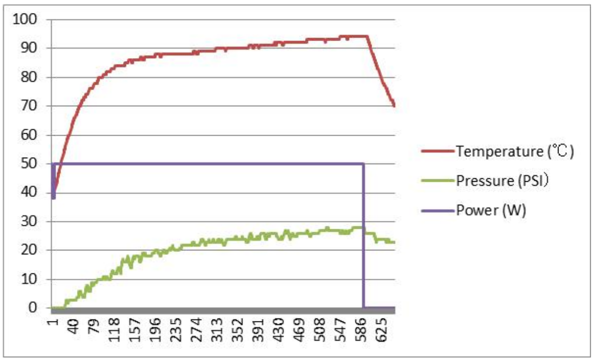


Table 2, entry 3

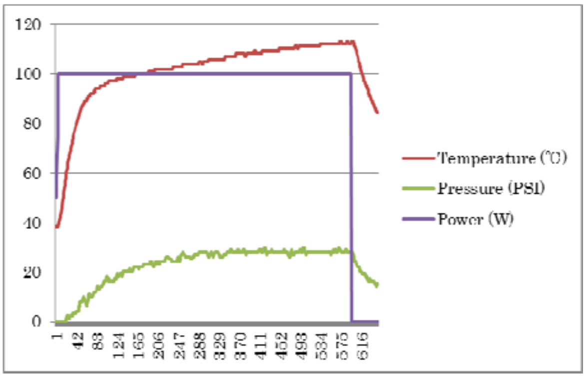


Table 2, entry 4

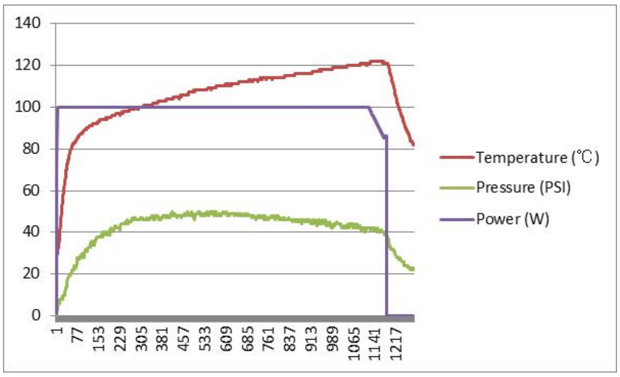


Table 2, entry 5

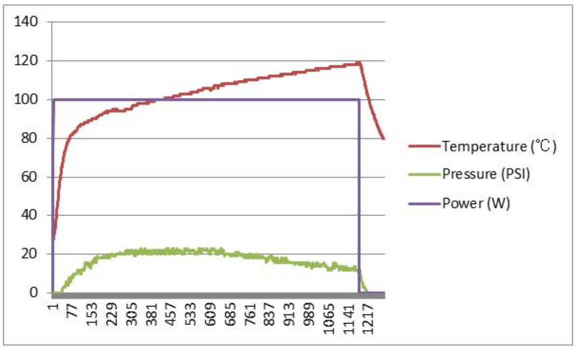
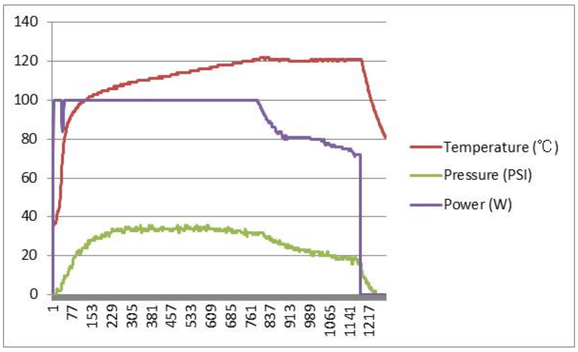


Table 2, entry 6



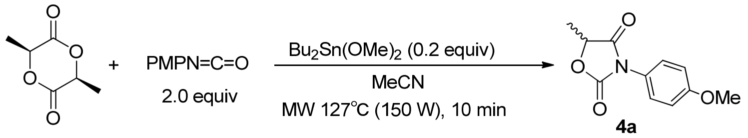
Other profiles corresponding to give novel products, **2a-2d**, **3a-3d**, **4a-4f** are listed after spectral charts.

Enantiomeric purity (Scheme 4)

Enantio-excess value of product **4a** was measured by HPLC. (TOSOH CCPS-UV8020 system using Daicel CHIRALPAK IA (0.46 cmD x 25cmL) detected at 254 nm eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50).

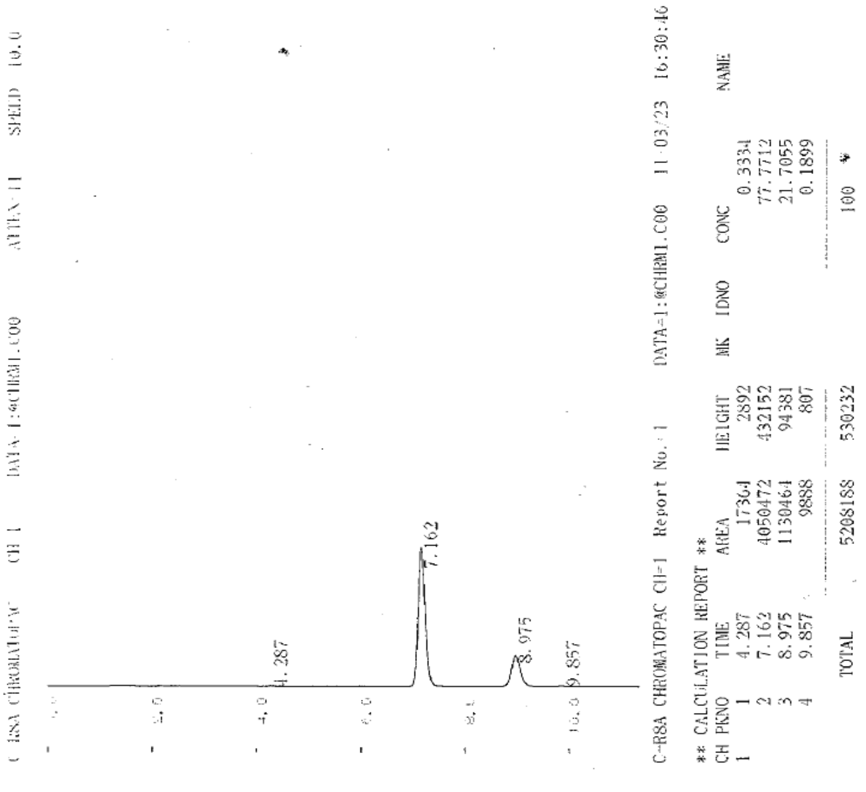
Products obtained using $Sn(OCOC_7H_{17})_2$ catalyst indicated high *ee* values which HPLC charts are shown in this SI. Other HPLC corresponding to novel products, **4a-4f**, with high *ee* are listed after spectral charts.

On the other hand, product obtained using $Bu_2Sn(OMe)_2$ catalyst (Scheme 4, eq. 1) indicated low *ee*. value as shown in the following chart.



L-lactide **1c**

4a
99% 56%ee



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** CALCULATION REPORT **
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       2   7.162    4050472     432152                  77.7712
       3   8.975    1130464      94381                  21.7055
       4   9.857       9888        807                   0.1899
           ----------------------------------------------------
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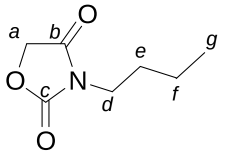
Analytical data for Products

3-Butyloxazolidine-2,4-dione (2a)



Colorless liquid.

Rf= 0.52 (in hexane : ethyl acetate = 7 : 3).

IR (neat) 1743 (C=O) cm^{-1}, 1736 (C=O) cm^{-1}.

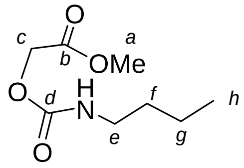
^{1}H NMR (CDCl$_3$, 400 MHz) δ4.70 (s, 2H, *a*), 3.56 (t, *J*= 7.3 Hz, 2H, *d*), 1.64 (m, 2H, *e*), 1.36 (m, 2H, *f*), 0.95 (t, *J*= 7.3 Hz, 3H, *g*).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 170.4 (*b*), 155.9 (*c*), 67.7 (*a*), 39.8 (*d*), 29.4 (*e*), 19.7 (*f*), 13.4 (*g*)

MS (EI, 70 eV) m/z 157 (M$^+$, 6), 115 (35), 102 (100).

HRMS calcd for $C_7H_{11}NO_3$: 157.0739, found: m/z 157.0744 (EI, (M$^+$), +0.5 mmu).

Butylcarbamoyloxy-acetic acid methyl ester (2a')



Pale yellow liquid.

Rf= 0.83 (in hexane : ethyl acetate = 7 : 3).

IR (neat) 1731 (C=O) cm^{-1}, 3350 (NH) cm^{-1}.

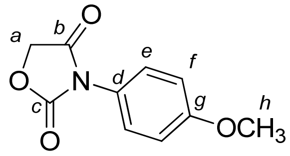
^{1}H NMR (CDCl$_3$, 400 MHz) δ4.60 (s, 2H, *c*), 3.77 (s, 3H, *a*), 3.19-3.24 (m, 2H, *e*), 1.47-1.52 (m, 2H, *f*), 1.31-1.39 (m, 2H, *g*), 0.93 (t, *J*= 7.2 Hz, 3H, *h*).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 169.3 (*b*), 155.4 (*d*), 60.8 (*c*), 52.0 (*a*), 40.8 (*e*), 31.7 (*f*), 20.0 (*g*), 13.6 (*h*)

MS (EI, 70 eV) m/z 157 (M$^+$, 6), 115 (35), 102 (100).

HRMS calcd for $C_8H_{15}NO_4$: 189.1001, found: m/z 189.1001 (EI, (M$^+$), +0.0 mmu).

3-(4-Methoxyphenyl)-oxazolidine-2,4-dione (2b)



Colorless solid.

mp. 120-121 °C.

IR (KBr) 1740 (C=O) cm^{-1}, 1736 (C=O) cm^{-1}.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.33 (d, J = 8.9 Hz, 2H, *e*), 7.01 (d, J = 8.9 Hz, 2H, *f*), 4.87 (s, 2H, *a*), 3.84 (s, 3H, *h*).

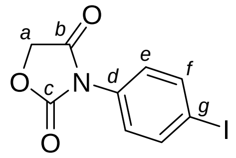
^{13}C NMR (CDCl$_3$, 100 MHz) δ 169.5 (*b*), 159.8 (*g*), 154.8 (*c*), 127.0 (*e*), 123.0 (*d*), 114.6 (*f*), 67.7 (*a*), 55.5 (*h*).

MS (EI, 70 eV) m/z 207 (M$^+$, 100), 149 (42), 135 (66), 120 (55).

HRMS calcd for $C_{10}H_9NO_4$: 207.0532, found: m/z 207.0528 (EI, (M$^+$), -0.4 mmu).

Anal. Calcd for $C_{10}H_9NO_4$: H, 4.38; C, 57.97; N, 6.76, found: H, 4.24; C, 57.92; N, 6.61.

3-(4-Iodo-phenyl)-oxazolidine-2,4-dione (2c)



Pale yellow solid.

mp. 166 °C.

IR (KBr) 1750 (C=O) cm^{-1}, 1748 (C=O) cm^{-1}.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.84 (d, J = 8.8Hz, 2H, *e*), 7.22 (d, J= 8.8 Hz, 2H, *f*), 4.87 (s, 2H, *a*).

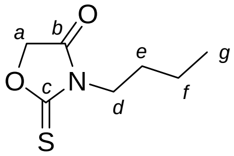
^{13}C NMR (CDCl$_3$, 100 MHz) δ 168.7 (*b*), 153.6 (*c*), 138.6 (*f*), 130.3 (*d*), 127.0 (*e*), 94.4 (*g*), 67.7 (*a*)

MS (EI, 70 eV) m/z 303 (M$^+$, 100), 245 (25), 231 (31), 90 (12).

HRMS calcd for $C_9H_6INO_3$: 303.9393, found: m/z 303.9391 (EI, (M$^+$), -0.2 mmu).

Anal. Calcd for $C_9H_6INO_3$: H, 2.00; C, 35.67; N, 4.62, found: H, 2.08; C, 35.82; N, 4.62.

3-Butyl-2-thioxo-oxazolidin-4-one (3a)



Pale yellow liquid.

Rf = 0.67 (in hexane:ethyl acetate= 7:3).

IR (neat) 1767 (C=O) cm^{-1}, 1373 (C=S) cm^{-1}.

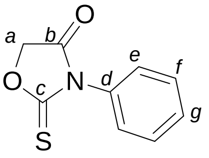
^{1}H NMR (CDCl$_3$, 400 MHz) δ 4.79 (s, 2H, *a*), 3.82 (t, J= 7.5 Hz, 2H, *d*), 1.65-1.72 (m, 2H, *e*), 1.32-1.41 (m, 2H, *f*), 0.96 (t, J= 7.2 Hz, 3H, *g*).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 190.7 (*b*), 171.0 (*c*), 69.64 (*a*), 42.8 (*d*), 20.6 (*e*), 19.8 (*f*), 13.5 (*g*).

MS (EI, 70 eV) m/z 173 (M$^+$, 42), 140 (31), 118 (100).

HRMS calcd for $C_7H_{11}NO_2S$: 173.0510, found: m/z 173.0511 (EI, (M$^+$), +0.1 mmu).

3-Phenyl-2-thioxooxazolidin-4-one (3b)



Pale yellow solid.

mp. 163-164 °C.

IR (KBr) 1771 (C=O) cm^{-1}, 1320 (C=S) cm^{-1}.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.57-7.49 (m, 3H, *f* and *g*), 7.33 (d, J = 7.0 Hz, 2H, *e*), 5.01 (s, 2H, *a*).

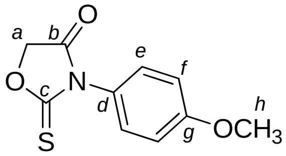
^{13}C NMR (CDCl$_3$, 100 MHz) δ 190.0 (*c*), 170.3 (*b*), 132.0 (*d*), 129.9 (*g*), 129.6 (*f*), 127.5 (*e*), 70.3 (*a*).

MS (EI, 70 eV) m/z 193 (M$^+$, 100), 135 (34), 105 (26), 104 (21), 77 (35).

HRMS calcd for $C_9H_7NO_2S$: 193.0197, found: m/z 193.0205 (EI, (M$^+$), +0.7 mmu).

Anal. Calcd for $C_9H_7NO_2S$: H, 3.65; C, 55.94; N, 7.25, found H, 3.79; C, 56.17; N, 7.18.

3-(4-Methoxy-phenyl)-2-thioxo-oxazolidin-4-one (3c)



Pale yellow solid.

mp. 108 °C.

IR (KBr) 1780 (C=O) cm^{-1}, 1320 (C=S) cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.24 (d, *J*= 8.9 Hz, 2H, *e*), 7.04 (d, *J*= 8.9 Hz, 2H, *f*), 5.00 (s, 2H, *a*), 3.96 (s, 3H, *h*).

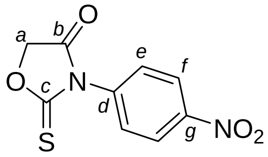
^{13}C NMR ($CDCl_3$, 100 MHz) δ 190.5 (*c*), 170.5 (*b*), 160.4 (*g*), 128.6 (*e*), 124.4 (*d*), 114.8 (*f*), 70.2 (*a*), 55.5 (*h*).

MS (EI, 70 eV) m/z 270 (M^+, 100), 143 (53), 107 (40).

HRMS calcd for $C_{10}H_9NO_3S$: 223.0303, found: m/z 223.0304 (EI, (M^+), +0.1 mmu).

Anal. Calcd for $C_{10}H_9NO_3S$: H, 4.06; C, 53.80; N, 6.27, found: H, 4.08; C, 53.75; N, 6.22.

3-(4-Nitro-phenyl)-2-thioxo-oxazolidin-4-one (3d)



Pale yellow solid.

mp.193 °C.

IR (KBr) 1783 (C=O) cm^{-1}, 1350 (C=S) cm^{-1}.

^{1}H NMR (acetone-*d*, 400 MHz) δ 8.41 (d, *J*= 9.2 Hz, 2H, *f*), 7.62 (d, *J*= 9.2 Hz, 2H, *e*), 5.07 (s, 2H, *a*).

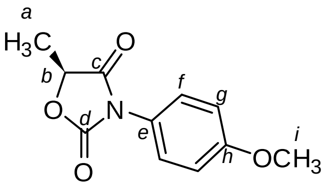
^{13}C NMR (acetone-*d*, 100 MHz) δ 191.5 (*c*), 171.6 (*b*), 148.7 (*g*), 139.5 (*d*), 130.2 (*e*), 125.1 (*f*), 72.1 (*a*).

MS (EI, 70 eV) m/z 238 (M^+, 100).

HRMS calcd for $C_9H_6N2O_4S$: 238.0049, found: m/z 238.0045 (EI, (M^+), -0.4 mmu).

Anal. Calcd for $C_9H_6N_2O_4S$: H, 2.54; C, 45.38; N, 11.76, found: H, 2.84; C, 45.18; N, 11.63.

3-(4-Methoxy-phenyl)-5-methyl-oxazolidine-2,4-dione (4a)



Colorless solid.

mp. 125-126 °C.

