

# Platinum(II)-catalyzed intermolecular hydroarylation of unactivated alkenes with indoles†

Zhibin Zhang, Xiang Wang and Ross A. Widenhofer\*

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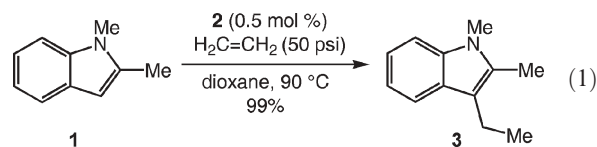
Ethylene,  $\alpha$ -olefins, and vinyl arenes undergo platinum-catalyzed hydroarylation with substituted indoles in moderate to good yield.

The intermolecular hydroarylation of unactivated alkenes has attracted considerable attention as an atom-economical approach to the functionalization of arenes. However, despite prolonged effort in this area, general and effective methods for the selective intermolecular hydroarylation of unactivated alkenes remain scarce.<sup>1</sup> Strong Lewis acids such as AlCl<sub>3</sub> catalyze the hydroarylation of unactivated alkenes, but these approaches suffer from poor selectivity and limited functional group compatibility.<sup>2</sup> Ru(II)-<sup>3</sup> and Rh(I)-<sup>4</sup> phosphine complexes catalyze the intermolecular hydroarylation of unactivated alkenes with arenes that possess a suitable directing group or that are predisposed to the formation of a stabilized carbene intermediate, respectively. Ir(III),<sup>5</sup> cationic Pt(II),<sup>6</sup> and Ru(II) hydridotris(pyrazolyl)borate complexes<sup>7</sup> catalyze the hydroarylation of unactivated alkenes with benzene, but require forcing reaction conditions ( $\geq 180$  °C) or a large excess of benzene. Brønsted acids catalyze the addition of aniline to norbornene and vinyl arenes to form mixtures of hydroarylation and hydroamination products.<sup>8</sup> The cationic zirconocene complex Cp<sub>2</sub>Zr(CH<sub>3</sub>)(THF)<sup>+</sup> catalyzes the hydroarylation of propene with  $\alpha$ -picoline but is restricted to this lone example.<sup>9</sup>

Absent from the catalytic systems noted in the preceding paragraph are examples of the intermolecular hydroarylation of unactivated alkenes with electron-rich arenes such as indoles. Rather, hydroarylation of alkenes with indoles requires either an electron-deficient Michael acceptor<sup>1</sup> or prolonged heating under highly acidic conditions.<sup>10</sup> We recently reported effective Pt(II)-catalyzed protocols for the intramolecular hydroarylation of unactivated alkenes with indoles<sup>11,12</sup> and for the intermolecular hydroalkylation of ethylene with  $\beta$ -diketones.<sup>13</sup> On the basis of these two precedents, we considered that Pt(II) complexes might also catalyze the intermolecular hydroarylation of unactivated alkenes with indoles. Indeed, here we report the platinum-catalyzed hydroarylation of ethylene,  $\alpha$ -olefins, and vinyl arenes with substituted indoles.

Reaction of 1,2-dimethylindole (**1**), ethylene (50 psi), and a catalytic amount of [PtCl<sub>2</sub>(H<sub>2</sub>C=CH<sub>2</sub>)<sub>2</sub>] (**2**; 0.5 mol %) in dioxane at 90 °C for 6 h led to isolation of 3-ethyl-1,2-dimethylindole (**3**) in 99% yield (eqn (1)).‡ The efficiency of the platinum-catalyzed

conversion of **1** to **3** was such that 0.05 mol% of **2** was sufficient to achieve 90% isolated yield of **3** (TON = 900; Table 1, entry 1). The Pt-catalyzed hydroarylation of ethylene tolerated the presence of either an electron-donating or electron-withdrawing group at the C(5) position of the indole moiety or a phenyl group at the C(2) position of the indole moiety (Table 1, entries 2–5). Substitution at the C(2) position of the indole appeared to facilitate intermolecular hydroarylation, but was not required (Table 1, entry 6).



