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Preparation of Heterocyclic Amines by an Oxidative Amination of Zinc Organometallics Mediated by Cu^{I}: A New Oxidative Cycloamination for the Preparation of Annulated Indole Derivatives

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Dedicated to Professor Eiichi Nakamura on the occasion of his 60th birthday

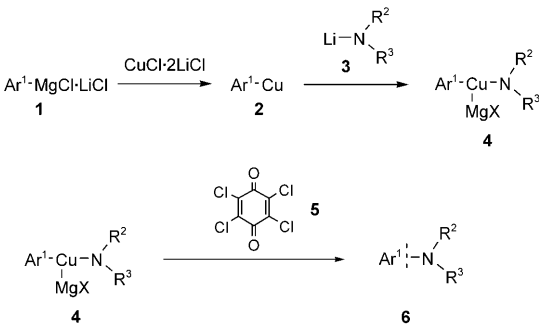
Abstract: Functionalized heterocyclic zinc reagents are easily aminated by an oxidative amination reaction of zinc amidocuprates prepared from various lithium amides. For the oxidation step, $PhI(OAc)_2$ proved to be the best reagent. The required heterocyclic zinc organometallics can be prepared either by direct metalation, by magnesium insertion in the presence of $ZnCl_2$, or by transmetalation of a suitable magnesium reagent. Furthermore, we report a new ring-closing reaction involving an intramolecular oxidative amination reaction. This reaction allows the preparation of tetracyclic heterocycles containing furan, thiophene, or indole rings.

Keywords: amination · cross-coupling · heterocycles · lithium amides · zinc organometallics

Introduction

Heteroaromatics are important classes of structures in medicinal chemistry.[1] Heteroaromatic amines are widely found in natural products[2] and are frequent target molecules in organic synthesis, owing to their potential applications as pharmaceuticals, xerographic and photographic materials, conducting polymers, or material precursors.[3] Owing to the pioneering work of Buchwald, Hartwig, and Beller[4,5] many functional five- and six-membered heterocyclic amines are nowadays available.[6] Although much progress has been made for these transition metal-catalyzed aminations of aryl and heteroaryl halides, these reactions still have some limitations. Particularly, the mono-functionalization of dihaloarenes (e.g., diiodo-, dibromo-, and dichloroarenes) results in the formation of product mixtures. Some disadvantages for aminations with sterically hindered amines are the long reaction times required and the use of strong bases. Finally, triarylamines cannot always efficiently be prepared by using these methods. Inspired by the work of Yamamoto and Ricci,[7] we recently reported an oxidative amination reaction of functionalized amidocuprates.[8] Thus, the preparation of primary, secondary, and tertiary arylamines was achieved by the oxidative coupling of polyfunctional aryl and heteroaryl amidocuprates (Scheme 1). A suitable magnesium reagent **1** is transmetalated to the corresponding copper species **2** using the complex CuCl·2 LiCl. After addition of a lithium amide **3**, a magnesium amidocuprate of type **4** is formed. Subsequent oxidation using chloranil (**5**) furnishes the desired amines of type **6**.

More recently, we have reported an extension of this protocol using functionalized heteroarylzinc reagents for the



Scheme 1. General scheme for the oxidative amination of organomagnesium reagents by using chloranil.

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Cu^I-mediated amination.[9] The oxidative amination of zinc reagents failed using chloranil, however $PhI(OAc)_2$[10] gave much better results and furnished the desired amines in moderate to good yields. Although the present method requires stoichiometric amounts of CuCl·2 LiCl, the procedure allows the selective amination of various sensitive heterocycles.

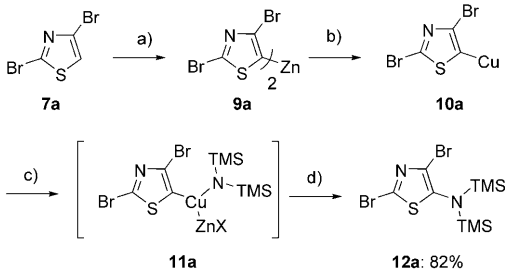
Herein, we wish to report the scope and limitations of this oxidative amination reaction using mostly zinc organometallics. A new ring-closure leading to condensed indoles will also be reported. Furthermore, the scale-up of this oxidative cross-coupling reaction will be described in detail.

