

A Copper-Catalyzed Tandem Synthesis of Indolo- and Pyrrolo[2,1-*a*]isoquinolines**

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Dedicated to Professor Alan R. Katritzky on the occasion of his 80th birthday

Transition-metal-catalyzed tandem reactions have emerged as a useful tool for the synthesis of multiring heterocyclic compounds because of the intriguing selectivity, atom economy,^[1] and exceptional ability to activate π systems, especially alkynes, towards intermolecular and intramolecular nucleophilic attack.^[2] Among the transition-metal-catalyzed reactions, palladium is extensively used because of its tolerance of many functional groups and its low toxicity.^[3] However, in recent years copper-catalyzed reactions have received considerable attention because of their efficiency and low costs.^[2f,4,5] The reported annulation chemistry for the synthesis of heterocycles from alkynes proceeds through π complexation of the alkyne and subsequent attack of the resulting η^2 -metal complex onto the appropriate adjacent functionalized arene.^[2a,6] However, the synthesis of polyheterocycles by the nucleophilic addition of N heterocycles onto alkynes and subsequent in situ ring closure by C–C bond formation is still unknown.

Indolo[2,1-*a*]isoquinolines and pyrrolo[2,1-*a*]isoquinolines have unique nitrogen-containing tetracyclic and tricyclic structures, and their reduced and oxidized forms occur widely among natural products,^[7] biologically active pharmaceuticals,^[8] and π -conjugated functional materials, such as organic semiconductors and luminescent materials.^[9] The reported methods for the syntheses of indolo- and pyrrolo[2,1-*a*]isoquinolines, typically require multistep syntheses and expensive reagents.^[10,11] Methods for the construction of these structures include well known benzyne reactions^[10d] or the oxidative couplings of 1-benzylisoquinoline.^[12] Fürstner and

co-workers reported the synthesis of analogous isoquinolines by the cycloisomerization of biaryl alkynes using PtCl₂, AuCl, AuCl₃, GaCl₃, or InCl₃.^[2a] Herein, we report the first copper-catalyzed synthesis of this class of heterocycles by the tandem addition of N heterocycles onto alkynes and subsequent intramolecular cyclization of the in situ generated enamine by C2 arylation.

In continuation of recently developed methods for the copper-catalyzed N-arylation using benzotriazole as a ligand^[13] and the electrophilic cyclization of alkynes,^[14,15] we hypothesized that the direct synthesis of polycyclic heteroaromatic compound **6** could occur in a one-pot reaction of N heterocycle **1** with *ortho*-haloarylalkyne **2** by sequential N–C and C–C bond formation under the proper conditions such that intermediate **5** would not have to be isolated (Scheme 1, route A). We also anticipated the possible formation of regioisomer **3** by initial arylation of N heterocycle **1** at the C2-position by the *ortho*-haloarylalkyne **2** and subsequent intramolecular attack of the N heterocycle onto the carbon–carbon triple bond of the in situ generated intermediate **4** (Scheme 1, route B). This designed tandem reaction features the use of benzotriazole (**L1**) and benzotriazol-1-ylmethanol (**L2**) as novel and inexpensive ligands in copper-catalyzed reactions.

