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Benzimidazole Nitrogen-Directed, Regiocontrolled, Lithiation of Ferrocenyl- and Phenyl-*N*-*n*-butylbenzimidazoles

Damien Hérault,[†] Karel Aelvoet,[†] Alexandrea J. Blatch,[†] Abdullah Al-Majid,[‡] Christian A. Smethurst,[§] and Andrew Whiting*,[†]

Department of Chemistry, Durham University, Sciences Laboratories, South Road, Durham DH1 3LE, U.K., Chemistry Department, College of Science, King Saud University, PO Box 2455, Riyadh 11451, Saudi Arabia, and GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, U.K.

Andy.whiting@durham.ac.uk

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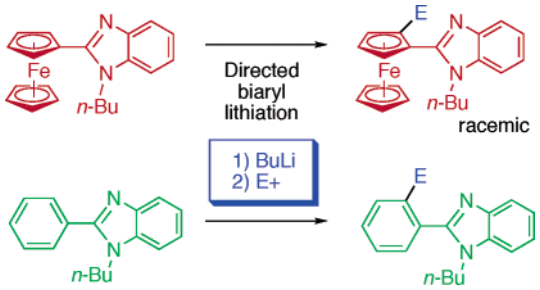

2-Ferrocenyl- and 2-phenyl-*N*-*n*-butylbenzimidazoles were synthesized to evaluate the influence of the benzimidazole functional group upon their directed lithiation. The regiochemistry of lithiation was studied, as well as the effect of stabilization of the lithiated species by diamine coordination using tetramethylethylenediamine and (−)-sparteine. The lithiations were followed by reaction with a variety of electrophiles to give the disubstituted 2-ferrocenyl- and 2-phenyl-*N*-*n*-butylbenzimidazoles compounds. This study showed that despite a simple *n*-butyl function on the benzimidazole, directed lithiation was readily achieved with high regiocontrol on the ferrocenyl and phenyl groups. (−)-Sparteine failed to provide asymmetric induction in the ferrocene system, and its inefficiency is explained by intramolecular coordination of the lithiated species by the benzimidazole nitrogen, which is preferred over sparteine coordination.

Introduction

The lithiation of phenyl and ferrocenyl groups is very common in the synthesis of di- or trisubstituted aromatic compounds[1−3] or chiral planar ferrocene derivatives.[4] In particular, for the regioselective lithiation of, for example, monosubstituted phenyl and ferrocene derivatives, the directing groups frequently used are functionals such as amides,[5] carboxylic acids,[6] amines,[7] imidazoles,[8] imidazolines,[9] methoxyls,[10] and oxazolines.[11] In ferrocene systems, there are numerous directing groups used to provide ring substitution in an enantioselective manner, including ferrocene chiral acetals,[12] oxazolines,[13]

* To whom correspondence should be addressed. Tel: +44-191-334-2081. Fax: +44-191-384-4737.
[†] Department of Chemistry, Durham University.
[‡] Chemistry Department, King Saud University.
[§] GlaxoSmithKline Pharmaceuticals, Essex.

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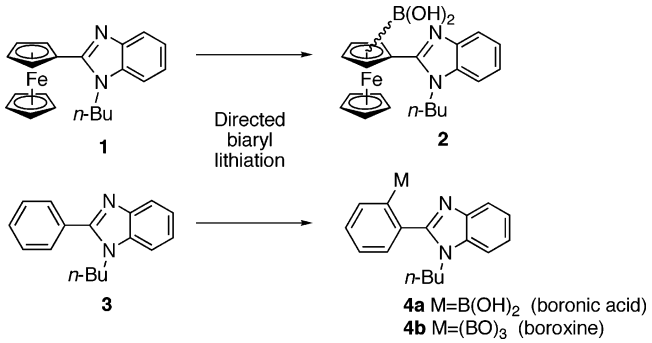
SCHEME 1. Synthesis of Boronic Acid Derivatives by Directed Lithiation

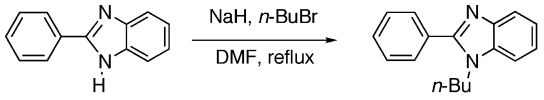


amines,[14] sulfoxides,[15] imidazolines,[16] and oxazaphospholodine-oxides.[17] To synthesize chiral planar ferrocene systems, external chiral auxiliaries were generally employed to induce enantioselectivity. Because diamines, such as TMEDA, are often employed to stabilize the product of directed lithiation,[1] enantioselective lithiation can also be effected by directed enantioselective deprotonation using chiral diamines, (−)-sparteine being a most efficient auxiliary for the *ortho*-lithiation of ferrocene carboxamides.[18] In addition, amide anions can be used to temporarily protect aromatic aldehydes via formation of the aldehyde−amide adduct,[19] and both (*S*)-(+)-1-(2-pyrrolidinylmethyl)pyrrolidine[20] and chiral cyclohexanediamines[21] have provided temporary protection with concomitant *ortho*-lithiation of a ferrocene carboxaldehyde and a benzaldehyde chromium tricarbonyl complex.

