A Novel Approach to Substituted 2*H*-Azirines

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Supporting Information

General procedure for the oximes **2a c**.

To a solution of hydroxylamine hydrochloride (30 mmol) in water (50 mL), was added a solution of benzotriazolymethylketone **1** (15 mmol) in ethanol (50 mL) followed by dropwise addition of 10% NaOH (30 mmol) solution at room temperature. After addition, the yellow or off-white colored mixture was stirred under reflux overnight. Upon cooling to room temperature, white crystals of the product formed and were collected by filtration with no further purification necessary.

2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-phenyl-1-ethanoneoxime (2a). White prisms (93%), mp 234–236 °C (lit.¹ 223–225 °C, 56%); ¹H NMR (DMSO-*d*₆) 12.2 (s, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.73–7.70 (m, 2H), 7.55 (dd, *J* = 7.2, 7.9 Hz, 1H), 7.40–7.32 (m, 4H), 6.09 (s, 2H); ¹³C NMR (DMSO-*d*₆) 151.2, 145.3, 134.4, 133.3, 129.6, 128.8, 127.9, 126.7, 124.5, 119.6, 110.9, 41.5.

2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-(4-chlorophenyl)-1-ethanoneoxime (2b). White needles (91%), mp 226–227 °C; ¹H NMR (DMSO-*d*₆) 12.33 (s, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.58 (dd, *J* = 7.8, 7.0 Hz, 1H), 7.43–7.37 (m, 3H), 6.10 (s, 2H); ¹³C NMR (DMSO-*d*₆) 149.9, 144.8, 134.0, 132.8, 128.4, 128.0, 127.4, 124.0, 119.1, 110.4, 41.0. Anal. Calcd for C₁₅H₁₄N₄O: C, 67.65; H, 5.31; N, 21.04. Found: C, 67.43; H, 5.47; N, 21.02.

2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-(4-methylphenyl)-1-ethanoneoxime (2c). White microcrystals (92%), mp 185–188 °C; ¹H NMR (DMSO-*d*₆) 12.11 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.62–7.53 (m, 3H), 7.37 (dd, *J* = 8.0, 7.3 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.07 (s, 2H), 2.24 (s, 3H); ¹³C NMR (DMSO-*d*₆) 150.6, 144.9, 138.8, 132.8, 131.1, 128.9, 127.4, 126.2, 124.0, 119.1, 110.4, 41.0, 20.7. Anal. Calcd for C₁₄H₁₁ClN₄O: C, 58.65; H, 3.87; N, 19.54. Found: C, 58.47; H, 3.92; N, 19.49.

General procedure for 2-(benzotriazol-1-yl)-2*H*-azirines **4a c**.

To a solution of oxime **2** (20 mmol) in a mixture of ethyl ether (150 mL) and chloroform (50 mL), was added dropwise aqueous KOH (11.2 g KOH dissolved in 50 mL of water) at 0 °C. After the addition of the base solution, the mixture was stirred vigorously at this temperature for 30 min, and then a catalytic amount of Bu₄NHSO₄ was added. A solution of *p*-toluenesulfonyl chloride (TsCl) in Et₂O (50 mL) was added dropwise at 0 °C. After this addition, the final mixture was stirred at 0–5 °C for 6h until the solid reactants disappeared. The reaction mixture was transferred into a separatory funnel and extracted with ethyl ether. The combined organic layer was washed with water and dried over MgSO₄. The residue on removal of solvents was purified by column (hexane-ethyl acetate) to give the desired products **4a c**.

1-(3-Phenyl-2*H*-aziren-2-yl)-1*H*-1,2,3-benzotriazole (4a). White needles (40%), mp 99–100 °C; ¹H NMR 8.15 (d, *J* = 6.7 Hz, 2H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.73–7.62 (m, 4H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.37 (dd, *J* = 7.9, 7.3 Hz, 1H), 5.19 (s, 1H); ¹³C NMR 164.6, 146.1, 134.4, 132.8, 130.5, 129.5, 127.8, 124.2, 123.0, 120.1, 109.8, 42.7. Anal. Calcd for C₁₄H₁₀N₄: C, 71.78; H, 4.30; N, 23.92. Found: C, 71.81; H, 4.39; N, 23.92.

1-[3-(4-Chlorophenyl)-2*H*-aziren-2-yl]-1*H*-1,2,3-benzotriazole (4b). Yellow prism (58%), mp 158–160 °C; ¹H NMR 8.10 (d, *J* = 8.5 Hz, 2H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 8.0, 7.3 Hz, 1H), 5.17 (s, 1H); ¹³C NMR 163.8, 146.2, 140.9, 132.9, 131.7, 130.0, 127.9, 124.3, 121.6, 120.2, 109.7, 42.4. Anal. Calcd for C₁₄H₉ClN₄: C, 62.58; H, 3.38; N, 20.85. Found: C, 62.81; H, 3.34; N, 20.84.

