Tetrahedron Letters 51 (2010) 3141–3145

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Indium(III) bromide-catalyzed hydroarylation of alkynes with indoles

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ARTICLE INFO

Article history:
Received 10 February 2010
Revised 8 April 2010
Accepted 10 April 2010
Available online 14 April 2010

ABSTRACT

Indium(III) bromide-catalyzed hydroarylation of alkynes with indoles leading to the synthesis of 3-vinylindoles in good to excellent yields was achieved. The *E*/*Z* ratio of the products depends on the substituents on the indole. This protocol is efficient and atom-economic from the synthetic point of view.

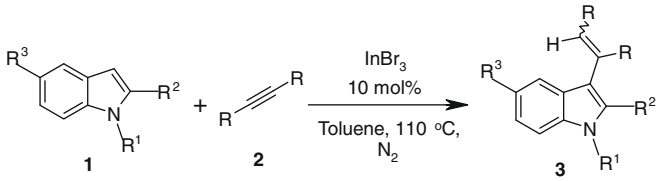
1. Introduction

Development of heteroarene functionalization has attracted much attention in view of the wide range of useful applications such as fluorescent dyes, synthetic analogues of natural products, and pharmaceuticals. Addition of an aromatic C–H bond to an unsaturated C–C bond is a useful functionalization method for introducing carbon framework on to the heteroarenes and leads to the formation of multi-substituted olefins. The success of such processes would provide convenient, clean, and economic methodologies for the synthesis of aryl-substituted compounds directly from simple arenes without requiring arene prefunctionalization such as halogenation.[1] Moreover the regio- and stereoselective synthesis of multi-substituted olefins has been a challenge for synthetic organic chemists for many years.[2] Lewis acid catalysts,[3] transition metal catalysts such as rhodium,[4] ruthenium,[5–7] platinum,[8,9] palladium,[10] gold,[11–13] rhenium,[14] rare-earth metals,[15] $FeCl_3$,[16] and transition metal triflates[17–21] in the presence of ionic liquid media also promote the alkenylation of arenes. However, some of these methods employ expensive, moisture sensitive catalysts and also produce undesired side products. Moreover the alkynes involved in the hydroarylation process need to be electron-deficient and the reaction requires longer time.

The indole ring system exists ubiquitously in natural products, and exhibits important biological and pharmaceutical properties.[22] Echavarren and co-workers reported a systematic investigation on the gold-catalyzed intra- and intermolecular addition of indoles to alkynes.[23] Cheng and co-workers investigated the reaction of indoles with alkynyl alcohols employing platinum as catalyst.[24] These studies demonstrate that a range of substituted indoles could be accessed through the reaction of indoles with alkynes. Recently, there has been considerable interest in the catalytic use of indium(III) halides in organic synthesis,[25] due to their unique properties such as non-toxicity, stability in air, and water tolerance.[26] Indium(III) bromide is known to catalyze intramolecular cyclization of 2-alkynylanilines.[27] As part of our ongoing interest in the catalytic applications of indium(III) halides for various organic transformations,[28] herein we report a hydroarylation reaction of unactivated internal and terminal alkynes with various substituted indoles in the presence of indium(III) bromide. (Scheme 1).

2. Results and discussion

To begin our study, 1-methylindole (**1b**) and diphenyl acetylene (**2a**) were allowed to react in equimolar quantities in toluene at room temperature for 24 h. The reaction does not proceed at all as indicated by TLC. Refluxing for 10 h under N_2 atmosphere also did not yield fruitful results. However, the use of indium(III) bromide (5 mol %) at reflux condition drove the reaction to form the desired product 3-vinylindole (**3b**) in 67% yield within 24 h. The ^{1}H NMR spectrum of the product exhibited two sets of signals corresponding to two diastereomers (*E*/*Z*, 90:10). The major *E*-isomer was separated by crystallization and the stereochemistry was confirmed by X-ray diffraction analysis. The ORTEP diagram for the major isomer is shown in Figure 1. In order to improve the yield of the product, we increased the catalyst to substrate ratio to 10 mol % and obtained **3b** in 78% in 3.5 h. We noticed that when the same reaction was carried out with 1.5 equiv of diphenylacetylene, for 2 h, it gave 89% yield. Further increasing of alkyne ratio had no significant effect on the reaction time and yield. Hence this optimized condition was executed for other indole derivatives to explore the substrate scope of the reaction (Scheme 1, Table 1). All the compounds were obtained in good to excellent yields



Scheme 1.