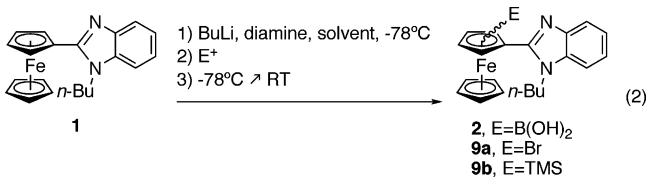
We are interested in the synthesis of amino-boronic acid compounds which have potential as bifunctional and organic catalysts.[22] In particular, we focused our attention on the preparation of 2-(2-boronoferrocenyl)-*N*-*n*-butylbenzimidazole (**2**) and 2-(2-boronophenyl)-*N*-*n*-butylbenzimidazole (**4a**), which we argued would be available via the directed lithiation of 2-ferrocenyl-*N*-*n*-butylbenzimidazole (**1**) and 2-phenyl-*N*-*n*-butylbenzimidazole (**3**) (Scheme 1), assuming that regiocontrolled metalation could be accomplished across the biaryl ring system, as opposed to alpha to nitrogen, i.e., on the benzimidazole benzene ring. In this paper, we report the successful application of the strategy, the conditions for the optimization of the lithiation of these two systems, and the results obtained with the different electrophiles.

Results and Discussion

First, we synthesized **1** and **3**. In the case of the ferrocene derivative, we applied Beaulieu's method[23] involving oxidative coupling between the (*N*-*n*-butylamine)aniline and the ferrocene carboxaldehyde in the presence of Oxone. The preparation of the *N*-*n*-butylaniline precursor (**7**) was realized in two steps, as shown in Scheme 2, involving aromatic nucleophilic substitution of *n*-butylamine on 2-bromonitrobenzene, followed by hydrogenation of the nitro-function, as reported.[24] After coupling with the ferrocene carboxaldehyde, the substituted ferrocene **1** was obtained in an overall yield of 63% (Scheme 2). **3** can also be prepared by a similar route or by using more conventional polyphosphoric acid-catalyzed cyclocondensation methods;[24] however, for this study it was readily prepared by N-alkylation of the commercial 2-phenylbenzimidazole in 88% (eq 1).[25] With



access to both benzimidazoles **1** and **3** achieved, the lithiation of these systems was examined with the aim of synthesizing the chiral planar 1,2-ferrocene and *ortho*-disubstituted benzene derivatives as typified by the boronic acid derivatives **2** and **4**, respectively. To achieve the synthesis of systems related to the ferrocene system **2**, the direct lithiation of **1** was attempted by the method of Snieckus et al. (eq 2).[17] Treatment with 1.3 equiv of *n*-butyllithium and 1.3 equiv of (−)-sparteine was used to form the lithiated ferrocene, followed by quenching with excess electrophile. With the use of trimethylborate as the electrophile, **2** was obtained in an inadequate 23% yield and with no asymmetric induction (zero rotation by optical rotation).



To confirm the inefficiency of (−)-sparteine to direct asymmetric induction in competition with the benzimidazole, 2-(2-bromoferrocenyl)-*N*-*n*-butylbenzimidazole (**9a**) was synthesized directly using both TMEDA-*n*-BuLi (Table 1, entry 4) and (−)-sparteine-*n*-BuLi (entry 3) in 41 and 47% yields, respectively. Chiral HPLC analysis again showed the absence of any

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SCHEME 2. Synthesis of 2-Ferrocenyl-*N*-*n*-butylbenzimidazole (1)

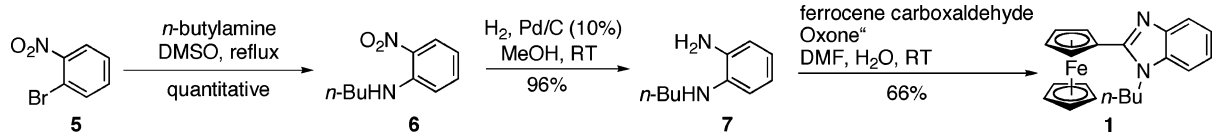
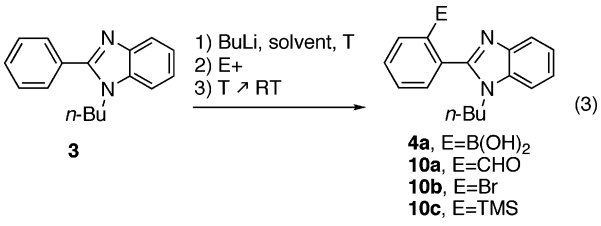


