Supporting Information

A mild method for synthesizing carboxylic acids by oxidation of aldoximes using hypervalent iodine reagents

Akira Nakamura,[a] Hodaka Kanou,[a] Junki Tanaka,[a] Akira Imamiya,[a] Tomohiro Maegawa[a] and Yasuyoshi Miki*[a,b]*

[a.] *School of Pharmaceutical Sciences, Kindai University, 3-4-1 Kowakae, Higashi-osaka, Osaka 577-8502, Japan.*

[b.] *Research Organization of Science and Technology, Research Center for Drug Discovery and pharmaceutical Science, Ritsumeikan University, 1-1-1 Nojihigashi, Kusatsu, Shiga 525-8577, Japan.*

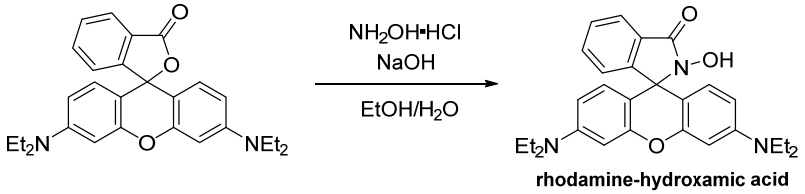
Experimental Section

General. ^{1}H NMR spectra were recorded on the JEOL JMN-400 spectrometer in $CDCl_3$ or DMSO-d_6 with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (δ), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant (Hz).

Materials: Unless otherwise noted, all reagents, including $PhI(OCOCH_3)_2$, PhI(OH)OTs and $PhI(OCOCF_3)_2$, and solvents were purchased from commercial suppliers and used without further purification.

General Oxidation Procedure: To a DMSO-H_2O (50:1, 2 mL) solution of aldoxime **1** (0.2 mmol) was added PhI(OH)OTs (0.21 mmol) at room temperature, and another amount of PhI(OH)OTs (0.21 mmol) was added in 30 min. After completion of the reaction as indicated by TLC monitoring, the reaction mixture was poured into 10% aq. Na_2CO_3 and then EtOAc was added. The organic layer was extracted with 10% aq. Na_2CO_3. The combined aqueous layers were acidified by addition of aq. HCl, and then extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to afford pure carboxylic acid **2** with no need for further purification.

Preparation of rhodamine-hydroxamic acid[1]

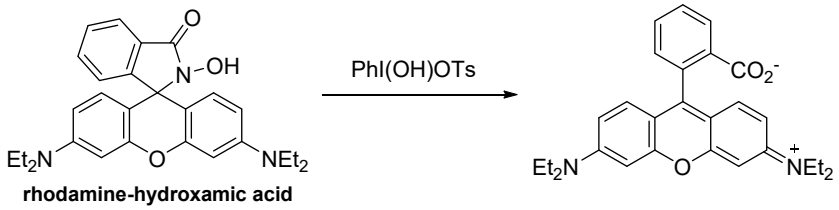


rhodamine-hydroxamic acid

To a solution of rhodamine B base (221 mg, 0.5 mmol) and hydroxylamine hydrochloride (0.347 g, 5 mmol) in EtOH (5 mL) was added NaOH (200 mg, 5 mmol) dissolved in water (2 mL). The reaction mixture was refluxed for 10 h, and then poured into water (20 mL). The solution was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and then concentrated *in vacuo*. The crude was purified by column chromatography (silica gel, ethyl acetate) to give product (208 mg, 91%) as a beige colored solid.

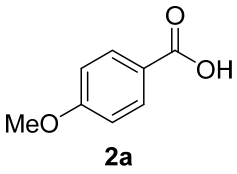
^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.84 (dd, *J* = 6.0, 1.6 Hz, 1H), 7.44–7.40 (m, 2H), 7.07 (d, *J* = 6.8 Hz, 1H), 6.51 (d, *J* = 8.8 Hz, 2H), 6.40 (d, *J* = 2.4 Hz, 2H), 6.27 (dd, *J* = 8.8 ,2.8 Hz, 2H), 3.32 (q, *J* = 7.2 Hz, 8H), 1.15 (t, *J* = 7.2 Hz, 12H).

Signaling experiment[1]



Solution of rhodamine-hydroxamic acid (5.0×10^{-4} M) and PhI(OH)OTs (5.0×10^{-2} M) were prepared in DMSO. The solution of rhodamine-hydroxamic acid (30 μL) was diluted to 3.0 mL with DMSO and pH 4.8 acetate buffer solution to make a composition of 1:9, v/v (colorless solution). The solution of PhI(OH)OTs (30 μL) was added and the resulting solution was fluoresced in a second.

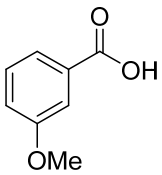
NMR data



2a

4-Methoxybenzoic acid (2a)[2]

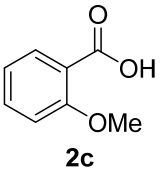
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 9.2 Hz, 1H), 6.95 (d, *J* = 9.2 Hz, 1H), 3.86 (s, 3H).



2b

3-Methoxybenzoic acid (2b)[3]

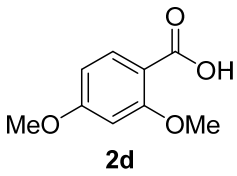
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.61 (s, 1H), 7.37 (dd, *J* = 8.4, 7.6 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.85 (s, 3H).



2c

2-Methoxybenzoic acid (2c)[3]

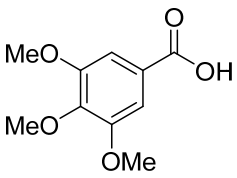
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.57 (ddd, *J* = 8.4, 7.6, 1.6 Hz, 1H), 7.13 (ddd, *J* = 8.8, 7.6, 0.8 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 4.07 (s, 3H).



2d

2,4-Dimethoxybenzoic acid (2d)[4]

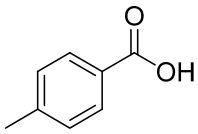
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.8 Hz, 1H), 6.64 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.52 (d, *J* = 2.4 Hz, 1H), 4.03 (s, 3H), 3.86 (s, 3H).



2e

3,4,5-Trimethoxybenzoic acid (2e)[2]

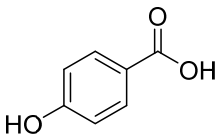
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 2H), 3.914 (s, 3H), 3.907 (s, 6H).



2f

4-Methylbenzoic acid (2f)[2]

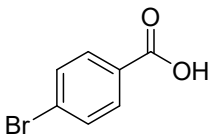
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 2.41 (s, 3H).



2g

4-Hydroxybenzoic acid (2g)[3]

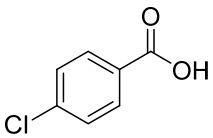
^{1}H NMR (400 MHz, DMSO-d_6): δ 12.44 (brs, 1H), 10.2 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H).



