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OPTIONAL SYNTHESIS OF 2- OR 5-SUBSTITUTED 3-BROMOPYRROLES *VIA* BROMINE–LITHIUM EXCHANGE OF *N*-BENZENESULFONYL-2,4-DIBROMOPYRROLE

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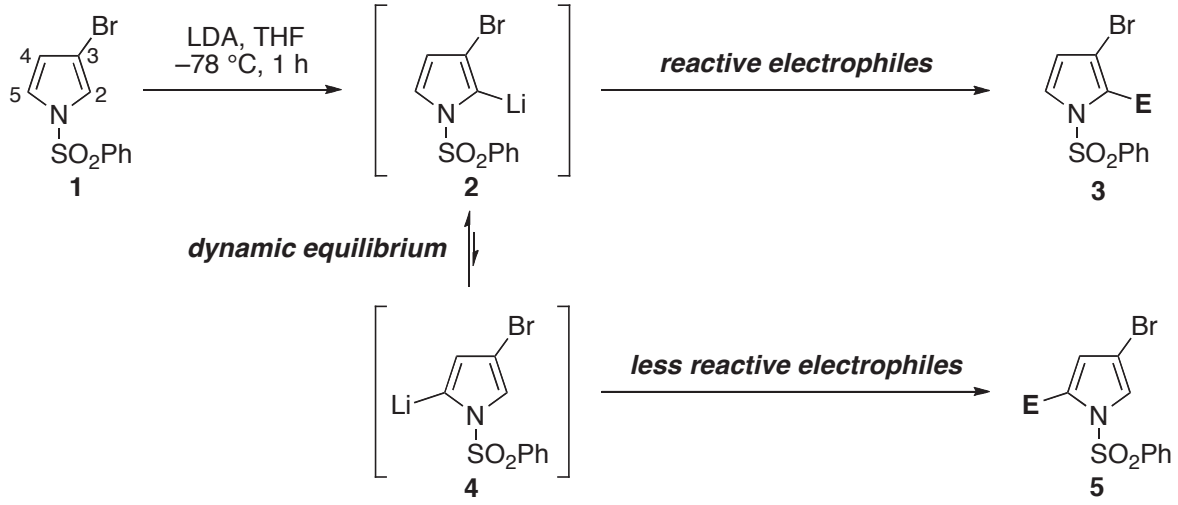
Abstract – The regioselective bromine–lithium exchange of *N*-benzenesulfonyl-2,4-dibromopyrrole (**6**) with *n*-BuLi followed by treatment with various electrophiles gave 5-substituted 3-bromopyrroles (**5**) in excellent yields. In contrast, the sequential treatment of **6** with *n*-BuLi and diisopropylamine followed by quenching with electrophiles produced regioisomeric 2-substituted 3-bromopyrroles (**3**) selectively. The latter reaction can be rationalized by the rapid equilibration of the C-5 lithio species (**4**) to the more stable C-2 lithio species (**2**) in the presence of diisopropylamine.

INTRODUCTION

The directed lithiation[1] of *N*-protected pyrroles followed by reaction with electrophiles has frequently been employed in the synthesis of 2-substituted pyrroles.[2] During our investigation of the directed lithiation of *N*-benzenesulfonyl-3-bromopyrrole (**1**),[3] we encountered an interesting phenomenon involving a dynamic equilibrium between C-2 and C-5 lithio species (Scheme 1).[3b] Thus, the treatment of **1** with lithium diisopropylamide regioselectively generated C-2 lithio species (**2**). When **2** was treated with reactive electrophiles such as methyl chloroformate and chlorotrimethylsilane, 2-substituted 3-bromopyrroles (**3**) were obtained in good yields. On the other hand, when **2** was treated with less reactive electrophiles such as dimethylcarbamoyl chloride and chlorotriisopropylsilane, unexpected 5-substituted 3-bromopyrroles (**5**) were produced. The electrophile-controlled regioselective functionalization of **2** was rationalized by a dynamic equilibrium between the C-2 lithio species (**2**) and C-5 lithio species (**4**).

This paper is dedicated to Professor Dr. Ei-ichi Negishi on the occasion of his 77th birthday.