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doi:10.1016/j.tetlet.2010.04.036

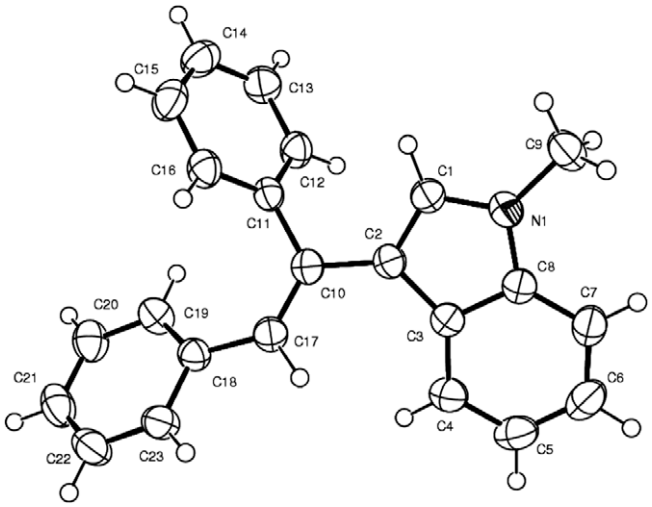


Figure 1. ORTEP diagram of **3b**.

(74–92%). These results are summarized in Table 1. There is no obvious effect on the yield of the products by changing the substituents on the indole.

The stereochemistry of the products was highly dependent on the nature of the substituents on the indole (**3a**–**k**). The reaction of 2-methylindole with diphenylacetylene gave *Z* isomer as the major product (*E*/*Z*, 6/94), which was confirmed by X-ray diffraction analysis (Fig. 2). This observation was controversial to that of the previously noticed stereoselectivity for 1-methylindole. The similar selectivities were observed for other 2-substituted indoles (**1g** and **1h**). These results prompted us to proceed with other substituted indoles.

The indole, N-substituted, and 5-substituted indoles (**1a**,**1d**, **1e**, **1f**, **1i**, and **1j**) reacted with diphenylacetylene (**2a**) to afford good yield of products (**3a**, **3d**, **3e**, **3f**, **3j**, and **3k**) and the stereoselectivity was same as in the case of 1-methylindole. The *E*-isomer was obtained as the major product, when indole, N-substituted, and 5-substituted indoles were used, and the *Z* isomer was obtained as the major product, when 2-substituted indoles were used. There was no change of *E*/*Z* selectivity and product (**3i**) yield, when

Table 1
$InBr_3$-catalyzed hydroarylation of internal alkynes (**2**) with indoles (**1**)