2h

4-Bromobenzoic acid (2h)[3]

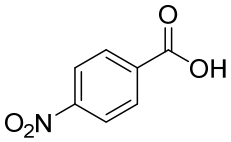
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.14 (brs, 1H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H).



2i

4-Chlorobenzoic acid (2i)[2]

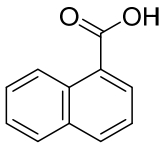
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.93 (d, *J* = 11.6 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H).



2j

4-Nitrobenzoic acid (2j)[3]

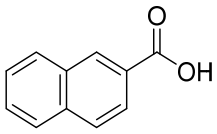
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.32 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.0 Hz, 2H).



2k

1-Naphthoic acid (2k)[2]

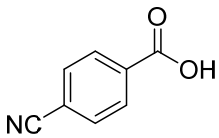
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.85 (d, J = 8.8 Hz, 1H), 8.16-8.13 (m, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.65-7.56 (m, 3H).



2l

2-Naphthoic acid (2l)[2]

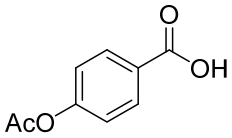
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.61 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.97-8.02 (m, 3H), 7.59-7.68 (m, 2H).



2m

4-Cyanobenzoic acid (2m)[2]

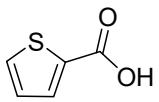
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H).



2n

4-Acetoxybenzoic acid (2n)[5]

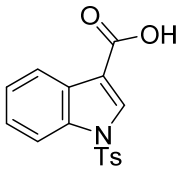
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.8 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H), 2.32 (s, 3H).



2o

Thiophene-2-carboxylic acid (2o)[6]

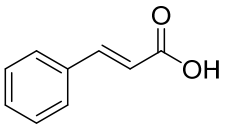
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.88 (m, 1H), 7.64-7.63 (m, 1H), 7.14-7.12 (m, 1H).



2p

1-Tosyl-1*H*-indole-3-carboxylic acid (2p)[7]

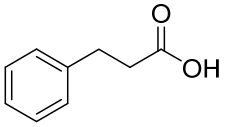
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.15-8.13 (m, 1H), 7.97-7.95 (m, 1H), 7.83 (d, J = 8.4 Hz, 2H), 7.38-7.34 (m, 2H), 7.27 (d, J = 8.4 Hz, 1H), 2.35 (s, 3H).



2q

Cinnamic acid (2q)[2]

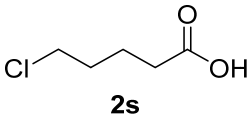
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 16.0 Hz, 1H), 7.56-7.37 (m, 5H), 6.45 (d, *J* = 16.0 Hz, 1H).



2r

3-Phenylpropanoic acid (2r)[8]

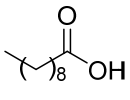
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.21 (m, 5H), 2.97 (t, *J* = 7.8 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H).



2s

5-Chloropentanoic acid (2s)[9]

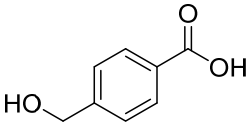
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.54 (t, *J* = 6.8 Hz, 2H), 2.39 (t, *J* = 6.8 Hz, 2H), 1.83-1.78 (m, 4H).



2t

Decanoic acid (2t)[10]

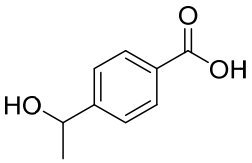
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (t, *J* = 7.2 Hz, 2H), 1.63-1.59 (m, 2H), 1.28-1.20 (m, 12H), 0.86 (t, *J* = 6.4 Hz, 3H).



2u

4-(Hydroxymethyl)benzoic acid (2u)[11]

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.8 (brs, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 5.36 (brs, 1H), 4.57 (s, 2H).

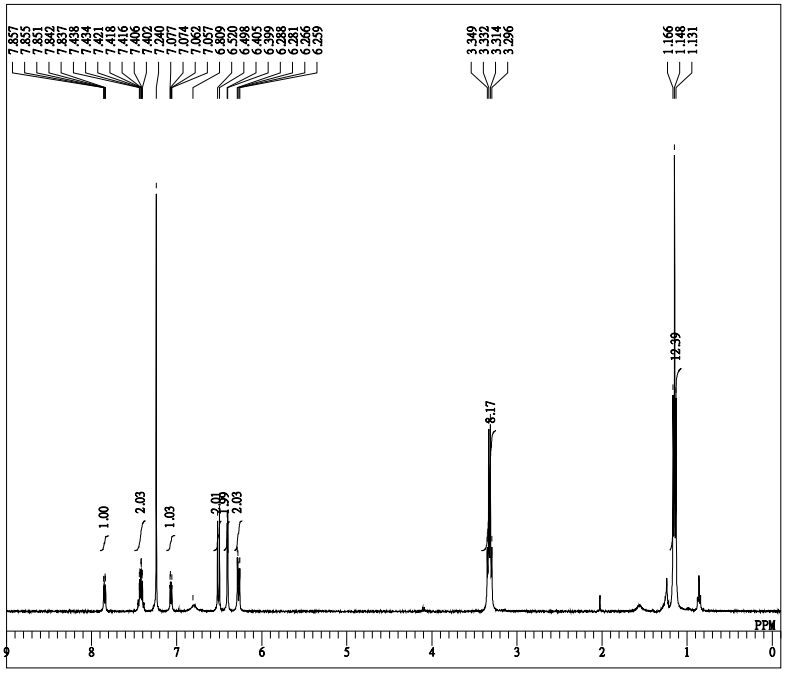


2v

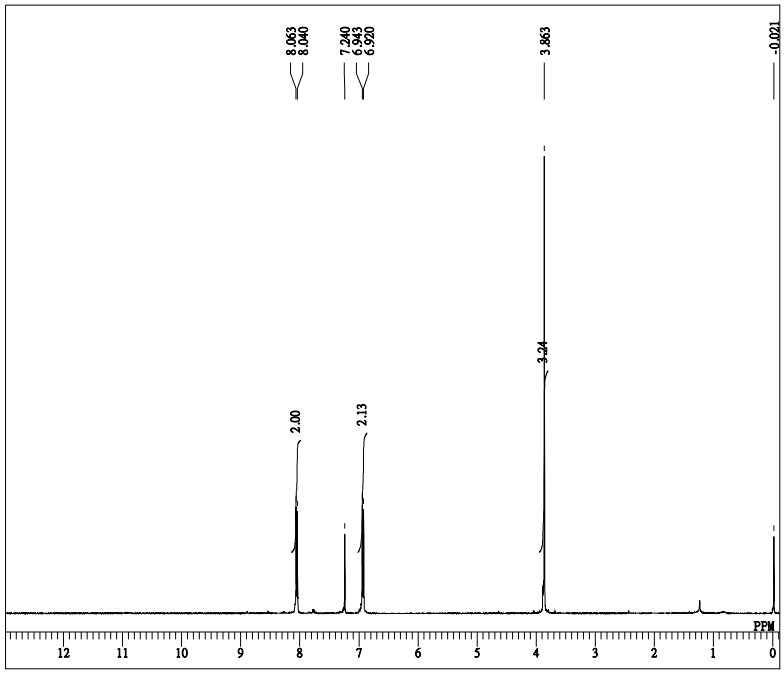
4-(1-Hydroxyethyl)benzoic acid (2v)[12]

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 4.97 (q, *J* = 6.4 Hz, 1H), 1.50 (d, *J* = 6.4 Hz, 3H).