1-[3-(4-Methylphenyl)-2*H*-aziren-2-yl]-1*H*-1,2,3-benzotriazole (4c). Yellow microcrystals (66%), mp 101–102 °C; ¹H NMR 8.07–8.02 (m, 3H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.50–7.44 (m, 3H), 7.37 (dd, *J* = 7.8, 7.4 Hz, 1H), 5.18 (s, 1H), 2.5 (s, 3H). ¹³C NMR 164.1, 146.1, 145.6, 132.8, 130.6,

130.2, 127.7, 124.2, 120.3, 120.1, 109.9, 42.6, 22.0. Anal. Calcd for $C_{15}H_{12}N_4$: C, 72.56; H, 4.87; N, 22.57. Found: C, 72.63; H, 4.96; N, 24.46.

General procedure for 2*H*-azirine 5a f.

Under N_2 , activated Mg powder (2 mmol) was added into a dried two-necked flask equipped with a condenser and magnetic stirrer. Then 5 mL of Et_2O was added. With the starting of the stirrer, 3–4 drops of a solution of the bromide (2 mmol) in 5 mL of Et_2O was added by syringe, and several minutes later, the remaining bromide solution was added dropwise. The mixture was heated and refluxed slowly for 1 h. Upon cooling to $-18\text{ }^{\circ}C$ (ice-salt bath), $ZnCl_2$ solution (1.0 M, 2.0 mL) was added, and 30–40 minutes later, a solution of starting 2*H*-azirine **4** (0.5 mmol) in 5 mL of toluene was added at this temperature. After these additions, the final mixture was stirred at $-18\text{ }^{\circ}C$ to room temperature overnight (around 24 h). TLC showed almost no starting material. The reaction was quenched with water, and the reaction mixture was diluted with Et_2O , washed with water, and dried over $MgSO_4$. The residue on removal of solvents was purified by column (hexane-ethyl acetate) to give the desired products **5a f**.

2-Benzyl-3-phenyl-2*H*-azirine (5a). Oil (70%); 1H NMR δ 7.77–7.75 (m, 2H), 7.55–7.47 (m, 3H), 7.31–7.21 (m, 5H), 3.06 (dd, J = 14.6, 5.1, 1H), 2.76 (dd, J = 14.6, 5.1 Hz, 1H), 2.51 (t, J = 5.1 Hz, 1H); ^{13}C NMR δ 171.6, 139.3, 132.8, 129.3, 129.0, 128.9, 128.5, 126.3, 125.5, 40.1, 33.2.

2-(4-Methylbenzyl)-3-phenyl-2*H*-azirine (5b). Oil (70%); 1H NMR δ 7.86–7.83 (m, 2H), 7.65–7.55 (m, 3H), 7.25 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 3.08 (dd, J = 14.6–4.9 Hz, 1H), 2.77 (dd, J = 14.6, 5.3 Hz, 1H), 2.55 (t, J = 5.1 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR δ 171.7, 136.2, 135.8, 132.8, 129.4, 129.2, 129.0, 128.8, 125.6, 39.7, 33.4, 21.0. Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.53; H, 7.24; N, 6.20.

2-Benzyl-3-(4-chlorophenyl)-2H-azirine (5c). Oil (70%); ^1H NMR 7.67 (d, $J = 8.5$ Hz, 2H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.33–7.20 (m, 5H), 3.09 (dd, $J = 14.6, 4.9$ Hz, 1H), 2.73 (dd, $J = 14.6, 5.1$ Hz, 1H), 2.54 (t, $J = 5.1$ Hz, 1H); ^{13}C NMR 170.9, 139.1, 139.0, 130.5, 129.5, 128.9, 128.6, 126.4, 124.0, 40.0, 33.5. Anal. Calcd for $\text{C}_{15}\text{H}_{12}\text{ClN}$: C, 74.53; H, 5.00; N, 5.79. Found: C, 74.55; H, 5.37; N, 5.76.

3-(4-Chlorophenyl)-2-(4-methylbenzyl)-2H-azirine (5d). White prism (80%), mp 93–95 °C; ^1H NMR 7.69 (d, $J = 8.5$ Hz, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.17–7.09 (m, 4H), 3.05 (dd, $J = 14.6, 4.8$ Hz, 1H), 2.68 (dd, $J = 14.6, 5.4$ Hz, 1H), 2.51 (dd, $J = 5.1, 4.8$ Hz, 1H), 2.33 (s, 3H); ^{13}C NMR 171.0, 139.0, 136.0, 135.9, 130.5, 129.5, 129.2, 128.8, 124.1, 39.6, 33.6, 21.0. Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{ClN}$: C, 75.14; H, 5.52; N, 5.48. Found: C, 75.18; H, 5.65; N, 5.32.

2-Benzyl-3-(4-methylphenyl)-2H-azirine (5e). Oil (71%); ^1H NMR 7.57 (d, $J = 7.8$ Hz, 2H), 7.24–7.14 (m, 7H), 2.97 (dd, $J = 14.6, 5.1$ Hz, 1H), 2.65 (dd, $J = 14.6, 5.1$ Hz, 1H), 2.40 (t, $J = 5.1$ Hz, 1H), 2.35 (s, 3H). ^{13}C NMR 171.1, 143.6, 139.5, 129.7, 129.4, 128.9, 128.5, 126.2, 122.7, 40.2, 32.9, 21.8. Anal. Calcd for $\text{C}_{16}\text{H}_{15}\text{N}$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.67; H, 7.23; N, 6.02.

