Supporting Information

An efficient and convenient protocol for the synthesis of 3,5-disubstituted 1,2,4-oxadiazoles using $\text{HClO}_4\text{-SiO}_2$ as a heterogeneous recyclable catalyst

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1. General Methods:

Melting points were recorded on a Mel-Temp melting point apparatus, in open capillaries and are uncorrected. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AMX 400 MHz spectrometer using TMS as internal standard and the values for chemical shifts (δ) being given in ppm and coupling constants (J) in Hertz (Hz). Mass spectra were recorded on an Agilent 1100 LC/MSD. Acme silica gel G and silica gel (100-200 mesh) were used for analytical TLC and column chromatography, respectively. Silica-supported perchloric acid ($\text{HClO}_4\text{-SiO}_2$)^[1] and compounds **3a-b**,^[2] mixed anhydride (**4f**),^[3a] **4h**^[3b] and 3-chloropropanoic anhydride^[3c] were prepared according to the literature procedure. Other chemicals were purchased from Sigma Aldrich and used without further purification. All yields refer to isolated ones.

2. General experimental procedure for the synthesis of 3,5-disubstituted 1,2,4-oxadiazoles

A mixture of amidoxime (1.47 mmol), anhydride (1.77 mmol) and $\text{HClO}_4\text{-SiO}_2$ (5 mol%) was stirred at 80 °C for the specified time (Table 2). After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane, and the combined organic layers were washed with saturated aq. NaHCO_3 and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel (Merck, 100–200 mesh) using hexane/EtOAc as eluents. The recovered catalyst was activated by heating at 80 °C under vacuum for 2 h and reused three times with a slight variation in the yields of the products.

3. Synthesis of 3,5-disubstituted 1,2,4-oxadiazoles and characterization data

5-Methyl-3-phenyl 1,2,4-oxadiazole (Table 2, 5a):^[4]

A mixture of benzamidoxime (1.47 mmol), acetic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol%) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **5a**.

Mp: 35-37 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 2.63 (s, 3H), 7.50-7.57 (m, 3H), 7.98-8.00 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 11.8, 126.3, 126.8, 129.0, 131.2, 167.6, 177.2; LC-MS: *m/z* 161 [M + H]⁺; Anal. Calcd. for C₉H₈N₂O: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.44; H, 5.09; N, 17.45.

2-(5-Methyl-1,2,4-oxadiazol-3-yl)pyridine (Table 2, 5b):

A mixture of compound **3b** (1.47 mmol), acetic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to get pure compound **5b**.

Mp: 70-72 °C; ¹H NMR (400 MHz, CDCl₃): δ 2.24 (s, 3H), 7.35-7.38 (m, 1H), 7.71-7.76 (m, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.7, 121.3, 125.4, 136.7, 148.3, 153.5, 168.1, 177.4; LC-MS: *m/z* 162 [M + H]⁺; Anal. Calcd. for C₈H₇N₃O: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.58; H, 4.44; N, 26.03.

5-Ethyl-3-phenyl-1,2,4-oxadiazole (Table 2, **5c**):

A mixture of benzamidoxime (1.47 mmol), propionic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol%) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated

under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **5c**.

Mp: 87-89 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 1.32 (t, *J* = 7.6 Hz, 3H), 2.97 (q, *J* = 7.6 Hz, 2H), 7.54 (m, 3H), 8.01 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 10.3, 19.5, 126.4, 126.8, 129.0, 131.2, 167.4, 181.0; LC-MS: *m/z* 175 [M+H]⁺; Anal. Calcd. for C₁₀H₁₀N₂O: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.91; H, 5.84; N, 16.04.

2-(5-Ethyl-1,2,4-oxadiazol-3-yl)pyridine (Table 2, **5d**):

A mixture of compound **3b** (1.47 mmol), propionic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 6 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃, water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to get pure compound **5d**.

