An Unexpected Disproportional Reaction of 2H-Azirines Giving (1E,3Z)-2-Aza-1,3-dienes and Aromatic Nitriles in the Presence of Nickel Catalysts

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Supporting Information

1. General. NMR spectra were recorded on JEOL EX-400 spectrometer (400 MHz for ¹H NMR and 100 MHz for ¹³C NMR). Chemical shifts are reported in δ ppm referenced to CDCl₃ (δ 7.26 for ¹H NMR and δ 77.00 for ¹³C NMR). IR spectra were recorded with an FT-IR spectrometer (JASCO FT/IR-460 Plus). Melting points (mp) are uncorrected. High-resolution mass spectra (HRMS) were measured with JEOL JMX-SX 102A spectrometer. Toluene and THF were purified by passed through a neutral alumina column under argon atmosphere. DMF was distilled over CaH₂. Silica gel 60 NH₂ was purchased from Kanto Chemicals. All other materials were purchased and used without further purification.

2. Preparation of Substrates.

A typical procedure for the synthesis of azirines **1** is shown below.¹ **2,3-Diphenyl-2***H***-azirine (1b)** [CAS 16483-98-0]



To a solution of benzyl phenyl ketone (19.6 g, 100 mmol) *N*,*N*-dimethylhydrazine (15.2 mL, 200 mmol) in benzene (150 mL) was added trifluoroacetic acid (0.15 mL). The solution was heated to reflux with Dean-Stark apparatus for 4 h. The reaction mixture was poured into H_2O (50 mL) and the aqueous layer was extracted with 30 mL of Et₂O three times. The combined organic layer was dried over MgSO₄, filtered, and concentrated under vacuum to give 25.0 g of the crude hydrazine, which was used to the next step without further purification. A solution of the hydrazone in MeI (30 mL) was stirred at 40 °C for 13 h. The solution was diluted with Et₂O and the

⁽¹⁾ A. Padwa, P. H. J. Carlsen, J. Am. Chem. Soc. 1977, 99, 1514.

resulting precipitate was filtered to give 37.2 g of the corresponding hydrazonium salt (98.0 mmol, 98% yield) as a yellow solid.

To a suspension of NaH (~60 wt%, 1.60 g, 40.0 mmol) in DMF (10 mL) was added the hydrazoniuim salt (13.8 g, 36.0 mmol) in one portion at 0 °C and the mixture was stirred at 0 °C for 1 h. Then the reaction mixture was quenched with H₂O and extracted with Et₂O three times. The combined organic layer was dried over MgSO₄, filtered, and concentrated under vacuum. The residue was subjected to column chromatography on silica gel (hexane/EtOAc = 10/1) followed by reprecipitation from hexane/CH₂Cl₂ to give 3.79 g of azirine **1b** (19.6 mmol, 54% yield) as a pale yellow solid. ¹H NMR (CDCl₃): δ 3.32 (s, 1H), 7.16 (d, *J* = 6.3 Hz, 2H), 7.23–7.31 (m, 3H), 7.52–7.57 (m, 3H), 7.91 (d, *J* = 6.6 Hz, 2H). ¹³C NMR (CDCl₃): δ 34.4, 124.0, 126.1, 127.1, 128.3, 129.2, 129.9, 133.2, 140.8, 163.5.

2,2-Diphenyl-3-methyl-2H-azirine (1a) [CAS 65817-54-1]



A colorless oil. ¹H NMR (CDCl₃): δ 2.59 (s, 3H), 7.21 (d, J = 7.3 Hz, 4H), 7.26 (t, J = 6.8 Hz, 2H), 7.32 (t, J = 6.8 Hz, 4H). ¹³C NMR (CDCl₃): δ 12.8, 42.7, 126.9, 127.9, 128.3, 141.8, 167.4.

2-(4-tert-Butylphenyl)-3-phenyl-2H-azirine (1c)



A white solid. Mp 44–45 °C. ¹H NMR (CDCl₃): δ 3.28 (s, 1H), 7.15 (d, J = 6.8 Hz, 2H), 7.22-7.29 (m, 3H), 7.56 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H). ¹³C NMR (CDCl₃): δ 31.1, 34.1, 35.3, 121.2, 126.1, 126.2, 126.9, 128.2, 129.7, 141.1, 157.1, 162.9. HRMS (FAB) calcd for C₁₈H₂₀N (M+H)⁺ 250.1596, found 250.1592.

2-(4-Methoxyphenyl)-3-phenyl-2*H*-azirine (1d)



A white solid. Mp 46–47 °C. ¹H NMR (CDCl₃): δ 3.27 (s, 1H), 3.89 (s, 3H), 7.04 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 6.8 Hz, 2H), 7.22-7.28 (m, 3H), 7.85 (d, J = 8.8 Hz, 2H). ¹³C NMR (CDCl₃): δ 34.0, 55.5, 114.7, 116.3, 126.0, 126.8, 128.2, 131.8, 141.2, 162.0, 163.4. HRMS (FAB) calcd for C₁₅H₁₄NO (M+H)⁺ 224.1075, found 224.1073.

