Regioselective Protection at N-2 and Derivatization at C-3 of Indazoles

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Experimental procedures for the new reactions and full characterization of compounds **1b**, **2a**, **2b**, **3a-3i**, **8-10**, **12a-12h** and **13**.

General Details.

¹H and ¹³C NMR spectra were recorded on a 400 MHz Bruker spectrometer. In ¹H and ¹³C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from CHCl₃ (7.26 ppm) and CDCl₃ (77.0 ppm), respectively. Mass spectra were recorded by electron impact or chemical ionization. Column chromatography was performed on silica gel packed in Biotage Horizon columns.

Indazoles **1a**, **1c**, **1e-1i**, and 3-methyl pyrazole **4** were commercially available. Indazole **1d** was prepared by literature methods.¹ All reagents, anhydrous grade solvents, and

(1) Dell'Erba, C.; Novi, M; Petrillo, G.; Tavani, C. *Tetrahedron* **1994**, *50*, 3529.

starting materials were used as received from commercial sources. Reactions that required anhydrous conditions were conducted under an atmosphere of dry nitrogen with oven-dried flasks.

Preparation of 7-methylindazole-5-carboxaldehyde (1b).

5-Bromo-7-methylindazole (**1d**) (6.10 g, 28.9 mmol) and sodium hydride (60% in mineral oil, 1.27 g, 1.1 equiv) were weighed into a flame-dried round-bottom flask containing a magnetic stir bar. Under a nitrogen atmosphere at room temperature, dry tetrahydrofuran (30 mL) was added. The mixture was stirred at room temperature for 15 min, during which time it became homogeneous. The stirred mixture was cooled to -70°C and a solution of *sec*-butyllithium in cyclohexane (1.4M, 45 mL, 2.2 equiv) was added over several minutes. After 1 h at -70°C , dimethylformamide (10 mL) was added over several minutes. The mixture was allowed to warm to room temperature and was stirred overnight. It was then cooled to 0°C and carefully treated with 1N hydrochloric acid (60 mL). After a few minutes, solid sodium bicarbonate was added to basify the mixture to pH 9-10. The layers were separated and the aqueous phase washed twice with ethyl acetate. The combined organic phases were extracted with 0.8M sodium hydrogen sulfate (3 x 125 mL). The combined aqueous phases were washed with ethyl acetate (100 mL) and then the pH was adjusted to ca. 10 with solid sodium hydroxide. The resulting suspension was extracted with ethyl acetate (3 x 150 mL). The combined organic phases were washed with brine, dried (magnesium sulfate) and evaporated to give the product as a light-tan solid (3.01 g, 65%). $^1\text{H-NMR}$ (MeOD- D_4 , 500 MHz) δ 2.58 (3H, s), 7.65 (1H, s), 8.18 (1H, s), 8.24 (1H, s), 9.93 (1H, s). MS m/e 161.06 ($\text{M}+\text{H}$) $^{+}$.

1b

Acquisition Time (sec)	3.2768	Comment	7-methylindazolealdehyde proton_d MeOD v chenling 41
Date	09 Jan 2006 18:05:41		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\CwingBruker500\2006_data\data\chenling\nmr\7-methylindazolealdehyde\10\7-methylindazolealdehyde_10.jdx		
Frequency (MHz)	500.03	Nucleus	1H
Number of Transients	16	Origin	7-methylindazolealdehyde
Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	MeOD
Spectrum Offset (Hz)	4000.3115	Sweep Width (Hz)	10000.00
Temperature (degree C)	27.000

Protection of indazoles using NaH/SEM-Cl in THF.**1-((2-(Trimethylsilyl)ethoxy)methyl)-1H-indazole (2a)****and 2-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (3a).**

To an oven-dried flask was charged indazole **1a** (121 mg, 1.03 mmol) and powdered NaH (95%, 50 mg, 1.2 equiv.). Anhydrous THF (10 mL) was slowly introduced via syringe under nitrogen. After the mixture was stirred for 5 min, SEM-Cl (0.22 mL, 1.2 equiv.) was added via syringe. The mixture was left stirring overnight (16 h). The reaction mixture was diluted with ethyl acetate and quenched with 0.5 N NaOH. The layers were separated and the organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (linear gradient: 0-50%, ethyl acetate/hexanes) to afford 147 mg (58% yield) of **2a** and 20 mg (8% yield) of **3a** as colorless oils. Structures of **2a** and **3a** were assigned unequivocally by NOE studies.

2a: NOE (0.5%) between methylene group of SEM and 7-H; ¹H NMR (400 MHz, CDCl₃) δ 8.01(1 H, s), 7.73 (1 H, d, J = 8.8 Hz), 7.58 (1 H, d, J = 9.2 Hz), 7.40 (1 H, t, J = 8.4 Hz), 7.18 (1 H, t, J = 8.0 Hz), 5.735 (2 H, s), 3.55 (2 H, t, J = 8.0 Hz), 0.88 (2 H, t, J = 8.0 Hz), 0.02 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 139.8, 134.0, 126.7, 124.8, 121.3, 121.0, 109.7, 77.7, 66.4, 17.8, -1.2; HRMS m/e 249.1435 (M + H)⁺, calcd. 249.1423.

3a: NOE (0.5%) between methylene group of SEM and 3-H; analytical data was the same as reported in the experimental section of the paper.

