Electronic Supplementary Information

Synthesis and diverse general oxidative cyclization catalysis of high-valent $Mo^{VI}O_2(HL)$ to ubiquitous heterocycles and their chiral analogues with high selectivity

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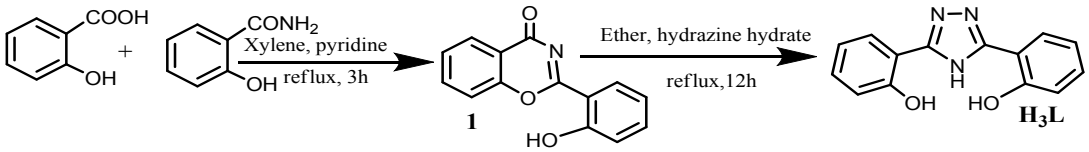
1. Materials and methods.

All reagents were purchased from commercial suppliers and used without further purification, unless otherwise specified. Commercially supplied ethyl acetate and petroleum ether were distilled before use. Acetonitrile, diethyl ether, and CH_2Cl_2 were dried by distillation over P_2O_5, toluene over sodium and DMF over calcium hydride. Tetrahydrofuran (THF) was dried by distillation from sodium benzophenone ketyl. Petroleum ether used in our experiments was in the boiling range of 60-80^{o}C. Column chromatography was performed on basic alumina (70-230mesh, pH 8.5-10) and silica gel (60-120mesh, 0.12mm-0.25mm). Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Melting points are reported uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 300 MHz spectrometers (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shift is reported in ppm from internal reference tetramethylsilane and coupling constant in Hz. Proton multiplicities are presented as br (broad), s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), and m (multiplet). Infrared spectra were recorded on FT-IR spectrometer as KBr pellets or thin film from $CHCl_3$ on the NaCl window. Optical rotation of the chiral compounds was measured in a polarimeter using standard 10 cm quartz cell in sodium-D lamp at ambient temperature. Mass spectrometry was performed on a gas chromatography-mass spectroscopy system using helium as a carrier gas for electron impact (EI) at 70eV. Exact mass measurements were obtained using ESIMS Qtof instrument.

2. Synthesis of high-valent $MoO_2(HL)(H_2O)(DMF)$

(i) Preparatrion of ligand 2-(2-hydroxyphenyl)-4*H*-1,3-benzoxazin-4-one[1]:



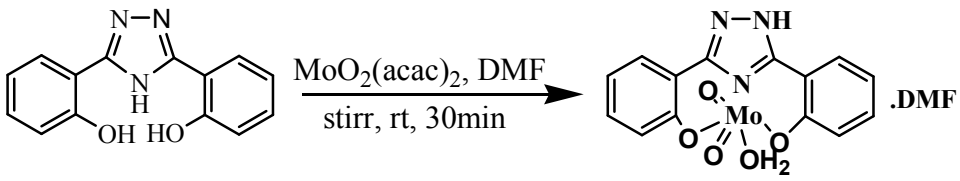
Salicylic acid (24.9 g, 0.18mol), salicylamide (20.6 g, 0.15mol) and pyridine (0.019mol, 1.5mL) were mixed in xylene (30mL). The suspension was heated to boiling with continuous stirring till a clear solution was obtained. Thionyl chloride (23.7mL; 0.33mol) was added very

slowly from a dropping funnel over a period of 4h. A vigorous evolution of SO_2 and HCl gas occurred. At the end of the reaction yellow solid separated out in the reaction mixture. Stirring was continued for another 30min and cooled to room temperature. The solvent was removed, EtOH (60mL) and acetic acid (1.5mL) were added. The suspension was heated to boiling for about 15min and cooled to room temperature. The separated solid was filtered and crystallized from methoxy ethanol to obtain the pure product (**1**, 27.29g, 0.11mol, 77%).

(ii) **Preparation of 3,5-bis(2-hydroxyphenyl)-1,2,4-triazole**[1] **(H_3L):** The compound **1** was prepared by dissolving hydrazine hydrate (0.2mL, 4.18mmol) in dry diethyl ether (25mL), the solution was heated to boiling and stirred under reflux for about 20 min. 2-(2-Hydroxyphenyl)-4*H*-1,3-benzoxazin-4-one (1g, 4.18mmol) was added to the mixture in portions and stirring was continued for 12 hour under reflux. A colourless solid was separated out, which was filtered and washed with chilled ether to afford HL (0.82g, 3.44mmol, 80%).

(iii) **Preparation of $MoO_2(acac)_2$**[2]**:** Ammonium molybdate (12.35g, 0.01mol) was dissolved in warm distilled water (60mL) and diluted nitric acid was added to control the pH = 3. Acetyl acetone (9.5mL, 0.105mol) was added and stirred contentiously for 3h. The separated out yellow solid was filtered, washed with water, 1:1 aqueous EtOH, finally with diethyl ether, air dried and used for next step without further purification.

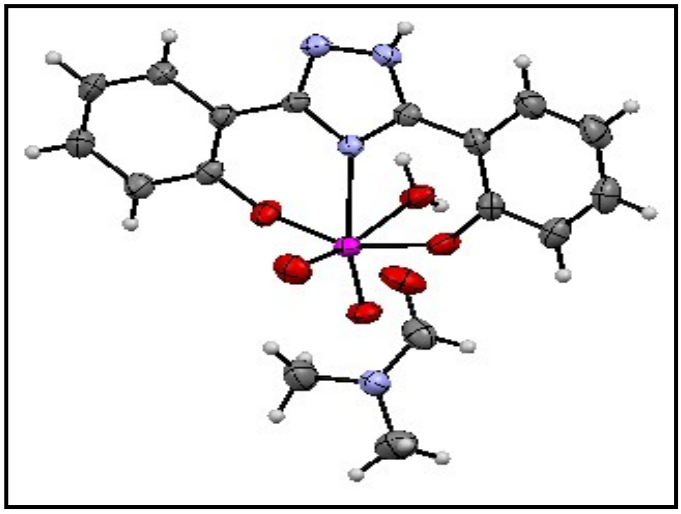
(iv) **Preparation of $MoO_2(HL)(H_2O)(DMF)$:** $MoO_2(acac)_2$ (328mg, 1mmol) was dissolved in dry DMF (25mL), and 3,5-bis(2-hydroxyphenyl)-1,2,4-triazole (278mg, 1.1mmol) was added and stirred continuously for 30 min at room temperature. The solid was filtered off through a Whattman-41 filter paper. The clear orange yellow filtrate was allowed for the slow evaporation. The bright yellow crystal was found after 72h.The crystal was used for the single crystal XRD study to establish the structure.



^{1}H NMR (300 MHz, DMSO-d6): δ 2.01 (2H, s), 3.29 (6H, s), 6.92 (2H, dd, *J* = 7.8, 7.5 Hz), 7.39 (1H, t, *J* = 7.5 Hz), 7.76 (1H, d, *J* = 7.8 Hz). 11.3 (1H, s), 11.9 (1H, Brs); ^{13}C NMR (75 MHz, DMSO-d6): δ 40.5, 116.5, 118.4, 119.1, 130.0, 133.7, 156.3, 164.0; FT-IR (KBr, cm^{-1}): 747,

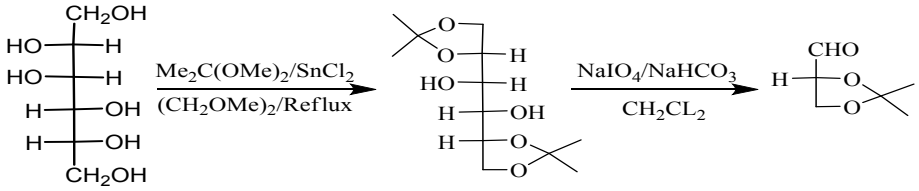
878, 1095, 1250, 1306, 1459, 1645, 3271; HRMS (ESI) $[M]^+$ Calcd for $C_{17}H_{18}MoN_4O_5$: 456.0331, Found: 456.0303.

3. Selected single crystal XRD data of the high-valent molybdenum complex



- Chemical formula and formula weight (M): C17 H18 Mo N4 O5and 456.03
- Crystal system: Triclinic
- Unit-cell dimensions (angstrom or pm, degrees) and volume, with edges: a 9.2570(15), b 9.9830(16), c 10.7891(17), 114.336(2), 90.211(2), 91.610(2), 908.0(3)
- Temperature: 293K
- Space group symbol: P-1
- No. of formula units in unit cell (Z): 3
- Number of reflections measured and/or number of independent reflections, Rint: 2825
- Final R values (and whether quoted for all or observed data): 0.0342

4. Synthesis of (2S)-2,3-O-isopropylideneglyceraldehyde



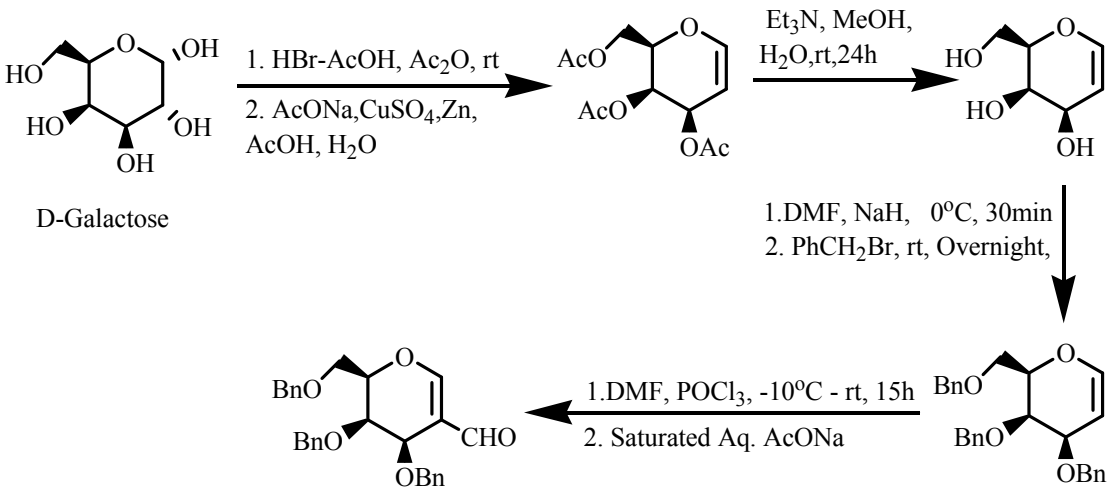
(i) **Preparation of 1,2,5,6-di-O-isopropylidine-D-mannitol:** This compound was prepared by modified Chittenden[3] method from readily available D-mannitol. D-(+)-mannitol was suspended in ethylene glycol dimethyl ether (75mL, 0.49mol) containing freshly distilled methanol free acetone dimethyl acetal (48mL, 0.39mol) and catalytic amount of tin(II) chloride (30mg), and

the slurry was heated under reflux with continuous stirring for about 4h, until a clear solution was obtained. The solution was cooled to room temperature and a calculated amount of pyridine (0.3mL) was added for complexing the metal chloride. A very small amount of solid material was separated out. It was filtered off and identified as 1,2-monoisopropylidene-D-mannitol. The filtrate was concentrated with the help of a rotary evaporator and poured in cyclohexane (100mL). The separated out crystal was filtered and crystallized from acetone as a colourless solid. Yield: 75%; mp: 122 ^{o}C [Lit. mp: 122 ^{o}C]; Optical rotation: $[\alpha]_D^{24}$ = +1.82 [c 3.5, EtOH].

(ii) **Synthesis of (2S)-2,3-O-isopropylideneglyceraldehyde:** It was prepared by oxidative cleavage of 1,2:5,6-di-O-isopropylidine-D-mannitol by using sodium periodate. 1,2:5,6-Di-O-isopropylidine-D-mannitol (2.27g, 8.5mmol) was dissolved in a mixture of dichloromethane (50mL) and saturated solution of sodium bicarbonate (4mL) and stirred continuously with the help of a mechanical stirrer. Solid sodium periodate (2.8g, 13mmol) was added portion wise for about 20 min. Stirring was continued for two and half hour and anhydrous sodium sulphate (5g) was added with vigorous stirring. After another one hour it was filtered and residue was washed with dry dichloromethane. The filtrate was concentrated in a rotary evaporator at below 30 ^{o}C under reduced pressure and to furnish crude (2S)-2,3-O-isopropylideneglyceraldehyde, which was used for the next step. The FTIR spectroscopy of the product showed removal of –OH band (3317 cm^{-1}) and appearance of –CHO band (1739 cm^{-1}).

5. Synthesis of benzyl protected glycal aldehydes

(i) **Synthesis of 2-*C*-galactal aldehyde**



(a) **Preparation of HBr-AcOH:** Distilled tetraline (150mL) was placed in a two necked round bottomed flask equipped with a pressure equalizer. The content was stirred with a magnetic

stirrer and bromine (35mL) was added drop wise during 3h.The evolved HBr was passed through two traps filled with tetraline to remove any trace of Br_2 present in HBr vapour. A two necked round bottomed flask fitted with a calcium chloride guard tube was utilized as the receiving vessel containing AcOH(42.2g), which was placed on a water bath (20 °C). Percentage of HBr in acetic acidthus formed was nearly 36.4% (may slightly change from time to time). This solution was diluted with AcOH to 31% before using in the synthesis of the galactal acetate.

(b) **Preparation of 3,4,6-tri-O-acetyl-D-galactal:** To a suspension of D-(+)-galactose (3.0 g, 16.7mmol) in distilled Ac_2O (11.0mL), 31% HBr-AcOH (4.0mL)was added dropwise at 0 °C. The reaction mixture was stirred at ambient temperature for about 45min until the suspended solid dissolved. Another portion of 31% HBr-AcOH (14.0mL) was added dropwise from a pressure equalizer and the resulting mixture was stirred overnight at ambient temperature. Anhydrous NaOAc (6.0g, 73.2mmol) was added slowly to the ice cold reaction mixture to neutralize the excess HBr. The reaction mixture was added to a suspension of pulverized $CuSO_4.5H_2O$ (0.5g, 2mmol) and Zn-dust (37.8g, 581.5mmol) in a buffer containing $NaOAc.3H_2O$ (28.4g, 208.8mmol), water (30.0mL) and AcOH (45.0mL) under vigorous stirring maintaining temperature at 15-20 °C. After 2h the reaction mixture was filtered through a celite bed and washed well with ethyl acetate and ice cold water. The organic portion was separated and washed with water (1x100.0mL), aqueous saturated $NaHCO_3$ solution (4x50mL), and water (2x100mL). The organic portion was separated and dried over anhydrous Na_2SO_4. The solvent was removed in a rotary evaporator under reduced pressure at room temperature. Purification of thecrude product by column chromatography on silica gel (60-120 mesh) using ethylacetate-petroleum ether (1:5) as eluting solvents afforded solid compound, 3,4,6-tri-*O*-acetyl-D-galactal (2.9 g, 10.9mmol, 66%).

