Accepted Manuscript

One-pot Preparation of 2,5-Disubstituted and 2,4,5-Trisubstituted Oxazoles from Aromatic Ketones with Molecular Iodine, Oxone, and Trifluoromethanesulfonic Acid in Nitriles

Sho Imai, Hiroki Kikui, Katsuhiko Moriyama, Hideo Togo

PII: S0040-4020(15)00877-7

DOI: 10.1016/j.tet.2015.06.022

Reference: TET 26857

To appear in: *Tetrahedron*

Received Date: 7 May 2015

Revised Date: 3 June 2015

Accepted Date: 4 June 2015

Please cite this article as: Imai S, Kikui H, Moriyama K, Togo H, One-pot Preparation of 2,5-Disubstituted and 2,4,5-Trisubstituted Oxazoles from Aromatic Ketones with Molecular Iodine, Oxone, and Trifluoromethanesulfonic Acid in Nitriles, Tetrahedron (2015), doi: 10.1016/j.tet.2015.06.022.

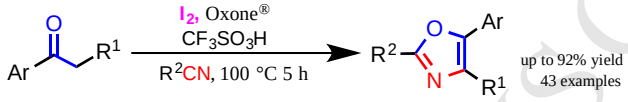
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

One-pot Preparation of 2,5-Disubstituted and 2,4,5-Trisubstituted Oxazoles from Aromatic Ketones with Iodine, Oxone, and Trifluoromethanesulfonic Acid in Nitriles

Leave this area blank for abstract info.

Sho Imai, Hiroki Kikui, Katsuhiko Moriyama, and Hideo Togo*
Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522 Japan



Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-$O_2NC_6H_4$, *etc.*
R^1 = H, CH_3, CH_3CH_2, $CH_3(CH_2)_2$, $CH_3(CH_2)_5$, $CH_3(CH_2)_7$, $CH_3(CH_2)_9$
R^2 = CH_3, CH_3CH_2, $CH_3CH_2CH_2$, $(CH_3)_2CH$, Ph

Pergamon

TETRAHEDRON

One-pot Preparation of 2,5-Disubstituted and 2,4,5-Trisubstituted Oxazoles from Aromatic Ketones with Molecular Iodine, Oxone, and Trifluoromethanesulfonic Acid in Nitriles

Sho Imai, Hiroki Kikui, Katsuhiko Moriyama, and Hideo Togo*

Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522 Japan

Abstract—Alkyl aryl ketones were successfully converted into the corresponding 2,5-disubstituted and 2,4,5-trisubstituted oxazoles in good to moderate yields in a one-pot manner, utilizing iodine, Oxone®, and trifluoromethanesulfonic acid in nitriles under transition-metal-free conditions. The present method could be used for the preparation of Oxaprozin from benzyl phenyl ketone and succinonitrile. A possible reaction mechanism was proposed in which the key intermediates were α-iodoalkyl aryl ketones and α-iodosylalkyl aryl ketones.

Keywords: Ketone, Molecular Iodine, Oxazole, Nitrile, One-Pot Reaction

* Corresponding author. Tel.: 81-43-290-2792; fax:81-43-290-2792; e-mail: togo@faculty.chiba-u.jp..

1. Introduction

Oxazoles are one of the most important heterocyclic compounds, as the oxazole unit is found in many natural products,[1] and many biologically active compounds bearing an oxazole unit,[2] *i.e.*, Inthomycin C (antineoplastic),[2j] Oxaprozin (anti-inflammatory),[2k] Bengazole A (antibiotic),[2l] *etc*., are known. They can be also used as versatile synthetic intermediates.[3] Therefore, many methods for the synthesis of oxazoles have been developed, although most invole multi-step reactions and/or require harsh reaction conditions.[4] For example, the intramolecular dehydration of α-acylaminoketones,[5] the Rh-catalyzed reaction of α-diazo-β-ketocarbonyl compounds with nitriles or amides,[6] the cyclization of *N*-propargylamides,[7] the copper/iodine-catalyzed tandem oxidative cyclization of vinyl halides and amides,[8] the aza-Wittig reaction of iminophosphoranes bearing on acyl group at α-position with acyl chlorides,[9] the reaction of α-bromoketones and amides,[10] and the Au-catalyzed reaction of alkynes and nitriles[11] were reported. Studies on the direct preparation of oxazoles from easily available compounds have continued actively, examples of which are the preparation of 2,4,5-trisubstituted oxazoles from diethyl *trans*-2-aryl-3-nitrocyclopropane-1,1-dicarboxylates and nitriles in the presence of $SnCl_4$ in 1,2-dichloroethane at room temperature,[12a] the preparation of 2,5-diaryloxazoles from chalcone and benzylic amines in toluene in the presence of $CuBr_2$ and pyridine under oxygen atmosphere at 110 °C,[12b] the preparation of 2,5-diaryloxazoles bearing an amide group at 4-position from *N*-acyl-2-bromoenamides in the presence of CuI in 1,4-dioxane at 80 °C,[12c] the preparation of 2,5-diaryloxazoles bearing an ester group at 4-position from 3-arylpropargyl ester and benzylic amines in the presence of $Pd(CH_3CN)_2Cl_2$ and $CuBr_2$ in DMSO at 100 °C under air,[12d] and the preparation of 2,4-disubstituted and 2,4,5-trisubstituted oxazoles from α-bromoketones and amides in the presence of silver trifluoromethanesulfonate in ethyl acetate at 50 °C.[12e] As recent reports of the transition-metal-free preparation of oxazoles include the preparation of 2,5-disubstituted oxazoles by the reaction of aryl methyl ketones and primary benzylic amines with molecular iodine in DMSO at 100 °C,[13a] the preparation of 2,4,5-trisubstituted oxazoles by the reaction of 1,3-diynes and nitriles in the presence of cesium hydroxide in dioxane at 100 °C,[13b] and the preparation of 2,4,5-trisubstituted oxazoles by the reaction of 1,3-diynes with *N*,*O*-bis(trimethylsilyl)acetamide in the presence of *t*-BuOK at 120 °C.[13c]

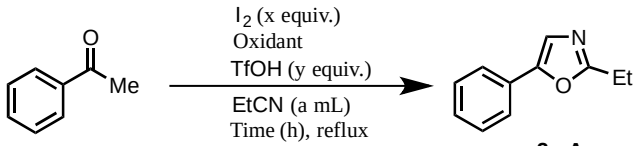
Despite the emergence of a number of reports, new synthetic methods for the direct preparation of oxazoles from easily available or commercially available compounds are highly required.

The preparation of oxazoles from easily available ketones and nitriles under transition-metal-free conditions is very attractive in view of process chemistry. Here, as part of our basic study of molecular iodine for organic synthesis,[14] and of our recent report of the preparation of α-sulfonyloxyketones from alkyl aryl ketones, sulfonic acids, molecular iodine, and Oxone®,[14u] we would like to report a one-pot transformation of alkyl aryl ketones into the corresponding 2,5-disubstituted and 2,4,5-trisubstituted oxazoles with molecular iodine, Oxone®, and TfOH (trifluoromethanesulfonic acid) in nitrile solvents.

2. Results and Discussion

To a solution of acetophenone **1a** in propionitrile (6 mL) were added aq. H_2O_2 (ca 30%, 1.1 equiv.), *m*CPBA (1.1 equiv.) or Oxone® (1.1 equiv.), and molecular iodine (0.7 equiv.) and TfOH (8.0 equiv.), and the reaction mixture was stirred for 5 h under refluxing conditions to provide corresponding oxazole **2a-A** in low yields (entries 1, 2, and 4). The results indicated that Oxone® was the most effective oxidant, and that corresponding oxazole **2a-A** was not formed at all in the absence of an oxidant (entry 3). Then, various reactions with Oxone® were performed in an attempt to increase the yield of oxazole **2a-A**. By changing the amounts of TfOH and molecular iodine, and the reaction time (entries 5~21), it was found that the treatment of acetophenone **1a** with molecular iodine (0.7 equiv.), Oxone® (1.1 equiv.), and TfOH (8.0 equiv.) for 5 h under refluxing conditions provided oxazole **2a-A** in 61% yield (entry 9). Reducing the amounts of molecular iodine and propionitrile decreased the yield of the oxazole, and the use of TsOH or MsOH instead of TfOH also gave oxazole **2a-A** in extremely poor yields (< 2% yield). When a mixed solvent of propionitrile (3 mL or 2 mL) and 1,2-dichloropropane (3 mL or 4 mL) was used under the same reaction conditions, the yield of oxazole **2a-A** was also decreased (entries 22 and 23).

Table 1. Preparation of 2-Ethyl-5-phenyloxazole with Acetophenone, Molecular Iodine, Oxone®, and TfOH in Propionitrile



1a 1.0 mmol **2a-A**

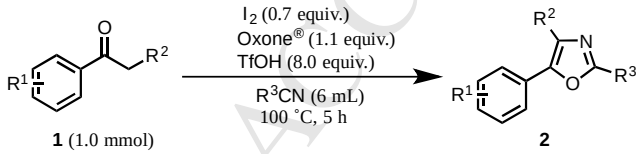
Entry	x (equiv.)	y (equiv.)	Oxidant (equiv.)	a (mL)	Time (h)	Yield[a] (%)
1	0.7	8.0	aq.H_2O_2 (1.1)	6.0	5	8
2	0.7	8.0	*m*CPBA (1.1)	6.0	5	19
3	0.7	8.0	-	6.0	5	0
4[b]	0.7	8.0	Oxone® (1.1)	6.0	2	37
5	0.7	6.0	Oxone® (1.1)	6.0	2	52
6	0.7	6.0	Oxone® (1.1)	6.0	3	52

7	0.7	6.0	Oxone® (1.1)	6.0	4	50
8	0.7	6.0	Oxone® (1.1)	6.0	5	54
9	0.7	8.0	Oxone® (1.1)	6.0	5	61
10	0.7	1.0	Oxone® (1.1)	6.0	5	3
11	0.7	10.0	Oxone® (1.1)	6.0	5	49
12	0.7	8.0	Oxone® (1.5)	6.0	5	51
13	0.7	8.0	Oxone® (2.0)	6.0	2	24
14	0.5	8.0	Oxone® (1.1)	6.0	5	55
15	0.6	8.0	Oxone® (1.1)	6.0	5	60
16	1.0	6.0	Oxone® (1.1)	6.0	3	30
17	0.2	6.0	Oxone® (1.1)	6.0	3	35
18	0.2	6.0	Oxone® (2.0)	6.0	3	29
19	0.7	6.0	Oxone® (1.1)	6.0	3	34
20	0.7	6.0	Oxone® (1.1)	6.0	3	39
21	0.7	6.0	Oxone® (1.1)	6.0	3	22
22	0.7	8.0	Oxone® (1.1)	3.0[c]	5	29
23	0.7	8.0	Oxone® (1.1)	2.0[d]	5	26

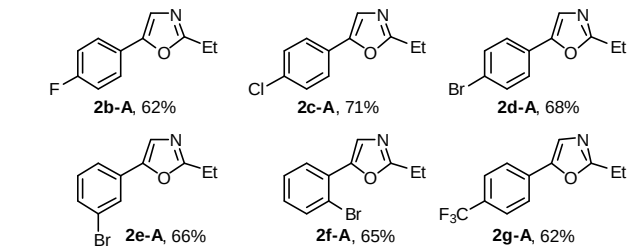
[a] Isolated yield [b] Reaction was carried out at 80 ºC. [c] 1,2-Dichloropropane (3.0 mL) was added. [d] 1,2-Dichloropropane (4.0 mL) was added.

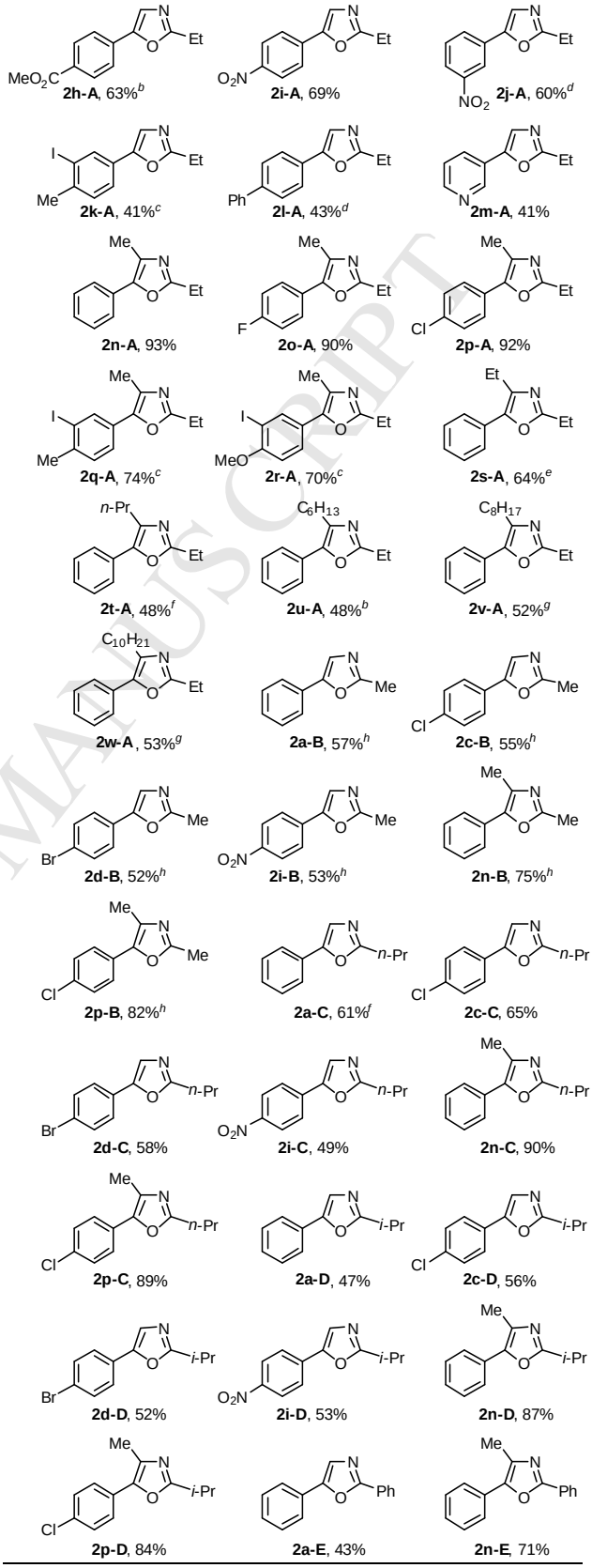
Based on the optimum reaction conditions, various substituted acetophenone derivatives **1** were treated with molecular iodine (0.7 equiv.), Oxone® (1.1 equiv.), and TfOH (8.0 equiv.) in propionitrile under refluxing

Table 2 Preparation of 2,5-Disubstituted and 2,4,5-Trisubstutited Oxazoles with Alkyl Aryl Ketones, Molecular Iodine, Oxone®, and TfOH in Nitriles



product, yield (%)[a]



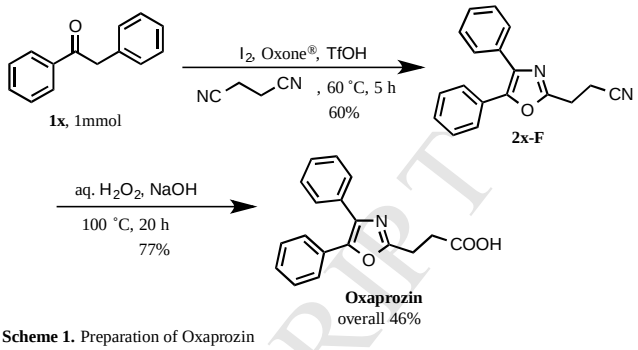


[a] isolated yield. [b] I_2 (0.7 equiv.), Oxone® (1.5 equiv.) and TfOH (10 equiv.) were used. [c] I_2 (3.0 equiv.), Oxone® (2.0 equiv.) and TfOH (12 equiv.) were used. [d] I_2 (1.0 euivq.) and Oxone® (1.5 equiv.) were used. [e] I_2 (0.7 equiv.) and Oxone® (1.7 equiv.) were used. [f] I_2 (0.7 equiv.) and Oxone® (1.5 equiv.) were used. [g] I_2 (1.0 equiv.), Oxone® (2.0 equiv.) and TfOH (10 equiv.) were used. [h] Reaction was carried out at 80 ºC.

conditions, and the results are shown in Table 2.

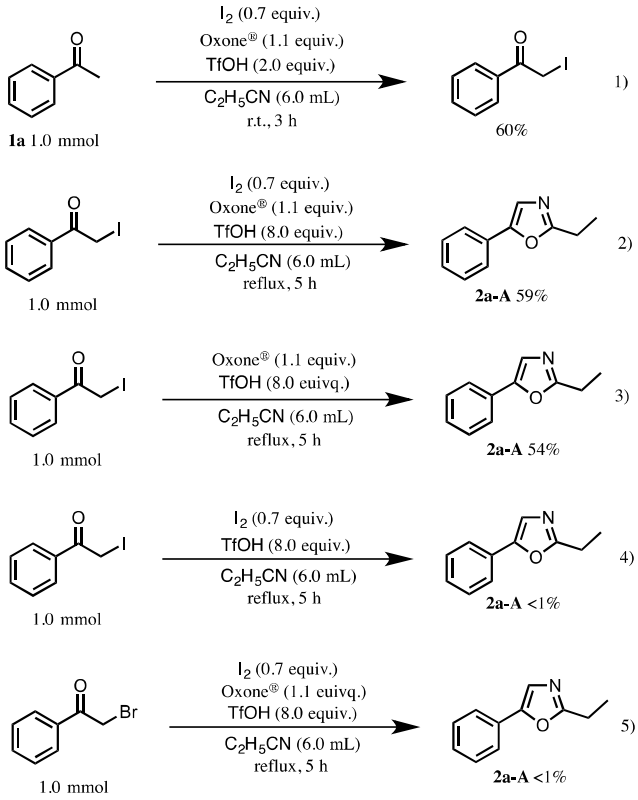
Treatment of *p*-fluoroacetophenone **1b**, *p*-chloroacetophenone **1c**, *p*-bromoacetophenone **1d**, *m*-bromoacetophenone **1e**, *o*-bromoacetophenone **1f**, *p*-(trifluoromethyl)acetophenone **1g**, *p*-(ethoxycarbonyl)acetophenone **1h**, *p*-nitroacetophenone **1i**, and *m*-nitroacetophenone **1j** under the same conditions provided corresponding 2,5-disubstituted oxazoles **2b-A**~**2j-A** in good yields, respectively. However, the same treatment of *p*-methylacetophenone **1k**, *p*-phenylacetophenone **1l**, and *m*-acetylpyridine **1m** gave corresponding 2,5-disubstituted oxazoles **2k-A**~**2m-A** in moderate yields, respectively, and the *p*-methylphenyl group in compound **2k-A** was iodinated. On the other hand, the same treatment of propiophenone **1n**, *p*-fluoropropiophenone **1o**, and *p*-chloropropiophenone **1p** with molecular iodine, Oxone®, and TfOH in propionitrile under refluxing conditions provided corresponding 2-ethyl-4-methyl-5-aryloxazoles **2n-A**~**2p-A** in good yields, respectively. When *p*-methylpropiophenone **1q** and *p*-methoxypropiophenone **1r** were subjected to the same procedure and conditions using excess amounts of molecular iodine and Oxone®, the iodinated 2-ethyl-4-methyl-5-aryloxazoles **2q-A** and **2r-A** were obtained in good yields, respectively, due to the iodination of the electron-rich aromatic ring. When butyrophenone **1s**, pentanophenone **1t**, octanophenone **1u**, decanophenone **1v**, and dodecanophenone **1w** were used as substrates under the same conditions, corresponding oxazoles **2s-A**~**2w-A** were obtained in moderate yields. The reason for the moderate yields of the oxazoles may be the steric hindrance caused by the long alkyl side chain groups. Then, the solvent was changed to acetonitrile, and the same treatment of acetophenone **1a**, *p*-chloroacetophenone **1c**, *p*-bromoacetophenone **1d**, *p*-nitroacetophenone **1i**, propiophenone **1n**, and *p*-chloropropiophenone **1p** under refluxing conditions provided corresponding 2,5-disubstituted and 2,4,5-trisubstituted oxazoles **2a-B**, **2c-B**, **2d-B**, **2i-B**, **2n-B**, and **2p-B** in moderate to good yields, respectively. Moreover, when butyronitrile and isobutyronitrile were used with acetophenone **1a**, *p*-chloroacetophenone **1c**, *p*-bromoacetophenone **1d**, *p*-nitroacetophenone **1i**, propiophenone **1n** and *p*-chloropropiophenone **1p** under same reaction conditions at 100 °C, corresponding 2-propyl-5-aryloxazoles (**2a-C**, **2c-C**, **2d-C**, and **2i-C**), 2-propyl-4-methyl-5-aryloxazoles (**2n-C** and **2p-C)**, 2-isopropyl-5-aryloxazoles (**2a-D**, **2c-D**, **2d-D**, and **2i-D**), and 2-isopropyl-4-methyl-5-aryloxazoles **(2n-D** and **2p-D**), were obtained in moderate to good yields, respectively. Finally, when benzonitrile was used as the nitrile and the same procedure was applied to acetophenone **1a** and propiophenone **1n** at 100 °C, corresponding 2,5-diphenyloxazole **2a-E** and 2,5-diphenyl-3-methylphenyloxazole **2n-E** were obtained in moderate to good yields, respectively.

As a synthetic use of the present method, Oxaprozin was prepared in 2 steps in 46% overall yield from benzyl phenyl ketone **1x**, as shown in Scheme 1. Moreover, as a semi-large-scale reaction, when benzyl phenyl ketone **1x** (10 mmol) was used as the substrate, Oxaprozin was obtained in 45% overall yield.



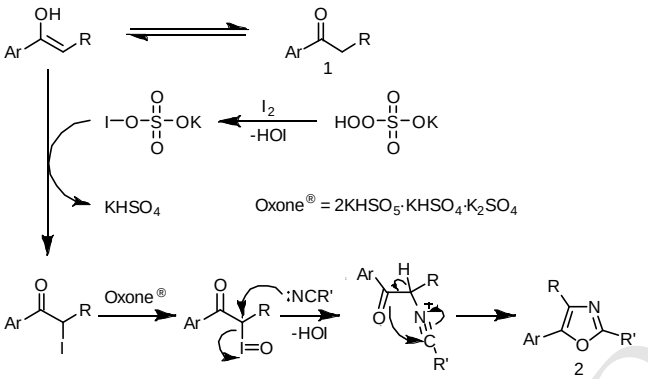
Scheme 1. Preparation of Oxaprozin

To elucidate the reaction mechanism, the present reaction with acetophenone **1a**, molecular iodine, Oxone®, and TfOH in propionitrile was carried out at room temperature, not refluxing conditions, to give α-iodoacetophenone in 60% yield, as shown in eq. 1. When α-iodoacetophenone was treated with molecular iodine, Oxone®, and TfOH in propionitrile under refluxing conditions, 2-ethyl-5-phenyloxazole **2a-A** was obtained in 59% yield (eq. 2). Moreover, refluxing treatment of α-iodoacetophenone with Oxone® and TfOH in propionitrile without molecular iodine provided 2-ethyl-5-phenyloxazole **2a-A** in 54% yield (eq. 3). On the other hand, treatment of α-iodoacetophenone with molecular iodine and TfOH without Oxone® did not give 2-ethyl-5-phenyloxazole **2a-A** (eq. 4). To clarify the specific character of iodine, α-bromoacetophenone was



treated with molecular iodine, Oxone®, and TfOH in propionitrile under refluxing conditions. However, 2-ethyl-5-phenyloxazole **2a-A** was not obtained (eq. 5). Based on those blank experiments, we conclude that molecular iodine plays an important role in this reaction. However, it does not work as a catalyst, as shown in Table 1.

Today, it is well known that Oxone® is a powerful oxidant; iodoarenes and perfluoroiodoalkanes (monovalent iodine)[15] are oxidized into trivalent iodine species by Oxone®. Therefore, we believe that the present oxazole **2** formation reaction proceeds through the α-iodination of the enol form of ketone **1** with a hypoiodite–sulfate species (*i.e.*, $IOSO_3$–). That is formed by the reaction of molecular iodine with Oxone®. Once the α-iodoketone is formed, it is smoothly oxidized into an α-iodosylketone, a very reactive intermediate, which reacts rapidly with the nitriles to produce corresponding oxazoles **2**, as shown in Scheme 2.



Scheme 2 Plausible Reaction Pathway

3. Conclusion

In conclusion, 2,5-disubstituted and 2,4,5-trisubstituted oxazoles have been prepared in moderate to good yields via the reactions of alkyl aryl ketones with Oxone® and TfOH in the presence of molecular iodine in acetonitrile, propionitrile, butyronitrile, isobutyronitrile, and benzonitrile. We believe that the present method for the preparation of oxazoles is very useful because of its simplicity, and may open new possibilities in the reactions of alkyl iodides with Oxone®.

4. Experimental

4.1. General. ^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400, JEOL-JNM-ECS400, and JEOL-JNM-ECA500 spectrometers. Chemical shifts are expressed in ppm downfield from TMS in δ units. Mass spectra were recorded on JMS-T100GCV, JMS-HX110, and Thermo LTQ Orbitrap XL spectrometers. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography.

4.2 Typical Procedure for Preparation of 2-Ethyl-5-phenyloxazole 2a-A: To a solution of acetophenone **1a** (120 mg, 1 mmol) in CH_3CH_2CN (6 mL) were added TfOH (0.70 mL, 8 mmol), molecular iodine (178 mg, 0.7 mmol), and Oxone® (676 mg, 1.1 mmol). The mixture was stirred for 5 h at 100 °C under an Ar atmosphere. After the reaction, the reaction mixture was poured into a sat. aq Na_2SO_3 and sat. aq $NaHCO_3$ solution, and extracted with EtOAc (3 × 30 mL). The organic layer was dried over Na_2SO_4. After being filtration and removal of the solvent under reduced pressure, the residue was purified by short flash column chromatography on silica gel (EtOAc–hexane, 1:4) to give 2-ethyl-5-phenyloxazole **2a-A** in 61% yield.

4.3 Typical Procedure for Preparation of Oxaprozin: To a solution of benzyl phenyl ketone **1x** (196 mg, 1 mmol) in succinonitrile (6 mL) were added TfOH (0.35 mL, 4 mmol), molecular iodine (178 mg, 0.7 mmol), and Oxone® (676 mg, 1.1 mmol). The mixture was stirred for 5 h at 60 °C under an Ar atmosphere. After the reaction, the reaction mixture was poured into a sat. aq Na_2SO_3 and sat. aq $NaHCO_3$ solution, and extracted with EtOAc (3 × 30 mL). The organic layer was dried over Na_2SO_4. After being filtration and removal of the solvent under reduced pressure, the residue was purified by short flash column chromatography on silica gel (EtOAc–hexane, 1:4) to give 2-cyanoethyl-4,5-diphenyloxazole **2x-E** in 60% yield. Then, **2x-E** (55 mg, 0.2 mmol) in 1,4-dioxane (1 mL) was added to a mixture of 4 M NaOH (2 mL) and aq. H_2O_2 (concentration: 30.0-35.5 %, 1 mL). The mixture was stirred for 20 h at 100 °C under an Ar atmosphere. After cooling to room temperature, the reaction mixture was diluted with 1 M HCl (20 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was dried over Na_2SO_4. After being filtration and removal of the solvent under reduced pressure, the residue was purified by short flash column chromatography on silica gel (EtOAc–hexane, 1:2) to give Oxaprozin in 77% yield.

2-Ethyl-5-phenyloxazole 2a-A
Oil. IR (neat): 2980, 1557, 1489, 1448, 1132, 759, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.6 Hz, 3 H), 2.86 (q, *J* = 7.6 Hz, 2 H), 7.22 (s, 1 H), 7.30 (tt, *J* = 7.6 and 1.4 Hz, 1 H), 7.40 (dd, *J* = 8.0 and 7.6 Hz, 2 H), 7.61 (dd, *J* = 1.4, 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 150.8, 128.8, 128.2, 128.0, 123.9, 121.7, 21.8, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{12}ON$ = 174.0913, Found = 174.0914.

2-Ethyl-5-(4'-fluorophenyl)oxazole 2b-A
Oil. IR (neat): 2981, 1571, 1509, 1233, 1028, 834, 597 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.4 Hz, 3 H), 2.85 (q, *J* = 7.4 Hz, 2 H), 7.06-7.12 (m, 2 H), 7.55-7.60 (m, 2 H), 7.15 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 162.3 (d, J_{C-F} = 248.0 Hz), 150.0, 125.7 (d, J_{C-F} = 7.6 Hz), 124.5 (d, J_{C-F} = 2.9 Hz), 115.8, 121.3 (d, J_{C-F} = 21.9 Hz), 21.7, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONF$ = 192.1819, Found = 192.0817.

2-Ethyl-5-(4'-chlorophenyl)oxazole 2c-A

Oil. IR (neat): 2981, 1572, 1485, 1133, 1092, 955, 819, 738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.7 Hz, 3 H), 2.85 (q, *J* = 7.7 Hz, 2 H), 7.20 (s, 1 H), 7.37 (d, *J* = 8.5 Hz, 2 H), 7.53 (d, *J* = 8.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 149.9, 133.8, 129.1, 126.7, 125.2, 122.1, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONCl$ = 208.0524, Found = 208.0523.

2-Ethyl-5-(4'-bromophenyl)oxazole 2d-A

Mp 50-51 °C. IR (neat): 2360, 1573, 1481, 1402, 1132, 954, 812 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.8 Hz, 3 H), 2.85 (q, *J* = 7.8 Hz, 2 H), 7.23 (s, 1 H), 7.48 (d, *J* = 8.9 Hz, 2 H), 7.53 (d, *J* = 8.9 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 149.9, 132.0, 127.2, 125.4, 122.2, 121.9, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONBr$ = 252.0019, Found = 252.0016.

2-Ethyl-5-(3'-bromophenyl)oxazole 2e-A

Mp 44-45 °C. IR (neat): 2980, 1582, 1550, 1281, 1133, 957, 780 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.5 Hz, 3 H), 2.86 (q, *J* = 7.5 Hz, 2 H), 7.24 (s, 1 H), 7.27 (t, *J* = 7.9 Hz, 1 H), 7.42 (dt, *J* = 7.9, 0.9 Hz, 1 H), 7.53 (dd, *J* = 7.9, 0.9 Hz, 1 H), 7.76 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 149.4, 130.9, 130.3, 130.1, 126.8, 123.0, 122.7, 122.4, 21.8, 11.1. . HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONBr$ = 252.0019, Found = 252.0016.

2-Ethyl-5-(2'-bromophenyl)oxazole 2f-A

Oil. IR (neat): 2939, 1578, 1551, 1141, 1020, 843, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.6 Hz, 3 H), 2.87 (q, *J* = 7.6 Hz, 2 H), 7.16 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.38 (td, *J* = 7.5, 1.1 Hz, 1 H), 7.66 (dd, *J* = 8.1, 1.1 Hz, 1 H), 7.72-7.76 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 148.4, 134.1, 128.9 (2C), 128.3, 127.5, 126.5, 119.7, 21.7, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONBr$ = 252.0019, Found = 252.0018.

2-Ethyl-5-(4'-trifluoromethylphenyl)oxazole 2g-A

Oil. IR (neat): 2985, 2359, 1621, 1558, 1416, 1043, 956, 798, 594 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, *J* = 7.6 Hz, 3 H), 2.88 (q, *J* = 7.6 Hz, 2 H), 7.33 (s, 1 H), 7.65 (d, *J* = 8.3 Hz, 2 H), 7.72 (d, *J* = 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 149.5, 131.4, 129.7 (q, J_{C-F} = 32.4 Hz), 125.8 (q, J_{C-F} = 3.8 Hz), 123.9, 123.9 (q, J_{C-F} = 271.8 Hz), 123.5, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{11}ONF_3$ = 242.0787, Found = 242.0784.

2-Ethyl-5-(4'-ethoxycarbonylphenyl)oxazole 2h-A

Mp 90-91 °C. IR (neat): 2359, 1717, 1557, 1281, 1111, 957, 829, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, *J* = 7.6 Hz, 3 H), 2.88 (q, *J* = 7.6 Hz, 2 H), 3.93 (s, 3 H), 7.35 (s, 1 H), 7.68 (d, *J* = 8.3 Hz, 2 H), 8.07 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 166.3, 149.9, 132.2, 130.2, 129.3, 123.8, 123.6, 52.2, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{14}O_3N$ = 232.0968, Found = 232.0964.

2-Ethyl-5-(4'-nitrophenyl)oxazole 2i-A

Mp 81-82 °C. IR (neat): 2359, 1684, 1557, 1506, 1327, 1145, 1043, 951, 849, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, *J* = 7.7 Hz, 3 H), 2.90 (q, *J* = 7.7 Hz, 2 H), 7.44 (s, 1 H), 7.76 (d, *J* = 9.0 Hz, 2 H), 8.28 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2, 148.8, 146.9. 133.9, 125.3, 124.4, 124.2, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}O_3N_2$ = 219.0764, Found = 219.0762.

2-Ethyl-5-(3'-nitrophenyl)oxazole 2j-A

Oil. IR (neat): 2359, 1559, 1520, 1346, 1137, 963, 739, 681 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, *J* = 7.7 Hz, 3 H), 2.90 (q, *J* = 7.7 Hz, 2 H), 7.38 (s, 1 H), 7.60 (t, *J* = 7.9 Hz, 1 H), 7.92 (d, *J* = 8.0 Hz, 1 H), 8.13-8.17 (m, 1 H), 8.46 (t, *J* = 1.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 148.6, 148.6, 129.9, 129.8, 129.3, 123.8, 122.4, 118.6, 21.8, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}O_3N_2$ = 219.0764, Found = 219.0760.

2-Ethyl-5-(3'-iodo-4'-methylphenyl)oxazole 2k-A

Oil. IR (neat): 2978, 1562, 1478, 1130, 1028, 957, 879, 812, 671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.6 Hz, 3 H), 2.44 (s, 3 H), 2.85 (q, *J* = 7.6 Hz, 2 H), 7.18 (s, 1 H), 7.23-7.27 (m, 1 H), 7.48 (dd, *J* = 8.1, 1.8 Hz, 1 H), 8.06 (d, *J* = 1.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5, 149.1, 141.2, 134.1, 129.8, 127.5, 123.7, 121.9, 101.3, 27.9, 21.7, 11.1.

2-Ethyl-5-(*p*-biphenyl)oxazole 2l-A

Mp 105-107 °C. IR (neat): 2359, 1557, 1388, 1132, 997, 732, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, *J* = 7.7 Hz, 3 H), 2.88 (q, *J* = 7.7 Hz, 2 H), 7.26 (s, 1 H), 7.37 (tt, *J* = 1.1, 7.6 Hz, 1 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.61-7.70 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 150.4, 139.8, 139.5, 137.9, 128.7, 127.6, 127.2, 124.4, 122.1, 93.3, 21.8, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{17}H_{16}ON$ = 250.1226, Found = 250.1220.

2-Ethyl-5-(3'-pyridyl)oxazole 2m-A

Mp 192-195 °C. IR (neat): 3649, 2359, 1734, 1254, 1037, 767, 631 cm^{-1}. ^1H NMR (400 MHz, DMSO-d6): δ = 1.28 (t, *J* = 7.7 Hz, 3 H), 2.83 (q, *J* = 7.7 Hz, 2 H), 7.48 (ddd, *J* = 7.9, 4.8, 0.9 H), 7.68 (s, 1 H), 8.04 (dt, *J* = 7.9, 1.8 Hz, 1 H), 8.52 (dd, *J* = 5.0, 1.6 Hz, 1 H), 8.91 (d, *J* = 1.6 Hz). ^{13}C NMR (100 MHz, DMSO-d6): δ = 165.7, 149.0, 147.5, 144.9, 131.0, 124.1, 124.0, 123.8, 21.1, 11.0 HRMS (ESI) $[M + H]^+$ Calcd for $C_{10}H_{11}ON_2$ = 175.0866, Found = 175.0863.

2-Ethyl-4-methyl-5-phenyloxazole 2n-A

Oil. IR (neat): 2979, 2360, 1568, 1242, 1017, 763, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.5 Hz, 3 H), 2.40 (s, 3 H), 2.81 (q, *J* = 7.5 Hz, 2 H), 7.29 (t, *J* = 8.0 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 144.8, 131.4, 129.4, 128.7, 127.2, 125.1, 21.6, 13.2, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{14}ON$ = 188.1070, Found = 188.1073.

2-Ethyl-4-methyl-5-(4'-fluorophenyl)oxazole 2o-A

Oil. IR (neat): 2982, 2361, 1560, 1500, 1230, 1132, 955, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.5 Hz, 3H), 2.37 (s, 3 H), 2.80 (q, *J* = 7.5 Hz, 2H), 7.09-7.15 (m, 2 H), 7.51-7.57 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 161.8 (d, J_{C-F} = 248.0 Hz), 144.0, 130.9, 126.8 (d, J_{C-F} = 8.6 Hz), 125.5 (d, J_{C-F} = 3.8 Hz), 115.7 (d, J_{C-F} = 21.9 Hz), 21.5, 13.0, 11.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONF$ = 206.0976, Found = 206.0981.

2-Ethyl-4-methyl-5-(4'-chlorophenyl)oxazole 2p-A
Oil. IR (neat): 2981, 1573, 1491, 1244, 1093, 827, 714 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.8 Hz, 3 H), 2.38 (s, 3 H), 2.81 (q, *J* = 7.8 Hz, 2 H), 7.39 (d, *J* = 8.9 Hz, 2 H), 7.50 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0, 143.9, 133.0, 131.9, 128.9, 127.8, 126.2, 21.6, 13.3, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONCl$ = 222.0680, Found = 222.0685.

2-Ethyl-4-methyl-5-(3'-iodo-4'-methylphenyl)oxazole 2q-A
Oil. IR (neat): 2978, 1571, 1486, 1380, 1239, 1023, 817, 702, 665 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.6 Hz, 3 H), 2.37 (s, 3 H), 2.45 (s, 3 H), 2.80 (q, *J* = 7.6 Hz, 2 H), 7.24-7.29 (m, 1 H), 7.44 (dd, *J* = 8.1, 1.6 Hz, 1 H), 8.02 (d, *J* = 1.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 143.2, 140.3, 135.2, 131.8, 129.7, 128.6, 124.8, 101.3, 27.9, 21.6, 13.2, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{15}ONI$ = 328.0193, Found = 328.0192.

2-Ethyl-4-methyl-5-(3'-iodo-4'-methoxyphenyl)oxazole 2r-A
Oil. IR (neat): 2978, 1573, 1491, 1283, 1254, 1108, 1031, 809, 731, 621 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.5 Hz, 3 H), 2.35 (s, 3 H), 2.79 (q, *J* = 7.5 Hz, 2 H), 3.91 (s, 3 H), 6.86 (d, *J* = 8.6 Hz, 1 H), 7.50 (d, *J* = 8.6 Hz, 1 H), 7.99 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 157.2, 143.2, 136.2, 130.6, 126.4, 124.0, 110.7, 86.3, 56.4, 21.6, 13.0, 11.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{15}O_2NI$ = 344.0142, Found = 344.0142.

2,4-Diethyl -5-phenyloxazole 2s-A
Oil. IR (neat): 2976, 2359, 1698, 1567, 1220, 1014, 665 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.6 Hz, 3 H), 1.37 (t, *J* = 7.6 Hz, 3 H), 2.75 (q, *J* = 7.6 Hz, 2 H), 2.82 (q, *J* = 7.4 Hz, 2 H), 7.29 (tt, *J* = 7.4, 1.3 Hz, 1 H), 7.42 (t, *J* = 7.6 Hz, 2 H), 7.56 (d, *J* = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 144.2, 137.2, 129.4, 128.6, 127.3, 125.2, 21.7, 20.4, 13.3, 11.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{16}ON$ = 202.1226, Found = 202.1222.

2-Ethyl-4-propyl-5-phenyloxazole 2t-A
Oil. IR (neat): 2964, 2359, 1698, 1449, 1260, 1175, 764, 670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.5 Hz, 3 H), 1.37 (t, *J* = 7.7 Hz, 3 H), 1.76 (sext, *J* = 7.4 Hz, 2 H), 2.70 (t, *J* = 7.5 Hz, 2 H), 2.81 (q, *J* = 7.7 Hz, 2 H), 7.28 (t, *J* = 7.5 Hz, 1 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.57 (d, *J* = 8.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 144.6, 135.9, 129.4, 128.6, 127.2, 125.2, 29.0, 22.1, 21.7, 13.9, 11.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{14}H_{18}ON$ = 216.1383, Found = 216.1379.

2-Ethyl-4-hexyl-5-phenyloxazole 2u-A
Oil. IR (neat): 2928, 1702, 1568, 1495, 1448, 1238, 1016, 763, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.6 Hz, 3 H), 1.28-1.44 (m, 9 H), 1.67-1.76 (m, 2 H), 2.71 (t, *J* = 7.9 Hz, 2H), 2.82 (q, *J* = 7.7 Hz, 2 H), 7.29 (t, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* = 7.5 Hz, 2 H), 7.56 (d, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 144.5, 136.2, 129.4, 128.7, 127.3, 125.3, 31.6, 29.2, 28.9, 27.2, 22.6, 21.7, 14.0, 11.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{17}H_{24}ON$ = 258.1852, Found = 258.1853.

2-Ethyl-4-octyl-5-phenyloxazole 2v-A
Oil. IR (neat): 2925, 2854, 1721, 1569, 1462, 1220, 1065, 1014, 762, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.6 Hz, 3 H), 1.21-1.41 (m, 13 H), 1.67-1.76 (m, 2 H), 2.71 (t, *J* = 8.2 Hz, 2 H), 2.82 (q, *J* = 7.7 Hz, 2 H), 7.29 (tt, *J* = 7.2, 1.5 Hz, 1 H), 7.42 (tt, *J* = 7.2, 1.5 Hz, 2H), 7.56 (dt, *J* = 7.2, 1.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 144.5, 136.2, 129.4, 129.2, 128.7, 127.3, 125.3, 31.8, 29.6, 29.4, 28.9, 27.2, 22.6, 21.8, 14.1, 11.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{19}H_{28}ON$ = 286.2165, Found = 286.2164.

2-Ethyl-4-decyl-5-phenyloxazole 2w-A
Oil. IR (neat): 2924, 2853, 2360, 1700, 1569, 1463, 1240, 1015, 692, 671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.21-1.42 (m, 17 H), 1.66-1.75 (m, 2 H), 2.70 (t, *J* =7.9 Hz, 2 H), 2.82 (q, *J* = 7.5 Hz, 2 H), 7.29 (t, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* =7.5 Hz, 2 H), 7.56 (d, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 144.5, 136.2, 129.4, 128.7, 127.3, 125.3, 31.9, 29.6 (3C), 29.4, 29.3, 28.9, 27.2, 22.7, 21.8, 14.1, 11.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{21}H_{32}ON$ = 314.2478, Found = 314.2478.