Mp: 97-99 °C; ¹H NMR (400 MHz, CDCl₃): δ 1.25 (t, *J* = 7.6 Hz, 3H), 2.55 (q, *J* = 7.6 Hz, 2H), 7.36 (m, 1H), 7.73 (m, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.54 (d, *J* = 4.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 9.1, 26.3, 121.1, 125.3, 136.6, 148.2, 153.4, 168.2, 177.4; LC-MS: *m/z* 176

$[M+H]^+$; Anal. Calcd. For $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.65; H, 5.23; N, 23.94.

3-(Phenyl)-5-(*n*-propyl)-1,2,4-oxadiazole (Table 2, 5e):^[5]

A mixture of benzamidoxime (1.47 mmol), butyric anhydride (1.77 mmol) and $HClO_4 \cdot SiO_2$ (5 mol%) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. $NaHCO_3$ and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **5e**.

Colourless oil; 1H NMR (400 MHz, $CDCl_3$) : δ 1.01 (t, J = 7.6 Hz, 3H); 1.76 (m, 2H); 2.46 (t, J = 7.6 Hz, 2H), 7.37-7.48 (m, 3H), 7.68 (d, J = 7.2 Hz, 2H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 13.7, 24.9, 35.0, 126.7, 128.6, 130.9, 131.2, 168.5, 180.6; LC-MS: m/z 189 $[M+H]^+$; Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.15; H, 6.49; N, 14.84.

2-(5-Propyl-1,2,4-oxadiazol-3-yl)pyridine (Table 2, 5f):

A mixture of compound **3b** (1.47 mmol), butyric anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to get pure compound **5f**.

Mp: 45-47 °C; ¹H NMR (400 MHz, CDCl₃) : δ 1.01 (t, *J* = 7.6 Hz, 3H), 1.72-1.81 (m, 2H), 2.48 (t, *J* = 7.2 Hz, 2H), 7.32-7.42 (m, 1H), 7.71-7.75 (m, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 4.4 Hz, 1H); ¹³C NMR(100 MHz, CDCl₃): δ 13.6, 28.4, 34.9, 121.2, 125.4, 136.7, 148.3, 153.5, 168.0, 180.6; LC-MS: *m/z* 190 [M+H]⁺; Anal. Calcd. for C₁₀H₁₁N₃O: C, 63.48; H, 5.86; N, 22.2. Found: C, 63.42; H, 5.92; N, 22.16.

5-Pentyl-3-phenyl-1,2,4-oxadiazole (Table 2, **5g**):^[6]

A mixture of benzamidoxime (1.47 mmol), hexanoic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol%) was stirred at 80 °C for 4 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq.

NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (9:1) as eluents to get pure compound **5g**.

Mp: 85-87 °C; ¹H NMR (400 MHz, CDCl₃): δ 0.91 (t, *J* = 6.8 Hz, 3H), 1.35 (m, 4H), 1.69 (m, 2H), 2.45 (t, *J* = 7.6 Hz, 2H), 7.42 (m, 3H), 7.66 (d, *J* = 6.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 13.8, 22.3, 24.7, 31.3, 33.1, 126.7, 128.6, 130.8, 131.0, 168.2, 180.0; LC-MS: *m/z* 217 [M+H]⁺; Anal. Calcd. for C₁₃H₁₆N₂O: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.15; H, 7.49; N, 12.90.

2-(5-Pentyl-1,2,4-oxadiazol-3-yl)pyridine (Table 2, **5h):**

A mixture of compound **3b** (1.47 mmol), hexanoic anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to get pure compound **5h**.

Mp: 44-46 °C; ¹H NMR (400 MHz, CDCl₃): δ 0.96 (t, *J* = 6.8 Hz, 3H), 1.36-1.72 (m, 4H), 1.74-1.78 (m, 2H), 2.50 (t, *J* = 7.6 Hz, 2H), 7.35-7.38 (m, 1H), 7.71-7.76 (m, 1H), 8.17 (d, *J* = 8.0 Hz,

1H), 8.54 (d, $J = 4.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 13.8, 22.2, 24.7, 31.3, 33.0, 121.3, 125.4, 136.7, 148.3, 153.5, 168.1, 177.4; LC-MS: m/z 218 $[\text{M}+\text{H}]^+$; Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}$: C, 66.34; H, 6.96; N, 19.34. Found: C, 66.30; H, 7.01; N, 19.29.