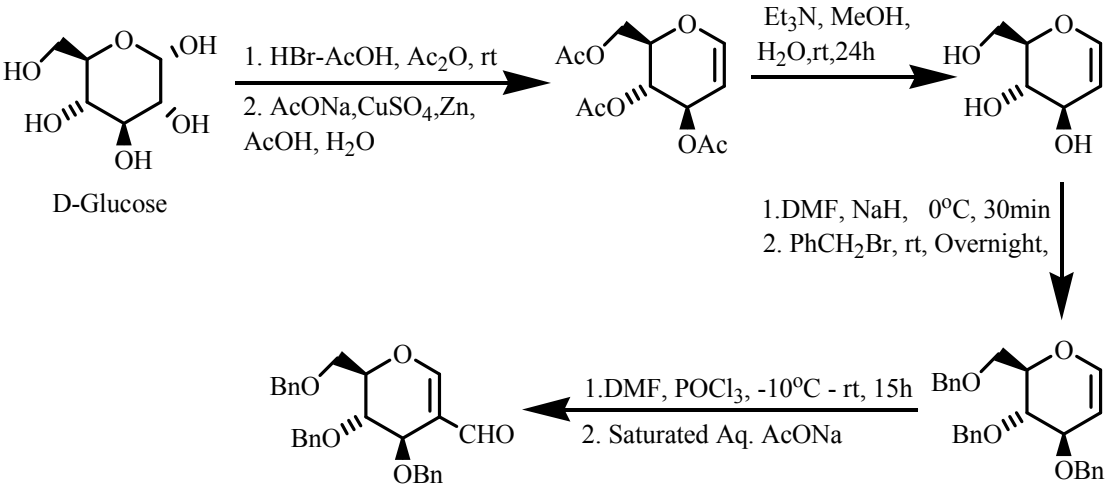
(c) **Deacetylation of 3,4,6-tri-O-acetyl-D-galactal:** 3,4,6-Tri-*O*-acetyl-D-galactal (2.0g, 7.4mmol), MeOH (10mL), Et_3N (6.1 mL) and H_2O (0.8 mL) were taken together in an around bottom flask (25 mL) and the content of the reaction mixture was stirred overnight at ambient temperature. After completion of the reaction (monitored by TLC) the solvent was removed under reduced pressure at ambient temperature. The crude product was dried by making

azeotropic mixture using dry toluene and simultaneous removal of the solvent under reduced pressure for at least 7 times to afford pure galactal (92%, 1.0g, 6.8mmol).

(d) **Preparation of 3,4,6-tri-O-benzyl-D-galactal:** The D-galactal (2.0g, 13.7mmol) was dissolved in dry DMF (8.0 mL) and NaH (2.02 g, 60% oil suspension, 50.5 mmol) was added in portions over a period of 15min. maintaining the temperature between 0-5 ^{o}C and stirred for half an hour. Benzyl chloride (6.3g, 49.8mmol) was added drop wise over a period of 20min. The content of the reaction mixture was stirred overnight at room temperature. The excess NaH present in the reaction mixture was decomposed by adding dry MeOH (2.0mL) under the ice cold condition and stirred for another 30 min. It was transferred into a separating funnel and extracted with ethyl acetate (5x30.0mL). The combined organic portion was washed with brine (2x30.0mL), dried over anhydrous Na_2SO_4 and the solvent was removed in a rotary evaporator under reduced pressure at room temperature. The crude product was purified by column chromatography on silica gel (80-120mesh) using ethyl acetate and petroleum ether (1:10). Thus 3,4,6-tri-*O*-benzyl-D-galactal was afforded in 73% (4.2g, 10mmol) yield.

(e) **Formylation of 3,4,6-tri-O-benzyl-D-galactal:** 3,4,6-Tri-*O*-benzyl-D-galactal was subsequently converted into the corresponding 2-C-formyl galactal by Vilsmeier Haak reaction through the following procedure. 3,4,6-Tri-O-benzyl-D-galactal (1.0g, 2.4mmol) was dissolved in dry DMF (4.0mL, 3.8g, 52mmol) and cooled in an ice bath. Freshly distilled $POCl_3$ (2.5 mL, 4.0g, 26.1mmol) was added drop wise to the reaction mixture over a period of 40min. The reaction mixture was stirred at 0 ^{o}C for 30 min and allowed to attain room temperature. After 12h, the reaction mixture was poured into a mixture of ice (20.0g) and $NaOAc.3H_2O$ (60.0g, 441.2 mmol) taken in a 250mL conical flask and it was stirred for 1h at 20 °C. The post reaction mixture was taken in a separating funnel and extracted with ethyl acetate (5x20mL). Organic portion was washed with saturated aqueous $NaHCO_3$ solution (1x30.0mL), water (3x30mL), dried over anhydrous Na_2SO_4 and the solvent was removed in a rotary evaporator under reduced pressure at room temperature. The crude product was purified by column chromatography on silica gel using ethyl acetate and petroleum ether (1:6). Thus 2-*C*-2-formyl-3,4,6-tri-*O*-benzyl-D-galactal was afforded 75% (0.8g, 1.8mmol) yield.

(b) **Synthesis of 2-*C*-glucal aldehyde:** 2-*C*-2-formyl-3,4,6-tri-*O*-benzyl-D-glucal was synthesized exactly similar procedure as described for 2-*C*-2-formyl-3,4,6-tri-*O*-benzyl-D-galactal.

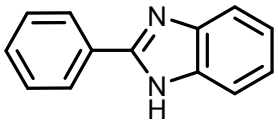


6. **General procedure for synthesis of 2-substituted benzimidazoles (3)**

Benzaldehyde (108mg, 1mmol), o-phenylenediamine (119mg, 1.1mmol), THF (5.0mL), $MoO_2(HL)(H_2O)(DMF)$ catalyst (38mg, 8mol%) and magnesium sulphate (0.5g) were taken together in a round-bottomed flask at 0 °C and stirred magnetically. The content of the reaction mixture was allowed to attain room temperature. The reaction was monitored by TLC (SiO_2 plate, petroleum ether/ethyl acetate (2:1) and the spots were developed in an iodine chamber. The reaction was complete in 7h. THF was removed from the post reaction mixture in a rotary evaporator under reduced pressure at room temperature. The residue was extracted with ethyl acetate (2x25mL). The organic portion was washed with water (3x25mL), dried on activated sodium sulphate, and concentrated in a rotary evaporator under reduced pressure at room temperature. The crude product was washed with diethyl ether to afford the pure 2-(phenyl)-1*H*-benzimidazole (**3a**) in a yield of 86% (166mg, 0.86mmol).

7. Characterization data of the synthesized benzoimidazoles (3a-p)

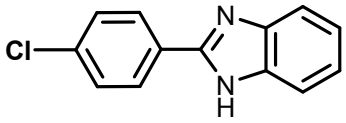
2-phenyl-1*H*-benzimidazole (3a)



3a

Yield: 86% (166 mg, 0.86mmol).
Characteristic: Yellow solid.
Melting point**:** 302-304ºC. [Lit.[4], 302-303 ºC].
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (2H, dd, *J* = 3.0, 6.0 Hz), 7.44-7.51 (2H, m), 7.60 (2H, s), 8.19 (2H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ113.5, 120.6, 125.1, 126.7, 127.2, 128.2, 128.7, 137.8, 150.1; FT-IR (KBr, cm^{-1}): 620, 740, 1116, 1409, 1447, 1624, 2373, 2670, 2856, 2925, 3050,3450. Spectroscopic data was compared with that previously reported.[4]

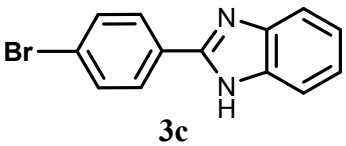
2-(4-Chlorophenyl)-1*H*-benzimidazole (3b)



3b

Yield: 81% (184mg, 0.81mmol).
Characteristic: Yellow solid.
Melting point**:** 302-304^{o}C. [Lit.[5], 303-304 ºC].
^{1}H NMR (300 MHz, $CDCl_3$): δ- 7.17-7.22 (2H, m), 7.45 (2H, d, *J* = 8.4 Hz), 7.57-7.62 (2H, m), 8.15 (2H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 121.8, 127.5, 128.2, 134.8, 150.1; FT-IR (KBr, cm^{-1}): 739, 828, 961, 1012, 1091, 1270, 1316, 1430, 1588, 2375, 2699, 2851, 3053. Spectroscopic data was compared with that previously reported.[5]

2-(4-Bromophenyl)-1*H*-benzimidazole (3c)

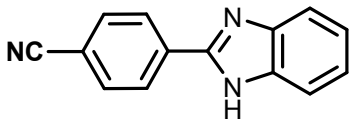


3c

Yield: 83% (224 mg, 0.83mmol).
Characteristic: Light Yellow solid.

Melting point: 298-299 °C. [Lit.[6], 299-300 ºC].
^{1}H NMR (300 MHz, DMSO-d6): δ 7.19 (2H, d, *J* = 5.4 Hz), 7.49 (1H, d, *J* = 7.2 Hz), 7.63 (1H, d, *J* = 6.6 Hz), 7.72 (2H, d, *J* = 8.4 Hz), 8.08 (2H, d, *J* = 8.4 Hz), 12.9 (1H, s); ^{13}C NMR (75MHz, DMSO-d6): δ121.8, 123.1, 127.7, 128.7, 131.2, 150.2; FT-IR (KBr, cm^{-1}): 961, 1011, 1112, 1273, 1318, 1429, 1590, 2782, 2855, 2933, 3052. Spectroscopic data was compared with that previously reported.[6]

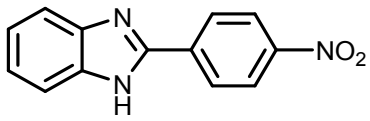
4-(1*H*-Benzoimidazol-2-yl)-benzonitrile (3d)



3d

Yield: 79% (172 mg, 0.79 mmol).
Characteristic: Light grey solid.
Melting point**:** 263-265 °C. [Lit.[7], 260-262 ºC].
^{1}H NMR (300 MHz, DMSO-d6): δ7.16 (2H, s), 7.50 (1H, s), 7.61 (1H, s), 7.94 (2H, d, *J* = 6.0 Hz), 8.26 (2H, d, *J* = 9.0 Hz), 13.11 (1H, s); ^{13}C NMR (75 MHz, DMSO-d6): δ112.2, 112.3, 119.0, 119.8, 122.6, 123.8, 127.4, 133.4, 134.7, 149.8; FT-IR (KBr, cm^{-1}): 1031, 1179, 1255, 1293, 1400, 1431, 1478, 1613, 1745, 2230, 2372, 3035, 3423. Spectroscopic data was compared with that previously reported.[7]

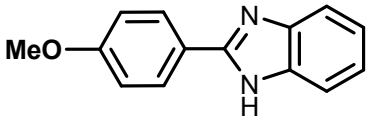
2-(4-Nitrophenyl)-1*H*-benzimidazole (3e)



3e

Yield: 79% (189 mg, 0.79mmol).
Characteristic: Yellow solid.
Melting point: 310-311 °C. [Lit.[8], 308-310 °C].
^{1}H NMR (300 MHz, DMSO-d6): δ 7.41 (2H, s), 7.54 (1H, d, J = 6.3 Hz), 7.69 (1H, d, *J* = 6.6 Hz), 8.36 (4H, s), 13.2 (1H, s); ^{13}C NMR (75 MHz, DMSO-d6): δ 111.8, 119.5, 122.3, 123.6, 124.0, 124.3, 127.4; FT-IR (KBr, cm^{-1}): 1100, 1335, 1433, 1513, 1597, 1704, 1933, 2375, 2750, 2854, 2917, 3437. Spectroscopic data was compared with that previously reported.[8]

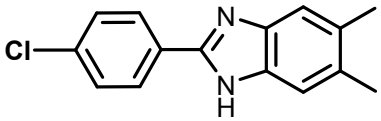
2-(4-Methoxyphenyl)-1*H*-benzimidazole(3f)



3f

Yield: 82% (183 mg, 0.82 mmol).
Characteristic: Colourless solid.
Melting point**:** 223-224 °C. [Lit.[9], 222-225 ºC]
^{1}H NMR (300 MHz, DMSO-d6): δ- 3.80 (3H, s), 7.07 (2H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 5.7 Hz), 7.44 (1H, d, *J* = 4.8 Hz), 7.56 (1H, s), 8.07 (2H, d, *J* = 8.7 Hz), 12.68 (1H, s); ^{13}C NMR (75 MHz, DMSO-d6): δ 55.1, 114.1, 114.6, 121.8, 122.8, 128.1, 139.3, 151.7, 160.7; FT-IR (KBr, cm^{-1}): 1031, 1179, 1255, 1293, 1400, 1442, 1499, 1609, 1750, 3055. Spectroscopic data was compared with that previously reported.[9]

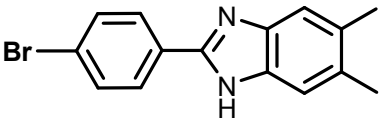
2-(4-Chlorophenyl)-5,6-dimethyl-1*H*-benzimidazole (3g)



3g

Yield: 77% (197 mg, 0.77 mmol).
Characteristic: Light grey solid.
Melting point**:** 260-263 °C. [Lit.[8] 262-264 ºC].
^{1}H NMR (300 MHz, DMSO-d6): δ 2.29 (6H, s), 7.24 (1H, s), 7.37 (1H, s), 7.51 (2H, dd, *J* = 8.4 Hz), 8.13 (2H, d, *J* = 8.4 Hz), 12.63 (1H, s); ^{13}C NMR (75 MHz, DMSO-d6): δ 130.21, 131.54, 133.62, 134.11, 142.52, 149.31; FT-IR (KBr, cm^{-1}): 534, 725, 834, 1011, 1092, 1437, 1593, 2374, 2925. Spectroscopic data was compared with that previously reported.[8]

2-(4-Bromophenyl)-5,6-dimethyl-1*H*-benzimidazole (3h)

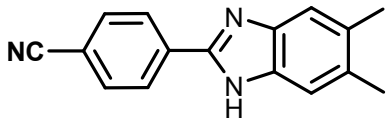


3h

Yield: 74% (222 mg, 0.74 mmol).
Characteristic: Yellow solid.

Melting point**:** 272-273 °C. [Lit.[6], 272-274 ºC].
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (6H, s), 7.34 (2H, s), 7.59 (2H, d, *J* = 7.8 Hz), 8.06 (2H, d, *J* = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.1, 122.0, 126.9, 128.5, 130.0, 130.5, 148.6; FT-IR (KBr, cm^{-1}): 719, 824, 1010, 1440, 1577, 1655, 2374, 2928, 3423. Spectroscopic data was compared with that previously reported.[6]

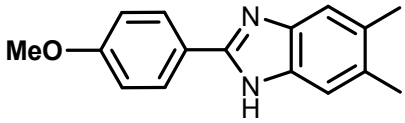
4-(5,6-Dimethyl-1*H*-benzimidazol-2-yl)-benzonitrile (3i).