TABLE 1. Lithiation of 2-(Ferrocenyl)-*N*-*n*-butyl-benzimidazole (1)

entry	E^+	BuLi (equiv)	diamine (1.3 equiv)	solvent	E (product)	yield (%)	ee (%)
1	$B(OMe)_3$	*n*-(1.3)	(−)-sparteine	Et_2O	$B(OH)_2$-**2**	23	0
2	$B(OMe)_3$	*t*-(1.5)		THF	$B(OH)_2$-**2**	87	
3	$(BrCCl_2)_2$	*n*-(1.3)	(−)-sparteine	Et_2O	Br-**9a**	47	0
4	$(BrCCl_2)_2$	*n*-(1.3)	TMEDA	Et_2O	Br-**9a**	41	
5	$(BrCCl_2)_2$	*t*-(1.5)		THF	Br-**9a**	85	
6	TMSCl	*t*-(1.5)		THF	TMS-**9b**	25	

asymmetric induction in the latter case. Indeed, further studies showed that the addition of a diamine was not required during the lithiation. In addition, lithiation of **1** with 1.5 equiv of *t*-BuLi followed by quenching with either trimethylborate or 1,2-dibromotetrachloroethane gave the boronic acid **2** and the bromide **9a** in yields of 87 and 85%, respectively. This proved the ability of a simple *N*-alkyl-substituted benzimidazole group to direct the lithiation onto the neighboring ring of a biaryl system and to stabilize the resulting lithiated intermediate without any external diamine additive; i.e., the lack of asymmetric induction is presumably a direct result of the preferred metalation reaction being an intramolecular delivery of a benzimidazole-*n*-butyllithium species which does not require sparteine. With the use of the same conditions as those for the bromination of ferrocene **1**, the corresponding TMS derivative (Table 1, entry 6) was also isolated, albeit only with a yield of 25%.

The lithiation of benzimidazole **2** was also realized according to the method of Demuth and Molina/Foces-Foces[8] using different electrophiles, as outlined in eq 3 and Table 2. In this case, the conditions were optimized in a manner which depended upon the type of electrophile used. First, lithiation of benzimi-



(3)

dazole **3** was developed for the synthesis of the boronic acid derivative **4**. It was found that the efficiency of the lithiation did not depend upon the solvent, since under the same reaction conditions (temperature, equivalents, and type of lithiating agent), the yields were similar in diethyl ether or THF, i.e., 65 and 67%, respectively (Table 2, entries 1 and 2). Thus, the preferred conditions involved THF at −78 °C with 1.5 equiv of *t*-BuLi, which gave the pure *single* regioisomer boroxine **4b**. When the reaction was run at −25 °C using 2 equiv of *n*-BuLi, a mixture of compounds (Table 2, entry 3) was clearly indicated by ^{1}H NMR. Indeed, this was reinforced by ^{11}B NMR which showed three peaks at 8, 19, and 33 ppm, corresponding to the intramolecular chelated derivative,[24] the boroxine **4b**, and the boronic acid **4a**, respectively.

It was also interesting to investigate the same reaction using different electrophiles, i.e., DMF, 1,2-dibromotetrachloroethane,

TABLE 2. Lithiation of 2-(Phenyl)-*N*-*n*-butyl-benzimidazole (3)

entry	E^+ (equiv)	BuLi (equiv)	solvent	*T* (°C)	E (product)	yield (%)
1	$B(O\text{-}iPr)_3$ (2)	*t*-(1.5)	Et_2O	−78	$(RBO)_3$-boroxine **4b**	65
2	$B(O\text{-}iPr)_3$ (2)	*t*-(1.5)	THF	−78	$(RBO)_3$-boroxine **4b**	67
3	$B(O\text{-}iPr)_3$ (3)	*n*-(2)	THF	−25	mixture of ester/acid	ND
4	DMF (8)	*n*-(1.5)	THF	−78	CHO **10a**	SM
5	DMF (8)	*n*-(1.5)	THF	−42	CHO **10a**	31
6	DMF (8)	*n*-(2)	THF	−25	CHO **10a**	87
7	$(BrCCl_2)_2$ (2)	*n*-(1.5)	THF	−78	Br **10b**	SM
8	$(BrCCl_2)_2$ (2)	*n*-(1.5)	THF	−42	Br **10b**	ND (32[a])
9	$(BrCCl_2)_2$ (2)	*n*-(2)	THF	−25	Br **10b**	5 (64[a])
10	Br_2 (2)	*n*-(2)	THF	−25	Br **10b**	9 (55[a])
11	TMSCl (2)	*n*-(2)	THF	−42	TMS **10c**	87
12	TMSCl (2)	*n*-(2)	THF	−25	mixture	ND