Results and Discussion

Direct Zincation of Heteroaromatics and Subsequent Oxidative Amination Reaction

2,4-Dibromothiazole (**7a**) was zincated within 45 min at 25 °C by using $[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$[11] (**8**, 0.55 equiv; TMP = 2,2,6,6-tetramethylpiperidyl)[12] furnishing the diarylzinc **9a**. This zinc reagent was very stable and did not undergo halogen-dance reactions, as is usual for electron-rich heteroaromatic organometallics.[13] After the addition of CuCl·2 LiCl (1.1 equiv), the corresponding copper derivative **10a** was obtained after 30 min at −50 °C. Further addition of $LiN(SiMe_3)_2$ (2.0 equiv, −50 °C, 1 h) afforded the amidocuprate **11a**. The subsequent oxidation of **11a** by using $PhI(OAc)_2$ (1.1 equiv, −78 °C, 1 h) provided the amino thiazole **12a** in 82 % yield (Scheme 2). Interestingly, if chloranil (**5**) was used for the oxidation step, large amounts of the corresponding homocoupling product of the zinc reagent were obtained. Of all amination reactions performed with a zinc reagent, $PhI(OAc)_2$ was the best oxidant.

A range of thiazoles were aminated in 61–76 % yield by this procedure (Table 1). Thus, the copper derivative **10a** was also reacted with lithium morpholide or lithium *N*-methylpiperazide, leading to the tertiary amines **12b** and **12c** in 61–70 % yield (Table 1, entries 1–2). 2-Bromothiazole (**7b**) was smoothly zincated within 2 h at 25 °C by using



Scheme 2. Cu^I-mediated oxidative amination of a zinc reagent obtained by direct zincation. Conditions: a) $[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$ **8** (0.55 equiv), THF, 25 °C, 45 min; b) CuCl·2 LiCl (1.1 equiv), −50 °C, 30 min; c) $LiN(SiMe_3)_2$, (2.0 equiv), −50 °C, 1 h; d) $PhI(OAc)_2$ (1.1 equiv), −78 °C, 1 h.

$[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$. The corresponding amidocuprates were obtained after transmetalation with CuCl·2 LiCl and the addition of various cyclic and acyclic amines. Subsequent oxidation with $PhI(OAc)_2$ furnished the 5-amino-2-bromothiazoles **12d–f** in 63 %–75 % yield (entries 3–6). Using this method, 4-aminothiazoles can also be prepared. Thus, the zincation and subsequent transmetalation of 2-bromo-5-trimethylsilylthiazole (**7c**) gave the corresponding copper reagents. Oxidative amination with suitable lithium amides furnished the tertiary amines **12g–h** in 73–75 % yield and the triarylamine **12i** in 76 % yield (entries 7–9). 2-(Phenylthio)thiazole (**7d**) was also successfully aminated, providing the amines **12j–k** in 72–75 % yield (entries 10–11). These (phenylthio)thiazoles may be further functionalized, since the phenylthio group can serve as a leaving group in cross-coupling reactions.[14]

Furthermore, we have applied this method to the amination of other heteroaromatics, such as benzothiazole (**13a**), benzothiophene (**13b**), benzofuran (**13c**), and 2,5-dibromothiophene (**13d**). Benzothiazole (**13a**) was smoothly zincated at 25 °C using $[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$ (**8**). Subsequent oxidative amination with lithium morpholide and LiTMP furnished the tertiary amines **14a–b** in 60 %–73 % yield (Table 2, entries 1–2). Remarkably, the steric hindrance of the TMP moiety did not hamper the oxidative amination.[15] Benzothiophene (**13b**) was metalated by using $[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$ (**8**) within 24 h at 25 °C. The oxidative amination with different lithium amides gave the amines **14c–d** in 67–73 % yield (entries 3–4).

