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Domino C–N Coupling/Annulation *versus* C–N Coupling/Hydroamination of 2-Alkynyl-3-bromobenzothiophenes and 2-Alkynyl-3-bromothiophenes. Highly Efficient Synthesis of Benzothieno[3,2-*b*]quinolines and Thieno[3,2-*b*]pyrroles

Ghazwan Ali Salman,[a] Munawar Hussain,[a] Viktor Iaroshenko,[a] Alexander Villinger,[a] and Peter Langer[a,b,*]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany
Fax: (+49)-381-498-6412; e-mail: peter.langer@uni-rostock.de
[b] Leibniz-Institut für Katalyse e. V. an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany

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Abstract: While the palladium-catalyzed reaction of 2-alkynyl-3-bromothiophenes with anilines afforded thienopyrroles by a domino C–N coupling/hydroamination process, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines resulted, under identical conditions, in the formation of benzothienoquinolines by a domino C–N coupling/annulation process. The electronic character of the aniline also has an influence on the product distribution.

Keywords: catalysis; cyclizations; heterocycles; palladium; regioselectivity

Nitrogen-containing heterocycles are of great importance in the field of medicinal chemistry and material sciences.[1] In recent years, transition metal-catalyzed syntheses of heterocycles have been developed which nicely complement classic synthetic approaches because they proceed under mild conditions and show a high degree of chemoselectivity and functional group tolerance.[2] A variety of palladium-catalyzed syntheses of indoles and carbazoles have been reported.[3] Ackermann and co-workers reported the synthesis of carbazoles and related molecules by palladium-catalyzed cyclization of 1,2-dihalides with anilines by domino[4] N–H/C–H activation reactions.[5] Stepwise syntheses following this strategy have also been reported.[6] Ackermann et al. reported the synthesis of indoles and various other ring systems by domino *N*-arylation/hydroamination reactions.[7] They also developed an efficient approach to indoles by Pd- or Cu-catalyzed domino C–N coupling/hydroamination reactions of *ortho*-alkynylated aryl halides.[8] Buchwald et al. reported the synthesis of pyrroles and pyrazoles by a related strategy.[9,10]

The development of regioselective palladium-catalyzed coupling reactions of dihalogenated heterocycles is of considerable current interest.[11] In the course of our own studies in this field,[12] we have studied the reaction of 2-alkynyl-3-bromothiophenes and 2-alkynyl-3-bromobenzothiophenes with anilines. Herein, we report the results of our efforts. The reaction of 2-alkynyl-3-bromothiophenes with anilines afforded, as expected, thienopyrroles by a domino C–N coupling/hydroamination process. In contrast, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines surprisingly resulted in the formation of benzothienoquinolines by a domino C–N coupling/annulation process. This type of palladium-catalyzed domino reaction has, to the best of our knowledge, not been previously reported and provides a convenient approach to pharmacologically relevant molecules which are not readily available by other methods. We believe that this type of cyclization is mechanistically interesting and has the potential to be extended to other heterocyclic systems in the future.

Cryptolepsis sanguinolenta is a shrub found along the west coast of Africa and is still being used significantly in the traditional medicine in Ghana. Its strong antimalarial activity has been proved in clinical trials. Furthermore, it has been been shown to possess a considerable antibiotic activity against Gram-positive and Gram-negative bacteria. Major alkaloids, cryptolepine (**1**) and quindoline (**2**), have been isolated along with some minor alkaloids from *Cryptolepsis sanguinolenta* (Figure 1).[13] Benzothienoquinolines are sulfur analogues of these alkaloids and represent