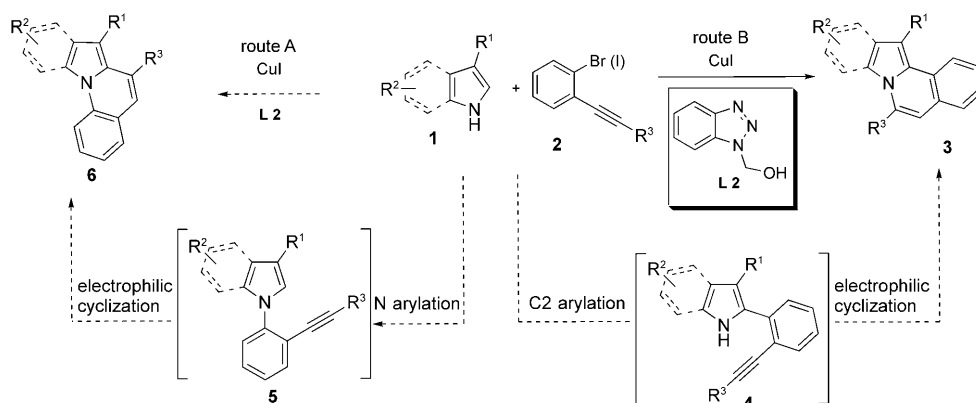
To identify the optimal reaction conditions for the reaction, a number of copper catalysts, including CuI, CuCl, CuBr, Cu₂O, and Cu(OAc)₂, and several different organic solvents and ligands were examined in the reaction of 3-methylindole (**1a**) with 2-bromophenyl-4-methoxyphenylethyne (**2a**; Table 1). Interesting observations emerge from the data in Table 1. We first reacted **1a** (0.5 mmol) with 1.1 equivalents of **2a**, 10 mol % of CuI, and 1.4 equivalents of KO^tBu in 1.0 mL of DMF at 110 °C for 24 hours—the desired coupling product **3a** was not observed (Table 1, entry 1). However, the addition of 20 mol % of ligand **L1** to the reaction afforded the desired product **3a** in a 65 % yield (Table 1, entry 2). The designed ligand **L2**, was subsequently found to be more effective than ligand **L1** (Table 1, entry 3), and from entries 4 and 5 in Table 1 it is apparent that the solvent has a significant influence on the reaction. DMSO was found to be quite successful for the transformation as compound **3a** was obtained in an 82 % yield when DMSO was used as the solvent instead of DMF (Table 1, entry 4). When we used toluene as the solvent, the desired product **3a** was obtained in only a 38 % yield (Table 1, entry 5). Different bases were tested in this reaction system, but KO^tBu proved to be most effective (Table 1, entries 4, 6, and 7). The yield of

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[**] The research work was supported by the Department of Science and Technology (DST) Government of India and the National Institute of General Medical Science (GM 070620 and GM 079593). A.K.V. was awarded a BOYSCAST Fellowship from the DST, Ministry of Science and Technology, Government of India for the Promotion of Science for Young Scientists. J.S. is thankful to CSIR. We thank Dr. Ellern Arkady, Iowa State University, for X-ray crystallographic data.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.200804427>.



Scheme 1. The design of direct synthesis of polycyclic heteroaromatic molecules by a tandem reaction.

Table 1: Optimization of the reaction conditions.^[a]

Entry	Cu cat. (mol %)	L (mol %)	Base	Solvent	t [h]	Yield [%] ^[b]
1	CuI (10)	—	KOtBu	DMF	24	0
2	CuI (10)	L1 (20)	KOtBu	DMF	30	65
3	CuI (10)	L2 (20)	KOtBu	DMF	24	72
4	CuI (10)	L2 (20)	KOtBu	DMSO	24	82
5	CuI (10)	L2 (20)	KOtBu	toluene	24	38
6	CuI (10)	L2 (20)	NaOtBu	DMSO	24	55
7	CuI (10)	L2 (20)	CS ₂ CO ₃	DMSO	24	47
8	CuI (5)	L2 (10)	KOtBu	DMSO	24	80
9	CuI (2.5)	L2 (5)	KOtBu	DMSO	36	42
10	CuCl (5)	L2 (10)	KOtBu	DMSO	36	39
11	CuBr (5)	L2 (10)	KOtBu	DMSO	36	45
12	Cu ₂ O (5)	L2 (10)	KOtBu	DMSO	24	22
13	Cu(OAc) ₂ (5)	L2 (10)	KOtBu	DMSO	24	48
14	Cu(OAc) ₂ (10)	L2 (20)	KOtBu	DMSO	24	46

[a] All reactions were performed with **1a** (0.5 mmol) and 1-bromo-2-(4-methoxyphenyl)ethynylbenzene **2a** (1.1 equiv), under standard conditions at 110 °C under an argon atmosphere. [b] Yield of isolated products. DMF = *N,N*-dimethylformamide; DMSO = dimethyl sulfoxide.