2a

Acquisition Time (sec)	4.0894	Comment	57557-044-1 proton1f_d
Date	26 Jan 2004 15:36:54		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-044-1\30\57557-044-1_30.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5366	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

2a

Acquisition Time (sec)	1.2976	Comment	57557-044-1 c13_d
Date	26 Jan 2004 16:21:17		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-044-1\40\57557-044-1_40.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11069.1318	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

2a - NOE experiment

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Acquisition Time (sec)	4.0894	Comment	57557-044-1 selnogg_d
Date	26 Jan 2004 16:27:08		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\DwingBruker400\2004\data\chenling\nmr\57557-044-1\41\57557-044-1_41.jdx		
Frequency (MHz)	400.13	Nucleus	1H
Origin	CDCI3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Sweep Width (Hz)	8012.82	Temperature (degree C)	27.000
		Number of Transients	64
		Owner	v
		Spectrum Offset (Hz)	3201.0972

No.	(ppm)	Value	Absolute Value
1	[5.46 .. 6.14]	100.000	7.08560e+9
2	[7.45 .. 7.78]	-0.458	-3.24245e+7

No	Color	Structure	Visible
1			True

3a

Acquisition Time (sec)	4.0894	Comment	57557-045-1_proton1f_d		
Date	16 Jan 2004 14:52:15				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-045-1\10\57557-045-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	CDCI3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	3187.5366	Sweep Width (Hz)	8012.82	Temperature (degree C)	27.000

3a

Acquisition Time (sec)	1.2976	Comment	57557-045-1 c13_d		
Date	16 Jan 2004 14:59:54				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-045-1\11\57557-045-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	CDCI3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	11069.1318	Sweep Width (Hz)	25252.53	Temperature (degree C)	27.000

3a - NOE experiment

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luogu

Acquisition Time (sec)	4.0894	Comment	57557-045-1 selnogg_d
Date	16 Jan 2004 15:16:21		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\DwingBruker400\2004\data\chenling\nmr\57557-045-1\20\57557-045-1_20.jdx		
Frequency (MHz)	400.13	Nucleus	1H
Origin	CDCI3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Sweep Width (Hz)	8012.82	Temperature (degree C)	27.000
		Number of Transients	64
		Owner	v
		Spectrum Offset (Hz)	3201.0972

No.	(ppm)	Value	Absolute Value
1	[5.49 .. 5.99]	100.000	6.63464e+9
2	[8.02 .. 8.22]	-0.491	-3.26045e+7

No	Color	Structure	Visible
1			True

7-Methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole-5-carbaldehyde (2b)
 and **7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole-5-carbaldehyde (3b)**.

To an oven-dried flask was charged 7-methylindazole-5-carboxaldehyde **1b** (712 mg, 4.45 mmol) and powdered NaH (95%, 135 mg, 5.34 mmol, 1.2 equiv.). Anhydrous THF (10 mL) was slowly introduced via syringe under nitrogen. After the mixture was stirred for 5 min, SEM-Cl (0.83 mL, 1.05 equiv.) was added via syringe. The mixture was left stirring overnight (16 h). The reaction mixture was diluted with ethyl acetate and quenched with 0.5 N NaOH. The layers were separated and the organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (linear gradient: 5-40%, ethyl acetate/hexanes) to afford 0.50 g (39% yield) of **2b** as a light yellow oil and 0.35 g (27% yield) of **3b** as an off-white solid. Structures of **2b** and **3b** were assigned unequivocally by NOE studies.

2b: NOE (2.7%) between 7-CH₃ and methylene group of SEM; R_f = 0.39 (20% ethyl acetate/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 9.84 (1 H, s), 7.98 (1 H, s), 7.90 (1 H, s), 7.53 (1 H, s), 5.71 (2 H, s), 3.43 (2 H, br.), 2.64 (3 H, s), 0.74 (2 H, br.), -0.20 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 191.2, 141.5, 135.6, 131.2, 126.7, 125.4, 124.8, 122.3, 79.4, 66.2, 18.6, 17.6, -1.5; MS m/e 291.16 (M + H)⁺.

3b: NOE (1.1%) between 3-H and methylene group of SEM; R_f = 0.23 (20% ethyl acetate/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 9.85 (1 H, s), 8.26 (1 H, s), 7.98 (1 H, s), 7.47 (1 H, s), 5.68 (2 H, s), 3.62 (2 H, t, J = 8.0 Hz), 2.55 (3 H, s), 0.88 (2 H, t, J = 8.0 Hz), -0.10 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 191.8, 151.1, 132.2, 129.2, 127.7, 126.1, 121.8, 121.2, 81.9, 67.7, 17.8, 17.0, -1.5; HRMS m/e 291.1533 (M + H)⁺, calcd. 291.1529.

2b

Acquisition Time (sec)	4.0894	Comment	55624-141-1 proton_d
Date	08 Sep 2003 18:13:18		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2003\data\luogu\nmr\55624-141-1\10\55624-141-1_10.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

2b

Acquisition Time (sec)	1.2976	Comment	55624-141-1 c13_d
Date	08 Sep 2003 18:21:07		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2003\data\luogu\nmr\55624-141-1\11\55624-141-1_11.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11069.1318	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

2b- NOE experiment

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Acquisition Time (sec)	4.0894	Comment	55624-141-1 selnogp_d		
Date	08 Sep 2003 21:11:44				
File Name	C:\Documents and Settings\luogu\My Documents\My Documents\publications\Indazoles\55624-141-1_40.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	64
Origin	CDCI3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	3201.0972	Sweep Width (Hz)	8012.82	Temperature (degree C)	27.000

No.	(ppm)	Value	Absolute Value	No	Color	Structure	Visible
1	[2.58 .. 2.81]	-2.675	-4.06966e+8	1			True
2	[5.52 .. 6.09]	100.000	1.52157e+10				

3b

Acquisition Time (sec)	4.0894	Comment	55624-141-2 proton. d
Date	08 Sep 2003 18:36:18		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2003\data\luogu\nmr\55624-141-2\10\55624-141-2_10.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

3b

Acquisition Time (sec)	1.2976	Comment	55624-141-2 c13_d
Date	08 Sep 2003 18:44:47		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2003\data\luogu\nmr\55624-141-2\11\55624-141-2_11.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11069.1318	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

3b- NOE experiment

5/1/2006 10:14 AM
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Acquisition Time (sec)	4.0894	Comment	55624-141-2 selnogp_d
Date	08 Sep 2003 21:58:55		
File Name	C:\Documents and Settings\luogu\My Documents\My Documents\publications\Indazoles\55624-141-2_40.jdx		
Frequency (MHz)	400.13	Nucleus	1H
Origin	CDCI3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3201.0972	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

No.	(ppm)	Value	Absolute Value
1	[5.46 .. 5.96]	99.999	8.69008e+9
2	[8.18 .. 8.42]	-1.142	-9.92611e+7

No	Color	Structure	Visible
1			True

Regioselective protection of indazoles using dicyclohexylmethyl amine/SEM-Cl in THF.**2-((2-(Trimethylsilyl)ethoxy)methyl)-1H-indazole (3a).**

General procedure A. See the Experimental Section in the paper.