2-Methyl-5-phenyloxazole 2a-B
Mp 57-58.5 °C. IR (neat): 1558, 1484, 1215, 1129, 941, 763, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3 H), 7.20 (s, 1 H), 7.30 (t, *J* = 7.5 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 7.60 (d, *J* = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 151.0, 128.8, 128.1, 128.0, 123.9, 121.8, 14.0. HRMS (ESI) $[M + H]^+$ Calcd for $C_{10}H_{10}ON$ = 160.0757, Found = 160.0755.

2-Methyl-5-(4′-chlorophenyl)oxazole 2c-B
Mp 59-60 °C. IR (neat): 2359, 1552, 143, 1129, 1091, 938, 816, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3 H), 7.20 (s, 1 H), 7.38 (d, *J* = 8.9 Hz, 2 H), 7.54 (d, *J* = 8.9 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 150.1, 133.8, 129.1, 126.6, 125.1, 122.2, 14.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{10}H_9ONCl$ = 194.0367, Found = 194.0365.

2-Methyl-5-(4′-bromophenyl)oxazole 2d-B
Mp 81-83 °C. IR (neat): 2359, 1549, 1481, 1210, 1133, 939, 822, 671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3 H), 7.21 (s, 1 H), 7.47 (d, *J* = 8.9 Hz, 2 H), 7.53 (d, *J* = 8.9 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 150.1, 132.0, 127.1, 125.4, 122.4, 121.9, 14.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{10}H_9ONBr$ = 237.9862, Found = 237.9859.

2-Methyl-5-(4′-nitrophenyl)oxazole 2i-B
Mp 160-162 °C. IR (neat): 1557, 1504, 1327, 1102, 941, 850, 753, 688, 529 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3 H), 7.42 (s, 1 H), 7.76 (d, *J* = 9.0 Hz, 2 H), 8.28 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 149.0, 146.9, 133.8, 125.4, 124.4, 124.1, 14.2. HRMS (ESI) $[M + H]^+$ Calcd for $C_{10}H_9O_3N_2$ = 205.0608, Found = 205.0605.

2,4-Dimethyl-5-phenyloxazole 2n-B
Mp 88-90 °C. IR (neat): 2360, 1569, 1393, 1281, 1003, 824, 669, 531 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 2.48 (s, 3 H), 7.29 (t, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* = 7.5

Hz, 2 H), 7.57 (d, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 144.2, 137.8, 132.4, 128.7, 126.6, 92.5, 13.9, 13.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{12}ON$ = 174.0913, Found = 174.0911.

2,4-Dimethyl-5-(4′-chlorophenyl)oxazole 2p-B

Oil. IR (neat): 2360, 1712, 1491, 1264, 1090, 1009, 824, 755 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3 H), 2.47 (s, 3 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 7.50 (d, *J* = 8.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 144.1, 132.9, 131.9, 128.8, 127.6, 126.1, 13.8, 13.1. HRMS (ESI) $[M + H]^+$ Calcd for $C_{11}H_{11}ONCl$ = 208.0524, Found = 208.0521.

2-Propyl-5-phenyloxazole 2a-C

Oil. IR (neat): 2964, 1556, 1149, 1133, 941, 759, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.4 Hz, 3 H), 1.85 (sext, *J* = 7.4 Hz, 2 H), 2.81 (t, *J* = 7.4 Hz, 2 H), 7.22 (s, 1 H), 7.30 (t, *J* = 7.4 Hz, 1 H), 7.40 (t, *J* = 7.4 Hz, 2 H), 7.61 (d, *J* = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 150.8, 128.8, 128.2, 128.0, 123.9, 121.7, 30.1, 20.5, 13.7. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{14}ON$ = 188.1070, Found = 188.1066.

2-Propyl-5-(4’-chlorophenyl)oxazole 2c-C

Oil. IR (neat): 2964, 1569, 1485, 1186, 1092, 941, 819, 737 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.4 Hz, 3 H), 1.85 (sext, *J* = 7.4 Hz, 2 H), 2.80 (t, *J* = 7.4 Hz, 2 H), 7.21 (s, 1 H), 7.37 (d, *J* = 8.8 Hz, 2 H), 7.54 (d, *J* = 8.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 149.8, 133.7, 129.0, 126.7, 125.1, 122.1, 30.1, 20.5, 13.7. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONCl$ = 222.0680, Found = 222.0677.

2-Propyl-5-(4’bromophenyl)oxazole 2d-C

Oil. IR (neat): 2959, 1566, 1481, 1286, 1007, 940, 813, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.5 Hz, 3 H), 1.85 (sext, *J* = 7.5 Hz, 2 H), 2.80 (t, *J* = 7.4 Hz, 2 H), 7.23 (s, 1 H), 7.48 (d, *J* = 8.6 Hz, 2 H), 7.53 (d, *J* = 8.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 149.9, 132.0, 127.2, 125.4, 122.2, 121.8, 30.1, 20.5, 13.7. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONBr$ = 266.0175, Found = 266.0169.

2-Propyl-5-(4’-nitrophenyl)oxazole 2i-C

Mp 76-77 °C. IR (neat): 1607, 1506, 1328, 1104, 940, 851, 687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.5 Hz, 3 H), 1.88 (sext, *J* = 7.2 Hz, 2 H), 2.85 (t, *J* = 7.5 Hz, 2 H), 7.44 (s, 1 H), 7.76 (d, *J* = 9.1 Hz, 2 H), 8.28 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 148.8, 146.9, 134.0, 125.3. 124.4, 124.2, 30.2, 20.4, 13.7. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}O_3N_2$ = 233.0921, Found = 233.0916.

2-Propyl-4-methyl-5-phenyloxazole 2n-C

Oil. IR (neat): 2964, 1704, 1566, 1386, 1241, 1015, 762, 536 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.4 Hz, 3 H), 1.84 (sext, *J* = 7.6 Hz, 2 H), 2.40 (s, 3H), 2.76 (t, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.4 Hz, 1 H), 7.42 (t, *J* = 7.9 Hz, 2 H), 7.58 (d, *J* = 7.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 144.8, 131.4, 129.4, 128.7, 127.2, 125.0, 30.1, 20.6, 13.7, 13.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{16}ON$ = 202.1226, Found = 202.1223.

2-Propyl-4-methyl-5-(4’-chlorophenyl)oxazole 2p-C

Oil. IR (neat): 2965, 1620, 1572, 1491, 1241, 827, 713 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.4 Hz, 3 H), 1.83 (sext, *J* = 7.4 Hz, 2 H), 2.37 (s, 3 H), 2.75 (t, *J* = 7.6 Hz, 2 H), 7.38 (d, *J* = 8.8 Hz, 2 H), 7.49 (d, *J* = 8.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 143.8, 132.9, 131.9, 128.8, 127.8, 126.1, 30.0, 20.5, 13.9, 13.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{15}ONCl$ = 236.0837, Found = 236.0833.

2-Isopropyl-5-phenyloxazole 2a-D

Oil. IR (neat): 2974, 1697, 1554, 1288, 1138, 940, 761, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 6.9 Hz, 6 H), 3.15 (sep, *J* = 6.9 Hz, 1 H), 7.21 (s, 1 H), 7.30 (t, *J* = 7.4 Hz, 1 H), 7.40 (t, *J* = 7.8 Hz, 2 H), 7.62 (d, *J* = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 150.6, 128.8, 128.3, 128.0, 123.9, 121.5, 28.5, 20.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{14}ON$ = 188.1070, Found = 188.1066.

2-Isopropyl-5-(4’-chlorophenyl)oxazole 2c-D

Oil. IR (neat): 2974, 1567, 1485, 1407, 1139, 1092, 961, 819, 739 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (d, *J* = 7.0 Hz, 6 H), 3.15 (sep, *J* = 7.0 Hz, 1 H), 7.21 (s, 1 H), 7.37 (d, *J* = 8.8 Hz, 2 H), 7.55 (d, *J* = 8.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 149.7, 133.7, 129.0, 126.8, 125.2, 122.0, 28.5, 20.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONCl$ = 222.0680, Found = 222.0678.

2-Isopropyl-5-(4’-bromophenyl)oxazole 2d-D

Oil. IR (neat): 2974, 1696, 1550, 1480, 1106, 1072, 940, 817 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (d, *J* = 7.0 Hz, 6 H), 3.14 (sep, *J* = 7.0 Hz, 1 H), 7.22 (s, 1 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 7.53 (d, *J* = 8.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 149.7, 132.0, 127.2, 125.4, 122.1, 121.8, 28.5, 20.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}ONBr$ = 266.0175, Found = 266.0169.

2-Isopropyl-5-(4’-nitrophenyl)oxazole 2i-D

Mp 75-76 °C. IR (neat): 1607, 1546, 1509, 1328, 1106, 852, 737, 687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 6.9 Hz, 6 H), 3.19 (sep, *J* = 7.0 Hz, 1 H), 7.43 (s, 1 H), 7.76 (d, *J* = 9.0 Hz, 2 H), 8.28 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 148.7, 146.9, 134.0, 125.2, 124.4, 124.2, 28.6, 20.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{12}H_{13}O_3N_2$ = 233.0921, Found = 233.0916.

2-Isopropyl-4-methyl-5-phenyloxazole 2n-D

Oil. IR (neat): 2973, 1564, 1445, 1243, 1015, 764, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (d, *J* = 6.8 Hz, 6 H), 2.40 (s, 3 H), 3.10 (sep, *J* = 7.0 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1 H), 7.42 (t, *J* = 7.9 Hz, 2 H), 7.58 (d, *J* = 7.3 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 144.6, 131.3, 129.4, 128.6, 127.2, 125.1, 28.3, 20.5, 13.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{16}ON$ = 202.1226, Found = 202.1224.

2-Isopropyl-4-methyl-5-(4’-chlorophenyl)oxazole 2p-D

Oil. IR (neat): 2974, 1569, 1490, 1388, 1245, 1010, 827, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (d, *J* = 7.0 Hz, 6 H), 2.38 (s, 3 H), 3.10 (sep, *J* = 6.8 Hz, 1 H), 7.39 (d, *J* = 8.9 Hz, 2 H), 7.50 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.1, 143.7, 132.9, 131.8, 128.9, 127.9, 126.2, 28.3, 20.5, 13.3. HRMS (ESI) $[M + H]^+$ Calcd for $C_{13}H_{15}ONCl$ = 236.0837, Found = 236.0832.

2,5-Diphenyloxazole 2a-E

Mp 66-69 °C. IR (neat): 2359, 1542, 1480, 1133, 1058, 760, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (t, *J* = 7.4 Hz, 1 H), 7.43-7.52 (m, 6 H), 7.73 (d, *J* = 7.4 Hz, 2 H), 8.12 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1,

151.2, 130.3, 128.9, 128.8, 128.4, 128.0, 127.4, 126.3, 124.2, 123.4. HRMS (ESI) $[M + H]^+$ Calcd for $C_{15}H_{12}ON$ = 222.0913, Found = 222.0910.

2,5-Diphenyl-4-methyloxazole 2n-E

Mp 79-80 °C. IR (neat): 1483, 1442, 1067, 777, 763, 738, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H), 7.33 (t, *J* = 7.2 Hz, 1 H), 7.43-7.49 (m, 5 H), 7.68 (d, *J* = 7.4 Hz, 2 H), 8.07-8.11 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 145.4, 133.3, 130.1, 129.1, 128.8, 128.7, 127.6, 127.4, 126.2, 125.3, 13.5. HRMS (ESI) $[M + H]^+$ Calcd for $C_{16}H_{14}ON$ = 236.1070, Found = 236.1065.

2-(2'-Cyaboethyl)-4,5-diphenyloxazole 2x-F

Mp 107-109 °C. IR (neat): 2987, 2359, 2254, 1585, 1439, 1216, 1058, 765, 593 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.95 (t, *J* = 7.5 Hz, 2 H), 3.24 (t, *J* = 7.5 Hz, 2 H), 7.31-7.41 (m, 6 H), 7.55- 7.66 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 146.1, 135.3, 132.0, 128.8, 128.7, 128.6, 128.5, 128.3, 127.8, 126.5, 118.3, 24.5, 15.0.

Oxaprozin

Mp 157-158 °C (Mp 163 °C, commercially available) IR (neat): 2939, 1718, 1569, 1443, 1274, 965, 922, 693, 675 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.96 (t, *J* = 7.5 Hz, 2 H), 3.20 (t, *J* = 7.5 Hz, 2 H), 7.30-7.39 (m, 6 H), 7.54-7.64 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 161.8, 145.5, 134.8, 132.0, 128.7, 128.6, 128.6 (2C), 128.2, 127.9, 126.4, 30.9, 23.2.

Acknowledgments

Financial support in the form of a Grant-in–Aid for Scientific Research (No. 20550033) from the Ministry of Education, Culture, Sports, Science, and Technology in Japan, and Iodine Research Project in Chiba University, is gratefully acknowledged.

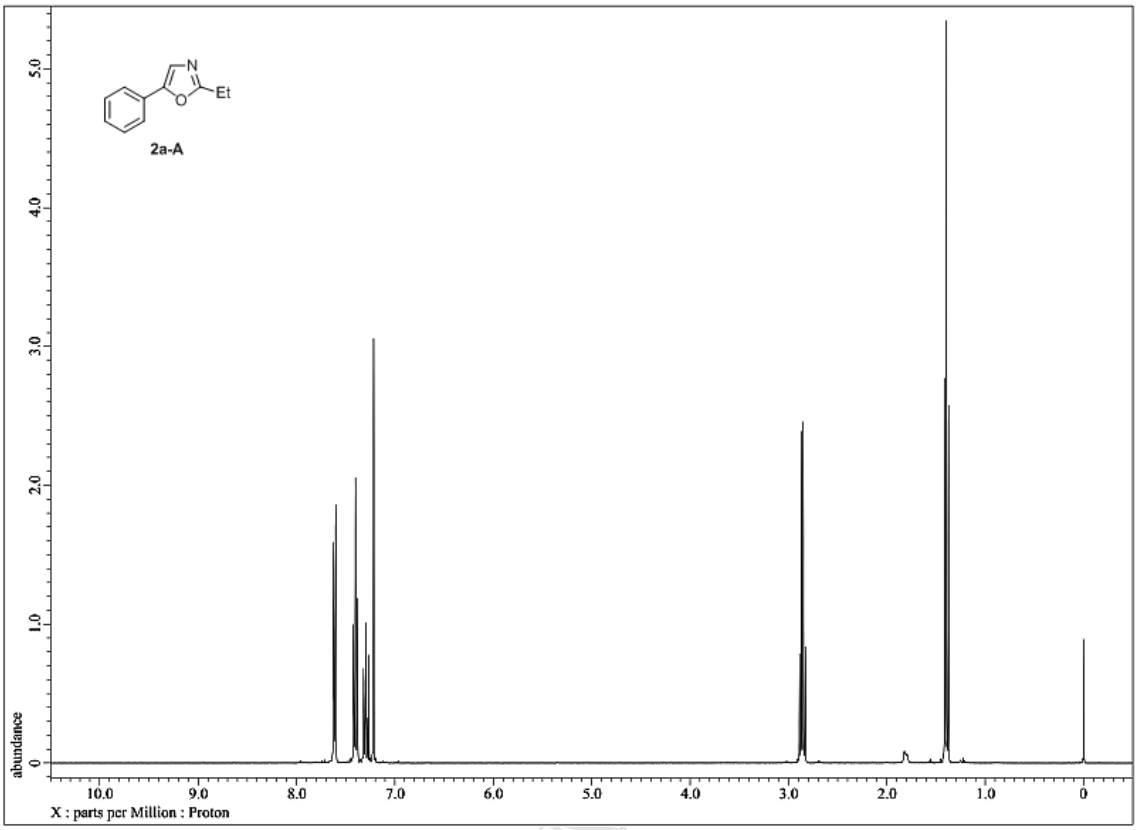
References

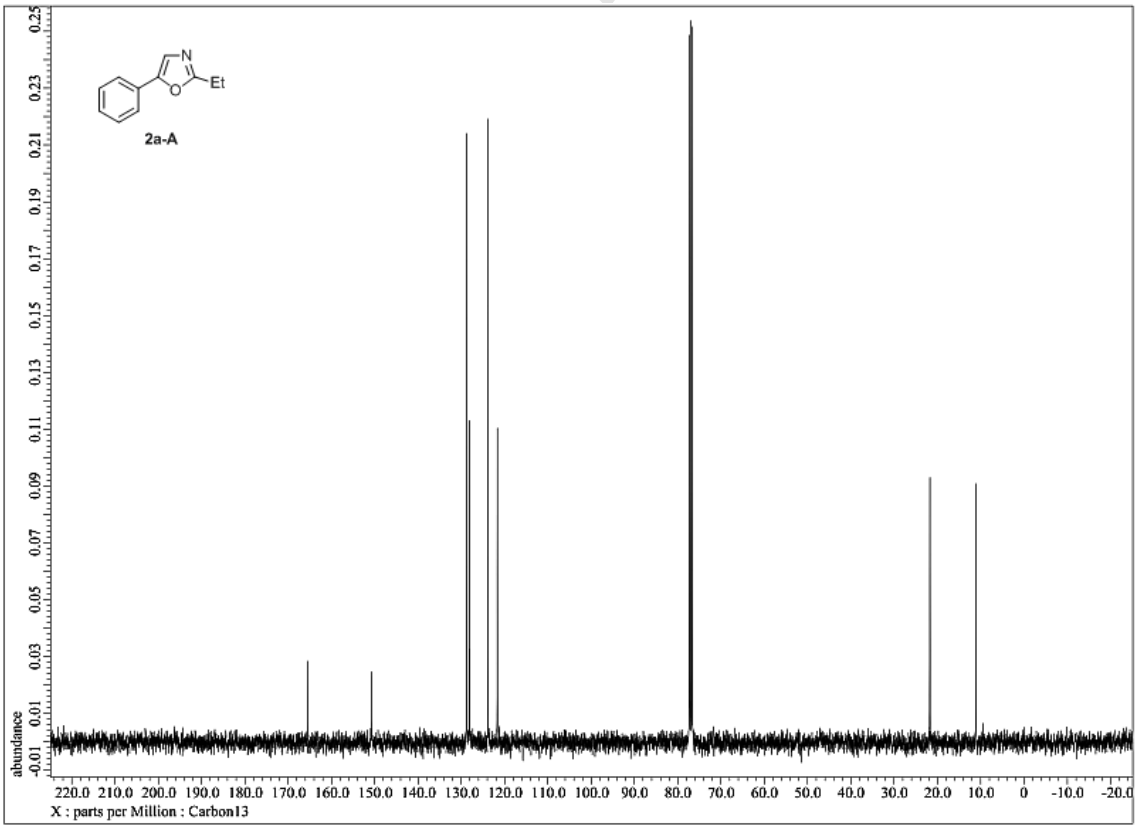
1. (a) Nicolaou, K. C.; Bella, M.; Chen, D. Y.; Huang, X.; Ling, T.; Snyder, S. A. *Angew. Chem. Int. Ed*. **2002**, *41*, 3495. (b) Yeh, V. S. C. *Tetrahedron*, **2004**, *60*, 11995. (c) Linder, J.; Blake, A. J.; Moody, C. J. *Org. Biomol. Chem*. **2008**, *6*, 3908. (d) Pattenden, G.; Ashweek, N. J.; Baker-Glenn, C. A. G.; Walker, G. M.; Yee, J. G. K. *Angew. Chem. Int. Ed*. **2007**, *46*, 4359. (e) Jin, Z. *Nat. Prod. Rep*. **2011**, *28*, 1143. (f) *Oxazoles: Synthesis, Reactions, and Spectroscopy, Part A*; Palmer, D. C.; Ed.; John Wiley & Sons: Hoboken, NJ, 2003. (g) *Oxazoles: Synthesis, Reactions, and Spectroscopy, Part B*; Palmer, D. C.; Ed.; John Wiley & Sons: Hoboken, NJ, 2004.
2. (a) Jin, Z. *Nat. Prod. Rep*. **2005**, *22*, 196. (b) Jin, Z. *Nat. Prod. Rep*. **2006**, *23*, 464. (c) Jin, Z. *Nat. Prod. Rep*. **2009**, *26*, 382. (d) Desroy, N.; Moreau, F.; Briet, S.; Le Fralliec, G.; Floquet, S.; Durant, L.; Vongsouthi, V.; Gerusz, V.; Denis, A.; Escaich, S. *Bioorg. Med. Chem*. **2009**, *17*, 1276. (e) Heng, S.; Gryncel, K. R.; Kantrowitz, E. R. *Bioorg. Med. Chem*. **2009**, *17*, 3916. (f) Perner, R. J.; Koenig, J. R.; DiDomenico, S.; Gomtsyan, A.; Schmidt, R. G.; Lee, C.; Hsu, M. C.; McDonald, H. A.; Gauvin, D. M.; Joshi, S.; Turner, T. M. Reilly, R. M.; Kyn, P. R.; Kort, M. E. *Bioorg. Med. Chem*. **2010**, *18*, 4821. (g) Choi, M. J.; No, E. S.; Thorat, D. A.; Jang, J. W.; Yang, H.; Lee, J.; Choo, H.; Kim, S. J.; Lee, C. S.; Ko, S. Y.; Lee, J.; Nam, G.; Pae, A. N. *J. Med. Chem*. **2013**, *56*, 9008. (h) Jin, Z. *Nat. Prod. Rep*. **2013**, *30*, 869. (i) Rai, G.; Joshi, N.; Jung, J. E.; Liu, Y.; Schultz, L.; Yasgar, A.; Perry, S.; Diaz, G.; Zhang, Q.; Kenyon, V.; Jadhav, A.; Simeonov, A.; Lo, E. H.; Leyen, K. V.; Maloney, D. J.; Holman, T. R. *J. Med. Chem.* **2014**, *57*. 4035. (j) Hale, K. J.; Grabski, M.; Manaviazar, S.; Maczka, *Org. Lett*. **2014**, *16*, 1164. (k) Wenlock, M. C.; Barton, P.; Luker, T. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 3550. (l) Chandrasekhar, S,; Sudhakar, A. *Org. Lett*. **2010**, *12*, 236.
3. (a) Vedejs, E.; Barda, D. A. *Org. Lett.* **2000**, *2*, 1033. (b) Mann, E.; Kessler, H. *Org. Lett*. **2003**, *5*, 4567. (c) Wang, Q.; Xia, Q.; Ganem, B. *Tetrahedron Lett.* **2003**, *44*, 6825. (d) Atkins, J. M.; Vedejs, E. *Org. Lett*. **2005**, *7*, 3351. (e) Zhang, J.; Polishchuk, E. A.; Chen, J.; Ciufolini, M. A. *J. Org. Chem.* **2009**, *74*, 9140. (f) Zhang, J.; Ciufolini, M. A. *Org. Lett*. **2009**, *11*, 2389. (g) Jouanno, L.; Mascio, V. D.; Tognetti, V.; Joubert, L.; Sabot, C.; Renaud, P. *J. Org. Chem*. **2014**, *79*, 1303.
4. Typical reviews: (a) Turchi, I. J.; Dewar, M. J. *Chem. Rev*. **1975**, *75*, 389. (b) Wiley, R. H. *Chem. Rev*. **1945**, *37*, 401.
5. (a) Cornforth, J. W.; Cornforth, R. H. J. Chem. Soc. 1947, 96. (b) Robinson, R. J. *J. Chem. Soc., Trans* **1909**, 95, 2167 (c) Gabriel, S. Ber. Bunsen-Ges. *Phys. Chem*. **1910**, *43*, 134. (d) Brain, C. T.; Paul, J. M. *Synlett* **1999**, 1642. (e) Wipf, P.; Miller, C. P. *J. Org. Chem*. **1993**, *58*, 3604. (f) Morwick, T.; Hrapchak, M.; DeTuri, M.; Campbell, S. *Org. Lett*. **2002**, *4*, 2665.
6. (a) Moody, C. J.; Doyle, K. J. Prog. *Heterocycl. Chem.* **1997**, *9*, 1. (b) Bagley, M. C.; Buck, R. T.; Hind, S. L.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 591. (c) Doyle, K. J.; Moody, C. J. *Tetrahedron Lett*. **1992**, *33*, 7769. (d) Davies, J. R.; Kane, P. T.; Moody, C. J. *J. Org. Chem.* **2005**, *70*, 7305. (e) Shi, B.; Blake, A. J.; Lewis, W.; Campbell, I. B.; Judkins, B. D.; Moody, C. J. *J. Org. Chem*. **2010**, *75*, 152.
7. (a) Senadi, G. C.; Hu, W.-P.; Hsiao, J.-S.; Vandavasi, J. K.; Chen, C.-Y.; Wang, J.-J. *Org. Lett*. **2012**, *14*, 4478. (b) Wipf, P.; Aoyama, Y.; Benedum, T. E. *Org. Lett*. **2004**, *6*, 3593. (c) Arcadi, A.; Cacchi, S.; Cascia, L.; Fabrizi, G.; Marinelli, F. *Org. Lett.* **2001**, *3*, 2501. (d) Saito, A.; Iimura, K.; Hanzawa, Y. *Tetrahedron. Lett.* **2010**, *51*, 1471. (e) Beccalli, E. M.; Borsini, E.; Broggini, G.; Palmisano, G.; Sottocornola, S. *J. Org. Chem*. **2008**, *73*, 4746. (f) Nilsson, B. M.; Hacksell, U. *J. Heterocyclic Chem*. *1989*, **26**, 269. (g) Wipf, P.; Rahman, L. T.; Rector, S. R. *J. Org. Chem*. **1998**, *63*, 7132. (h) Coqueron, P.-Y.; Didier, C.; Ciufolini, M. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1411.
8. (a) Martin, R.; Cuenca, A.; Buchwald, S. L. *Org. Lett.* **2007**, *9*, 5521. (b) Schuh, K.; Glorius, F. *Synthesis* **2007**, 2297.

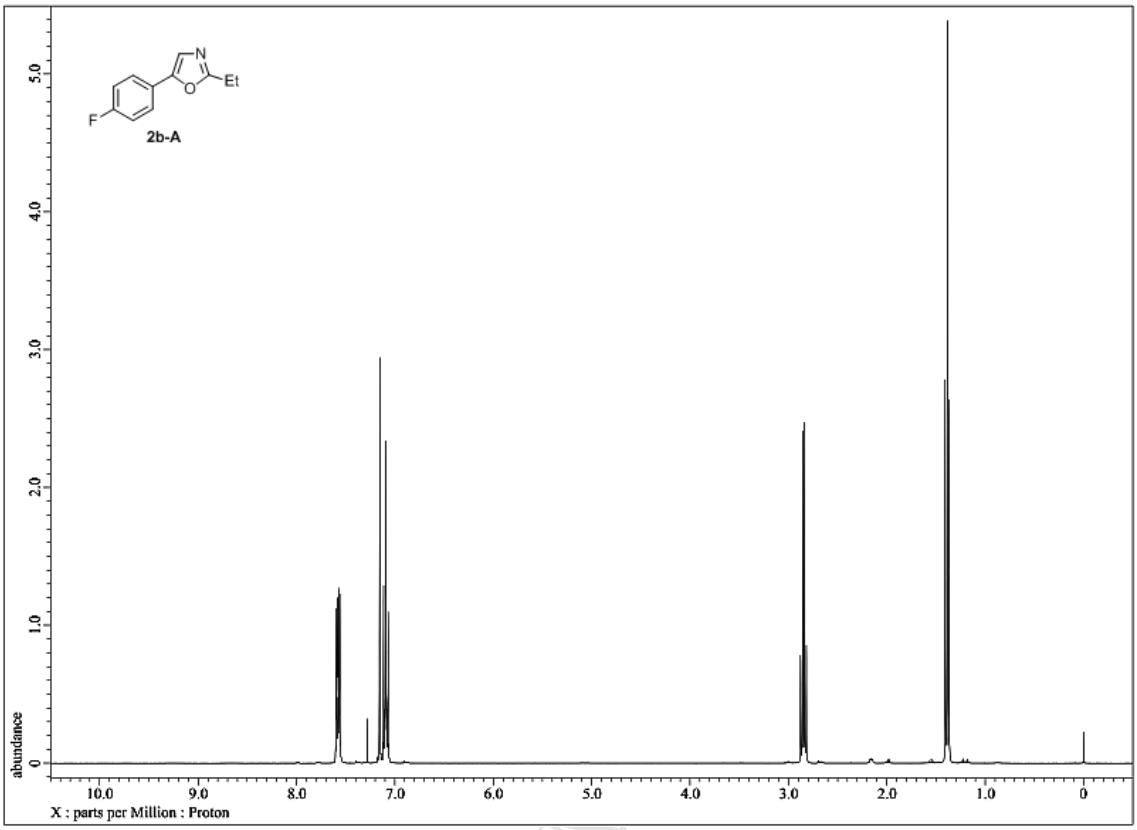
9. (a) Fresneda, P. M.; Molina, P. *Synlett* **2004**, 1. (b) Xie, H.; Yuan, D.; Ding, M.-W. *J. Org. Chem*. **2012**, *77*, 2954. (c) Fresneda, P. M.; Castaneda, M.; Blug, M.; Molina, P. *Synlett* **2007**, 324. (d) Huang, N.-Y.; Nie, Y.-B.; Ding, M.-W. *Synlett* **2009**, 611. (e) Takeuchi, H.; Yanagida, S.-I.; Ozaki, T.; Hagiwara, S.; Eguchi, S. *J. Org. Chem*. **1989**, *54*, 431.
10. (a) Moody, C. J.; Swann, E. *J. Med. Chem*. **1995**, *38*, 1039. (b) Panek, J. S.; Beresis, R. T. *J. Org. Chem*. **1996**, *61*, 6496.
11. (a) Milton, M. D.; Inada, Y.; Nishibayashi, Y.; Uemura, S. *Chem. Comm*. **2004**, *23*, 2712. (b) He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc*. **2011**, *13*3, 8482. (c) Hashmi, A. S.; Schuster, A. M.; Schmuck, M.; Rominger, F. *Eur. J. Org. Chem.* **2011**, 4595. (d) Egorova, O. A.; Seo, H.; Kim, Y.; Moon, D.; Rhee, Y. M.; Ahn, K. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 11446. (e) Hashmi, A. S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5232. (f) Luo, Y.; Ji, K.; Li, Y.; Zhang, L. *J. Am. Chem. Soc*. **2012**, *134*, 17412.
12. (a) Selvi, T.; Srinivasan, K. *Chem. Commun*. **2014**, *50*, 10845. (b) Liu, D.; Yu, J.; Cheng, J. *Tetrahedron* **2014**, *70*, 1149. (c). Liu, B.; Zhang, Y.; Huang, G.; Zhang, X.; Niu, P.; Wu, J.; Yu, W.; Chang, J. *Org. & Biomol. Chem*. **2014**, *12*, 3912. (d). Zheng, J.; Zhang, M.; Huang, L.; Hu, X.; Wu. W.; Huang, H.; Jiang, H. *Chem. Commun*. **2014**, *50*, 3609. (e). Bailey, J. L.; Sudini, R. R. *Tetrahedron Lett.* **2014**, *55*, 3674.
13 (a) Gao, Q.; Fei, Z.; Zhu, Lian, M.; Y.; Jia, F.; Liu, M.; She, N.; Wu, A. *Tetrahedron* **2013**, *69*, 22. (b) Ming, L.; Tang, J.; Zhao, X. *Synthesis* **2014**, *46*, 2499. (c) Zhang, L.; Zhao, X. J. *Org. Lett*. **2015**, *17*, 184.
14 *Reviews*: (a) Togo, H.; Iida, S. *Synlett*. **2006**, 2159. (b) Togo, H. *J. Synth. Org. Chem*. **2008**, *66*, 652; *Papers*: (c) Mori, N.; Togo, H. *Synlett* **2004**, 880. (d) Mori, N.; Togo, H. *Tetrahedron.* **2005**, *61*, 5915. (e) Ishihara, M.; Togo, H. *Synlett* **200**6, 227. (f) Iida, S.; Togo, H. *Synlett* **2006**, 2633. (g) Ishihara, M.; Togo, H. *Tetrahedron* **2007**, *63*, 1474. (h) Iida, S.; Togo, H. *Synlett* **2007**, 407. (i) Iida, S.; Togo, H. *Synlett* **2008**, 1639. (j) Iida, S.; Ohmura, H. Togo, *Tetrahedron* **2009**, *65*, 6257; (k) Ohmura, H.; Takahata, M.; Togo, H. *Tetrahedron Lett*. **2010**, *51*, 4378. (l) Suzuki, Y.; Ishiwata, Y.; Moriyama, K.; Togo, H. *Tetrahedron Lett*. **2010**, *51*, 5950. (m) Takahashi, S.; Togo, H. *Heterocycles* **2010**, *82*, 593. (n) Suzuki, Y.; Yoshino, T.; Moriyama, K.; Togo, H. *Tetrahedron*. **2011**, *67*, 3809. (o) Baba, H.; Moriyama, K.; Togo, H. *Tetrahedron Lett*. **2011**, *52*, 4303. (p) Suzuki, Y.; Moriyama, K.; Togo, H. *Tetrahedron* **2011**, *67*, 7956. (q) Ushijima, S.; Dohi, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2012**, *68*, 1436. (r) Baba, H.; Moriyama, K.; Togo, H. *Synlett.* **2012**, *23*, 1175. (s) Ushijima, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2012**, *68*, 4701. (t) Dohi, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2012**, *68*, 6557. (u) Kikui, H.; Moriyama, K.; Togo, H. *Synthesis*, **2013**, 791. (v) Ishii, G.; Harigae, R.; Moriyama, K.; Togo, H. *Tetrahedron*, **2013**, *69*, 1462. (w) Shimojo, H.; Moriyama, K.; Togo, H. *Synthesis*, **2013**, *45*, 2155. (x) Miyagi, K.; Moriyama, K.; Togo, H. *Eur. J. Org. Chem*., **2013**, 5886. (y) Tsuchiya, D.; Kawagoe, Y.; Moriyama, K.; Togo, H. *Org. Lett.*, **2013**, *15*, 4194. (z) Dohi, S.; Moriyama, K.; Togo, H. *Eur. J. Org. Chem.*, **2013**, 7815. (za) Kawagoe, Y.; Moriyama, K. Togo, H. *Eur. J. Org. Chem.*, **2014**, 4115.
15. (a) Thottumkara, A. P.; Bowsher, M. S.; Vinod, T. K. *Org. Lett*. **2005**, *7*, 2933. (b) Yakura, T.; Konishi, T. *Synlett* **2007**, 765. (c) Chen, C.; Feng, X.; Zhang, G.; Zhao, Q.; Huang, G. *Synthesis* **2008**, 3205. (d) Uyanik, M.; Akakura, M.; Ishihara, K. *J. Am. Chem. Soc*. **2009**, *131*, 251. (e) Uyanik, M.; Fukatsu, R.; Ishihara, K. *Org. Lett.* **2009**, *11*, 3470. (f) Tanaka, A.; Togo, H. *Synlett*, **2009**, 3360.

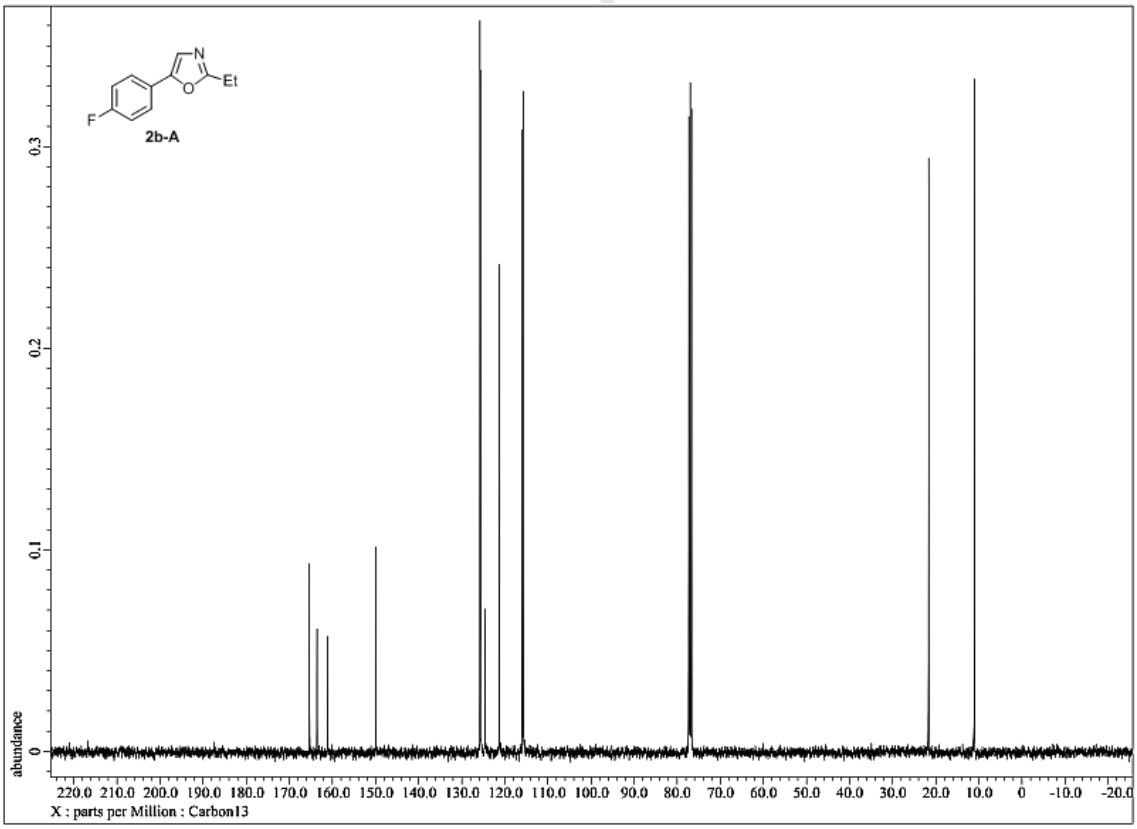
Supplementary Material

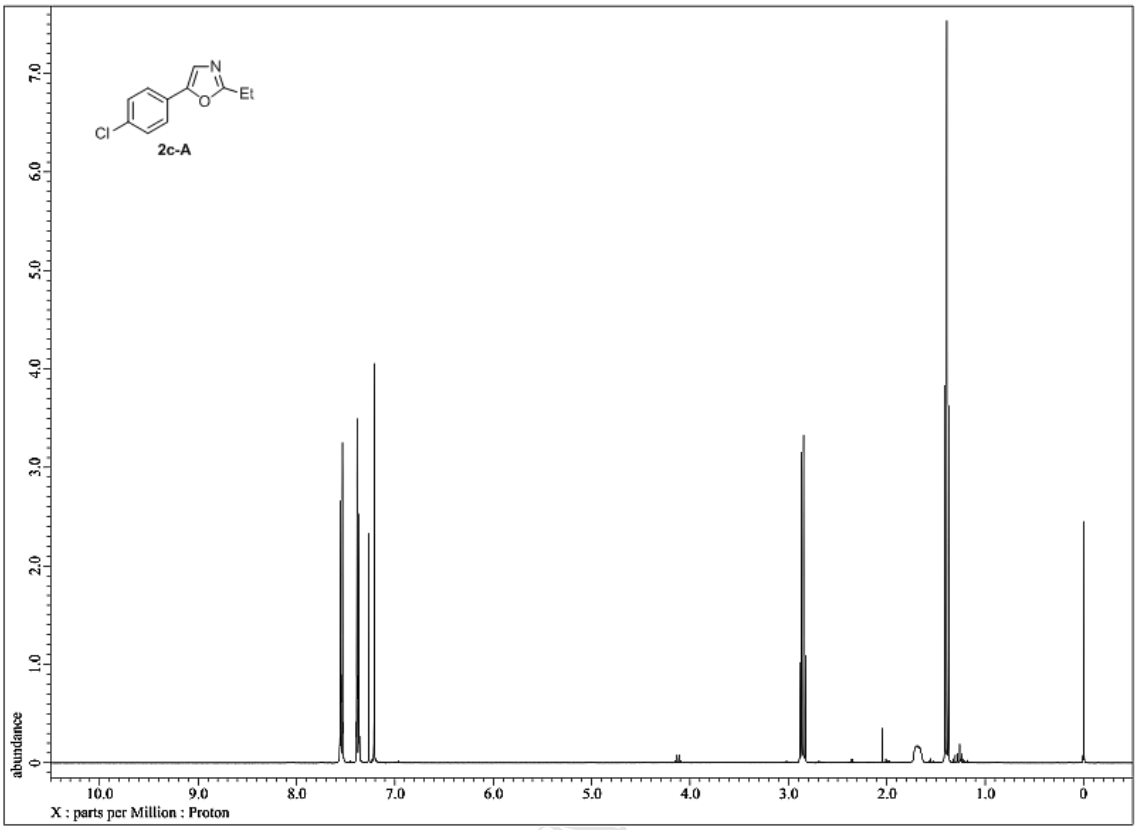
H-NMR and C-NMR charts of all oxazoles.