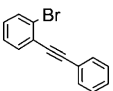
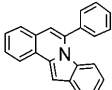
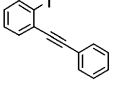
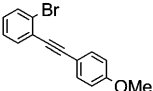
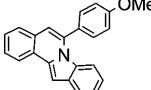
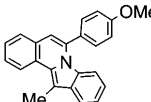
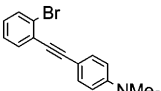
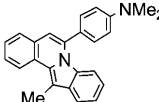
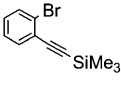
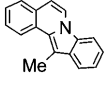
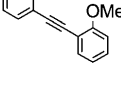
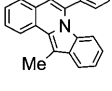
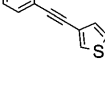
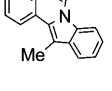
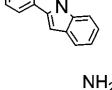
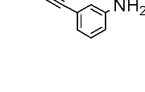
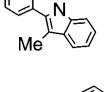
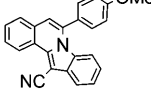
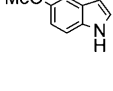
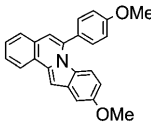
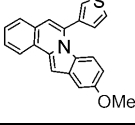
the desired product **3a** remained almost the same upon decreasing the Cu^I catalyst loading from 10 to 5 mol % (Table 1, entry 8). However, decreasing the catalyst loading from 5 to 2.5 mol % adversely affected the yield of the product as compound **3a** was obtained in only a 42 % yield (Table 1, entry 9). As in our recent report,^[13a] copper(I) complexes generally give superior results when compared to copper(II) catalysts in terms of conversion and yield. In fact, we focused on the use of CuI, since other copper precursors, such as CuCl, CuBr, Cu₂O, and Cu(OAc)₂, were found to be inferior (Table 1, entries 10–14).

The 2-haloarylalkynes **2a–h** required for examining the scope of this synthesis were readily prepared by the standard Sonogashira coupling of the commercially available 2-bromiodobenzene or 1,2-diiodobenzene and terminal alkynes. We avoided the use of 2-iodoarylalkynes because of their cost and the low yield initially observed when using such a substrate. However, with our optimized reaction conditions, they appear to provide results comparable

to the corresponding bromoarylalkynes (see Table 2, compare entries 1 and 2). The polycyclic product of the reaction was fully characterized by ¹H and ¹³C NMR methods and mass spectroscopic data. The disappearance of the two characteristic peaks of an alkyne in the ¹³C NMR spectrum confirmed the formation of either compound **3a** or **6a**, but initially it was difficult to confirm the structure of the regioisomer as either **3a** or **6a**. X-ray crystallographic analysis of the product confirmed the presence of **3a**, and not **6a**.

The scope and limitations of this copper-catalyzed tandem process were next examined by employing various *ortho*-haloarylalkynes and substituted *N*-heterocycles. The nature of the heteroarenes and the substituents attached to the triple bond has a major impact on the success of the process. The presence of a methoxy group on the arene, *para* to the triple bond, increases the electron density on the distal end of the triple bond, which favors attack at that position and favors a 6-*endo-dig* cyclization. This effect, in turn, increased the efficiency of the reaction and the products **3** were obtained in good yields (Table 2, entries 3, 4, 12, and 15). Alkyne **2f** having an *ortho*-methoxy group gave an inseparable mixture (Table 2, entry 7), and an alkyne bearing an electron-rich heterocycle, such as a thiophene, proved favorable for the reaction (Table 2, entries 8, 9, 13, and 16). The presence of a methyl group in the 3-position of the indole was found to increase the efficiency of the transformation, which may be because of the formation of a more stable transient tertiary carbocation (Table 2, entries 4–8, and 10). However, the presence of an electron-withdrawing cyano group in the 3-position of the indole (Table 2, entry 11) provided an inseparable mixture of unidentifiable compounds, which may be the result of the reduced nucleophilicity of the indole or the formation of a relatively unstable carbocation. The presence of an electron-donating group in the 5-position of the indole ring was found to increase the efficiency of the process, which may be because of an increase in the electron density at the 2-position of the indole ring, favoring electrophilic attack onto the alkyne (Table 2, entries 12 and 13), whereas electron-withdrawing groups gave an unsatisfactory result (Table 2, entry 14). The reaction of the iodoalkyne **2c** takes place at a lower temperature (100 °C) than the corresponding bromo derivative **2b** (110 °C), and affords the

Table 2: Tandem synthesis of diversely substituted indolo- and pyrrolo[2,1-a]isoquinolines catalyzed by CuI/L2.^[a]

Entry	Heterocycle	Alkyne	Product	Yield [%] ^[b]
1				62
2				64 ^[c]
3				76
4				82
5				72
6				52
7				— ^[d]
8				80
9				72
10				53 ^[e]
11				— ^[d]
12				85
13				84

desired cyclized product in a comparable yield (Table 2, entry 2).