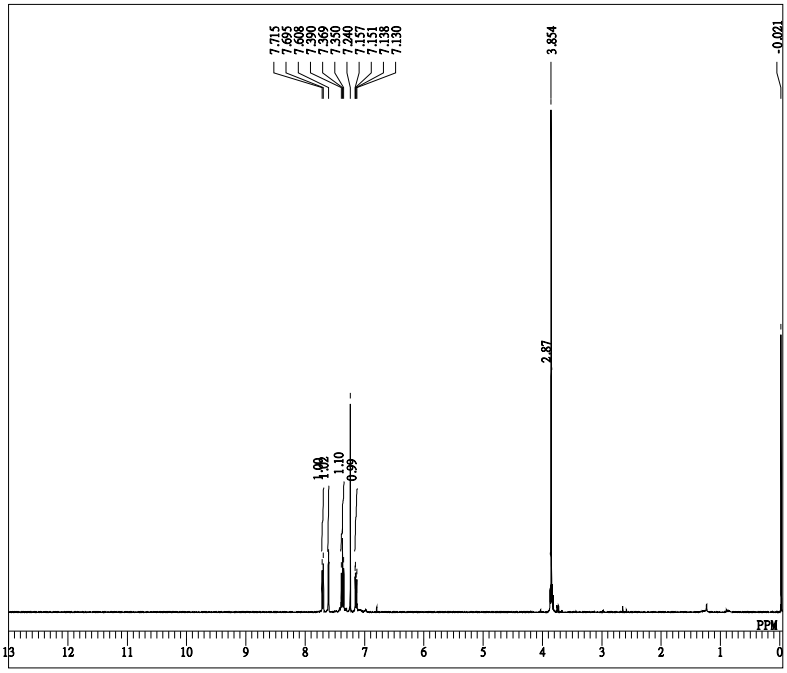
Rhodamine-hydroxamic acid ^{1}H NMR



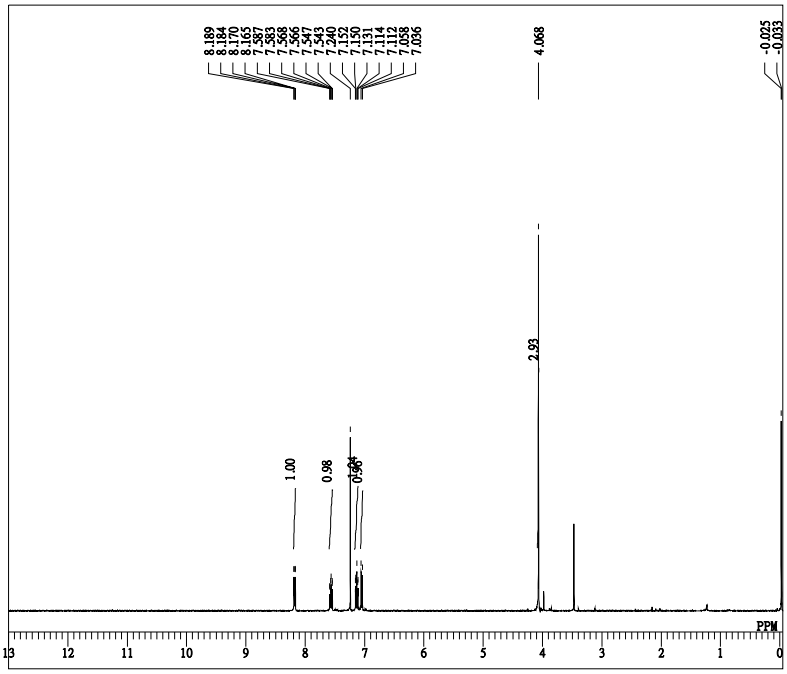
2a ^{1}H NMR



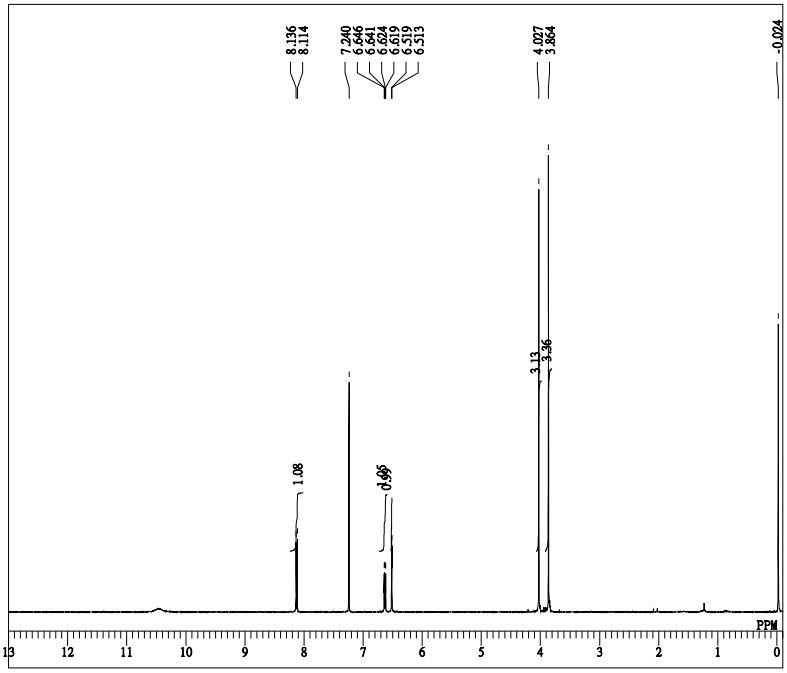
2b ^{1}H NMR



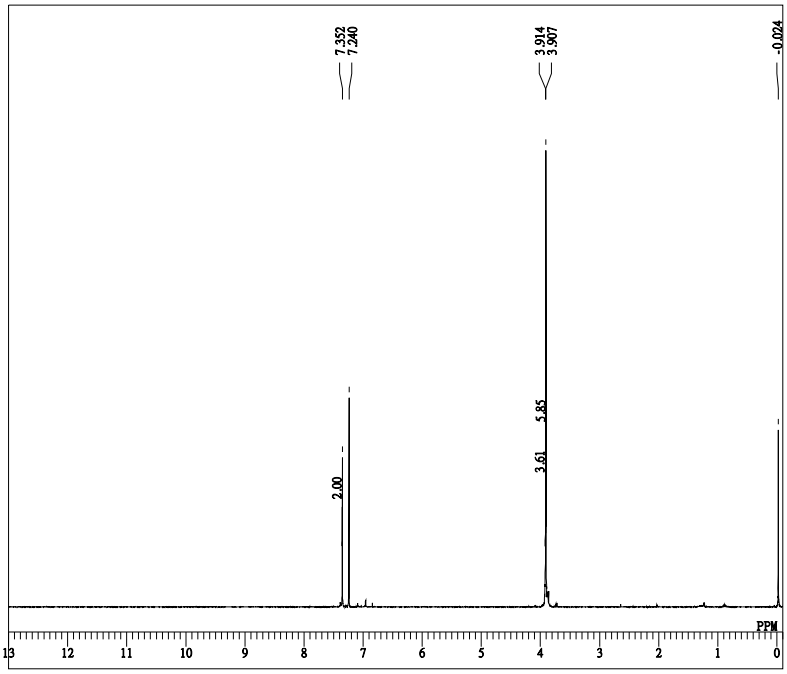
2c ^{1}H NMR



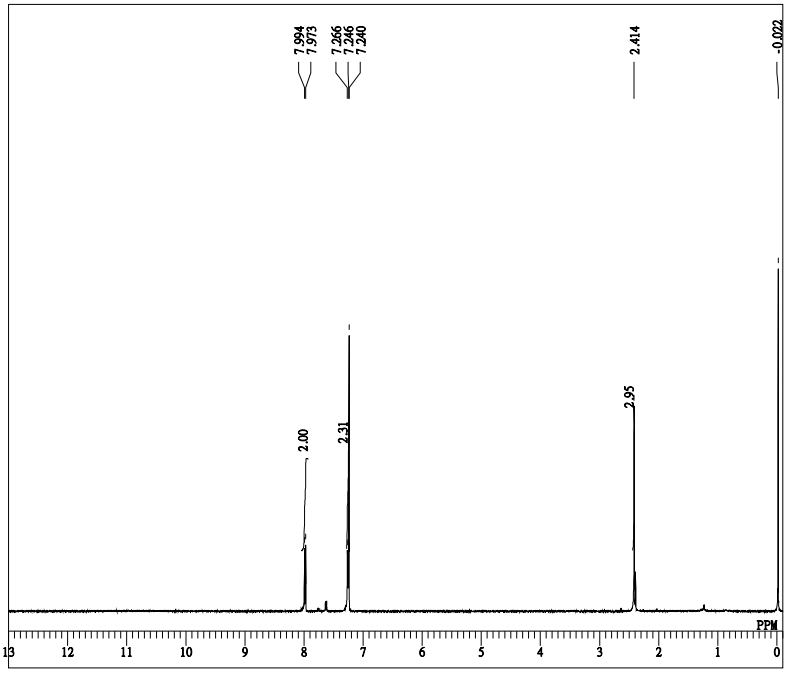
2d ^{1}H NMR



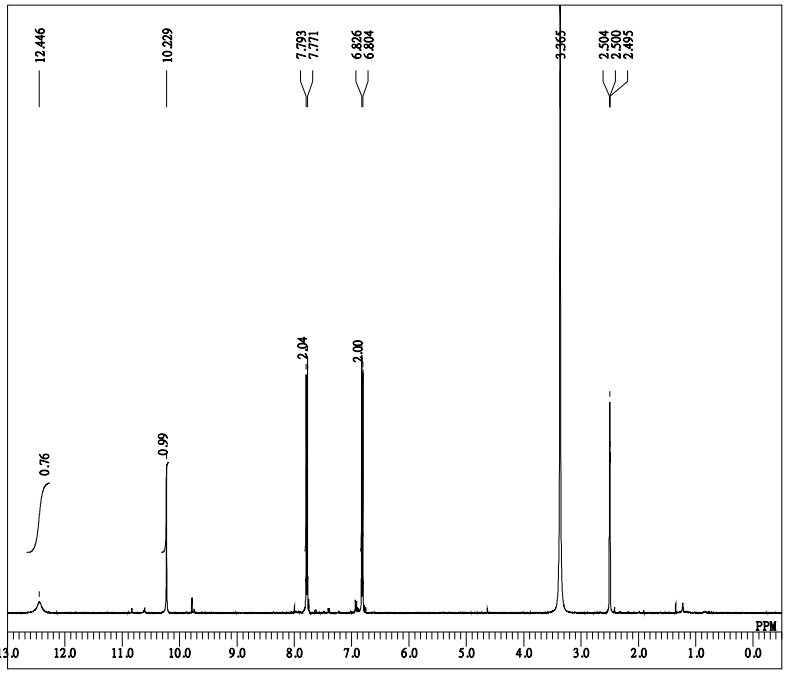
2e ^{1}H NMR



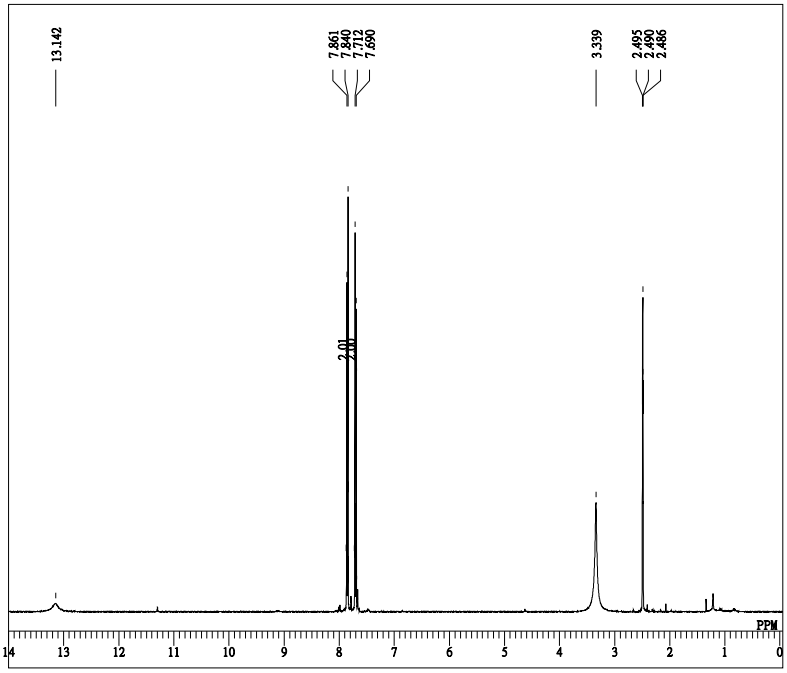