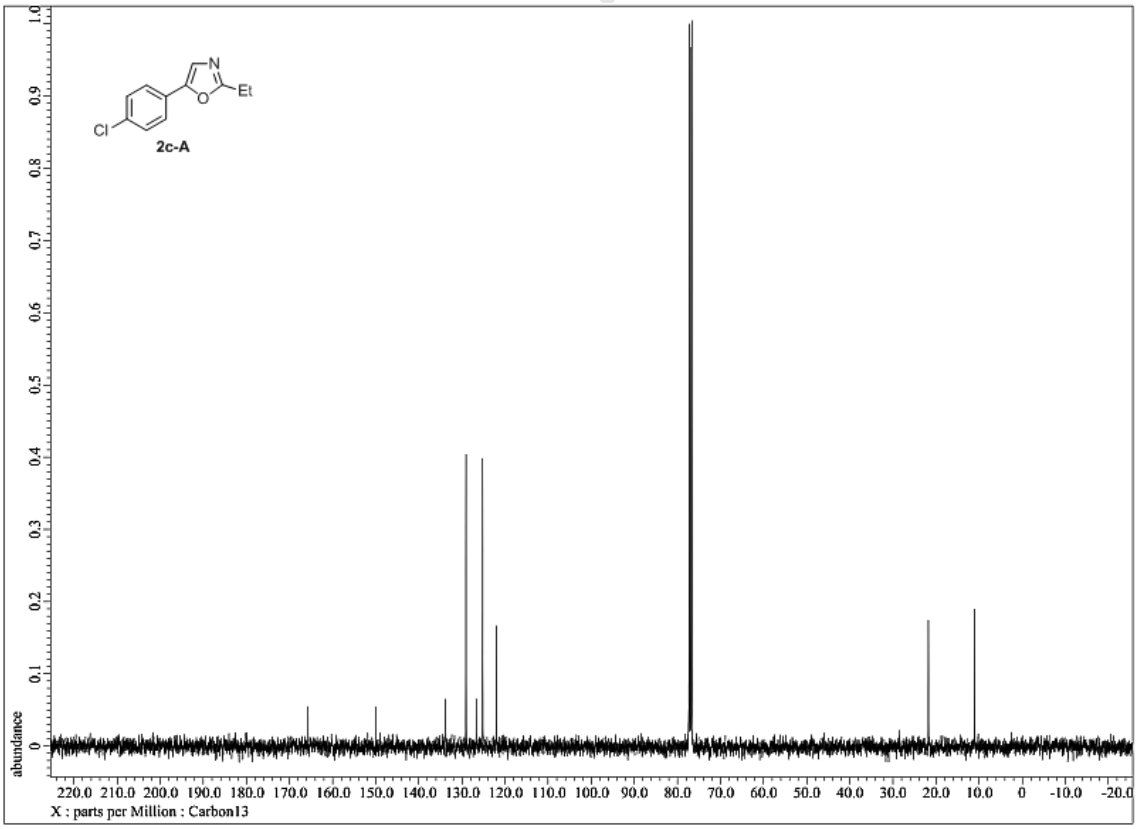

N
O
Et
2a-A
abundance
X : parts per Million : Proton

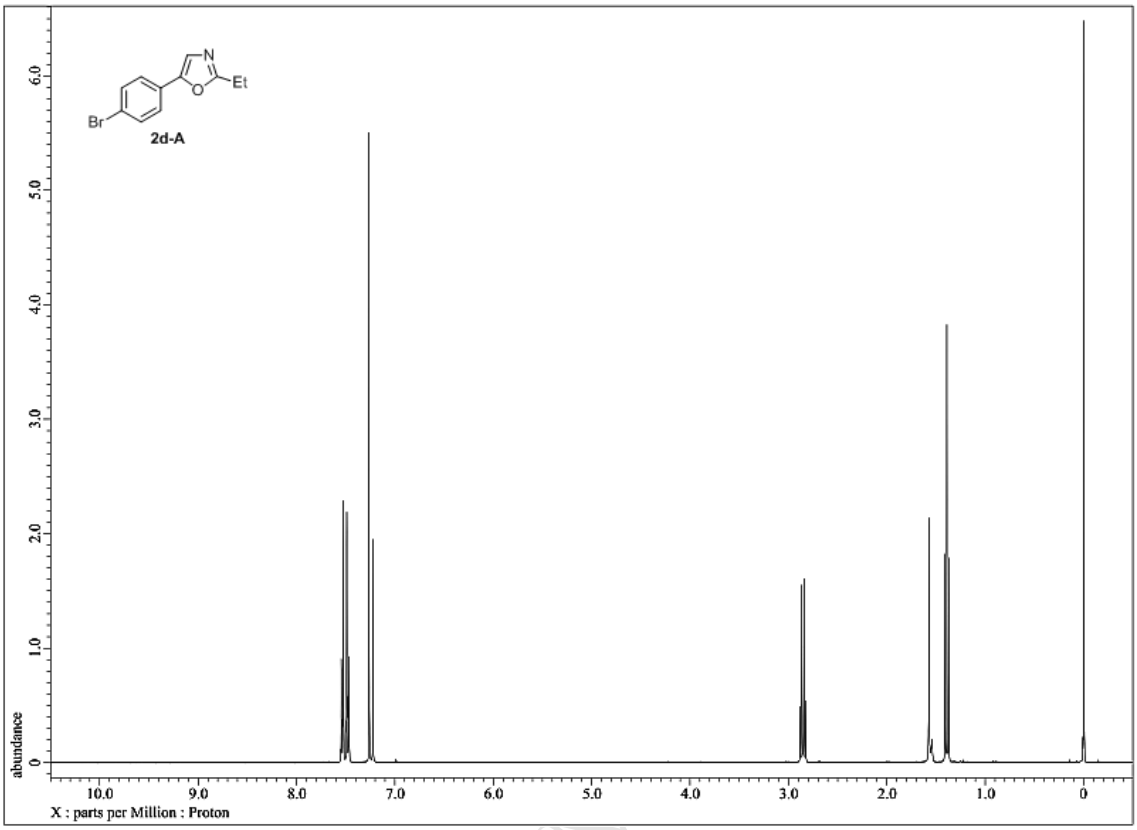

N
O
Et
2a-A
abundance
X : parts per Million : Carbon13

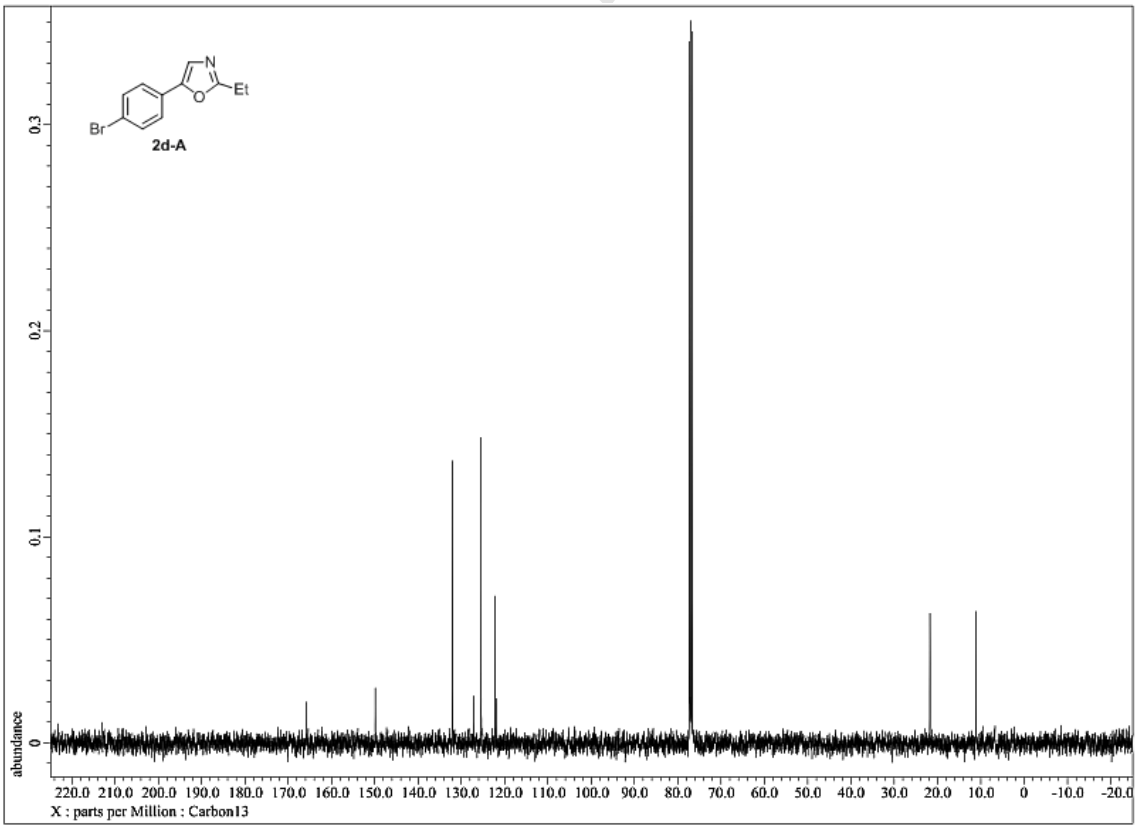

2b-A
abundance
X : parts per Million : Proton

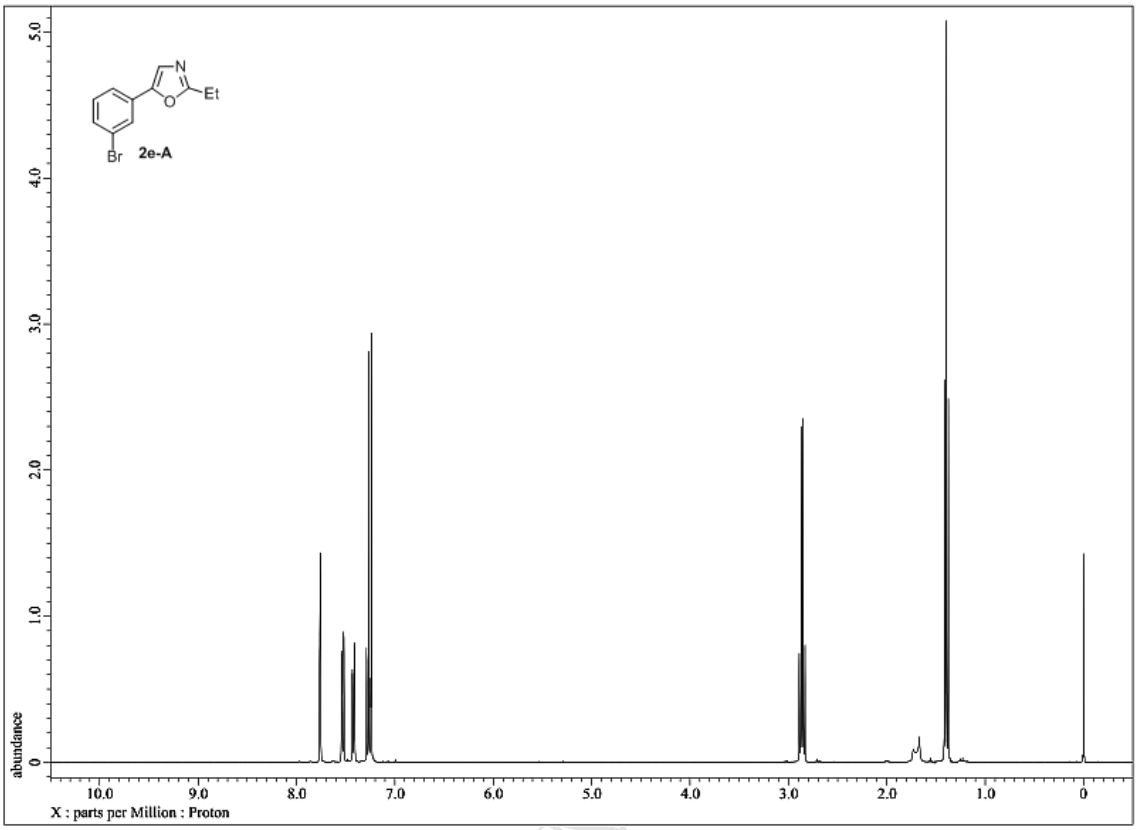

2b-A
abundance
X : parts per Million : Carbon13

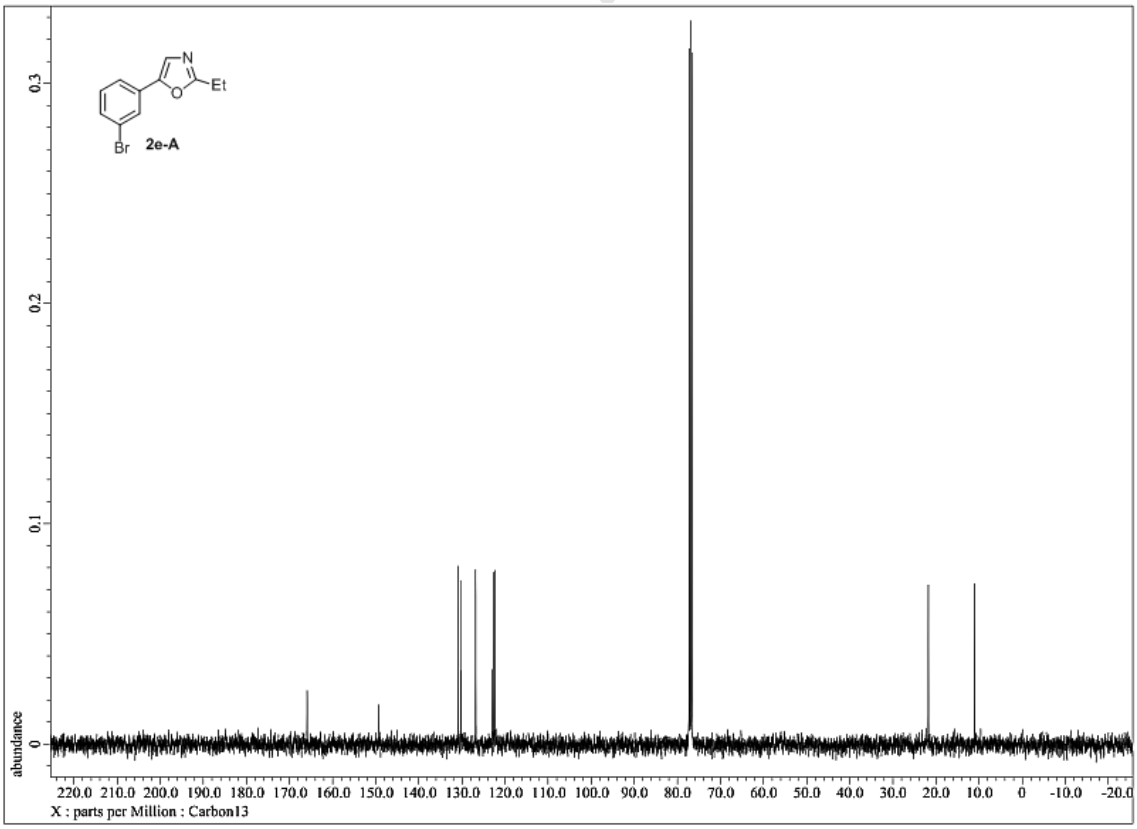

2c-A
abundance
X : parts per Million : Proton

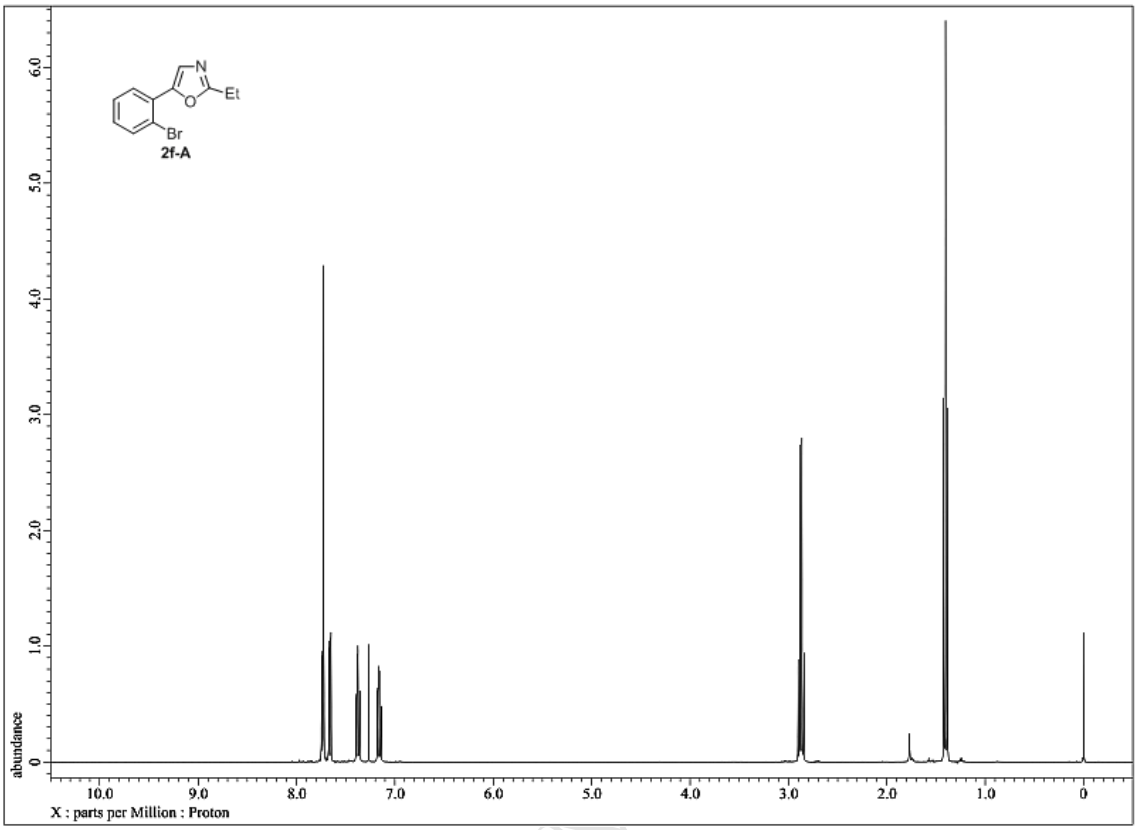

2c-A
abundance
X : parts per Million : Carbon13

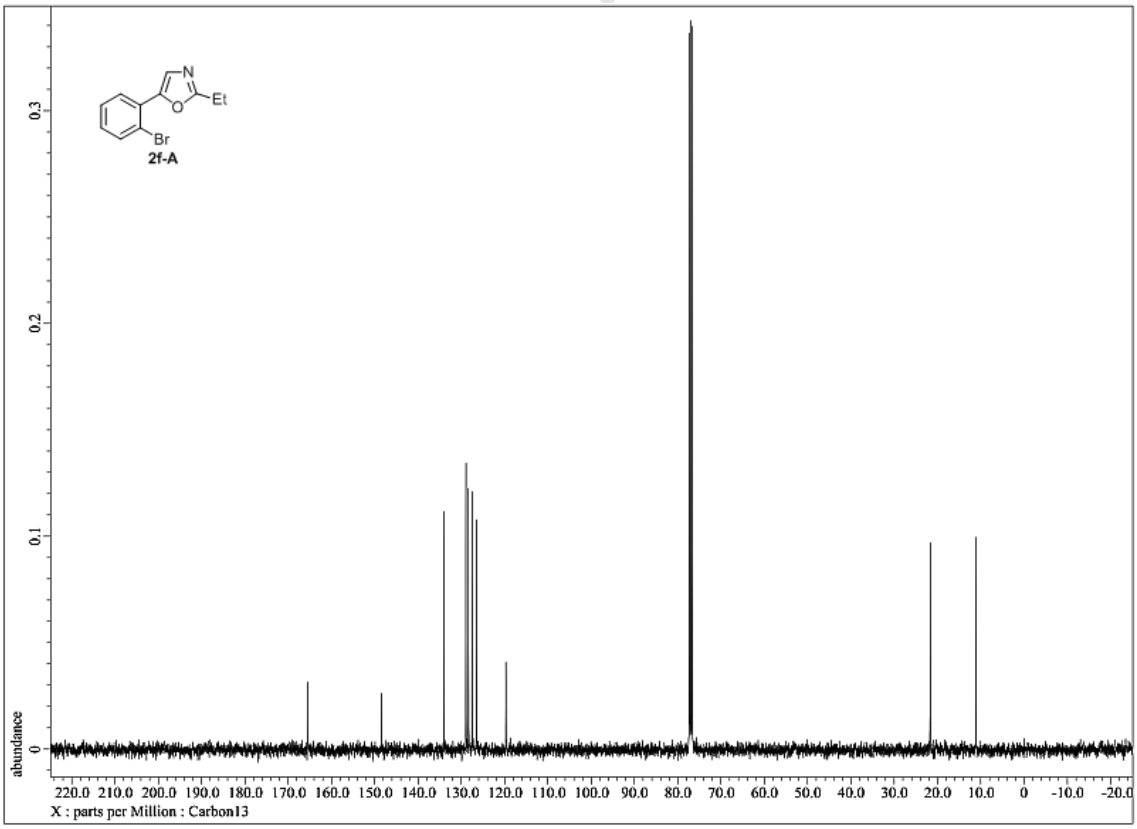

Br
N
O
Et
2d-A
abundance
X : parts per Million : Proton

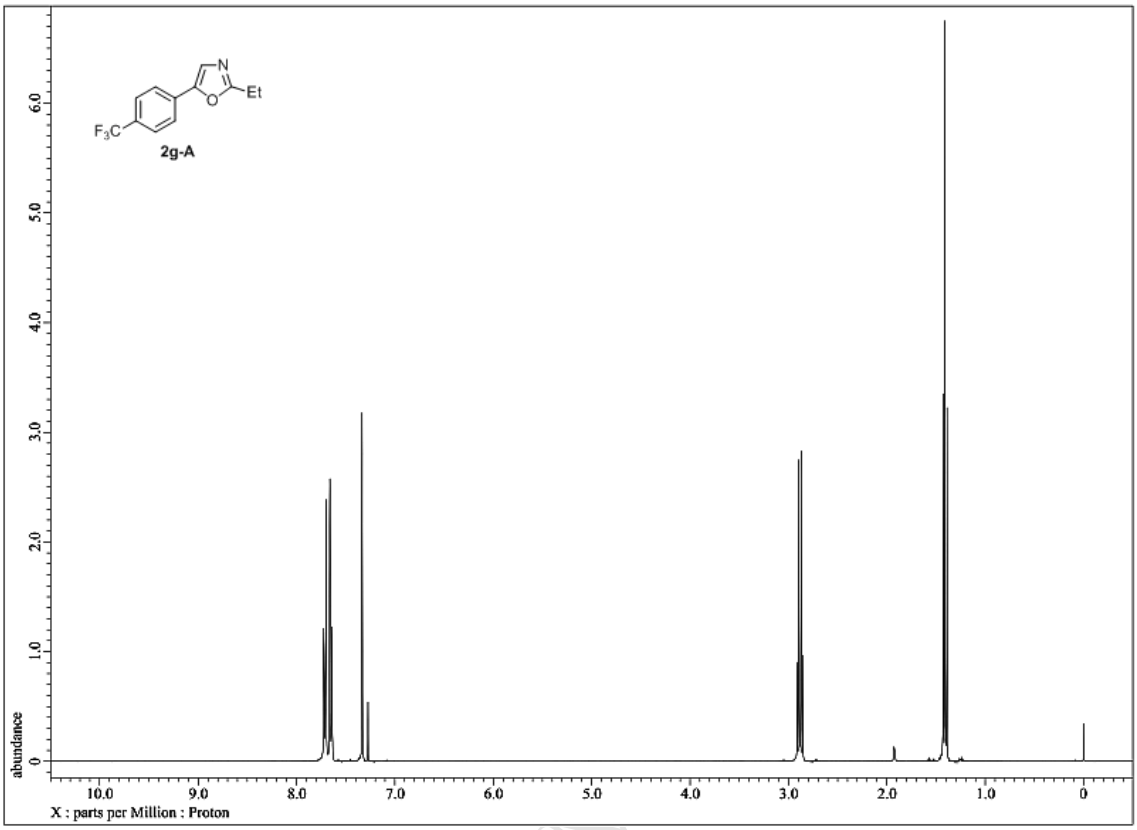

Br
N
O
Et
2d-A
abundance
X : parts per Million : Carbon13

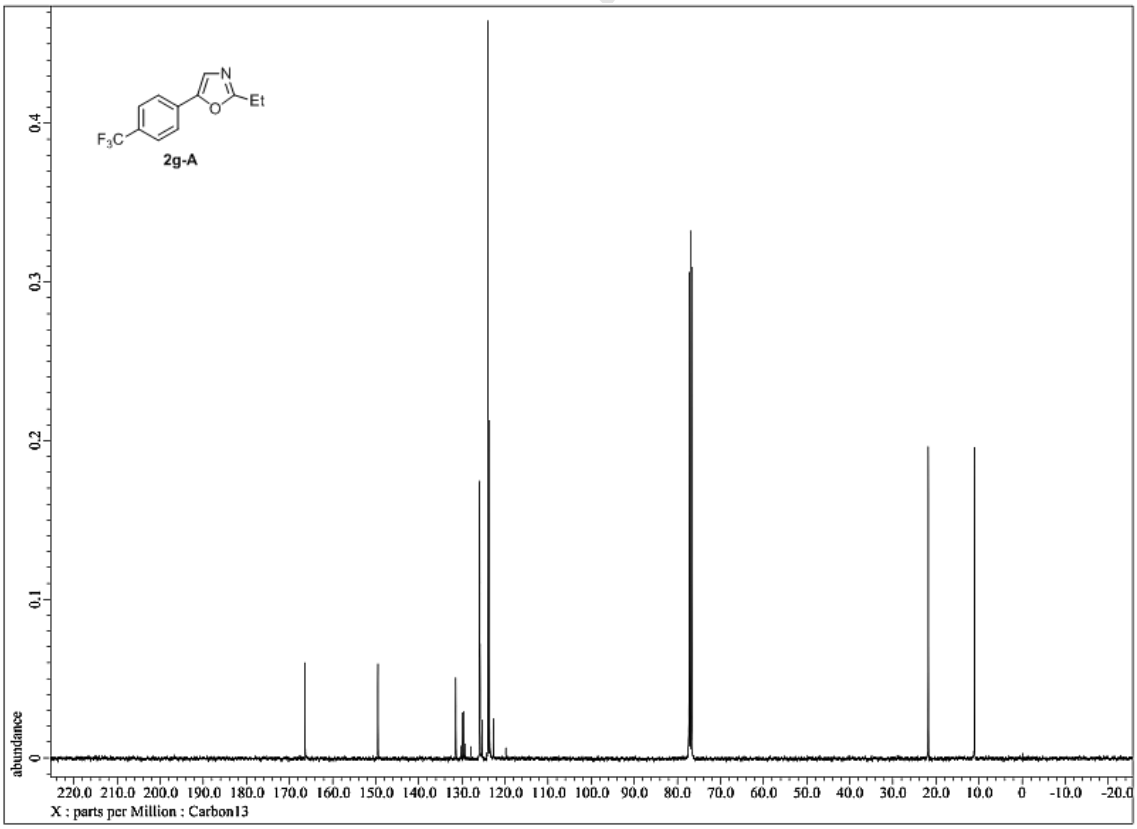

N
Et
O
Br
2e-A
abundance
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

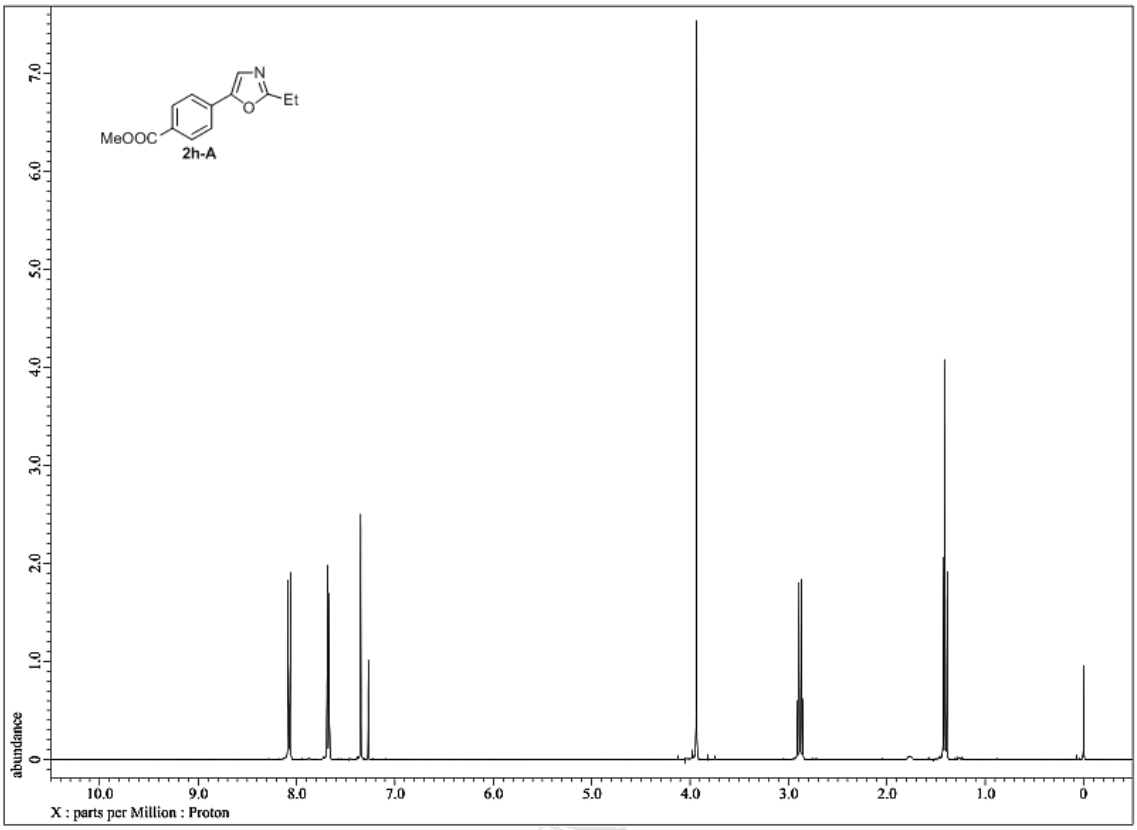

N
Et
O
Br
2e-A
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
X : parts per Million : Carbon13

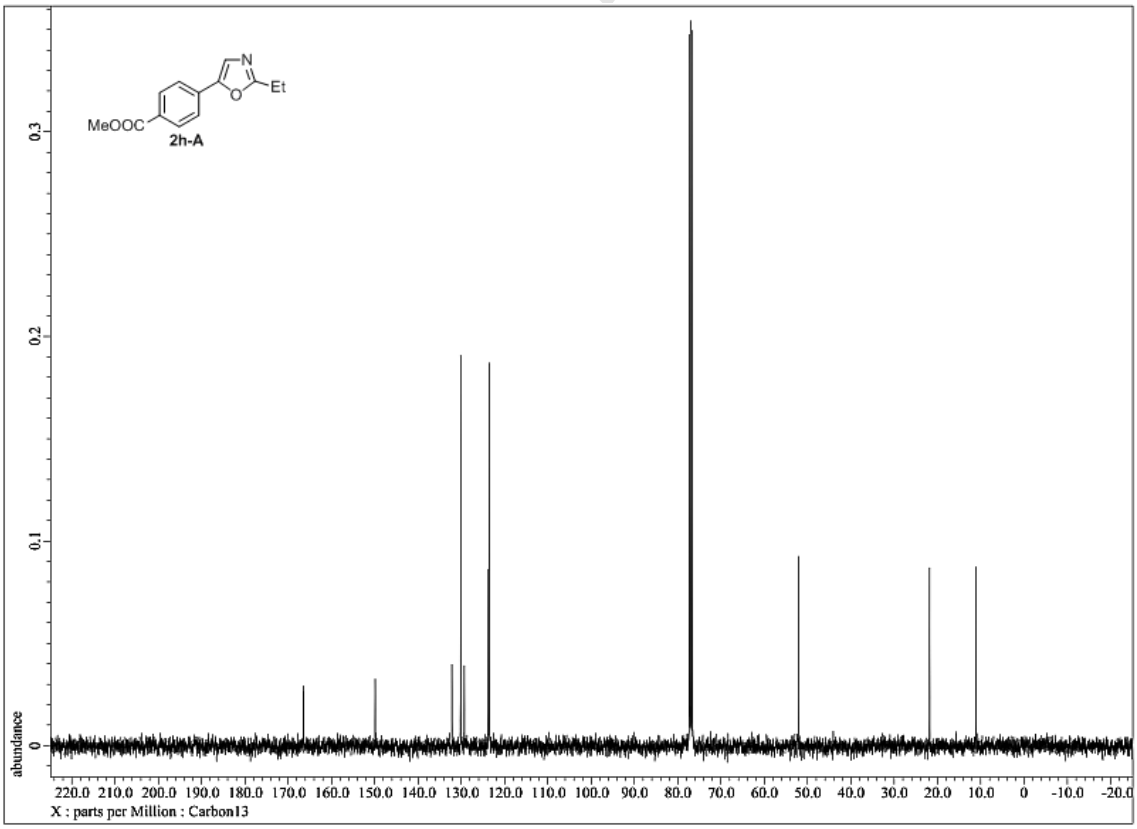

N
Et
O
Br
2f-A
abundance
X : parts per Million : Proton

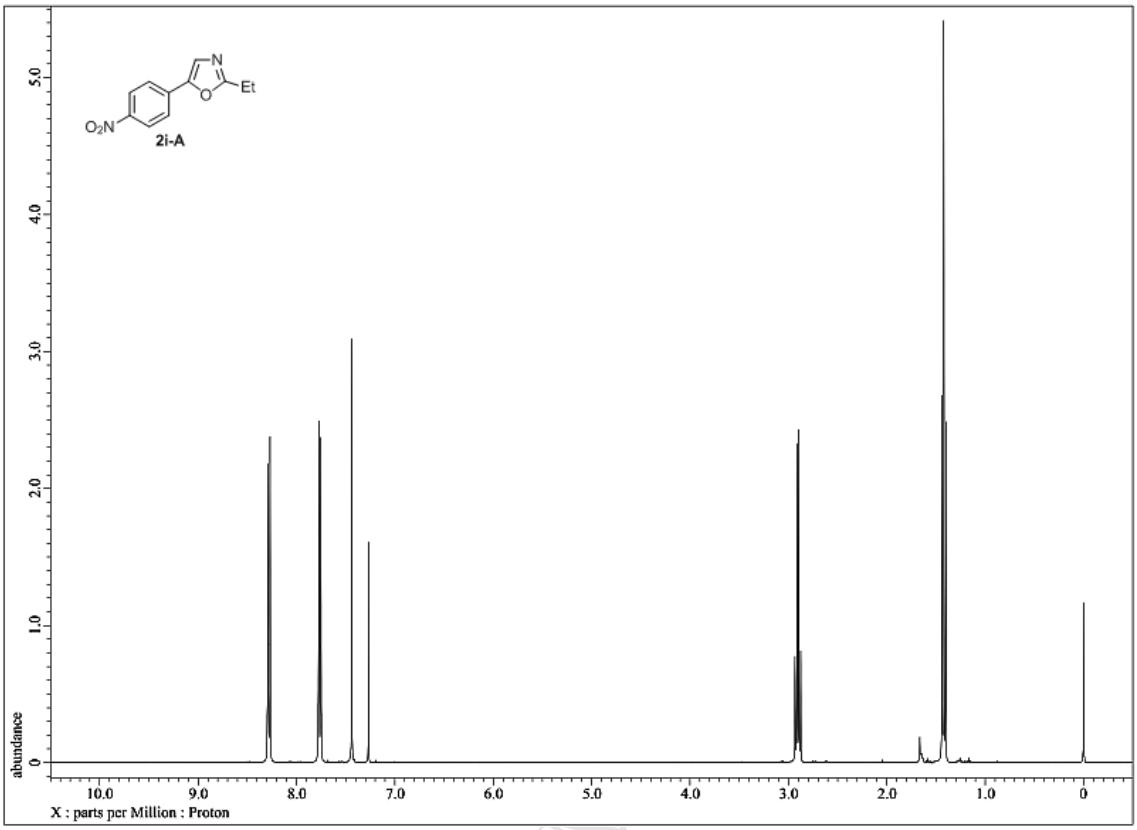

N
Et
O
Br
2f-A
abundance
X : parts per Million : Carbon13

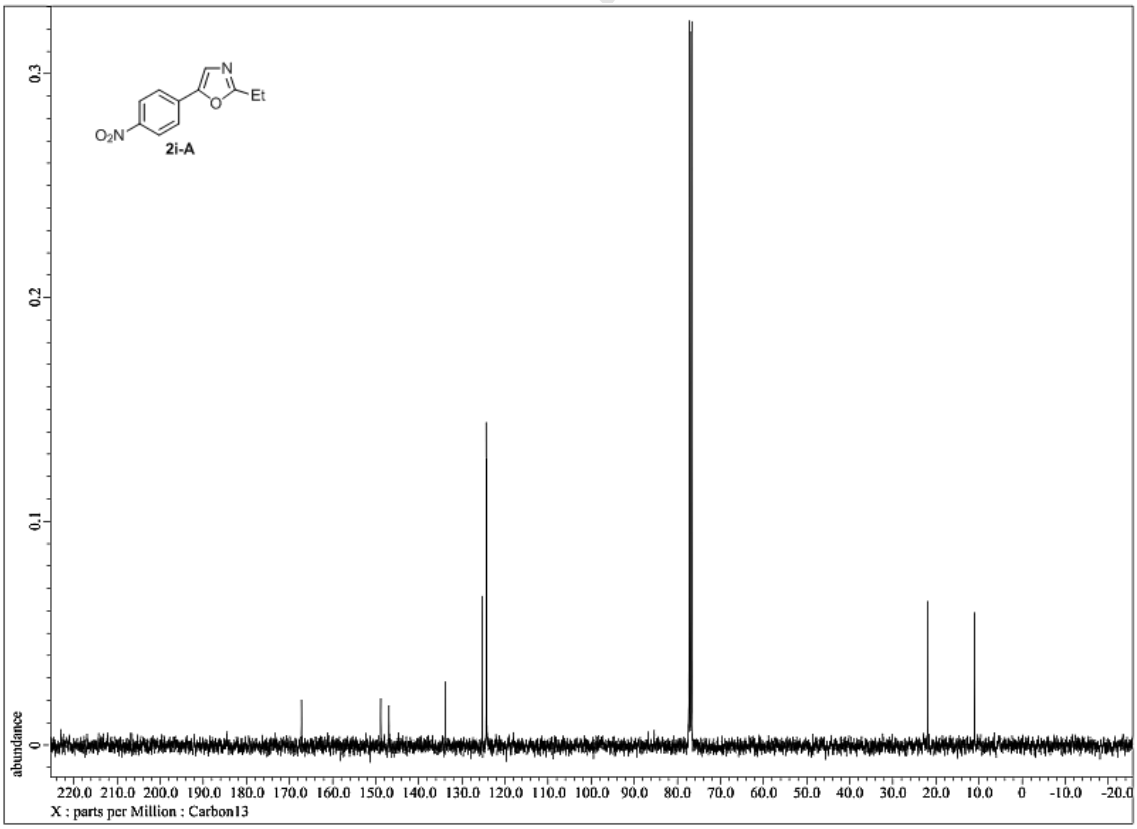

N
O
Et
F3C
2g-A
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

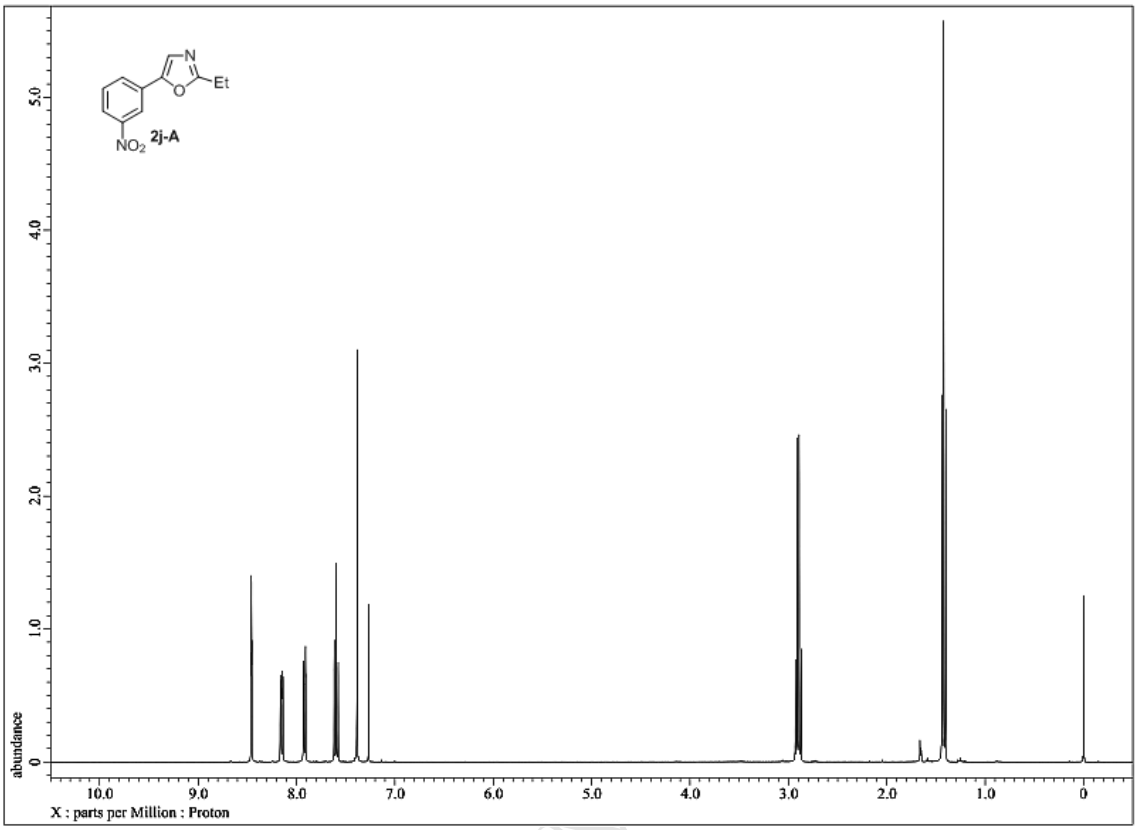

N
O
Et
F3C
2g-A
abundance
0
0.1
0.2
0.3
0.4
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
X : parts per Million : Carbon13