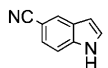
The trimethylsilyl-substituted alkyne **2e** afforded the desired cyclization product **3e** in a 52 % yield with removal of the trimethylsilyl group, presumably because of the basic conditions employed (Table 2, entry 6). We extended the scope of the reaction by employing alkynes having amino substituents (Table 2, entries 5, 10, and 17). The reaction of aminoalkyne **2h** with heterocycle **1a**, using KO^tBu as the base, gave an inseparable mixture of products. However, replacing KO^tBu with Cs₂CO₃ (2.5 equiv) afforded the desired product **3i** in a 53 % yield (Table 2, entry 10). We have extended the substrate scope of this reaction by replacing the indole with a pyrrole, therefore treatment of **1f** with alkynes **2a**, **2g**, and **2d** afforded the corresponding products **3n**, **3o**, and **3p** in 78, 72, and 53 % yields, respectively (Table 2, entries 15–17).

The structure of the products **3** was confirmed by the X-ray crystallographic analysis of compounds **3h** and **3n** (Figure 1). The X-ray crystallographic results rule out the formation of product **6** by route A, and clearly suggest that the product **3** must arise through initial arylation at the C2-position of the indole and subsequent attack of the nitrogen nucleophile onto the carbon–carbon triple bond (Scheme 1, route B).

To additionally validate the formation of products **3** by route B, we carried out a control experiment, which involved the coupling of 4-bromoanisole (**7**) with indole **1b** and pyrrole **1f** under identical reaction conditions (Scheme 2), which afforded the N-arylated coupling product in excellent yield instead of C2-arylation products.

After ruling out both of the routes shown in Scheme 1, we proposed another possibility for the formation of the products **3** (Scheme 3). The formation of the product **3** takes place by initial attack of the N heterocycle onto

Table 2: (Continued)

Entry	Heterocycle	Alkyne	Product	Yield [%] ^[b]
14		2a	3m	— ^[d]
15		2a	3n	78
16	1f	2g	3o	72
17	1f	2d	3p	53

[a] All the reactions were carried out using 0.5 mmol of N heterocycle **1** and 1.1 equivalent of 2-haloarylalkyne **2** in the presence of CuI (5.0 mol%), **L2** (10 mol%), and the base (1.4 equiv), in 1 mL DMSO at 110 °C. [b] The yields are based on the product isolated after column chromatography. [c] The reaction was carried out at 100 °C. [d] An inseparable mixture of products was obtained. [e] 2.5 equivalents of Cs₂CO₃ was used as a base.

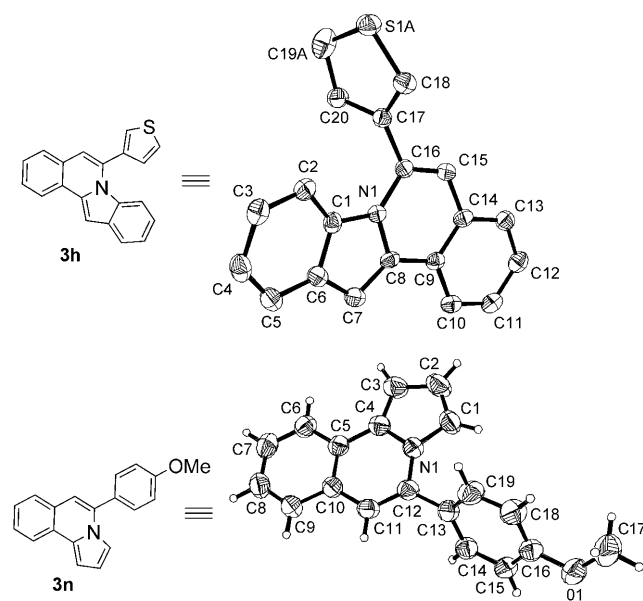
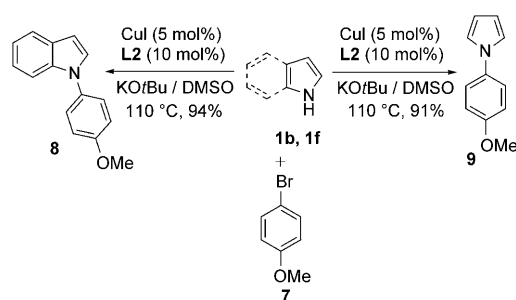


Figure 1. X-ray crystallographic ORTEP drawings of compounds **3h** and **3n** drawn at the 50% probability level.