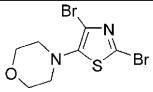
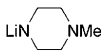
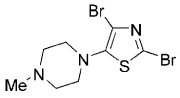
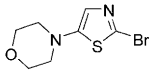
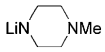
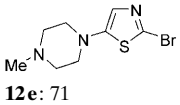
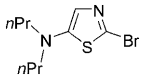
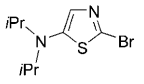
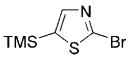
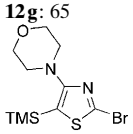
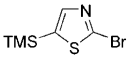
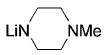
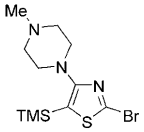
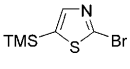
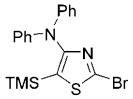
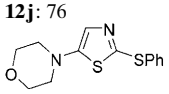
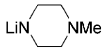
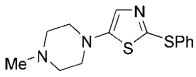
Benzofuran (**13c**), as well as 2,5-dibromothiophene (**13d**), was zincated by treatment with $[(TMP)_2Zn]\cdot 2\,MgCl_2\cdot 2\,LiCl$ (**8**) by using microwave irradiation (100 °C, 1 h)[16] followed by an oxidative amination with suitable lithium amides, yielding the corresponding amines **14e–g** in 60–70 % yield (entries 5–7).

Magnesium Insertion in the Presence of $ZnCl_2$ into Various Heterocyclic Halides and Subsequent Oxidative Amination Reaction

Recently, we reported a novel Mg-insertion into aromatic and heterocyclic bromides and chlorides in the presence of

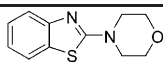
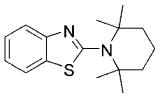
Abstract in German: Funktionalisierte heterozyklische Amine können durch oxidative Aminierung von Zink-Amidocupraten dargestellt warden, welche durch die Reaktion einer Reihe von Lithiumamiden mit funktionalisierten Zinkreagenzien zugänglich sind. Dabei hat sich Iodbenzoldiacetat $PhI(OAc)_2$ als optimales Oxidationsmittel herausgestellt. Die notwendigen Organozinkverbindungen können durch direkte Metallierung, Magnesiuminsertion in Gegenwart von $ZnCl_2$ oder durch Transmetallierung geeigneter Organomagnesiumreagenzien dargestellt werden. Darüber hinaus berichten wir von einer neuen Ringschlussreaktion mittels intramolekularer oxidativer Aminierung. Diese Reaktion ermöglicht die Darstellung tetrazyklischer Heterozyklen mit Furan-, Thiophen-, oder Indolgerüsten.

Table 1. Oxidative amination of various functionalized thiazoles after zincation with $[(TMP)_2Zn]\cdot 2MgCl_2\cdot 2LiCl$ (**8**).

Entry	Substrate (T [°C], t [h])[a]	Lithium amide	Product yield [%][b]
1			
	7a: 25, 0.75		**12b**: 70
2			
	7a: 25, 0.75		**12c**: 61
3			
	7b: 25, 2		**12d**: 75
4			
	7b: 25, 2		**12e**: 71
5			
	7b: 25, 2		**12f**: 63
6			
	7b: 25, 2		**12g**: 65
7			
	7c: 25, 8		**12h**: 73
8			
	7c: 25, 8		**12i**: 75
9			
	7c: 25, 8		**12j**: 76
10			
	7d: 25, 2		**12k**: 75
11			
	7d: 25, 2		**12l**: 72

[a] Reaction conditions for the direct zincation using $[(TMP)_2Zn]\cdot 2MgCl_2\cdot 2LiCl$; [b] Yield of analytically pure product.

Table 2. Oxidative amination of various heterocycles leading to tertiary and protected secondary amines.

Entry	Substrate[a] (T [°C], t [h])[b]	Lithium amide	Product yield [%][c]
1			
	13a: 25, 1		**14a**: 73
2			
	13a: 25, 1		**14b**: 60
3			
	13b: 25, 24		**14c**: 73
4			
	13b: 25, 24		**14d**: 67
5			
	13c: 100, 1 (MW)		**14e**: 60
6			
	13d: 100, 1 (MW)		**14f**: 70
7			
	13d: 100, 1 (MW)		**14g**: 67

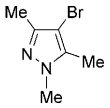
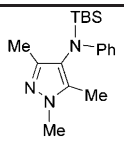
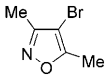
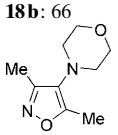
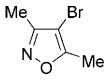
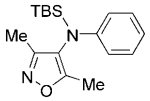
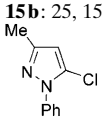
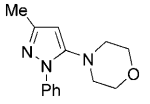
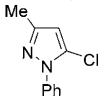
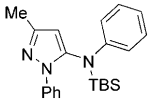
[a] Reaction conditions for the direct zincation using $[(TMP)_2Zn]\cdot 2MgCl_2\cdot 2LiCl$; [b] Yield of analytically pure product.