3i

Yield: 83% (204 mg, 0.83 mmol).
Characteristic: Light yellow solid.
Melting point**:** 199-202 °C [Lit.[10], 199-202 °C].
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (6H, m), 7.38 (2H, s), 7.79 (2H, d, *J* = 7.8 Hz), 8.30 (2H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.2, 109.7, 116.7, 124.8, 129.6, 130.8, 132.6; FT-IR (KBr, cm^{-1}): 1000, 1281, 1444, 1610, 2225, 2370, 2925, 3067, 3423. Spectroscopic data was compared with that previously reported.[10]

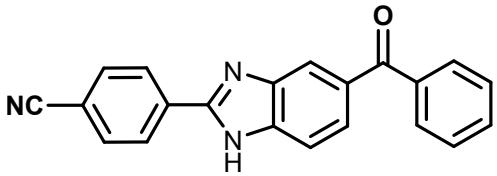
2-(4-Methoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (3j)



3j

Yield: 83% (205 mg, 0.83 mmol).
Characteristic: Light gray solid.
Melting point**:** Mp 196-199 °C. [Lit.[4,11]; 198-200 ºC].
^{1}H NMR (300 MHz, DMSO-d6): δ 2.37 (6H, s), 3.76 (3H, s), 7.03 (2H, d, *J* = 8.7),7.24 (1H, s), 7.35 (1H, s), 8.05 (2H, d, *J* = 8.6 Hz), 12.4 (1H, s); ^{13}C NMR (75 MHz, DMSO d6): δ 20.4, 55.3, 111.7, 114.7, 119.2, 123.5, 128.4, 130.1, 131.2, 133.9, 143.1, 151.1, 160.7; FT-IR (KBr, cm^{-1}): 836, 1026, 1178, 1254, 1448, 1498, 1611, 2927. Spectroscopic data was compared with that previously reported.[4,11]

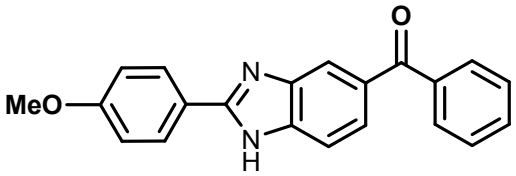
4-(5-Benzoyl-1*H*-benzimidazol-2-yl)-benzonitrile (3k)



3k

Yield: 86% (277 mg, 0.86mmol).
Characteristic: Light grey solid.
Melting point**:** 237-238 ^{o}C. [Lit.[10], 238-240 ^{o}C]
^{1}H NMR (300 MHz, DMSO-d6): δ 7.43-7.66 (3H, m), 7.72 (2H, d, *J* = 7.2 Hz), 7.85-7.90 (3H, m), 7.99 (2H, d, *J* = 8.4 Hz), 8.30 (2H, d, *J* = 8.4 Hz), 13.51 (1H, s); ^{13}C NMR (75 MHz, DMSO-d6): δ 111.9, 112.5, 114.5, 118.5, 119.1, 122.2, 125.2,127.3, 128.4, 129.5, 132.2, 132.8, 133.6, 138.0, 195.5; FT-IR (KBr, cm-1): 1080, 1282, 1282, 1316, 1418, 1603, 1640, 2227, 2376, 3213. Spectroscopic data was compared with that previously reported.[10]

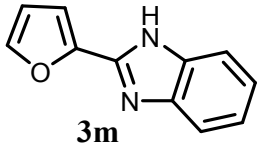
[2-(4-Methoxyphenyl)-1*H*-benzimidazol-5-yl]-phenyl-methanone (3l)



3l

Yield: 83% (272mg, 0.83 mmol).
Characteristic: Grey solid.
Melting point: 178-181 ^{o}C [Lit.[10], 180-182 ^{o}C].
^{1}H NMR (300 MHz, $CDCl_3$): δ 3.00 (3H, s), 6.15 (2H, d, *J* = 8.4 Hz), 6.60-6.65 (2H, m), 6.70-6.81 (2H, m), 6.87-6.93 (3H, m), 7.18 (1H, s), 7.32 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.4, 113.3, 113.4, 117.0, 120.6, 123.7, 127.2, 127.8, 128.7, 130.6, 130.9, 137.4, 137.6, 141.1, 153.2, 160.6, 195.3; FT-IR (KBr, cm^{-1}): 712, 829, 1026, 1117, 1178, 1251, 1311, 1427, 1491, 1613, 2043, 2378, 2837, 2957, 3064, 3275. Spectroscopic data was compared with that previously reported.[10]

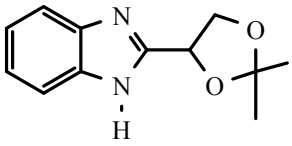
2-Furan-2-yl-1*H*-benzimidazole (3m)



3m

Yield: 82% (159 mg, 0.82 mmol).
Characteristic: Light yellow solid.
Melting point**:** 286-288 ^{o}C [Lit.[12], 286 ºC].
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.57 (1H, d, *J* = 1.5 Hz) 7.17-7.20 (3H, m), 7.55-760 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$):δ 109.1, 110.9, 114.0, 121.2, 142.5, 142.9, 144.6; FT-IR (KBr, cm^{-1}): 1012, 1114, 1167, 1229, 1274, 1364, 1414, 1523, 1624, 1720, 2376, 2662, 2925, 3059. Spectroscopic data was compared with that previously reported.[12]

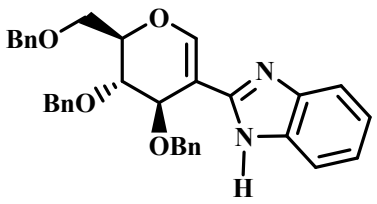
2-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-1*H*-benzimidazole (3n)



3n

Yield: 82% (132 mg, 0.82 mmol).
Characteristic: Colourless solid.
Melting Point: 237-238^{o} C
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47 (3H, s), 1.49 (3H, s), 4.25 (1H, dd, *J* = 8.7, 6.0 Hz), 4.49 (1H, dd, *J* = 8.4, 6.9 Hz), 5.39 (1H, t, *J* = 6.3 Hz), 7.21-7.27 (4H, m), 7.58 (1H, brs); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 26.3, 69.2, 72.3, 110.7, 121.7, 122.9, 125.0, 126.0, 143.2; Ft-IR (KBr, cm^{-1}): 1066, 1220, 1272, 1382, 1427, 1455, 1621, 2984; HR-MS (*m*/*z*) for $C_{12}H_{14}N_2O_2$ (M+H): Calculated 219.1134, found 219.1139.

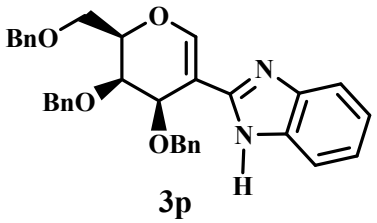
(-)-2-(4R,5R-dibenzyloxy-6R-benzyloxymethyl-5,6-dihydro-4*H*pyran-3-yl)-1*H*-benzimidazole (3o)



3o

Yield: 77% (409 mg, 0.77 mmol).
Characteristic: Viscous yellow liquid.
$[\alpha]_D^{20}$ -10.5° (*c* 0.4, CH_3OH).
^1H NMR (300 MHz, $CDCl_3$): δ 3.72 (1H, dd, *J* = 4.2, 10.8 Hz), 3.80 (1H, dd, *J* = 5.1,10.5 Hz), 4.12 (1H, dd, *J* = 6.0, 10.5 Hz), 4.29-4.44 (2H, m), 4.49 (2H, s), 4.53 (2H,q, *J* = 5.0 Hz), 4.67 (2H, s), 7.03-7.32 (20H, m), 7.66 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.7, 70.5, 71.8, 72.6, 73.4, 73.5, 77.4, 103.8, 122.1,127.8, 127.9, 128.0, 128.4, 128.5, 128.6, 128.9, 137.2, 137.6, 137.7, 149.3, 150.4; FT-IR (neat, cm^{-1}): 1072, 1189, 1274, 1364, 1450, 1642, 2370, 2866, 3034, 3398. Spectroscopic data was compared with that previously reported.[10]

(-)-2-(4R,5S-dibenzyloxy-6R-benzyloxymethyl-5,6-dihydro-4*H*pyran-3-yl)-1*H*-benzimidazole[10] (3p)



3p

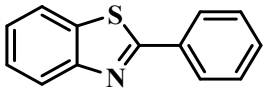
Yield: 79% (419 mg, 0.79 mmol).
Characteristic: Yellow viscous liquid.
$[\alpha]_D^{20}$ -5.6° (*c* 0.5, CH_3OH).
^1H NMR (300 MHz, $CDCl_3$):δ 3.78-3.87 (2H, m), 4.12 (1H, t, *J* = 6.6 Hz), 4.34-4.67 (6H, m), 4.80 (2H, dd, *J* = 9.3, 11.7 Hz), 7.02-7.07 (2H, m), 7.11-7.34 (18H, m), 7.45 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.7, 71.5, 72.1, 73.2, 73.4, 73.5, 77.4, 104.4, 122.0, 127.7, 127.8, 127.9, 128.4, 128.4, 128.5, 128.9, 137.5, 137.8, 148.3, 150.7; FT-IR (KBr, cm^{-1}): 1083, 1185, 1270, 1349, 1450, 1526, 1638, 2374, 2865, 3033, 3396. Spectroscopic data was compared with that previously reported.[10]

8. General procedure for synthesis of 2-substituted benzothiazoles (6)

Benzaldehyde (105mg, 1.0mmol), o-aminothiophenol (138 mg, 1.1mmol), THF (5.0 mL), $MoO_2(HL)(H_2O)(DMF)$ catalyst (38mg, 8mol%), anhydrous Ce(III)chloride (30 mg, 10mol%), Urea-hydrogen peroxide (282 mg, 3mmol) and magnesium sulphate (0.5 g) was stirred in a round-bottomed flask at 0°C. The content of the reaction mixture was allowed to attain room temperature. The reaction was monitored by TLC (SiO_2 plate, petroleum ether/ethyl acetate (3.5:1) and the spots were developed in an iodine chamber. The reaction was complete in 4 h. THF was removed from the post reaction mixture in a rotary evaporator under reduced pressure at room temperature. The residue was extracted with ethyl acetate (2x25mL). The organic portion was washed with water (3x5mL), dried on activated sodium sulphate, and concentrated in a rotary evaporator under reduced pressure at room temperature. The product was separated by the column chromatography to afford the pure 2-(phenyl)-1*H*-benzothiazole in 84% (177 mg, 0.84mmol) yield.

9. Characterization data of synthesized benzothiazoles (6a-h)

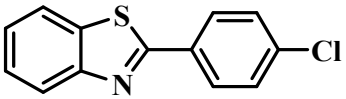
2-Phenyl benzothiazole (6a)



6a

Yield: 84% (177 mg, 0.84 mmol).
Characteristics: Colourless solid.
Melting point: 110-112 ºC [Lit.[13]112 °C].
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.60 (5H, m), 8.01-8.12 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 121.6, 123.2, 125.4, 126.5, 128.7, 129.3, 132.0, 135.0, 137.1, 153.9, 166.6; FT-IR (KBr, cm^{-1}): 871, 959, 1015, 1077, 1253, 1436, 1469, 2368, 2843, 2938. Spectroscopic data was compared with that previously reported.[13]

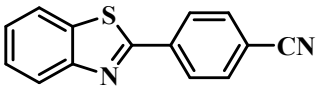
2-(4-Chlorophenyl)-benzothiazole (6b)



6b

Yield: 82% (201 mg, 0.82 mmol).
Characteristics: Colourless solid.
Melting point: 110-112 ºC [Lit.[14]112 °C].
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.46 (4H, m), 7.84 (1H, d, *J* = 7.8 Hz), 7.94-8.04 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 121.6, 123.2, 125.4, 126.5, 128.7, 129.3, 132.0, 135.0, 137.1, 153.9, 166.6; FT-IR (KBr, cm^{-1}): 964, 1012, 1089, 1250, 1434, 1474, 2364, 2851, 2924. Spectroscopic data was compared with that previously reported.[14]

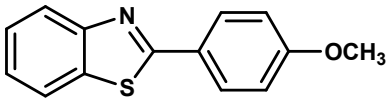
4-Benzothiazol-2-yl-benzonitrile (6c)



6c

Yield: 84% (198 mg, 0.84 mmol).
Characteristics: Colourless solid.
Melting point: 168-170 °C [Lit.[15]171°C].
^{1}H NMR (300 MHz, $CDCl_3$): δ7.43-7.48 (1H, m), 7.52-7.58 (1H, m), 7.77-7.81 (2H, m), 7.95 (1H, dd, *J* = 7.8, 0.6 Hz), 8.20 (1H, d, *J* = 7.8 Hz), 8.19-8.22 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 114.1, 118.2, 121.7, 123.8, 126.0, 126.8, 127.9, 132.7, 135.3, 154.0, 165.3; FT-IR (KBr, cm^{-1}): 831, 1223, 1740, 2986. Spectroscopic data was compared with that previously reported.[13,15]

2-(4-Methoxyphenyl)-benzothiazole (6d)

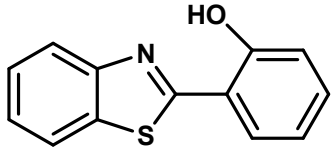


6d

Yield: 84% (202 mg, 0.84 mmol).
Characteristics: Colourless solid:
Melting point:130-132°C [Lit.[16]134°C].

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (3H, s), 6.92 (2H, dd, *J* = 6.9, 2.1 Hz), 7.25-7.30 (1H, m), 7.36-7.42 (1H, m), 7.75-7.81 (2H, m), 7.96 (2H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4, 114.4, 121.5, 122.7, 124.8, 126.2, 129.2, 134.6, 153.8, 162.0, 167.9; FT-IR (KBr, cm^{-1}): 759, 832, 968, 1027, 1171, 1225, 1260, 1310, 1434, 1484, 1521, 1605, 2926. Spectroscopic data was compared with that previously reported.[16]

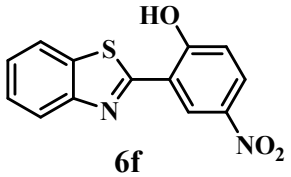
2-Benzothiazol-2-yl-phenol (6e)



6e

Yield: 81% (182 mg, 0.81 mmol).
Characteristics: Colourless solid.
Melting point: 129 °C (Lit.[17] 131-132 °C)
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80-6.93 (1H, m), 7.04 (1H, d, *J* = 8.4Hz), 7.27- 7.47 (3H, m), 7.66 (1H, d, *J* = 8.1 Hz) 7.82 (1H, d, *J* = 7.8 Hz), 7.93 (1H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.8, 117.8, 119.5, 121.5, 122.1, 125.5, 126.7, 128.4, 132.6, 132.7, 151.8, 157.9, 169.4; FT-IR (KBr, cm^{-1}): 741, 756, 973, 1219, 1271, 1315, 1438, 1487, 1589, 1622, 2851, 2922. Spectroscopic data was compared with that previously reported.[17,18]

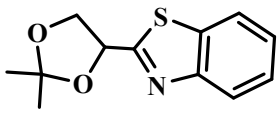
2-Benzothiazole-2-yl-4-nitro-phenol (6f)



6f

Yield: 86% (234mg.0.86mol).
Characteristics: White solid
Melting point: 198 ^{o}C (Lit.[19] 197-199 °C)
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.18 (1H, d, *J* = 9.4Hz), 7.47- 7.52 (1H, m), 7.53- 7.62 (1H, m), 7.96- 8.05 (2H, m), 8.24- 8.28 (1H, m), 8.61 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.8, 122.1, 122.8, 124.7, 126.7, 127.5, 127.9, 132.7, 140.5, 151.4, 163.6, 167.5; FT-IR (KBr, cm^{-1}): 984, 1102, 1210, 1271, 1312, 1380, 1485, 1525, 1578, 1626, 1736, 2425, 2855, 2924, 3065, 3434. Spectroscopic data was compared with that previously reported.[19]

2-(2,2-dimethyl-1,3-dioxolan-4-yl)benzo[d]thiazole (6h)



6h

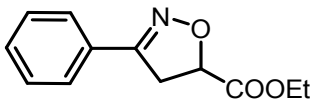
Yield: 79% (199 mg, 0.79 mmol).
Characteristics: Colourless solid.
Melting Point: 235-236^{o} C
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.60 (3H, s), 1.61 (3H, s), 4.20 (1H, dd, *J* = 8.7, 5.4 Hz), 4.52 (1H, dd, *J* = 8.4, 6.6 Hz), 5.48 (1H, dd, *J* = 6.9, 5.7 Hz), 7.36-7.41 (1H, m), 7.45-7.51 (1H, m), 7.90 (1H, d, *J* = 7.8 Hz), 7.97 (1H, d, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 26.3, 70.1, 75.8, 111.3, 121.7, 122.9, 125.0, 126.0, 134.7, 153.5, 173.2; FT-IR (KBr, cm^{-1}): 831, 1223, 1740, 2986. HR-MS (*m*/*z*) for $C_{12}H_{14}NO_2$ S(M+H): Calculated 236.0745, found 236.0749

10. **General procedure for synthesis of isoxazolines (9)**

Benzaldoxime (**7a**, 122 mg, 1.0 mmol), vinyl acetate (172mg, 2.0mmol), MoO_2(HL)(H_2O)(DMF) (38mg, 8mol%), anhydrous $CeCl_3$ (30mg, 10mol%), urea-hydrogen peroxide (282mg, 3mmol), THF (15mL) and magnesium sulphate (0.5g) were stirred in a round-bottomed flask at 0 ^{o}C. The content of the reaction mixture was allowed to attain room temperature with continuous stirring. Progress of the reaction was monitored by TLC (SiO_2 plate, petroleum ether/ethyl acetate: 7:2) and developed in an iodine chamber. The reaction was complete in 4 h. THF was removed from the post reaction mixture in a rotary evaporator under the reduced pressure at room temperature. The residue was extracted with ethyl acetate (2x25 mL). The organic portion was washed with water (3x25mL), dried on activated sodium sulphate, and concentrated in a rotary evaporator under reduced pressure at room temperature. The product was separated by the column chromatography to afford the pure 3-(phenyl)-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (**9a**,199 mg, 0.79 mmol) with 79% yield.