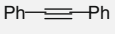
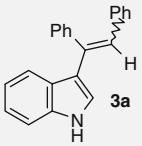
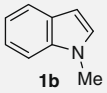
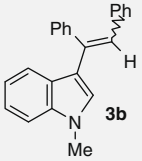
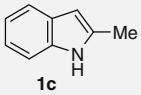
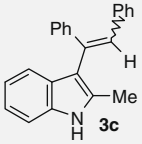
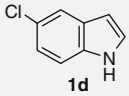
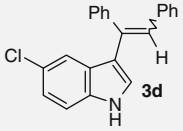
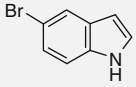
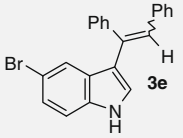
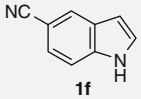
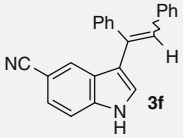
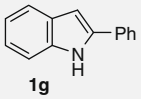
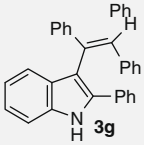
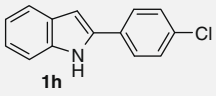
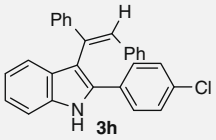
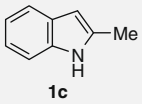
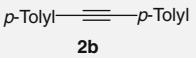
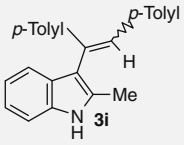
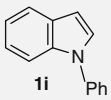
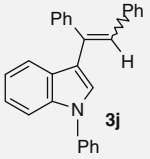
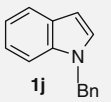
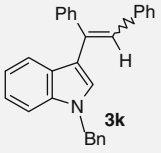
Entry	Indole (**1**)	Alkyne (**2**)	Product[a] (**3**)	Time (h)	(*E*/*Z*)[b]	Yield[c] (%)
1	 **1a**	 **2a**	 **3a**	4.0	78/22	74
2	 **1b**	**2a**	 **3b**	2.0	90/10	89
3	 **1c**	**2a**	 **3c**	2.0	6/94	92
4	 **1d**	**2a**	 **3d**	2.5	84/16	86
5	 **1e**	**2a**	 **3e**	2.5	86/14	90
6	 **1f**	**2a**	 **3f**	2.5	82/18	86
7	 **1g**	**2a**	 **3g**	2.5	>99 (*Z*)	81

Table 1 (*continued*)

Entry	Indole (**1**)	Alkyne (**2**)	Product[a] (**3**)	Time (h)	(*E*/*Z*)[b]	Yield[c] (%)
8	 **1h**	**2a**	 **3h**	2.5	>99 (*Z*)	79
9	 **1c**	 **2b**	 **3i**	2.0	8/92	90
10	 **1i**	**2a**	 **3j**	2.0	86/14	87
11	 **1j**	**2a**	 **3k**	2.0	88/12	85

[a] All products were characterized by IR, ^{1}H, ^{13}C NMR, and Mass.
[b] Isomeric ratio (*E*/*Z*) analyzed by GC and ^{1}H NMR.
[c] Isolated yield.

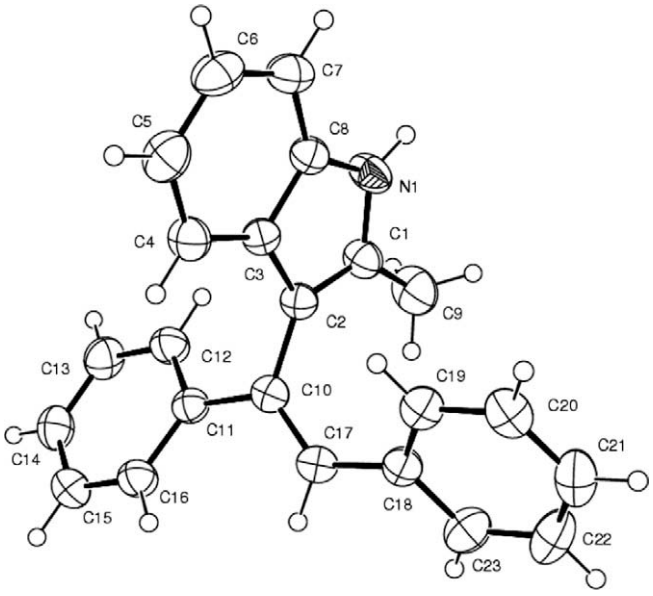


Figure 2. ORTEP diagram of **3c**.

substituted diphenylacetylene (**2b**) was used. The stereoselectivity of the reaction was in good agreement with other hydroarylation protocol.[10]

The ratio of product distribution of *E*/*Z* isomers might be rationalized based on thermodynamic stability of the products. The proposed mechanism involves zwitterionic intermediate[3a] **6** (Fig. 3), which leads to the formation with a *E*/*Z* ratio of 1:1. But the experimental results indicate that 2-substituted indoles gave Z as the major isomer and other indoles afford E as the major isomer. This might be explained through the formation of an alkyl cation **7** (Fig. 4) by the reaction of **8** with indium bromide and subsequent single bond rotation followed by the elimination of the indium

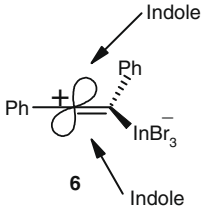


Figure 3.

