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A simple synthesis of 2-arylbenzothiazoles and its application to palladium-catalyzed Mizoroki–Heck reaction

Yuka Kawashita, Chigusa Ueba and Masahiko Hayashi*

Department of Chemistry, Faculty of Science, Kobe University, Nada, Kobe 657-8501, Japan

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Abstract—A variety of 2-arylbenzothiazoles were prepared by the direct reaction of 2-aminobenzenethiol and aryl aldehydes by the aid of activated carbon (Shirasagi KL or Darco® KB) under oxygen atmosphere. 2-Pyridylbenzothiazole, thus obtained, was proved to work as an efficient ligand in palladium-catalyzed Mizoroki–Heck reaction.

2-Arylbenzoxazoles, -benzimidazoles and -benzothiazoles are a remarkably important class of biologically active compounds.[1–5] Among these, 2-arylbenzothiazoles and their derivatives have attracted much attention not only in pharmaceutical but also in material fields. Therefore, there have been some reports for the synthetic procedures of these compounds. Oxidative cyclization of the corresponding Schiff base provides a general method.[6] Recently, Ohsawa and his co-workers reported one-step synthesis of 2-arylbenzothiazoles and imidazoles using scandium triflate ($Sc(OTf)_3$) as a catalyst.[7] They described that $Sc(OTf)_3$ worked as a catalyst for both ring-closing and oxidation steps.

On the other hand, we recently reported that direct synthesis of 2-arylbenzoxazoles and 2-arylbenzimidazoles (or 1,2-phenylenediamines) from substituted 2-aminophenols and aldehydes in the presence of activated carbon in xylene under an oxygen atmosphere.[8] In this letter, we report an ultimately simple and efficient synthesis of 2-arylbenzothiazoles by the reaction of 2-aminobenzenethiol and aryl aldehydes in the presence of activated carbon under oxygen or air atmosphere. Also, we will reveal that 2-pyridylbenzothiazole obtained by the reaction of 2-aminobenzenethiol and 2-pyridylaldehyde proved to serve as an efficient ligand in palladium-catalyzed Mizoroki–Heck reaction.

A variety of 4-substituted benzaldehydes reacted with 2-aminobenzenethiol to produce the corresponding 2-arylbenzothiazoles in the presence of activated carbon (Shirasagi KL; Japan EnviroChemicals, Ltd or Darco® KB; Aldrich, Inc.) under oxygen atmosphere in high yield (Table 1). The reactions took place at 50 °C, under milder conditions compared with the case of the synthesis of 2-arylbenzoxazoles and 2-arylbenzimidazoles.[8] The reaction also proceeded under air atmosphere instead of oxygen, though it took longer time, for example, in the reaction of 2-aminobenzenethiol and benzaldehyde (50 °C, 13 h, 82%), 4-methylbenzaldehyde (50 °C, 13 h, 82%) and 4-chlorobenzaldehyde (50 °C, 13 h, 76%).

It should be mentioned that the reaction of 2-aminobenzenethiol with formaldehyde (37 wt % solution in water containing 7–8% methanol) also took place to afford the benzothiazole in moderate yield (52% isolated yield) (Scheme 1). Benzothiazole is known as a very important intermediate compound, because many functional groups will be introduced to these as the second position.[9]

The Mizoroki–Heck reaction has been widely used for the construction of carbon–carbon bonds since 1971.[10] As ligands, phosphine and related compounds are often used. Recently, electron-rich and bulky alkyl phosphines, such as $P(t\text{-}Bu)_3$, were developed as highly effective ligands.[11] Especially, the advancement in the field of palladacycles,[12] *N*-heterocyclic carbene-complexes, should be noteworthy.[13] We also have interest in the development of an active and simple catalyst system in Mizoroki–Heck reactions, and especially, we have focused on imidazole derivatives, because their structures are simple, stable and inexpensive. The reaction

* Corresponding author. Tel.: +81 78 803 5687; fax: +81 78 803 5688; e-mail: mhayashi@kobe-u.ac.jp