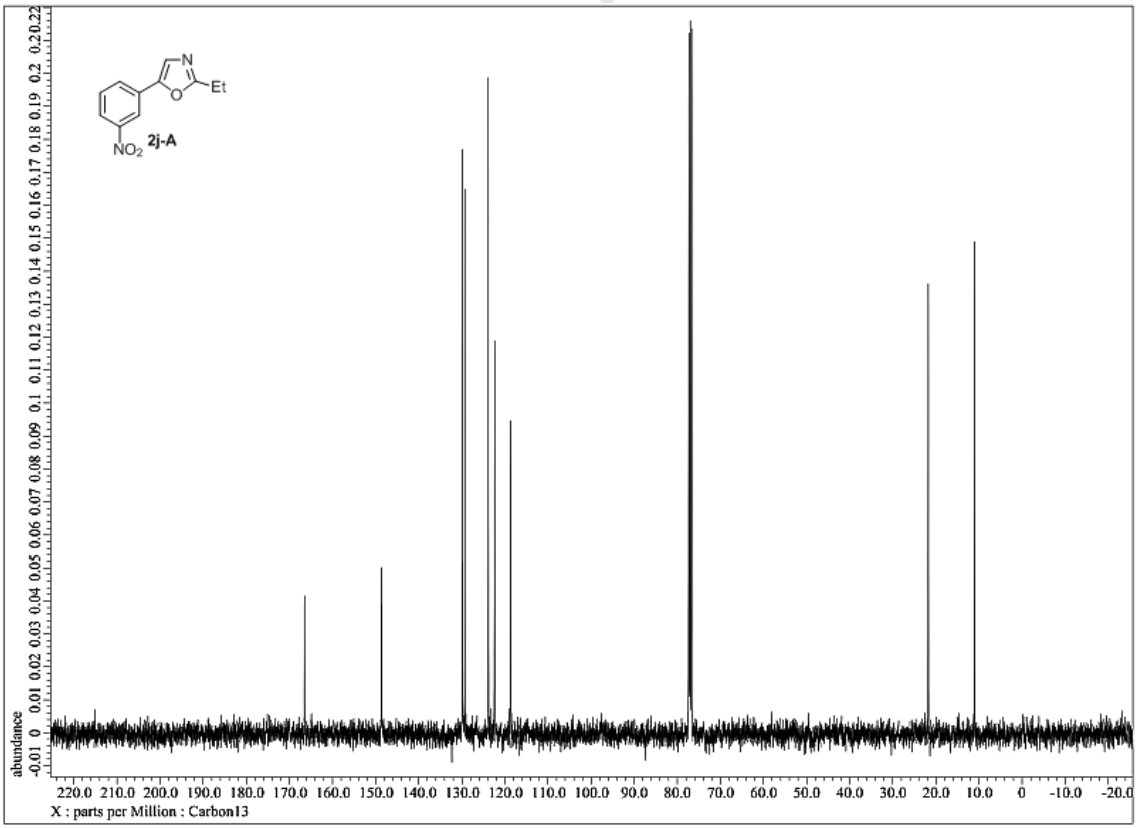

MeOOC
Et
N
O
2h-A
abundance
X : parts per Million : Proton

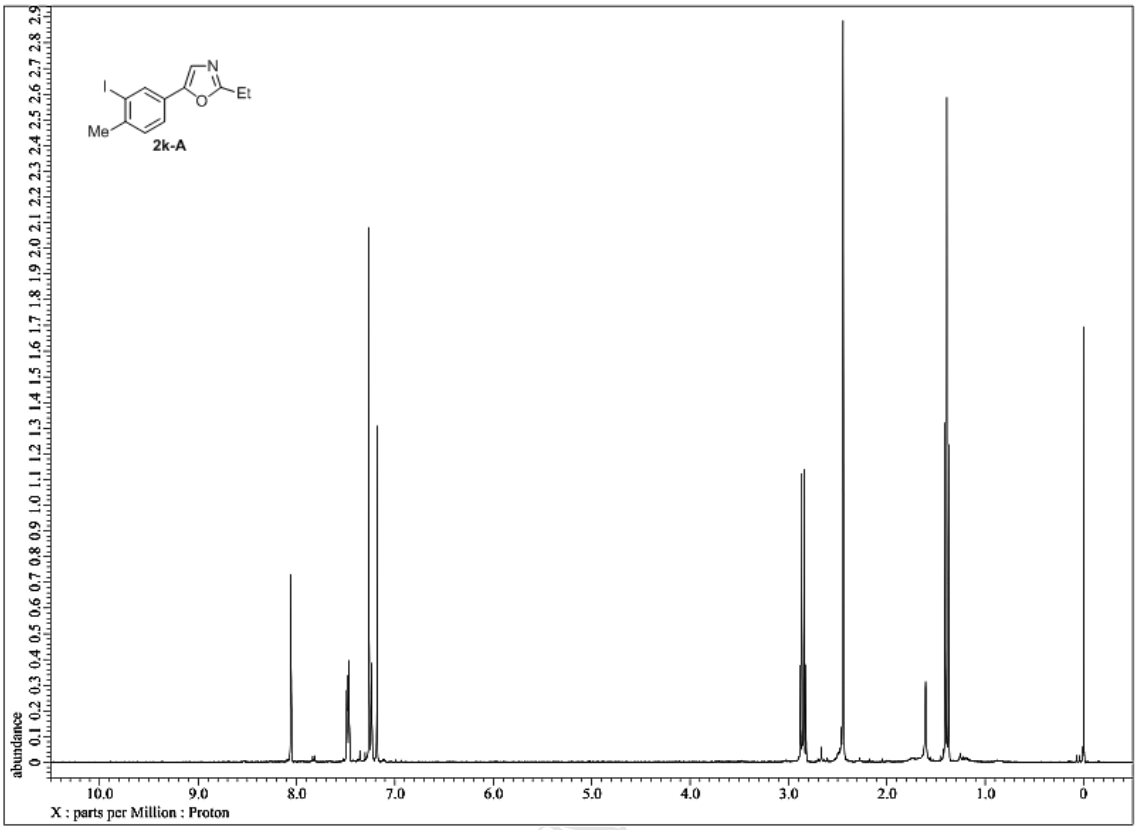

MeOOC
Et
N
O
2h-A
abundance
X : parts per Million : Carbon13

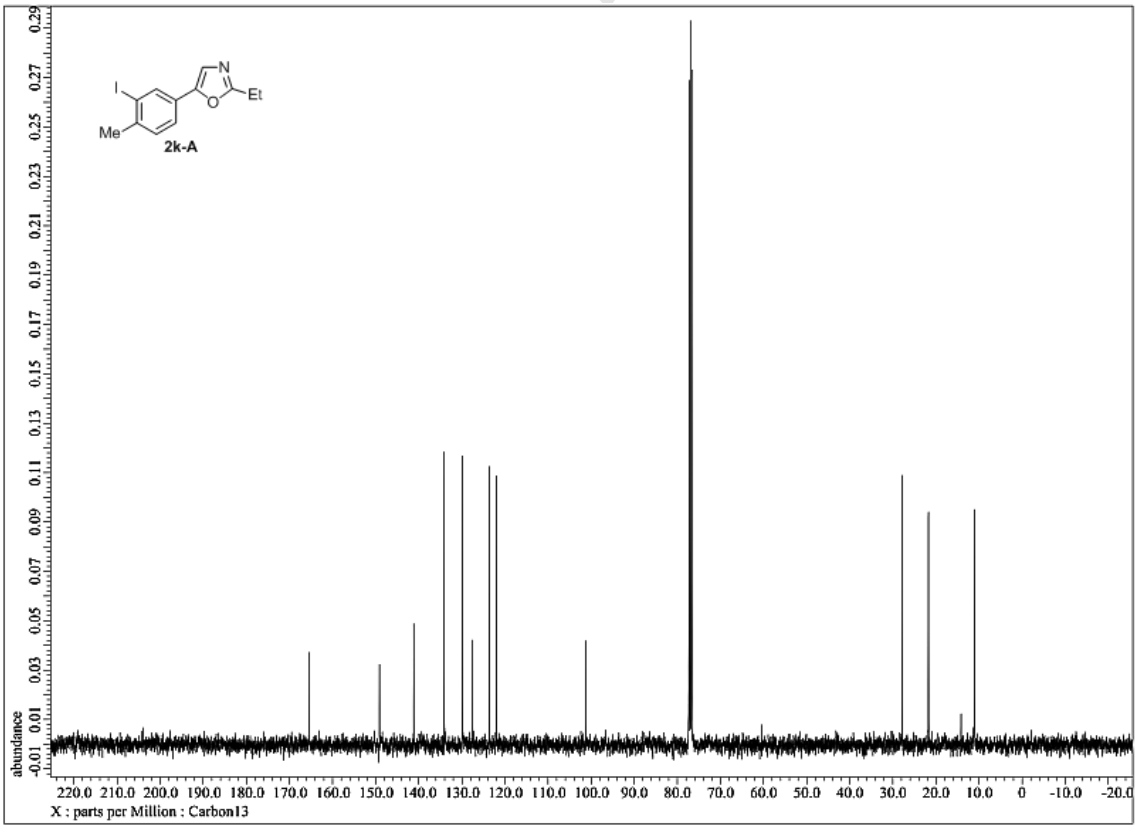

2i-A
abundance
X : parts per Million : Proton

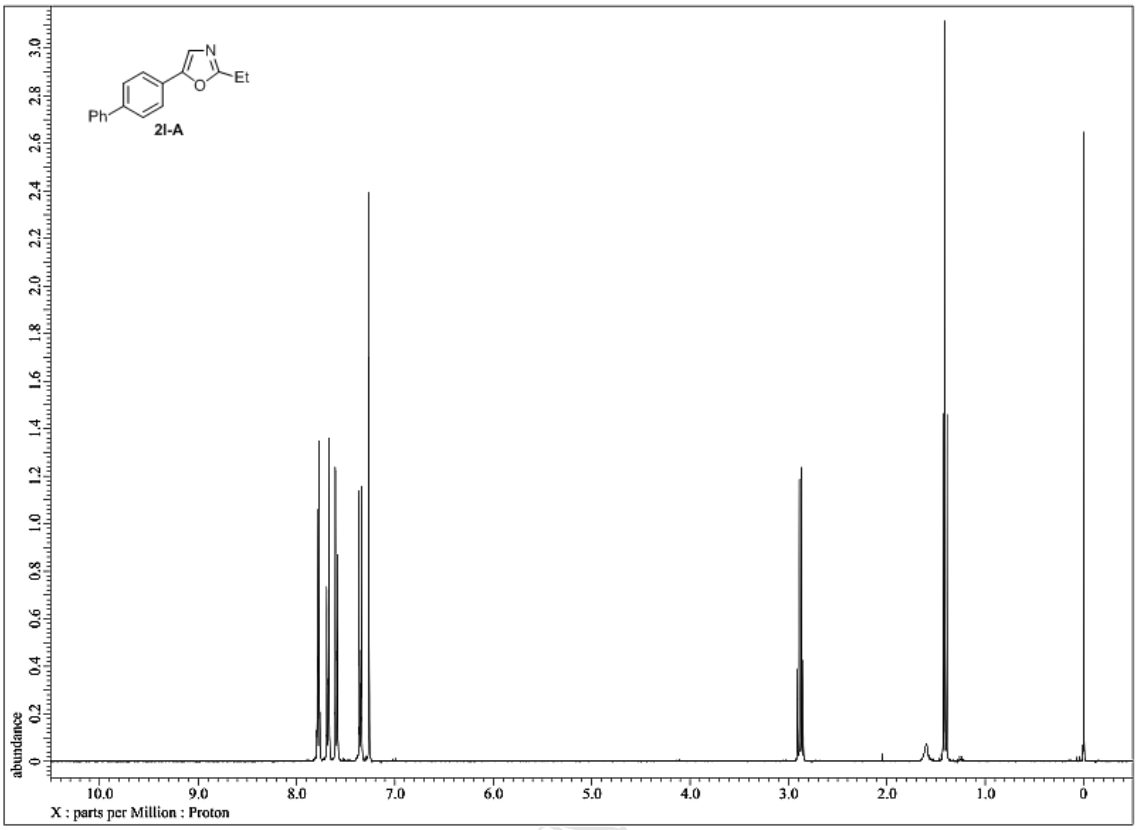

2i-A
abundance
X : parts per Million : Carbon13

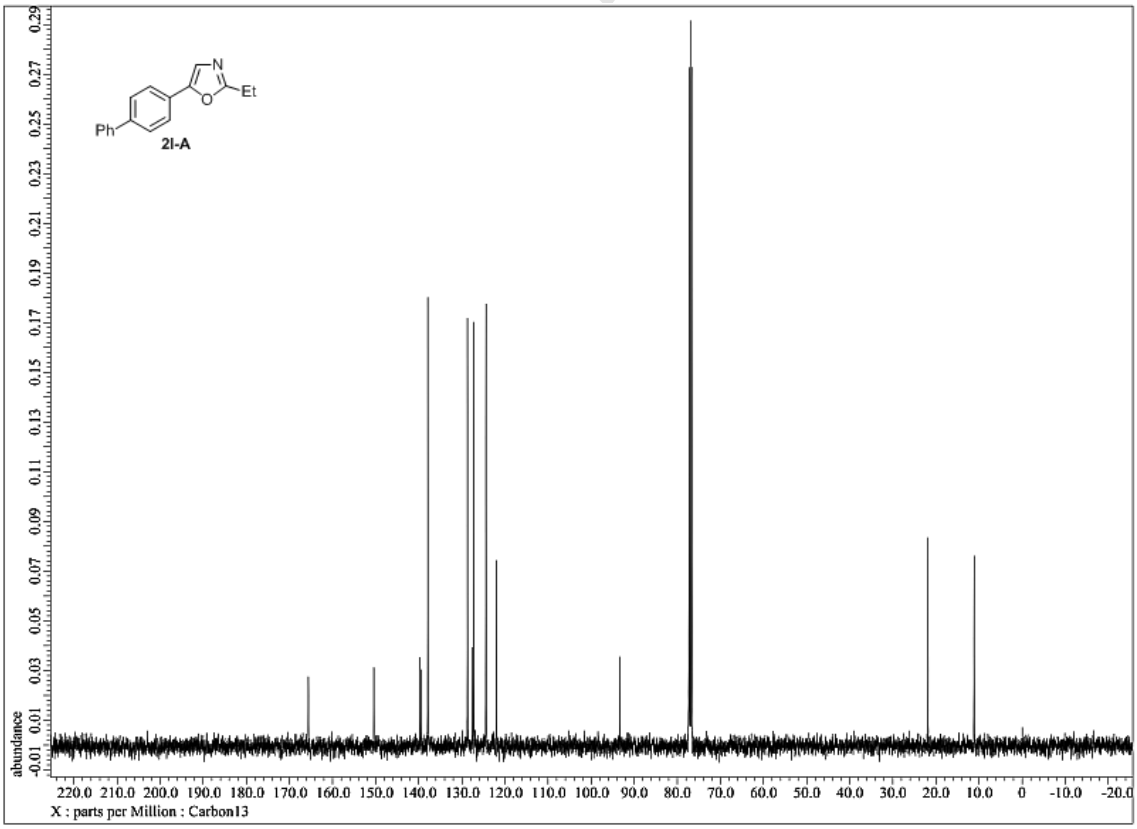

2j-A
abundance
X : parts per Million : Proton

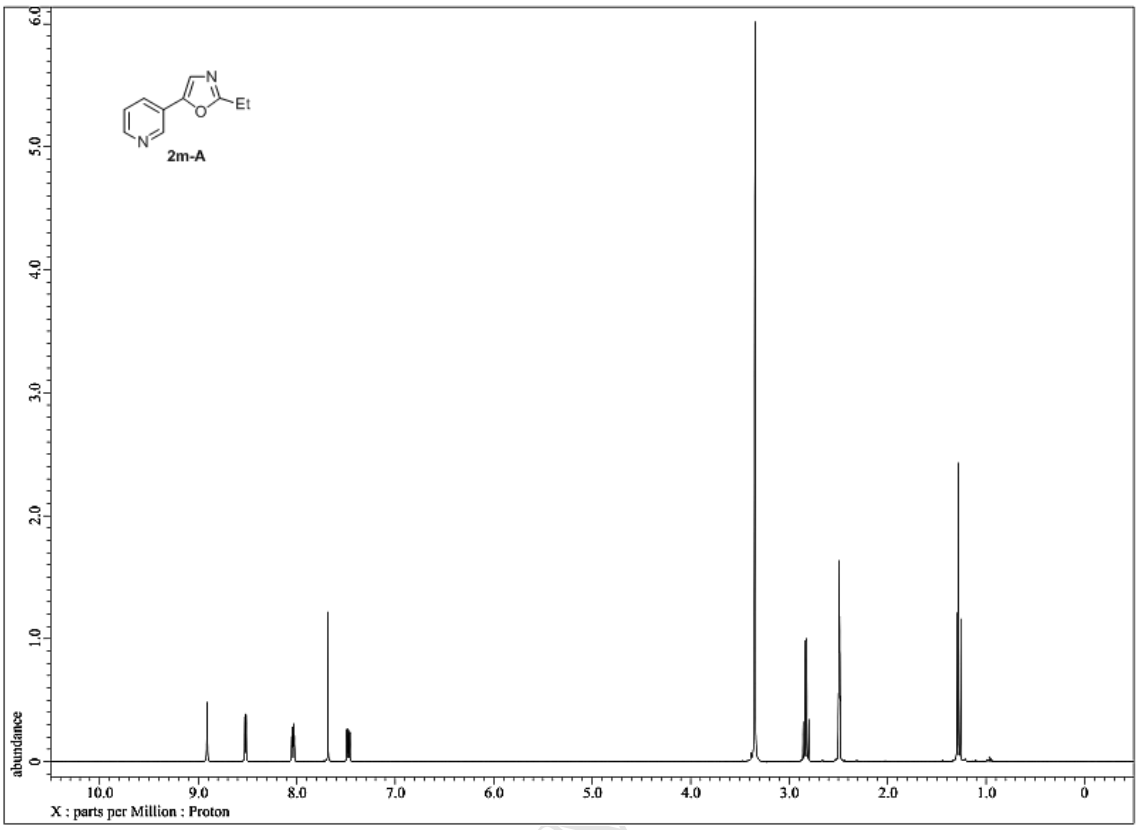

2j-A
abundance
X : parts per Million : Carbon13

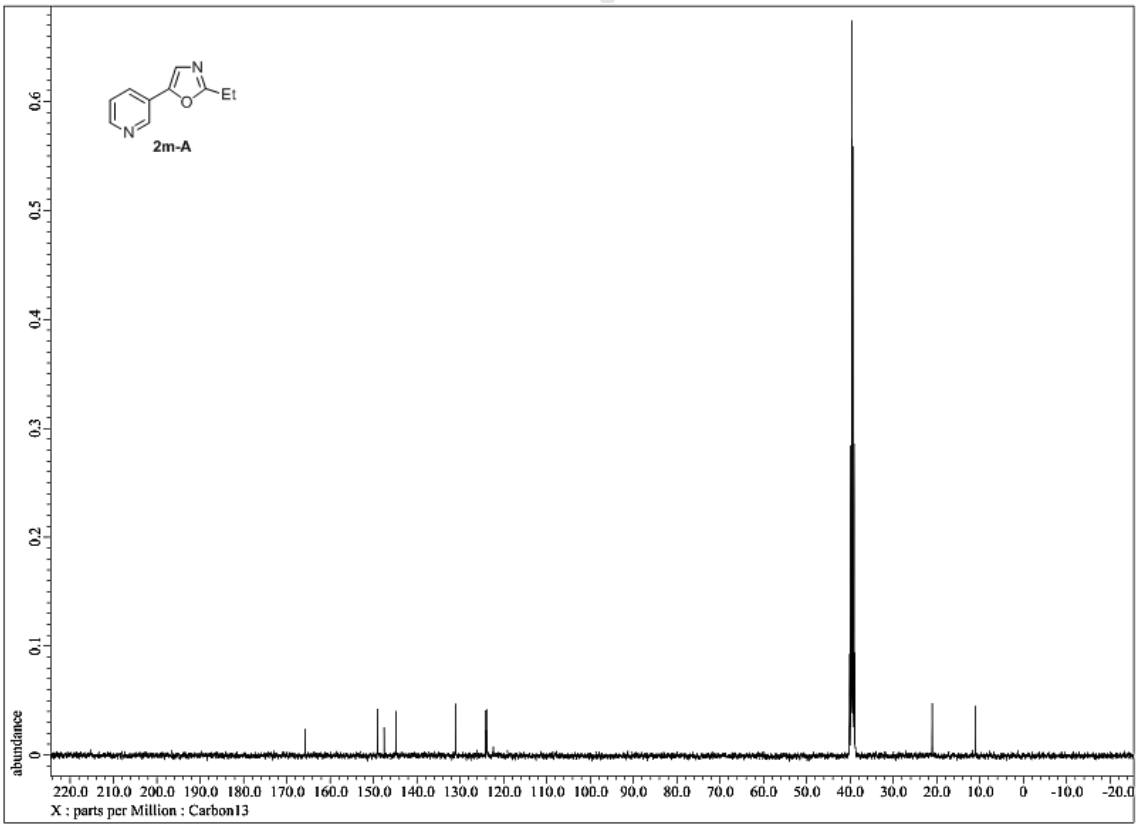

I
Me
N
O
Et
2k-A
abundance
X : parts per Million : Proton

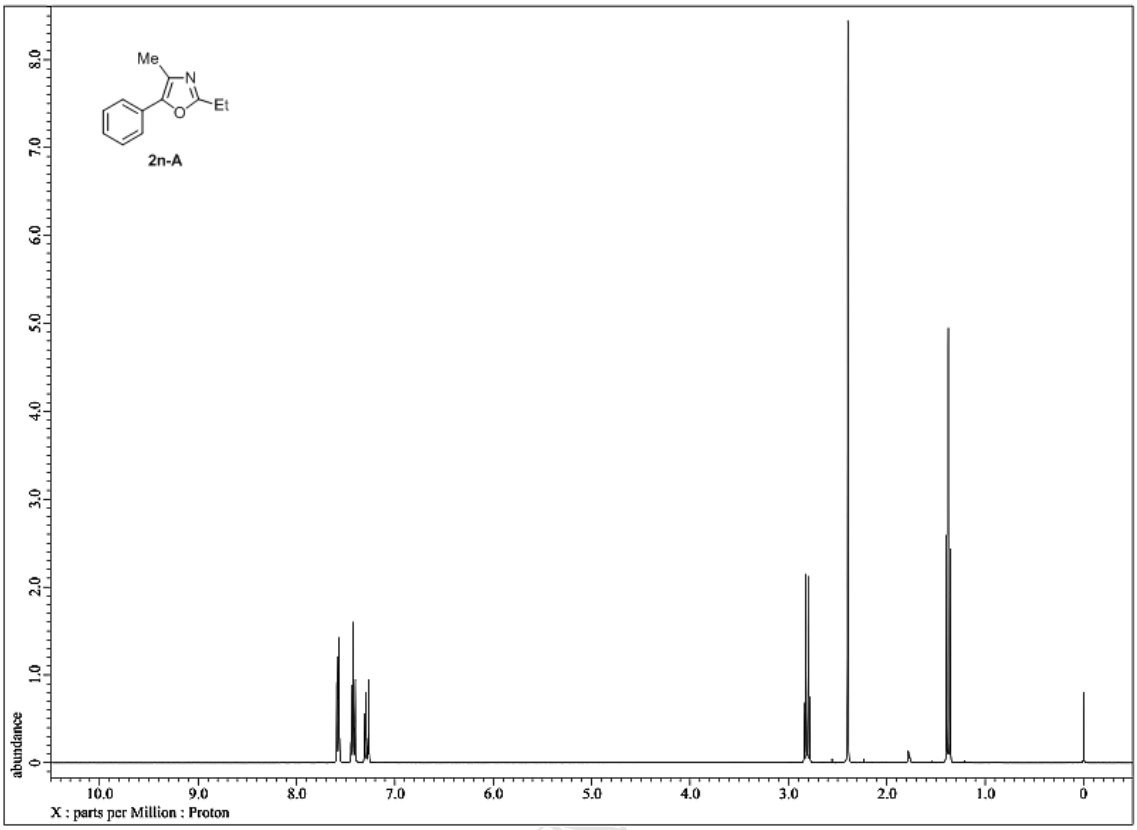

I
Me
N
O
Et
2k-A
abundance
X : parts per Million : Carbon13

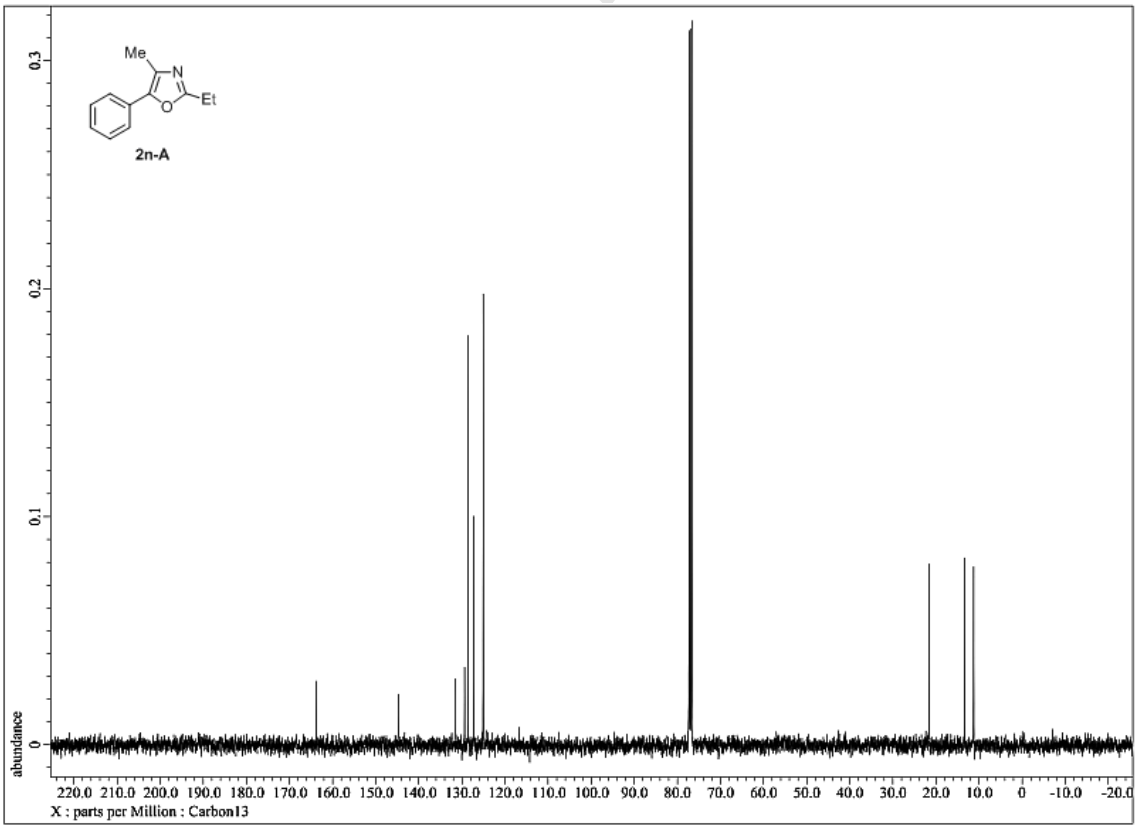

N
O
Et
Ph
2l-A
abundance
X : parts per Million : Proton

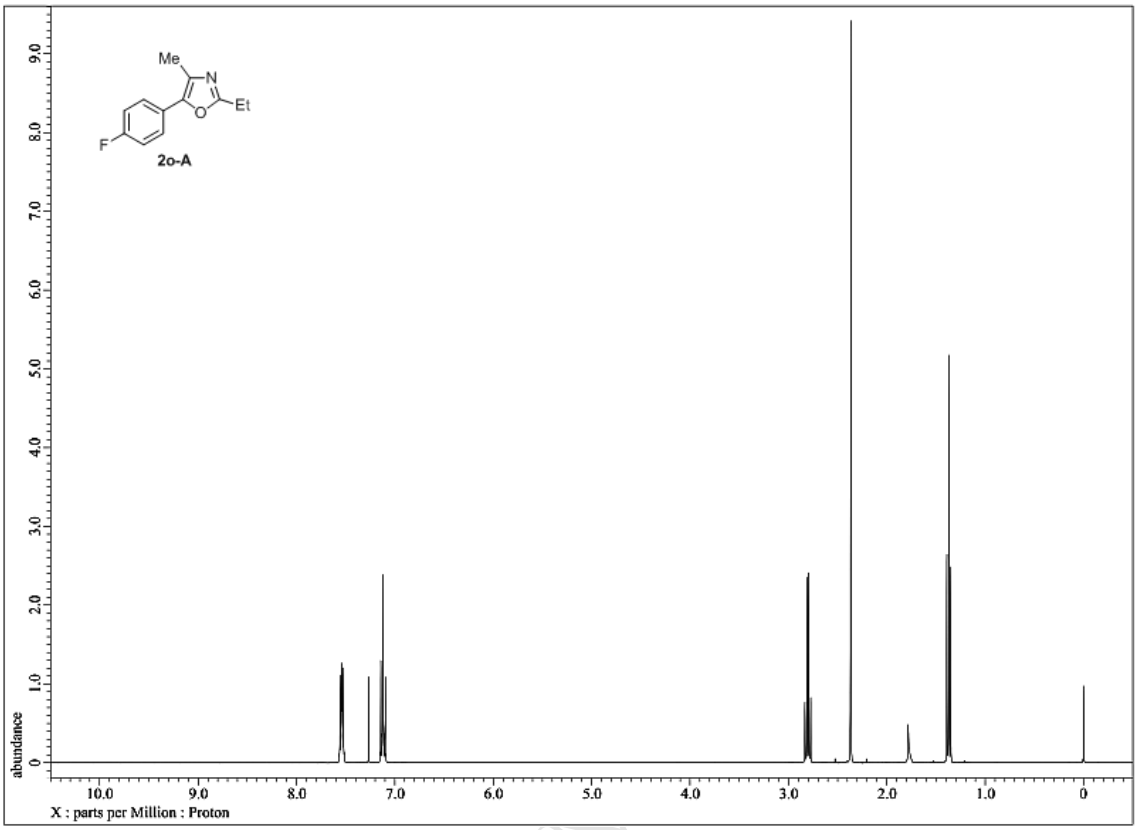

N
O
Et
Ph
2l-A
abundance
X : parts per Million : Carbon13

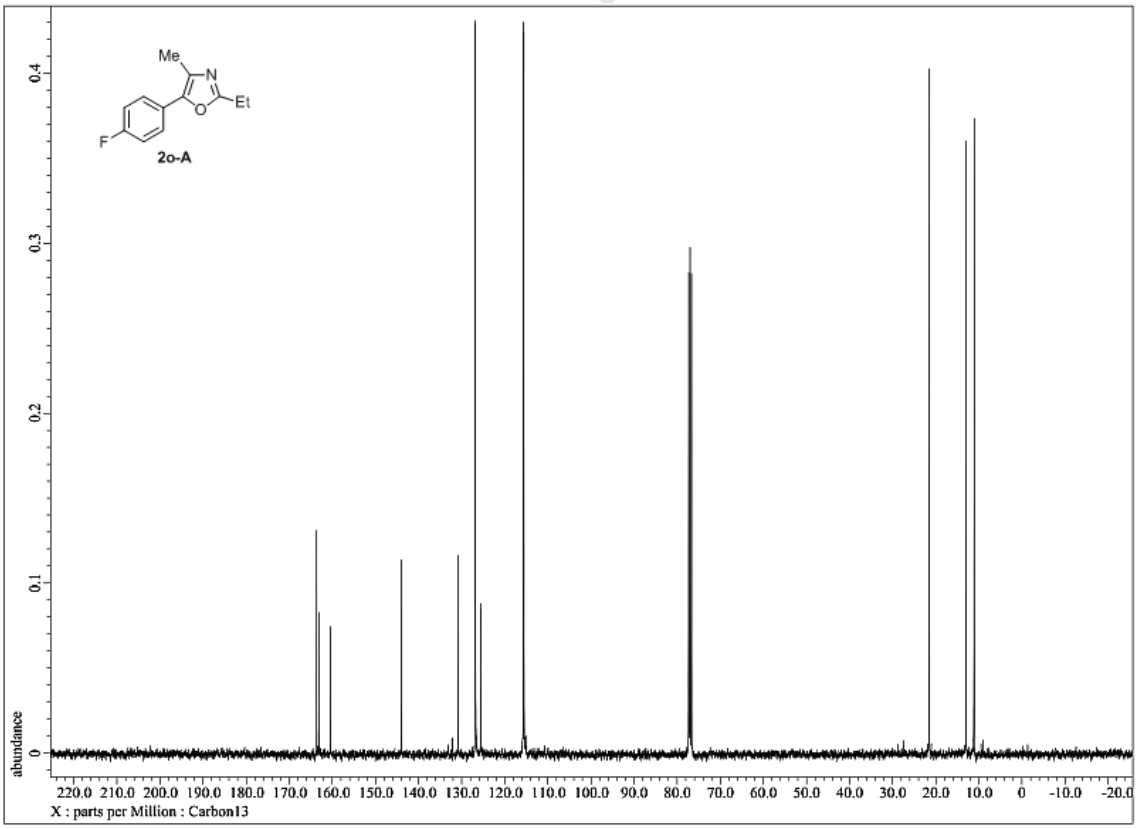

2m-A
abundance
X : parts per Million : Proton

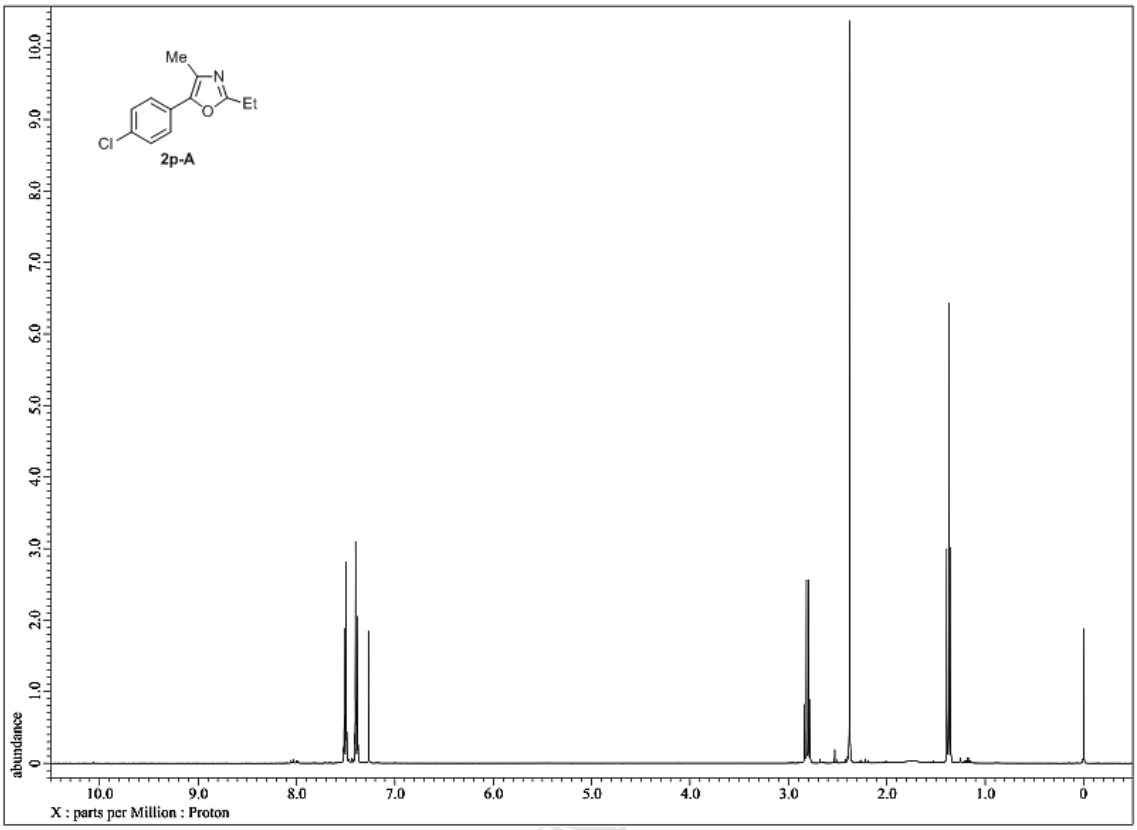

2m-A
abundance
X : parts per Million : Carbon13

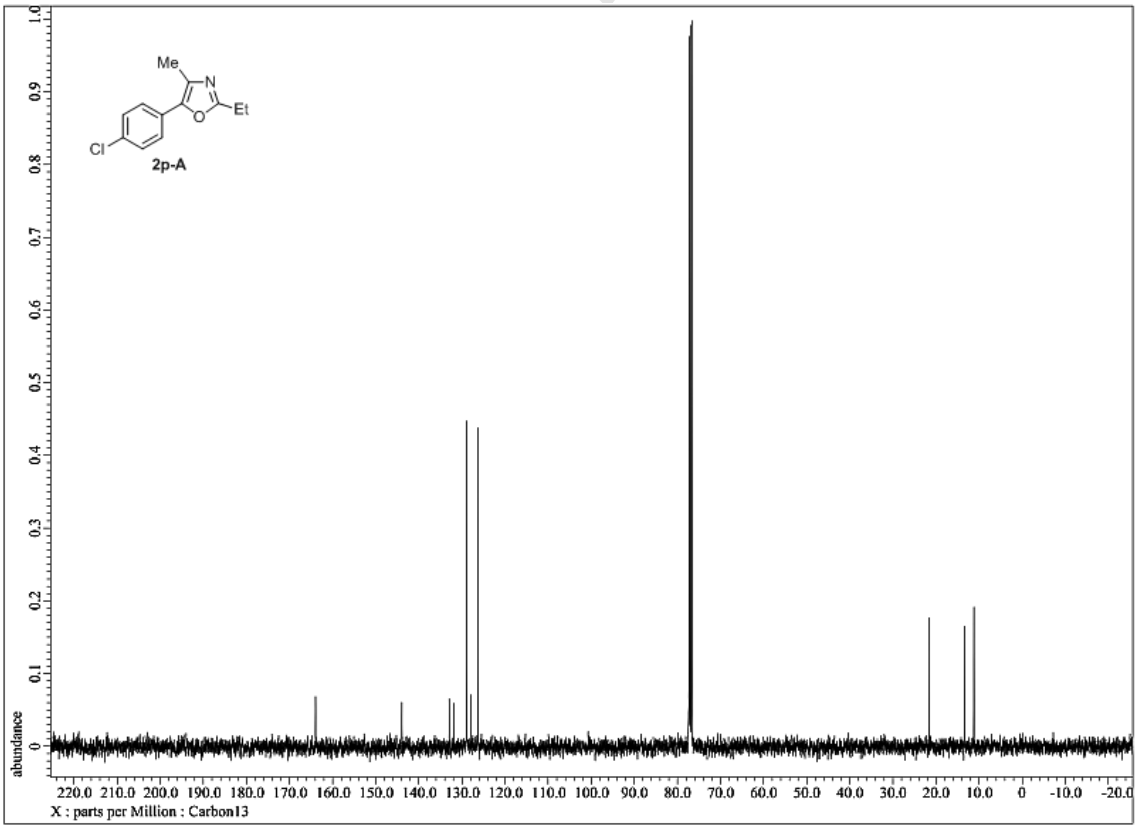

Me
N
O
Et
2n-A
abundance
X : parts per Million : Proton

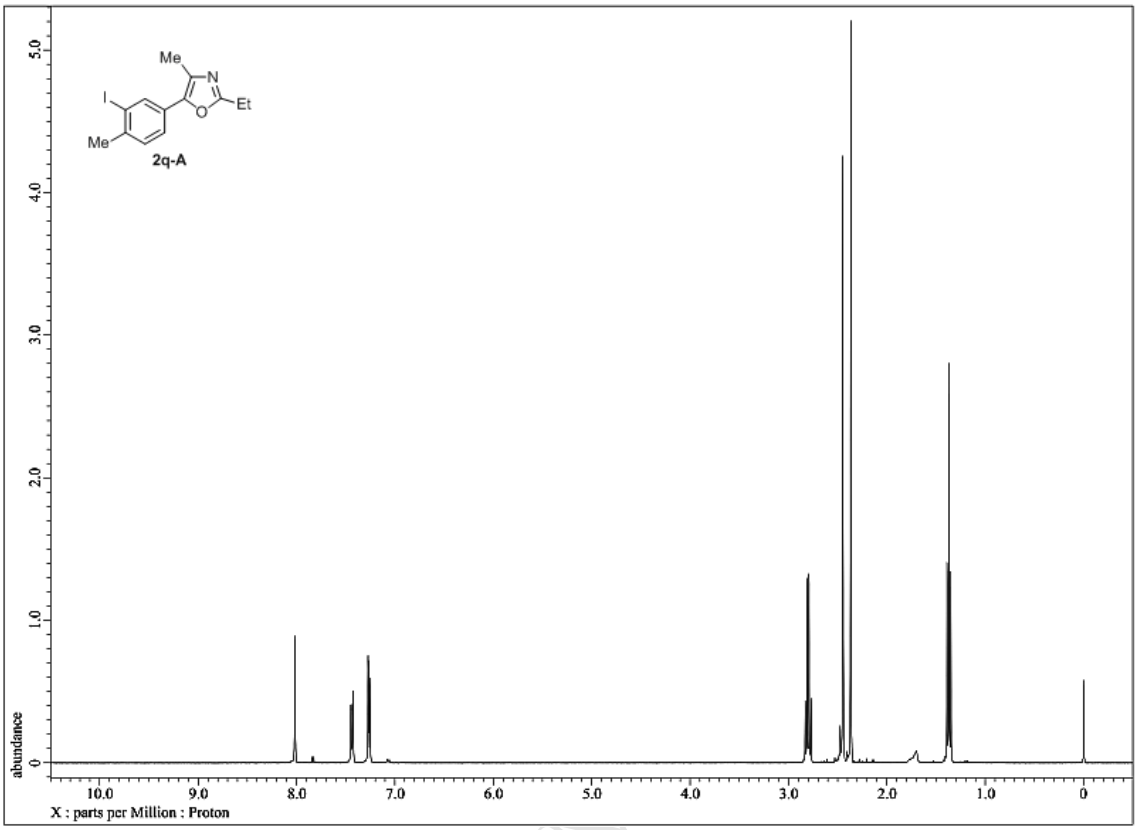

Me
N
O
Et
2n-A
abundance
X : parts per Million : Carbon13

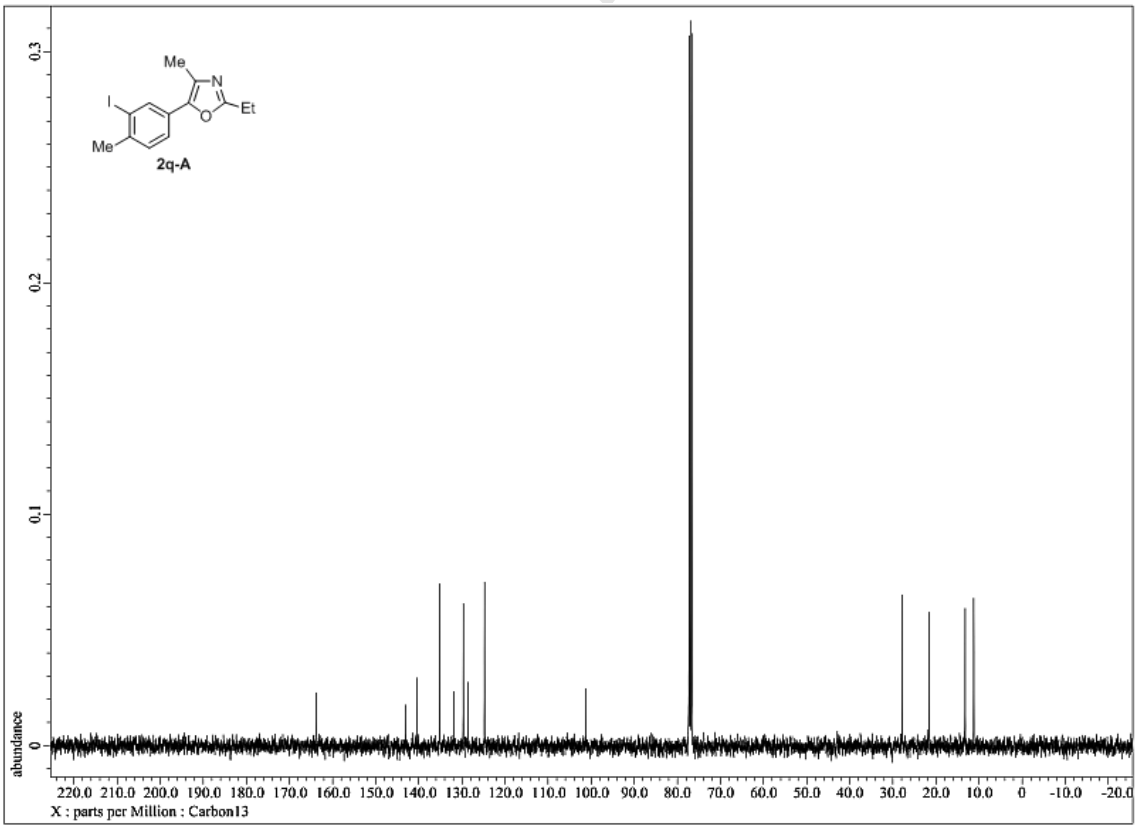

Me
N
Et
O
F
2o-A
abundance
X : parts per Million : Proton

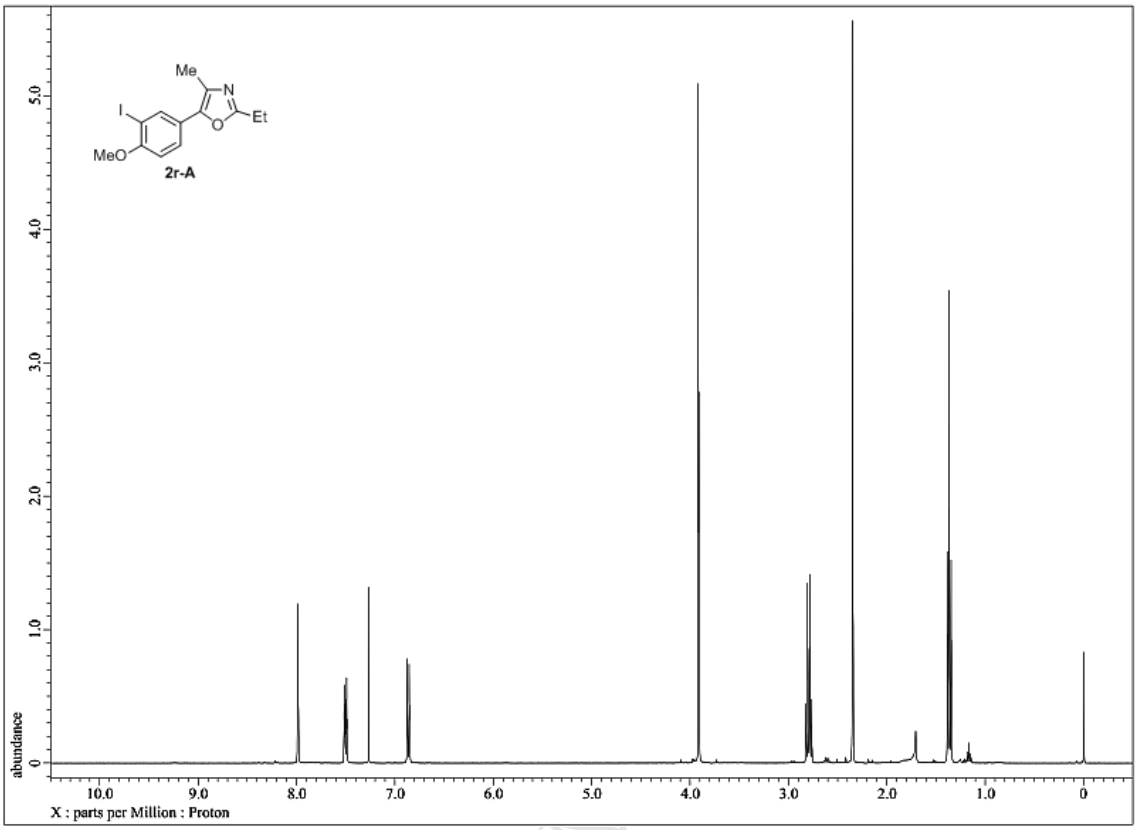

Me
N
Et
O
F
2o-A
abundance
X : parts per Million : Carbon13

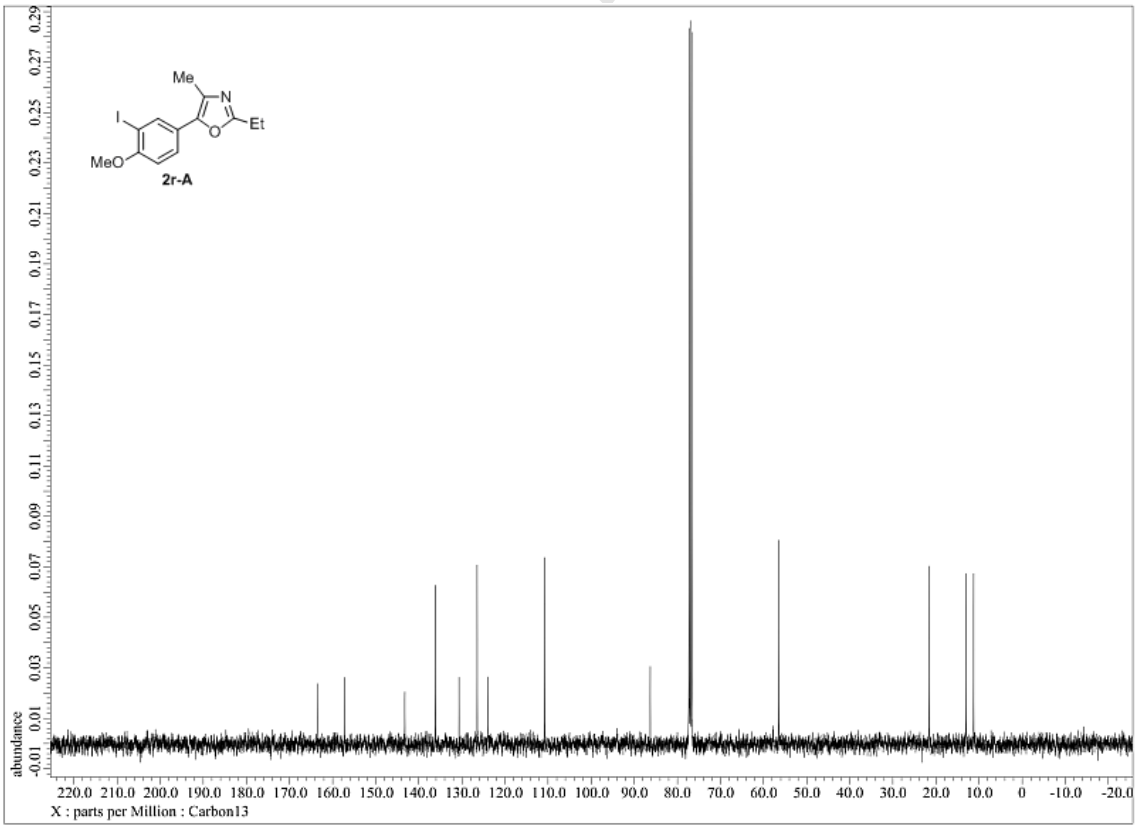

Me
N
Et
O
Cl
2p-A
abundance
X : parts per Million : Proton

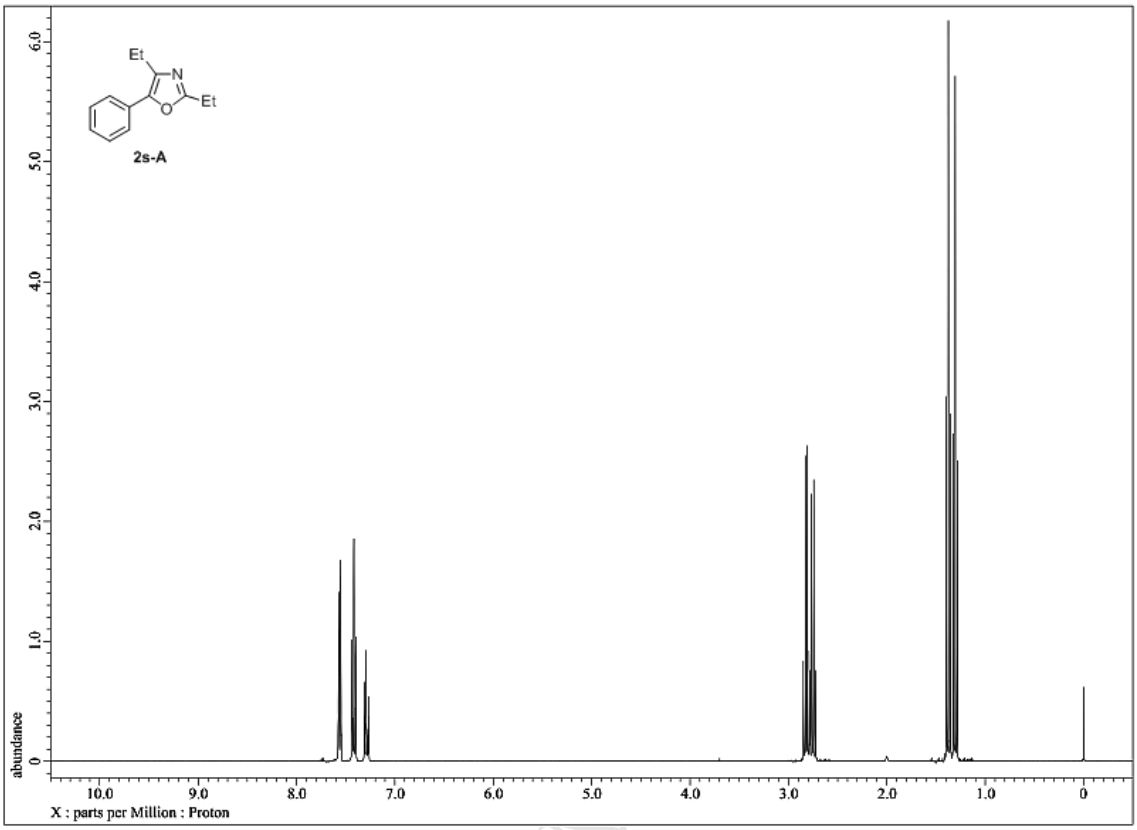

Me
N
Et
O
Cl
2p-A
abundance
X : parts per Million : Carbon13

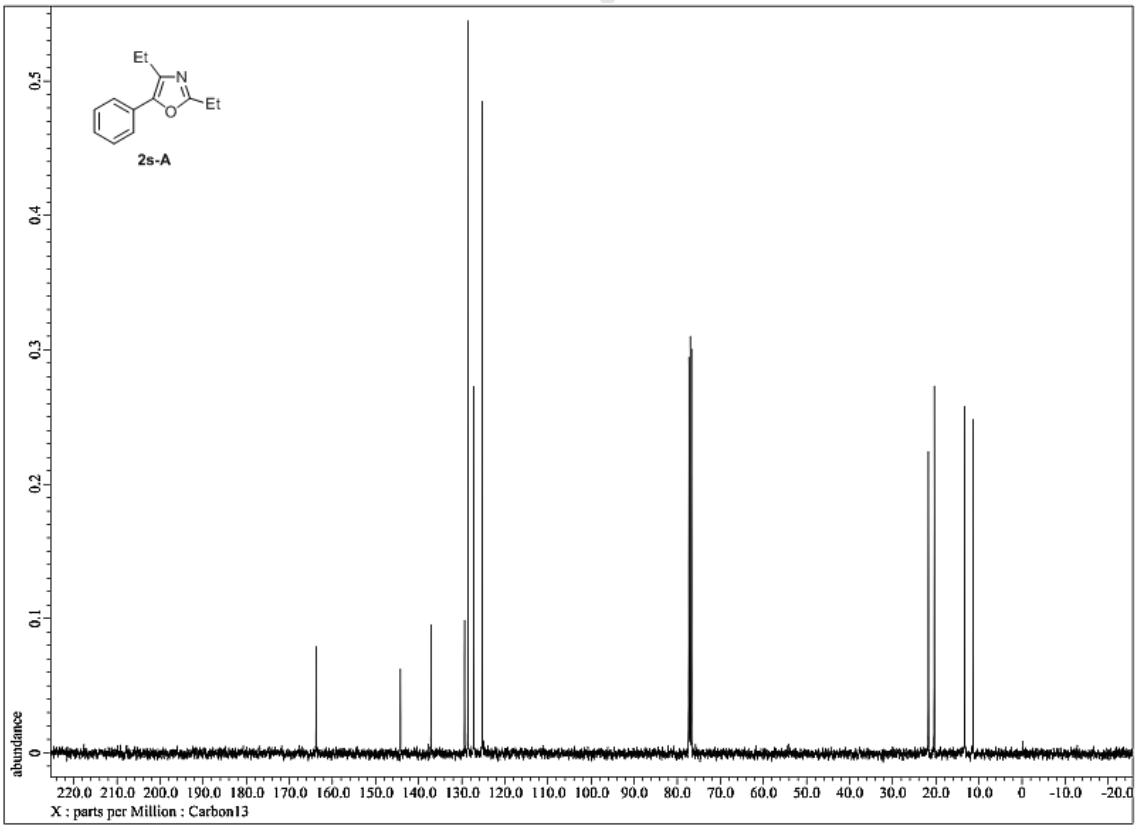

Me
N
I
Et
O
Me
2q-A
abundance
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

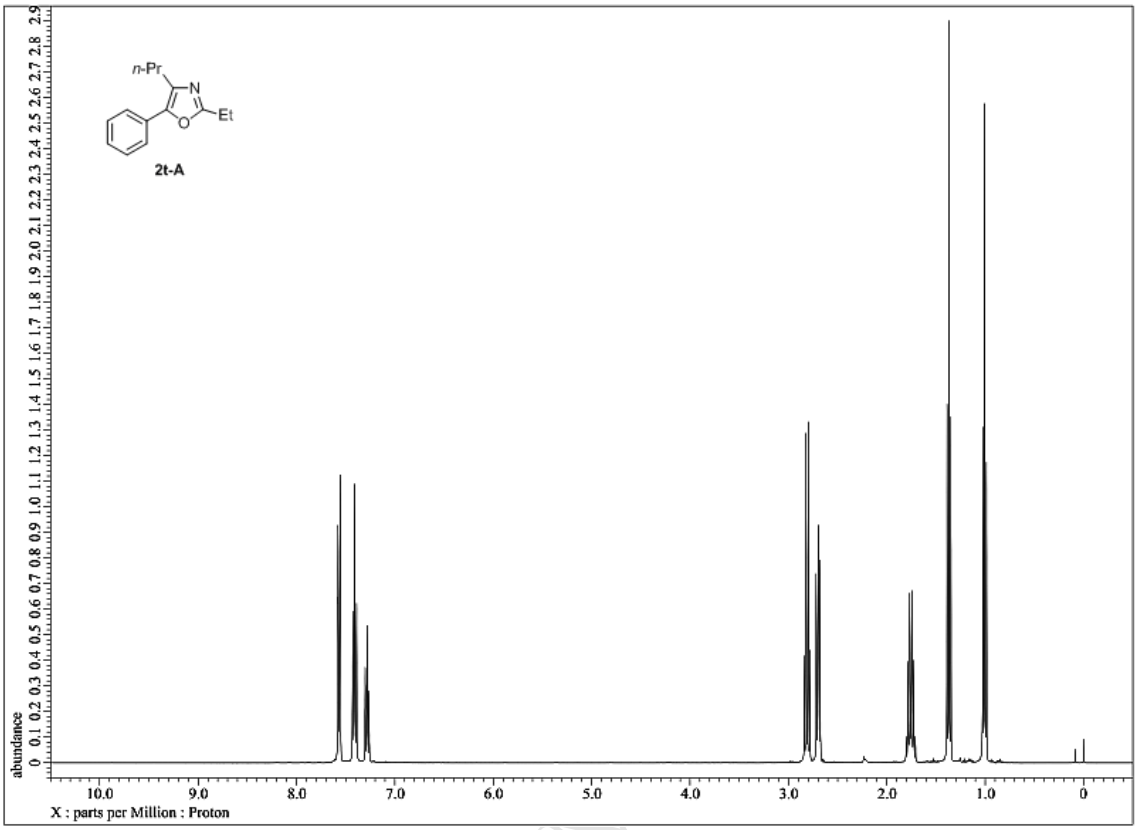

Me
N
I
Et
O
Me
2q-A
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
X : parts per Million : Carbon13