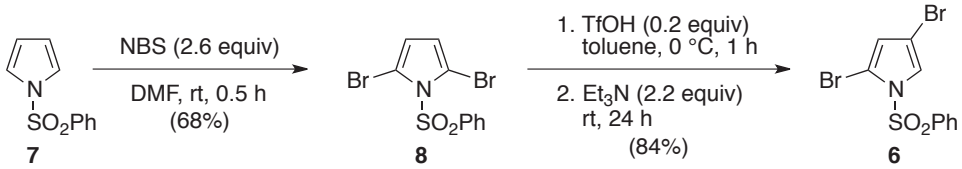


Scheme 1

From a practical viewpoint, the reactions shown in Scheme 1 are useful for the synthesis of 2-substituted 3-bromopyrroles (**3**). However, they are impractical for the synthesis of 5-substituted 3-bromopyrroles (**5**) because of the limited number of suitable electrophiles. In the previous *Letter*,[3b] we described briefly that the lithio species (**4**) can be generated alternatively by the selective bromine–lithium exchange of *N*-benzenesulfonyl-2,4-dibromopyrrole (**6**). In addition, we also indicated that the C-5 lithio species (**4**) thus generated could rearrange to the more stable C-2 lithio species (**2**) in the presence of diisopropylamine.[4] In this paper, we describe the application of these reactions for the practical synthesis of **5** and **3**.

RESULTS AND DISCUSSION

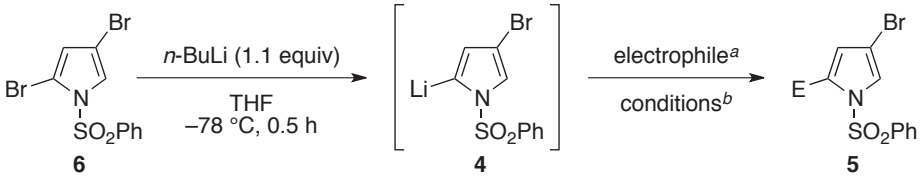
The synthesis of *N*-benzenesulfonyl-2,4-dibromopyrrole (**6**) is shown in Scheme 2. *N*-Benzenesulfonylpyrrole (**7**) was brominated with 2.6 equiv of NBS to give *N*-benzenesulfonyl-2,5-dibromopyrrole (**8**). Reaction of this compound with a catalytic amount of trifluoromethanesulfonic acid followed by treatment with triethylamine provided **6** in 84% yield.



Scheme 2

N-Benzenesulfonyl-2,4-dibromopyrrole (**6**) thus synthesized was treated with 1.1 equiv of *n*-BuLi in THF at –78 °C for 0.5 h, and the resulting C-5 lithio species (**4**) was reacted with 1.8 equiv of an appropriate electrophile under conditions A (–78 °C, 1 h) or B (–78 °C, 1 h → 0 °C, 1 h). After the usual work-up, the product was isolated by column chromatography. As shown in Table 1, various 5-substituted 3-bromopyrroles (**5**) were obtained in excellent yields.

Table 1. Bromine–lithium exchange of **6** followed by reactions with electrophiles