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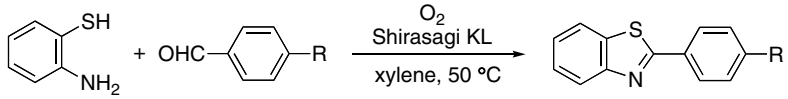
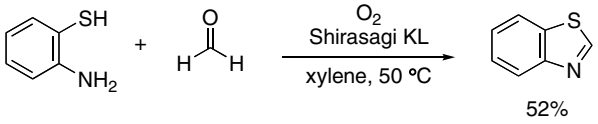
Table 1. Direct Synthesis of 2-Arylbenzthiazole[a]



Entry	R	Time/h	% Yield[b]
1	H	3	79
2	CH_3	3	82[c]
3	OCH_3	3	81[c]
4	Cl	4	72
5	CN	4	82
6	NO_2	4	86

[a] The ratio of 2-aminobenzenethiol and aldehydes was 1:1. Shirasagi KL (625 mg) was used per 5 mmol (626 mg) of 2-aminobenzenethiol.
[b] Isolated yield by recrystallization unless otherwise noted.
[c] Isolated yield by silica-gel column chromatography.

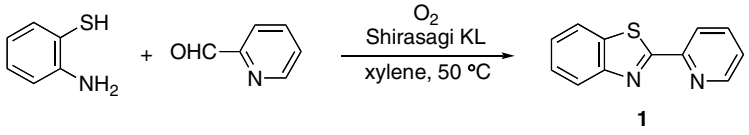


Scheme 1.

of 2-aminobenzenethiol with 2-pyridylaldehyde, by the aid of an activated carbon–oxygen system, produced 2-pyridylbenzothiazole in 82% yield (Scheme 2). We then examined the reaction of 4-bromotoluene with methyl acrylate using 1 mol % of a palladium catalyst and 1 mol % of ligands under various conditions (Table 2).

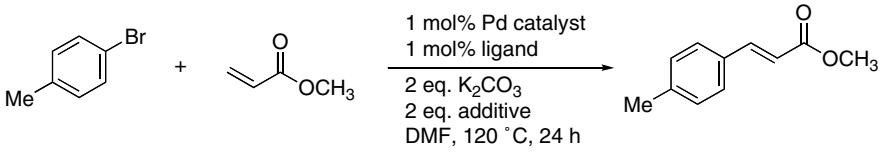
As shown in Table 2, the combination of $PdCl_2$ and the 2-pyridylbenzothiazole (entry 6) and 2-pyridylbenzimidazole system (entry 8) exhibited higher reactivity in Mizoroki–Heck reaction compared with Jefferry's conditions.[13]

In conclusion, we have disclosed a simple and direct synthesis of 2-arylbenzothiazole by the aid of activated carbon and the utility of 2-pyridylbenzothiazole as a ligand in palladium-catalyzed Mizoroki–Heck reaction. We are now investigating simple imidazole-containing nitrogen coordinated palladium complexes in coupling reactions encouraged by the result of entry 8, which will be published in the near future.[14–16]



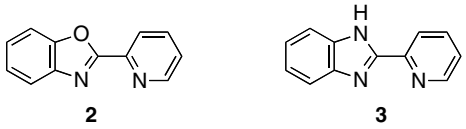
Scheme 2.

Table 2. Mizoroki–Heck reaction using 2-pyridylbenzothiazole, -benzoxazole and -benzimidazole ligands



Entry	Pd catalyst	Ligand	Additive	% Yield[a]
1	$Pd(OAc)_2$	None	*n*-Bu_4NBr	34
2	$Pd(OAc)_2$	**1**	*n*-Bu_4NBr	24
3	$Pd(OAc)_2$	**2**	*n*-Bu_4NBr	26
4	$Pd(OAc)_2$	**3**	*n*-Bu_4NBr	64
5	$PdCl_2$	None	None	9
6	$PdCl_2$	**1**	None	79
7	$PdCl_2$	**2**	None	42
8	$PdCl_2$	**3**	None	84

[a] Isolated yield.