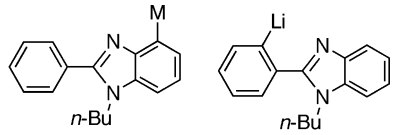
[a] Percentage of **10b** in the crude product was determined by ^{1}H NMR, on the basis of the relative integrations of the CH_2N groups.

and TMSCl. First, the DMF quenched reaction (Table 2, entries 4−6) was carried out at −78 °C using 1.5 equiv of *n*-BuLi (entry 4). However, only starting material **3** was observed; hence, the reaction temperature was increased to −42 °C to promote the lithiation and subsequent reaction with DMF (entry 5). In this case, 31% of the benzaldehyde derivative **10a** was isolated. Raising the temperature again to −25 °C gave a further increase in yield to 87% (entry 6) of the corresponding aldehyde **10a**. It is also interesting to note that the percentage of side products observed in the crude NMR also decreased with increasing temperature.

For the bromination of **3** to give **10b** (Table 2, entries 7−10), the initial reaction was carried out at −78 °C using 1.5 equiv of *n*-BuLi; however, only starting material **3** was recovered (entry 7). When the temperature was increased to −42 °C (entry 8), complete conversion of **3** was achieved; however, separation of the starting material and product **10b** was difficult due to their similar retention times. With the use of 2 equiv of *n*-BuLi at −25 °C (entry 9), the conversion of **3** was improved to an estimated 67%; however, again due to separation problems, only 5% of **10b** was isolated after silica gel chromatography. A marginal improvement in yield to 9% was possible using Br_2 as the electrophile (entry 10), though the conversion was lower (55%). In contrast, the lithiation of benzimidazole **3** and reaction with TMSCl gave the corresponding trimethylsilyl compound **10c** in a much more straightforward manner (Table 2, entries 11 and 12). Carrying out the reaction at −25 °C using 2 equiv of *n*-BuLi (entry 12), followed by quenching with TMSCl, gave a crude product which by ^{1}H NMR also showed the presence of a major side product. This side product may well be the *ortho*-trimethylsilylated derivative **11a**; however, it could not be isolated in a pure state. The directed metalation was substantially improved to give regioselective trimethylsilylation when the reaction was carried out at a lower temperature (−42 °C), resulting in 87% yield of **10c** (entry 11).

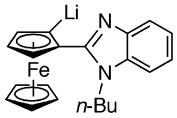
Conclusions

It is clear that neighboring group electron-donor systems attached to nitrogen functions such as N-Boc, for example,[5]



11a, M=TMS
11b, M=Li

12



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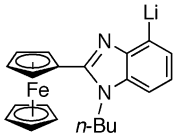

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assist the directed lithiation and subsequent stabilization of the aryl lithium. The present study shows that *N*-alkyl benzimidazole systems alone can direct metalation with reasonable-to-good facility, even with a simple alkyl group attached to nitrogen. However, the subsequent reaction with an external electrophile does vary in efficiency and it is therefore necessary to optimize reaction conditions to reflect this. From the results presented here, it is clear that directed metalation of biaryl−benzimidazole systems is not necessarily completely regioselective; however, with a suitable choice of reaction conditions, lithiated species such as **12** or **13** do predominate over **11b** or **14**, respectively. Overall, this directed metalation is a useful way to rapidly functionalize biaryl−benzimidazole systems, and although the enantioselective metalation is not possible on the ferrocene system **1** by sparteine-directed metalation, the resulting racemic products, such as **2**, could be subjected to resolution as a route to novel axially chiral catalysts and ligands.