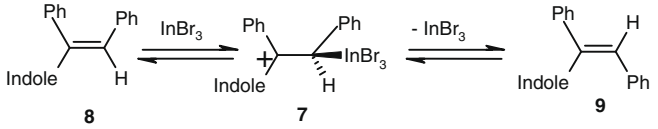
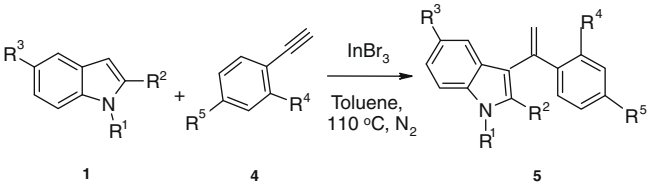


Figure 4.

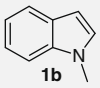
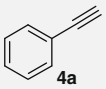
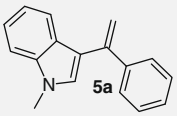
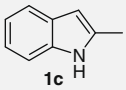
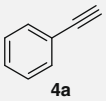
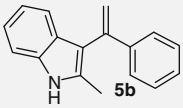
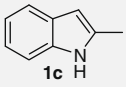
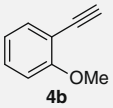
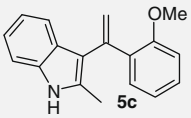
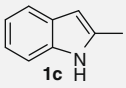
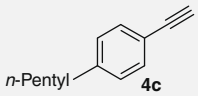
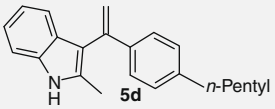
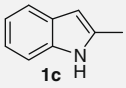
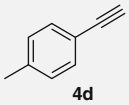
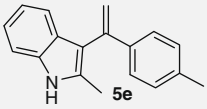
bromide which would induce the isomerization between the two isomers **8** and **9** this equilibrium allows the formation of the thermodynamically favored product.

To investigate the scope and generality of this methodology, various terminal alkynes were tested with indoles (Scheme 2, Table 2).



Scheme 2.

Table 2
InBr3-catalyzed hyrdroarylation of terminal alkynes (**4**) with indoles (**1**)[a]

Entry	Indole (**1**)	Terminal alkyne (**4**)	Product[b] (**5**)	Time (min)	Yield[c] (%)
1	 **1b**	 **4a**	 **5a**	15	87
2	 **1c**	 **4a**	 **5b**	15	91
3	 **1c**	 OMe **4b**	 OMe **5c**	15	84
4	 **1c**	 *n*-Pentyl **4c**	 *n*-Pentyl **5d**	15	85
5	 **1c**	 **4d**	 **5e**	15	87

[a] All the reactions were carried out using 1 equiv of indole and 1.2 equiv of terminal alkyne.
[b] All products were characterized by IR, NMR, and Mass.
[c] Isolated yield.

Initially we carried out the reaction between 2-methylindole (1.0 mmol) and phenylacetylene (1.2 mmol) with 10 mol % of $InBr_3$ in toluene at 110 °C under N_2 atmosphere. The reaction proceeded well and furnished 3-vinylindole product in good yield within 15 min. Terminal alkynes generally gave good yields at a shorter reaction time than internal alkynes. Similarly 1-methyl and 2-methylindoles reacted very smoothly with various terminal alkynes to afford the corresponding vinyl indole products in good to excellent yield (Table 2). There is no obvious effect on the reaction time and yields with substituents present on the indoles and alkynes.