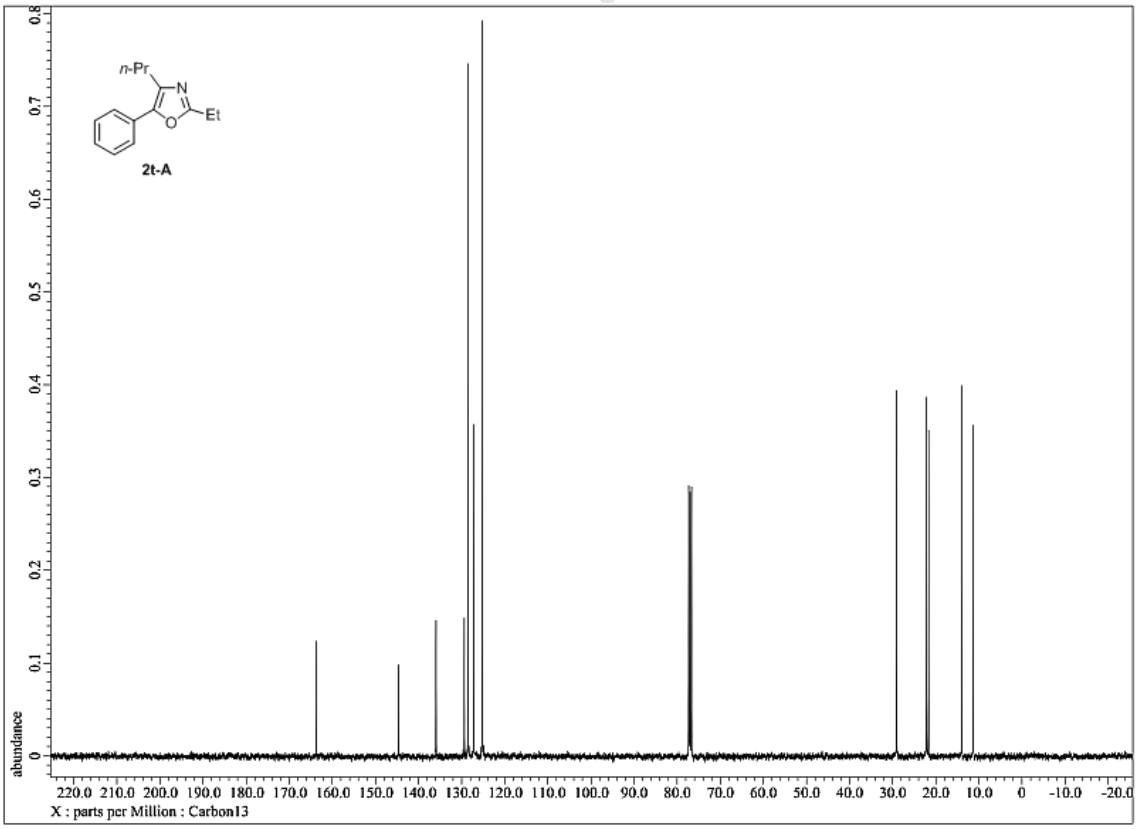

Me
N
Et
O
I
MeO
2r-A
abundance
X : parts per Million : Proton

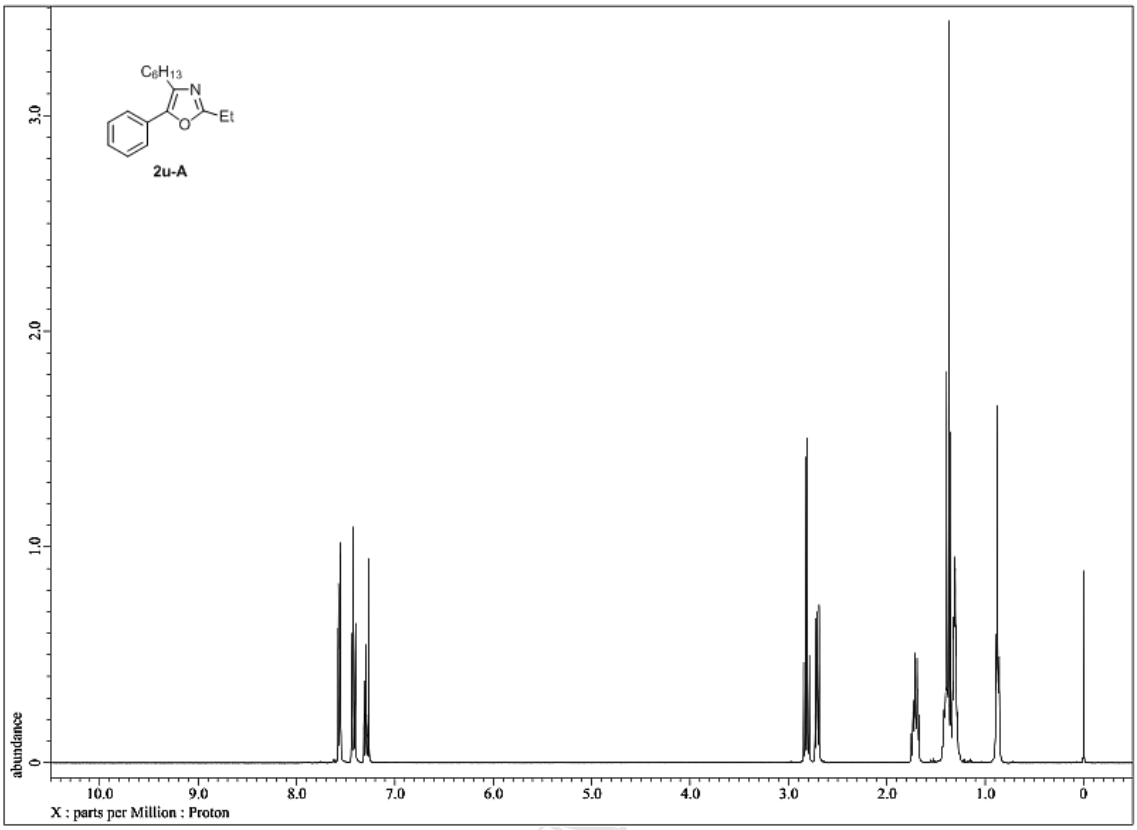

Me
N
Et
O
I
MeO
2r-A
abundance
X : parts per Million : Carbon13

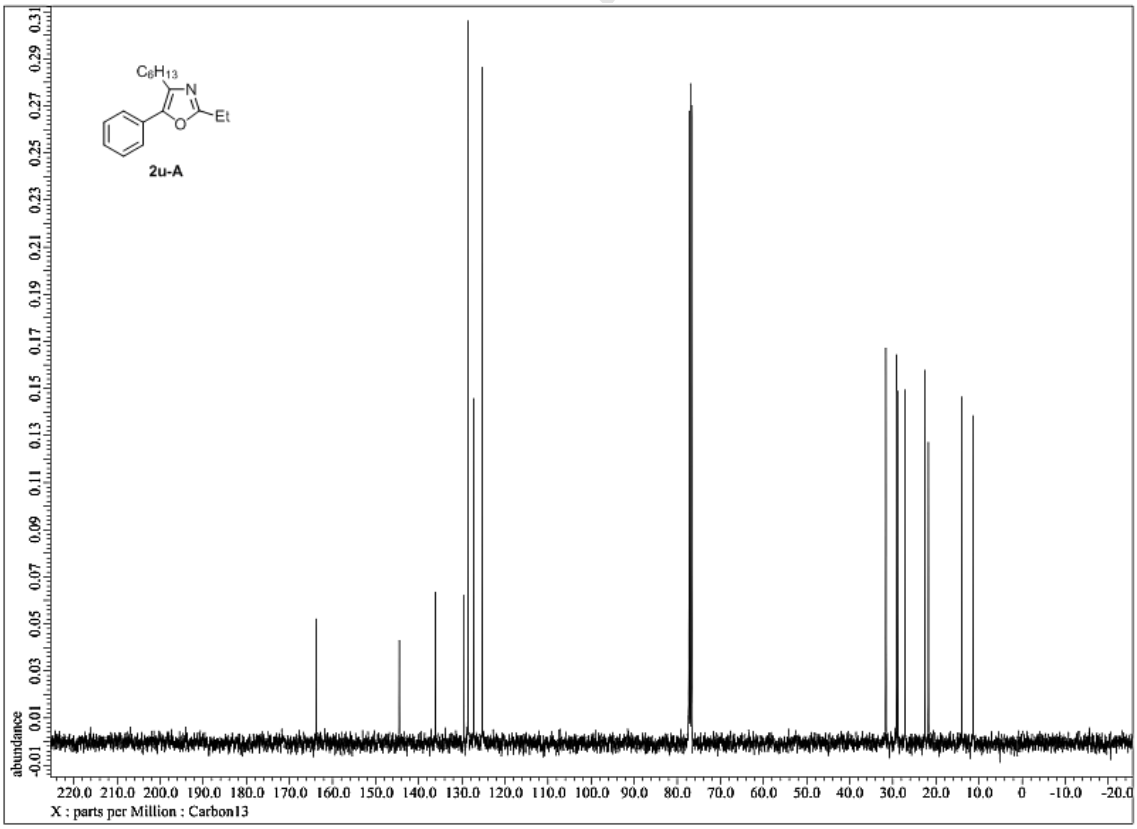

Et
N
Et
O
2s-A
abundance
X : parts per Million : Proton

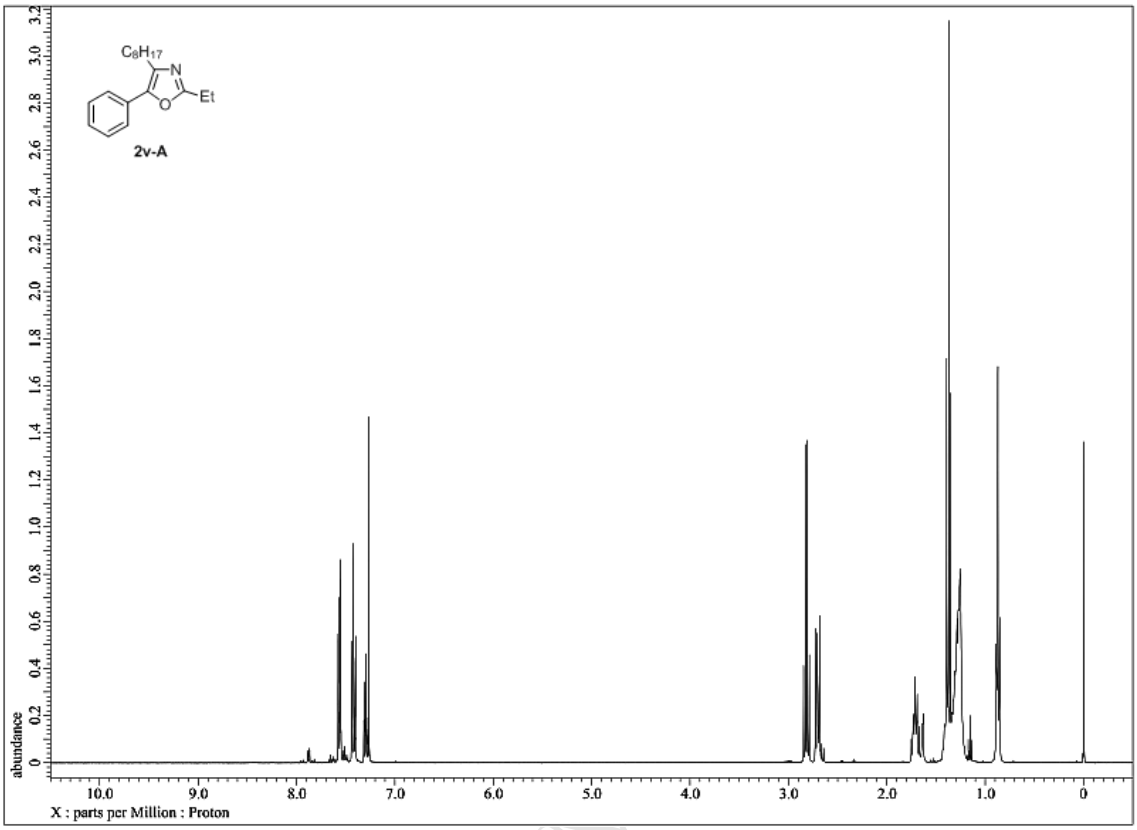

Et
N
Et
O
2s-A
abundance
X : parts per Million : Carbon13

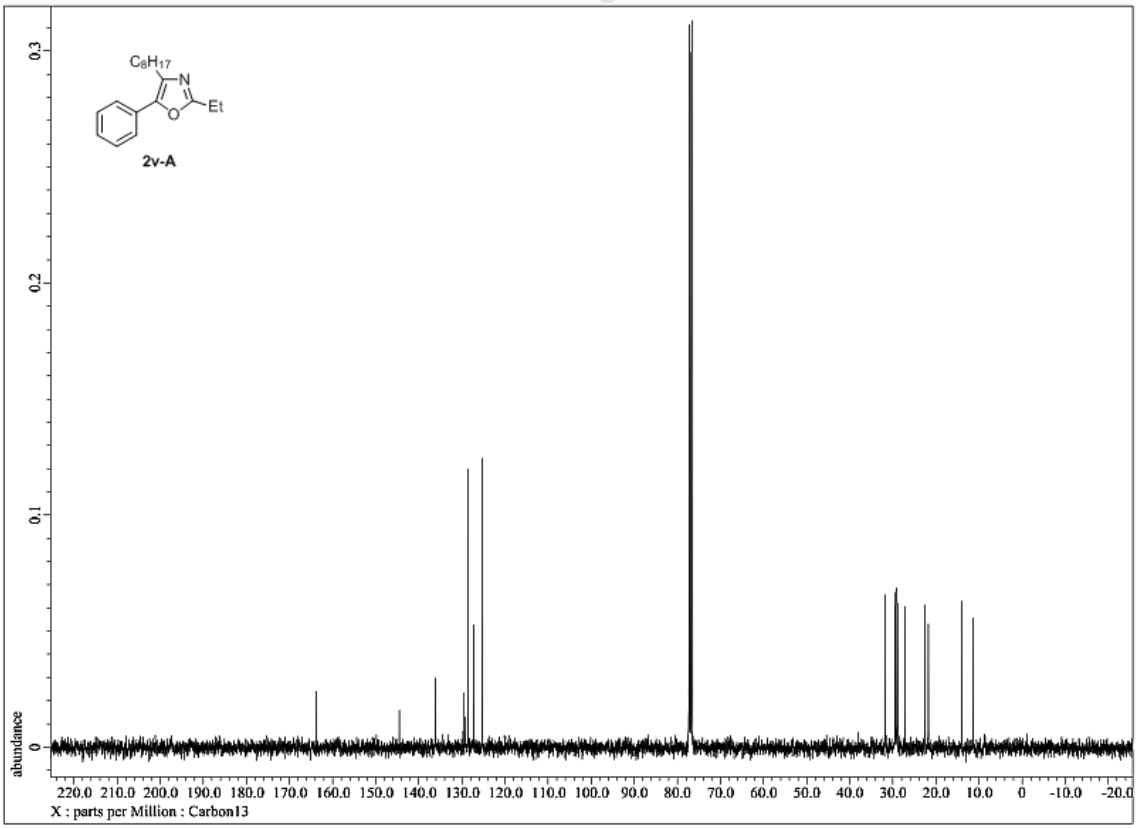

n-Pr
N
O
Et
2t-A
abundance
X : parts per Million : Proton

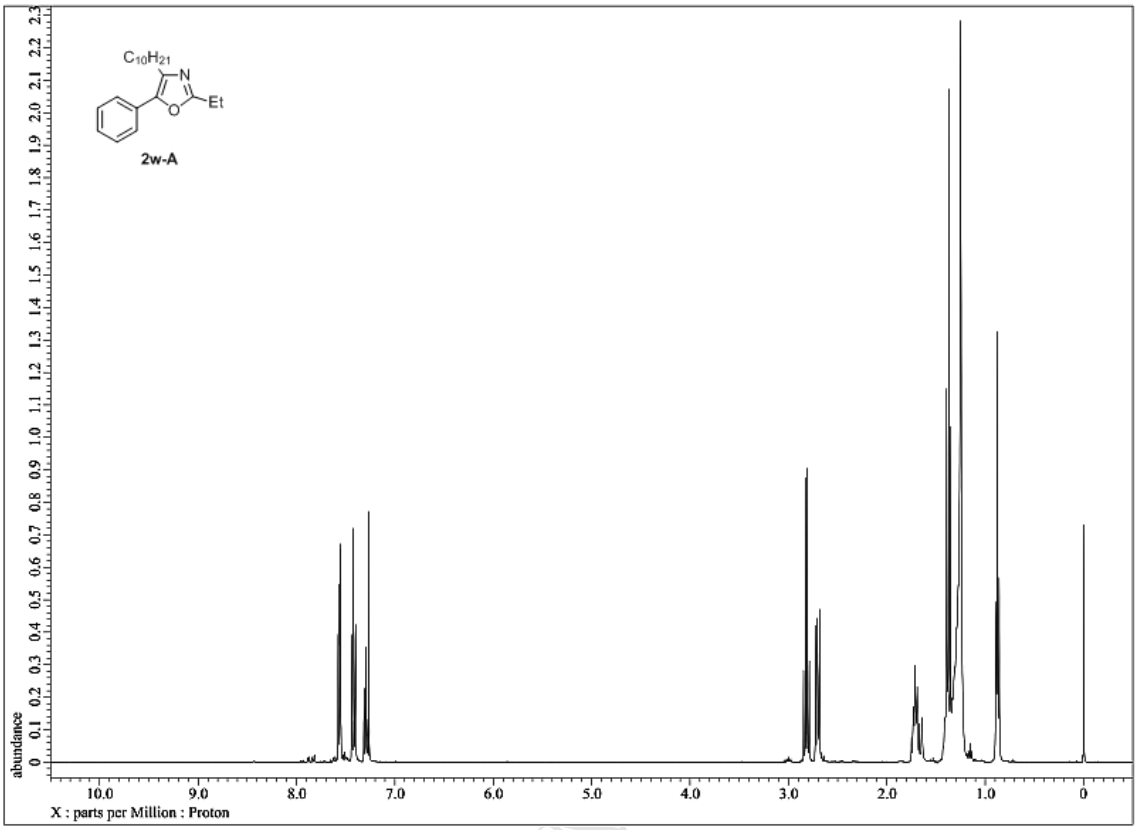

n-Pr
N
O
Et
2t-A
abundance
X : parts per Million : Carbon13

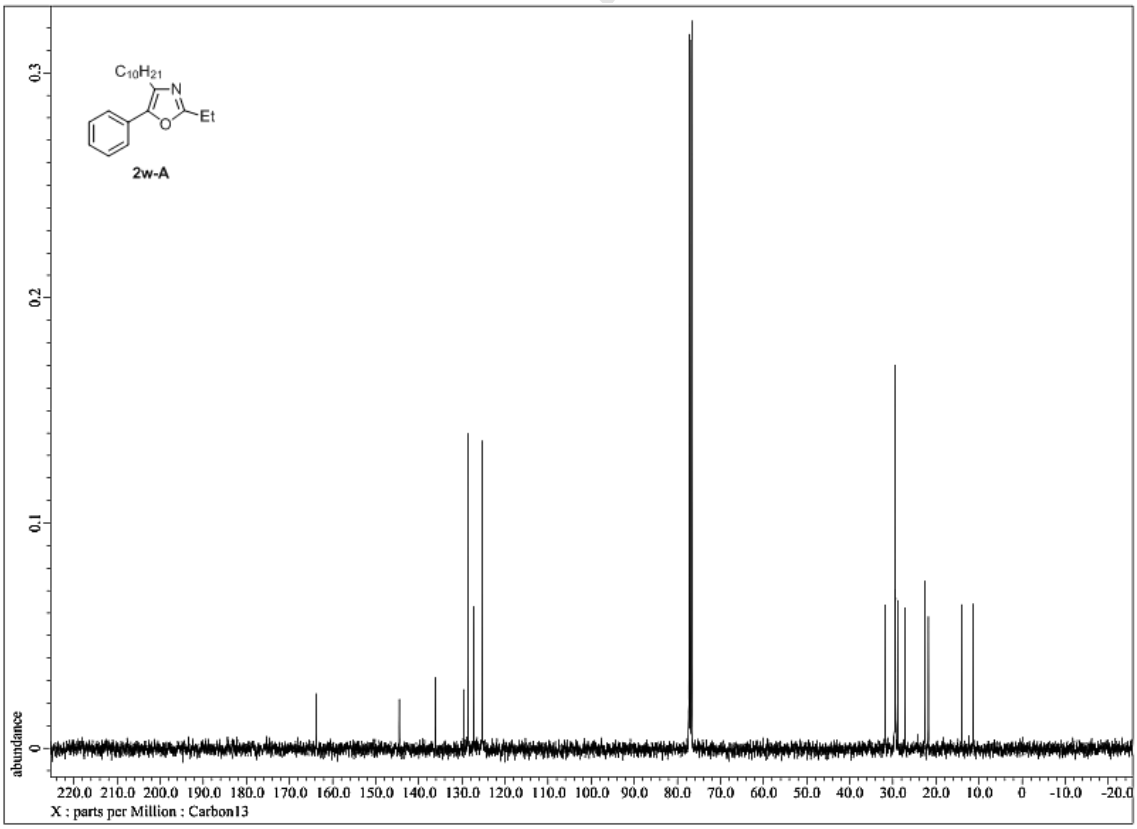

C6H13
N
O
Et
2u-A
abundance
X : parts per Million : Proton

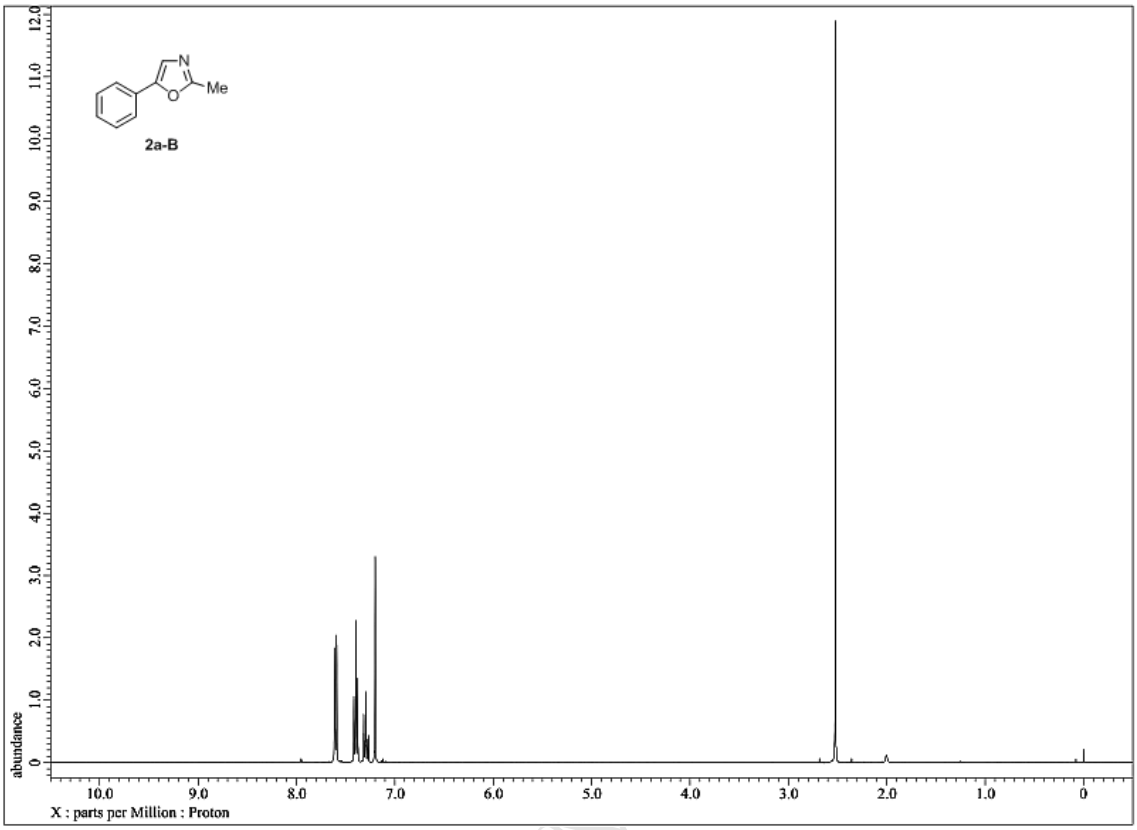

C6H13
N
O
Et
2u-A
abundance
X : parts per Million : Carbon13

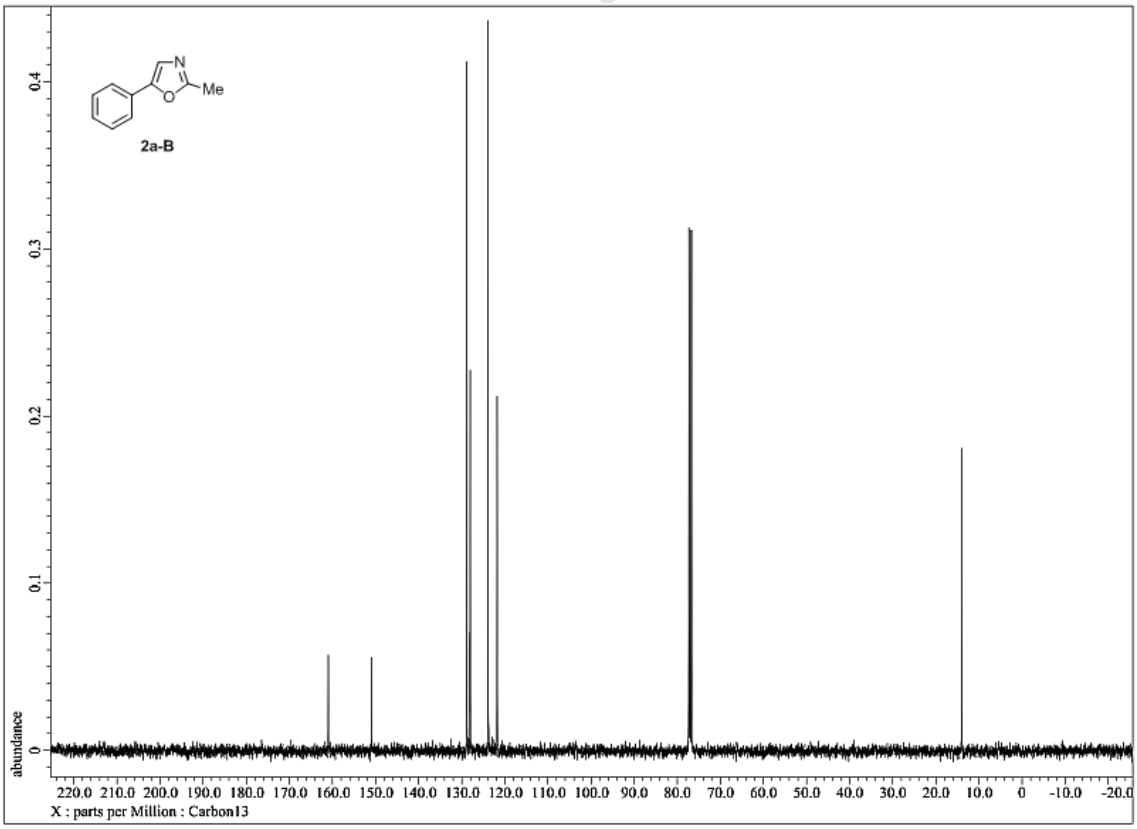

C8H17
N
O
Et
2v-A
abundance
X : parts per Million : Proton

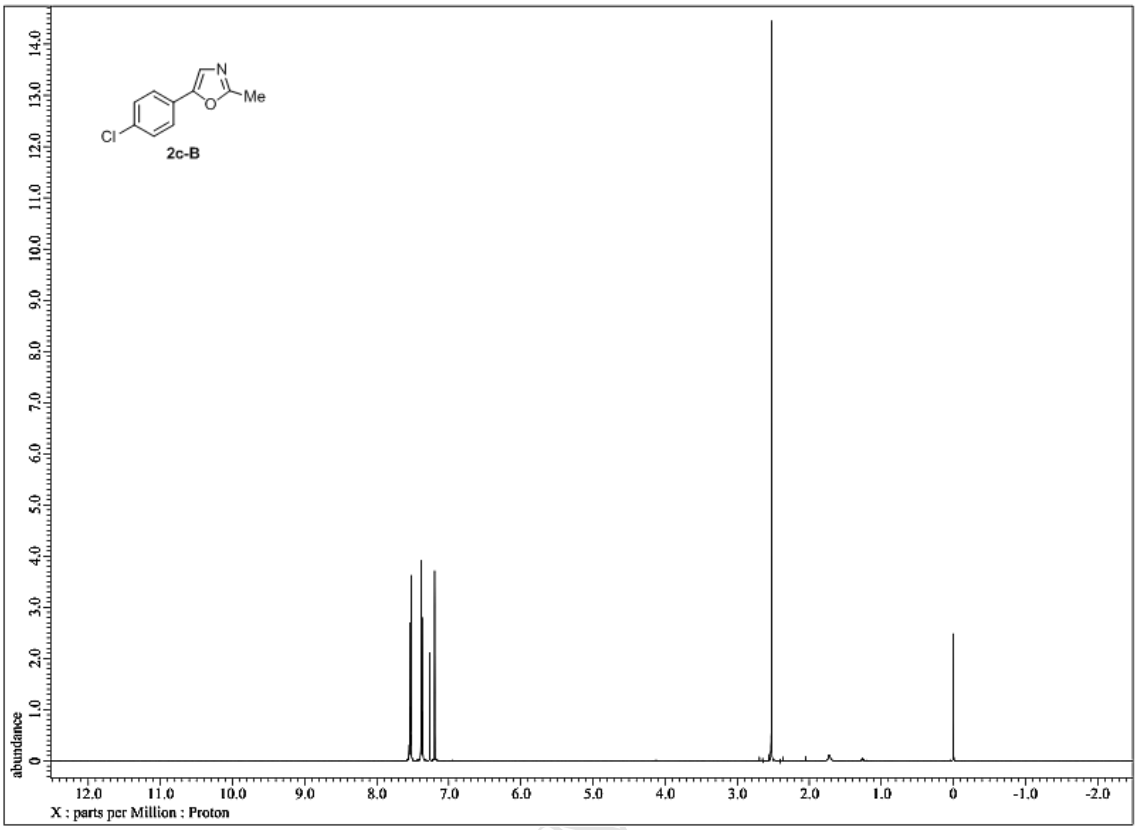

C8H17
N
O
Et
2v-A
abundance
X : parts per Million : Carbon13

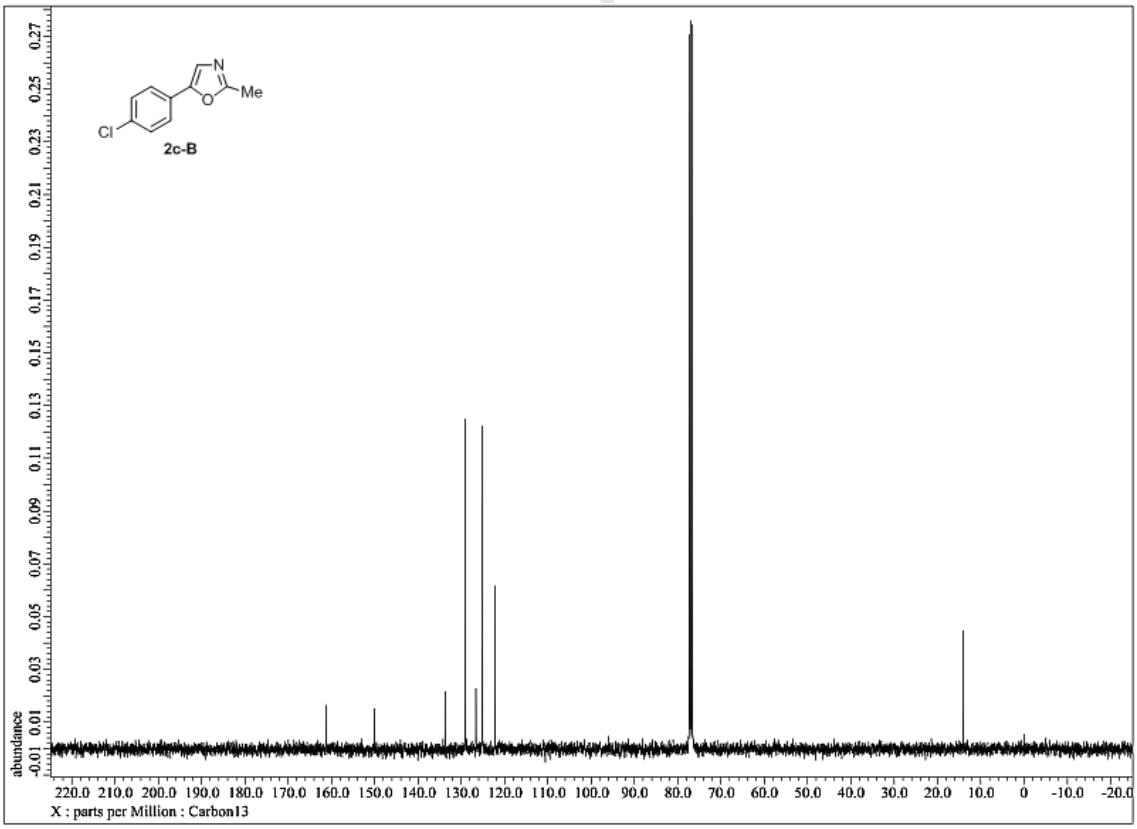

C10H21
N
O
Et
2w-A
abundance
X : parts per Million : Proton

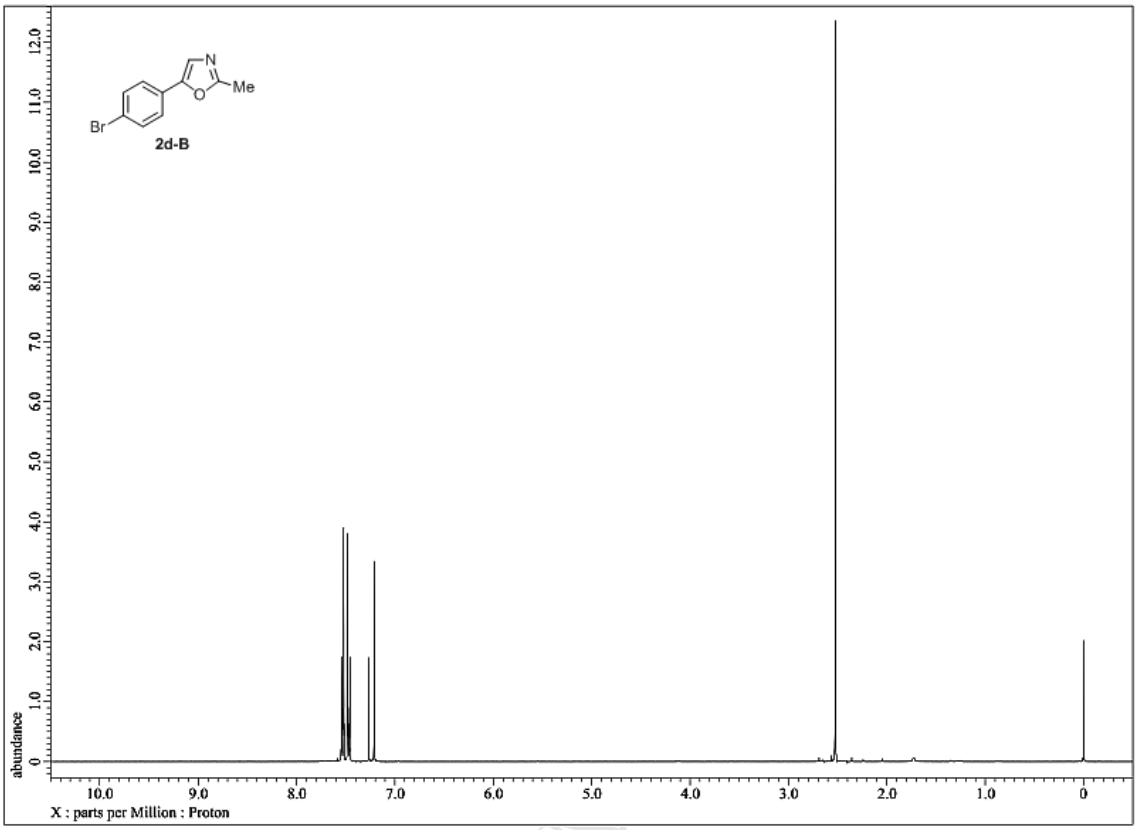

C10H21
N
O
Et
2w-A
abundance
X : parts per Million : Carbon13

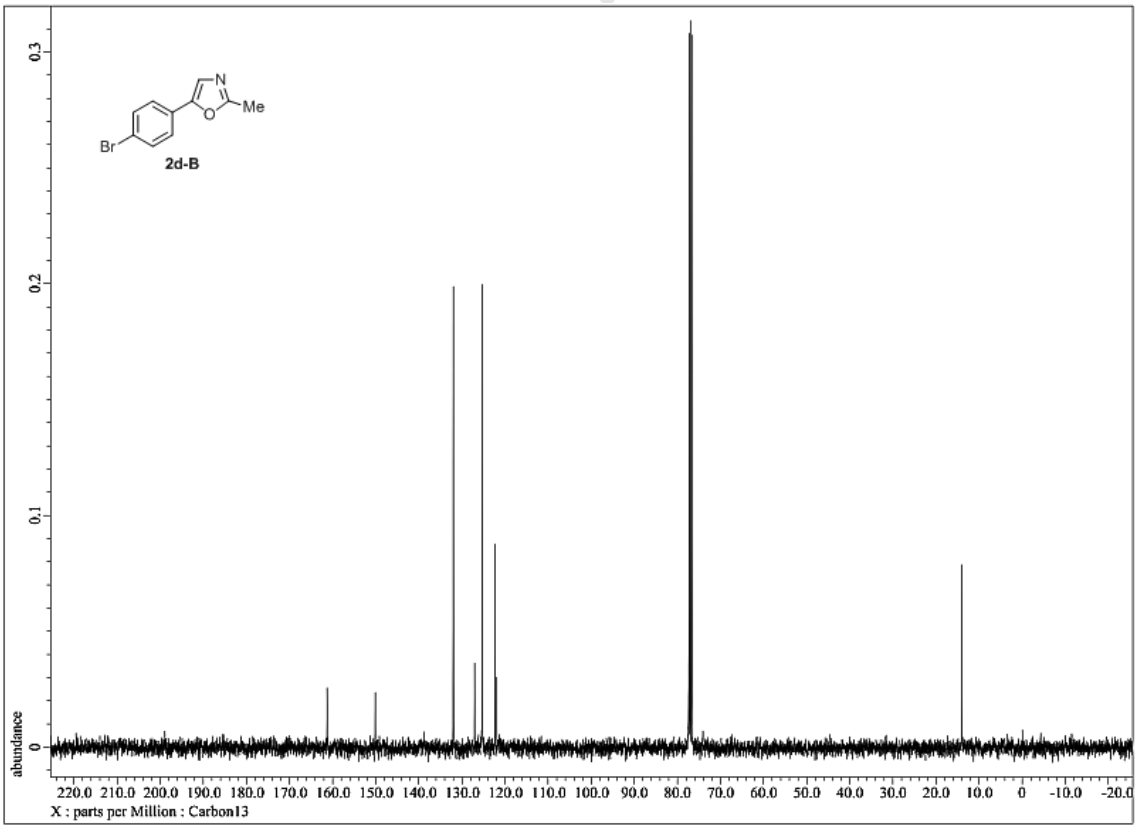

N
O
Me
2a-B
abundance
X : parts per Million : Proton

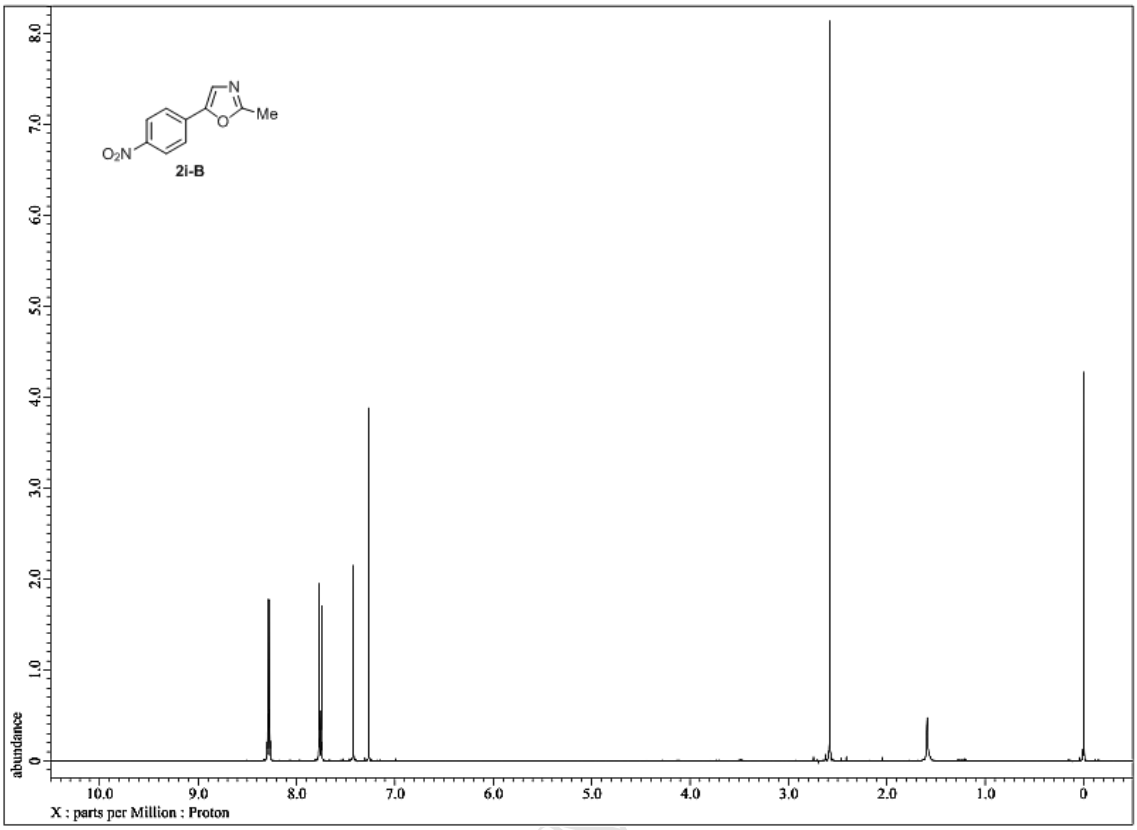