5-Cyclohexyl-3-phenyl-1,2,4-oxadiazole (Table 2, 5i):

A mixture of benzamidoxime (1.47 mmol), cyclohexanecarboxylic acid anhydride (1.77 mmol) and $\text{HClO}_4\text{-SiO}_2$ (5 mol%) was stirred at 80°C for 6 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO_3 and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **5i**.

Colourless oil; ^1H NMR (400 MHz, CDCl_3) : δ 1.25-1.47 (m, 4H), 1.65-1.74 (m, 2H), 1.84-1.88 (m, 2H), 2.11-2.15 (m, 2H), 2.96-3.04 (m, 1H), 7.43-7.47 (m, 3H), 8.06-8.09 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) : δ 25.3, 25.5, 30.2, 36.4, 127.2, 127.4, 128.7, 130.9, 168.1, 182.9; LC-MS: m/z 229 $[\text{M}+\text{H}]^+$; Anal. Calcd. for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.62; H, 7.12; N, 12.23.

2-(5-Cyclohexyl-1,2,4-oxadiazol-3-yl)pyridine (Table 2, 5j):

A mixture of compound **3b** (1.47 mmol), cyclohexanecarboxylic acid anhydride (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 5 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to get pure compound **5j**.

Mp : 75-77 °C; ¹H NMR (400 MHz, CDCl₃) : δ 1.22-1.37 (m, 3H), 1.55-1.70 (m, 3H), 1.80-1.89 (m, 2H), 2.00-2.03 (m, 2H), 2.49-2.56 (m, 1H), 7.35-7.38 (m, 1H), 7.72-7.76 (m, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 8.56 (d, *J* = 4.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) : δ 25.4, 25.6, 29.2, 42.5, 121.3, 125.3, 136.6, 148.3, 153.7, 168.2, 177.3; LC-MS: *m/z* 230 [M+H]⁺; Anal. Calcd. for C₁₃H₁₅N₃O: C, 68.10; H, 6.59; N, 18.33. Found: C, 68.05; H, 6.64; N, 18.30.

(Z)-3-(3-Phenyl-1,2,4-oxadiazol-5-yl)acrylic acid (Table 2, 5k):

A mixture of benzamidoxime (1.47 mmol), maleic anhydride (2.64mmol) and $\text{HClO}_4\text{-SiO}_2$ (5 mol %) was stirred at 80 °C for 8 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO_3 and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (3:7) as eluents to get pure compound **5k**.

Mp: 120-122 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 6.82 (d, J = 12.4Hz, 1H), 6.97 (d, J = 12.4Hz, 1H), 7.57-7.58 (m, 3H), 8.00-8.02 (m, 2H), 10.76 (s, 1H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$): δ 118.4, 128.5, 129.2, 130.4, 131.4, 134.7, 167.9, 172.8, 180.6; LC-MS: m/z 215 $[\text{M-H}]^+$; Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_3$: C, 61.11; H, 3.73; N, 12.96. Found: C, 61.07; H, 3.78; N, 12.92.

(Z)-3-(3-(Pyridine-2-yl)-1,2,4-oxadiazol-5-yl)acrylic acid (Table 2, 5l):

A mixture of compound **3b** (1.47 mmol), maleic anhydride (2.64mmol) and $\text{HClO}_4\text{-SiO}_2$ (5 mol %) was stirred at 80 °C for 8 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO_3 and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated

under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (2:8) as eluents to get pure compound **5l**.

Mp: 135-137 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 6.78 (d, *J* = 12.4 Hz, 1H), 6.89 (d, *J* = 12.4 Hz, 1H), 7.29-7.37 (m, 1H), 7.71-7.76 (m, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 4.8 Hz, 1H), 10.86 (s, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 120.1, 121.1, 125.3, 136.6, 145.2, 148.2, 153.4, 168.2, 177.3, 181.3; LC-MS: *m/z* 216 [M-H]⁺; Anal. Calcd. for C₁₀H₇N₃O₃: C, 55.30; H, 3.25; N, 19.35. Found: C, 55.24; H, 3.31; N, 19.31.