7-Methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole-5-carbaldehyde (3b).

According to general procedure A, 7-methylindazole-5-carbaldehyde **1b** (185 mg, 1.15 mmol) was allowed to react with SEM-Cl (0.29 mL) to afford, after purification, 277 mg (87% yield) of **3b** as a white solid. Analytical data of **3a** matched these of **3a** previously prepared by NaH/SEM-Cl/THF treatment..

6-Bromo-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (3c).

According to general procedure A, 6-bromoindazole (**1c**) (153 mg, 0.78 mmol) was allowed to react with SEM-Cl for 3 h to afford, after purification, 158 mg (62% yield) of **3c** as a brown oil. ^1H NMR (400 MHz, CDCl_3) δ 8.07 (1 H, s), 7.89 (1 H, s), 7.54 (1 H, d, J = 8.8 Hz), 7.15 (1 H, d, J = 9.2 Hz), 5.68 (2 H, s), 3.60 (2 H, t, J = 8.0 Hz), 0.92 (2 H, t, J = 8.0 Hz), -0.43 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 149.5, 126.0, 123.1, 121.9, 120.8, 120.5, 120.4, 81.9, 67.7, 17.8, -1.4; HRMS m/e 327.0531 ($M + H$) $^+$, calcd 327.0528.

3c

Acquisition Time (sec)	3.9715	Comment	57557-090-1 proton, d CDCl3 v chenling 57		
Date	15 Mar 2004 13:58:46				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-090-1\10\57557-090-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-090-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	24.460

3c

Acquisition Time (sec)	1.2976	Comment	57557-090-1 c13_d CDCI3 v chenling 57		
Date	15 Mar 2004 14:06:32				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-090-1\11\57557-090-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-090-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	26.160

5-Bromo-7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (3d).

According to general procedure A, 5-bromo-7-methyl-indazole (**1d**) (202 mg, 0.96 mmol) was allowed to react with SEM-Cl for 3 h to afford, after purification, 263 mg (81% yield) of **3d**. ^1H NMR (400 MHz, CDCl_3) δ 8.01 (1 H, s), 7.66 (1 H, s), 7.12 (1 H, s), 5.69 (2 H, s), 3.61 (2 H, t, $J = 8.0$ Hz), 2.59 (3 H, s), 0.92 (2 H, t, $J = 8.0$ Hz), -0.04 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 147.7, 130.3, 128.8, 123.0, 122.2, 120.0, 115.7, 81.8, 67.5, 17.8, 16.9, -1.4; HRMS m/e 341.0696 ($\text{M} + \text{H}$) $^+$, calcd: 341.0607.

3d

Acquisition Time (sec)	3.9715	Comment	57557-096-1 proton, d CDCl3 v chenling 48		
Date	23 Mar 2004 14:02:08				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-096-1\10\57557-096-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-096-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	23.960

3d

Acquisition Time (sec)	1.2976	Comment	57557-096-1 c13_d CDCI3 v chenling 48
Date	23 Mar 2004 14:09:54		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-096-1\11\57557-096-1_11.idx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	57557-096-1	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.760
		Number of Transients	128
		Owner	chenling
		Spectrum Offset (Hz)	11030.1299

Ethyl 2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole-5-carboxylate (3e**).**

According to general procedure A, ethyl indazole-5-carboxylate (**1e**) (175 mg, 0.92 mmol) was allowed to react with SEM-Cl for 3 h to afford, after purification, 261 mg (89% yield) of **3e** as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 8.52 (1 H, s), 8.23 (1 H, s), 7.90 (1 H, d, $J = 9.2$ Hz), 7.70 (1 H, d, $J = 9.2$ Hz), 5.72 (2 H, s), 4.38 (2 H, q, $J = 6.8$ Hz), 3.62 (2 H, t, $J = 8.0$ Hz), 1.38 (3 H, t, $J = 7.2$ Hz), 0.92 (2 H, t, $J = 8.0$ Hz), 0.00 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 166.9, 150.0, 126.2, 125.1, 125.0, 124.7, 121.6, 117.8, 82.0, 67.8, 60.9, 17.9, 14.4, -1.5; HRMS m/e 321.1637 ($\text{M} + \text{H}$) $^+$, calcd: 321.1635.

3e

Acquisition Time (sec)	3.9715	Comment	57557-089-1 proton d CDCl3 v chenling 14		
Date	12 Mar 2004 14:07:21				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-089-1\10\57557-089-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-089-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	24.760

3e

Acquisition Time (sec)	1.2976	Comment	57557-089-1 c13_d CDCI3 v chenling 14		
Date	12 Mar 2004 14:15:07				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-089-1\11\57557-089-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-089-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	26.460

6-Nitro-2-((2-(trimethylsilyl)ethoxy)methyl)-2*H*-indazole (3f).