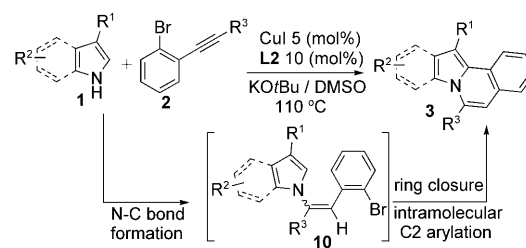
the carbon–carbon triple bond to generate *N*-alkenyl intermediate **10**, which subsequently cyclizes intramolecularly at the C2-position of the N heterocycle. Formation of product **3** was confirmed by treating compound **1a** with diphenylacetylene **11** under similar reaction conditions (Scheme 4). As expected, spectroscopic identification of the product indicated the formation of the reaction product **12** in an 82% yield as a mixture of *E* and *Z* isomers. This result clearly supports 1) initial attack of the N nucleophile onto the distal end of the triple bond (activated by copper), which favors a 6-

endo-dig cyclization product; and 2) intramolecular copper-catalyzed C–C bond formation.

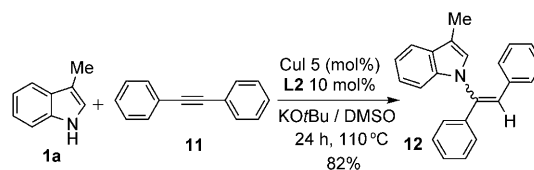
A plausible catalytic cycle for the above transformation based on the copper chemistry reported by Knochel and co-workers^[4b], is shown in Scheme 5. Presumably, CuI and ligand **L2** generates the copper complex **13**, which upon oxidative addition and subsequent complexation with the alkyne results in the formation of intermediate **14**. π Complexation between the alkyne and the copper renders haloalkyne complex **14** susceptible to attack by the heterocyclic nucleophile. Thus, copper complex **15** is formed by intermolecular attack of nucleophile **1**, which then undergoes intramolecular attack by C2 of the N heterocycle and subsequent



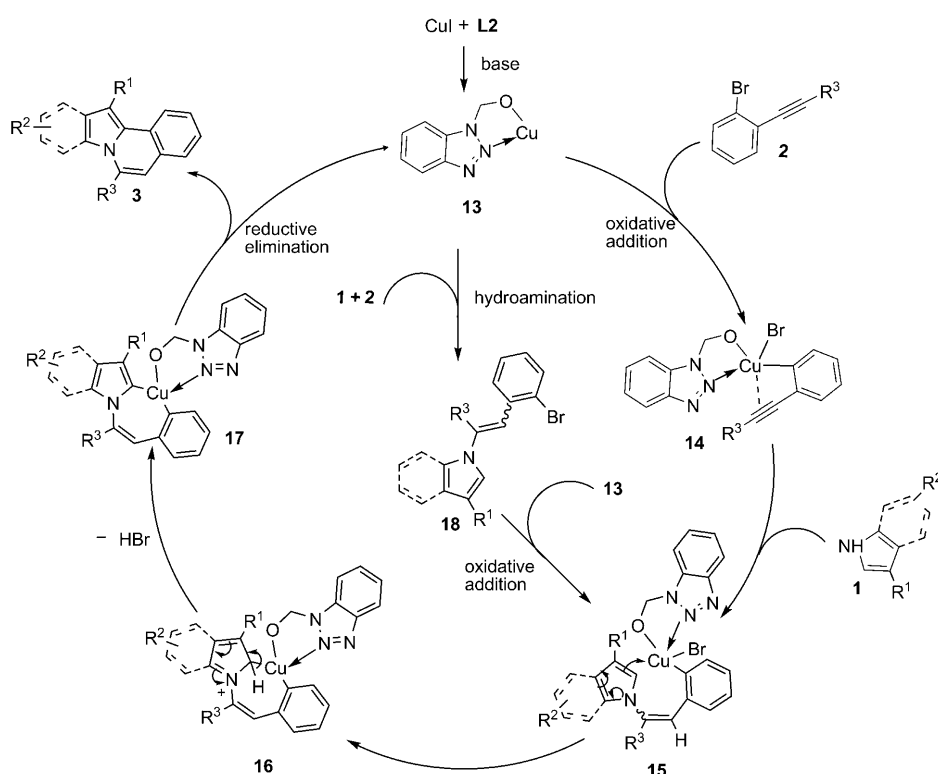
Scheme 2. Control experiment confirming N arylation



Scheme 3. A possible pathway.



Scheme 4. Control experiment confirming the attack of the nucleophile onto the triple bond.