Experimental Section

2-Ferrocenyl-*N*-*n*-butylbenzimidazole (1). To a solution of 2-(*N*-*n*-butylamine)aniline (**7**) (1.0 g, 6 mmol) in DMF/water (15 mL:0.5 mL) was added the ferrocene carboxaldehyde (1.30 g, 6 mmol) and Oxone (2.43 g, 4 mmol). The reaction mixture was stirred at room temperature overnight, quenched with a saturated solution of K_2CO_3 (5 mL), extracted with ethyl acetate (3 × 15 mL), dried, evaporated, and purified by silica gel chromatography (ethyl acetate/hexane, 1:9 as eluent) to give **1** (1.43 g, 66%) as orange needles. Mp: 73−74°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.98 (t, 3H, J = 7.2 Hz), 1.46 (sextet, 2H, J = 7.2, 14.8 Hz), 1.81−1.89 (m, 2H), 4.12 (s, 5H), 4.32−4.37 (m, 2H), 4.40 (t, 2H, J = 1.6 Hz), 4.85 (t, 2H, J = 2.0 Hz), 7.15−7.21 (m, 2H), 7.23−7.28 (m, 1H), 7.65−7.72 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 20.4, 32.4, 44.3, 69.1, 69.7, 70.0, 74.2, 109.1, 119.1, 121.9, 122.0, 136.0, 143.2, 152.9. IR (KBr, cm^{-1}): 3088, 2957, 2927, 2860, 2905, 1535, 1459, 1428, 1363, 742. HRMS (ES+): $C_{21}H_{23}N_2{}^{54}Fe$ *m*/*z* calcd 357.1252 (M + H$^+$), found 357.1255

2-Phenyl-*N*-*n*-butylbenzimidazole (3). Sodium hydride (300 mg of 60% oil suspension, 7.5 mmol) was washed with dry hexane (3 × 10 mL) and dissolved in anhydrous DMF (25 mL) under argon. 2-Phenyl-*1H*-benzimidazole (**8**) (971 mg, 5.0 mmol) was added and stirred for 10 min at room temperature. The *n*-butylbromide (0.54 mL, 5.0 mmol) was added dropwise over 15 min, and the reaction mixture was heated to reflux. After 6 h, ethanol (0.5 mL) was added to quench the reaction and the mixture was stirred for an extra 10 min at room temperature. The solvent was evaporated, and the mixture was redissolved in diethyl ether (20 mL), washed with 20% NaOH (3 × 10 mL), dried, and evaporated to give **3** (1.10 g, 88%) as a dark yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.69 (t, 3H, J = 7.2 Hz), 1.09 (hextet, 2H, J = 7.6 Hz), 1.62 (quintet, 2H, J = 7.6 Hz), 4.04 (t, 2H, J = 7.2 Hz), 7.14−7.16 (m, 2H), 7.24−7.26 (m, 1H), 7.34−7.36 (m, 3H), 7.55−7.57 (m, 2H) and 7.70−7.73 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.4, 18.7, 30.7, 43.4, 109.1, 118.6, 121.2, 121.6, 127.7 (2C), 128.2 (2C), 128.6, 129.8, 134.6, 142.1, 152.6. IR (neat, cm^{-1}): 3157, 2978, 2905, 1453, 1314. HRMS (ES+): $C_{17}H_{19}N_2$ *m*/*z* calcd 251.1543 (M + H$^+$), found 251.1542. Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.56; H, 7.25; N, 11.19. Found C, 80.25; H, 7.21; N, 11.16.

2-(2-Boronoferrocenyl)-*N*-*n*-butylbenzimidazole (2). Method A: To a solution of (−)-sparteine (1.19 mL, 5.2 mmol) in dry diethyl ether (20 mL) under argon stirred at −78 °C was added *n*-butyllithium (3.25 mL of a 1.6 M solution in hexane, 5.2 mmol). The resulting solution was stirred for 30 min. Then, a solution of **1** (1.43 g, 3.9 mmol) in diethyl ether (15 mL) was added and the mixture was stirred at −78 °C, followed by addition of trimethylborate (0.894 mL, 7.98 mmol). After 30 min, the mixture was warmed to room temperature, quenched with saturated NH_4Cl solution (10 mL), and extracted with diethyl ether (3 × 15 mL). The combined organic extracts were washed with H_2O (3 × 15 mL) and brine (3 × 15 mL), dried, evaporated, and purified by silica gel chromatography (hexane, hexane/ethyl acetate, ethyl acetate, ethyl acetate/methanol, methanol, gradient elution) to give a solid which was recrystallized from acetonitrile/water to give **2** (341 mg, 23%) as orange needles. Mp: 143−145 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, 3H, J = 6.8 Hz), 1.41 (hextet, 2H, J = 6.8, 14.8 Hz), 1.75−1.90 (m, 2H), 4.09 (s, 5H), 4.14−4.21 (m, 1H), 4.32−4.40 (m, 1H), 4.59 (s br, 1H), 4.79 (s br, 1H), 4.88 (s br, 1H), 7.12−7.28 (m, 3H), 7.60−7.70 (m, 1H), 9.80 (s br, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.8, 20.3, 32.2, 44.8, 70.7, 71.6, 73.1, 76.4, 78.0, 109.5, 118.5, 122.6, 122.7, 135.4, 140.8, 154.6. ^{11}B NMR ($CDCl_3$, 128 MHz): δ 29.6. IR (neat, cm^{-1}): 3323, 2954, 2924, 2361, 1518, 1398, 1289. MS (ES+, *m*/*z*, %): 403.1 (M + H$^+$, 100), 346.9 (15), 232.0 (15). Anal. Calcd for $C_{21}H_{23}BFeN_2O_2$: C, 62.73; H, 5.77; N, 6.97. Found C, 62.33; H, 5.81; N, 6.76.