***tert*-Butyl (3-phenyl-1,2,4-oxadiazol-5-yl)methyl carbamate (Table 2, **5m**):**

A mixture of benzamidoxime (1.47 mmol), compound **4h** (1.77 mmol) and HClO₄-SiO₂ (5 mol %) was stirred at 80 °C for 7 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO₃ and water. The obtained organic layer was dried over anhy. Na₂SO₄ and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **5m**.

Mp: 74-76 °C; ¹H NMR (400 MHz, DMSO-*d*₆) : δ 1.47 (s, 9H), 4.62 (s, 2H), 5.34 (bs, 1H), 7.44-7.50 (m, 3H), 8.05-8.07 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) : δ 28.2, 37.2, 80.6, 126.5,

127.4, 128.8, 131.2, 155.4, 168.4, 176.5; LC-MS: m/z 298 $[M+Na]^+$; Anal. Calcd. for $C_{14}H_{17}N_3O_3$: C, 61.08; H, 6.22; N, 15.26. Found: C, 61.04; H, 6.31; N, 15.22.

***tert*-Butyl (3-(pyridine-2-yl)-1,2,4-oxadiazol-5-yl)methyl carbamate (Table 2, 5n):**

A mixture of compound **3b** (1.47 mmol), compound **4h** (1.77 mmol) and $HClO_4-SiO_2$ (5 mol %) was stirred at 80 °C for 8 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. $NaHCO_3$ and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (2:8) as eluents to get pure compound **5n**.

Mp: 85-87 °C; 1H NMR (400 MHz, $DMSO-d_6$) : δ 1.46 (s, 9H), 4.69 (s, 2H), 5.59 (bs, 1H), 7.43 (m, 1H), 7.85 (m, 1H), 8.11(m, 1H), 8.79 (m, 1H); ^{13}C NMR (100 MHz, $DMSO-d_6$) : δ 28.2, 37.1, 80.5, 123.1, 125.5, 136.9, 146.0, 150.3, 155.3, 168.1, 177.4; LC-MS: m/z 277 $[M+H]^+$; Anal. Calcd. for $C_{13}H_{16}N_4O_3$: C, 56.51; H, 5.84; N, 20.28. Found: C, 56.48; H, 5.89; N, 20.24.

Oxolamine (7):

A mixture of benzamidoxime (1.47 mmol), 3-chloropropanoic anhydride (1.77 mmol) and $\text{HClO}_4\text{-SiO}_2$ (5 mol%) was stirred at 80 °C for 8 min. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, diluted with dichloromethane (5 mL) and the catalyst was allowed to settle down. Then the reaction mixture was filtered, washed with dichloromethane (5 mL), and the combined organic layers were washed with saturated aq. NaHCO_3 and water. The obtained organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude compound. The crude was then purified by column chromatography on silica gel using hexane/EtOAc (8:2) as eluents to get pure compound **6**. Then, a mixture of compound-**6** (1.05 mmol) and KI (1.05 mmol) in CH_3CN was stirred at room temperature for 30 min. To the reaction mixture, K_2CO_3 (2.64 mmol) and $\text{Et}_2\text{NH.HCl}$ (1.58 mmol) were added and reaction was stirred under reflux conditions for 2.5 h. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature, water was added and extracted with ethyl acetate. The organic layer was dried over anhy. Na_2SO_4 and concentrated under reduced pressure to get crude. The crude was purified by using column chromatography on silica gel using hexane/EtOAc (7:3) as eluents to afford pure oxolamine as brown colour liquid.