In summary, we developed a method for the synthesis of 3-vinylindoles by hydroarylation of indoles with unactivated internal and terminal alkynes using indium bromide as the catalyst. This methodology is simple, efficient, and atom-economic from the synthetic point of view.

3. General experimental procedure for compounds 3a–k

A mixture of diphenylacetylene (**2**) (3.0 mmol), indole (**1**) (2.0 mmol), and indium bromide (0.2 mmol) in toluene (4 mL) was stirred at 110 °C for the appropriate time (see Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by column chromatography on silica gel (Merck, 100–200 mesh) to afford a mixture of *E* and *Z* isomers. These isomers were separated by crystallization using ethyl acetate/petroleum ether. Spectroscopic data for selected products.

3.1. 3-((*E*)-1,2-Diphenylvinyl)-1-methyl-1*H*-indole (3b)

Colorless solid. Mp = 182–184 °C. IR (KBr): ν_{max}: 3023, 1952, 1642, 1519, 1452, 1014, 733 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$): δ 3.73 (3H, s), 6.78 (1H, s), 7.03 (2H, d, J = 7.6 Hz), 7.07 (1H, d, J = 6.9 Hz), 7.10–7.16 (4H, m), 7.27 (1H, d, J = 7.7 Hz), 7.32 (1H, s), 7.34 (5H, s) 7.71 (1H, d, J = 8.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 32.9, 109.2, 109.6, 119.3, 120.0, 121.1, 122.1, 124.4, 125.9, 127.3, 127.9, 128.6, 129.3, 129.7, 130.3, 137.1, 137.7, 138.1, 141.4. MS (ES) = 310 (M^++H^+).

3.2. 3-((Z)-1,2-Di-*p*-tolylvinyl)-2-methyl-1*H*-indole (3i)

Colorless solid. Mp = 131–133 °C. IR (KBr) ν_{max}: 3404, 3004, 2910, 1911, 1605, 1446, 1288, 1115, 1012, 820, 736 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.99 (3H, s), 2.27 (3H, s), 2.38 (3H, s), 6.93 (2H, d, J = 8.5 Hz), 6.98 (1H, t, J = 7.6 Hz), 7.01–7.06 (2H, m), 7.09–7.17 (5H, m), 7.31–7.37 (3H, m), 7.84 (1H, NH, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.6, 21.3, 110.2, 112.2, 119.6, 120.1, 121.2, 127.1, 127.7, 128.7, 128.8, 129.0, 133.0, 134.0, 135.8, 135.9, 136.0, 137.1, 140.4. MS (ES) = 338 (M^++H^+).

4. General experimental procedure for compounds 5a–e

A mixture of terminal alkyne (**4**) (2.4 mmol), indole (**1**) (2.0 mmol), and indium bromide (0.2 mmol) in toluene (4 mL) was stirred at 110 °C for the appropriate time (see Table 2). After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by column chromatography on silica gel (Merck, 100–200 mesh) to afford pure products **5a**–**e**.

4.1. 2-Methyl-3-(1-phenylvinyl)-1*H*-indole (5b)

Brown viscous liquid. IR (neat) ν_{max}: 3401, 3055, 2920, 1681, 1609, 1450, 898, 747 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.28 (3H, s), 5.41 (1H, d, J = 1.6 Hz), 5.81 (1H, d, J = 1.6 Hz), 7.08 (1H, t, J = 7.6 Hz), 7.19 (1H, t, J = 6.9 Hz), 7.31 (2H, t, J = 7.6 Hz), 7.35–7.39 (3H, m), 7.47–7.51 (2H, m), 7.91 (1H, NH, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.9, 110.4, 114.0, 115.0, 119.8 (2C), 121.3, 127.5, 127.7, 128.4, 128.5, 133.4, 135.3, 142.0, 142.7. MS (ES) = 234 (M^++H^+).