According to general procedure A, 6-nitroindazole (**1f**) (162 mg, 1.0 mmol) was allowed to react with SEM-Cl for 20 h to afford, after purification, 229 mg (78% yield) of **3f** as a yellow wax. ^1H NMR (400 MHz, CDCl_3) δ 8.71 (1 H, s), 8.23 (1 H, s), 7.90 (1 H, d, $J = 9.2$ Hz), 7.78 (1 H, d, $J = 9.2$ Hz), 5.77 (2 H, s), 3.64 (2 H, t, $J = 8.4$ Hz), 0.94 (2 H, t, $J = 8.4$ Hz), 0.00 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 146.9, 146.8, 124.5, 123.4, 121.9, 116.2, 116.1, 82.5, 68.1, 17.9, -1.5; HRMS m/e 294.1279 ($\text{M} + \text{H}$) $^+$, calcd: 294.1274.

3f

Acquisition Time (sec)	3.9715	Comment	57557-103-1 proton, d CDCl3 v chenling 18		
Date	25 Mar 2004 14:53:45				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-103-1\10\57557-103-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-103-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	24.260

3f

Acquisition Time (sec)	1.2976	Comment	57557-103-1 c13_d CDCl3 v chenling 18		
Date	25 Mar 2004 15:01:31				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-103-1\11\57557-103-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-103-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.960

5-Nitro-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (3g).

According to general procedure A, 5-nitroindazole (**1g**) (169 mg, 1.0 mmol) was allowed to react with SEM-Cl for 20 h to afford, after purification, 228 mg (75% yield) of **3g** as a light yellow wax. ^1H NMR (400 MHz, CDCl_3) δ 8.73 (1 H, s), 8.39 (1 H, s), 8.06 (1 H, d, $J = 9.6$ Hz), 7.75 (1 H, d, $J = 9.6$ Hz), 5.74 (2 H, s), 3.64 (2 H, t, $J = 8.4$ Hz), 0.93 (2 H, t, $J = 8.4$ Hz), -0.05 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 149.7, 143.5, 126.8, 120.6, 120.4, 119.8, 119.0, 82.3, 68.2, 17.8, -1.2; HRMS m/e 294.1276 ($\text{M} + \text{H}$) $^+$, calcd:296.1274.

3g

Acquisition Time (sec)	3.9715	Comment	57557-104-1 proton, d CDCl3 v chenling 55		
Date	26 Mar 2004 13:39:59				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-104-1\10\57557-104-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-104-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	23.960

3g

Acquisition Time (sec)	1.2976	Comment	57557-104-1 c13_d CDCl3 v chenling 55		
Date	26 Mar 2004 13:47:47				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-104-1\1\57557-104-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-104-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.660

7-Nitro-2-((2-(trimethylsilyl)ethoxy)methyl)-2*H*-indazole (3h).

According to general procedure A, 7-nitroindazole (**1h**) (342 mg, 2.1 mmol) was allowed to react with SEM-Cl for 20 h to afford, after purification, 342 mg (56% yield) of **3h** as an orange solid, 84 mg (14%) of the isomer of **3h** as a brown oil, and 98 mg (29%) of recovered **1h**. Structures of both isomers were unequivocally assigned by GHMBC NMR studies.

3h: ^1H NMR (400 MHz, CDCl_3) δ 8.37 (1 H, s), 8.25 (1 H, d, $J = 8.4\text{ Hz}$), 8.03 (1 H, d, $J = 8.4\text{ Hz}$), 7.13 (1 H, t, $J = 8.4\text{ Hz}$), 5.79 (2 H, s), 3.64 (2 H, t, $J = 8.4\text{ Hz}$), 0.89 (2 H, t, $J = 8.4\text{ Hz}$), -0.11 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 140.5, 137.9, 129.3, 125.7, 125.5, 124.8, 120.4, 82.5, 68.1, 17.9, -1.5; HRMS m/e 294.1288 ($\text{M} + \text{H}$) $^+$, calcd: 294.1274.

Isomer of **3h** (7-nitro-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indazole): ^1H NMR (400 MHz, CDCl_3) δ 8.16 (1 H, s), 8.08 (1 H, d, $J = 8.8\text{ Hz}$), 8.03 (1 H, d, $J = 8.8\text{ Hz}$), 7.26 (1 H, t, $J = 8.0\text{ Hz}$), 5.96 (2 H, s), 3.22 (2 H, t, $J = 8.0\text{ Hz}$), 0.72 (2 H, t, $J = 8.0\text{ Hz}$), -0.16 (9 H, s). ^{13}C NMR (100.6 MHz, CDCl_3) δ 136.2, 134.7, 130.0, 129.5, 127.5, 124.5, 120.7, 81.2, 66.0, 17.6, -1.6; HRMS m/e 294.1285 ($\text{M} + \text{H}$) $^+$, calcd: 294.1274.

3h

Acquisition Time (sec)	3.9715	Comment	61322-135-1 proton, d CDCl3 v chenling 2		
Date	08 Dec 2005 14:49:22				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2005\data\chenling\nmr\61322-135-1\30\61322-135-1_30.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	61322-135-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	25.160

3h

Acquisition Time (sec)	1.2976	Comment 61322-135-1 c13_d CDCl3 v chenling 117			
Date	08 Dec 2005 14:11:43				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2005\data\chenling\nmr\61322-135-1\22\61322-135-1_22.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	61322-135-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.160

isomer of 3h

Acquisition Time (sec)	3.9715	Comment	61322-135-2 protonlf d CDCl3 v chenling 61		
Date	07 Dec 2005 12:08:49				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2005\data\chenling\nmr\61322-135-2\10\61322-135-2_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	61322-135-2	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	25.160

isomer of 3h

Acquisition Time (sec)	1.2976	Comment	61322-135-2 c13_d CDCI3 v chenling 61		
Date	07 Dec 2005 15:25:51				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2005\data\chenling\nmr\61322-135-2\11\61322-135-2_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	61322-135-2	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.160

3-Chloro-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (3i).