Method B: To a solution of **1** (100 mg, 0.28 mmol) in dry THF (2 mL) under argon stirred at −78 °C was added *tert*-butyllithium (0.279 mL of a 1.5 M solution in pentane, 0.418 mmol). The resulting solution was stirred for 2 h followed by the addition of trimethylborate (0.062 mL, 0.56 mmol). After 1 h, the mixture was warmed to room temperature and stirred for 2 h, the reaction was quenched with saturated NH_4Cl solution (2 mL), and the product was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with brine (3 × 5 mL), dried, evaporated, and purified by silica gel chromatography as in the previous experiment to give **2** (98 mg, 87%) as orange needles.

2-(2-Bromoferrocenyl)-*N*-*n*-butylbenzimidazole (9a). Method A: To a solution of (−)-sparteine (0.083 mL, 0.36 mmol) in dry THF (2 mL) under argon stirred at −78 °C was added *n*-butyllithium (0.226 mL of a 1.6 M solution in hexane, 0.36 mmol). The resulting solution was stirred for 30 min. Then, a solution of **1** (100 mg, 0.28 mmol) in THF (2 mL) was added, and the mixture was stirred at −78 °C. After 1 h, a solution of dibromotetrachloroethane (181 mg, 0.56 mmol) in THF (2 mL) was added. After 30 min, the mixture was warmed to room temperature, the reaction was quenched with saturated NH_4Cl solution (2 mL), and the product was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with H_2O (3 × 5 mL) and brine (3 × 5 mL), dried, evaporated, and purified by silica gel chromatography (hexane/ethyl acetate, 8:2 as eluent) to give **9a** (57 mg, 47%) as brown-green solid. Mp: 92−93 °C. Enantiomeric ratio = 1, Chiralcel OD, hexane/isopropanol: 95/5, 1 mL/min, λ = 254 nm, 8.35 min, 9.62 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.71 (t, 3H, J = 7.2 Hz), 1.07 (hextet, 2H, J = 7.6, 14.4 Hz), 1.49−1.58 (m, 2H), 3.90−3.98 (m, 1H), 4.00−4.09 (m, 1H), 4.26 (s br, 1H), 4.41 (s br, 1H), 4.43 (s, 5H), 4.59 (s br, 1H), 7.15−7.32 (m, 3H), 7.81−7.85 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.5, 19.8, 31.5, 44.1, 67.3, 69.4, 70.1, 71.2, 72.9, 79.4, 109.7, 120.2, 121.9, 122.4, 135.5, 143.1, 149.8. IR (neat, cm^{-1}): 3104, 2938, 2874, 1541, 1451, 1241. MS (ES+, *m*/*z*, %): 437.0 (M + H$^+$, 100), 439.0 (M + H$^+$ + 2), 346.9 (25), 232.0 (20). Anal. Calcd for $C_{21}H_{21}BrFeN_2$: C, 57.70; H, 4.84; N, 6.41. Found C, 57.75; H, 4.91; N, 6.10.

Method B: To a solution of **1** (100 mg, 0.28 mmol) in dry THF (2 mL) under argon stirred at −78 °C was added *tert*-butyllithium (0.279 mL of a 1.5 M solution in pentane, 0.418 mmol). The resulting solution was stirred for 2 h. Then a solution of 1,2-dibromotetrachloroethane (181 mg, 0.56 mmol) in dry THF (2 mL) was added, and the mixture was stirred at −78 °C. After 1 h, the mixture was warmed to room temperature and stirred over 2 h, the reaction was quenched with saturated NH_4Cl solution (2 mL), and the product was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with brine (3 × 5 mL), dried, evaporated, and purified as in the previous experiment to give **9a** (103 mg, 85%) as a brown-green solid.