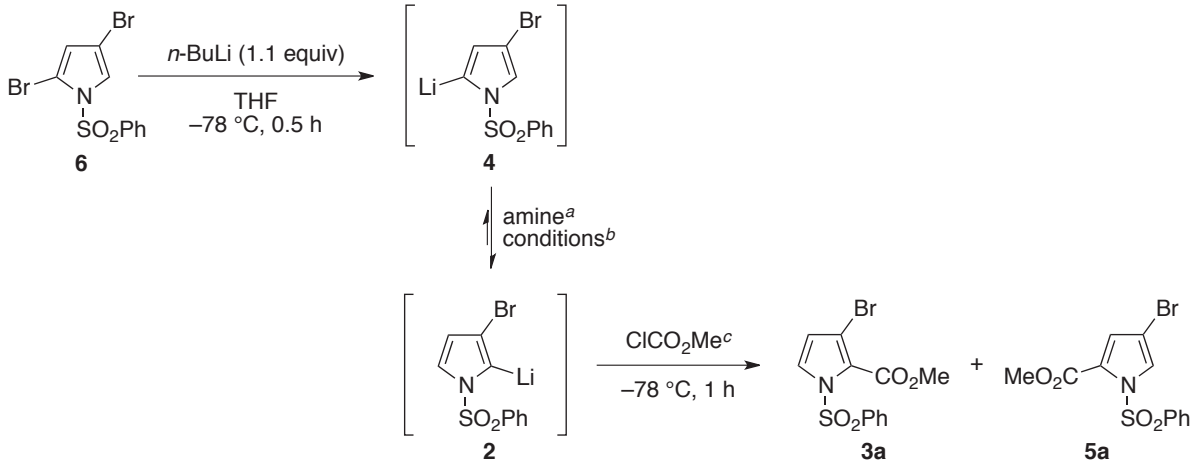
entry	electrophile[a]	conditions[b]	product	E	yield (%)[c]
1	$ClCO_2Me$	A	**5a**	CO_2Me	97
2	TMS-Cl	A	**5b**	TMS	93
3	PhSSPh	A	**5c**	SPh	92
4	ICH_2CH_2I	A	**5d**	I	97
5	*p*-$MeOC_6H_4CHO$	A	**5e**	CH(OH)(C_6H_4OMe-*p*)	89
6	HCO_2Et	A	**5f**	CHO	73
7	*p*-$MeOC_6H_4COCl$	A	**5g**	COC_6H_4OMe-*p*	78
8	TIPS-OTf	A	**5h**	TIPS	80
9	*t*-BuNCO	A	**5i**	CONH*t*-Bu	50
10	*t*-BuNCO	B	**5i**	CONH*t*-Bu	82

[a] Electrophile (1.8 equiv) was added as a THF solution.
[b] A: –78 °C, 1 h; B: –78 °C, 1 h → 0 °C, 1 h.
[c] Isolated yield.

Next, the reaction conditions for the amine-mediated rearrangement of the C-5 lithio species (**4**) to the C-2 lithio species (**2**) were investigated (Table 2). To this end, the C-5 lithio species (**4**) was treated with 1.0 equiv of a secondary amine in THF under conditions A (–78 °C, 1 h → 0 °C, 0.5 h) and then reacted with 1.8 equiv of methyl chloroformate, and the products were analyzed. The use of dimethylamine or diethylamine did not produce the desired product (**3a**) but provided the corresponding benzenesulfonamides (**9** or **10**) by the nucleophilic attack of the *in situ* generated lithium amides on the substrate (entries 1 and 2). When diisopropylamine was used for the reaction, a 97:3 mixture of **3a** and **5a** was obtained in 95% yield (entry 3). On the other hand, in the reactions with more bulky

2,2,6,6-tetramethylpiperidine (TMP) or *N*-*t*-butyl-*N*-tritylamine (TBTA),[5] C-2 selectivity was decreased (entries 4 and 5). The amines, especially TBTA, may not be efficiently incorporated in the dynamic equilibrium because of their much lower kinetic acidities. To improve the C-2 selectivity of the products, longer reaction times (entries 6 and 7) and an increased amount of diisopropylamine (entry 8) were also tested, but regioselectivity was not improved (entries 6–8). The reaction conditions shown in entry 3 were estimated to be the most optimal.

Table 2. Examination of reaction conditions for the generation of **2**

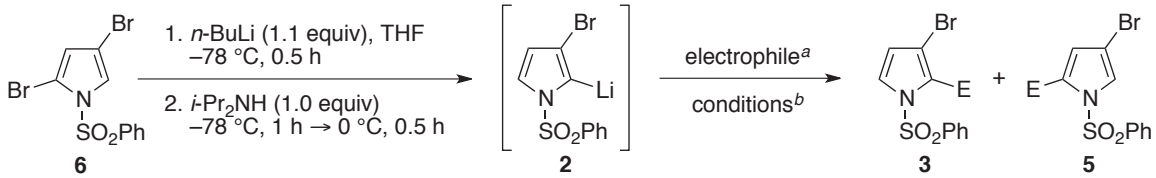


entry	amine[a]	conditions[b]	yield (%)[d]	ratio (**3a**:**5a**)[e]
1	Me_2NH[f]	A	–[g]	–
2	Et_2NH	A	–[h]	–
3	*i*-Pr_2NH	A	95	97:3
4	TMP	A	86	93:7
5	TBTA[i]	A	80	41:59
6	*i*-Pr_2NH	B	86	97:3
7	*i*-Pr_2NH	C	74	97:3
8	*i*-Pr_2NH[j]	A	89	97:3