Scheme 5. A plausible mechanism.

elimination of HBr from complex **16**, resulting in the formation of intermediate **17**. Reductive elimination of **17** affords product **3** and regenerates copper complex **13**. The other possibility for the formation of **15** involves oxidative addition of aryl halide **18** to **13**. Intermediate **18** could be obtained by hydroamination of bromoalkyne **2** with indole. The regioselectivity in the formation of **18** can be explained by steric effects as observed by Ackermann and Kaspar in their hydroamination reactions.^[17]

In summary, the chemistry described herein provides a facile and direct synthesis of diversely-substituted, medicinally-useful indolo- and pyrrolo[2,1-*a*]isoquinolines in good yields with excellent regioselectivity. This chemistry appears to involve the preferential nucleophilic addition of indoles and pyrroles onto the *ortho*-haloarylalkynes over *N* arylation of the aryl halide. From a synthetic point of view the net transformation involves a one-step conversion of simple, readily available starting materials into an interesting class of heterocyclic derivatives in good yields. An inexpensive compound, hydroxymethyl benzotriazole, is used as a ligand along with inexpensive CuI, thereby increasing the overall utility of this reaction. This process is expected to find applications in organic synthesis in general, and in the construction of a variety of interesting polycyclic heterocycles.

Experimental Section

General procedure: An oven-dried Schlenk tube with a Teflon screw valve was charged with CuI (5.0 mol %), **L2** (10 mol %), *N* hetero-

cycle **1** (0.5 mmol), 2-haloarylalkyne **2** (1.1 equiv), and base KO^tBt (1.4 equiv). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon, and DMSO (1 mL) was then added by syringe through the septum. The septum was then replaced with a Teflon screw valve and the Schlenk tube was sealed. The reaction mixture was heated to 110 °C until 2-haloarylalkyne **2** had been completely consumed (as determined by TLC) and was then cooled to room temperature. The reaction solution was diluted with ethyl acetate (10 mL) and water (15 mL). The layers were separated and the organic layer was dried over Na₂SO₄, and then concentrated under reduced pressure. The crude material obtained was then purified by using flash chromatography on silica gel (hexanes).

Received: September 8, 2008
Published online: December 29, 2008

Keywords: alkynes · benzotriazoles · C–C coupling · copper · cyclization

- [1] a) X.-Y. Liu, C.-M. Che, *Angew. Chem.* **2008**, *120*, 3865–3870; *Angew. Chem. Int. Ed.* **2008**, *47*, 3805–3810. For recent reviews, see: b) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; c) J. M. Lee, Y. Na, H. Han, S. Chang, *Chem. Soc. Rev.* **2004**, *33*, 302–312; d) A. Ajamian, J. L. Gleason, *Angew. Chem.* **2004**, *116*, 3842–3848; *Angew. Chem. Int. Ed.* **2004**, *43*, 3754–3760; e) J.-C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1001–1020; f) A. de Meijere, P. von Zezschwitz, S. Bräse, *Acc. Chem. Res.* **2005**, *38*, 413–422.
- [2] a) V. Mamane, P. Hännel, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556–4575, and references therein; b) J. Takaya, S. Udagawa, H. Kusama, N. Iwasawa, *Angew. Chem.* **2008**, *120*, 4984–4987; *Angew. Chem. Int. Ed.* **2008**, *47*, 4906–4909; c) H. Kusama, K. Ishida, H. Funami, N. Iwasawa, *Angew. Chem.* **2008**, *120*, 4981–4983; *Angew. Chem. Int. Ed.* **2008**, *47*, 4903–4905; d) N. Umeda, H. Tsurugi, T. Satoh, M. Miura, *Angew. Chem.* **2008**, *120*, 4083–4086; *Angew. Chem. Int. Ed.* **2008**, *47*, 4019–4022; e) S. Bhunia, K.-C. Wang, R.-S. Liu, *Angew. Chem.* **2008**, *120*, 5141–5144; *Angew. Chem. Int. Ed.* **2008**, *47*, 5063–5066; f) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 2074–2075.
- [3] a) M. Pfeffer, *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 567–576; b) J. Spencer, M. Pfeffer, A. DeCian, J. Fisher, *J. Org. Chem.* **1995**, *60*, 1005–1012; c) J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, New York, **1996**.
- [4] a) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; b) C. Koradin, K. Polborn, P. Knochel, *Angew. Chem.* **2002**, *114*, 2651–2654; *Angew. Chem. Int. Ed.* **2002**, *41*, 2535–2538; c) F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 210–216; d) A. Kondoh, H. Yorimitsu, K. Oshima, *J.*