Brown colour liquid; ^1H NMR (400 MHz, CDCl_3): δ 1.06 (t, J = 6.8 Hz, 6H), 2.60 (q, J = 7.2 Hz, 4H), 3.04 (t, J = 4.8 Hz, 2H), 3.09 (t, J = 1.6 Hz, 2H), 7.48-7.50 (m, 3H), 8.07-8.10 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) : δ 11.9, 29.6, 46.8, 49.5, 126.9, 127.4, 128.8, 131.0, 168.2, 178.9; LC-MS: m/z 246 $[\text{M}+\text{H}]^+$; Anal. Calcd. for $\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}$: C, 68.54; H, 7.81; N, 17.13. Found: C, 68.5; H, 7.86; N, 17.09.

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Current Data Parameters
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PROCNO              1
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F2 - Processing parameters
SI                      32768
SF                      400.1299793 MHz
WDW                      EM
SSB                      0
LB                      0.30 Hz
GB                      0
PC                      1.00
```

```
Current Data Parameters
NAME                R-4
EXPNO                2
PROCNO              1
```

```

F2 - Acquisition Parameters
Date_      20120502
Time_      11.24
INSTRUM    spect
PROBH      5 mm BBO BB-1H
PULPROG    zgpg30
TD          65536
SOLVENT    CDCl3
NS          300
DS          4
SWH         24038.461 Hz
FIDRES     0.366798 Hz
AQ         1.3632196 sec
RG          2300
DW          20.800 usec
DE          6.00 usec
TE          300.0 K
d1          2.00000000 sec
d11         0.03000000 sec
DELTA      1.89999998 sec
TDO        1

```

```

                                CHANNEL f1
NUC1                            13C
P1                               7.00 usec
PL1                             0.00 dB
SFO1                          100.6228298 MHz

```

```
===== CHANNEL f2 =====
CPDPRG2          waltz16
NUC2              1H
PCPD2            80.00 usec
PL2              -2.00 dB
PL12             15.64 dB
PL13             16.50 dB
SFO2            400.1316005 MHz
```

```
F2 - Processing parameters
SI                      32768
SF                      100.6127690 MHz
WDW                      EM
SSB                      0
LB                      1.00 Hz
GB                      0
PC                      1.40
```


5c 1H DMSO

8.018
8.014
8.000
7.994
7.577
7.561
7.549
7.531
7.517
7.509

3.374
3.008
2.989
2.970
2.951

1.348
1.329
1.310

Current Data Parameters
NAME S8
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20120110
Time 12.20
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 45.2
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.0000000 sec
TDO 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

5c 13C DMSO

181.03
167.47

131.22
129.02
126.88
126.42

40.20
39.99
39.78
39.57
39.36
39.15
38.94
19.54
10.32

Current Data Parameters
NAME S8
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date 20120110
Time 12.25
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 256
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 2890
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.0000000 sec
d11 0.0300000 sec
DELTA 1.89999998 sec
TDO 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5d 1H CDCl3

Current Data Parameters
NAME R-7
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120317
Time 9.11
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 71.8
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TDO 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1299931 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

5d 1H CDCl3

Current Data Parameters
NAME R-7
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120317
Time 9.17
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 550
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 181
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TDO 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127766 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5f 1H CDCl3

Current Data Parameters
NAME R-2
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120628
Time_ 11.50
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 114
DE 60.600 usec
TE 6.00 usec
DE 300.0 K
D1 2.00000000 sec
TDO 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1299815 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

R-2 13C CDCl3
5f 13C CDCl3

Current Data Parameters
NAME R-2
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120628
Time_ 11.17
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 640
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 16400
DE 20.800 usec
TE 6.00 usec
DE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TDO 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5h

5b

```

Current Data Parameters
NAME          R-4
EXPNO        5336
PROCNO       1

F2 - Acquisition Parameters
Date_         20120502
Time          11.44
INSTRUM       spect
PROBHD        5 mm BBO BB-1H
PULPROG       zg30
TD            65536
SOLVENT       CDCl3
NS            16
DSW           2
H1FREQ        8250.825 Hz
F2FREQ        0.125898 Hz
RG            3.971592 sec
AQ            71.8
DE            60.600 usec
WDW           6.00 usec
GB            300.0 K
TE            2.0000000 sec
D1            1

```