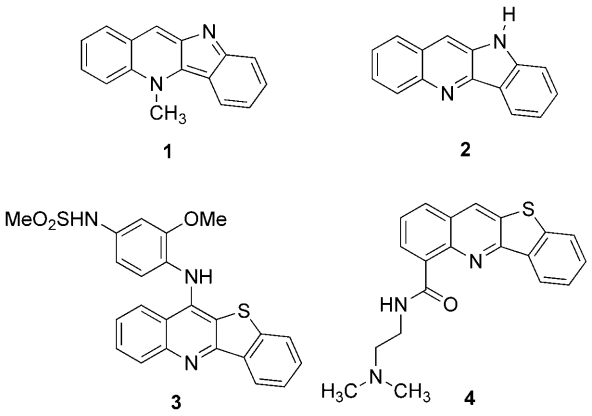


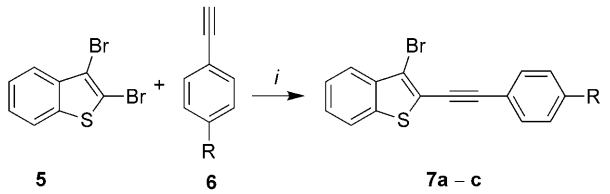
Figure 1. Alkaloids cryptolepine (**1**) and quindoline (**2**) isolated from *Cryptolepsis sanguinolenta* and bioactive benzothienoquinolines **3** and **4**.

interesting target molecules, due to their broad spectrum of antimicrobial, anticancer and cytotoxic activities. For example, benzothienoquinoline **3** has been reported to show antitumor activity *in vivo*, while derivative **4** possesses significant cytotoxic activity.[14,15]

Due to their biological relevance, a number of syntheses of benzothienoquinolines have been reported. Many of them represent modifications of the Pfitzinger synthesis which relies on the base-mediated cyclocondensation of isatin with ketones.[16] Recently, Zhu et al. reported a multistep synthesis of benzothienoquinolines from substituted anthranilic acids, acyl chlorides and thiophenols.[15] The above-mentioned syntheses of thienopyrroles and benzothienoquinolines proceed under harsh conditions or require several synthetic steps. Therefore, the development of alternative synthetic strategies is of considerable interest.

The regioselective synthesis of 2-alkynyl-3-bromothiophenes[17] and 2-alkynyl-3-bromobenzothiophenes[18] by Sonogashira reactions of 2,3-dibromothiophene and 2,3-dibromobenzothiophene with alkynes has been previously reported. The reaction of 2,3-dibromobenzothiophene (**5**) with alkynes **6**, in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol%), afforded the 2-alkynyl-3-bromobenzothiophenes **7a–c** (Scheme 1, Table 1).

The palladium-catalyzed reaction of 2-alkynyl-3-bromobenzothiophenes **7a–c** with anilines **8a–m** afforded the benzothienoquinolines **9a–m** in 60–70% yields (Scheme 2, Table 2). The synthesis of derivative **9j** was optimized by variation of the reaction conditions. The best yield of **9j** was obtained when $Pd(OAc)_2$ (10 mol%) in the presence of P(*t*-Bu)$_3$·HBF_4 (20 mol%) was used as the catalyst and when KO-*t*-Bu (2 equiv.) and CuI (25 mol%) were employed. The use of stoichiometric amounts of CuI in the absence of a palladium catalyst failed to give

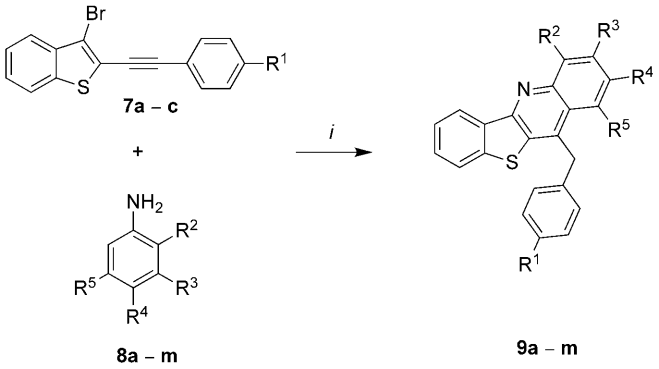


Scheme 1. Synthesis of **7a–c**. *Reaction conditions: i*, **6a–c** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (10 mol%), triethylamine, 20 °C, 24 h.