[a] Amine (1.0 equiv) was added as a neat liquid unless otherwise mentioned.
[b] A: –78 °C, 1 h → 0 °C, 0.5 h; B: –78 °C, 1 h → 0 °C, 1 h; C: –78 °C, 1 h → 0 °C, 3 h.
[c] Methyl chloroformate (1.8 equiv) was added as a THF solution.
[d] Isolated yield.
[e] Determined by ^{1}H NMR analysis (400 MHz).
[f] Dimethylamine was added as a 2.0 M solution in THF.
[g] *N*,*N*-Dimethylbenzenesulfonamide (**9**) was obtained in 86% yield.
[h] *N*,*N*-Diethylbenzenesulfonamide (**10**) was obtained in 89% yield.
[i] *N*-*t*-Butyl-*N*-tritylamine (TBTA) was added as a 0.5 M solution in THF.
[j] 1.5 equiv of diisopropylamine.

After obtaining the optimized conditions for generating the C-2 lithio species (**2**), we performed functionalization. The lithio species (**2**) was reacted with 1.8 equiv of an appropriate electrophile under conditions A (–78 °C, 1 h) or B (–78 °C, 1 h → 0 °C, 3 h). As shown in Table 3, highly regioselective 2-substituted 3-bromopyrroles (**3**) were obtained in good yields. Pure 2-substituted *N*-benzenesulfonyl-3-bromopyrroles (**3**) were readily obtained by column chromatography or recrystallization.

Table 3. Synthesis of 2-substituted 3-bromopyrroles (**3**)



entry	electrophile[a]	conditions[b]	product	E	yield (%)[c]	ratio (**3**:**5**)[d]
1	$ClCO_2Me$	A	**3a**	CO_2Me	95	97:3
2	TMS-Cl	A	**3b**	TMS	91	97:3
3	PhSSPh	A	**3c**	SPh	94	98:2
4	ICH_2CH_2I	A	**3d**	I	97	97:3
5	(*p*-$MeOC_6H_4$)CHO	A	**3e**	CH(OH)(C_6H_4OMe-*p*)	92	97:3
6	HCO_2Et	A	**3f**	CHO	67	97:3
7	(*p*-$MeOC_6H_4$)COCl	B	**3g**	COC_6H_4OMe-*p*	74	97:3
8	TIPS-OTf	B	**3h**	TIPS	72	97:3
9	*t*-BuNCO	B	**3i**	CONH*t*-Bu	91	97:3

[a] Electrophile (1.8 equiv) was added as a THF solution.
[b] A: –78 °C, 1 h; B: –78 °C, 1 h → 0 °C, 1 h.
[c] Isolated yield.
[d] Determined by ^{1}H NMR analysis (400 MHz).

In conclusion, we have developed an efficient procedure to produce 5- or 2-substituted *N*-benzenesulfonyl-3-bromopyrroles using *N*-benzenesulfonyl-2,4-dibromopyrrole (**6**) as a common starting material. The lithio species (**4**) generated by the selective bromine–lithium exchange of *N*-benzenesulfonyl-2,4-dibromopyrrole (**6**) was quenched with a number of electrophiles to give C-5 functionalized 3-bromopyrroles (**5**) in excellent yields. Moreover, quenching the lithio species (**4**) after diisopropylamine-mediated isomerization produced the C-2 functionalized product (**3**) with excellent selectivity. The reactions described in this paper could aid the synthesis of more complex pyrrole

derivatives because further regioselective functionalization of the pyrrole ring is possible at the bromine positions.[6,7]

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained using a Thermo Nicolet Nexus 670 NT FT-IR instrument and are reported in terms of wave number (cm^{-1}). NMR spectra were recorded on a JEOL JNM-AL400 instrument (400 MHz for ^1H and 100 MHz for ^{13}C) using tetramethylsilane as an internal standard (δ 0.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift. High-resolution mass spectra were recorded on a JEOL JMS-700N spectrometer. Elemental analysis was performed for C, H, and N using a Perkin Elmer 2400II instrument. Column chromatography was conducted using silica gel 60 N, 63–210 μm (Kanto Chemical Co., Inc.). *n*-Butyllithium was used after titration with 2,5-dimethoxybenzyl alcohol. Solvents were dried and distilled by standard methods if necessary.