2-(4-Methylbenzyl)-3-(4-methylphenyl)-2H-azirine (5f). Oil (50%); ^1H NMR 7.67 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 3.01 (dd, $J = 14.6, 4.9$ Hz, 1H), 2.68 (dd, $J = 14.6, 5.4$ Hz, 1H), 2.46–2.44 (m, 4H), 2.34 (s, 3H). ^{13}C NMR 171.3, 143.6, 136.4, 135.7, 129.8, 129.4, 129.2, 128.8, 122.9, 39.9, 33.1, 21.8, 21.0. HRMS (FAB) Calcd for $\text{C}_{17}\text{H}_{17}\text{N}$ [M^+]: 235.1361. Found: 235.1359.

General procedure for 2H-azirine 6a–c.

To a solution of potassium phthalimide (0.5 mmol) in DMF (5 mL), was added dropwise a solution of starting 2H-azirine **4** (0.5 mmol) in DMF (5 mL) at room temperature. After addition, the reaction mixture was stirred at room temperature overnight (around 18h). Crushed ice was added to

quench the reaction, then the mixture was transferred to a separatory funnel and extracted with ether. The organic layer was washed with water, dried over MgSO_4 . The residue on the removal of Et_2O was purified by column to give yellow oil. Recrystallization was carried out in hexane/ethyl acetate.

2-(3-Phenyl-2*H*-aziren-2-yl)-1*H*-isoindole-1,3(2*H*)-dione (6a). Yellow microcrystals (70%), mp 139–140 °C; ^1H NMR 8.10–8.07 (m, 2H), 7.82–7.80 (m, 2H), 7.72–7.70 (m, 2H), 7.66–7.58 (m, 3H), 4.27 (s, 1H); ^{13}C NMR 167.9, 165.3, 134.3, 133.4, 131.7, 130.2, 128.9, 124.7, 123.3, 35.6. Anal. Calcd for $\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}$: C, 73.27; H, 3.84; N, 10.68. Found: C, 73.16; H, 3.83; N, 10.58.

2-[3-(4-Chlorophenyl)-2*H*-aziren-2-yl]-1*H*-isoindole-1,3(2*H*)-dione (6b). Yellow needles (57%), mp 182.5–184.5 °C; ^1H NMR 8.03 (d, $J = 8.4$ Hz, 2H), 7.85–7.81 (m, 2H), 7.75–7.72 (m, 2H), 7.60 (d, $J = 8.4$ Hz, 2H), 4.27 (s, 1H). ^{13}C NMR 167.9, 164.7, 139.9, 134.4, 131.8, 131.5, 129.5, 123.5, 123.3, 35.7. HRMS (FAB) Calcd for $\text{C}_{16}\text{H}_9\text{N}_2\text{O}_2$ [M^+]: 296.0353. Found: 296.0351.

2-[3-(4-Methylphenyl)-2*H*-aziren-2-yl]-1*H*-isoindole-1,3(2*H*)-dione (6c). Yellow needles (79%), mp 145–146 °C; ^1H NMR 7.97 (d, $J = 8.1$ Hz, 2H), 7.83–7.79 (m, 2H), 7.72–7.70 (m, 2H), 7.41 (d, $J = 8.0$ Hz, 2H), 4.24 (s, 1H), 2.48 (s, 3H). ^{13}C NMR 168.0, 164.8, 144.4, 134.3, 131.8, 130.3, 129.7, 123.4, 122.0, 35.5, 21.9. Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_2$: C, 73.90; H, 4.38; N, 10.14. Found: C, 73.79; H, 4.21; N, 10.10.

The procedure for 2*H*-azirine 7.

To a solution of sodium salt of benzenethiol (0.5 mmol) in DMF (5 mL) cooled at 0 °C, was added dropwise a solution of starting 2*H*-azirine **4a** (0.5 mmol) in DMF (5 mL). After addition, the reaction mixture quickly turned purple and was stirred at 0 °C for 1h. Crushed ice was added to quench the reaction, then the mixture was transferred to a separatory funnel and extracted with ether. The organic layer was washed with water, dried over MgSO_4 . The residue on the removal of Et_2O was purified by column to give green oil. This compound is not stable at room temperature.

Phenyl 3-phenyl-2*H*-aziren-2-ylsulfide 7. Green oil (70%); ^1H NMR 7.87 (d, $J = 8.4$ Hz, 2H), 7.67 7.55 (m, 5H), 7.36 7.24 (m, 3H), 3.84 (s, 1H); ^{13}C NMR 166.4, 136.3, 133.6, 130.1, 129.8, 129.2, 129.0, 126.8, 124.0, 37.6. HRMS (FAB) Calcd for $\text{C}_{14}\text{H}_{11}\text{NS}$ $[\text{M}+2\text{H}]$: 227.0769. Found: 227.0764.

References

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