Table 1. Regioselective alkynylation of 2,3-dibromobenzothiophene.

6, **7**	R	Yield [%] of **7**[a]
a	H	80
b	Me	90
c	OCH_3	87

[a] Yields of isolated products.



Scheme 2. Synthesis of **9a–m**. *Reaction conditions: i*, **8a–m** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), P(*t*-Bu)$_3$·HBF_4 (20 mol%), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105 °C, 12 h.

Table 2. Synthesis of **9a–m**.

8, **9**	R^1	R^2	R^3	R^4	R^5	Yield [%] of **9**[a]
a	H	H	H	OCH_3	H	60
b	H	H	OCH_3	H	H	65
c	H	H	H	CH_3	H	61
d	H	H	H	C_2H_5	H	60
e	H	H	H	OC_2H_5	H	65
f	H	H	CH_3	H	CH_3	61
g	H	H	OCH_3	H	OCH_3	67
h	CH_3	OCH_3	H	OCH_3	H	70
i	CH_3	OCH_3	H	H	H	64
j	CH_3	H	H	OC_2H_5	H	60
k	OCH_3	H	H	$CH(CH_3)_2$	H	63
l	CH_3	H	H	F	H	60
m	OCH_3	H	CF_3	H	H	55

[a] Yields of isolated products.

the product. No reaction was observed when DMSO and THF were used as solvents. In fact, toluene proved to be the best solvent. The employment of dioxane afforded only trace amounts of product. Likewise, the use of Cs_2CO_3 instead of KO-*t*-Bu provided only traces of **9j**. The use of SPhos, XPhos or $P(Cy)_3$ instead of $P(t\text{-Bu})_3{\cdot}HBF_4$ again resulted in low yields. The best yield of **9j** (60%) was obtained when 20 mol% of the ligand $P(t\text{-Bu})_3{\cdot}HBF_4$ was used. The yield decreased to 30% when only 10 mol% of the ligand was employed. The moderate yields of products **9a–m** can be explained by the fact that small amounts of different side-products were formed (TLC of the crude product) which resulted in some practical difficulties during the chromatographic purification.

The structures of all products were established by spectroscopic methods. The structure of **9a** was independently confirmed by an X-ray crystal structure analysis (Figure 2).[19]

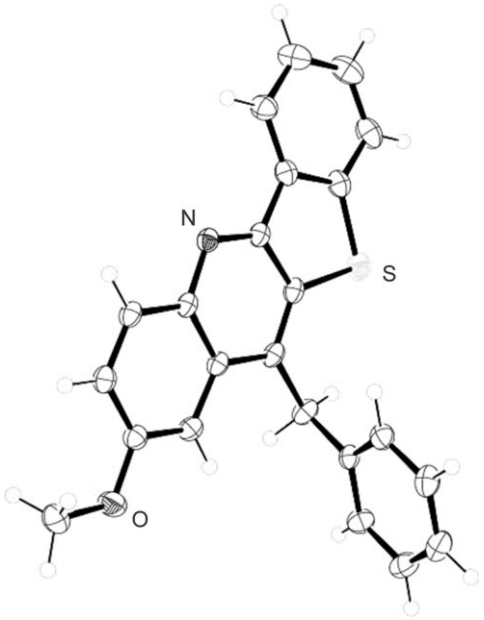


Figure 2. Crystal structure of **9a**.