11. **Characterization data for the synthesized isoxazolines (9a-i)**

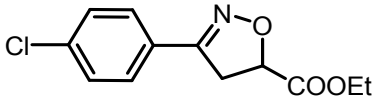
3-Phenyl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester[20] (9a)



9a

Yield: 79% (199 mg, 0.79 mmol).
Characteristics: Gray white solid.
Melting point: 58-61°C [Lit.[20] 64-65.5°C].
^{1}H NMR (300 MHz, $CDCl_3$): δ1.32 (3H, t, *J* = 7.2 Hz), 3.53-3.59 (2H, m), 4.24 (2H, q, *J* = 7.2 Hz), 7.31 (3H, m), 7.60(2H, d, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ16.2, 33.6, 58.1, 73.2, 127.8, 129.4, 131.5. Spectroscopic data was compared with that previously reported.[20]

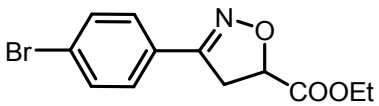
3-(4-Chlorophenyl)-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester[21] (9b)



9b

Yield: 79% (199 mg, 0.79 mmol).
Characteristics: Yellow solid.
Melting point: 63-65°C [Lit[21].64-65.5°C].
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (3H, t, *J* = 7.2 Hz), 3.52-3.59 (2H, m), 4.21 (2H, q, *J* = 7.2 Hz), 5.10 (1H, dd, *J* = 7.8, 10.5 Hz), 7.31 (2H, d, *J* = 8.1 Hz), 7.60(2H, d, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ14.1, 38.6, 62.1, 78.2, 126.8, 127.8, 128.9, 131.5, 136.5, 155.1, 172.5; FT-IR (KBr, cm^{-1}): 831, 1223, 1740, 2986. Spectroscopic data was compared with that previously reported.[21]

3-(4-Bromophenyl)-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester[22] (9c)

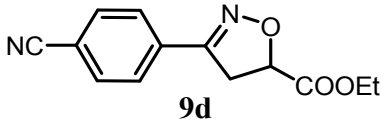


9c

Yield: 81% (228 mg, 0.81 mmol).
Characteristic: Pale yellow solid.
Melting point: 75 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.08 (3H, s), 3.32 (1H, dd, *J* = 1.2, 17.7 Hz), 3.58 (1H, dd, *J* = 6.6, 17.7 Hz), 6.83 (1H, dd, *J* = 1.5, 6.6 Hz), 7.57 (4H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 41.1, 95.9, 125.2, 127.2, 128.4, 132.1, 156.1, 169.5; FT-IR (KBr, cm^{-1}): 860, 961, 1067, 1229, 1367, 1751; Elemental analysis calculated for $C_{11}H_{10}BrNO_3$: C 46.50, H 3.55, Br 28.12, N 4.93; Found C 46.44, H 3.51, Br 28.10, N 4.95. Spectroscopic data was compared with that previously reported.[22]

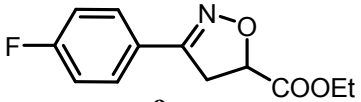
3-(4-Cyanophenyl)-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester[23] (9d)



9d

Yield: 79% (192 mg, 0.79 mmol).
Characteristics: Colourless solid.
Melting point: 76-82 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ1.25 (3H, t, *J* = 7.2 Hz), 3.51-3.58 (2H, m), 4.20 (2H, q, *J* = 7.2 Hz), 5.15 (1H, dd, *J* = 10.8, 7.8 Hz), 7.62 (2H, d, *J* = 8.4 Hz), 7.70 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ14.1, 38.5, 62.3, 78.3, 126.7, 127.8, 128.9, 131.7, 136.6, 155.5, 172.3; FT-IR (KBr, cm^{-1}): 841, 1227, 1740, 2983.

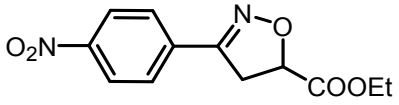
3-(4-Fluorophenyl)-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (9e)



9e

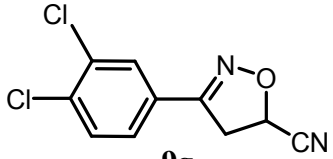
Yield: 81% (191 mg, 0.81 mmol).
Characteristics: Yellow solid.
Melting point: 40-43 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ1.24 (3H, t, *J* = 7.2 Hz), 3.50-3.56 (2H, m), 4.20 (2H, q, *J* = 7.2 Hz), 5.06-5.12 (1H, m), 6.98-7.11 (2H, m), 7.57-7.68 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ14.0, 38.8, 62.0, 78.1, 115.8, 116.1, 128.8, 128.9, 155.0, 162.3, 165.6, 170.0; FT-IR (KBr, cm^{-1}): 841, 1022, 1214, 1603, 1747; EI-MS (*m/z*): 237 (M^+), 164, 136, 95, 75; HR-MS (*m/z*) for $C_{12}H_{13}FNO_3$ (M+H): Calculated 238.0879, found 238.0877 (One of the major peaks).

3-(4-Nitrophenyl)-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester[24] (9f)



Yield: 81% (214 mg, 0.81 mmol).
Characteristics: Yellow solid.
Melting point: 112-114 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (3H, t, *J* = 7.2 Hz), 3.58-3.64 (2H, m), 4.22 (2H, q, *J* = 7.2 Hz), 5.16-5.25 (1H, m), 7.77-7.82 (2H, m), 8.19-8.22 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ14.0, 38.6, 62.2, 78.4, 115.9, 116.3, 128.9, 129.1, 155.2, 162.5, 165.4, 171.0. Spectroscopic data was compared with that previously reported.[24]

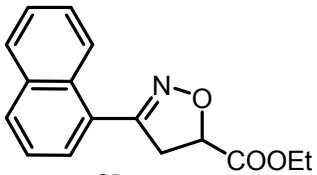
3-(3,4-Dichlorophenyl)-4,5-dihydroisoxazole-5-carbonitrile (9g)



9g

Yield: 85% (204 mg, 0.85 mmol).
Characteristics: Colourless solid; m.p. 110º-112 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62-3.69 (2H, m), 5.31-5.37 (1H, m), 7.45 (2H, s), 7.67 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.7, 66.9, 116.6, 126.0, 127.3, 128.8, 131.1, 133.5, 135.5, 154.5; FT-IR (KBr, cm^{-1}): 888, 1356, 2374; EI-MS (*m/z*): 241 (M^+), 207, 118, 105, 77, 51, 44. HR-MS (*m/z*) for $C_{10}H_7Cl_2N_2O$ (M+H): Calculated 240.9935, found 240.9938 (One of the major peaks).

3-Naphthalen-2-yl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (9h).

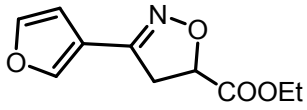


9h

Yield: 80% (215 mg, 0.80 mmol).
Characteristics: Colourless solid.
Melting point: 71-73 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (3H, t, *J* = 7.2 Hz), 3.64- 3.71 (2H, m), 4.21 (2H, q, *J* = 7.2 Hz), 5.11-5.17 (1H, m), 7.44-7.51 (3H, m), 7.76-7.91 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 38.8, 62.0, 78.3, 123.6, 126.2, 126.8, 127.3, 127.8, 128.4, 128.6, 132.9, 134.2, 156.1,

170.2; FT-IR (KBr, cm^{-1}): 475, 749, 1200, 1745, 2926; EI-MS (*m/z*): 269(M+), 182, 104, 103, 102, 77, 51, 50, 44; HR-MS (*m/z*) for $C_{16}H_{16}NO_3$ (M+H): Calculated 270.1130, found 270.1132.

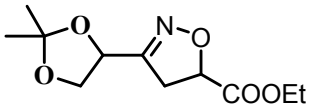
3-furan-2-yl-4,5-dihydro-oxazole-5-carboxylic acid ethyl ester (9i)



9i

Yield: 81% (169 mg, 0.81 mmol).
Characteristics: Yellow liquid.
^{1}H NMR (300 MHz, CDCl3): δ 1.32 (3H, t, *J* = 7.2 Hz), 3.56-3.68 (2H, m), 4.26 (2H, q, *J* = 7.2 Hz), 5.12 (1H, dd, *J* = 10.8, 7.5 Hz), 6.50 (1H, dd, *J* = 1.8, 3.3 Hz), 6.77 (1H, dd, *J* = 3.3, 0.9 Hz), 7.53 (1H, d, *J* = 1.8 Hz); ^{13}C NMR (75 MHz, CDCl3): δ 14.0, 38.7, 62.0, 77.7, 111.8, 112.4, 143.9, 144.6, 148.2, 169.9; FT-IR (KBr, cm-1): 757, 886, 1016, 1210, 1302, 1469, 1664, 1737; HR-MS (*m/z*) for $C_{10}H_{12}NO_4$(M+H): Calculated 210.0766, found 210.0769.

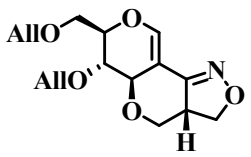
3-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-4,5-dihydro-isoazole-5-carboxylic acid ethyl ester (9j & 9k)



9j & 9k

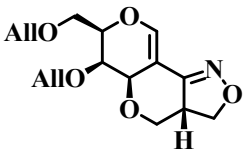
Mixture of two diastereoisomers (dr = 70: 30)
Yield: 84% (204 mg, 0.84 mmol).
Characteristic: Colourless solid.
Melting point: 90-92 ºC.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25-1.34 (2H, m), 1.39 (3H, s), 1.45 (3H, s), 3.31-3.39 (2H, m), 3.99-4.06 (1H, m), 4.21-4.29 (3H, m), 4.94-5.06 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 25.0, 25.1, 37.7, 38.1, 38.9, 39.0, 61.9, 64.2, 67.0, 67.1, 68.0, 68.1, 70.6, 70.7, 110.5, 157.6, 157.7, 169.9, 170.1; FT-IR (KBr, cm^{-1}): 830, 870, 1014, 1072, 1355, 1407, 1645, 1736; HR-MS (*m/z*) for C11H18NO5(M+): Calculated 244.1185, found 244.1181.

(+)-(3aS,5aR,6S,7R)-6-allyloxy-7-allyloxymethyl-3a,4,6,7-tetrahydro-3*H*,5a*H*-2,5,8-trioxa-1-aza-cyclopenta[*a*]naphthalene (9l)



Yield: 79 (242mg, 0.79mmol); Characteristics: Yellow liquid; Optical rotation: $[\alpha]_D^{20}$ (+) 40.2º (*c* 0.20, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) : δ 3.43 - 3.45 (2H, m), 3.62 - 3.80 (4H, m), 3.92-4.12 (4H, m), 4.20 - 4.22 (4H, m), 5.16 - 5.33 (4H, m) 5.87-5.95 (2H, m), 7.26 (1H, s); ^{13}C NMR (300 MHz, $CDCl_3$): δ 47.2, 67.9, 69.1, 70.1, 72.6, 73.2, 73.4, 77.4, 77.3, 101.3, 117.0, 117.4, 134.7, 134.3, 143.0, 154.0; FT- IR (neat, cm^{-1}): 730, 822, 923, 1010, 1093, 1184, 1439, 1469, 1573, 1653, 1703, 2856, 2921. Spectroscopic data was compared with that previously reported.[25]

(+)-(3aS,5aR,6R,7R)-6-Allyloxy-7-allyloxymethyl-3a,4,6,7-tetrahydro-3*H*,5a*H*-2,5,8-trioxa-1-aza-cyclopenta[*a*]naphthalene (9m)



Yield: 76 (233mg, 0.76mmol); Characteristics: Yellow semi solid; Optical rotation: $[\alpha]_D^{20}$ +79.7º (*c* 1.08, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 3.39-3.44 (2H, m), 3.61-3.69 (3H, m), 3.98-4.24 (6H, m), 4.37-4.54 (3H, m), 5.13-5.33 (4H, m), 5.83-5.94 (2H, m), 7.04 (1H, s); ^{13}C NMR (75MHz MHz, $CDCl_3$): δ 46.9, 68.2, 69.1, 69.8, 72.4, 72.9, 73.9, 76.4, 100.8, 117.4, 117.6, 134.1, 134.9, 143.0, 154.4.; FT-IR (neat, cm^{-1}): 925, 1003, 1091, 1146, 1196, 1647, 1725, 2861, 2922. Spectroscopic data was compared with that previously reported.[25]

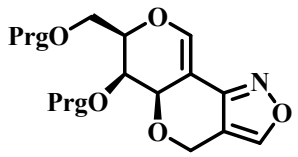
12. General procedure for synthesis of isoxazoles (12)

O-Propargyl galactal aldoxime (**11a**, 305mg, 1.0mmol), $MoO_2(HL)(H_2O)(DMF)$ (38mg, 8mol%), anhydrous $CeCl_3$ (30mg, 10mol%), urea-hydrogenperoxide (282mg, 3mmol), THF (15 mL) and magnesium sulfate (0.5 g) were stirred in a round-bottomed flask at 0° C. The content of the reaction mixture was allowed to attain room temperature with continuous stirring. The progress of the reaction was monitored by TLC (through charring on a hot plate with dilute H_2SO_4 using spray gun). After completion of the reaction the solvent was removed in a rotary evaporator at room temperature under reduced pressure. The reaction mixture was filtered

through a sintered funnel and washed with a mixture of ethyl acetate and cold water. The filtrate was transferred to a separating funnel and extracted with EtOAc (3 x 30mL). The combined EtOAc layer was washed with water (2 x 30mL), brine solution (1 x 30mL) and dried over anhydrous Na_2SO_4. Removal of the solvent in a rotary evaporator left the crude product which was purified by column chromatography over silica gel (60-120 mesh) using ethyl acetate-petroleum ether as eluent to afford the pure fused-isoxazoles **12a** (217mg, 0.73 mmol) with 73% yield.

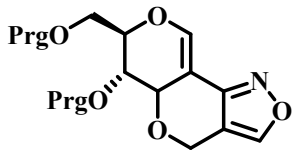
13. Characterization data of the synthesized isoxazoles (12a-d)

(+)-(5aR,6S,7R)-6-Prop-2-ynyloxy-7-prop-2-ynyloxymethyl-6,7-dihydro-4*H*,5a*H*-2,5,8-trioxa-1-aza-cyclopenta[*a*]naphthalene (12a).