```
===== CHANNEL f1 =====
NUC1          1H
P1            10.50 usec
PL1           -2.00 dB
SFO1          400.1324710 MHz
```

```
F2 - Processing parameters
SI                      32768
SF                      400.1299933 MHz
WDW                      EM
SSB                      0
LB                      0.30 Hz
GB                      0
PC                      1.00
```

CCCCC1=NC(=N2C(=N1)C(=O)N2)c3ccncc3

5h

5h

```
Current Data Parameters
NAME                R-4
EXPNO                2
PROCNO              1
```

```

F2 - Acquisition Parameters
Date=                20120502
Time=                11.24
INSTRUM              5 mm BBO BH-1H
PROBHD               zgpg30
PULPROG              zgpg30
TD                   65536
SOLVENT              CDCl3
NS                   300
DS                   4
SWH                  24038.461 Hz
FIDRES              0.366779 Hz
AQ                  1.363219 sec
RG                   2300
DW                  20.800 usec
DE                   6.00 usec
TE                   300.0 K
D1                   2.0000000 sec
d11                  0.0300000 sec
DELTA                1.89999998 sec
TDO                  1

```

```

===== CHANNEL f1 =====
NUC1          13C
P1             7.00 usec
PL1            0.00 dB
SFO1          100.6228298 MHz

```

```
===== CHANNEL f2 =====
CPDPRG2          waltz16
NUC2              1H
PCPD2            80.00 usec
PL2              -2.00 dB
PL12             15.64 dB
PL13             16.50 dB
SFO2            400.1316005 MHz
```

```
F2 - Processing parameters
SI              32768
SF              100.6127690 MHz
WDW              EM
SSB              0
LB              1.00 Hz
GB              0
PC              1.40
```

Si 1H CDCl3

Current Data Parameters
NAME TR-II
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20111223
Time 14.07
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 80.6
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TDO 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300992 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Si 13C CDCl3

Current Data Parameters
NAME TR-II
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20111223
Time 14.18
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1021
DS 4
SWH 24038.463 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 181
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999999 sec
TDO 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5j ¹H CDC13

5j ¹³C CDC13

5k 1H DMSO

Current Data Parameters
 NAME RA-2
 EXPNO 2
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20120223
 Time 10.31
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 16
 DS 2
 SWH 8250.825 Hz
 FIDRES 0.125898 Hz
 AQ 3.9715922 sec
 RG 64
 DW 60.600 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec
 TDO 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -2.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

5k 13C DMSO

Current Data Parameters
 NAME RA-2
 EXPNO 3
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20120223
 Time 10.38
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 1024
 DS 4
 SWH 24038.461 Hz
 FIDRES 0.366798 Hz
 AQ 1.3632196 sec
 RG 3250
 DW 20.800 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TDO 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 7.00 usec
 PL1 0.00 dB
 SFO1 100.6228298 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 80.00 usec
 PL2 -2.00 dB
 PL12 15.64 dB
 PL13 16.50 dB
 SFO2 400.1316005 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6128193 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Current Data Parameters
NAME RA-2
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date 20120223
Time 10.31
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125896 Hz
AQ 3.9715922 sec
RG 64
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Current Data Parameters
NAME RA-2
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date 20120223
Time 10.38
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 3250
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5m 1H

Current Data Parameters
NAME S5
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20111119
Time 14.11
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 144
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

5m 13C CDCl3

Current Data Parameters
NAME S5
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20111119
Time 14.14
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 4100
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5n 1H CDC13

Current Data Parameters
NAME S10
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120110
Time 13.02
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8250.825 Hz
FIDRES 0.125898 Hz
AQ 3.9715922 sec
RG 144
DW 60.600 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TDO 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -2.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1299924 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

5n 13C CDC13

Current Data Parameters
NAME S10
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120110
Time 14.01
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3632196 sec
RG 1440
DW 20.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TDO 1

===== CHANNEL f1 =====
NUC1 13C
P1 7.00 usec
PL1 0.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 15.64 dB
PL13 16.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127734 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Oxolamine (7)

oxolamine 13C

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