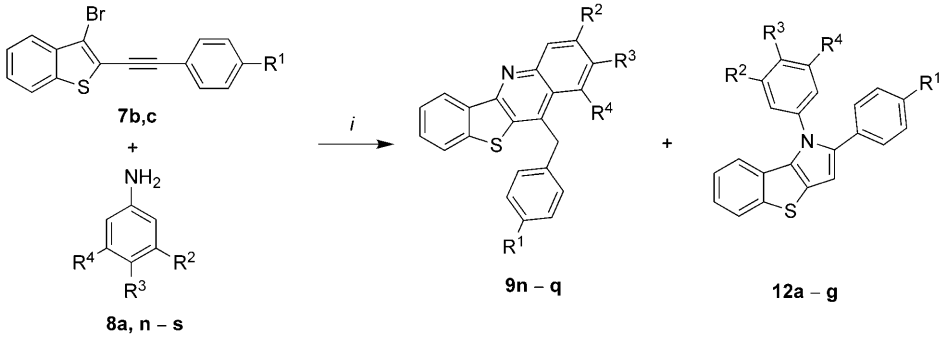
The palladium-catalyzed reaction of 2-alkynyl-3-bromobenzothiophenes **7b**, **c** with anilines **8a**, **n–p** afforded separable mixtures of benzothienoquinolines **9n–q** and benzothienopyrroles **12a–d** in 50–60 and 30–40% yields, respectively (Scheme 3, Table 3). The reactions were carried out under identical conditions as described for the synthesis of products **9a–m**. The cyclization of anilines **8q–s**, containing strong π-acceptor substituents (nitro, ester, cyano), resulted in exclusive formation of benzothienopyrroles **12e–g**. Thus, the electronic character of the starting materials seems to have an influence on the product distribution. It is a striking observation that the combined yields of products **9n–q** and **12a–g** were higher than the yields of products **9a–m** given in Table 2. This can be explained by the fact that several side products were formed during the synthesis of **9a–m** (resulting in a difficult chromatographic purification), while the reactions leading to those products listed in Table 3 proceeded more cleanly and the chromatographic purification was relatively easy.

The formation of benzothienoquinolines **9a–m** can be explained by a domino C–N coupling/annulation reaction and isomerization of a double bond (Scheme 4). This type of reaction has, to the best of our knowledge, not been previously reported. The formation of **9a** may proceed by initial palladium-catalyzed C–N coupling and subsequent annulation or by

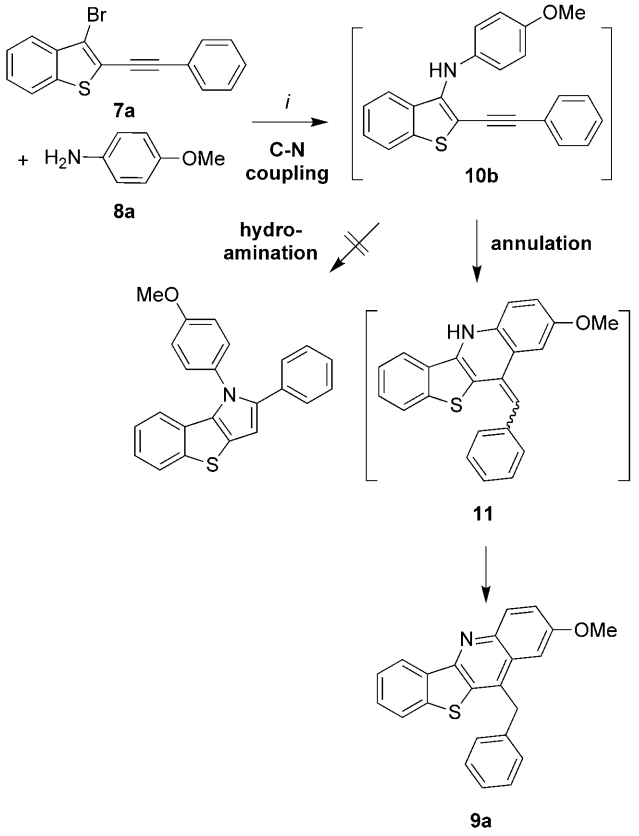
Table 3. Synthesis of **9n–t** and **12a–g**.