Yield: 73 % (217 mg, 0.73 mmol); Characteristics: Colourless solid; Melting point: 120°- 122°; Optical rotation: $[\alpha]_D^{20}$: +18.8° (*c* 0.5, $CHCl_3$); ^{1}H NMR (300MHz, $CDCl_3$): δ 2.47 (2H, s), 3.89 (2H, t, *J* = 5.7Hz), 4.24 (2H, d, *J* = 2.4 Hz), 4.26 (1H, d, *J* = 5.4 Hz), 4.30 (2H, d, *J* = 3.3 Hz), 4.5 (1H, dd, *J* = 2.4, 10.5 Hz), 4.63 (1H, d, *J* = 1.2Hz), 4.96 (1H, d, *J* = 14.1 Hz), 7.80 (1H, s), 8.09 (1H, s); ^{13}CNMR (75MHz, $CDCl_3$): δ 58.7, 59.6, 61.1, 68.2, 68.7, 72.1, 74.9, 79.1, 80.0, 99.5, 111.9, 142.7, 150.4, 153.6; FT-IR (KBr, cm^{-1}): 944, 1064, 1106, 1146, 1197, 1366, 1412, 1610, 1655, 2111, 2369, 2860, 2929, 3259; HR-MS (*m*/*z*) for $C_{16}H_{16}NO_5$ (M+H): Calculated 302.0950, found 302.0955.

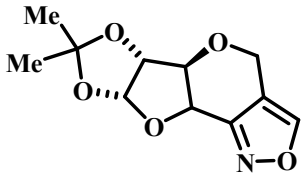
(-)-(5aR,6R,7R)-6-Prop-2-ynyloxy-7-prop-2-ynyloxymethyl-6,7-dihydro-4*H*,5a*H*-2,5,8-trioxa-1-aza-cyclopenta[*a*]naphthalene (12b).



Yield: 72% (208 mg, 0.72 mmol); Characteristics: Yellow viscous liquid; Optical rotation: $[\alpha]_D^{20}$: -6.25° (*c* 0.5, $CHCl_3$); ^{1}H NMR (300MHz, $CDCl_3$): δ 2.31 (2H, s), 3.59-3.64 (1H, m), 3.74-3.77(2H, m), 4.05 (1H, d, *J* = 4.5 Hz), 4.21 (2H, t, *J* = 9.9 Hz), 4.27-4.40 (3H, m), 5.86 (1H, s), 6.07 (1H, s), 6.63 (1H, d, *J* = 17.4 Hz);

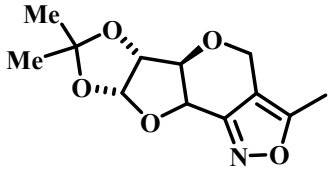
^{13}CNMR (75 MHz, $CDCl_3$): δ 58.0, 58.2, 58.6, 67.3, 69.5, 71.5, 73.6, 74.9, 75.6, 75.8, 83.3, 107.8, 115.0, 142.4, 144.1; FT-IR (neat, cm^{-1}): 1097, 1384, 1596, 2363, 2924, 3442; HR-MS (*m*/*z*) for $C_{16}H_{16}NO_5$ (M+H): Calculated 302.0950, found 302.0952.

(+)-(5aS,5bR,8aR,9aR)-7,7-Dimethyl-5a,5b,8a,9a-tetrahydro-4*H*-2,5,6,8,9-pentaoxa-1-azacyclopenta[*b*]-as-indacene (12c).



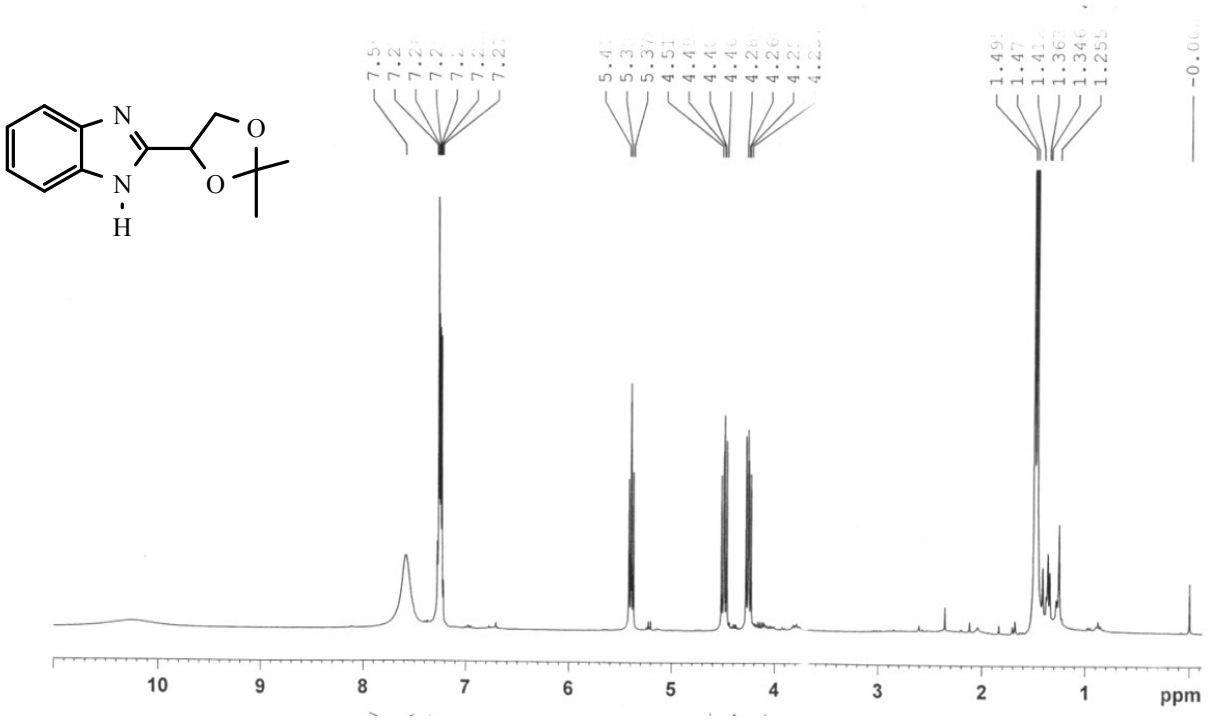
Yield: 75 % (180 mg, 0.75 mmol); Characteristics: Colorless solid; Melting point: 151-152 °C; Optical rotation: $[\alpha]_D^{20}$: +41.50° (*c* 0.7, $CHCl_3$); ^{1}H NMR (300MHz, $CDCl_3$): δ 1.37 (3H, s), 1.57 (3H, s), 4.13 (1H, d, *J* = 2.1 Hz), 4.55 (1H, dd, *J* = 0.9, 14.4 Hz), 4.71 (1H, d, *J* = 3.6 Hz), 4.92 (1H, d, *J* = 14.4 Hz), 5.21 (1H, d, *J* = 2.1 Hz), 6.00 (1H, d, *J* = 3.6 Hz), 8.25 (1H, s).
^{13}CNMR(75MHz,$CDCl_3$): δ 26.2, 26.8, 60.5, 68.4, 80.4, 83.4, 106.4, 112.4, 112.5, 151.4, 154.6; FT-IR (KBr, cm^{-1}): 799, 859, 1013, 1092, 1228, 1381, 1428, 1616, 1721, 2859, 2991, 3117; HR-MS (*m*/*z*) for $C_{11}H_{14}NO_5$ (M+H): Calculated 240.0872, found 240.0870.

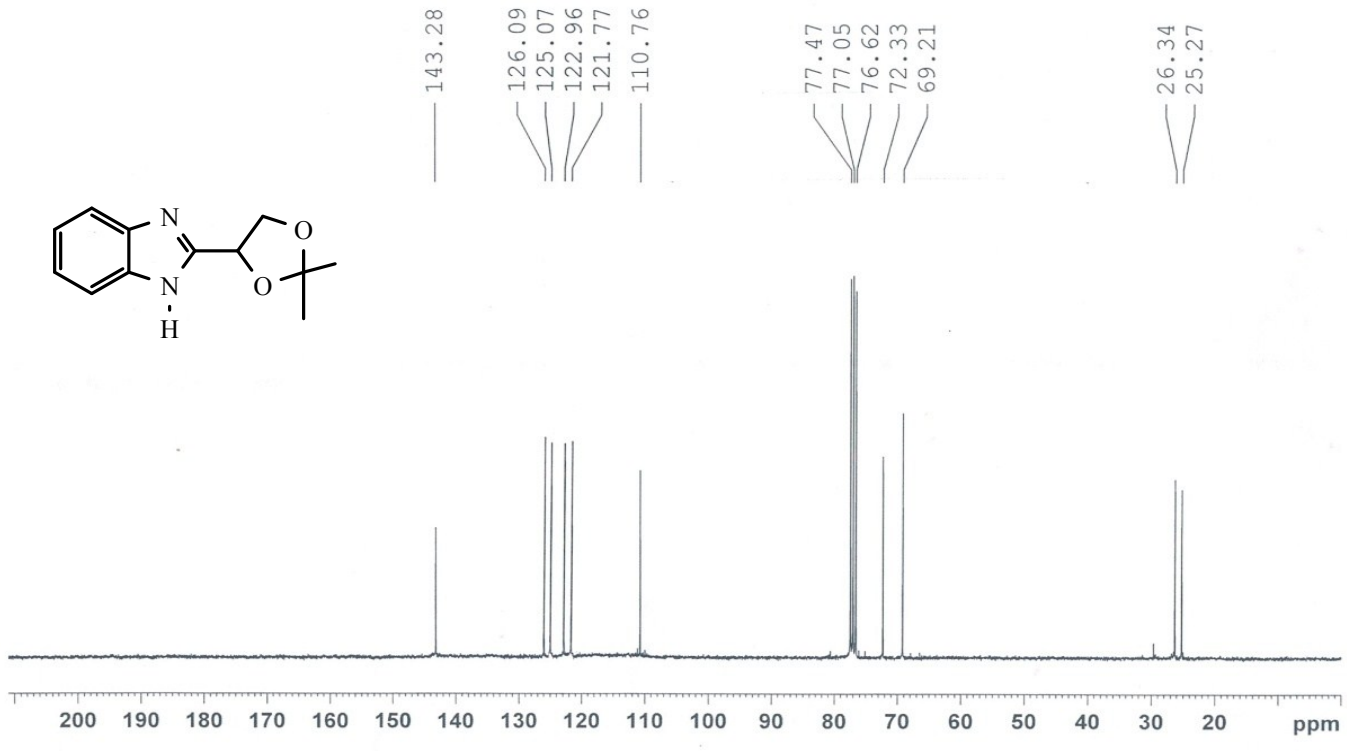
(+)-(5aS,5bR,8aR,9aR)-3,7,7-Trimethyl-5a,5b,8a,9a-tetrahydro-4*H*-2,5,6,8,9-pentaoxa-1-azacyclopenta[*b*]-as-indacene (12d).

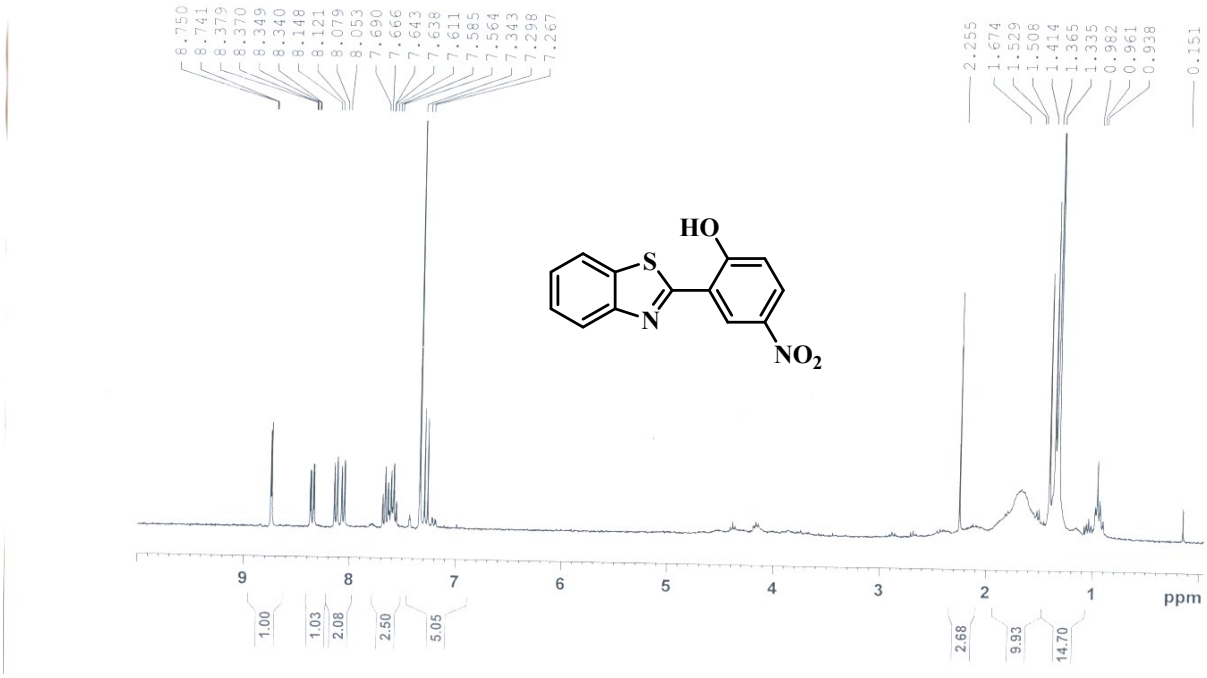


Yield: 76% (192 mg, 0.76 mmol); Characteristics: Colorless solid; Melting point: 134-135 °C; Optical rotation: $[\alpha]_D^{20}$: +30.94° (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (3H, s), 1.52 (3H, s), 2.31 (3H, s), 4.04 (1H, d, *J* = 1 Hz), 4.42(1H, d, *J* = 13.8 Hz), 4.64 (1H, d, *J* = 3.3 Hz), 4.72 (1H, d, *J* = 14 Hz), 5.10 (1H, d, *J* = 2 Hz), 5.94 (1H, d, *J* = 3.6Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 26.2, 26.8, 60.7, 68.8, 80.2, 83.4, 105.9, 108.4, 112.3, 155.4, 162.0; FT-IR (KBr, cm^{-1}): 852, 1017, 1094,1360, 1458, 1652, 2864, 2929, 2991; HR-MS (*m*/*z*) for $C_{12}H_{16}NO_5$ (M+H): Calculated 254.1028, found 254.1024.