According to general procedure A, 3-chloroindazole (**1i**) (324 mg, 2.1 mmol) was allowed to react with SEM-Cl for 72 h to afford, after purification, 485 mg (81% yield) of **3i** as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.66 (1 H, d, $J = 8.8$ Hz), 7.55 (1 H, d, $J = 8.8$ Hz), 7.29 (1 H, t, $J = 8.8$ Hz), 7.10 (1 H, t, $J = 8.8$ Hz), 5.75 (2 H, s), 3.67 (2 H, t, $J = 8.4$ Hz), 0.92 (2 H, t, $J = 8.4$ Hz), 0.01 (9 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 148.1, 127.4, 122.7, 119.9, 119.3, 118.9, 118.4, 78.7, 67.4, 18.0, -1.2; HRMS m/e 283.1033 ($\text{M} + \text{H}$) $^+$, calcd: 283.1033.

3i

Acquisition Time (sec)	4.0894	Comment	57557-055-1 proton_d
Date	11 Feb 2004 14:18:21		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-055-1\10\57557-055-1_10.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

3i

Acquisition Time (sec)	1.2976	Comment	57557-055-1 c13_d		
Date	11 Feb 2004 14:25:59				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-055-1\11\57557-055-1_11.idx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	CDCI3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53	Temperature (degree C)	27.000

Acylation of indazoles.**2-((2-(Trimethylsilyl)ethoxy)methyl)-1H-indazole (8).**

Procedure for preparation of **8**: To the solution of anhydrous CH_2Cl_2 (10 mL) solution of indazole (146 mg, 1.2 mmol) and triethylamine (0.19 mL, 1.1 eq, 1.4 mmol) was added phenylacetylchloride (0.18 mL, 1.1 eq, 1.4 mmol) at 0 °C under N_2 . The reaction was stirred overnight. The reaction mixture was washed by 1N NaOH (1 x 10 mL) and water (2 x 10 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*. Flash column chromatography by ethyl acetate/hexane from 0-20 % gave the desired product (275 mg, 94%). ^1H NMR (400 MHz, CDCl_3) δ 8.47 (1 H, d, $J = 8.4$ Hz), 8.17 (1 H, s), 7.72 (1 H, d, $J = 8.0$ Hz), 7.55 (1 H, t, $J = 8.4$ Hz), 7.47 - 7.29 (6 H, m), 4.56 (2 H, s); ^{13}C NMR (100.6 MHz, CDCl_3) δ 171.5, 140.0, 139.3, 134.1, 129.9, 129.5, 128.8, 128.7, 127.2, 127.1, 126.5, 124.6, 120.9, 115.7 , 41.7. The position of the acyl group was assigned by GHMBC NMR studies.

8

Acquisition Time (sec)	4.0894	Comment	57557-081-1 protonlf_d
Date	05 Mar 2004 19:25:37		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-081-1\10\57557-081-1_10.jdx		
Frequency (MHz)	400.13	Nucleus	1H
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5366	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

8

Acquisition Time (sec)	1.2976	Comment	57557-081-1 c13_d CDC13 v chenling 4
Date	09 Mar 2004 13:12:52		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\400a\2004\data\chenling\nmr\57557-081-1\40\57557-081-1_40.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	57557-081-1	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Sweep Width (Hz)	25252.53	Temperature (degree C)	23.660
		Number of Transients	128
		Owner	chenling
		Spectrum Offset (Hz)	11030.1299

Protection of indazole using Cyhex₂NMe/BOM-Cl in THF.**1-(Benzyloxymethyl)-2*H*-indazole (**9**) and 2-(benzyloxymethyl)-2*H*-indazole (**10**).**

According to general procedure A, started from indazole (116 mg, 1.0 mmol) to give **9** (169 mg, 72%) and **10** (58 mg, 25%) as colorless oils. The structures of **9** and **10** were unequivocally assigned by NOE and GHMBC NMR studies.

9: ¹H NMR (400 MHz, CDCl₃) δ 8.12 (1 H, s), 7.77 (1 H, d, J = 8.0 Hz), 7.79 (1 H, d, J = 8.0 Hz), 7.33 (6 H, m), 7.12 (1 H, m), 5.79 (2 H, s), 4.58 (2 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 149.0, 136.5, 128.5, 128.1, 127.6, 127.0, 126.6, 123.0, 123.3, 120.6, 118.0, 81.2, 65.2; HRMS m/e 239.1190(M + H)⁺, calcd: 239.1185.

10: ¹H NMR (400 MHz, CDCl₃) δ 8.06 (1 H, s), 7.76 (1 H, d, J = 8.0 Hz), 7.58 (1 H, d, J = 8.4 Hz), 7.44 (1 H, t, J = 6.4 Hz), 7.33 - 7.20 (6 H, m), 5.83 (2 H, s), 4.51 (2 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 139.9, 137.1, 134.4, 128.4, 128.0, 127.9, 126.9, 124.9, 121.4, 121.1, 109.7, 70.4, 77.4; HRMS m/e 239.1190 (M + H)⁺, calcd: 239.1184.

9

Acquisition Time (sec)	4.0894	Comment	57557-067-2 proton_d	
Date	20 Feb 2004 14:48:06			
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-067-2\10\57557-067-2_10.jdx			
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients 16
Origin	CDCI3	Original Points Count	32768	Owner v
Points Count	32768	Solvent	CHLOROFORM-D	
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82	Temperature (degree C) 27.000

9

Acquisition Time (sec)	1.2976	Comment	57557-067-2 c13_d
Date	20 Feb 2004 14:55:46		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-067-2\11\57557-067-2_11.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

10

Acquisition Time (sec)	4.0894	Comment	57557-067-1 proton.d		
Date	23 Feb 2004 14:21:03				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-067-1\30\57557-067-1_30.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	CDCl3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82	Temperature (degree C)	27.000

10

Acquisition Time (sec)	1.2976	Comment	57557-067-1 c13_d
Date	23 Feb 2004 14:28:44		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-067-1\31\57557-067-1_31.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