2f ^{1}H NMR



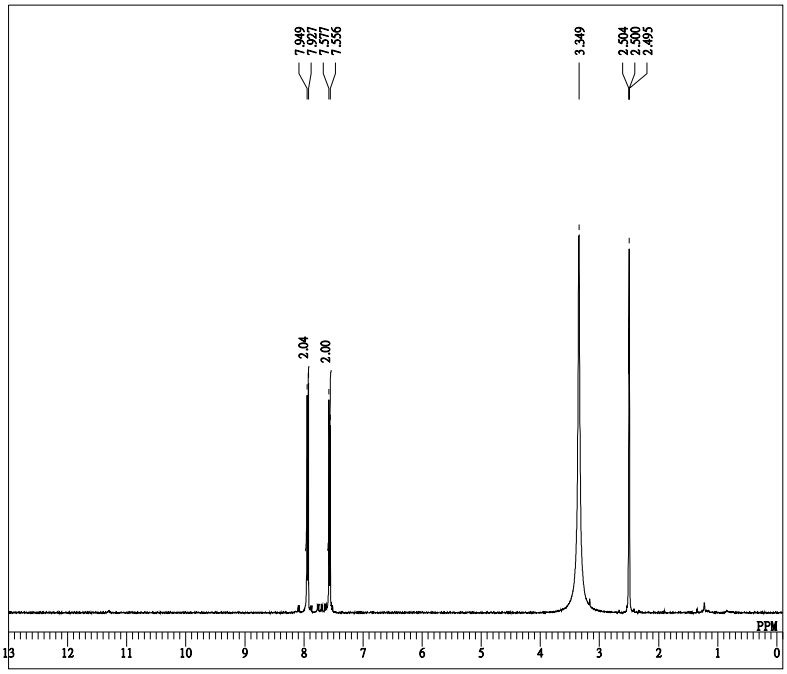
2g ^{1}H NMR



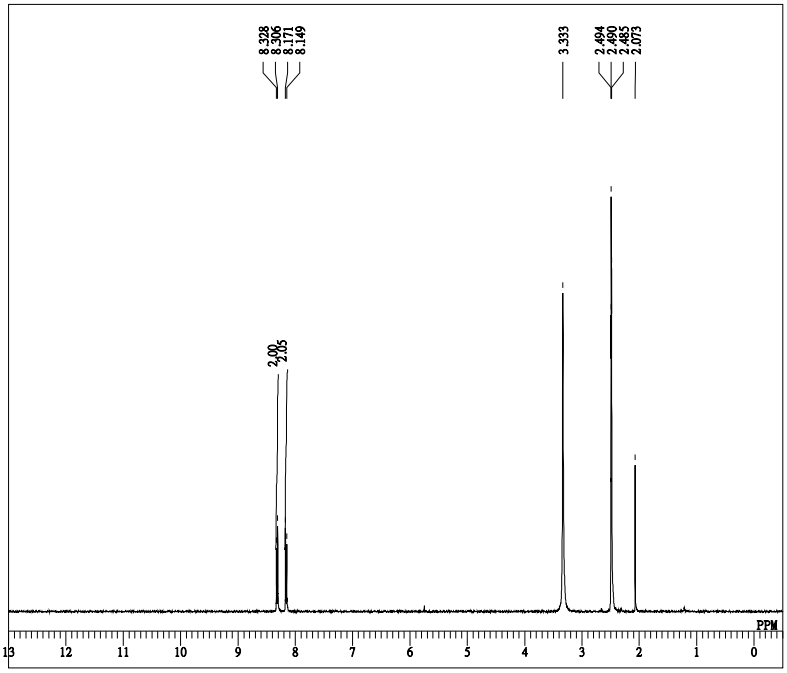
2h ^{1}H NMR



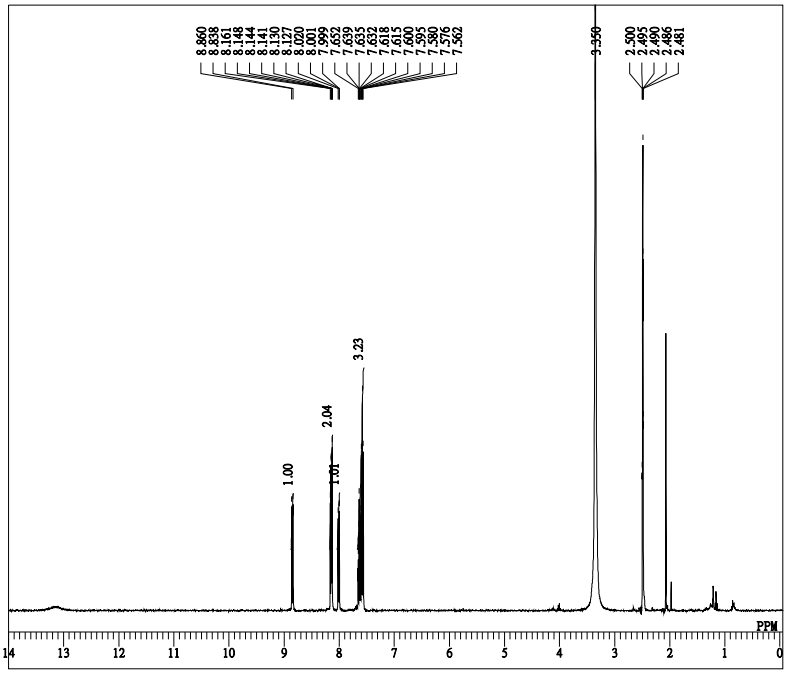
2i ^{1}H NMR



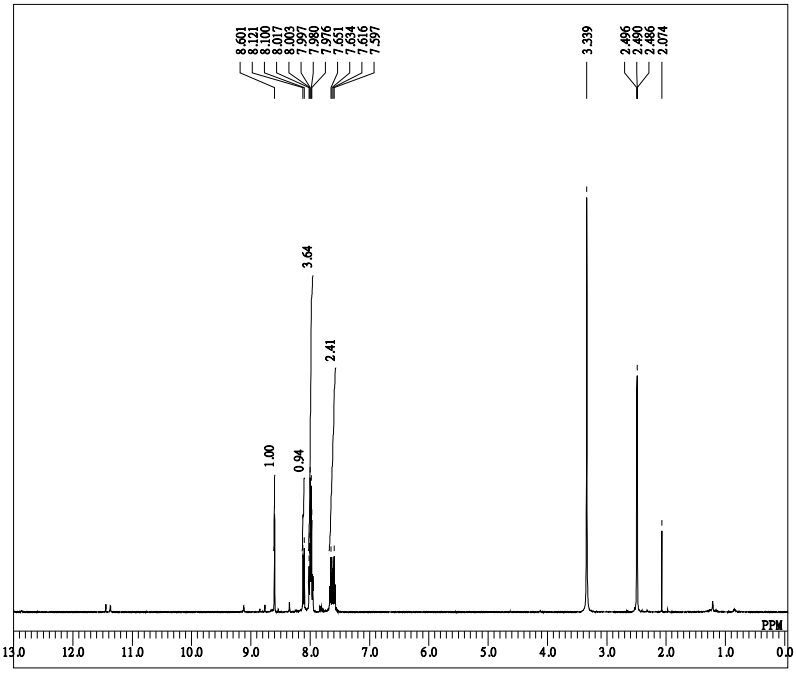
2j ^{1}H NMR



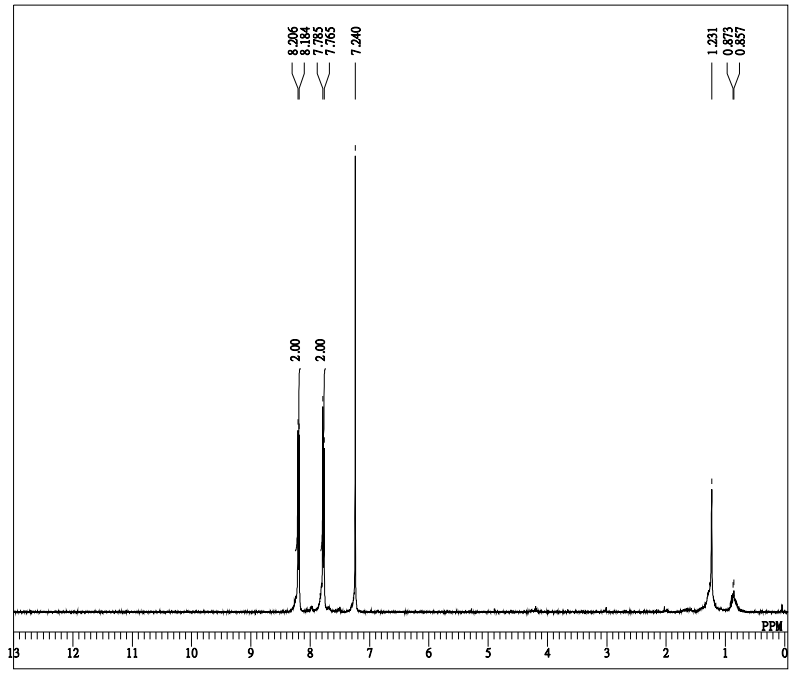
2k ^{1}H NMR



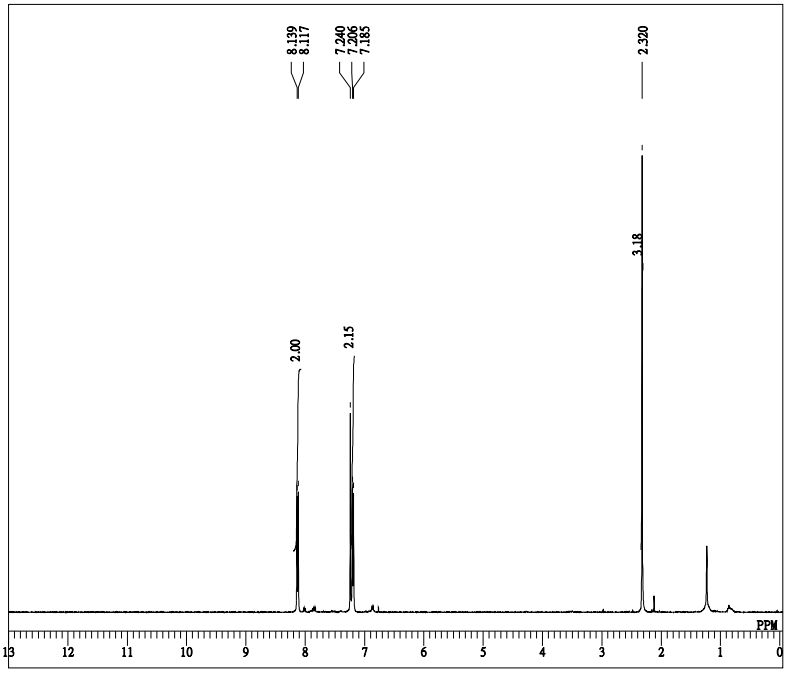
2l ^{1}H NMR



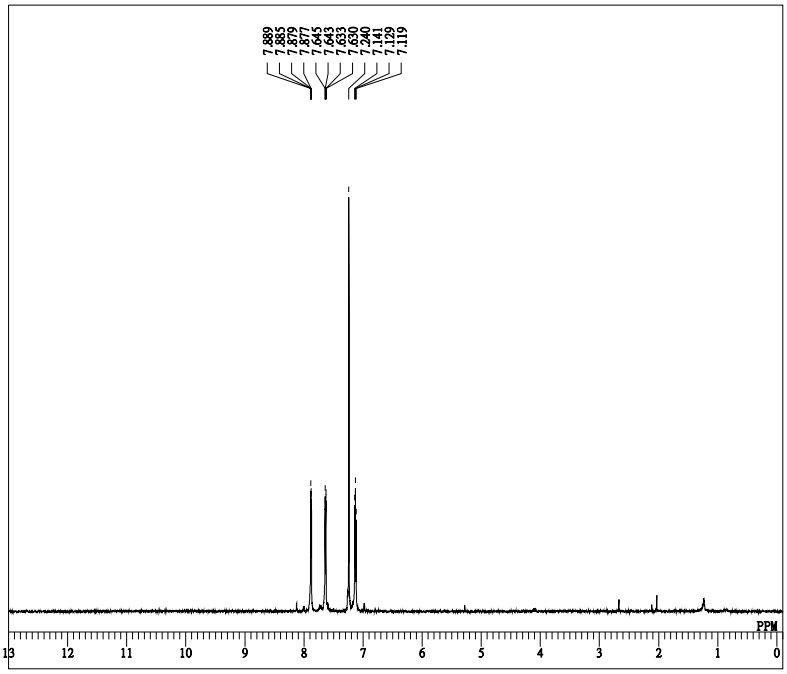
2m ^{1}H NMR