					Yield [%][a]	
12	R^1	R^2	R^3	R^4	of **9**	of **12**
a	OCH_3	H	OCH_3	H	60	30
b	CH_3	OCH_3	OCH_3	OCH_3	53	35
c	CH_3	OCH_3	OCH_3	H	50	40
d	OCH_3	H	Cl	H	55	32
e	OCH_3	NO_2	H	H	0	78
f	OCH_3	H	CN	H	0	84
g	CH_3	H	CO_2Me	H	0	45

[a] Yields of isolated products.



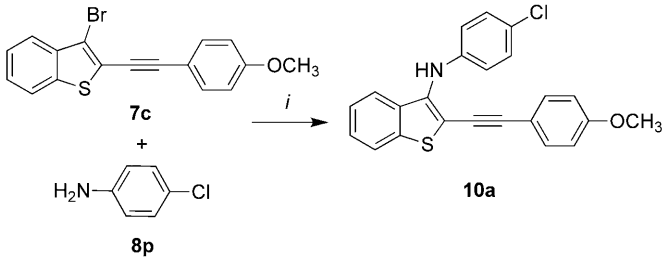
Scheme 3. Synthesis of **9n–q** and **12a–g**. *Reaction conditions: i*, **8a**, **n–s** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-Bu})_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105 °C, 12 h.



Scheme 4. Formation of **9a**. *Reaction conditions: i*, **8a** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 105 °C, 12 h.

the opposite order of events. Buchwald and co-workers showed that (copper-catalyzed) domino C–N coupling/hydroamination reactions proceed with the C–N coupling as the first step.[7] Therefore, we believe that this is the case also in our transformation. While the C–N coupling must proceed by palladium catalysis, the subsequent annulation may proceed either by a palladium-catalyzed or by a thermal process. A thermal mechanism may involve intermediate **10b** (Scheme 4), its isomerization to a 5-aza-1,2,4,6-tetraene containing an allene unit and subsequent electrocyclization.

To study the mechanism of the cyclization reaction, we tried to isolate the intermediate **10** formed by initial C–N coupling. The reaction of **7c** with **8p**, carried out at at 40 °C (4 h) instead of 105 °C (12 h), afforded the desired product **10a** (Scheme 5). Simple stirring of a toluene solution of **10a** at 105 °C for 12 h, in the absence of a catalyst, failed to give any type of cyclization (decomposition). In contrast, a cyclization could be successfully induced when the reaction was carried out in the presence of $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.), and CuI (25 mol%). This result shows that the cyclization step



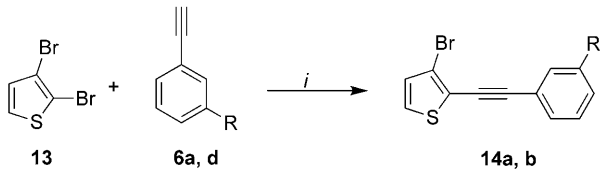
Scheme 5. Synthesis of intermediate **10a**. *Reaction conditions: i*, **8p** (1.3 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.), CuI (25 mol%), toluene, 40 °C, 4 h.

of the one-pot synthesis of products **9** (and **12**) is a palladium-catalyzed process and not a thermal electrocyclization.

2-Alkynyl-3-bromothiophenes **14a**, **b** were regioselectively prepared in very good yields by Sonogashira reactions of 2,3-dibromothiophene (**13**) with alkynes **6a**, **d** (Scheme 6, Table 4). The best yields were obtained when $Pd(PPh_3)_2Cl_2$ (5 mol%) was used.

The palladium-catalyzed reaction of 2-alkynyl-3-bromothiophenes **14a**, **b** with anilines **8a**, **c**, **d**, **e**, **g**, **n**, and **t** afforded the thienopyrroles **15a–h** in 55–75% yields (Scheme 7, Table 5).