2-(4-Chlorophenyl)-3-phenyl-2*H*-azirine (1e)



A white solid. Mp 37–38 °C. ¹H NMR (CDCl₃): δ 3.33 (s, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.24-7.31 (m, 3H), 7.52 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H). ¹³C NMR (CDCl₃): δ 34.63, 122.5, 126.0, 127.2, 128.3, 129.7, 131.0, 139.5, 140.4, 162.8. HRMS (FAB) calcd for C₁₄H₁₁NCl (M+H)⁺ 228.0580, found 228.0580.

3-(4-Chlorophenyl)-2-phenyl-2H-azirine (1f)



A pale yellow solid. Mp 51–52 °C. ¹H NMR (CDCl₃): δ 3.29 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.51-7.63 (m, 3H), 7.88 (d, *J* = 6.6 Hz, 2H). ¹³C NMR (CDCl₃): δ 33.7, 123.6, 127.2, 128.3, 129.2, 129.8, 132.7, 133.3, 139.4, 163.2. HRMS (FAB) calcd for C₁₄H₁₁NCl (M+H)⁺ 228.0580, found 228.0580.

3. Nickel-catalyzed formation of indole 2a (eq. 1).



To a solution of Ni(cod)₂ (5.5 mg, 20 μ mol) and PCyp₃ (9.9 μ L, 40 μ mol) in toluene (1.0 mL) was added azirine **1a** (41.5 mg, 0.20 mmol) and the mixture was stirred at 80 °C for 12 h. The reaction mixture was filtered through a pad of Florisil and the filtrate was concentrated under vacuum. The residue was subjected to column chromatography on Florisil (hexane/EtOAc = 20/1) to give 18.8 mg of 2-methyl-3-phenylindole (**2a**) [CAS 4757-69-1] (0.090 mmol, 45% yield) as a pale

yellow oil. ¹H NMR (CDCl₃): δ 2.50 (s, 3H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.16 (t, *J* = 6.8 Hz, 1H), 7.26–7.36 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.92 (br s, 1H). ¹³C NMR (CDCl₃): δ 12.5, 110.3, 114.5, 118.8, 119.9, 121.5, 125.8, 127.8, 128.5, 129.4, 131.4, 135.2, 135.4.

4. Nickel-catalyzed disproportionation of azirines 1 (Tables 1 and 2).



A typical procedure for Table 1, entry 3 is shown below. To a solution of Ni(cod)₂ (5.5 mg, 20 µmol) and PCyp₃ (9.9 µL, 40 µmol) in toluene (1.0 mL) was added azirine **1b** (38.6 mg, 0.20 mmol) and the mixture was stirred at 40 °C for 1 h. The reaction mixture was filtered through a pad of Florisil and the filtrate was concentrated under vacuum. The yields were estimated by ¹H NMR of the crude product to which nitromethane (10.8 µL, 0.20 mmol) was added. The residue was subjected to column chromatography on Florisil (hexane/EtOAc = 20/1) to give 13.6 mg of (1*E*,3*Z*)-1,3,4-triphenyl-2-aza-1,3-butadiene² (**3b**) [CAS 185623-84-1] (0.048 mmol, 48% yield) as a pale yellow oil. ¹H NMR (CDCl₃): δ 6.46 (s, 1H), 7.02-7.25 (m, 9H), 7.41 (d, *J* = 6.8 Hz, 2H), 7.67-7.71 (m, 2H), 7.84 (d, *J* = 7.8 Hz, 2H), 8.16 (s, 1H). ¹³C NMR (CDCl₃): δ 119.1, 126.6, 127.7, 127.9, 128.2, 128.5, 128.8, 128.9, 130.2, 131.4, 136.3, 136.7, 139.3, 149.5, 162.4. HRMS (FAB) calcd for C₂₁H₁₈N (M+H)⁺ 284.1439, found 284.1433.

(1*E*,3*Z*)-1,4-Diphenyl-3-(4-*tert*-butylphenyl)-2-aza-1,3-butadiene (3c)



19.7 mg, 0.058 mmol, 58% yield. A colorless oil. ¹H NMR (CDCl₃): δ 1.35 (s, 9H), 6.40 (s, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.41 (s, 4H), 7.42–7.50 (m, 2H), 7.65 (d, J = 7.3 Hz, 2H), 7.82–7.91 (m, 2H), 8.31 (s, 1H). ¹³C NMR (CDCl₃): δ 31.3, 34.6, 118.3, 125.4, 126.4, 127.3, 128.1, 128.8, 128.9, 130.2, 131.4, 136.4, 136.8, 149.6, 151.0, 162.4. HRMS (FAB) calcd for C₂₅H₂₆N (M+H)⁺ 340.2065, found 340.2060.

⁽²⁾ F. Palacious, C. Alonso, G. Rubiales, J. Org. Chem. 1997, 62, 1146.