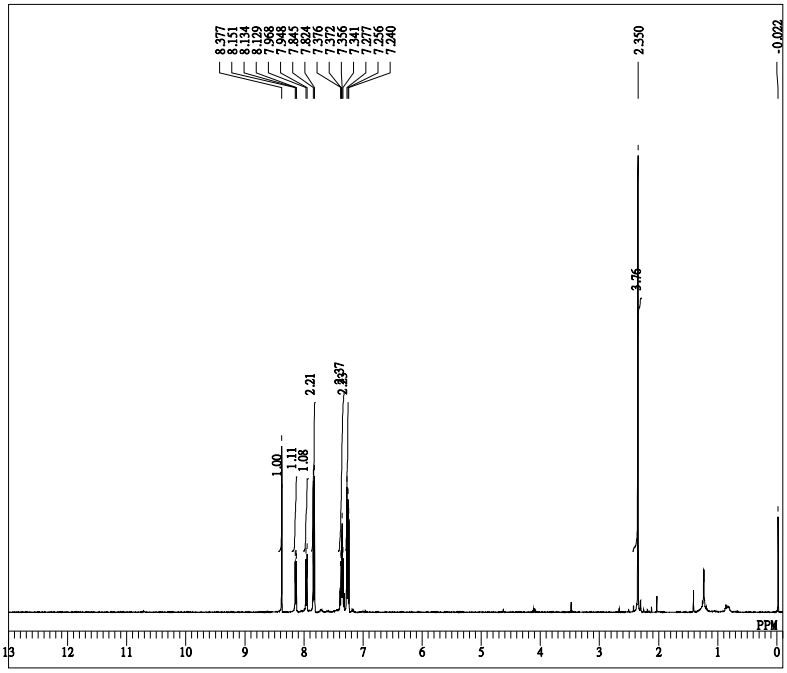
2n ^{1}H NMR



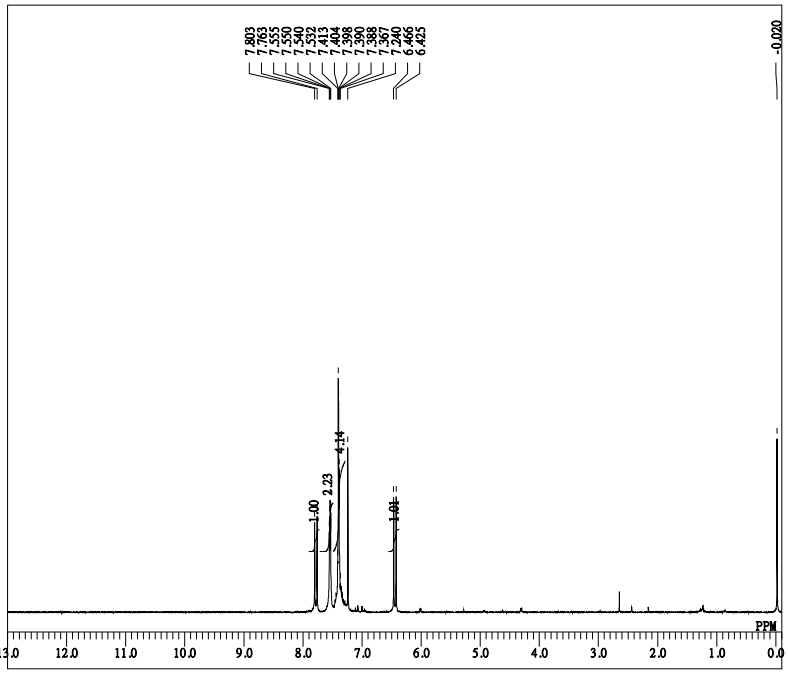
2o ^{1}H NMR



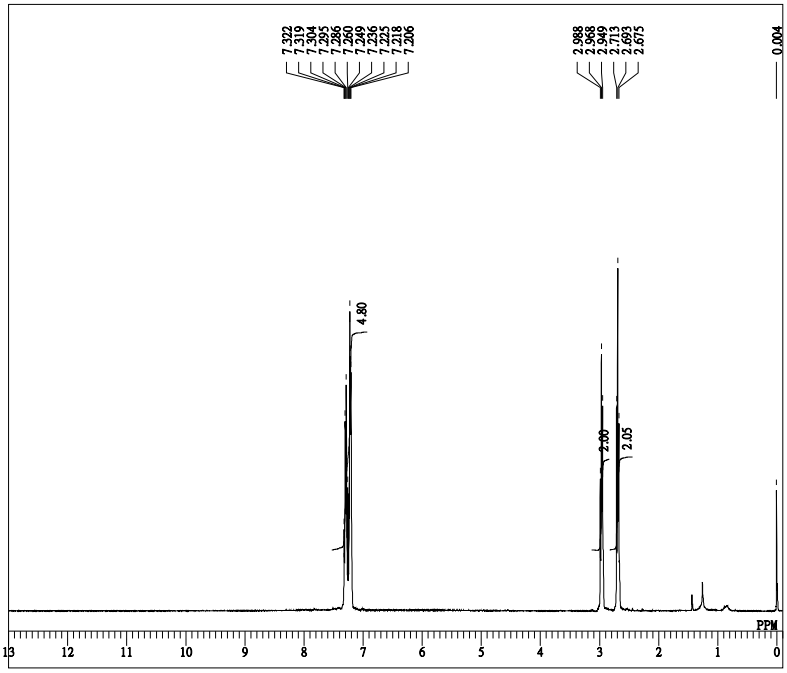
2p ^{1}H NMR



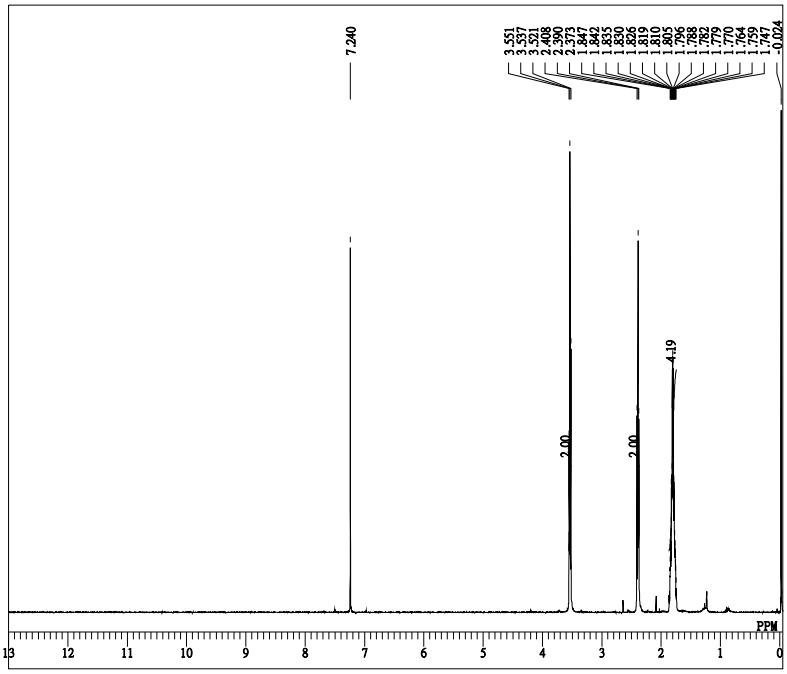
2q ^{1}H NMR



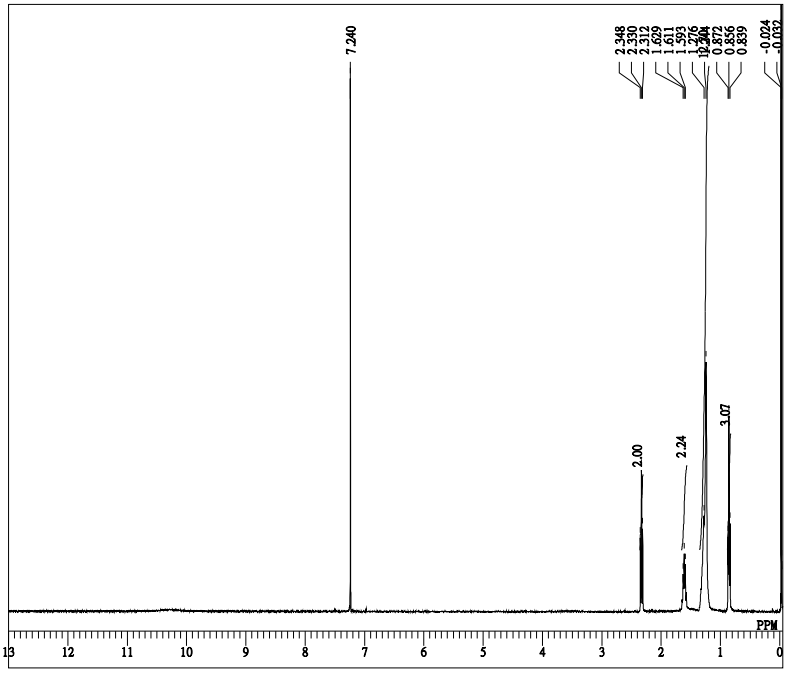
2r ^{1}H NMR



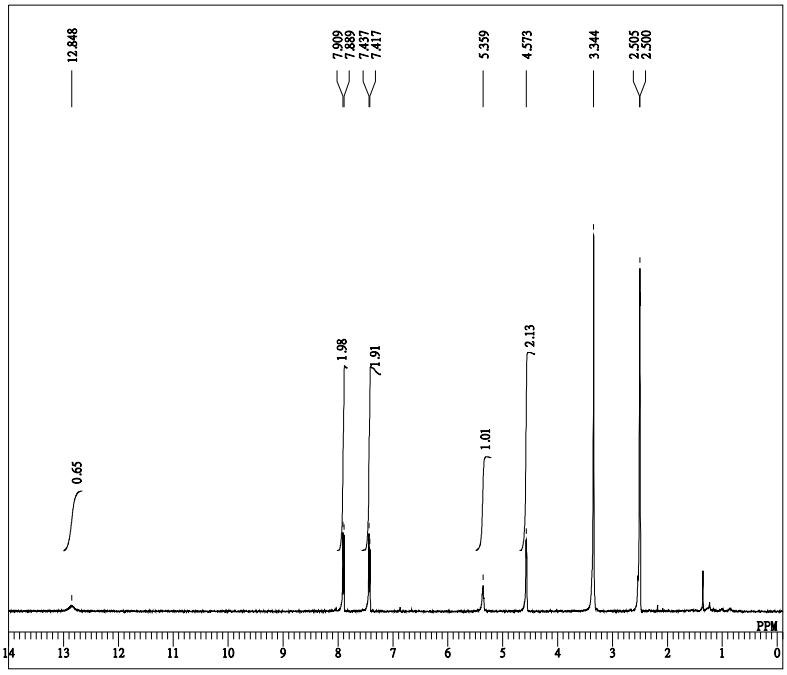
2s ^{1}H NMR



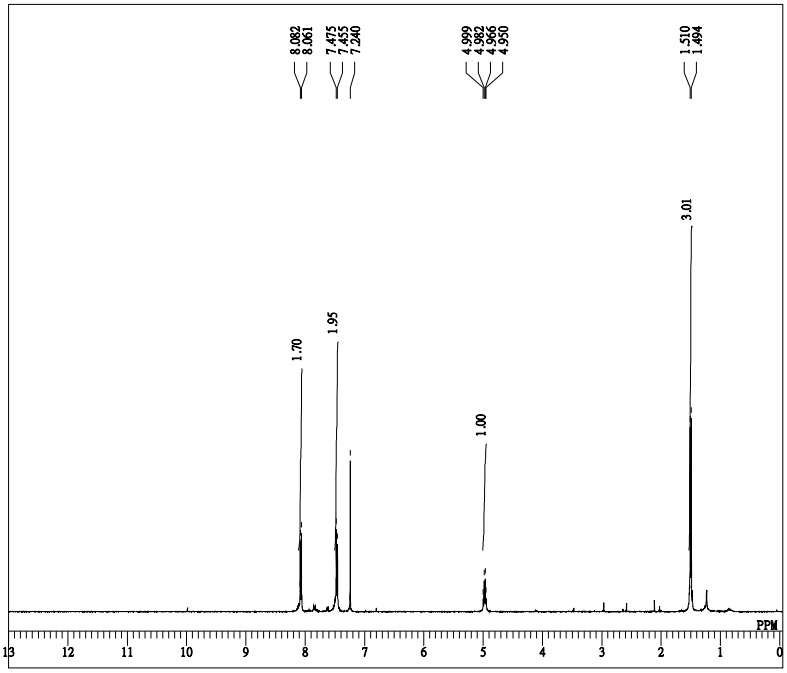
2t ^{1}H NMR



2u ^{1}H NMR