IR (KBr) 1771 (C=O) cm^{-1}.

$[\alpha]_D^{13}$= -32.8 (*c* = 0.0101 in $CHCl_3$, 99%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, *J*= 9.2 Hz, 2H, *f*), 7.00 (d, *J*= 9.2 Hz, 2H, *g*), 5.01 (q, *J* = 7.0 Hz, 1H, *b*), 3.84 (s, 3H, *i*), 1.71 (d, *J*= 7.0 Hz, 3H, *a*).

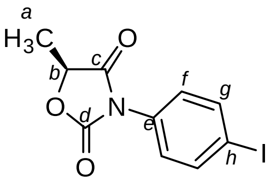
^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6(*c*), 159.6(*h*), 154.1(*d*), 126.9(*f*), 123.2(*e*), 114.5(*g*), 75.9(*b*), 55.5(*i*), 16.7(*a*).

MS (EI, 70 eV) m/z 221 (M^+, 100), 149 (99), 134 (85).

HRMS calcd for $C_{11}H_{11}NO_4$: 221.0688, found: m/z 221.0691 (EI, (M^+), + 0.3 mmu).

Anal. Calcd for $C_{11}H_{11}NO_4$: H, 5.01; C, 59.73; N, 6.33, found: H, 5.01; C, 59.82; N, 6.35.

3-(4-Iodo-phenyl)-5-methyl-oxazolidine-2,4-dione (4b)



White solid.

mp. 182-183 °C.

IR (KBr) 1747 (C=O) cm^{-1}

$[\alpha]_D^{13}$= -26.2 (*c*= 0.00943 in $CHCl_3$, 98%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, *J* = 8.9 Hz, 3H, *g*), 7.22 (d, *J* = 8.9 Hz, 2H, *f*), 5.02 (q, *J* = 7.0 Hz, 1H, *b*), 1.71 (d, *J* = 7.0 Hz, 3H, *a*).

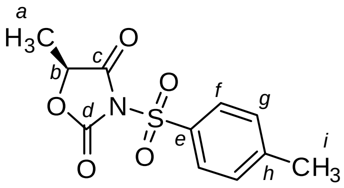
^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9(*c*), 153.4(*d*), 138.4(*g*), 130.6(*e*), 126.9(*f*), 94.2(*h*), 75.9(*b*), 16.7(*a*).

MS (EI, 70 eV) m/z 317 (M^+, 100), 245 (66), 230 (29).

HRMS calcd for $C_{10}H_8INO_3$: 316.9549, found: m/z 316.9550 (EI, (M^+), + 0.1 mmu).

Anal. Calcd for $C_{10}H_8INO_3$: H, 2.54; C, 37.88; N, 4.42, found: H, 2.53; C, 37.92; N, 4.41.

5-Methyl-3-(toluene-4-sulfonyl)-oxazolidine-2,4-dione (4c)



Colorless solid.

mp. 103 °C.

IR (KBr) 1779 (C=O) cm^{-1}, 1738 (C=O) cm^{-1}.

$[\alpha]_D^{13}$= -47.8 (*c*= 0.0105 in $CHCl_3$, 98%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, *J*= 8.4 Hz, 2H, *f*), 7.41 (d, *J*= 8.4 Hz, 2H, *g*), 4.80 (q, *J*= 7.0 Hz, 1H, *b*), 2.48 (s, 3H, *i*), 1.58 (d, *J* = 7.0 Hz, 3H, *a*).

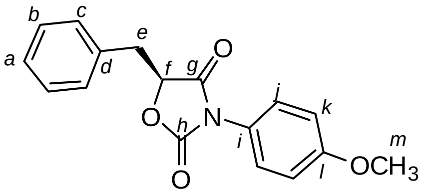
^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5(*c*), 160.4(*d*), 135.5(*h*), 128.6(*g*), 124.4(*e*), 114.8(*f*), 70.2(*b*), 55.5(*i*), 30.9(*a*).

MS (EI, 70 eV) m/z 205 (M$^+$, 46), 177 (36), 155 (32), 118 (48), 91 (100), 70 (69).

HRMS calcd for $C_{11}H_{11}NO_5S$: 269.0358, found: m/z 269.0357 (EI, (M$^+$), - 0.1 mmu).

Anal. Calcd for $C_{11}H_{11}NO_5S$: H, 4.12; C, 49.06; N, 5.20, found: H, 4.01; C, 48.90; N, 4.91.

5-Benzyl-3-(4-methoxy-phenyl)-oxazolidine-2,4-dione (4d)



White solid.

mp. 119 °C.

IR (KBr) 1750 (C=O) cm^{-1}, 1727 (C=O) cm^{-1}.

$[\alpha]_D^{13}$= -151.4 (*c* = 0.0123 in $CHCl_3$, 94%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.35 (m, 5H, Ar), 6.83-6.89 (m, 4H, Ar), 5.21 (t, *J*= 4.3 Hz, 1H, *f*), 3.79 (s, 3H, *m*), 3.42 (dd, *J*= 4.3 and 10.1 Hz, 1H, *e*), 3.29 (dd, *J*= 4.3 and 14.5 Hz, 1H, *e*).

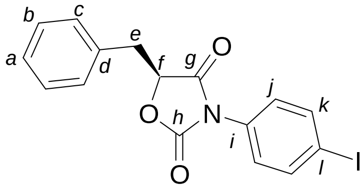
^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2(*g*), 159.8(*l*), 154.1(*h*), 132.5(*d*), 123.0, 128.7, 127.8(*i*), 127.0, 122.8(*a*), 114.5(*k*), 79.3(*f*), 55.4(*m*), 36.7(*e*).

MS (EI, 70 eV) m/z 297 (M$^+$, 100), 149 (87), 134 (84), 91(27).

HRMS calcd for $C_{17}H_{15}NO_4$: 297.1001, found: m/z 297.1000 (EI, (M$^+$), - 0.1 mmu).

Anal. Calcd for $C_{17}H_{15}NO_4$: H, 5.09; C, 68.68; N, 4.71, found: H, 5.11; C, 68.84; N, 4.59.

5-Benzyl-3-(4-iodo-phenyl)-oxazolidine-2,4-dione (4e)



White solid.

mp. 193 °C.

IR (KBr) 1740 (C=O) cm^{-1}, 1720 (C=O) cm^{-1}.

$[\alpha]_D^{13}$= -140.5 (c = 0.00974 in $CHCl_3$, 97%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, *J*= 8.7 Hz, 2H, *k*), 7.15-7.40 (m, 5H, *a*-*c*), 6.73 (d, *J*= 8.7 Hz, 2H, *j*), 5.20 (t, *J*= 4.3 and 14.7 Hz, 1H, *f*), 3.43 (dd, *J*= 4.3 and 14.7 Hz, 1H, *e*), 3.23 (dd, *J*= 4.3 and 14.7 Hz , 1H, *e*).

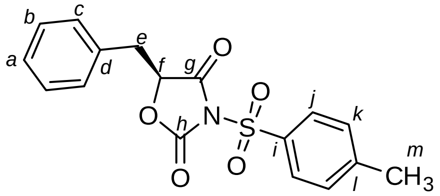
^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6(*g*), 153.3(*h*), 138.4(*k*), 132.3(*d*), 130.1(*i*), 129.9(*b*), 128.8(*c*), 127.9(*a*), 127.2(*j*), 94.4(*l*), 79.3(*f*), 36.7(*e*).

MS (EI, 70 eV) m/z 393 (M^+, 100), 91 (87).

HRMS calcd for $C_{16}H_{12}INO_3$: 392.9862, found: m/z 392.9865 (EI, (M^+), + 0.3 mmu).

Anal. Calcd for $C_{16}H_{12}INO_3$: H, 3.08; C, 48.88; N, 3.56, found H, 3.35; C, 48.89; N, 3.41.

5-Benzyl-3-(toluene-4-sulfonyl)-oxazolidine-2,4-dione (4f)



White solid.

mp. 128 °C.

IR (KBr) 1773 (C=O) cm^{-1}

$[\alpha]_D^{1}$ = -54.0 (c = 0.00974 in $CHCl_3$, 92%*ee*).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06-7.78 (m, 9H, Ph), 5.02 (t, *J*= 4.6 Hz, 1H, *f*), 3.28 (dd, *J*= 4.6 and 14.7 Hz, 1H, *e*), 3.16 (dd, *J*= 4.6 and 14.7 Hz, 1H, *e*), 2.48 (s, 3H, *m*).

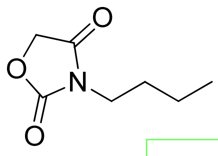
^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1(*g*), 148.5(*h*), 146.8(*l*), 133.4(*d*), 131.7(*i*), 130.0, 129.6, 128.7, 128.5, 127.7(*a*), 78.7(*f*), 36.2(*e*), 21.2(*m*).

MS (EI, 70 eV) m/z 91 (M^+, 100).

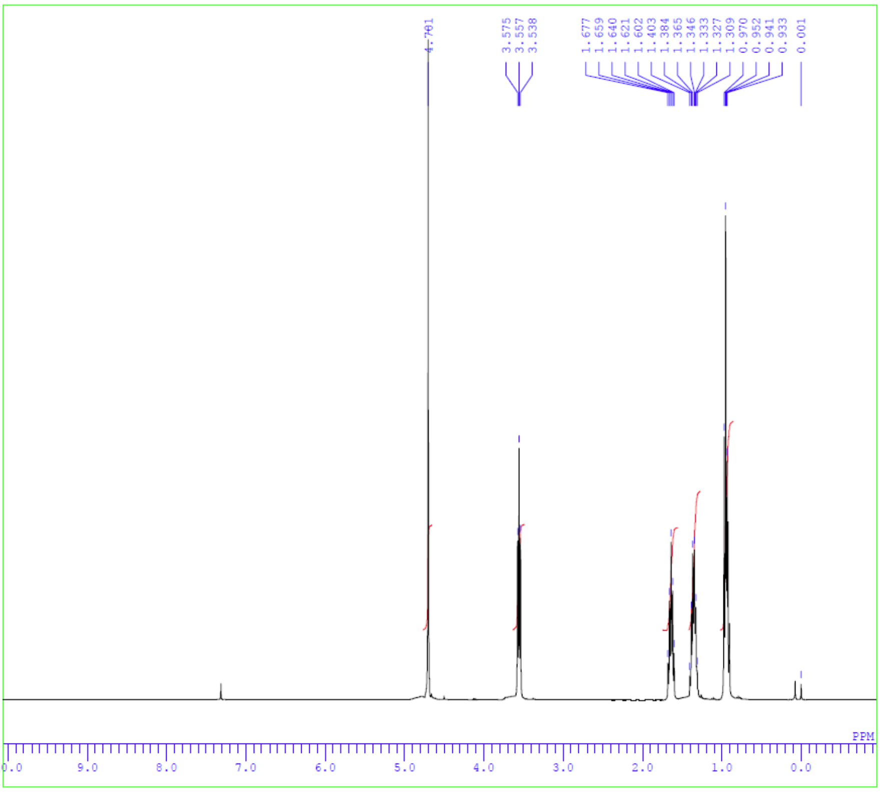
HRMS calcd for $C_{17}H_{15}NO_5S$: 345.0671, found: m/z 345.0671 (EI, (M^+), ± 0.0 mmu).

Anal. Calcd for $C_{17}H_{15}NO_5S$: H, 4.38; C, 59.12; N, 4.06, found: H, 4.70; C, 59.48; N, 3.95.

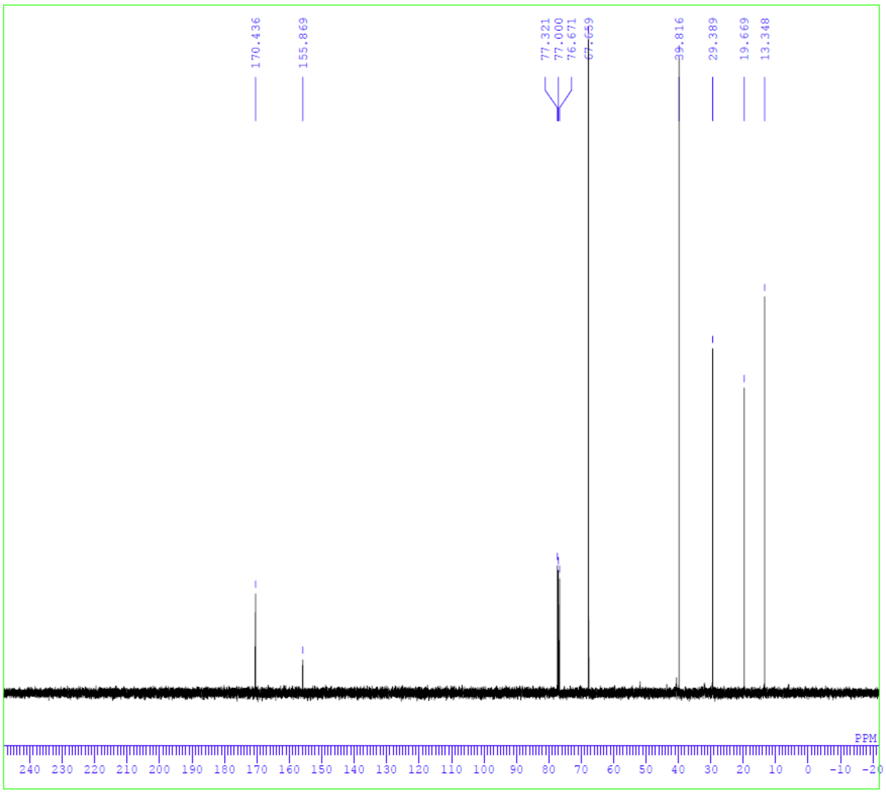
2a



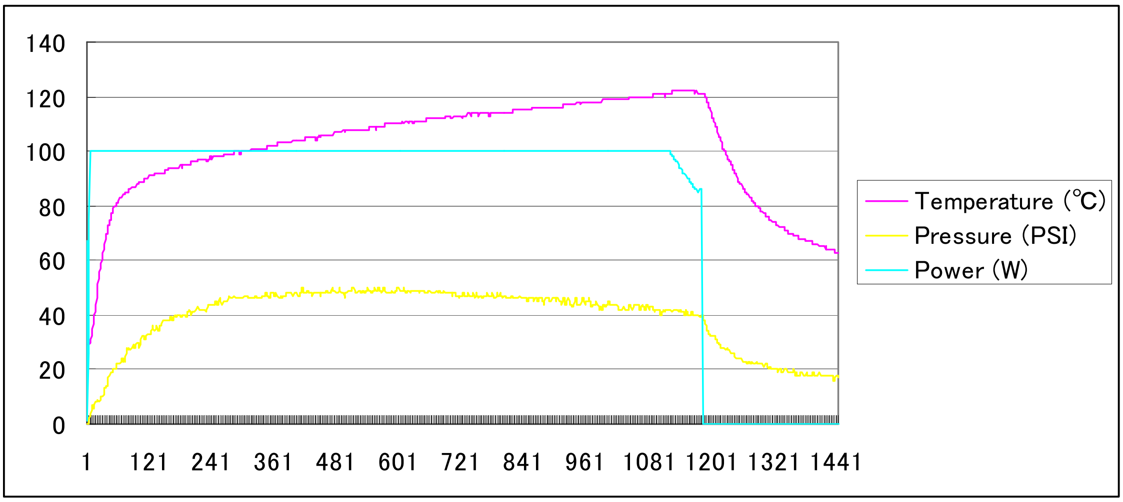
^{1}H NMR



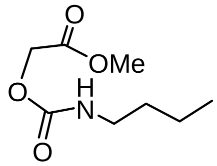
^{13}C NMR



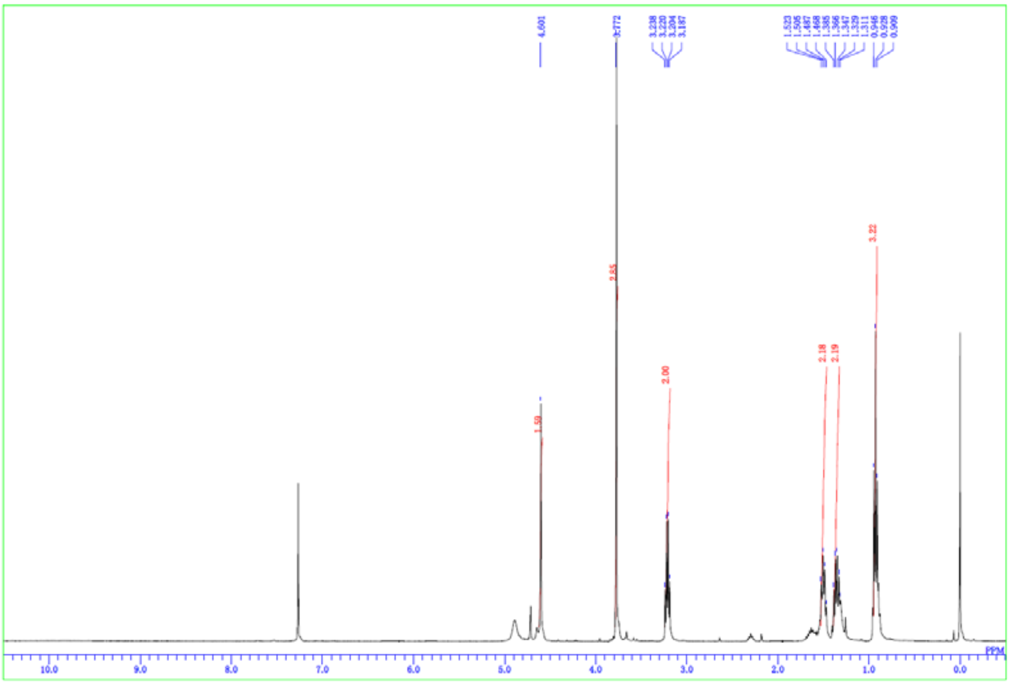
MW Profile (Table 2, entry 4)