Selective lithiation of 1a and subsequent electrophilic reactions.**Phenyl(2-((2-(trimethylsilyl)ethoxy)methyl)-2*H*-indazol-3-yl)methanol (12a).**

General procedure B. To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indazole (**3a**) (99 mg, 0.4 mmol) in THF (2 mL) at -65 °C under nitrogen was added *n*-BuLi (2.5 M in hexanes, 0.18 mL, 0.44 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and re-cooled to -70 °C. Benzaldehyde (0.045 mL, 0.44 mmol, 1.1 equiv.) was added via syringe and the yellow color disappeared. After 30 min., the reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and ethyl acetate. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The crude product was purified using silica gel column chromatography (step gradient up to 1:1 hexane/ethyl acetate) to afford 125 mg (89% yield) of **12a** as a colorless oil. *R*_f = 0.15 (20% ethyl acetate/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.65 (1 H, d, *J* = 8.8 Hz), 7.44 – 7.20 (7 H, m), 6.99 (1 H, t, *J* = 7.6 Hz), 6.45 (1 H, s), 5.61 (1 H, d, *J* = 10.8 Hz), 5.52 (1 H, d, *J* = 10.8 Hz), 4.10 (1 H, br.), 3.52 (2 H, t, *J* = 8.0 Hz), 0.95 – 0.75 (2 H, m), -0.06 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 147.6, 140.5, 136.8, 128.6, 128.0, 126.7, 126.1, 122.3, 121.4, 120.5, 117.8, 80.2, 67.4, 67.3, 17.8, -1.5; HRMS *m/e* 355.1852 (*M* + *H*)⁺, calcd: 355.1842.

12a

Acquisition Time (sec)	4.0894	Comment	57555-081 proton.d	
Date	11 Feb 2004 20:15:47			
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-081\10\57555-081_10.jdx			
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients 16
Origin	CDCl3	Original Points Count	32768	Owner v
Points Count	32768	Solvent	CHLOROFORM-D	
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82	Temperature (degree C) 27.000

12a

Acquisition Time (sec)	1.2976	Comment	57555-081 c13 d	Date	11 Feb 2004 20:23:22
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-081\11\57555-081_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	CDCI3	Original Points Count	32768	Owner	v
Points Count	32768	Solvent	CHLOROFORM-D		
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53	Temperature (degree C)	27.000

Phenyl(2-((2-(trimethylsilyl)ethoxy)methyl)-2*H*-indazol-3-yl)methanone (12b).

According to the general procedure B, started from **3a** (86 mg) to give **12b** (121 mg, 99%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.87-7.82 (3 H, m), 7.65 -7.08 (6 H, m), 6.15 (2 H, s), 3.65 (2 H, t, J = 8.0 Hz), 0.89 (2 H, t, J = 8.0 Hz), 0.07 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 186.1, 147.6, 138.4, 133.3, 131.5, 129.8, 128.6, 126.5, 125.0, 123.7, 120.8, 118.9, 81.0, 67.4, 17.8, -1.5; HRMS m/e 351.1690 (M + H)⁺, calcd: 351.1685.

12b

Acquisition Time (sec)	4.0894	Comment	57557-077-1 proton_d
Date	01 Mar 2004 15:17:53		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-077-1\10\57557-077-1_10.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

12b

Acquisition Time (sec)	1.2976	Comment	57557-077-1 c13_d
Date	01 Mar 2004 15:25:33		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-077-1\11\57557-077-1_11.jdx		
Frequency (MHz)	100.62	Nucleus	¹³ C
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

***N*-Phenyl-2-((2-(trimethylsilyl)ethoxy)methyl)-2*H*-indazole-3-carboxamide (12c).**

Procedure: See the Experimental Section in the paper.

12c

Acquisition Time (sec)	4.0894	Comment	57555-091-1 proton_d
Date	02 Mar 2004 15:05:53		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-091-1\10\57555-091-1_10.jdx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

12c

Acquisition Time (sec)	1.2976	Comment	57555-091-1 c13_d
Date	02 Mar 2004 15:13:33		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-091-1\11\57555-091-1_11.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

3-(Phenylthio)-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (12d).

To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (**3a**) (94 mg, 0.38 mmol) in THF (2 mL) at -70 °C under nitrogen was added n-BuLi (2.5 M in hexanes, 0.17 mL, 0.42 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and re-cooled to -70 °C. Phenyl disulfide (91 mg, 0.42 mmol, 1.1 equiv.) was added in one portion. Cooling bath was removed and after 30 min, the reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and ethyl acetate. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (step gradient up to 1:1 hexane/ethyl acetate) with contamination of thiophenol. The recovered crude product was further purified by methylene chloride/hexane system (1:1 up to 1:0) to afford 114 mg (85% yield) of **12d** as a colorless oil. R_f = 0.56 (20% ethyl acetate/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.81 (1 H, d, J = 8.0 Hz), 7.66 (1 H, J = 8.0 Hz), 7.50 – 7.30 (1 H, m), 7.22 – 7.09 (5 H, m), 7.09 – 7.02 (2 H, m), 5.89 (2 H, s), 3.59 (2 H, t, J = 9.0 Hz), 0.82 (2 H, t, J = 9.0 Hz), -0.07 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 148.6, 135.6, 129.2, 127.3, 127.0, 126.5, 123.6, 120.2, 118.8, 79.1, 67.3, 17.8, -1.5; HRMS *m/e* 357.1470 (M + H)⁺, calcd: 357.1457.

12d

Acquisition Time (sec)	4.0894	Comment	57555-091-2 proton. d
Date	02 Mar 2004 15:27:46		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-091-2\10\57555-091-2_10.idx		
Frequency (MHz)	400.13	Nucleus	¹ H
Origin	CDCl ₃	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	3187.5293	Sweep Width (Hz)	8012.82
		Temperature (degree C)	27.000

12d

Acquisition Time (sec)	1.2976	Comment	57555-091-2 c13_d
Date	02 Mar 2004 15:35:25		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-091-2\11\57555-091-2_11.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

3-Bromo-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (12e).