In conclusion, we have studied the reaction of 2-alkynyl-3-bromothiophenes and 2-alkynyl-3-bromobenzothiophenes with anilines. While the reaction of 2-alkynyl-3-bromothiophenes with anilines afforded thienopyrroles by a domino C–N coupling/hydroamination process, the reaction of 2-alkynyl-3-bromobenzothiophenes with anilines resulted, under identical conditions, in the formation of benzothienoquinolines by a domino C–N coupling/annulation process. The type of starting material (both the heterocyclic moiety

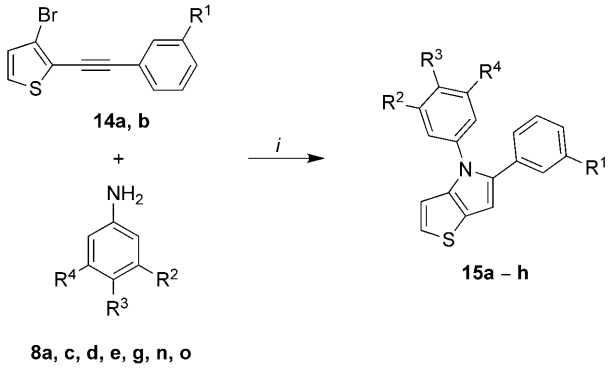


Scheme 6. Synthesis of **14a**, **b**. *Reaction conditions: i*, **6a**, **d** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (10 mol%), diisopropylamine (DIPA), 45 °C, 24 h.

Table 4. Regioselective alkynylation of 2,3-dibromothiophene.

6	14	R	Yield [%] of 14[a]
a	**a**	H	75
d	**b**	OCH_3	80

[a] Yields of isolated products.



Scheme 7. Synthesis of **15a–h**. *Reaction conditions: i*, **8a**, **c**, **d**, **e**, **g**, **n**, **t** (1.2 equiv.), $Pd(OAc)_2$ (10 mol%), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%),KO-*t*-Bu (2.0 equiv.), CuI (25 mol%), toluene, 90 °C, 12 h.

Table 5. Synthesis of **15a–h**.

15	R^1	R^2	R^3	R^4	Yield [%] of **15**[a]
a	H	H	OCH_3	H	65
b	H	H	CH_3	H	64
c	H	H	C_2H_5	H	60
d	H	H	OC_2H_5	H	65
e	OCH_3	H	OC_2H_5	H	75
f	H	OCH_3	H	OCH_3	63
g	H	OCH_3	OCH_3	OCH_3	60
h	H	H	NO_2	H	55

[a] Yields of isolated products.

and the aniline) plays an important role for the product distribution. As mentioned above, Buchwald and co-workers reported the synthesis of thienopyrroles by copper-catalyzed domino C–N coupling/hydroamination reaction of 2-alkynyl-3-bromothiophenes with $(BOC)NH_2$.[7] On the one hand, annulation reactions are, of course, only possible for anilines, but not for alkylamines or $(BOC)NH_2$. On the other hand, the different chemical behaviour of 2-alkynyl-3-bromobenzothiophenes and 2-alkynyl-3-bromothiophenes in their reaction with anilines is surprising. The most important difference between thiophene and its benzo analogue lies in the fact that the aromatic character of thiophene is much stronger than the aromaticity of the five-membered ring of benzothiophene. The alkene character of the double bond of the bromoenyne system of compounds **7** is, thus, higher than in case of derivatives **14**. It might be that this difference plays a role for the two different reaction paths. The type of aniline employed also has an influence on the product distribution. While 6-membered rings are formed in case of electron-rich anilines, 5-membered rings are formed in case of anilines containing strong π-acceptor substituents. This can be explained by the fact that, as shown above, the cyclization proceeds by palladium-catalyzed attack of the *ortho* carbon atom or of the nitrogen atom of the aniline to the alkyne. The nucleophilicity of the aromatic carbon atom is reduced when electron-withdrawing substituents are present and, thus, the cyclization proceeds *via* the (more nucleophilic) nitrogen atom.