Acknowledgements

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References and notes

1. Shi, D.-F.; Bradshaw, T. D.; Wrigley, S.; McCall, C. J.; Lelieveld, P.; Fichtner, I.; Stevens, M. F. G. *J. Med. Chem.* **1996**, *39*, 3375–3384.
2. Lezcano, M.; Al-Soufi, W.; Novo, M.; Rodriguez-Núñez, E.; Vázquez Tato, J. *J. Agric. Food Chem.* **2002**, *50*, 108–112.
3. Zhuang, Z.-P.; Kung, M.-P.; Wilson, A.; Lee, C.-W.; Plössl, K.; Hou, C.; Holtzman, D. M.; Kung, H. F. *J. Med. Chem.* **2003**, *46*, 237–243.
4. Wells, G.; Berry, J. M.; Bradshaw, T. D.; Burger, A. M.; Seaton, A.; Wang, B.; Westwell, A. D.; Stevens, M. F. G. *J. Med. Chem.* **2003**, *46*, 532–541.
5. Skalitzky, D. J.; Marakovits, J. T.; Maegley, K. A.; Ekker, A.; Yu, X.-H.; Hostomsky, Z.; Webber, S. E.; Eastman, B. W.; Almassy, R.; Li, J.; Curtin, N. J.; Newell, D. R.; Calvert, A. H.; Griffin, R. J.; Golding, B. T. *J. Med. Chem.* **2003**, *46*, 210–213.
6. (a) Chang, J.; Zhaob, K.; Pana, S. *Tetrahedron Lett.* **2002**, *43*, 951–954; (b) Ranu, B. C.; Jana, R.; Dey, S. S. *Chem. Lett.* **2004**, *33*, 274–275; (c) Chang, W.-C.; Hu, A. T.; Duan, J.-P.; Rayabarapu, D. K.; Cheng, C.-H. *J. Organomet. Chem.* **2004**, *689*, 4882–4888; (d) Kodomari, M.; Tamaru, Y.; Aoyama, T. *Synth. Commun.* **2004**, *34*, 3029–3036.
7. Itoh, T.; Nagata, K.; Ishikawa, H.; Ohsawa, A. *Heterocycles* **2004**, *63*, 2769–2783, and references cited therein.
8. Kawashita, Y.; Nakamichi, N.; Kawabata, H.; Hayashi, M. *Org. Lett.* **2003**, *5*, 3713–3715.
9. For example, Jin, L.; Song, B.; Zhang, G.; Xu, R.; Zhang, S.; Gao, X.; Hu, D.; Yang, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1537–1543.
10. (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581–583; (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320–2322; (c) Tsuji, J. *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*; John Wiley & Sons, 2004; Chapter 3.
11. (a) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844–1848; (b) Herrmann, W. A.; Böhm, V. P. W.; Reisinger, C.-P. *J. Organomet. Chem.* **1999**, *576*, 23–41; (c) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989–7000; (d) Stambuli, J. P.; Stauffer, S. R.; Shaughnessy, K. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 2677–2678.
12. (a) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309; (b) Hillier, A. C.; Grasa, G. A.; Viciu, M. S.; Lee, H. M.; Yang, C.; Nolan, S. P. *J. Organomet. Chem.* **2002**, *653*, 69–82.
13. (a) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287–1289; (b) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113–10130.
14. Ueba, C.; Eda, K.; Hayashi, M., submitted for publication.
15. General procedure for the synthesis of 2-arylbenzothiazoles (Table 1); A mixture of 2-aminothiophenol (5 mmol), aldehyde (5 mmol) and Shirasagi KL (625 mg) in xylene (8 mL) was placed in a 100 mL three-necked flask under oxygen atmosphere (using 1 L of balloon) and stirred at 50 °C for 3–4 h. The reaction mixture was then filtered using Celite. After the filtrate was concentrated, the product was isolated by recrystallization or silica-gel column chromatography.
16. Experimental of Mizoroki–Heck reaction (Table 2): In an 80-mL Schlenk tube were placed $PdCl_2$ (3.55 mg, 0.01 mmol), 2-pyridylbenzothiazole (4.24 mg, 0.01 mmol) and K_2CO_3 (552.8 mg, 4 mmol) in DMF (10.0 mL) and the mixture was stirred at 50 °C for 1 h. 4-Bromotoluene (246.1 μL, 2 mmol) and methyl acrylate (358.7 μL, 4 mmol) in 1 mL of DMF were added. The mixture was then stirred at 120 °C for 24 h. The reaction mixture was cooled, and then the precipitates were removed by filtration and extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After evaporation, the obtained residue was purified by silica-gel column chromatography to give methyl *trans*-4-methylcinnamate in 79% yield (277.5 mg).