$\alpha$ -Olefins also underwent Pt-catalyzed hydroarylation with indoles with predominant formation of the Markovnikov addition product. For example, reaction of **1** with propene (50 psi) and a catalytic amount of PtCl<sub>2</sub> (5 mol%) in dioxane that contained a trace (5 mol%) of HCl at 90 °C for 14 h led to isolation of a 6 : 1 mixture of 3-isopropyl-1,2-dimethylindole (**4a**) and 3-*n*-propyl-1,2-dimethylindole (**4b**) in 88% combined yield (Table 2, entry 1).§ Likewise, Pt-catalyzed reaction of **1** with 1-butene (30 psi) led to isolation of a 6 : 1 mixture of **5a** and **5b** in 74% combined yield (Table 2, entry 2). Vinyl arenes also underwent Pt-catalyzed hydroarylation with indoles. In an initial experiment, reaction of **1** and *p*-chlorostyrene with a catalytic amount of PtCl<sub>2</sub> (5 mol %) in dioxane at 120 °C for 16 h led to >95% conversion to form a 6.5 : 10.3 : 1.0 mixture of Markovnikov adduct **6a**, anti-Markovnikov adduct **6b**, and oxidized Markovnikov product **6c** in 89% combined yield (GC, Scheme 1). Unfortunately, neither unreacted **1** nor **6c** could be separated from **6a** and **6b** by flash chromatography. Thus, the crude reaction mixture was first treated with 1,4-benzoquinone to consume unreacted **1** and then hydrogenated to convert **6c** to **6a**. Subsequent chromatography led to isolation of a 1 : 1.6 mixture of **6a** and **6b** in 79% combined yield (Table 2, entry 3).¶

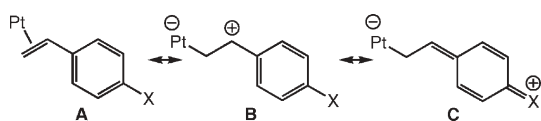
A number of styrene derivatives underwent platinum-catalyzed hydroarylation with **1** in moderate yield (Table 2, entries 4–8). Noteworthy was that the Markovnikov/anti-Markovnikov (**a** : **b**) selectivity of the Pt-catalyzed hydroarylation of **1** increased from 2.0 : 1 for the hydroarylation of *p*-methylstyrene to 1 : 5.8 for the hydroarylation of *p*-nitrostyrene (Table 2, entries 4–8). A plot of the log of the Markovnikov/anti-Markovnikov (**a** : **b**) ratio versus the Hammett  $\sigma$ -parameter was linear with slope  $\rho = -0.98$  (see Supporting Information†), which points to the increasing contribution of the zwitterionic resonance structures **B** and **C** with the increasing electron donating ability of the *para* substituent. ||<sup>14</sup>

P. M. Gross Chemical Laboratory, Duke University, Durham, North Carolina, USA. E-mail: rwidenho@chem.duke.edu; Fax: +1-919-6601605; Tel: +1-919-6601533

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**Table 1** Reaction of ethylene with indoles catalyzed by [PtCl<sub>2</sub>(H<sub>2</sub>C=CH<sub>2</sub>)<sub>2</sub>] (**2**) at 90 °C for 3–6 h

Entry	Indole	Cat load (mol %)	Product	Yield (%) <sup>a</sup>
1	R <sup>1</sup> = Me, R <sup>2</sup> = H ( <b>1</b> )	0.05	<b>3</b>	90
2	R <sup>1</sup> = Me, R <sup>2</sup> = OMe	0.5		99
3	R <sup>1</sup> = Me, R <sup>2</sup> = Cl	0.5		99
4	R <sup>1</sup> = Ph, R <sup>2</sup> = H	0.5		76
5	R <sup>1</sup> = Et, R <sup>2</sup> = Ph	0.5		86
6	R <sup>1</sup> = Me, R <sup>2</sup> = H	0.5		71

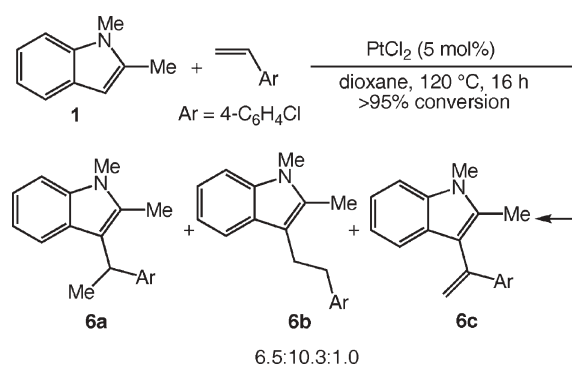
<sup>a</sup> Isolated yield of >95% purity.

In summary, we have developed effective Pt(II)-catalyzed protocols for the intermolecular hydroarylation of ethylene,  $\alpha$ -olefins and vinyl arenes with indoles. We continue to work toward the development of more active and more selective hydroarylation catalysts.