^{1}H and ^{13}C NMR spectra of the new compounds (3, 6, 9 and 12)



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7.638
7.611
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7.564
7.343
7.298
7.267
2.255
1.674
1.529
1.508
1.414
1.365
1.335
0.982
0.961
0.938
0.151
HO
S
N
NO2
9
8
7
6
5
4
3
2
1
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2.50
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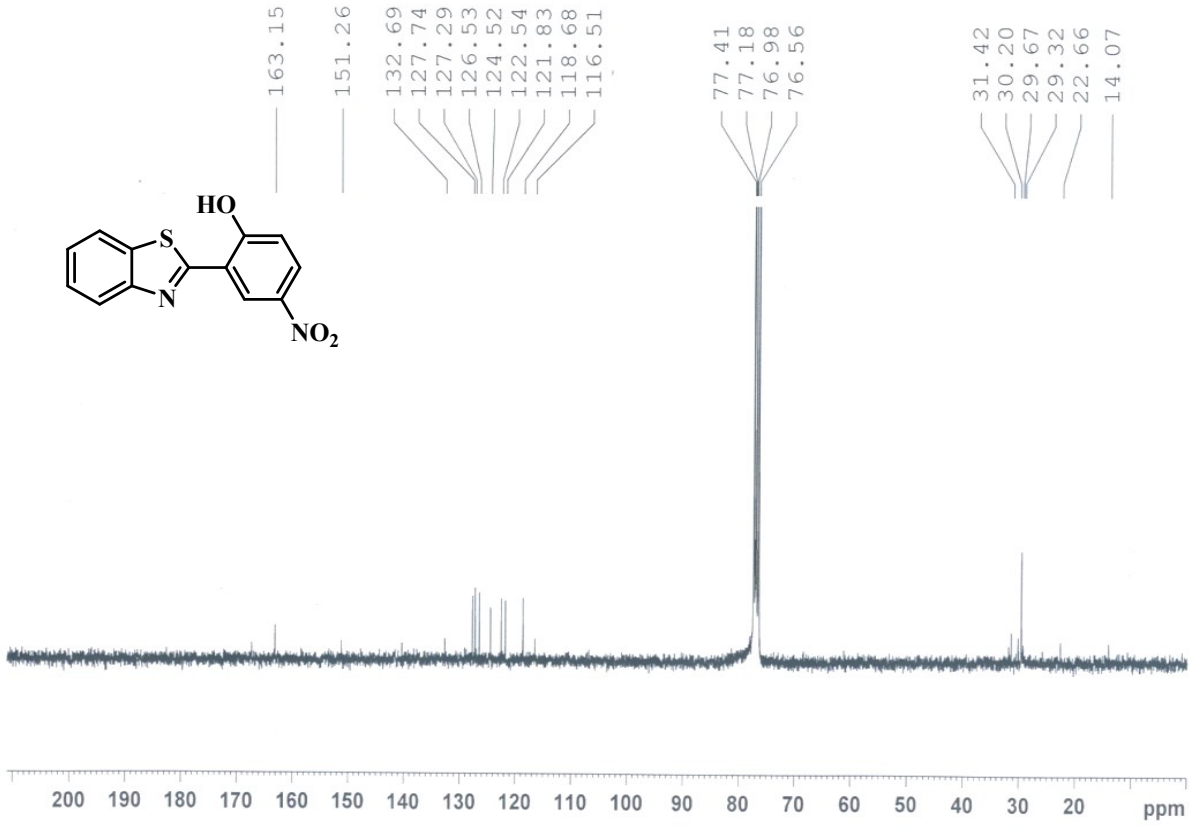
14.70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127.29
126.53
124.52
122.54
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118.68
116.51
77.41
77.18
76.98
76.56
31.42
30.20
29.67
29.32
22.66
14.07
HO
S
N
NO2
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80
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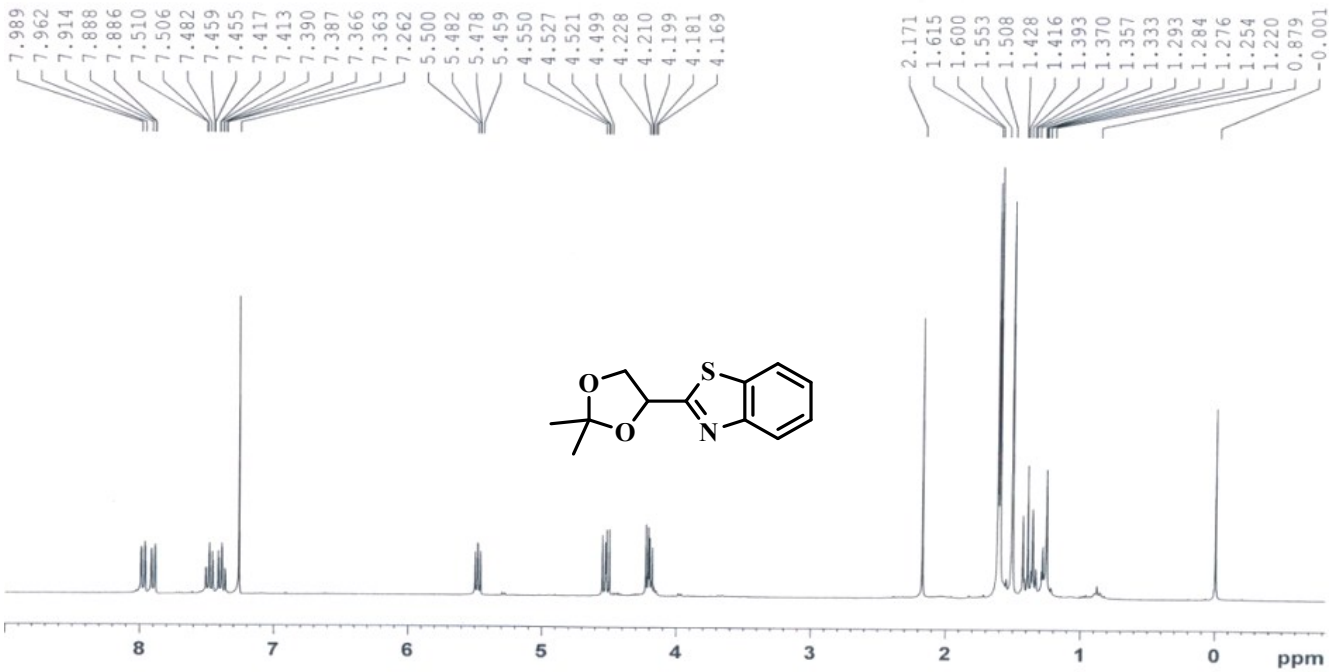
50
40
30
20
ppm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7.482
7.459
7.455
7.417
7.413
7.390
7.387
7.366
7.363
7.262
5.500
5.482
5.478
5.459
4.550
4.527
4.521
4.499
4.228
4.210
4.199
4.181
4.169
2.171
1.615
1.600
1.553
1.508
1.428
1.416
1.393
1.370
1.357
1.333
1.293
1.284
1.276
1.254
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O
S
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6
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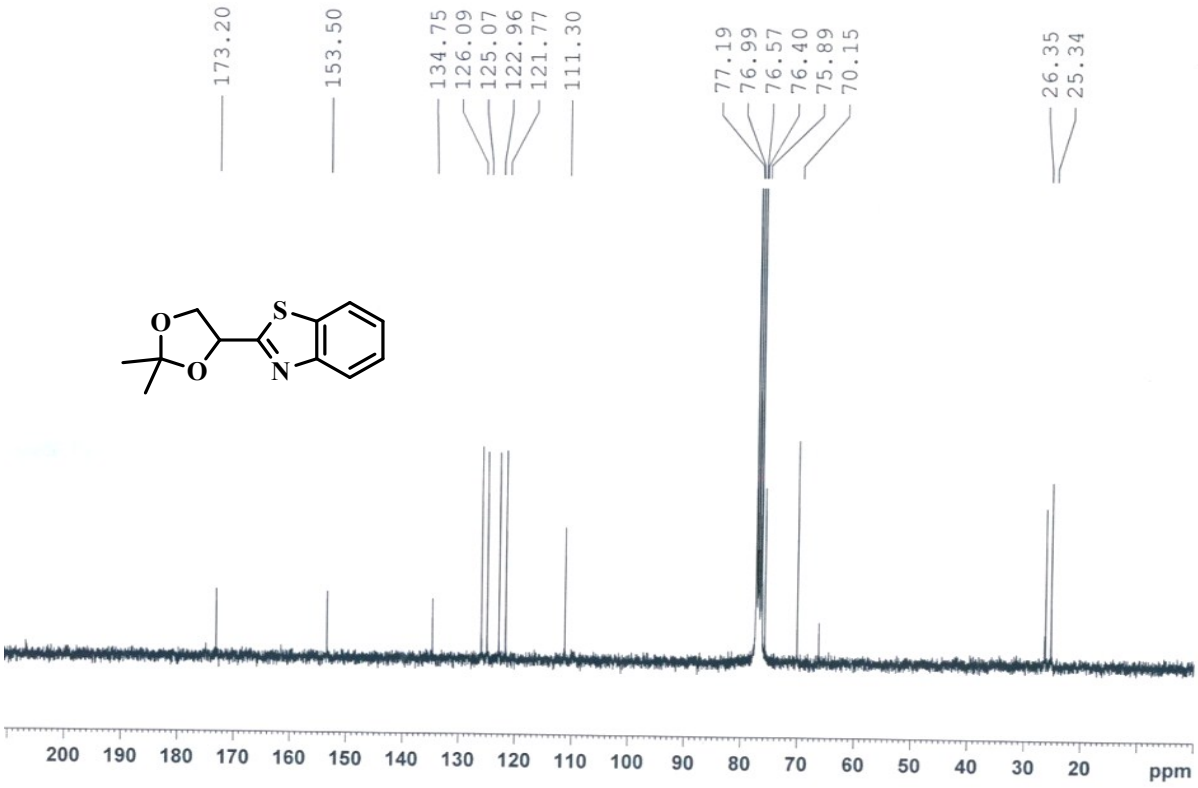
3
2
1
0
ppm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153.50
134.75
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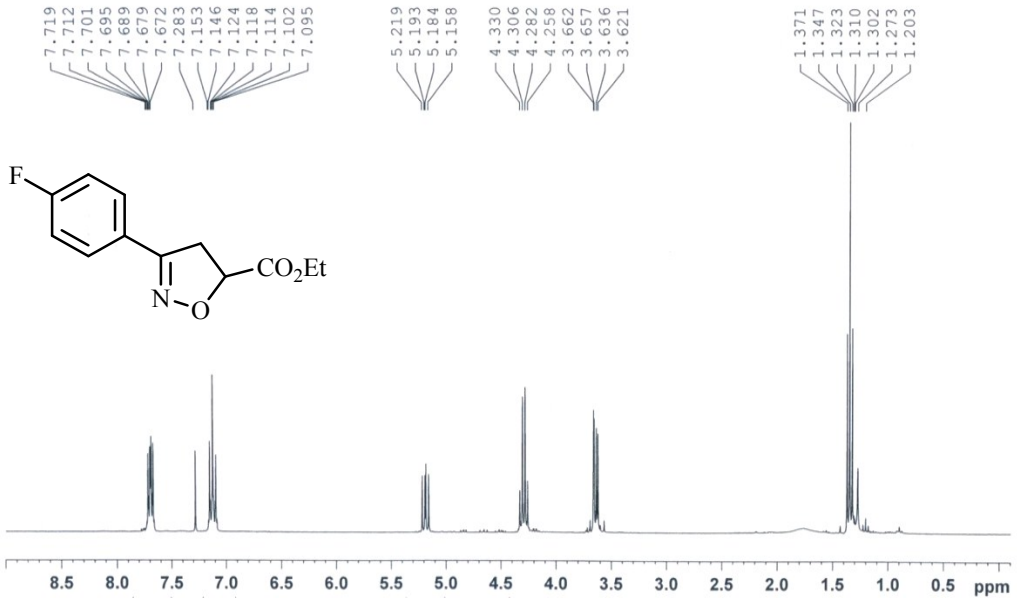
125.07
122.96
121.77
111.30
77.19
76.99
76.57
76.40
75.89
70.15
26.35
25.34
O
O
S
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.153
7.146
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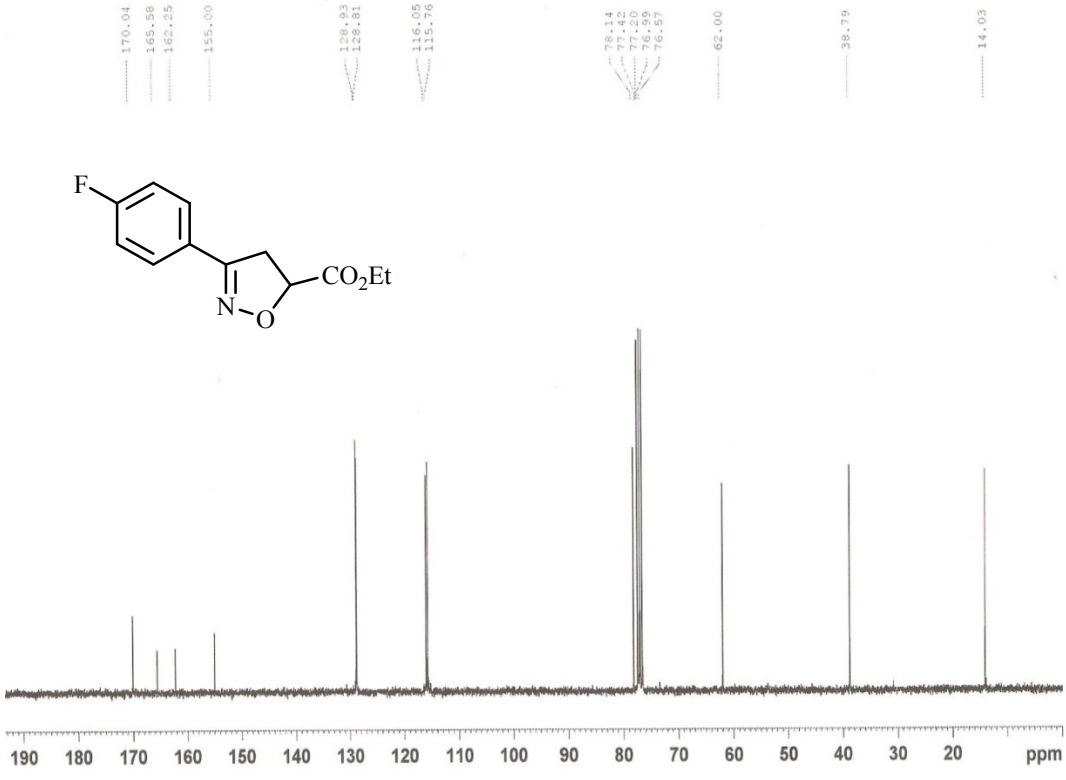
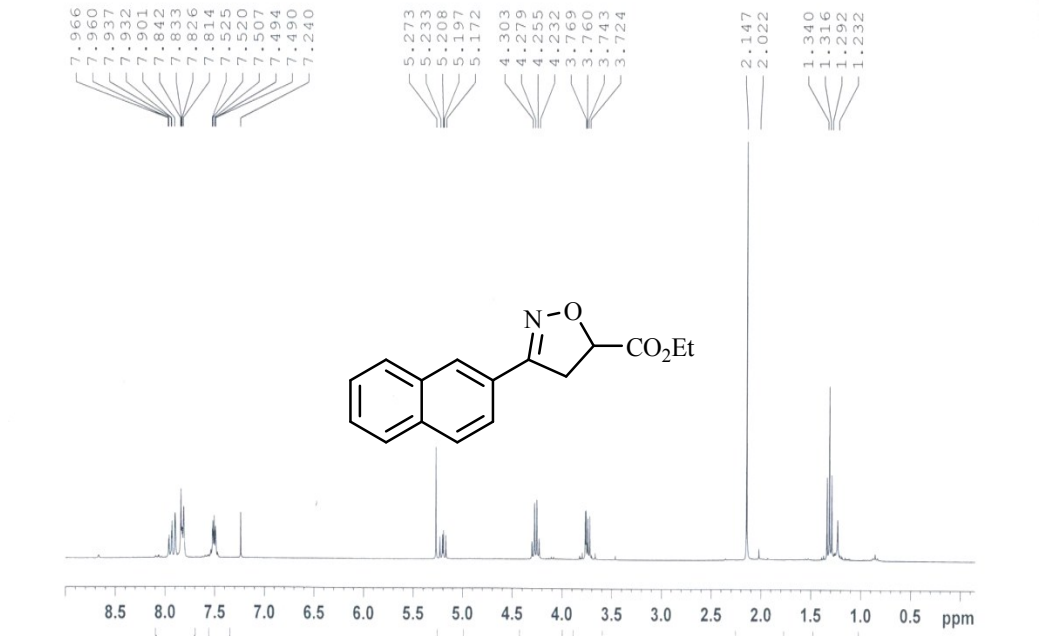
7.118
7.114
7.102
7.095
5.219
5.193
5.184
5.158
4.330
4.306
4.282
4.258
3.662
3.657
3.636
3.621
1.371
1.347
1.323
1.310
1.302
1.273
1.203
F
CO2Et
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