- Am. Chem. Soc.* **2007**, *129*, 4099–4104; e) H. Isobe, K. Cho, N. Solin, D. B. Werz, P. H. Seeberger, E. Nakamura, *Org. Lett.* **2007**, *9*, 4611–4614; f) S. Kamijo, Y. Sasaki, Y. Yamamoto, *Tetrahedron Lett.* **2004**, *45*, 35–38; g) A. Klapars, S. Parris, K. W. Anderson, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 3529–3533; h) M. Periasamy, P. Vairaprakash, M. Dalai, *Organometallics* **2008**, *27*, 1963–1966; i) L. Ackermann, H. K. Potukuchi, D. Landsberg, R. Vicente, *Org. Lett.* **2008**, *10*, 3081–3084.
- [5] a) B. H. Yang, S. L. Buchwald, *J. Organomet. Chem.* **1999**, *576*, 125–146; b) J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154–2177; *Angew. Chem. Int. Ed.* **1998**, *37*, 2046–2067; c) A. R. Muci, S. L. Buchwald, *Top. Curr. Chem.* **2002**, *219*, 131–209.
- [6] a) Z. Liu, R. C. Larock, *J. Org. Chem.* **2007**, *72*, 223–232; b) Q. Tian, R. C. Larock, *Org. Lett.* **2000**, *2*, 3329–3332.
- [7] J. Ewing, G. K. Hughes, E. Ritchie, W. C. Taylor, *Nature* **1952**, *169*, 618–619.
- [8] a) W. K. Anderson, A. R. Heider, N. Raju, J. A. Yucht, *J. Med. Chem.* **1988**, *31*, 2097–2102; b) M. Goldbrunner, G. Loidl, T. Polossek, A. Mannschreck, E. von Angerer, *J. Med. Chem.* **1997**, *40*, 3524–3533; c) R. Ambros, S. von Angerer, W. Wiegerebe, *Arch. Pharm.* **1988**, *321*, 743–747; d) R. Ambros, S. von Angerer, W. Wiegerebe, *Arch. Pharm.* **1988**, *321*, 481–486.
- [9] a) N. Boden, R. Bissell, J. Clements, B. Movaghar, *Liq. Cryst. Today* **1996**, *6*, 1–4; b) E. Ahmed, A. L. Briseno, Y. Xia, S. A. Jenekhe, *J. Am. Chem. Soc.* **2008**, *130*, 1118–1119. For reviews, see: c) M. D. Watson, A. Fechtenkötter, K. Müllen, *Chem. Rev.* **2001**, *101*, 1267–1300; d) S. Chandrasekhar, *Liq. Cryst.* **1993**, *14*, 3–14; e) D. Pérez, E. Guitián, *Chem. Soc. Rev.* **2004**, *33*, 274–283.
- [10] a) K. Orito, R. Harada, S. Uchiito, M. Tokuda, *Org. Lett.* **2000**, *2*, 1799–1801; b) R. Ambros, M. R. Schneider, S. von Angerer, *J. Med. Chem.* **1990**, *33*, 153–160; c) K. Orito, S. Uchiito, Y. Satoh, T. Tatsuzawa, R. Harada, M. Takuda, *Org. Lett.* **2000**, *2*, 307–310; d) A. I. Meyers, T. M. Sielecki, *J. Am. Chem. Soc.* **1991**, *113*, 2789–2790; e) Z. Vincze, A. B. Bíró, M. Csékei, G. Timári, A. Kotschy, *Synthesis* **2006**, 1375–1385; f) O. Barun, S. Chakrabarti, H. Ila, H. Junjappa, *J. Org. Chem.* **2001**, *66*, 4457–4461; g) F. J. Reboredo, M. Treus, J. C. Estévez, L. Castedo, R. J. Estévez, *Synlett* **2003**, 1603–1606; h) M. Menes-Arzate, R. Martínez, R. Cruz-Almanza, J. M. Muchowski, Y. M. Osornio, L. D. Miranda, *J. Org. Chem.* **2004**, *69*, 4001–4004; i) N. M. Elwan, H. A. Abdelhadi, T. A. Abdallah, H. M. Hassaneen, *Tetrahedron* **1996**, *52*, 3451–3456; j) B.-X. Zhao, Y. Yu, S. Eguchi, *Tetrahedron* **1996**, *52*, 12049–12060; k) A. R. Katritzky, G. Qiu, B. Yang, H.-Y. He, *J. Org. Chem.* **1999**, *64*, 7618–7621.
- [11] A. N. C. Lötter, R. Pathak, T. S. Sello, M. A. Fernandes, W. A. L. van Otterlo, C. B. de Koning, *Tetrahedron* **2007**, *63*, 2263–2274, and references therein.