2v ^{1}H NMR


8.082
8.061
7.475
7.455
7.240
4.999
4.982
4.966
4.950
1.510
1.494
3.01
1.95
1.70
1.00
PPM
13
12
11
10
9
8
7
6
5
4
3
2
1
0

References

1. T. Sun, J. O. Moon, M. G. Choi, Y. Cho, S. W. Ham and S. K. Chang, *Sensors Actuators B Chem.*, 2013, **182**, 755.
2. Z.-B. Chen, K. Liu, F.-L. Zhang, Q. Yuan and Y.-M. Zhu, *Org. Biomol. Chem.*, 2017, **15**, 8078
3. A. K. Shil, S. Kumar, C. B. Reddy, S. Dadhwal, V. Thakur and P. Das, *Org. Lett.*, 2015, **17**, 5352.
4. P. Pahari, U. P. Saikia, T. P. Das, C. Damodaran and J. Rohr, *Tetrahedron,* 2016, **72**, 3324.
5. J. N. Moorthy and K. N. Parida, *J. Org. Chem.*, 2014, **79**, 11431.
6. N. Jiang and A. J. Ragauskas, *J. Org. Chem.*, 2007, **72**, 7030.
7. G. J. P. Perry, J. M. Quibell, A. Panigrahi and I. Larrosa, *J. Am. Chem. Soc.*, 2017, **139**, 11527.
8. A. C. Schmidt and C. B. W. Stark, *Org. Lett.*, 2011, **13**, 4164.
9. M. Prashad, Y. Lu, H.-Y. Kim, B. Hu, O. Repic and T. J. Blacklock, *Synth. Commun.*, 1999, **29**, 2937.
10. M. Zeng and S. B. Herzon, *J. Org. Chem.*, 2015, **80**, 8604.
11. M. Trincado, H. Grtzmacher, F. Vizza and C. Bianchini, *Chem. Eur. J.*, 2010, **16**, 2751.
12. C. K. Savile and R. J. Kazlauskas, *J. Am. Chem. Soc.,* 2005, **127**, 12228.