LiCl and $ZnCl_2$, leading to aromatic and heteroaromatic zinc organometallics.[17] We have applied this method to the zincation of several heterocycles followed by an oxidative amination. Thus, 4-bromo-1,3,5-trimethyl-1*H*-pyrazole (**15a**) was treated with Mg turnings (2.5 equiv) in the presence of LiCl (2.5 equiv) and $ZnCl_2$ (1.0 equiv), furnishing the zinc species **16a** within 30 min at 25 °C. The amidocuprate **17a** was obtained after transmetalation with CuCl·2 LiCl (1.1 equiv) and the addition of lithium diphenylamide (2.0 equiv). Oxidation of **17a** by using $PhI(OAc)_2$ (1.1 equiv) led to the desired tertiary amine **18a** in 70% yield (Scheme 3).

In a similar manner, the heterocycle **15a** was converted to the protected secondary amine **18b** in 66% yield (Table 3,

Scheme 3. Mg-insertion to the 4-bromopyrazole (**15a**) in the presence of LiCl and $ZnCl_2$ followed by an oxidative amination with $PhI(OAc)_2$.

Table 3. Oxidative amination of zinc reagents obtained by magnesium insertion in the presence of LiCl and $ZnCl_2$.

Entry	Substrate (T [°C], t [min])[a]	Lithium amide	Product yield [%][b]
1			
	15a: 25, 15		**18b**: 66
2			
	15b: 25, 15		**18c**: 66
3			
	15b: 25, 15		**18d**: 60
4			
	15c: 25, 60		**18e**: 67
5			
	15c: 25, 60		**18f**: 57

[a] Reaction conditions for the Mg insertion in the presence of LiCl and $ZnCl_2$ [b] Yield of analytically pure product.

entry 1). Other chloro- or bromo-*N*-heterocycles, such as **15b** and **15c**, led to the corresponding zinc compounds by using the previously described Mg insertion in the presence of $ZnCl_2$. These zinc reagents were then aminated by using the oxidative amination, yielding the protected secondary and tertiary amines **18c–f** in 57–67% yield (entries 2–5).

Oxidative Cycloamination

We have found that the oxidative amination can also be used for performing an oxidative ring closure leading to indole derivatives. Furo[2,3-*b*]indoles of type **A** are recurring structural motifs in natural products[19] and thieno[2,3-*b*]indoles of type **B** find application in treating diseases of the human central nervous system.[20] Benzofuro[2,3-*b*]indole derivatives, such as **C**, have not been described and only the unsubstituted benzothieno[2,3-*b*]indole **D** has been prepared (Figure 1).[21] The inversely condensed benzofuro-[3,2-*b*]indoles of type **E** show high activity in opening Ca-

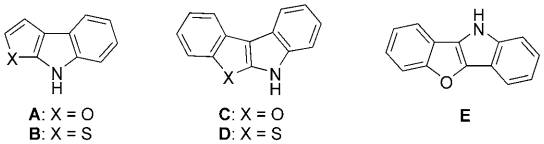
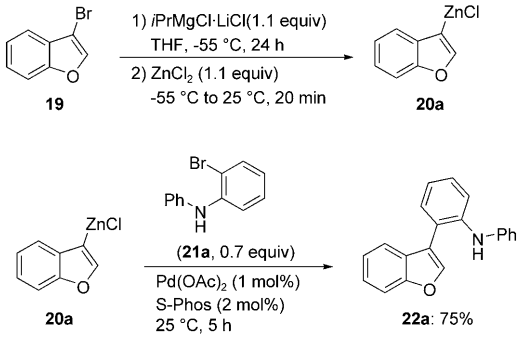


Figure 1. Condensed indole derivatives of type **A**–**E**.

controlled K channels in eukaryotic cells[22] explaining our interest for preparing their undescribed [2,3-*b*]-fused analogs.

Thus, a Br/Mg-exchange on 3-bromobenzofuran (**19**) with *i*PrMgCl·LiCl (−55°C, 24 h) provided the corresponding magnesium reagent. A higher temperature for the exchange reaction resulted in the decomposition of the metalated species. This magnesium reagent was transmetalated to the zinc species **20a** using $ZnCl_2$ (1.1 equiv, −55°C to 25°C, 20 min). A subsequent Negishi cross-coupling with the bromoaniline **21a** in the presence of $Pd(OAc)_2$ (1 mol%) and S-Phos[18] (2 mol%) furnished the desired benzofuran derivative **22a** within 5 h at 25°C in 75% yield (Scheme 4).