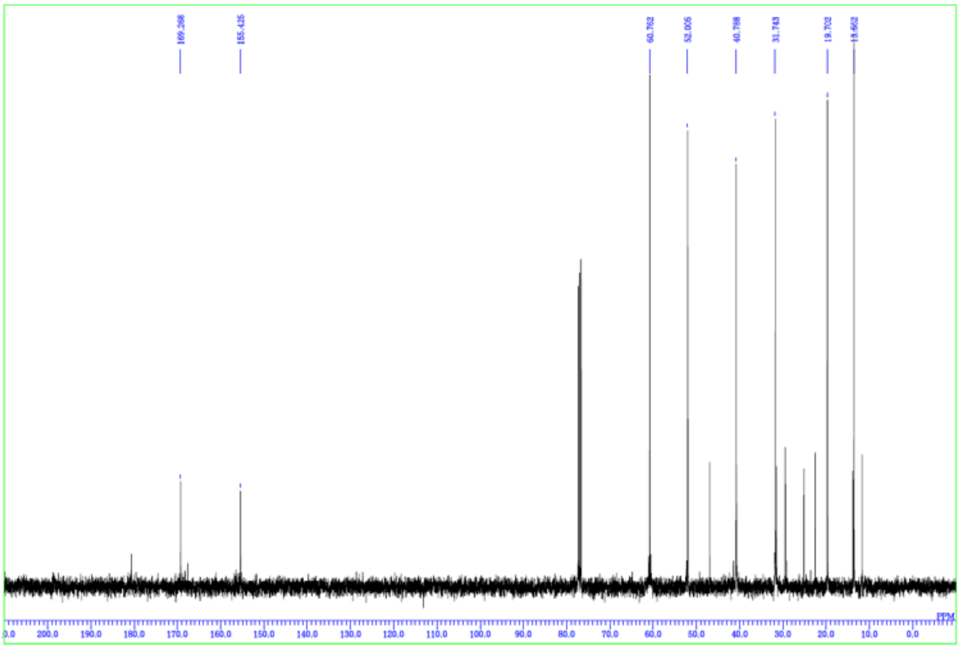
2a'



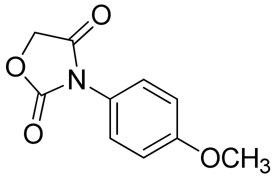
^{1}H-NMR



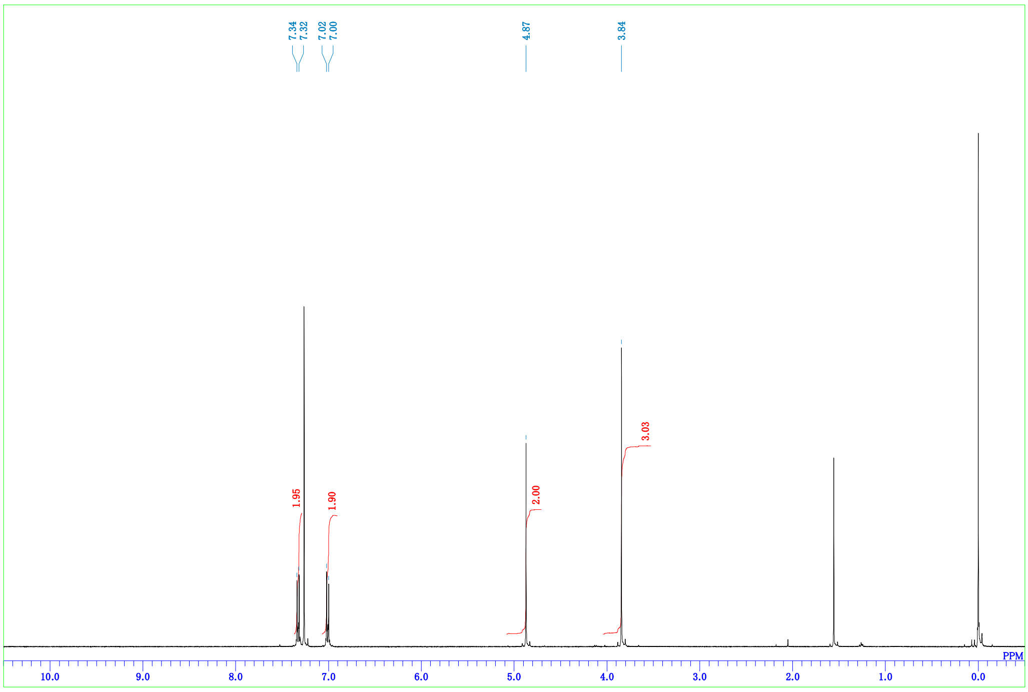
^{13}C-NMR



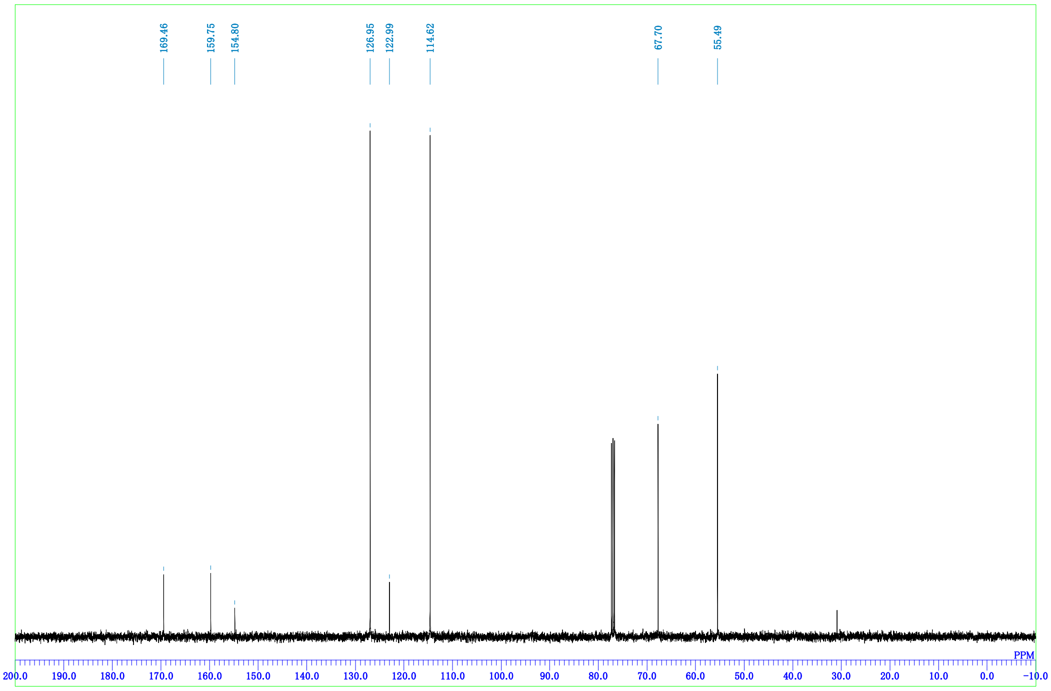
2b



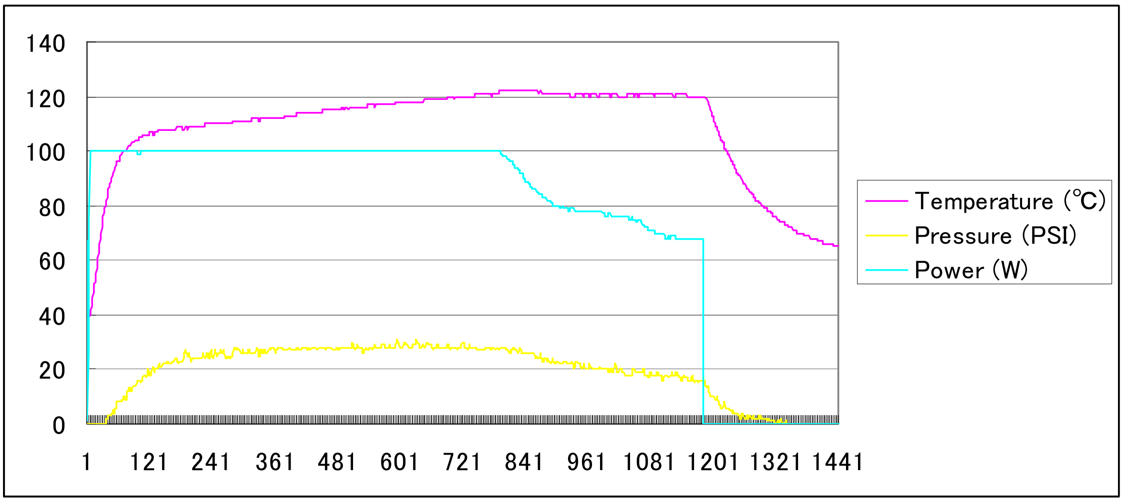
^{1}H NMR



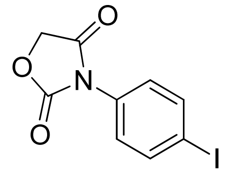
^{13}C NMR



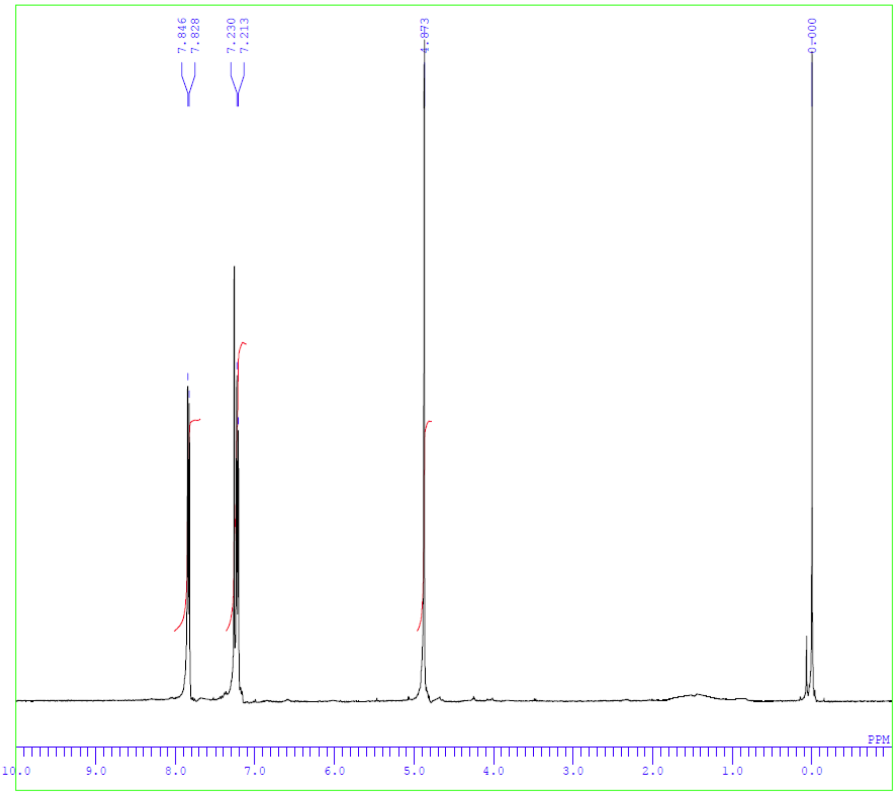
MW profile (Table 2, entry 7)



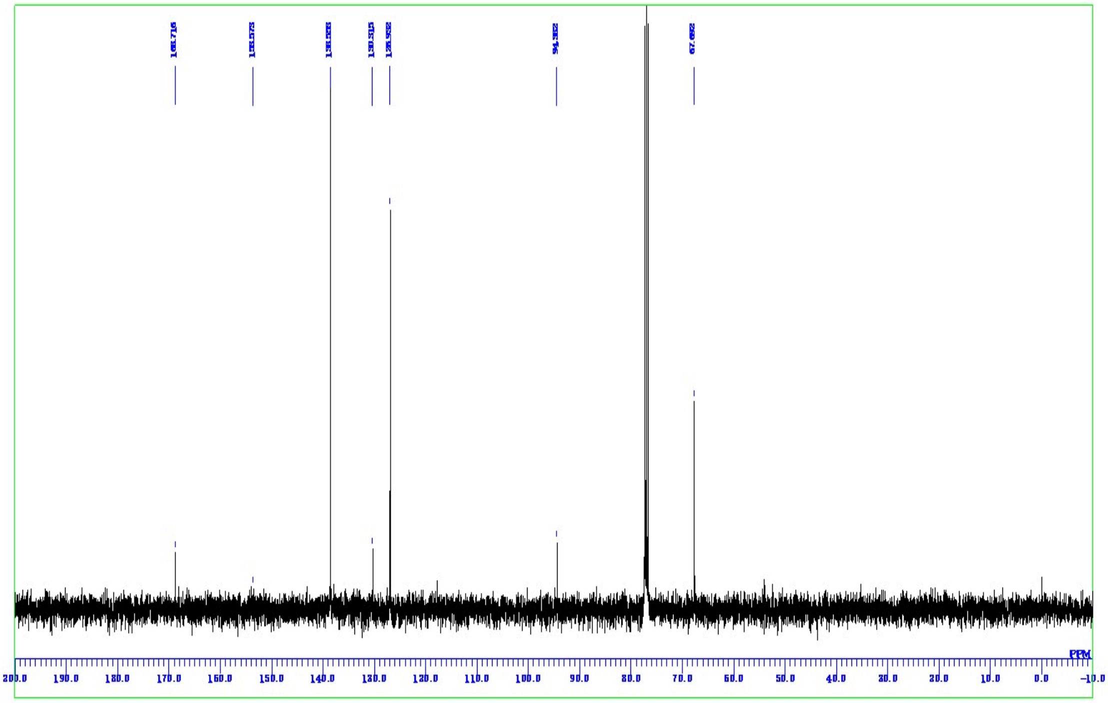
2c



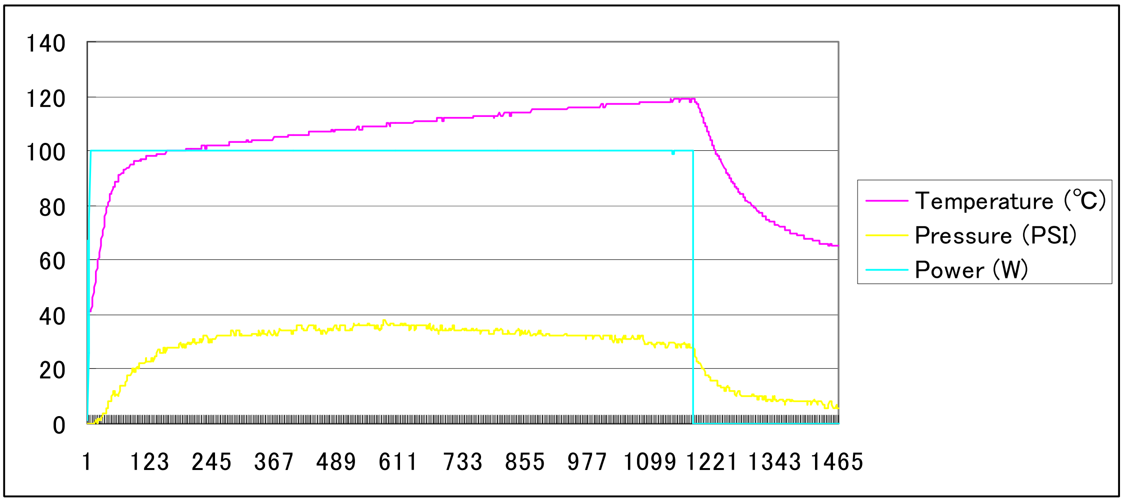
^{1}H NMR



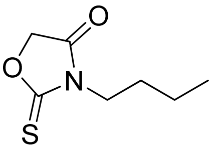
^{13}C NMR



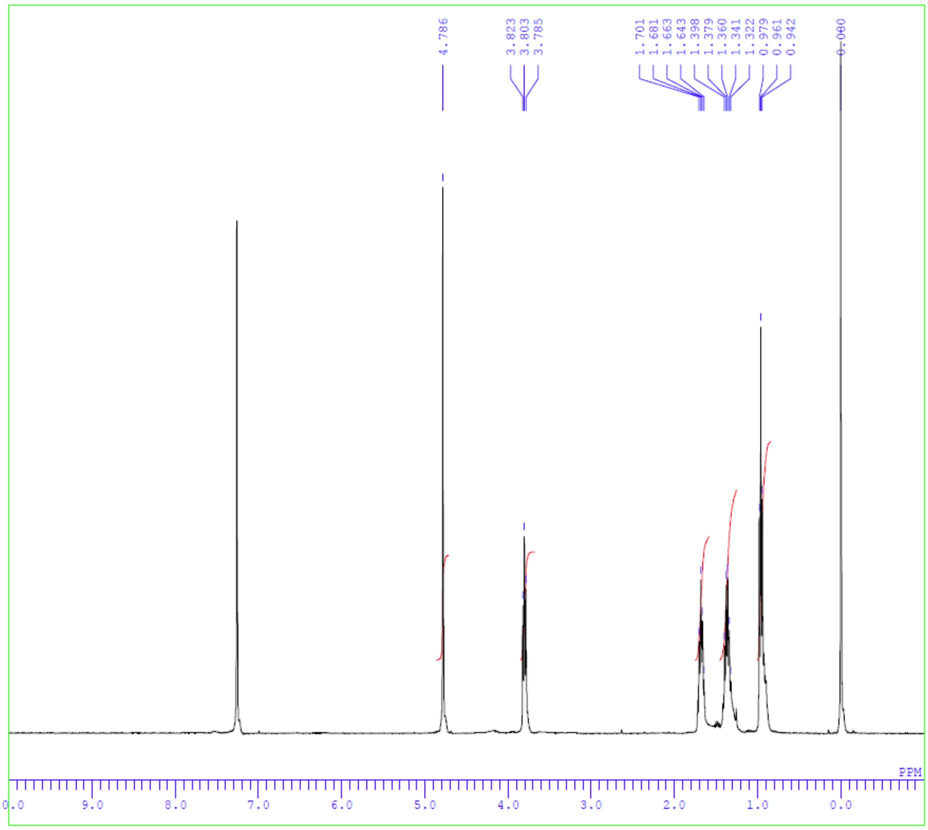
MW Profile (Table 2, entry 9)