To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (**3a**) (76 mg, 0.31 mmol) in THF (2 mL) at -65 °C under nitrogen was added n-BuLi (2.5 M in hexanes, 0.13 mL, 0.34 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and recooled to -70 °C. N-bromosuccinamide (60 mg, 0.34 mmol, 1.1 equiv.) was added in one portion and the yellow color turned to reddish. After 30 min., the reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and ethyl acetate. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (step gradient up to 1:1 hexane/ethyl acetate) to afford 72 mg (72% yield) of **12e** as a colorless oil and 20 mg of recovered **3a** (98% yield of **12e**). ¹H NMR (400 MHz, CDCl₃) δ 7.68 (1 H, d, J = 8.8 Hz), 7.52 (1 H, d, J = 8.4 Hz), 7.36 – 7.27 (1 H, m), 7.16 – 7.08 (1 H, m), 5.79 (2 H, s), 3.66 (2 H, t, J = 8.0 Hz), 0.92 (2 H, t, J = 8.0 Hz), -0.06 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 148.7, 127.4, 122.9, 122.3, 119.6, 118.4, 106.4, 79.8, 67.4, 17.7, -1.5; MS m/e 349.66 (M + H)⁺.

12e

Acquisition Time (sec)	4.0894	Comment	57555-094-1 proton1f_d	
Date	03 Mar 2004 15:27:07			
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-094-1\10\57555-094-1_10.jdx			
Frequency (MHz)	400.13	Nucleus	¹ H	Number of Transients 16
Origin	CDCl ₃	Original Points Count	32768	Owner v
Points Count	32768	Solvent	CHLOROFORM-D	
Spectrum Offset (Hz)	3187.5366	Sweep Width (Hz)	8012.82	Temperature (degree C) 27.000

12e

Acquisition Time (sec)	1.2976	Comment	57555-094-1 c13_d
Date	03 Mar 2004 17:03:37		
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-094-1\21\57555-094-1_21.jdx		
Frequency (MHz)	100.62	Nucleus	13C
Origin	CDCl3	Original Points Count	32768
Points Count	32768	Solvent	CHLOROFORM-D
Spectrum Offset (Hz)	11026.3857	Sweep Width (Hz)	25252.53
		Temperature (degree C)	27.000

Ethyl 2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole-3-carboxylate (12f**).**

To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (**3a**) (76 mg, 0.31 mmol) in THF (2 mL) at -65 °C under nitrogen was added n-BuLi (2.5 M in hexanes, 0.14 mL, 0.34 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and re-cooled to -70 °C. Ethyl cyanofomate (0.033 mL, 0.34 mmol, 1.1 equiv.) was added via syringe. After 30 min., the reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and ethyl acetate. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (step gradient from 20% up to 100% methylene chloride in hexane) to afford 75 mg (77% yield) of **12f** as a colorless oil and 14 mg of recovered **3a** (91% yield of **12f**). ¹H NMR (400 MHz, CDCl₃) δ 8.04 (1 H, d, J = 8.4 Hz), 7.79 (1 H, d, J = 8.8 Hz), 7.39 – 7.25 (2 H, m), 6.18 (2 H, s), 4.49 (2 H, q, J = 7.1 Hz), 3.64 (2 H, t, J = 8.2 Hz), 1.48 (3 H, t, J = 7.2 Hz), 0.91 (2 H, t, J = 8.4 Hz), -0.08 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 159.9, 147.7, 126.8, 125.4, 124.3, 123.9, 121.8, 118.8, 81.0, 67.3, 61.2, 17.8, 14.4, -1.5; MS m/e 342.75 (M + Na)⁺.

12f

Acquisition Time (sec)	3.9715	Comment	57555-094-2 proton. d CDCl3 v luogu 28	
Date	19 Mar 2004 18:10:38			
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-094-2\10\57555-094-2_10.jdx			
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients 16
Origin	57555-094-2	Original Points Count	32768	Owner luogu
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz) 2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	24.760

12f

Acquisition Time (sec)	1.2976	Comment	57555-094-2 c13_d CDCl3 v luogu 28	
Date	19 Mar 2004 18:18:23			
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\luogu\nmr\57555-094-2\11\57555-094-2_11.jdx			
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients 128
Origin	57555-094-2	Original Points Count	32768	Owner luogu
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz) 11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	26.460

3-Methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (12g).

To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indazole (**3a**) (91 mg, 0.32 mmol) in THF (3 mL) at -78 °C under nitrogen was added *n*-BuLi (2.5 M in hexanes, 0.16 mL, 0.35 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and re-cooled to -78 °C. CH₃I (0.046 mL, 0.35 mmol, 2.0 equiv.) was added via syringe. Cooling bath was removed and after 5 min and the reaction was left to room temperature for 1 hour. The reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and methylene chloride. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (linear gradient up to 1:4 hexane/ethyl acetate) to give **12g** (86 mg, 90%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.64 (1 H, d, *J* = 8.8 Hz), 7.56 (1 H, d, *J* = 8.6 Hz), 7.25 (1 H, t, *J* = 8.8 Hz), 7.02 (1 H, t, *J* = 8.8 Hz), 5.70 (2 H, s), 3.59 (2 H, t, *J* = 8.4 Hz), 2.67 (3 H, s), 0.88 (2 H, t, *J* = 8.4 Hz), -0.07 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 147.8, 132.1, 126.5, 121.6, 120.8, 120.0, 117.7, 79.4, 66.9, 17.8, 9.6, -1.4; HRMS *m/e* 263.1570 (*M* + *H*)⁺, calcd: 263.1590.