Scheme 4. Negishi cross-coupling of the zinc reagent **20a** with the bromoaniline **21a**.

Using the same conditions, the zinc reagent **20a** was coupled with various bromoanilines to give the corresponding biaryls **22b–d** in 86–91% yield (Table 4, entries 1–3). The related 3-bromobenzothiophene was converted to the corresponding zinc reagent **20b**. Thus, treatment of 3-bromobenzothiophene with *i*PrMgCl·LiCl (1.1 equiv, −55°C, 24 h) and subsequent addition of $ZnCl_2$ (1.1 equiv) furnished the zinc species **20b**. This reagent reacted with various bromoanilines under Pd-catalysis ([$Pd(OAc)_2$] (1 mol%) and S-Phos[18] (2 mol%)) providing the corresponding coupling products **22e–h** in 43–81% yield (entries 4–7).

These primary amines **22d** and **22h** were then protected with various protecting groups. Thus, deprotonation of **22d** and **22h** with *n*BuLi (1.1 equiv, −30°C, 30 min) gave the corresponding lithium species. Subsequent addition of an electrophile (e.g., MeI, allyl bromide, or TIPS-Cl (ClSi-(iPr)$_3$), 1.1 equiv, −30°C to 25°C, 30 min) gave the desired secondary amines **22i–n** in 30–96 yield (Table 5, entries 1–6).

Having the secondary amines **22a–n** in hand, we examined the oxidative ring closure of these compounds for the formation of annulated indole derivatives. Thus, the benzofuran derivative **22a** was deprotonated by using *n*BuLi (2.0 equiv, −78°C to −30°C, 5 h) to give the corresponding *bis*-metalated species. After transmetalation with CuCl·2 LiCl (1.1 equiv, −50°C, 20 min), the resulting copper species underwent a ring closure mediated by chloranil (**5**, 1.1 equiv, −78°C, 1 h) furnishing the desired indole derivative **23a** in 80% yield (Scheme 5). The best results for this ring closure

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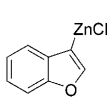
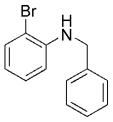
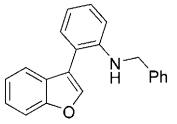
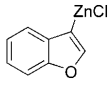
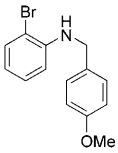
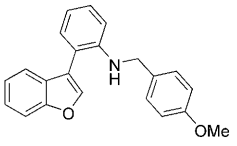
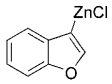
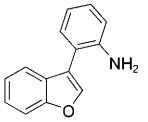
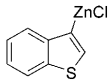
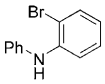
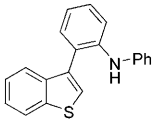
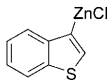
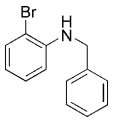
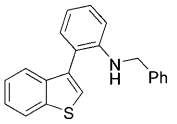
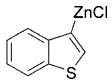
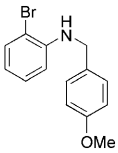
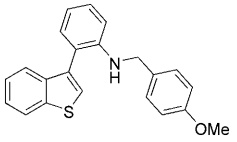
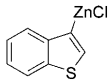
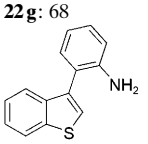
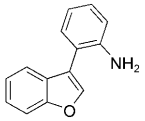
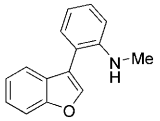
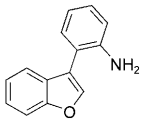
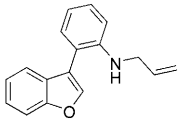
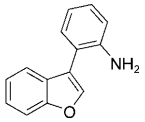
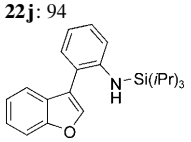
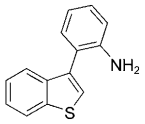
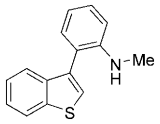
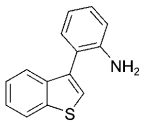
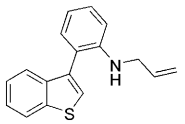
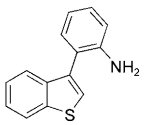
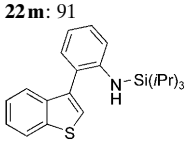
Table 4. Negishi cross-coupling of zinc reagents with various bromoanilines.