2-(2-Trimethylsilylferrocenyl)-*N*-*n*-butylbenzimidazole (9b). To a solution of **1** (200 mg, 0.56 mmol) in dry THF (8 mL) under argon stirred at −78 °C was added *tert*-butyllithium (0.56 mL of a 1.5 M solution in pentane, 0.84 mmol). The resulting solution was stirred for 3.5 h. Then, trimethylsilylchloride (0.15 mL, 1.12 mmol) was added dropwise, and the mixture was stirred at −78 °C. After 2 h, the mixture was gradually warmed to room temperature and stirred for 15 h. The reaction was then quenched with saturated NH_4Cl solution (9 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (2 × 10 mL), dried, evaporated, and purified by silica gel chromatography (hexane/ethyl acetate, 2:1 as eluent) to give **9b** (92 mg, 25%) as a red oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.21 (s, 9H), 0.93 (t, 3H, J = 7.2 Hz), 1.36 (hextet, 2H, J = 7.2, 14.8 Hz), 1.62−1.84 (m, 2H), 3.96−4.05 (m, 1H), 4.34 (s, 5H), 4.36 (dd, 1H, J = 1.2, 2.4 Hz), 4.37−4.47 (m, 1H), 4.53 (t, 1H, J = 2.4 Hz), 4.62 (dd, 1H J = 1.2, 2.4 Hz), 7.20−7.27 (m, 2H), 7.29−7.34 (m, 1H), 7.71−7.80 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 0.0, 13.1, 19.6, 31.4, 43.4, 69.3, 70.6, 71.7, 74.1, 74.7, 108.6, 119.0, 120.9, 121.2, 130.8, 146.6, 151.9. IR (KBr, cm^{-1}): 2958, 2926, 2852, 1531, 1457, 1243, 838, 743. HRMS (ES+): $C_{24}H_{31}N_2{}^{54}FeSi$ *m*/*z* calcd 429.1646 (M + H$^+$), found 429.1647.

2-(*N*-*n*-Butylbenzimidazole)phenylboroxine (4b). To a solution of **3** (338 mg, 1.35 mmol) in dry THF (14 mL) under argon stirred at −78 °C was added dropwise *tert*-butyllithium (1.35 mL of a 1.5 M solution in pentane, 2.02 mmol) over 40 min. After the solution was stirred for 2 h at −78 °C, triisopropylborate (0.63 mL, 2.69 mmol) was added dropwise. The reaction mixture was stirred 1 h at −78 °C and then was allowed to warm to room temperature overnight. The reaction mixture was quenched with a 10% solution of NaOH (8 mL) and neutralized to a pH of 7 with a 10% solution of HCl. After evaporation of the THF, a precipitate was formed and removed by filtration. The resulting solid was purified by chromatography on aluminum oxide (ethyl acetate, then acetonitrile and acetonitrile/methanol, 9:1, as eluent) giving the boroxine **4b**[24] (248 mg, 67%) as a white powder. Mp: 238−239 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.77 (t, 9H, J = 7.2 Hz), 1.21 (hextet, 6H, J = 8 Hz), 1.60 (quintet, 6H, J = 7.6 Hz), 3.96 (t, 6H, J = 7.2 Hz), 7.02 (d, 3H, J = 8 Hz), 7.09−7.19 (m, 12H), 7.27−7.30 (m, 3H), 7.53−7.55 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 20.1, 31.5, 44.5, 109.7, 117.3, 122.3, 122.9, 124.5, 127.6, 130.1, 132.2, 132.4, 135.6, 136.6, 149.1 (br), 155.2. ^{11}B NMR ($CDCl_3$, 128 MHz): δ 18.0. IR (neat, cm^{-1}): 3055, 2957, 2931, 2869, 1459, 1433, 1397, 1358, 1297, 737. HRMS (ES+): $C_{51}H_{52}N_6O_3B_3$ *m*/*z* calcd 829.4364 (M + H$^+$), found 829.4375. Anal. Calcd for $C_{51}H_{51}B_3N_6O_3$: C, 73.94; H, 6.21; N, 10.14. Found C, 72.26; H, 6.10; N, 9.86.