N-Benzenesulfonyl-2,4-dibromopyrrole (6)

A solution of NBS (13.9 g, 78.0 mmol) in DMF (30 mL) was added dropwise to a solution of *N*-benzenesulfonylpyrrole (**7**)[3a] (6.22 g, 30.0 mmol) in DMF (60 mL) at room temperature, and the mixture was stirred for 0.5 h. The solution was quenched with 10% aq. Na_2SO_3 and the product was extracted with EtOAc. The extract was washed with water and brine, then dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography using silica gel 60 N (hexane–EtOAc = 5:1) to give the colorless solid *N*-benzenesulfonyl-2,5-dibromopyrrole (**8**) (7.49 g, 68%). This compound was partially unstable and was used for the next reaction without further purification. Mp 102.5–104.5 °C; IR (KBr): 1448, 1385, 1196, 1141, 1096 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.31 (s, 2H), 7.53–7.59 (m, 2H), 7.64–7.69 (m, 1H), 8.02–8.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 101.8, 118.9, 127.7, 129.4, 134.5, 138.3. *Anal*. Calcd for $C_{10}H_7Br_2NO_2S$: C, 32.90; H, 1.93; N, 3.84. Found: C, 32.96; H, 1.67; N, 3.64.

Under an argon atmosphere, neat liquid trifluoromethanesulfonic acid (354 μL, 4.00 mmol) was added to a solution of **8** (7.30 g, 20.0 mmol) in toluene (1.00 L) at 0 °C. The mixture was stirred for 1 h at 0 °C. Triethylamine (6.1 mL, 44.0 mmol) was then added to the solution and the mixture was allowed to warm to room temperature. The solution was stirred for 24 h, washed with sat. aq. $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography using silica gel 60 N (hexane–toluene = 2:1) to give the colorless solid **6** (6.16 g, 84%). Recrystallization from Et_2O –pentane

gave colorless granules. Mp 87–88 °C; IR (KBr): 1445, 1379, 1187, 1136, 1091 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.29 (d, J = 2.0 Hz, 1H), 7.50 (d, J = 2.0 Hz, 1H), 7.53–7.59 (m, 2H), 7.65–7.71 (m, 1H), 7.93–7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 100.6, 100.8, 120.0, 123.2, 128.0, 129.5, 134.7, 137.5. *Anal*. Calcd for $C_{10}H_7Br_2NO_2S$: C, 32.90; H, 1.93; N, 3.84. Found: C, 32.81; H, 1.69; N, 3.53.

Bromine–lithium exchange of *N*-benzenesulfonyl-2,4-dibromopyrrole (6) followed by reactions with electrophiles (Table 1)

General procedure

Under an argon atmosphere, a hexane solution of *n*-butyllithium (1.60 M, 688 μL, 1.10 mmol) was added dropwise to a solution of **6** (365 mg, 1.00 mmol) in THF (5.0 mL) at –78 °C. After stirring for 30 min, a solution of an appropriate electrophile (1.80 mmol) in THF (2.0 mL) was added dropwise and the mixture was treated under the conditions described in Table 1 (A: –78 °C, 1 h; B: –78 °C, 1 h → 0 °C, 1 h). The reaction mixture was quenched with sat. aq. NH_4Cl, allowed to warm to room temperature, and evaporated. The products were extracted with Et_2O and the extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography using silica gel 60 N to give **5**.