4.2. 3-(1-(2-Methoxyphenyl)vinyl)-2-methyl-1*H*-indole (5c)

Brown viscous liquid. IR (neat) ν_{max}: 3396, 3053, 2936, 1682, 1599, 1452, 1246, 1027, 896, 751, 593 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.20, (3H, s), 3.68 (3H, s), 5.58 (1H, d, J = 2.3 Hz), 5.67 (1H, d, J = 2.0 Hz), 6.92–6.96 (2H, m), 7.02 (1H, t, J = 6.9 Hz), 7.11 (1H, t, J = 7.1 Hz), 7.21 (1H, d, J = 8.4 Hz), 7.29 (2H, d, J = 7.6 Hz), 7.35 (1H, d, J = 6.5 Hz), 7.77 (1H, NH, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.8, 55.9, 110.2, 111.7, 114.9, 117.1, 119.6 (2C), 120.7, 121.0, 128.2, 128.5, 130.9, 132.2, 132.5, 135.1, 139.8, 157.4. MS (ES) = 264 (M^++H^+).

4.3. 2-Methyl-3-(1-(4-pentylphenyl)vinyl)-1*H*-indole (5d)

Yellow viscous liquid. IR (neat) ν_{max}: 3041, 3039, 2928, 2860, 1676, 1606, 1450, 839, 744 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, J = 6.8 Hz), 1.32–1.38 (4H, m), 1.58–1.68 (2H, m), 2.28 (3H, s), 2.60 (2H, t, J = 7.6 Hz), 5.27 (1H, d, J = 2.3 Hz), 5.72 (1H, d, J = 2.2 Hz), 6.99 (1H, t, J = 8.4 Hz), 7.11 (3H, d, J = 8.4 Hz), 7.24 (1H, d, J = 7.6 Hz), 7.29 (1H, d, J = 7.6 Hz), 7.33 (2H, t, J = 8.4 Hz), 7.94 (1H, NH, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.8, 14.1, 22.6, 31.2, 31.6, 35.7, 110.2, 114.2, 114.3, 119.6, 119.8, 121.2, 127.2, 128.3, 128.6, 133.1, 135.2, 139.2, 142.3, 142.4. MS (ES) = 304 (M^++H^+).

Acknowledgment

One of the authors, G.B., thanks the Council of Scientific and Industrial Research, New Delhi, India, for the research fellowship.