N
O
Me
2a-B
abundance
X : parts per Million : Carbon13

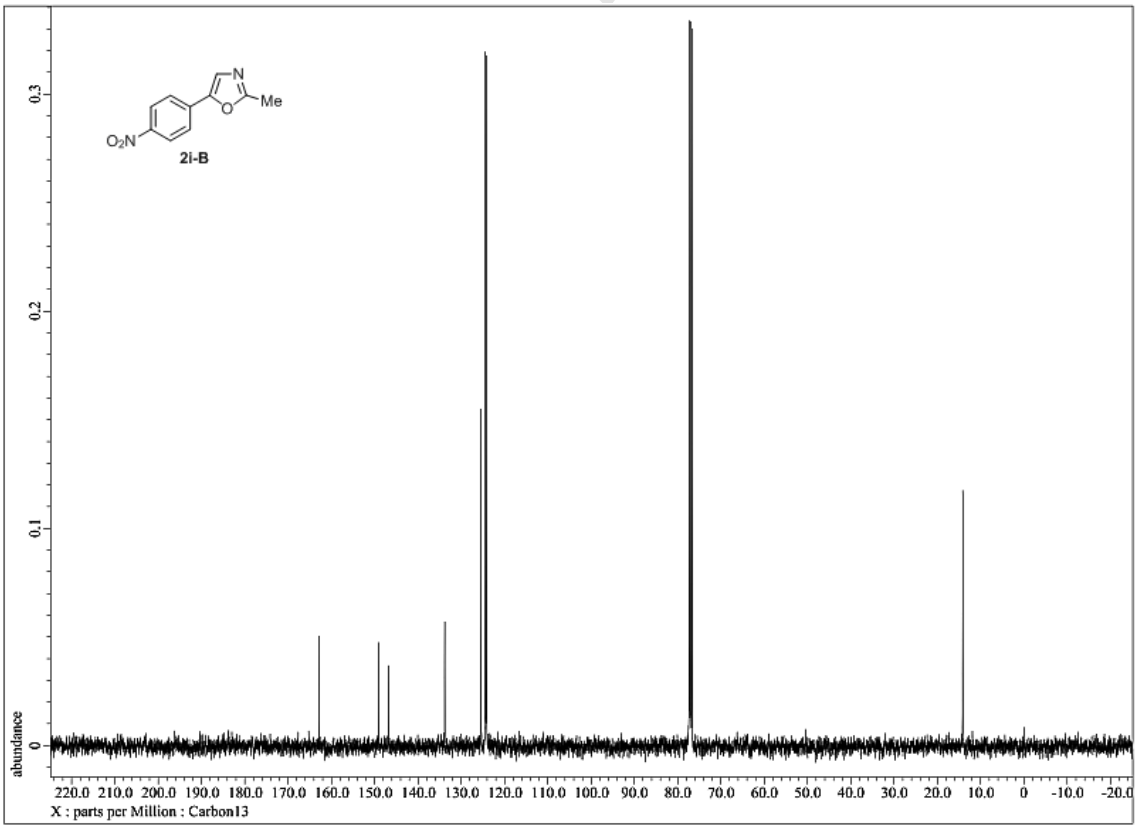

Cl
N
O
Me
2c-B
abundance
X : parts per Million : Proton

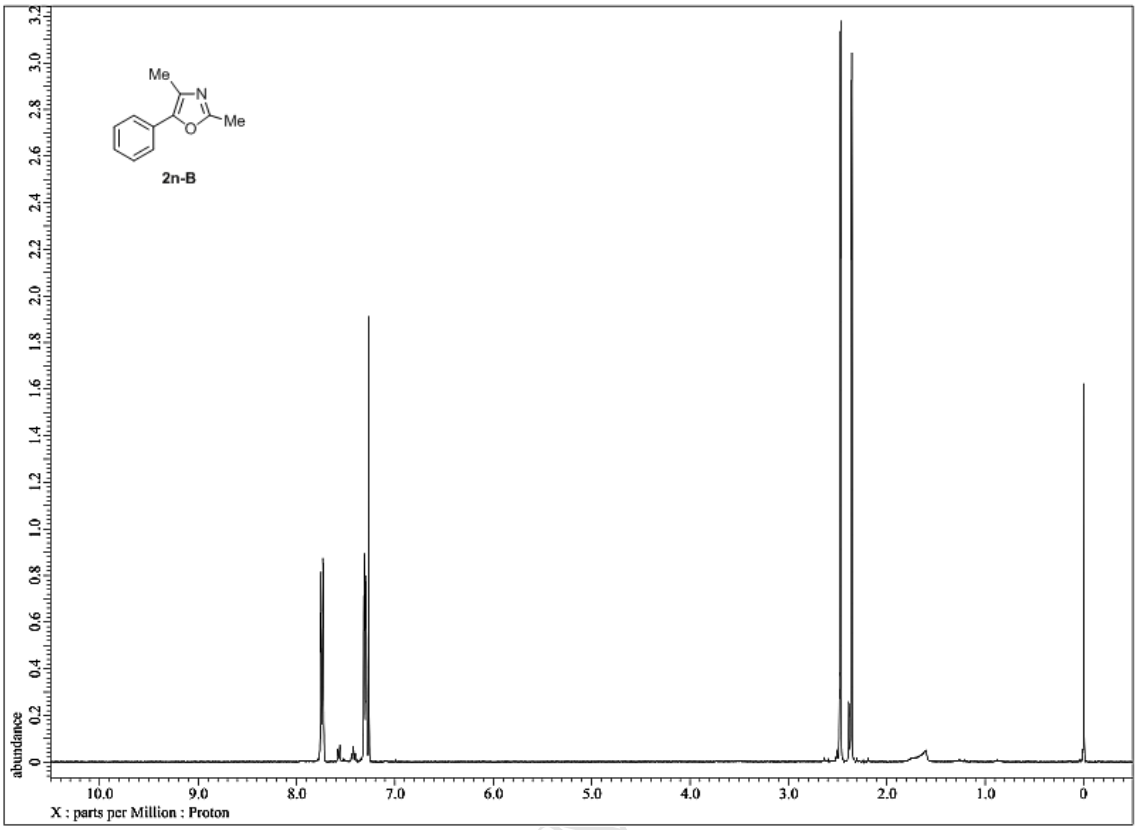

Cl
N
O
Me
2c-B
abundance
X : parts per Million : Carbon13

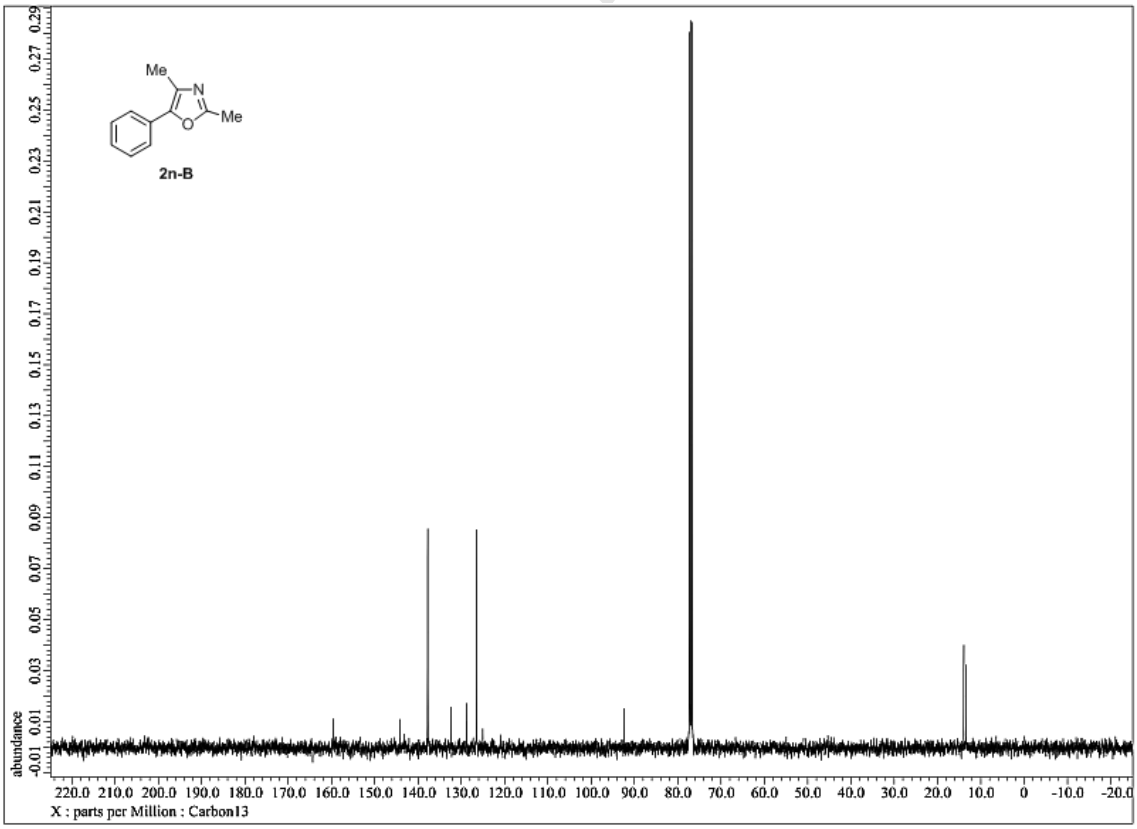

2d-B
Br
N
O
Me
abundance
X : parts per Million : Proton

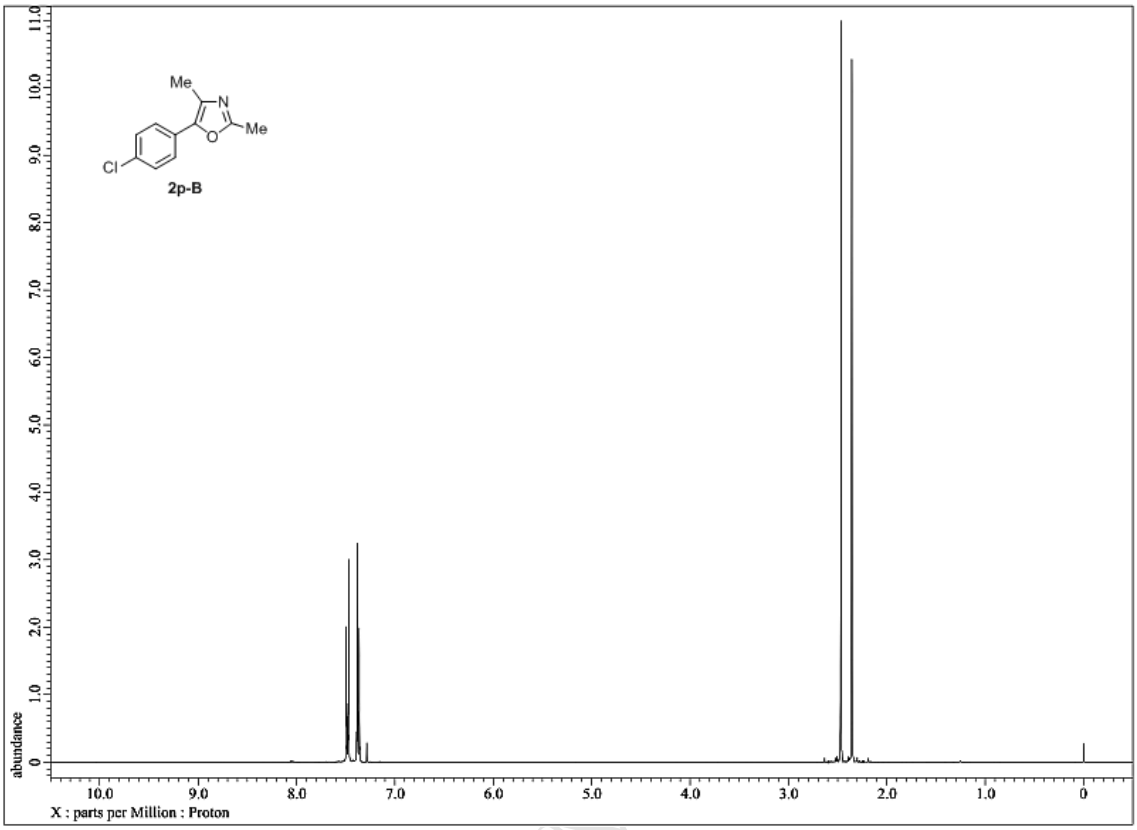

2d-B
Br
N
O
Me
abundance
X : parts per Million : Carbon13

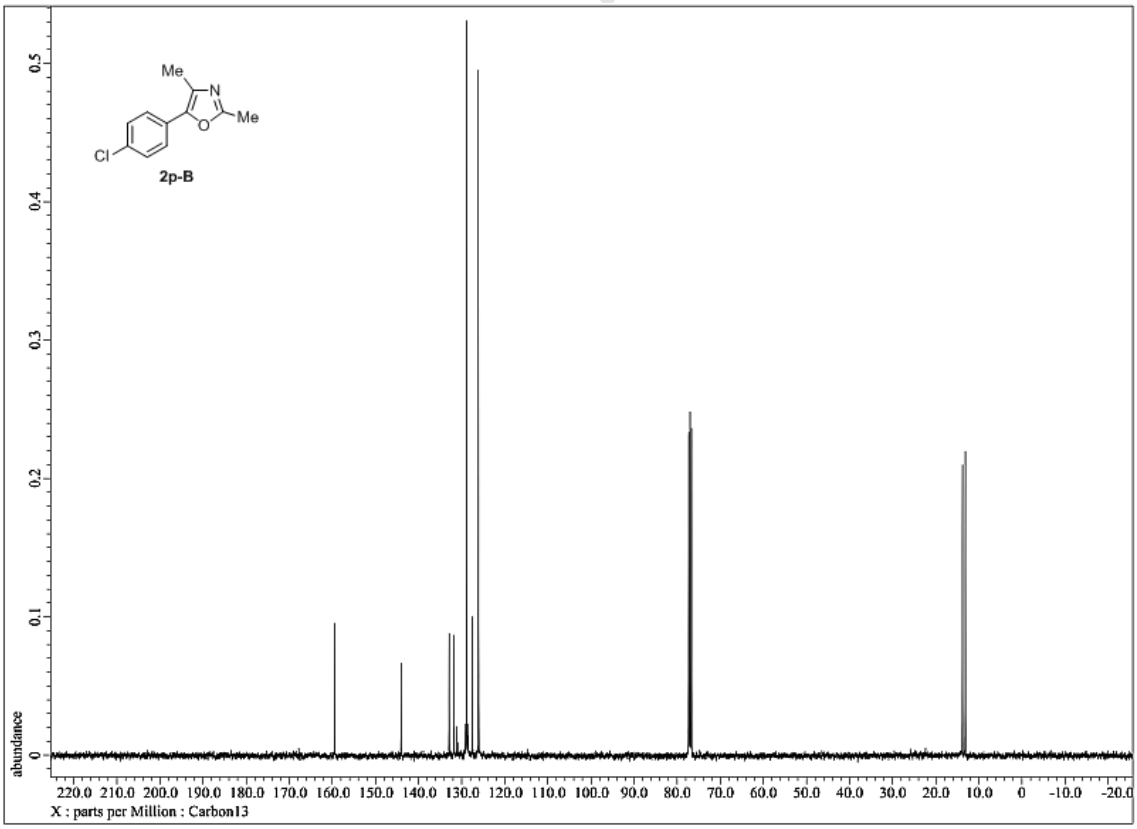

2i-B
abundance
X : parts per Million : Proton

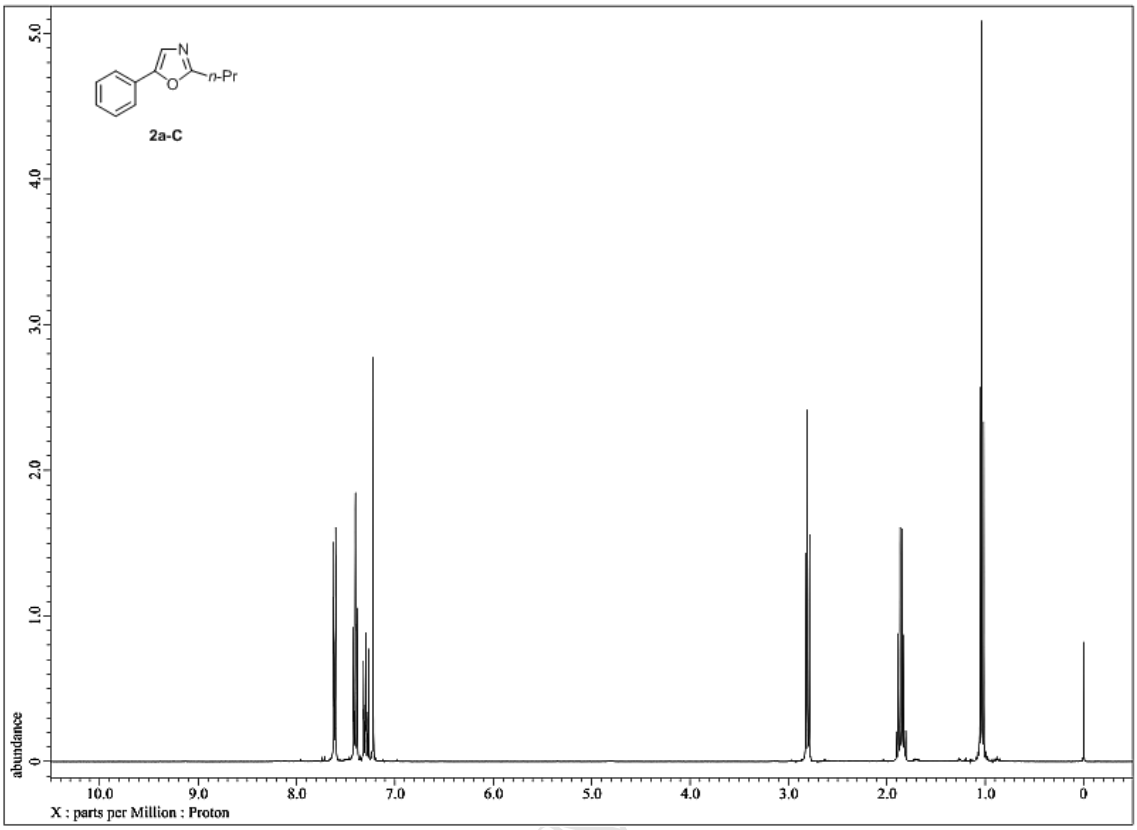

2i-B
abundance
X : parts per Million : Carbon13

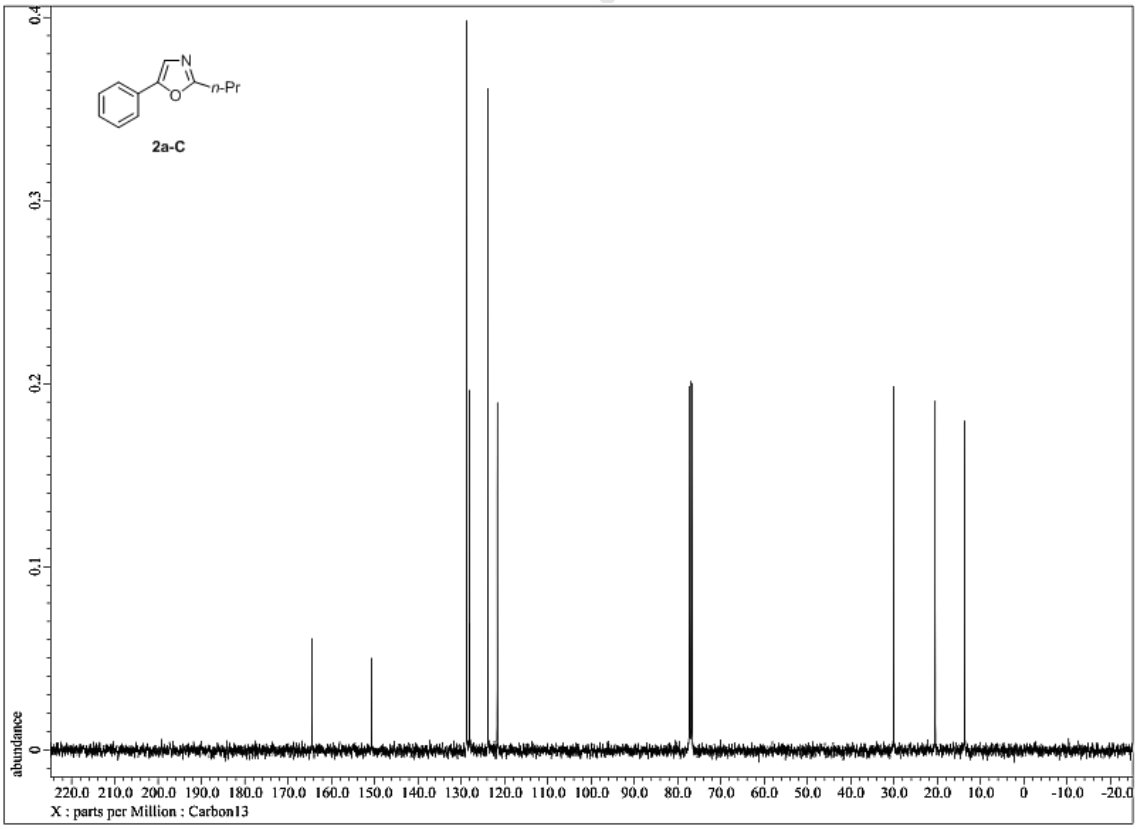

Me
N
O
Me
2n-B
abundance
X : parts per Million : Proton

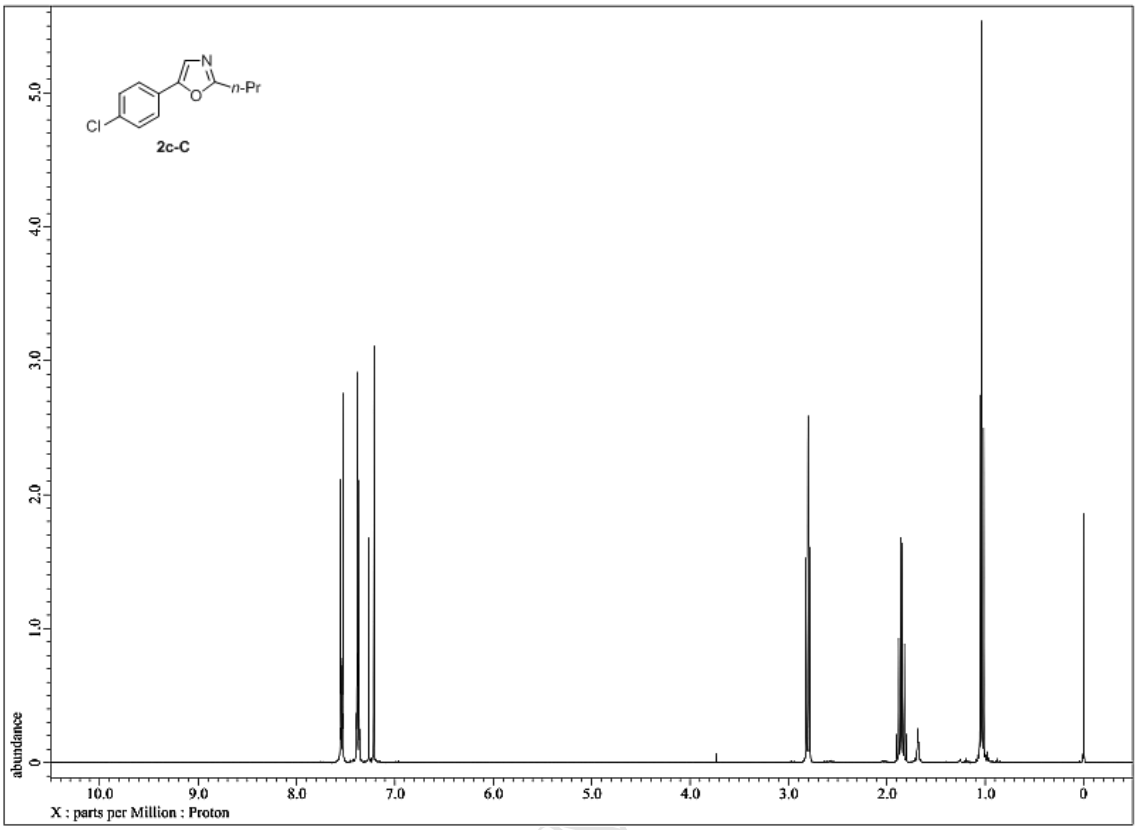

Me
N
O
Me
2n-B
abundance
X : parts per Million : Carbon13

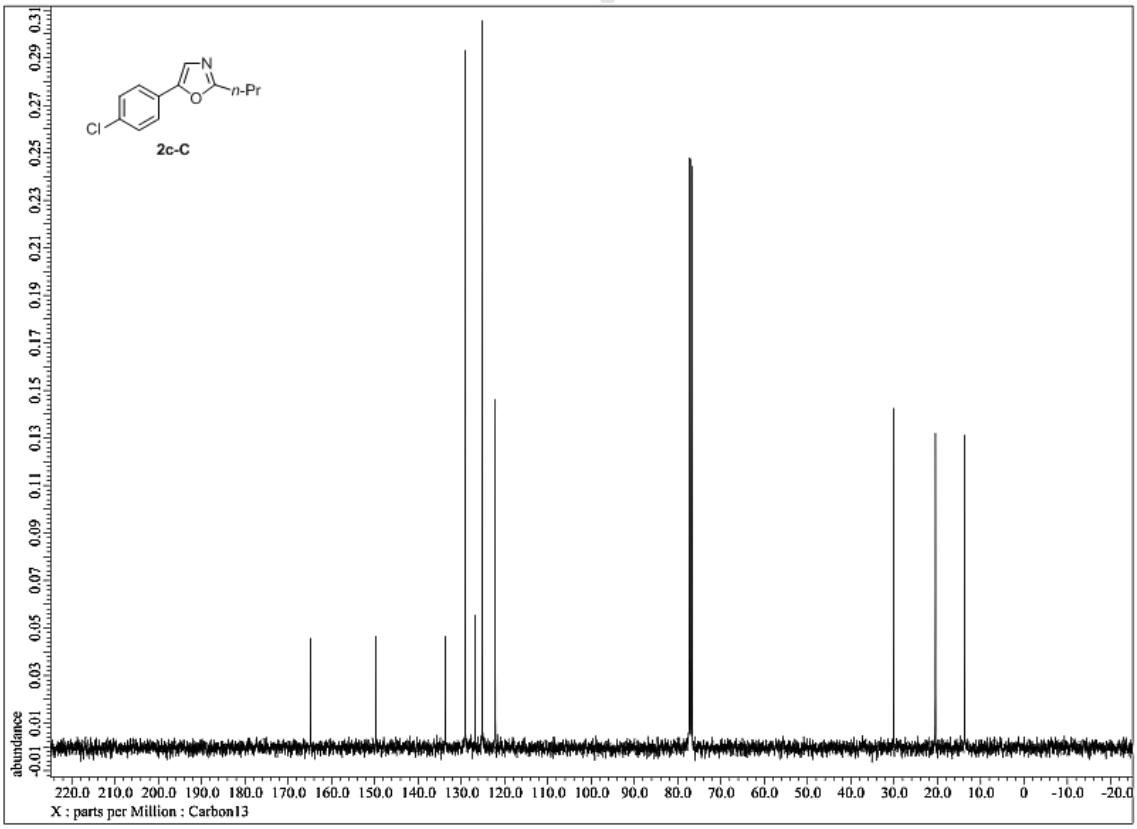

Me
N
Me
O
Cl
2p-B
abundance
X : parts per Million : Proton

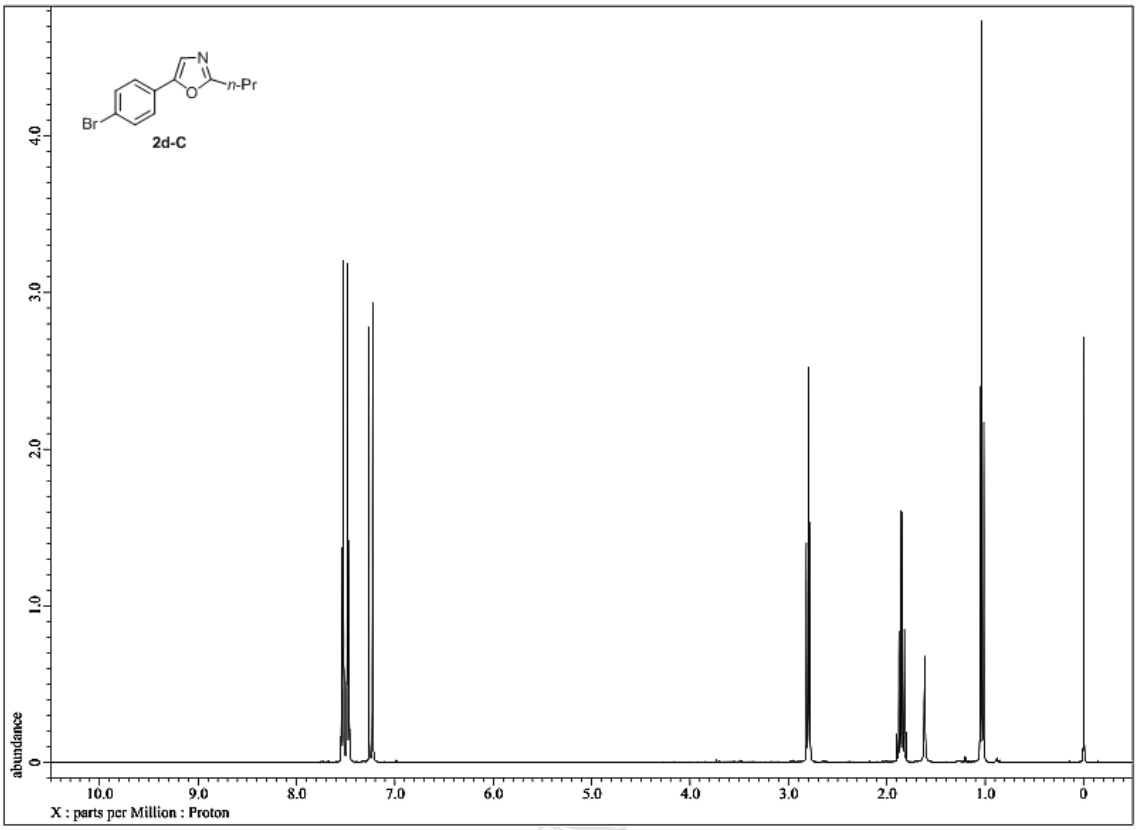

Me
N
Me
O
Cl
2p-B
abundance
X : parts per Million : Carbon13

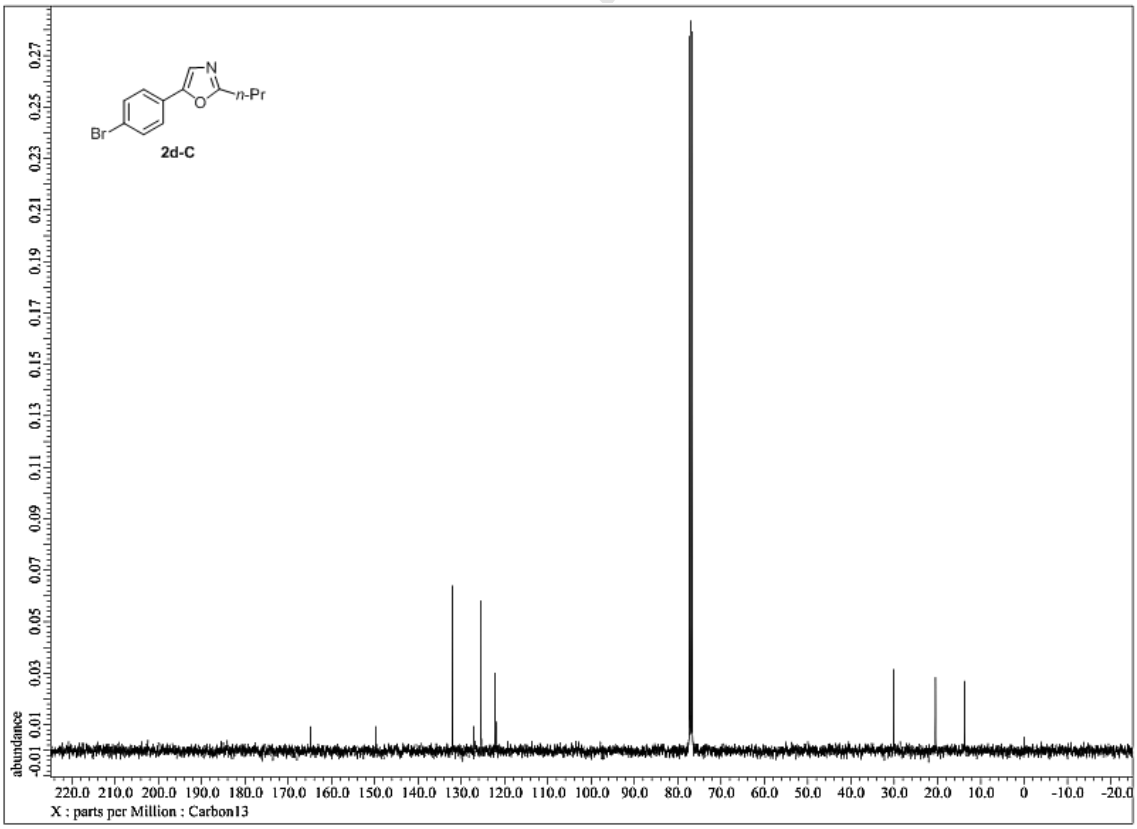

n-Pr
2a-C
abundance
X : parts per Million : Proton

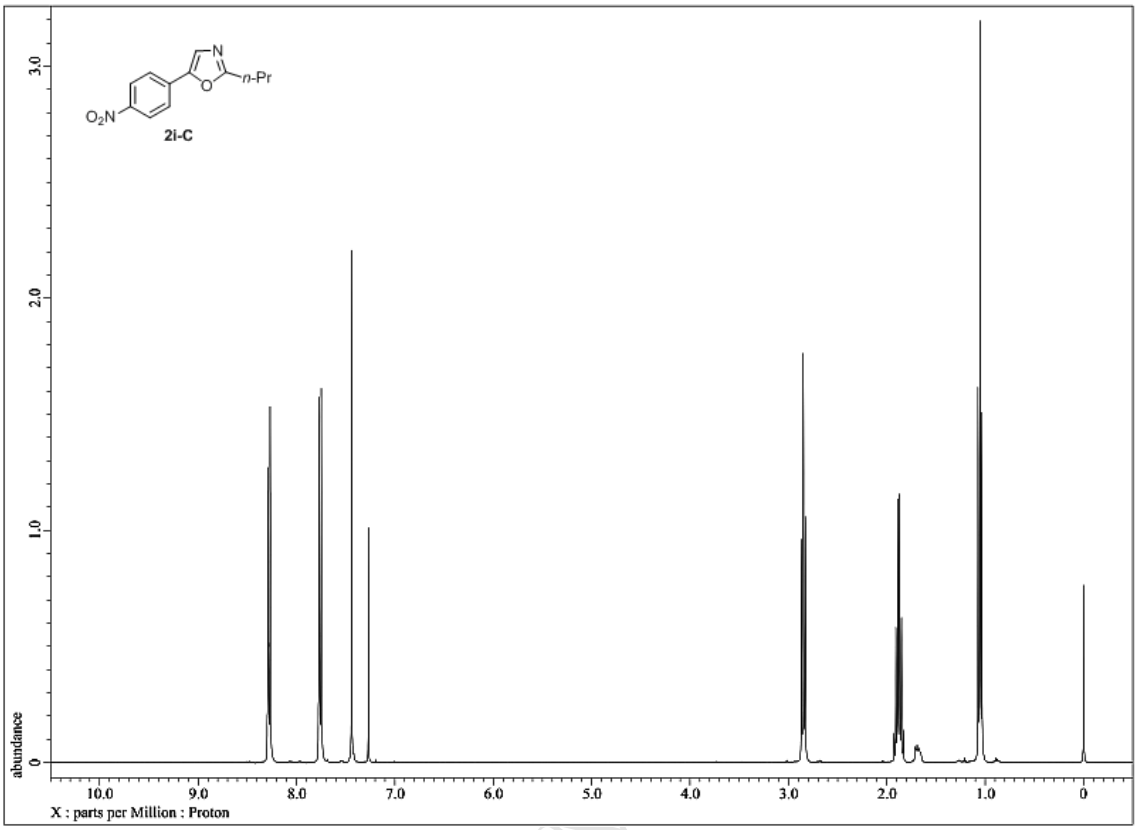

n-Pr
2a-C
abundance
X : parts per Million : Carbon13

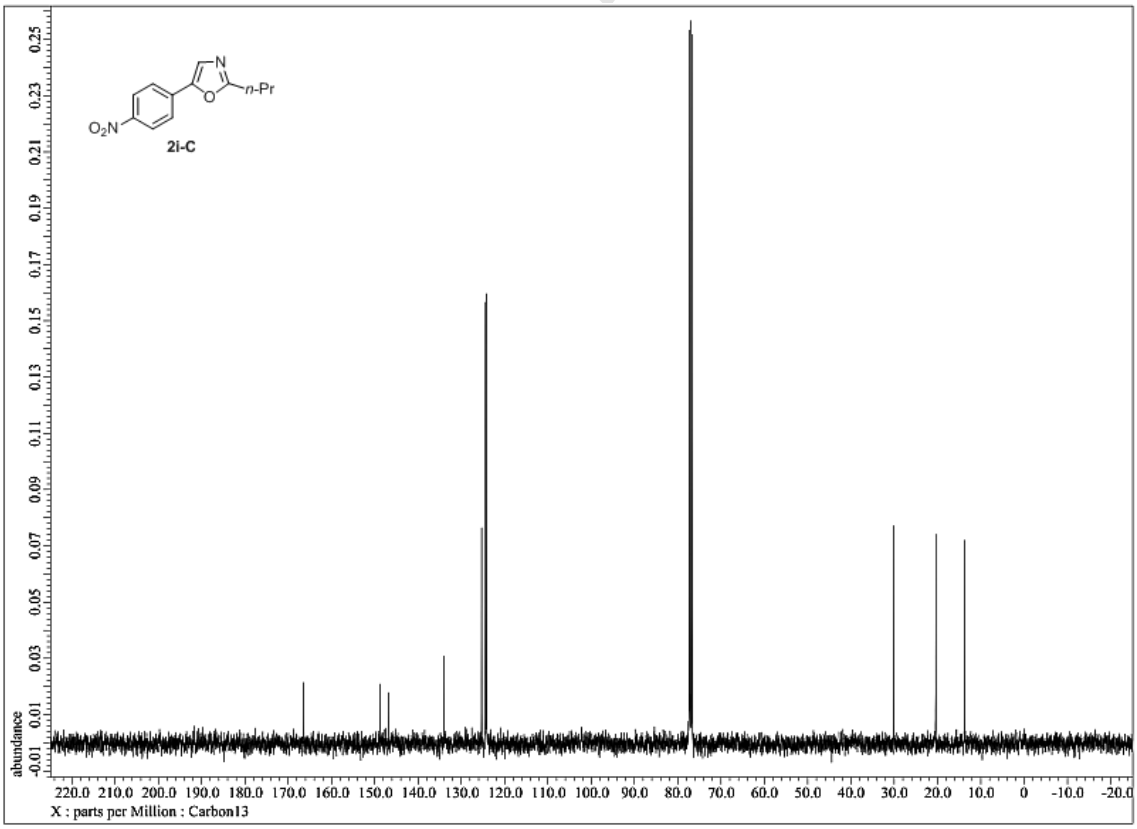

N
O
n-Pr
Cl
2c-C
abundance
X : parts per Million : Proton

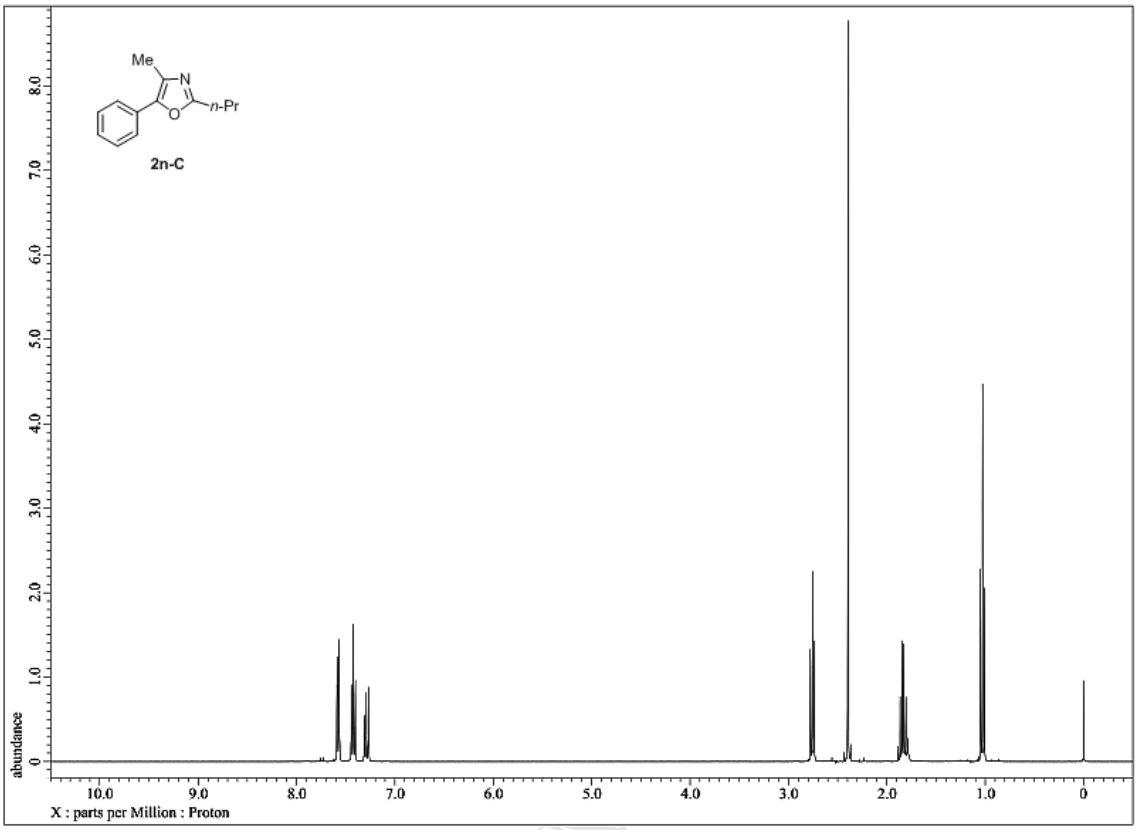