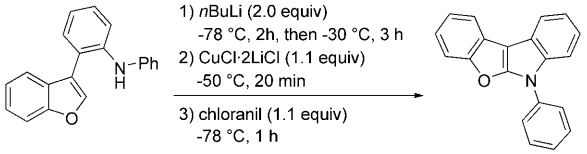
Entry	Substrate[a]	Lithium amide	Product yield [%][b]
1			
	20a		**22b**: 86
2			
	20a		**22c**: 91
3			
	20a		**22d**: 89
4			
	20b		**22e**: 43
5			
	20b		**22f**: 62
6			
	20b		**22g**: 68
7			
	20b		**22h**: 81

[a] Reaction conditions for the cross-coupling reaction: 25 °C, 5 h; [b] Yield of analytically pure product.

Table 5. Monoprotection of the primary amines **22d** and **22h**.

Entry	Substrate[a]	Electrophile	Product yield [%][b]
1		MeI	
	22d		**22i**: 62
2		allyl bromide	
	22d		**22j**: 94
3		TIPS-Cl	
	22d		**22k**: 48
4		MeI	
	22h		**22l**: 96
5		allyl bromide	
	22h		**22m**: 91
6		TIPS-Cl	
	22h		**22n**: 30

[a] Reaction conditions for the protection step; i) *n*BuLi (1.1 equiv, −30 °C, 30 min); ii) electrophile (1.1 equiv, −30 °C to 25 °C, 30 min). [b] Yield of analytically pure product.



22a **23a**: 80%

Scheme 5. Oxidative cycloamination for the synthesis of annulated indole derivatives.

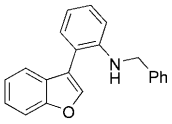
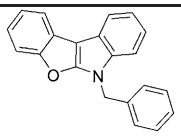
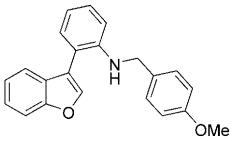
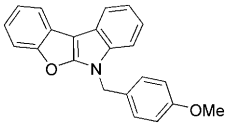
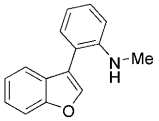
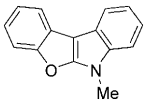
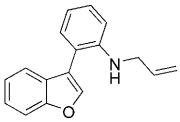
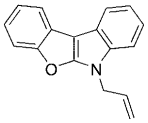
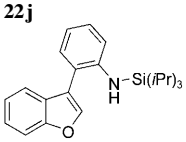
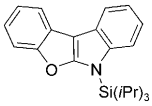
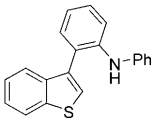
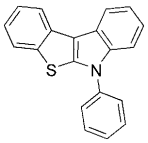
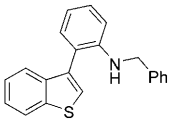
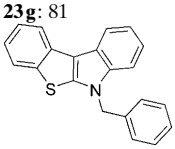
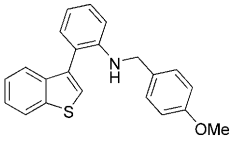
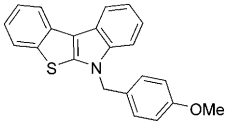
were obtained, when the precursors were diluted in THF (0.1 M). By running the oxidation cross-coupling reaction at a 1.0 M concentration in THF, large amounts of undesired by-products were obtained.

The reaction conditions detailed above proved to be general for such ring closing reactions, both for non-donating and donating substituents on the aniline nitrogen. Also, steric factors seemed to play a negligible role even with bulky substituents, such as TIPS. Thus, deprotonation of the benzofuran derivatives **22b–c** and **22i–k** was achieved with *n*BuLi (2.0 equiv, −78 °C, 1 h, then −30 °C, 3 h). After transmetalation with CuCl·2 LiCl, the corresponding copper species were oxidized with chloranil leading to the indole derivatives **23b–f** in 50–84 % yield (Table 6, entries 1–5). Similarly, the related benzothiophene derivatives **22e–g** and **22l–n** gave the corresponding tetracyclic heterocycles **23g–l** in 51–89 % yield (entries 6–11).