(1*E*,3*Z*)-1,4-Diphenyl-3-(4-methoxyphenyl)-2-aza-1,3-butadiene (3d)



16.9 mg, 0.054 mmol, 54% yield. A colorless oil. ¹H NMR (CDCl₃): δ 6.36 (s, 1H), 6.92 (d, J = 8.8 Hz, 2H), 7.17 (t, J = 7.3 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 7.45-7.52 (m, 3H), 7.64 (d, J = 7.3 Hz, 2H), 7.85-7.91 (m, 2H), 8.29 (s, 1H). ¹³C NMR (CDCl₃): δ 55.3, 113.9, 117.6, 126.3, 128.1, 128.78, 128.83, 128.9, 130.1, 131.4, 131.8, 136.3, 136.9, 149.3, 159.5, 162.4. HRMS (FAB) calcd for C₂₂H₂₀NO (M+H)⁺ 314.1545, found 314.1538.

(1*E*,3*Z*)-1,4-Diphenyl-3-(4-chlorophenyl)-2-aza-1,3-butadiene (3e)



13.0 mg, 0.041 mmol, 41% yield. A pale yellow oil. ¹H NMR (CDCl₃): δ 6.39 (s, 1H), 7.17-7.49 (m, 10H), 7.65 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 6.4 Hz, 2H), 8.25 (s, 1H). ¹³C NMR (CDCl₃): δ 118.9, 126.8, 128.2, 128.7, 128.8, 128.9, 130.2, 131.6, 133.4, 133.8, 136.1, 136.4, 137.8, 148.5, 162.7. HRMS (FAB) calcd for C₂₁H₁₇NCl (M+H)⁺ 318.1050, found 318.1053.

(1E,3Z)-1,4-Diphenyl-3-(4-chlorophenyl)-2-aza-1,3-butadiene (3f)



10.9 mg, 0.031 mmol, 31% yield. A pale yellow oil. ¹H NMR (CDCl₃): δ 6.36 (s, 1H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.33-7.50 (m, 7H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 8.22 (s, 1H). ¹³C NMR (CDCl₃): δ 119.0, 127.8, 128.2, 128.3, 128.6,

129.2, 130.0, 131.5, 132.4, 134.6, 135.1, 137.7, 138.8, 149.7, 161.0. HRMS (FAB) calcd for $C_{21}H_{16}NCl_2$ (M+H)⁺ 352.0660, found 352.0665.

5. Palladium-catalyzed dimerization of azirine 1b (eq. 4).



To a solution of $Pd(dba)_2$ (11.5 mg, 20 µmol) and $P(2-furyl)_3$ (9.3 mg, 40 µmol) in THF (1.5 mL) was added azirine **1b** (41.5 mg, 0.20 mmol) and the mixture was stirred at 40 °C for 2 h. The reaction mixture was filtered through a pad of Florisil and the filtrate was concentrated under vacuum. The residue was subjected to column chromatography on Florisil (hexane/EtOAc = 20/1) to give 32.1 mg of a mixture of azirine dimers **5b** (0.057 mmol, 57% yield) and **6b** (0.026 mmol, 26% yield). Analytically pure samples were obtained by further purification by column chromatography followed by recrystallization. Relative configurations of two dimers were not determined.

5b: A colorless oil. ¹H NMR (CDCl₃): δ 4.50 (s, 1H), 5.41 (s, 1H), 7.16–7.30 (m, 10H), 7.36 (t, J = 7.3 Hz, 2H), 7.44 (t, J = 7.3 Hz, 1H), 7.47–7.56 (m, 3H), 8.01 (d, J = 7.3 Hz, 1H), 8.45 (d, J = 7.8 Hz, 1H). ¹³C NMR (CDCl₃): δ 45.3, 65.8, 126.5, 127.4, 127.45, 127.48, 127.9, 128.3, 128.4, 128.6, 128.7, 129.2, 130.8, 132.2, 136.8, 137.2, 138.4, 140.0, 159.7, 172.5. HRMS (FAB) calcd for C₂₈H₂₃N₂ (M+H)⁺ 387.1868, found 387.1866.

6b: A white solid. Mp 148–150 °C. ¹H NMR (CDCl₃): δ 4.37 (d, J = 6.8 Hz, 1H), 5.09 (d, J = 6.8 Hz, 1H), 6.55 (d, J = 7.8 Hz, 1H), 6.95 (t, J = 7.3 Hz, 2H), 7.04 (t, J = 7.8 Hz, 1H), 7.20–7.28 (m, 6H), 7.42 (t, J = 7.8 Hz, 2H), 7.46–7.55 (m, 4H), 8.16 (d, J = 7.8 Hz, 2H), 8.50 (d, J = 7.3 Hz, 2H). ¹³C NMR (CDCl₃): δ 44.0, 62.5, 126.9, 127.1, 127.9, 128.1, 128.2, 128.25, 128.31, 128.7, 129.0, 130.8, 132.1, 132.3, 136.5, 136.7, 139.9, 161.2, 174.9. HRMS (FAB) calcd for C₂₈H₂₃N₂ (M+H)⁺ 387.1868, found 387.1851.

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