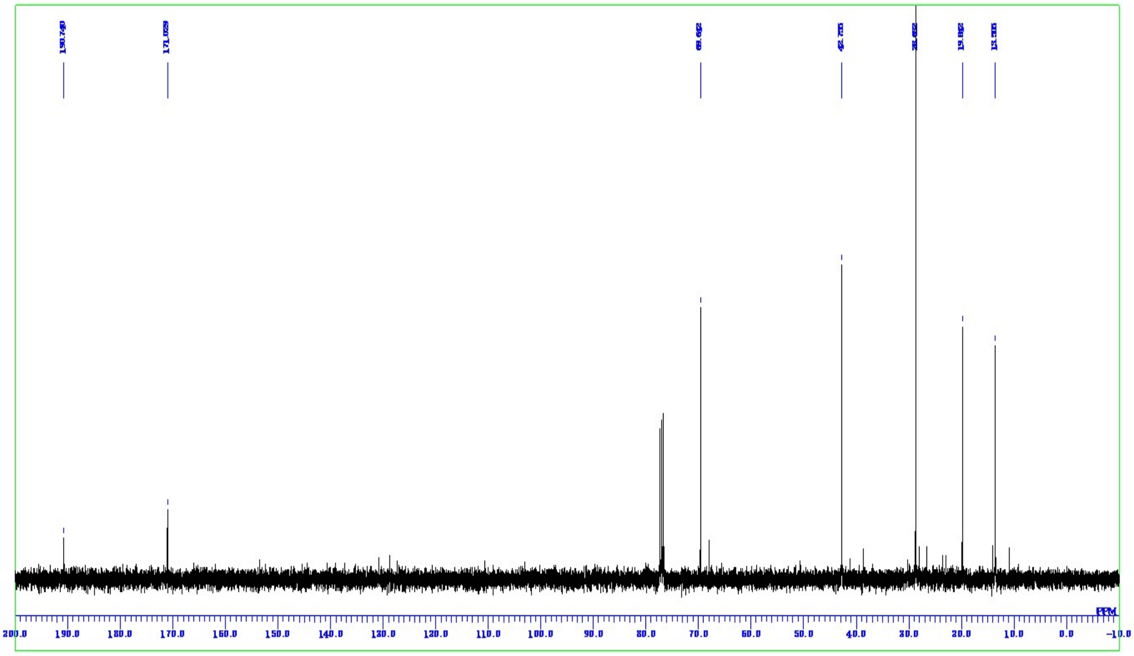
3a



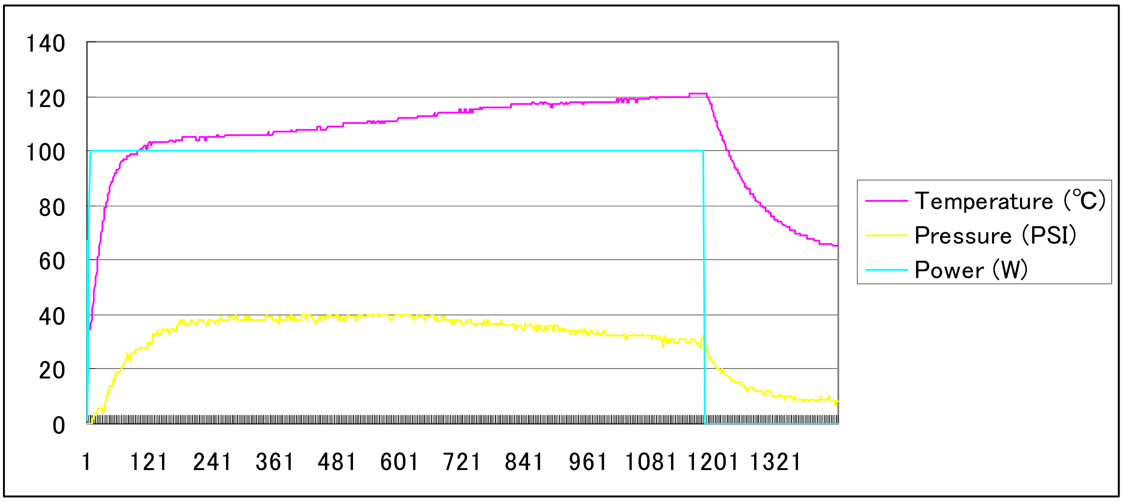
^{1}H NMR



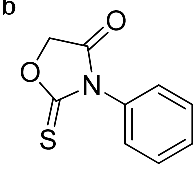
^{13}C NMR



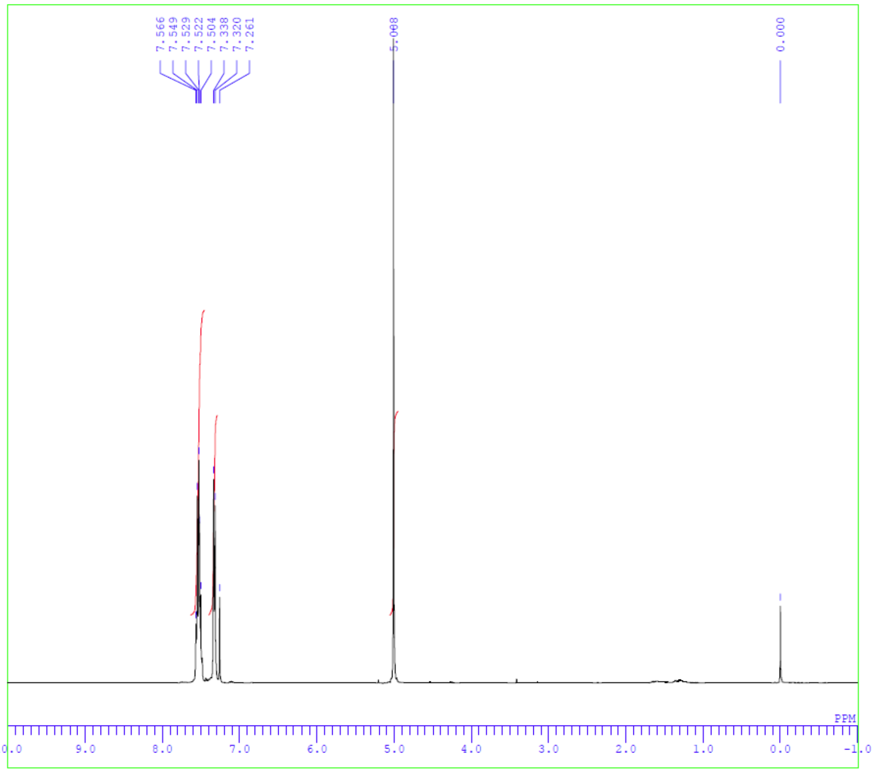
MW Profile (Table 3, entry 1)



3b



^{1}H NMR



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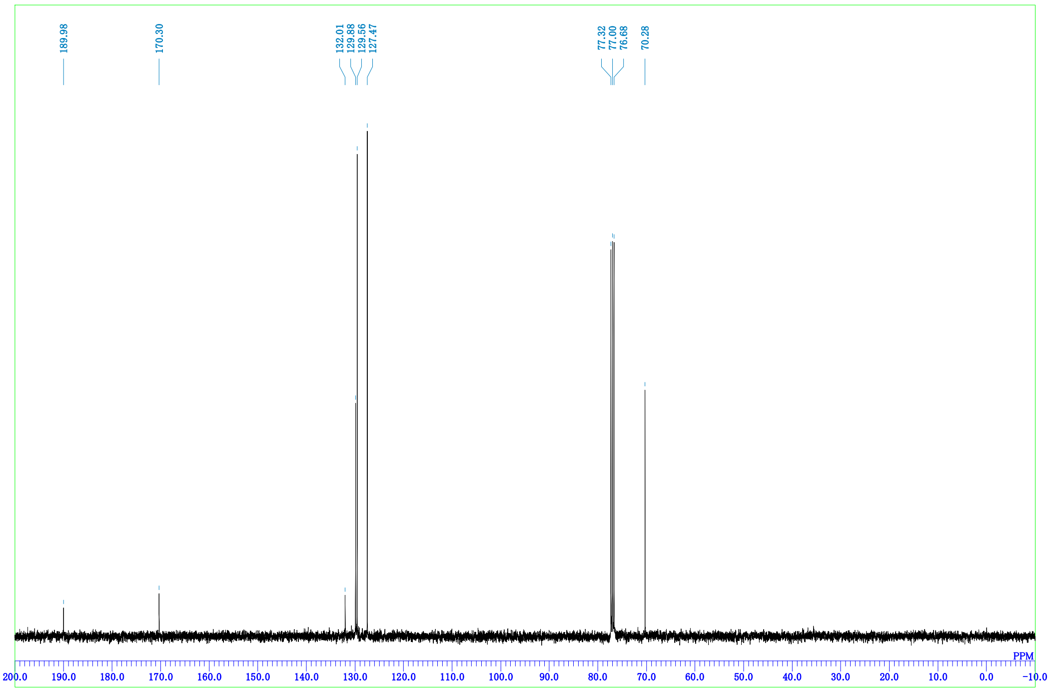
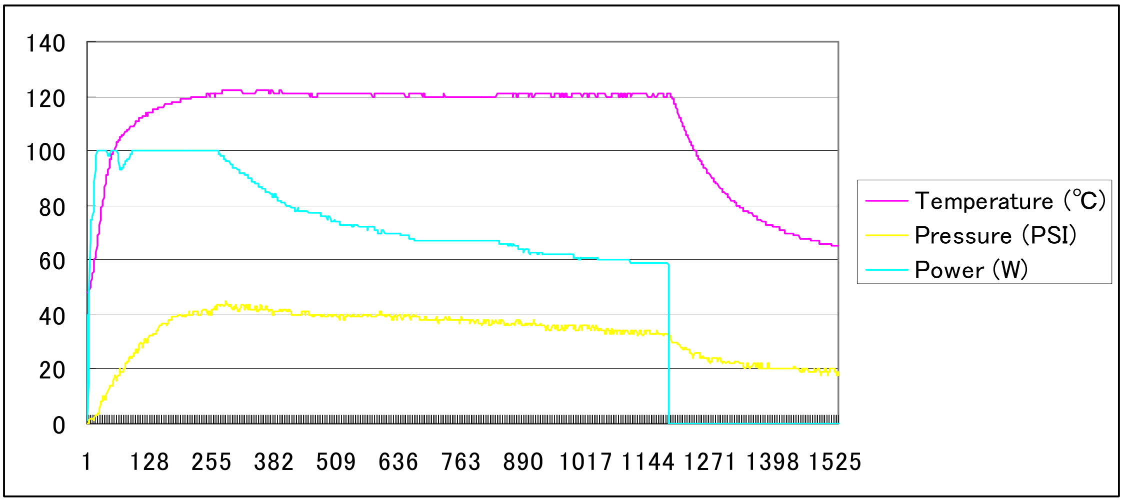
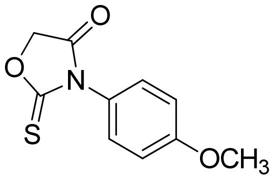


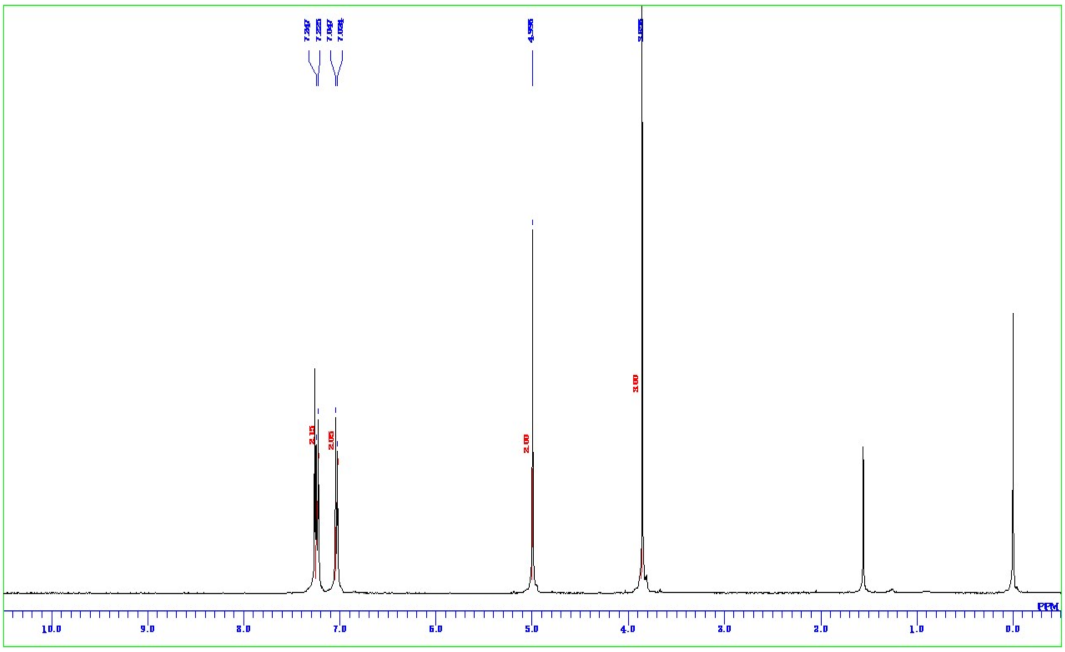
MW Profile (Table 3, entry 3)