2-(*N*-*n*-Butylbenzimidazole)benzaldehyde (10a). To a solution of **3** (186 mg, 0.74 mmol) in dry THF (7 mL) under argon stirred at −25 °C was added dropwise *n*-butyllithium (0.927 mL of a 1.6 M solution in hexane, 1.483 mmol) over 20 min. After the solution was stirred for 3 h at −25 °C, anhydrous DMF (0.459 mL, 5.93 mmol) was added dropwise. The reaction mixture was stirred 1 h at −25 °C and then was allowed to warm to room temperature overnight, quenched with a saturated solution of NH_4Cl (10 mL), and extracted with diethyl ether (3 × 7 mL). The combined organic extracts were dried, evaporated, and purified by silica gel chromatography (hexane/ethyl acetate, 9:1, then ethyl acetate as eluent) to give **10a** (179 mg, 87%) as a yellow thick oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.69 (t, 3H, J = 7.6 Hz), 1.08 (hextet, 2H, J = 7.2 Hz), 1.61 (quintet, 2H, J = 7.6 Hz), 4.01 (t, 2H, J = 7.6 Hz), 7.24−7.31 (m, 2H), 7.37−7.40 (m, 1H), 7.53 (d, 1H, J = 7.6 Hz), 7.60 (t, 1H, J = 7.6 Hz), 7.67 (t, 1H, J = 7.6 Hz), 7.76 (dd, 1H, J = 6.6, 2 Hz), 8.04 (d, 1H, J = 7.6 Hz), 9.88 (1H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.4, 18.8, 30.6, 43.4, 109.2, 119.2, 121.6, 122.2, 127.6, 129.3, 130.0, 132.3, 132.5, 134.0, 134.6, 142.1, 149.0, 189.9. IR (neat, cm^{-1}): 3059, 2957, 2930, 2870, 1693, 1453, 1385, 1329, 743. HRMS (ES+): $C_{18}H_{19}N_2O$ *m*/*z* calcd 279.1492 (M + H$^+$), found 279.1494. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found C, 76.56; H, 6.82; N, 9.63.

2-(2-Bromophenyl)-*N*-*n*-butylbenzimidazole (10b). To a solution of **3** (307 mg, 1.23 mmol) in dry THF (10 mL) under argon stirred at −25 °C was added dropwise *n*-butyllithium (1.54 mL of a 1.6 M solution in hexane, 2.46 mmol) over 20 min. After the solution was stirred for 3 h at −25 °C, a solution of 1,2-dibromotetrachloroethane (0.800 g, 2.46 mmol) in dry THF (1.5 mL) was added dropwise. The reaction mixture was stirred 1 h at −25 °C, allowed to warm to room temperature overnight, quenched with a saturated solution of NH_4Cl (10 mL), and extracted with diethyl ether (3 × 7 mL). The combined organic extracts were dried, evaporated, and purified by silica gel chromatography (hexane/ethyl acetate, 9:1, then ethyl acetate as eluent) to give **10b** (20 mg, 5%) as a red thick oil. All spectroscopic and analytical properties were identical to those reported in the literature.[24]

2-(2-Trimethylsilanylphenyl)-*N*-*n*-butylbenzimidazole (10c). To a solution of **3** (393 mg, 1.57 mmol) in dry THF (13 mL) under argon stirred at −42 °C was added dropwise *n*-butyllithium (1.96 mL of a 1.6 M solution in hexane, 3.136 mmol) over 30 min. After the solution was stirred for 2 h at −42 °C, anhydrous TMSCl (0.397 mL, 3.14 mmol) was added dropwise. The reaction mixture was stirred 1 h at −42 °C, allowed to warm to room temperature overnight, quenched with a saturated solution of NH_4Cl (10 mL), and extracted with diethyl ether (3 × 10 mL). The combined organic extracts were dried, evaporated, and purified by silica gel chromatography (hexane/ethyl acetate, 9:1, then ethyl acetate as eluent) to give **10c** (438 mg, 87%) as a yellow thick oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.00 (s, 9H), 0.85 (t, 3H, J = 7.6 Hz), 1.28 (hextet, 2H, J = 8 Hz), 1.72 (quintet, 2H, J = 7.2 Hz), 3.94 (t, 2H, J = 7.6 Hz), 7.26−7.32 (m, 2H), 7.37−7.49 (m, 4H), 7.69−7.72 (m, 1H), 7.78−7.82 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 0.00 (3C), 13.6, 20.5, 32.2, 44.7, 110.3, 120.4, 122.4, 122.9, 128.7, 129.1, 130.1, 135.0, 135.4, 136.5, 141.9, 143.2, 154.8. IR (neat, cm^{-1}): 3051, 2955, 2896, 2872, 1454, 1385, 1328, 835, 750. HRMS (ES+): $C_{20}H_{27}N_2Si$ *m*/*z* calcd 323.1938 (M + H$^+$), found 323.1940. Anal. Calcd for $C_{20}H_{26}N_2Si$: C, 74.48; H, 8.12; N, 8.69. Found C, 73.17; H, 7.70; N, 8.59.

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Supporting Information Available: General experimental methods and ^{1}H and ^{13}C NMR spectra for compounds **1** and **9b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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