References and notes

1. (a) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731–1769; (b) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698; (c) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**, *345*, 1077; (d) Kakiuchi, F.; Murai, S. Activation of C–H bonds: Catalytic Reactions. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S., Ed.; Springer: Berlin, 1999; pp 47–79; (e) Shilov; Shul.'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879; (f) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013.
2. (a) Denmark, S. E.; Amburgey, J. *J. Am. Chem. Soc.* **1993**, *115*, 10386; (b) Creton, I.; Marek, I.; Normant, J. F. *Synthesis* **1996**, 1499; (c) Brown, S. D.; Armstrong, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 6331; (d) Organ, M. G.; Cooper, J. T.; Rogers, L. R.; Soleymanzadeh, F.; Paul, T. *J. Org. Chem.* **2000**, *65*, 7959.
3. (a) Tsuchimoto, F.; Maeda, T.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2000**, 1573; (b) Reilly, A. J. A.; Nieuwland, J. A. *J. Am. Chem. Soc.* **1928**, *50*, 2564; (c) Pasha, Nayeem.; Seshu Babu, N.; Venkateswara Rao, K. T.; Sai Prasad, P. S.; Lingaiah, N. *Tetrahedron Lett.* **2009**, *50*, 1714.
4. Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731.
5. Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.
6. Merlic, C. A.; Pauly, M. E. *J. Am. Chem. Soc.* **1996**, *118*, 11319.
7. Murakami, M.; Hori, S. *J. Am. Chem. Soc.* **2003**, *125*, 4720.
8. Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992.
9. Jia, C.; Lu, W.; Oyamada, J.; Kitamura, T.; Matsuda, K.; Irie, M.; Fujiwara, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7252.
10. Lu, W.; Jia, C.; Kitamura, T.; Fujiwara, Y. *Org. Lett.* **2000**, *2*, 2927.
11. Reet, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485.
12. Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669.
13. Ne-vado, C.; Echavarren, A. M. *Chem. Eur. J.* **2005**, *11*, 3155.
14. Kuninobu, Y.; Kikuchi, K.; Tokunaga, Y.; Nishina, Y.; Takai, K. *Tetrahedron* **2008**, *64*, 5974.
15. Song, C.; Jung, D.; Choung, S.; Roh, E.; Lee, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 6183.
16. Nakao, Y.; Kanyiva, K.; Oda, S.; Hiyama, T. *J. Am. Chem. Soc.* **2006**, *128*, 8146.
17. Bolm, C.; Legros, J.; Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217.
18. Jovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3913.
19. Kischel, J.; Jovel, I.; Mertins, K.; Zapf, A.; Beller, M. *Org. Lett.* **2006**, *8*, 19.
20. Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 978.
21. Komeyama, K.; Morimoto, T.; Takaki, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2938.
22. Sundberg, R. J. *Indoles*; Academic: London, 1996.
23. Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M. *Chem. Eur. J.* **2007**, 1358.
24. Bhuvaneswari, S.; Jeganmohan, M.; Cheng *Chem. Eur. J.* **2007**, *13*, 8285.
25. For review see: (a) Nair, V.; Ros, S.; Jayan, C. N.; Pillai, B. S. *Tetrahedron* **2004**, *60*, 1959; (b) Tocco, G.; Begala, M.; Delogu, G.; Picciau, C.; Podda, G. *Tetrahedron Lett.* **2004**, *45*, 6909; (c) Fringuell, F.; Peirmatt, O.; Pizz, O. F.; Vaccaro, L. *Curr. Org. Chem.* **2003**, *7*, 1661; (d) Frost, C. G.; Hartly, J. P. *Mini-Rev. Org. Chem.* **2004**, *1*, 1; (e) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347; (f) Auge, J.; Lubin, N.; Germain; Uziel, J. *Synthesis* **2007**, 1739.
26. (a) Sakai, N.; Annaka, K.; Konakahara, T. *Tetrahedron Lett.* **2006**, *47*, 631; (b) Martins, M. A. P.; Teixeira, M. V. M.; Cunico, W.; Scapin, E.; Mayer, R.; Pereira, C. M. P.; Zanatta, N.; Bonacorso, H. G.; Peppe, C.; Yua, Y.-F. *Tetrahedron Lett.* **2004**, *45*, 8991; (c) Sakai, N.; Annaka, K.; Konakahara, T. *J. Org. Chem.* **2006**, *71*, 3653; (e) Ghosh, R.; Maiti, S. *J. Mol. Catal. A: Chem.* **2007**, *264*, 1; (f) Endo, K.; Hatekeyama, T.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2007**, *129*, 5264; (g) Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 793. and the references cited therein.
27. Sakai, N.; Annaka, K.; Fujita, A.; Sato, A.; Konakahara, T. *J. Org. Chem.* **2008**, *73*, 4160.
28. (a) Elamparithi, E.; Anniyappan, M.; Muralidharan, D.; Perumal, P. T. *ARKIVOC* **2005**, *XI*, 6–16; (b) Sridharan, V.; Perumal, P. T.; Avendan, O. C.; Mene'ndez, C. *J. Org. Biomol. Chem.* **2007**, 1351; (c) Hemanth, K.; Muralidharan, D.; Perumal, P. T. *Synthesis* **2004**, *1*, 0063; (d) Shanthi, G.; Perumal, P. T. *Tetrahedron Lett.* **2007**, *48*, 6785; (e) Shanthi, G.; Perumal, P. T. *Tetrahedron* **2007**, *63*, 2057; (f) Shanthi, G.; Perumal, P. T. *Tetrahedron Lett.* **2008**, *49*, 7139; (g) Shanthi, G.; Perumal, P. T. *Tetrahedron Lett.* **2008**, *50*, 3959; (h) Thirumurugan, P.; Perumal, P. T. *Tetrahedron* **2009**, *65*, 7620.