170.04
165.58
162.25
155.00
129.93
128.81
116.05
115.76
78.14
77.42
77.20
76.99
76.57
62.00
38.79
14.03
F
CO2Et
N
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.932
7.901
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7.833
7.826
7.814
7.525
7.520
7.507
7.494
7.490
7.240
5.273
5.233
5.208
5.197
5.172
4.303
4.279
4.255
4.232
3.769
3.760
3.743
3.724
2.147
2.022
1.340
1.316
1.292
1.232
N
O
CO2Et
8.5
8.0
7.5
7.0
6.5
6.0
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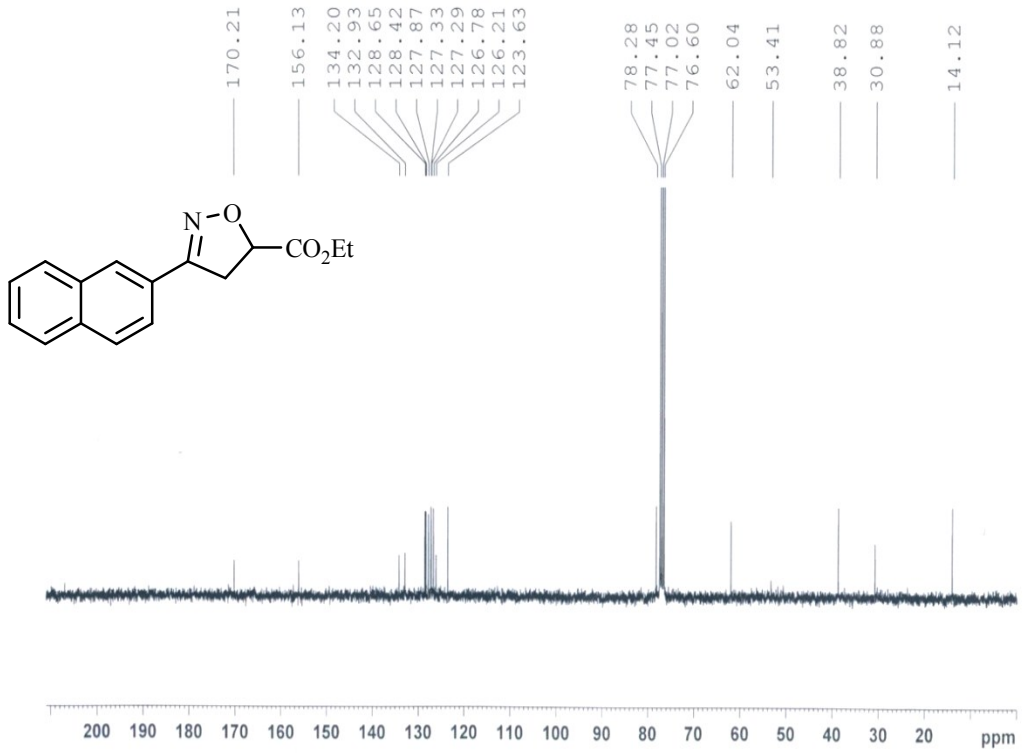
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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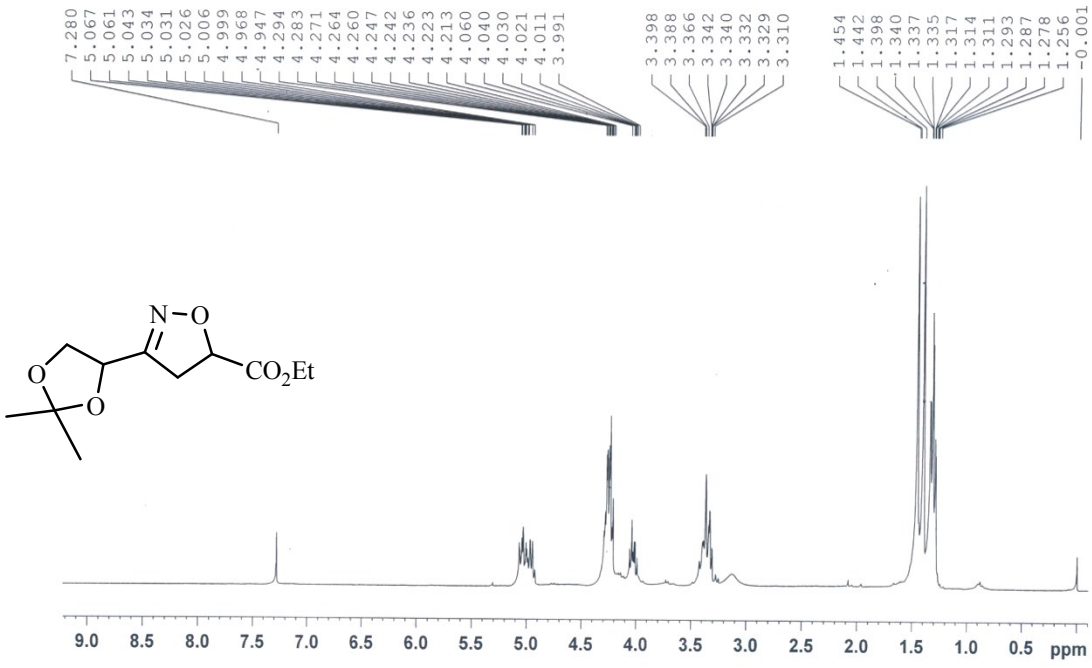
156.13
134.20
132.93
128.65
128.42
127.87
127.33
127.29
126.78
126.21
123.63
78.28
77.45
77.02
76.60
62.04
53.41
38.82
30.88
14.12
N
O
CO2Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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5.061
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5.034
5.031
5.026
5.006
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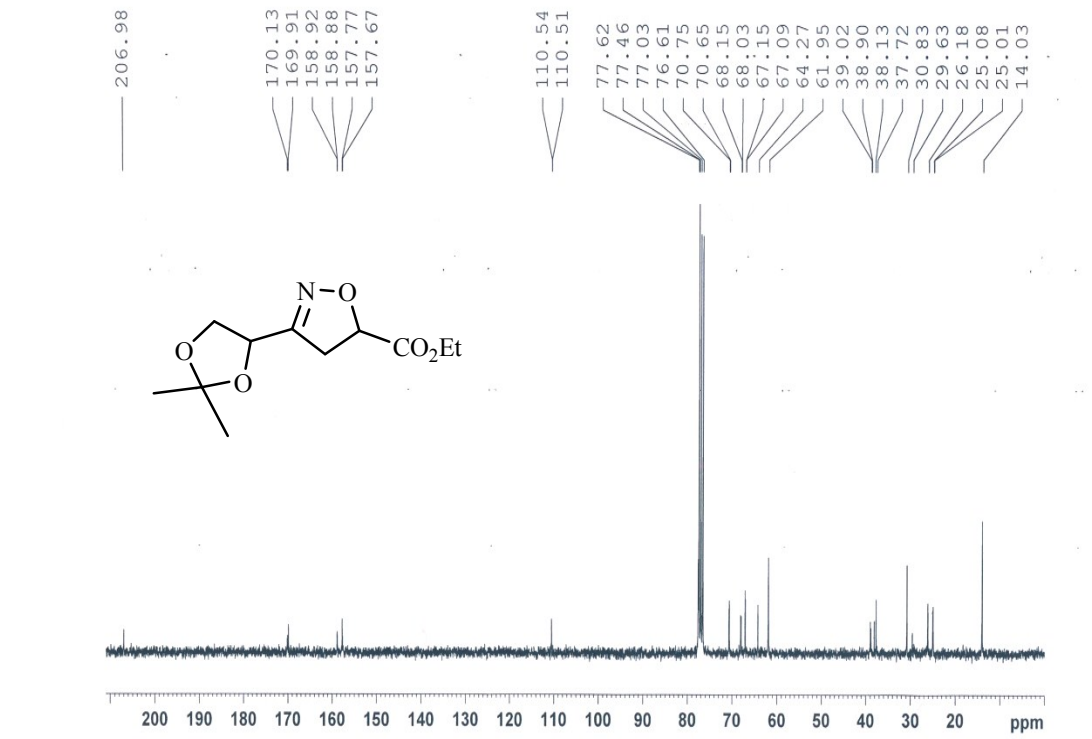
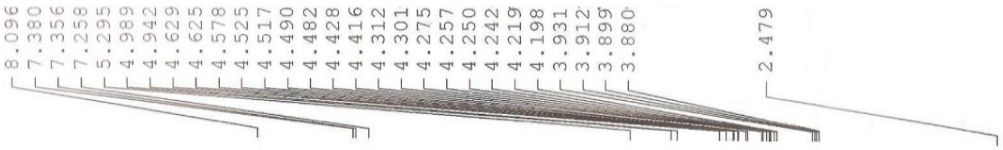
4.968
4.947
4.294
4.283
4.271
4.264
4.260
4.247
4.242
4.236
4.223
4.213
4.060
4.040
4.030
4.021
4.011
3.991
3.398
3.388
3.366
3.342
3.340
3.332
3.329
3.310
1.454
1.442
1.398
1.340
1.337
1.335
1.317
1.314
1.311
1.293
1.287
1.278
1.256
-0.001
N–O
O
O
CO2Et
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


206.98
170.13
169.91
158.92
158.88
157.77
157.67
110.54
110.51
77.62
77.46
77.03
76.61
70.75
70.65
68.15
68.03
67.15
67.09
64.27
61.95
39.02
38.90
38.13
37.72
30.83
29.63
26.18
25.08
25.01
14.03
N–O
O
O
CO2Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.258
5.295
4.989
4.942
4.629
4.625
4.578
4.525
4.517
4.490
4.482
4.428
4.416
4.312
4.301
4.275
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4.250
4.242
4.219
4.198
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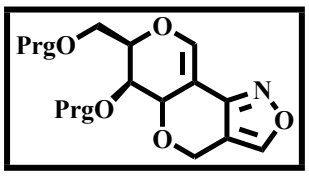
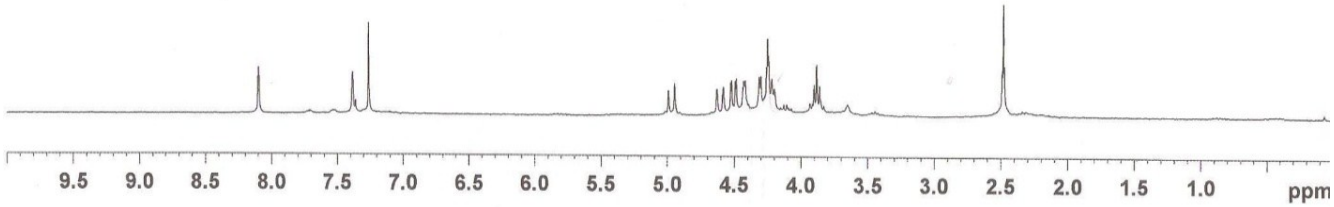
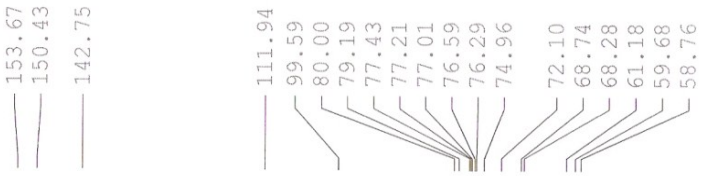
3.899
3.880
2.479


PrgO
PrgO
O
O
N
O


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


153.67
150.43
142.75
111.94
99.59
80.00
79.19
77.43
77.21
77.01
76.59
76.29
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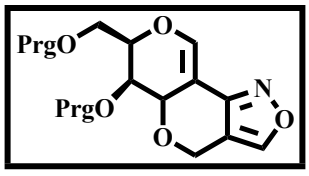
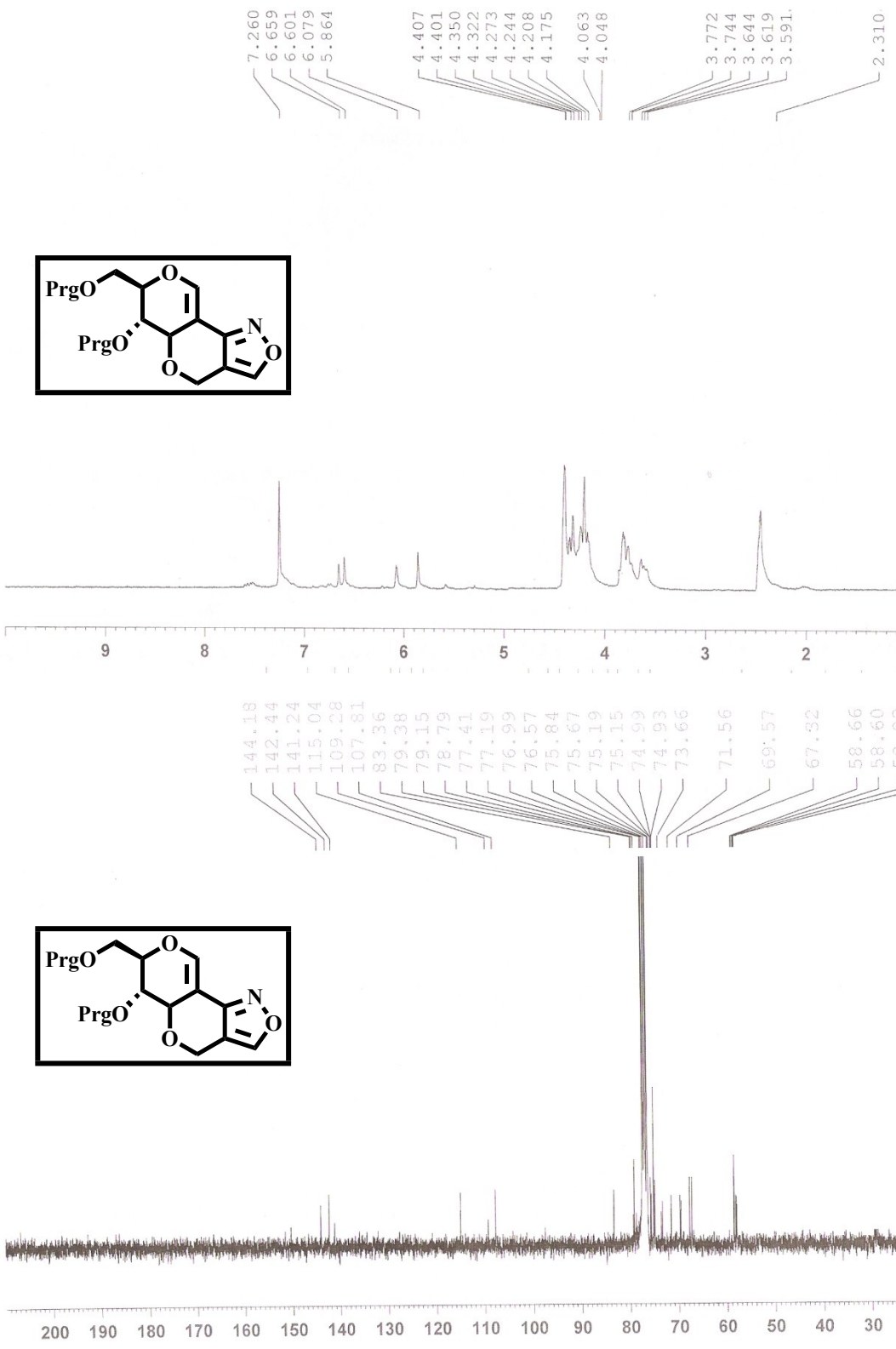
72.10
68.74
68.28
61.18
59.68
58.76