Methyl *N*-benzenesulfonyl-4-bromopyrrole-2-carboxylate (5a)

Methyl chloroformate (138 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (toluene), **5a** was obtained as colorless solid (332 mg, 97%). Recrystallization from Et_2O–hexane gave colorless prisms. Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-4-bromo-2-(trimethylsilyl)pyrrole (5b)**

Chlorotrimethylsilane (228 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1), **5b** was obtained as colorless oil (332 mg, 93%). IR (KBr): 1371, 1176, 1132, 1076, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.29 (s, 9H), 6.51 (d, J = 1.6 Hz, 1H), 7.39 (d, J = 1.6 Hz, 1H), 7.47–7.53 (m, 2H), 7.57–7.64 (m, 1H), 7.64–7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.0, 102.3, 125.7, 126.2, 127.5, 129.4, 133.8, 137.8, 139.6; HRFABMS *m*/*z*. Calcd for $C_{13}H_{17}BrNO_2SSi$ [$(M+H)^+$]: 357.9933. Found: 357.9921.

***N*-Benzenesulfonyl-4-bromo-2-(phenylthio)pyrrole (5c)**

Diphenyl disulfide (393 mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1), **5c** was obtained as pale purple oil (361 mg, 92%). IR (KBr): 1378,

1188, 1135, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.49 (d, J = 2.0 Hz, 1H), 6.88–6.92 (m, 2H), 7.07–7.16 (m, 3H), 7.34–7.40 (m, 2H), 7.48–7.53 (m, 1H), 7.62 (d, J = 2.0 Hz, 1H), 7.88–7.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 100.0, 122.1, 125.2, 126.3, 126.6, 127.2, 128.1, 128.9, 129.1, 134.2, 136.2, 137.5; HRFABMS *m/z*. Calcd for $C_{16}H_{12}BrNO_2S_2$ (M^+): 392.9493. Found: 392.9522.

_N_-Benzenesulfonyl-4-bromo-2-iodopyrrole (5d)

1,2-Diiodoethane (507 mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1), **5d** was obtained as colorless solid (398 mg, 97%). Recrystallization from Et_2O–pentane gave colorless granules. Mp 87.0–88.0 °C; IR (KBr): 1377, 1184, 1134, 609 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.50 (d, J = 1.9 Hz, 1H), 7.53–7.59 (m, 2H), 7.60 (d, J = 1.9 Hz, 1H), 7.64–7.70 (m, 1H), 7.93–7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 64.2, 102.5, 125.6, 128.1, 128.2, 129.4, 134.6, 137.6. *Anal*. Calcd for $C_{10}H_7BrINO_2S$: C, 29.15; H, 1.71; N, 3.40. Found: C, 29.13; H, 1.33; N, 3.32.

_N_-Benzenesulfonyl-4-bromo-2-(α-hydroxy-4-methoxybenzyl)pyrrole (5e)

p-Methoxybenzaldehyde (219 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (toluene to toluene–EtOAc = 5:1), **5e** was obtained as pale purple oil (375 mg, 89%). IR (KBr): 3421, 1512, 1372, 1251, 1175 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3, 67.7, 100.9, 113.7, 117.6, 122.4, 126.8, 127.9, 129.5, 132.3, 134.2, 138.5, 139.1, 159.4; HRFABMS *m/z*. Calcd for $C_{18}H_{16}BrNO_4S$ (M^+): 420.9983. Found: 420.9990.

_N_-Benzenesulfonyl-4-bromopyrrole-2-carbaldehyde (5f)

Ethyl formate (145 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1 to toluene), **5f** was obtained as pale brown solid (229 mg, 73%). Recrystallization from Et_2O–hexane gave pale brown needles. The spectroscopic data are identical with those previously reported.[3b]

_N_-Benzenesulfonyl-4-bromo-2-(4-methoxybenzoyl)pyrrole (5g)

p-Methoxybenzoyl chloride (307 mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (toluene), **5g** was obtained as pale yellow oil (330 mg, 78%). IR (KBr): 1650, 1600, 1376, 1257, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.87 (s, 3H), 6.62 (d, J = 1.8 Hz, 1H), 6.91–6.96 (m, 2H), 7.56–7.62 (m, 2H), 7.64–7.70 (m, 1H), 7.69 (d, J = 1.8 Hz, 1H), 7.81–7.85 (m, 2H), 8.11–8.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6, 99.4, 113.7, 124.3, 126.9, 128.4, 129.0, 129.9, 132.3, 133.3, 134.2, 138.8, 163.9, 182.8; HRFABMS *m/z*. Calcd for $C_{18}H_{15}BrNO_4S$ [$(M+H)^+$]: 419.9905.