N
O
n-Pr
Cl
2c-C
abundance
X : parts per Million : Carbon13

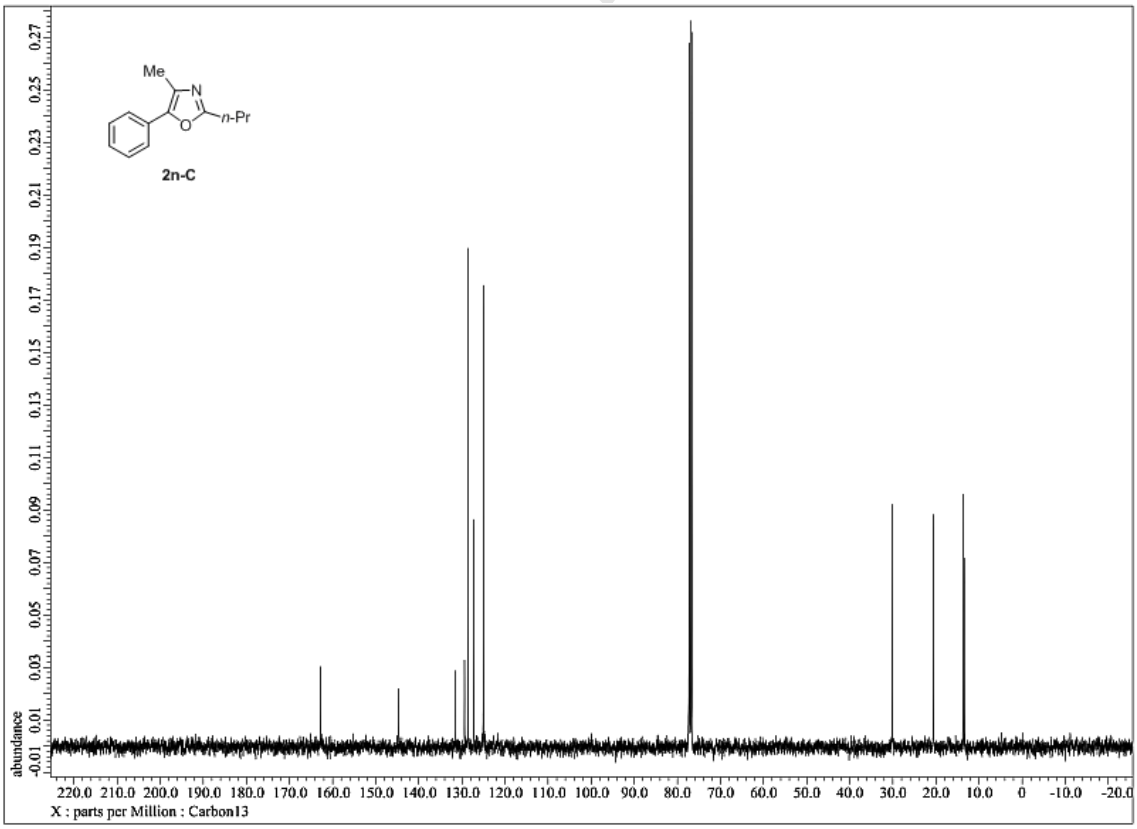

N
O
n-Pr
Br
2d-C
abundance
X : parts per Million : Proton

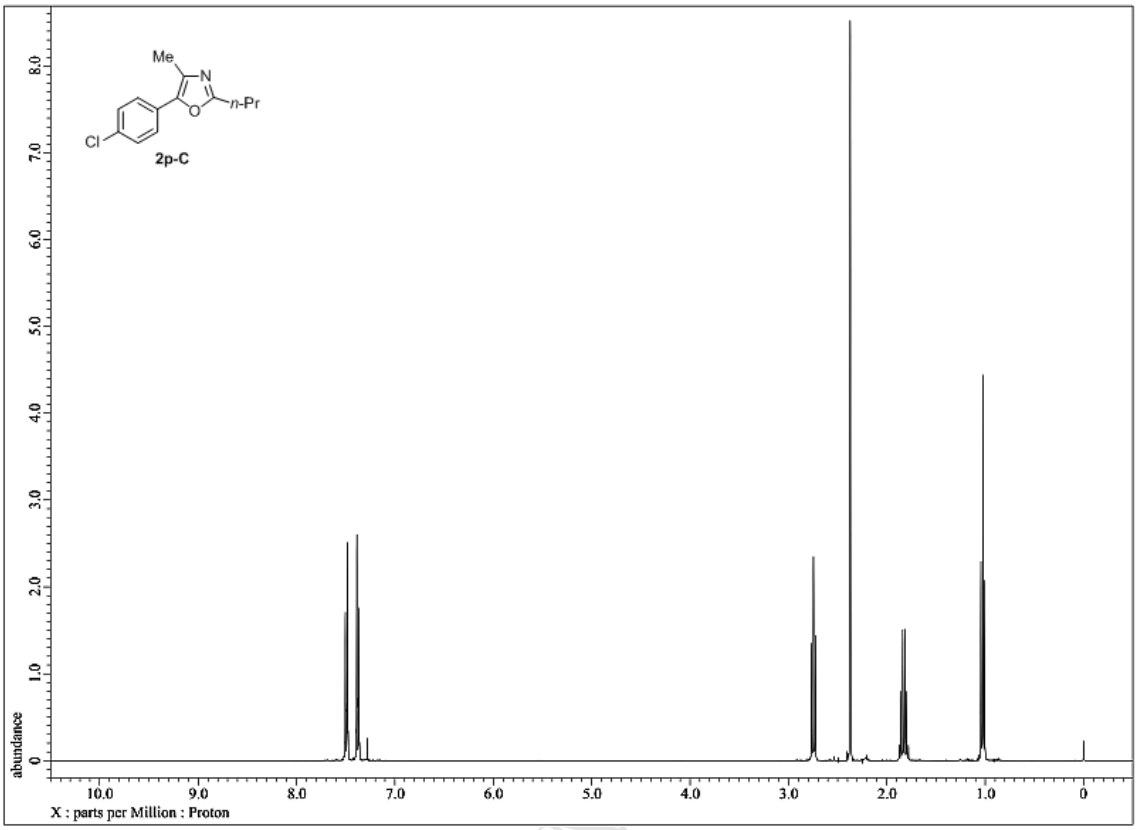

N
O
n-Pr
Br
2d-C
abundance
X : parts per Million : Carbon13

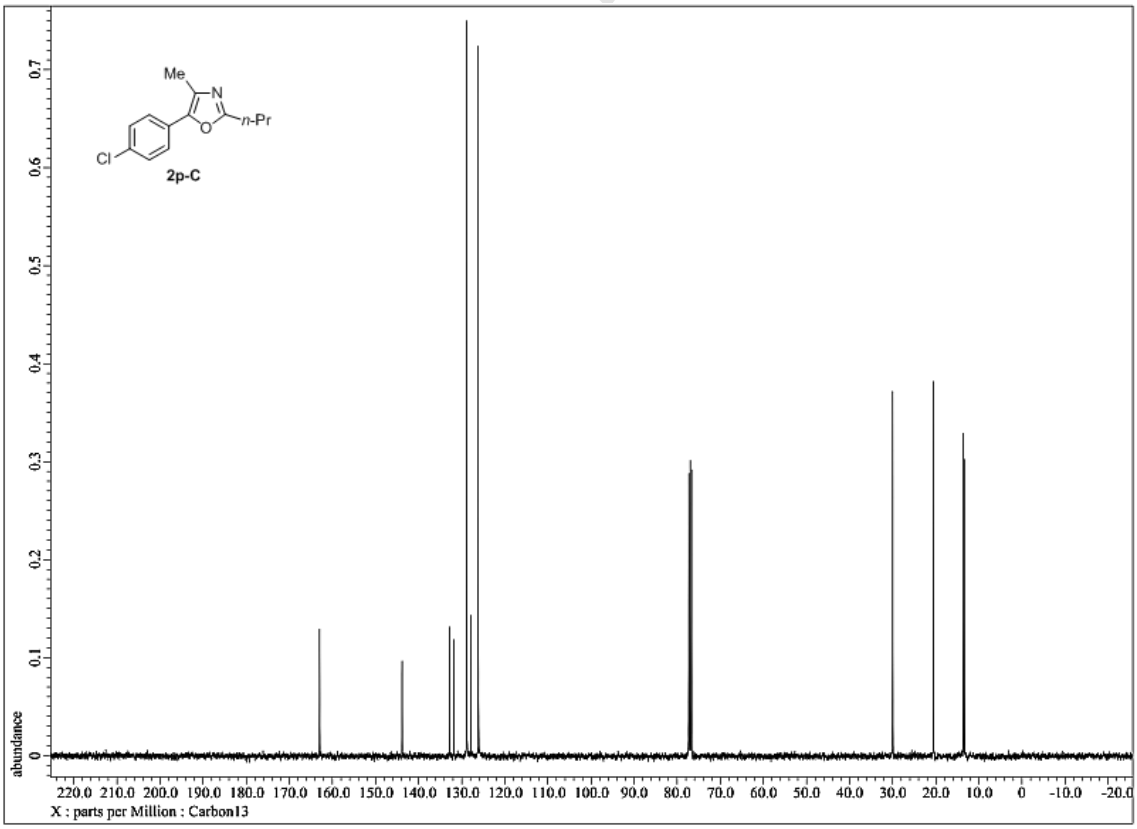

n-Pr
O2N
2i-C
abundance
X : parts per Million : Proton

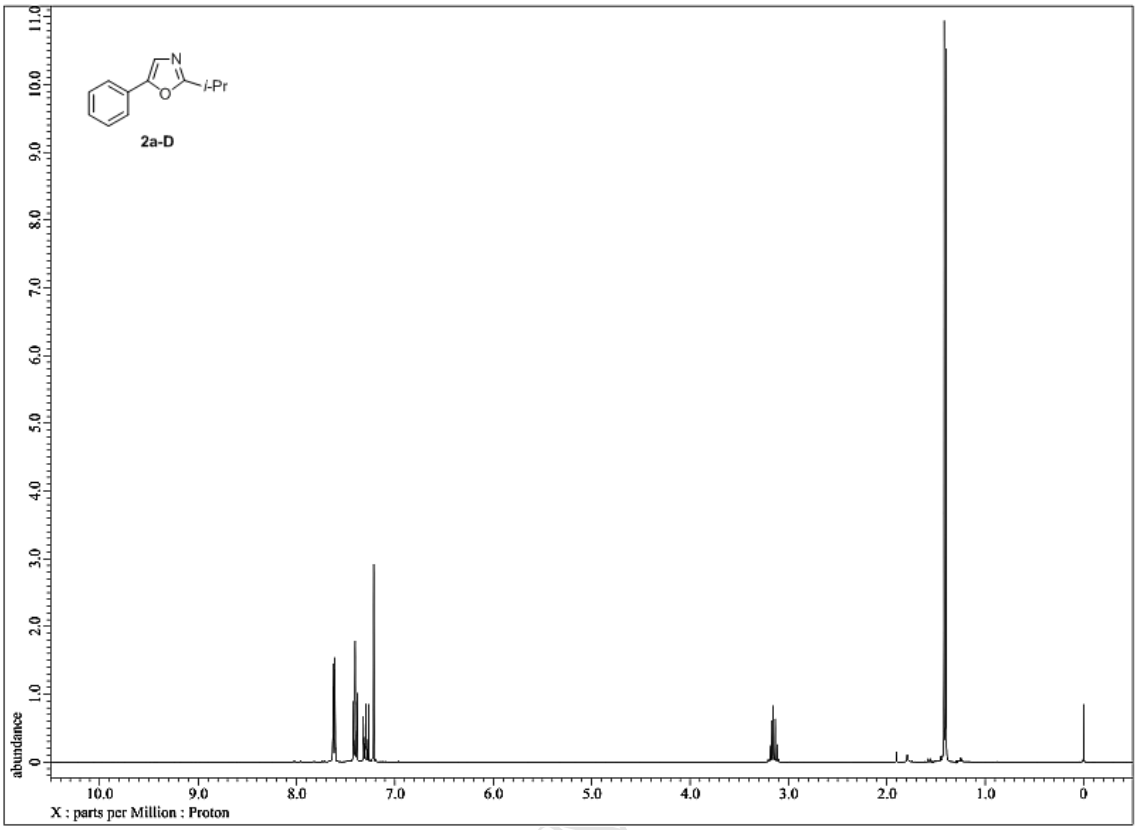

n-Pr
O2N
2i-C
abundance
X : parts per Million : Carbon13

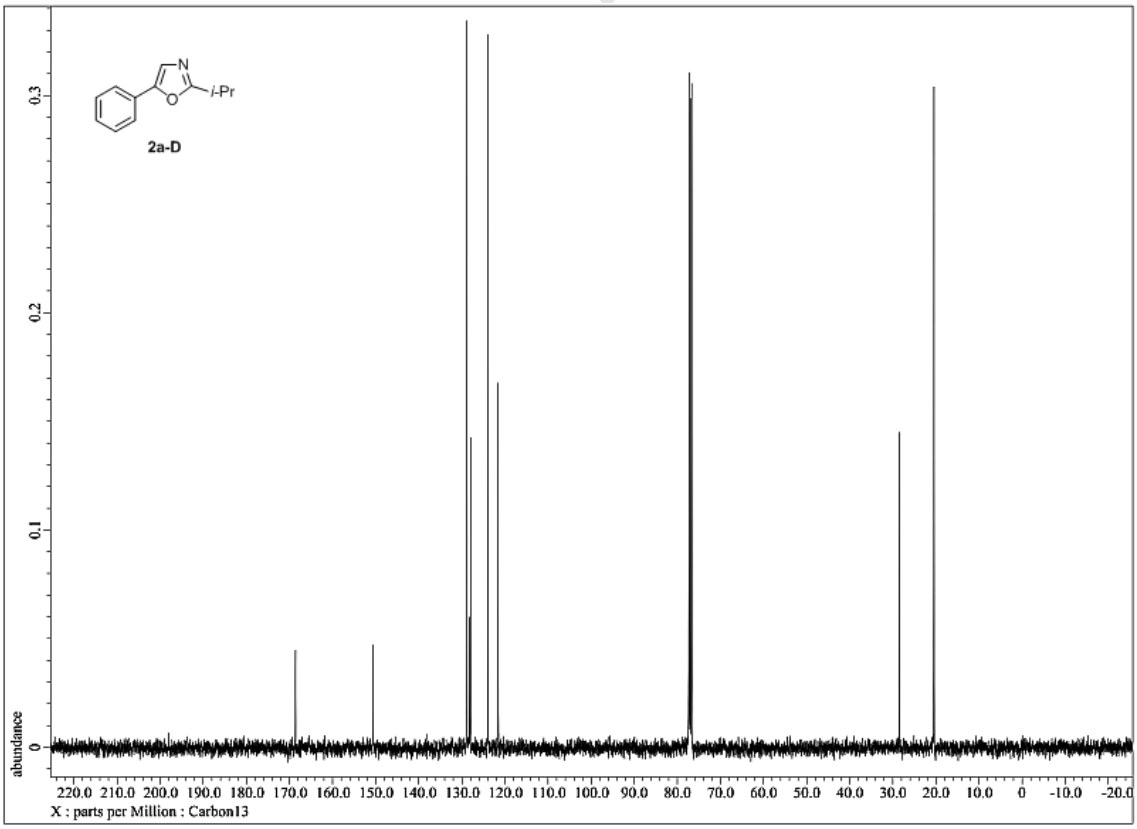

Me
N
O
n-Pr
2n-C
abundance
X : parts per Million : Proton

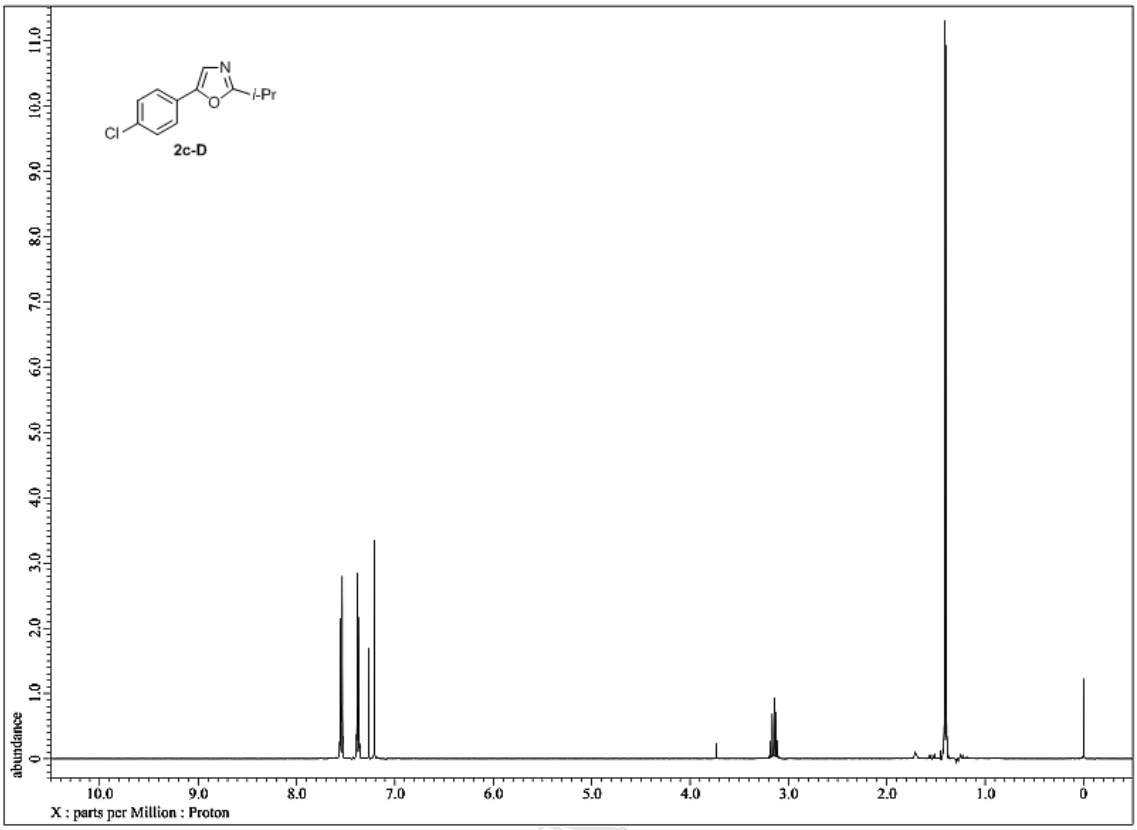

Me
N
O
n-Pr
2n-C
abundance
X : parts per Million : Carbon13

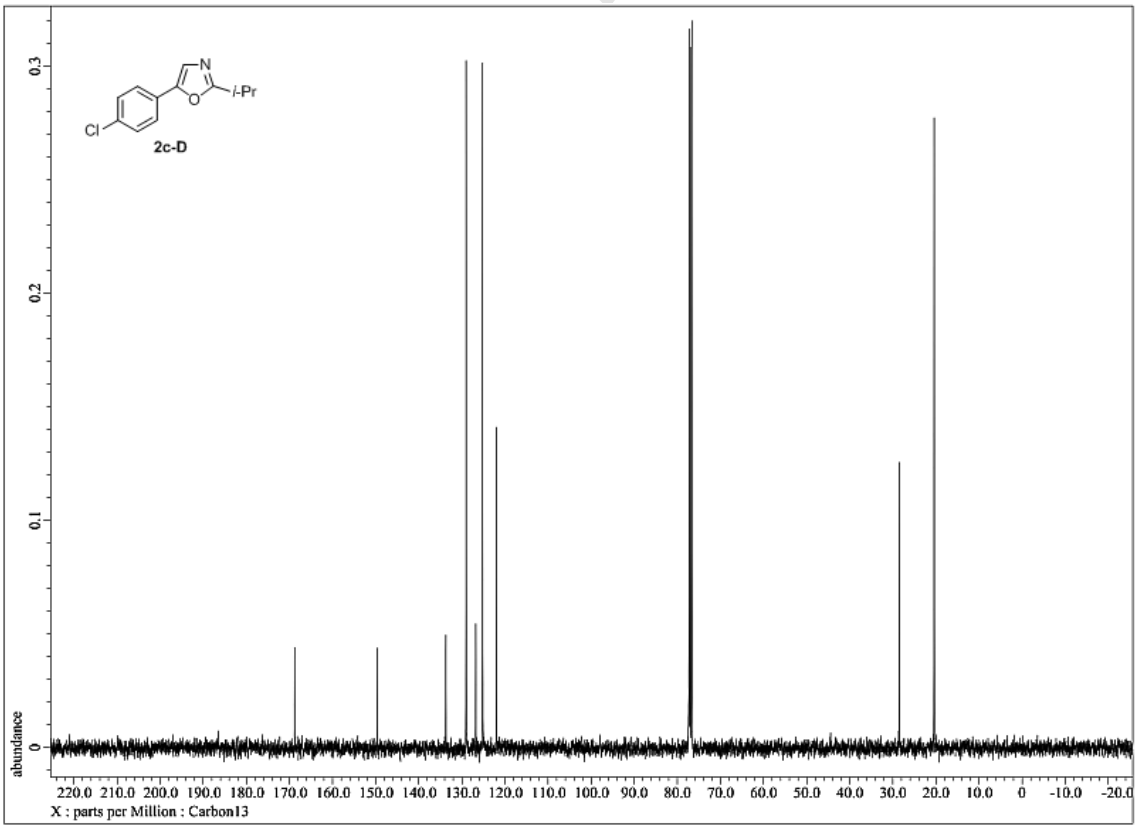

Me
N
O
n-Pr
Cl
2p-C
abundance
X : parts per Million : Proton

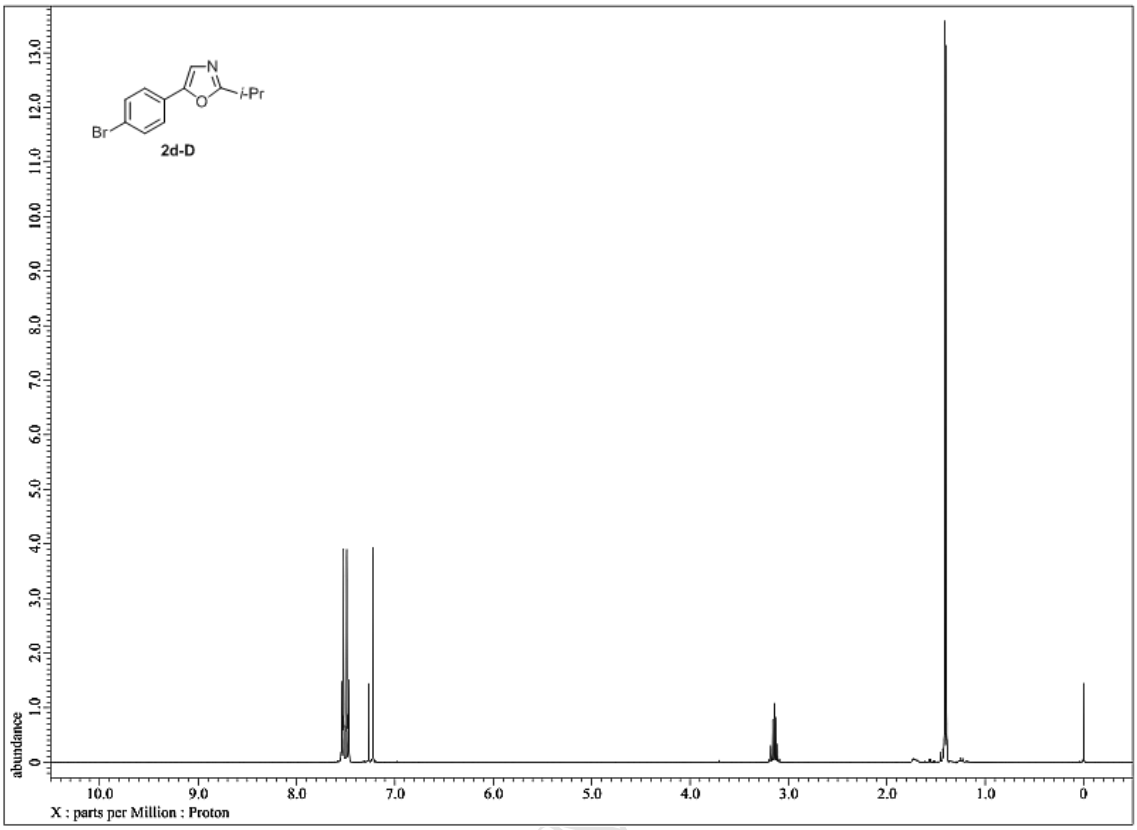

Me
N
O
n-Pr
Cl
2p-C
abundance
X : parts per Million : Carbon13

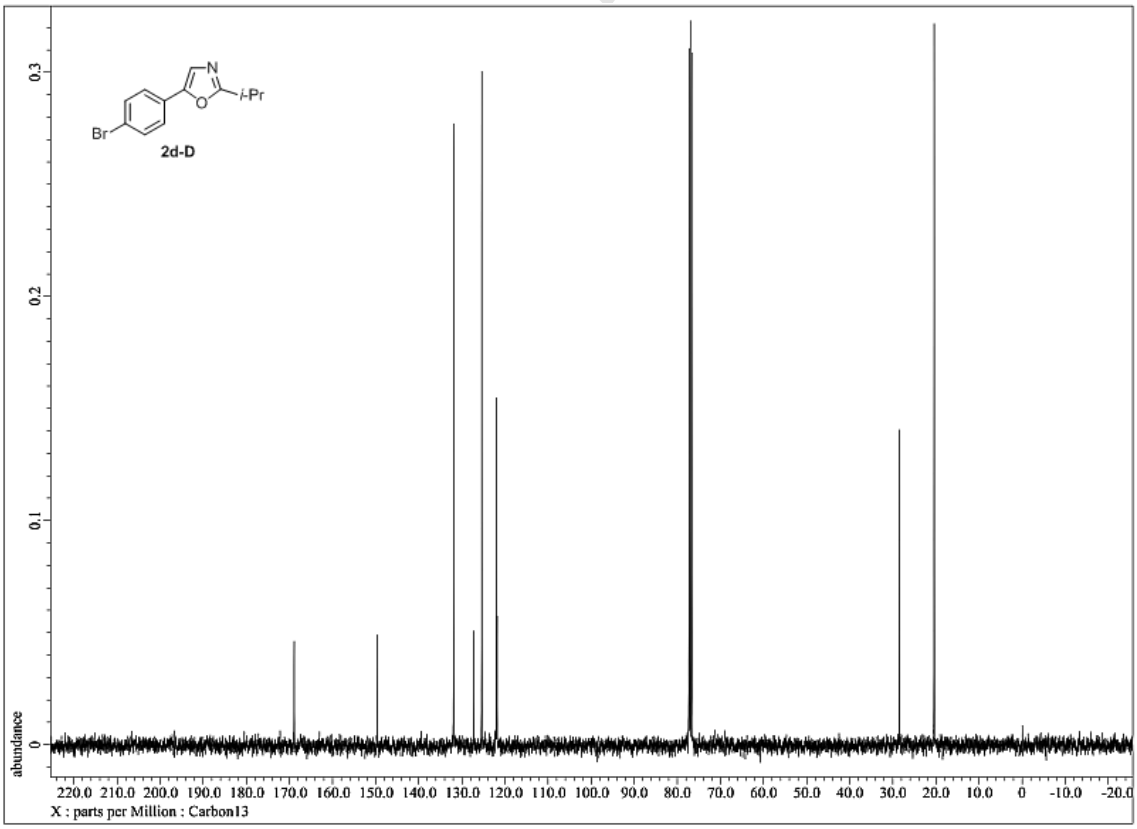

i-Pr
2a-D
abundance
X : parts per Million : Proton

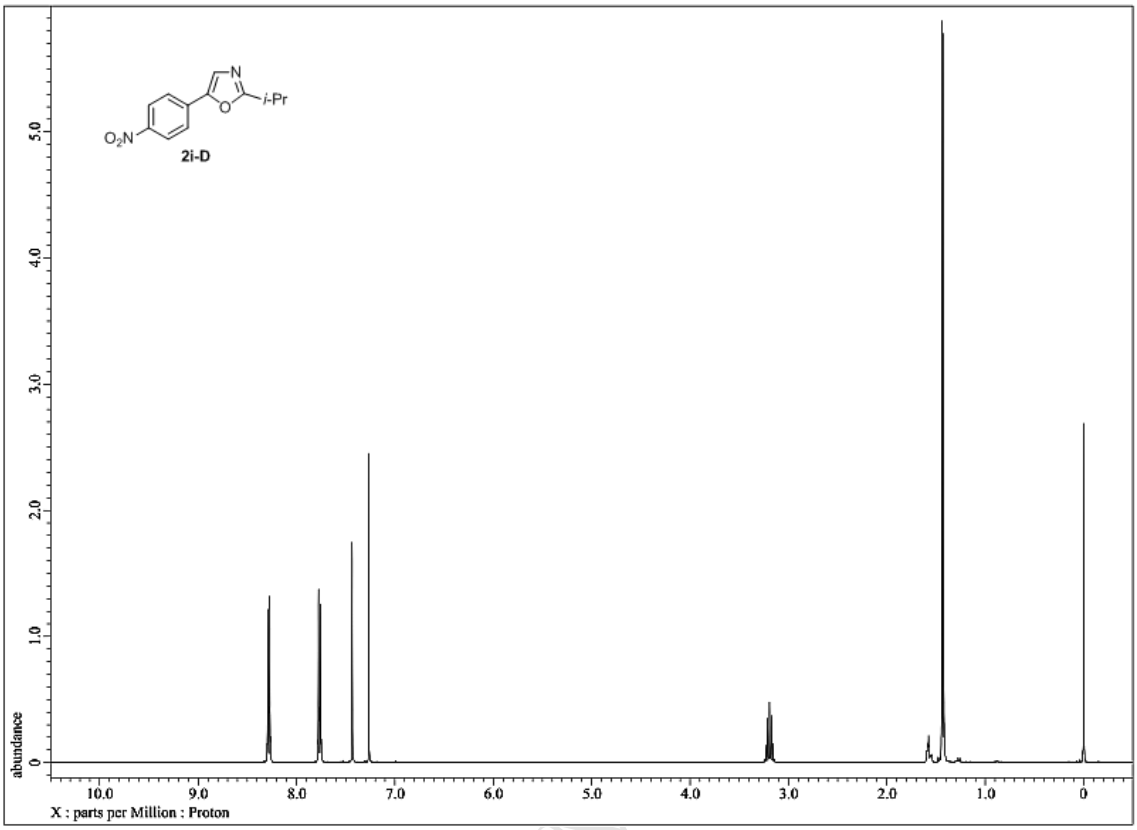

i-Pr
2a-D
abundance
X : parts per Million : Carbon13

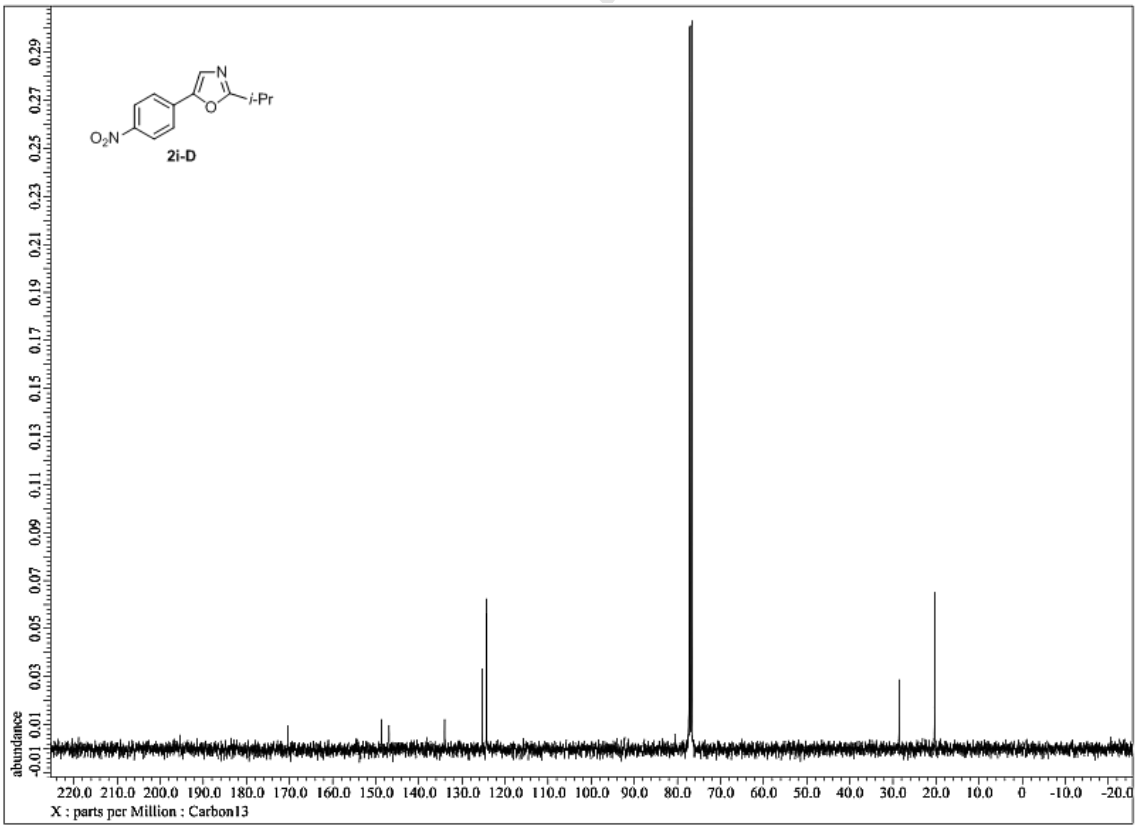

N
O
i-Pr
Cl
2c-D
abundance
X : parts per Million : Proton

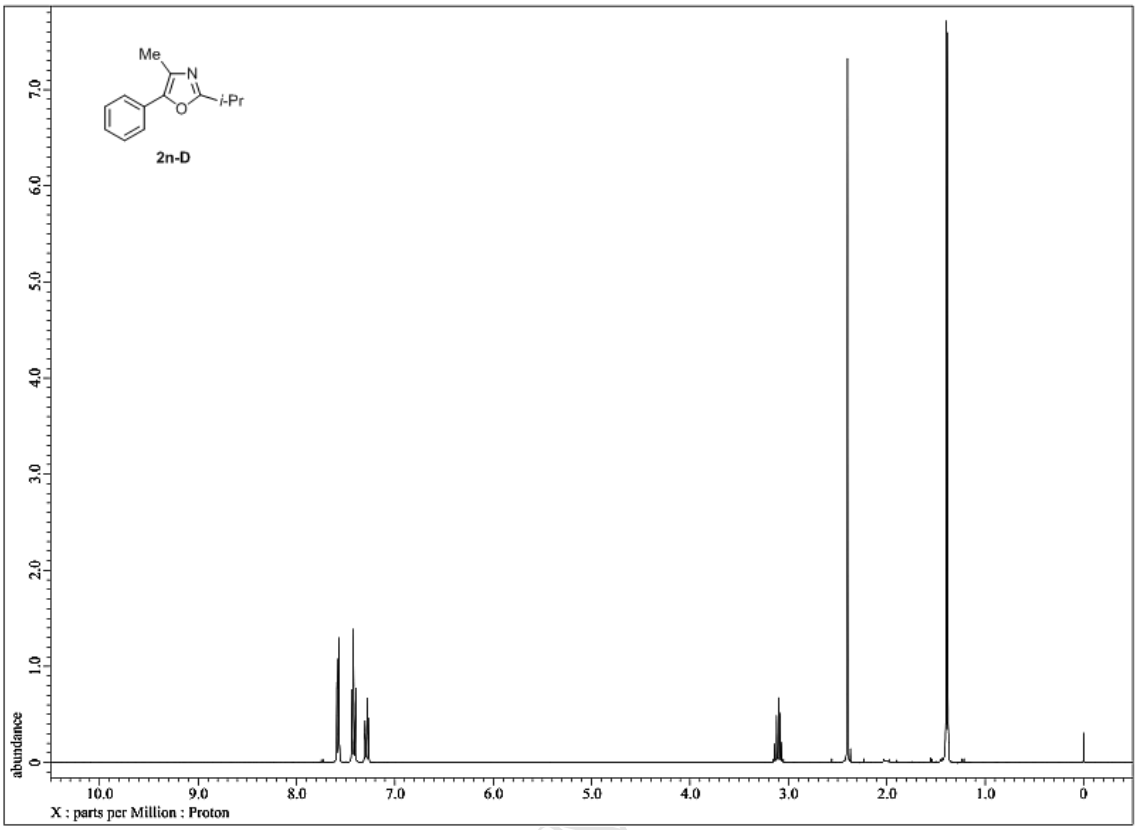

N
O
i-Pr
Cl
2c-D
abundance
X : parts per Million : Carbon13

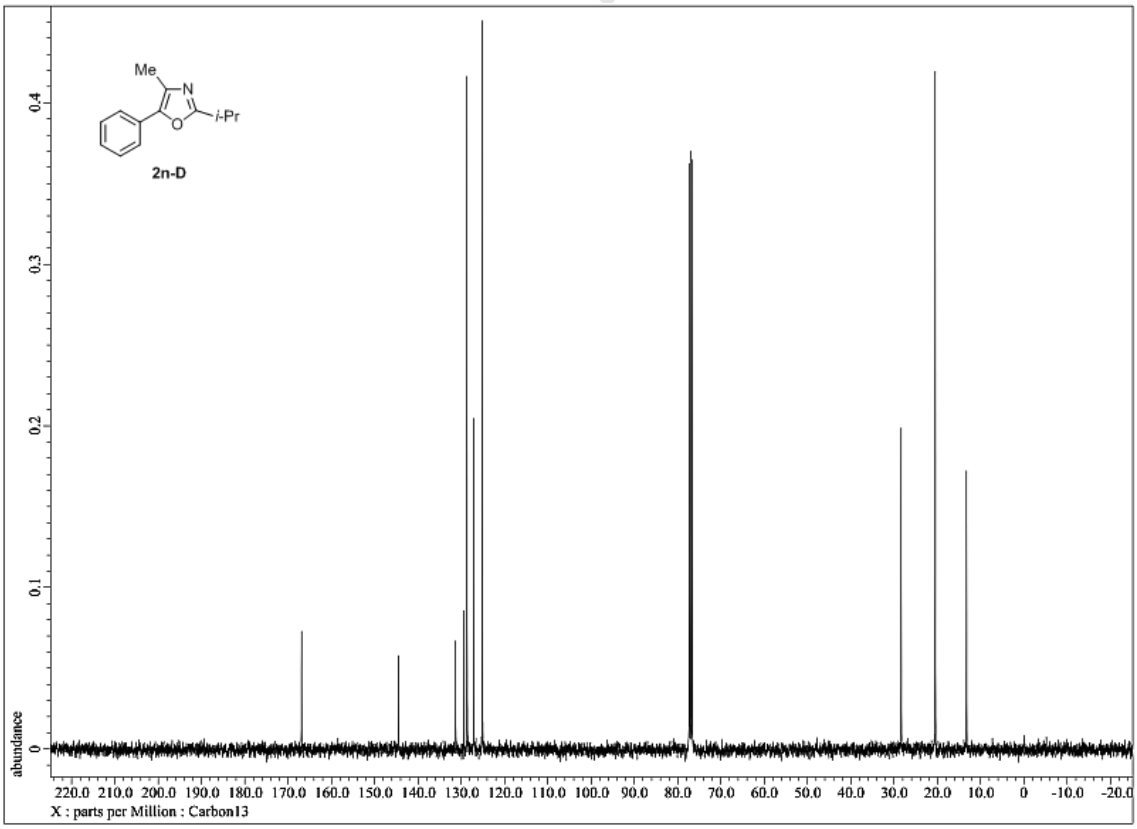

N
O
i-Pr
Br
2d-D
abundance
X : parts per Million : Proton