In conclusion, we have reported what are, to the best of our knowledge, the first domino C–N coupling/annulation reactions. These reactions provide a convenient approach to pharmacologically relevant molecules which are not readily available by other methods. A detailed study of the scope and limitations and the isolation of an intermediate allowed us to draw some conclusions regarding the mechanism of cyclization.

Experimental Section

General Procedure for the Synthesis of 9, 12 and 15

In a pressure tube (glass bomb) a suspension of $Pd(OAc)_2$ (10 mol%), $Pd(t\text{-}Bu)_3{\cdot}HBF_4$ (20 mol%), KO-*t*-Bu (2 equiv.) in toluene (5 mL) was purged with argon and stirred at 20 °C to give a brownish clear solution. To the stirred solution was added **7a–c** or **14a**, **b** (1.0 equiv.), aniline **8a–s** (1.3 equiv.) and CuI (25 mol%). The reaction mixture was heated at 105 °C for 12 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were dried (Na_2SO_4), concentrated under vacuum, and the residue was purified by chromatography (flash silica gel, heptanes-EtOAc) to give **9** and/or **12** and **15**.

References

[1] a) T. Eicher, S. Hauptmann, *The Chemistry of Heterocycles: Structure, Reactions, Synthesis and Application*, (translated by H. Suschitzky, J. Suschitzky), VCH, Weinheim, **2003**; b) M. S. Butler, *J. Nat. Prod.* **2004**, *67*, 2141; c) J. A. Joule, K. Mills, *Heterocyclic Chemistry*, Blackwell Science, Oxford, **2000**.

[2] For general reviews on the metal-catalyzed synthesis of heterocycles, see: a) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127; b) T. L. Gilchrist, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2849; c) J. F. Hartwig, *Synlett* **2006**, 1283; d) L. Jiang, S. L. Buchwald, in: *Metal-Catalyzed Cross-Coupling Reactions*, 2nd edn., (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**, p 699.

[3] a) R. B. Bedford, C. S. J. Cazin, *Chem. Commun.* **2002**, 2310; b) R. B. Bedford, M. Betham, C. S. J. Cazin, in: *Handbook of C–H Transformations*, (Ed.: G. Dyker), Wiley-VCH, Weinheim, **2005**, p 238; c) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303; d) H.-J. Knölker, J. Knöll, *Chem. Commun.* **2003**, 1170; e) K. Nozaki, K. Takahashi, K. Nakano, T. Hiyama, H.-Z. Tang, M. Fujiki, S. Yamaguchi, K. Tamao, *Angew.*

Chem. **2003**, *115*, 2097; *Angew. Chem. Int. Ed.* **2003**, *42*, 2051; f) W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 14560; g) M. P. Krahl, A. Jäger, T. Krause, H.-J. Knölker, *Org. Biomol. Chem.* **2006**, *4*, 3125, and references cited therein; h) L.-C. Campeau, K. Fagnou, *Chem. Commun.* **2006**, 1253.

[4] For reviews of domino reactions, see: a) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115; b) A. de Meijere, P. von Zezschwitz, S. Kse, *Acc. Chem. Res.* **2005**, *38*, 413; c) L. F. Tietze, G. Brasche, K. M. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**.

[5] L. Ackermann, A. Althammer, *Angew. Chem.* **2007**, *119*, 1652; *Angew. Chem. Int. Ed.* **2007**, *46*, 1627.

[6] a) T. Iwaki, A. Yasuhara, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1505; b) I. C. F. R. Ferreira, M.-J. R. P. Queiroz, G. Kirsch, *Tetrahedron* **2003**, *59*, 3737.

[7] a) L. Ackermann, S. Barfüßer, H. K. Potukuchia, *Adv. Synth. Catal.* **2009**, *351*, 1064; b) L. Ackermann, R. Sandmann, A. Villar, L. T. Kaspar, *Tetrahedron* **2008**, *64*, 769.