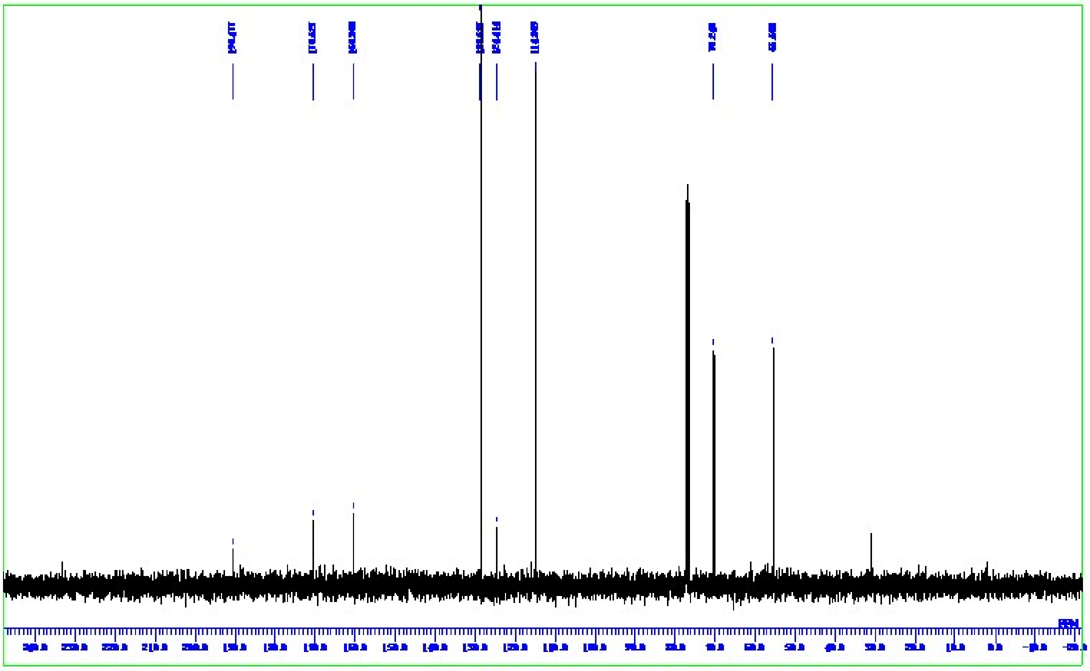
3c



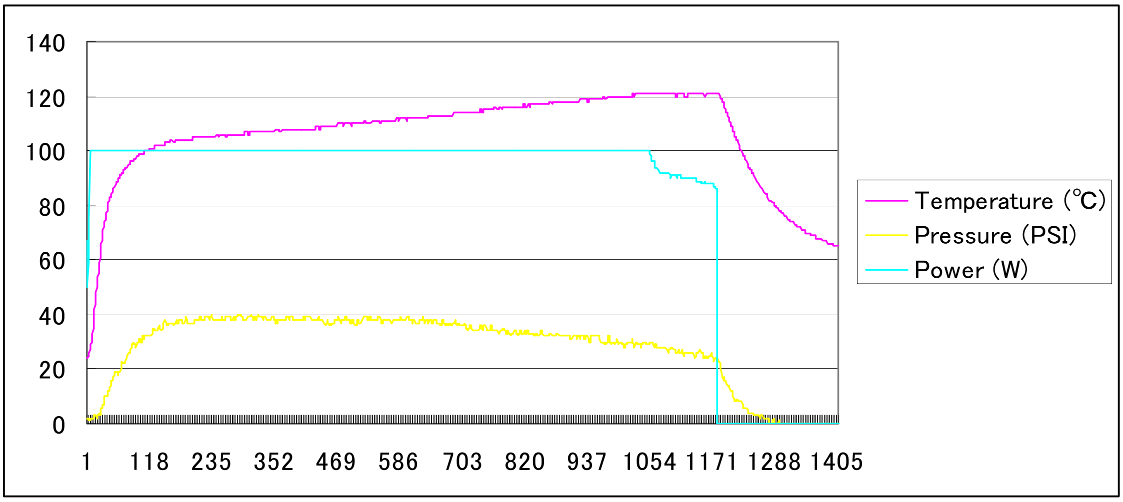
^{1}H NMR



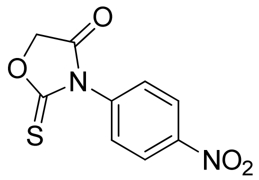
^{13}C NMR



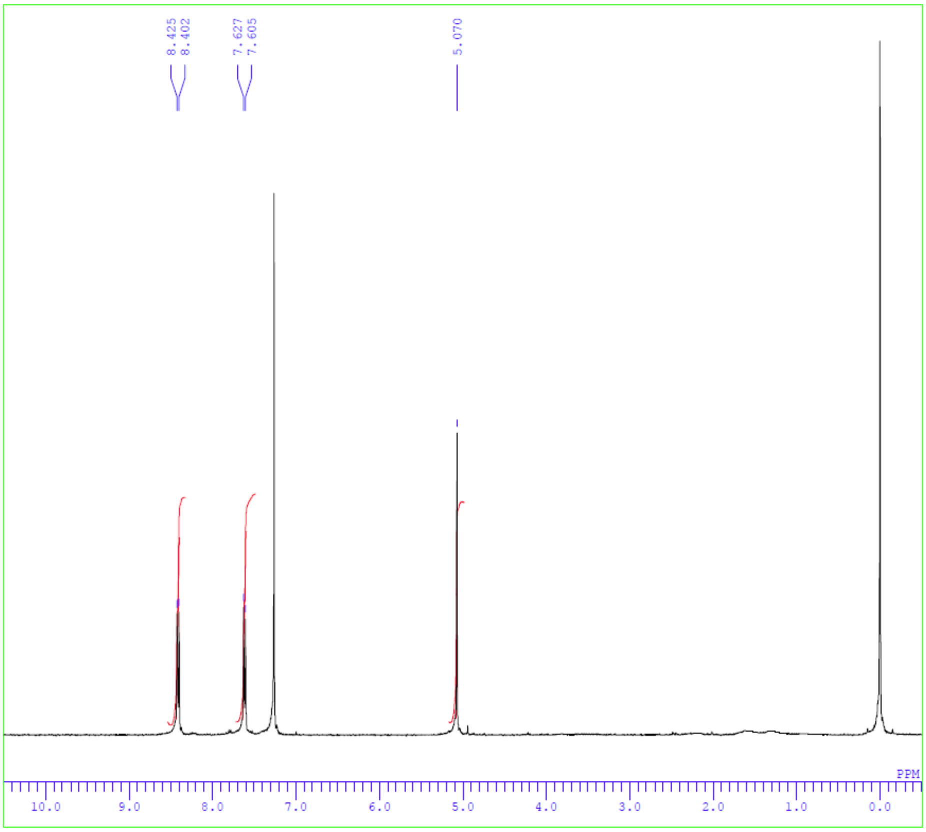
MW Profile (Table 3, entry 5)



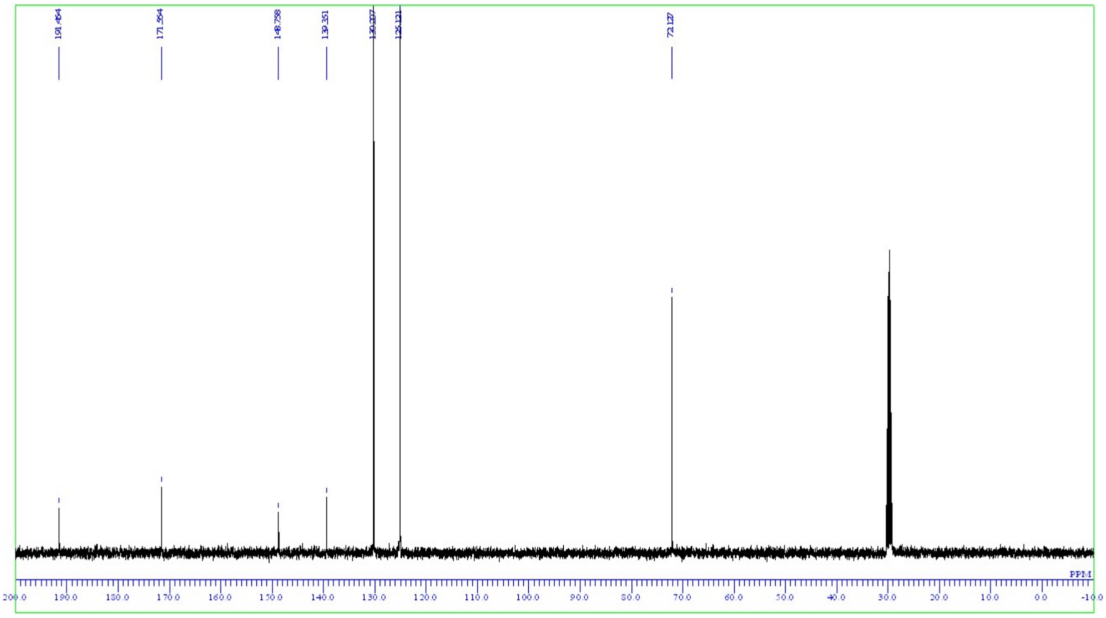
3d



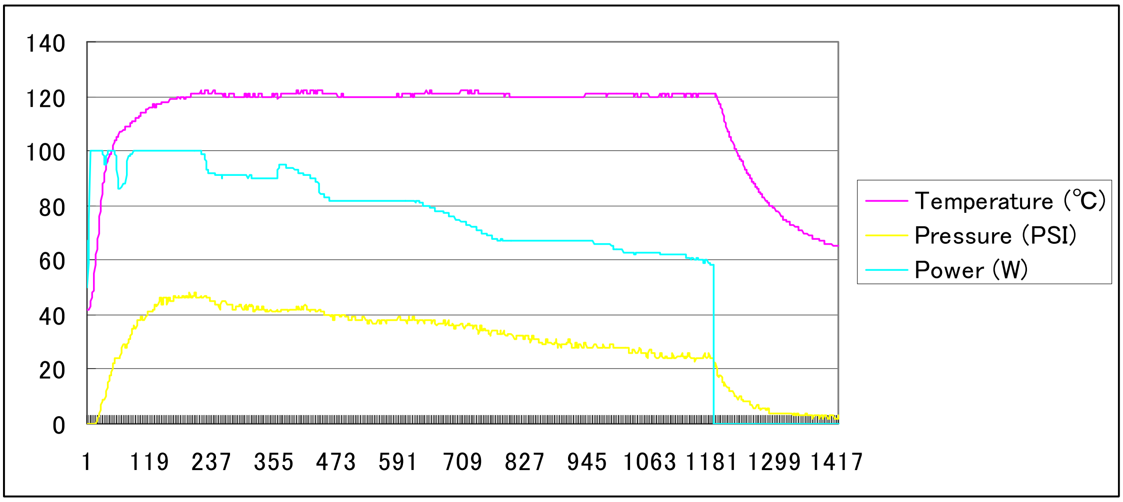
^{1}H NMR



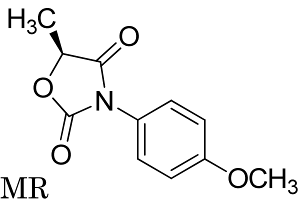
^{13}C NMR



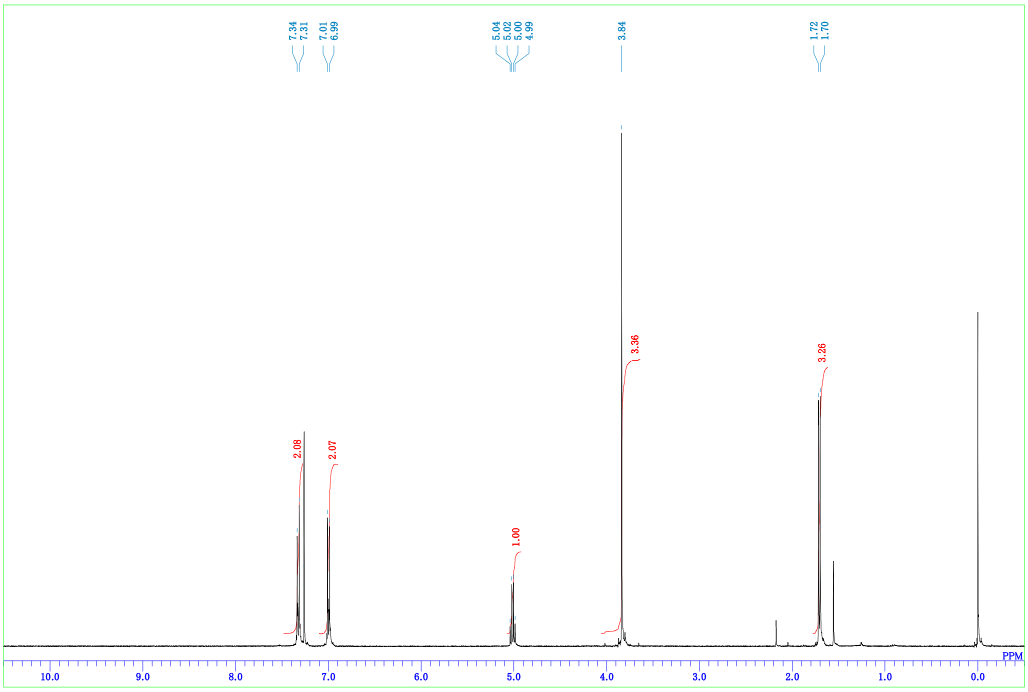
MW Profile (Table 3, entry 7)



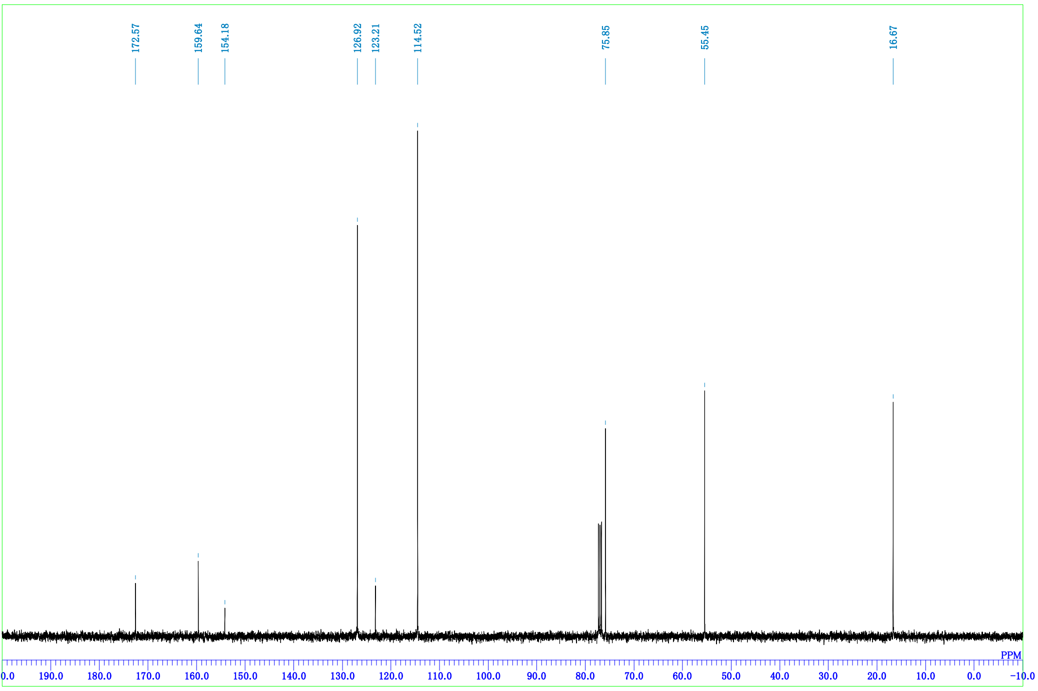
4a



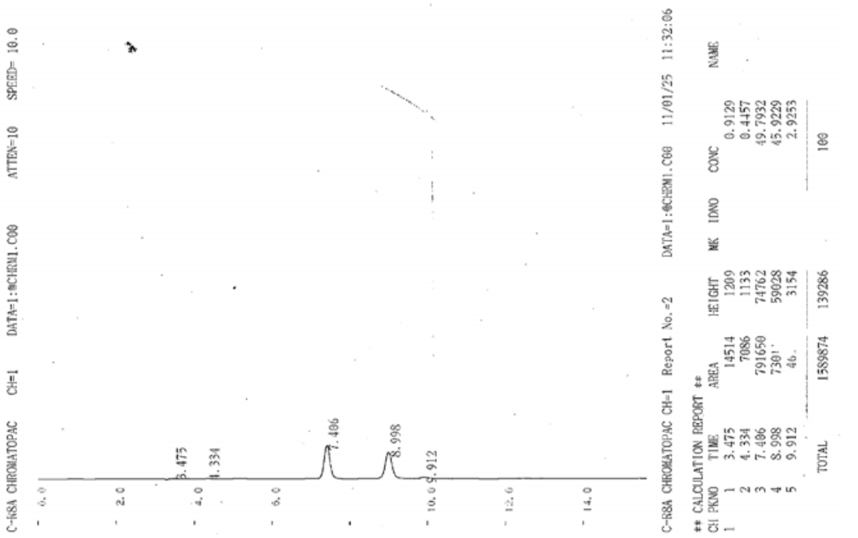
^{1}H NMR



^{13}C NMR



HPLC (racemic sample)



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C-R8A CHROMATOPAC CH=1  Report No.=2   DATA=1:@CHRM1.C00   11/01/25  11:32:06

** CALCULATION REPORT **
CH PKNO   TIME      AREA    HEIGHT   MK  IDNO   CONC       NAME
1    1    3.475     14514    1209               0.9129
     2    4.334      7086    1133               0.4457
     3    7.406    791650   74762              49.7932
     4    8.998     730''   59028              45.9229
     5    9.912       46.    3154               2.9253
     
     TOTAL        1589874  139286             100
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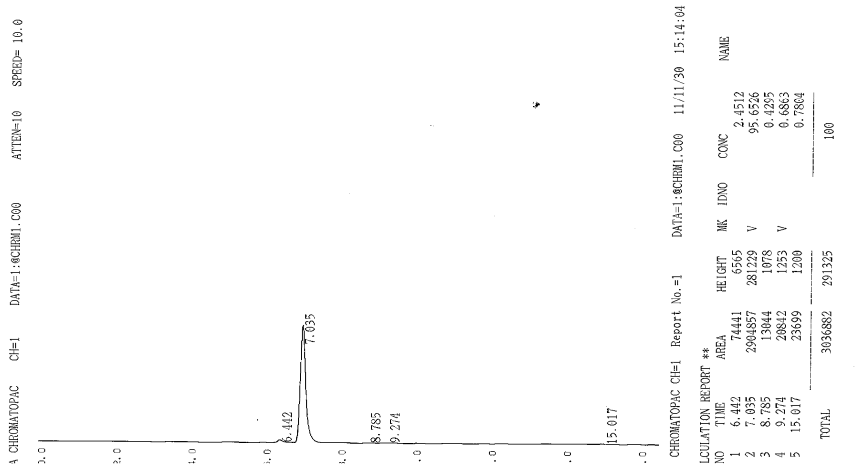
(Isolated sample in Table4 entry 1)



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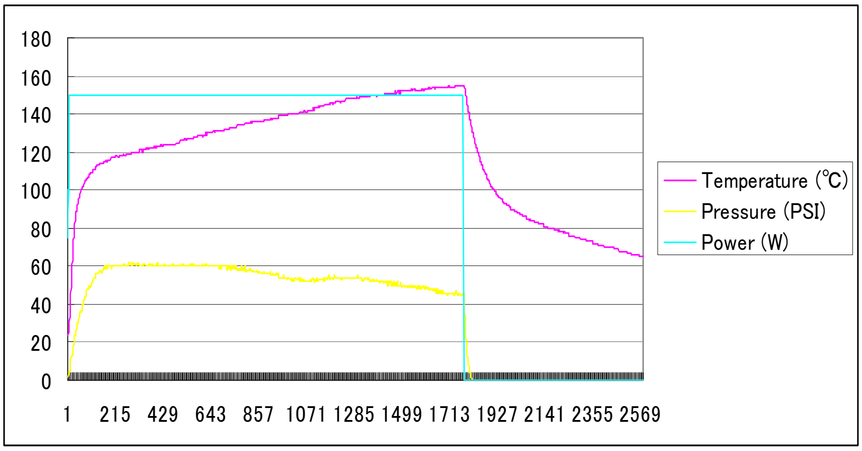
CHROMATOPAC CH=1  Report No.=1   DATA=1:@CHRM1.C00   11/11/30  15:14:04