Conclusions

In summary, we have shown that amidocuprates obtained from organozinc reagents can be smoothly oxidized by PhI(OAc)$_2$. A range of heterocycles was successfully aminated by this protocol. The organozinc reagents required for the amination show a remarkable thermal stability and are supe-

Table 6. Cu^{I}-mediated oxidative cycloamination.

Entry	Substrate	Product yield [%][a]
1		
	22b	**23b**: 84
2		
	22c	**23c**: 50
3		
	22i	**23d**: 50
4		
	22j	**23e**: 70
5		
	22k	**23f**: 81
6		
	22e	**23g**: 81
7		
	22f	**23h**: 58
8		
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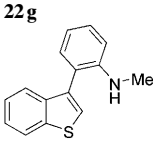
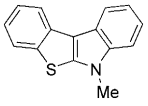
9		
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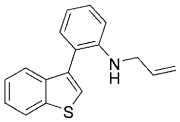
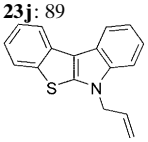
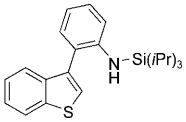
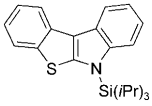
10		
	22m	**23k**: 62
11		
	22n	**23l**: 71

[a] Yield of analytically pure product.

rior to the corresponding magnesium reagents. Furthermore, we applied the oxidative amination reaction to the synthesis of indole derivatives. A range of tetracyclic heterocycles was synthesized by a new oxidative ring closing reaction. Further extensions of this methodology, as well as applications in natural material chemistry, are currently underway in our laboratories.

Experimental Section

*2,4-Dibromo-N,N-bis(trimethylsilyl)-1,3-thiazol-5-amine (**12a**)*

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with 2,4-dibromo-1,3-thiazole (**7a**) (243 mg, 1.0 mmol) and THF (1 mL). To the resulting mixture was added dropwise $[(TMP)_2Zn]\cdot 2MgCl_2\cdot 2LiCl$ (**8**, 1.30 mL, 1.68 M in THF, 0.55 mmol) and the reaction mixture was stirred for 45 min. CuCl·2 LiCl (1.1 mL, 1.0 M in THF, 1.1 mmol) was added dropwise to **9a** at −50 °C under argon and the mixture was stirred for 30 min. $LiN(SiMe_3)_2$ (2 mmol, 1 M in THF) was added dropwise to the resulting cuprate **10a**, and the mixture was stirred for 1 h at −50 °C. The reaction mixture was cooled to −78 °C, then a solution of $PhI(OAc)_2$ (354 mg, 1.1 mmol) in dry THF (10 mL) was added slowly over a period of 60 min. The reaction mixture was then warmed to −50 °C and stirred for an additional 3 h. Et_2O (100 mL) was poured into the crude reaction mixture. The organic phase was washed with 2×10 mL portions of aqueous NH_4OH (2.0 M) and extracted with Et_2O. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane; Al_2O_3 III) yielded **12a** (331 mg, 80 %) as a colorless oil. IR (ATR): $\tilde{\nu}$ = 2950, 1499, 1412, 1251, 1204, 1154, 1009, 909, 869, 837, 816, 790, 753, 684, 666, 632 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.17 ppm (s, 18H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.3, 127.7, 119.8, 1.5 ppm; MS (70 eV, EI): *m*/*z* (%) = 402 (18), 399 (18), 387 (32), 385 (14), 323 (15), 321 (14), 125 (12), 123 (11), 97 (11), 83 (11), 73 (100); HRMS (EI): *m*/*z* calc. for $[C_9H_{18}{}^{79}Br_2N_2SSi_2]$ 399.9096, found: 399.9086.