[8] L. Ackermann, *Org. Lett.* **2005**, *7*, 439.

[9] a) R. Martin, M. Rodriguez Rivero, S. L. Buchwald, *Angew. Chem.* **2006**, *118*, 7237; *Angew. Chem. Int. Ed.* **2006**, *45*, 7079; b) R. Martin, C. H. Larsen, A. Cuenca, S. L. Buchwald, *Org. Lett.* **2007**, *9*, 3379.

[10] For related transformations, see: a) Z.-Y. Tang, Q.-S. Hu, *Adv. Synth. Catal.* **2006**, *348*, 846; b) Y. Yu, G. A. Stephenson, D. Mitchell, *Tetrahedron Lett.* **2006**, *47*, 3811; c) K. Hiroya, S. Itoh, T. Sakamoto, *J. Org. Chem.* **2004**, *69*, 1126; d) L. Xu, I. R. Lewis, S. K. Davidsen, J. B. Summers, *Tetrahedron Lett.* **1998**, *39*, 5159.

[11] For reviews of cross-coupling reactions of polyhalogenated heterocycles, see: a) S. Schröter, C. Stock, T. Bach, *Tetrahedron* **2005**, *61*, 2245; b) M. Schnürch, R. Flasik, A. F. Khan, M. Spina, M. D. Mihovilovic, P. Stanetty, *Eur. J. Org. Chem.* **2006**, 3283.

[12] a) T. T. Dang, T. T. Dang, R. Ahmad, H. Reinke, P. Langer, *Tetrahedron Lett.* **2008**, *49*, 1698; b) T. T. Dang, A. Villinger, P. Langer, *Adv. Synth. Catal.* **2008**, *350*, 2109; c) M. Hussain, T. H. Nguyen, P. Langer, *Tetrahedron Lett.* **2009**, *50*, 3929; d) S.-M. Tengho Toguem, M. Hussain, I. Malik, A. Villinger, P. Langer, *Tetrahedron Lett.* **2009**, *50*, 4962; e) T. T. Dang, T. T. Dang, N. Rasool, A. Villinger, P. Langer, P. *Adv. Synth. Catal.* **2009**, *351*, 1595; f) M. Hussain, T. H. Nguyen, R. A. Khera, I. Malik, D. S. Zinad, P. Langer, *Adv. Synth. Catal.* **2010**, *352*, 1429.

[13] S. Radl, P. Konvicka, P. Vachal, *J. Heterocycl. Chem.* **2000**, *37*, 855, and references cited therein.

[14] J. Chen, L. W. Deady, J. Desneves, A. J. Kaye, G. J. Finlay, B. C. Baguley, W. A. Denny, *Bioorg. Med. Chem.* **2000**, *8*, 2461.

[15] X. Y. Zhu, L. G. Mardenborough, S. Li, A. Khan, W. Zhang, P. Fan, M. Jacob, L. Walker, S. Y. Ablordeppey, *Bioorg. Med. Chem.* **2007**, *15*, 686, and references cited therein.

[16] L. W. Deady, A. J. Kaye, G .J. Finlay, B. C. Baguley, W. A. Denny, *J. Med. Chem.* **1997**, *40*, 2040.

[17] a) R. Pereira, B. Iglesias, A. R. de Lera, *Tetrahedron* **2001**, *57*, 7871; b) K. Morimitsu, S. Kobatake, M. Irie, *Tetrahedron Lett.* **2004**, *45*, 1155; c) K. Yumoto, K. Matsuda, M. Irie, *Org. Lett.* **2008**, *10*, 2051.

[18] a) J. Bussenius, N. L aber, T. Müller, W. Eberbach, *Chem. Ber.* **1994**, *127*, 247; b) V. Lyaskovskyy, R. Fröhlich, E.-U. Würthwein, *Chem. Eur. J.* **2007**, *13*, 3113.

[19] CCDC 805300 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