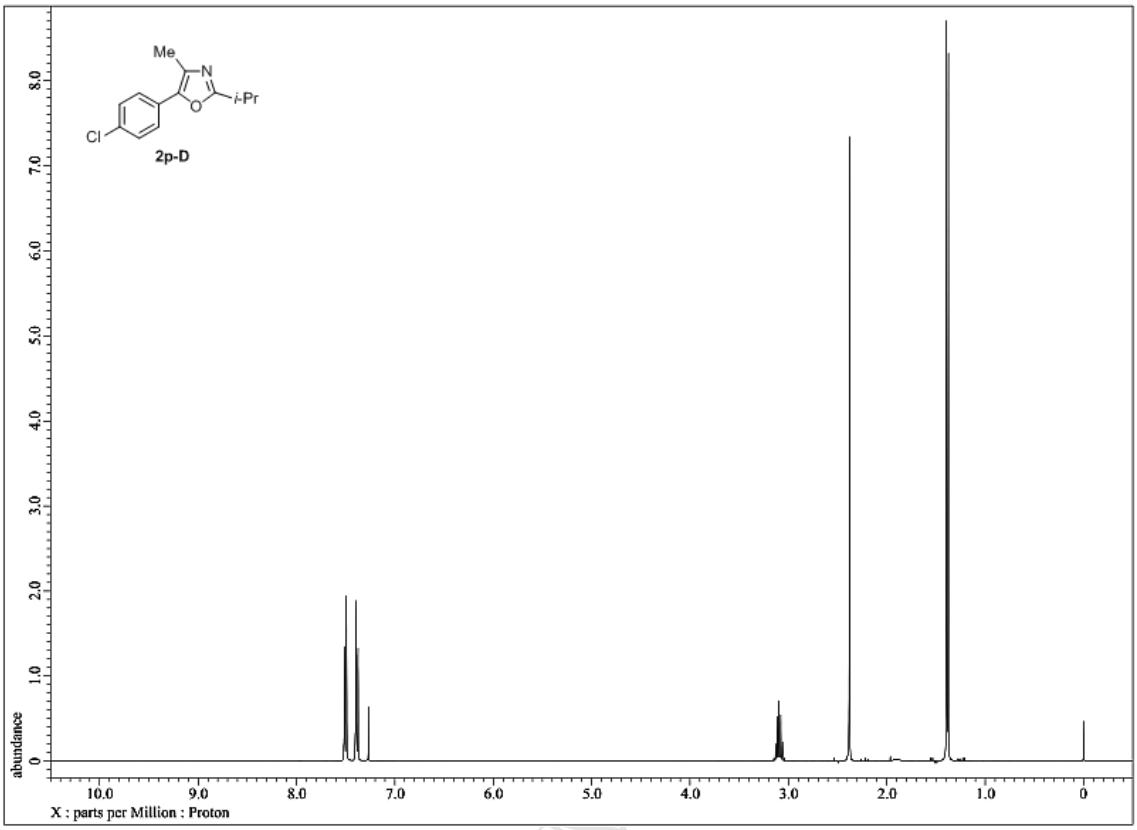

N
O
i-Pr
Br
2d-D
abundance
X : parts per Million : Carbon13

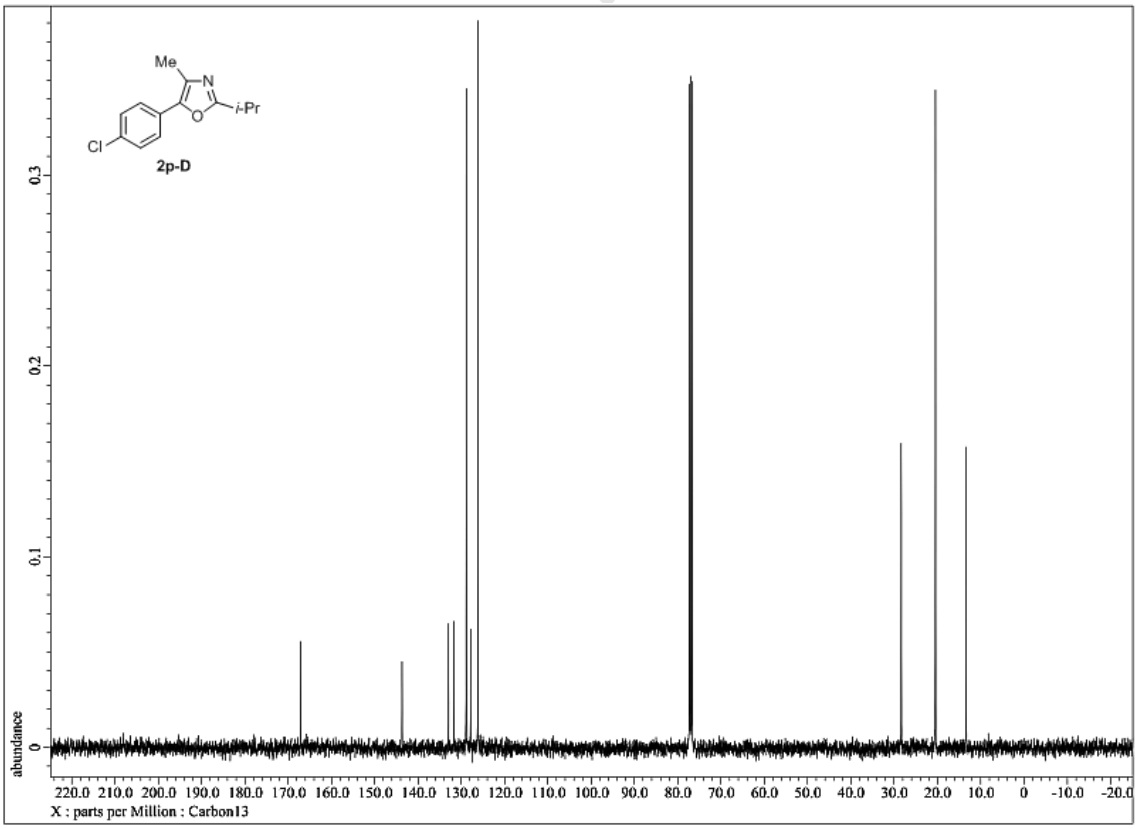

i-Pr
O2N
2i-D
abundance
X : parts per Million : Proton

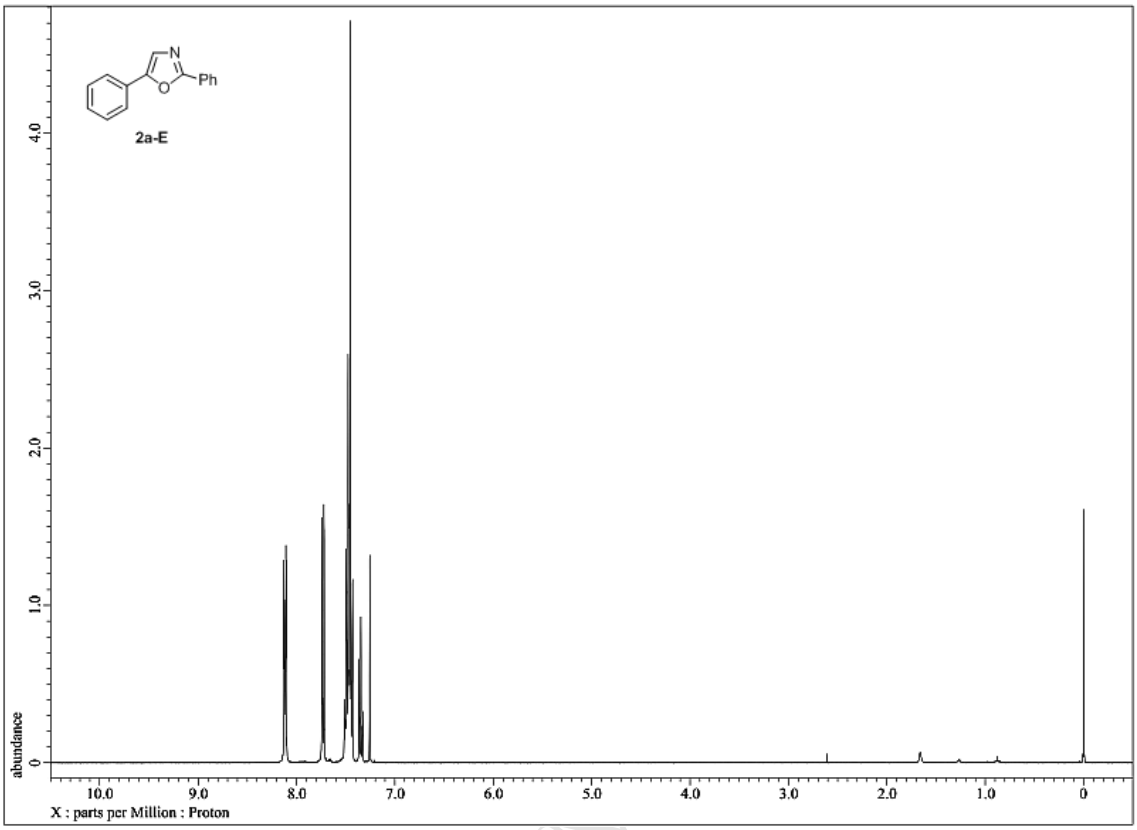

i-Pr
O2N
2i-D
abundance
X : parts per Million : Carbon13

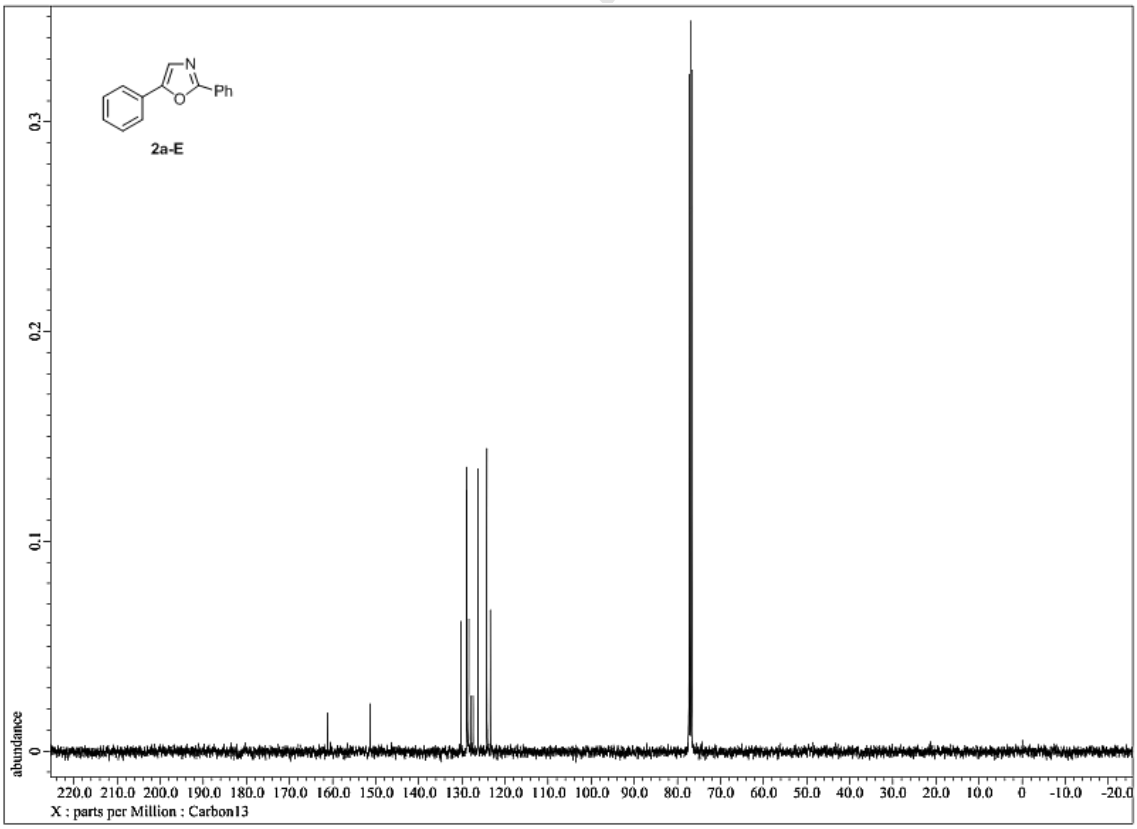

Me
N
O
i-Pr
2n-D
abundance
X : parts per Million : Proton

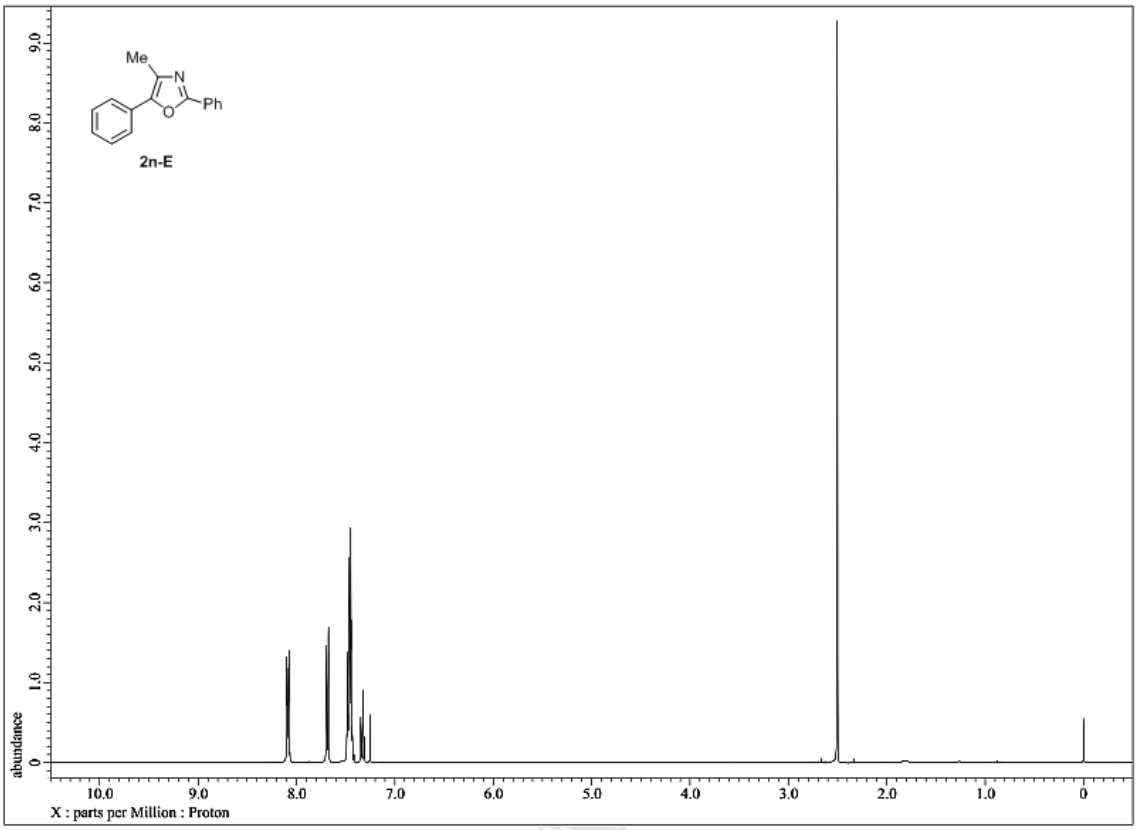

Me
N
O
i-Pr
2n-D
abundance
X : parts per Million : Carbon13

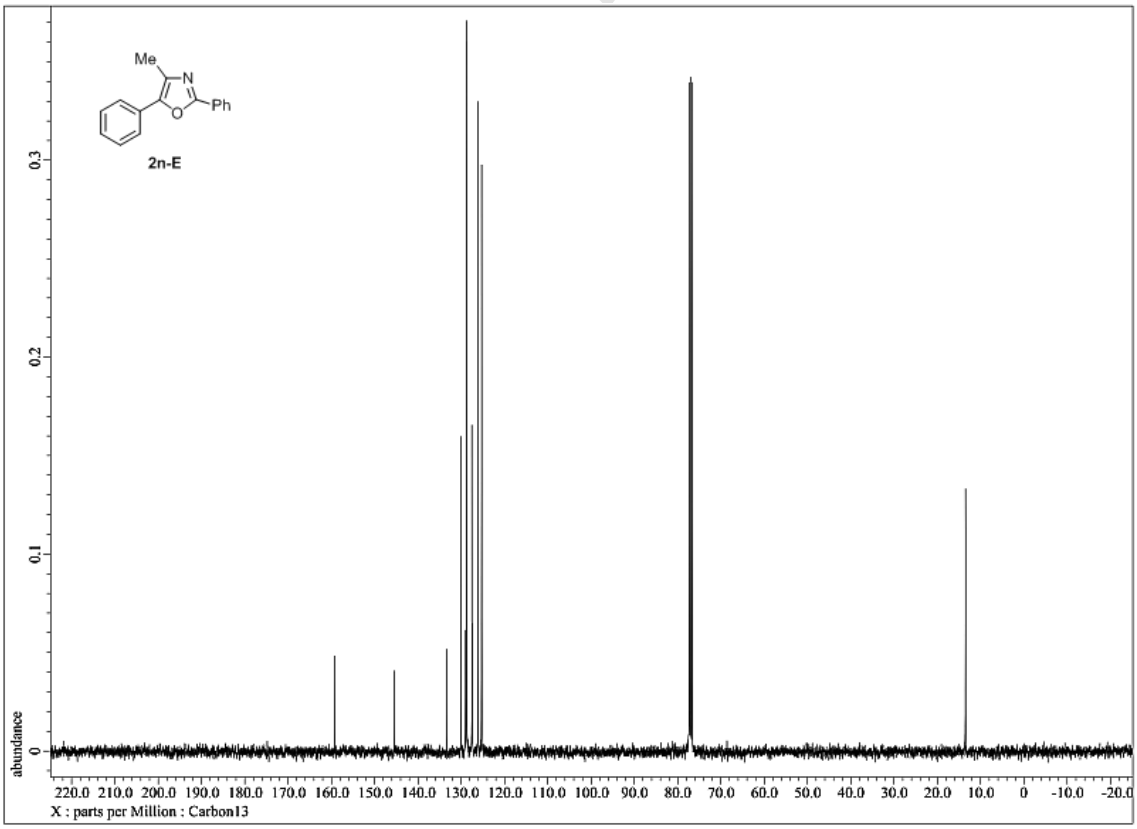

Me
N
O
i-Pr
Cl
2p-D
abundance
X : parts per Million : Proton

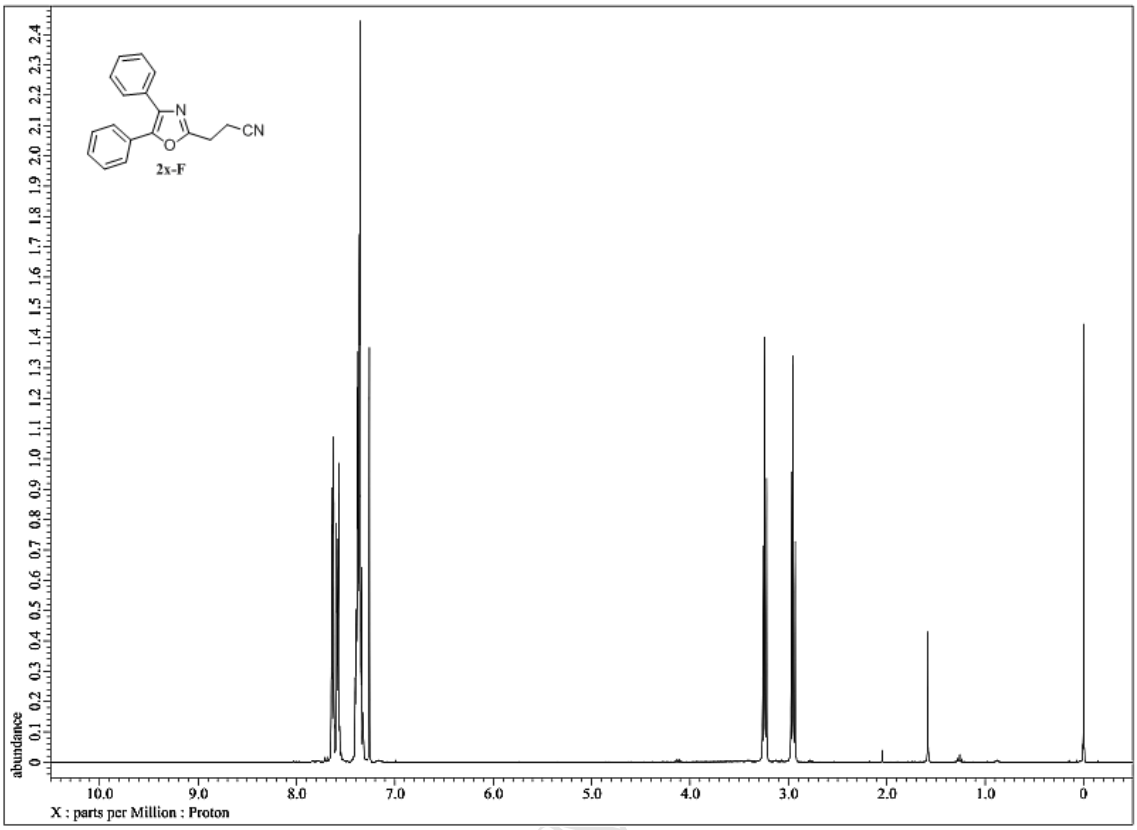

Me
N
O
i-Pr
Cl
2p-D
abundance
X : parts per Million : Carbon13

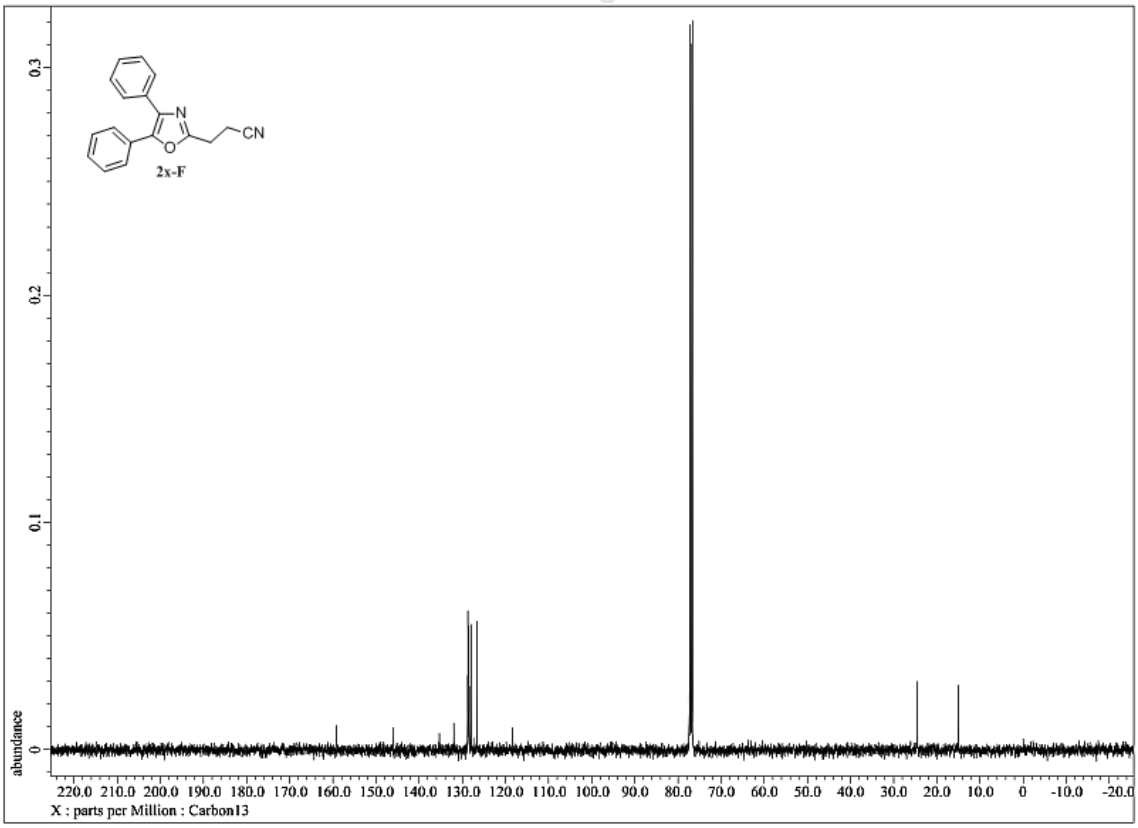

N
O
Ph
2a-E
abundance
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

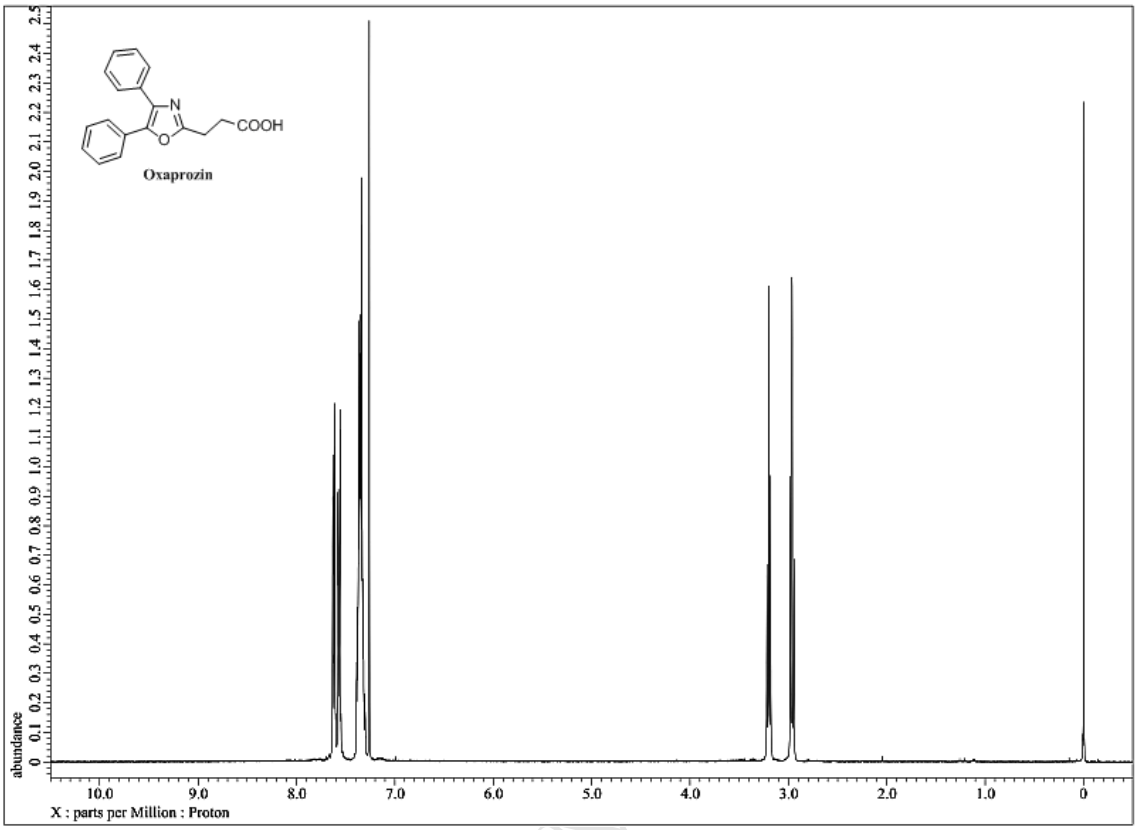

N
O
Ph
2a-E
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
X : parts per Million : Carbon13

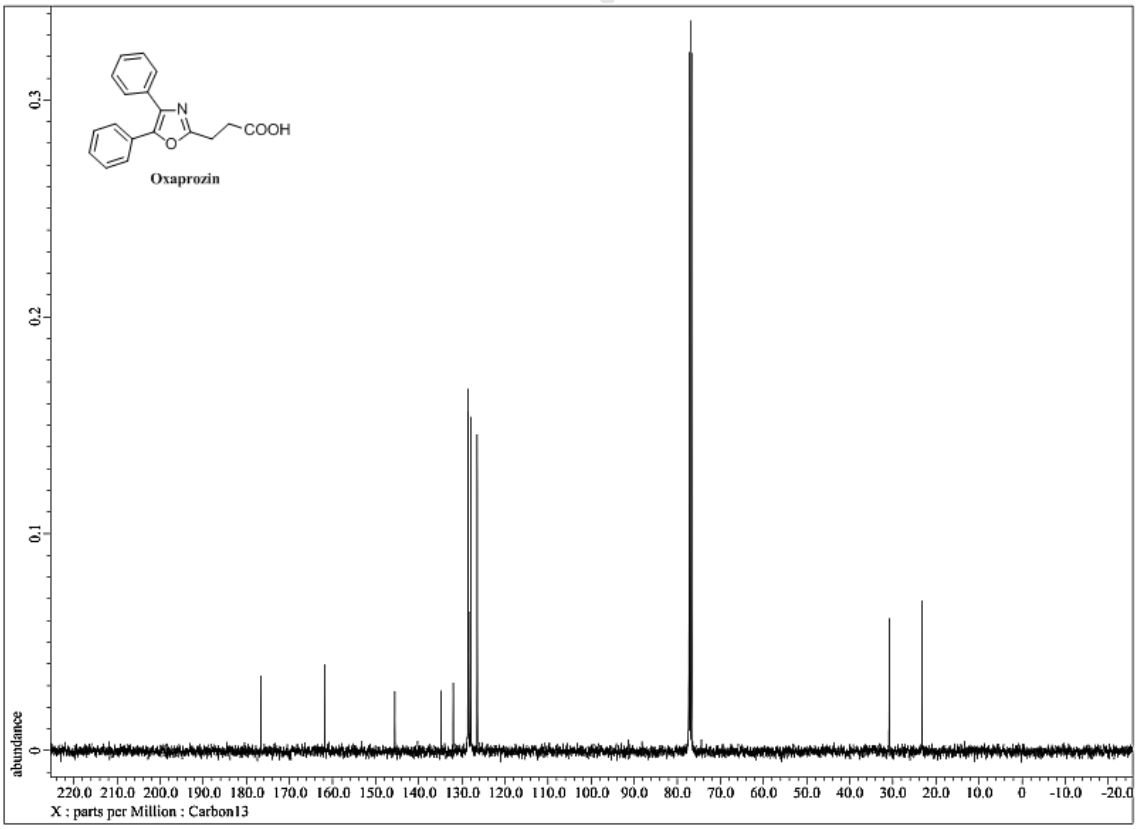

Me
N
O
Ph
2n-E
abundance
X : parts per Million : Proton


Me
N
O
Ph
2n-E
abundance
X : parts per Million : Carbon13


2x-F
CN
abundance
X : parts per Million : Proton


2x-F
CN
abundance
X : parts per Million : Carbon13


N
O
COOH
Oxaprozin
abundance
X : parts per Million : Proton


N
O
COOH
Oxaprozin
abundance
X : parts per Million : Carbon13