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**Table 2** Platinum-catalyzed reaction of 1,2-dimethylindole (**1**) (0.5 M) with  $\alpha$ -olefins and vinyl arenes

Entry	R	Conditions <sup>a</sup>	Product	Yield (a + b) <sup>b</sup>	Ratio (a:b)
1	Me	A	<b>4</b>	88	6 : 1
2	Et	A	<b>5</b>	74	6 : 1
3	4-C <sub>6</sub> H <sub>4</sub> Cl	B	<b>6</b>	79	1 : 1.6
4	4-C <sub>6</sub> H <sub>4</sub> H	B	<b>7</b>	55	1.1 : 1
5	4-C <sub>6</sub> H <sub>4</sub> Me	B	<b>8</b>	43	2.0 : 1
6	4-C <sub>6</sub> H <sub>4</sub> CN	B	<b>9</b>	56	1 : 2.5
7	4-C <sub>6</sub> H <sub>4</sub> CF <sub>3</sub>	B	<b>10</b>	51	1 : 3.1
8	4-C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	B	<b>11</b>	39	1 : 5.8

**Scheme 1**

## Notes and references

‡ Control experiments ruled out the possibility of acid-catalyzed background reactions for the hydroarylation of ethylene,  $\alpha$ -olefins, and vinyl arenes with indoles (see Supporting Information†).

§ Employment of **2** as a catalyst for the hydroarylation of  $\alpha$ -olefins or vinyl arenes led to contamination of the product with small amounts of the corresponding 3-ethyl indole.

¶ PtCl<sub>4</sub> is also an effective catalyst for the hydroarylation of vinyl arenes (see Supporting Information†) and for the intramolecular hydroarylation of alkynes.<sup>15</sup>

|| We have previously shown that the Pt(II)-catalyzed intramolecular hydroarylation of alkenes with indoles occurs *via* outer-sphere attack of the indole on a Pt-complexed alkene.<sup>11</sup>

- G. A. Olah, R. Krishnamurti and G. K. S. Prakash, *Friedel–Crafts Alkylations in Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 3, pp. 293–339.
- (a) G. A. Olah and S. J. Kuhn, *J. Org. Chem.*, 1964, **29**, 2317; (b) G. A. Olah, *Friedel–Crafts and Related Reactions*, vol. 1, Interscience, New York, 1963.
- F. Kakiuchi and S. Murai, *Acc. Chem. Res.*, 2002, **35**, 826 and references therein.
- (a) K. L. Tan, R. G. Bergman and J. A. Ellman, *J. Am. Chem. Soc.*, 2002, **124**, 13964; (b) C. P. Lenges and M. Brookhart, *J. Am. Chem. Soc.*, 1999, **121**, 6616; (c) S. H. Wiedemann, J. A. Ellman and

- R. G. Bergman, *J. Org. Chem.*, 2006, **71**, 1969; (d) K. L. Tan, S. Park, J. A. Ellman and R. G. Bergman, *J. Org. Chem.*, 2004, **69**, 7329.
- 5 (a) T. Matsumoto, D. J. Taube, R. A. Periana, H. Taube and H. Yoshida, *J. Am. Chem. Soc.*, 2000, **122**, 7414; (b) T. Matsumoto, R. A. Periana, D. J. Taube and H. Yoshida, *J. Mol. Catal. A: Chem.*, 2002, **180**, 1.
- 6 D. Karshedt, A. T. Bell and T. D. Tilley, *Organometallics*, 2004, **23**, 4169.
- 7 M. Lail, B. N. Arrowood and T. B. Gunnoe, *J. Am. Chem. Soc.*, 2003, **125**, 7506.
- 8 L. L. Anderson, J. Arnold and R. G. Bergman, *J. Am. Chem. Soc.*, 2005, **127**, 14542.
- 9 R. F. Jordan and D. F. Taylor, *J. Am. Chem. Soc.*, 1989, **111**, 778.
- 10 G. C. Morrison, R. O. Waite, F. Serafin and J. Shavel, *J. Org. Chem.*, 1967, **32**, 2551.
- 11 C. Liu, X. Han, X. Wang and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2004, **126**, 3700.
- 12 For a related transformation see: S. W. Youn, S. J. Pastine and D. Sames, *Org. Lett.*, 2004, **6**, 581.
- 13 X. Wang and R. A. Widenhoefer, *Chem. Commun.*, 2004, 660.
- 14 For similar behavior see: (a) H. Van der Poel and G. Van Koten, *Inorg. Chem.*, 1981, **20**, 2941; (b) H. Kurosawa, T. Majima and N. Asada, *J. Am. Chem. Soc.*, 1980, **102**, 6996; (c) H. Kurosawa, A. Urabe and M. Emoto, *J. Chem. Soc., Dalton Trans.*, 1986, 891; (d) K. Miki, O. Shiotani, Y. Kai, N. Kasai, H. Kanatani and H. Kurosawa, *Organometallics*, 1983, **2**, 585.
- 15 S. J. Pastine, S. W. Youn and D. Sames, *Org. Lett.*, 2003, **5**, 1055.

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