LCULATION REPORT **
NO    TIME      AREA    HEIGHT   MK  IDNO   CONC       NAME
1    6.442     74441     6565               2.4512
2    7.035   2904857   281229    V         95.6526
3    8.785     13044     1078               0.4295
4    9.274     20842     1253    V          0.6863
5   15.017     23699     1200               0.7804

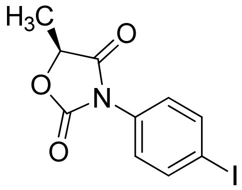
     TOTAL   3036882   291325             100
```

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

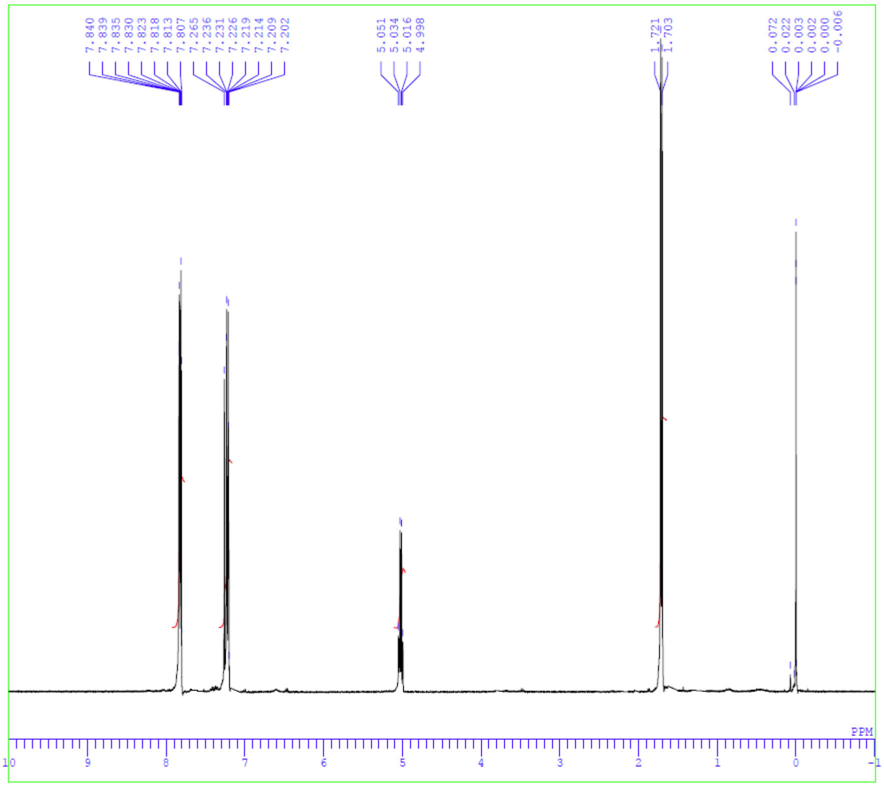
MW Profile (Table 4, entry 1)



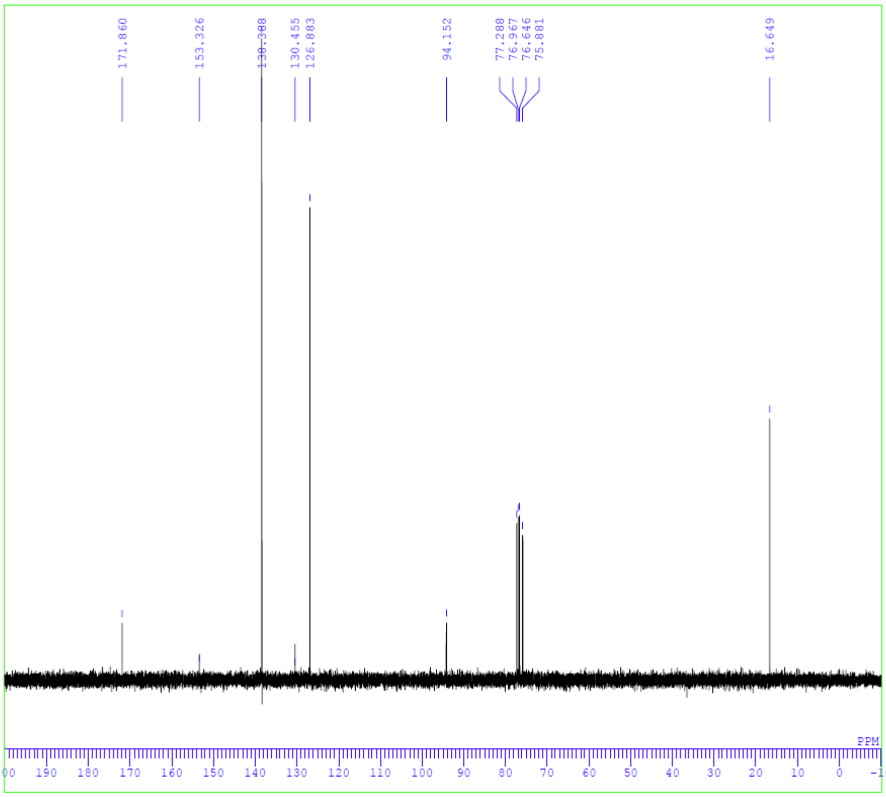
4b



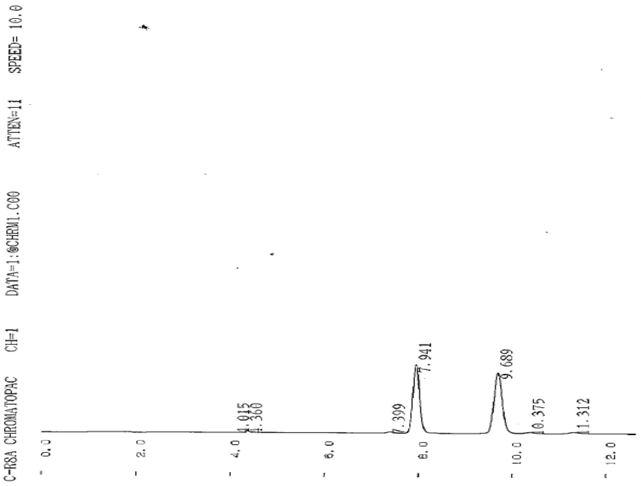
^{1}H NMR



^{13}C NMR



HPLC (racemic sample)



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C-R8A CHROMATOPAC CH=1  Report No.=3        DATA=1:@CHRM1.C00    11/03/03  12:05:00

** CALCULATION REPORT **
CH PKNO   TIME       AREA      HEIGHT   MK  IDNO    CONC          NAME
1     1   4.015       3481        390                 0.0484
      2   4.36       59805       9375                 0.8315
      3   7.399      53577       5894                 0.7449
      4   7.941    3266273     327209                45.4119
      5   9.689    3614533     288076                50.2539
      6  10.375      94631       6217   V             1.3157
      7  11.312     100246       6374                 1.3937
              ---------------------------    -------------
      TOTAL        7192544     643534               100
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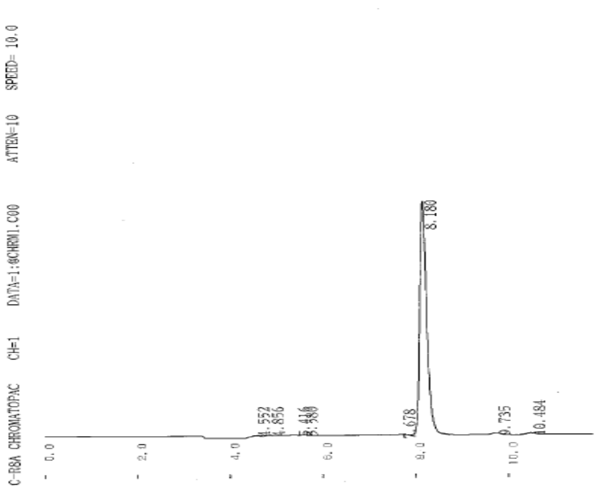
(Isolated sample in Table4 entry 2)



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C-R8A CHROMATOPAC CH=1  Report No.=1        DATA=1:@CHRM1.C00    11/12/07  17:11:36

** CALCULATION REPORT **
CH PKNO   TIME       AREA      HEIGHT   MK  IDNO    CONC          NAME
1     1   4.552      64967       4843   E             1.0422
      2   4.856      26707       2153   V             0.4284
      3   5.416       9166        836                 0.147
      4   5.58        9021       1102   V             0.1447
      5   7.678      17311       1328                 0.2777
      6   8.18     5994942     573331   V            96.1686
      7   9.735      57372       4411                 0.9203
      8  10.484      54298       3790                 0.871
              ---------------------------    -------------
      TOTAL        6233783     591793               100
```
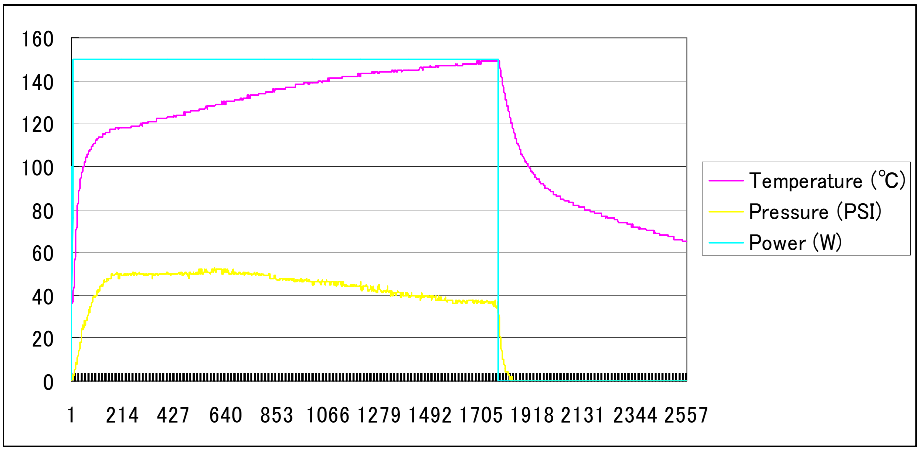
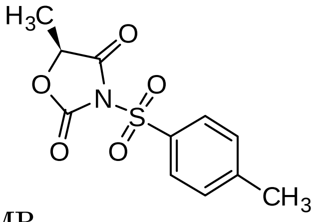

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

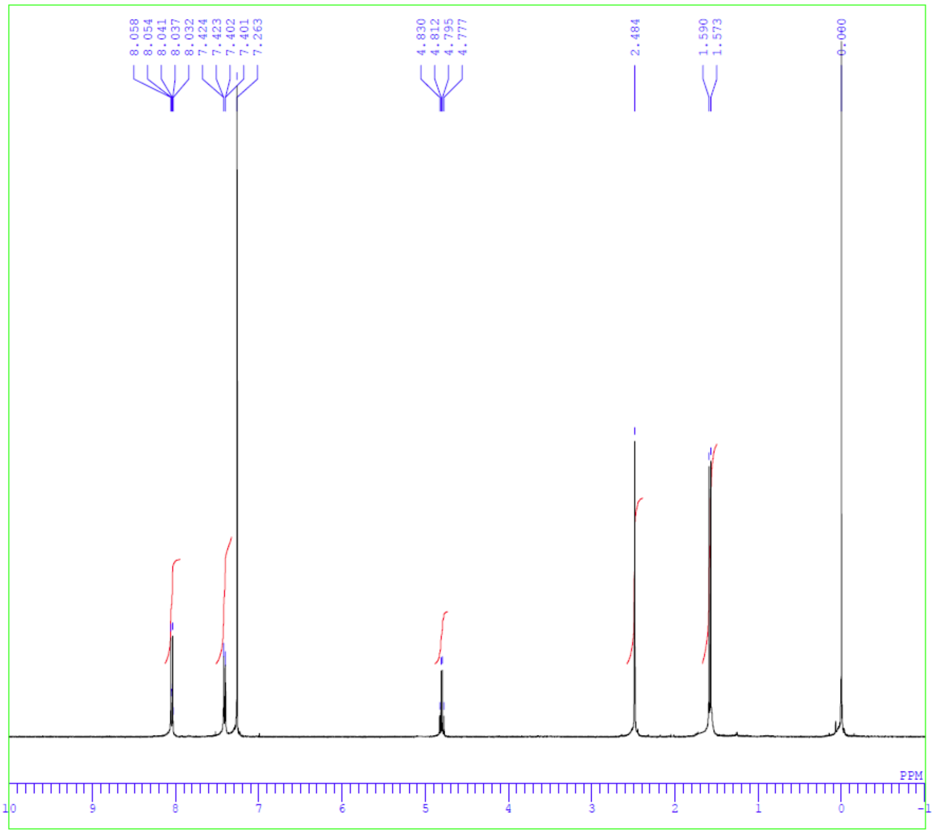
MW Profile (Table 4, entry 2)



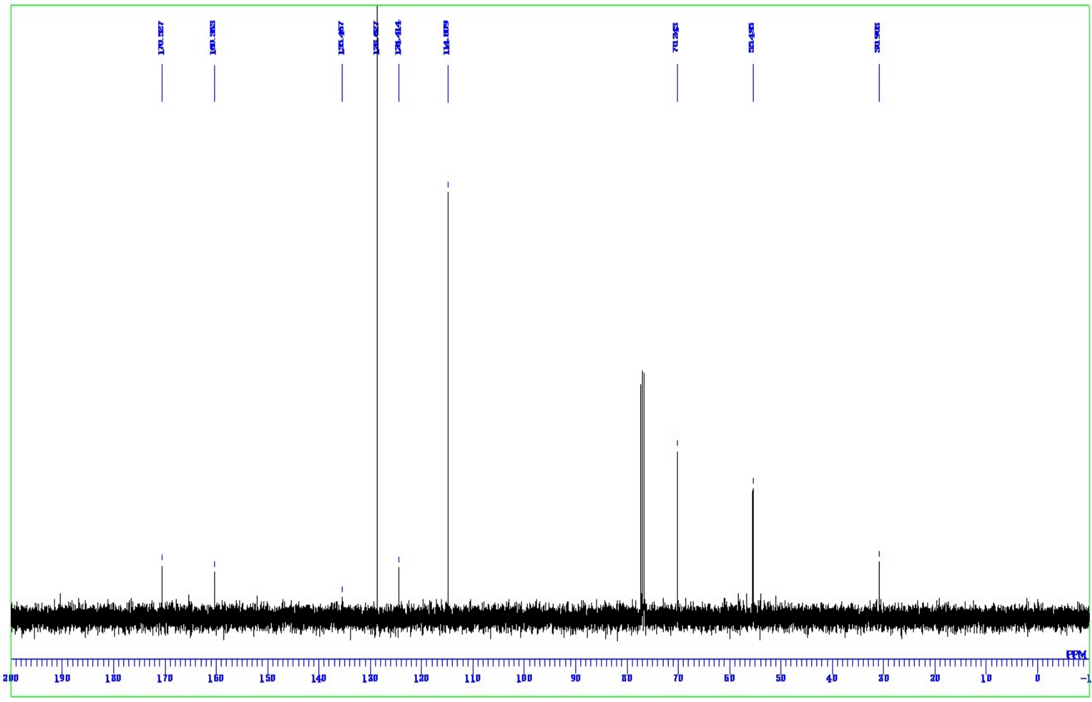
4c



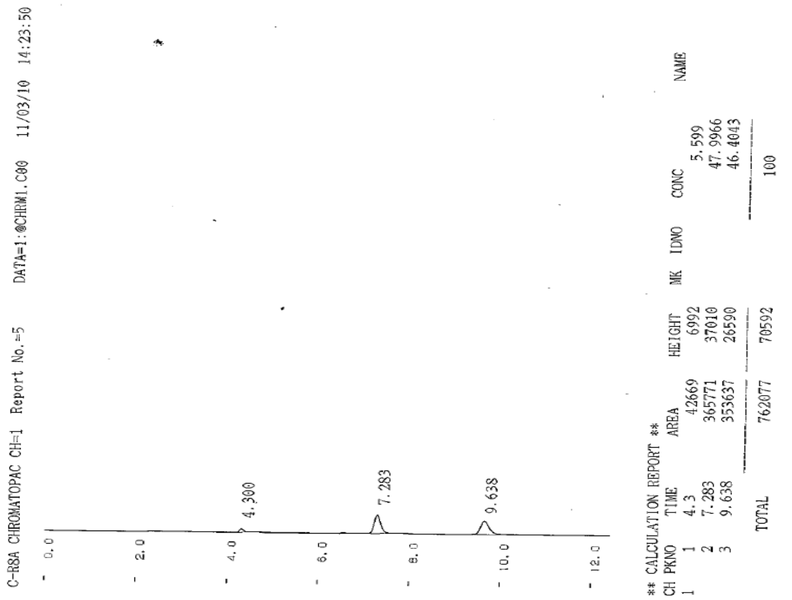
^{1}H NMR



^{13}C NMR



HPLC (racemic sample)