12g

Acquisition Time (sec)	3.9715	Comment	57557-109-1 proton, d CDCl3 v chenling 75		
Date	01 Apr 2004 13:57:56				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-109-1\10\57557-109-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-109-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	23.860

12g

Acquisition Time (sec)	1.2976	Comment	57557-109-1 c13_d CDCI3 v chenling 75		
Date	01 Apr 2004 14:05:42				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-109-1\11\57557-109-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-109-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.660

3-(Trimethylsilyl)-2-((2-(trimethylsilyl)ethoxy)methyl)-2H-indazole (12h).

To a solution of 2-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole (**3a**) (86 mg, 0.32 mmol) in THF (3 mL) at -78 °C under nitrogen was added n-BuLi (2.5 M in hexanes, 0.15 mL, 0.35 mmol, 1.1 equiv.) dropwise via syringe. After the resulting bright yellow solution was stirred at the same temperature for 10 min, it was briefly warmed up to room temperature for 5 min and re-cooled to -78 °C. TMSCl (0.049 mL, 0.35 mmol, 1.1 equiv.) was added via syringe. Cooling bath was removed and after 5 min and the reaction was lift to room temperature for 1 hour. The reaction was quenched by NH₄Cl solution. THF was stripped off and the residue was partitioned between water and methylene chloride. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel column chromatography (linear gradient up to 1:4 hexane/ethyl acetate) to give **12h** (89 mg, 80%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (1 H, d, J = 8.0 Hz), 7.78 (1 H, d, J = 8.0 Hz), 5.79 (2 H, s), 3.55 (2 H, t, J = 8.0 Hz), 0.89 (2 H, t, J = 8.0 Hz), 0.51 (9 H, s), -0.06 (9 H, s); ¹³C NMR (100.6 MHz, CDCl₃) δ 148.2, 135.7, 130.4, 125.8, 121.9, 121.7, 118.2, 82.0, 66.8, 17.9, 0.24, -1.4; HRMS m/e 321.1812 (M + H)⁺, calcd: 321.1818.

12h

Acquisition Time (sec)	3.9715	Comment	57557-114-1 proton. d CDCl3 v chenling 38		
Date	05 Apr 2004 13:36:09				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-114-1\10\57557-114-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	16
Origin	57557-114-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83	Temperature (degree C)	24.260

12h

Acquisition Time (sec)	1.2976	Comment	57557-114-1 c13_d CDCI3 v chenling 38		
Date	05 Apr 2004 13:43:55				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\d400a\2004\data\chenling\nmr\57557-114-1\11\57557-114-1_11.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	128
Origin	57557-114-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53	Temperature (degree C)	25.960

***N*-Phenyl-1*H*-indazole-3-carboxamide (13).**

Procedures: See the Experimental Section in the paper.

5/2/2006 2:24 PM
luogu

Acquisition Time (sec)	3.9715	Comment			65165-098-1 protonlf_d CDCl3 v chenling 71
Date	28 Apr 2006 20:41:53				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\lDwingBruker400\2006_data\data\chenling\nmr\65165-098-1\10\65165-098-1_10.jdx				
Frequency (MHz)	400.13	Nucleus	1H	Number of Transients	32
Origin	65165-098-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	2454.8384
Sweep Width (Hz)	8250.83

No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	Value	Absolute Value	No.	Color
1	7.12	2847.0	0.1316	14	7.44	2975.2	0.1381	1	[1.44 .. 1.79]	0.590	1.66135e+9	1	
2	7.13	2854.3	0.2908	15	7.45	2982.5	0.2519	2	[7.03 .. 7.19]	1.044	2.94218e+9		
3	7.15	2861.9	0.1775	16	7.46	2983.8	0.2282	3	[7.28 .. 7.56]	5.160	1.45363e+10		
4	7.24	2898.1	1.0000	17	7.47	2989.3	0.1850	4	[7.68 .. 7.81]	2.039	5.74502e+9		
5	7.31	2924.8	0.1425	18	7.47	2990.5	0.1817	5	[8.38 .. 8.52]	0.998	2.81235e+9		
6	7.33	2931.9	0.2717	19	7.51	3005.9	0.4074	6	[8.79 .. 8.98]	0.971	2.73509e+9		
7	7.34	2938.9	0.2012	20	7.53	3014.2	0.2292	7	[10.20 .. 10.49]	0.899	2.53246e+9		
8	7.35	2939.9	0.2037	21	7.73	3092.5	0.4727						
9	7.36	2943.2	0.3412	22	7.75	3100.1	0.4426						
10	7.38	2951.5	0.4708	23	8.45	3381.1	0.3014						
11	7.39	2957.1	0.1105	24	8.47	3389.4	0.3010						
12	7.40	2959.1	0.3206	25	8.89	3556.9	0.1225						
13	7.43	2974.2	0.1358	26	10.35	4143.1	0.0409						

13

5/2/2006 2:27 PM
luogu

Acquisition Time (sec)	1.2976	Comment 65165-098-1 c13_n CDCl3 v.chenling 109			
Date	02 May 2006 03:52:09				
File Name	\\cruncher.wfd.pri.bms.com\nmrread1\lDwingBruker400\2006_data\data\chenling\nmr\65165-098-1\20\65165-098-1_20.jdx				
Frequency (MHz)	100.62	Nucleus	13C	Number of Transients	5120
Origin	65165-098-1	Original Points Count	32768	Owner	chenling
Points Count	32768	Solvent	CHLOROFORM-D	Spectrum Offset (Hz)	11030.1299
Sweep Width (Hz)	25252.53

No.	(ppm)	Height	No.	(ppm)	Height
1	76.72	0.9935	9	123.23	0.0785
2	77.04	0.9392	10	124.20	0.0848
3	77.24	0.0386	11	127.69	0.0757
4	77.35	1.0000	12	129.13	0.1548
5	109.87	0.0868	13	137.86	0.0335
6	119.82	0.1903	14	139.67	0.0206
7	122.11	0.0237	15	141.54	0.0286
8	122.75	0.0892	16	160.50	0.0305

No	Color	Structure	Visible
1			True