- [12] a) T. Kametani, K. Ogasawara, *J. Chem. Soc. C* **1967**, 2208–2212; b) F. Benington, R. D. Morin, *J. Org. Chem.* **1967**, *32*, 1050–1053; c) J. M. Boente, L. Castedo, A. Rodriguez de Lera, J. M. Saa, R. Suau, M. C. Vidal, *Tetrahedron Lett.* **1983**, *24*, 2295–2298; d) J. Harley-Mason, *J. Chem. Soc.* **1953**, 1465–1466; e) U. Hess, K. Hiller, R. Schroeder, E. Gründmann, *J. Prakt. Chem.* **1977**, *319*, 568–572.
- [13] a) A. K. Verma, J. Singh, V. K. Sankar, R. Chaudhary, R. Chandra, *Tetrahedron Lett.* **2007**, *48*, 4207–4210; b) A. K. Verma, J. Singh, R. Chaudhary, *Tetrahedron Lett.* **2007**, *48*, 7199–7202. For other ligands, see review: c) S. V. Ley, A. W. Thomas, *Angew. Chem.* **2003**, *115*, 5558–5607; *Angew. Chem. Int. Ed.* **2003**, *42*, 5400–5449.
- [14] a) Z. W. Just, R. C. Larock, *J. Org. Chem.* **2008**, *73*, 2662–2667, and references therein; b) X. Zhang, M. A. Campo, T. Yao, R. C. Larock, *Org. Lett.* **2005**, *7*, 763–766; c) J. P. Waldo, R. C. Larock, *Org. Lett.* **2005**, *7*, 5203–5205; d) J. P. Waldo, R. C. Larock, *J. Org. Chem.* **2007**, *72*, 9643–9647; e) T. Yao, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 1432–1437; f) D. Yue, T. Yao, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 62–69; g) T. Yao, D. Yue, R. C. Larock, *J. Comb. Chem.* **2005**, *7*, 809–812; h) C. Zhou, A. V. Dubrovsky, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 1626–1632; i) D. Yue, N. Della Cá, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3381–3388; j) X. Zhang, S. Sarkar, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 236–243; k) D. Yue, T. Yao, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 10292–10296; l) T. Yao, X. Zhang, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 7679–7685; m) T. Yao, M. A. Campo, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 3511–3517; n) T. Kesharwani, S. A. Worlikar, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 2307–2312.
- [15] a) J. Barluenga, M. Trincado, E. Rublio, J. M. González, *Angew. Chem.* **2003**, *115*, 2508–2511; *Angew. Chem. Int. Ed.* **2003**, *42*, 2406–2409; b) M. Amjad, D. W. Knight, *Tetrahedron Lett.* **2004**, *45*, 539–541; c) J. Barluenga, H. Vázquez-Villa, A. Ballesteros, J. M. González, *J. Am. Chem. Soc.* **2003**, *125*, 9028–9029; d) A. Sniady, K. A. Wheeler, R. Dembinski, *Org. Lett.* **2005**, *7*, 1769–1772; e) Y. Liu, S. Zhou, *Org. Lett.* **2005**, *7*, 4609–4611; f) M. Biagetti, F. Bellina, A. Carpita, P. Stabile, R. Rossi, *Tetrahedron* **2002**, *58*, 5023–5038; g) R. Rossi, A. Carpita, F. Bellina, P. Stabile, L. Mannina, *Tetrahedron* **2003**, *59*, 2067–2081; h) A. Arcadi, S. Cacchi, S. Di Giuseppe, G. Fabrizi, F. Marinelli, *Org. Lett.* **2002**, *4*, 2409–2412; i) B. L. Flynn, P. Verdier-Pinard, E. Hamel, *Org. Lett.* **2001**, *3*, 651–654; j) L. Ackermann, *Org. Lett.* **2005**, *7*, 439–442; k) L. T. Kaspar, L. Ackermann, *Tetrahedron* **2005**, *61*, 11311–11316; l) R. Martin, M. R. Rivero, S. L. Buchwald, *Angew. Chem.* **2006**, *118*, 7237–7240; *Angew. Chem. Int. Ed.* **2006**, *45*, 7079–7082.
- [16] T. Imahori, C. Hori, Y. Kondo, *Adv. Synth. Catal.* **2004**, *346*, 1090–1092.
- [17] L. Ackermann, L. T. Kaspar, *J. Org. Chem.* **2007**, *72*, 6149–6153.