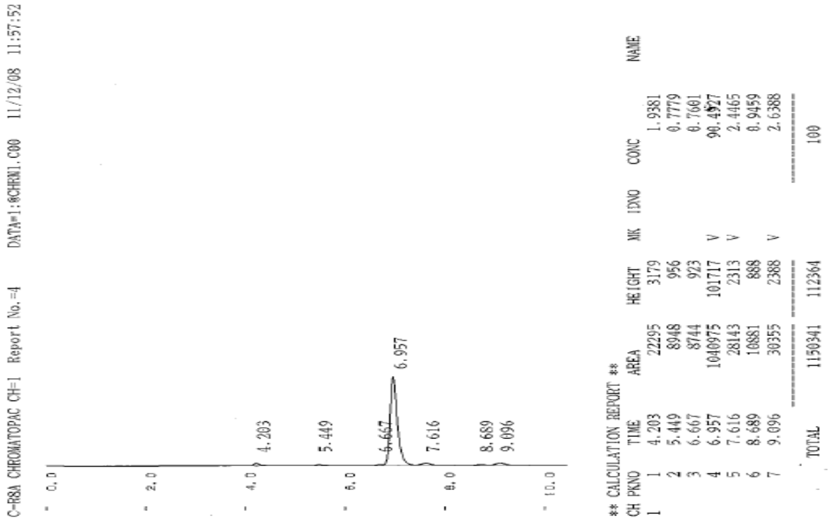


C-R8A CHROMATOPAC CH=1 Report No.=5 DATA=1:@CHRM1.C00 11/03/10 14:23:50

** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	4.3	42669	6992			5.599	
	2	7.283	365771	37010			47.9966	
	3	9.638	353637	26590			46.4043	
		TOTAL	762077	70592			100	

(Isolated sample in Table4 entry 3)



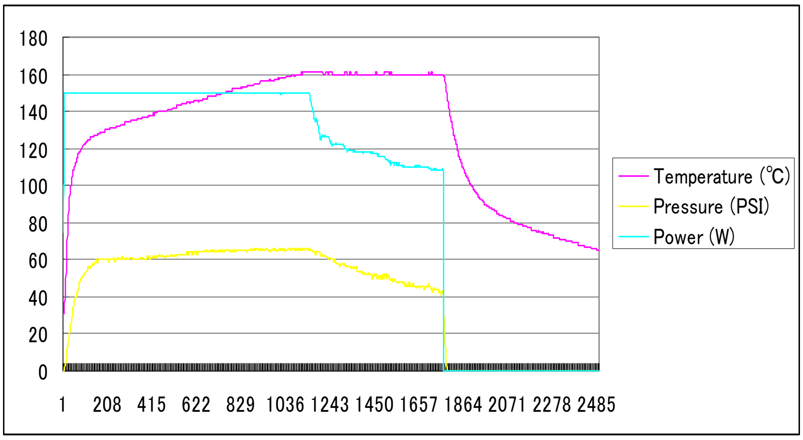
C-R8A CHROMATOPAC CH=1 Report No.=4 DATA=1:@CHRM1.C00 11/12/08 11:57:52

** CALCULATION REPORT **

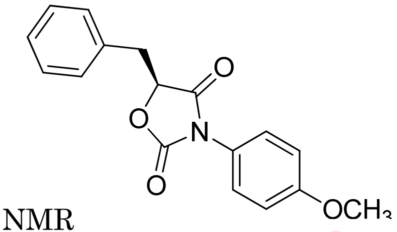
CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	4.203	22295	3179			1.9381	
	2	5.449	8948	956			0.7779	
	3	6.667	8744	923	V		0.7601	
	4	6.957	1040975	101717	V		90.4927	
	5	7.616	28143	2313			2.4465	
	6	8.689	10881	888	V		0.9459	
	7	9.096	30355	2388			2.6388	
		TOTAL	1150341	112364			100	

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

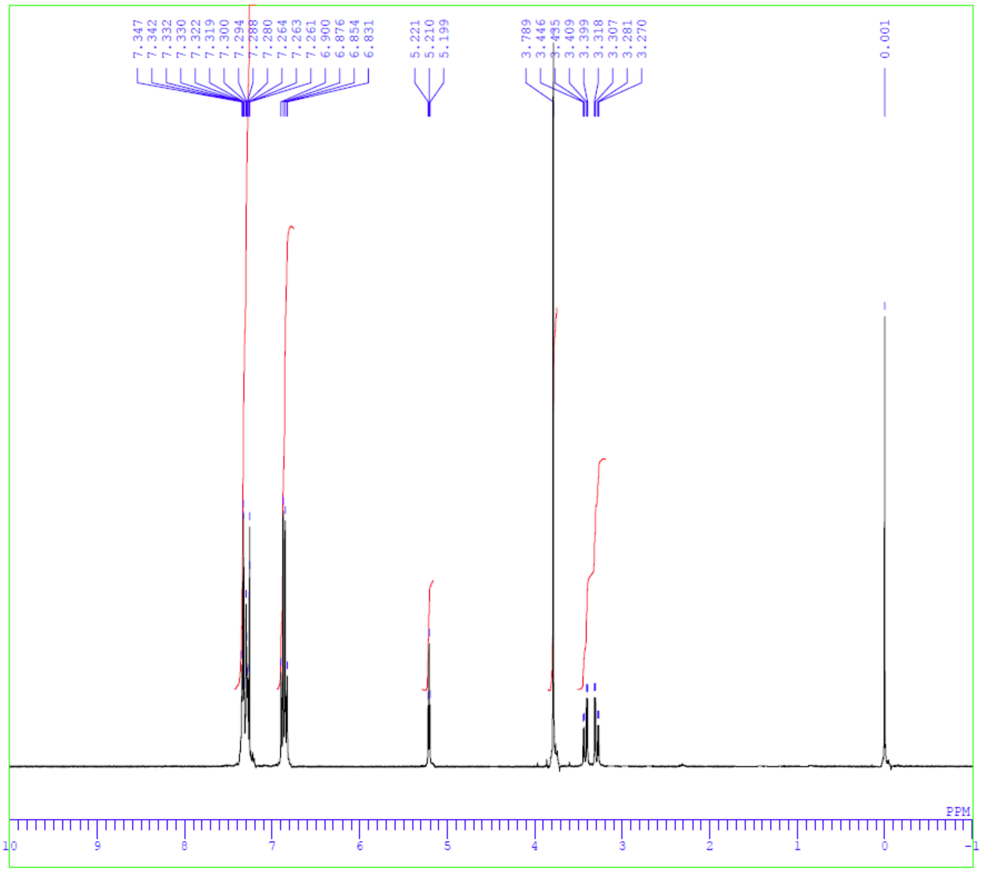
MW Profile (Table 4, entry 3)



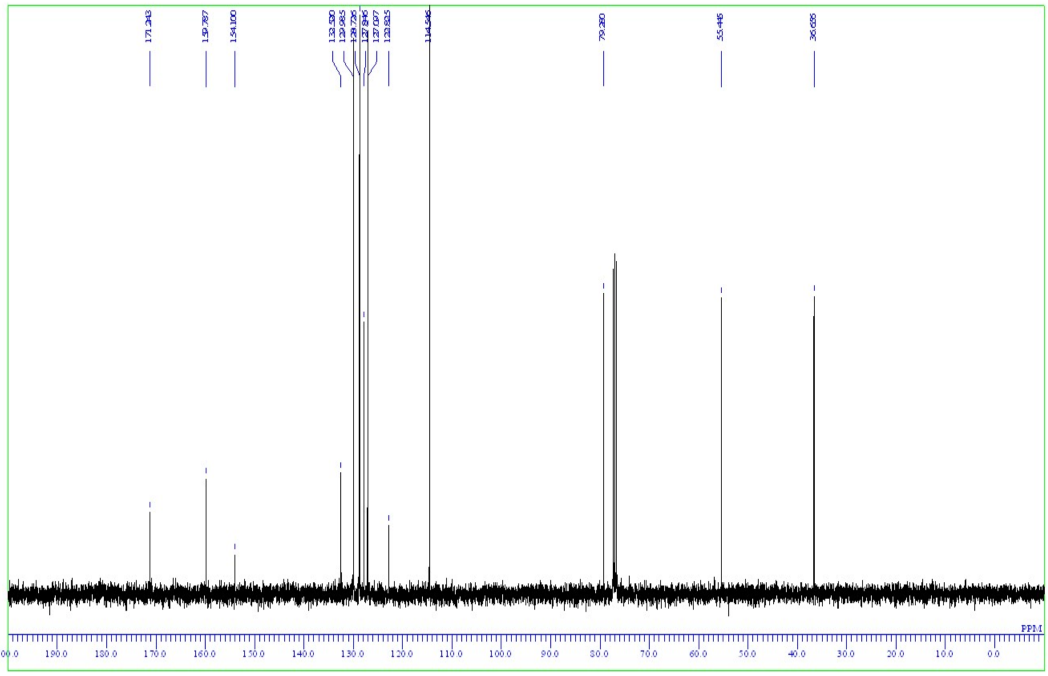
4d



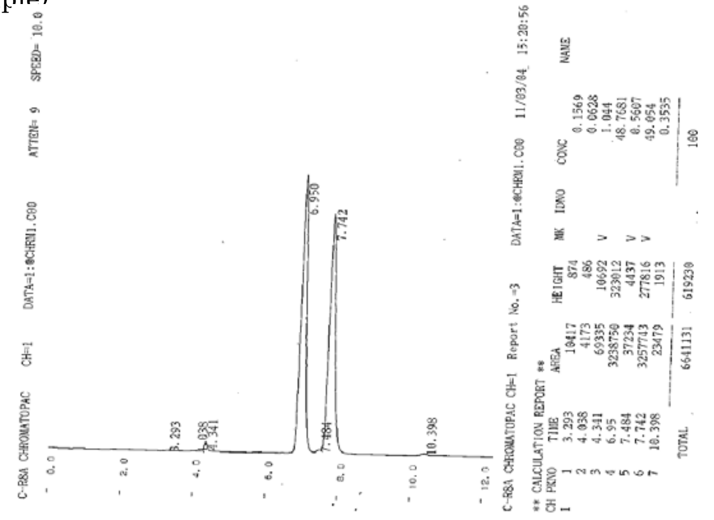
^{1}H NMR



^{13}C NMR

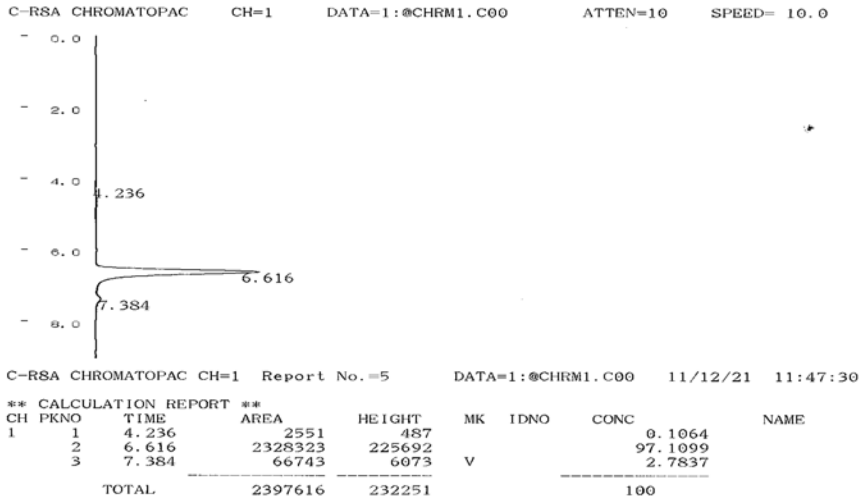


HPLC (racemic sample)



```
C-R8A CHROMATOPAC   CH=1   DATA=1:@CHRM1.C00   ATTEN= 9   SPEED= 10.0

C-R8A CHROMATOPAC CH=1  Report No.=3      DATA=1:@CHRM1.C00    11/03/04  15:20:56

** CALCULATION REPORT **
CH PKNO   TIME      AREA      HEIGHT   MK  IDNO   CONC          NAME
1    1    3.293      10417       874               0.1569
     2    4.038       4173       486               0.0628
     3    4.341      69335     10692   V           1.044
     4    6.95     3238750    323012              48.7681
     5    7.484      37234      4437   V           0.5607
     6    7.742    3257743    277816   V          49.054
     7   10.398      23479      1913               0.3535
                 ---------  --------          ---------
          TOTAL    6641131    619230             100
```

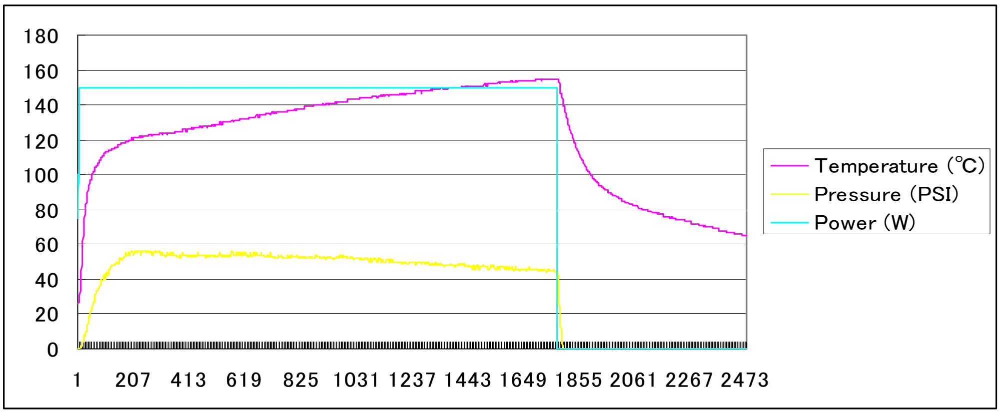
(Isolated sample in Table4 entry 4)



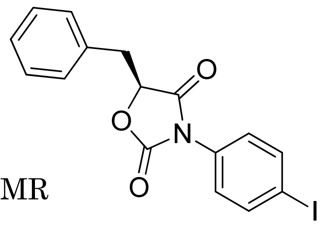
```
C-R8A  CHROMATOPAC     CH=1      DATA=1:@CHRM1.C00        ATTEN=10      SPEED= 10.0

C-R8A CHROMATOPAC CH=1    Report No.=5          DATA=1:@CHRM1.C00      11/12/21    11:47:30

** CALCULATION REPORT **
CH  PKNO       TIME          AREA        HEIGHT     MK    IDNO      CONC               NAME
1      1       4.236          2551          487                        0.1064
       2       6.616       2328323       225692                       97.1099
       3       7.384         66743         6073      V                 2.7837
                         -----------   ----------             ----------------
             TOTAL         2397616       232251                      100
```

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

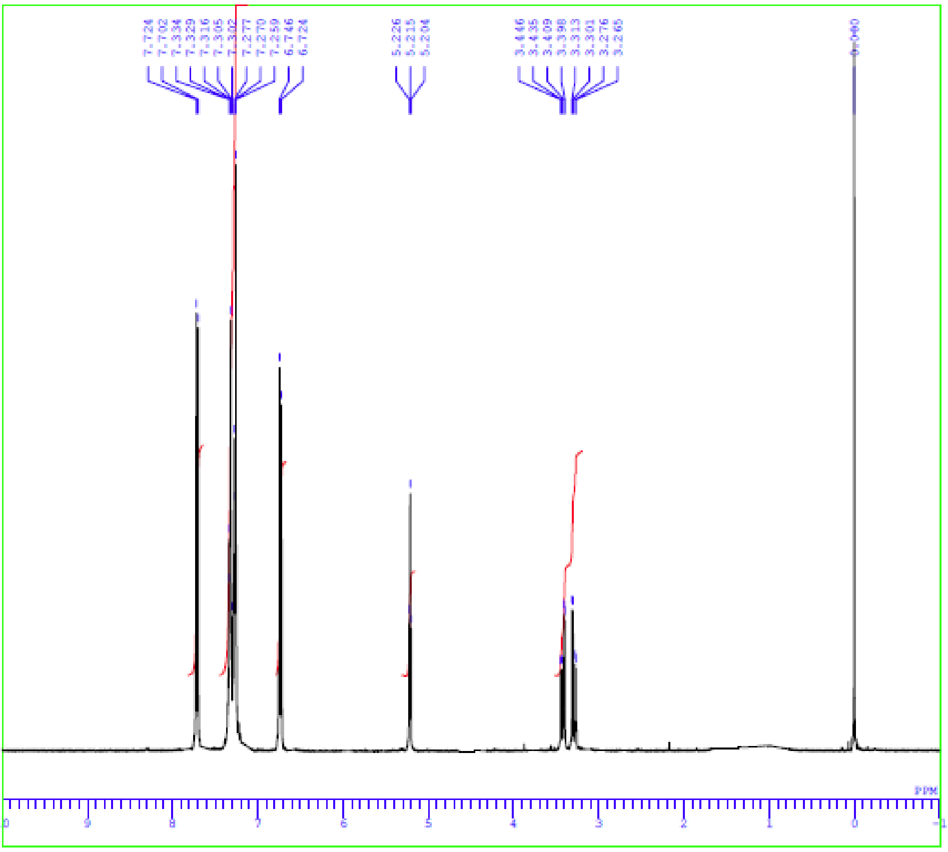
MW Profile (Table 4, entry 4)