Found: 419.9898.

***N*-Benzenesulfonyl-4-bromo-2-(triisopropylsilyl)pyrrole (5h)**

Triisopropylsilyl trifluoromethanesulfonate (484 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 2:1), **5h** was obtained as colorless solid (355 mg, 80%). Recrystallization from MeOH gave colorless plates. The spectroscopic data are identical with those previously reported.[3b]

***N*-*tert*-Butyl-1-benzenesulfonyl-4-bromopyrrole-2-carboxamide (5i)**

tert-Butyl isocyanate (206 μL, 1.80 mmol) was reacted under the conditions B. After chromatographic purification using different solvent systems (hexane–toluene = 1:1 and toluene–EtOAc = 10:1), **5i** was obtained as colorless solid (316 mg, 82%). Recrystallization from Et_2O–hexane gave colorless needles. Mp 81.5–83.0 °C; IR (KBr): 3275, 1665, 1643, 1560, 1379, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 9H), 6.09 (br s, 1H), 6.53 (d, J = 1.9 Hz, 1H), 7.35 (d, J = 1.9 Hz, 1H), 7.51–7.57 (m, 2H), 7.61–7.67 (m, 1H), 8.00–8.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 52.1, 99.9, 119.0, 123.7, 128.1, 129.2, 131.9, 134.5, 137.9, 158.7. *Anal*. Calcd for $C_{15}H_{17}BrN_2O_3S$: C, 46.76; H, 4.45; N, 7.27. Found: C, 46.79; H, 4.18; N, 7.27.

Examination of reaction conditions for the generation of 2 (Table 2)

General procedure

Under an argon atmosphere, a hexane solution of *n*-butyllithium (1.60 M, 689 μL, 1.10 mmol) was added dropwise to a solution of **6** (365 mg, 1.00 mmol) in THF (5.0 mL) at –78 °C. After stirring for 30 min, an appropriate secondary amine (1.00 mmol or 1.50 mmol) was added as a neat liquid or a THF solution, and the mixture was reacted under the conditions described in Table 2 (A: –78 °C, 1 h → 0 °C, 0.5 h; B: –78 °C, 1 h → 0 °C, 1 h; C: –78 °C, 1 h → 0 °C, 3 h). After the reaction mixture was recooled to –78 °C, a solution of methyl chloroformate (138 μL, 1.80 mmol) in THF (2.0 mL) was added dropwise and the mixture was stirred for 1 h at –78 °C. The reaction mixture was quenched with sat. aq. NH_4Cl, allowed to warm to room temperature, and evaporated. The products were extracted with Et_2O and the extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography using silica gel 60N (hexane–toluene = 1:1 to toluene) to give a mixture of the colorless solids **3a** and **5a**. The regioisomeric ratio was determined by integration of the ^1H NMR absorption of the methyl protons for each regioisomer (δ Me of **3a**: 3.80; δ Me of **5a**: 3.73).

***N*,*N*-Dimethylbenzenesulfonamide (9)**

A THF solution of dimethyamine (2.0 M, 500 μL, 1.00 mmol) was reacted under the conditions A. After chromatographic purification using different solvent systems (hexane–toluene = 1:1 and toluene–EtOAc = 5:1), **9** was obtained as yellow oil (160 mg, 86%). IR (KBr): 1446, 1339, 1167, 954, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.71 (s, 6H), 7.53–7.59 (m, 2H), 7.59–7.65 (m, 1H), 7.76–7.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.9, 127.7, 129.0, 132.8, 135.4. HREIMS *m*/*z*. Calcd for $C_8H_{11}NO_2S$ (M^+): 185.0510. Found: 185.0483. These spectroscopic data are identical with those previously reported.[8]

***N*,*N*-Diethylbenzenesulfonamide (10)**

Diethyamine (103 μL, 1.00 mmol) was reacted under the conditions A. After chromatographic purification using different solvent systems (hexane–toluene = 1:1 and toluene–EtOAc = 5:1), **10** was obtained as yellow oil (190 mg, 89%). IR (KBr): 1446, 1333, 1155, 1017, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.12 (t, J = 7.2 Hz, 6H), 3.24 (q, J = 7.2 Hz, 4H), 7.47–7.52 (m, 2H), 7.53–7.58 (m, 1H), 7.79–7.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 42.0, 126.9, 129.0, 132.3, 140.3. HRFABMS *m*/*z*. Calcd for $C_{10}H_{16}NO_2S$ [$(M+H)^+$]: 214.0902. Found: 214.0910. These spectroscopic data are identical with those previously reported.[9]

