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

Kazuhiro Okamoto, Ayano Mashida, Masahito Watanabe, and Kouichi Ohe* Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan e-mail: ohe@scl.kyoto-u.ac.jp

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.

azirine(Me-Ph,Ph)	10.11 10.18 10.18 10.18 10.18 10.18 10.18			DFILE COMNT DEFAULT.ALS DATIM Mon Jan 30 12:27:01 2012 OBNUC 1H EXMOD NON OBSET 124.00 KHz OBFIN 10500.00 Hz POINT 16384 FREQU 7992.01 Hz SCANS 16 ACQTM 2.0501 sec PW1 7.20 usec IRNUC 1H CTEMP 27.2 c SLVNT CDCL3 EXREF 0.00 ppm BF 1.02 Hz RGAIN 16
		3.00		Me Ph
		2.58671	1.56789	1a <u>M</u>

	2H-azirine(Me-Ph,Ph)	- 128.2642 - 127.8532 - 126.9078	•	MENUF BCM OBNUC 13C OFR 75.45 MHz OBSET 124.00 KHz OBSET 1840.00 Hz
				PW1 4.50 usec DEADT 27.20 usec PREDL 0.20000 msec IWT 1.0000 msec POINT 32768 TIMES 1000 DIMMY 1
				DOMMI 1 FREQU 20356.23 Hz FLT 10200 Hz DELAY 19.60 usec ACQTM 1.6097 sec PD 1.3900 sec ADBIT 16 RGAIN 28 BF 0.10 Hz T1 0.00
			•	12 0.00 T3 90.00 T4 100.00 EXMOD BCM EXPCM Bilevel.complete.decoupling:Se IRNUC 1H IFR 300.40 MHz IRSET 130.00 KHz IRRFIN 1150.00 Hz IRRPW 50 usec IRATNU E11
				IRAIN 511 DFILE DEFAULT.ALS SF TH5 LKSET 25.60 KHz LKFIN 52.0 Hz LKLEV 200 LGAIN 25 LKPHS 201 LKSIG 578 CSPED 12 Hz
				FILDC FILDF
		128 127		Me Ph 1a
. 2			андатьданный антериалания и продоктали и продоктивной самонали и продоктивной самонали и продоктивной самонали 7 75 50 25	
	167.3700 - 167.3700 - 141.7872 - 121.2632 - 127.8532 -	126.9078 -	77,4193 - 77,4193 - 76,5725 - 76,5725 - 42,6951 - 42,6951 -	12.8129











Electronic Supplementary Material (ESI) for Chemical Communications This journal is C The Royal Society of Chemistry 2012







いてててててててて





single pulse decoupled gated NOE





Electronic Supplementary Material (ESI) for Chemical Communications This journal is © The Royal Society of Chemistry 2012



1

125.351 125.351 125.351 129.350 129.350 121.151 122.7651 123.7655 123.7655 123.7655 123.7655 123.7655 124.755 124.755 124.755 125.7555 125.7555 125.7555 125.7555 125.7555 125.7555 125.7555 125.7555 125.7555 125.75555 125.75555 125.7555 125.75555 125.75	118.7611 114.4699 110.2856				DFILE DEFAULT.ALS COMNT Exp-237(1) DATIM Tue May 17 21:11:50 2011 OBNUC 13C EXMOD BCM OBFRQ 75.45 MHz OBSET 124.00 KHz OBFIN 1840.00 Hz POINT 32768 FREQU 20356.23 Hz SCANS 512 ACQTM 1.6097 sec PD 1.3900 sec PW1 4.50 usec IRNUC 1H CTEMP 22.7 c SLVNT CDCL3 EXREF 77.00 ppm BF 0.10 Hz RGAIN 28
				·	Me K Ph 2a
land and have no an a state of the state of					
0 175			75 50		PPM T
	55.3998 11.3778 11.3778 11.3778 23.4697 25.7651 25.7651	10.2856 11 10.2856 11 10.2856 11 10.2856 11 10.2856 11 10.2856 11 10.285556 11 10.28556 110.285556 11 10.285556 110.285556 110.285556 110.285556 110.285556 110.285556 110.285556 110.285556 110.285556 110.2855556 110.285555556 110.2855555555 110.2	1,4193 1,0000 6.58007	2.5005	

Ph Ph

.

OMePh Ph

.

Electronic Supplementary Material (ESI) for Chemical Communications This journal is © The Royal Society of Chemistry 2012 <u>CTPDocuments and Settings (ECLEMy Documents Falcet DEFAULT.ALS</u>

Electronic Supplementary Material (ESI) for Chemical Communications This journal is © The Royal Society of Chemistry 2012

Electronic Supplementary Material (ESI) for Chemical Communications This journal is © The Royal Society of Chemistry 2012