*2-(1-Benzo[b]furan-3-yl)-N-phenylaniline (**22a**)*

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with 3-bromobenzofuran (**22a**) (295 mg, 1.5 mmol) and THF (0.75 mL). The solution was cooled to −55 °C, then *i*PrMgCl·LiCl (1.65 mmol, 1.30 M in THF, 1.27 mL) was added and the resulting mixture was stirred for 24 h. Then, $ZnCl_2$ (1.5 mmol, 1 M in THF, 1.5 mL) was added and the solution was warmed up to −10 °C within 20 min. A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with 2-bromoaniline (172 mg, 1.0 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol) and S-Phos (8.2 mg, 0.02 mmol) in THF (1 mL). To this mixture, the freshly prepared zinc reagent was added within 10 min at 25 °C. The resulting solution was stirred at 25 °C for additional 5 h to obtain full conversion. The reaction mixture was quenched by the addition of sat. NH_4Cl-solution (5 mL) and the product was extracted with EtOAc (3×25 mL). The combined organic phases were successively washed with sat. thiourea solution (2×10 mL) and sat. NaCl solution (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography (pentane/Et_2O; 9:1) yielded **22a** (213 mg, 75 %) as white solid. IR (ATR): $\tilde{\nu}$ = 3392, 3036, 1588, 1500, 1452, 1420, 1336, 1304, 1220, 1200, 1164, 1100, 1080, 964, 856, 800, 740, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.77 (s, 1H), 7.56 (t, ^3J = 9.3 Hz, 2H), 7.42 (ddd, ^3J = 15.7 Hz, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 2H), 7.36–7.33 (m, 1H), 7.31–7.29 (m, 1H), 7.27–7.22 (m, 3H), 7.06–7.04 (m, 2H), 7.00 (td, ^3J = 7.5 Hz, ^4J = 1.3 Hz, 1H), 6.94 (tt, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 5.69 ppm (br. s, 1H, N*H*); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 155.6, 143.1, 142.9, 141.8, 131.5, 129.6, 129.0, 127.2, 125.0, 123.3, 121.7, 121.0, 120.8, 120.5, 119.0, 116.7, 112.0, 105.0 ppm; MS (70 eV, EI): *m*/*z* (%) = 286 (21), 285 (100), 284 (14), 256 (12), 254 (11); HRMS (EI): *m*/*z* calc. for $[C_{20}H_{15}NO]$ 285.1154, found: 285.1145.

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*6-Phenyl-6H-[1]benzo[4,5]furo[2,3-b]indole (**23a**)*

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with 2-(1-benzofuran-3-yl)-*N*-phenylaniline (285 mg, 1 mmol) and THF (10 mL). The solution is cooled to −78 °C and *n*BuLi (0.87 mL, 2.30 M in pentane, 2.0 mmol) was added dropwise. The mixture was stirred for 1 h at −78 °C and for additional 3 h at −30 °C. Then, the mixture was cooled to −50 °C and CuCl·2 LiCl (1.1 mL, 1.0 M in THF, 1.1 mmol) was added and stirred for 20 min. After cooling to −78 °C, THF (9 mL) was added followed by the dropwise addition of chloranil (270 mg, 0.1 M in THF, 1.1 mmol). Diethyl ether was added to the crude reaction mixture and it was filtered through Celite, washed with ether thoroughly, and the filtrate was washed with 2×10 mL portions of aqueous NH_4OH (2.0 M). The organic extract was dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography (pentane) afforded **23a** (192 mg, 68%) as colorless solid. IR (ATR): $\tilde{\nu}$ = 3184, 3052, 2920, 2852, 1912, 1872, 1624, 1592, 1560, 1500, 1448, 1400, 1328, 1300, 1204, 1176, 1148, 1108, 1076, 1012, 960, 916, 852, 784, 748, 724, 696, 676 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.90 (t, ^3J = 7.8 Hz, 1H), 7.82 (d, ^3J = 7.8 Hz, 1H), 7.72 (d, ^3J = 7.8 Hz, 2H), 7.64–7.60 (m, 3H), 7.53 (d, ^3J = 7.8 Hz, 1H), 7.45 (t, ^3J = 7.5 Hz, 1H), 7.38–7.32 (m, 2H), 7.28–7.26 (m, 1H), 7.22 ppm (t, ^3J = 8.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.0, 156.0, 137.5, 136.0, 130.1, 127.4, 125.0, 124.7, 124.0, 121.9, 121.8, 121.7, 121.2, 119.6, 119.0, 112.1, 111.6, 99.5 ppm; MS (70 eV, EI): *m*/*z* (%) = 284 (21), 283 (100), 254 (32), 179 (8); HRMS (EI): *m*/*z* calc. for $[C_{20}H_{13}NO]$ 283.0997, found: 283.0987.

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