Synthesis of 2-substituted 3-bromopyrroles (3) (Table 3)

General procedure

Under an argon atmosphere, a hexane solution of *n*-butyllithium (1.60 M, 688 μL, 1.10 mmol) was added dropwise to a solution of **6** (365 mg, 1.00 mmol) in THF (5 mL) at –78 °C. After stirring for 30 min, neat liquid diisopropylamine (140 μL, 1.00 mmol) was added. After stirring for 1 h at –78 °C, the mixture was allowed to warm to 0 °C, stirred for 0.5 h at 0 °C, and then recooled to –78 °C. A solution of an appropriate electrophile (1.8 mmol) in THF (2.0 mL) was added dropwise and the mixture was treated under the conditions described in Table 3 (A: –78 °C, 1 h; B: –78 °C, 1 h → 0 °C, 1 h). The reaction mixture was quenched with sat. aq. NH_4Cl, allowed to warm to room temperature, and evaporated. The products were extracted with Et_2O and the extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography using silica gel 60 N to give a 97:3–98:2 mixture of **3** and **5**.

Methyl *N*-benzenesulfonyl-3-bromopyrrole-2-carboxylate (3a)

Methyl chloroformate (138 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1 to toluene), a 97:3 mixture of **3a** and **5a** was obtained as colorless solid (327 mg, 95%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-(trimethylsilyl)pyrrole (3b)**

Chlorotrimethylsilane (228 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 3:1 – 1:1), a 97:3 mixture of **3b** and **5b** was obtained as colorless solid (326 mg, 91%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-(phenylthio)pyrrole (3c)**

Diphenyl disulfide (393 mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1), a 98:2 mixture of **3c** and **5c** was obtained as colorless solid (372 mg, 94%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-iodopyrrole (3d)**

1,2-Diiodoethane (507 mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification over Silica Gel 60N (hexane–toluene = 1:1), a 97:3 mixture of **3d** and **5d** was obtained as colorless solid (401 mg, 97%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-(α-hydroxy-4-methoxybenzyl)pyrrole (3e)**

p-Methoxybenzaldehyde (219 μL mg, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (toluene to toluene–EtOAc = 10:1), a 97:3 mixture of **3e** and **5e** was obtained as colorless solid (599 mg, 84%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromopyrrole-2-carbaldehyde (3f)**

Ethyl formate (145 μL, 1.80 mmol) was reacted under the conditions A. After chromatographic purification (hexane–toluene = 1:1 to toluene), a 97:3 mixture of **3f** and **5f** was obtained as colorless solid (210 mg, 67%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-(4-methoxybenzoyl)pyrrole (3g)**

p-Methoxybenzoyl chloride (307 mg, 1.80 mmol) was reacted under the conditions B. After chromatographic purification (hexane–toluene = 1:1–1:2 to toluene), a 97:3 mixture of **3g** and **5g** was obtained as colorless solid (309 mg, 74%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N*-Benzenesulfonyl-3-bromo-2-(triisopropylsilyl)pyrrole (3h)**

Chlorotriisopropylsilane (484 μL, 1.80 mmol) under the conditions B. After chromatographic purification (hexane–toluene = 1:1), a 97:3 mixture of **3h** and **5h** was obtained as colorless solid (319 mg, 72%). Physical and spectroscopic data of this compound were reported previously.[3b]

***N-tert*-Butyl-1-benzenesulfonyl-3-bromopyrrole-2-carboxamide (3i)**

tert-Butyl isocyanate (206 μL, 1.80 mmol) was reacted under the conditions B. After chromatographic purification using different solvent systems (hexane–toluene = 1:1, toluene, and toluene–EtOAc = 10:1), a 97:3 mixture of **3i** and **5i** was obtained as colorless solid (351 mg, 91%). Physical and spectroscopic data of this compound were reported previously.[3b]

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