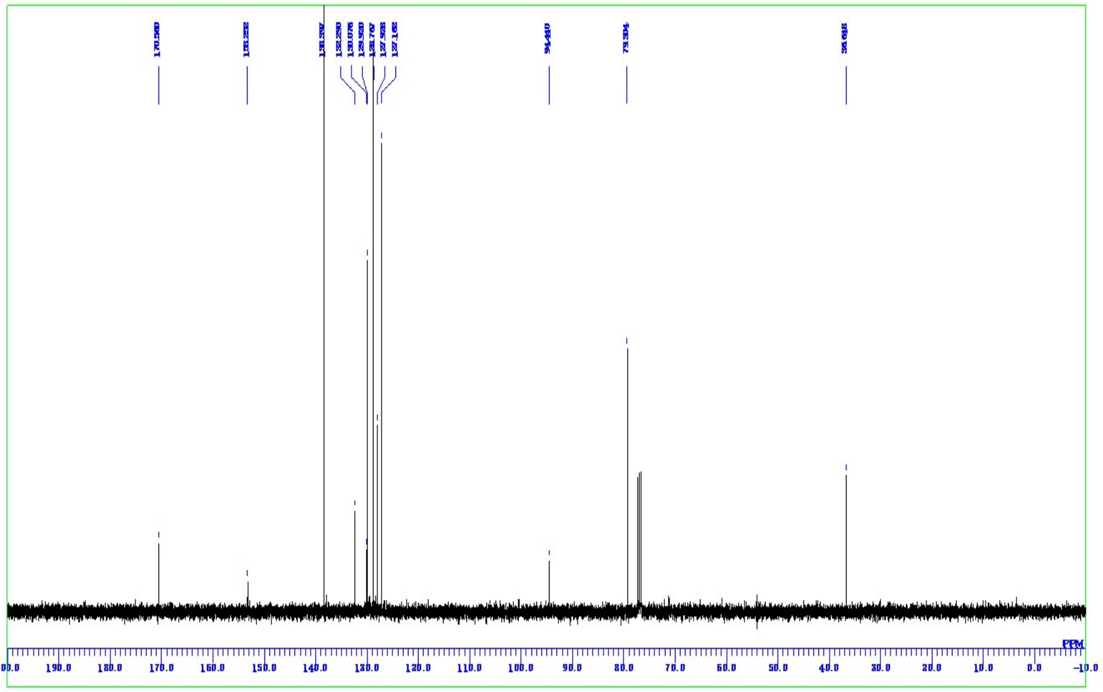
4e



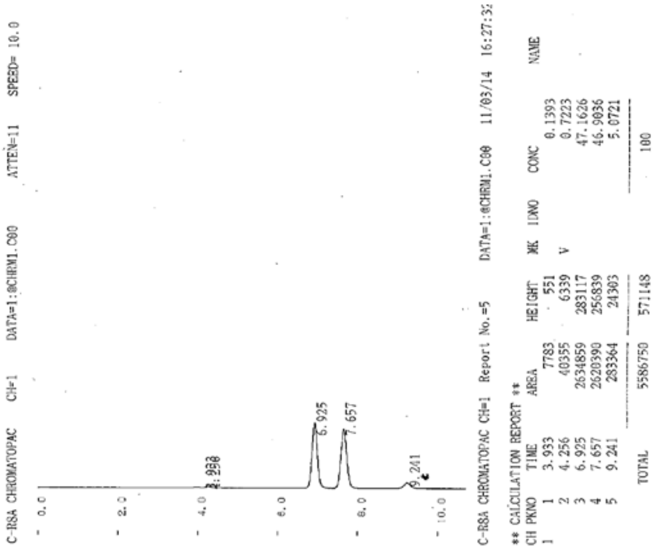
^{1}H NMR



^{13}C NMR

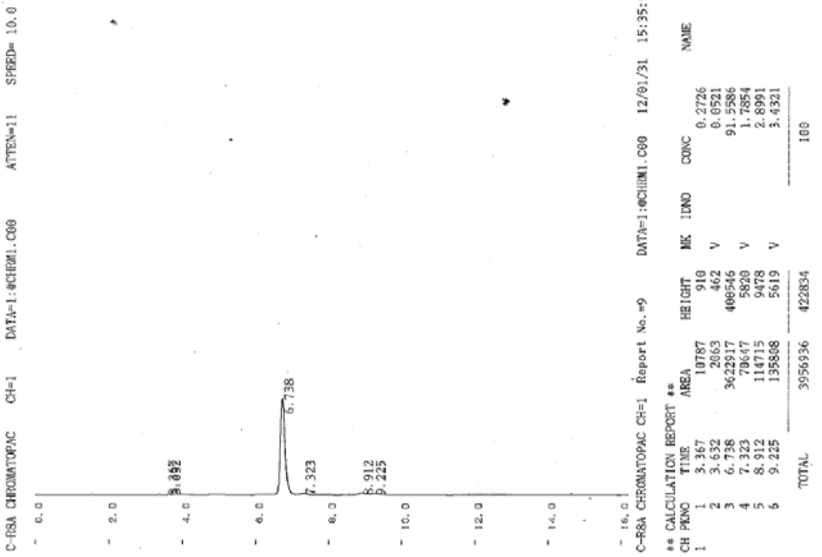


HPLC (racemic sample)



```
C-R8A CHROMATOPAC   CH=1   DATA=1:@CHRM1.C00   ATTEN=11   SPEED= 10.0

C-R8A CHROMATOPAC CH=1  Report No.=5     DATA=1:@CHRM1.C00   11/03/14  16:27:32

** CALCULATION REPORT **
CH PKNO    TIME       AREA     HEIGHT  MK  IDNO   CONC      NAME
1     1   3.933       7783        551             0.1393
      2   4.256      40355       6339  V          0.7223
      3   6.925    2634859     283117            47.1626
      4   7.657    2620390     256839            46.9036
      5   9.241     283364      24303             5.0721
          ---------------------------------   ----------
        TOTAL      5586750     571148           100
```

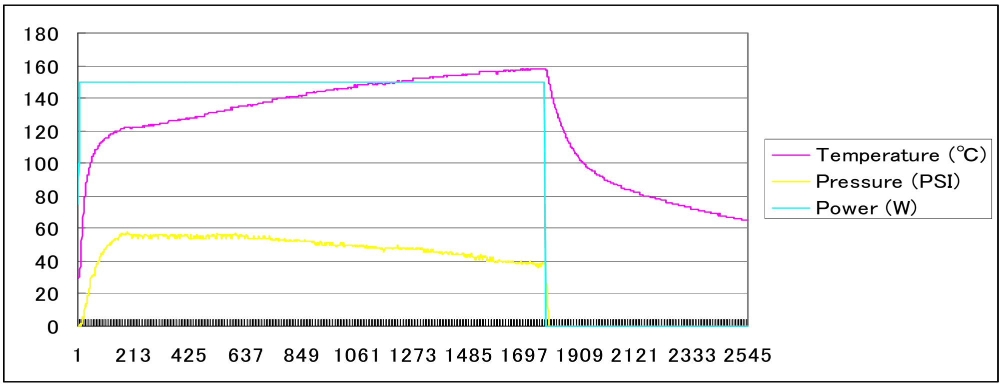
(Isolated sample in Table4 entry 5)



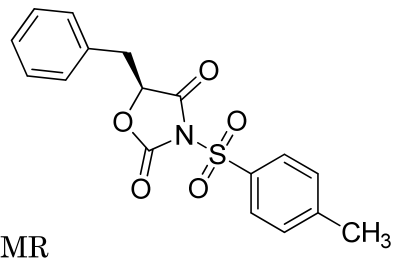
```
C-R8A CHROMATOPAC   CH=1   DATA=1:@CHRM1.C00   ATTEN=11   SPEED= 10.0

C-R8A CHROMATOPAC CH=1  Report No.=9     DATA=1:@CHRM1.C00   12/01/31  15:35:56

** CALCULATION REPORT **
CH PKNO    TIME       AREA     HEIGHT  MK  IDNO   CONC      NAME
1     1   3.367      10787        910             0.2726
      2   3.632       2063        462  V          0.0521
      3   6.738    3622917     400546            91.5586
      4   7.323      70647       5820  V          1.7854
      5   8.912     114715       9478             2.8991
      6   9.225     135808       5619  V          3.4321
          ---------------------------------   ----------
        TOTAL      3956936     422834           100
```

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

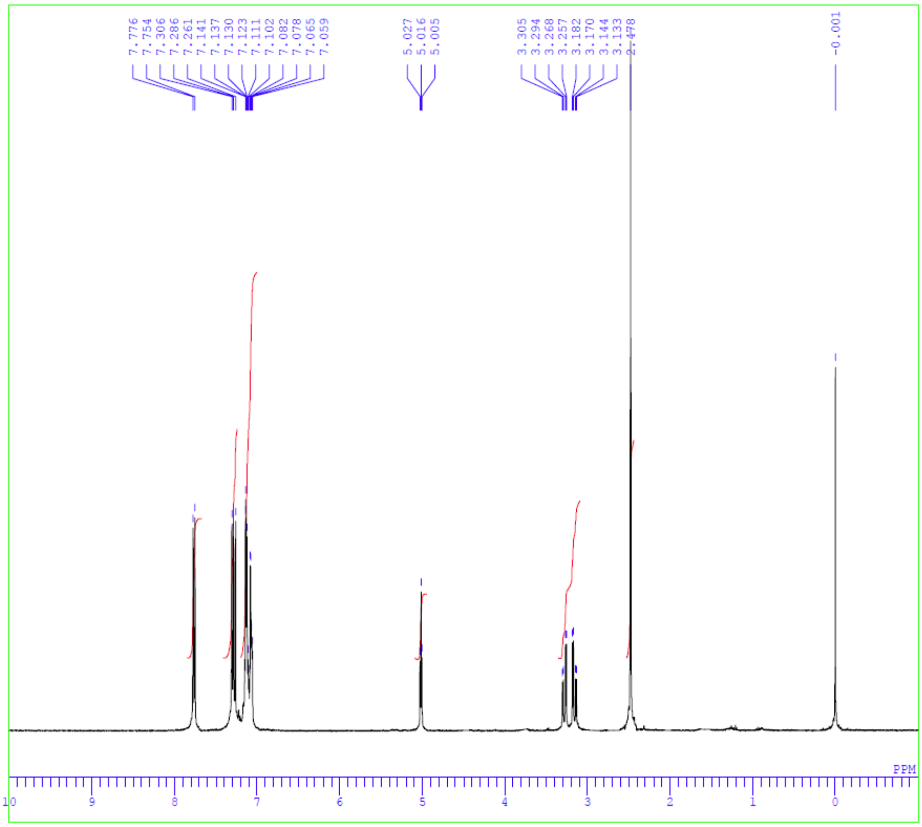
MW Profile (Table 4, entry 5)



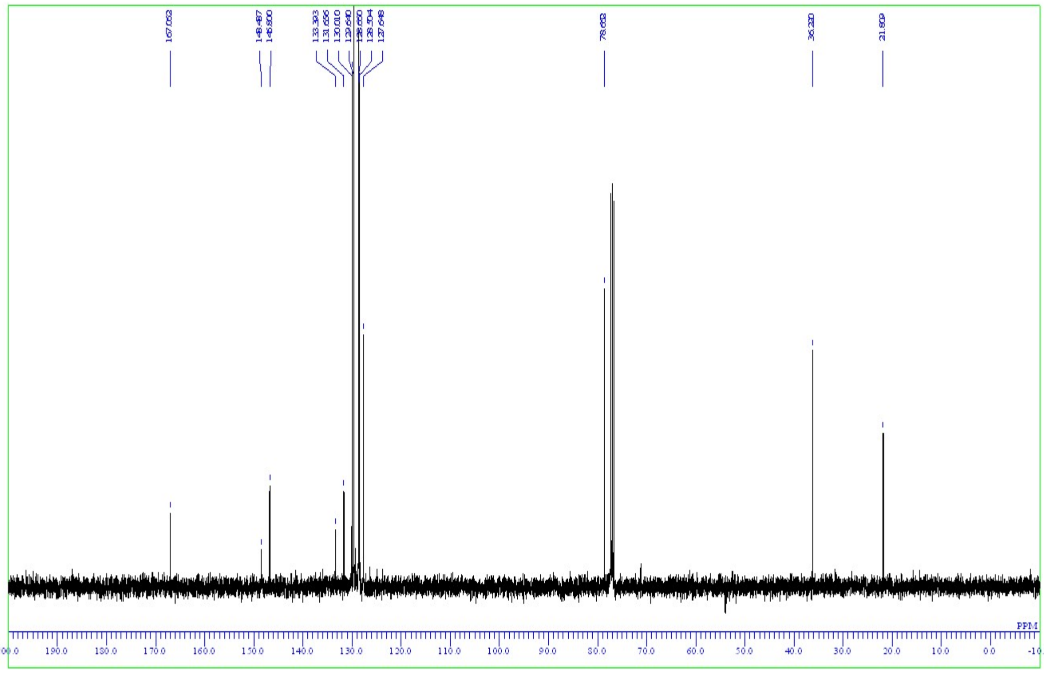
4f



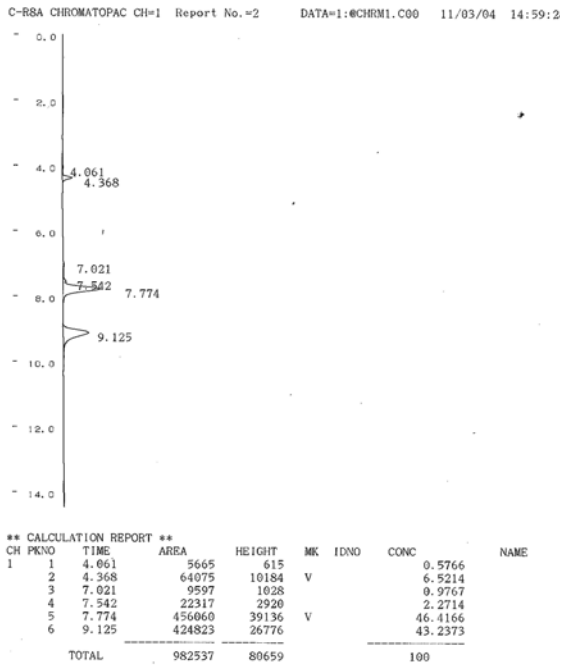
^{1}H NMR



^{13}C NMR



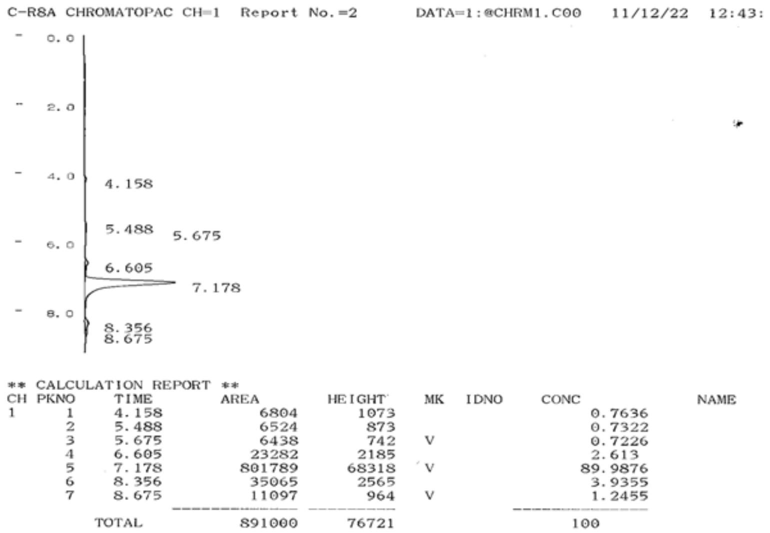
HPLC (racemic sample)



```
C-R8A CHROMATOPAC CH=1  Report No.=2      DATA=1:@CHRM1.C00   11/03/04  14:59:2
```

```
** CALCULATION REPORT **
CH PKNO    TIME        AREA      HEIGHT    MK  IDNO    CONC          NAME
1     1    4.061       5665        615                 0.5766
      2    4.368      64075      10184     V           6.5214
      3    7.021       9597       1028                 0.9767
      4    7.542      22317       2920                 2.2714
      5    7.774     456060      39136     V          46.4166
      6    9.125     424823      26776                43.2373
                   ----------  ---------          -------------
        TOTAL        982537      80659              100
```

(Isolated sample in Table4 entry 6)



```
C-R8A CHROMATOPAC CH=1  Report No.=2      DATA=1:@CHRM1.C00   11/12/22   12:43:
```

```
** CALCULATION REPORT **
CH PKNO    TIME       AREA     HEIGHT    MK   IDNO    CONC          NAME
1     1    4.158      6804      1073                 0.7636
      2    5.488      6524       873                 0.7322
      3    5.675      6438       742     V           0.7226
      4    6.605     23282      2185                 2.613
      5    7.178    801789     68318     V          89.9876
      6    8.356     35065      2565                 3.9355
      7    8.675     11097       964     V           1.2455
                 -----------  ---------          -----------
        TOTAL       891000     76721               100
```

Daicel CHIRALPAK IA detected at 254 nm (UV) eluted by 1.0 mL/min Hexane/$CHCl_3$=50/50.

MW Profile (Table 4, entry 6)