PrgO
PrgO
O
O
N
O

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.260
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6.601
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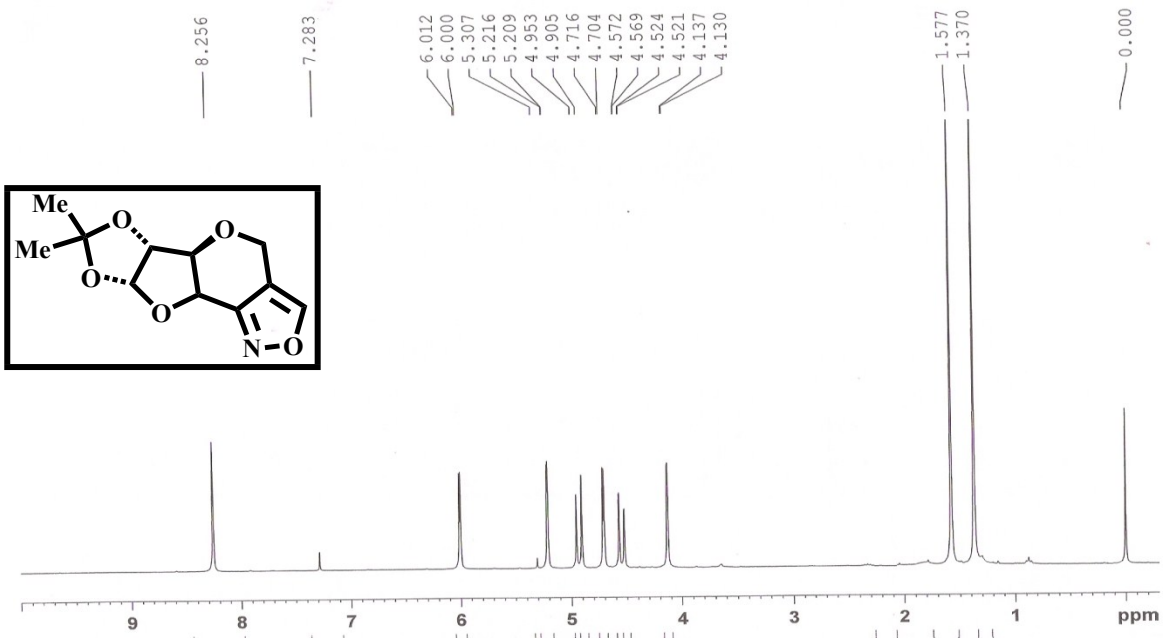
5.864
4.407
4.401
4.350
4.322
4.273
4.244
4.208
4.175
4.063
4.048
3.772
3.744
3.644
3.619
3.591
2.310
PrgO
PrgO
O
N
O
O
9
8
7
6
5
4
3
2
1
ppm
144.18
142.44
141.24
115.04
109.28
107.81
83.36
79.38
79.15
78.79
77.41
77.19
76.99
76.57
75.84
75.67
75.19
75.15
74.99
74.93
73.66
71.56
69.57
67.32
58.66
58.60
58.23
58.09
PrgO
PrgO
O
N
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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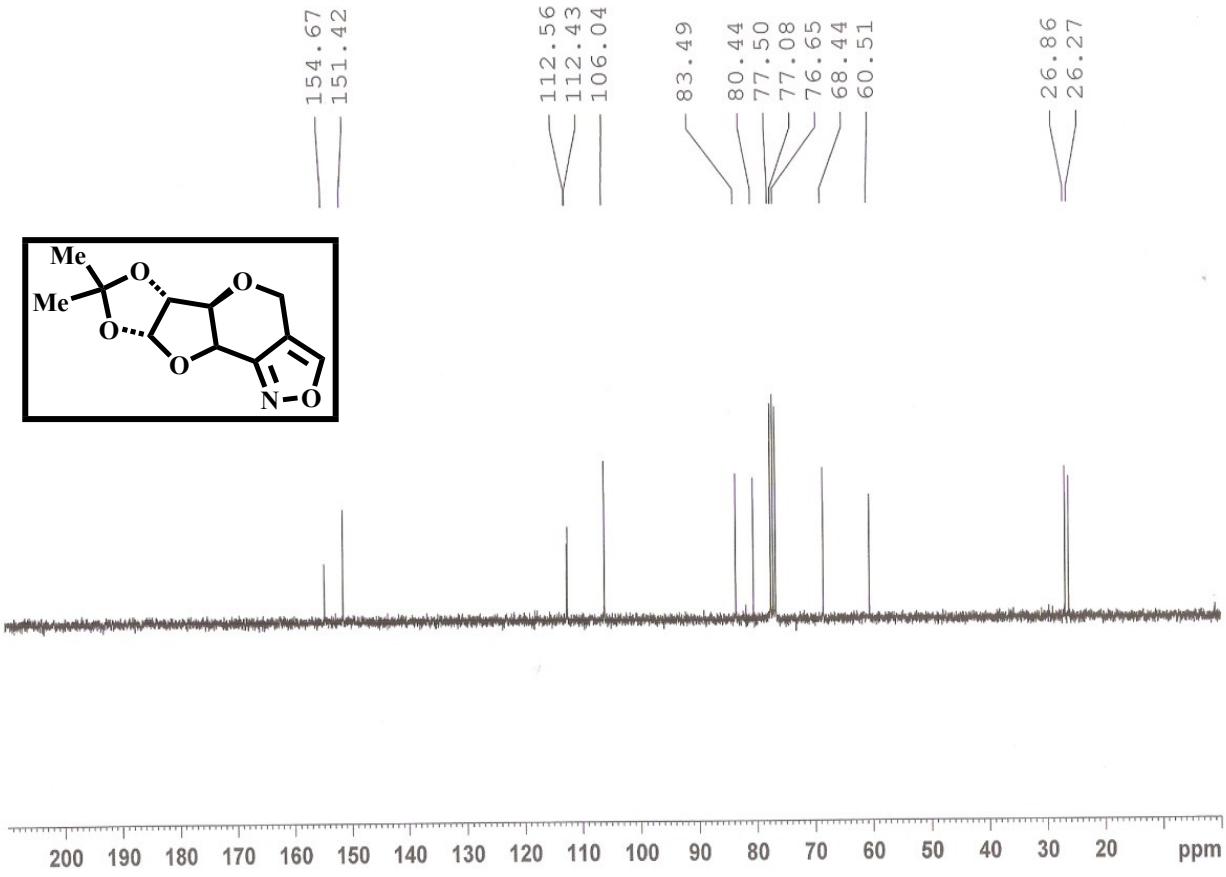
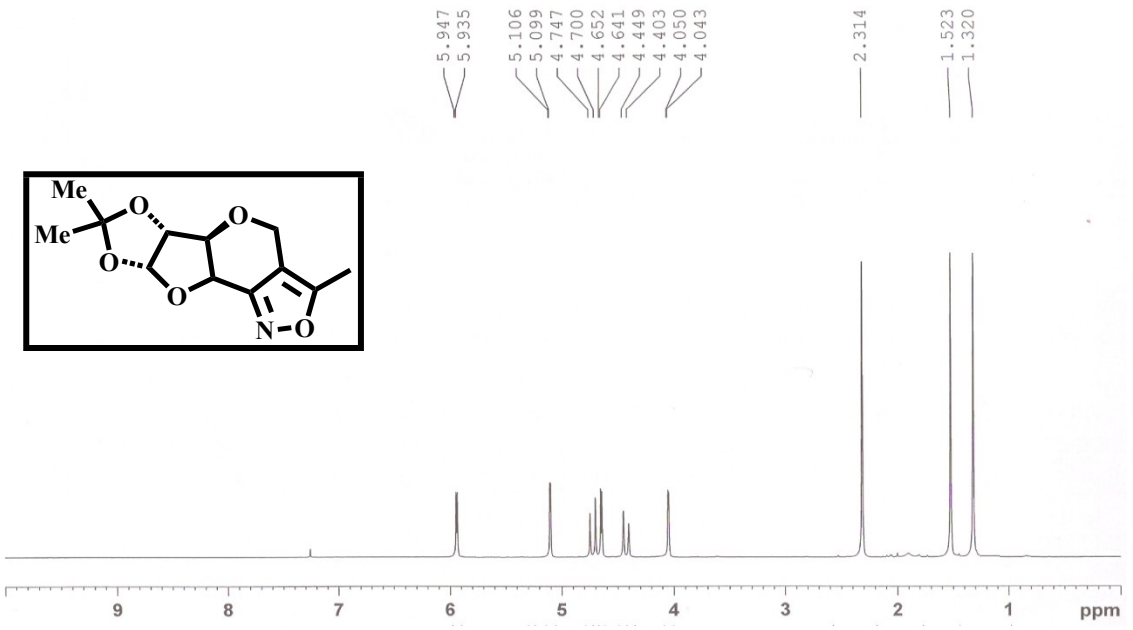
4.716
4.704
4.572
4.569
4.524
4.521
4.137
4.130
1.577
1.370
0.000
Me
Me
O
O
O
O
N
O
9
8
7
6
5
4
3
2
1
ppm


154.67
151.42
112.56
112.43
106.04
83.49
80.44
77.50
77.08
76.65
68.44
60.51
26.86
26.27
Me
Me
O
O
O
O
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


5.947
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5.106
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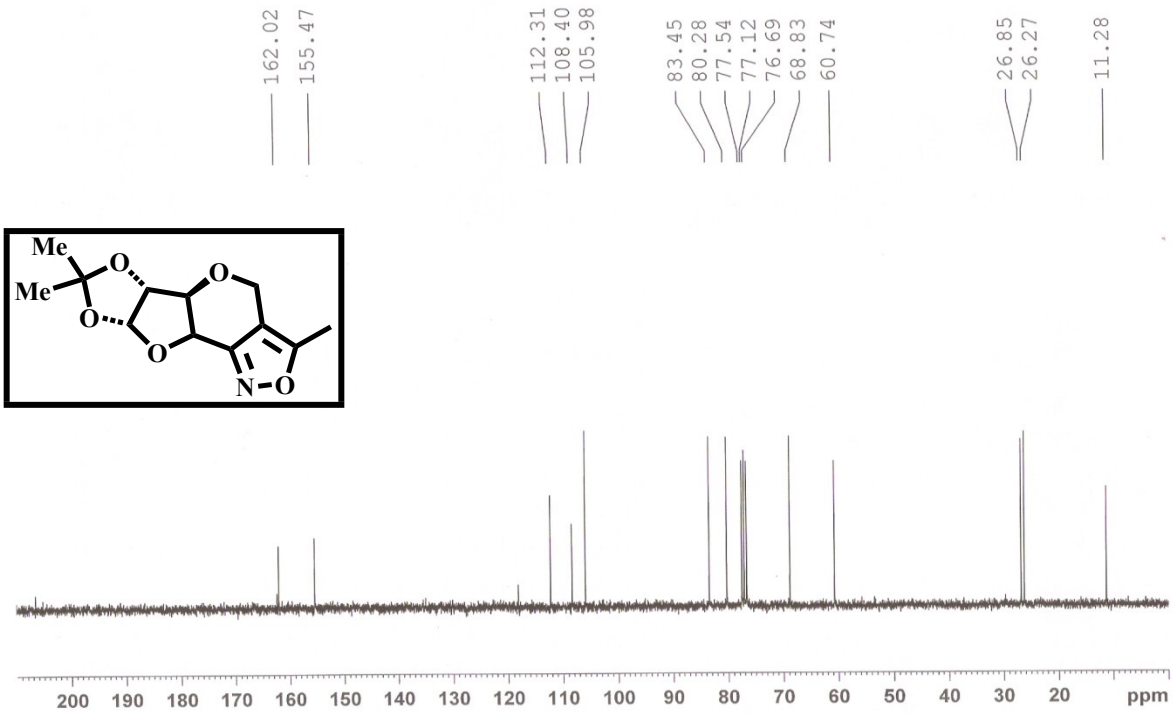
4.700
4.652
4.641
4.449
4.403
4.050
4.043
2.314
1.523
1.320
Me
Me
O
O
O
O
O
N-O
9
8
7
6
5
4
3
2
1
ppm


162.02
155.47
112.31
108.40
105.98
83.45
80.28
77.54
77.12
76.69
68.83
60.74
26.85
26.27
11.28
Me
Me
O
O
O
O
O
N-O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

References

1. (a) Y. I. Ryabukhin, L. N. Faleeva and V. G. Korobkova, *Chem. Heterocycl. Comp*., 1983, **19**, 332; (b) J. G. Haasnoot, *Coord. Chem. Rev*., 2000, **200**, 131; (c) M. H. Klingele and S. Brooker, *Coord. Chem. Rev*., 2003, **241**, 131.

2. G. J. Chen, J. W. Mc Donald and W. E. Newton, *Inorg. Chem.*, 1976, **15**, 2612.

3. G. F. Chittenden, *Carbohydr. Res.,* 1980, **87**, 219-226.

4. H. Ma, X. Han and Y. Wang, *J. Heterocycles,* 2007, **71**, 1821-1825.

5. K. Leroy, *J. Org. Chem*. 1964, **29**, 3630–3632.

6. M. Shen and T. G. Driver, *Org. Lett.* **2008***, 10*, 3367-3370.

7. M. Vojtech, M. Petrušová, E. Sláviková, S. Bekešová and L. Petrus, *Carbohydr. Res.,* 2007, **342**, 119-123.

8. (a) M. Chakrabarty, S. Karmakar, A. Mukherji, S. Arima, Y. Harigaya, *Heterocycles,* 2006, **68**, 967-974; (b) H. Ma and Y. Wang, *J. Heterocycles,* 2006, **68**, 1669-1673. (c) H. Ma, X. Han and Y. Wang, *J. Heterocycles* 2007, **71**,1821-1825.

9. J. W. Hubbard, *Tetrahedron,* 2007, **63**, 7077-7085.

10. D. K. Maiti, S. Halder, P. Pandit, N. Chatterjee, D. De Joarder, N. Pramanik, Y. Saima, A. Patra and P. K. Maiti. *J. Org. Chem.,* 2009*,***74***,* 8086-8097.

11. B. M. Savall, *Tetrahedron Lett.,* 2008, **47**, 6667-6669.

12. R. Schiffmann, *J. Med.Chem*., 2006, **49**, 511-22.

13. V. Prabhakar, K. Babu, Sudhakar; L. K. Ravindranath, J. Latha, *World J. Pharm. Pharmaceutical Sc.,* 2015, **4,** 1605-1614.

14. T. Guntreddi, R. Vanjari and K. N. Singh, *Organic Letters* 2015, **17**, 976-978

15 V. S. Goud and M. Boruah, *PharmaChemica,* 2014, **6**, 388-395

16. T. Nguyen, L. Ermolenko, P. Retailleau and A. Al-Mourabit, *Angew. Chem. Int. Ed.* 2014, **53,** 13808-13812.

17. H. Naeimi and A. Heidarnezhad *J. Chinese Chem. Soc.,* 2014, **61**, 1004-1008.

18. S. Rahmani, A. Amoozadeh and E. Kolvari, *Catal. Commun.* 2014, **56**,184-188

19. A. K.; Chakraborti, S. Rudrawar, K. B. Jadhav, G. Kaur and S. V. Chankeshwara,*Green Chem.,*2010, **9,**1335-1340.

20. S. D. Sharma, *Indian J. Heterocycl. Chem.*, 2005, **14**, 209-212;

21. F. Ono, Y. Ohta, M. Hasegawa and S. Kanemasa, *Tetrahedron Lett.,* 2009, **50**, 2111-2114.

22. M. A. Weidner-Wells, S. A. Fraga-Spano and I. J. Turchi, *J. Org. Chem.* 1998, **63**, 6319.

23. G. Bianchi, A. Cogoli, P. Gruenanger, *J. Organomet. Chem.*1966, **6**, 598-602.

24. J. W. Bode and E. M. Carreira, *J. Am. Chem. Soc.,* 2001, **123**, 3611-3612.

25. N. Chatterjee, P. Pandit, S. Halder, A. Patra and D. K. Maiti, *J. Org. Chem.*, 2008, **73**, 7775-7778